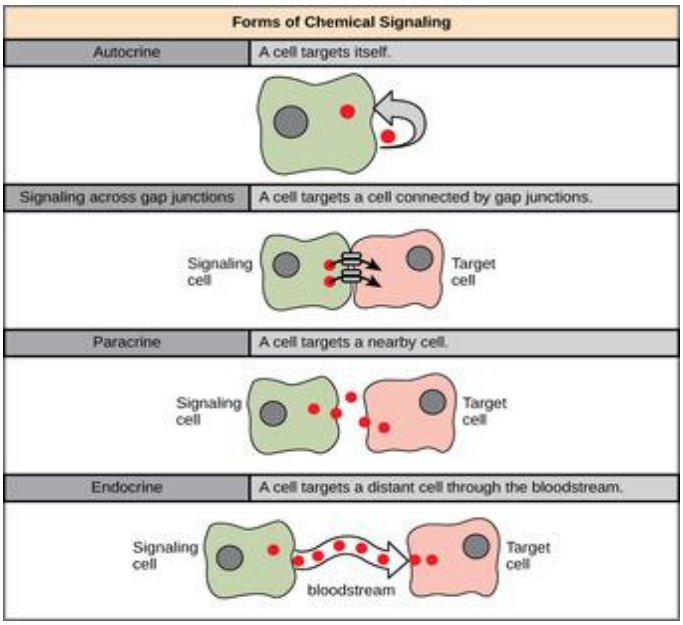
Lecture (6) Cellular communication

Signaling Molecules and Cellular Receptors

Cells have developed complex mechanisms of communication that can receive a message, transfer the information across the plasma membrane, and then produce changes within the cell in response to the message.

Forms of Signaling



1. Autocrine signaling

Signaling molecules produced by cells to act on these releasing cells or on other similar cells (prefix auto- means self)

2. Endocrine signaling

Signaling molecules produced by cells to act on distant cells. Endocrine signaling slower than neuronal signaling but its effect is long-lasting. The endocrine signaling molecules called hormones.

3. Paracrine signaling

Signaling molecules produced and released by cells to locally act on nearby cells by diffusion through the extracellular matrix. (para = near). Paracrine signaling produce quick responses but quickly degraded by enzymes or removed by neighboring cells which makes it short-lasting.

4. Direct Signaling Across Gap Junctions

Signaling molecules transfer between the plasma membranes of neighboring adjacent cells through water-filled channels connections called Gap junctions. Gap junctions allow passage of small messengers but not large molecules likes proteins and genetic materials and this maintaining the specificity of cells. Gap junctions allow quick signaling and coordination of group of cells to single stimulus.

Types of Receptors

Receptors are protein molecules inside the target cell or on its surface that bind ligands. There are two types of receptors: **internal receptors** and **cell-surface receptors**.

1. Internal receptors (Intracellular or Cytoplasmic receptors)

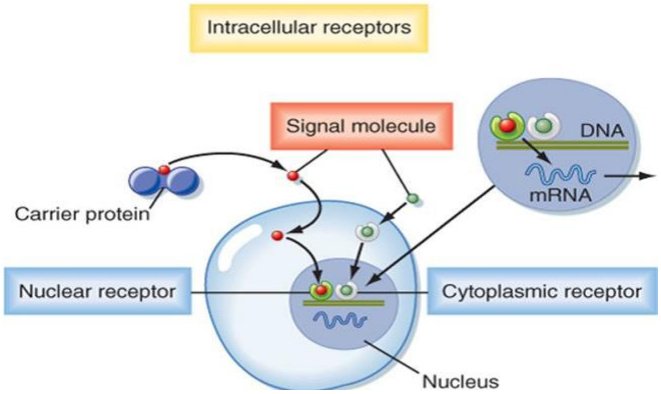
Protein structures founded **in the cytoplasm** of the cell and **respond to hydrophobic ligand molecules (hormones)** which has ability to passively cross the plasma membrane. The **ligand-receptor complex** moves into the nucleus, not need signaling molecules for signal

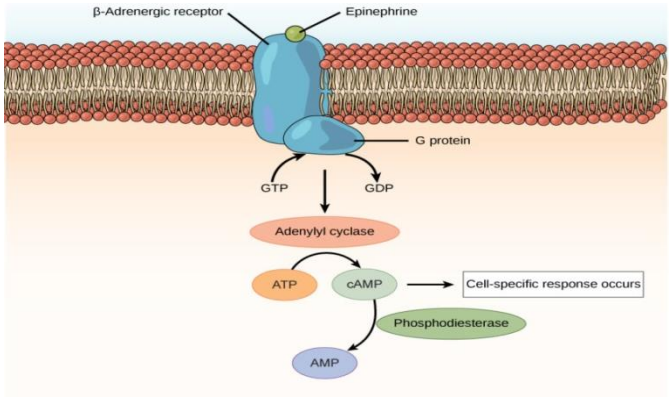
transduction, directly influence gene expression and promotes the initiation of gene transcription.

