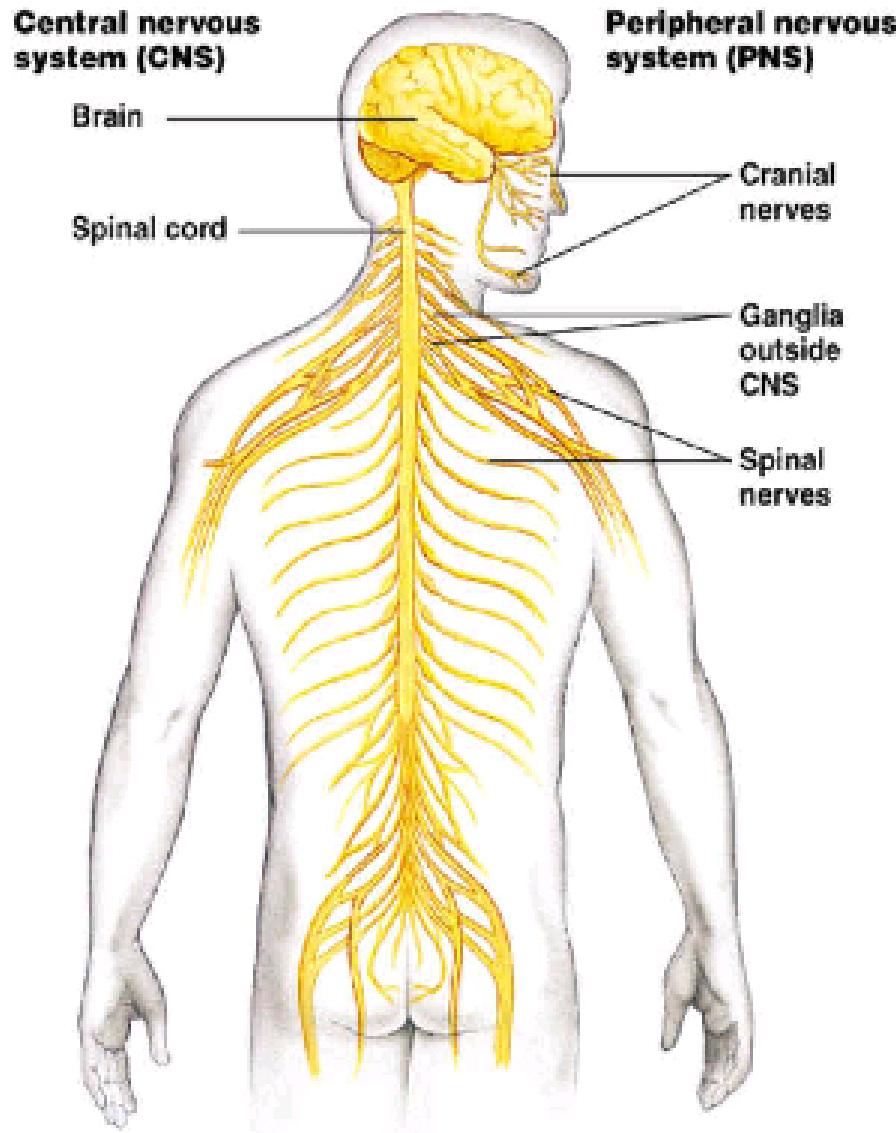


Introduction:
organization of Nervous
system, neurons,
classification of nerves,
neuroglia

Organization of Nervous System



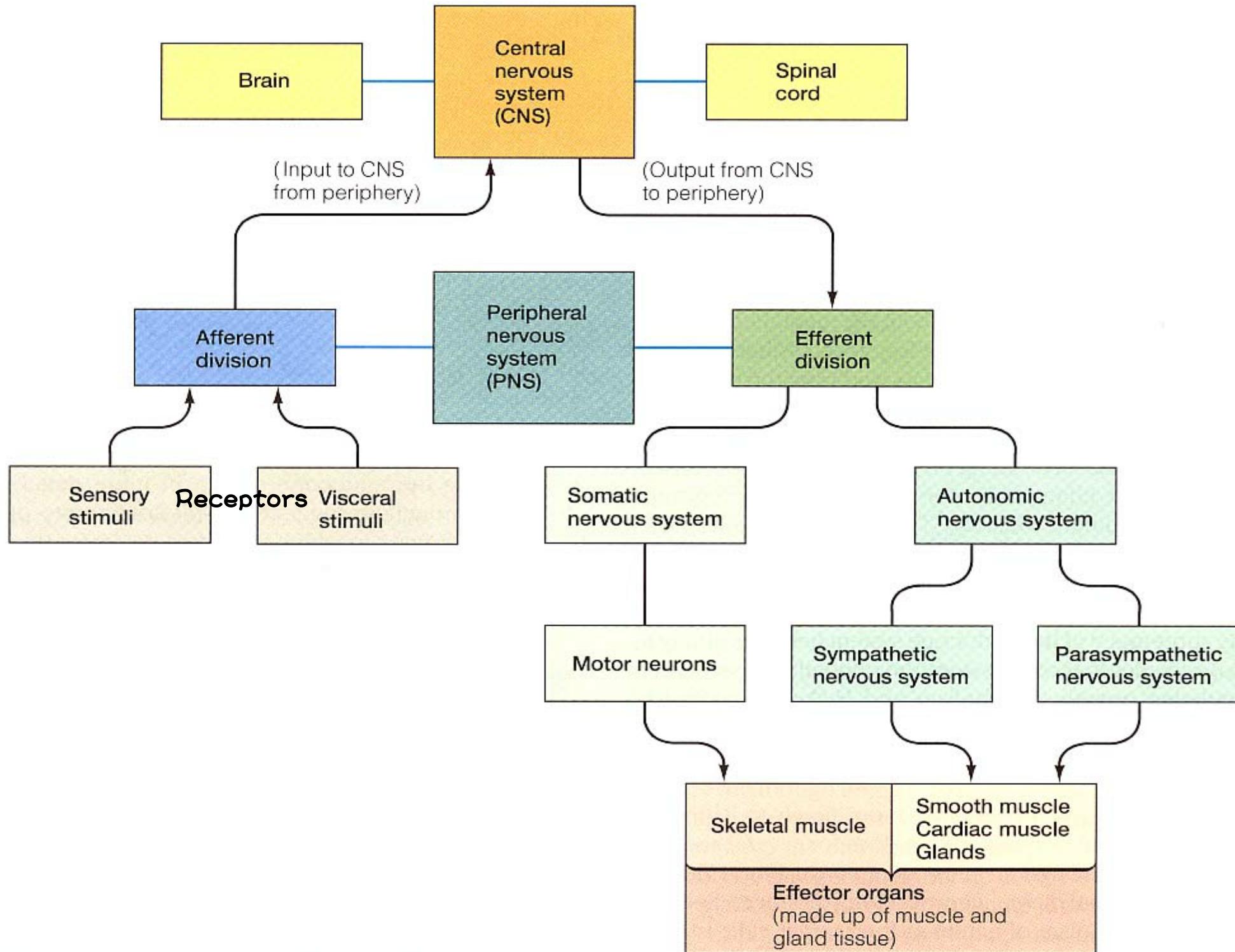
(reception, integration,
interpretation and transmission of
information)

Central Nervous system

Brain
Spinal cord

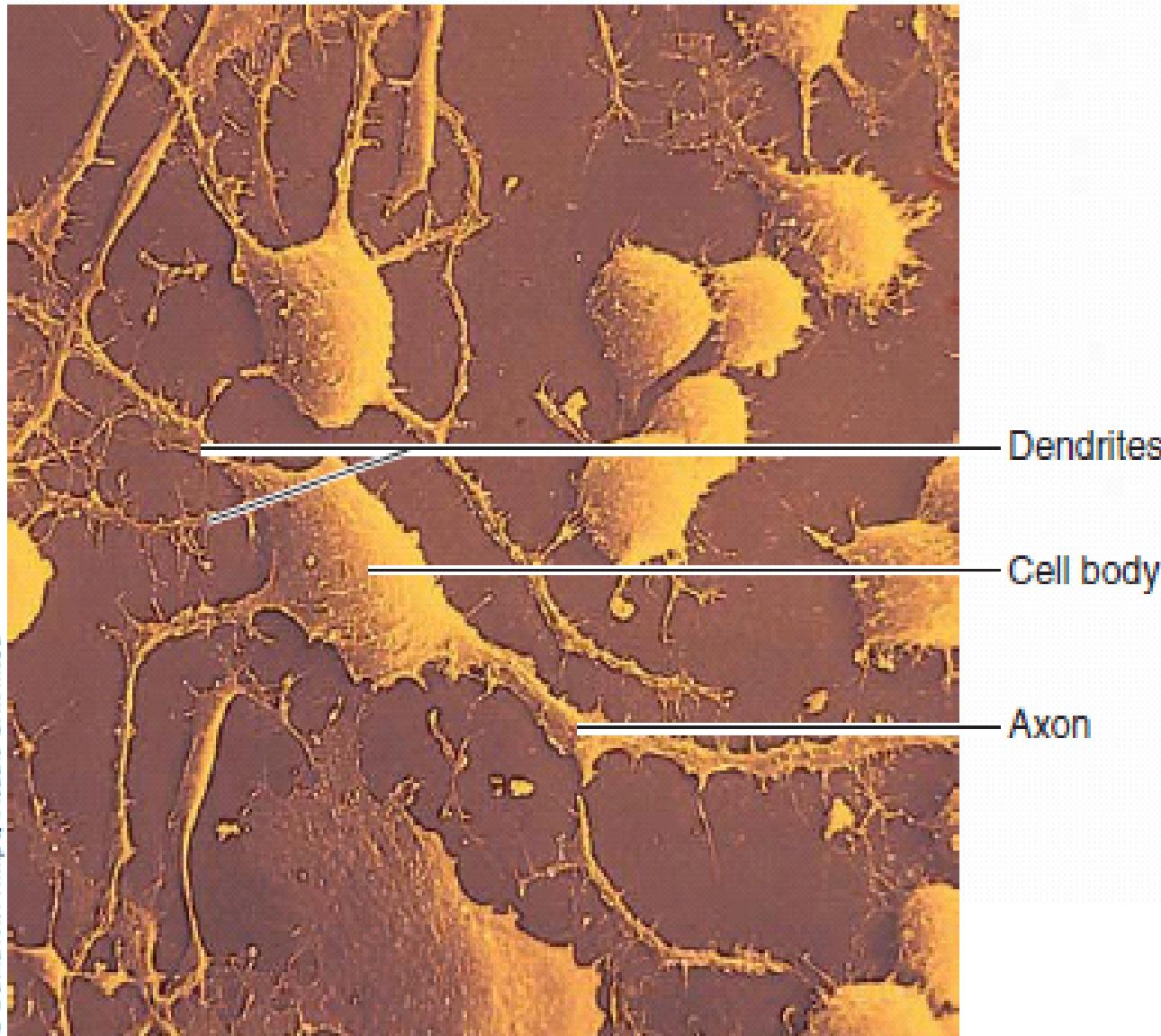
Peripheral Nervous system

Somatic nervous



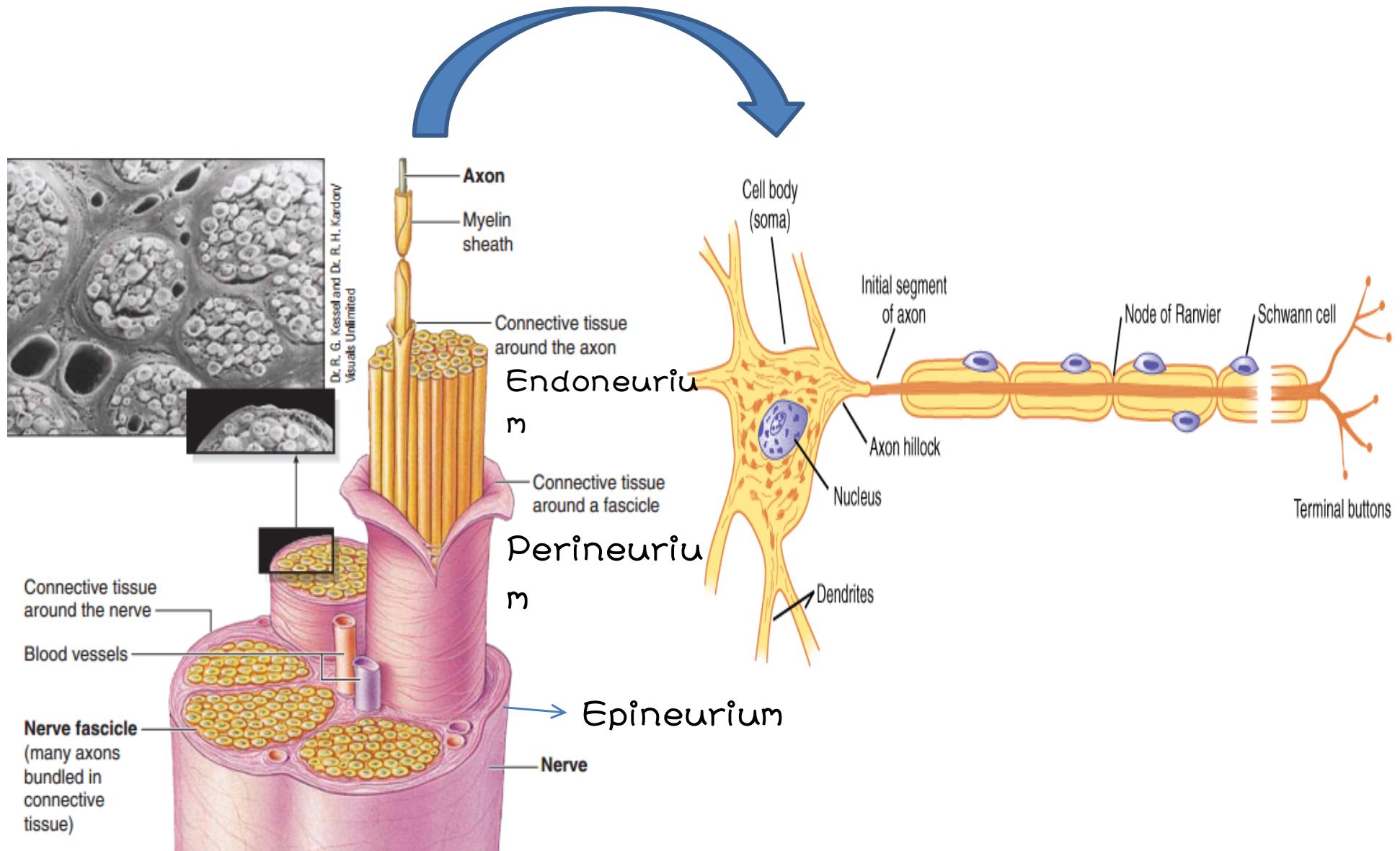
• FIGURE 5–1 Organization of Nervous System

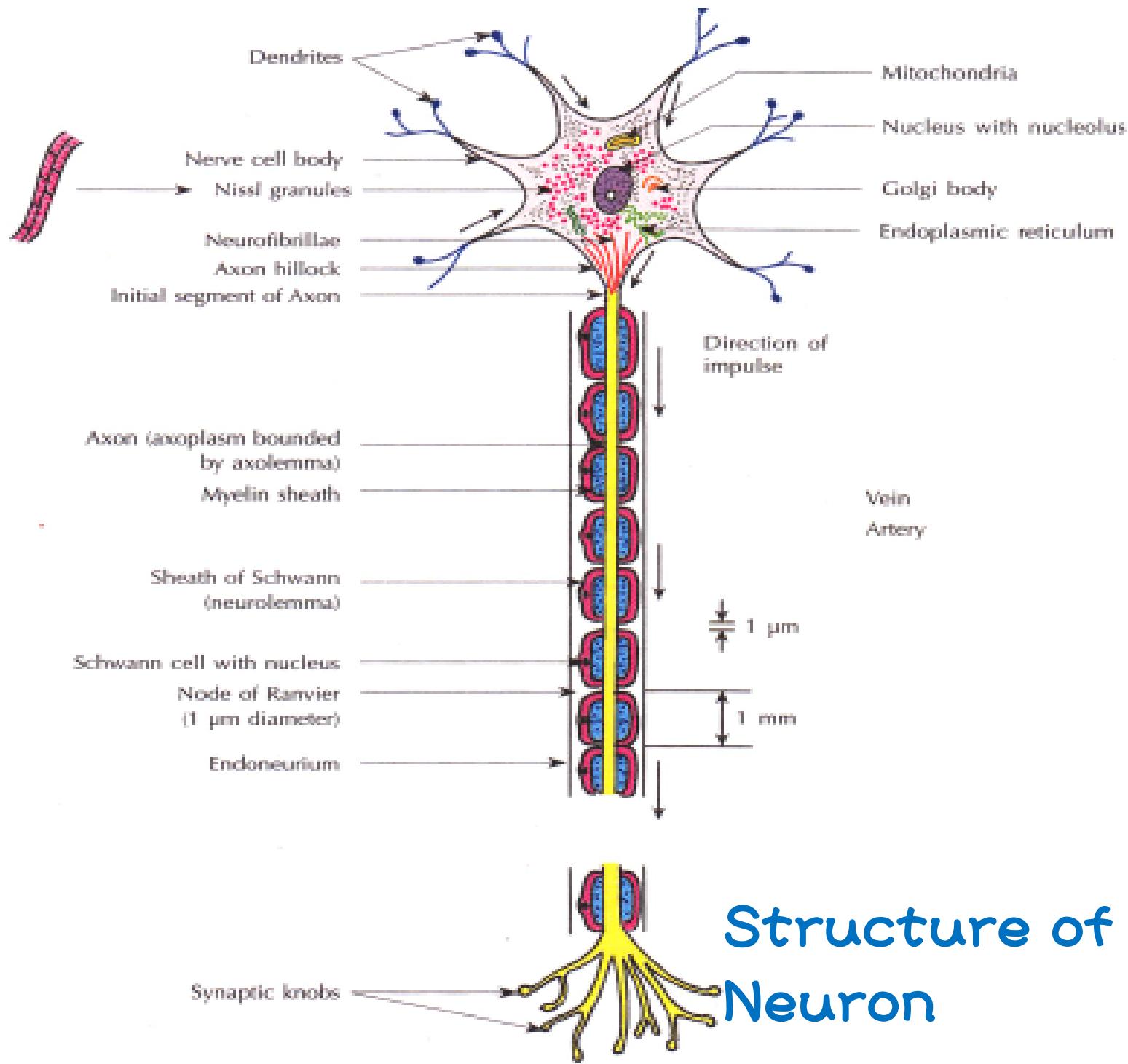
Anatomy of most common type of neuron



- Structural and functional unit of the nervous system
- $> 10^{12}$ neurons
- CNS - Nucleus
- Outside - Ganglia

Structure of the Neuron



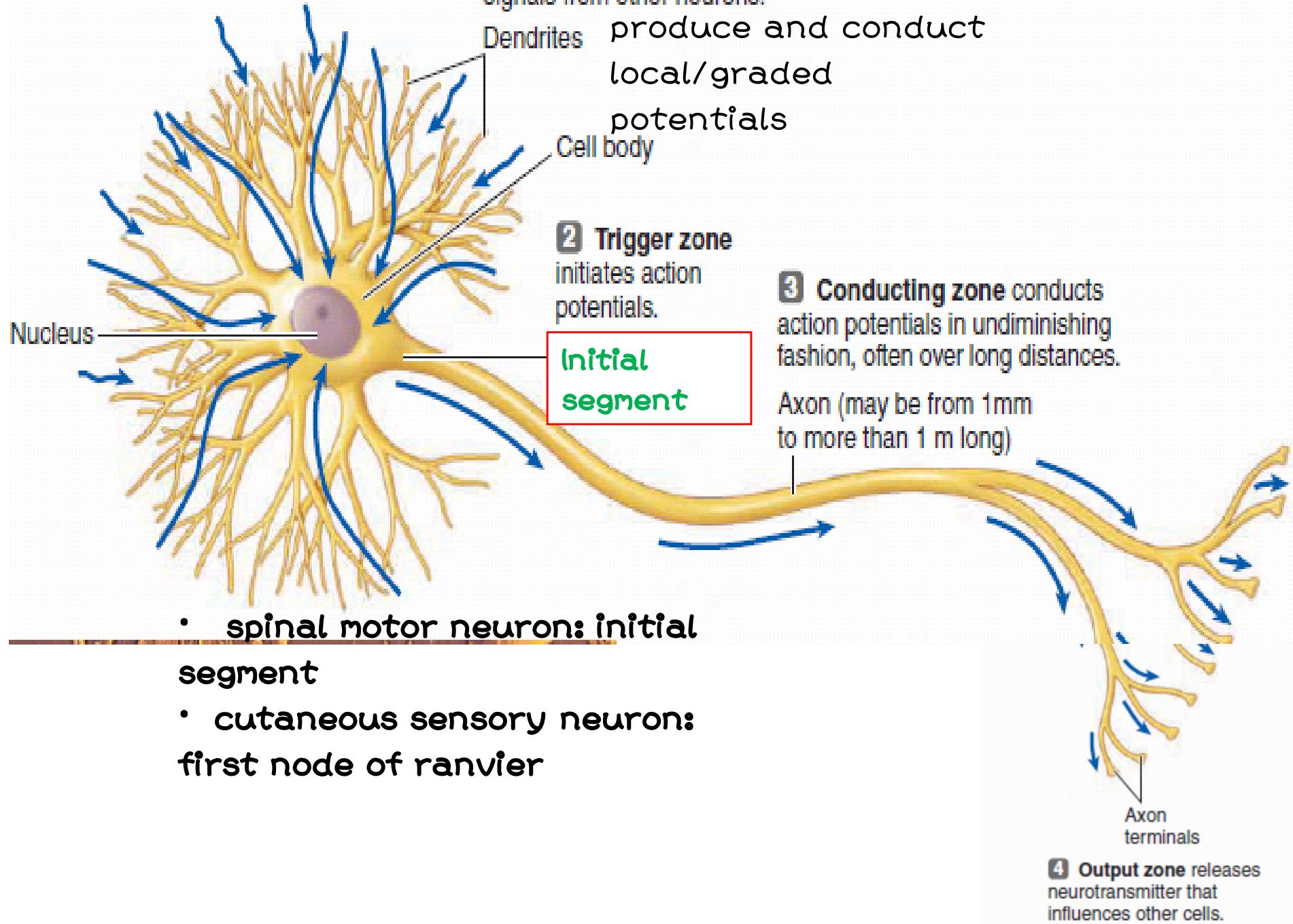


Cell body or soma

- Cytoplasm
 - Nissl body
 - Organelles
 - Neurofibrillae
- Nucleus
- Centrosome: absent
- A Nissl bodies, also known as **Nissl or tigroid substance**, is a large granular body, which are rough endoplasmic reticulum (RER) with rosettes of free ribosomes, and are the site of protein synthesis. Nissl bodies under pathological conditions may dissolve and disappear (chromatolysis).

