2018

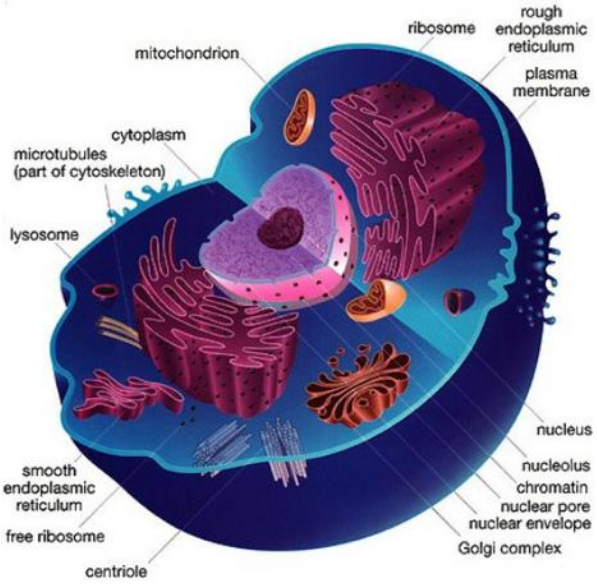
PHSI3009

FULL SUMMARY NOTES

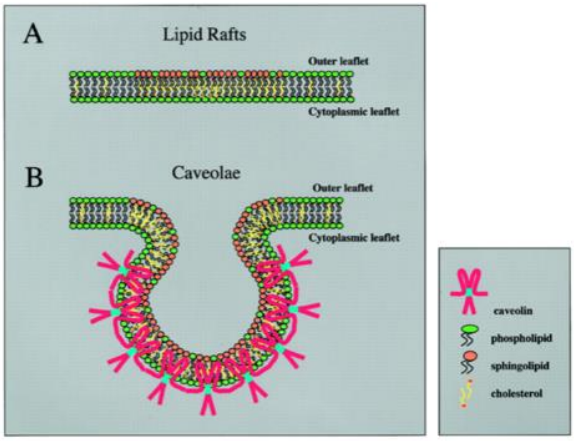
Cell Signalling

Cell Membranes:

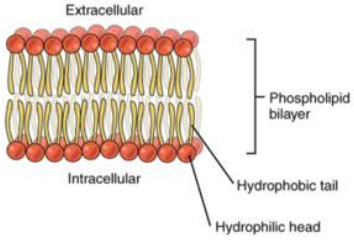
- Separate the interior and exterior environments and form functional, closed compartments, called **Organelles.**
    - Biological reactions occur within them and they provide the surface area to facilitate them.



- 2D fluid, lipid and protein layer than can move freely and has many functions.
- **Lipid Rafts** are cholesterol and **Sphingolipid** rich, rigid regions.
- **Caveolae** are small cave-like pits (60-80nm diameter) involved in **Endocytosis** and signal transduction and have a signature protein, called **Caveolin.**

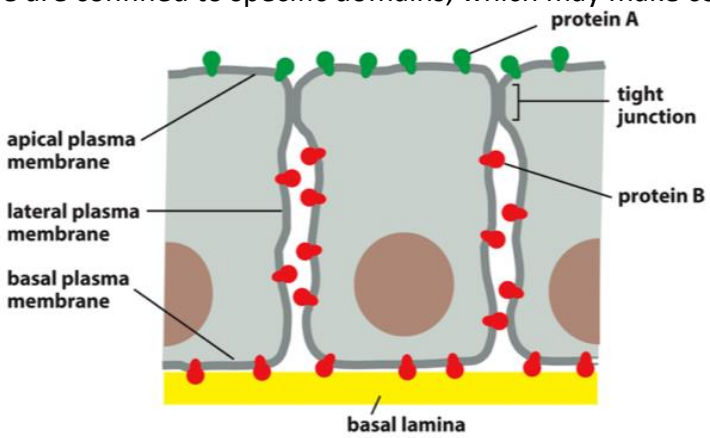


- The **Plasma Membrane** is a **Phospholipid Bilayer** composed of cholesterol and **Glycolipids**.

