IPAM Cells and Materials:
At the Interface between Mathematics, Biology and Engineering

Tutorial 1, The Cells

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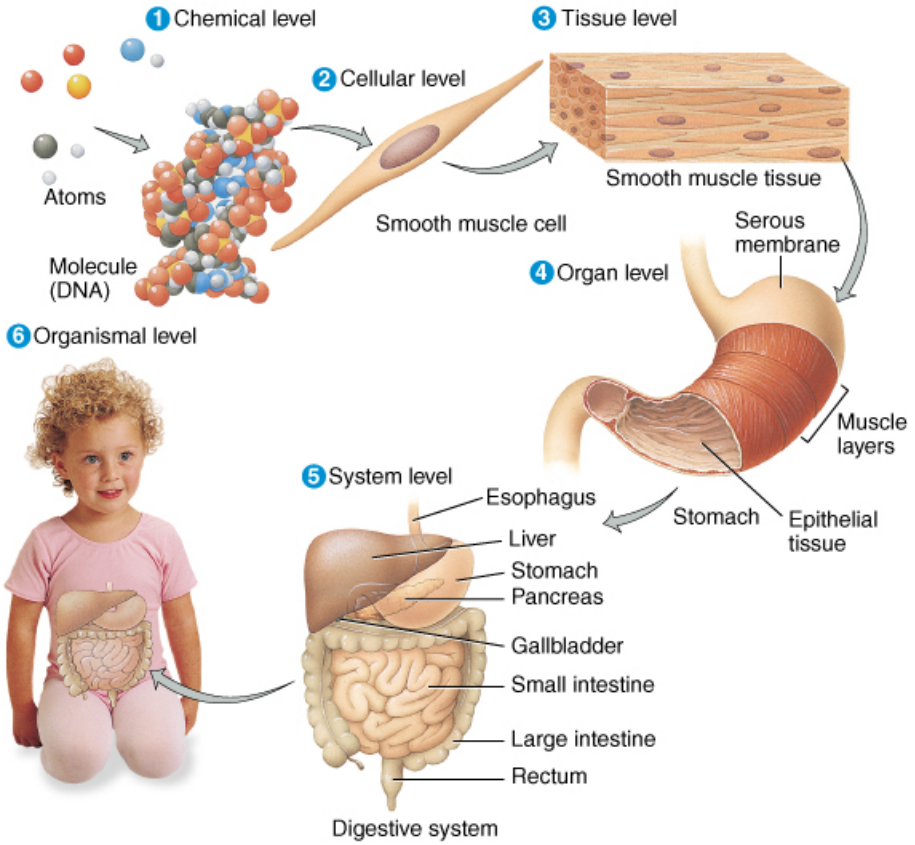
Human Body: Levels of Organization



A human body consists of :

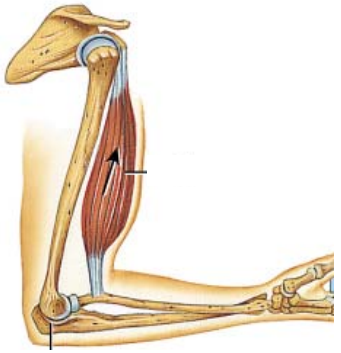
- **Cells (live or dead)**
- **Extracellular Matrix**
  ***e.g.* Basal lamina, Collagen ...**
- **Extracellular Fluid (ECF)**
  ***e.g.* Blood plasma, Lymph, CSF …**

- Organismic Level
  -one living individual.
- System Level
  collection of related organs with a common function
  Digestive system
  sometimes an organ is part of more than one system
  Pancreas – digestive, endocrine
- Organs
  grouping of 2 or more tissue types into a recognizable structure w/ a specific function.
- Tissue
  4 basic tissue types -- epithelium, muscle, connective tissue, nerve tissue
- **Cellular**
  smallest living unit of the body
- Chemical
  atomic and molecular level

Amplification of an activity through the levels

e.g. Muscle activities

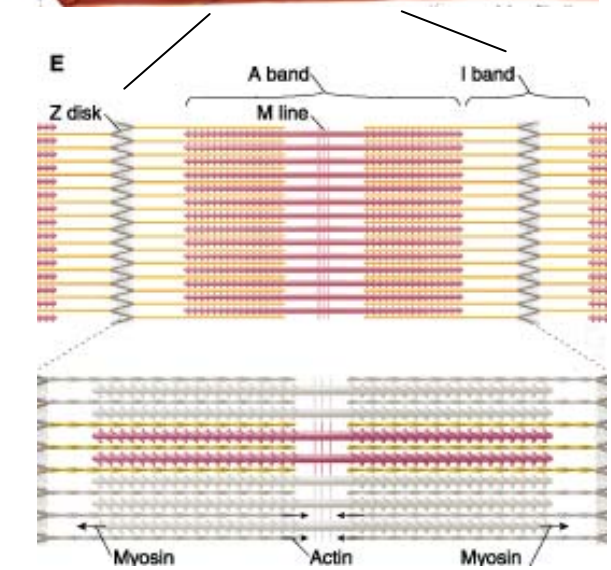
Skeletal - Muscle system



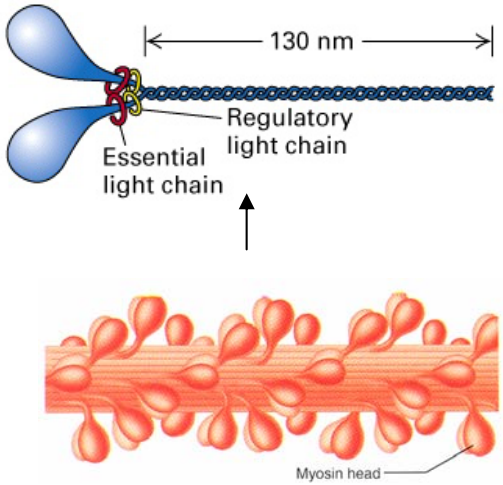
Skeletal muscle tissue

Muscle cell (Muscle fiber)

Myofibril (Molecular assembly of actin-myosin)



Myosin molecule (Myosin II) [Biomolecular motor]

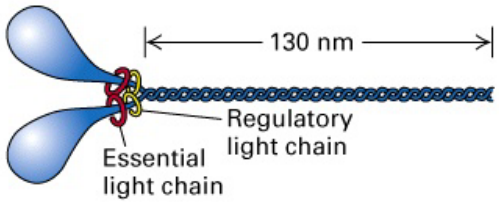


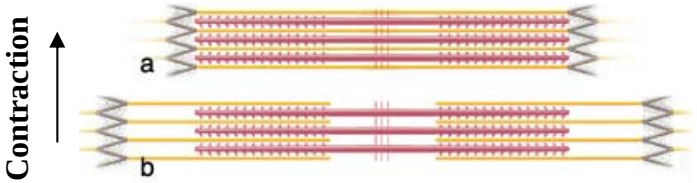
Myosin (Thick) filament

Amplification of an activity through the levels

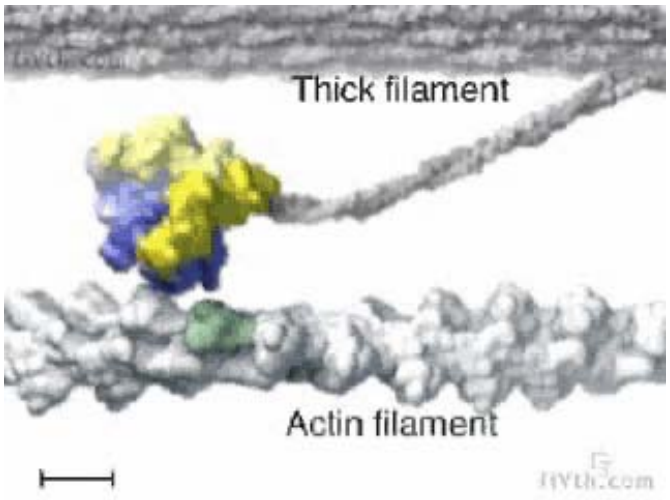
e.g. Muscle activities

Myosin molecule (Myosin II)

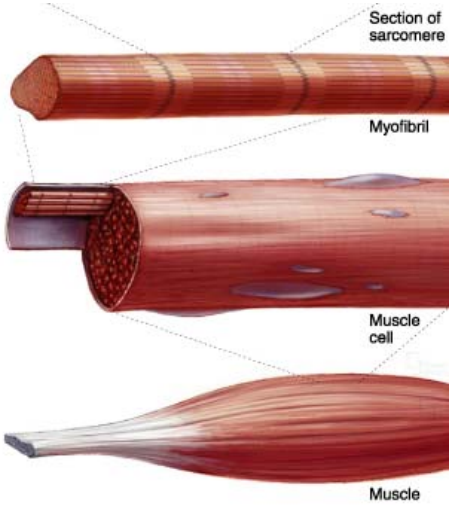


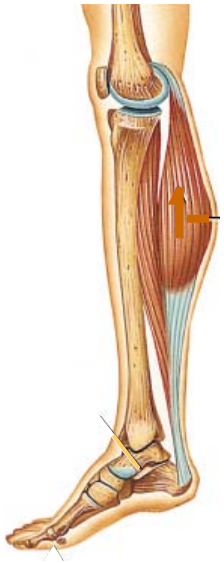


Shortening of sarcomere



Molecular assembly
Cell assembly
Tissue assembly





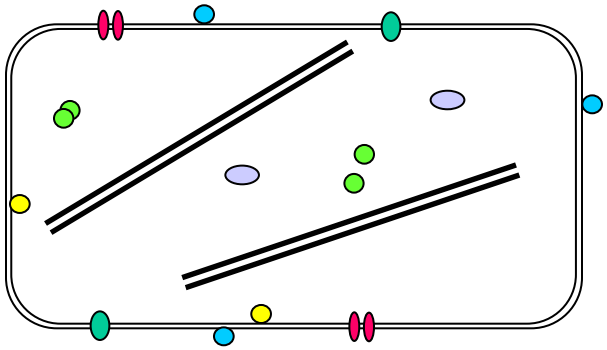
Actomyosin interaction

Each cycle produces 5(~10) nm step.
A head cycles no more than 20 /Sec (in physiological conditions).

300 nm /s ≈ 1mm /h
(typical)

10 mph
(A Marathon runner)

Cell (Human cell) = smallest <u>living unit</u> of the body

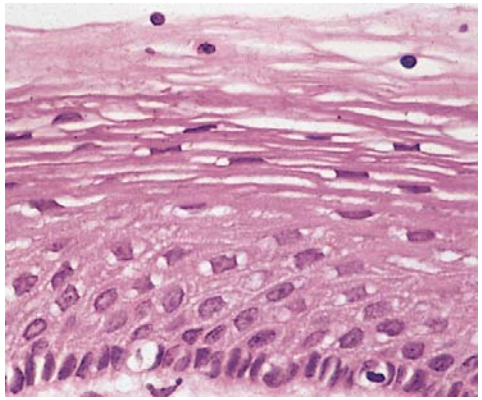


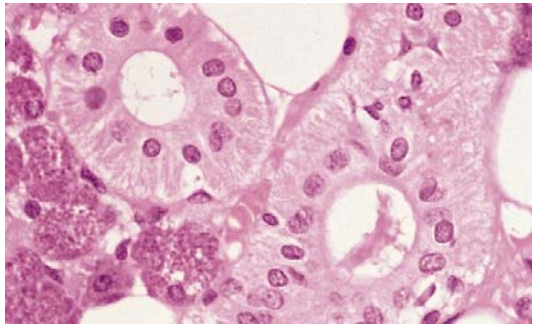
Minimal common components

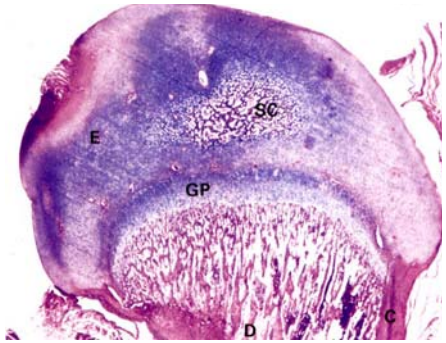
- Cell (plasma) membrane
  The boundary that separates
  ionic constituents (environment)
- Membrane proteins
- Cytoplasm
  Proteins, other molecules, ions, water
- Cytoskeleton

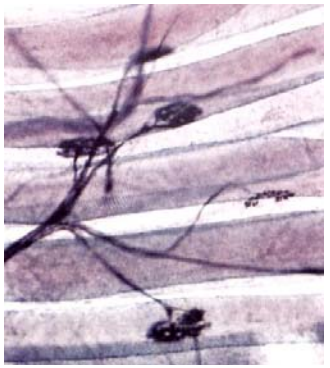
Various size, shape, components, organization, function, life span

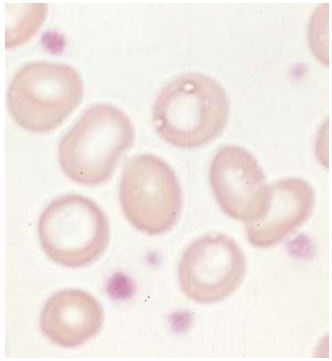
❖Some cells are partially to completely missing organelles (such as red blood cells)





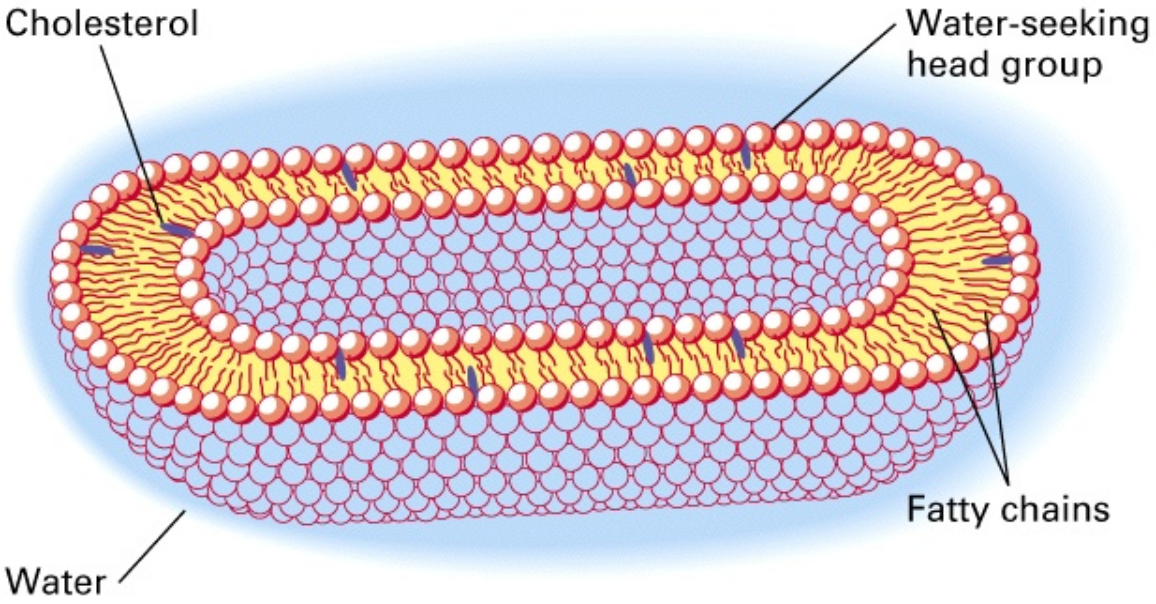






Plasma Membrane

separates the cell from the environment (“Barrier”)



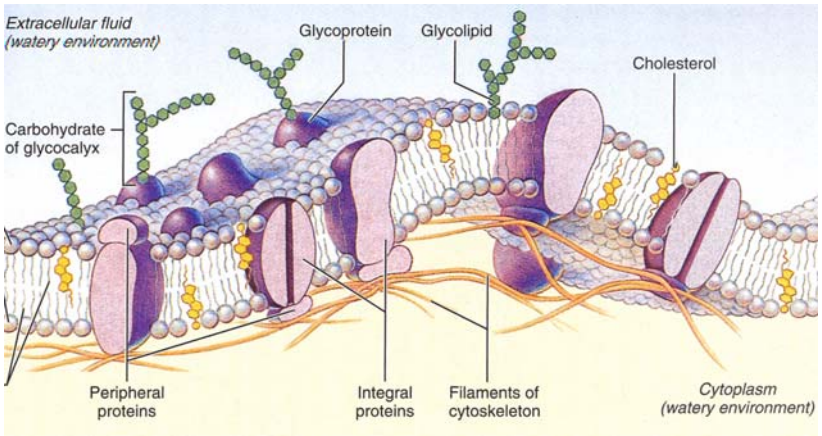
Lipid Bi-layer

Hydrophobic Barrier

Ions (Na^+, K^+, Ca^{2+} etc.) : Impermeable

Water : Permeable (poorly)

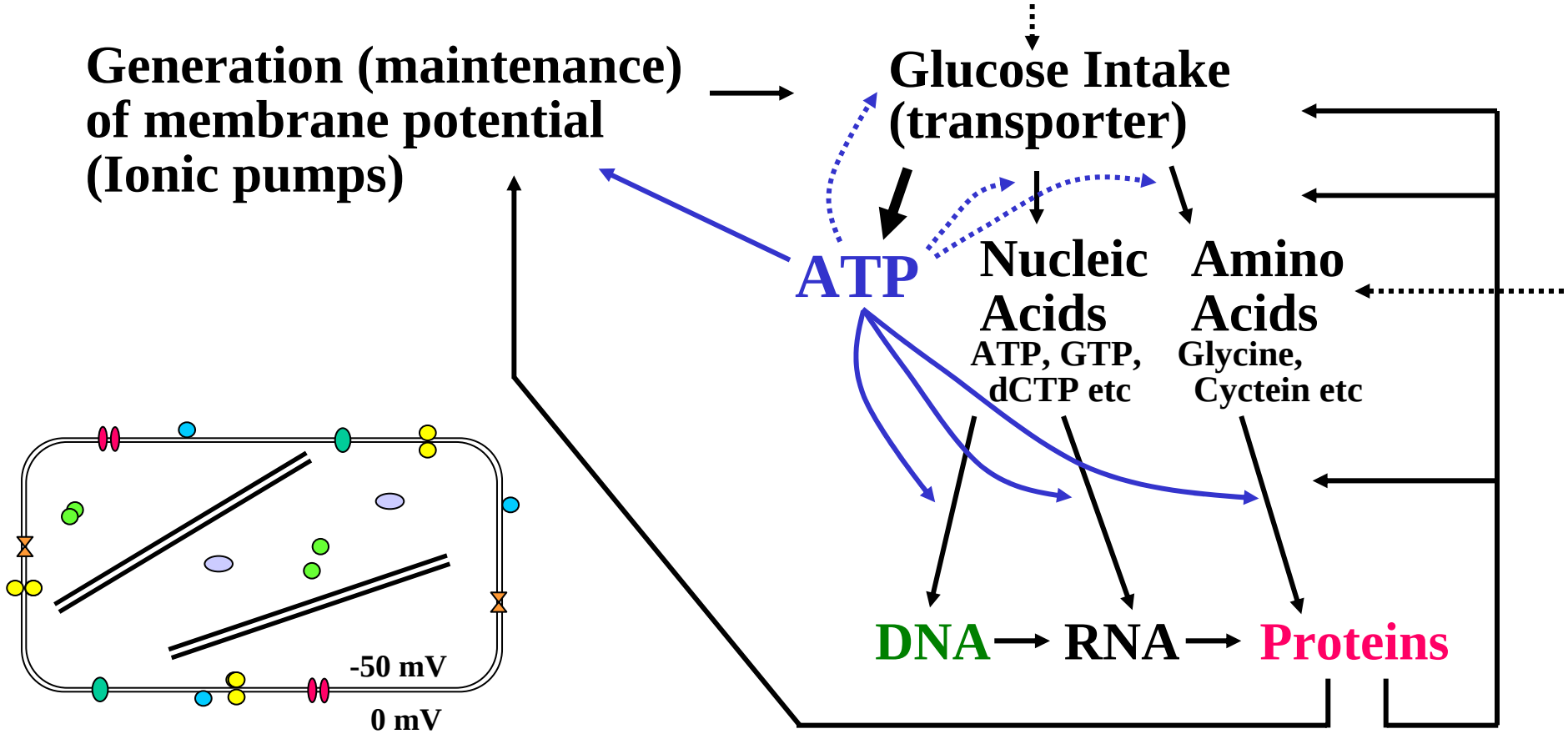
O_2, CO_2 : Permeable



[More on membranes : next lecture]

Intracellular Environment

Energy from ATP is used for (nearly) all the processes that maintain cell's 'LIFE'.