Axon

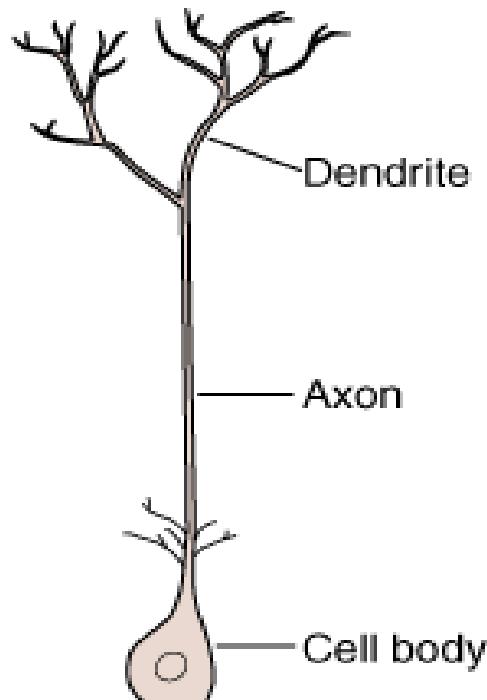
- Axolemma
- Terminal button or synaptic knob



Classification of Nerves

Depending upon number of poles

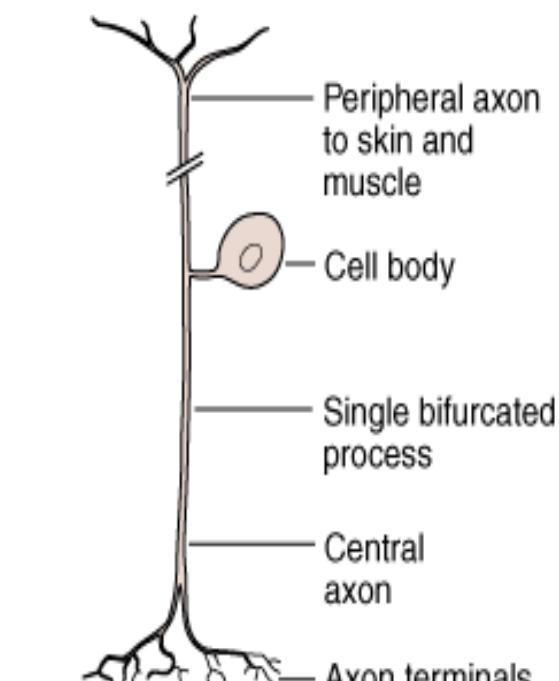
A Unipolar cell



Invertebrate neuron

Eg. Embryonic
stage in human
being

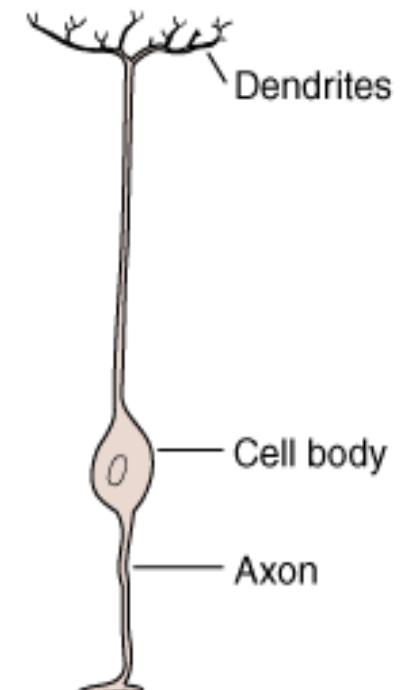
C Pseudo-unipolar cell



Ganglion cell of dorsal root

Sensory
neuron

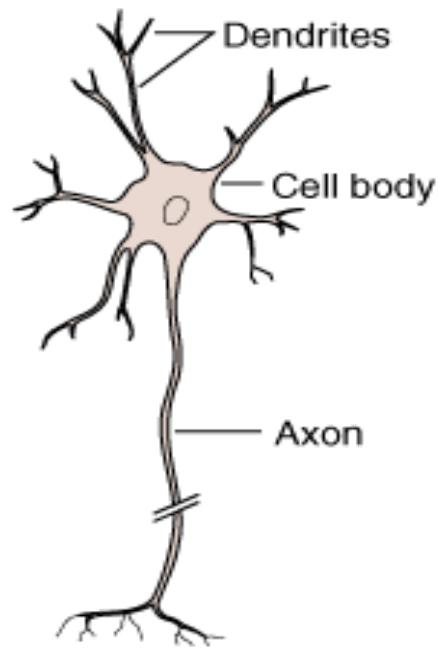
B Bipolar cell



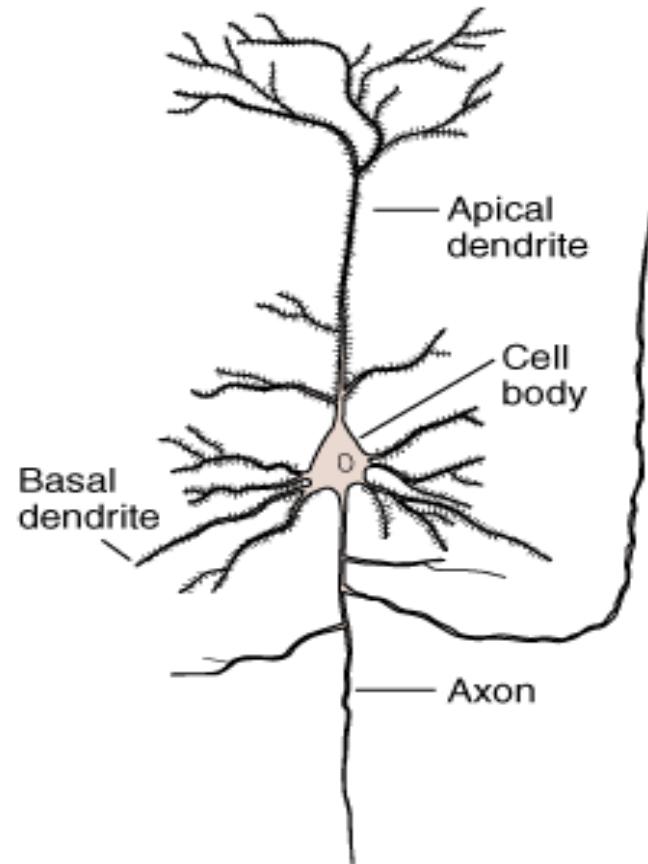
Bipolar cell of retina

Retina,
Vestibular
and cochlear
ganglia

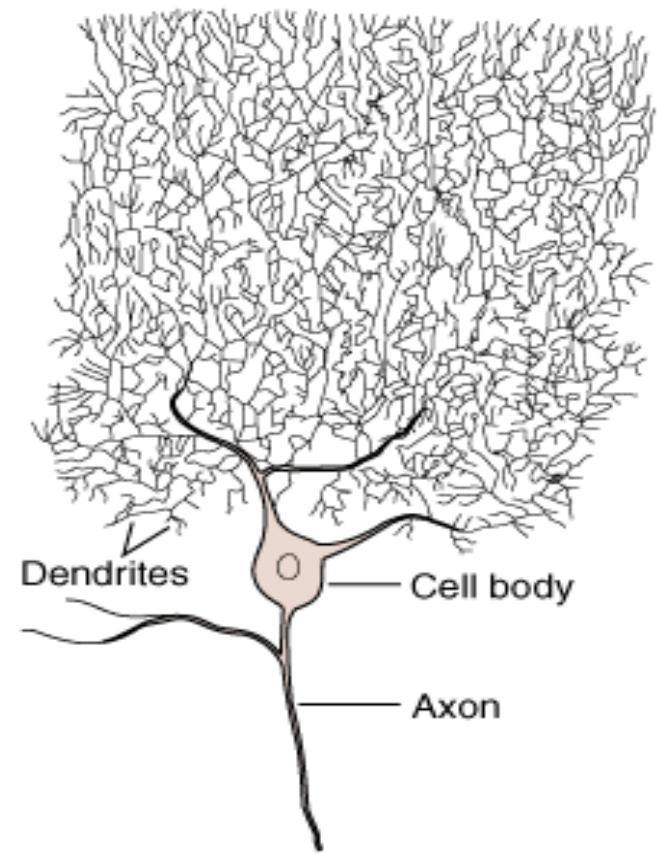
D Three types of multipolar cells



Motor neuron of
spinal cord



Pyramidal cell of
hippocampus



Purkinje cell of cerebellum

Depending upon functions

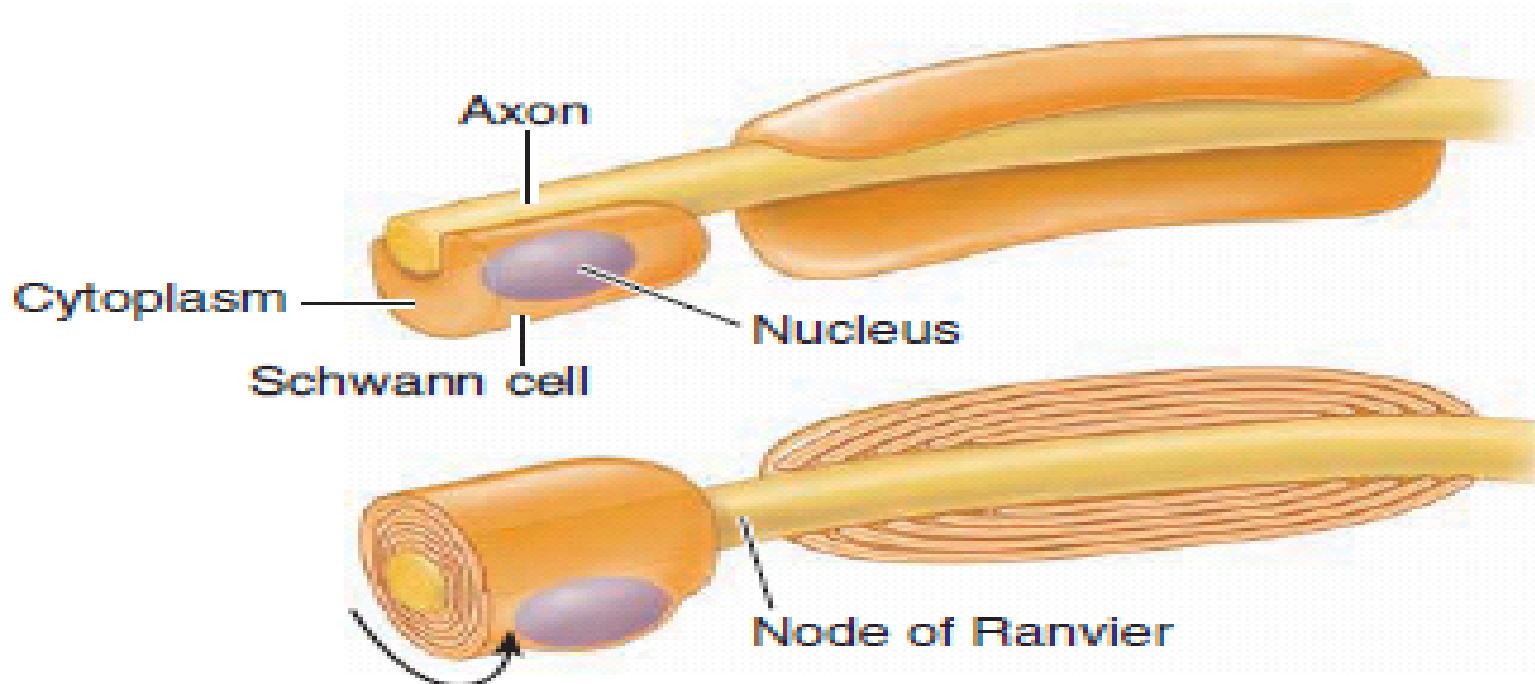
1. Motor or Efferent neuron

- Carry impulses from CNS to peripheral effector organs like muscles, glands, blood vessels, etc.

2. Sensory or Afferent neuron

- carry impulses from periphery to central nervous system

Motor neuron with a myelinated axon



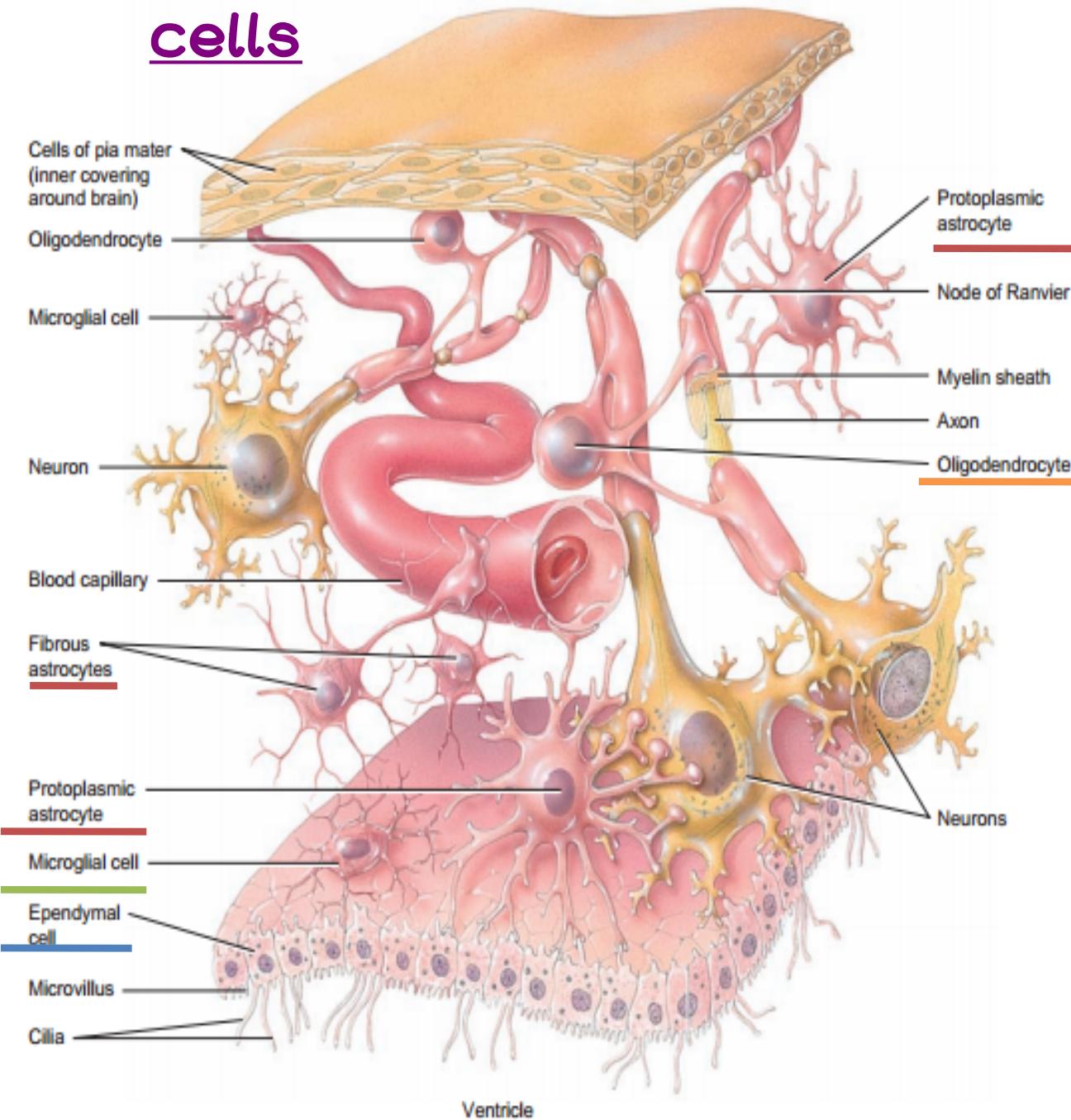
Myelin is a protein-lipid complex, produced by Schwann cell in PNS and oligodendrocytes in CNS that encircle the axon except at its ending and at periodic constrictions about 1mm apart called Nodes of Ranvier
functions: facilitates conduction of nerve impulse

In the PNS each patch of myelin is formed by a separate Schwann cell that wraps itself jelly-roll fashion around the nerve fiber.

Multiple sclerosis (MS)

- Multiple sclerosis (MS) is a pathophysiological condition in which nerve fibers **lose their myelin**.
- MS is an **autoimmune disease**.
- In MS, **antibodies and WBC** in immune system **attack myelin**, causing **inflammation and injury** to the sheath and eventually nerve that surround it. **Loss of myelin** leads **to leakage of K⁺** through voltage gated channels, **hyperpolarization** and **failure to conduct action potential**.

Neuroglia cells



- About 90% of neuronal cell are glial cell

- are the supporting cells present w/n the brain or spinal cord

1. Macrogliia

1. Astrocyte

- i) Fibrous
- ii)

Protoplasmic
c

2. Oligodendrocyt e

3. Ependidymal cell

Macroglia

- Blood brain barrier
- Metabolism of neurotransmitters & neuromodulators
- Regulation of synaptic activity
- Produce neurotrophins

Microglia

- Are scavenger cells that resembles tissue macrophage
- Remove debris from injury, infection and disease

Axonal transport

- **Anterograde (orthograde)transport:**
 1. Fast axonal transport - 400mm/day (vesicular cargoes)
 2. Slow axonal transport - 0.5-10mm/day (protein cargoes)

Retrograde transport,

- opposite direction
- occurs along microtubules at about 200 mm/day.
- carry tetanus toxin, neurotropic, virus (polio, rabies)

Types of nerve fiber

Fiber Type	Function	Fiber Diameter (μm)	Conduction Velocity (m/s)
A			
α	Proprioception; somatic motor	12-20	70-120
β	Touch, pressure	5-12	30-70
γ	Motor to muscle spindles	3-6	15-30
δ	Pain, cold, touch	2-5	12-30
B	Preganglionic autonomic	<3	3-15
C			
Dorsal root	Pain, temperature, some mechano-reception	0.4-1.2	0.5-2
Sympathetic	Postganglionic sympathetic	0.3-1.3	0.7-2.3

A and B fibers are myelinated; C fibers are unmyelinated.

