Ashur University
College of Medicine

Grade 2
Neuroscience
Physiology of Nervous System

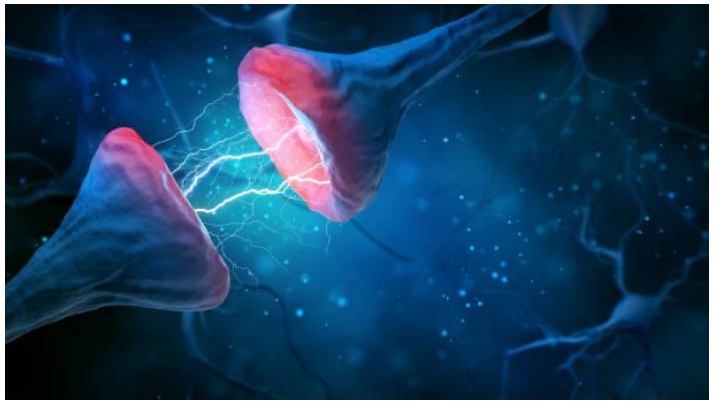
Types of Synapse



Ass. Professor Internal Medicine

Dr.Qasim Razzaq Radhi

14/10/2024

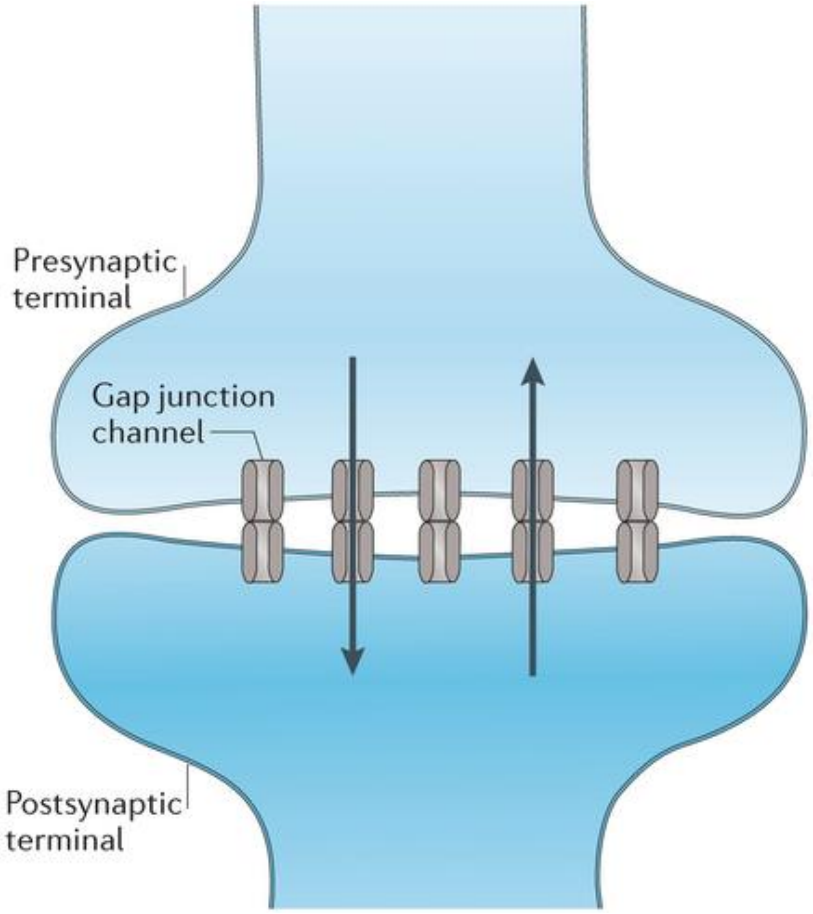


Type of Synapse
A- Electrical synapse (Gap junction)
(Intestine, Heart muscle)

The cytoplasms of adjacent cells are directly connected by clusters of ion channels called **gap junctions** that allow free movement of ions from the interior of one cell to the interior of the next cell.

Electrical synapses contain channels that allow charges (ions) to flow from one cell to another.

Gap junctions are present the **nervous system** , in **cardiac muscle** and **visceral smooth muscles** **, smooth muscle cells .**

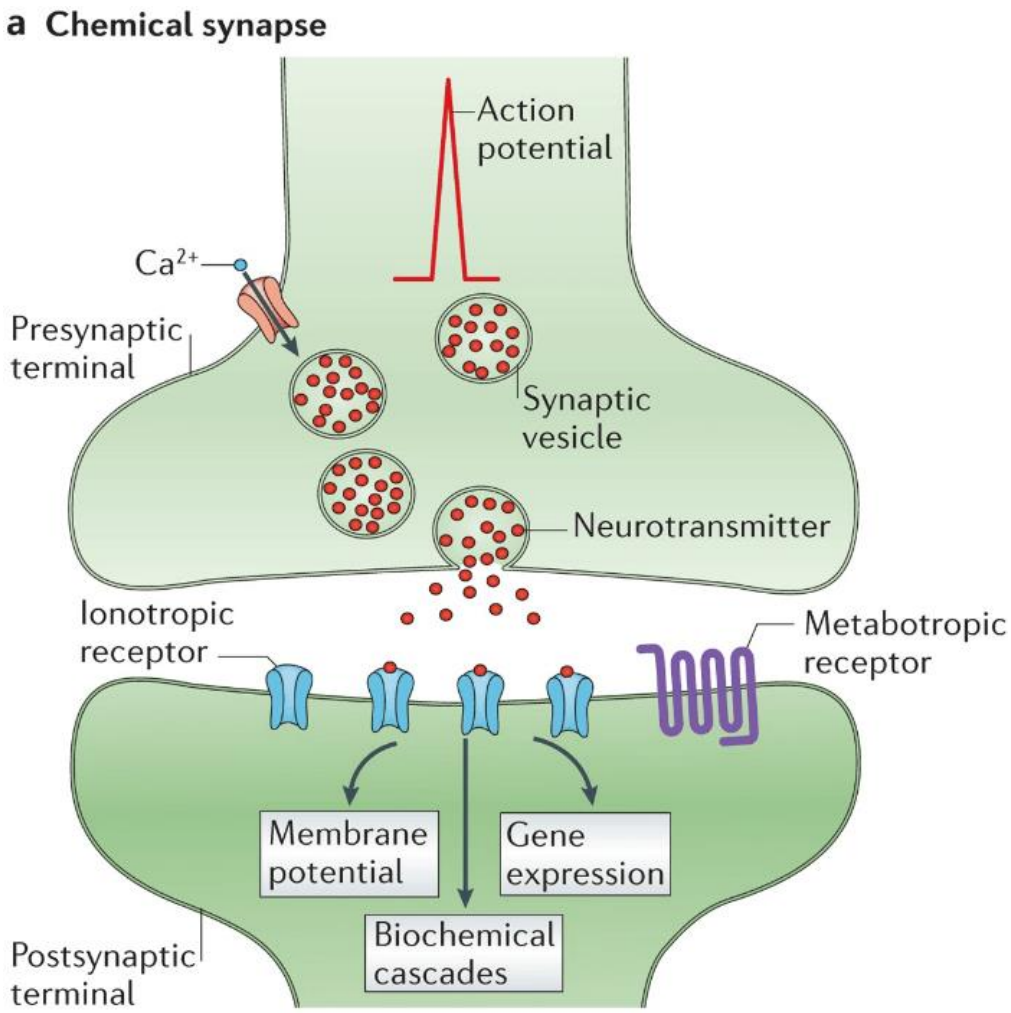


B. Chemical synapse (Neurotransmitter, One-way conduction)

Chemical synapses are specialized cell-to-cell junctions where nerve impulse is transmitted unidirectionally from one neuron to either another neuron or a non-neuronal target cell.

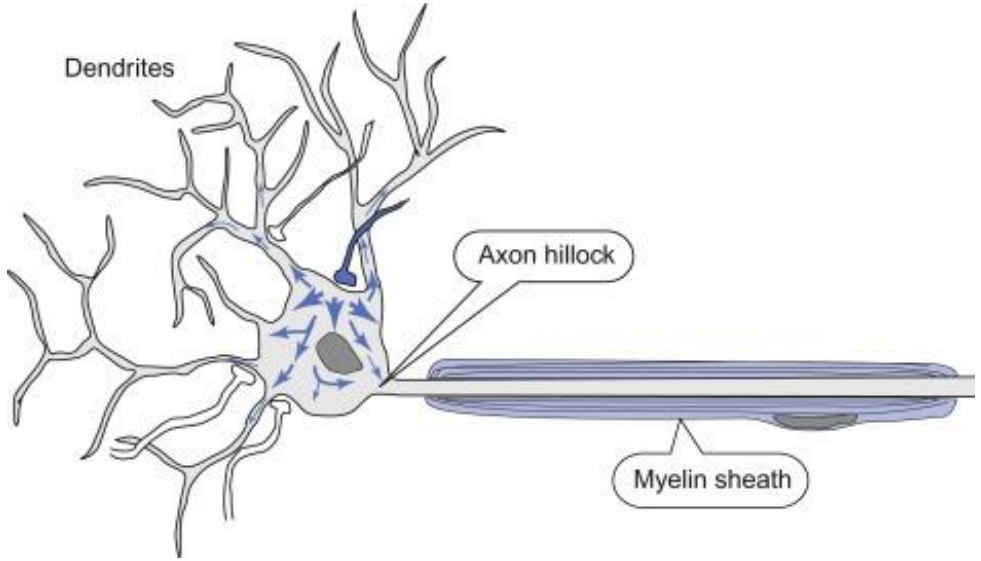
Chemical synapse allows unidirectional transmission by using chemicals called neurotransmitters to send signals along the neurons. Chemical synapse are the most common type of synapses in the body.

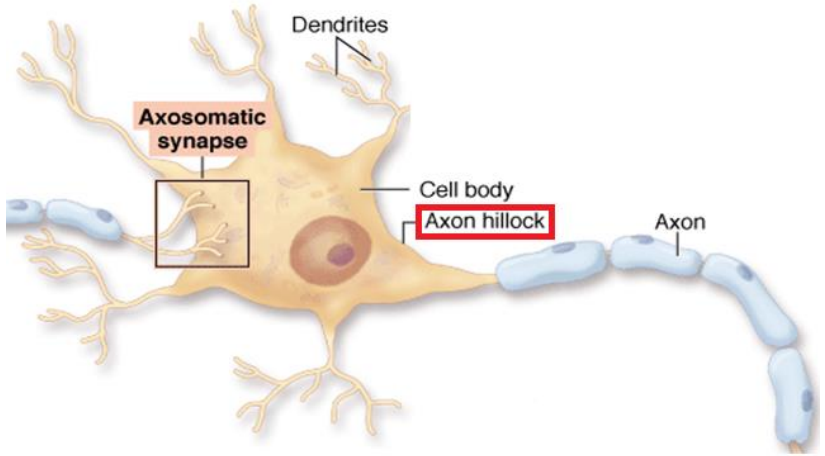
An example of chemical synapse by the release of neurotransmitters like **acetylcholine.**



The functional specialization of different regions in a multipolar neuron

- **Multipolar neurons** are typically characterized by a **single axon and two or more dendrites** arising from the cell body. Functionally, the dendrites serve as receptors, while the axon is the primary conducting pathway for electrical impulses.
- The integration of **Excitatory PostSynaptic Potentials (EPSPs)** and **Inhibitory PostSynaptic Potentials (IPSPs)** in a neuron occur at the **axon hillock**. This structure is located at the juncture where the cell body (soma) meets the axon of the neuron.