Ionic imbalance (particularly, Na^+ and K^+) b/w inside and outside a cell, created by membrane ionic pumps, ion exchangers and channels, establishes resting membrane potential. This is used to drive other process (such as molecule import), as well as for information processing (*e.g.* nerve cells).

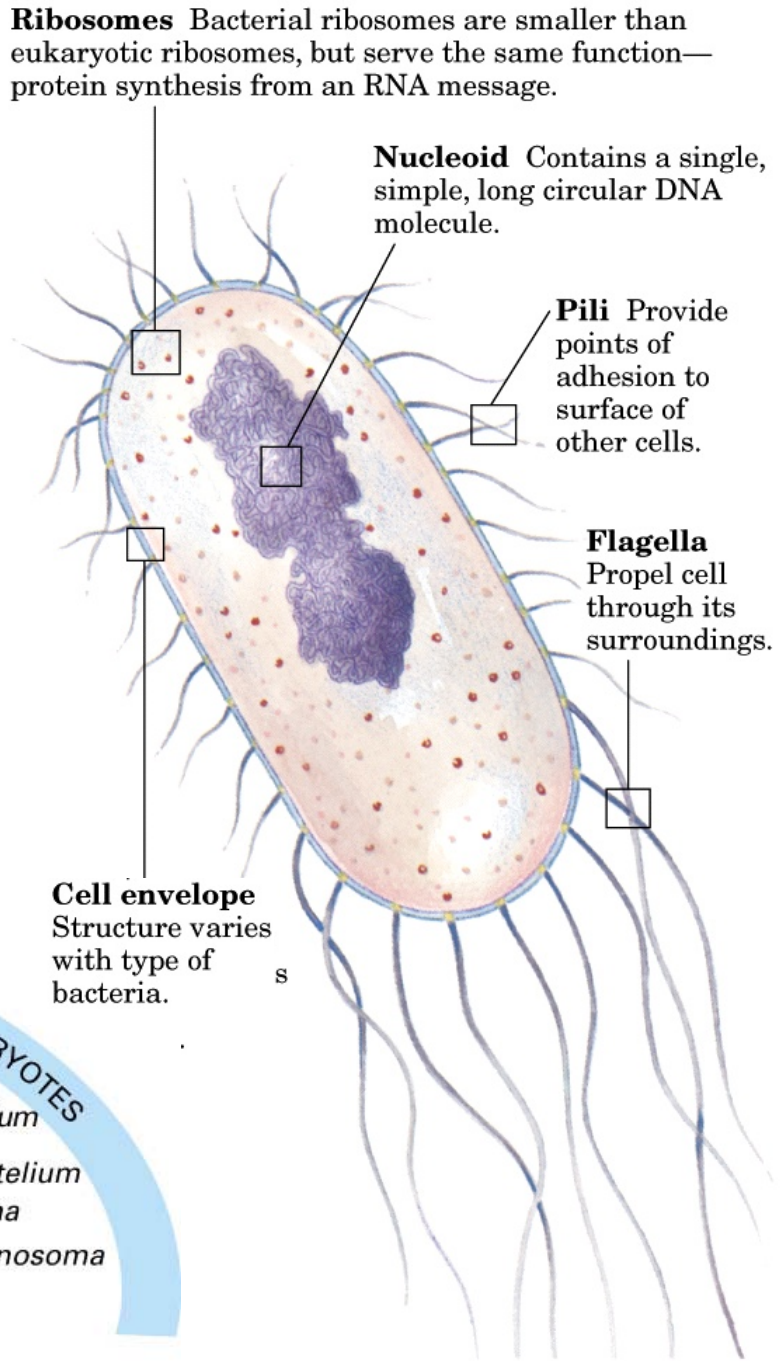
Cells

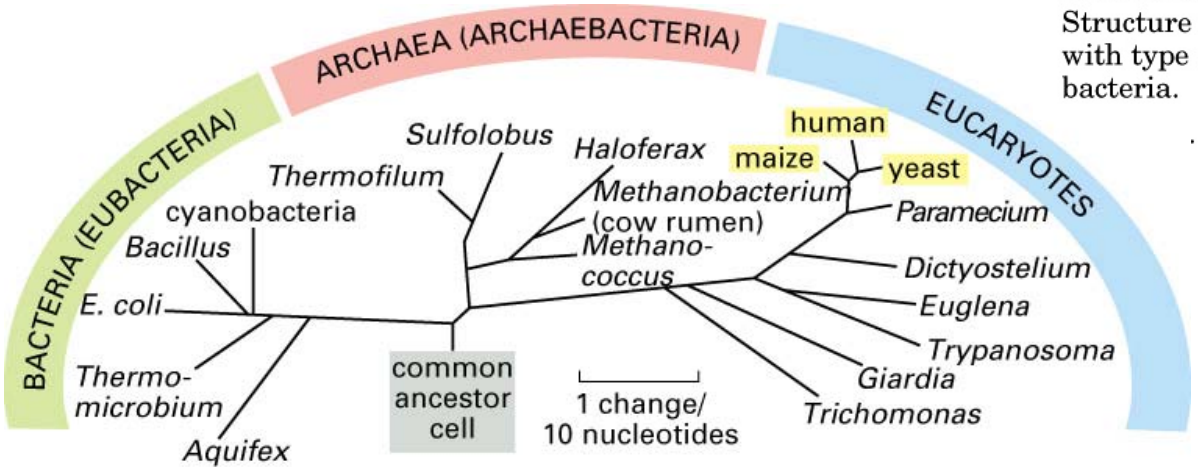
Prokaryotic cell (Bacteria)

Simple organization

No membrane-bound organelle
No nucleus
Primitive cytoskeleton
Bacterial flagella

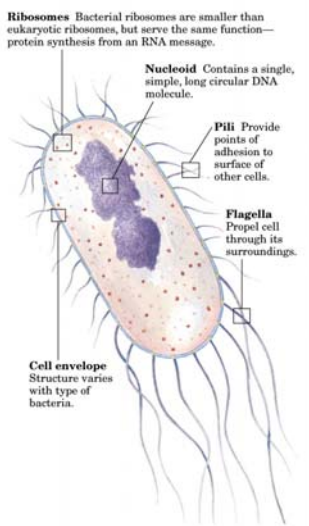
Generally smaller in size
(than an eukaryotic cell)



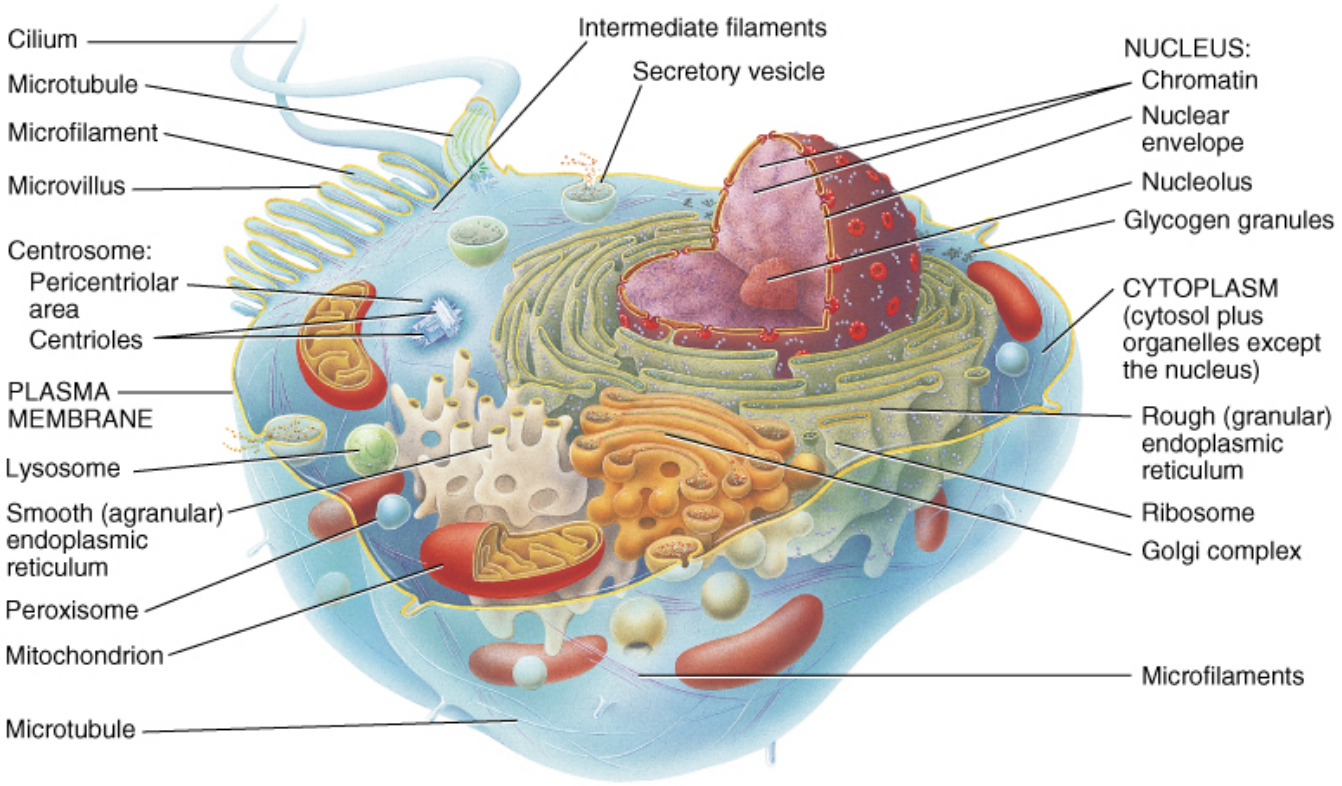


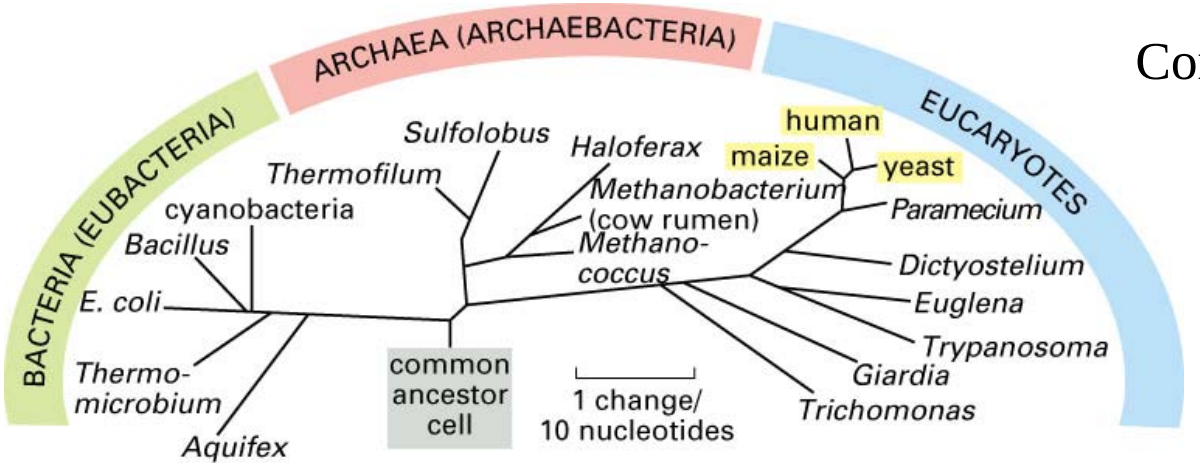
Prokaryotic cell

No membrane-bound organelle
No nucleus
Primitive cytoskeleton
Bacterial flagella



Eukaryotic cell: Subcellular Organization

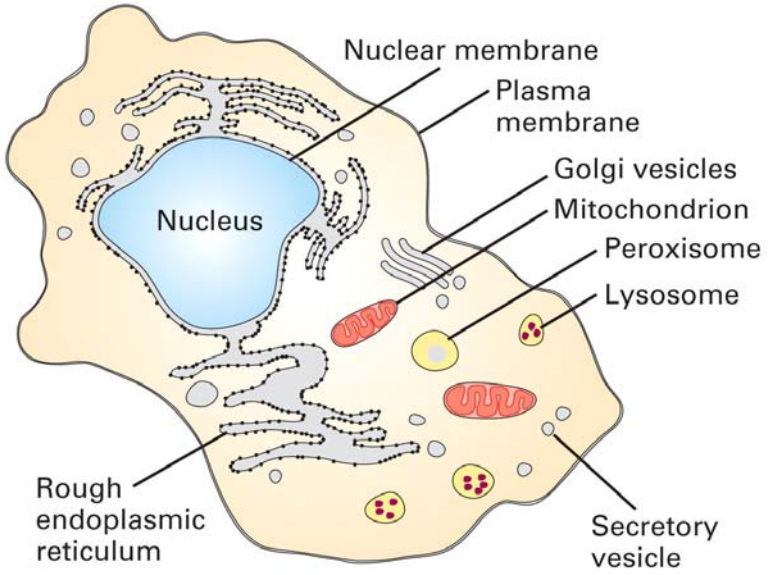




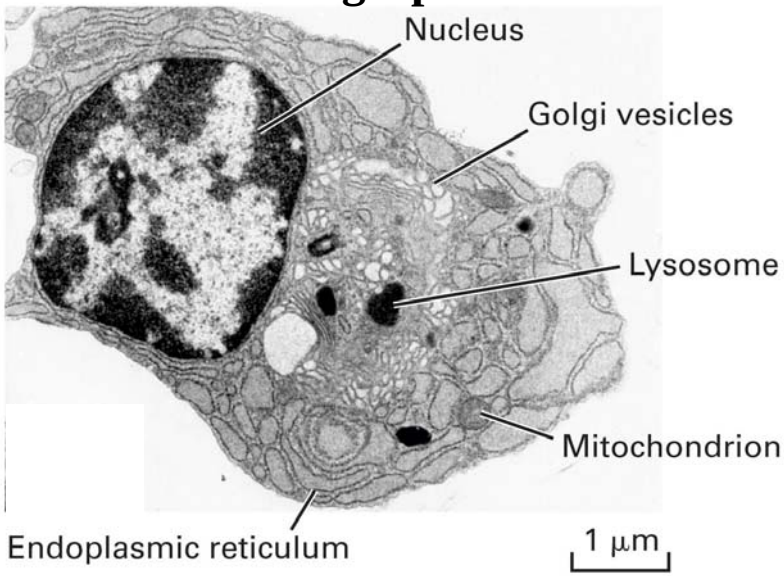
Complex organization inside cell :

Various **<u>organelles;</u>**
Nucleus
Mitochondria
Cytoskeleton

Eukaryotic cells



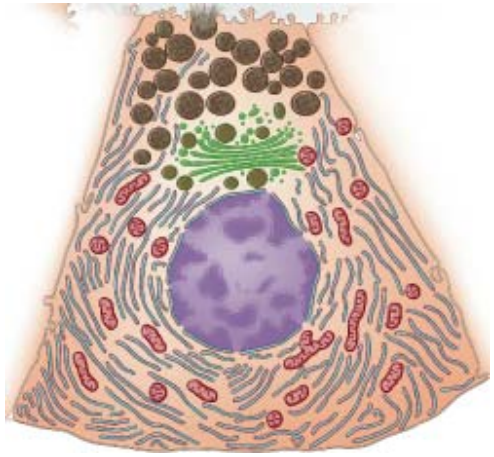
Electron Micrograph



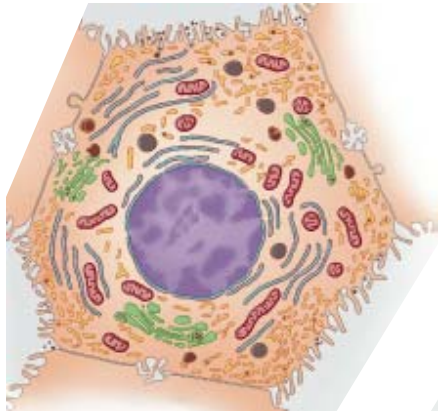
Various cell types; shape, size, intracellular organizations, <u>polarization</u> – Functions

These three cells all belong to "Intestinal Epithelial Cell" groups

Small Intestine (Absorptions)



Pancreatic Acinar cell (Digestive enzyme production)



Liver Hepatocyte (Metabolism, protein production, Bile secretion etc)

Comparison of Prokaryotic and Eukaryotic Cells

Characteristic	Prokaryotic cell	Eukaryotic cell
Size	Generally small (1–10 μm)	Generally large (5–100 μm)
Genome	DNA with nonhistone protein; genome in nucleoid, not surrounded by membrane	DNA complexed with histone and nonhistone proteins in chromosomes; chromosomes in nucleus with membranous envelope
Cell division	Fission or budding; no mitosis	Mitosis including mitotic spindle; centrioles in many species
Membrane-bounded organelles	Absent	Mitochondria, chloroplasts (in plants, some algae), endoplasmic reticulum, Golgi complexes, lysosomes (in animals), etc.
Nutrition	Absorption; some photosynthesis	Absorption, ingestion; photosynthesis in some species
Energy metabolism	No mitochondria; oxidative enzymes bound to plasma membrane; great variation in metabolic pattern	Oxidative enzymes packaged in mitochondria; more unified pattern of oxidative metabolism
Cytoskeleton	~~None~~ **(Exists during cell division)**	Complex, with microtubules, intermediate filaments, actin filaments
Intracellular movement	None **(?)**	Cytoplasmic streaming, endocytosis, phagocytosis, mitosis, vesicle transport

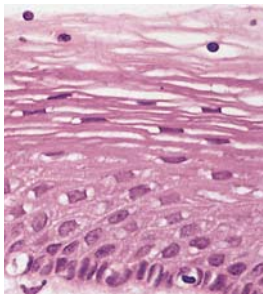
Source: Modified from Hickman, C.P., Roberts, L.S., & Hickman, F.M. (1990) *Biology of Animals,* 5th edn, p. 30, Mosby–Yearbook, Inc., St. Louis, MO.

