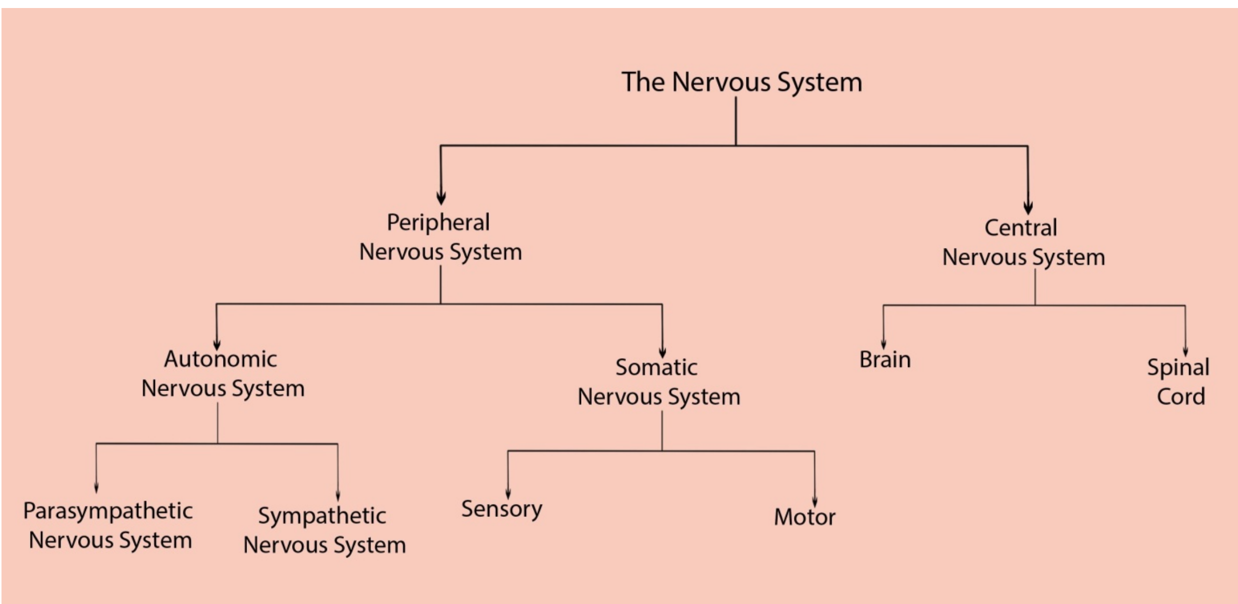
UNIT: I

ORGANIZATION OF NERVOUS SYSTEM

The organization of the nervous system refers to the structural and functional arrangement of its components that work together to control and coordinate body activities. It is designed in a highly systematic manner to efficiently receive sensory information, process it, and produce appropriate responses. This organization ensures rapid communication between different parts of the body and helps maintain internal balance (homeostasis).

The nervous system is broadly organized into two main divisions: the central nervous system, which acts as the control and integration center, and the peripheral nervous system, which connects the central system to the rest of the body. Functionally, it is further classified into sensory and motor divisions, allowing it to handle input and output processes effectively



The nervous system commands muscles, controls the functioning of all organs and provides information about the outside world through sensory information.

NEURON STRUCTURE AND CLASSIFICATION

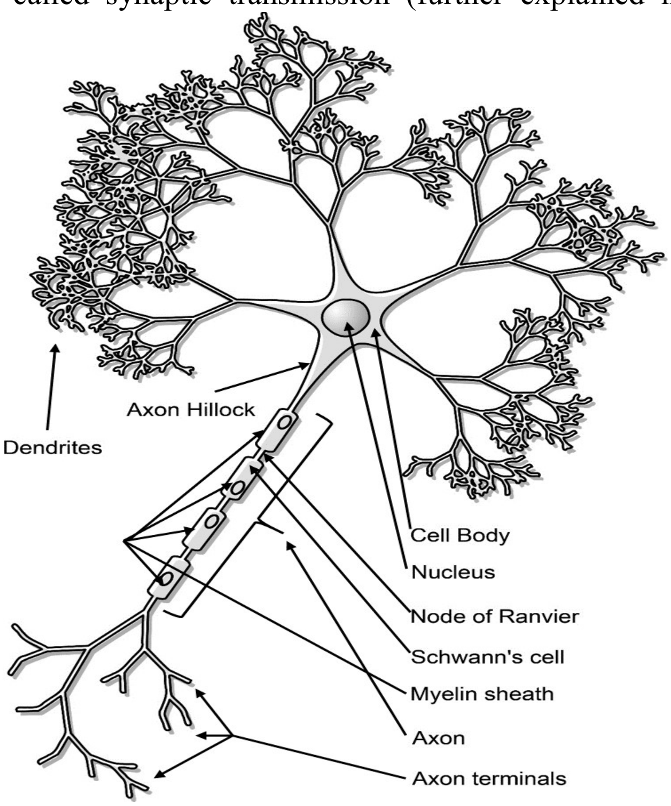
Neurons have four specialized structures that allow for the sending and receiving of information: the cell body (soma), dendrites, axon and axon terminals (see lowest figure).

Cell body or soma: The cell body is the portion of the cell that surrounds the nucleus and plays a major role in synthesizing proteins.

Dendrites: Dendrites are short, branched processes that extend from the cell body. Dendrites function to receive information, and do so through numerous receptors located in their membranes that bind to chemicals, called neurotransmitters.