Summation of action potential

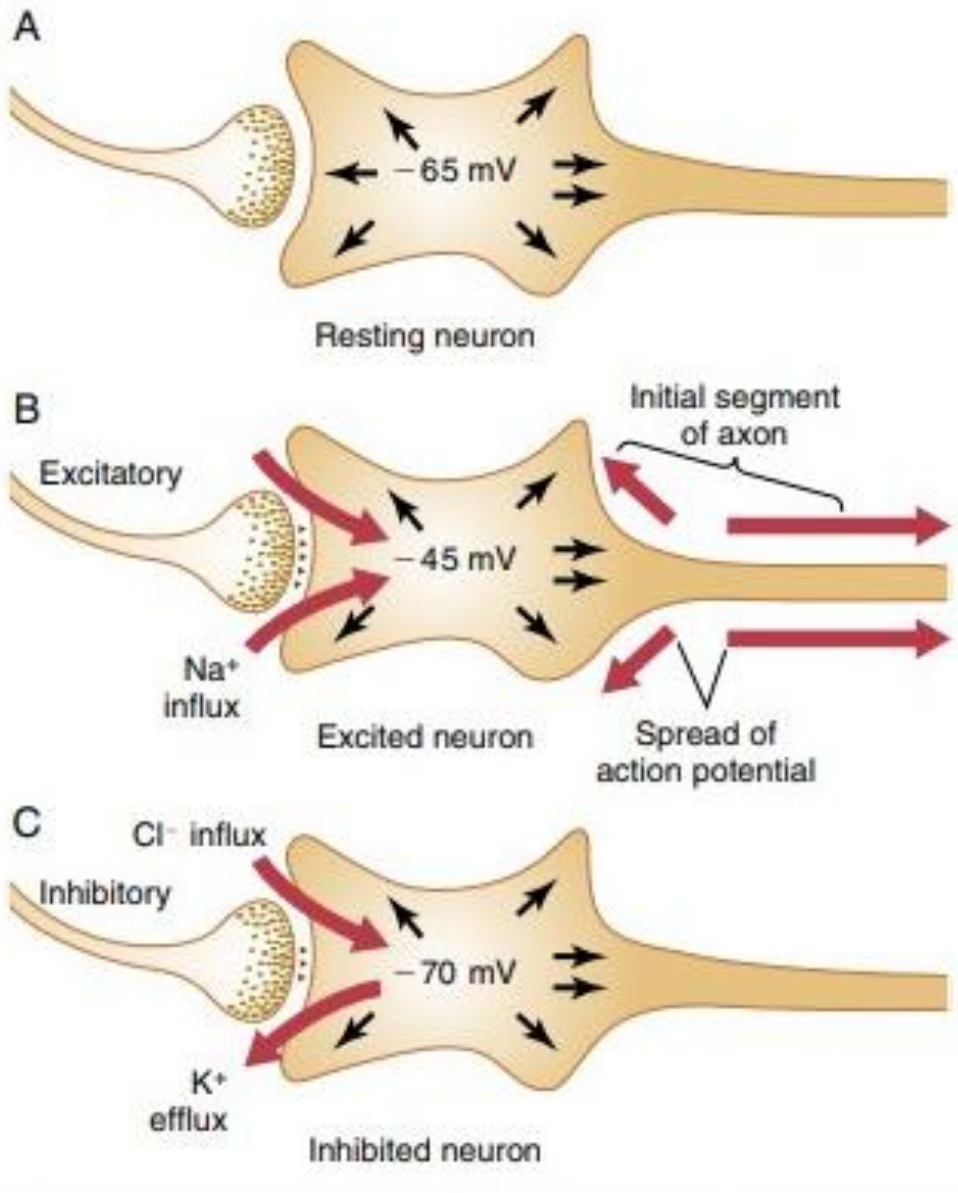
- **EPSPs stimulate** promote the firing of postsynaptic action potentials.
- **IPSPs suppress** the occurrence of postsynaptic action potentials.

EPSP: (20 mV)

- Opening of Na+ channels
- Depressed conduction through Cl- or K+ channels
- Increased internal metabolism of postsynaptic neuron

IPSP: (-5 mV)

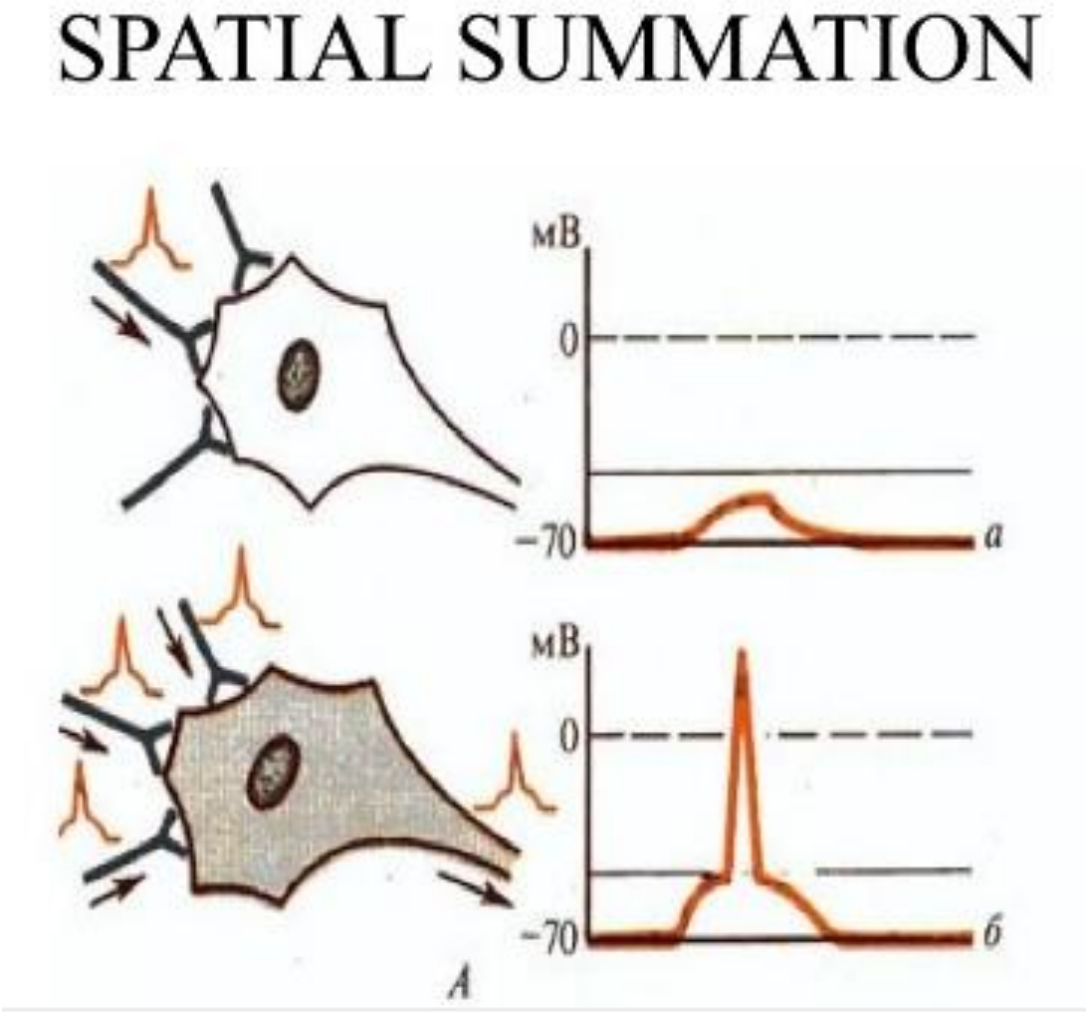
- Opening of Cl- channels
- Increased conduction of K+
- Activation of inhibitory enzyme



Types of summation:

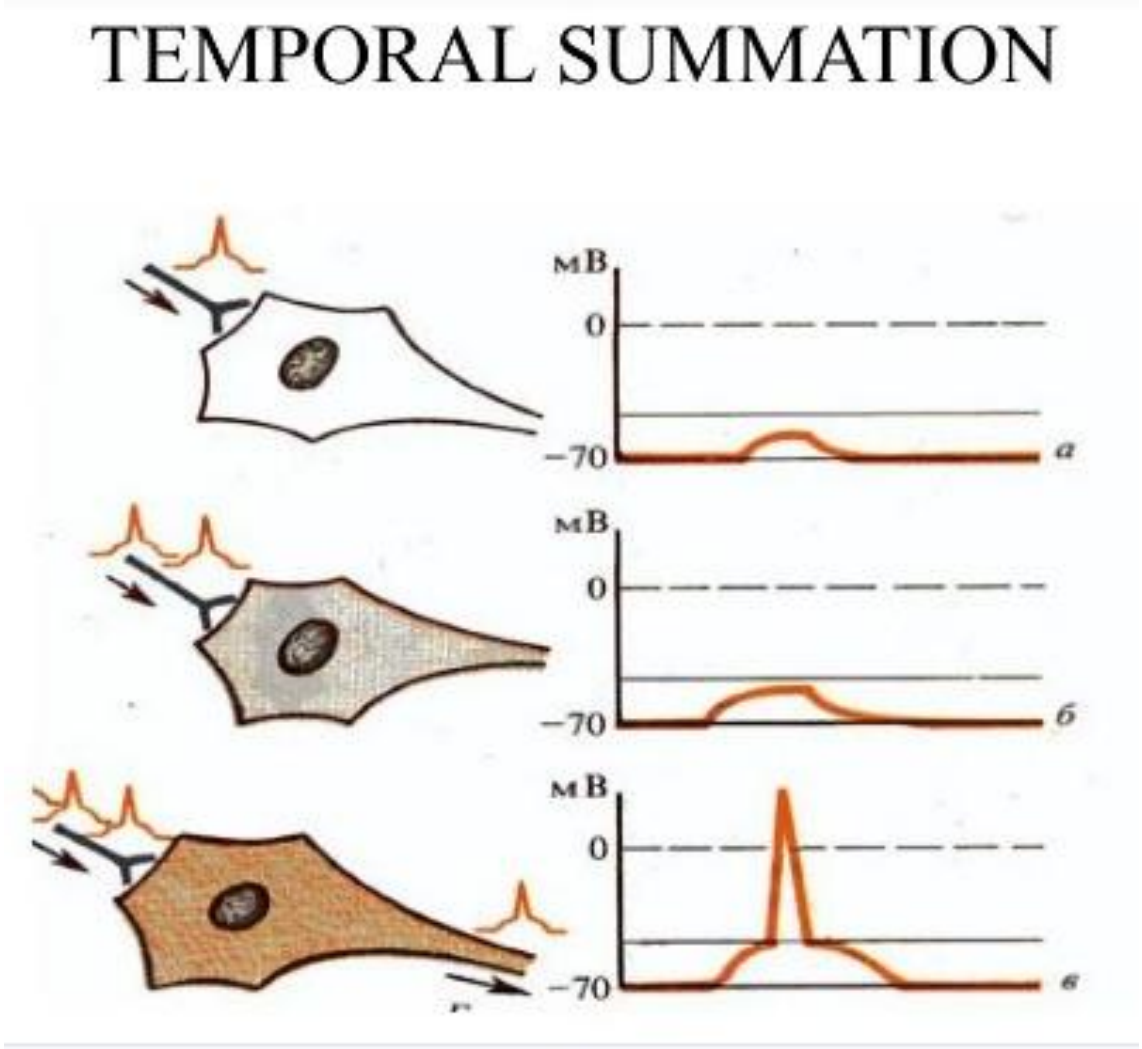
1-Spatial summation:

Spatial Summation: This occurs when **multiple presynaptic neurons release neurotransmitters simultaneously at different locations on the postsynaptic neuron**. The combined effect of these neurotransmitters can lead to the generation of an action potential if the total depolarization reaches the threshold. Spatial summation occurs when **stimuli are applied at the same time, but in different areas**, with a cumulative effect upon membrane potential. Spatial summation uses **multiple synapses** acting simultaneously.

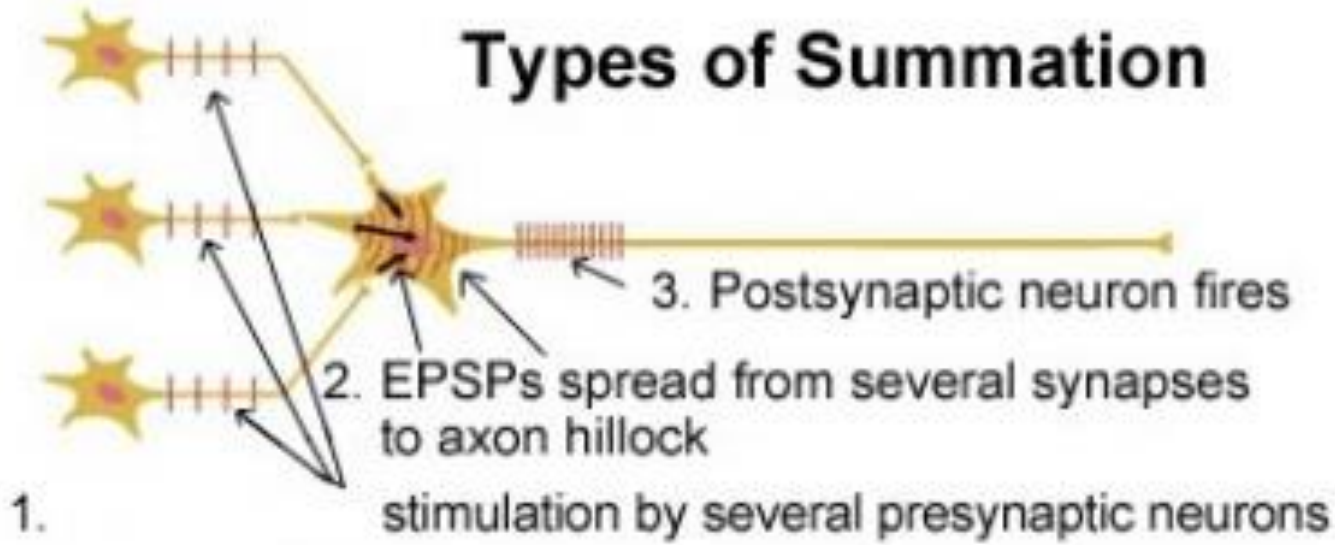


2-Temporal Summation

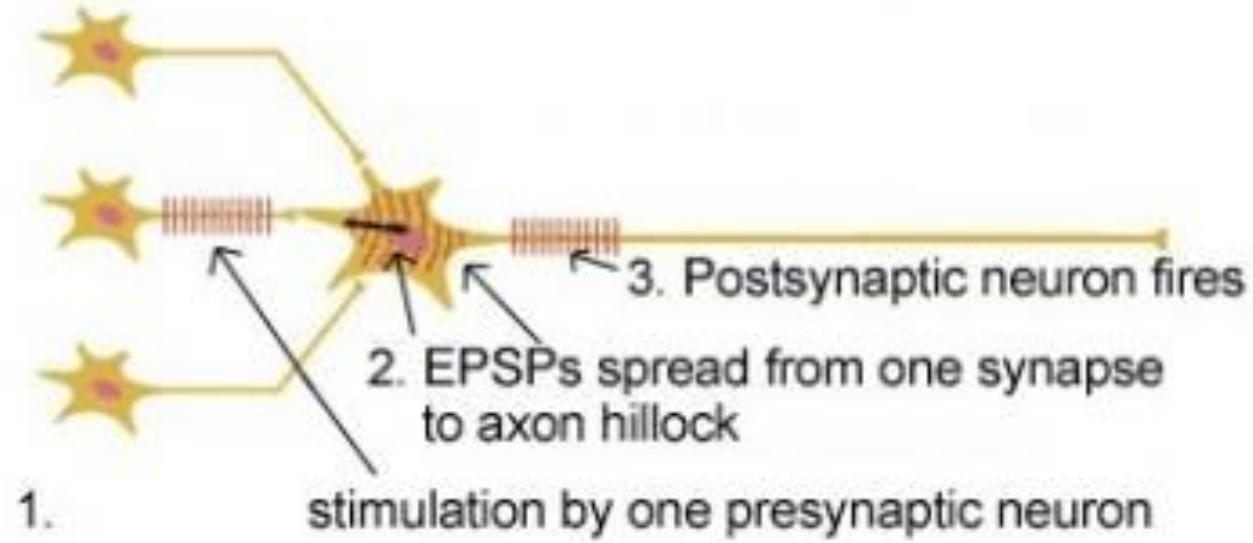
A **temporal summation occurs when one presynaptic neuron releases neurotransmitters several times over a specific period.** In this case, a **single presynaptic neuron is involved** in the production of multiple sub thresholds until it becomes sufficient to generate the firing of an action potential on the postsynaptic neuron.



Types of Summation



Spatial summation



Temporal summation

EPSPs- The current or electrical signals flowing through nerves

Axon Hillock- The region where the electrical impulse is formed in a neuron or nerve cell.

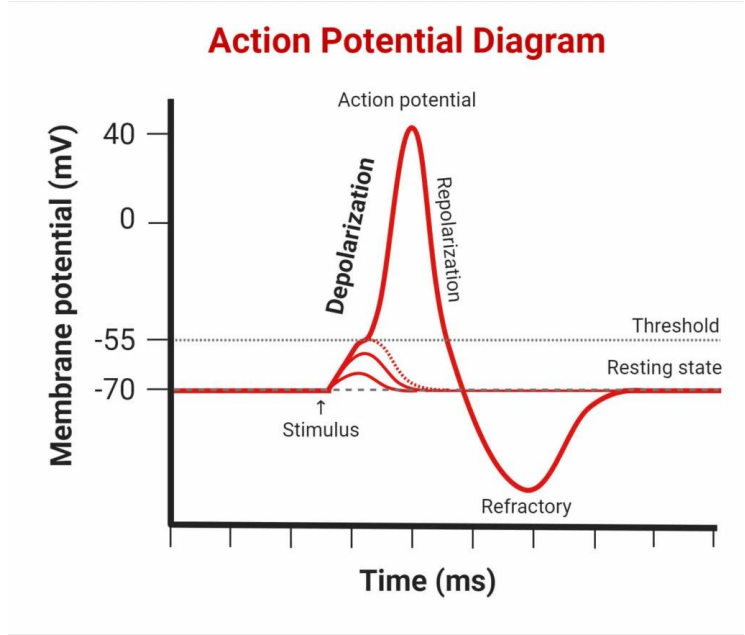
Spatial- Electrical signals flow from three or four synapses towrads the axon hillock.

Effect of Drugs on Synaptic Transmission

Many drugs are known to increase the excitability of neurons, and others are known to decrease excitability.

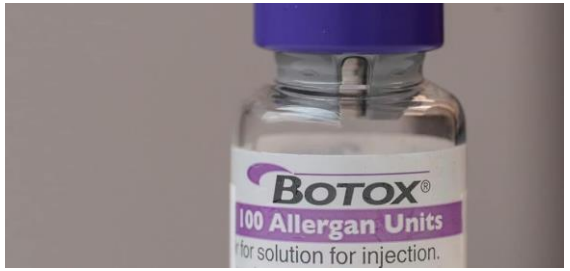
For example, **caffeine**, **theophylline**, and **theobromine**, which are found in **coffee**, **tea**, and **cocoa**, **respectively, all increase neuronal excitability**, presumably by **reducing the threshold for excitation of neurons**.

Most **anesthetics increase the neuronal membrane threshold for excitation** and thereby decrease synaptic transmission at many points in the nervous system.



BOTOX

- **Botulinum toxin (BTX)** is a neurotoxic protein produced by the bacterium ***Clostridium botulinum*** and related species.
- **It prevents the release of the neurotransmitter acetylcholine** from axon endings at the neuromuscular junction, thus **causing flaccid paralysis**. The toxin causes the **disease botulism**. The toxin is also used commercially for medical and cosmetic purposes.
- **Botulinum toxin is used** to treat certain **eye disorders** such as crossed eyes (strabismus) and uncontrolled blinking (blepharospasm), to treat **muscle stiffness/spasms** or movement disorders (such as cervical dystonia, torticollis), and to **reduce the cosmetic appearance of wrinkles**.
- In 2010, the FDA approved intramuscular botulinum toxin injections for prophylactic treatment of **chronic migraine headache.**





Neurotransmitters

- **Neurotransmitters are endogenous chemicals that allow neurons to communicate with each other throughout the body**. They enable the brain to provide a variety of functions, through the process of chemical synaptic transmission. The function of neurotransmitters is to carry chemical signals ("messages") from one neuron (nerve cell) to the next target cell. The next target cell can be another nerve cell, a muscle cell or a gland
- **Common neurotransmitters include**

Acetylcholine (associated with Alzheimer's disease and myasthenia gravis)

Serotonin (major depression)

Dopamine (Parkinson's disease)

Gamma-aminobutyric acid (GABA) and **Glutamate** (epilepsy and seizures)

Epinephrine (adrenaline) is part of the sympathetic nervous system.