Numerical Classification for Sensory Neuron

Number	Origin	Fiber Type
Ia	Muscle spindle, annulo-spiral ending	A α
Ib	Golgi tendon organ	A α
II	Muscle spindle, flower-spray ending; touch, pressure	A β
III	Pain and cold receptors; some touch receptors	A δ
IV	Pain, temperature, and other receptors	Dorsal root C

Table 3-1 Classification of Nerve Fibers

Classification	Type of Nerve Fiber	Example	Relative Diameter	Relative Conduction Velocity	Myelination
Sensory and Motor	A alpha (A α)	α Motoneurons	Largest	Fastest	Yes
	A beta (A β)	Touch, pressure	Medium	Medium	Yes
	A gamma (A γ)	γ Motoneurons to muscle spindles (intrafusal fibers)	Medium	Medium	Yes
	A delta (A δ)	Touch, pressure, temperature, fast pain	Small	Medium	Yes
	B	Preganglionic autonomic nerves	Small	Medium	Yes
	C	Slow pain; postganglionic autonomic nerves; olfaction	Smallest	Slowest	No
Sensory Only	Ia	Muscle spindle afferents	Largest	Fastest	Yes
	Ib	Golgi tendon organ afferents	Largest	Fastest	Yes
	II	Secondary afferents of muscle spindles; touch, pressure	Medium	Medium	Yes
	III	Touch, pressure, fast pain, temperature	Small	Medium	Yes
	IV	Pain, temperature; olfaction	Smallest	Slowest	No

Relative susceptibility of nerve fibers

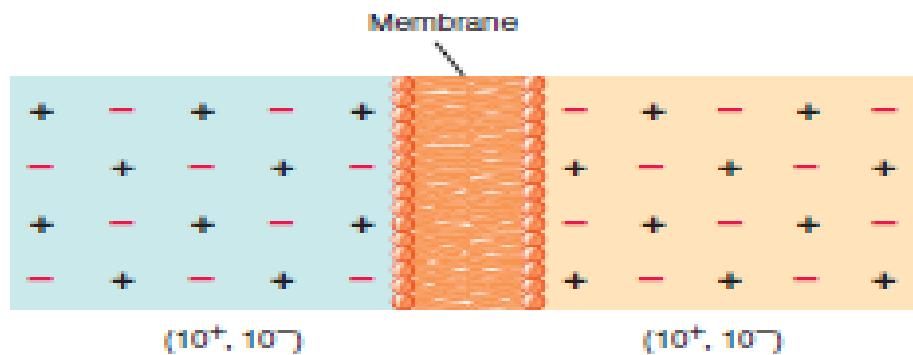
Sensitive to	Most susceptible	Intermediate susceptible	Least Susceptible
Hypoxia	B	A	C
Pressure	A	B	C
Local Anesthesia	C	C	A

Membrane Potential, Resting
membrane potential, Graded
potential, Action potential

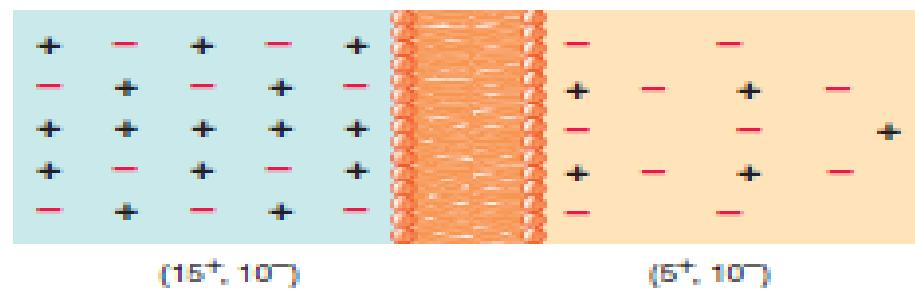
Excitable Tissues:-

The Excitable tissues are those tissues which can generate an Action Potential

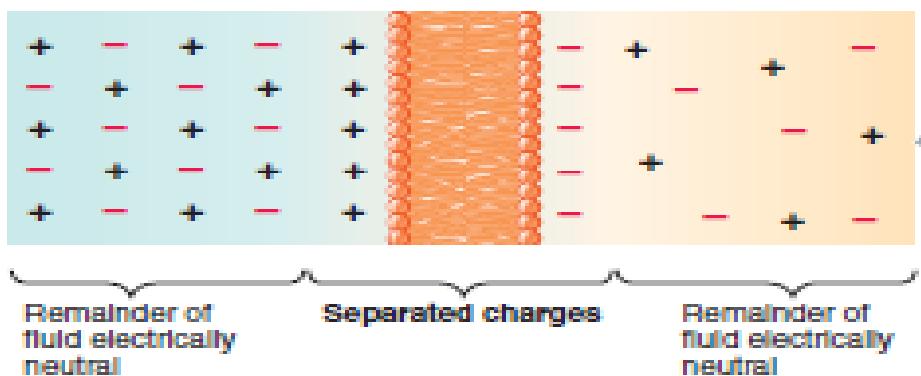
- Nervous tissue
- Muscle tissue



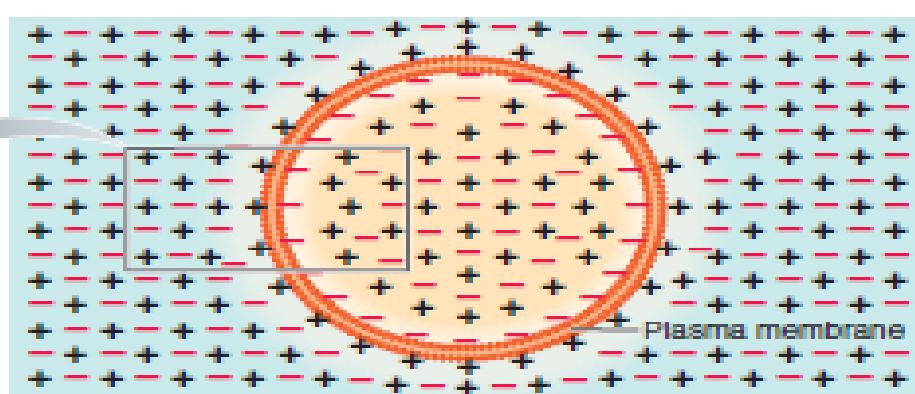
(a) Membrane has no potential



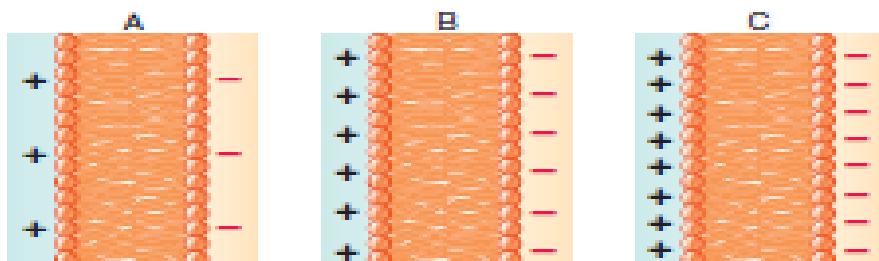
(b) Membrane has potential



(c) Separated charges responsible for potential



(d) Separated charges forming a layer along plasma membrane



(e) Magnitude of potential: membrane B has more potential than membrane A and less potential than membrane C

FIGURE 3-20 Determination of membrane potential by unequal distribution of positive and negative charges across the membrane. (a) When the positive and negative charges are equally balanced on each side of the membrane, no membrane potential exists. (b) When opposite charges are separated across the membrane, membrane potential exists. (c) The unbalanced charges responsible for the potential accumulate in a thin layer along opposite surfaces of the membrane. (d) The vast majority of the fluid in the ECF and ICF is electrically neutral. The unbalanced charges accumulate along the plasma membrane. (e) The greater the separation of charges across the membrane, the larger the potential.

- **Membrane potential:** It refers to a separation of opposite charges across the plasma membrane. It is measured in millivolts - mV
- The unequal distribution of a few key ions between the ICF and ECF and their selective movement through the plasma membrane is responsible for the generation of potential across the membrane.
- **Resting Membrane Potential [RMP]:** Potential across the membrane of an excitable cell in a resting state (unstimulated).
- **Action Potential:** The changes in the excitable cell's membrane potential that occurs when an appropriate stimulus is applied.

- Factors that helps to generate of Membrane potential are

- Selective permeability of cell membrane
- Gibbs Donnan equilibrium
- Nernst equation
- Goldmanns constant field equation
- Sodium potassium pump

Concentration and permeability of ions in resting nerve cells

CONCENTRATION (Millimoles/liter; mM)

ION	Extracellular	Intracellular	Relative Permeability
Na ⁺	150	15	1
K ⁺	5	150	25–30
A ⁻	0	65	0

- K^+ concentration is **higher inside** the cell.
- Under resting conditions **cell membrane is more permeable to K^+ and Cl^- than to Na^+ .**
- In the cell amino acids easily diffuse in the cell and form proteins which can not diffuse. At the pH of body these proteins are negatively charged.
- Presence of **nondiffusible negatively charged proteins lead to unequal distribution of diffusible ions which generate negativity inside the cell as compared to out side.** This - ve potential generated is called as the resting membrane potential.

Gibbs Donnan Equation

- Donnan and Gibbs showed that in presence of non diffusible ion, the diffusible ions distribute themselves so that at equilibrium, their concentration ratios are equal.

$$\frac{[K^+_x]}{[K^+_y]} = \frac{[Cl^-_y]}{[Cl^-_x]}$$

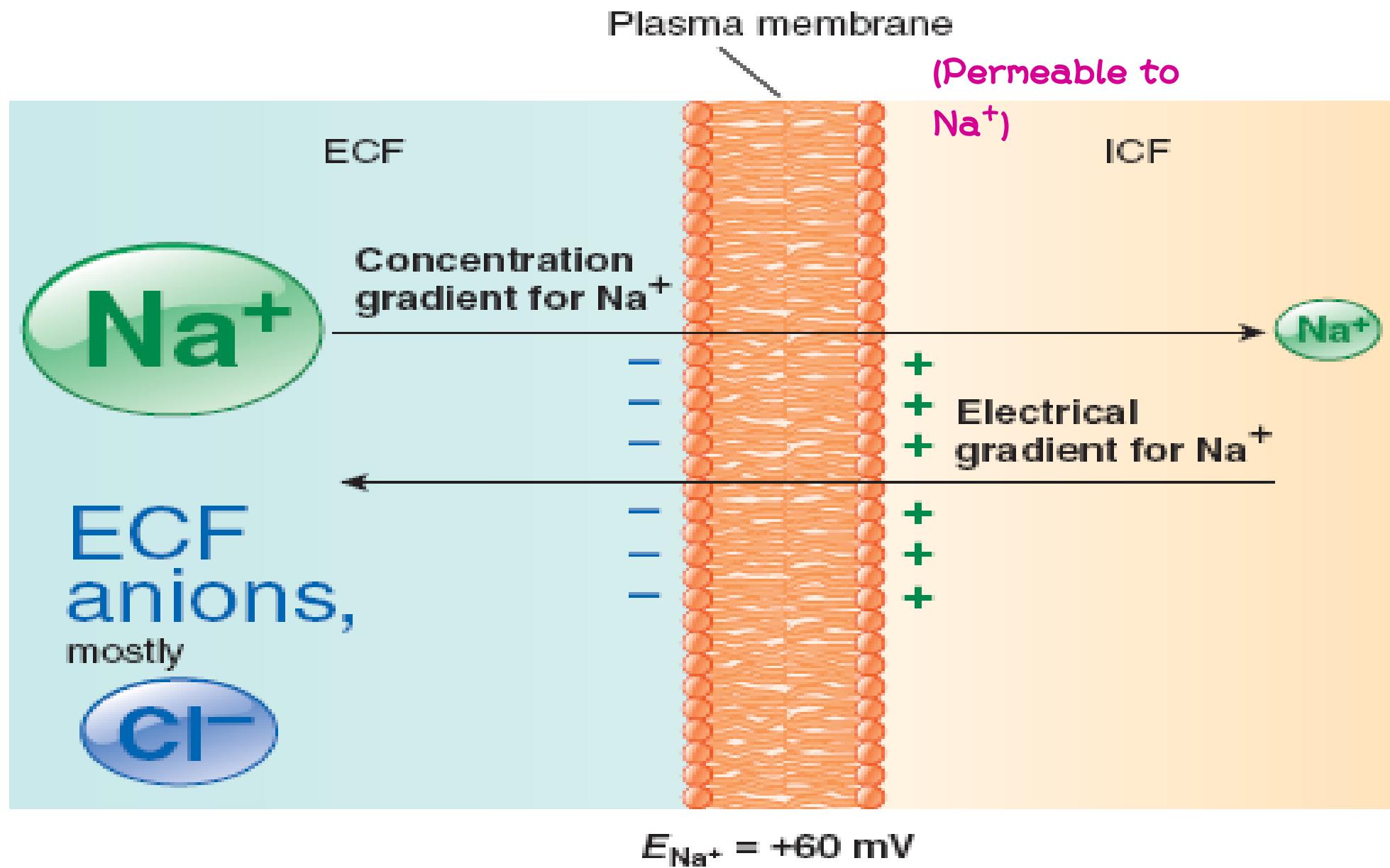
Cross-multiplying,

$$[K^+_x] [Cl^-_x] = [K^+_y] [Cl^-_y]$$

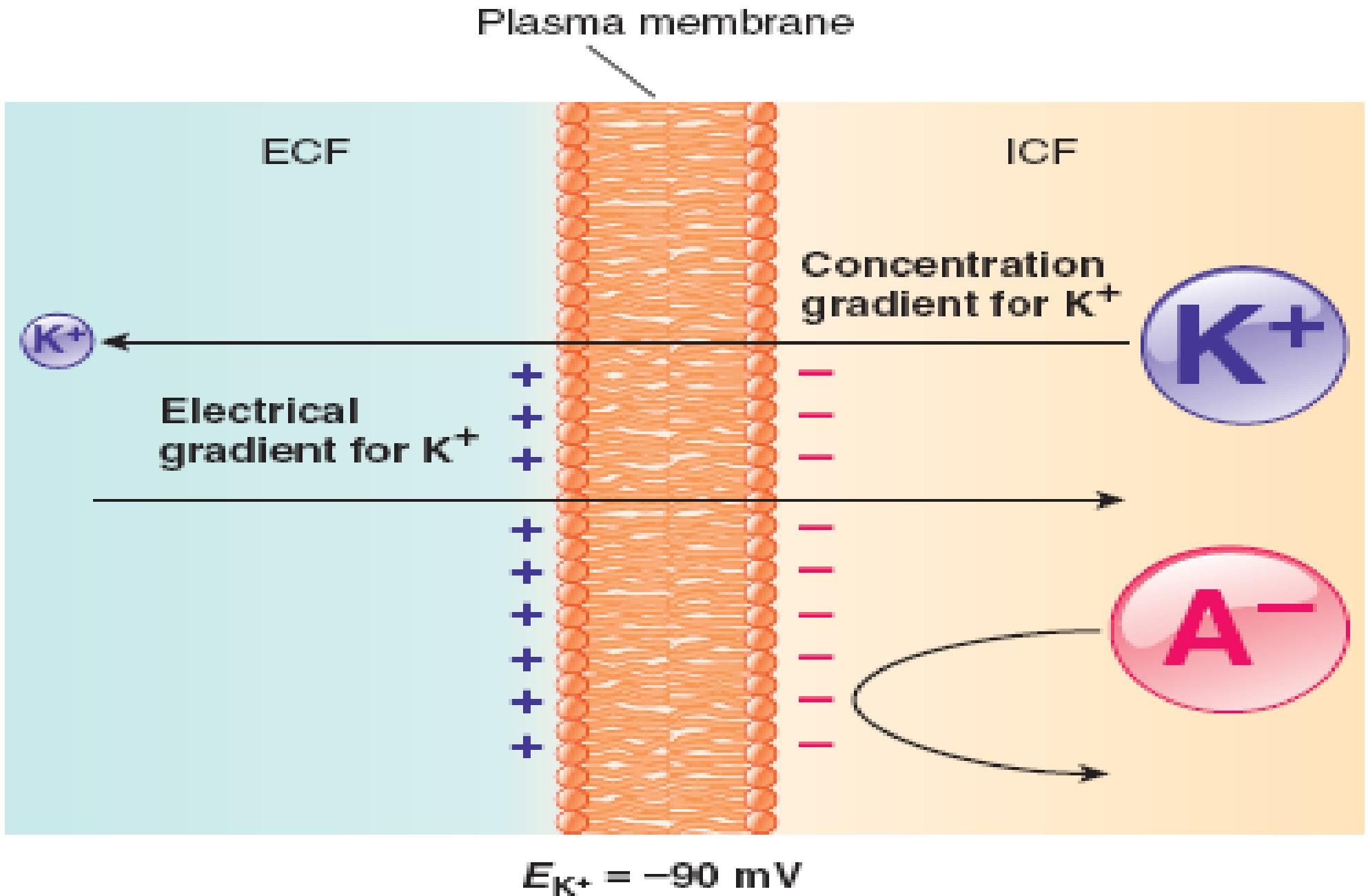
Equilibrium potential

An equilibrium potential for an ion across a permeable membrane is achieved when movement of that ion in one direction due to concentration gradient is balanced by the movement of that ion in the opposite direction due to electric gradient.

Equilibrium potential for sodium



Equilibrium potential for potassium



Nernst equation

- The magnitude of the equilibrium potential (E) for one ion can be calculated by Nernst equation.

$$E = \frac{RT \ln (\text{Conc})_o}{ZF (\text{Conc})^i}$$

At normal body temperature (37°C), equation can be simplified to

$$E_m = \pm 62 \log C_o/C_i$$

Note: \pm Sign of diffusion potential depends upon whether diffusing ion is positive or negative charge.

Given that ECF concentration of Na^+ is 150 mEq/liter and ICF concentration is 15 mEq/liter

$$\begin{aligned}E_{\text{Na}} &= 61 \log 250/15 \\&= 61 \log 20\end{aligned}$$

since $\log 20 = (2)$

$$\begin{aligned}&= 61 \times (2) \\&= +61 \text{ mV} \sim +60 \text{ mV}\end{aligned}$$

Given that ECF concentration of K^+ is 5 mM/liter and ICF concentration is 150 mM/liter

$$E_K = 62 \log 5/150$$

$$= 62 \log 1/30$$

since $\log 1/30 = -1.477$

$$= 62 \times (-1.477)$$

$$= -90mV$$

Goldman constant field equation

- When membrane is permeable to several different ions, the diffusion potential that develops can be calculated by Goldman equation

$$V = \frac{RT}{F} \ln \frac{P_{K^+}[K_o^+] + P_{Na^+}[Na_o^+] + P_{Cl^-}[Cl_i^-]}{P_{K^+}[K_i^+] + P_{Na^+}[Na_i^+] + P_{Cl^-}[Cl_o^-]}$$

V- Membrane potential

R- Gas constant

T- Absolute temperature

F- Faraday

P- Permeability of the membrane to various ions

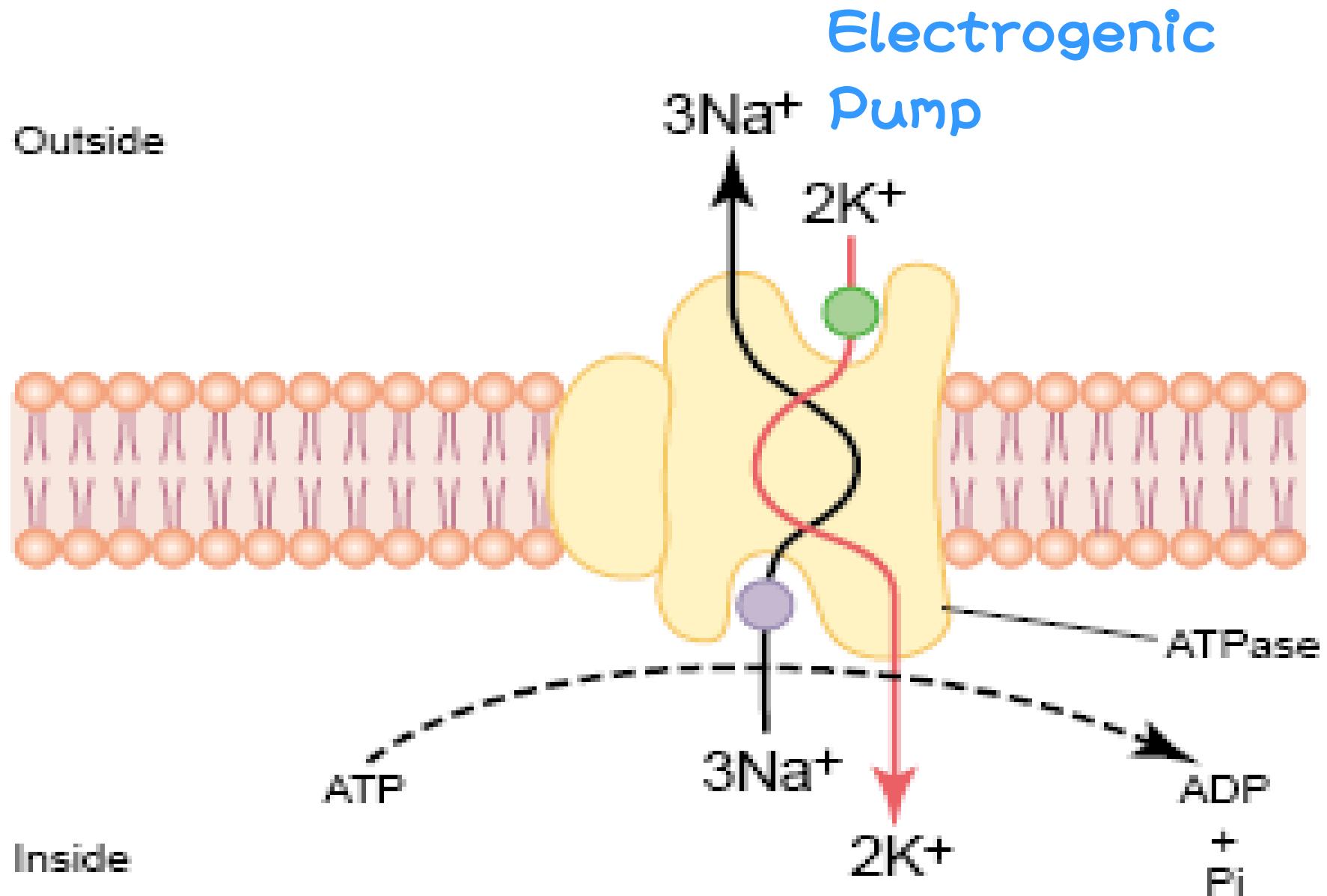
$$P_K^+ (K^+)_o + P_{Na}^+ (Na^+)_o$$

- $E = 61 \log \frac{P_K^+ (K^+)_i + P_{Na}^+ (Na^+)_i}{P_K^+ (K^+)_o + P_{Na}^+ (Na^+)_o}$
- 61 is a constant (RT/zF)
- Assume the resting membrane is $25x$ more permeable to K^+ than Na^+ .
- Then the relative permeability are $P_K^+ = 1.0$ and $P_{Na}^+ = 0.04$ ($1/25$ of 1.0)
$$(1)(5) + (0.04)(25)$$
- $E = 61 \log \frac{(1)(25) + (0.04)(1)}{(1)(1) + (0.04)(25)} = 61 \log 0.073$
$$\frac{(1)(25) + (0.04)(1)}{(1)(1) + (0.04)(25)} = \frac{25 + 0.04}{1 + 25} = \frac{25.04}{26} = 0.073$$

 $\log 0.073 = -1.237; E = 61(-1.237)$
$$= -69 \text{ mV}$$

= adding -1 mV of potential generated by Na^+ K^+ pump.
This value totals **-70mV** for resting membrane potential.