2. Cell-Surface Receptors (Trans-membrane receptors)

This type of **receptor integrates the plasma membrane** and **performs signal transduction**, **converting an extracellular signal into an intracellular signal**. Ligands that interact with cell-surface receptors do not have to enter the cell that they affect.

Each cell-surface receptor has three main components: an external ligand-binding domain (extracellular domain), a hydrophobic membrane-spanning region, and an intracellular domain inside the cell.





There are three general categories of cell-surface receptors: ion channel-linked receptors, G-protein-linked receptors, and enzyme-linked receptors.

2.1. Ion Channel-Linked Receptors are integral proteins formed pathways through the membrane which could be

Open channels: They are a leaky channel always remains open for substances and ions, smaller in diameter and less in number than other channels

Gated channels: They are closed during rest by protein acts as a gate and specifically allowing passage of only one type of molecules or ions. There are three types:

1. ***Ligand-Gated Channels***

Receptor opens because a signaling molecule, a ligand, binds to the extracellular region of the channel.

2. ***Mechanically-Gated Channels***

Receptor opens because of pressure/physical effect on the cell membrane. Many channels associated with the sense of touch.

3. ***Voltage-Gated Channels***

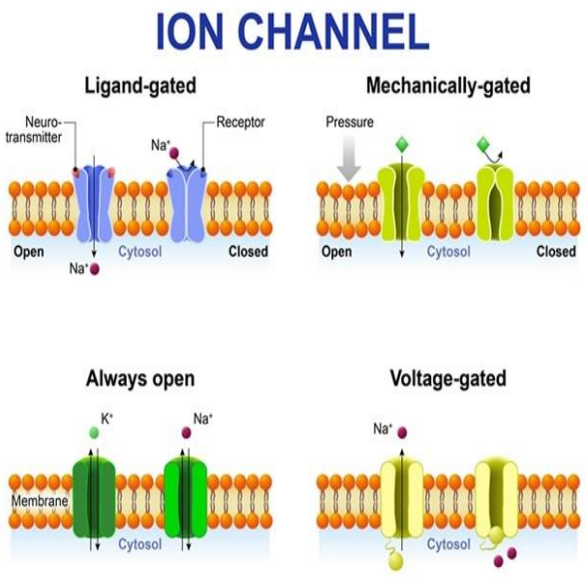
Receptor that responds to changes in the electrical properties of the membrane

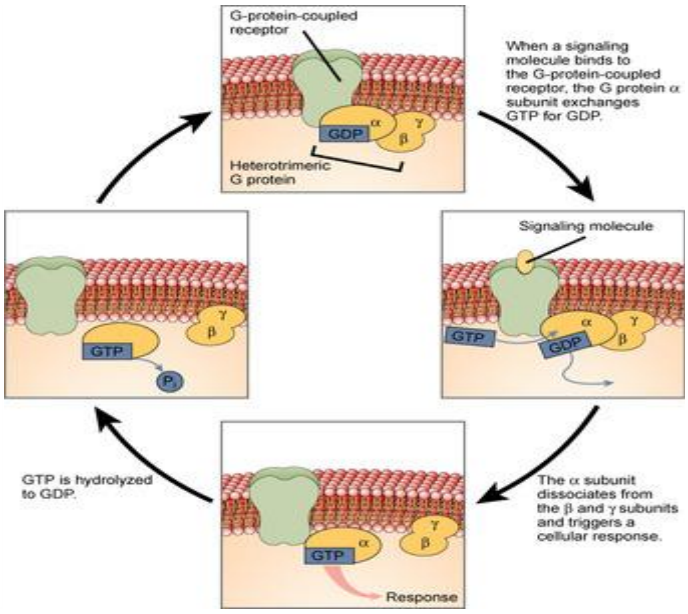
2.2.G-Protein Linked Receptors

Bind a ligand to this type of receptors activates intracellular membrane protein called a G-protein which dissociate from the receptor and starts intracellular signaling. G-protein-coupled receptors (GPCRs) mediate most of our physiological.

2.3.Enzyme-Linked Receptors

Cell-surface receptors with intracellular domains have enzymatic activity or bind to an enzyme. Ligand binding to these receptors activates the intracellular face enzymatic activity beginning a series of intracellular cascade.





