Kingdoms (Whittaker's classification)

Monera
(Carl Woese)
- Archae-bacteria
  - unicellular w/o nucleus & organelles
  - auto/hetero-trophic
  - prokaryotes
- Eubacteria

Protista
- unicellular
- eukaryotic
- auto/hetero-trophic

Fungi
- multicellular
- heterotropic
- cell wall

Plantae
- multicellular
- autotrophic
- cell wall

Undifferentiated body
Thallophyta
- aquatic predominantly
- Spirogyra, Ulothrix, Chara, Cladophora

Differentiated body
- with vascular tissue
  - No seeds
    - **Pteridophyta**
      - Horsetails
      - stems, roots, leaves
      - spores
      - (Cryptogamae)
  - Produce seeds - phanerogams
    - Naked seeds
      - **Gymnosperms**
      - eg. Pine, Deodar
    - Seeds inside fruits
      - **Angiosperms**
        - Monocots: maize
        - Dicots: wheat, gram
- without vascular tissue
  - **Bryophyta**
    - amphibians
    - Marchantia, Funaria

Animalia
- multicellular
- heterotrophic
- w/o cell wall

Porifera	Cnidaria / Coelentrata	Platy helminthes	Nema toda	Annelida	Arthro poda	Mollusca	Echino dermata	Protochor data
• pores	• aquatic	• triploblastic	• ✓	• ✓	• ✓	• ✓	• marine	• triploblastic
• marine mainly	• motile	• no true coelom	• tissues	• segmented	• ✓	• little segmentation	• spiny	• bilaterally symmetrical
• immotile	• some body diff. / cavity	• flattened	• pseudo coelom	• true body cavity	• ✓	• reduced coelom	• water driven tube system	• Coelom
• canal system		• bilaterally symmetrical	• cylindrical	• organs	• open circulatory system		• hard $CaCO_3$ skeleton	• Notochord
• no differentiation			• ✓	• ✓	• ✓	• ✓		• Marine
eg. Euplectella, Sycon, Spongilla	Sea anemone, hydra	Planaria, Liverfluke	Ascaris, Wuchereria	Nereis, Leech, Earthworm	• jointed legs Musca, Aranea	Unio, Pila	Sea urchin, Holothuria	Balanoglossus, Herdmania

Vertebrata

- true vertebral column
- internal skeleton
- coelomate / complex diff.
- triploblastic
- paired gill pouches

- **Pisces** — aquatic, scaly, streamlined, gills, cold blooded, two-chambered heart
- **Amphibia** — no scales, mucus glands in skin, 3-chambered heart, marine & terrestrial, eggs in water
- **Reptilia** — cold blooded, scales, lungs, 3-chambered ♡, (crocodile - 4 chambered ♡), shelled eggs
- **Aves** — birds, feathers, warm blooded, lungs, 4-chambered ♡, oviparous.
- **Mammalia** — warm blooded, 4 chambered ♡, mammary glands, viviparous mainly

CYTOLOGY → morphological features of a cell

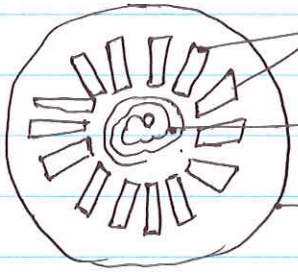
CELL BIOLOGY - cell organelles and morphological, biochemical, biophysical, bio physiological and genetic study of cells

CELL THEORY - Schleiden and Schwann

- → all organisms made up of cells
- → sum total of cellular interactions
- → generates life
- → independant life + interactions for organism as well
- → unit of heredity

VIRUS

- → macromolecules; can be crystallised
- → obligatory parasites
- → use host synthetic machinery to synthesise enzymes
- → VIRION - one intact non-dividing virus



Nucleic acid 3 - 300 kilo bases per strand

Types

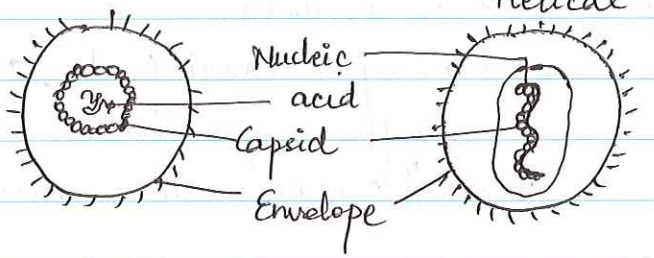
- DNA viruses
  - ss-DNA (papovirus)
  - ds-DNA (adenovirus)
- RNA viruses
  - ss-RNA (TMV)
  - ds-RNA (reovirus)

Capsid

- → protein coat arranged capsomeres
- → provides protection
- → recognizes few molecules
- → helps in adsorption
- → penetration in host cell
  - → viropexis (host phagocyte engulfs virus)
  - → penetration through sheath

Capsid symmetry

- Icosahedral
- Helical
- complex (bacteriophage)

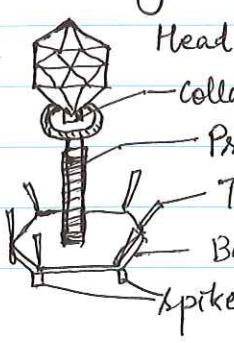


Envelope

- → only in large viruses
- → conceals the symmetry of virus capsid
- → made of lipid proteins
- → soluble in chloroform / ether

Types of viruses

- Bacteriophage (eg T4)
- Animal virus
- Plant virus



Animal virus
eg HIV, HPV
leukemia causing
reovirus / oncovirus

Plant virus
eg: Tobacco mosaic
Tobacco rattle

Types of cell

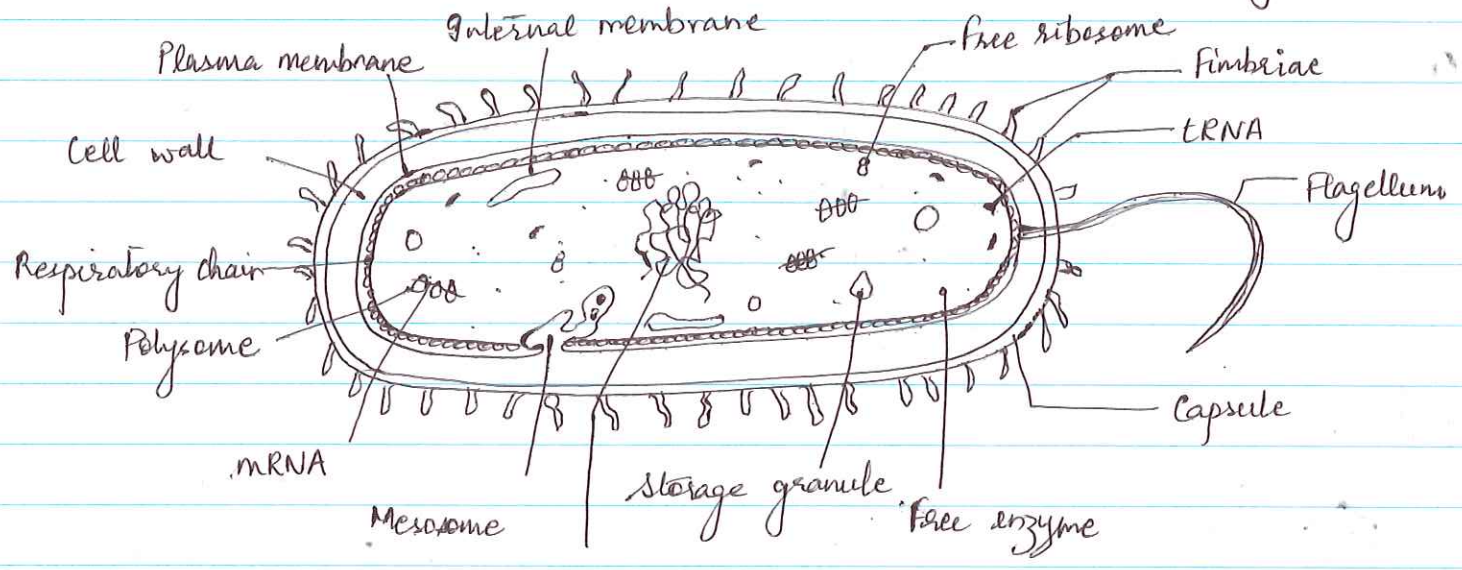
Prokaryotic
- → no nuclear membrane or organised nucleus
- eg. blue green algae, pleuropneumococci, bacteria

Mesokaryotic
- → nuclear membrane but no histones
- eg. dinoflagellate protozoans

Eukaryotic
- fully developed nucleus

Characteristics of prokaryotes

1) Very small in size
2) No nucleolus & nuclear membrane
3) single chromosome DNA material
4) no histones
5) Plasma membrane → without sterols
   - protein : phospholipid = 2 : 1
6) no endocytosis or exocytosis
7) Cell wall non cellulosic (amino acids & carbohydrates)
8) 70s ribosomes
9) plasma membrane folded as mesosomes & chromatophores
10) no organelles
11) store β-hydroxybutyrate, glycogen & phosphate granules.
12) no cytoplasmic streaming movement



Prokaryotic cell

STRUCTURE OF BACTERIAL CELL

1) **CAPSULE**
- slimy covering made of polysaccharides
- provides protection / outermost layer

2) **CELL WALL**
- strong & rigid
- carbohydrates, peptidoglycans, phosphorus, inorganic salts, teichoic acid., muramatic acid (derivate of glucose)
- Amino acid - diaminopimelic acid

3) **PLASMA MEMBRANE**
- does not contain sterols
- higher protein to phospholipid ratio (2:1)
- has a respiratory chain / oxidative chain
- can be folded or convoluted

Mesosomes / Chondroids
- invaginated plasma membrane
- site of synthesis of cell wall
- respiration & secretion
- receive DNA during conjugation
- site of DNA replication enzymes
- distribute chromosome to daughter cells

Desmosomes
- membrane sunk deep into cytoplasm
- multilayered
- eg. Thiovulum majus

4) **CYTOPLASM**
- contains granules of fats, glycogen, volutin, proteins
- can contain bacteriochlorophyll or carotenoids
- pigments can be associated with internal membranes arranged as vesicles / tubules
  - Chromatophores
- 70S ribosomes free or as polyribosomes (30S + 50S)

5) **NUCLEOID** - clear region of cytoplasm + nuclear material = GENOPHORE

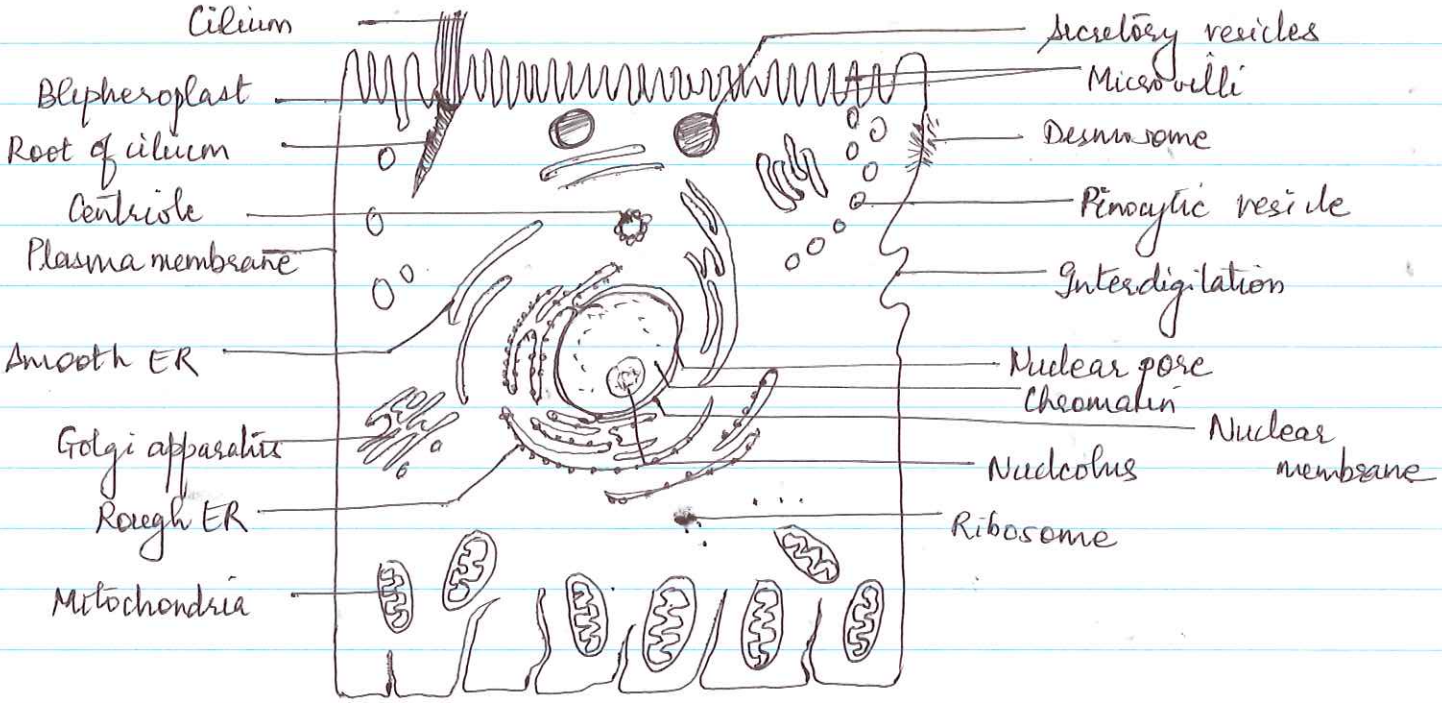
6) PLASMIDS - small double stranded circular DNA molecules
- replicate independantly
- plasmid DNA + nucleoid = EPISOME

eg. E. coli has 3 kinds of plasmids
- F factors - sex factor
- R factor - resistance against antibiotics
- Col factor - secrete colicins

7) FLAGELLA - thread like cytoplasmic outgrowth for motility
- formed of rounded subunits of flagellin
- units arranged spirally

- Atrichous: No flagella
- Monotrichous: One
- Lophotrichous: many at one end
- Amphitrichous: many at 2 ends
- Peritrichous: All over

8) PILLI / FIMBRIAE - fine outgrowths for attachment
- made of pilin protein



ANIMAL CELL

STRUCTURE OF EUKARYOTIC CELL

- Plasma membrane
- Nucleus
- Lytosome or Cytoplasm

1) **PLASMA MEMBRANE** → exceptionally thin made of lipoproteins
   - → double layer proteins sandwiching double layer of lipids (Protein = lipids)
   - → perforated & selectively permeable
   - → provides mechanical support & definite structure
   - → regulates the entry & exit of substances

2) **NUCLEUS**
   - central body in eukaryotic cells
   - spherical, oval or discoidal; may be lobed or ribbon-like
   - may be single body or formed of several bodies
   - may be diffused chromatin material in cell substance

Nuclear membrane
→ two membranes with perinuclear space

Nucleoplasm
→ Clear, homogenous, variable consistency

Nuclear reticulum
→ fine n/w of chromatin threads beaded with chromatin granules
   - histones
   - DNA
   - RNA

Nucleolus

Nucleus controls metabolic activities, cell division & hereditary transmission

3) **CYTOSOL / CYTOPLASM** → colourless, translucent, variable consistency

(a) Cytoplasmic fibrils or Cytoskeleton
   - thin, thick and intermediate filaments and microtubules
   - cytoskeletal filaments interconnected by network of thread like microtrabecular lattice
   - interconnects membranous organelles

(b) Endomembrane system

Endoplasmic Reticulum
- interconnected channels of vesicles or tubules
- not present in RBCs & prokaryotes
- bound by unit membranes

Functions
- provides mechanical support
- facilitates exchange & transport
- Protein synthesis — RER
- Cholesterol & steroid hormones — SER

Golgi complex
- Thick laminated flattened sacs/cisternae
- rich in fatty materials
- not present in RBCs

Function
- cell secretion
- processing & packaging of ER products
- form lysosomes & peroxisomes

Nuclear Envelope

(c) Membrane bound organelles

Lysosomes
- suicide bags
- hydrolytic enzymes
- cause autolysis
- intracellular digestion

Peroxisomes
- Smaller than lysosomes
- Single membrane
- Contain peroxidases that break peroxides

Mitochondria
- Constantly move
- Surrounded by double lipoprotein layer
- power house of cell
- Krebs cycle site

Plastids
- Contain pigments
- Chloroplasts or chromoplasts
- Store synthesised food

Vacuoles
- Hollow spaces
- maintain cell pressure
- digestion & excretion

(d) Non membranous organelles

Ribosomes
- protein synthesis
- composed of RNA + proteins

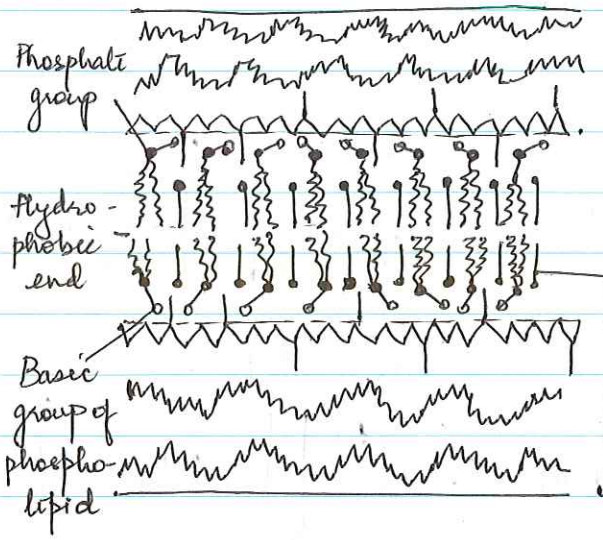
Zymogen granules
- Secretory granules
- preliminary stage of enzyme production