Sodium Potassium ATPase



Genesis of Resting Membrane Potential

- 1) Selective permeability of the cell membrane to some ions only. [It is the property of a living cell membrane].
- 2) Gibbs- Donnan equilibrium which causes unequal distribution of permeable ions across cell membrane due to the presence of non permeable protein anions in ICF.
- 3) Unequal distribution of permeant ions across the cell membrane [between ICF & ECF], creates **concentration and electrical gradient** across membrane which **causes movement of ions along their concentration and electrical gradient**.
- 4) Slow Na^+ ion influx occurs due to both concentration and electrical gradient. Their **accumulation** intracellularly is prevented by **$\text{Na}^+ - \text{K}^+$ ATPase or $\text{Na}^+ - \text{K}^+$ pump** which is electrogenic - i.e. it causes efflux of 3 Na^+ and influx of 2 K^+ . Thus it also helps to

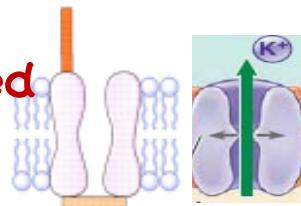
Irrespective of the nature of stimulus, the response is change in MP.

1). Graded Potentials: generated at the site of stimulation. They serve as short distance signals and their strength decreases with distance and time. When their magnitude is sufficient, they lead to generation of action potential. These are not propagated.

2). Action Potential: It refers to rapid depolarization followed by repolarization of the membrane after a threshold/supra-threshold stimulus is applied to an excitable membrane.

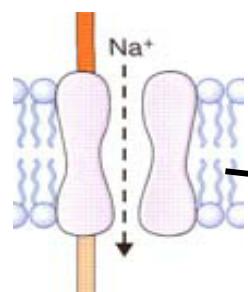
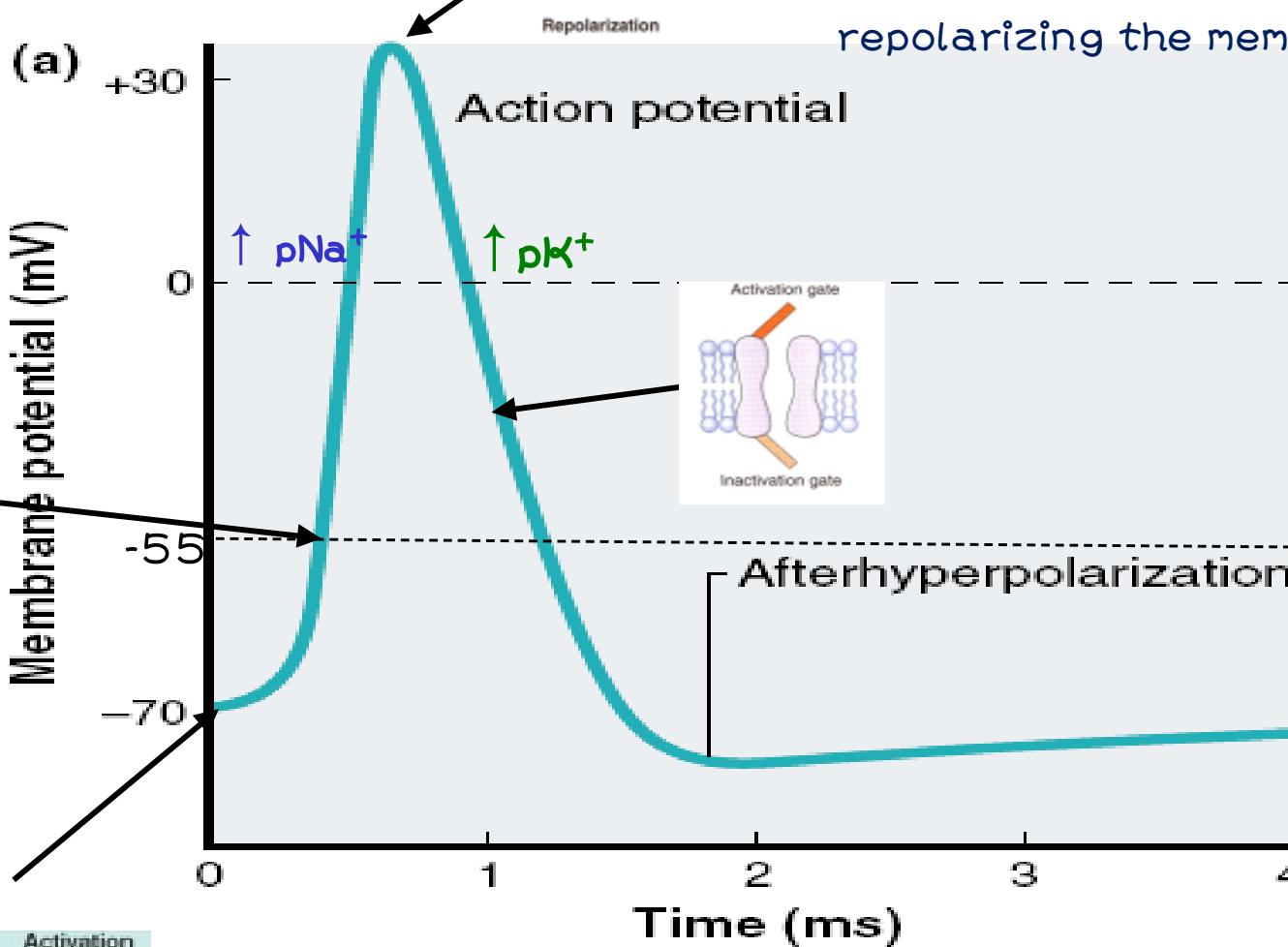
These potentials are transmitted or propagated over long distances with out decrement or change in the size or shape of action potential.

Na⁺ gate inactivated

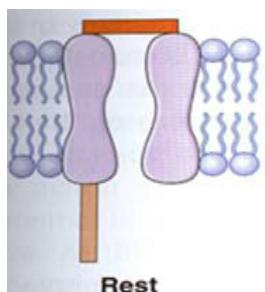


K⁺ gate open

The K⁺ efflux participates together with inactivation of the Na⁺ channels in repolarizing the membrane.



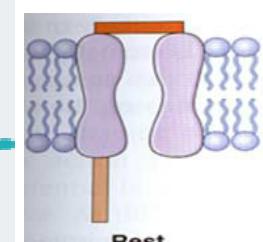
Na⁺ gates open during upstroke;
Na⁺ influx



Na⁺ gate closed



K⁺ gate closed



Na⁺ gate closed

Action potential exhibits all or none law: Once threshold potential is reached, the automatic changes in the permeability of the membrane leads to generation of an action potential. In an excitable tissue the magnitude, duration or shape of action potential does not change.

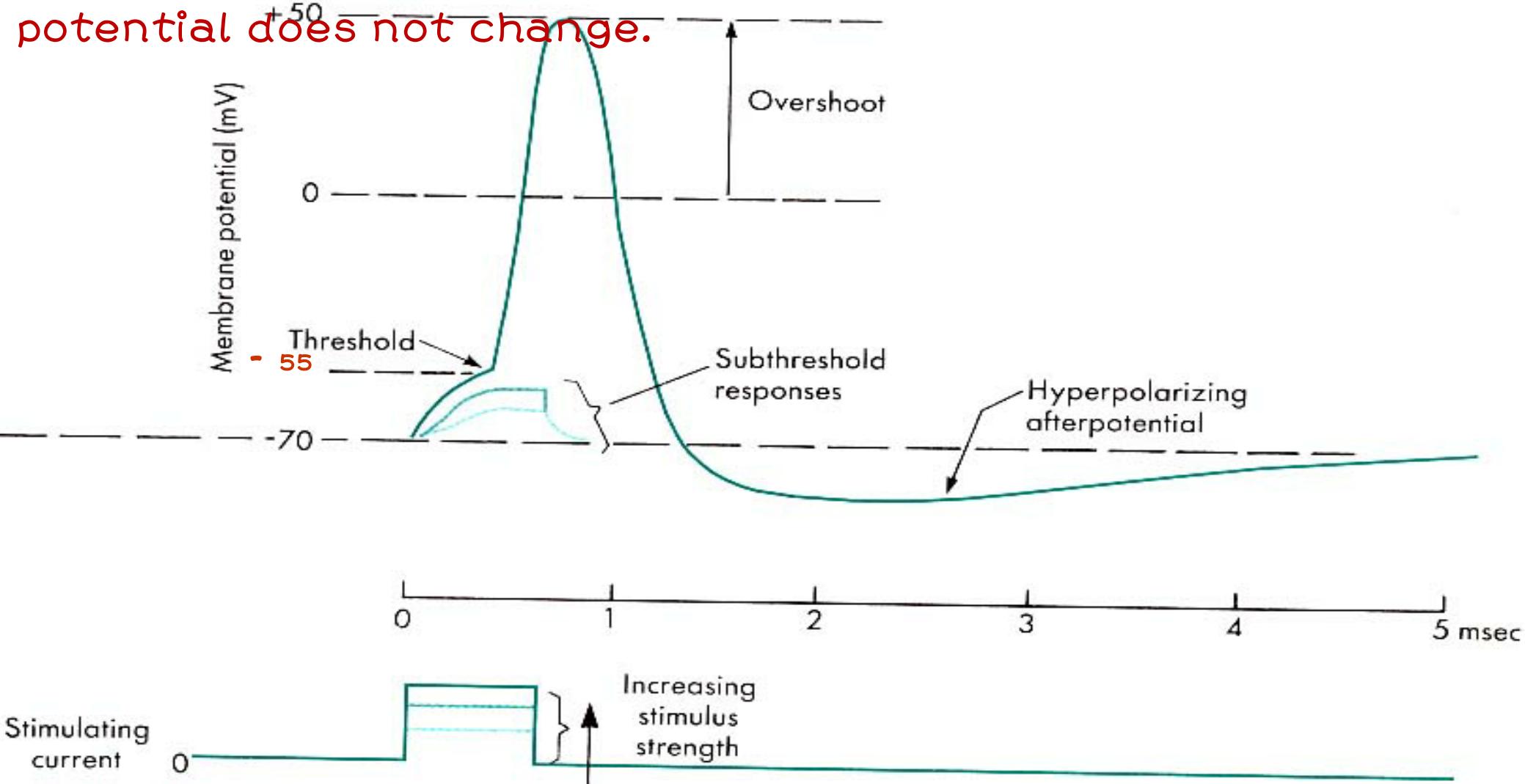


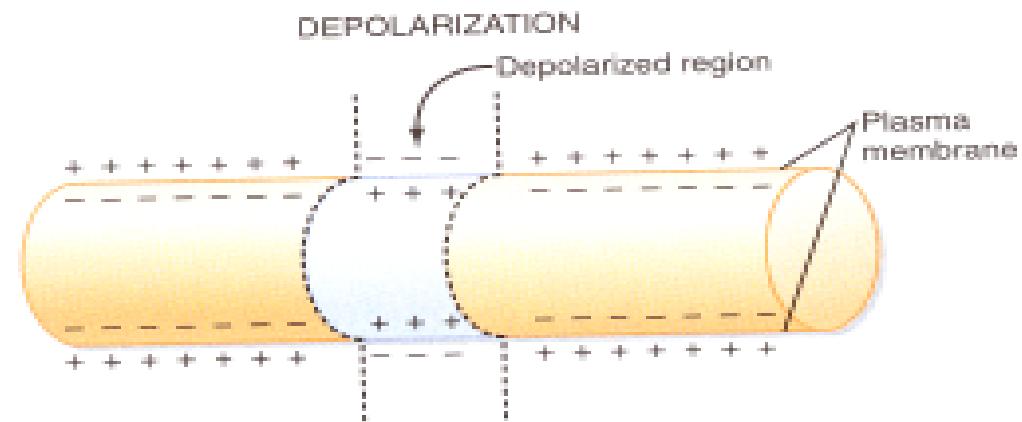
Fig. 3-4 Responses of the membrane potential of a squid giant axon to increasing pulses of depolarizing current. When the cell is depolarized to threshold, it fires an action potential.

Conduction of Action Potential

Conduction of AP along an axon is based on local current flow.

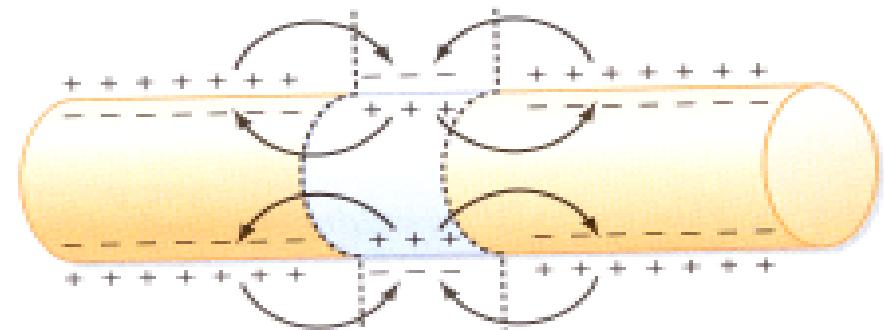
Conduction velocity depends on

- Fibers diameter
- Myelination



A

SPREAD OF DEPOLARIZATION



B

Unmyelinated nerve fiber: Point to point conduction

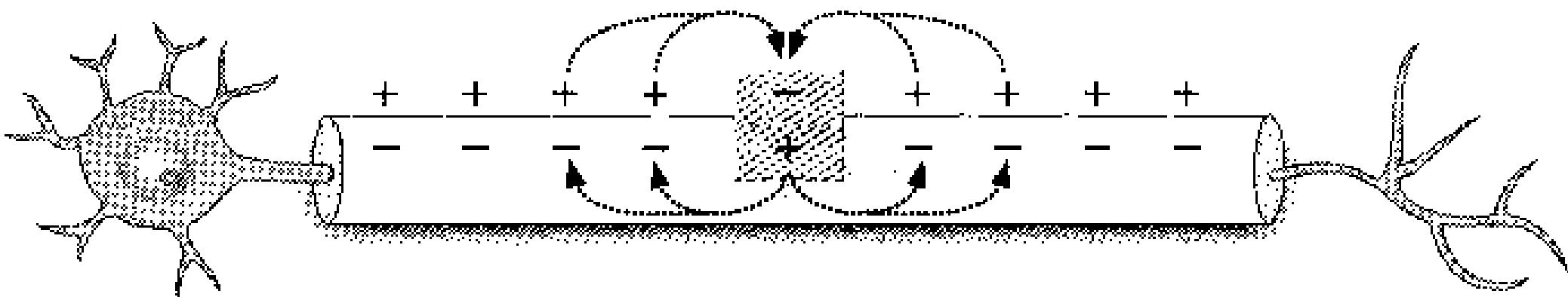


Figure 1-7 Unmyelinated axon showing spread of depolarization by local current flow.

Myelinated nerve fiber: Faster node to node (saltatory conduction) 50 times faster

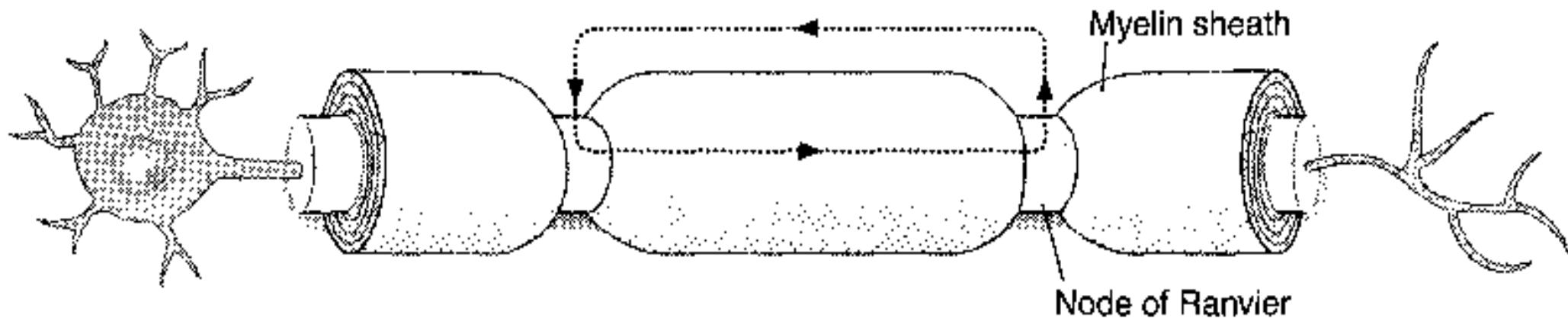


Figure 1-8 Myelinated axon. Action potentials can occur at nodes of Ranvier.

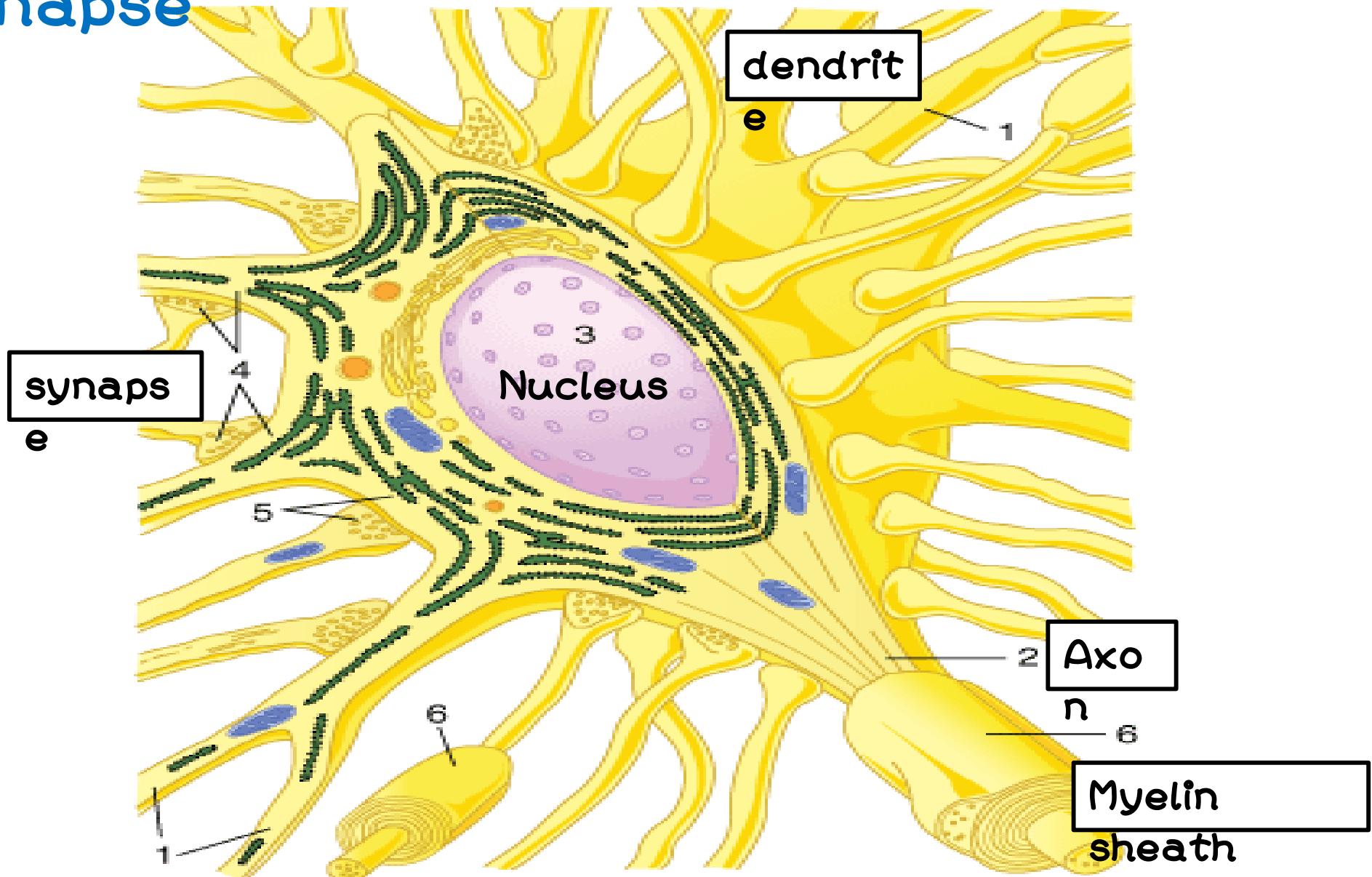
Number of Voltage gated Na⁺ Channels per square micrometer of membrane in Myelinated Neurons

- Cell body: 50 - 75
- Initial segment: 350 - 500
- On the surface of myelin: < 25
- **Nodes of Ranvier: 2000 - 12,000**
- Axon terminal: 20 - 75

