University of Baghdad
College of Veterinary Medicine
Department of Physiology and Pharmacology

Lecture- 2

Physiology of Nerve Cell

For Class- Two

By

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Physiology of Nerve Cell (or Physiology of Neuron)

In general the nervous system can be divided into:

- The central nervous system (CNS) which include: the brain and the spinal cord.
- The peripheral nervous system.
- (PNS) which include : the somatic and the autonomic nervous system(ANS).

Excitable cells: the ability of some cells to be electrically excited resulting in the generation (initiate) and propagate (transfer) of an action potentials.

e.g. neurons, muscle cells (skeletal, cardiac, and smooth) and some endocrine cells (e.g., pancreatic β cells) are excitable cells.

Neuron (or nerve cell): it is the basic unit of nervous system ,also called **"neuron".**

The neuron is composed of:

1- The soma: is the main part of the neuron (i.e. the body of neuron) contain nucleus ,cytoplasm ,organelles and granules called Nissl granules.

2- Dendrites: are structures of many number of projections branch out in tree like fashion from the soma.

3- Axon: it is a long prominent extending from the soma to distant regions from the cell body.

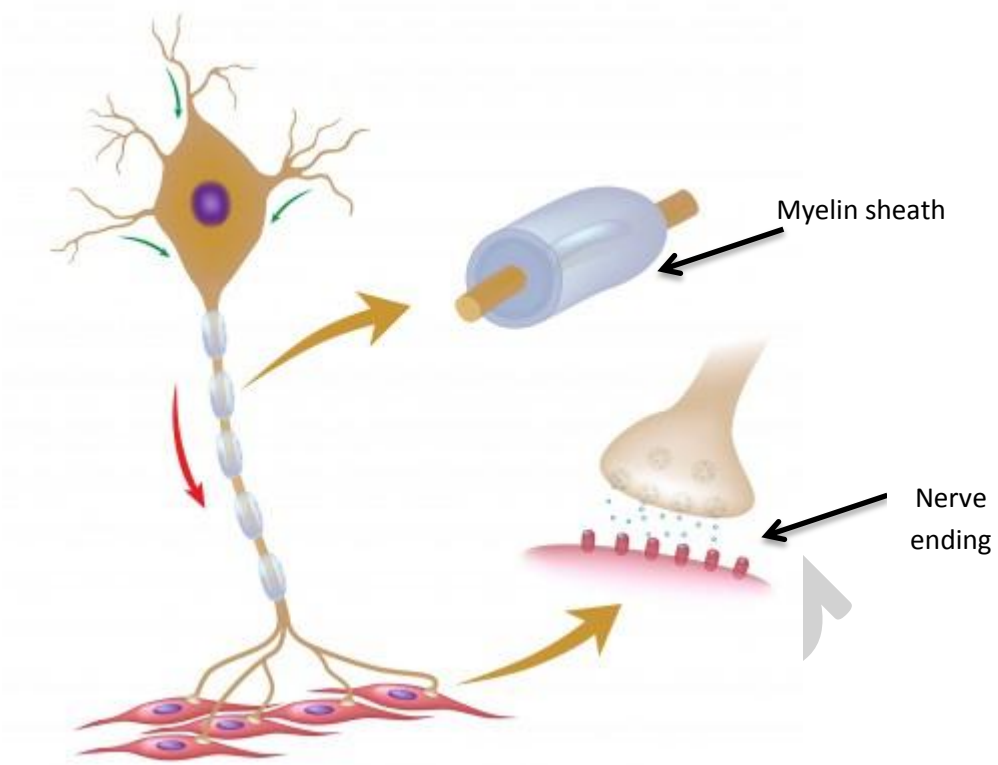
Myelinated Neuron:

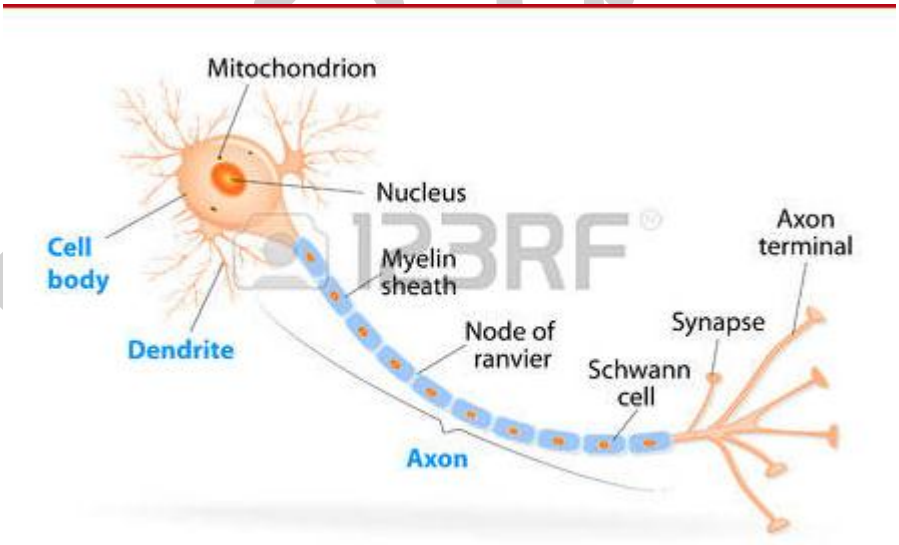
- The axons of many neurons are wrapped (covered) by series of **Schwann** cells to form several layers around the axon called "**myelin sheath**", which is composed of protein-lipid materials complex. The nerve cells which wrapped (covered) with myelin called "**Myelinated Neuron",** except at certain interval which is called **"Nodes of Ranvier"**.
- Shpingomyline, is a type of phospholipid in membrane of **Schwann** cell (myelin) act as electrical insulator to increase the velocity of conduction, rather than unmylinated neuron.

Functional Structure of Neuron

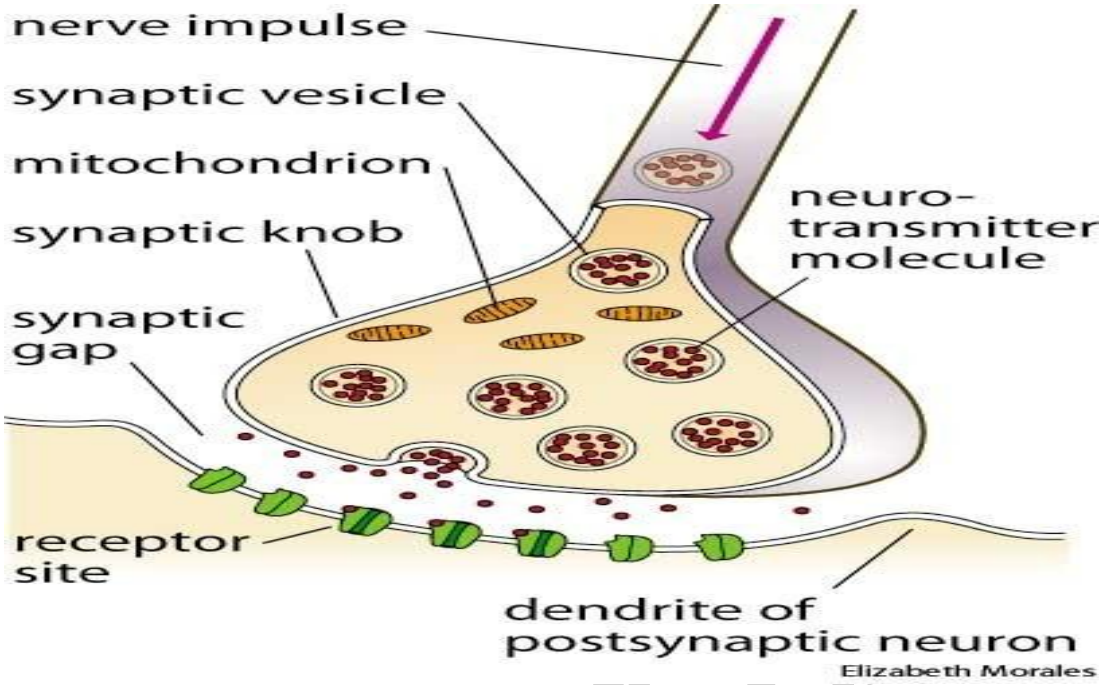
Different part of neuron has the following functions:

1) **The receptor zone or Dendritic zone (dendrites):** that received the incoming information (stimuli) from other cells and initiate a local potential in this area. Incoming signals can be either **excitatory** or **inhibitory** neuron.
2) **The initial segment**: is the site of origin of the impulse that is strong enough to be transmitted through the axon to the nerve endings.
3) **The axon**: it transmitting the impulses to the never endings , by an electrical mechanism.
4) **The nerve endings**: also called "**terminal buttons**" : are the sites for synthesis, storage and release of neurotransmitters to affect other neuron or muscle fiber.