Ergastic substances
- lifeless material
- Reserve food

CELL MEMBRANE

- Cell membrane or plasma membrane is the outermost covering of the cell cytoplasm
  - selectively permeable
  - controls the entry & exit of molecules & maintains the difference in ionic concentration of cytoplasm

ULTRASTRUCTURE



Thickness - ~75 Å

1) Outer protein layer = 20-25 Å
2) Bimolecular lipid layer = 30-35 Å
3) Inner protein layer = 20-25 Å

→ Unit membrane as mentioned by Robertson

CHEMICAL COMPOSITION

Composed of proteins, lipids and carbohydrates (2-10%)

(A) PROTEINS
- form main bulk
- proteins separated from RBCs - tektins

(a) Peripheral proteins
- aka extrinsic proteins
- form outer and inner layer
- loosely connected
- dissolve in aqueous solutions

eg. Spectrin - RBCs
Cytochrome C - mitochondria
acetylcholinestearase - electroplex membrane

(b) Intrinsic proteins - aka Integral proteins
- penetrate lipid layer partially or completely
- polar heads protrude from surface
- non-polar heads embedded in interior
- insoluble in water
- detergents / organic solvents can separate them
- attached to

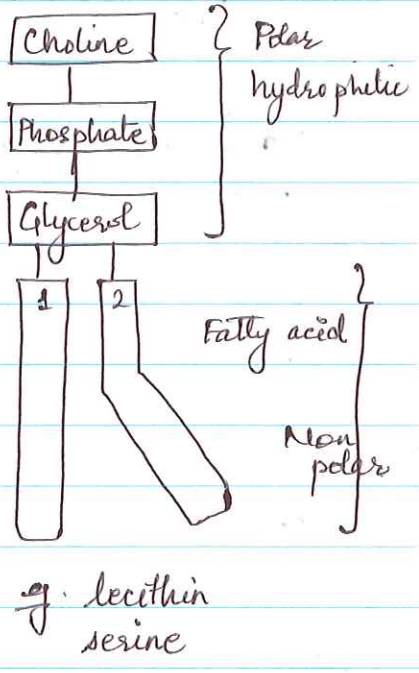
glycoproteins ← → lipoproteins
(oligosaccharides) (phospolipids)

(B) LIPIDS - 20-40% of the membrane

(a) Phospholipids - amphipathic → hydrophobic tail
↘ hydrophilic head

Hydrophilic head - polar end
- choline phosphate
- face protein layer or carbohydrates

Hydrophobic tail - non-polar end
- 2 molecules of fatty acids joined to backbone of glycerol through (-COOH) carboxyl group
- face each other



eg. lecithin
serine

(b) Cholesterol - found in plasma membrane & intracellular membranes only in eukaryotes
- mechanical strength & rigidity to fatty acid tails

(c) Glycolipids - outer lipid layer
- carry carbohydrate chains

Lipid layer - forms structural framework & permeability barrier

(c) CARBOHYDRATES - 2-10% of membrane

- eg. hexose, hexosamine, fucose, sialic acid

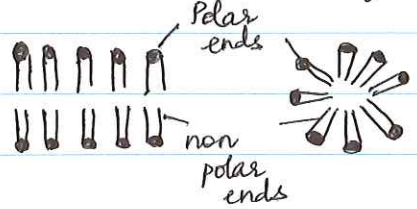
glycolipids — glycoproteins

MODELS OF PLASMA MEMBRANE STRUCTURE

Five models :- 1) Bimolecular lipid leaflet theory
2) Lamellar theory
3) Micelle theory
4) Unit membrane theory
5) Fluid Mosaic model

(1) Bimolecular lipid leaflet theory

- propounded by Gorter & Grendel
- measured lipid content of haemolyzed RBCs from mammals and found that membrane made primarily of phospholipids



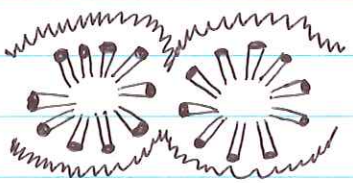
- arranged to form bimolecular lipid sheet
- polar ends towards water & cytoplasm
- non-polar ends facing each other.

(2) Lamellar Theory

- propounded by Danielle & Dawson
- lipoprotein model
- lipid layer sandwitched between β-folded proteins
- electrostatic attraction b/w polar lipid heads & charged amino acid side chains
- Variations

- β-folded proteins both sides
- globular proteins on both sides
- helical proteins both side
- globular & β folded on one side each
- β-folded on both with helical proteins extending to pores

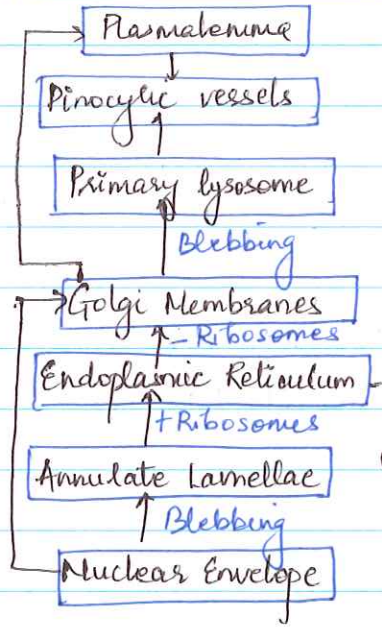
(3) MICELLAR THEORY



- propounded by Hillier & Hoffman
- mosaic of globular micelles of lipids with monolayer of globular proteins on both sides
- space b/w globular micelles represents poses bounded by polar groups of micelles & proteins

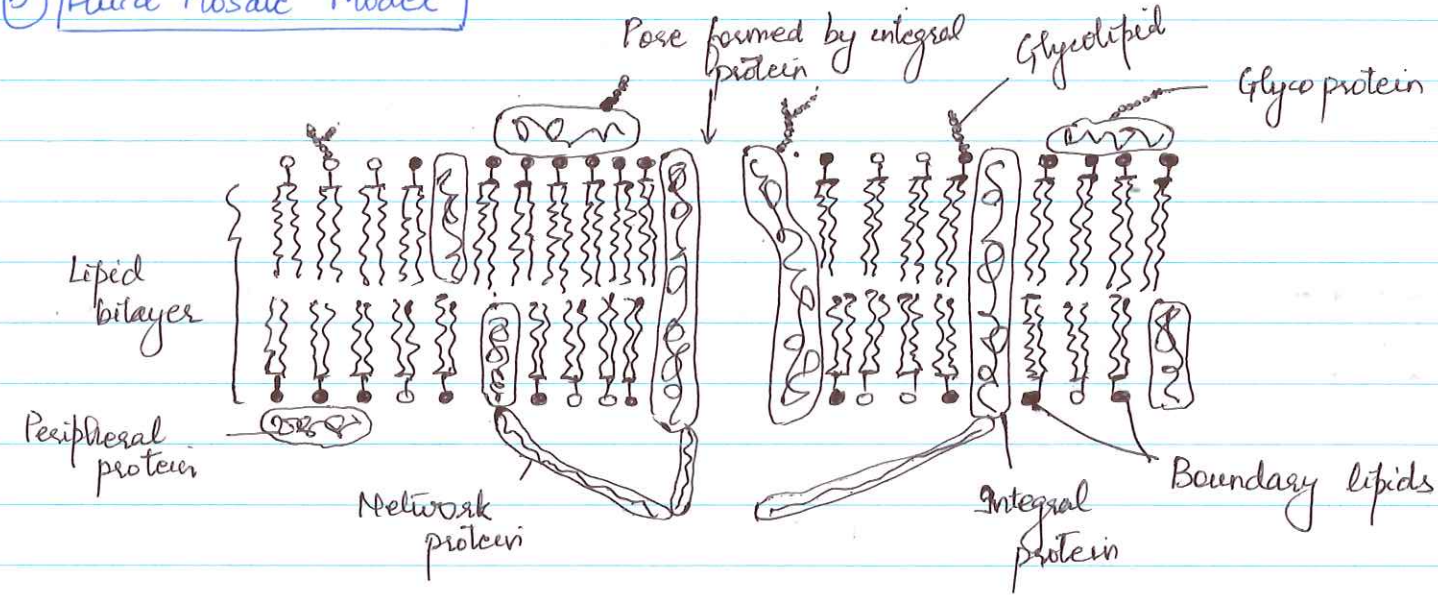
- micellar form can convert to lamellar form & vice versa

(4) UNIT MEMBRANE Model



- propounded by Robertson
- trilamellar structure with two osmophilic layers (protein) and a osmophobic layer (lipids)
- all cell organelles (ER, Golgi complex, lysosome, mitochondria, chloroplast & nuclear membrane) had similar structure
- various membranes are interrelated & derived from nuclear or plasma membrane

(5) Fluid Mosaic Model



- propounded by Singer & Nicholson
- Quasi fluid biological membrane

Features :- » lipids & integral proteins are amphipathic ⟨ hydrophobic / hydrophilic

» hydrophilic layer towards water phase
» hydrophobic region towards lipid bilayer
» arranged in mosaic fashion

» lipids, proteins and oligosaccharides held by non covalent interaction
» fluidity dependant on saturation of hydrocarbon chains of lipids

Non saturated (double / triple bonded) → Melting point low → Quasifluid at body temperature

Saturated (single bonded) → High melting points → less in amount

» lipids show lateral movement
- intra molecular (motion within lipid molecules)
- rotation on axis
- flip flop movements

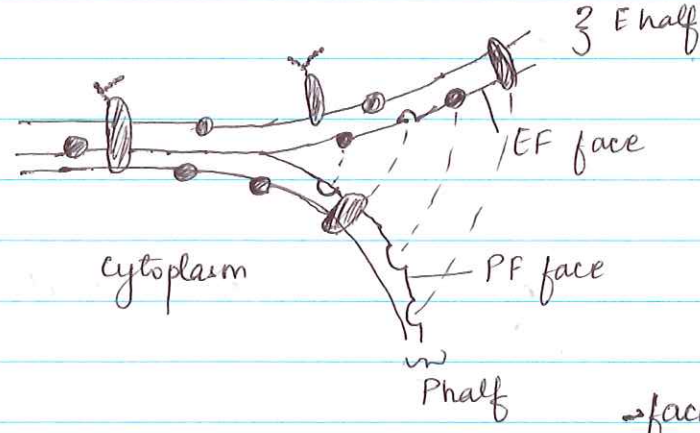
» proteins show movements
- lateral diffusion
- rotational diffusion ⊥ to P.M.
- rotational diffusion // to PM

» active sites of enzymes & antigenic glycoproteins on outer surface of membrane
» quasifluid nature allows diffusion of macromolecules through the membrane

Experimental Evidence in support of fluid Mosaic Model

Freeze-fracture model - from freeze fractured samples of RBCs
- by D. Branton

- membranes rapidly fracture along specific planes



- when plane of fracture intersects plane of membrane we get two half membranes

E-leaflet (Exoplasmic) → faces cell exterior

P-leaflet (protoplasmic) → faces protoplasm

Original membrane face = E face & P face
Fractured membrane face = EF face & PF face

Factors controlling fluidity

- Fluidity of plasma membrane means liquid crystalline structure at normal temperature
- provides flexibility
- facilitates transitional movement of lipids & integral proteins
- depends on transition of lipids from crystalline gel to liquid crystalline form

(a) degree of saturation of hydrocarbon chain
(b) cholesterol
↓
interferes with crystalline gel formation & provides fluidity

FUNCTIONS OF PLASMA MEMBRANE

1) Selective transport of substances and regulation of passage
   - selectively permeable
   - through : passive transport → diffusion, facilitated diffusion, osmosis
     active transport
     endocytosis → pinocytosis, phagocytosis
     exocytosis

2) Maintains differential distribution of ions
   - eg: K^+ inside cell & Na^+ / Cl^- outside cell
   - unequal distribution leads to a potential difference called membrane potential
   - happens with large amount of energy.

3) Response to environment
   - through receptor proteins
   - cell recognition through glycoproteins

4) Contact with neighbouring cells
   - structural & chemical relationships
   - communication through gap junctions

5) Cell recognition
   - distinguish between self & non self
   - glycocalyx on the surface provides molecular identity to cells

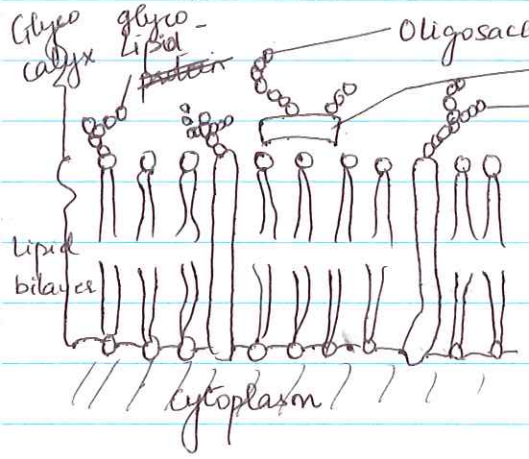
6) Cellular adhesion

7) Protection

8) Excretion

GLYCOCALYX

→ thin film all along cell surface except tight junctions
→ fuzzy coat on intestinal absorptive cells
- formed of mucopolysaccharides (eg. glycolipids, glycoproteins, polysaccharides)
- cell coat has (-)vely charged sialic acid
- can bind Na^+ & Ca^{2+} ions



FUNCTIONS

1) Stability
2) Protection - eg in gastrointestinal tract
3) Maintains microenvironment of cell - through pH & electrostatic charge
4) Filtration
5) Enzymes (contains) - eg microvilli
6) Antigenicity - in RBCs
7) Molecular recognition
8) Cellular recognition (biological compatibility)

Functions of membrane proteins

(a) Structural proteins - backbone of cell membrane
- elasticity & stability
- no catalytic functions

(b) Enzymes - catalytic proteins
- carry out biological reactions

(c) Membrane transport proteins - permeases
- for transport of polar molecules eg. ions, monosaccharides, nucleotides, metabolites

→ basically multipass transmembrane proteins projecting on both sides of lipid bilayer.

Types :- CARRIER PROTEINS - bind specific solute
- undergo conformational change
- help in active transport

CHANNEL PROTEINS - water filled poses extend across lipid bilayer
- when poses open, specific solutes pass

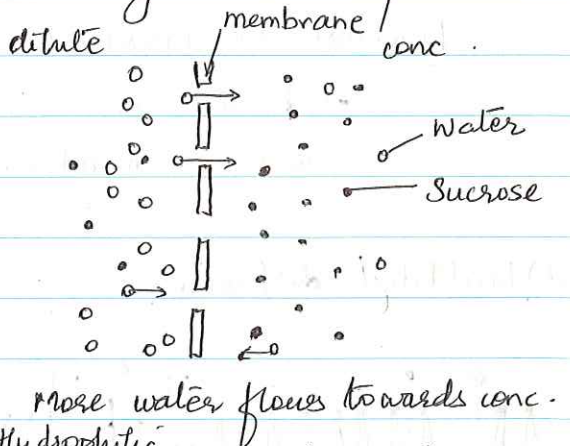
(d) Glycoproteins - cell receptors or cell antigens

(e) Lipoproteins - drug receptor proteins

Transport through Plasma Membrane

Transport of water - Osmosis

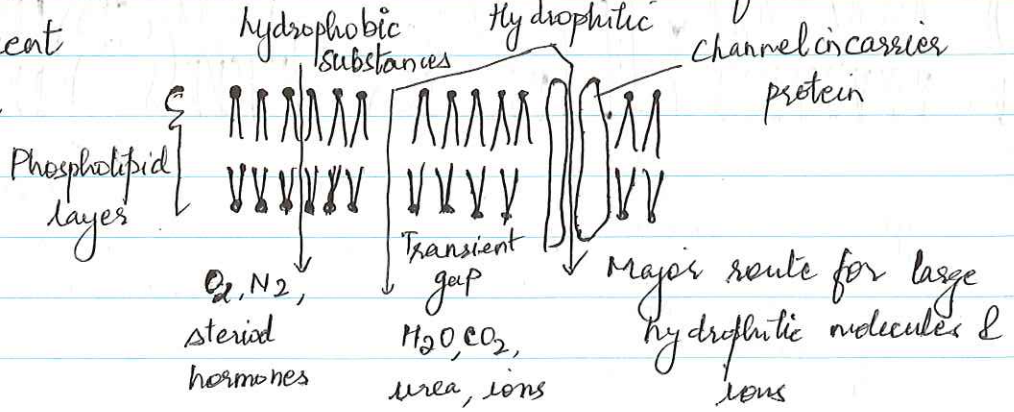
- diffusion of water or solvent molecules through plasma membrane from low osmolic pressure (dilute) to high osmotic pressure (concentrated)
- PM acts as differential membrane



Transport of ions & small molecules

Passive Transport

→ from high to low conc.
→ along conc. gradient
→ no energy required



Types of passive transport

(a) Simple diffusion
- along the conc. gradient
- without carrier molecule
- through gaps or channels or membrane proteins (channel proteins)

eg:
→ Lipid soluble molecules diffuse rapidly by dissolving through lipid bilayer