Along the axon of the unmyelinated fibers : 110

Synaptic transmission

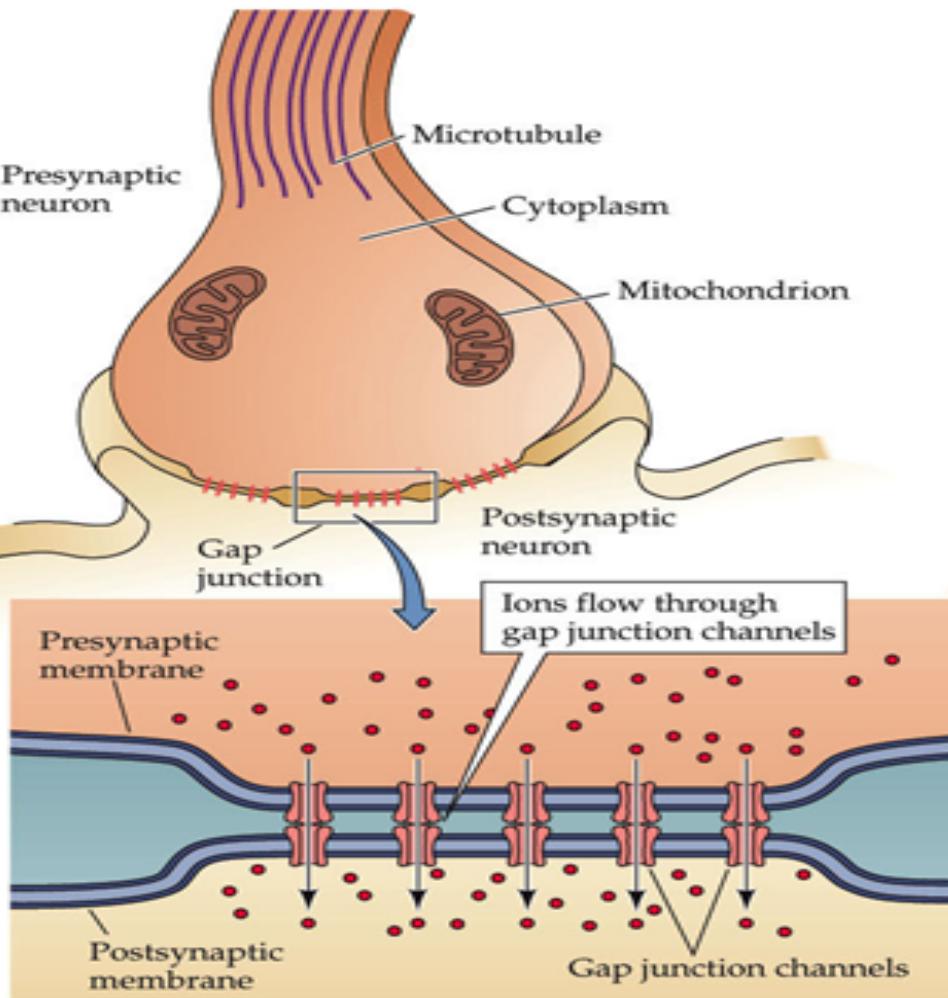
Synapse



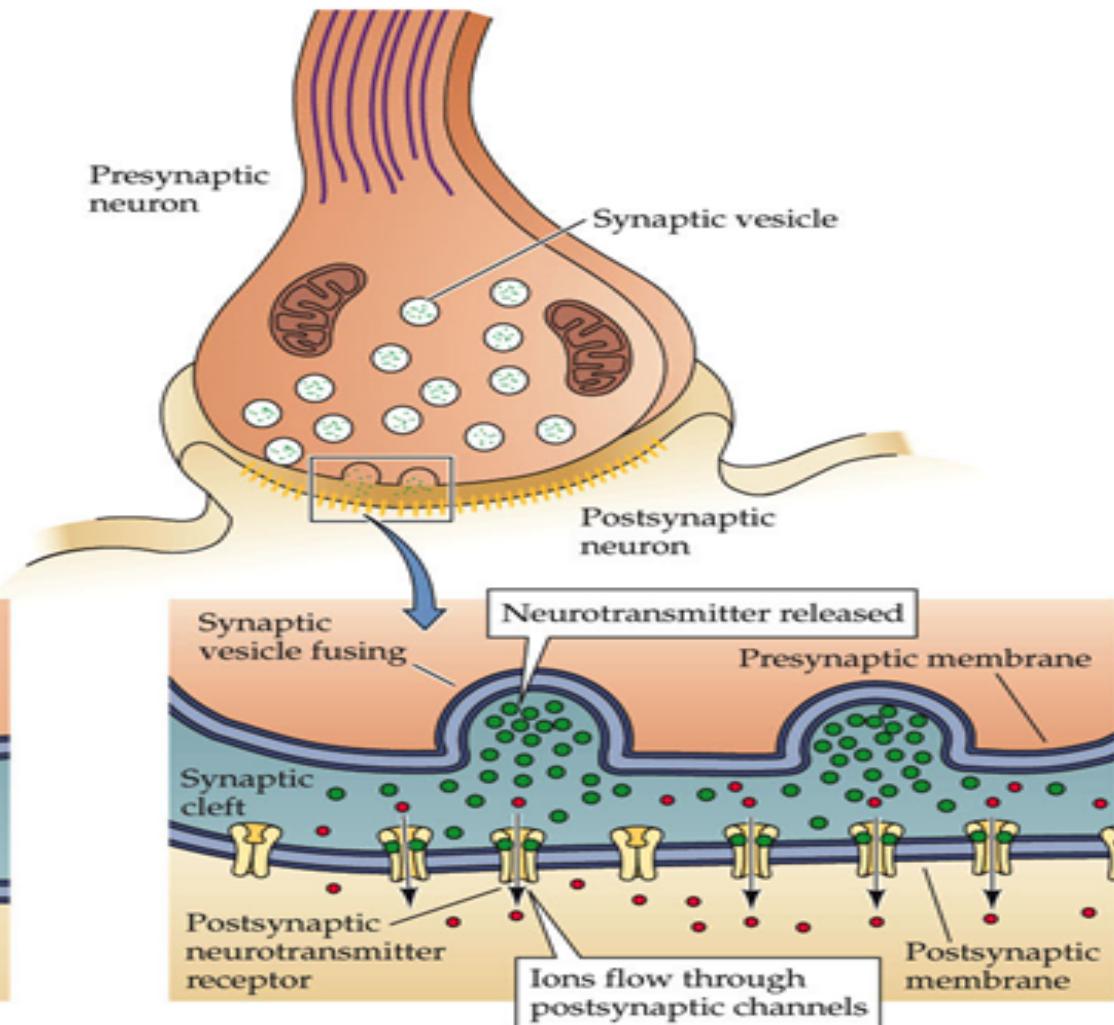
Synapse is a specialized region where excitable cells (neurons or muscle cells) communicate with each other or with a target organ's cell via action potentials

Functional classification of synapse

(A) ELECTRICAL SYNAPSE



(B) CHEMICAL SYNAPSE



when action potential generated in one cell is conducted to next cell via special “gap junctions” which allow easy passage to ions (e.g. conduction of action potentials in unitary smooth muscles and cardiac muscle fibers)

when an action potential leads to release of a chemical substance called neurotransmitter which acts on the next neuron. Here synapse acts as a transducer which converts electrical energy of action potential into chemical energy as released neurotransmitter (e.g. in CNS and at neuromuscular junction).

Structure of synapse

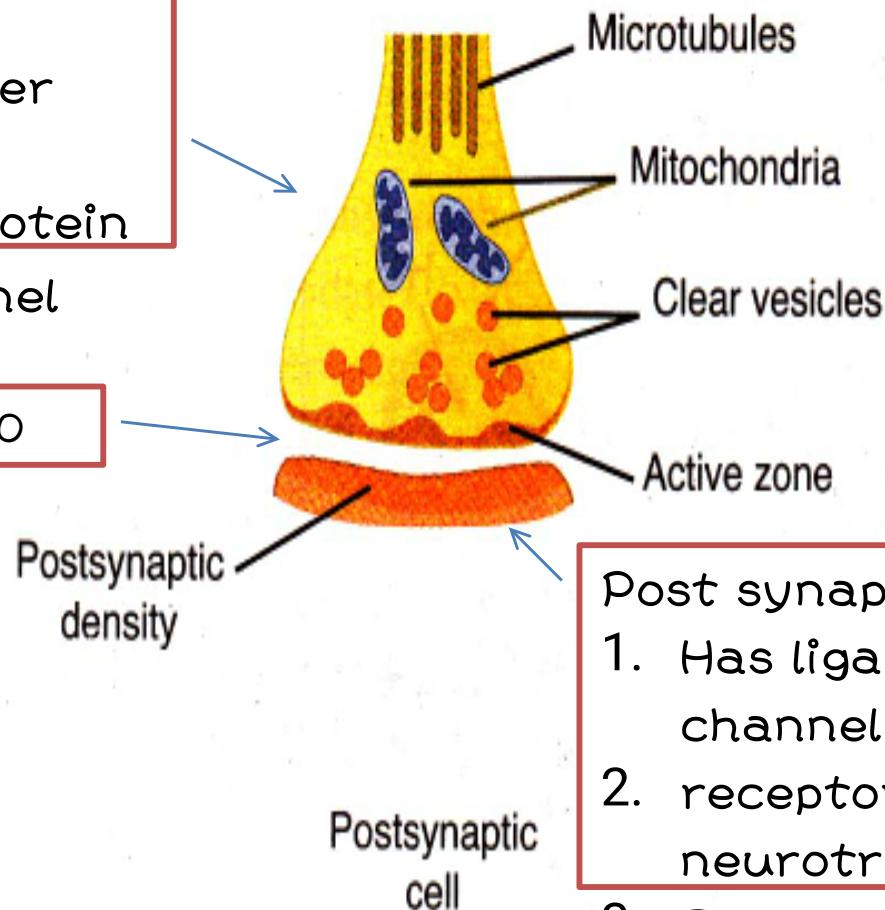
Presynaptic cell

1. Many vesicles which contain neurotransmitter
2. Mitochondria
3. Active zone: protein and Ca^{2+} channel

Presynaptic cell

Post synaptic cleft 20

- 40 nm



Post synaptic cell

1. Has ligand gate ion channels
2. receptors for neurotransmitters
3. Enzymes which can degrade the release of neurotransmitters

Sequence of events for synaptic transmission

1. Arrival of Impulse
2. Release of neurotransmitter
3. Development of postsynaptic potential (EPSP,IPSP)
4. Summation of postsynaptic potential
5. Generation of Action potential
6. Fate of neurotransmitter

Development of EPSP & IPSP

Excitatory

Synaptic vesicles in synaptic bouton

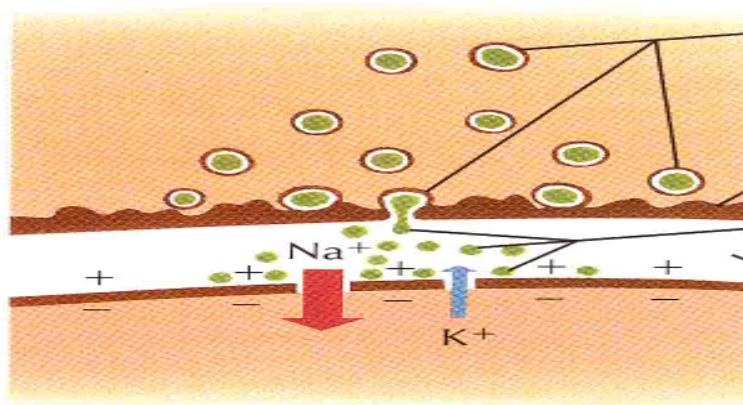
Presynaptic membrane

Transmitter substances

Synaptic cleft
Postsynaptic membrane

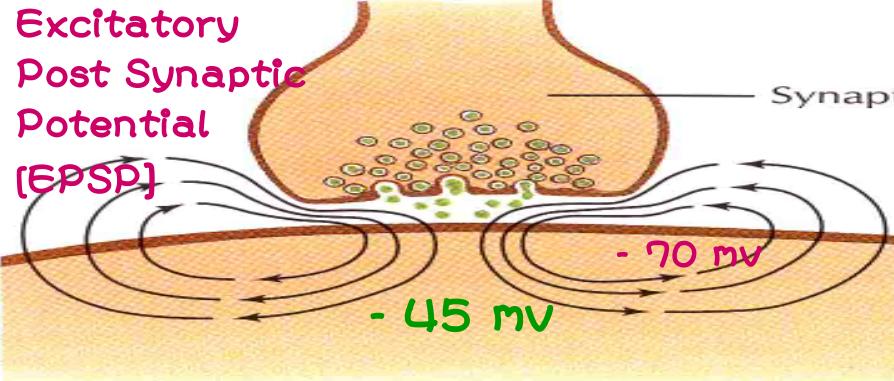
Inhibitory

Cl^-

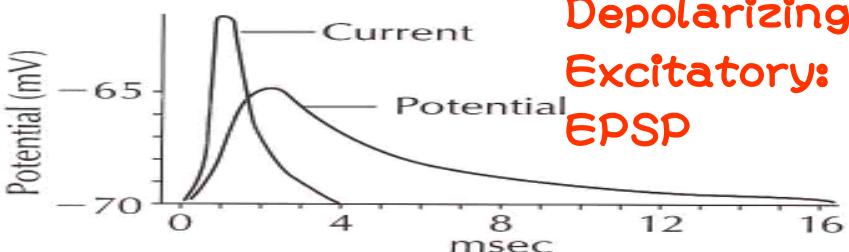


When impulse reaches excitatory synaptic bouton, it causes release of a transmitter substance into synaptic cleft. This increases permeability of postsynaptic membrane to Na^+ and K^+ . More Na^+ moves into postsynaptic cell than K^+ moves out, due to greater electrochemical gradient

Excitatory Post Synaptic Potential [EPSP]



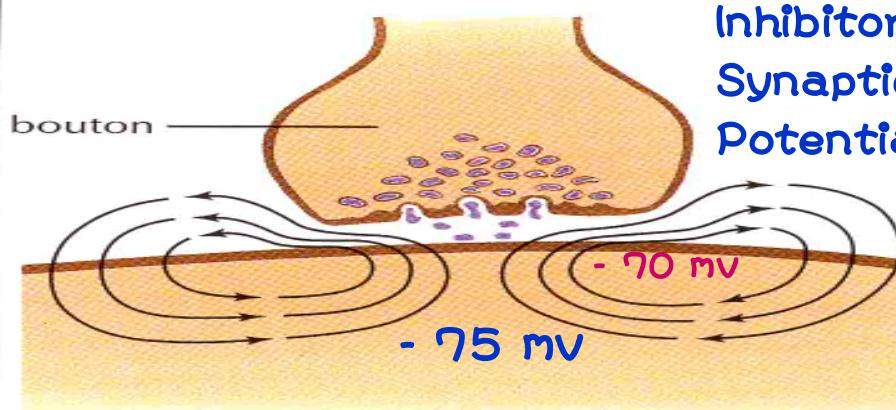
Resultant net ionic current flow is in a direction that tends to depolarize postsynaptic cell. If depolarization reaches firing threshold, an impulse is generated in postsynaptic cell



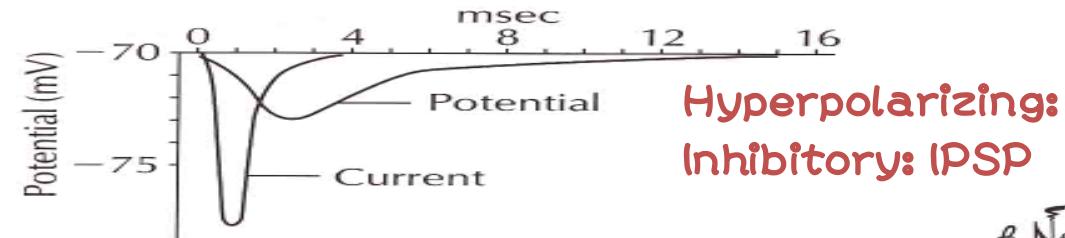
Depolarizing:
Excitatory:
EPSP

At inhibitory synapse, transmitter substance released by an impulse increases permeability of the postsynaptic membrane to Cl^- . K^+ moves out of post-synaptic cell but no net flow of Cl^- occurs at resting membrane potential

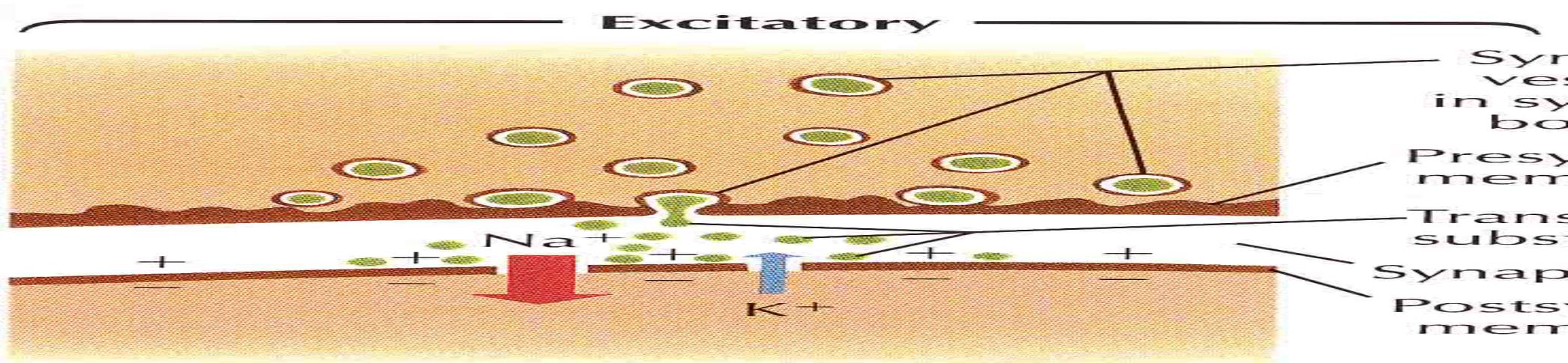
Inhibitory Post Synaptic Potential [IPSP]



Resultant ionic current flow is in direction that tends to hyperpolarize postsynaptic cell. This makes depolarization by excitatory synapses more difficult—more depolarization is required to reach threshold

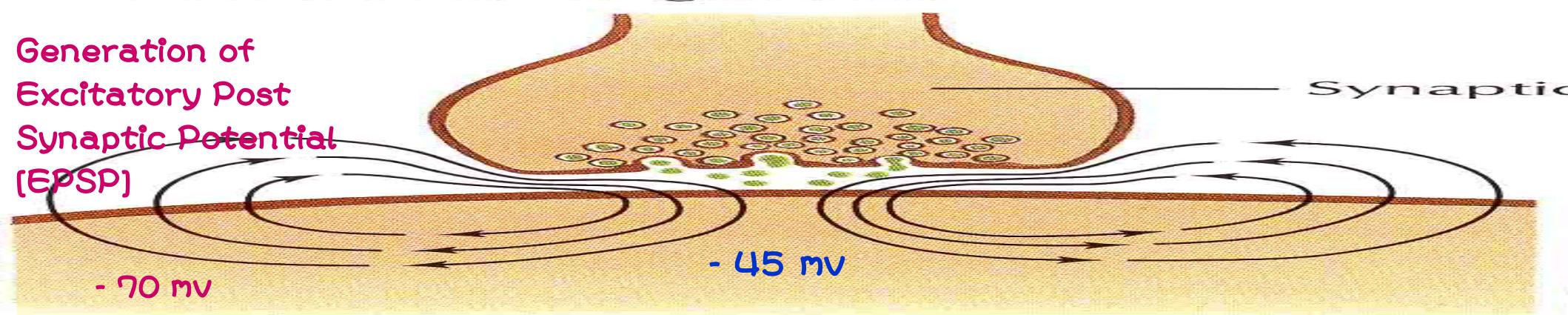


Hyperpolarizing:
Inhibitory: IPSP

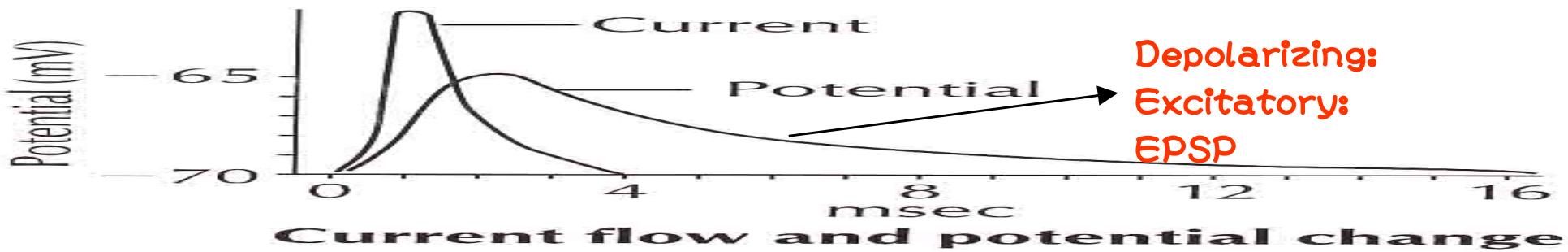


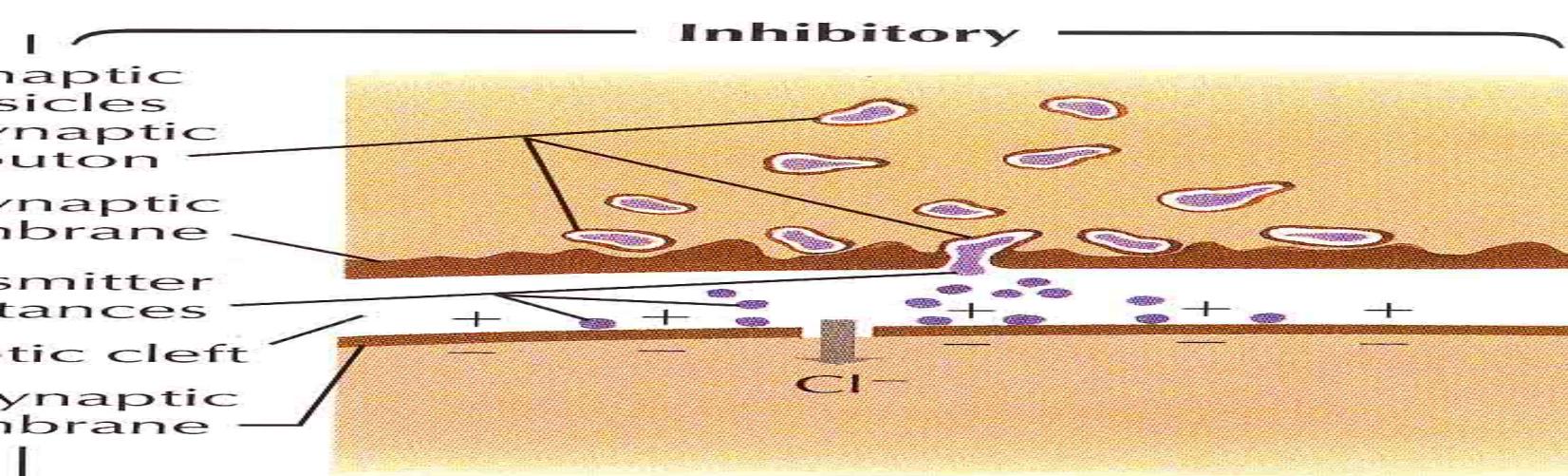
When impulse reaches excitatory synaptic bouton, it causes release of a transmitter substance into synaptic cleft. This increases permeability of postsynaptic membrane to Na^+ and K^+ . More Na^+ moves into postsynaptic cell than K^+ moves out, due to greater electrochemical gradient