Action of Neurotransmitters

- Neurotransmitters transmit one of **three possible actions** in their messages, depending on the specific neurotransmitter.

(1) Excitatory : Excitatory neurotransmitters **"excite" the neuron**.

Examples of excitatory neurotransmitters

glutamate, epinephrine and **norepinephrine**.

(2) Inhibitory : Inhibitory neurotransmitters **block or prevent the chemical message** from being passed along any farther.

e.g: **GABA** and **serotonin**.

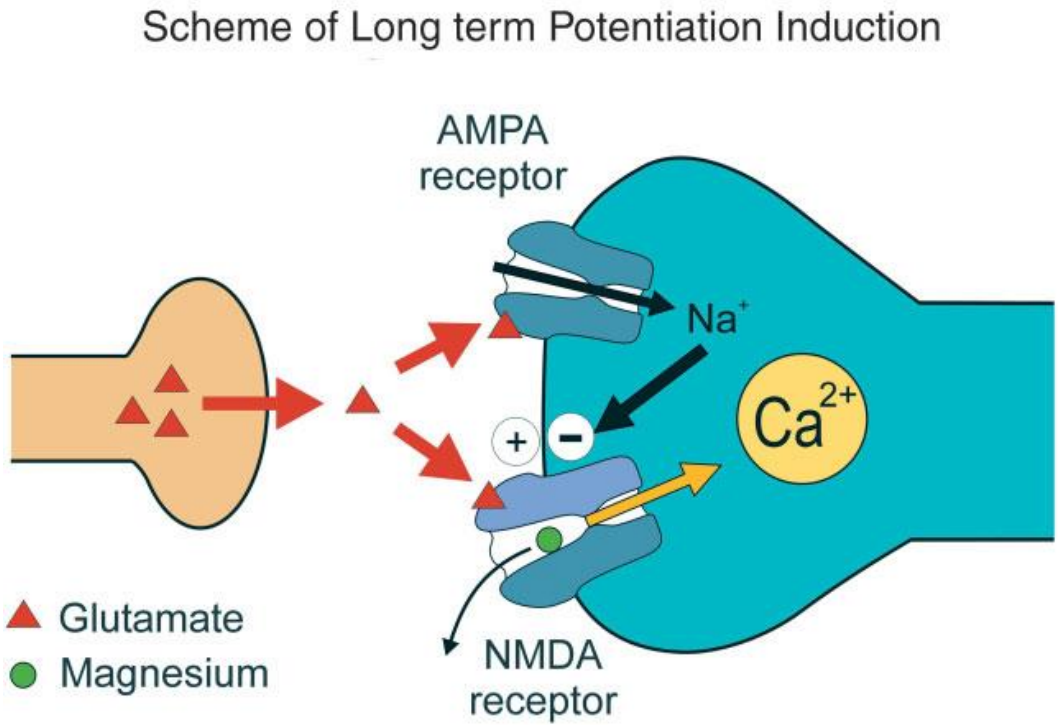
(3) Modulatory : Modulatory neurotransmitters **influence the effects of other chemical messengers**. They adjust how cells communicate at the synapse. e.g : **acetylcholine, dopamine, serotonin, histamine.**

Long-term potentiation (LTP)

Long-term potentiation (LTP) is a process by which **synaptic connections between neurons become stronger with frequent activation**. LTP is thought to be a way in which the **brain changes in response to experience, and thus may be an mechanism underlying learning and memory.**

N- methyl-D-aspartate (NMDA) receptor dependent LTP.

LTP is initiated when postsynaptic neurons become depolarized, **NMDA receptor channels are activated**, and Ca^{2+} flows into the postsynaptic neuron. NMDA receptor (in most hippocampal pathways) plays an integral role in synaptic plasticity (flexibility),a neuronal mechanism **believed to be the basis of memory formation**.



Characteristics of Neurotransmitters

Neurotransmitter	Secretion	Actions
Acetylcholine	Motor cortex, basal ganglia, motor neuron, preganglionic neuron of ANS, postganglionic neuron of parasympathetics	Mostly excitation, Inhibition in some parasympathetics
Norepinephrine	Brain stem, hypothalamus	Mostly excitation, some inhibition
Dopamine	Substantia nigra of basal ganglia	Inhibition
Glycine	Spinal cord	Inhibition
Glutamate	Sensory terminal, cerebral cortex	Excitation
GABA	Spinal cord, cerebellum, basal ganglia, cortex	Inhibition
Serotonin	Brain stem, spinal cord	Inhibition
Nitric oxide	Brain	Excitation (gas)
Neuropeptides	Synthesized by ribosome in the neuronal cell body	Much more prolonged action: Ca channel closure, metabolic change, gene activation/deactivation, alteration in number of receptors

Classifications of Neurotransmitter

- Neurotransmitters classified into two types:

(1) Small-molecule transmitters

(2) Large-molecule transmitters - Neuropeptides.

Synthesis and storage of neurotransmitter groups differ.

Small molecule neurotransmitters are synthesized and stored in the terminal for **fast release**.

Neuropeptides are synthesized in the cell body and must be transported to the terminal, which can lead **to slower release**.

Small-molecule transmitters :

dopamine , **glutamate**, **GABA**, **acetylcholine**, **serotonin** and **histamine**.

Class 1: Acetylcholine.

Class 2: different amines , norepinephrine, epinephrine, dopamine, serotonin, and histamine.

Class 3: different amino acids such as gamma-aminobutyric acid (GABA), glycine, glutamate, and aspartate.

Class 4: nitric oxide (NO). presents in areas of brain that are responsible for long-term behavior and memory.

Neuropeptides

Large-molecule transmitters – Neuropeptides

(A) Hypothalamic-releasing hormones.

(B) Pituitary peptides.

(C) Peptides that act on gut and brain (enkephalin, substance P, gastrin, Cholecystokinin (CCK), Vasoactive intestinal peptide (VIP) , insulin, glucagon).

(D) Neuropeptides from other tissues (angiotensin II, bradykinin, carnosine, sleep peptides, calcitonin).

Neuropeptides are different from small-molecule transmitters :

(A) They are not synthesized in the cytosol of the presynaptic terminals but by the ribosome in the soma.

(B) Neuropeptides are more potent as the small-molecule transmitters

(C) They usually cause much more prolonged action.

(D) The transmitter containing vesicles are autolyzed after the release of their transmitter and are not reused.

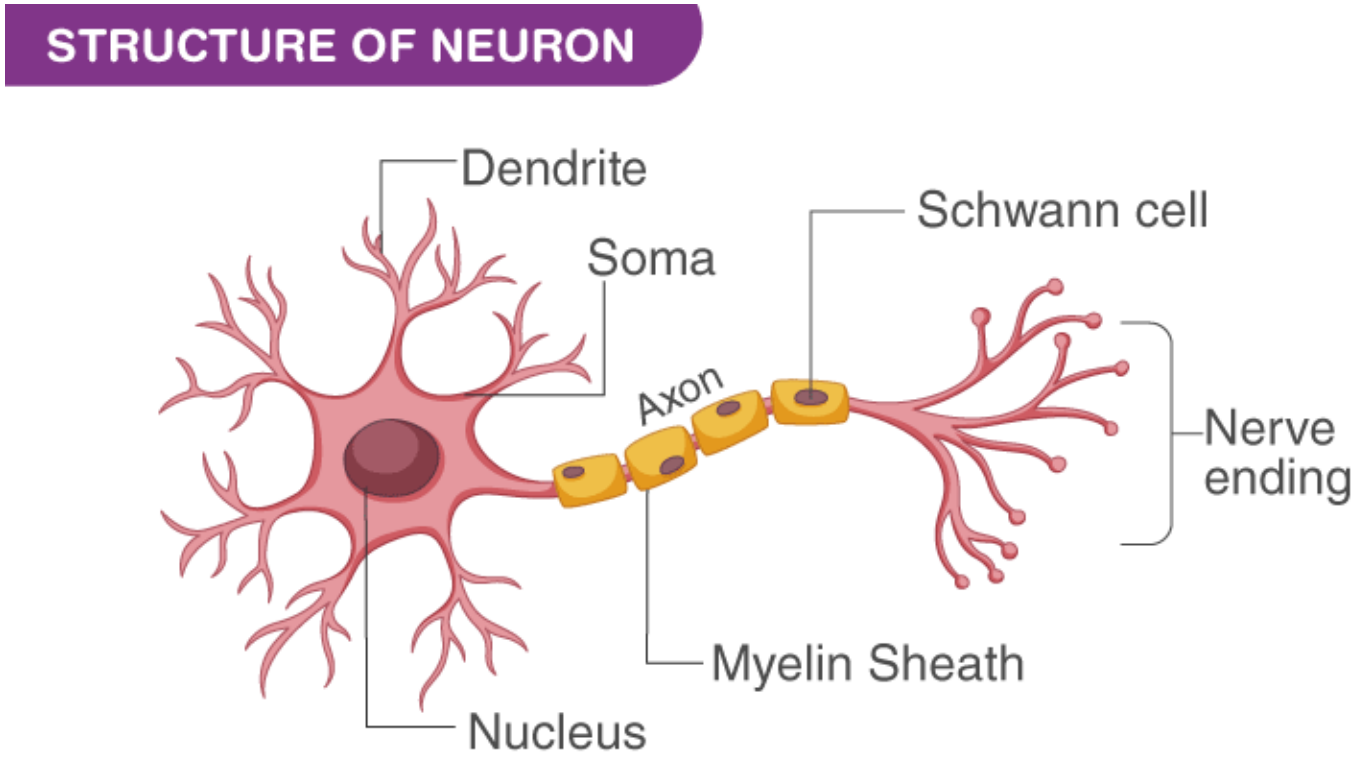
Structure of Neuron

A neuron has three main parts:

(1) Cell body or Soma

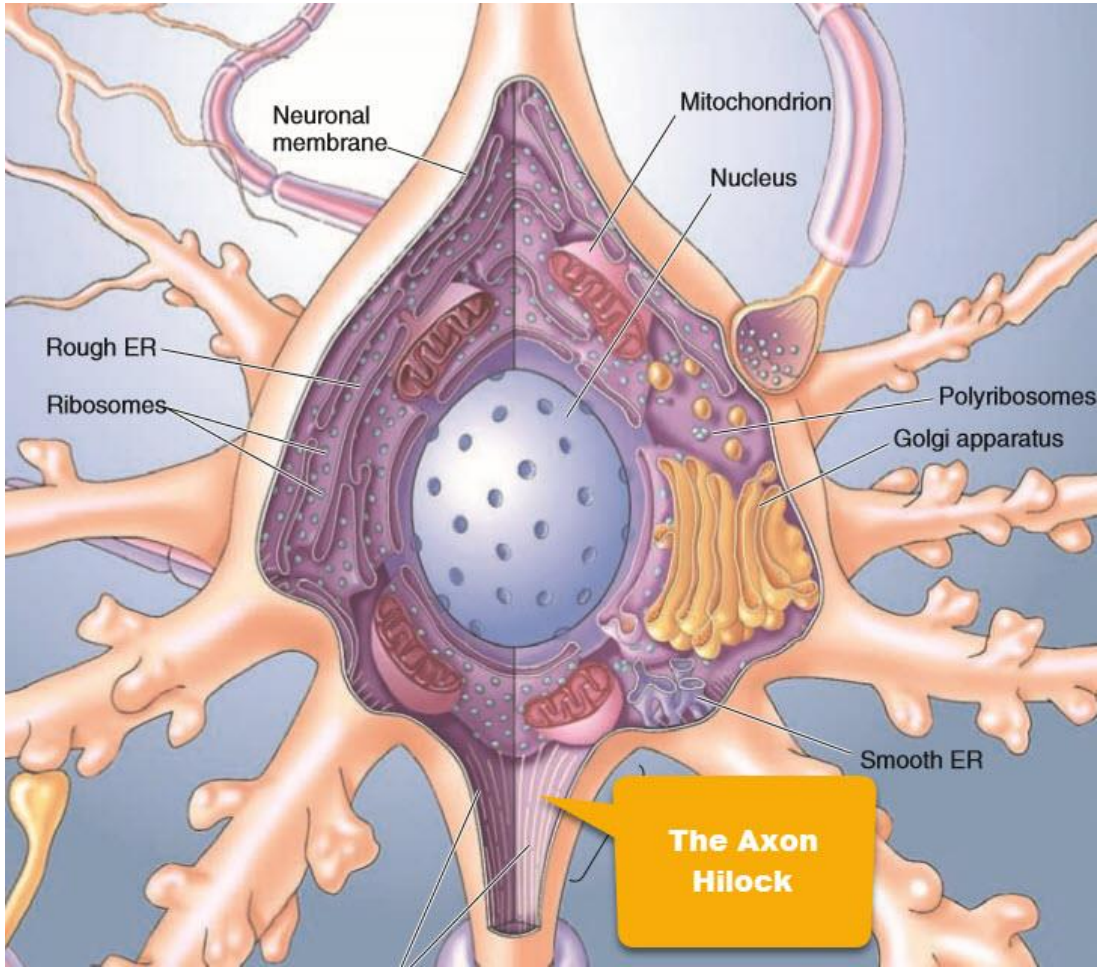
(2) Axon

(3) Dendrites



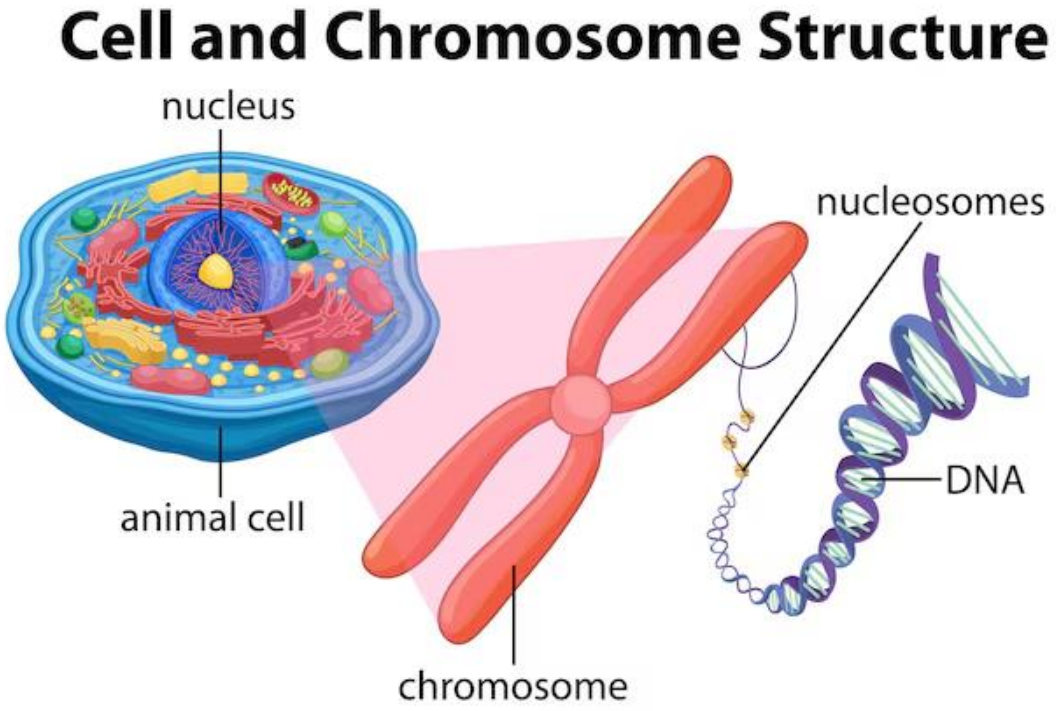
The Soma

- The **Soma (Latin, soma: body)** or cell body of a neuron.
- the main site within a neuron. It contains all the necessary organelles such as the **cellular nucleus, Golgi apparatus, mitochondria, polysomes, cytoskeletal elements, and lysosomes**.
- The watery fluid inside the cell, called the cytosol , is potassium rich solution. **Cytosol** also known as **cytoplasmic matrix** is one of the liquids found inside cells (intracellular fluid (ICF)).

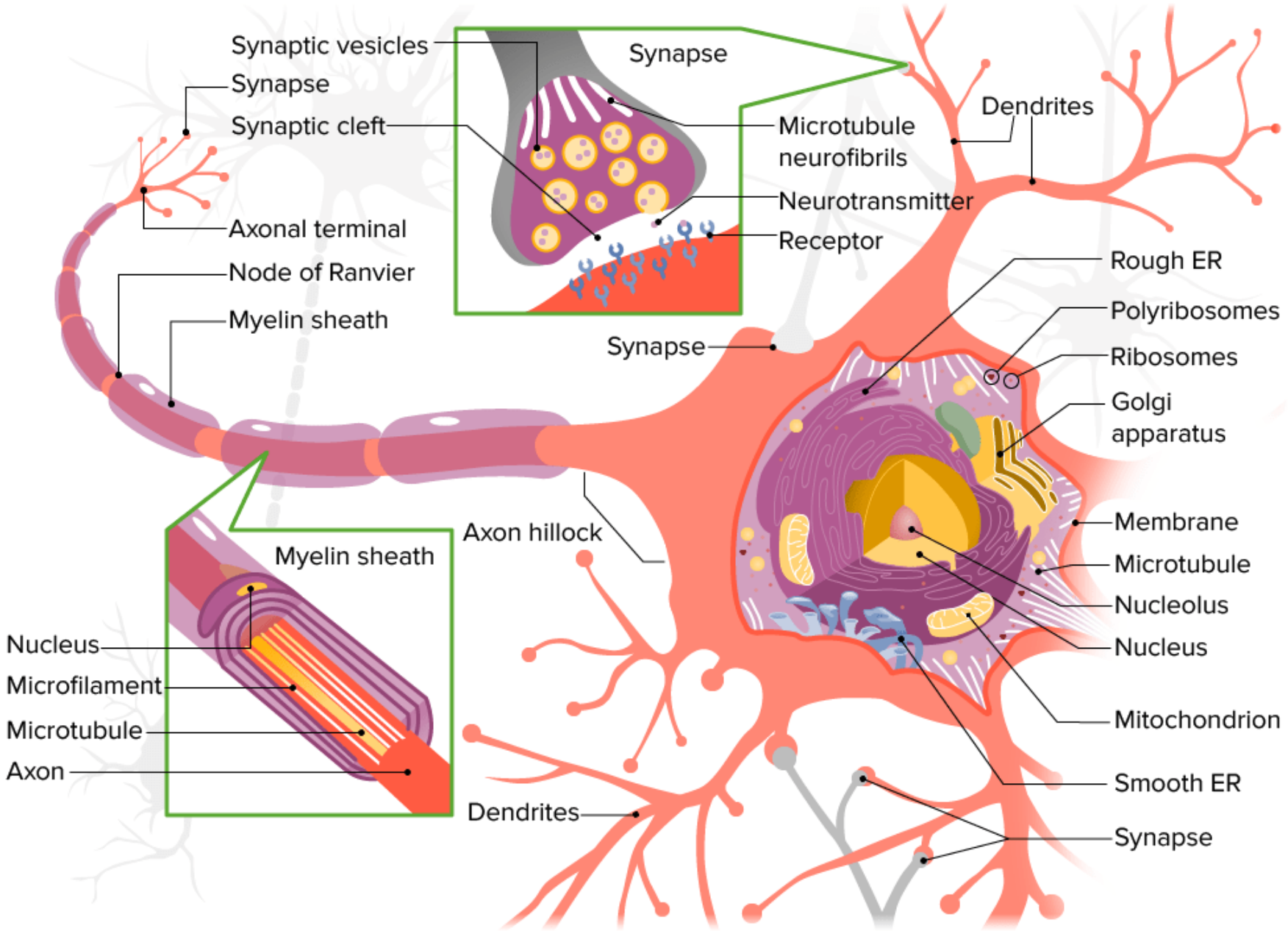


The Nucleus

- **Nucleus controls the cell's activities and contains the cell's genetic material , deoxyribonucleic acid, or DNA**. Each human cell contains around 2 meters (~6 feet) of DNA, wrapped up into structures called **chromosomes.**
- Some instances of serious psychiatric disorders, including **autism** and **schizophrenia,** were recently shown to be caused by gene copy number variations in the affected children.
- **Fragile X syndrome**, a disorder that manifests as intellectual disability and autism and is caused by disruption of a single gene.