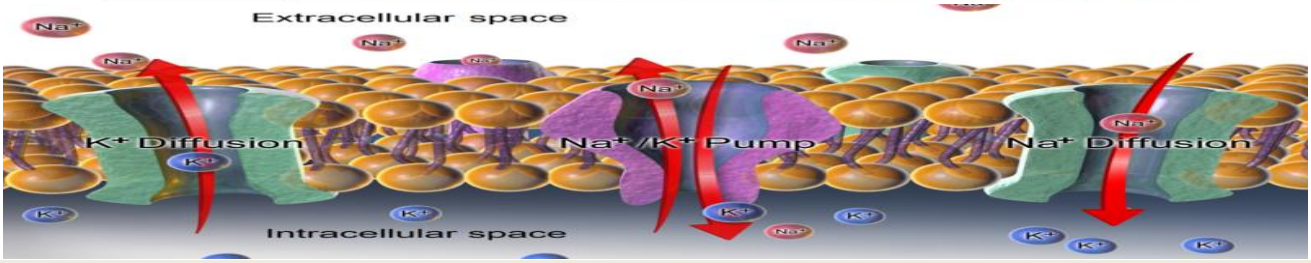
Electrically Active Cell Membranes

※Most cells in the body make use of charged particles, ions, to build up a charge across the cell membrane. The **cell membrane is a phospholipid bilayer**, so **only hydrophobic** substances **can pass directly** through while **charged particles**, which are **hydrophilic** by definition, **cannot pass without assistance**. **Transmembrane proteins, specifically channel proteins, make this possible**.

Hydrophobic (Lipophilic) means lacking an affinity for water; insoluble in water; repelling water. **Hydrophilic** means "of, relating to, or having a strong affinity for water.

※The concentration of **Na^+ outside the cell >inside** and the concentration of **K^+ is inside the cell >outside**. The carrier protein sodium/potassium pump (**Na^+/K^+ ATPase**) moves **(Na^+) ions out of a cell** and **(K^+) ions into a cell**, **against the concentration gradients for sodium and potassium**. This is why **Na^+/K^+ ATPase pump requires energy**. **Ion channels** are pores with **charge-specific** and **ion-selectivity**.

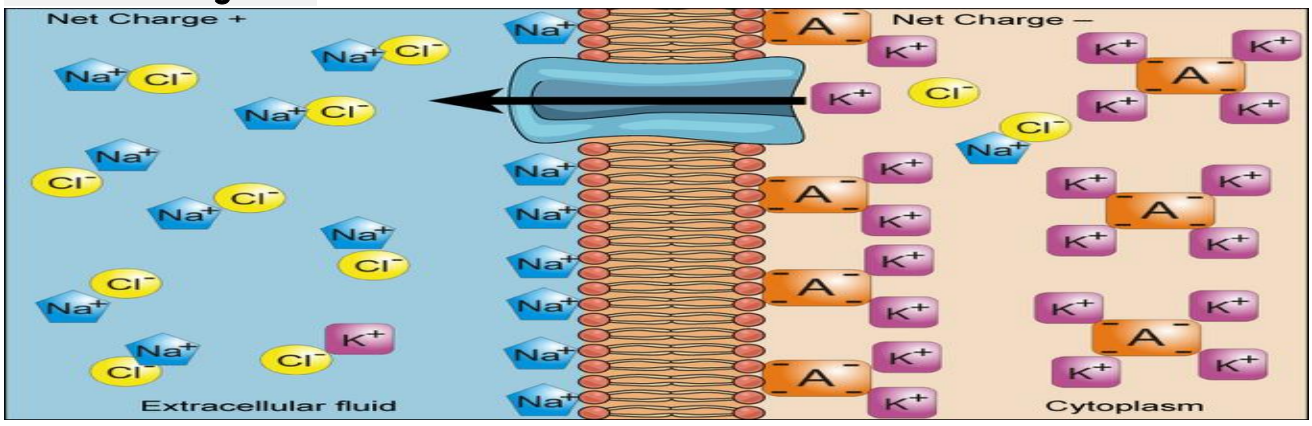
Reminder: **Active transport** forces molecules against the concentration gradient with help of ATP energy whereas **passive transport** let the molecules to pass across the membrane through a concentration channel, requiring no cellular energy.