Axon: An axon is a large process that extends from the cell body at a point of origin-called the axon hillock-and functions to send information. In contrast to the shorter dendrites, the axon can extend for more than a meter. Because of this length, the axon contains microtubules and is surrounded by myelin. Myelin consists of totally separate cells that coil and wrap their membranes around the outside of the axon. These are essential for electrical insulation and to speed up action potential propagation.

Axon terminals: Once an axon reaches a target, it terminates into multiple endings, called axon terminals. The axon terminal is designed to convert the electrical signal into a chemical signal in a process called synaptic transmission (further explained in the section "Physiology of the



Neuron").

CLASSIFICATION OF NEURONS

Structural classification of neurons is based upon the number of processes that extend out from the cell body.

STRUCTURAL CLASSIFICATION OF NEURONS.

1) Bipolar
2) Multipolar and

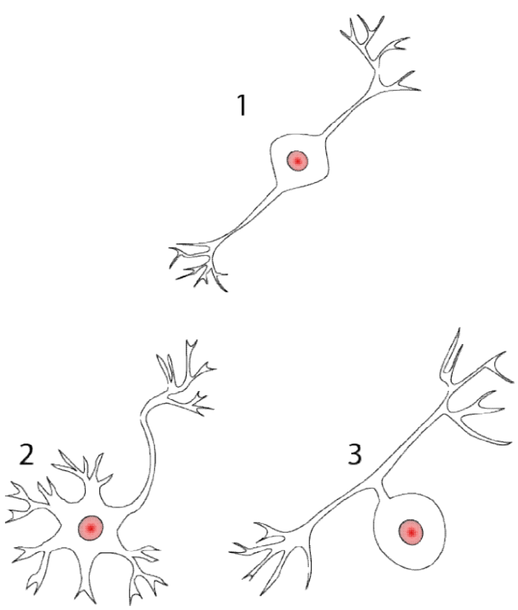
3) Unipolar.

Bipolar: Bipolar neurons have only two processes that extend in opposite directions from the cell body. One process is called a dendrite, and another process is called the axon. Although rare, these are found in the retina of the eye and the olfactory system.

Multipolar

Multipolar neurons are defined as having three or more processes that extend out from the cell body. They comprise of more than 99% of the neurons in humans, and are the major neuron type found in the CNS and the efferent division of the PNS.

Unipolar: Unipolar neurons have a single, short process that extends from the cell body and then branches into two more processes that extend in opposite directions. The process that extends peripherally is known as the peripheral process and is associated with sensory reception. The process that extends toward the CNS is the central process. Unipolar neurons are found primarily in the afferent division of the PNS.



GLIAL CELLS

Unlike neurons, the glial cells can be replaced if they are damaged. Glial cells compose half of the volume of the brain and are more numerous than neurons. There are four major types of glial cells in the CNS: the astrocyte, the oligodendrocyte, the ependymal, and the microglial cell.

The astrocyte: Astrocytes have an enormous amount of processes that wrap around blood vessels and neurons. Because of this arrangement, astrocytes are ideally positioned to control and modify the extracellular environment around neurons. Most of the functions of the astrocyte are attributed to controlling this environment.

Astrocyte characteristic	Function
Glycogen storage	Astrocytes store all the glycogen present in the CNS. This glycogen is used to help meet the high metabolic needs of the CNS. The main source is blood glucose, but glycogen levels can sustain the need for 5 to 10 min.
K+ permeability	Active neurons lose K^+ into the extracellular spaces, which would act as a positive feedback system for depolarization if the K+ was not trapped by the astrocytes. They take up K+ by a pump (Na^+/K^+ ATPase pump), and co-transporters ($Na^+/K^+/Cl^-$ and K^+/Cl^- exchangers).
Gap Junctions	Astrocytes are coupled to each other, as well as other glial cells and neurons through gap junctions. This may serve to help modulate activity and sensitivity in the CNS.
Neurotransmitters	Astrocytes synthesize over 20 different neurotransmitters and take up excess neurotransmitters to help terminate signals at the synapse.
Growth factors	Astrocytes secrete a variety of growth factors, which are important for the establishment of fully functioning excitatory synapses.
Blood flow	Astrocytes can modulate blood flow in the brain by inducing localized vasodilation or vasoconstriction. This modulation can occur through gap junctions between the astrocytes and the endothelial cells of brain blood vessels.

PROPERTIES OF NERVE FIBER:

i. Excitability:

When a stimulus is applied, the nerve fiber demonstrates a change in its electrical activity from its resting state.

ii. Conductivity:

It is the ability of the nerve fiber to transmit impulses all along the whole length of axon without any change in the amplitude of the action potential. This type of conduction is termed as decrementless conduction.

iii. Refractory period (Fig. 2.13):

It is the duration after an effective stimulus, when a second stimulus is applied, there will be no response for the second stimulus.