Myelinated neuron



Physiological Anatomy of Synapse

Types of neuron:

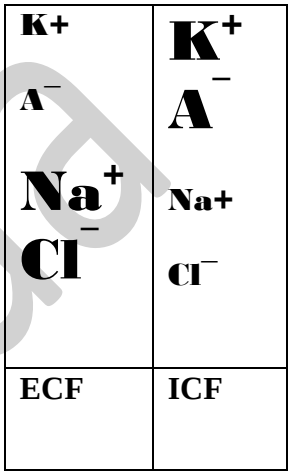
A- There are three types of neurons according to their shape:
1- Unipolar neurons, **2-** Bipolar neurons and **3**- Multipolar neurons

B- There are three types of neurons according to their function :
1- Sensory neurons, **2-** Motor neurons, and **3-** interneurons .

Distribution of Ions Across The Cell Membrane:

In living organisms there are different concentration gradients of ions across the cell membrane. The intracellular fluid **(ICF)** of living cells have higher concentrations of both potassium ions (cations) (K^+) and large organic anion ($\mathbf{A^-}$) , with lower concentrations of chloride (Cl^-) and sodium (Na^+). Whereas, the extracellular fluid **(ECF)** of living cells have higher concentrations of both sodium ions (cations) (Na^+) and chloride (Cl^-),with lower concentrations of both potassium ions (K^+) and large organic anion ($\mathbf{A^-}$).

Ions	Concentrations in ECF (meq/l)	Concentrations in ICF (meq/l)
Na^+	145	12
K^+	4	155
Cl^-	120	4
large organic anion (A^-)	7	155



These ions difference concentrations between outside and inside the cell produce (or initiate) a potential difference called " **Resting Membrane Potential** " and can be recorded by using oscilloscope with 2 electrodes.

- **Resting membrane potential (RMP):**

It is an electrical state difference between the interior and the exterior surface of the membrane when neuron is inactive, with inside (ICF) is relatively negative to the outside (ECF).

At resting state the values of membrane potential varies from tissue to another tissue:
e.g. skeletal muscle cells: **−90mV**; Neurons: **−70 mV**; Smooth muscle cells**: −50 mV**.

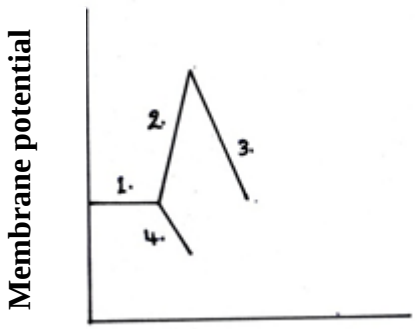
Factors affecting the generation of resting membrane potential:

1) The leakage or diffusion of potassium ions outside the cell according to concentration gradient because the membrane at resting state is permeable to potassium ions (i.e. the permeability of membrane to potassium ions (P K^+) about 100 times than that of sodium ions permeability (PNa^+).
2) Sodium ions try to pass inside the cell according to concentration gradient, but the membrane is impermeable to sodium ions at resting state (although the Na^+ ions are smaller than the K^+).

3) Large organic anion **(A^-)** cannot pass to the outside of the cell, so increasing the negative charge inside the cell.

4) Presence of Na-K pump, contribute to creates a concentration gradient by moving **$3Na^+$** out of the cell and **$2K^+$** moving inside the cell.

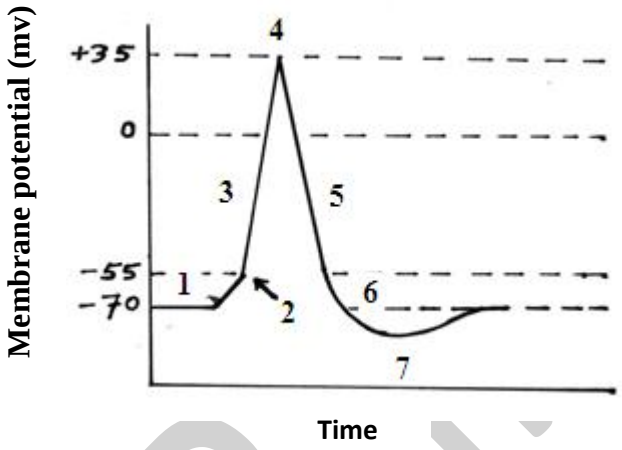
1. **Polarized state (RMP) :** at resting state the cell membrane of excitable cells with inside is negative to the ouside called to be "**Polarized state".**
2. **Depolarization**: is a state when the membrane potential becomes less negative than that of the resting state.
3. **Repolarization**: is a state when the membrane potential return to its polarized state.
4. **Hyperpolarization**: is a state when the membrane potential becomes more negative than that of the resting state.