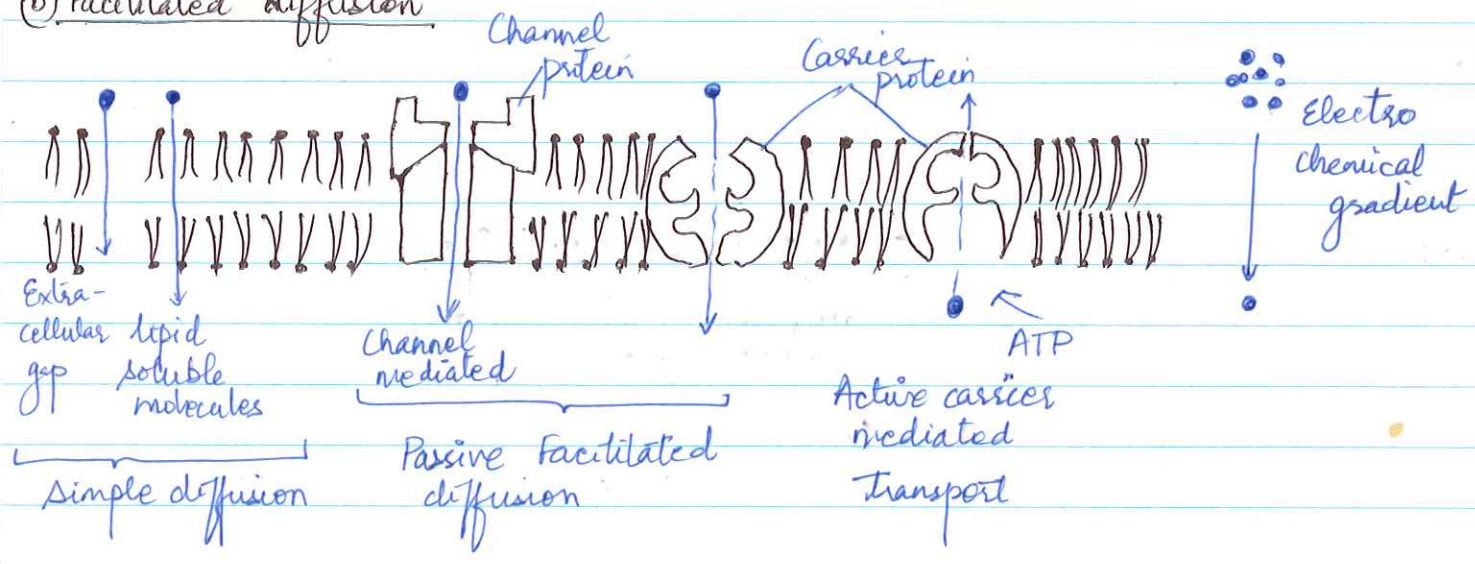
→ lipid insoluble small molecules (H_2O, CO_2, urea, glycerol) slowly diffuse through channel or tunnels (transient gap or carrier proteins)

→ Passive diffusion of ions depends on → chemical gradient
→ electrical gradient

It is a balancing act b/w these 2 forces
- cell contains (-)ve organic anions → show affinity to K^+ ions
- environment contains (+)ve inorganic cations

K^+ ions in excess inside cell so they diffuse outward till DONNAN EQUILIBRIUM is reached.
→ hence conc. of K^+ & Cl^- ions and a membrane potential

(b) Facilitated diffusion



→ metabolite diffusion facilitated by PM proteins w/o energy
→ proteins k/a permeases

STEPS :-

1. Diffusion molecules combine with cassies protein molecules (cassier - protein complexes)
2. Conformational change in cassier protein
3. Molecules pass to PM insides
4. Conformational change lowers the affinity to molecules
5. Molecule released inside cell
6. Original shape of cassies protein reached

Different from simple diffusion
→ stereospecific (either L or D isomer transported)
→ shows saturation kinetics
→ cassies proteins move to & fro through thermal diffusion

(c) Active Transport
- against conc. gradient
- requires energy (ATP)
- sugars, metabolites, Na^+ / K^+ / Cl^-, nucleotides etc participate.

CARRIER MOLECULE MECHANISM

→ cassies molecule from PM picks up the molecule & forms cassies transportant complex
for eg. for Na^+, Mg^{2+} activated ATPase functions as cassier.
→ carrier k/a translocase or permease

$Na^+ + Carrier \rightarrow Na^+C$

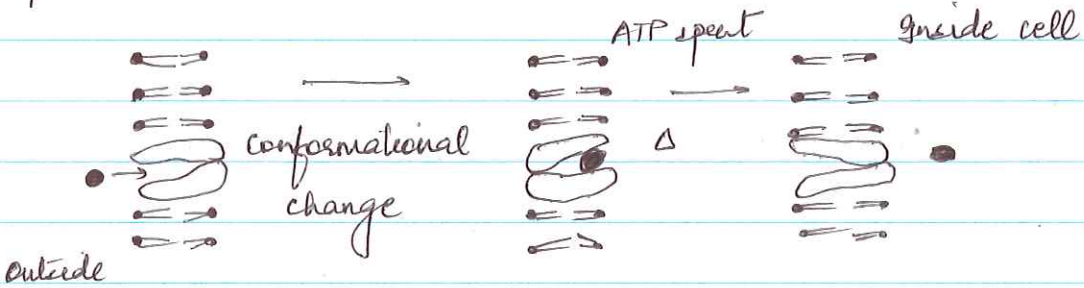
$Na^+C + ATP \longrightarrow ATP\text{-}C + Na^+$

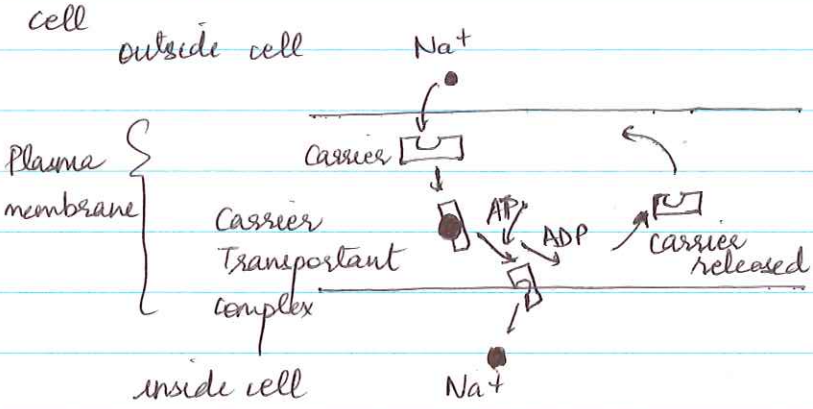
$ATP\text{-}C \xrightarrow{ATPase} ADP + C$

REVOLVING DOOR MODEL

- → explained by Monod & Cohen during lactose transport in E. coli
- carrier slot faces outside ; molecule fits in
- → carrier slot revolves & opens slot inside
- → molecule released
- → energy spent during rotation

Active transport helps maintain definite ionic concentration & osmotic pressure inside the cell.





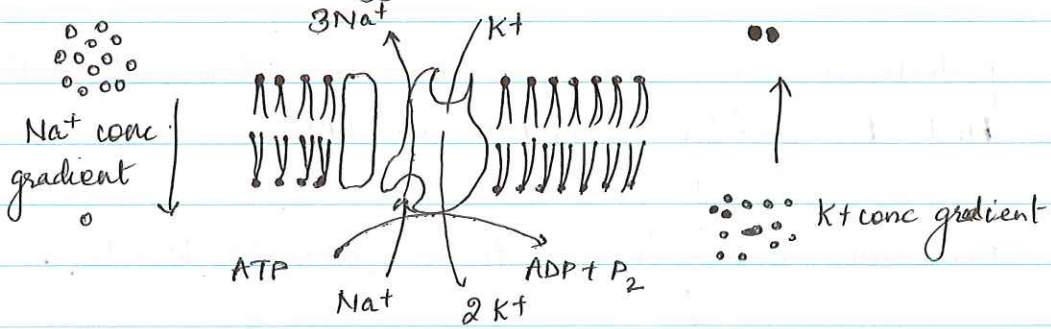
Transport of solid particles — Pinocytosis + Phagocytosis

↓ for high molecular wt. molecules like proteins that cannot pass through PM

↓ eg WBC engulfs foreign particles

SODIUM POTASSIUM PUMP

→ pumping of Na^+ & K^+ ions occurs <u>against</u> electrochemical gradient
→ through $Na^+ - K^+$ ATPase
→ Enzyme ATPase hydrolyses ATP to ADP to release energy
→ This energy used to pump 3 Na^+ out & get 2 K^+ inside.



<u>STEPS</u> :- $Na^+ - K^+$ - ATPase binds 3 Na^+ inside cell

↓

ATP hydrolysed to ADP & energy released

↓

Conformational change in receptor through <u>phosphorylation</u>

↓

Na^+ affinity lost & released outside cell

↓

K^+ ions taken up from outside cell

↓

Causes dephosphorylation of $Na^+ - K^+$ ATPase

↓

Original form of receptor

↓

K^+ released inside cell

Each pump transport 6000 K^+ ions per minute

Importance of active transport

- absorption of glucose in uriniferous tubules
- absorption of monosaccharides in intestine
- maintain $Na^+ - K^+$ pump for nerve impulse transmission
- pump solute against electrochemical gradient

PINOCYTOSIS

- uptake of fluid & aka "cell drinking"
- observed by Lewis
- induced by proteins, amino acids & ions
- in WBCs, kidney cells, intestinal mucosa & hepatic cells.

- proteins or amino acids in medium outside the cell bind to specific receptors in PM

↓

Membrane invaginates & forms Pinocytic vesicle.

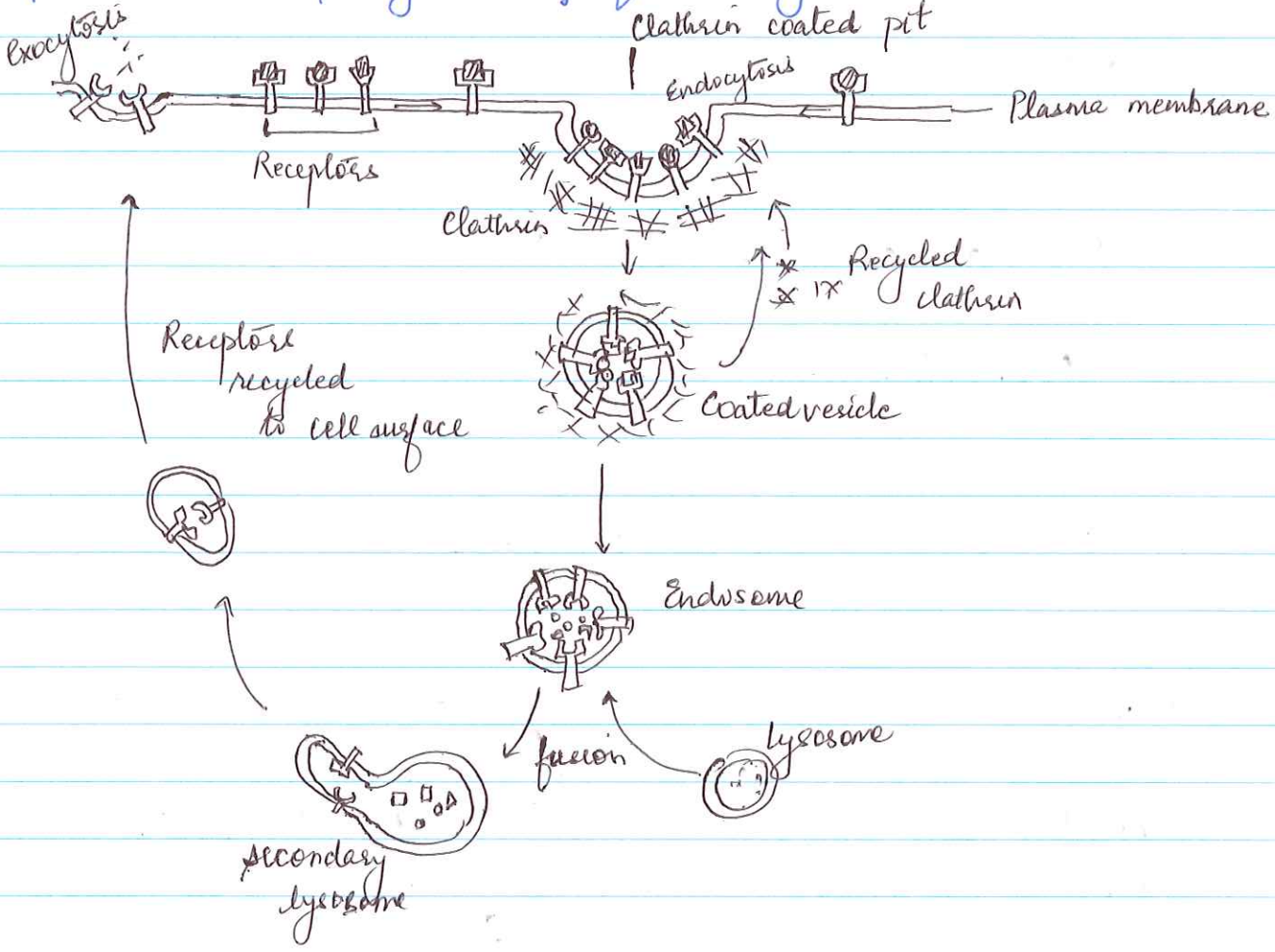
↓

Pinched off into the cytoplasm called pinosome

↓

Fuses with lysosome to form secondary lysosome.

Receptor mediated pinocytosis / specific endocytosis :-



→ for substances like yolk, cholesterol, steroid hormones, GH, insulin, low density lipoproteins (LDL)
→ selective swallowing even in extreme low conc.
→ coated pits formed by invagination of membrane.
↓
coat made of protein clathrin.

PHAGOCYTOSIS

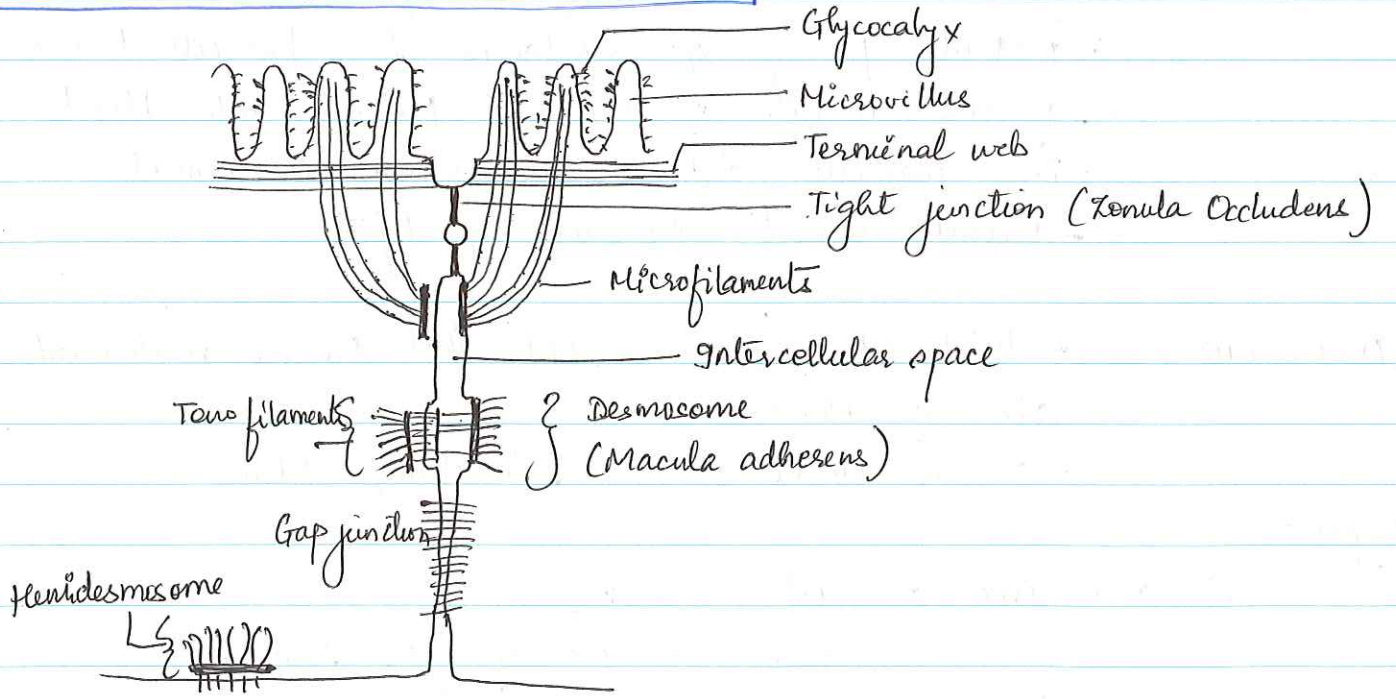
→ engulfing very large particles
→ eg. protozoa, leukocytes, macrophages

→ Adsorption → Pseudopodia extended → Engulfed to form phagosome.

EXOCYTOSIS

- cell vomiting
- undigested material from phago/pinocytes
- may be through direct sticking to membrane
- or packaged in secretory vesicles by Golgi complex.

SPECIALISATIONS OF PLASMA MEMBRANE



Plasma membrane may be specialised in relation to absorption, secretion or fluid transport.
Neighbouring cells connected through cell junctions, secretions, physiological processes, etc.