TISSUE = group of cells in similar type(s) , and perform (a) common (related) task(s).

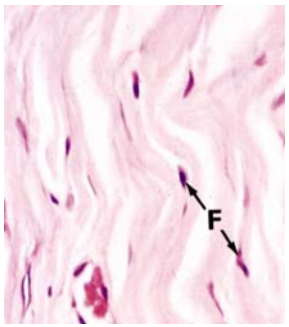
4 Basic tissue types:

(and that's all)

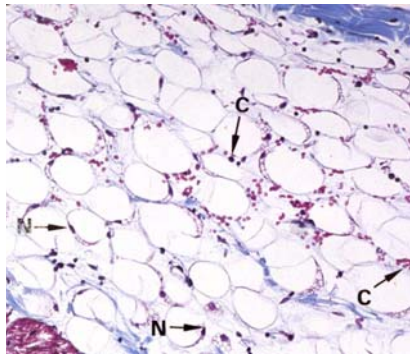
Epithelial tissue →



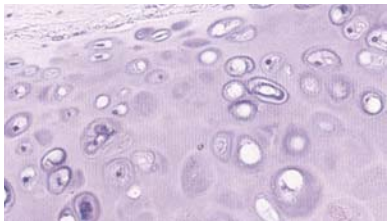
Connective tissue →



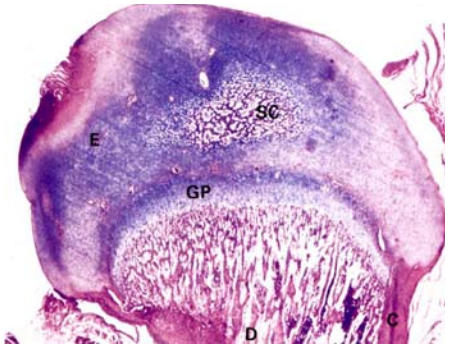
Adipose tissue →



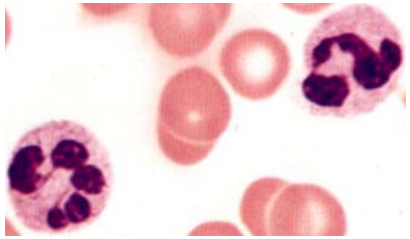
Cartilage →



Bone →

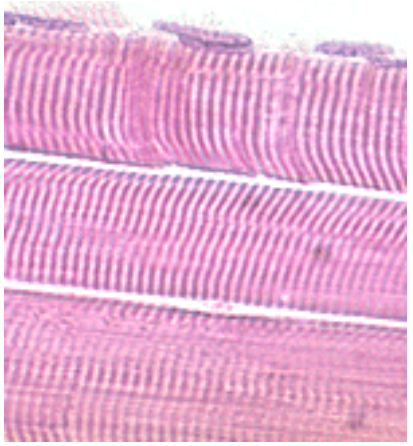


Blood →



Nervous tissue →

Muscle tissue →

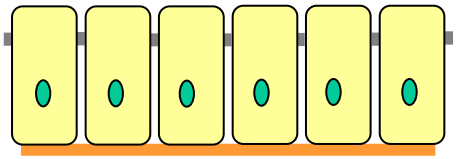


TISSUE

Cell organizations and Extracellular Matrix

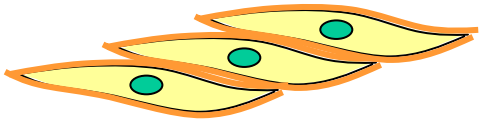
Cells are attached each other via junctional complex

***e.g.* Epithelial tissue**



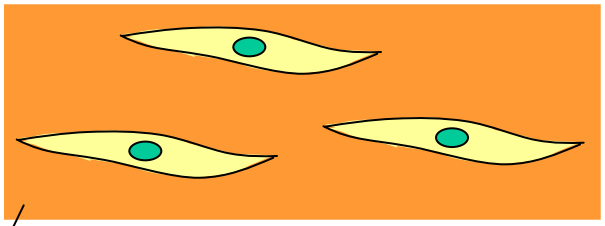
Cells are surrounded by extracellular matrix (Basal Lamina) and connected each other

***e.g.* Muscle tissue, Nervous Tissue**



Cells are scattered within the extracellular matrix

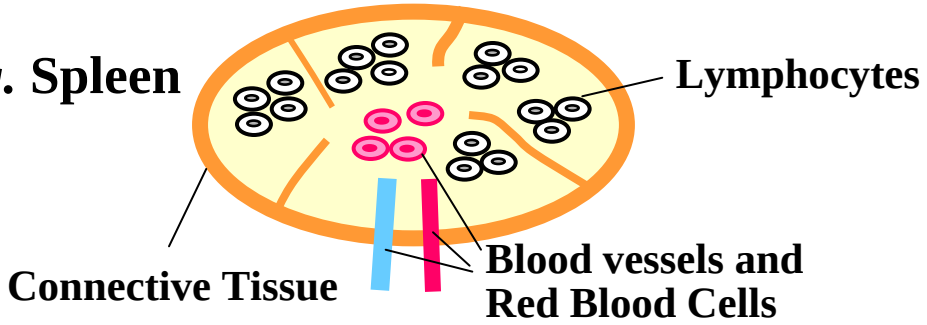
***e.g.* Connective tissues, Cartilage, Bone**



ORGAN

A Self-Closing unit, consists of tissues

***e.g.* Spleen**



Tissue: may consist of one type of cells, or various types of cells (together with extracellular matrix).

Different cells (types) within a tissue

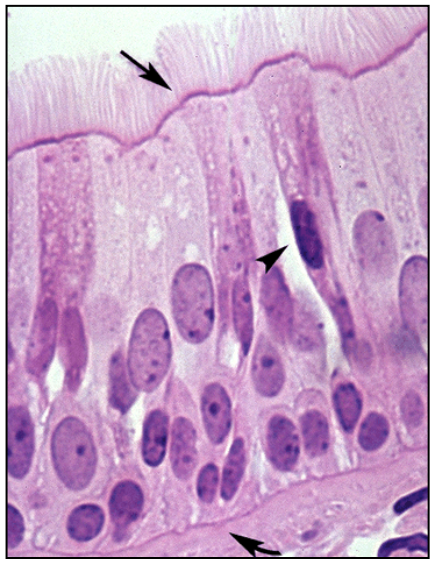
Same origin (stem cell) → different differentiation paths (1)

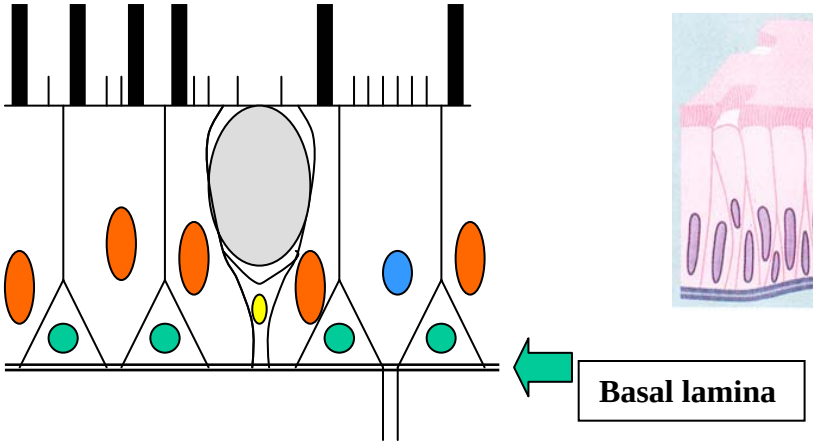
→ different stages of a differentiation (2)

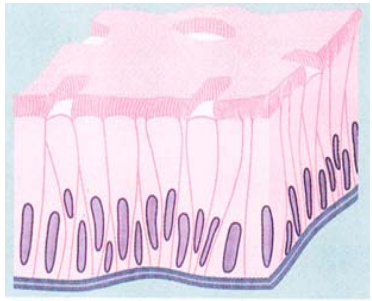
Different origin (3)

e.g. Tracheal epithelium

(Pseudostratified columnar ciliated epithelium)







Ciliated cell

Goblet cell

Basal cell

(precursor to either ciliated or goblet cell)

Brush cell

Diffuse endocrine cell

Tissue: may consist of one type of cells, or various types of cells (together with extracellular matrix).

Different cells (types) within a tissue

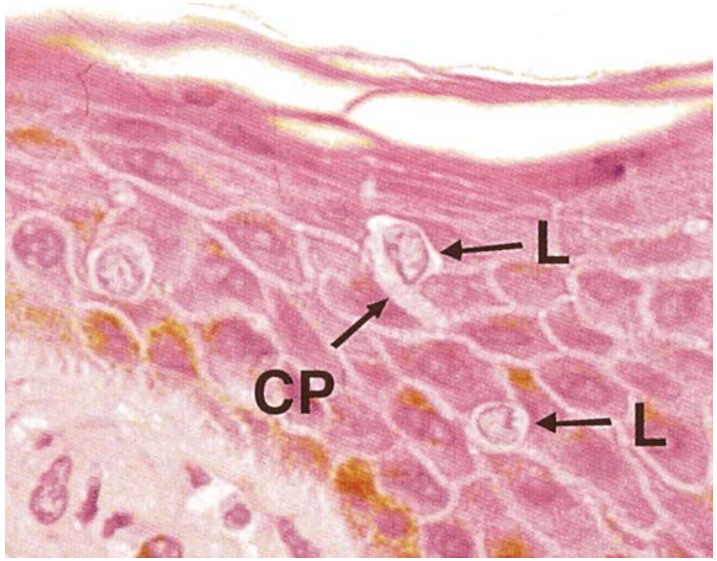
Same origin (stem cell) → different differentiation paths (1)

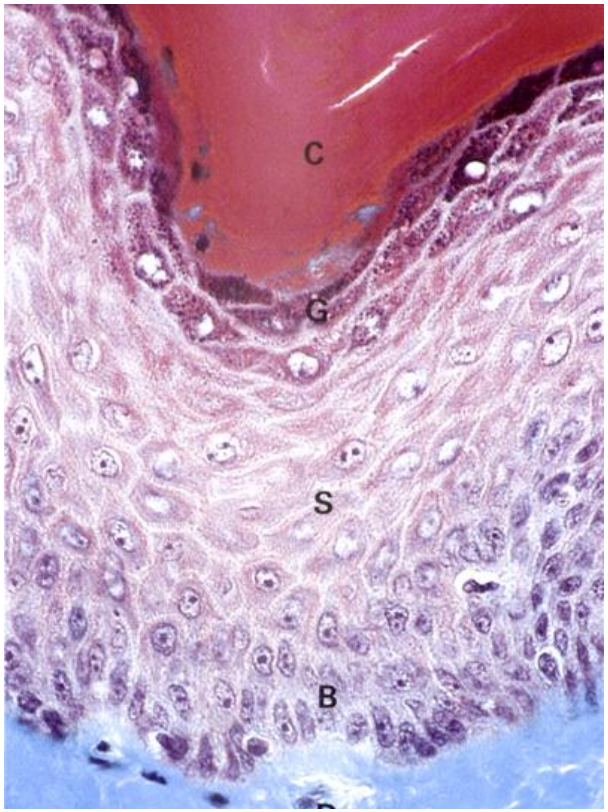
→ different stages of a differentiation (2)

Different origin (3)

***e.g.* Skin**

(Stratified squamous epithelium)





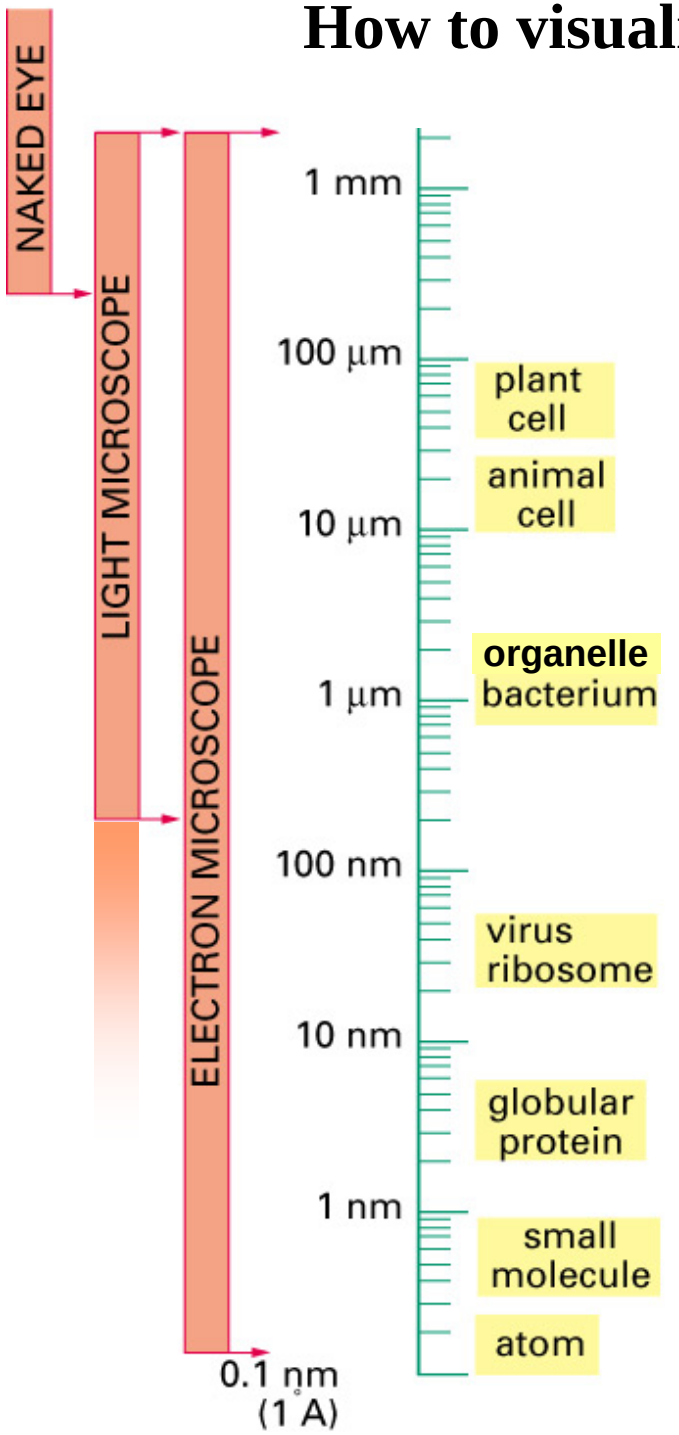
Different types of cells (functions):

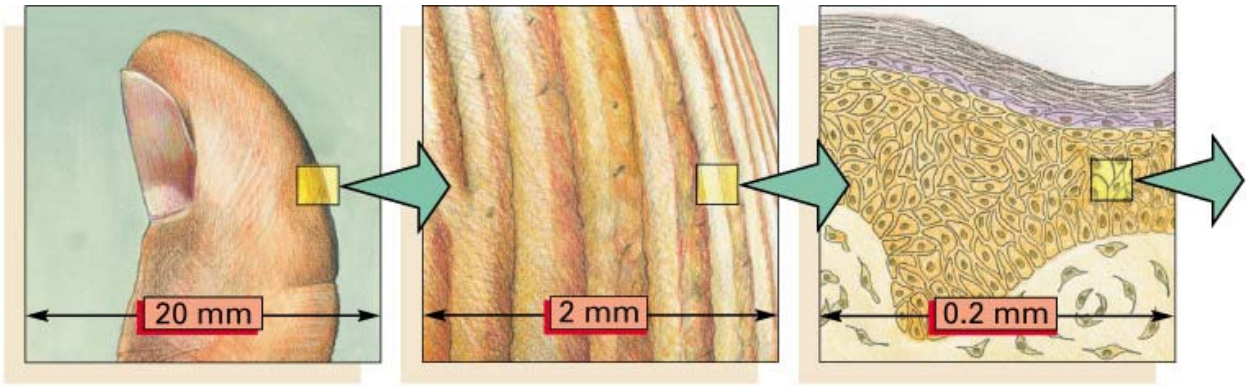
Keratinocyte
Melanocyte (produces melanin granules)
Langerhans cell
Markel's cell