1. **RMP.**
2. **Depolarization.**
3. **Repolarization.**
4. **Hyperpolarization**

Action potential

It is a rapid physico-chemical changes take place in the membrane potential of the axon of neuron in response to an appropriate stimulus such as electrical, chemical mechanical and thermal, when membrane potential reaches threshold, so a rapid electrical changes of membrane potential from -70mV to +35mv occur and the wave of an action potential appear as the following :



Action potential of a nerve cell

1. **RMP.**
2. **Threshold potential (firing level).**
3. **Depolarization**
4. **Spike potential.**
5. **Repolarization.**
6. **After depolarization.**
7. **After hyperpolarization**

Components of an action potential:

The changes in membrane potential of a nerve cell include**:**

1. **The resting membrane potential stage:** is the potential when membrane at a polarized state with value about **-70mv**.
2. **Threshold potential stage:** depending on stimulation of neuron , the membrane potential will be changes due to increase the permeability of membrane to sodium ions, (more positively charged inside) , when the membrane potential reaches a certain point of depolarization at **-55 mv** known as the **threshold potential** (or firing level) with value about **-15mv**. At this point the membrane will be fire; if it does not reach that point (-55mv), it will not fire.
3. **The depolarization stage:** it is caused when positively charged sodium ions (Na^+) suddenly rush through opening of voltage-gated sodium channels into a neuron and the value of membrane potential rehearing to +35 millivolts (**increased Na^+ influx**).
4. **Spike potential** , is a state occur in membrane potential with sharp rise and rapid fall of the action potential, where sodium ion channels will be **closed** and potassium ion channels will be **open** and the membrane potential not exceeds +35mv.
5. **The repolarization stage**: it is caused by **beginning of** the slow closing of sodium channels leading to **decrease the membrane permeability to Na^+** ions and the opening of voltage-gated potassium channels leading to **rapid diffusion of k^+ ions to the outside (**i.e. rush out of the cell**) .** As a result, **increased K^+ efflux**, and the membrane return to resting state.
6. **After depolarization**; also named "negative after potential " is the last 30% of repolarization, in this stage the membrane potential slowly return to RMP due to increase **K^+ efflux**.
7. **After hyperpolarization;** also named "positive after potential " in this period the membrane potential will not stop at the resting potential, but reduce below the resting potential (due to slow closure of K ion channels) and become more negative , then return to the resting potential by increasing the activity of Na-K pump.

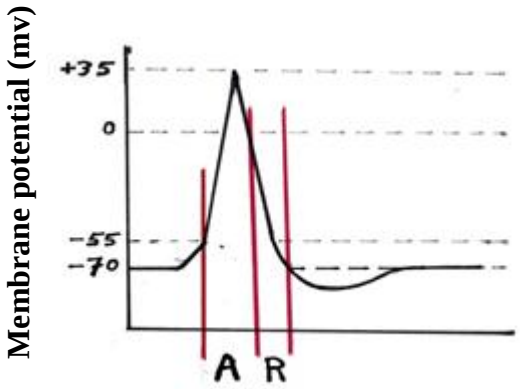
Periods of an action potential:

1- Absolute refractory period:

the amount of time that takes from the firing level up to end of the first third of repolarization ,(i.e. corresponds to depolarization and first 1/3 of repolarization) , during this period neuron cannot respond to another stimulus and no additional action potential can be produce (or initiate) regardless the strength of the second stimulus. The reason for that is that almost all Na channels are inactivated and no stimulus can reopen them.

2- Relative refractory period:

The relative refractory period immediately follows the absolute period. It extend from the end of absolute refractory period to start off after hyperpolarization . During this period a second action potential can be produce; if the stimulus stronger than that of threshold stimuli. The reason for that are that **a-** some of Na^+ channels are opened (activated) and **b-** increased the membrane permeability to K^+ ions.



Action potential of a nerve cell

A: Absolute refractory period.

R: Relative refractory period.

All or non-low

Means that the nerve or muscle fiber responds to a stimulus depending on the strength of the stimulus. If that stimulus exceeds the threshold potential, the nerve or muscle fiber will give a complete response; otherwise, there is no response. Therefore, the action potential produce or not.