- Rough Endoplasmic Reticulum (ER)
- Smooth endoplasmic reticulum (ER)
- Golgi Apparatus
- Mitochondria
- The Neuronal Membrane



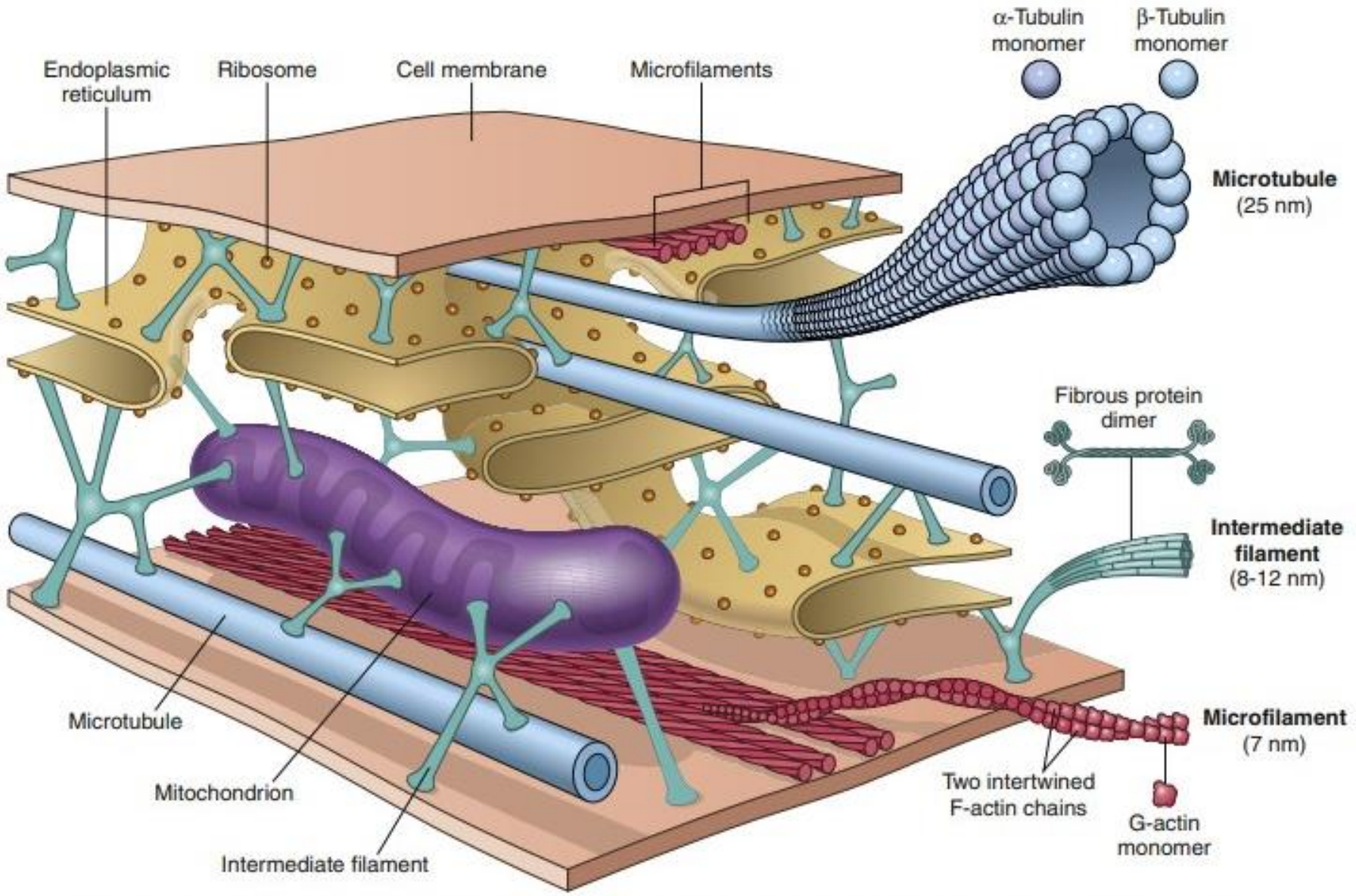
- **Figure**

Cell cytoskeleton composed of protein fibers called

(1)Microfilaments

(1) Intermediate filaments,

(3) Microtubules



Cytoskeleton

Neuronal cytoskeleton is composed by :

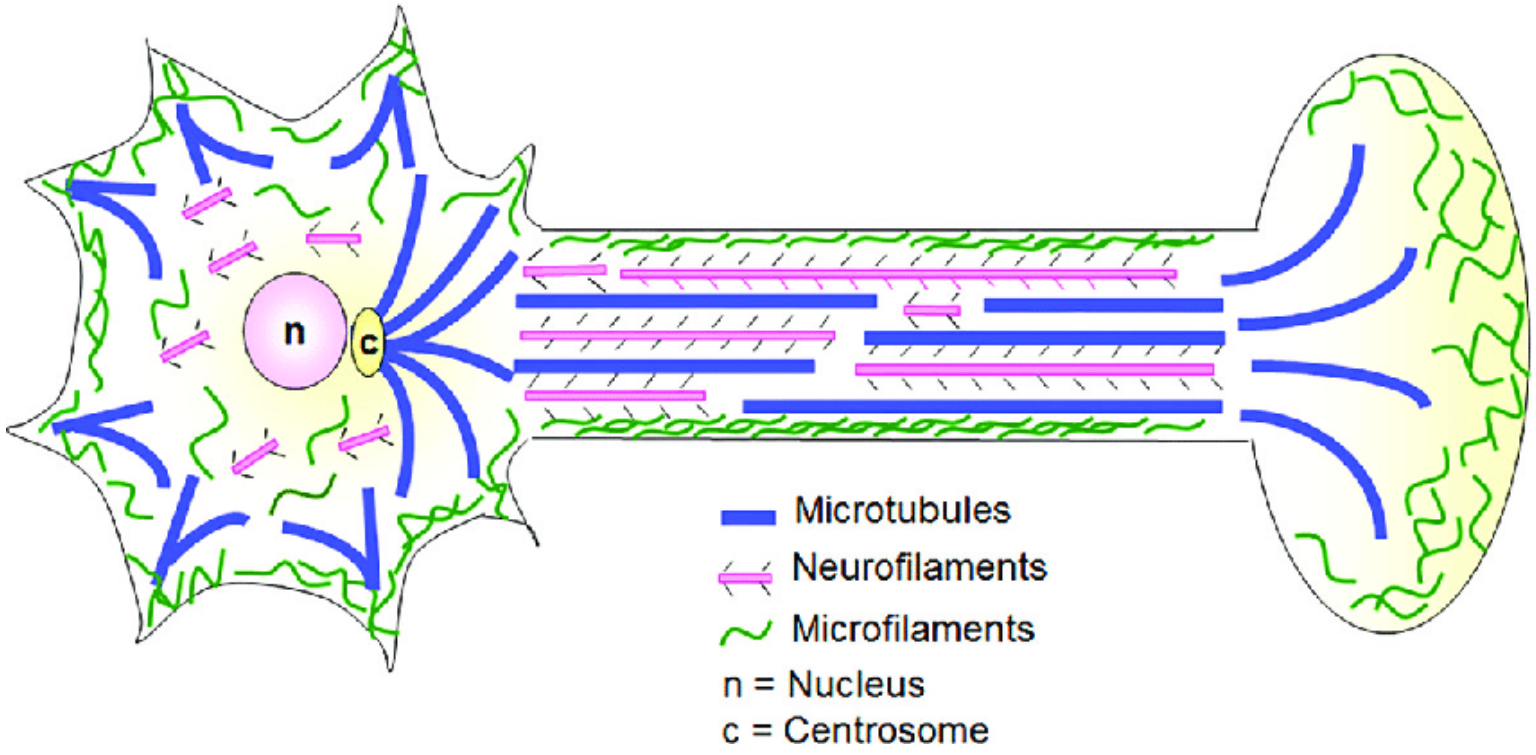
(1) Microfilaments

(2) Microtubules

(3) Intermediate filaments.

First, they provide **structural organization** for the cell interior, helping to establish metabolic compartments.

Second, cytoskeletal structures serve as **tracks** for intracellular transport.



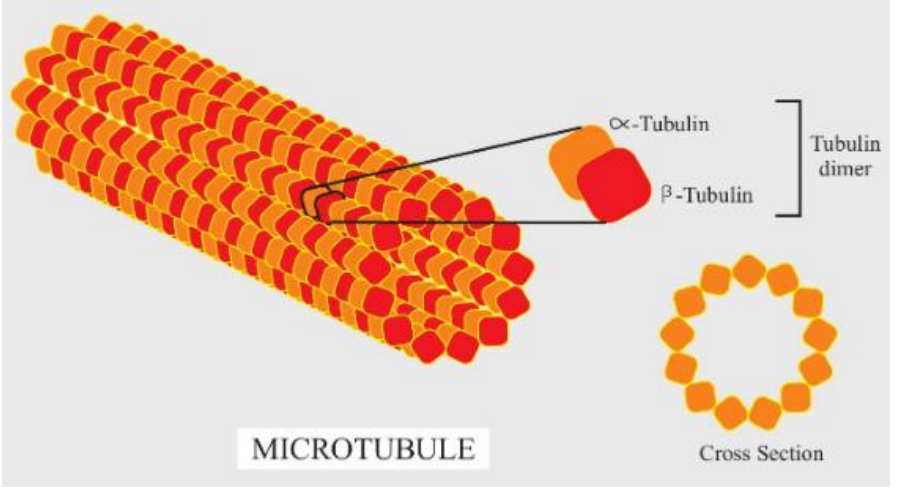
Microtubules (Neurotubules)

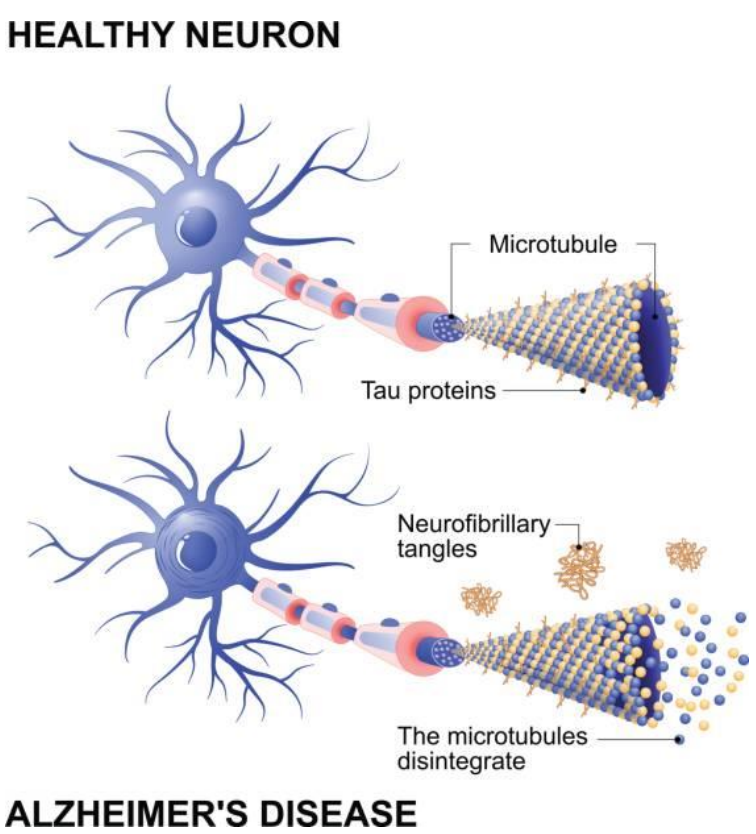
Microtubules : occupying axons and dendrites as paraxially (on axix) aligned arrays. These microtubule arrays **provide a structural backbone for axons and dendrites** that allows them to acquire and maintain their specialized morphologies.