(1) MICROVILLI
- minute finger like outpushings
- brush like border for increased surface area.
- inside intestinal epithelium, kidney tubules, uterus
- connected with transverse n/w of fibres called Terminal web

(2) TIGHT JUNCTION - aka Zona Occludens
- plasma membranes touch each other obliterating the intercellular space
- outer components of trilaminar membranes fused together
- form a band or girdle encircling a cell
- interlocking n/w of transmembrane linkers
- act as barriers to diffusion of macromolecules
- prevent passage of substances to & fro cell lumen.
- prevent leakage of pancreatic proteins into blood
- helps maintain different intercellular environment
- prevent lateral diffusion of lipids

(3) DESMOSOMES
- thickened regions of PM that provide mechanical adhesion b/w cells.
- act as anchorage to intercellular fibres

Types :-

Belt desmosomes - zonula adherens
- intermediate junctions or terminal bars
- just below tight junctions

- formed of → actin microfilaments (highly contractile)
  → intermediate filaments of actin binding proteins

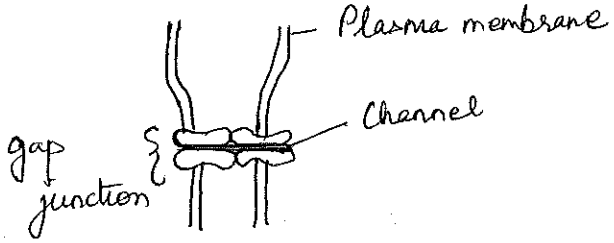
Spot desmosomes - aka macula adherens
- localized, circular or button like areas for mechanical attachment

contains → intercellular space
→ central stratum
→ Intracellular plaque
→ Tonofilaments
→ Transmembrane linkers

Hemidesmosomes - on the basal surface of some epithelial cells
- represented by one half

Septate desmosomes - in epithelial cells of invertebrates

④ GAP JUNCTION - appears as plaque like contact
- PM of adjacent cells in close approximation
- appears as annulus or cylinder
- rotation of connection proteins & closing of channels mediated by Ca^{2+} concentration



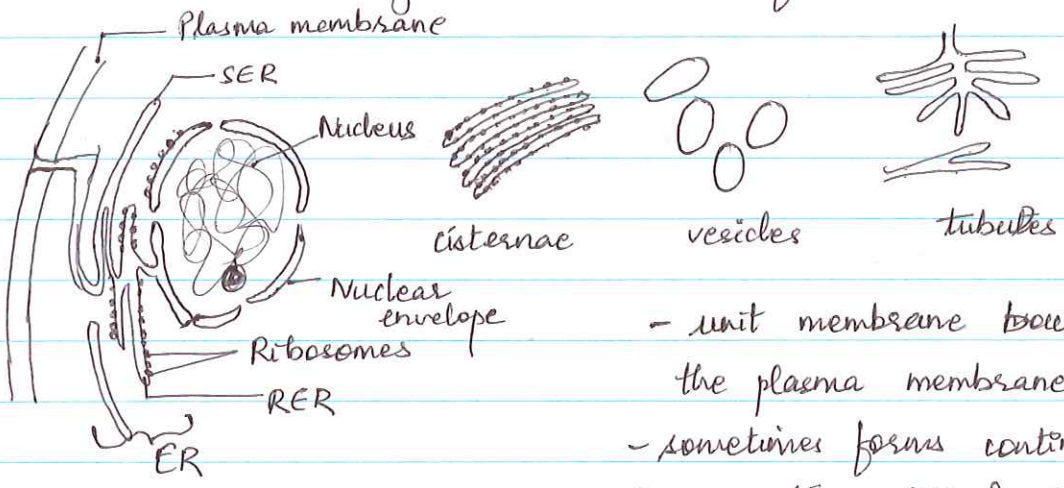
Functions :- Communication of electrical signals in cardiac muscles
metabolic cooperation
» widely observed in embryonic tissue

ENDOPLASMIC RETICULUM

Cytoplasmic Endomembrane System - aka **vacuolar system**

- represents the entire system of intracellular membranes and membrane bound vesicles traversing the cell cytoplasm
- Components :-
  (a) Nuclear envelope
  (b) ER
  (c) Golgi Apparatus
  (d) Lysosomes
  (e) Peroxisomes
  (f) Glyoxisomes
- packages, sequences & transports material within & outside cell

Endoplasmic Reticulum - elaborate system of flattened tubules or channels in ground substance of cell



- unit membrane bound similar to the plasma membrane
- sometimes forms continuous channels by connecting PM & nuclear envelope

3 components
- **cisternae** - long, flattened & lamellar vesicles
  - arranged in || rows
- **vesicles** - rounded, spheroidal or ovoidal
- **tubules** - irregularly branched
  - common in retinal epithelium & cells that synthesise steroids

ER Types

Agranular / SER
- without ribosomes
- lipid synthesis
- occurs in cells that donot synthesise proteins eg: adipose cells, muscle cells, glycogen storing cells

Granular / RER
- with ribosomes
- protein synthesis
- found in cells actively involved in protein synthesis eg: liver cells.

Enzymes associated with ER

- 30-40 enzymes located on ER membranes.
- may be associated with cytoplasmic or luminal surface

Enzymes :-
1. β-glucuronidase
2. Glucose-6-phosphatase
3. Mg-activated ATPase
4. Stearase
5. Cytochrome P-450
6. NADH Cytochrome b_5 reductase
7. NADPH Cytochrome C reductase
8. Nucleoside pyrophosphatases
9. NADH diaphorase

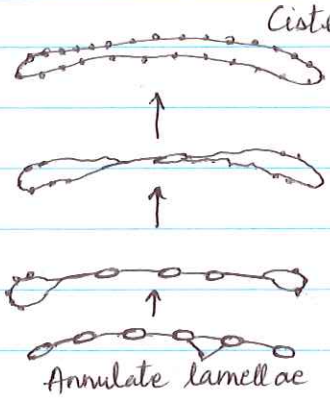
Enzyme functions :-
- Synthesis of - fatty acids
  - cholesterol
  - steroids
  - glycerides
  - phospholipids
  - L-Ascorbic acid
- Metabolism of - plasmalogen
  - UDP uronic acid
- UDP glucose dephosphorylation

Functions of ER

1) provides supplementary mechanical support to colloidal matrix
2) forms skeletal framework
3) Membranes of ER act as segregation apparatus & help regulate osmotic pressure
4) intracellular transport
5) increased surface area for metabolic activity
6) Protein synthesis through Microsome fractions
7) Glycogen metabolism (SER in liver cells)

8) Site of ATP synthesis
9) forms other cytomembranes eg Golgi body, mitochondria
10) Provides passage to RNAs from nucleus to various organelles

Annulate Lamellae



- usually ER membranes w/o pores
- in some cells, may contain pores & pore complexes
- these are annulate lamellae
- found in cells of invertebrates, immature oocytes & spermatocytes in vertebrates & foetal & embryonic cells (with fast metabolism)
- structually similar to nuclear membranes as it arises from it

Blebbing → finger like projections blebbed off from nuclear membrane to form ER & lamellae.

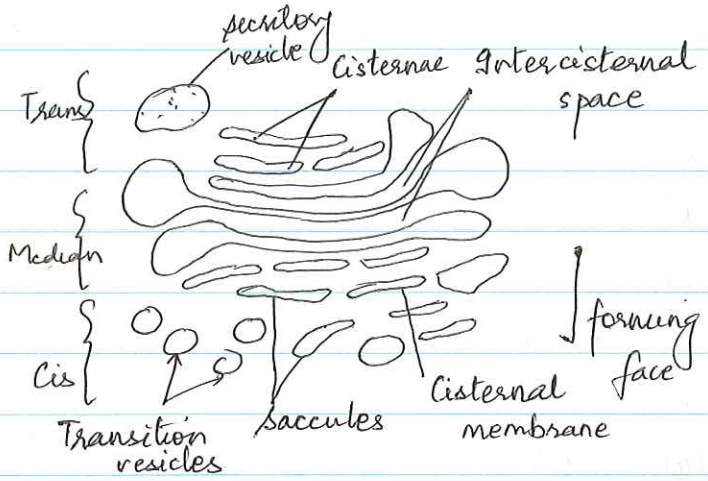
Microsomes

→ Lives homogenate in 25M sucrose solution
↓ differential centrifugation
nuclear membrane, mitochondria, cell debris removed
↓ spun at high speed
Microsomal fractions settle at the bottom

→ ribosomes isolated, membranes of ER & golgi body & attached ribosomes
→ heterogenous precipitate
→ constitute 15-20% of cell mass
→ consists of 50-60% RNA, lipids (few) & enzymes.

GOLGI COMPLEX

→ differentiated portion of vacuolar system
→ related to ER & secretory vesicles morphologically & functionally
→ discovered by Camillo Golgi
– occurs in all cells except – prokaryotic cells
– RBCs
– sperms & sieve tubes
– scattered in plant cells & k/a dictyosomes.



– stacks of membrane bound spaces

1) Cisternae – central plate-like part
– stacks of flattened compartments
– enclosed by unit membrane
– somewhat cresentic
– convex face towards ER or nuclear membrane
– concave face towards PM
– smaller towards convex face and elongated towards concave (maturing) face
– vesicles / vacuoles break off from tips due to concentration of secretory substances
– secretory vesicles form zymogen granules or lysosomes

2) Transition vesicles – drop like structures associated with forming face
– lie next to SER
– develop from cisternae of ER & fuse to form Golgi cisternae
– forms zone of exclusion or region of transition from ER to Golgi body

3) Secretory vesicles – present on maturing face

- pinched off from trans face of Golgi & form zymogen granules or lysosomes

4) Coated vesicles - coated with protein clathrin

5) Golgi vacuoles - large rounded sacs
- formed by expanded cisternae or fused vesicles
- filled with amorphous or granular substance

Polarity & membrane flow in Golgi

- polarised as they have a forming & a matured face
- vesicles break away from ER → fuse to form cisternae
  (zone of exclusion)
  ↓
  Form lysosomes ← Break off to form vesicles
- association veseble in GERL region
- GERL is region b/w PM & Golgi where secretory vesicles get converted to lysosomes by concentration of products synthesised in ER.

Chemical composition

(1) Phospholipids - membrane

(2) Enzymes - like acid phosphatases, Mg^{2+} ATPase, ADPase, galactosal transferase, glycosamine transferase

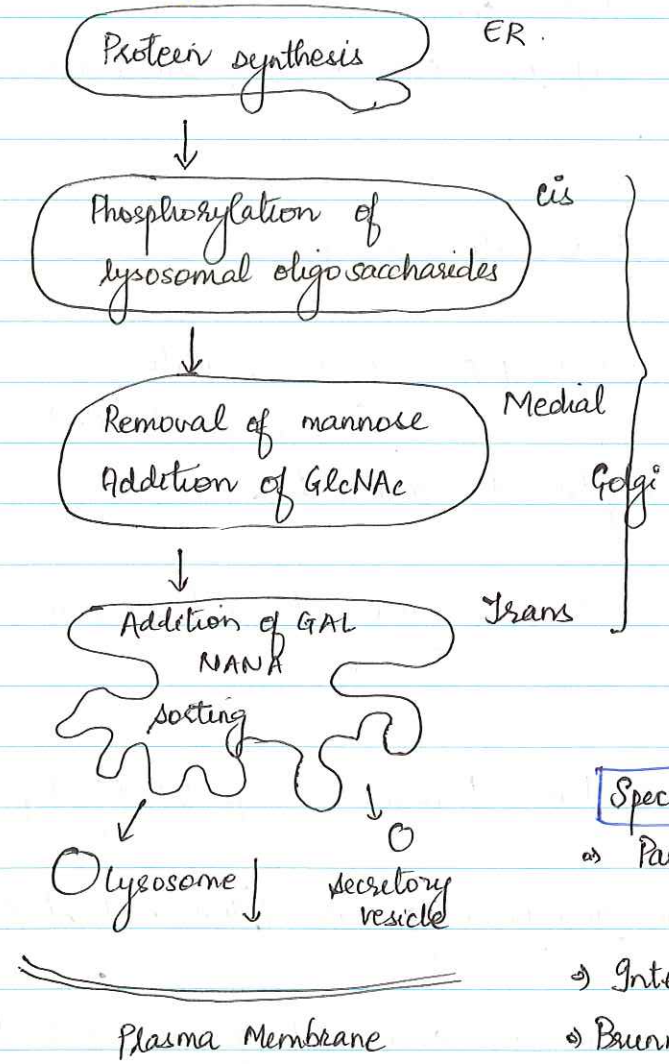
(3) Carbohydrates - glucose, mannose, galactose, glucosamine

Functions

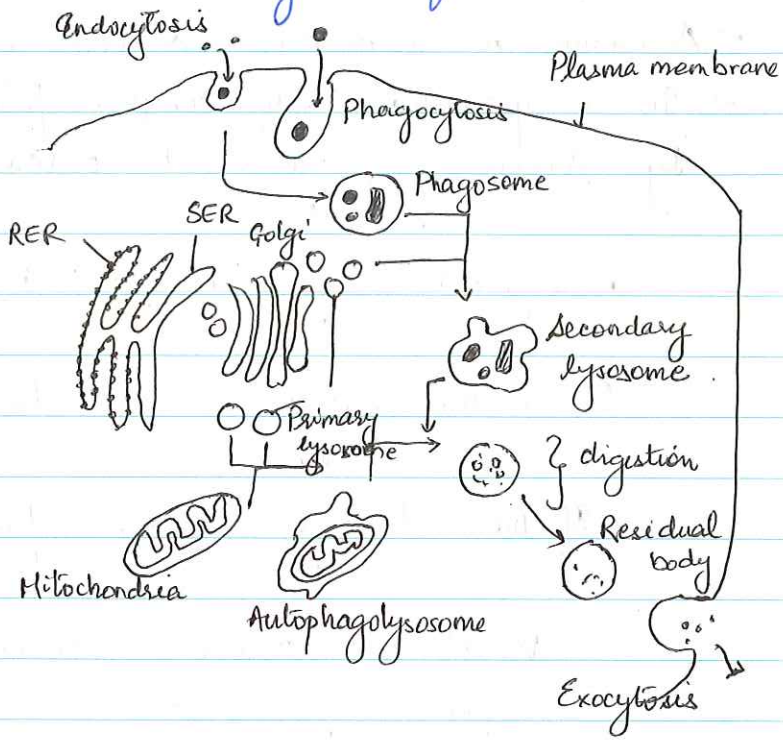
1) Secretion of substances synthesised elsewhere in cell
2) Packaging, concentration of modification of materials
   eg glycoproteins & lipoproteins

3) Forms primary lysosomes
4) Synthesis of glycoproteins
5) Synthesis of complex carbohydrates like pectin & polynucosaccharides.
6) Cell plate during anaphase of mitosis.
7) Formation of cell wall
8) Formation of acrosome of sperm.

Secretory Function



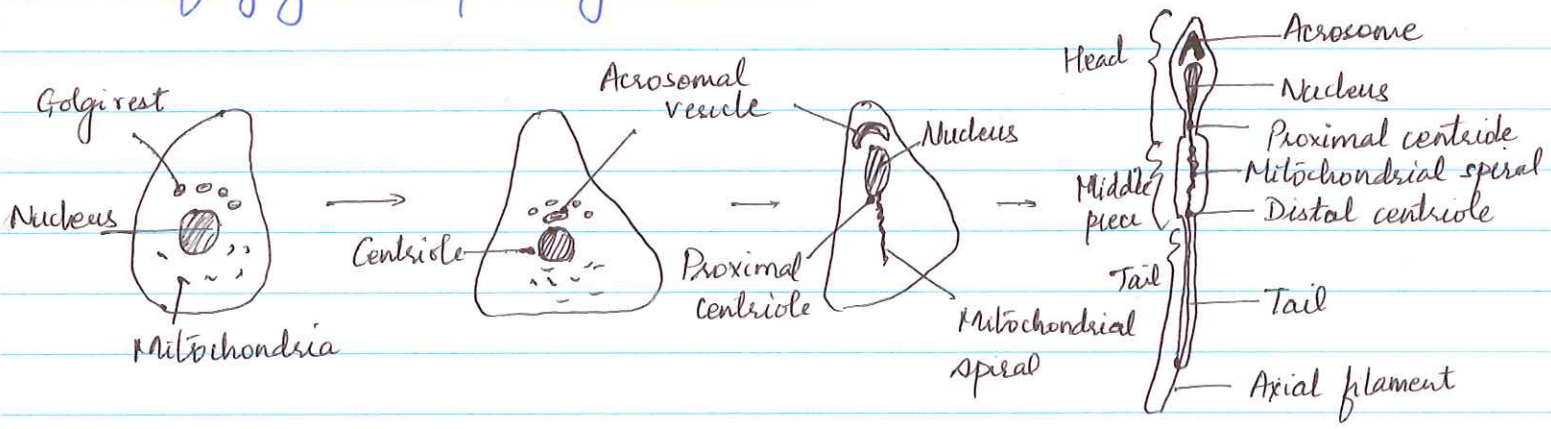
Lysosome formation



Specific functions

- Pancreas - secretion of protease, lipase & digestive enzymes
- Intestine - secretion of mucous
- Brunner's gland - secretion of mucopolysaccharides
- Liver - transformation of lipids
- Plasma - immunoglobulins
- Thyroid gland - prothyroglobulin

Role of golgi in spermatogenesis



→ Acrosome of spermatozoon derived from Golgi complex

→ In a spermatid, Golgi complex formed of numerous vesicles surrounded by concentrically arranged cisternae.

↓

arrangement becomes irregular, 2 or 1 vacuole enlarges

↓

Inside the vacuole, a dense body called proacrosomal granule (mucopolysaccharide)

↓

If more than one, vacuoles fuse together to form 1.

↓

Vacuole with acrosomal granule enlarges & move towards anterior region

↓

Attaches to tip of elongated nucleus forming a cap (caps stage)

↓

Proacrosomal granule enlarges to form acrosomal granule (acrosomal stage)

↓

Vacuole loses liquid content & spreads over acrosomal granule & half the nucleus to form a double sheath (acrosome cap)

↓

Remainder Golgi complex undergoes gradual regression & discarded as Golgi rest along with cytoplasm of spermatid

LYSOSOMES

- Small membrane bound organelles called 'suicide bags' of the cell
- discovered by Christian de Duve
- rounded or spherical
- can be enlarged eg. uriniferous tubule cells.
- bound by unit membrane.