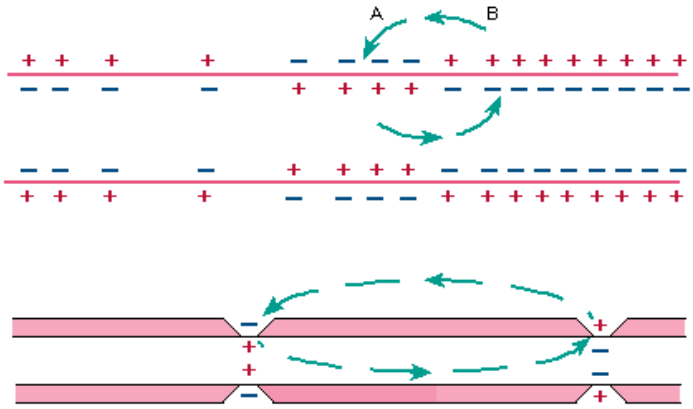
Propagation (or Conduction) of action potential

How does an action potential coduction in the neuron?

The action potential propagate along the axon by two methods:

1- Local circuit theory:

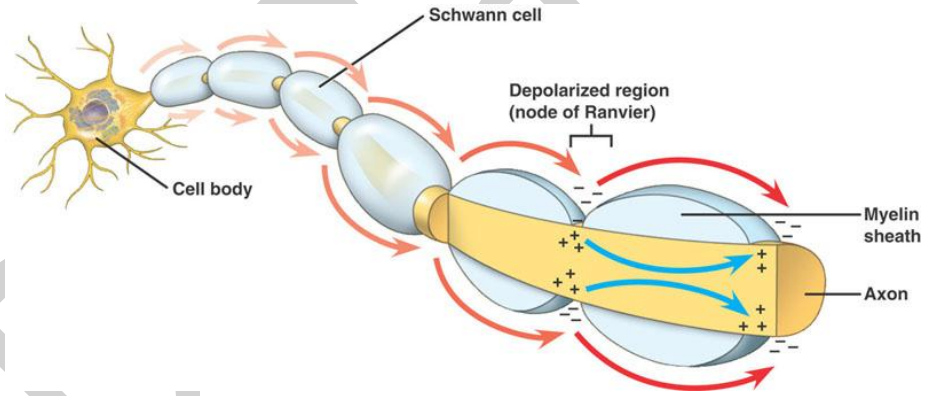
Stimulation of unmyelinated neuron caused an increases the membrane permeability to Na^+ ⟶ produce an active area with +ve charge inside the membrane and –ve charge outside and then a new area (or adjacent portions of axon) becomes depolarized, which lead to propagate or transported of an action potential in all direction as an electrical waves until the whole axon depolarized , this called "**local circuit theory**"



Local circuit theory

2- Saltatory conduction;

In myelinated nerve fibers, also the conduction depends on similar manner of a circular flow , but in presence of myelin the current is carried by the cytoplasm and depolarization jump from one node to another, ; this type of propagation of action potential is known as **Saltatory conduction**.



Saltatory conduction

Note:

a- Action potentials in **unmyelinated** neurons travel much more slowly than action potentials in **myelinated** neuron.

b- Action potentials in **myelinated** neuron can travel faster than that of **unmyelinated** neurons due to have large axons , wider diameter and low resistance.

Synaptic Transmission

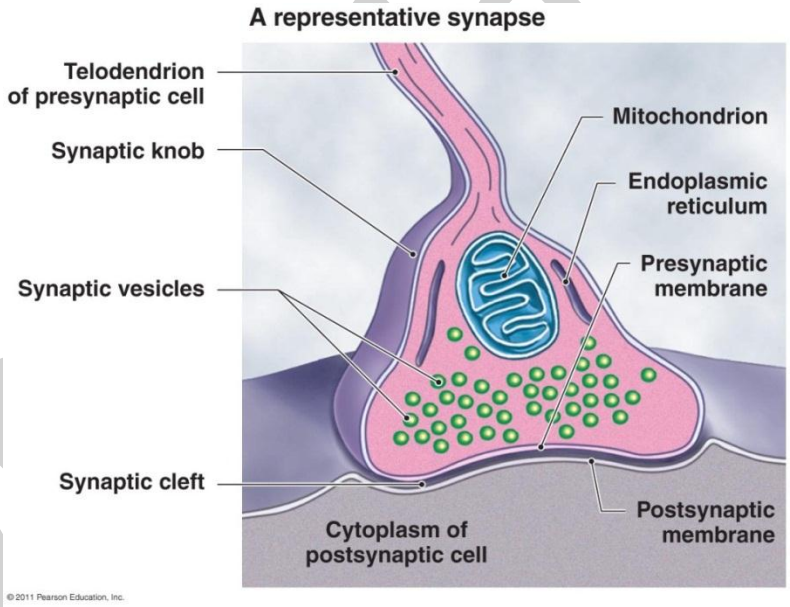
Synaptic transmission

How nerves communication between them?