Electro-chemical Gradient

Simple concentration gradients are differential concentrations of a substance across a membrane. Ions move into and out of cells and because cells contain proteins that do not move across the membrane and are mostly negatively charged, there is an **electrical gradient, a difference of charge,** across the plasma membrane. **The interior of living cells is electrically negative with respect to the extracellular fluid.** At the same time, cells have higher concentrations of potassium (K^+) and lower concentrations of sodium (Na^+) than does the extracellular fluid.

In a living cell, the **concentration gradient of Na^+ tends to drive it into the cell**, and the **electrical gradient of Na+ (a positive ion) also tends to drive it inward to the negatively-charged interior,** however for other elements such as potassium. The **electrical gradient of K+**, a positive ion, also **tends to drive it into the cell**, but the **concentration gradient of K+ tends to drive K+ out of the cell**. The **combined gradient of concentration and electrical charge that affects an ion is called its electrochemical gradient**.



EXCITABLE TISSUES

All cells within the body have a characteristic resting membrane potential. Some tissue have special types of voltage-gated ion channels embedded in their cell's plasma membrane allows their resting membrane potential to rapidly rises (depolarization) and falls (repolarization). This change in the membrane potential called action

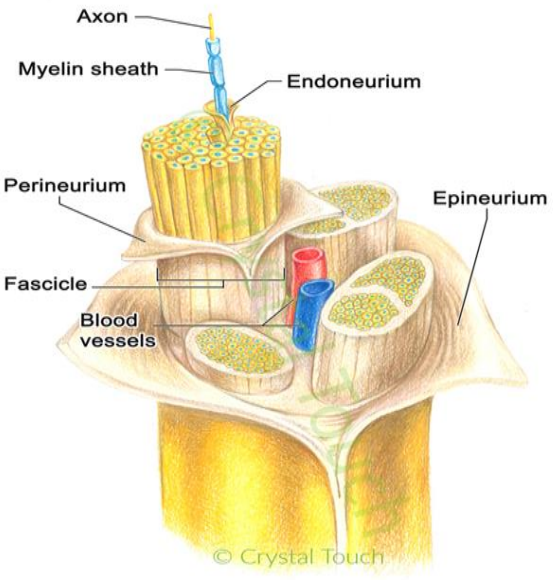
potential and this tissue called excitable tissue where this depolarization then causes and spread to adjacent tissue to similarly depolarize.

※ **Excitable tissues are:**

✓ Nerve ✓ Muscle ► Skeletal ► Cardiac ► Smooth

Nerve

The nerve is a bundle of neurons along with their connective tissue sheaths, blood vessels, and lymphatics whereas a neuron is a cell of the nervous system that conducts.



A nerve receives information in the form of electrochemical impulses (known as nerve impulses or action potentials) carried by the individual neurons that make up the nerve.

Reflex arc is the functional unit of nervous syste

Neuron is the structural unit of nervous system.

Nerves can be categorized into two groups based on function:

1. **Sensory neurons (afferent)** conduct sensory information from their receptors to the central nervous system, where the information is then processed.
2. **Motor neurons (efferent),** conduct signals from the central nervous system to muscles.

Motor neurons are either somatic or autonomic motor neurons. The somatic neurons **innervate skeletal muscle**, whereas the autonomic neurons innervate glands, neurons of the gastrointestinal tract, and cardiac and smooth muscles.

Formative Questions

✓ Which of the following statements is true?

A. Paracrine signaling refers to nearby cell communication
B. Autocrine signaling refers to distant cell communication
C. Gap junction signaling refers to the self-cell communication
D. Endocrine signaling refers to between cell plasma membrane communication

- ✓ All the following is true about internal receptors except:
  - A. They founded in cell cytoplasm
  - B. Influence gene expression
  - C. Respond to hydrophilic signaling molecules
  - D. Not need second messenger for signal transduction
- ✓ Excitable tissue has the ability to propagate action potential to surrounding tissue by
  - A. Enzyme linked receptors
  - B. Ligand gated ion channels
  - C. Voltage gated ion channels
  - D. G-protein coupled receptors
- ✓ Categorize the different types of receptors.
- ✓ True or False…….
  1. Only excitable tissue has membrane potential (….)
  2. Hydrophobic charged particles can pass directly through membrane phospholipid while hydrophilic cannot pass without assistance (….).
  3. The carrier protein sodium/potassium pump (Na^+ /K^+ ATPase) passively moves (Na^+) ions out of a cell and (K^+) ions into a cell (….).
  4. The interior of living cells is electrically negative with respect to the extracellular fluid (….).
- ✓ Complete the following sentences…
  1. The combined gradient of concentration and electrical charge that affects an ion is called …….
  2. Mechanically-Gated Channels opens in response to …….. on the cell membrane