Single cell type (Keratinocyte) in different stages (layers)

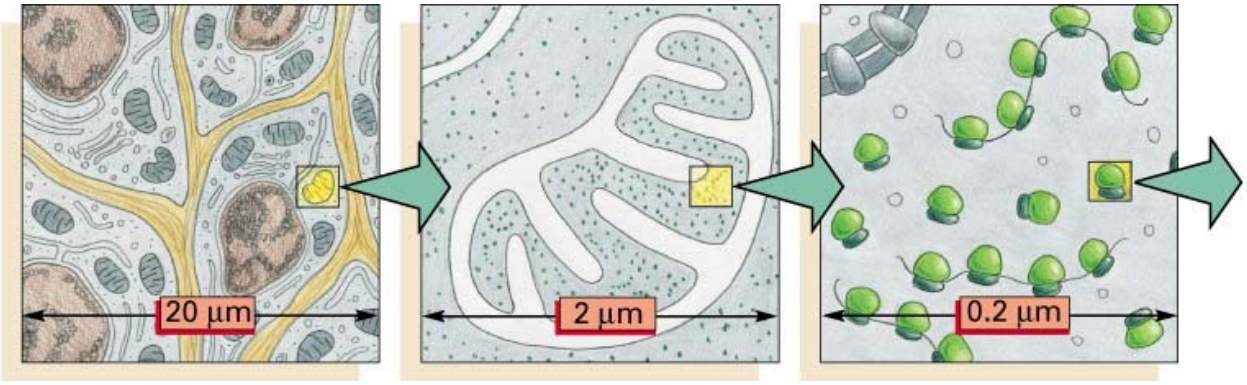
B → S → G → C → (skin surface)

How to visualize cells and Subcellular Components

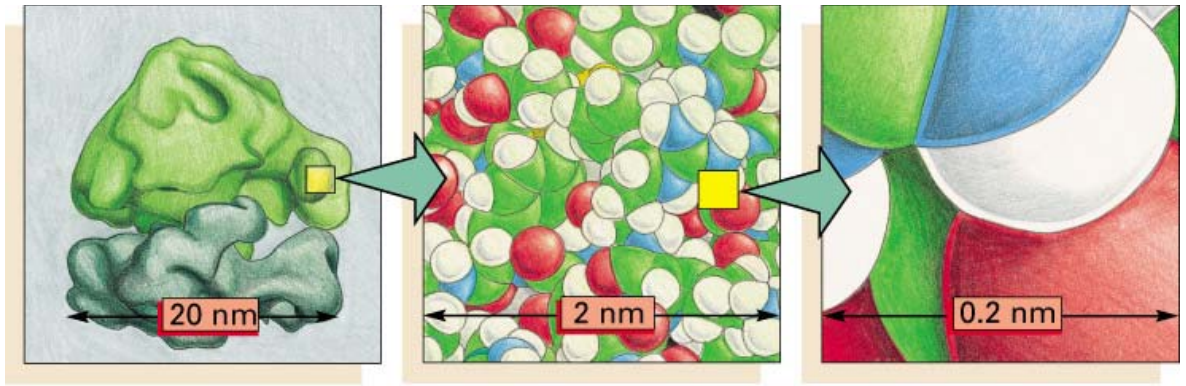




Finger **Epidermis (Tissue)**



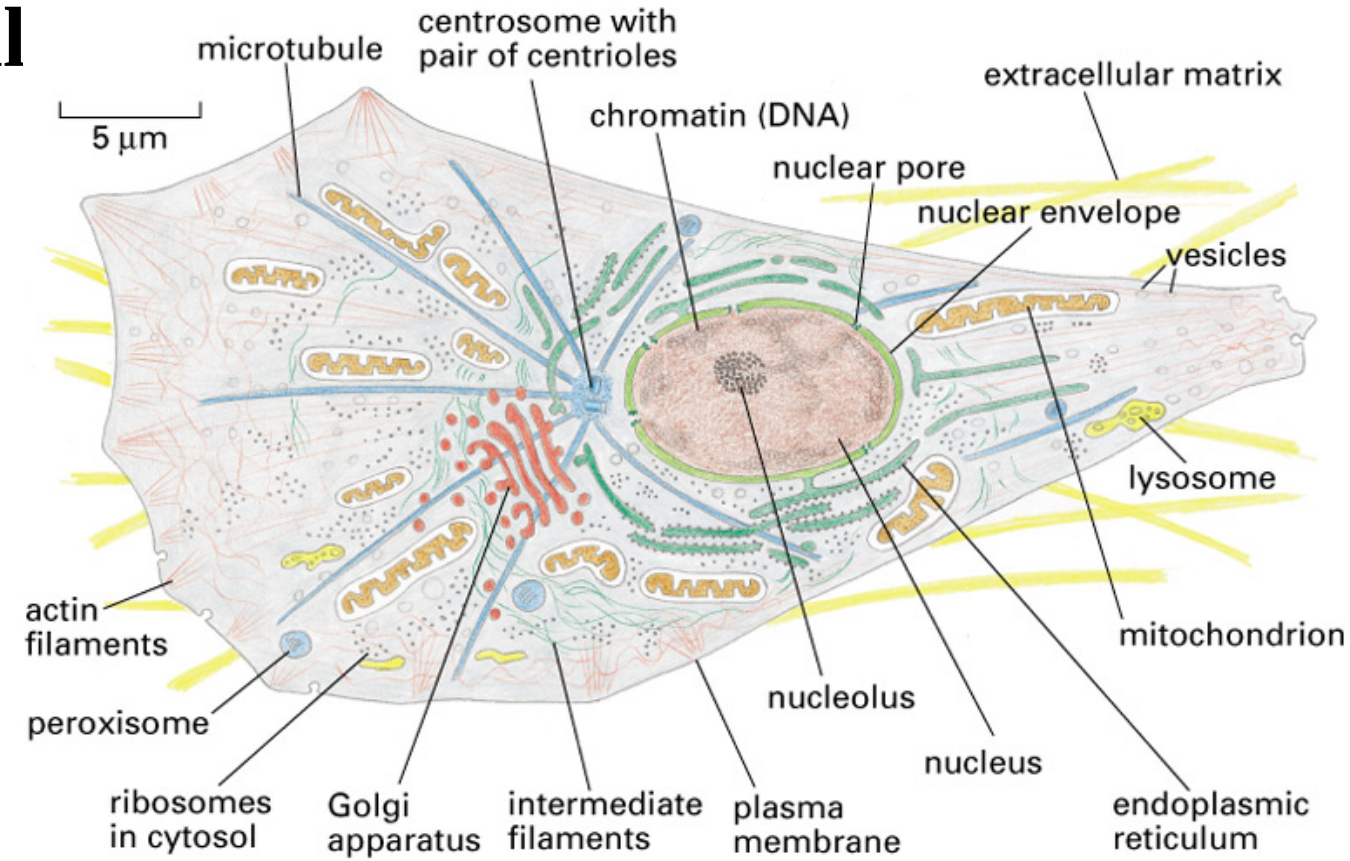
Cell (Organelle) **Mitochondrion** **Poly-Ribosomes (Multi-protein complex etc..)**



Ribosomes **Protein (structure)** **Atoms**

Prototypical mammalian cell

Organelles are not placed randomly throughout a cell; they are organized and localized (polarized).



Plasma Membrane
Membrane-bound Organelles
- **Mitochondria**
- **Rough-Endoplasmic Reticulum (rER)**
- **Smooth-Endoplasmic Reticulum (sER)**
- **Golgi Apparatus**
- **Lysosomes**
- **Peroxisomes**
- **Endosomes (Phagosomes)**
- **Exocytic vesicles**

Cytoplasmic components

Centriole(s)
Polysome (Poly-ribosome)

Nucleus
- **Nucleolus**

Cytoskeleton
- **Actin filaments**
- **Microtubules**
- **Intermediate filaments**

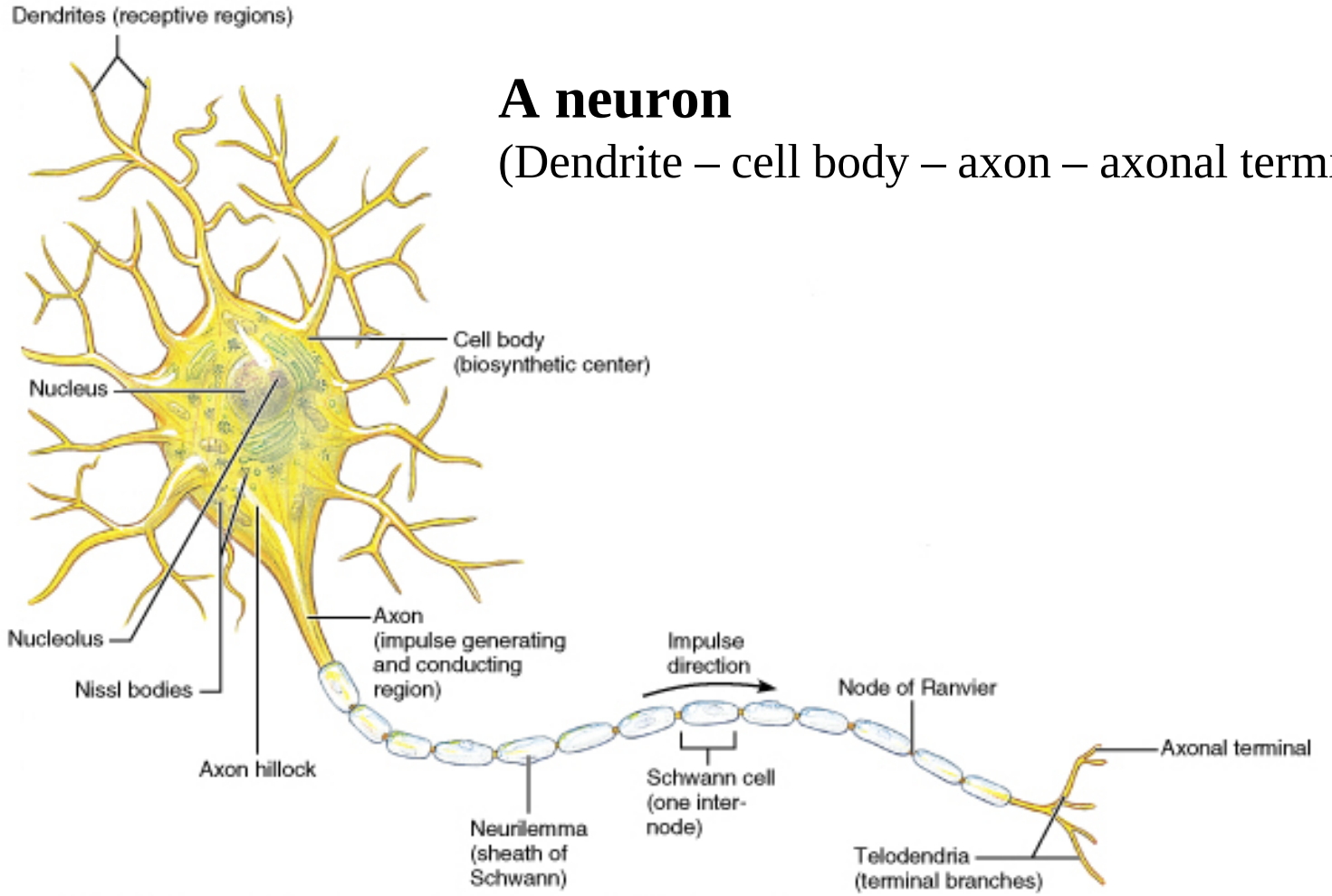
Cilia / Flagella
Microvilli

Cell Polarization

Positions of cellular components (organelles, plasma membrane sub-structures) are not randomly (uniformly) arranged throughout the cell;

➔ many cell types take <u>unique shape.</u>

- The shape of a cell, in many cases, is held by internal cytoskeletal proteins (actin filaments, intermediate filaments and microtubules.)



A neuron

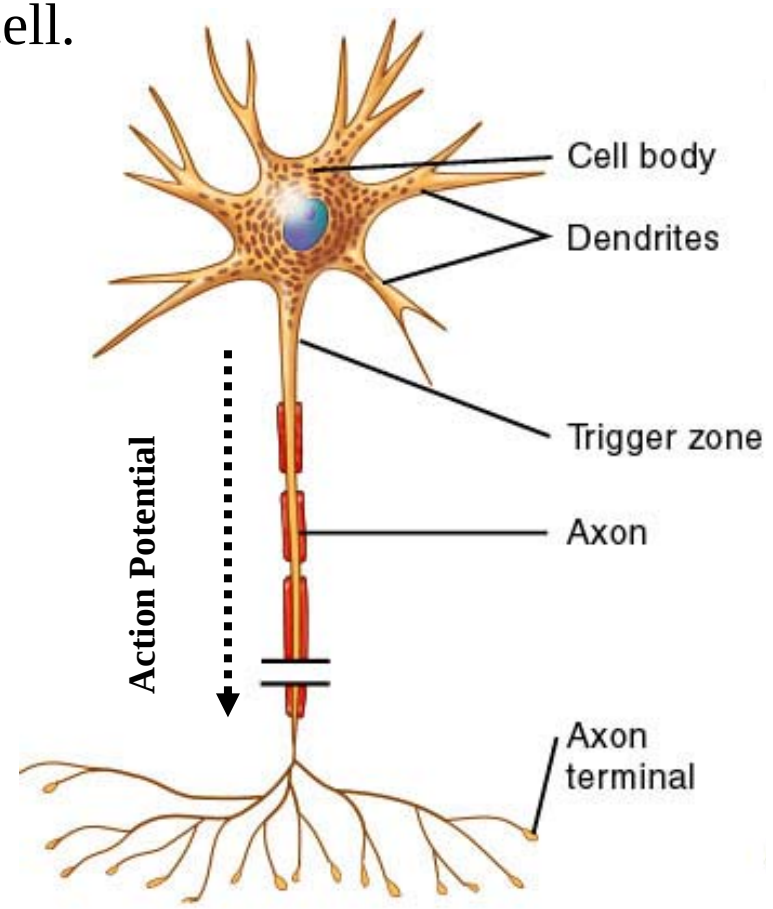
(Dendrite – cell body – axon – axonal terminal)

Subcellular specialization

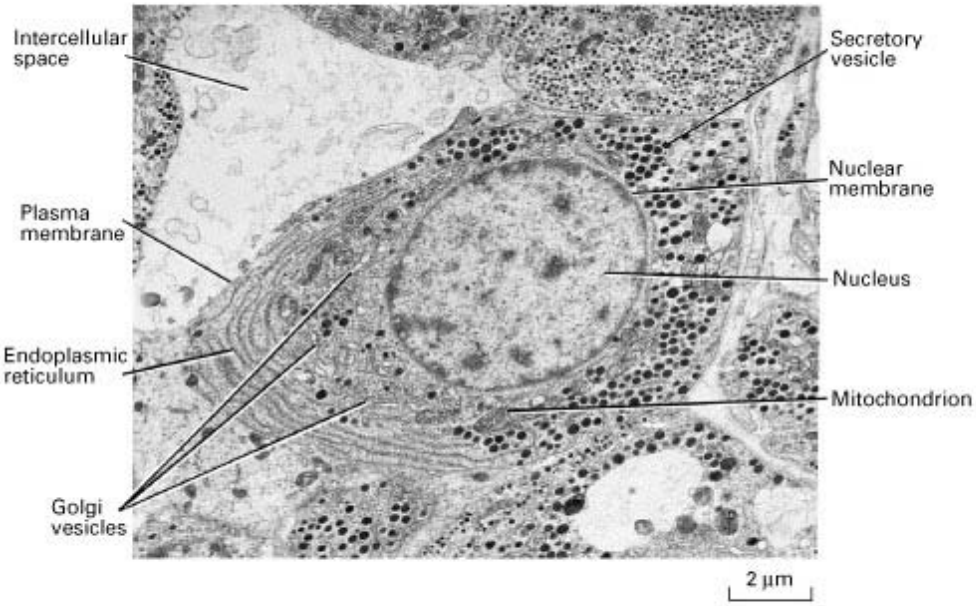
Arrangement of the cellular structures not only reflects the cell shape, but also unique function(s) within particular region(s) of the cell.