Chemical composition or enzymes

- matrix of lysosomes contains tissue dissolving enzymes - hydrolases & acid phosphatases

	Substrate	End product
(a) Nucleases		
- Acid ribonuclease	- RNA	
- Acid deoxyribonuclease	- DNA	
(b) Phosphatases		
- Acid phosphatases		
- Phosphodiesterase		
(c) Proteases & peptidases	- proteins	
- eg. Collegenase, peptidase, cathepsins		
(d) Glycosides	- carbs	
- α glucosidase		
- β glucosidase		
- α mannosidase		
(e) Sulphatases	- sulphate esters	
(f) Lipase	- fats	
(g) Esterase		
(h) Lysozyme	- mucopolysaccharides	(bacterial cell wall)
(i) Sphingomyelinase		

POLYMORPHISM

- various stages of digestion

1. PRIMARY LYSOSOME
- storage granules
- newly formed from Golgi complex
- contain only hydrolytic enzymes

2. SECONDARY LYSOSOME
- heterolysosomes or heterophagic vacuoles
- formed by fusion of lysosymes with phagosomes
- contain digestible material + enzymes

(a) Large digestive vacuoles - lysosome + phagosome
- phagolysosome

(b) Multivesicular body - endocytic vesicles + lysosome
- endolysosome

(c) Autophagic vacuoles - digest intracellular material or organelles
- present only under special physiological conditions
- autophagolysosome
- being autodissolution or autodigestion

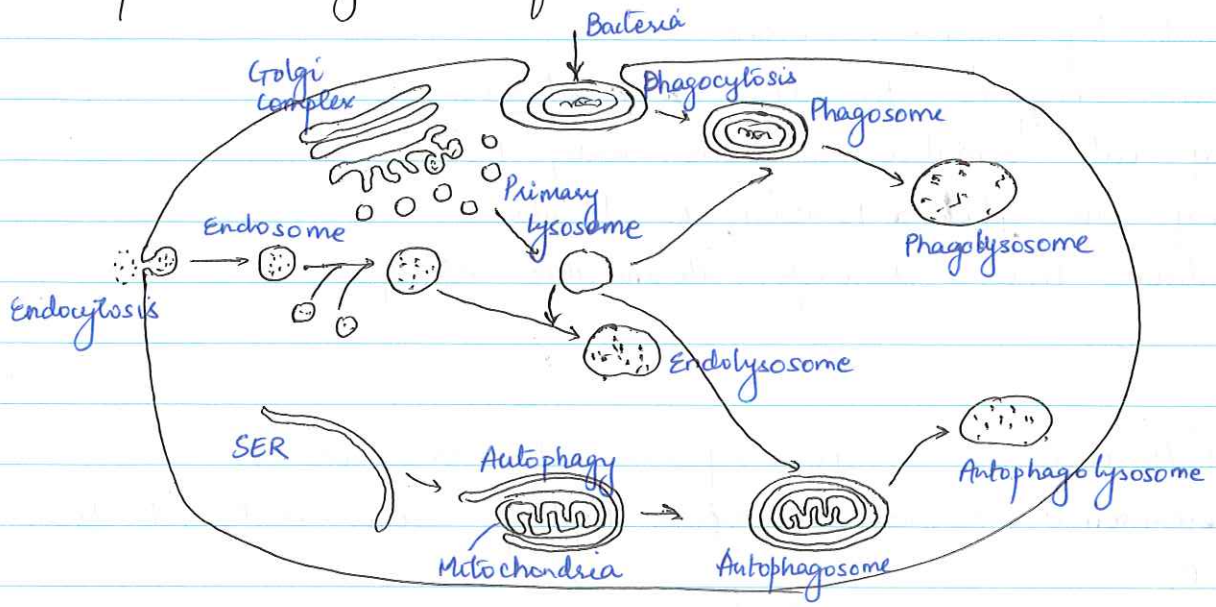
(d) Cytolysosomes - enlarged observed in dying cells

3. RESIDUAL BODIES
- exhausted lysosomes with undigested wastes
- aka telolysosomes.

Functions

1) Heterophagy or digestion of external particles (eg. protozoa, sponges, cnidarians)
2) Autophagy or autolysis
3) lysis of organelles during metamorphosis or differentiation
4) scavenging old parts of cell
5) bone resorption (osteolysis)
6) penetration of sperm into ovum.

7) digesting yolk during embryonic development
8) protection against infection



Lysosomal diseases

(a) Silicosis - inhalation of silica or asbestos fibres
↓
enclosed in secondary lysosomes but indigestible.
↓
rupture membrane of lysosomes & lung cells gets digested

(b) Rheumatoid arthritis - inflammation of body joints
- caused by release of lysosomal enzymes into extracellular space.

Why lysosomal enzymes inactive inside lysosome?

→ membrane resistant
→ membrane doesnot permit release of enzymes
→ do not act in acidic medium
→ cell cytoplasmic alkaline so can be digested

PEROXISOMES

- found in all eukaryotic cells
- bounded by single membrane
- contain enzymes peroxidases & catalases
- carry out oxidative reactions using O_2
- carry out photo respiration in plants
- produce H_2O_2 through degenerative activity

Functions :-

(a) Oxidation / Respiration :- cell respiration like mitochondria

(i) Peroxisomal oxidase transfers Hydrogen atoms to O_2 to form H_2O_2.

$$RH_2 + O_2 \xrightarrow{\text{Oxidase}} R + H_2O_2$$

(reduced substrate)

eg. uric acid oxidase, D-amino acid oxidase

(ii) Peroxisomal catalase immediately breaks down H_2O_2

$$2H_2O_2 \xrightarrow{\text{Catalase}} 2H_2O + O_2$$

or

$$H_2O_2 + R'H_2 \xrightarrow{\text{catalase}} R' + 2H_2O$$

(b) Permeability - membrane binding peroxisomes are highly permeable
- inorganic ions & low mol. wt substances pass easily

(c) Detoxification - in livers & kidney

(d) Metabolism of fatty acids - breakdown fatty acids to Acetyl CoA which begins Kreb's cycle.

GLYOXYSOMES

- similar to peroxisomes
- also contain enzymes of glyoxylate cycle.

- present in plant tissues
- enzymes eg. isocitrate lyase or malate synthetase
- help convert fatty acids to carbohydrates
- absent in animal cells.

SPHEROSOMES

- spherical & occur in most plant cells
- originate from ER
- contain lipids & proteins
- donot exhibit wide range of lytic action
- due to lipids, different from lysosome
- may contain hydrolytic enzymes eg. maize endosperm.

RIBOSOMES

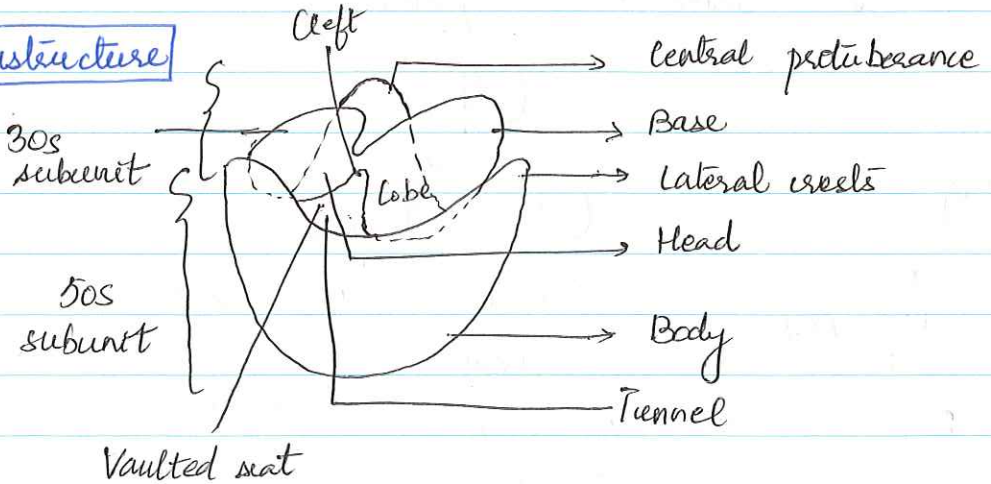
- submicroscopic granules found in all living cells
- attached to ER or scattered
- first observed by ~~Palade~~ Claude

70s (prokaryotes, mitochondrea, chloroplasts)

80s (eukaryotes)

based on sedimentation rate

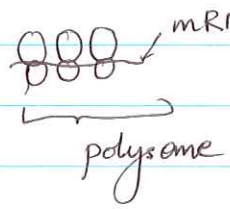
Ultrastructure



Lake model of prokaryotic (70S) ribosomes

(a) 30S small subunit → asymmetric / rod like
→ divided into two lobes by a deep groove / cleft
→ smaller head, larger base
- small outgrowth arises from base segment & is called platform.

wt. = 1·0 mn daltons
16S · rRNA + 21 proteins



(b) 50S large subunit → more or less spherical
→ 2 lateral & 1 central projection
→ flat anterior

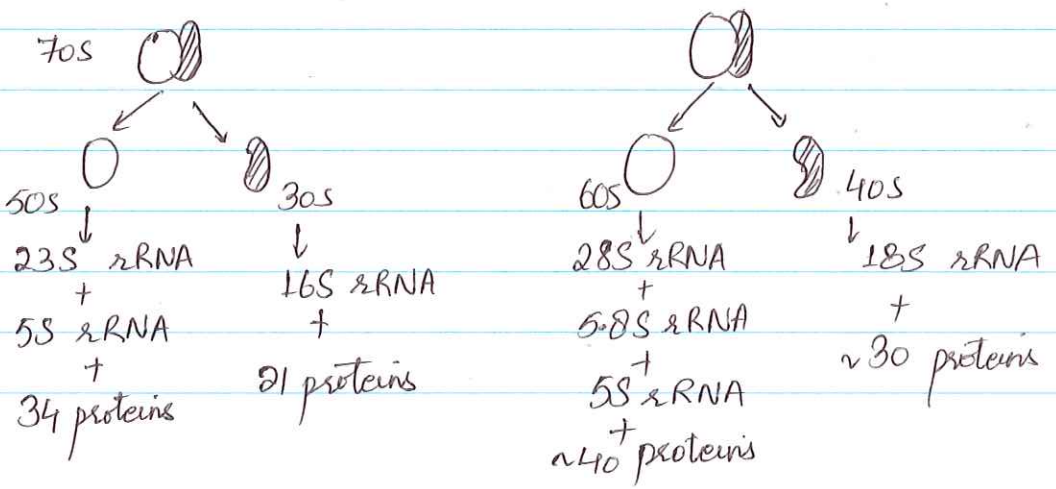
wt. = 1·8 mn Daltons
= 23S rRNA + 5S rRNA + 34 proteins

During protein synthesis, mRNA threaded through the tunnel.

Eukaryotic ribosome

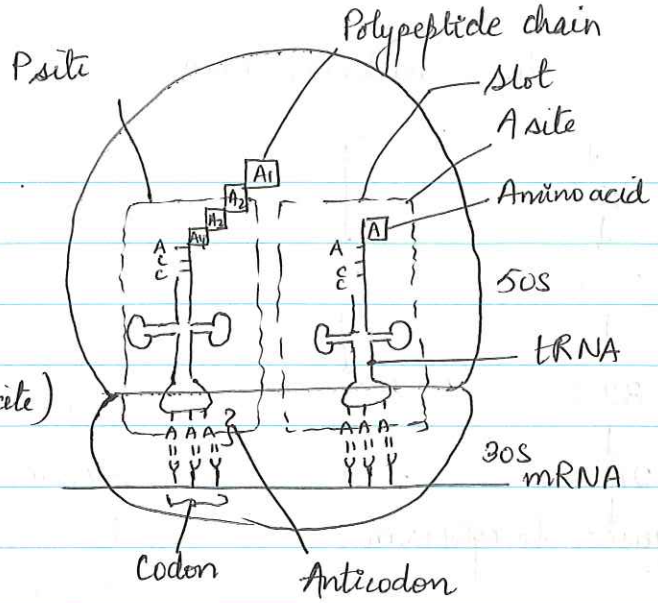
(a) 60S subunit - 2·7 mn Daltons
- 28S rRNA + 5·8S rRNA + 5S rRNA + ~40 proteins

(b) 40S subunit - 1·3 mn Daltons
- 18S rRNA + ~ 30 proteins



Attachment to ER

- large subunit attaches to ER
- two slots
  - P site (donor site) → Peptidyl site
  - A site (Acceptor site) → Aminoacyl site



⇒ Aminoacyl tRNA complex attached to A-site and t-RNA carrying polypeptide chain attached to P site.

↳ smaller subunit receives the mRNA.
- cleft separating two subunits lies parallel & remains attached to ER.

Chemical Composition :- Proteins + RNA

1. RNA – ribosomal RNA with different sedimentation rate

2. Proteins – About ~55.
   - Core proteins
     - bind directly to rRNA
     - → primary binding proteins
   - Split proteins → Acidic / Basic
     - ⇒ donot bind to rRNA
     - ⇒ interact with 1° binding proteins
     - ⇒ aka secondary binding proteins

BIOGENESIS OF RIBOSOMES

→ In prokaryotes, rRNA coded from specific cistrons of genome

→ In eukaryotes, rRNA synthesised in nucleolus.
→ Proteins synthesised in cytoplasm assemble in nucleolus
→ Attach to RNA to form RNP (ribonucleoprotein particles)

45S nucleolar RNA

↓ 42S

↓ 35S

↓ 32S

↓ 28S

↓ passes to cytoplasm

↓ 20S

↓ 18S

↓ passes to cytoplasm

Functions:-
- synthesis of proteins
- form long polypeptide chains with the help of mRNA & tRNA.

MITOCHONDRIAL RIBOSOMES

- occur freely in mitochondrial matrix or may be attached to membranes of cristae
- Yeast, fungi, protozoans & higher plants 70 - 80S
- animal cells - 50S - 80S
- synthesise mitochondrial proteins that form respiratory or oxidative enzymes

CHLOROPLAST RIBOSOMES

- similar to prokaryotic ribosomes
- 70S Type

POLYSOME

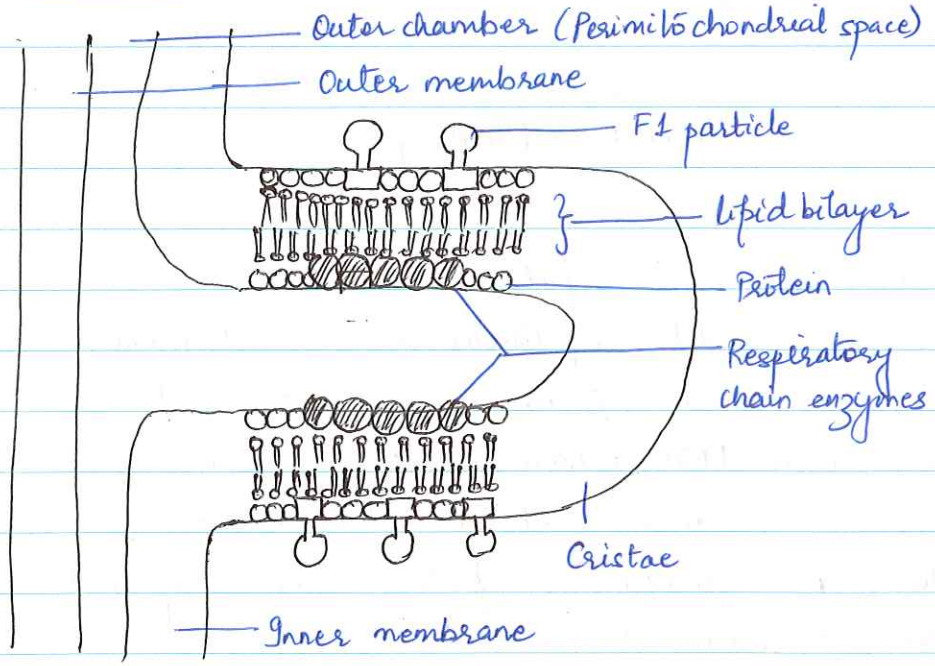
- aka polyribosome
- multiple ribosomes aligned in line on an mRNA
- dissociated after protein synthesis.

MITOCHONDRIA

→ membrane bound organelles that generate chemical energy as ATP
→ powerhouse of the cell
→ found in all eukaryotic cells except RBCs
→ first observed by Kollikar
→ term coined by Benda.

→ appear as thin filaments, granules or short rods
→ can be ribbon like, sausage or club-shaped
→ multiple per cell
→ only one per cell in few algae like Chlorella
→ more active cell, more mitochondria

STRUCTURE



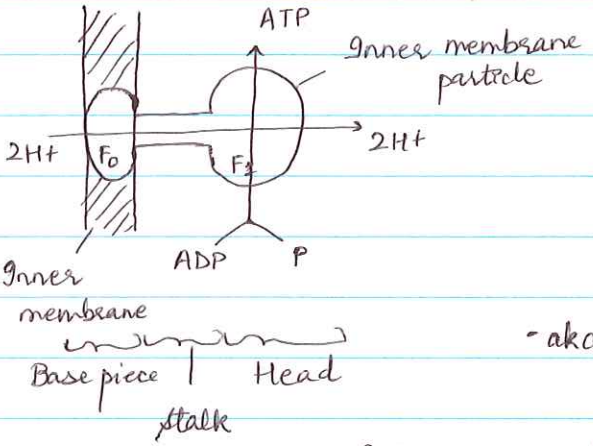
→ two membranes & two chambers
→ Outer membrane similar to ER membrane
→ Inner membrane projects into the matrix as ridges or septa = mitochondrial crests or cristae

→ increases the surface area
→ contains enzymes of e^- transfer system & ATP synthesis

→ Outer chamber aka perimitochondrial space.
→ Inner chamber filled with homogenous mitochondrial matrix.
→ Matrix contains - soluble proteins, some lipids, 70s ribosomes & a circular DNA, fine filaments for attaching Mg^{2+} & Ca^{2+}

Fernandes Mosan Particles

- F1 particles or mitochondrial particles
  - small particles situated in inner membrane & projecting into the matrix
  - seen only upon hypotonic treatment of mitochondria
  - 10^4 - 10^5 particles per mitochondria



- aka Fo-F1 complex or ATPase complex
  - Base piece lies in the inner mitochondrial membrane
  - forms proton translocating channel and acts as proton carrier
  - Head projects into the mitochondrial matrix
  - called ATPase as it synthesises ATP

Thus, enzymes contained in F1 particles → for electron transfer system; → oxidative phosphorylation

Chemical composition of Mitochondria

- 70% proteins & 25-30% lipids
- respiratory enzymes like cytochrome oxidase, cytochrome reductase, transaminase, coenzyme octanoxidase, etc.
- have their own DNA, mRNA, tRNA, ribosomes, RNA-polymerase & amino acid activating enzymes.
  - → have their own independant protein synthesising machinery
  - hence semiautonomous bodies.