Generation of Excitatory Post Synaptic Potential (EPSP)

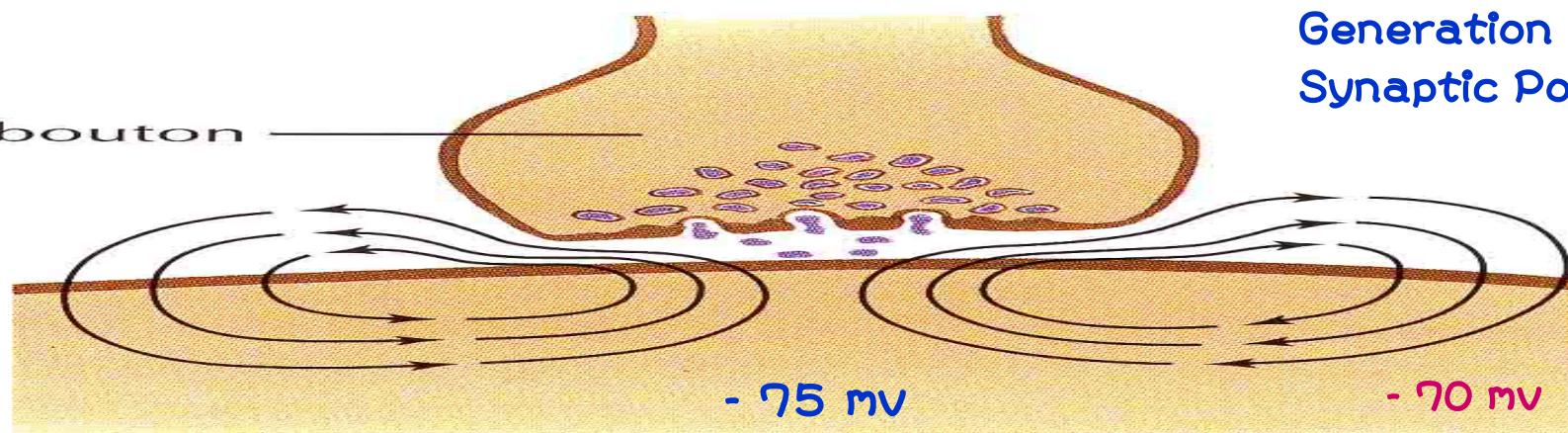


Resultant net ionic current flow is in a direction that tends to depolarize postsynaptic cell. If depolarization reaches firing threshold, an impulse is generated in postsynaptic cell



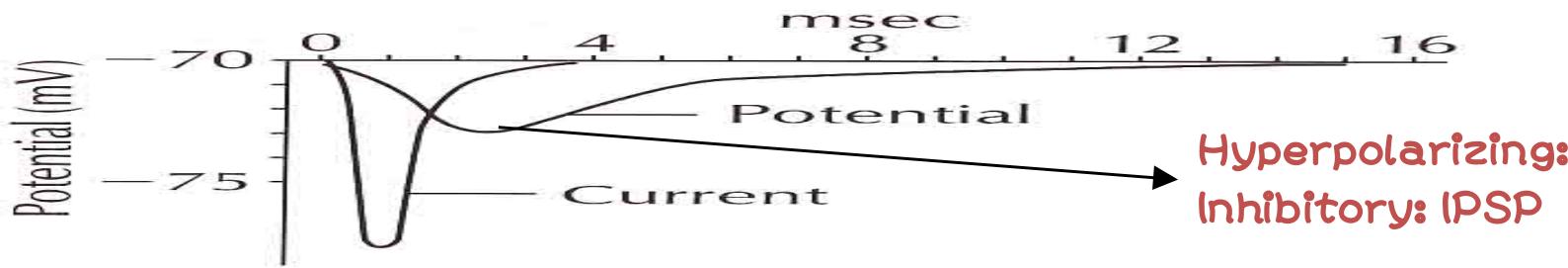


At inhibitory synapse, transmitter substance released by an impulse increases permeability of the postsynaptic membrane to Cl^- . K^+ moves out of post-synaptic cell but no net flow of Cl^- occurs at resting membrane potential



Generation of Inhibitory Post Synaptic Potential (IPSP)

Resultant ionic current flow is in direction that tends to hyperpolarize postsynaptic cell. This makes depolarization by excitatory synapses more difficult—more depolarization is required to reach threshold



Current flow and potential changes

Hyperpolarization (IPSP) produced due to influx of Cl^- ion via GABA_A receptors or due to efflux of K^+ through GABA_B receptors. These effects produce inhibition of the neuron where GABA (Gama Amino Butyric Acid) is the neurotransmitter.

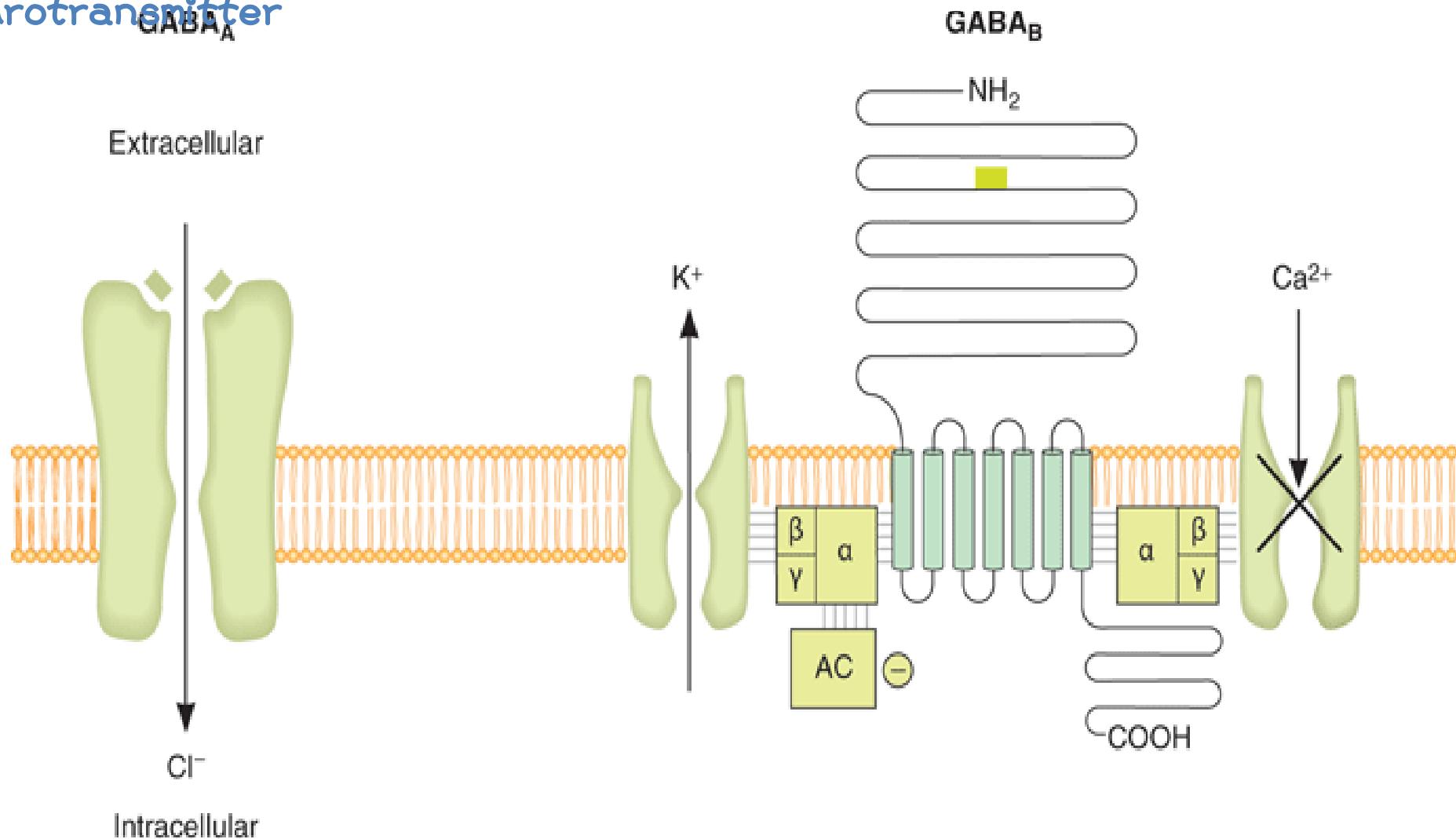
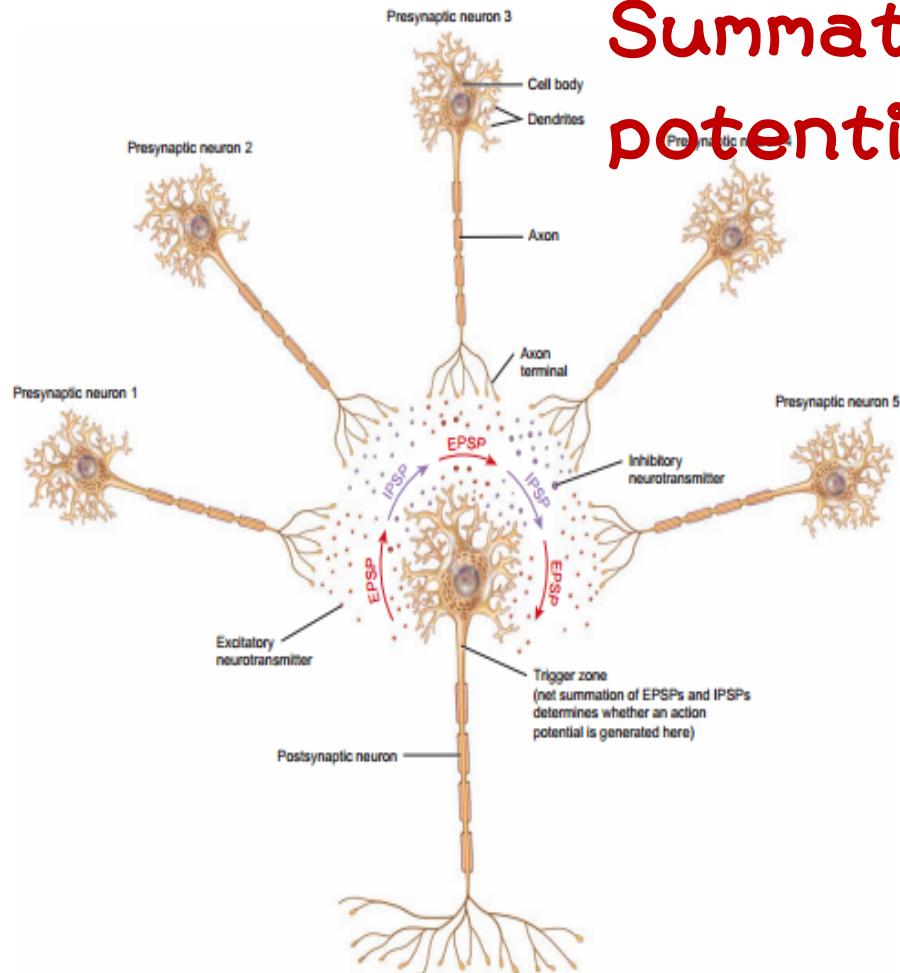


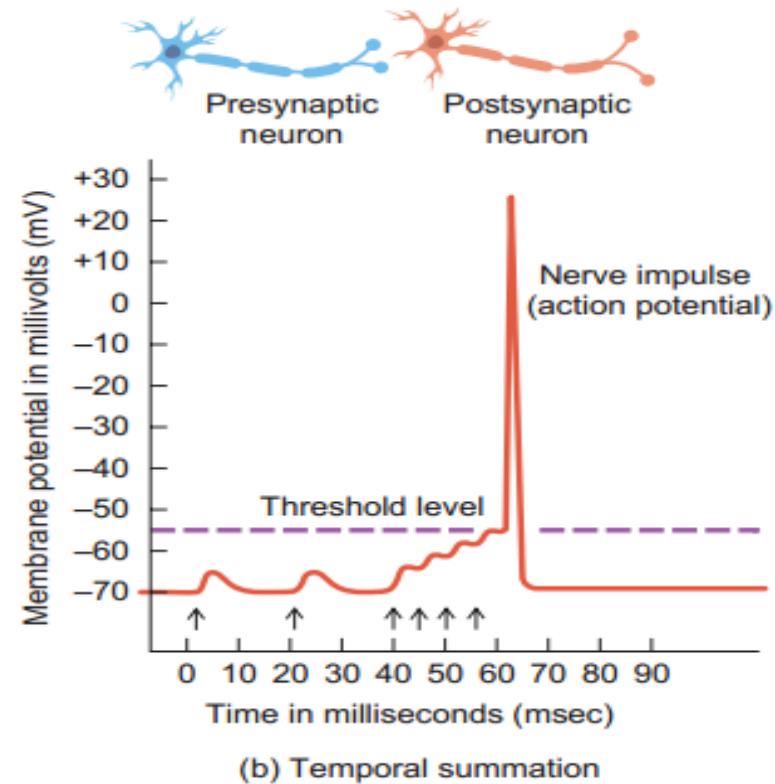
FIGURE 7-10 Diagram of GABA_A and GABA_B receptors, showing their principal actions. The G protein that mediates the effects of GABA_B receptors is a heterodimer. (Reproduced with permission from Bowery NG, Brown DA: The cloning of GABA_B receptors. Nature 1997;386:223. Copyright © 1997 by Macmillan Magazines.)

Summation of postsynaptic potential



Spatial summation

- Simultaneous stimulation of many synapse on the same neuron
- All impulses are added up

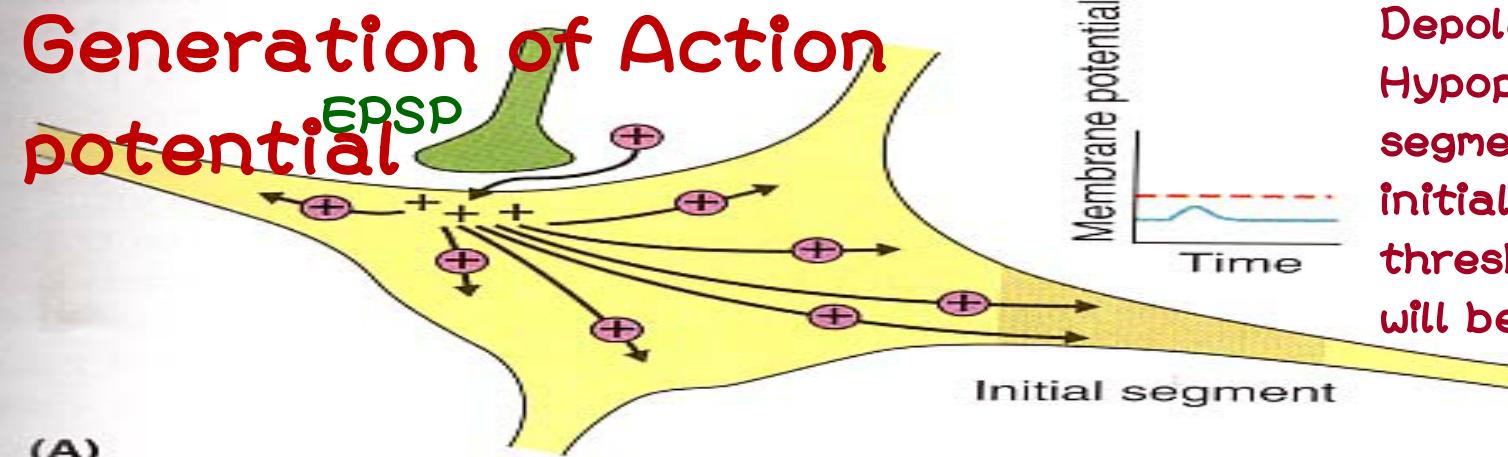


Temporal summation

- Repeated stimuli are applied at very short interval
 - The next stimulus add to previous post synaptic potential

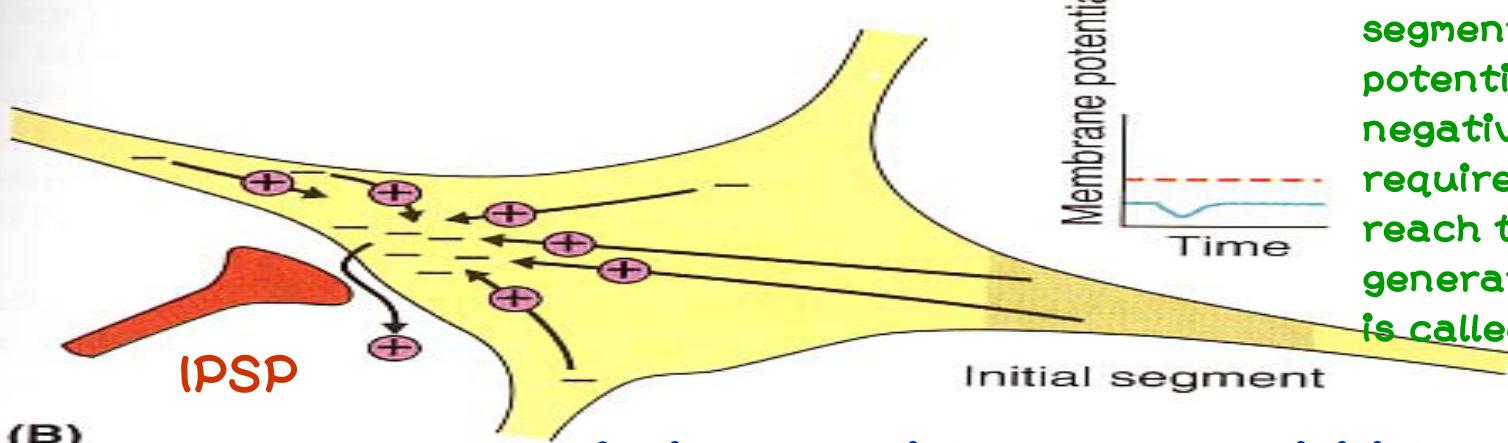
Generation of Action potential

EPSP



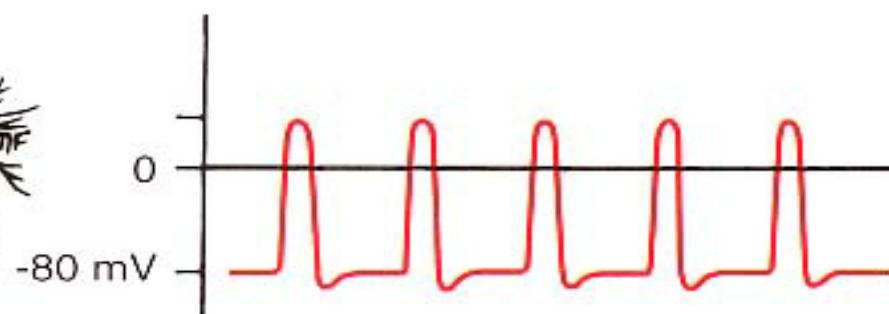
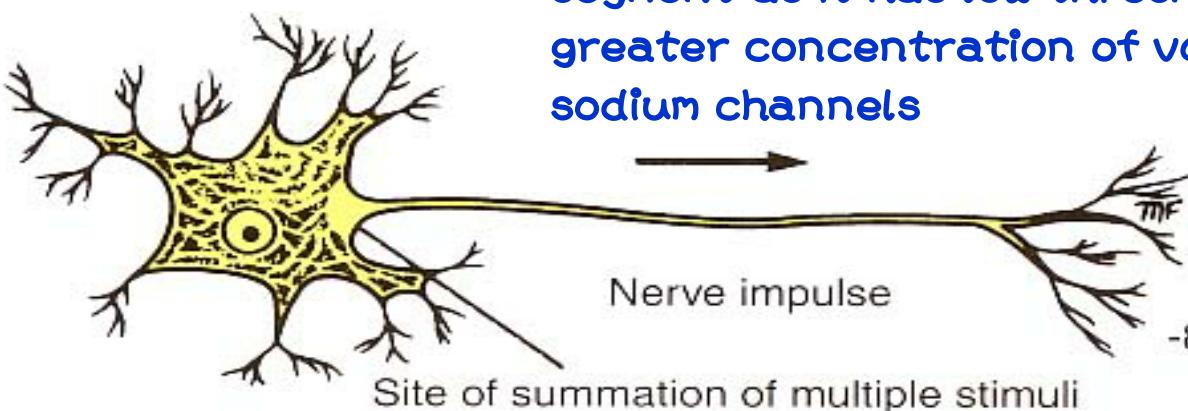
(A)