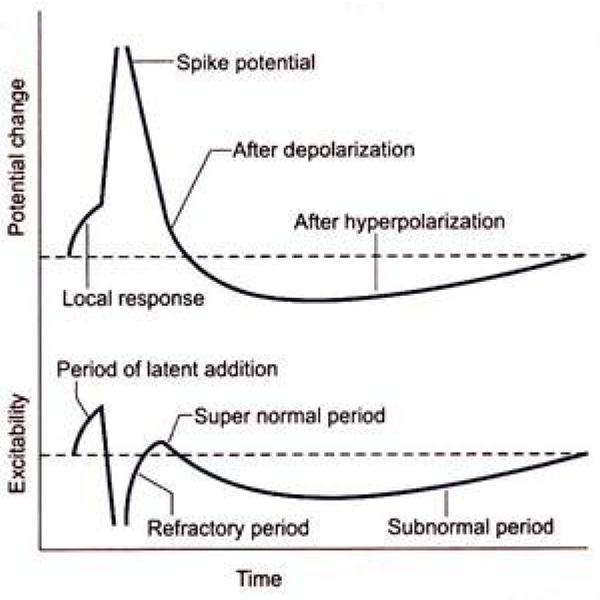


Fig. 2.13: Excitability of the nerve fiber during absolute and relative refractory periods

a. From the time of the application of the stimulus till the initial one-third of the repolarization phase, the nerve fiber excitability will be zero and is completely refractory for the second stimulus. This duration is known as absolute refractory period.

b. Relative refractory period is the duration after an effective stimulus, when a second stimulus, which is slightly above threshold, is applied there will be response for the second stimulus as well.

iv. All or none law:

It states that, when the tissue is stimulated with threshold or more than threshold strength, the amplitude of response will remain the same but for a stimulus of less than threshold strength, there will not be any response.

ELECTROPHYSIOOGY & ACTION POTENTIAL

Electrophysiology of the nerve studies the electrical properties and signals of neurons, primarily action potentials and graded potentials, to understand neural communication. It relies on measuring transmembrane voltage changes, caused by ion flux mainly and through specialized channels,

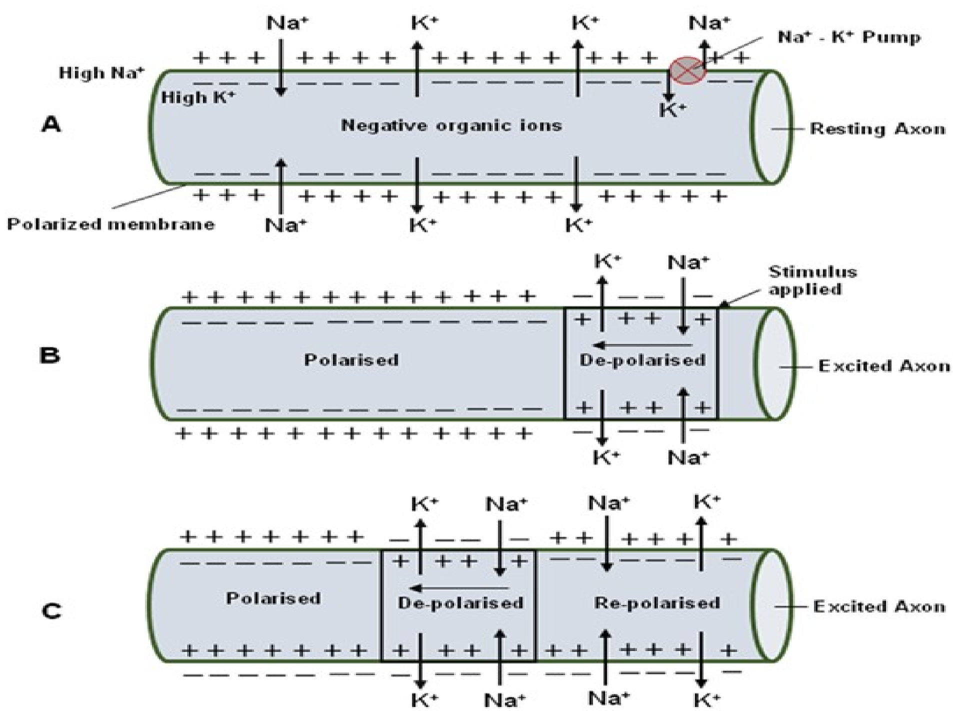
Nerve Impulse Conduction

Nerve impulse: Nerve impulse is an overall physiological changes that occur in a neuron due mechanical, chemical or electrical disturbance created by a stimulus. It propagation through axon, synapse and neuromuscular junction is called Nerve Impulse conduction.

Nerve Impulse transmission along Neuron

Transmission of nerve impulse along nerve fibre can be summarized in three steps

1. Polarization (Resting Potential)
2. Depolarization (Action Potential)
3. Repolarization



Polarization (Resting potetential):

- A neuron at resting is electrically charged but not conducting.
- The Axoplasm or plasma membrane of a resting neuron is negatively charged as compared to the interstitial fluid.
- The potential difference measured at this stage is called **resting potential** which is about **-70mV**. The interstitial fluid has high concentration of Na+ ion which is about 16 times higher outside the neuron than inside neuron. Similarly, the axoplasm has high concentration of K+ ion which is about 25 times higher inside than in outer interstitial fluids.
- Due to difference in concentration of ions, Na+ ion tends to diffuse into the axoplasm and K+ ion tends to diffuse outside the axoplasm.
- The membrane of neuron at resting is more permeable to K+ ion than Na+ ion. So, K+ leaves the neuron faster than Na+ enter the neuron.
- The difference in permeability results in accumulation of high concentration of cation (+ve charged ion) outside the neuron compared to the concentration of cation inside.
- This state of resting neuron is called **Polarized state** and it is electro-negatively charged.