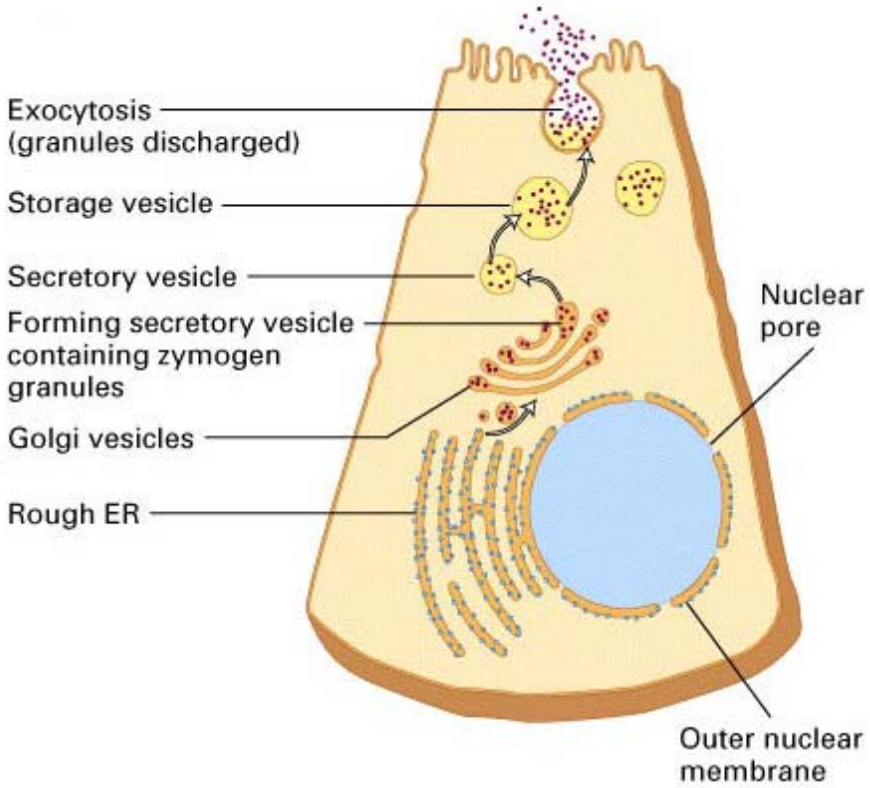
Different surface
- **– Different protein structures**
- **– Different role (activity)**

Cell junctions play key roles separating the surfaces (in Epithelial tissues)



Cell Polarization -- Subcellular specialization





e.g. a secretory cell

Exocytosis takes place only on the cell's apical surface

Note the locations of rER and Golgi vesicles

Positions of the organelles, as well as the direction of transport of the secretory vesicles are determined by network of cytoskeleton (actin filaments, microtubules and intermediate filaments).

Receptors / channels / pumps on the plasma membrane, in many cells, are also localized onto particular side (apical, basal, lateral.)

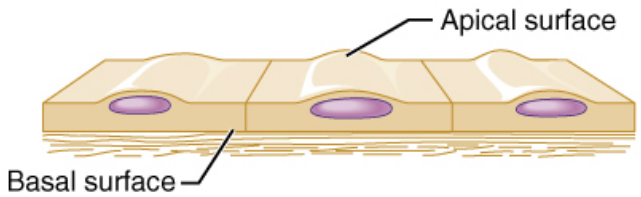
Cell polarization in epithelial tissues

Strategic localization of Cellular component;

Epical vs Basolateral surface

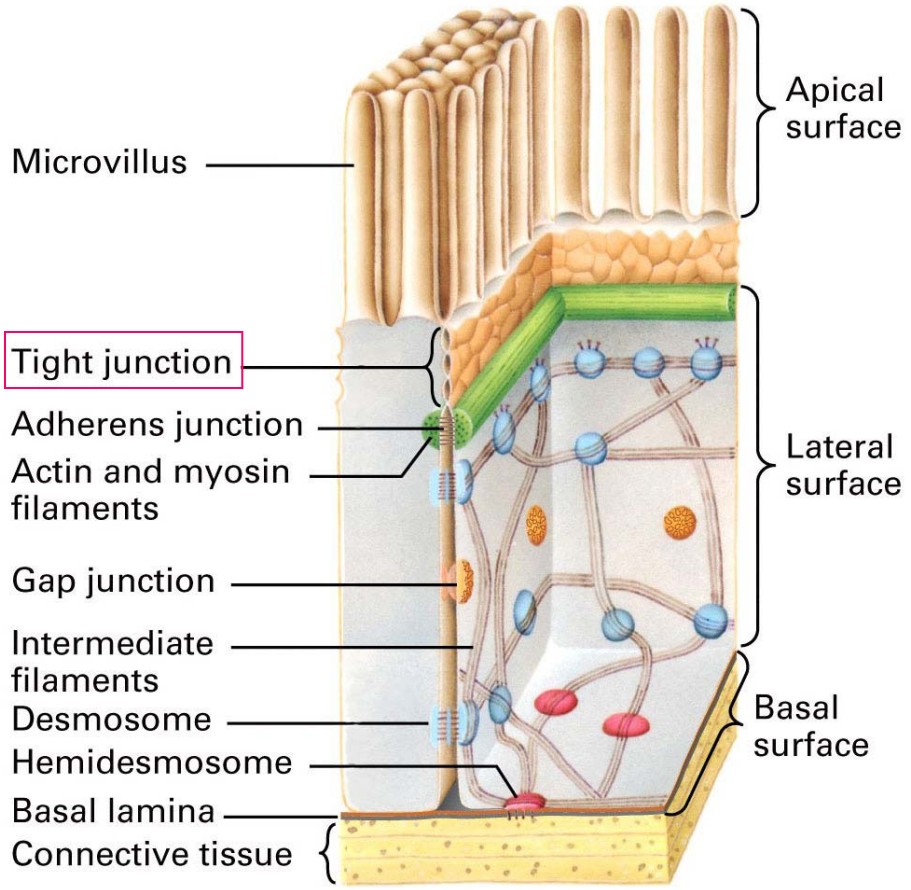
Different surface
- **Different protein compositions**
- **Different role (activity)**

Cell junctions play key roles separating the surfaces



(Outside)

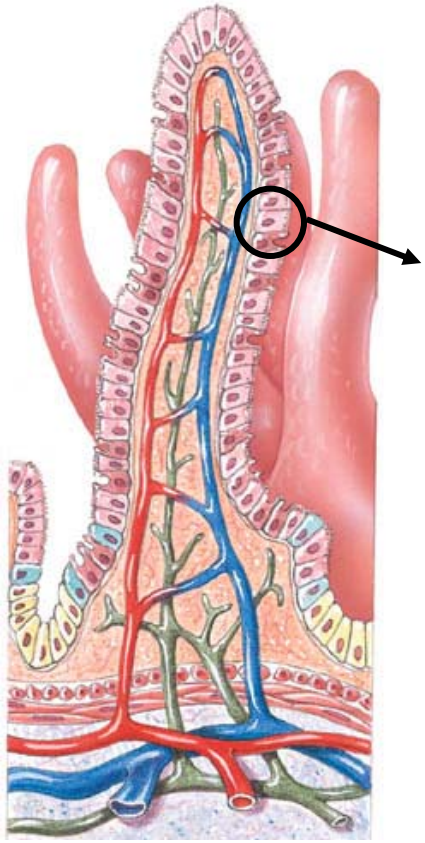
(Inside)

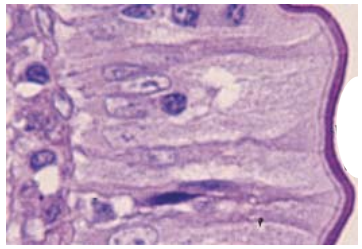


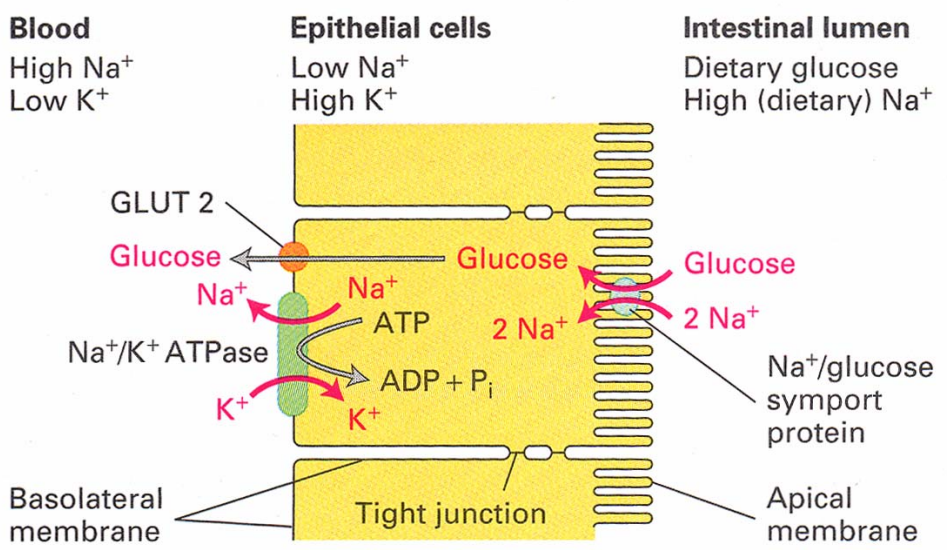
Prototypical epithelial cell

Epithelial cell polarization

Small intestine







Glucose intake

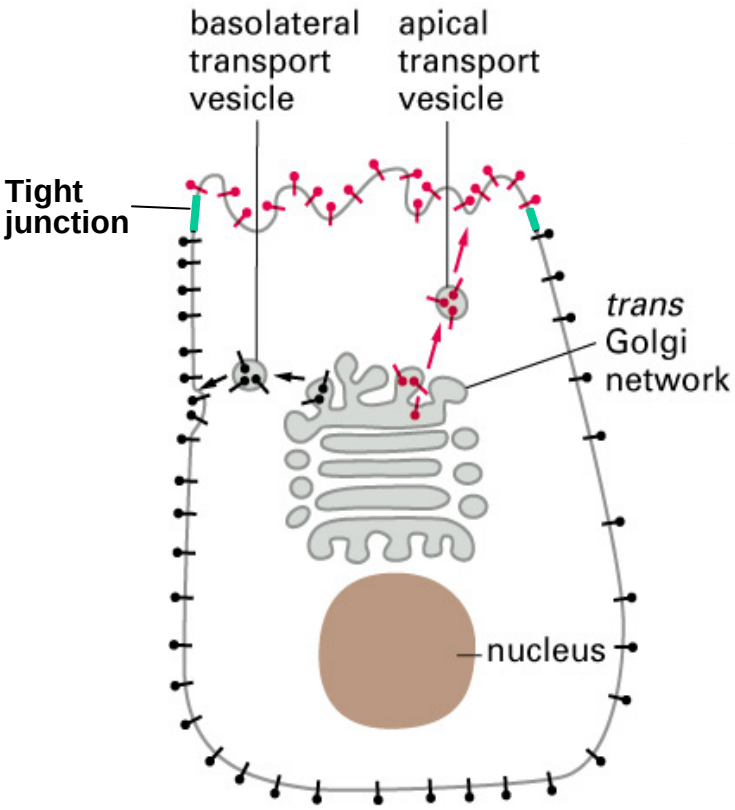
Basolateral vs Apical surfaces : Different <u>functions</u>

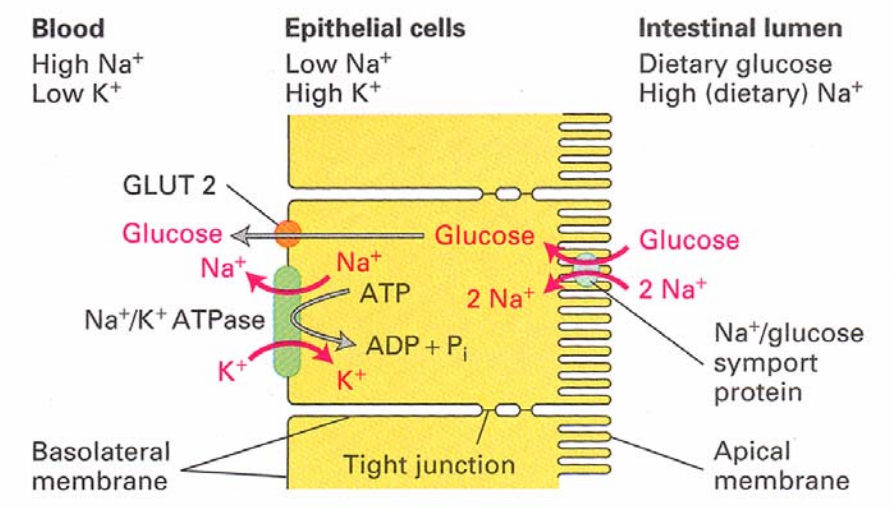
Membrane proteins, receptors, channels

Exocytosis/endocytosis

Epithelial cell polarization

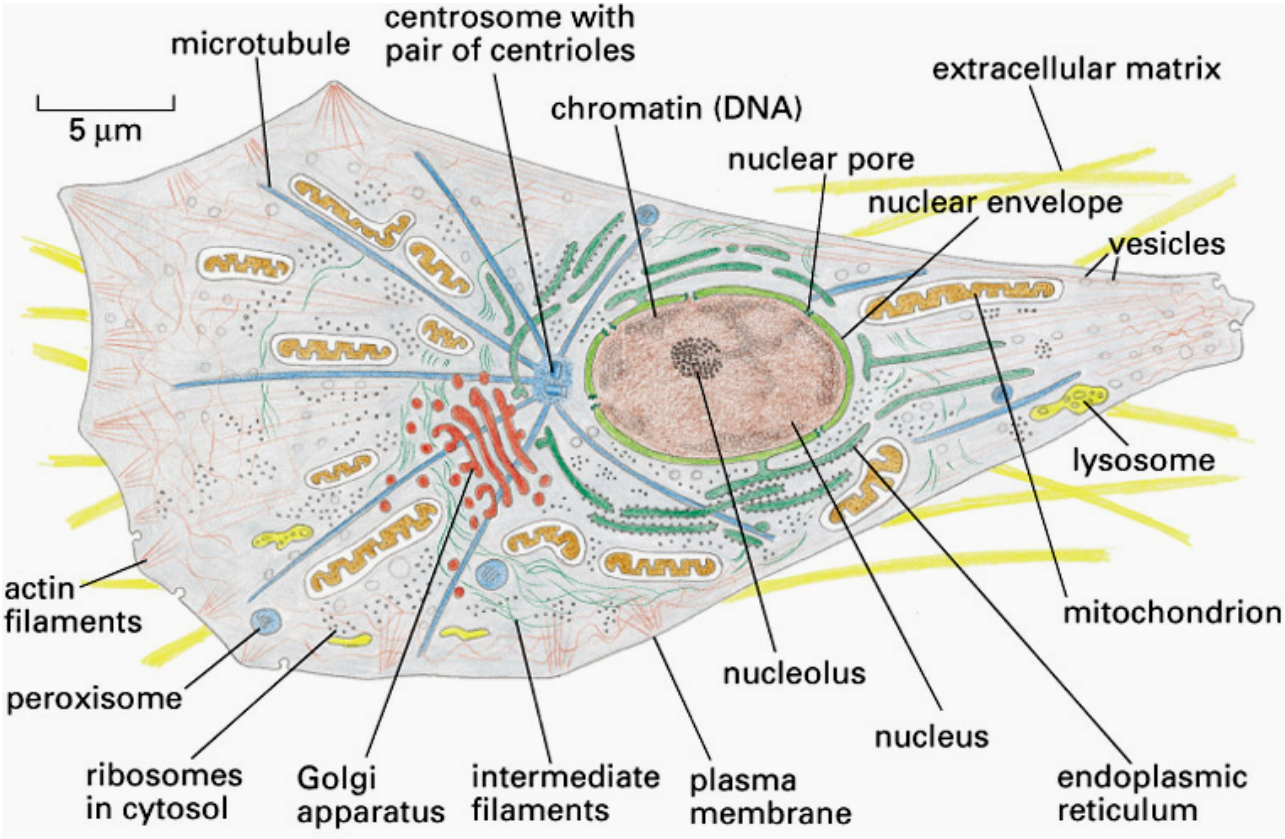
Small intestine





Specific sets of plasma membrane proteins / secretory proteins are transported to their <u>correct destination</u> by intracellular transport mechanisms.