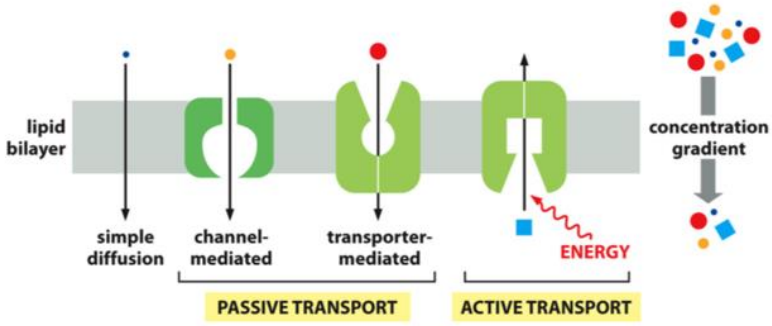


Membrane Transport & Proteins

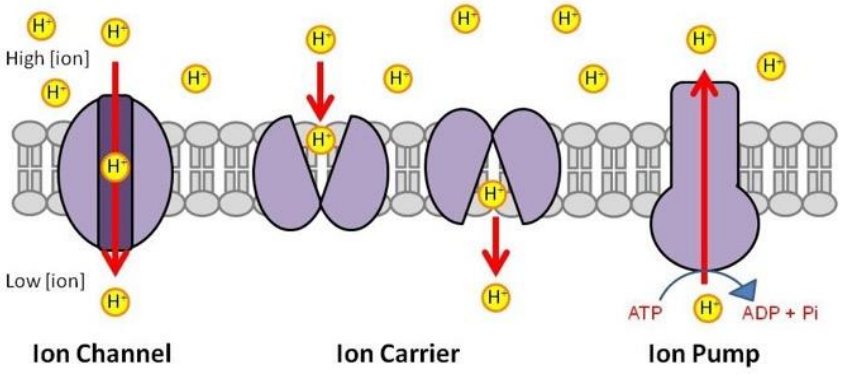
- **Integral Proteins** are always in the plasma membrane, some of which span its width and are called **Transmembrane Proteins.**
    - Some are confined to specific domains, which may make cells asymmetrical



- Small, non-charged and non-polar molecules can pass via diffusion.
- Most molecules move via **Active** or **Passive Transport**.



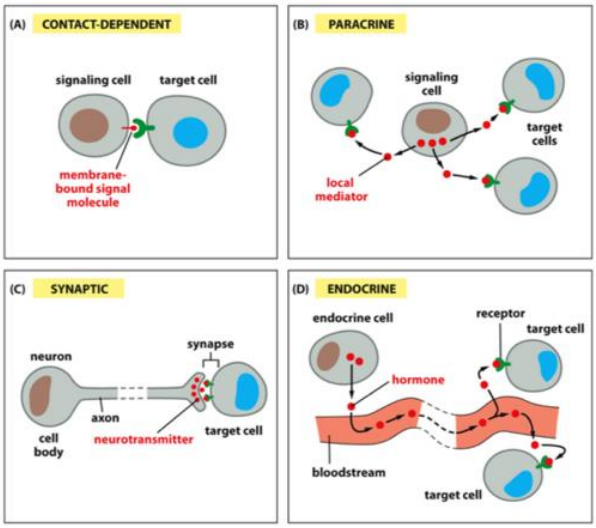
- Large molecules rely on endocytosis and **Exocytosis**.
- **Transporters**' binding to the solute induces a reversible conformational change, which exposes the solute to the other side of the membrane.
    - Transporters like the **Na^+-Glucose Co-Transporter (SGLT)** rely on **Secondary Active Transport**, which depends on solute's concentration gradient.
- Ion channels are either always open or require a stimulus to open them.
    - A **Selectivity Filter**, which is the narrow end towards the extracellular environment, ensures only a specific amount of the solute crosses.



- Movement across the membrane is also affected by the intracellular and extracellular environments.

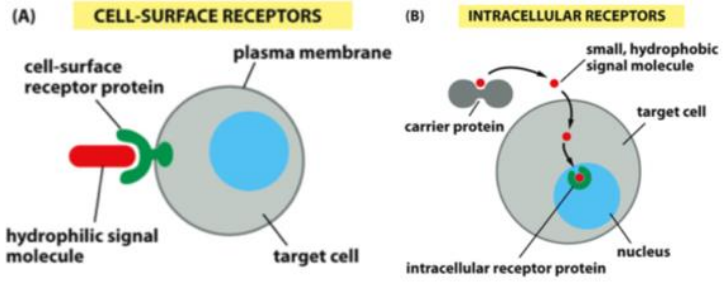
Cellular Communication & Interaction:

- Homeostasis requires the right number of cells performing the right task at the right time and place and are able to accommodate changes.
- Cells release wastes, obtain nutrients and growth factors, secrete extracellular matrix and may be subject to pathogens.
- Cells monitor the intracellular and extracellular environments and respond appropriately to any changes by changing protein activity and gene expression.
- **Contact Dependent Communication** relies on direct contact between a signalling cell's **Signal Molecule** and a target cell's receptor.
- **Paracrine Communication** results from the secretion of signalling molecules from one cell that act on receptors of neighbouring cells.
- **Synaptic Communication** relies on the release of neurotransmitters from the synaptic terminals of a neuron that act on receptors on the target cells.
- **Endocrine Communication** relies on the release of hormones from endocrine cells that travel through the blood to act on the receptor of target cells.
- Cells respond to a combination of signals and lack of them can lead to **Apoptosis.**



Receptors:

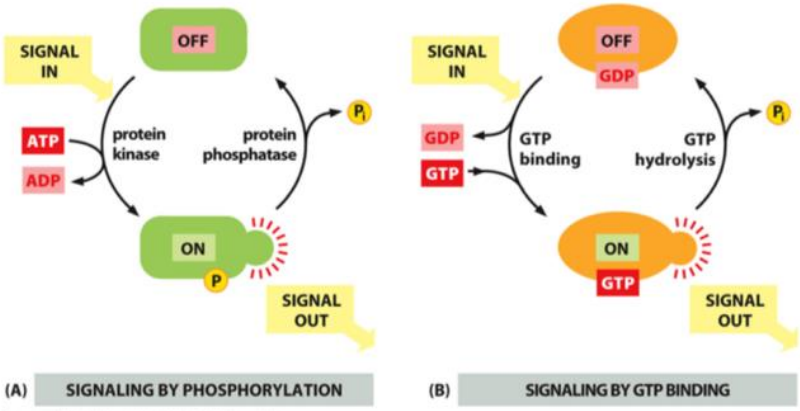
- **Cells Surface Receptors** are bound to the plasma membrane and have an exposed extracellular domain.
    - Hydrophilic signalling molecules act on these receptors.
    - They act through 2nd messengers to induce a response.
- **Intracellular Receptors** are within the cytosol or nucleus of the cell.
    - Hydrophobic signalling molecules, which are transported on **Carrier Proteins** pass through the plasma membrane and act on them.
    - They translocate to the nucleus and result in changes in gene expression.



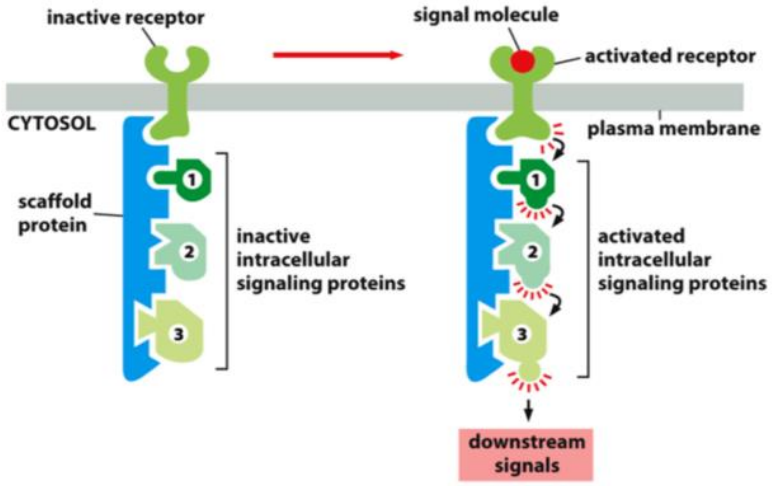
- **Ligand-Gated Ion Channels (Inotropic)** are ion-channel-coupled receptors open/close channels when they bind to their ligand.
- **G Protein-Coupled Receptors (GPCR)** are associated with a trimeric **GTP-Binding Protein**, composed of 7 transmembrane receptors.
- **Enzyme-Linked Receptors (Catalytic)** dimerise when a ligand is bound to their **Catalytic Domain** and either activate their own domain or an associated enzyme's.

Intracellular Signalling:

- Activation of a receptor leads to an activation cascade resulting in the activation of the effector proteins.
    - Effector proteins alter metabolism, gene expression and cell shape or movement.
- Signalling molecules have different effects on different cell types.
- Signalling by phosphorylation relies on **Kinase Proteins** to phosphorylate and activate proteins, while **Phosphatases** dephosphorylate and deactivate them.
- Signalling by GTP relies on GTP binding to activate the protein and GTP hydrolysis to deactivate them.



- Signal specificity can be enhanced when using a signalling complex.
    - **Scaffold Protein** are used to pre-form the signalling complex.



    - Signalling complex can also be assembled by recruiting the signalling proteins to be activated via phosphorylation by the activated receptor.