Depolarization (Action Potential):

- Any stimulus beyond the threshold can initiate an impulse.
- When such stimulus is applied in the resting neuron, it opens the sodium channel. Now the permeability of Na+ ion suddenly increases at the point of stimulus causing depolarization.
- The diffusion of Na+ ion increases by 10 times from outside to inside. As a result the axoplasm become positively charges, which is exact opposite to polarized state, so called as **depolarized state** or **reverse polarized state.**
- The depolarization of the membrane stimulates the adjacent voltage channel, so the action potential passes as a wave along the length of neuron.

Repolarization:

- When the concentration of Na+ ion inside axoplasm increases, the permeability to Na+ decreases and the sodium channel starts to close.

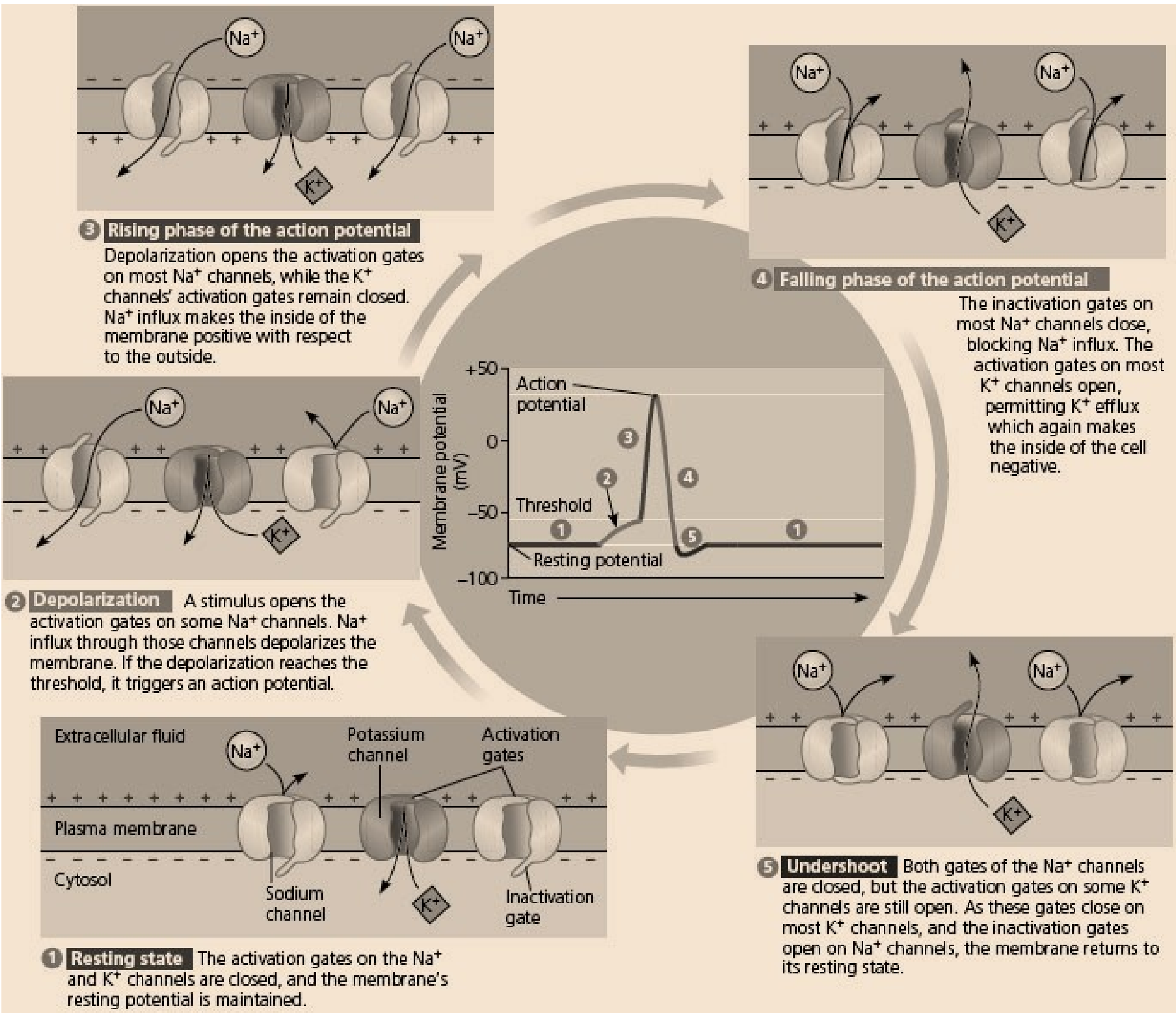
- The Na-K pump activates, so that Na+ are pumped out and K+ inside until the original resting potential is restored. The process is known as **repolarization** and it starts from the same point from where depolarization starts.
- The entire process of polarization, depolarization and repolarization occur within fraction **of seconds. Now, again the neuron is read for another impulse.**

Saltatory conduction:

- Transmission of nerve impulses is very rapid. However, nerve impulse conduction along unmyelinated neuron is slow than that of myelinated neuron. It is because, the myelin sheath act as insulator, so that the impulse have to jump from one node of Raniver to another.
- This speed up the conduction process, and this type of conduction is known as **Saltatory conduction.**

ACTION POTENTIALS

Action potentials are brief, rapid, large changes in the membrane potential in which the potential actually reverses. They are usually initiated as a result of spread from graded potentials.