SEMIAUTONOMOUS NATURE / SYMBIONT HYPOTHESIS

- → Altman described homology b/w bacteria & mitochondria
- → regarded as symbiotic bacteria inside eukaryotic cells because:-

1. Contains electron transfer enzymes similar to bacterial PM
2. Cristae similar to bacterial mesosomes and contain respiratory chain enzymes as in bacteria
3. Ribosomes are 70s type
4. Circular DNA molecule
5. Outer membrane similar to ER so original symbiont only had inner membrane
6. Chloramphenicol can inhibit protein synthesis in bacteria & mitochondria but not in cytoplasm
7. DNA dependant RNA synthesis

As per symbiont hypothesis, host cell = anaerobic, desiveng energy from glycolysis
parasite = completes Kreb's cycle & oxidative phosphorylation & respiration

FUNCTIONS

1. Cellular Respiration / Oxidation of Food.
   - mitochondria are sites of oxidation of food (Kreb's cycle)
   - convert potential energy of food to usable forms

(a) Glycolysis - occurs in cytoplasm

$$\text{Glucose} + 2NAD + 2ADP + 2P_i \longrightarrow 2 \text{ Pyruvic acid} + 2ATP + 2NADH_2$$

Nicotinamide Adenine Dinucleotide - captures 2 hydrogen ions

(b) Oxidation of pyruvic acid - occurs in mitochondria in O_2 presence

$$\text{Pyruvic acid} + NAD + \text{Coenzyme A} \xrightarrow[\text{dehydrogenase}]{\text{Pyruvate}} 2 \text{ Acetyl CoA} + NADH_2 + CO_2$$

Acetyl CoA with oxaloacetic acid forms citric acid & starts Kreb's cycle.

(C) Oxidative phosphorylation - $NADH_2$ & $FADH_2$ oxidised to remove Hydrogen.

$H^- \longrightarrow H^+ + 2e^-$

- These e^- transferred to O_2 through respiratory chain enzymes to for ETS or respiratory chain.

2. Thermogenesis or Heat production - ATP formation releases energy
   - part of this energy used to maintain body temp

3. Secretion of proteolytic enzymes.

4. Metabolism of fats

5. Myofibrils develop from mitochondria

6. Form mitochondrial spiral around flagellum in sperm.

ELECTRON TRANSPORT SYSTEM

- aka respiratory chain
- consists of enzymes & coenzymes in inner mitochondrial membrane

Components

5 complexes

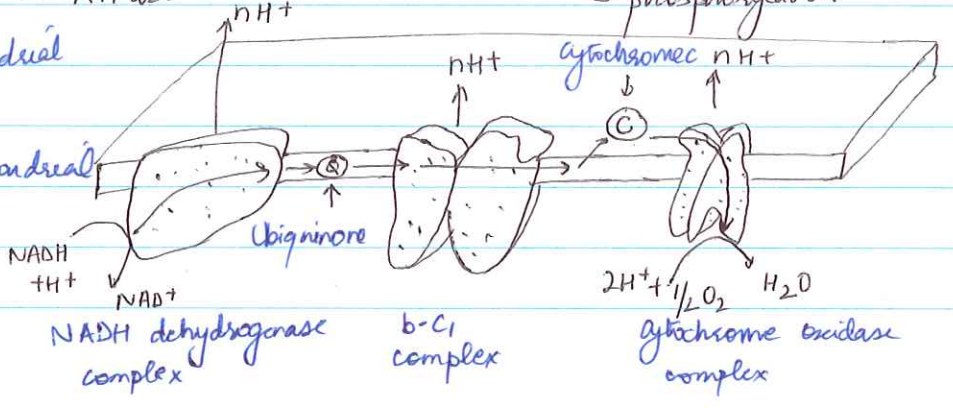
Complex I - NAD/NADH CoQ reductase
Complex II - Succinate CoQ reductase
Complex III - Cytochrome C reductase ($CoQH_2$)
Complex IV - Cytochrome C oxidase
Complex V - ATPase

} ETS

} Oxidative phosphorylation

2 mobile electron carriers

=> Coenzyme Q / Ubiquinone
=> Cytochrome - C.



1. **Complex I** :- Receives H^+ from NADH ⟶ Coenzyme Q (Ubiquinone)

Path:- NADH ⟶ FMN ⟶ Fe ⟶ CoQ
(Flavin mononucleotide) (Heme group)

2. **Complex II** :- Receives H^+ from succinic dehydrogenase ⟶ CoQ

Path:- Succinate ⟶ FAD ⟶ Fe ⟶ CoQ
(Flavin Adenine dinucleotide) (Heme group)

3. **Coenzyme Q / Ubiquinone (UQ)** :- mobile e^- carries b/w (Complex I & Complex III) & (complex II & complex III)

$FMNH_2 + CoQ \longrightarrow CoQH_2 + FMN$
(Complex I)

$FADH_2 + CoQ \longrightarrow CoQH_2 + FAD$
(Complex II)

4. **Complex III** :- Receives e^- from $CoQH_2$
- Contains cytochrome-b & cytochrome c_1 (reductase)

Path:- $CoQH_2$ ⟶ Cytochrome b ⟶ Cytochrome c_1 ⟶ Fe ⟶ Cytochrome C
(Heme part)
Complex III

5. **Cytochrome-C** :- mobile e^- carrier that is bounded to complex IV
transfers e^- to complex IV

6. **Complex IV** :- Cytochrome C-oxidase contains 2 heme & 2 Cu centres
Cytochrome a_1 (heme a_1) ↙ Cytochrome a_3 (heme a_3) ↘ Cu_1 Cu_2

Path:- Cytochrome-C → Cu_1 → Cyt a_1 → Cu_2 → Cyt a_3 → O_2

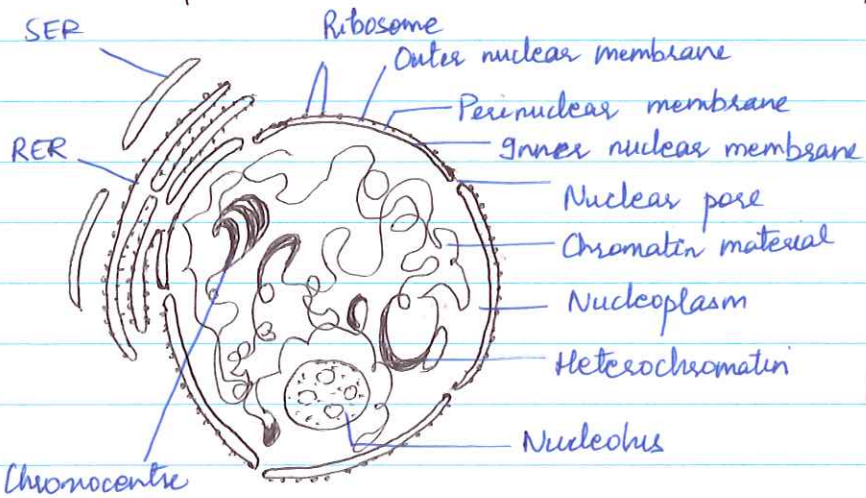
7. Complex V :- - ATPase complex present in F_0F_1 particle head piece
- has 4 coupling factors / coupling proteins

- head represents coupling factor F_1 ($\alpha, \beta, \delta, \gamma, \epsilon$) (subunits) + ATPase inhibitor protein
- stalk = F5 & F_6 factor
- base = F_0 factor containing hydrophobic proteins & phospholipids

NUCLEUS

- described as the control room of the cell
- controls and directs all cellular activity
- discovered by Robert Brown.
- occurs in 2 phases

interphase / metabolic phase division phase



•Interphase nucleus can be spherical, rounded, spheroidal, cylindrical, prismatic, branched, lobed

Nucleocytoplasmic ratio

$$NP = \frac{V_n}{V_c - V_n}$$

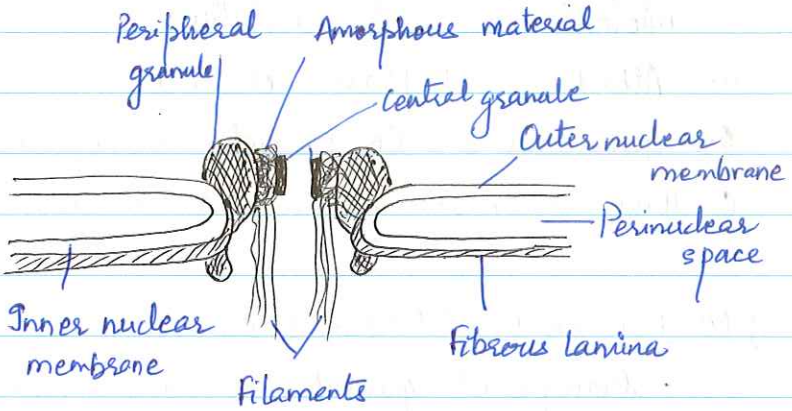
where V_n = volume of nucleus
V_c = volume of cytoplasm

STRUCTURE

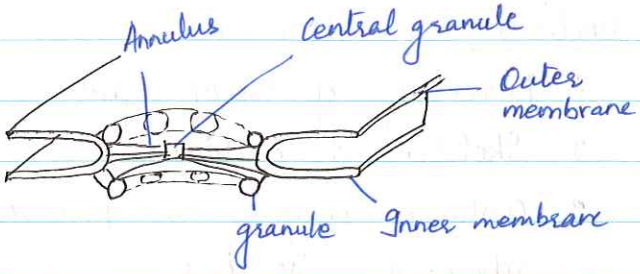
1) NUCLEAR ENVELOPE / KARYOTHECA

- double membranous sheath (2 unit membranes)
- dynamic gateway b/w nucleus & cytoplasm
- regulates nucleocytoplasmic interaction

(a) Nuclear membranes :- 2 membranes separated by perinuclear space
- outer membrane has attached ribosomes
- inner membrane coated with filaments k/a fibrous lamina or nuclear cortex



(b) Nuclear poses :- nuclear envelope is perforated by poses
- at the margins of the pores, outer & inner membranes are continuous
- circular channels occluded by e⁻ dense material
- projected outward into cytoplasm & inward into nucleoplasm
- k/a annuli
- electron dense material contains fibrous & particulate structures



(c) Annulus :- ring or cylinder of e⁻ dense material around nuclear pore.
- 2 sets of 8 set annular granules
- one central granule
- granules may be formed of compact fibrillar material
- fine fibres extend from central granule to peripheral annular granules
- regulate exchange of macromolecules

(d) Fibrous lamina: - inner surface of nuclear envelope coated with nuclear cortex
- fibres proteinaceous & similar to actin polymers
- form funnel shaped whorls
- direct material towards pores
- provides support

Functions of nuclear envelope :-

1. Separates genetic components
2. Pores serve to transfer macromolecules
3. Surface for attachment of structural elements of cytoplasm like myofilaments, microfilaments & microtubules
4. Attaches interphase chromatin
5. gives rise to ER & golgi membranes (participates in membrane flow)
6. Have enzymes of ETS as in ER

2) NUCLEOPLASM / KARYOLYMPH

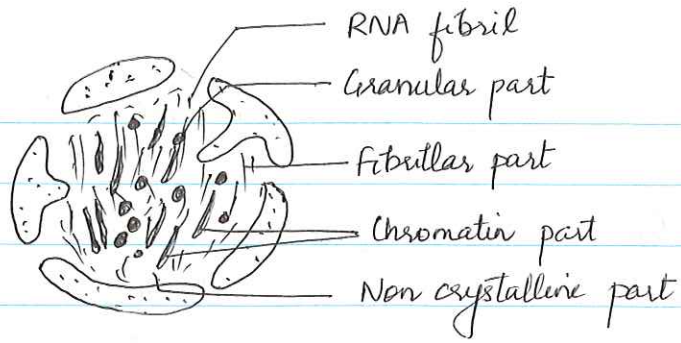
- transparent ground substance with suspended chromatin n/w
- contains proteins, large amount of Phosphorus & RNA
- hydrolytic enzymes like ribonuclease, alkaline phosphatase, dipeptidase.

Functions of nucleoplasm :-

1. Processing of newly synthesized RNA & transport to cytoplasm
2. Skeleton of nucleus
3. contains enzymes & proteins for DNA replication, RNA synthesis & ribosomal syntheses.

3) NUCLEOLUS

→ usually 2 nucleoli in diploid cells
→ 1 in gametes
→ larger in cells that are busy in protein synthesis



Structure :-

(a) Pars amphiosa – amorphous matrix
(b) Fibrillar zone – rRNA fibrils & ribonucleoproteins fibrils
(c) Granular zone – ribonucleoprotein (RNP) granules → precursor to ribosomes
(d) Perinucleolar chromatin – chromatin granules

- Nucleolus composed of RNA & proteins
  ribosomal ↙ ↘ phosphoproteins

- A ring of DNA represents heterochromatin regions of chromosomes associated with nucleolus.
- Enzymes – acid phosphatase, nucleoside phosphorylase & DPN synthetases

Functions of nucleolus :-

1. RNA synthesis – rRNA synthesised in nucleolus
   – nucleolar chromatin contains ribosomal genes or genes that code rRNA
   → rRNA synthesised as 28S & 18S

2. Biogenesis of ribosomes – two types of rRNA synthesised into nucleolus get associated with proteins and move to cytoplasm
   → ribonucleoprotein (RNP) granules are ribosome precursors
   → these RNP granules join to form ribosomes

Chromatin ⟶ Fibrils ⟶ Granules ⟶ Ribosomes

4) CHROMATIN NET

- consists of twisted filaments k/a chromonemata
- n/w k/a chromatin net or nuclear reticulum.

- chromatin net contracts and organises into chromosomes.

Euchromatin - fine thread like linen
- stains lightly with basic dyes

Heterochromatin - condensed chromatin that is darkly stained
- regions seen in interphase & prophase
- do not unravel during telophase like remaining euchromatin

Euchromatin → lightly stained threads (Achromatin) → stains with acidic dyes
→ darkly stained granules (Basichromatin)
chromomeres / chromatin proper

- Special sex chromatin bodies / Barr bodies at periphery of nucleus & well organized
  - more common in mammalian cells (esp. females)
  - no. depends on sets of X-chromosomes
  - one sex chromatin body for a diploid set of chromosomes

5) CHROMOCENTRES

- large regions of interphase nucleus that take dark stain
- heterochromatin region prone to premature condensation
- one or many per cell
- marked distinctly in nuclei of salivary glands of *Drosophila*

HAMMERLING EXPERIMENT

- to show importance of nucleus
- on a green alga *Acetabularia*
  - *mediterranea* (umbrella like cap)
  - *crenulata* (digitate cap)

NUCLEOLAR CYCLE

→ Nucleolus an unorganised body lacking continuity
→ During mitosis, undergoes cyclic changes
→ disappears at prophase
→ reappears at telophase
→ formed by one or more chromosomes of a haploid set k/a nucleolar chromosomes
→ In man, chromosomes 13, 14, 15, 21 & 22 participate in formation of nucleolus.
→ Specific regions of these chromosomes active in nucleolus formation are k/a nucleolar organizer zone.
→ masked by secondary constriction

Prophase :- amorphous part of nucleolus disappears
↓
Chromatin loop withdrawn into nucleolar organizer zone of corresponding chromosomes

Telophase :- Convoluted chromatin loop uncoils from nucleolar zone
↓
Surrounded by fibrillar & granular material
(materials produced from chromocentre of interphase nucleus)
↓
Nucleolus matrix and its basic proteins & RNA produced in chromocentre
↓
liberated in small perinucleolar bodies
↓
Fuse to form mature nucleolus.

NUCLEOPROTEINS

→ major component of nucleus
→ compounds of nucleic acids & proteins

(a) **Basic proteins** - low molecular weight & basic in nature
- ∝ to DNA amount with which they are intimately associated

Protamines
→ restricted distribution
→ mainly fish ~~sperm~~ spermatozoa
→ rich in arginine

Histones
→ widely distributed
→ composed of lysine & arginine
→ 55% of chromatin material

(b) **Acid proteins** - non histone proteins
- residual proteins of chromosomes
- contain tryptophan & Tyrosine (high content)
- amount depends on physiological activity of cell

Nucleoproteins provide framework to which nucleic acids attach.
Nucleohistones - associated with maintenance & reproduction of chromosomes.
Nucleonhistones - metabolic functions of the nucleus.

HETEROCHROMATIN

→ condensed regions of chromatin that are darkly stained
→ replicates during S- substage of interphase after replication of euchromatin.

Types :- (i) **Constitutive heterochromatin**
→ permanently inactive chromatin
→ occupies fixed position in interphase & chromosomes

→ occurs at same location in both chromosomes of a pair such as in centromeric region, at telomeres or adjacent to nucleolar organizer region
→ aka organiser heterochromatin

(ii) Facultative Heterochromatin :-

→ gets condensed for a short period only at certain stages of cell cycle
→ for eg. one of the 2 X chromosome in female human

In nucleolar organizer region, heterochromatin contains polygenes or repetitive DNA for rRNA, 5S RNA & tRNA.