Microtubules are hollow cylinders that are **made up of tubulin protein**.

Microtubule-associated proteins (MAPs) regulate the dynamic turnover of microtubules.

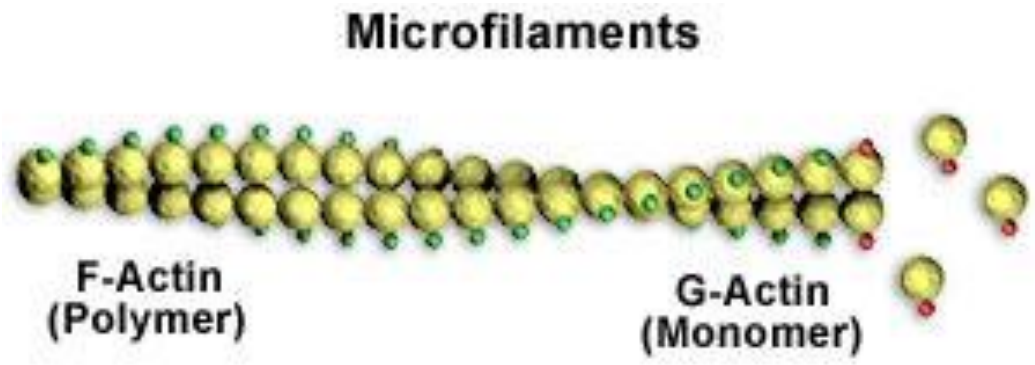
Tau is a microtubule-associated protein involved in regulating axon integrity and function. **Tau aggregation and deposition are hallmarks of Alzheimer's disease (AD).**

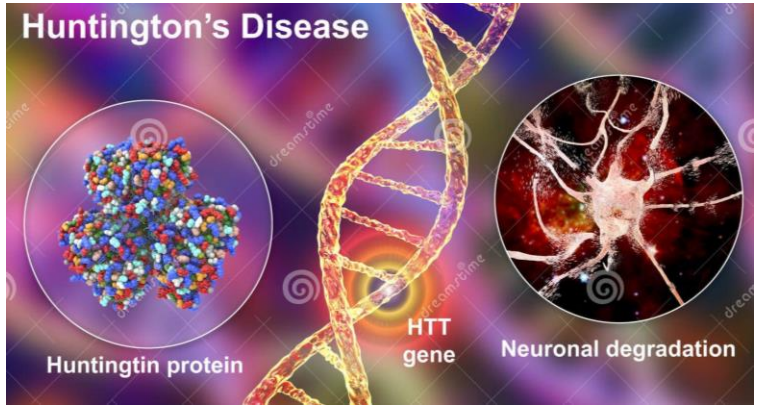


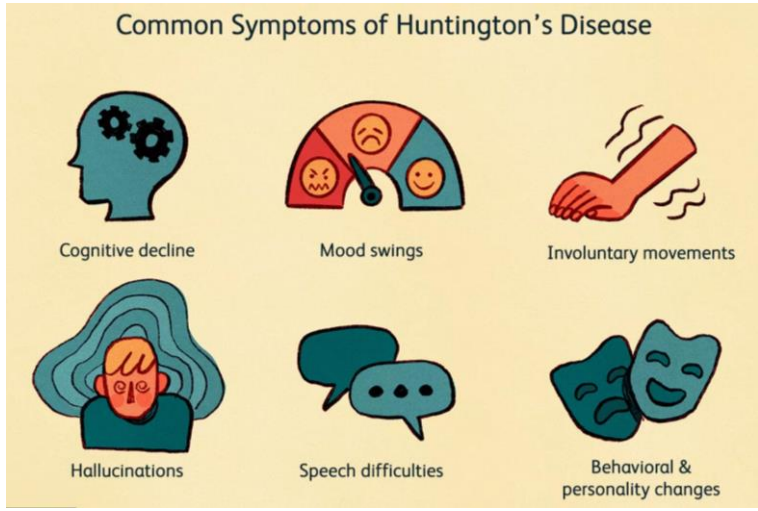


Microfilaments

- **Microfilaments are composed of two strands of actin monomers** twisted into helical filaments.
- Microfilaments well-developed immediately beneath the plasma membrane as the **cortical cytoskeleton.**
- Actin is believed to play a role in **changing cell shape**. Actin filaments are involved in the mechanism of **muscle contraction**.
- **Actin dysfunction** may result in age-associated diseases including **cancer**, **vascular diseases**, and **neurodegenerative diseases**.
- **Huntington's disease (HD)** is one of the inheritable neurodegerative disease.





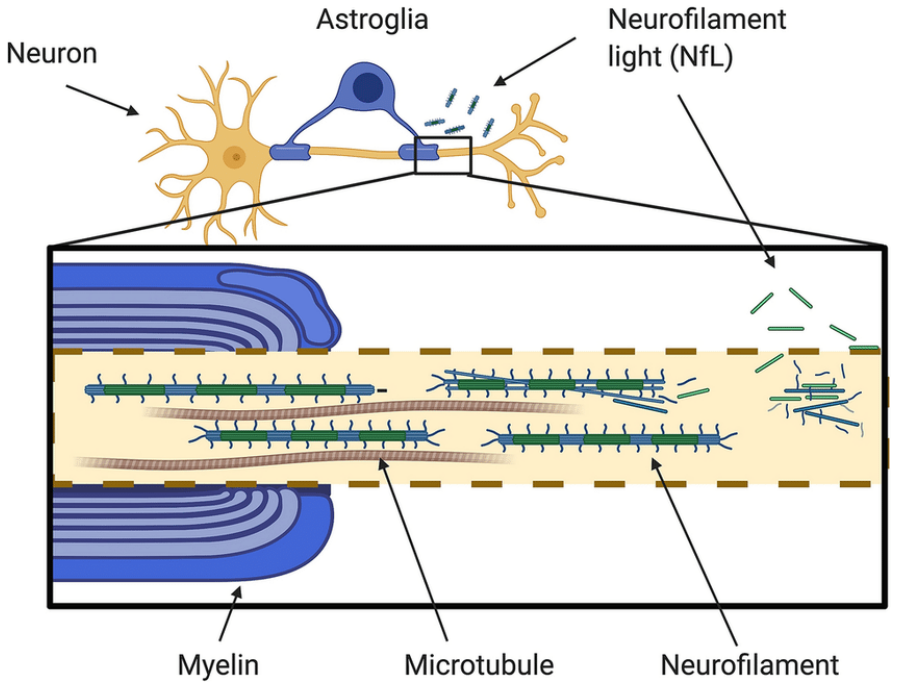


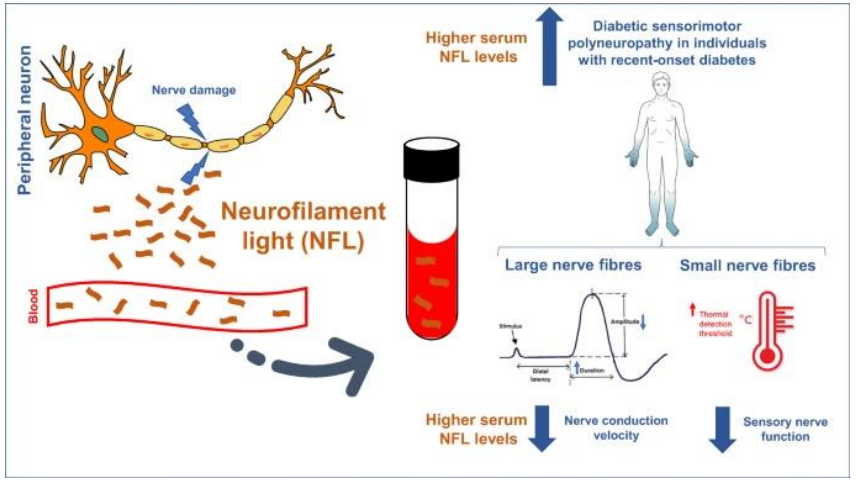
Neurofilaments (NF)

- **Neurofilaments** with a diameter of 10 nm, are intermediate in size between microtubules (20 nm) and microfilaments (5 nm).
- They exist in all cells of the body as **intermediate filaments**, only in neurons are they called neurofilaments.
- **Intermediate filaments** are generally strong ropelike filaments that often work together with microtubules, **providing strength and support for the fragile tubulin structures**. They are called intermediate because their average diameter is between that of narrower actin microfilaments and wider myosin filaments found in muscle cells.
- **Their functions are mainly mechanical** , provide structural support in neuronal axons.

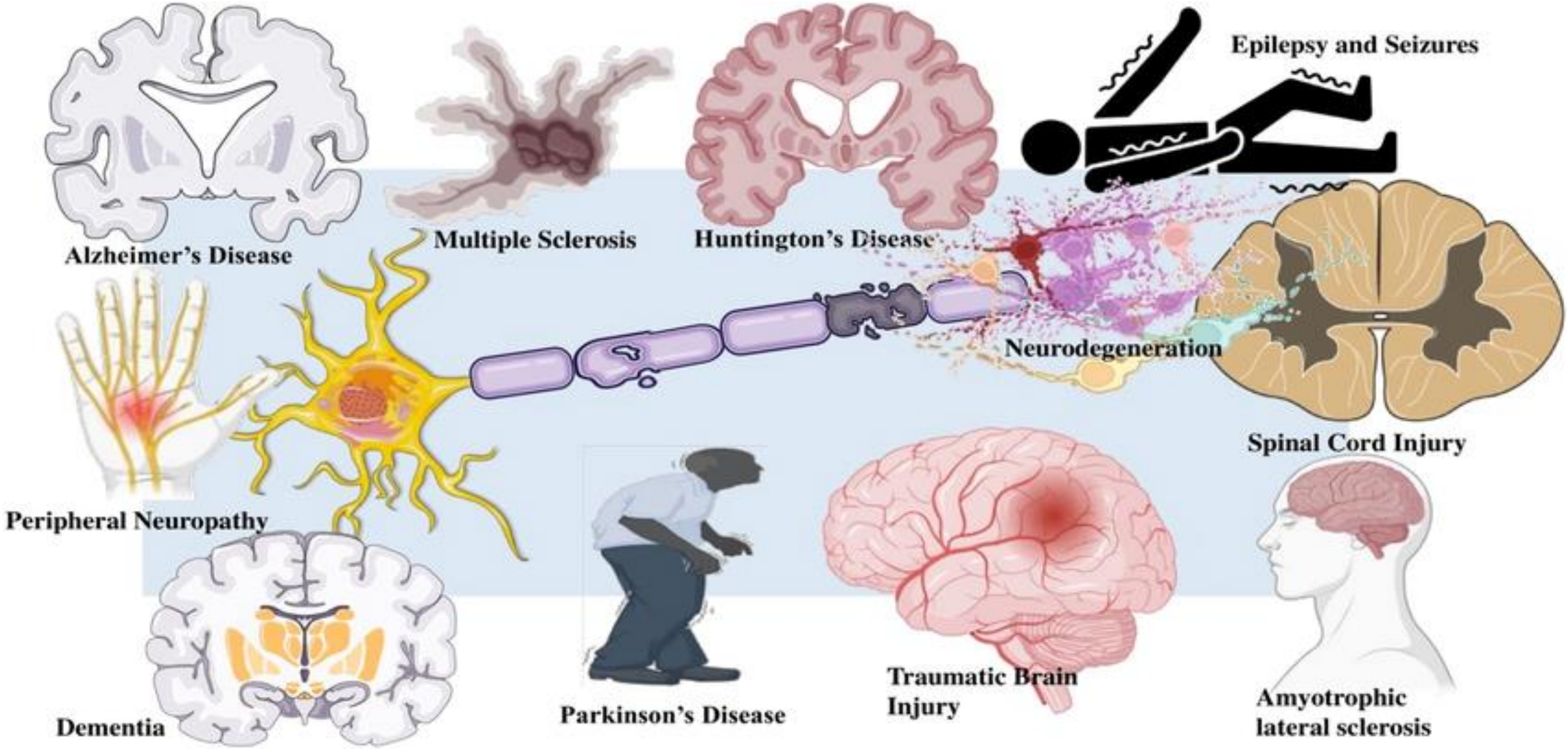
NFs represent very promising biomarkers for **Motor neuron diseases(MNDs).**