Neural Impulses in the Nervous System

The central nervous system (CNS) goes through a **three-step** process when it functions: **sensory input, neural processing, and motor output**.

STAGES OF NEURAL IMPULSES

"Resting potential" is the name for the electrical state when a neuron is not actively being signaled. A neuron at resting potential has a membrane with established amounts of sodium

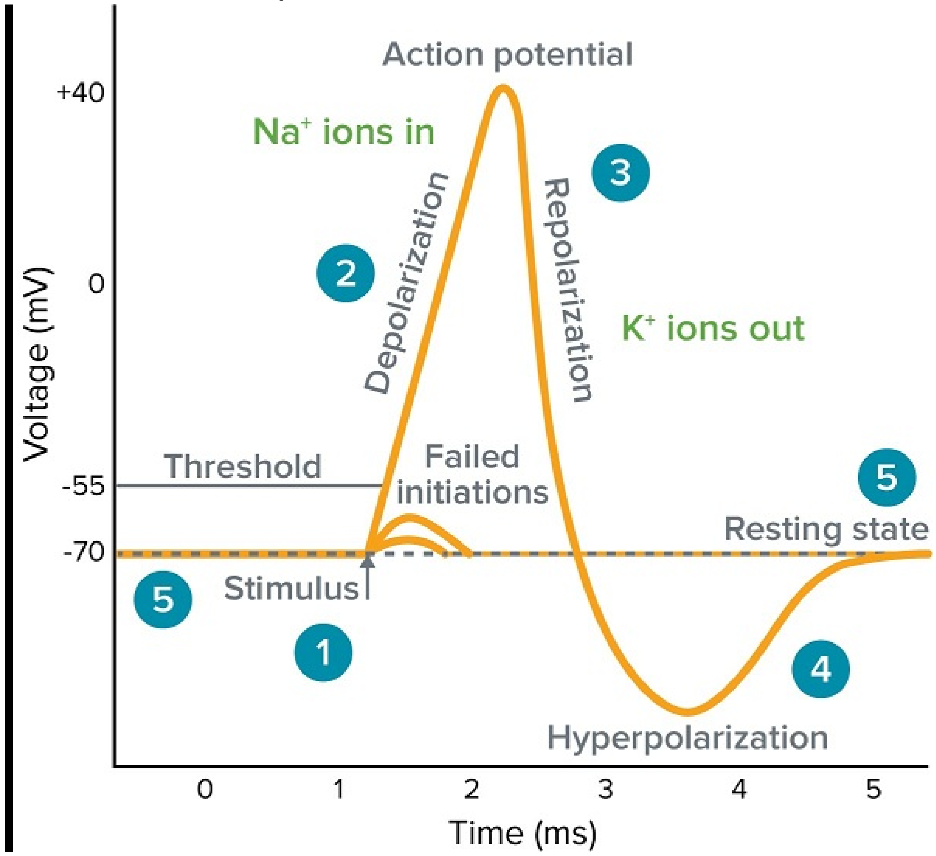
(Na+) and potassium (K+) ions on either side, leaving the inside of the neuron negatively charged relative to the outside.

The action potential is a rapid change in polarity that moves along the nerve fiber from neuron to neuron.

In order for a neuron to move from resting potential to action potential—a short-term electrical change that allows an electrical signal to be passed from one neuron to another—the neuron must be stimulated by pressure, electricity, chemicals, or another form of stimuli.

The action potential has several stages.

1. **Depolarization:** A stimulus starts the depolarization of the membrane. Depolarization, also referred to as the "upswing," is caused when positively charged sodium ions rush into a nerve cell. As these positive ions rush in, the membrane of the stimulated cell reverses its polarity so that the outside of the membrane is negative relative to the inside.
2. **Repolarization.** Once the electric gradient has reached the threshold of excitement, the "downswing" of repolarization begins. The channels that let the positive sodium ion channels through close up, while channels that allow positive potassium ions open, resulting in the release of positively charged potassium ions from the neuron. This expulsion acts to restore the localized negative membrane potential of the cell, bringing it back to its normal voltage.
3. **Refractory Phase**. The refractory phase takes place over a short period of time after the depolarization stage. Shortly after the sodium gates open, they close and go into an inactive conformation. The sodium gates cannot be opened again until the membrane is repolarized to its normal resting potential. The sodium-potassium pump returns sodium ions to the outside and potassium ions to the inside. During the refractory phase this particular area of the nerve cell membrane cannot be depolarized. Therefore, the neuron cannot reach action potential during this "rest period."