Functions of heterochromatin :-

1. Protects vital areas of genome against disruptive forces (eg 18S & 28S rRNA cistrons)
2. Centromeric heterochromatin participates in separation of chromosomes
3. Attracts homologous chromosomes for pairing during meiosis.
4. Establishes proximity b/w chromosomal regions that are functionally related
5. Role in replication & transcription of DNA
6. Provides fertility barrier for evolutionary diversity & speciation
7. Serves as transcription full stop.

CELL DIVISION

CELL CYCLE → At the end of a division of cell, daughter cells are formed
- → Daughter cells are smaller than parent cells with DNA content half that of parents
- → Cells grow in size by synthesising cytoplasmic material to reach 4X of their original volume
- → DNA content gets doubled by replication
- → Cell is now ready to undergo cell division

∴ Growth and division occur alternating in a cyclical fashion. This cycle is k/a cell cycle. It involves 2 phases :-

Growth phase / Interphase / Non-dividing phase → Division phase.

INTERPHASE

- Interphase is interval b/w 2 successive cell divisions
- Cell prepares itself by synthesising and storing substances essential for cell division
- Aka preparatory phase
- Non dividing cells remain permanently in this stage
- Biosynthetic activities of the cell are at a maximum
- ∴ Aka BIOSYNTHETIC PHASE or METABOLIC PHASE

- Further divided into 3 substages :-

1. G1 Phase or Post mitotic phase :-

- Young daughter cells grow in size by synthesising cytoplasm
- Synthesises & stores enzymes, mRNA, tRNA, ribosomes, proteins & nitrogenous bases needed for DNA replication
- Chromosomes extended & thread like to form chromatin n/w

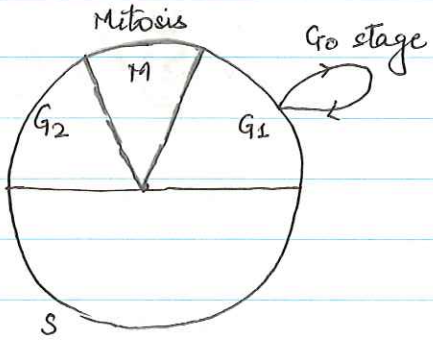
- takes 30-40% time of complete cell cycle
- In non-dividing cells (eg. mammalian lymphocytes), cell cycle stops at a point in this phase called G_0 phase (quiescent stage)
- When this cell is ready to divide, it enters G_1 phase

2. S- Substage or Synthesis Phase :-

- DNA replication takes place
- Synthesis of histones associated with DNA takes place
- 30 - 50% time of cell cycle

3. G_2 Substage or Premitotic Phase :-

- During this phase nucleus has double amount of DNA
- Nuclear volume increases due to synthesis of tRNA, mRNA & nucleolar RNA
- Cell synthesises proteins required during cell division
- 10 - 20% duration of cell cycle.



DIVISION PHASE

- last phase of cell cycle aka M-phase
- Mitosis or cell division occurs.

MITOSIS

- Mitotic division or somatic cell division is the process of division of a somatic cell into two maintaining same no. of chromosomes as present in the parent cell.
- Occurs in all cells except germ cells

1. Interphase

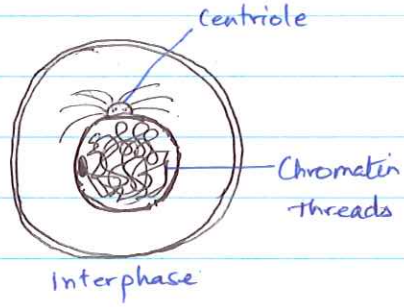
- Interval b/w 2 successive cell divisions
- Chromatin material remains highly attenuated
- preparatory phase as cytoplasmic & nuclear material is synthesised → G_1 phase, S phase, G_2 phase

2. Karyokinesis

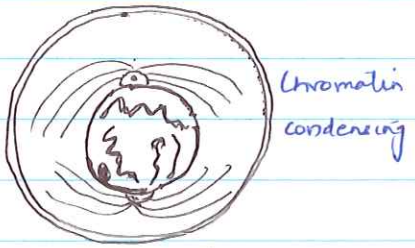
- Nuclear division and divided into following phases :-

A. PROPHASE

- Nuclear division (mitosis) begins with prophase
- Chromatin threads lose water & condense
- Chromatin threads coil like a cylindrical spring & become shorter & thicker to form chromosomes
- Each chromosome already doubled up due to DNA replication during S-substage
- By end of prophase, each chromatid splits lengthwise into two chromatids
- nucleolus & nuclear membrane disappears

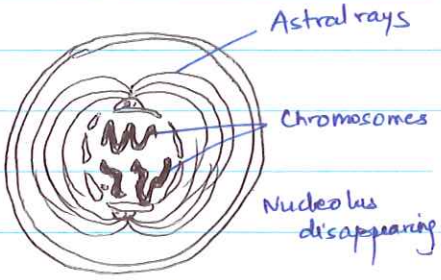


Interphase



Early Prophase

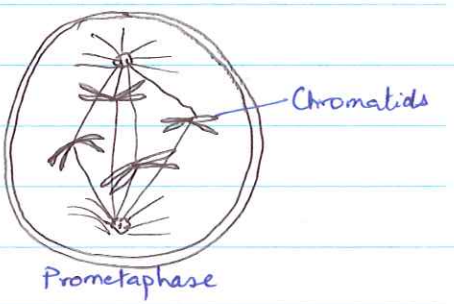
- centrioles divide into two & move towards opposite poles
- in the intervening cytoplasm, microtubules orient themselves b/w daughter centrioles and a spindle called amphiaster is formed
- By the end of prophase, nucleolus & nuclear membrane completely disappears



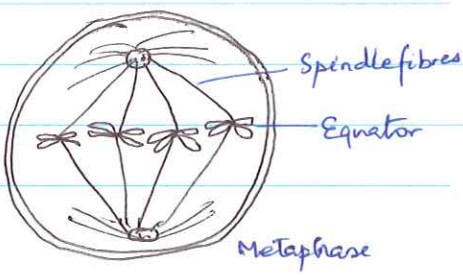
Late prophase

B. METAPHASE

- Each chromosome becomes more compact & short
- Chromatids separate except at centromere that has not divided so far
- chromosomes migrate towards the equator of the spindle
- arrange such that centromeres are at the equator &

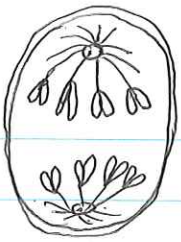


Prometaphase



Metaphase

arms directed towards the poles (plectonemic manner)
- Centromeres get attached to spindle fibres



Anaphase

C. ANAPHASE

- Centromere of each chromosome divides and daughter chromosomes formed by splitting of sister chromatids
- Daughter chromosomes move apart & pulled towards poles of spindle
- Chromosomal movement brought about by contraction of spindle fibres
- Centromeres pulled towards poles and arms dragged behind ∴ arms towards equator & centromeres towards poles

Telophase

Interphase

D. TELOPHASE

- Daughter chromosomes reach poles and form 2 groups - one at each pole
- Chromosomes uncoil to form chromatin net
- nuclear envelope & nucleolus reappear around each group.
- By end of telophase, two daughter nuclei are formed.
- Spindle fibres and astral rays disappear

3. Cytokinesis

- Division of cell cytoplasm into two separate cells
- Usually occurs in telophase alongside formation of daughter nuclei

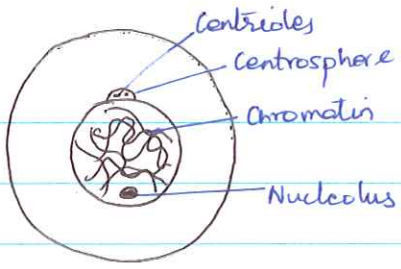
a. ANIMAL CELLS - a shallow groove appears in the cytoplasm at the equator of the spindle. It deepens and forms daughter cells

b. PLANT CELLS - cell plate is formed at the equator of the dividing cell.

Mitosis ensures growth of cells & organism.

MEIOSIS

- Reduction division occurs in the reproductive cells only at the time of gamete formation
- 4 daughter cells are formed from single parental cell
- chromosome no. in daughter cells reduced to half (haploid)

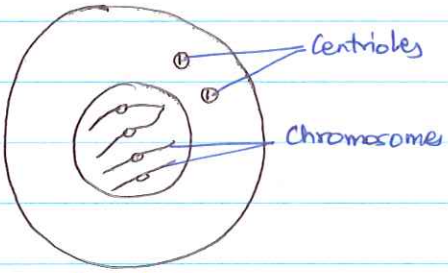


Interphase

1. Heterotypic / First Meiotic / Reduction Division

A. FIRST PROPHASE

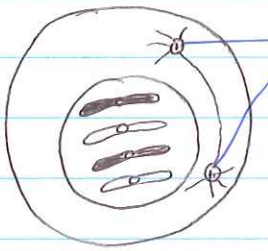
- Longer in duration as compared to mitosis and profoundly modified into 5 stages



Leptotene

(i) Leptotene stage

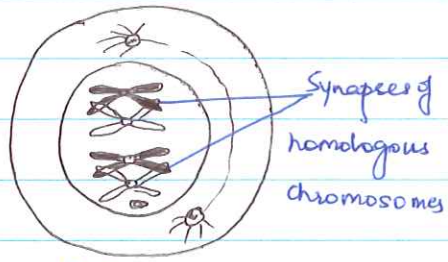
- this stage initiates meiosis
- meiotic cell is comparatively large with a large nucleus
- has diploid chromosome complement
- chromosomes long & thin and longitudinally single
- chromosome has beaded appearance due to presence of dense granules called chromomeres



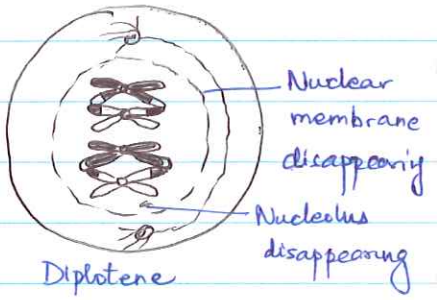
Zygotene

(ii) Zygotene stage

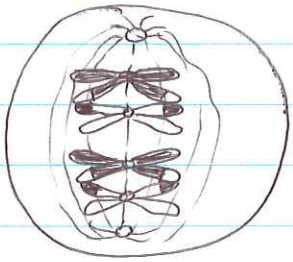
- commences with movement of chromosomes brought about by attraction b/w chromosomes of each homologous pair
- they approach each other and become intimately associated to form a bivalent
- pairing of homologous chromosomes b/a synapsis
- nucleus now appears to have haploid no. of chromosomes



Pachytene

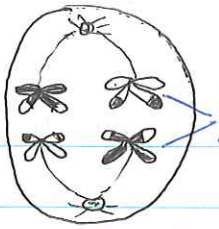


Diplotene

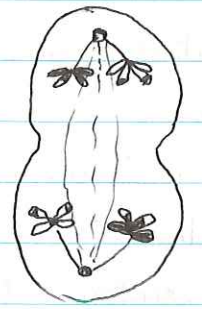

Diakineses

(iii) Pachytene stage

- stable period in the cell division
- each paired chromosome of a bivalent gets shortened & thickened & is more clearly visible
- homologous chromosomes start splitting into 2 sister chromatids by a longitudinal furrow

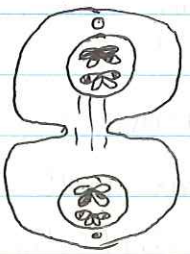


Metaphase I


Anaphase I

(iv) Diplotene stage

- splitting of chromosomes & separation of homologous chromosomes initiates diplotene
- bivalent consists of 4 chromatids
- synaptic forces lapse & homologous chromosomes uncoil & separate
- separation is incomplete and some points of contact called chiasmata remain
- exchange of chromatid parts b/w homologues occurs due breakage & rejoining of weaker chromatids at chiasmata
- This crossing over brings about exchange of hereditary material
- chiasmata begin to move from the centromere towards the ends of tetravalent - k/a TERMINALISATION


Telophase I

Prophase II


Metaphase II

(v) Diakinesis stage

- Nuclear membrane & nucleolus disappear
- Bivalents separate & chiasmata reach end of the chromosomes
- Nuclear spindle formation begins


Anaphase II

B. METAPHASE I

- movement of the bivalents towards the equator of the spindle (paranemic formation)


Telophase II

- bivalents orient themselves on the equator so that centromeres lie one on either side equidistant from the equatorial plate

C. ANAPHASE I

- chromatids separate into pairs and move towards opposite poles of the spindle
- two haploid chromosomes formed on either pole
- separation of tetrads into dyads or a pair of chromatids is k/a DISJUNCTION and involves the separation of chromosomes that were brought together during synapsis

D. TELOPHASE I

- nuclear wall forms, chromosomes uncoil & cytoplasm divides into Two
- 2 haploid daughter cells are thus formed

2. Second division

Interphase stage in these daughter cells may be absent or short

A. PROPHASE II

- Nuclear membrane ~~separates~~ disappears & spindle starts forming

B. METAPHASE II

- Chromatids connected only with centrioles and lie parallel to one another
- dyads move towards the centre and lie on the equator of the spindle

C. ANAPHASE II

- chromatids separate to form sister chromosomes & move towards two poles of the spindle

D. TELOPHASE II

- chromosomes uncoil and form 2 groups, nuclear membrane & nucleolus reappear 4 daughter cells formed from one cell.

CYTOKINESIS

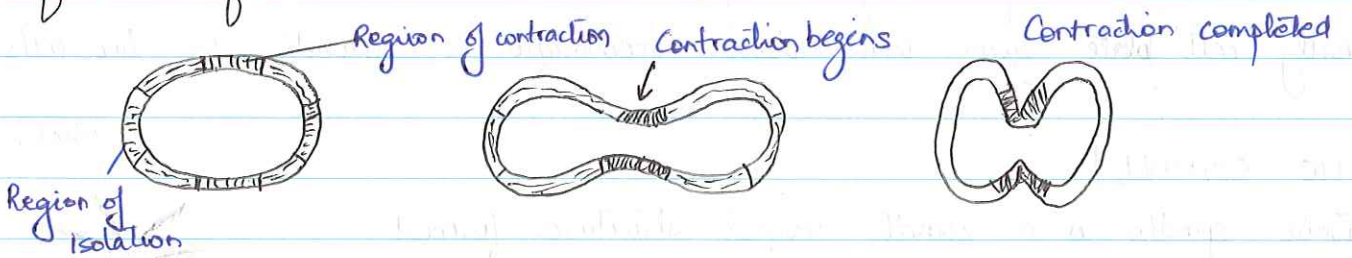
- Cytokinesis is the division of cell cytoplasm and cleavage of cell into 2 daughter cell.
- Occurs in telophase along with formation of daughter nuclei

A- CYTOKINESIS IN ANIMAL CELLS

- begins by appearance of a dense material around the microtubules at the equator of the spindle at late anaphase
- this dense material + microtubules of equatorial region = MIDBODY
- Simultaneously, a constriction appears at the cell surface at the equatorial region
- This constriction gradually deepens and constricts the cell into 2.

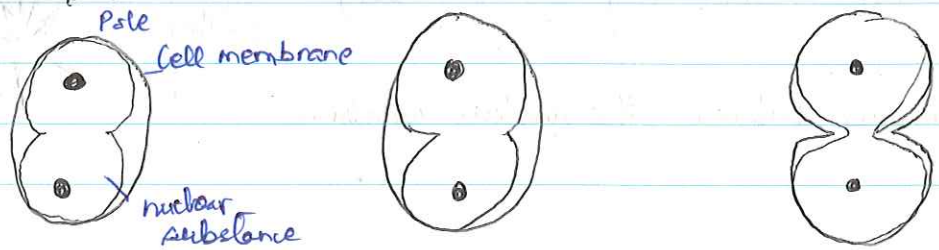
(1) Contractile Theory

→ A contractile protein (actinomyosin), forms a contractile ring at the equator in the cortex region of cell cytoplasm.
→ When the dividing cell elongates, the contractile ring contracts & forms a furrow.



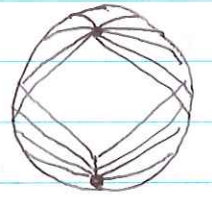
(2) Expanding surface Theory

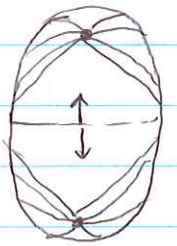
- Secretion of nuclear substance by chromosomes causes expansion of cell membrane at the pole
- As polar area expands, equator contracts & furrow starts dividing the cell into two



(3) Astral Relaxation Theory

- cell surface is under tension. When astral rays reach the pole, surface tension at the poles is lower
- Because of low surface tension polar regions expand & cause furrow to appear at the equator



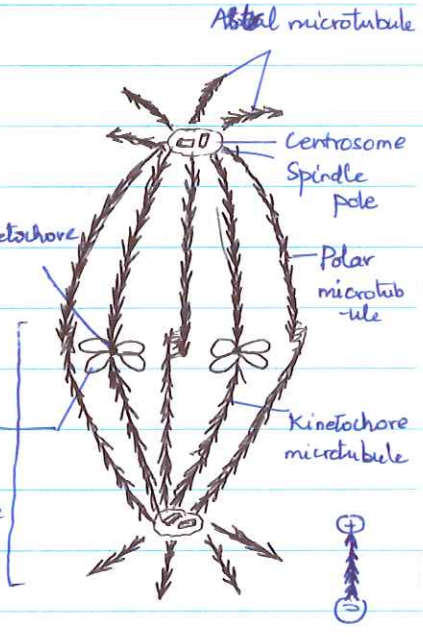


B. CYTOKINESIS IN PLANT CELLS

- In plant cell, cytokinesis is accomplished by formation of phragmoplast or cell plate at the equator of the dividing cell.
- During anaphase, phragmoplast is formed by accumulation of interzonal microtubules of spindle and Golgi vessels at equatorial plate
- These vesicles are filled with cellulose precursors
- Vesicles fuse to form a cell plate
- Cell plate grows by the fusion of more vesicles.
- Finally, cell plate fuses with plasma membrane to separate the two cells.