Synapse: The word **"synapse"** – meaning "conjunction",

Is the point of junction formed between two neurons or more, where an action potential transmitted from one neuron to another. So, the synapse consist from :

1) Presynaptic cell that contains neurotransmitters.
2) Synaptic cleft, a space between the two nerve cells.
3) Postsynaptic cell, that contains receptor sites.



Presynaptic ending (synaptic knobs) contains two main internal structures :

a) **synaptic vesicles :** contain chemical substance called " neurotransmitters " , which when released into synaptic cleft either; excites or inhibits of postsynaptic endings.
b) **mitochondria.**

How the neurotransmitter is released from the presynaptic nerve endings?

1) Presynaptic action potential (i.e. depolarization of nerve endings) causes opening of voltage- gates calcium ion channels causes increase the permeability of membrane to Ca^{+2} ions (**increase Ca^{++} influx**).
2) Increase **$[Ca^{+2}]_{ICF}$** promotes the fusion of synaptic vesicles with the presynaptic membrane.
3) Then vesicles release neurotransmitters into the synaptic cleft (via exocytosis)
4) .
5) These chemical messengers cross the synaptic cleft and connect to special receptors in the postsynaptic neuron triggering an electrical impulse known as an action potential.

There are two main types synapses:

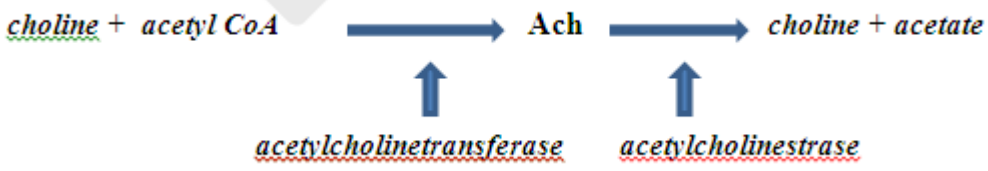
1) **The chemical synapse:** In this type , the electrical activity (action potential) in the presynaptic neuron causes secretion of neurotransmitters "chemical messengers ", that binds to receptors on the surface of postsynaptic cell, that either open or closed channels in the membrane of postsynaptic cell.
2) **The electrical synapses**: In this type, presynaptic cell and postsynaptic cell are connected by specialized protein channels known as **gap junctions**. These junctions form low-resistance bridges that allow the ions to flow quickly from the presynaptic neuron to the postsynaptic neuron easily.

Neurotransmitters:

Neurotransmitters: are endogenous chemical substances that transmit signals from a neuron to a target cell across a synapse. Neurotransmitters could also act as chemical messengers.

Types of Neurotransmitters:

1- **Acetylcholine(Ach),** it acts on the neuromuscular junction. It is synthesized from acetic acid and choline. Once released, acetylcholine binds to post-synaptic receptors and is degraded by acetylcholinesterase.



2- Monoamines: dopamine (DA), norepinephrine (NE) or noradrenaline(NA), epinephrine (adrenaline) and serotonin .

3- Amino acids, include glycin, glutamate, gamma-aminobutyric acid (GABA).

4- Neuropeptides, such as Substance P, endorphins , opioid peptides.

5- Enkephalins.

Neurotransmitters acts only in one of two ways, either ***excitation*** or ***inhibition*** and depending on these mechanisms, NTs classified into:

- **Excitatory Postsynaptic Potential(EPSP)**
  Excitatory neurotransmitters (such as Ach, NE and epinephrine) caused depolarization of the postsynaptic membrane due to increase flow of positively charged sodium ions (**Na^+ influx**) into the postsynaptic cell, as a result of opening ligand-gated ion channels, this will called **excitatory postsynaptic potential(EPSP).**

- **Inhibitory Postsynaptic Potential(IPSP)**
  Inhibitory neurotransmitters (GABA, dopamine ,glycine and serotonin) caused hyperpolarization of the postsynaptic membrane due to increase flow of negatively charged chloride ions (**Cl^- influx**) into the postsynaptic cell, as a result of opening ligand-gated ion channels, this will called **Inhibitory postsynaptic potential(IPSP).**