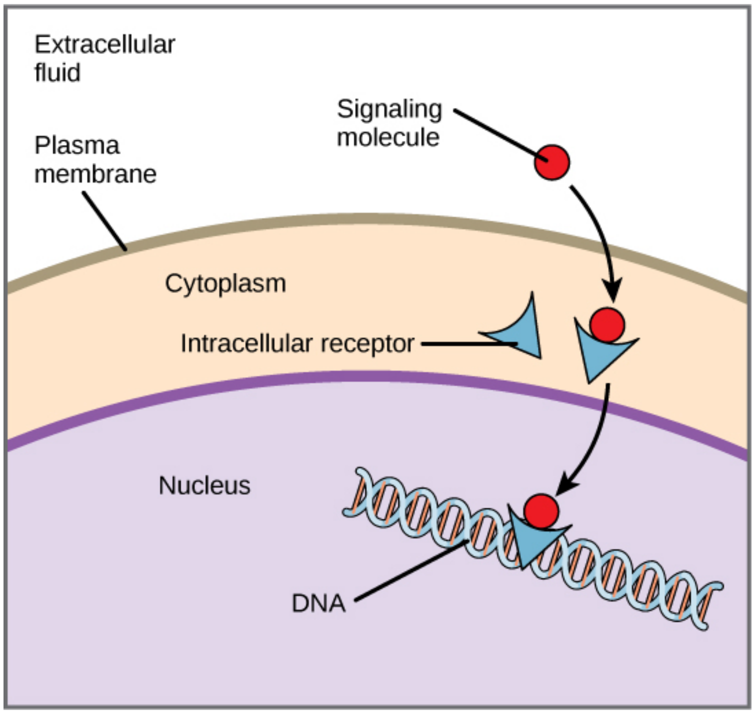
TYPES OF RECEPTORS

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

Internal receptors

Internal receptors, also known as intracellular or cytoplasmic receptors, are found in the cytoplasm of the cell and respond to hydrophobic ligand molecules that are able to travel across the plasma membrane.

Once inside the cell, many of these molecules bind to proteins that act as regulators of mRNA synthesis to mediate gene expression. Gene expression is the cellular process of transforming the information in a cell's DNA into a sequence of amino acids that ultimately forms a protein. When the ligand binds to the internal receptor, a conformational change exposes a DNA-binding site on the protein. The ligand-receptor complex moves into the nucleus, binds to specific regulatory regions of the chromosomal DNA, and promotes the initiation of transcription. Internal receptors can directly influence gene expression without having to pass the signal on to other receptors or messengers.



Cell-Surface Receptors

Cell-surface receptors, also known as transmembrane receptors, are cell surface, membrane-anchored, or integral proteins that bind to external ligand molecules. This type of receptor spans 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. Cell-surface receptors are also called cell-specific proteins or markers because they are specific to individual cell types.

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. The size and extent of each of these domains vary widely, depending on the type of receptor.

Cell-surface receptors are involved in most of the signaling in multicellular organisms. There are three general categories of cell-surface receptors: ion channel-linked receptors, G-protein-linked receptors, and enzyme-linked receptors.

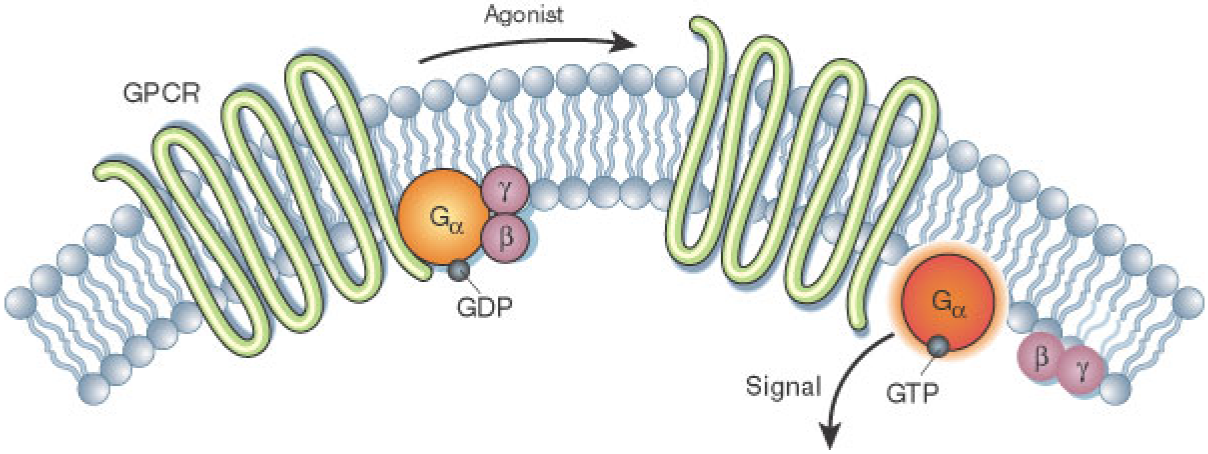
Ion Channel-Linked Receptors

Ion channel-linked receptors bind a ligand and open a channel through the membrane that allows specific ions to pass through. To form a channel, this type of cell-surface receptor has an extensive membrane-spanning region. In order to interact with the phospholipid fatty acid tails that form the center of the plasma membrane, many of the amino acids in the membrane-spanning region are hydrophobic in nature. Conversely, the amino acids that line the inside of the channel are hydrophilic to allow for the passage of water or ions. When a ligand binds to the extracellular region of the channel, there is a conformational change in the protein's structure that allows ions such as sodium, calcium, magnesium, and hydrogen to pass through.

G-Protein Linked Receptors

G-protein-linked receptors bind a ligand and activate a membrane protein called a G-protein. The activated G-protein then interacts with either an ion channel or an enzyme in the membrane. All G-protein-linked receptors have seven transmembrane domains, but each receptor has its own specific extracellular domain and G-protein-binding site.