Organelles



Major Functions of organelles

Protein synthesis and export
– rough Endoplasmic Reticulum (rER), Golgi Apparatus

Membrane lipid synthesis – smooth ER

Endocytosis, breakdown – endosome, phagosome, lysosome

Energy and metabolism – Mitochondrion, peroxizome

Genetic Information – Nucleus

Many Ornagelles would take more than one function:
***e.g.* Calcium storage – ER (SR), Mitochondrion**

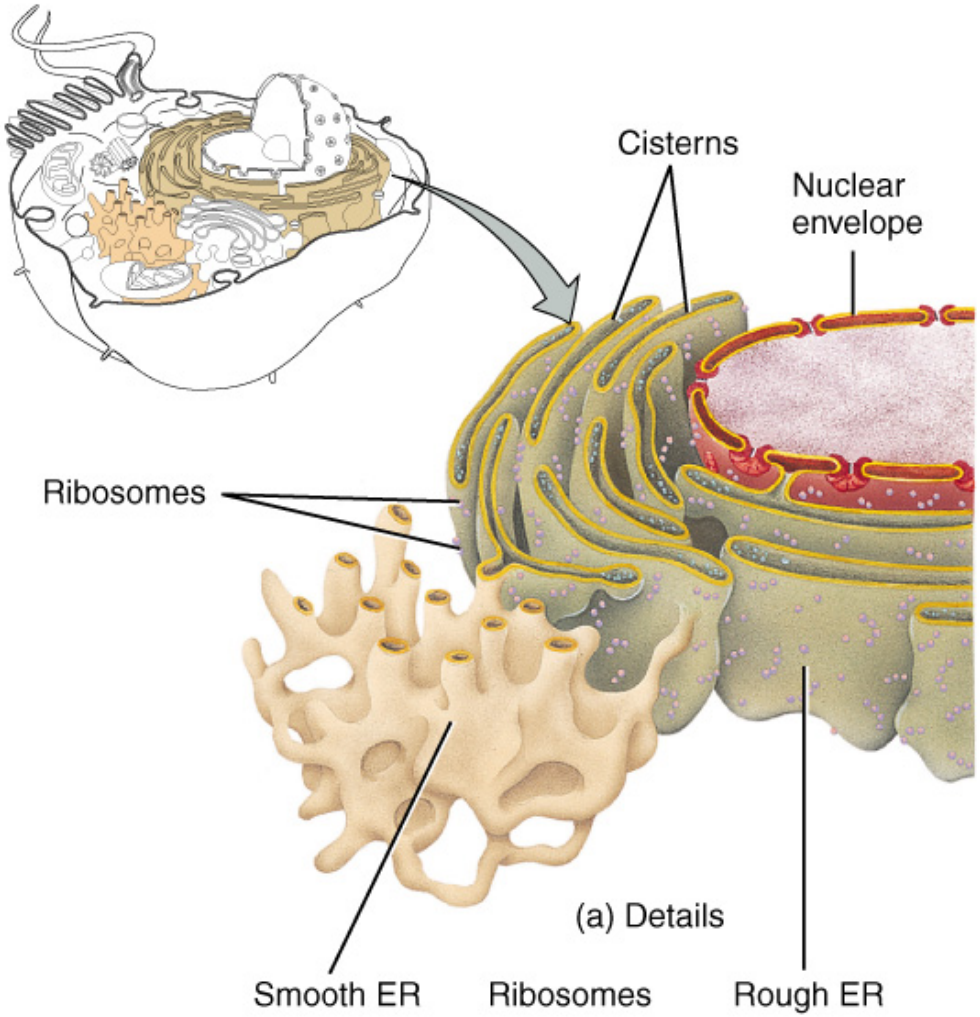
Membrane-bound Organelles

rER (rough Endoplasmic Reticulum) :
Protein synthesis
and modification
(Plasma membrane proteins, secretory proteins etc)

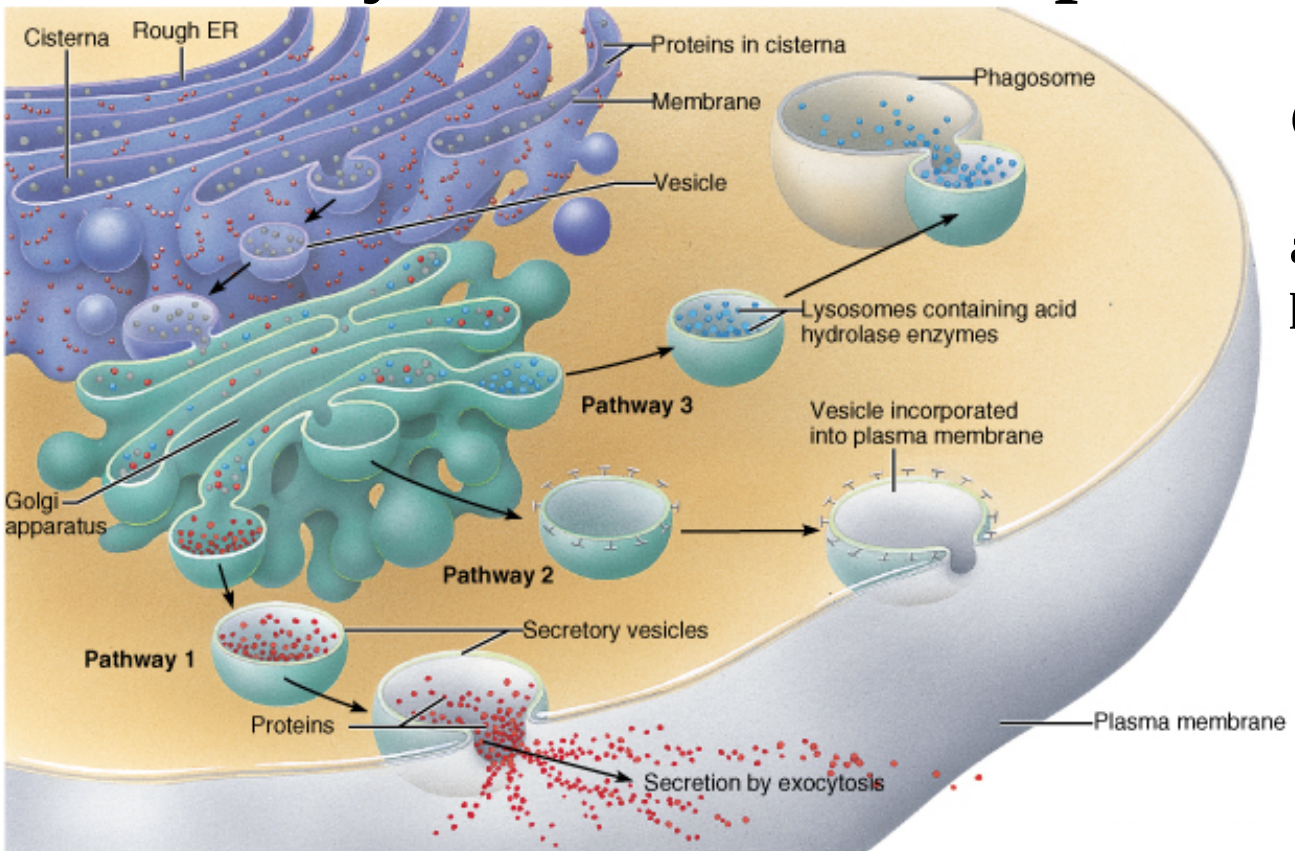
Lumen: ***Cistern(a)***
(environment of cisterna is, in many aspects, similar to outside cell; e.g. ion concentrations)

continuous:
Nuclear envelop – rER – sER

Smooth ER
Lipid Synthesis and Metabolism
(Fat metabolism)
Steroid Hormone Synthesis
Glycogen breakdown (liver)
Sarcoplasmic Reticulum
(Muscle cells; Ca^{2+} storage)



Protein Synthesis and Transport



Golgi Apparatus:

Sorting, modifications and concentration in protein synthesis

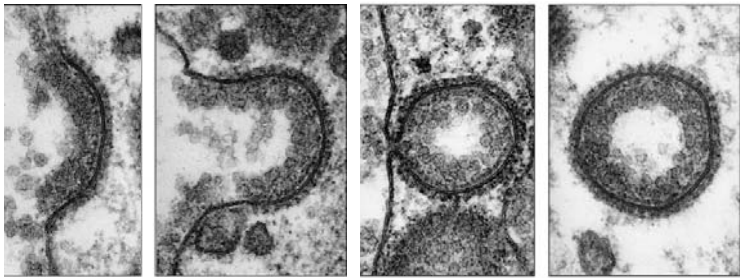
cis Golgi Network → cis Golgi → trans Golgi → TGN (Trans-golgi Network)

Each compartment is not continuous to the next one.

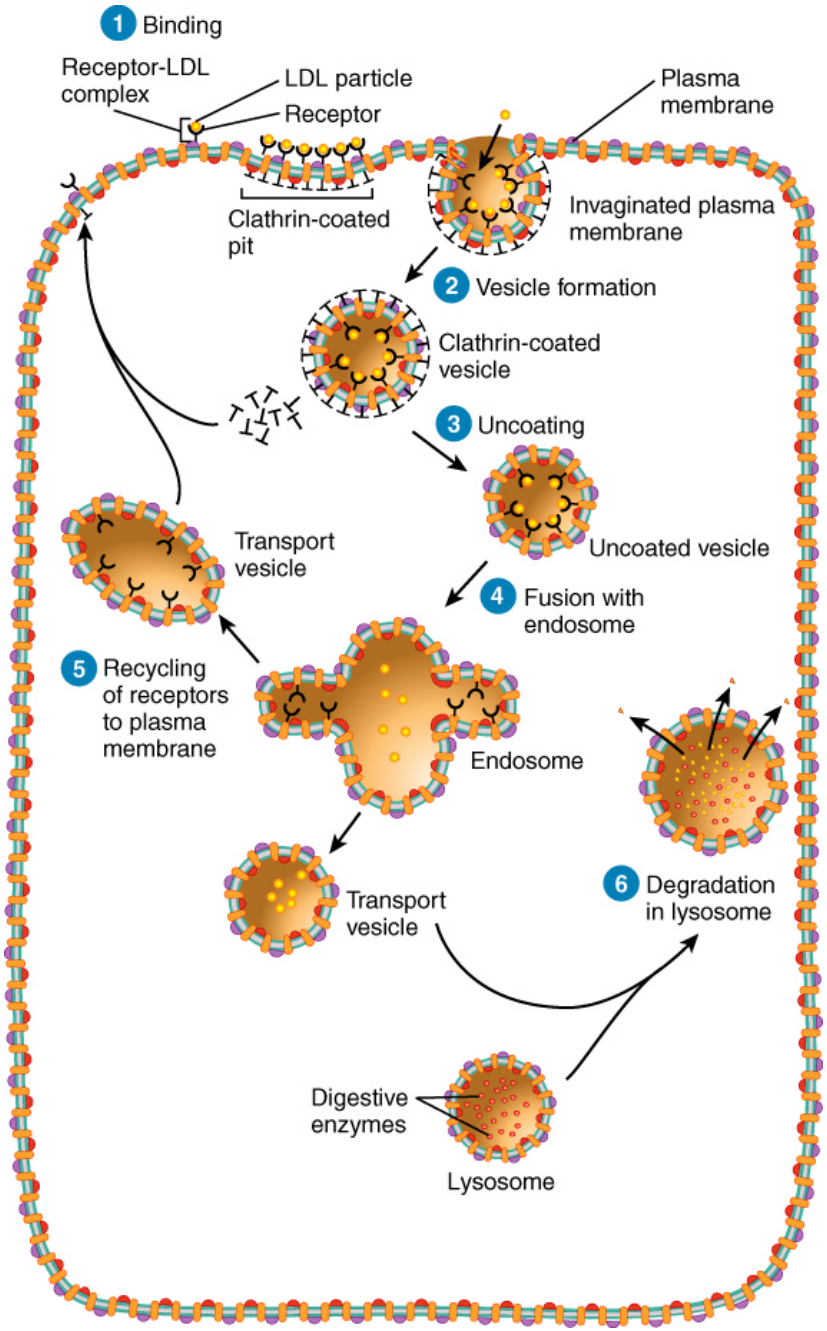
rER → Golgi complex → secretory vesicles
→ vesicle (organelle) membrane proteins
→ vesicle with membrane proteins
→ plasma membrane proteins
→ lysosomes (incl. Enzymes)

Examples of membrane trafficking

Receptor-mediated Endocytosis
Intake of small objects, proteins etc



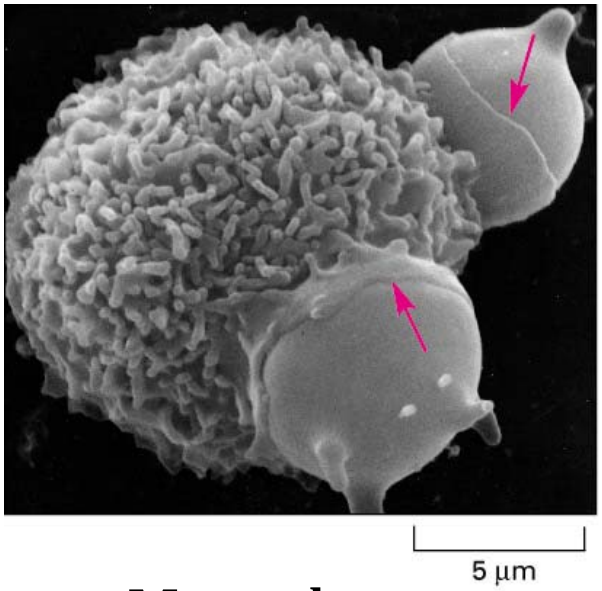
Receptor-mediated Endocytosis



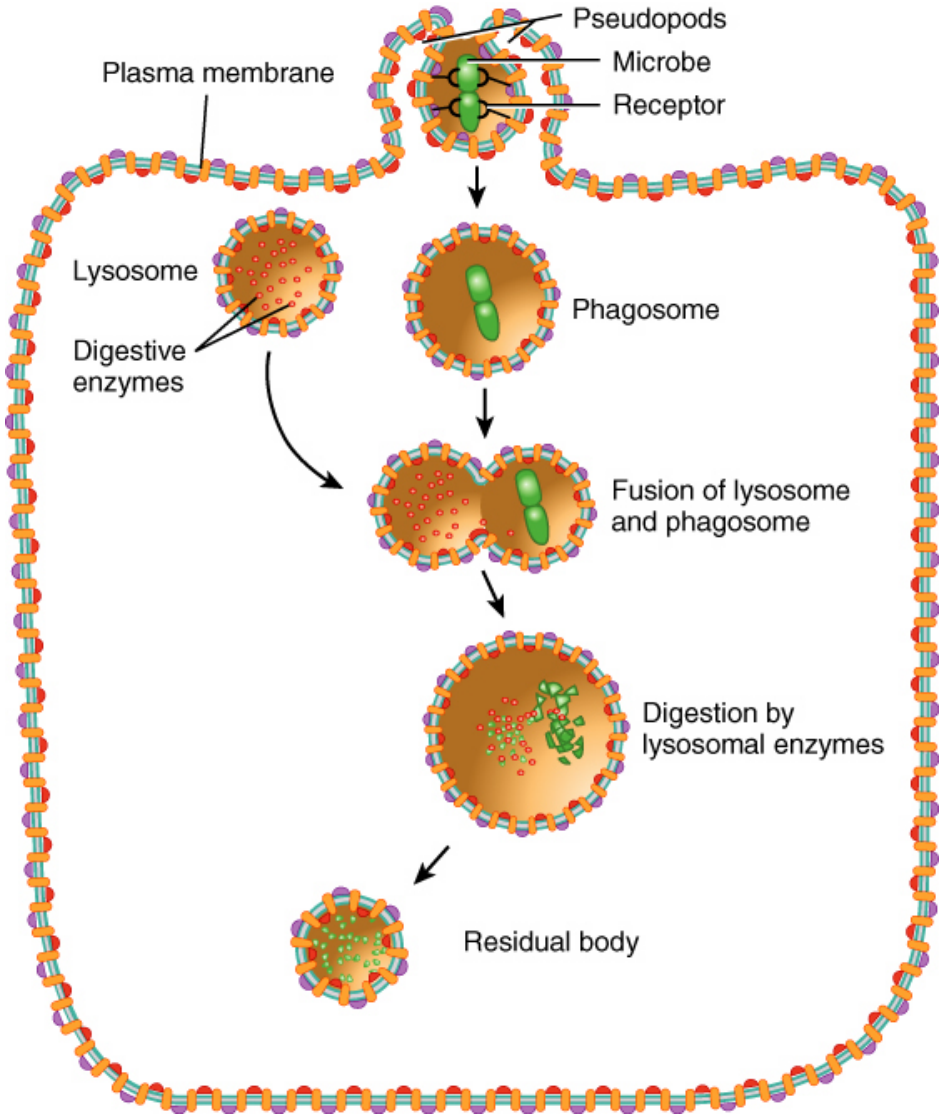
Examples of membrane trafficking and Organelles

Phagocytosis

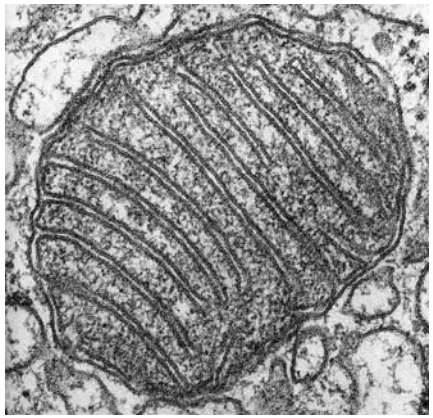
(For larger objects; bacteria, virus, damaged cells etc)

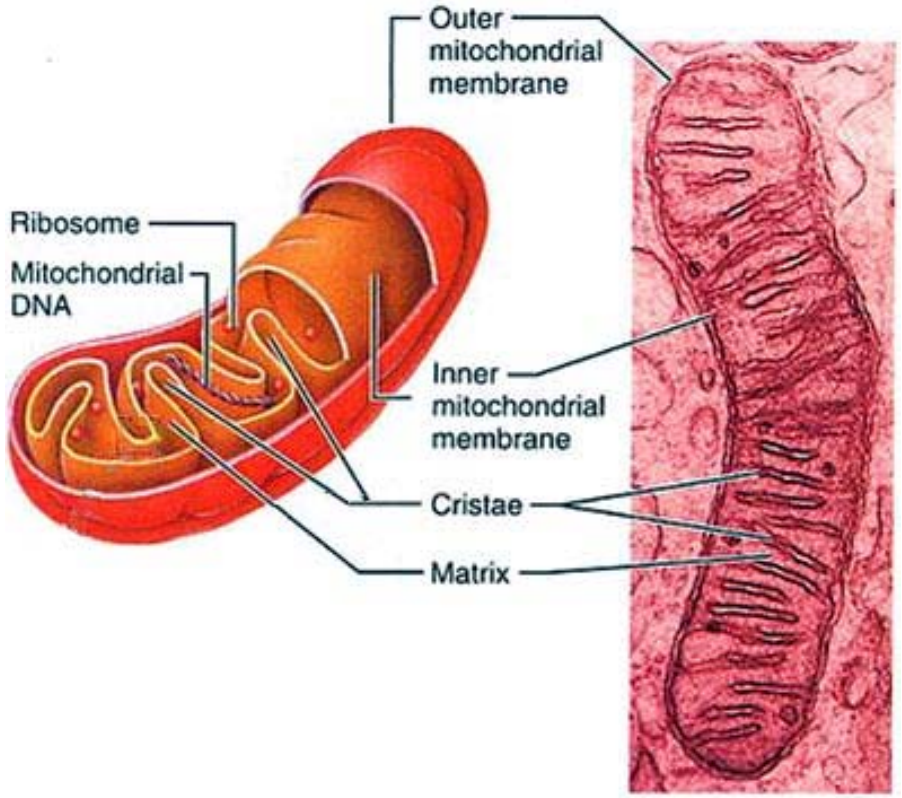


Macropharge engulfing two red blood cells



Mitochondrion



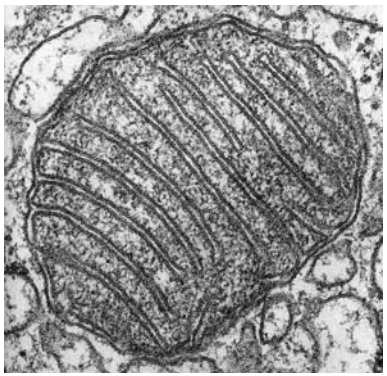


Double membrane system
Cristae (inner membrane-folding)
Matrix (Inside inner membrane
– <u>where ATP is synthesized</u>)