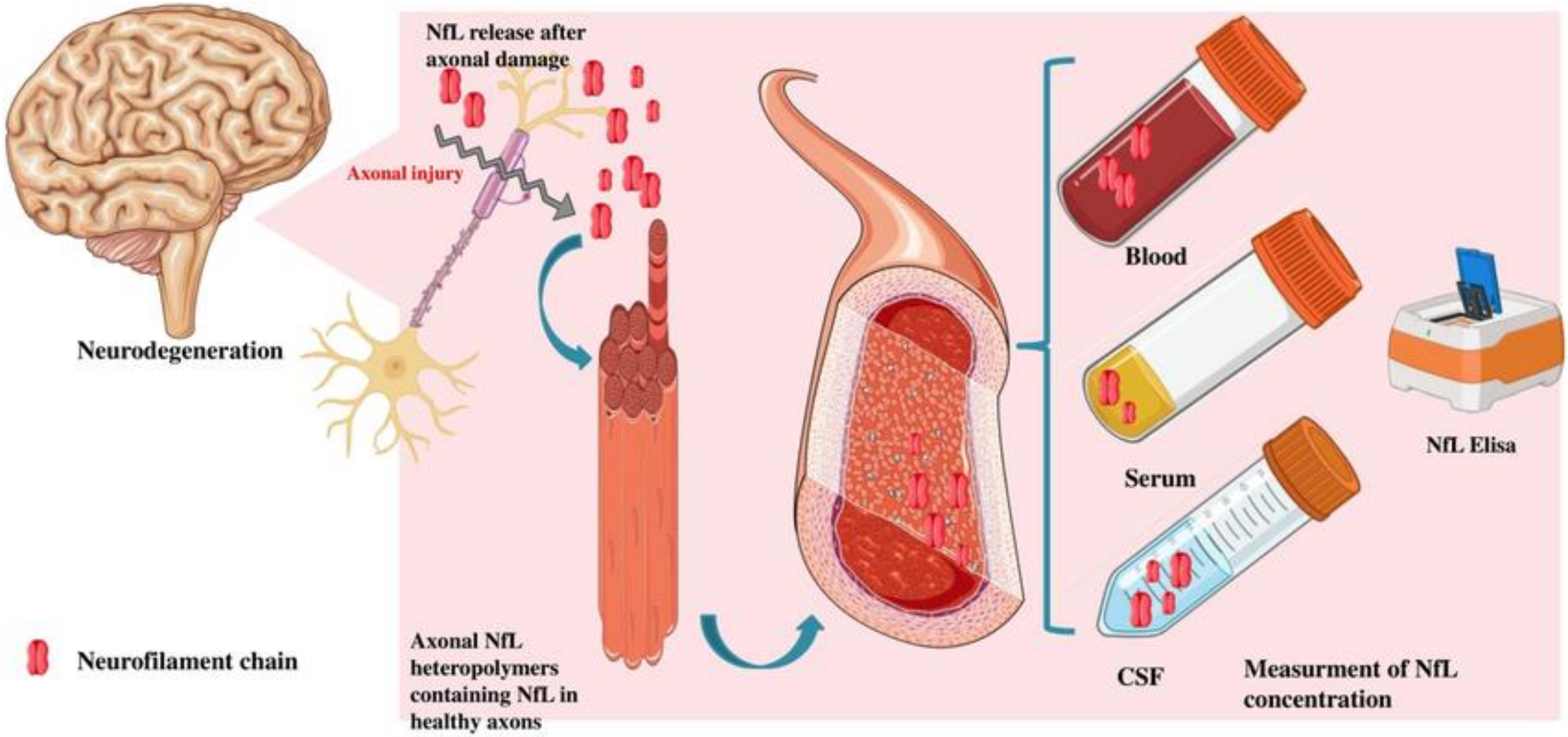
NF e.g Neurofilament light (NfL) elevated in multiple **neurodegenerative disorder** like **Alzheimer disease (AD) dementia** , **multiple sclerosis** and **Diabetic neuropathy**.





Neurofilament as biomarker in different neurological disorders




Neurodegeneration
NfL release after axonal damage
Axonal injury
Axonal NfL heteropolymers containing NfL in healthy axons
Blood
Serum
CSF
NfL Elisa
Measurment of NfL concentration
Neurofilament chain

Axoplasmic Transport

Axoplasmic transport also called **Axonal transport**.

Absence of ribosomes in the nerve terminal means that the proteins of the axon must be synthesized in the soma and then shipped down the axon.

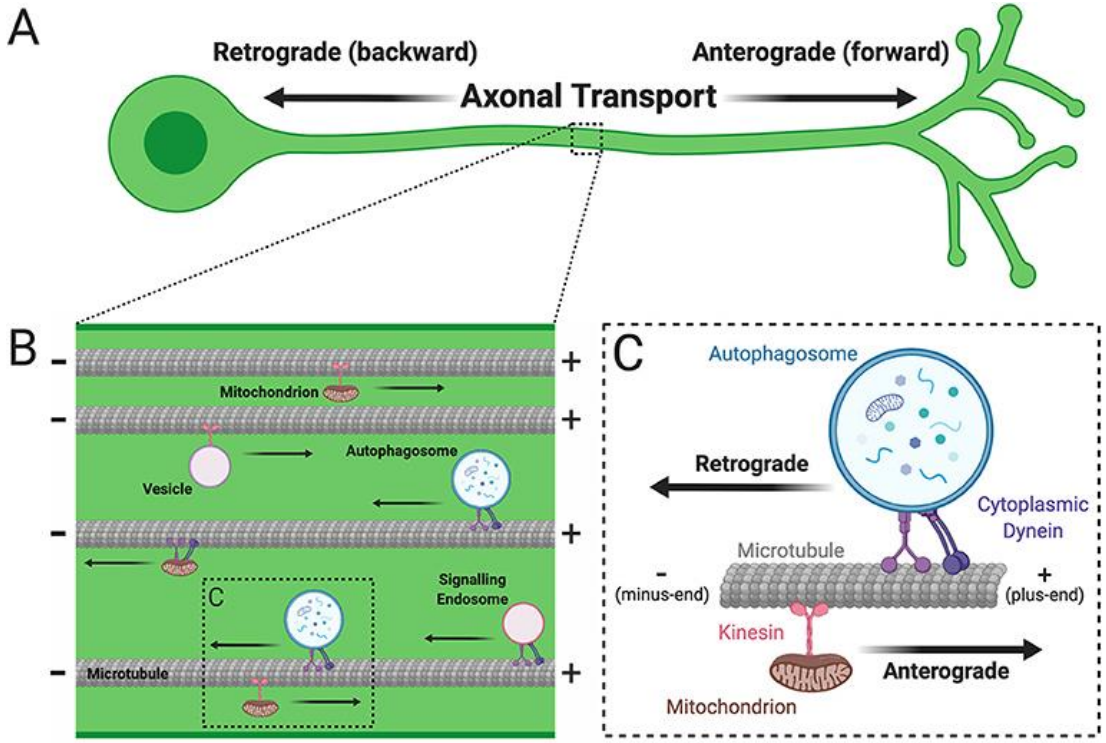
Axoplasm is the cytoplasm within the axon of a neuron.

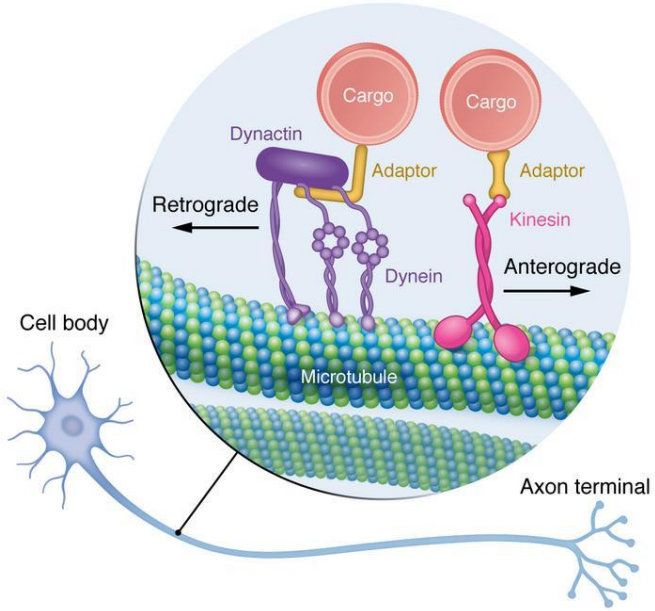
Axoplasmic transport refers to the dynamic flow of materials within the axon of a neuron. It involves the transportation of proteins and other organelles from the cell body (soma) to the distal end of the axon and vice versa.

Movement **toward the cell body (Soma)** is called **retrograde transport** and movement **toward the synapse** is called **anterograde transport.**

Dynein is the motor for **Retrograde** axonal transport of organelles. **(D-R) .**

Kinesins are responsible for the transport in an **Anterograde** manner. **(K-A) .**






THANK
YOU