Cell signaling using G-protein-linked receptors occurs as a cyclic series of events. Before the ligand binds, the inactive G-protein can bind to a newly-revealed site on the receptor specific for its binding. Once the G-protein binds to the receptor, the resultant shape change activates the G-protein, which releases GDP and picks up GTP. The subunits of the G-protein then split into the α subunit and the β subunit. One or both of these G-protein fragments may be able to activate other proteins as a result. Later, the GTP on the active α subunit of the G-protein is hydrolyzed to GDP and the β subunit is deactivated. The subunits reassociate to form the inactive G-protein, and the cycle starts over.

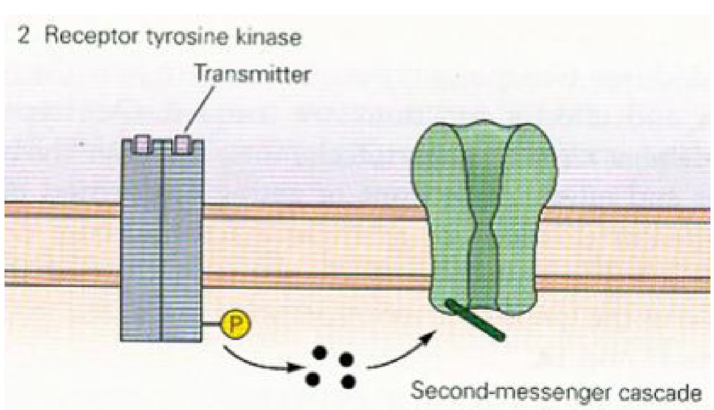


Enzyme-Linked Receptors

Enzyme-linked receptors are cell-surface receptors with intracellular domains that are associated with an enzyme. The enzyme-linked receptors normally have large extracellular and intracellular domains, but the membrane-spanning region consists of a single alpha-helical region of the peptide strand.

When a ligand binds to the extracellular domain, a signal is transferred through the membrane and activates the enzyme, which sets off a chain of events within the cell that eventually leads to a response.

An example of this type of enzyme-linked receptor is the tyrosine kinase receptor. The tyrosine kinase receptor transfers phosphate groups to tyrosine molecules. Signaling molecules bind to the extracellular domain of two nearby tyrosine kinase receptors, which then dimerize. Phosphates are then added to tyrosine residues on the intracellular domain of the receptors and can then transmit the signal to the next messenger within the cytoplasm.



SYNAPSE

A **synapse** is the functional junction between two neurons or between a neuron and an effector organ (such as a muscle or gland). It is the site where nerve impulses are transmitted from one cell to another. Synapses ensure proper communication within the nervous system and allow signals to be processed, modified, and directed.

Types of Synapse

Synapses are mainly classified into **electrical synapses** and **chemical synapses**.

Electrical synapses allow direct transmission of electrical impulses between adjacent neurons through specialized channels called gap junctions. These synapses are very fast, have minimal delay, and permit bidirectional transmission. They are found in areas where rapid and synchronized activity is required, such as in certain parts of the brain and cardiac muscle.

Chemical synapses are the most common type. In these synapses, transmission occurs through chemical messengers called neurotransmitters. They consist of three main parts: the presynaptic terminal, synaptic cleft, and postsynaptic membrane. Transmission is slower compared to electrical synapses and is usually unidirectional. Chemical synapses allow greater flexibility, modulation, and integration of signals.

Synapses can also be classified structurally as:

- **Axodendritic** (axon to dendrite)
- **Axosomatic** (axon to cell body)
- **Axoaxonic** (axon to axon)

Mechanism of Synaptic Transmission (Chemical Synapse)

The transmission of nerve impulses across a chemical synapse involves several steps:

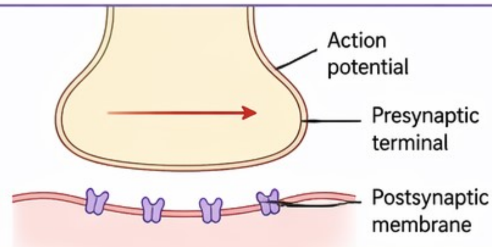
1. **Arrival of Action Potential:**
   When a nerve impulse reaches the presynaptic terminal, it causes depolarization of the membrane.
2. **Calcium Influx:**
   Voltage-gated calcium channels open, allowing Ca^{2+} ions to enter the presynaptic neuron.
3. **Release of Neurotransmitters:**
   The influx of calcium triggers synaptic vesicles to fuse with the presynaptic membrane and release neurotransmitters into the synaptic cleft.

4. **Diffusion Across Synaptic Cleft:**
   Neurotransmitters diffuse across the cleft and bind to specific receptors on the postsynaptic membrane.
5. **Generation of Postsynaptic Potential:**
   Binding of neurotransmitters opens ion channels, leading to either depolarization (excitatory) or hyperpolarization (inhibitory) of the postsynaptic membrane.
6. **Termination of Signal:**
   Neurotransmitters are removed by enzymatic degradation, reuptake into the presynaptic neuron, or diffusion away, ensuring that the signal does not persist indefinitely.

MECHANISM OF SYNAPTIC TRANSMISSION (CHEMICAL SYNAPSE)

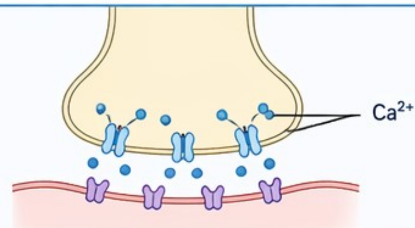
1 ARRIVAL OF ACTION POTENTIAL

When a nerve impulse (action potential) reaches the presynaptic terminal, it causes depolarization of the membrane.