Contains DNA (in the matrix) for some of its own components
This DNA is strictly maternal (from oocyte)

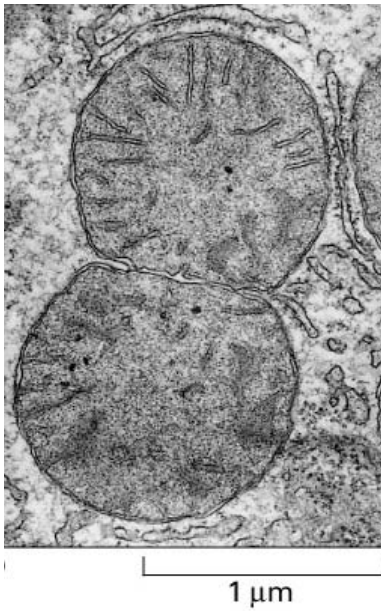
ATP synthesis
Amino acid metabolism

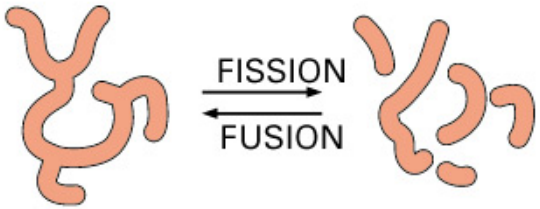
Mitochondrion

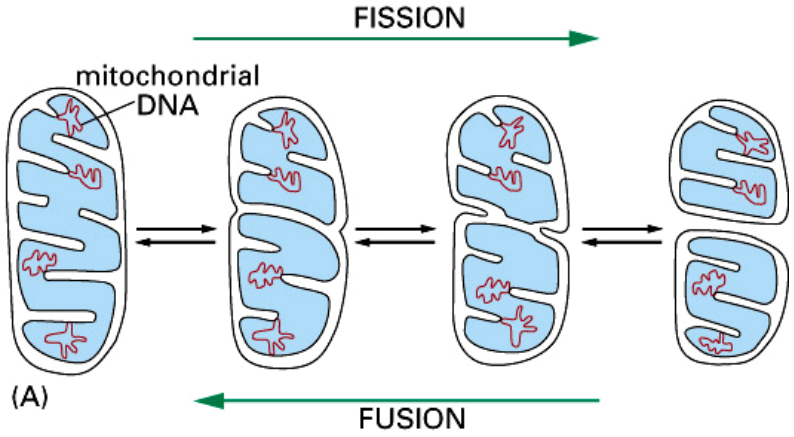


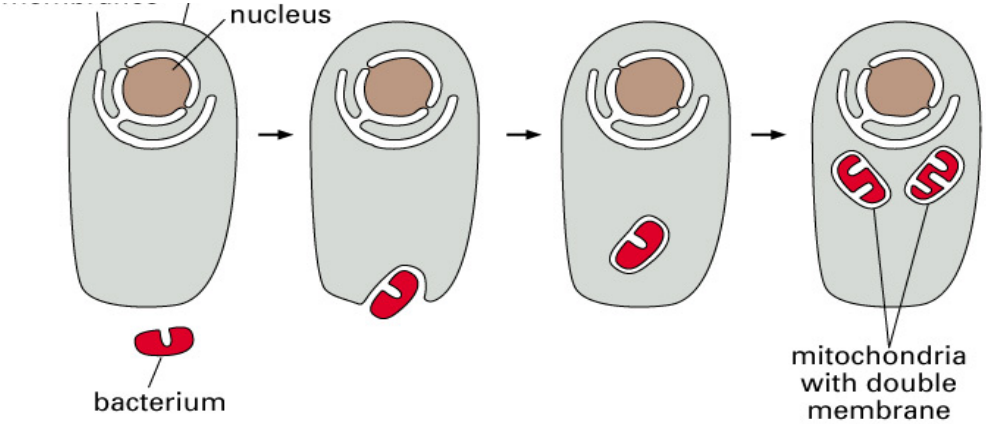
Mitochondria – its dynamic nature

Although mitochondria may seem small vesicles (especially on many textbook illustrations; above), they may be long, twisted (?) sausage-like shape. The shape changes dynamically. They divides, or, fuses together all the time, independently from the cell cycle (cell division).









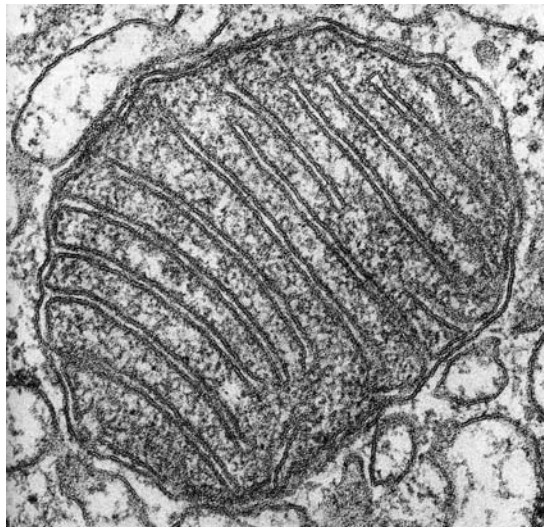
Evolutionally, mitochondrion is thought as a bacterial invader into an ancestral eukaryotic cell

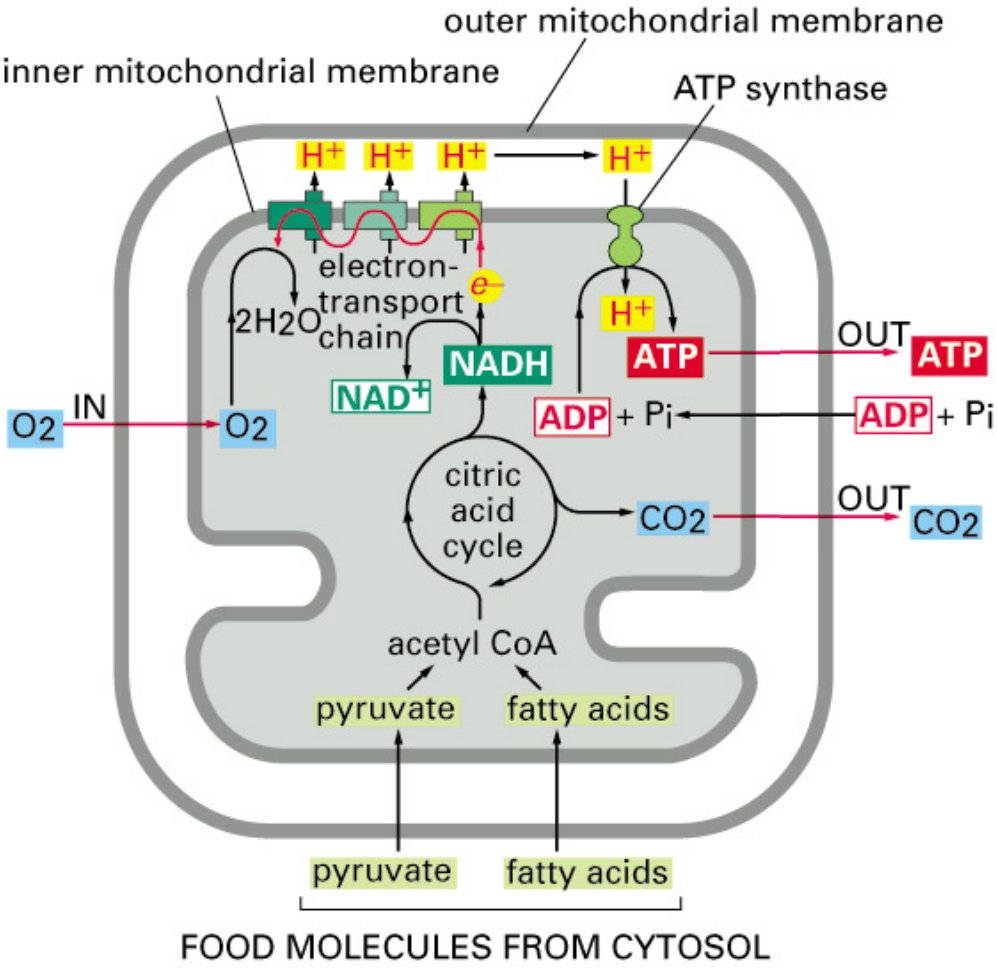
Mitochondrion

ATP production (Oxydative phosphorylation, citric acid cycle)

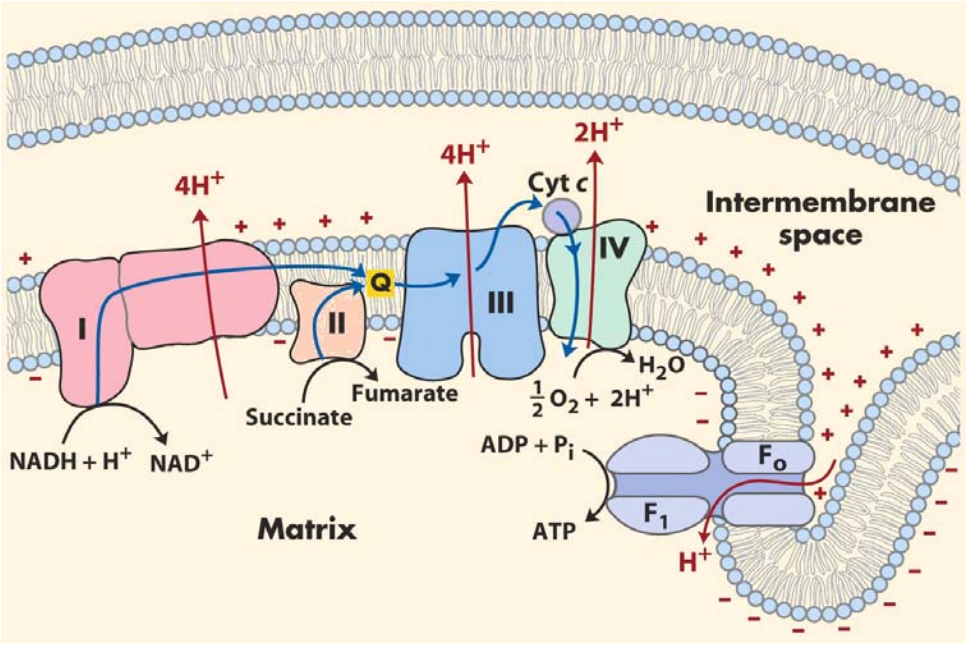
Glucose —[Glycolysis]→ Pyruvate
Fatty acids ⟶ ⟶ ⟶ ↘
Acetyl-CoA ⟶ [Citric Acid Cycle]

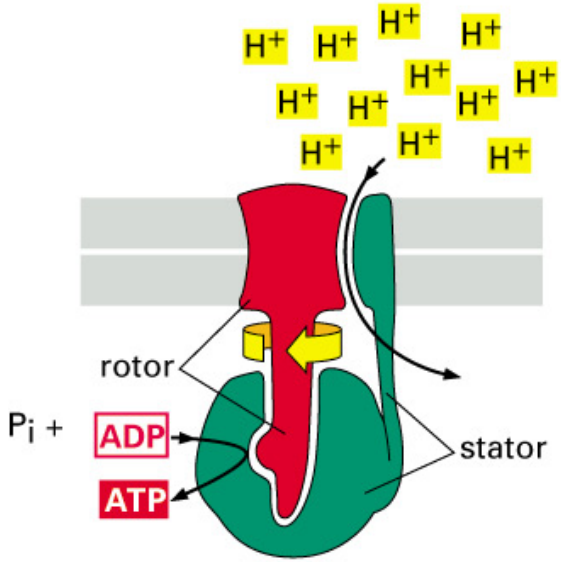
This is where O_2 is used.
Inner membrane
(consists cristae –
Cytochrome Complexes
& ATP synthase)





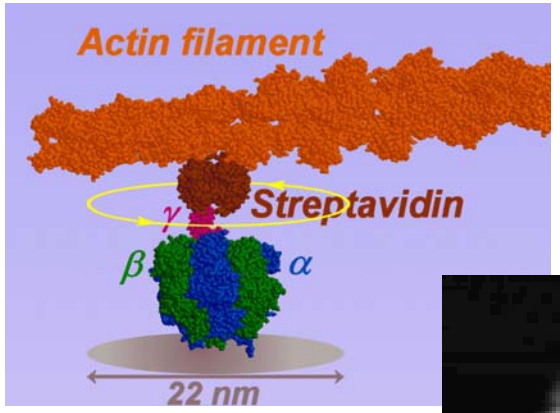
Mitochondrion Rotation of ATP synthase (a.k.a. F_oF_1 ATPase)

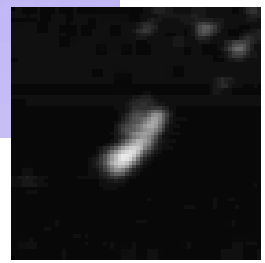




1 turn of the rotor required 3 H^+ movements across membrane (= 1 ATP synthesis) .

Alternatively, rotation of the rotor can be produced by uncoupling F_o and F_1 subunits, and adding ATP. (In this case, ATP hydrolysis takes place.)

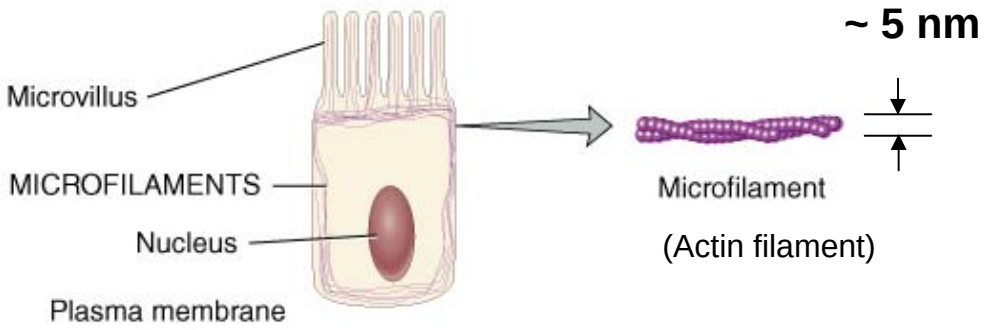




Cytoskeleton and Molecular Motors

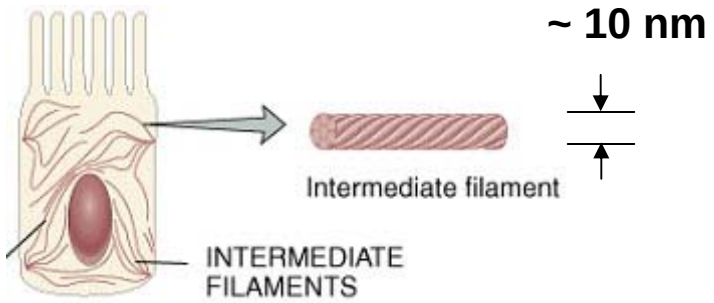
Protein fibers

Assembled from monomer subunits. (SELF ASEEMBLY)

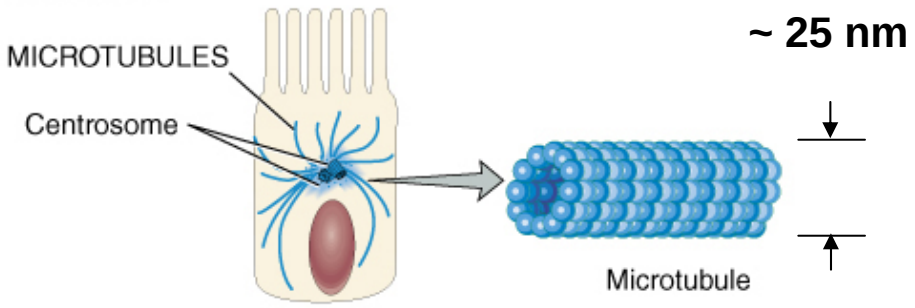


Holds cell's structural integrity

"Track" for biomolecular motors (Actin filaments, Microtubules)



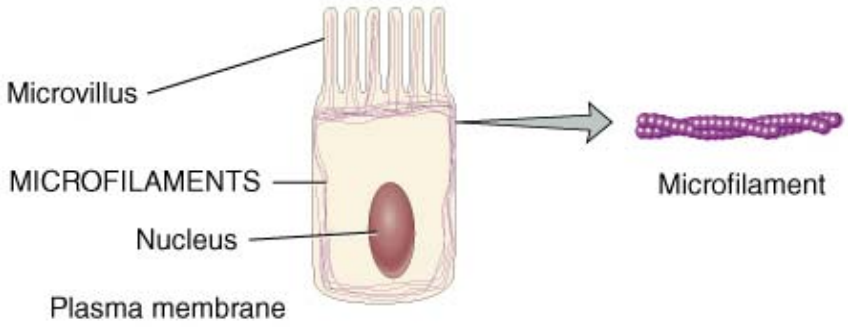
Dynamic changes during Various cellular activities (Actin filaments, Microtubules)



Cytoskeleton and Molecular Motors

Microfilaments (a.k.a Actin filaments, F-actions, Thin filaments) (Muscles)

Actin filaments — Associated Motor(s) → **Myosins**

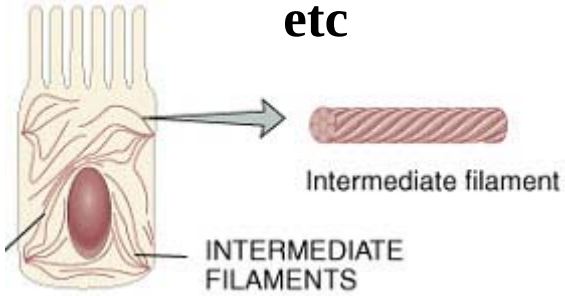


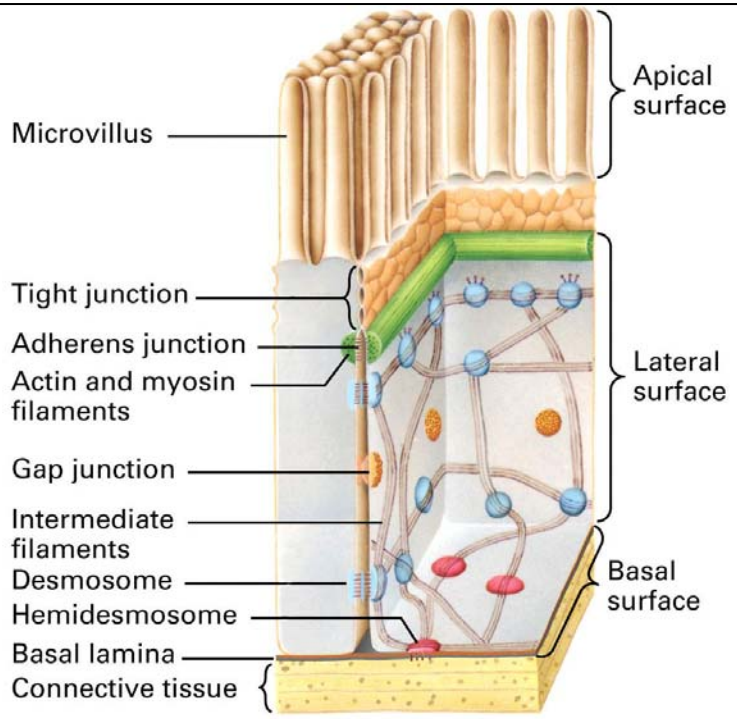
Actin filaments and Intermediate filaments are associated with plasma membrane via anchoring proteins, and they are associated with junctions and adhesion molecules.