MITOTIC SPINDLE

- Mitotic spindle is a spindle shaped structure formed by certain fibres in the cytoplasm of the dividing cell in late prophase or early metaphase of mitotic division
- Develops in the form of a bundle of fibres radiating in intervening cytoplasm b/w the centrioles
- Fibres develop by organisation of proteins (tubulin)
- Spindle formation begins outside the nuclear membrane



» Two centrioles situated at the opposite ends form the poles and the line joining two centrioles represents the axis
- Centre of the spindle marks the equator
- Spindle fibres are of 3 types:-
a) Continuous fibres extend from one pole to the other
b) Kinetochore fibres or chromosomal fibres extend from the spindle to the centromere of the chromosome
c) Interzonal fibres present b/w centromeres of separating chromosomes

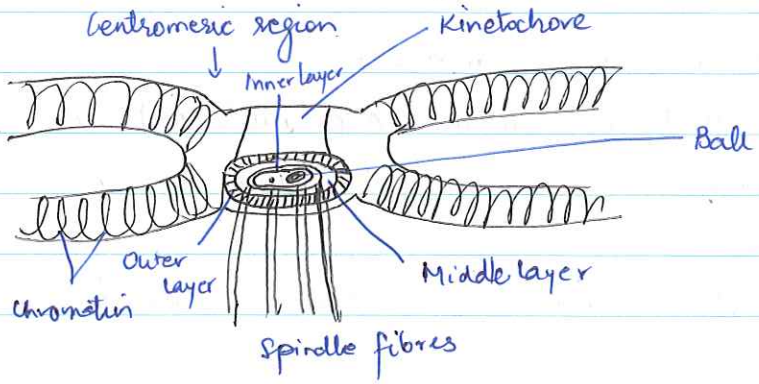
» Substance of spindle fibres is like an elastic gel but these are composed of protein groups linked by SH chains

» Each centrosome divides in a centrosome cycle to form 2 centrioles in S-phase These centrioles then migrate towards the poles. Three types of microtubules are present :-
(a) Astral microtubules - point outward towards the cell cortex to anchor the spindle apparatus to the axis

(b) Kinetochore microtubules - attach to kinetochore of chromatids

(c) Polar microtubules - oriented parallel to each other in opposite directions for pushing the spindle apparatus apart during mitosis

Where the microtubules from 2 Microtubule organizer centres (MTOCs) overlap it is known as zone of interdigitation



⇒ The central centromeric region is lightly stained. Each chromatid in this region consists of a small darkly stained granule called the spindle spherule.
⇒ Spindle fibres during cell division attach to these spherules f/a kinetochore

Organizing the spindle apparatus :-

⇒ In a properly formed mitotic spindle, bioriented chromosomes are aligned along the equator of the cell with spindle microtubules oriented roughly perpendicular to the chromosomes, their (+) end embedded in kinetochores & their (−) ends anchored at the cell poles

⇒ Two models to explain spindle formation & organisation :-

(a) Centrosome mediated "search & capture" model :-

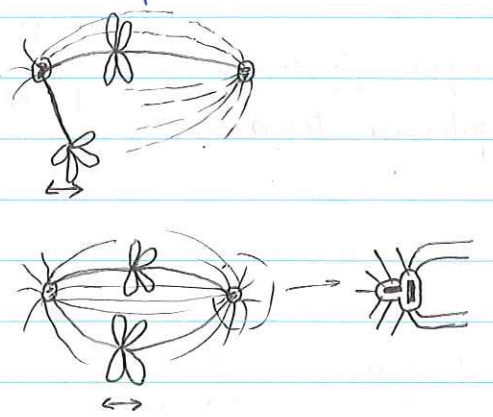
→ Microtubules are nucleated at MTOCs and undergo rapid growth & catastrophe to search the cytoplasm for kinetochores
→ Once they bind a kinetochore, they are stabelised and their dynamics is reduced
→ The newly monooriented chromosome oscillates in space near the pole to which it is attached until a microtubule from the opposite pole attaches the kinetochore
→ This second attachment further stabilises kinetochore attachment.
→ Gradually, bioriented chromosome is pulled towards the centre of the cell until microtubule tension is balanced on both sides of the centromere
⇒ The congressed chromosome oscillates at the metaphase plate until anaphase when the cohesion b/w sister chromatids is released.

(b) Chromatin mediated self organization model :-

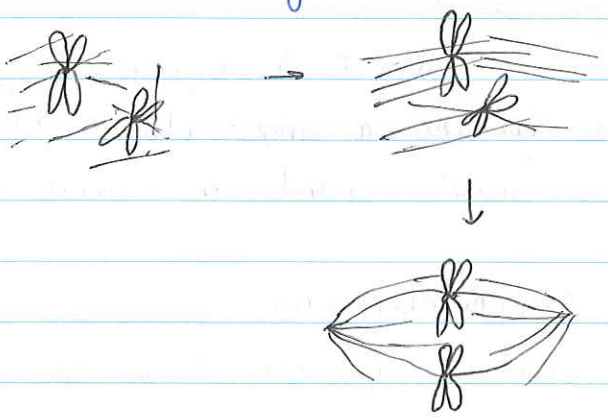
→ This model proposes that microtubules are nucleated acentrosomally near chromosomes and spontaneously arrange into anti-parallel bundles to adopt a spindle like structure
→ Proof :- Laser ablation of centrosome in vertebrate cells does not inhibit

chromosome segregation & spindle assembly

Search & capture model



Self organization model



⇒ Ran - GTP cascade releases spindle assembly factors and promotes the formation of spindle by organising microtubules in the vicinity of chromosomes

Functions of mitotic spindle :-

1. Chromosome alignment due to growth & shrinkage of microtubules and protein action
2. Chromosome segregation into sister chromatids during anaphase. All chromatids move at same speed due to shortening of kinetochore fibres through depolymerisation and spindle poles also move apart

CELL CYCLE REGULATION

→ Cell cycle is unidirectional and irreversible

→ There are checkpoints & gaps to ensure that the division happens correctly before going into the next stage.

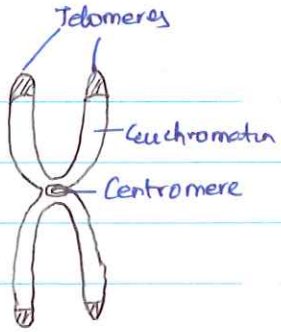
→

Controls of cell cycle

A. TELOMERES

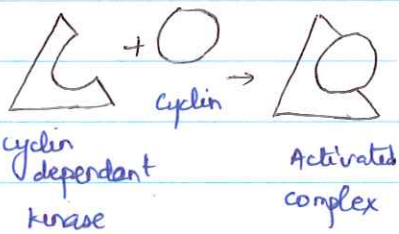
⇒ Mammalian cells typically divide only about 50 times due to limit set by presence of repeated DNA sequences

⇒ Example, in young cells, TTAGGG sequence is repeated 1000x times but



With each division 50-200 of these sepeats are lost.
» When the sequence of telomese is reduced to a certain size, cell division cannot occur.
» Telomeses are restored to original length by enzyme telomesase
» Telomesase contains a single strand RNA to synthesise telomeses.
» Telomesase usually found in gametes.

B. CYCLIN DEPENDANT KINASES



» Activated proteins are needed for cell to proceed from G1 to S and G2 to M phases.
» These proteins are activated by Kinases that transfer a phosphate group from ATP to simulate cell cycle.
» Kinases are themselves normally inactive and need other proteins to activate them eg cyclin

» At low level of cyclin, kinases inactive and cell cycle halted. As cyclin level increases, kinase activated and cell cycle resumes

C. GROWTH FACTORS

» Generally, cyclin binds with kinase only when growth factors are present

S-kinase + S-cyclin → S-kinase cyclin complex

↓

* Simulates DNA replication and cell cycle crosses through the checkpoint at G2 phase
* Activated S-kinase cyclin complex activates enzymes to destroy S-cyclin if checkpoint criteria not met

M-kinase + M-cyclin → Activated M-kinase cyclin complex

↓

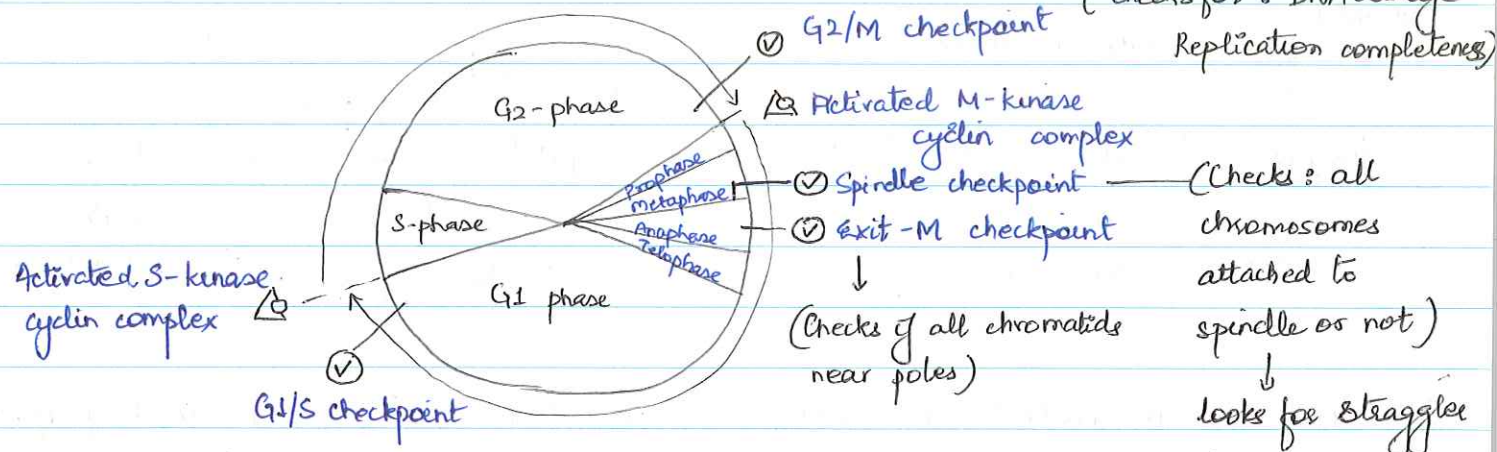
Initiates chromosome condensation, nuclear membrane disintegration & spindle

Damaged tissue
↓
Growth factors
↓
kinase + cyclin
↓
Activated cyclin dependant kinase complex
↓
* Activates enzymes for cell cycle
** Activates enzymes to destroy cyclin

apparatus synthesis.
It also activates enzymes that destroy M-cyclin

D. CELL CYCLE CHECK POINTS

- Checkpoints to monitor and regulate the process of cell cycle
- These checkpoints prevent the progress of cell cycle at specific points thereby allowing repair of DNA damage.
- Cell cycle cannot progress to next phase till the checkpoint criteria are met
- Major checkpoints are, G1/S checkpoint
  G2/M checkpoint
  Exit M phase checkpoint



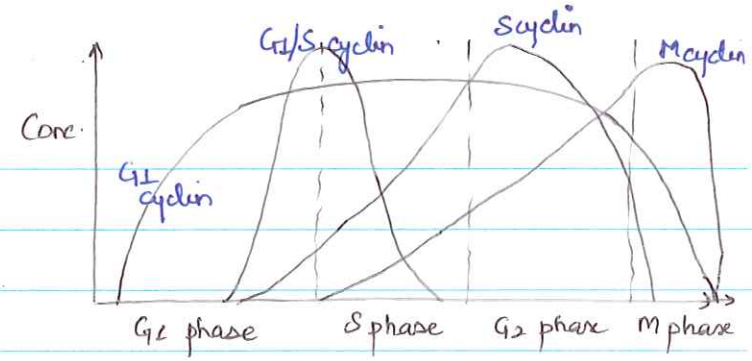
Checks for :-
- Cell size
- DNA Damage
- Growth factors
- Nutrients

CELL CYCLE REGULATORS

A. CYCLINS

- A group of proteins that activate cyclin dependant kinases
- Four basic types :- G1 cyclins
  G1/S cyclins
  S cyclins
  M cyclins

- A typical cyclin at low levels except the phase when it is needed.
- G1 cyclin needed throughout the cell cycle

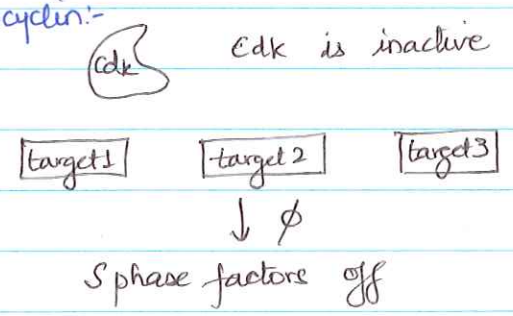


B. CYCLIN DEPENDANT KINASES

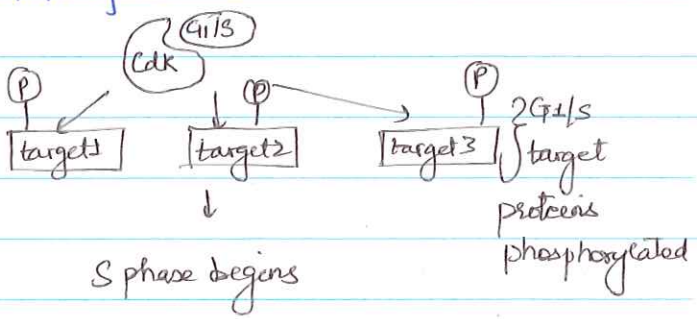
Cyclin expression cycle

- Cyclins drive the events of a cell cycle by partnering with enzymes called Cyclin-dependant kinases (CdKs)
- Lone Cdk is inactive but cyclin activates it
- Cdks when activated, phosphorylate target proteins (add phosphate groups)
- The phosphorylated protein that gets activated / deactivated further regulates cell cycle.

Nocyclin:-



+ G1/S cyclin



- Cdk levels remain constant and activation / deactivation controlled by level of cyclins
- Cdks are evolutionary conserved

MATURATION PROMOTING FACTOR

- MPF is a M-cyclin dependant Cdk
- M-cyclin remains low but builds up during G2/M transition
- M-cyclin now binds to Cdks to trigger the M-phase
- Once the activated complex receives additional signals (post checkpoint), M phase is set in motion
- MPF adds phosphate groups to proteins of the nuclear envelope resulting in its breakdown
- It also triggers chromosome condensation & spindle formation

ANAPHASE PROMOTING COMPLEX / CYCLOSOME

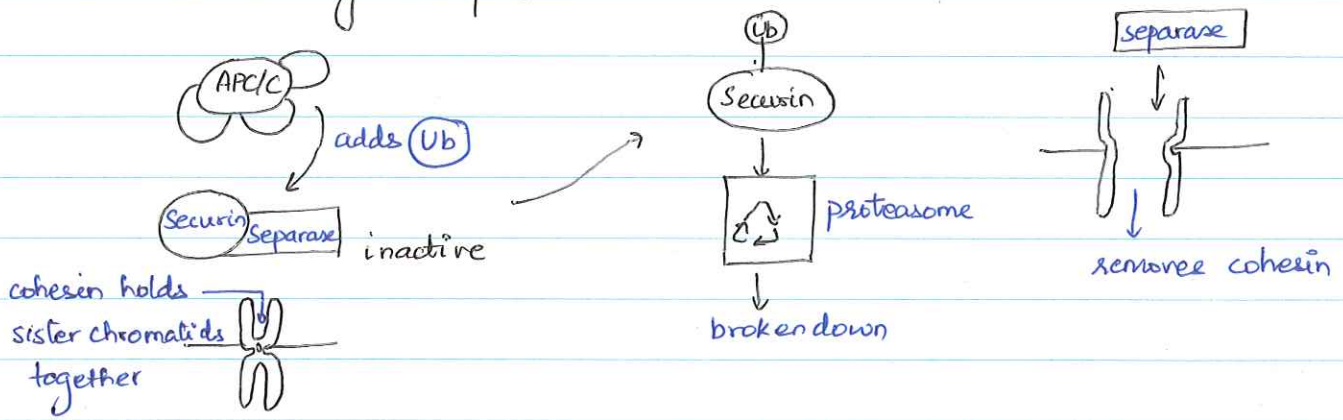
- MPF also triggers its own destruction by activating Anaphase Promoting Complex / Cyclosome (APC/C).
- APC/C causes M-cyclins to be destroyed starting in anaphase
- This allows daughter cells to push out of mitosis to G1 phase

- APC/C adds a small protein tag called Ubiquitin (Ub) to its targets.
- Targets tagged with Ub are sent for breakdown to proteasome
- APC/C → adds Ub to MPF tagged M-cyclins → M-cyclins shredded

- APC/C adds a Ub tag to securin (that binds to separase to inactive it)

↓

Securin broken down → separase breaks down cohesin to separate sister chromatids during anaphase



P53 - a tumour suppressor protein. If DNA damaged ~~not~~, it stops the cycle at G1 checkpoint through CDK inhibitor proteins (CDKI)
- → P53 then activates DNA repair enzymes
- → If DNA damage is irreparable, triggers programmed cell death → apoptosis

pRb - Retinoblastoma protein (gene RB) is another tumour suppressor protein
- phosphorylated if cell is ready to divide
- prevents progression from G1 to S stage
- binds to E2F-DP to stop transcription factors