IPSP



(B)

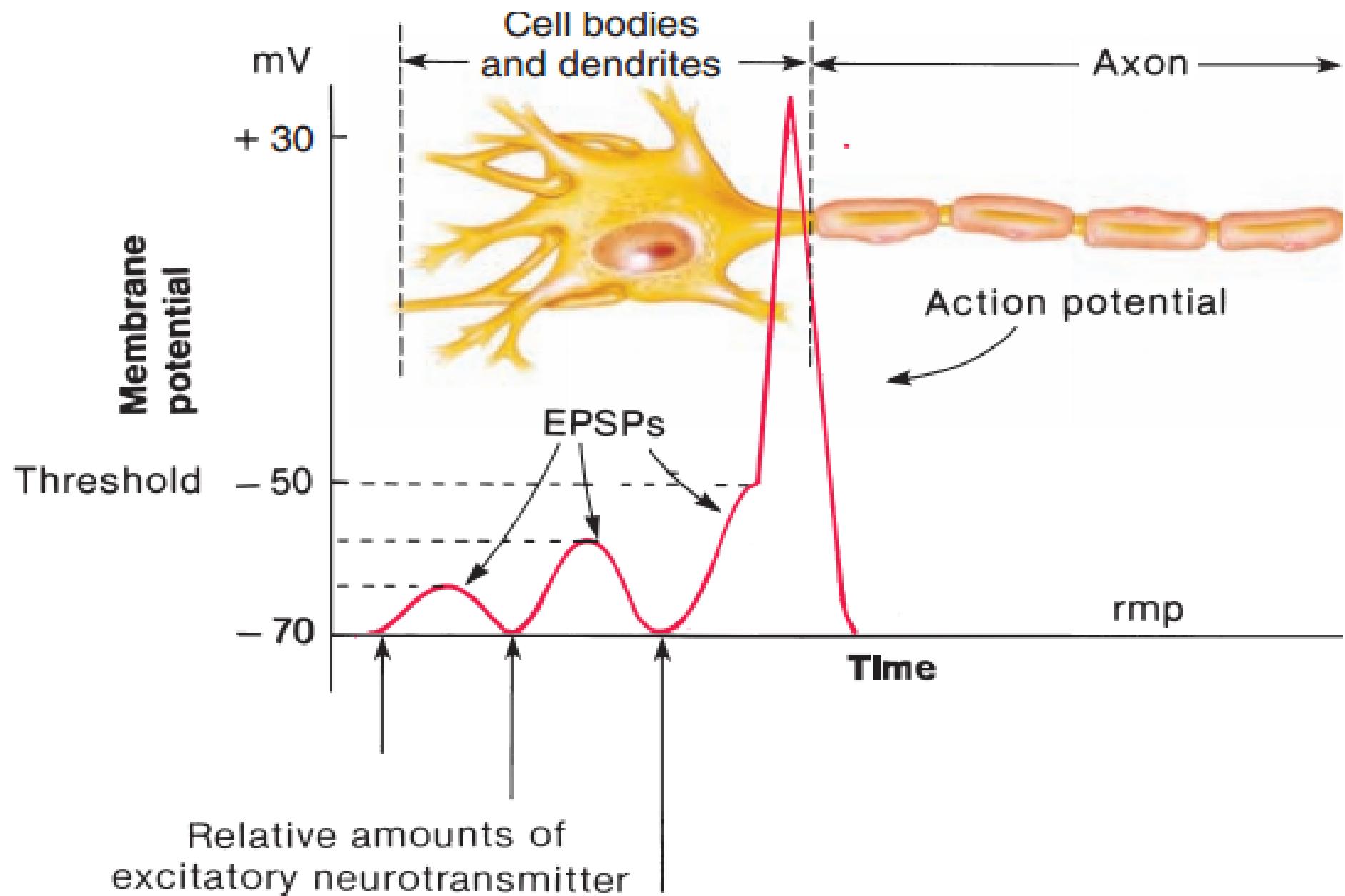
Action potentials generate at initial segment as it has low threshold and much greater concentration of voltage gated sodium channels



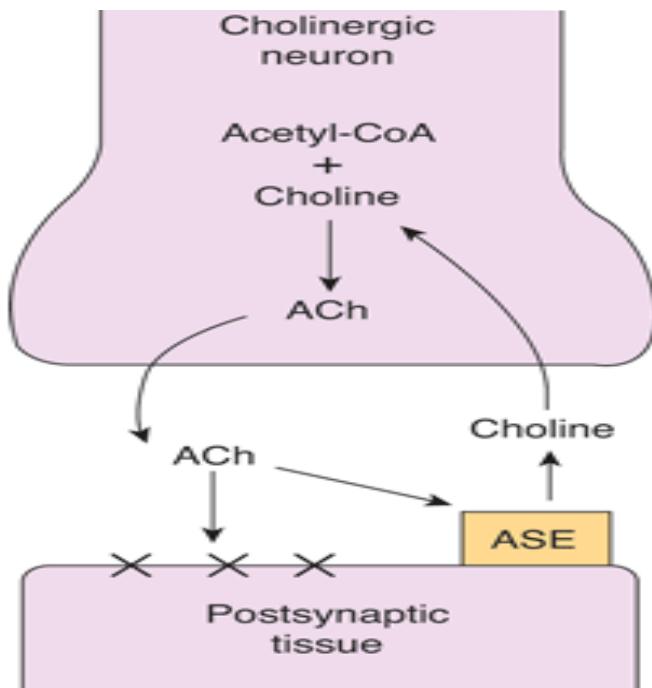
All-or-none action potentials with transient reversal of polarity

Depolarization/Hypopolarization of Initial segment. When depolarization of initial segment reaches threshold level, action potential will be generated

Generation of Action Potential

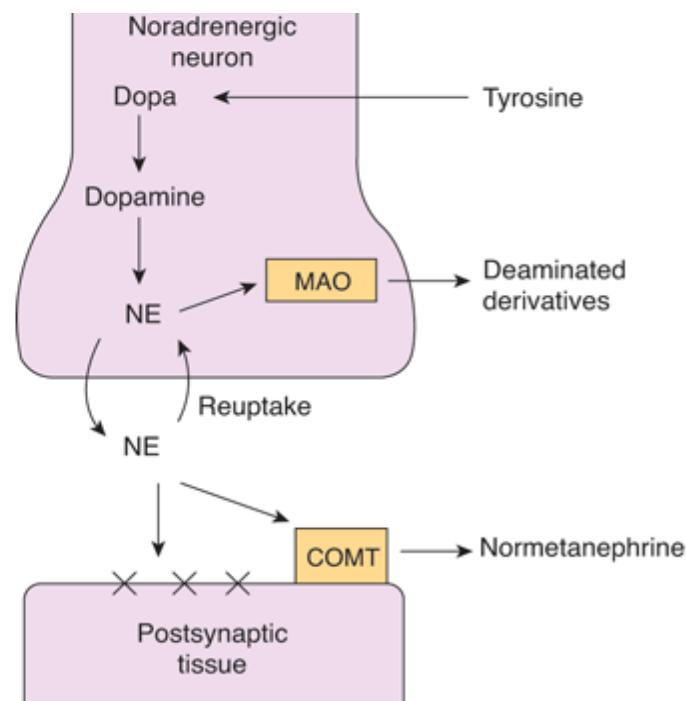


Fate of neurotransmitter

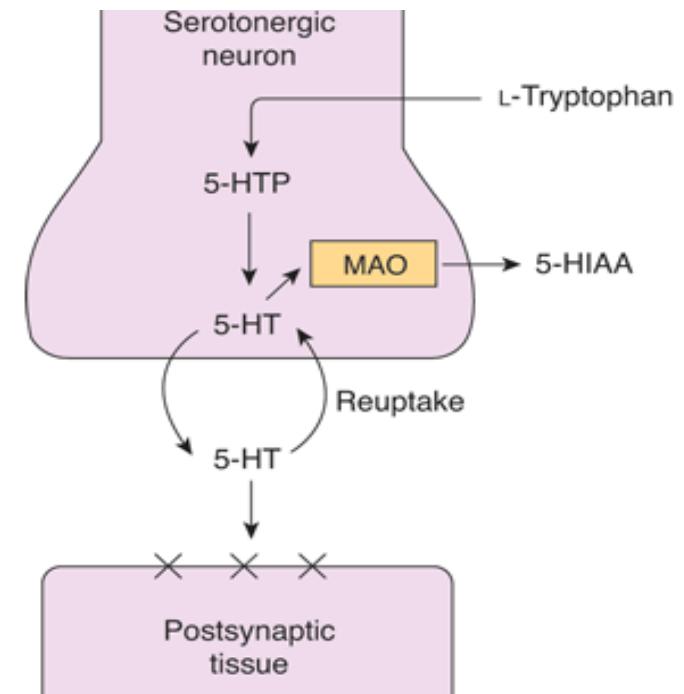


Acetylcholin

e



Catecholamine



Serotonin

MOTONEURON

MUSCLE

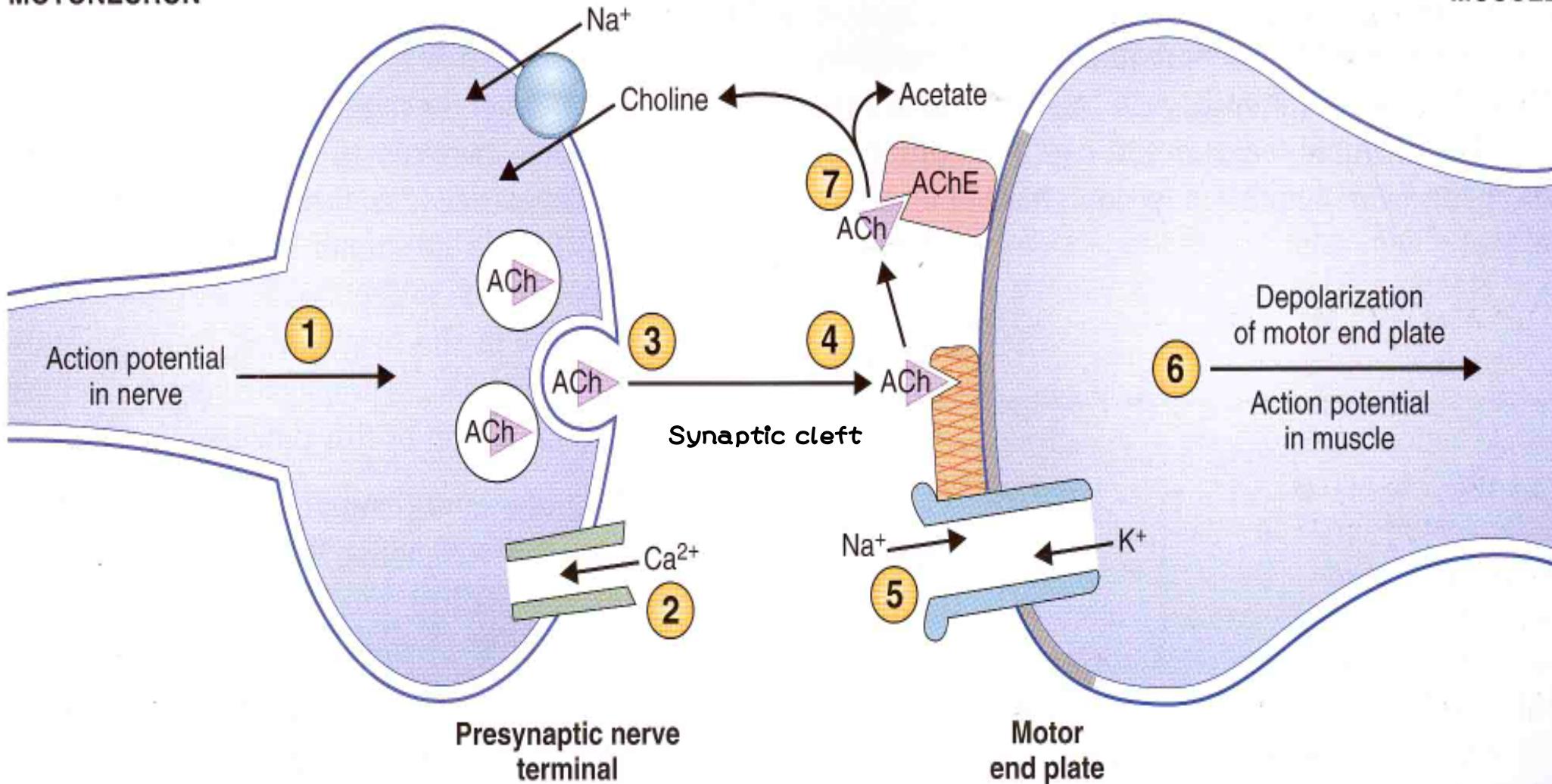
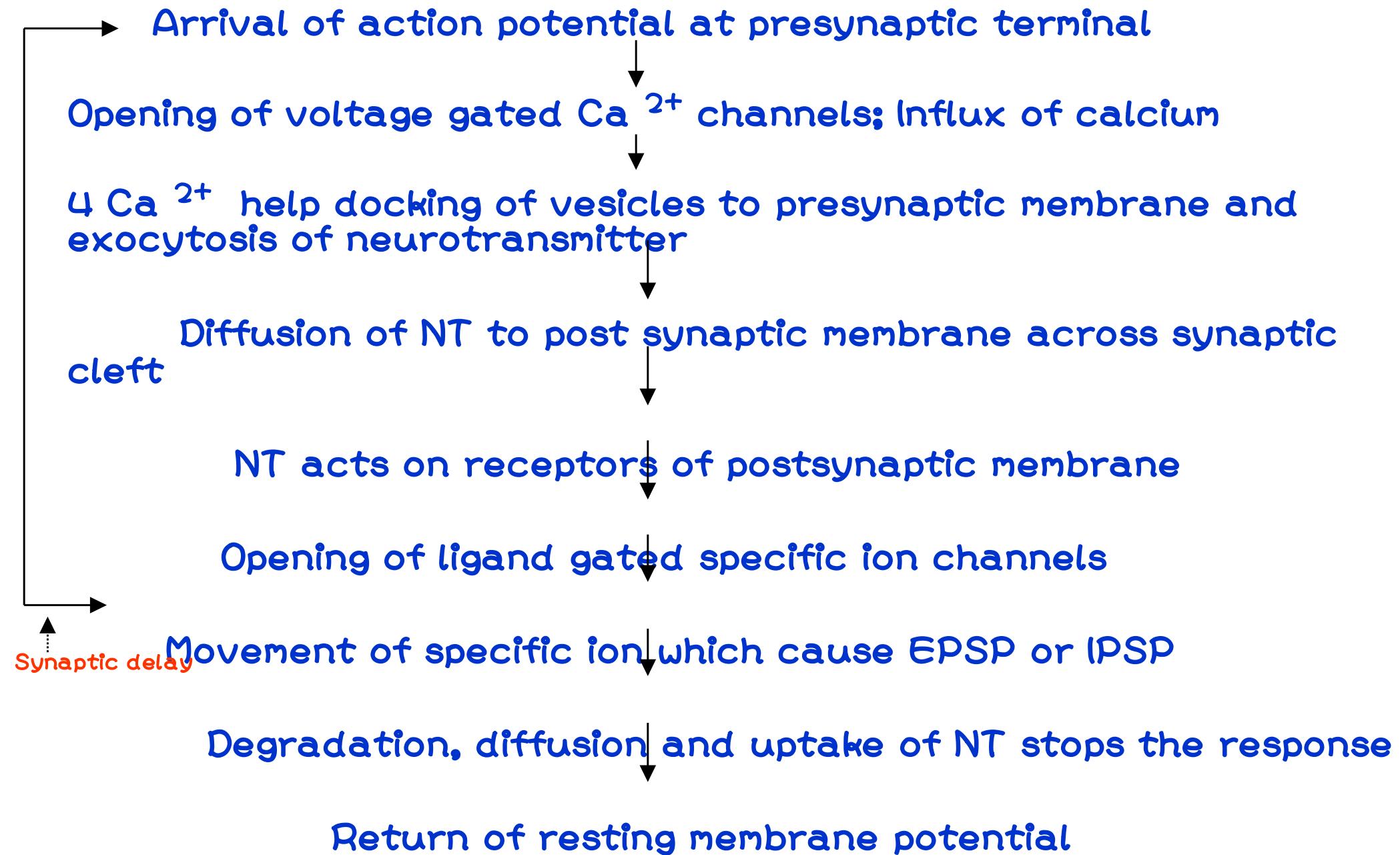


Figure 1-16 Sequence of events in neuromuscular transmission. 1, Action potential travels down the motoneuron to the presynaptic terminal. 2, Depolarization of the presynaptic terminal opens Ca^{2+} channels, and Ca^{2+} flows into the terminal. 3, Acetylcholine (ACh) is extruded into the synapse by exocytosis. 4, ACh binds to its receptor on the motor end plate. 5, Channels for Na^+ and K^+ are opened in the motor end plate. 6, Depolarization of the motor end plate causes action potentials to be generated in the adjacent muscle tissue. 7, ACh is degraded to choline and acetate by acetylcholinesterase (AChE); choline is taken back into the presynaptic terminal on an Na^+ -choline cotransporter.

Transmission across a Synapse



Properties of Synaptic transmission and Plasticity

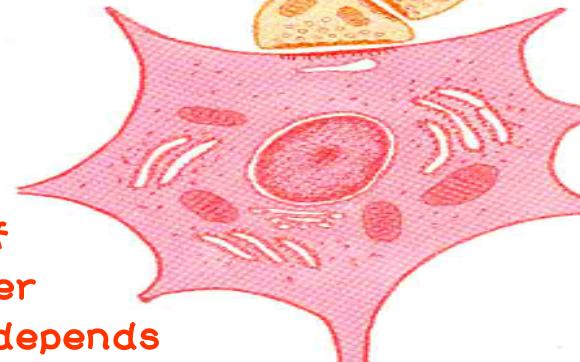
Synaptic inhibition

Presynaptic Inhibition

& Inhibition

(Excitatory fiber)

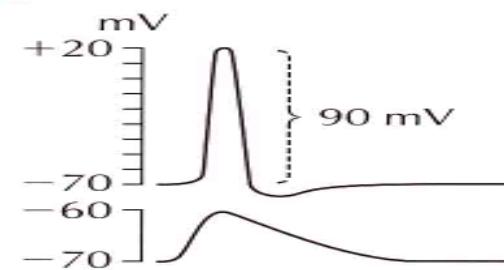
I
(Inhibitory fiber)



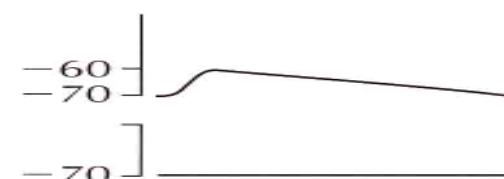
Amount of transmitter released depends on the magnitude of spike potential

A. Only E fires
90-mV spike in E terminal

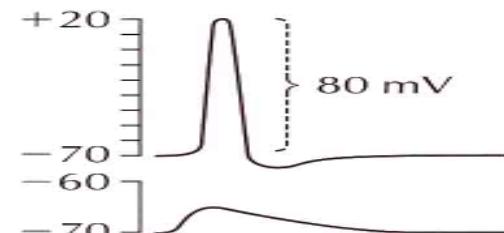
EPSP in motor neuron



B. Only I fires
Long-lasting partial depolarization in E terminal
No response in motor neuron

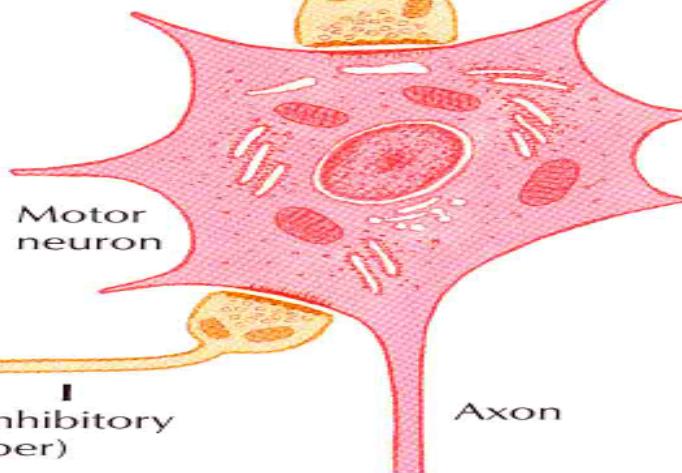


C. I fires before E
Partial depolarization of E terminal reduces spike to 80 mV, thus releasing less transmitter substance
Smaller EPSP in motor neuron