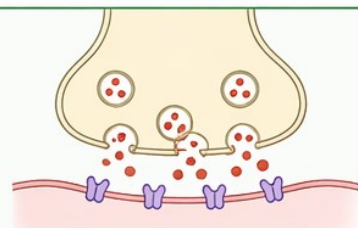
2 CALCIUM INFLUX

Voltage-gated calcium channels open, allowing Ca^{2+} ions to enter the presynaptic neuron.



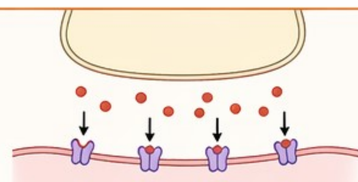
3 RELEASE OF NEUROTRANSMITTERS

The influx of calcium triggers synaptic vesicles to fuse with the presynaptic membrane and release neurotransmitters into the synaptic cleft.



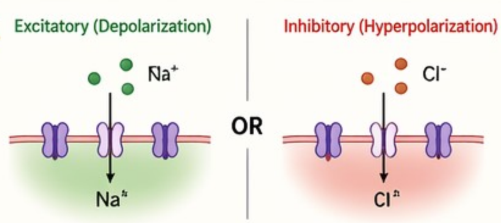
4 DIFFUSION ACROSS SYNAPTIC CLEFT

Neurotransmitters diffuse across the cleft and bind to specific receptors on the postsynaptic membrane.



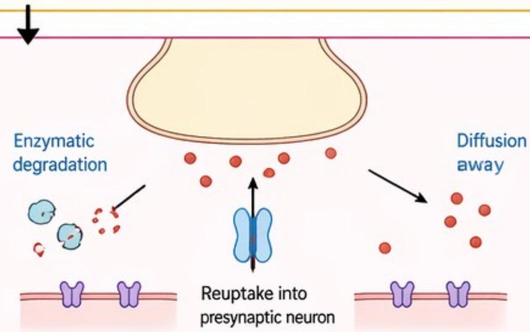
5 GENERATION OF POSTSYNAPTIC POTENTIAL

Binding of neurotransmitters opens ion channels, leading to either depolarization (excitatory) or hyperpolarization (inhibitory) of the postsynaptic membrane.



6 TERMINATION OF SIGNAL

Neurotransmitters are removed by enzymatic degradation, reuptake into the presynaptic neuron, or diffusion away, ensuring that the signal does not persist indefinitely.



NEUROTRANSMITTERS

Neurotransmitters are chemical substances released from the presynaptic neuron that transmit nerve impulses across a synapse to another neuron, muscle, or gland. **They play a crucial role in regulating** mood, movement, memory, and many body functions**.**

Types of Neurotransmitters

1. Based on Function

a) Excitatory Neurotransmitters

These increase the likelihood of generating an action potential (stimulate the next neuron).

Examples:

- **Glutamate** – major excitatory neurotransmitter in the brain
- **Acetylcholine** – involved in muscle contraction and memory

Function: Promote nerve impulse transmission

b) Inhibitory Neurotransmitters

These decrease the likelihood of generating an action potential (calm or suppress activity).

Examples:

- **GABA (Gamma-aminobutyric acid)** – main inhibitory neurotransmitter in CNS
- **Glycine** – acts in spinal cord

Function: Prevent over-excitation, maintain balance

c) Modulatory (Neuromodulators)

These influence or regulate the activity of neurons rather than directly exciting or inhibiting.

Examples:

- **Dopamine** – reward, motivation, movement
- **Serotonin** – mood, sleep, appetite
- **Norepinephrine** – alertness, stress response

Function: Modify and fine-tune neural responses

2. Based on Chemical Nature

a) Amino Acid Neurotransmitters

- **Glutamate** (excitatory)
- **GABA** (inhibitory)
- **Glycine** (inhibitory)

b) Monoamines

Derived from amino acids.

Types & Examples:

- **Catecholamines:**
  1. Dopamine
  2. Norepinephrine
  3. Epinephrine
- **Indolamine:**

  Serotonin

c) Peptide Neurotransmitters

Made of short chains of amino acids.

Examples:

- Endorphins – pain relief
- Substance P – pain transmission

d) Other Neurotransmitters

- **Acetylcholine** – first discovered neurotransmitter
- **Nitric oxide (NO)** – gaseous neurotransmitter

Neurotransmitters – Types, Examples and Functions

S. No.	Type of Neurotransmitter	Examples	Function
1.	Excitatory Neurotransmitters	• Glutamate • Acetylcholine	Stimulate neurons and promote nerve impulse transmission.
2.	Inhibitory Neurotransmitters	• GABA (Gamma-aminobutyric acid) • Glycine	Suppress neuronal activity and prevent over-excitation.
3.	Modulatory (Neuromodulators)	• Dopamine • Serotonin • Norepinephrine	Regulate mood, behavior and neural activity.
4.	Peptide Neurotransmitters	• Endorphins (Enkephalins, Dynorphins) • Substance P	Involved in pain relief, stress response and modulation of functions.
5.	Monoamines (Noradrenergic & Indolamines)	• Norepinephrine • Epinephrine • Serotonin	Control alertness, mood, motivation and stress response.