Intermediate filaments

Cell type-dependent

Keratin
Neurofilaments
etc



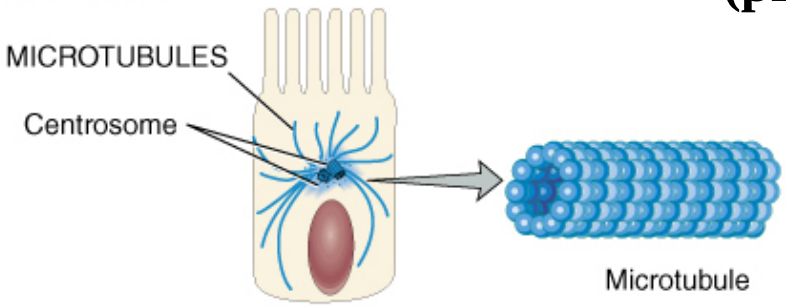


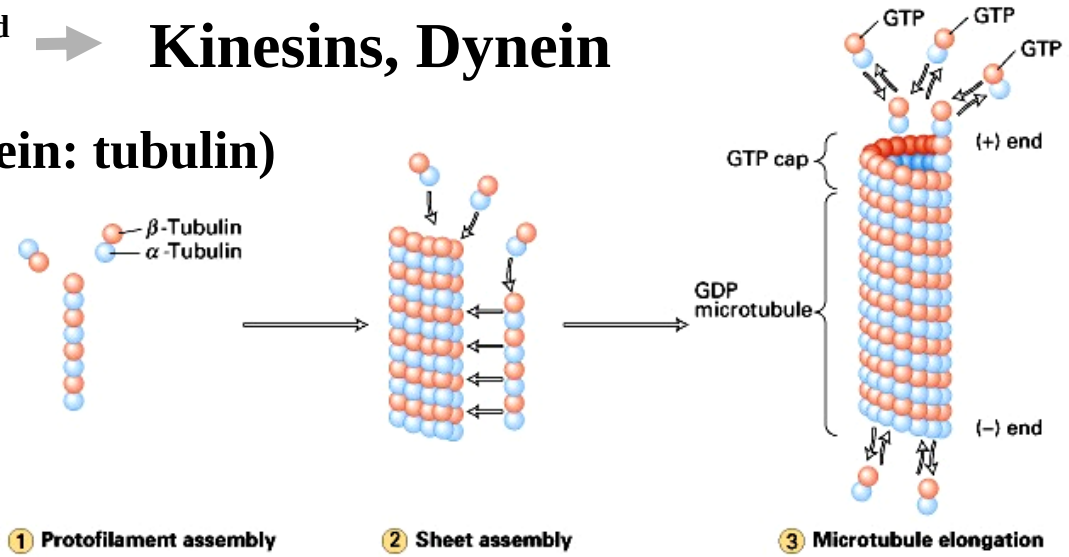
Prototypical epithelial cell

Cytoskeleton and Molecular Motors

Microtubules (MTs) — **Associated Motor(s)** → **Kinesins, Dynein**

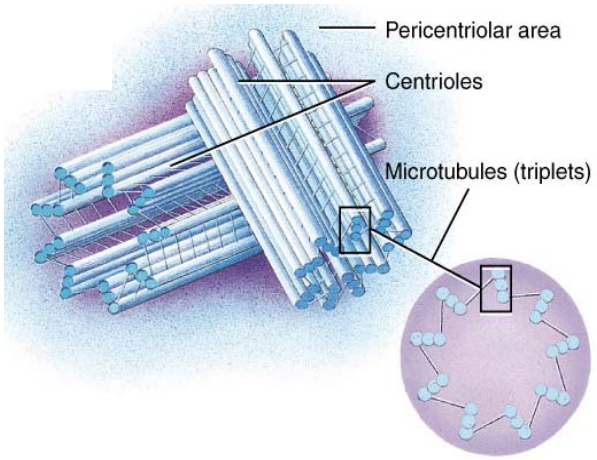
(protein: tubulin)



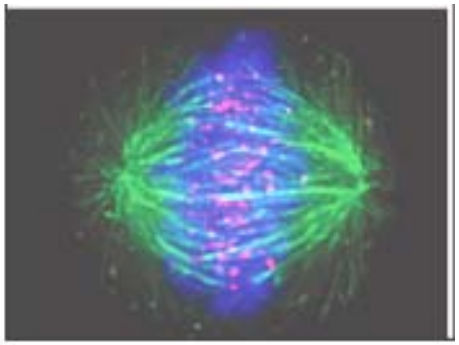


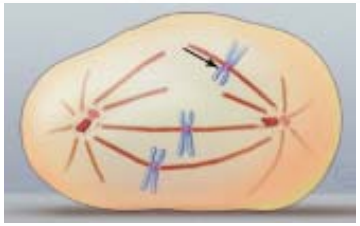
Microtubule-based Organelles

Centrosome

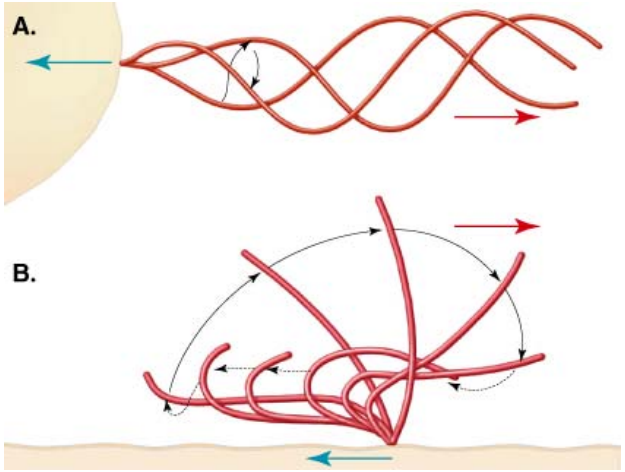


Mitotic Spindle

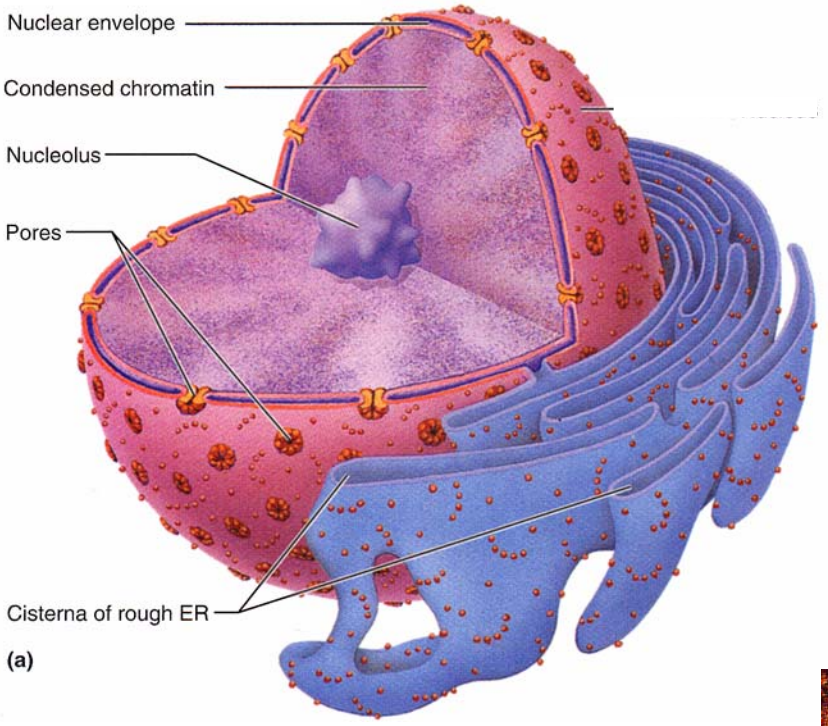




Cilium and Flagellum



Nucleus



Nuclear Envelopes

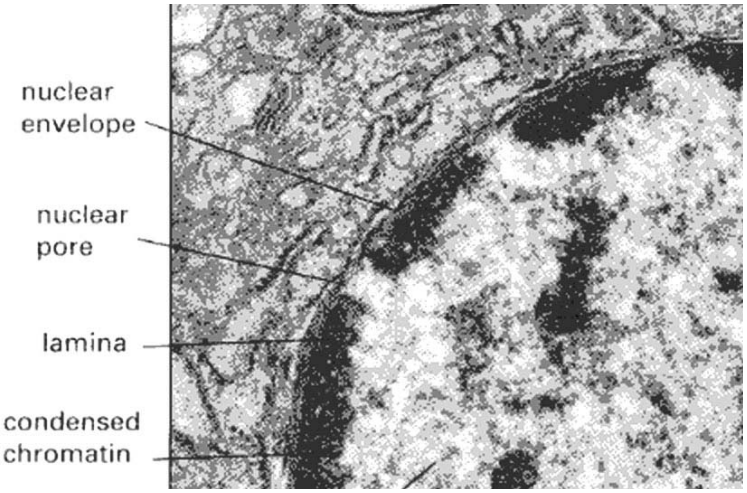
Double-membrane (just like collapsed bags)
Contentious to ER

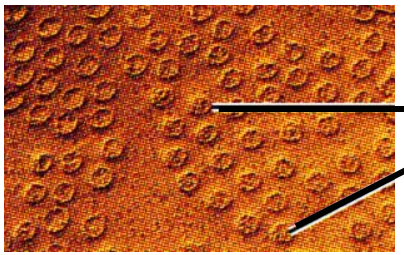
Nuclear pores

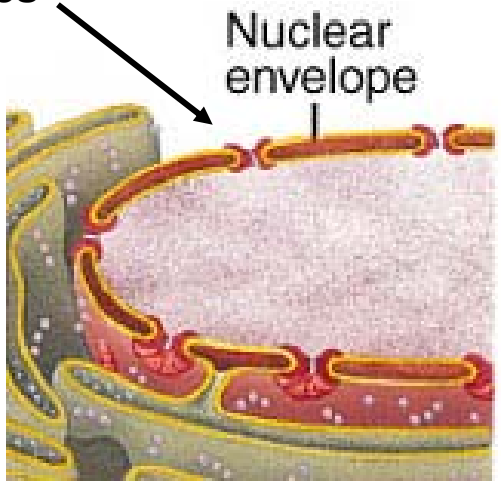
Gates to get into/exit from
nucleus to cytoplasm

Nucleolus

the site of ribosome subunit assembly

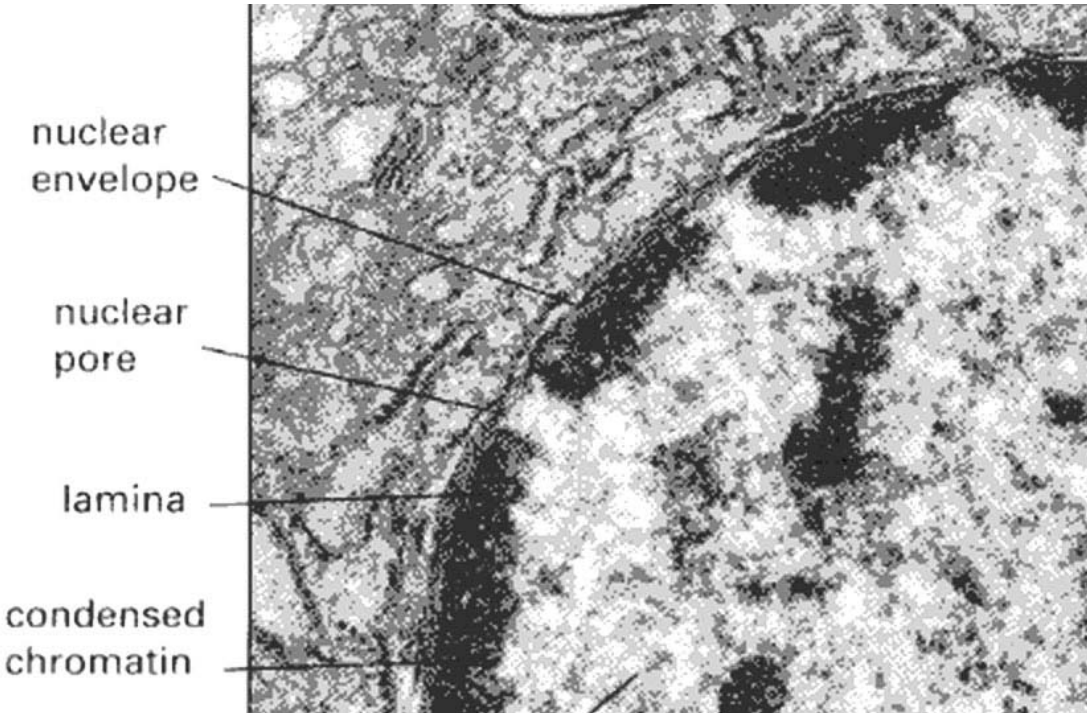




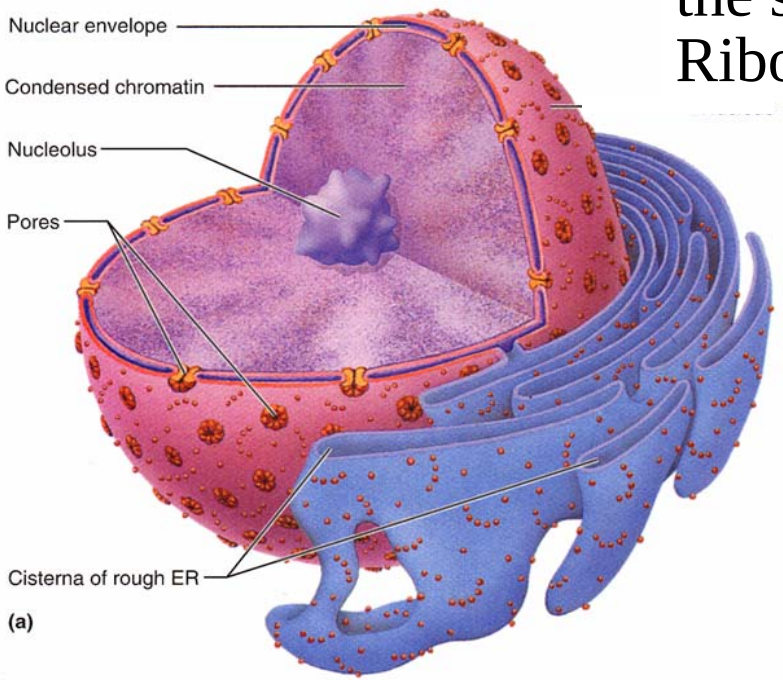


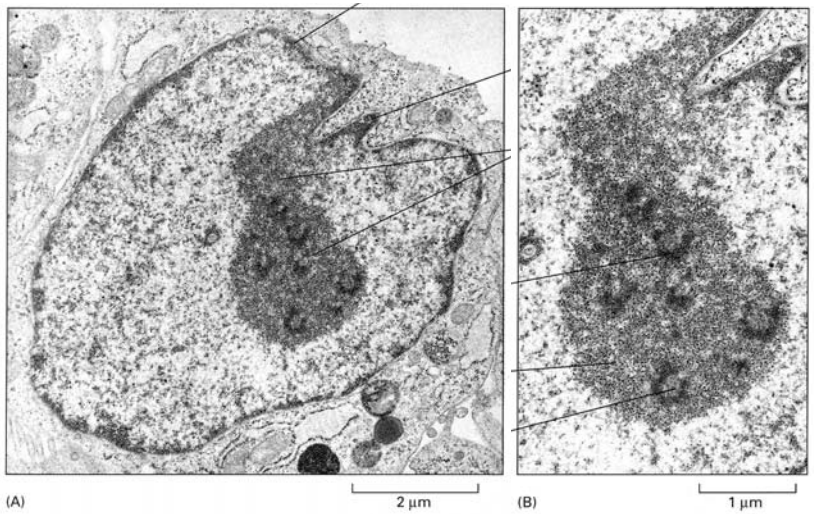
Nucleus

Chromosomes (Genes)
Gene Expression
Transcription (DNA ➔ Messenger RNA (mRNA)
active chromosomes – extended chromatin
inactive chromosomes – condensed chromatin



Nucleus





Nucleolus

the site of ribosome subunit assembly
Ribosomes = Protein synthesis machinery

Eukaryotic RIBOSOME components

4 ribosomal RNAs
> 80 proteins