Postsynaptic Excitation

E
(Excitatory fiber)



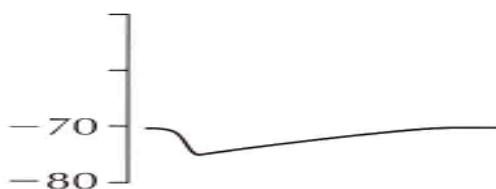
A'. Only E fires

EPSP in motor neuron



B'. Only I fires

Motor neuron hyperpolarized

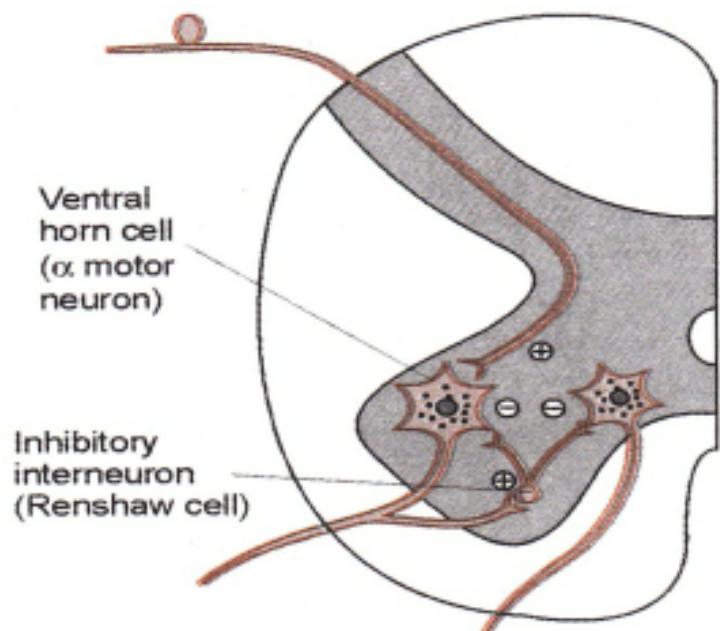


C'. I fires before E

Depolarization of motor neuron less than if only E fires



Negative feedback inhibition

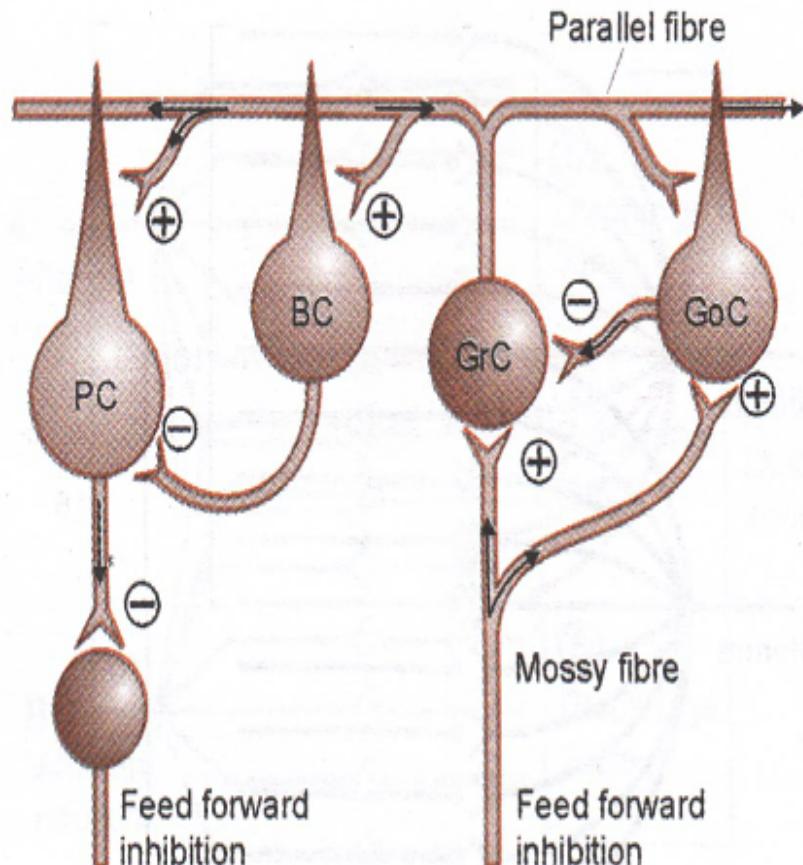


- Renshaw cells are inhibitory neurons in spinal cord
- Are activated by branches of motor cell axons
- Activated renshaw cell inhibit motor neuron which activate them and also neighboring motor neuron

Fig. 10.7-8. Renshaw cell when excited by a recurrent branch of an alpha motor neuron produces feedback inhibition of the soma of the same and other motor neurons.

Negative feedback inhibition of a spinal motor neuron via an inhibitory interneuron (Renshaw cell).

Feedforward inhibition



- Seen in cerebellum
- Neuron is connected through 2 pathway : one excitatory and other inhibitory
- Eg. In cerebellum, the granule cell excites purkinje cells which is soon inhibited by basket cells, which in turn was also excited by granule cell
- Limit duration of excitation
- Allow brief and precise timed excitation

Fig. 10.7-9. Feed forward inhibition of Purkinje cell (PC) by basket cell (BC). Note both Purkinje cell and basket cell are excited by the granule cell (GrC).

Properties of synaptic transmission

1. One way conduction
2. Synaptic delay
3. Summation
4. Convergence and divergence
5. Occlusion
6. Subliminal fringe
7. Fatigue
8. Synaptic plasticity and learning

1. One way conduction

- According to Bell Magendie law, the impulse are transmitted only in one direction

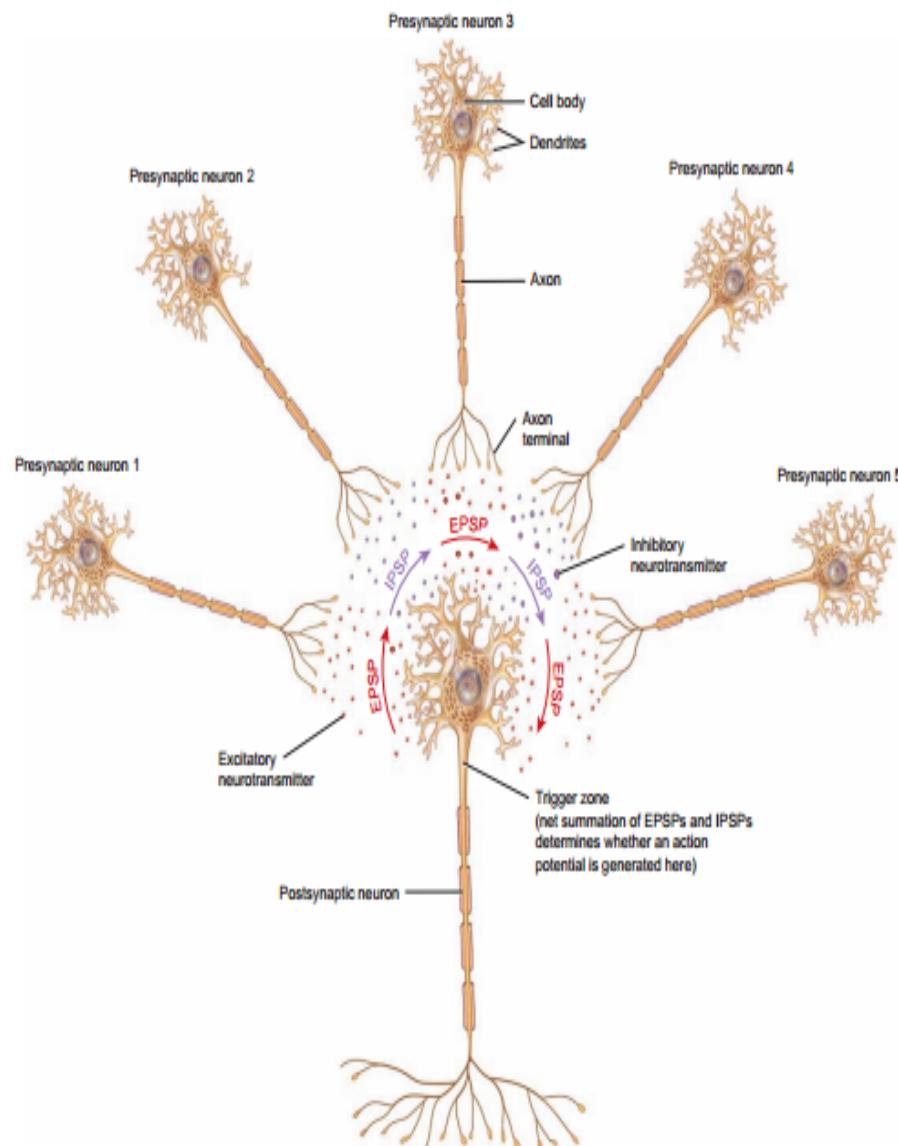
2. Synaptic delay

- Time lapse which occurs between arrival of impulse at presynaptic terminal and its passage to postsynaptic membrane
- Occurs approx. by 0.5 sec

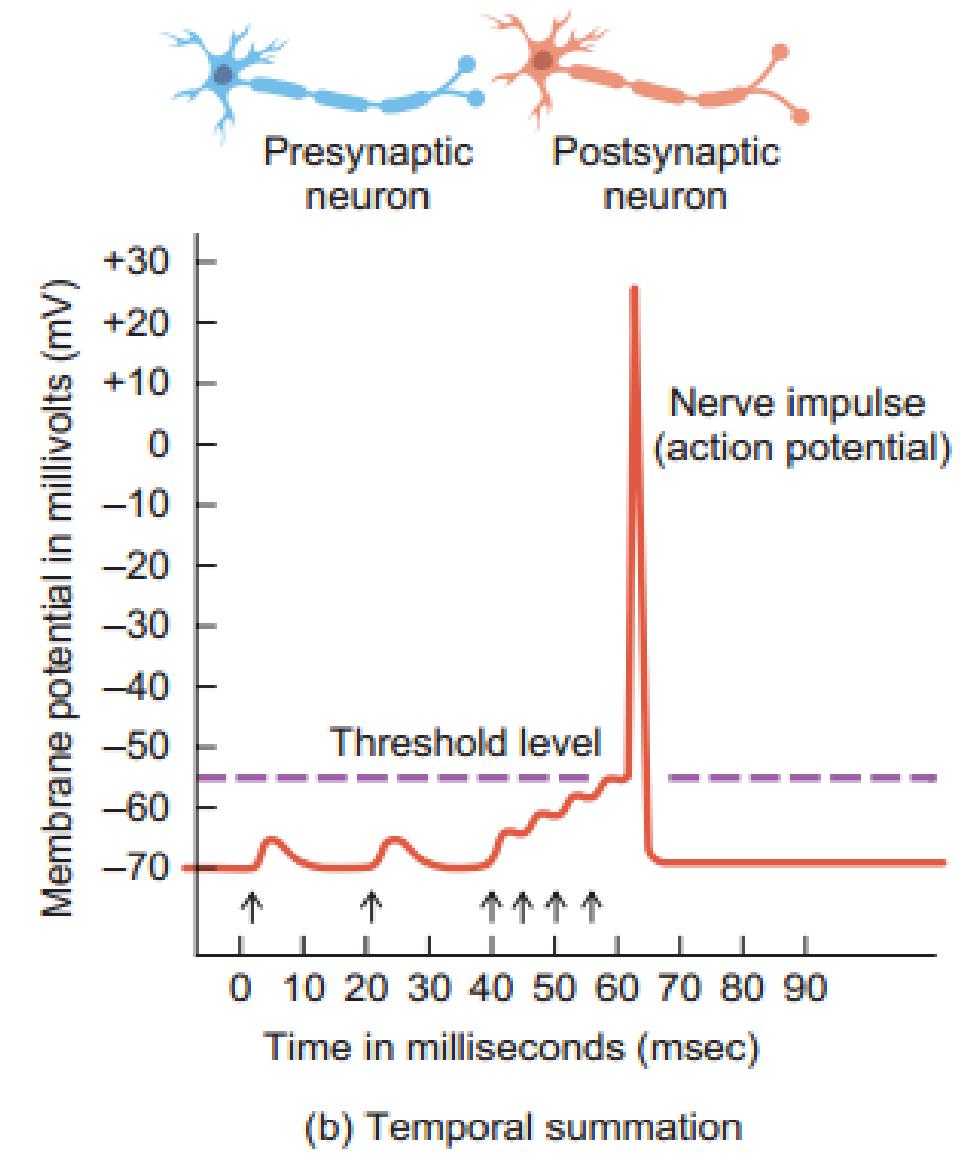
3. Summation

- Spatial summation
- Temporal summation

Summation of postsynaptic potential

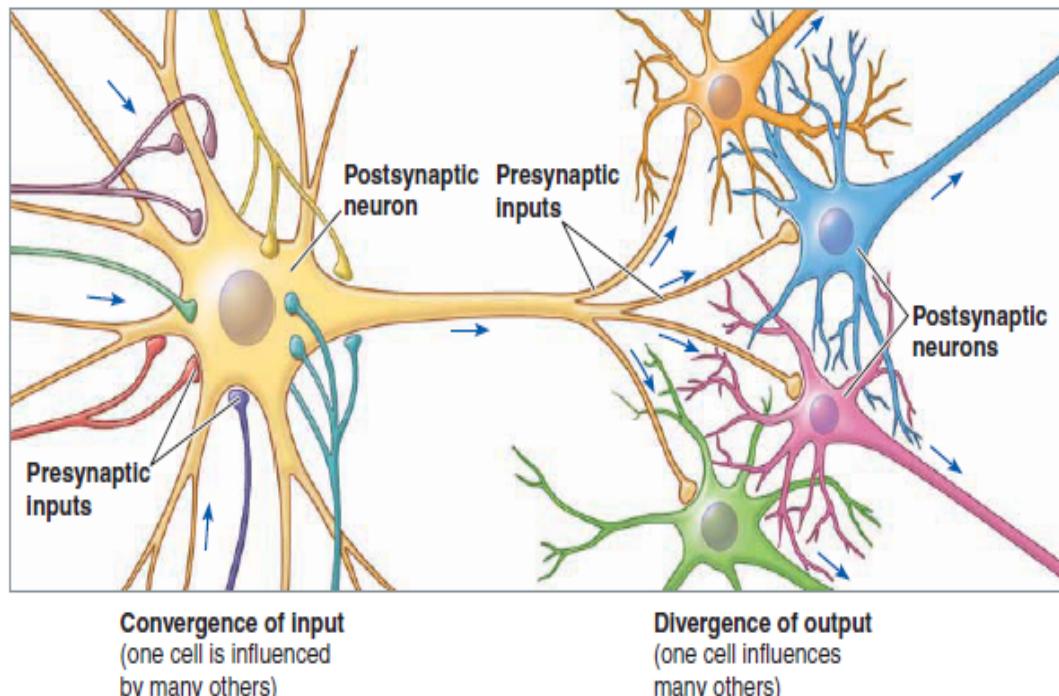


Spatial summation



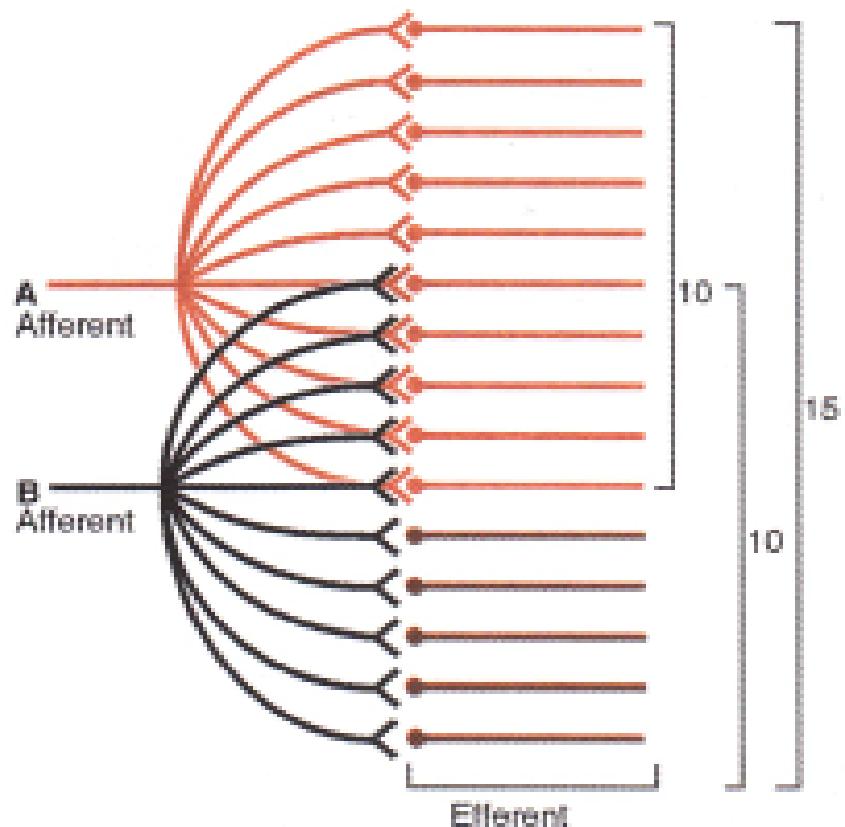
Temporal summation

4. Convergence and divergence



- Thousands of synapses from many different presynaptic cells can affect a single postsynaptic cell **convergence**
- Convergence allows information from many sources to influence a cell's activity
- A single presynaptic cell can send branches to many other postsynaptic cells **divergence**.
- divergence allows one information to affect multiple pathways.

5. Occlusion



Response to two presynaptic neuron is less than the sum of total of the response obtained when they are stimulated separately

Fig. 10.7-12. Occlusion phenomenon : Stimulation of afferent neuron A and B each excites 10 efferent neurons. Simultaneous stimulation of neuron A and B together excite 15 efferent neurons because 5 efferent neurons are common to both.

6. Subliminal fringe

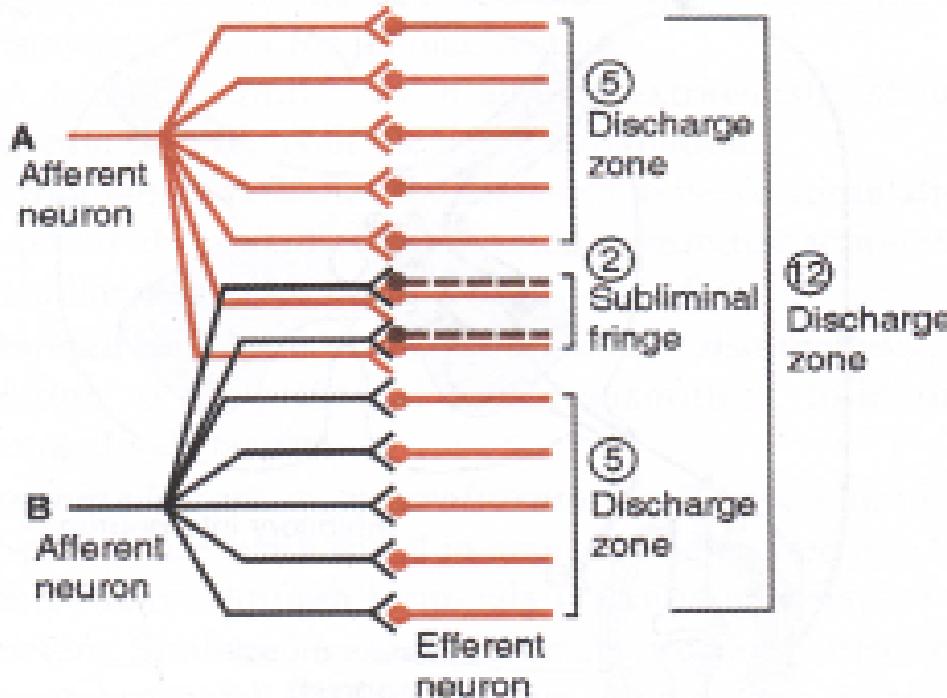


Fig. 10.7-13. Subliminal fringe effect: stimulation of afferent neuron A and B each excites 5 efferent neurons and subliminal fringe effect on 2 efferent neurons (which are common to both A and B neurons). Simultaneous stimulation of neuron A and B together excites 12 efferent neurons because the subliminal fringe effect on 2 neurons gets summated to produce threshold stimulation.

- Subliminal - below threshold, fringe - border
- An afferent nerve divides into many branches (100)
- Of this large number terminate on one efferent neuron while other terminate on near by
- When afferent neuron is stimulated, the efferent neuron w/c has many presynaptic terminal are excited to threshold level & AP is fired
- Other in the peripheral zone are excited to subthreshold level, AP is not fired, this is known as submininal fringe effect

7. Fatigue

- Repeated stimulation of presynaptic neuron leads to gradual decrease and finally disappearance of the response
- this is also called habituation
- is due to exhaustion of neurotransmitter

Plasticity of synaptic transmission

- Refers to modulation of outcome of synaptic activity by preceding effect

Following phenomenon contribute to plasticity

1. Post tetanic potentiation
2. Habituation
3. Sensitization
4. Long term potentiation
5. Long term depression

Post tetanic potentiation

- If rapidly repeated stimulus is followed by brief pause, the response to subsequent stimulus is frequently enhanced

Habituation

- Repeated stimulation of synapse leads to gradual diminution and finally disappearance of post synaptic response

Sensitization

- Increase in synaptic response as a result of exposure to noxious stimulus

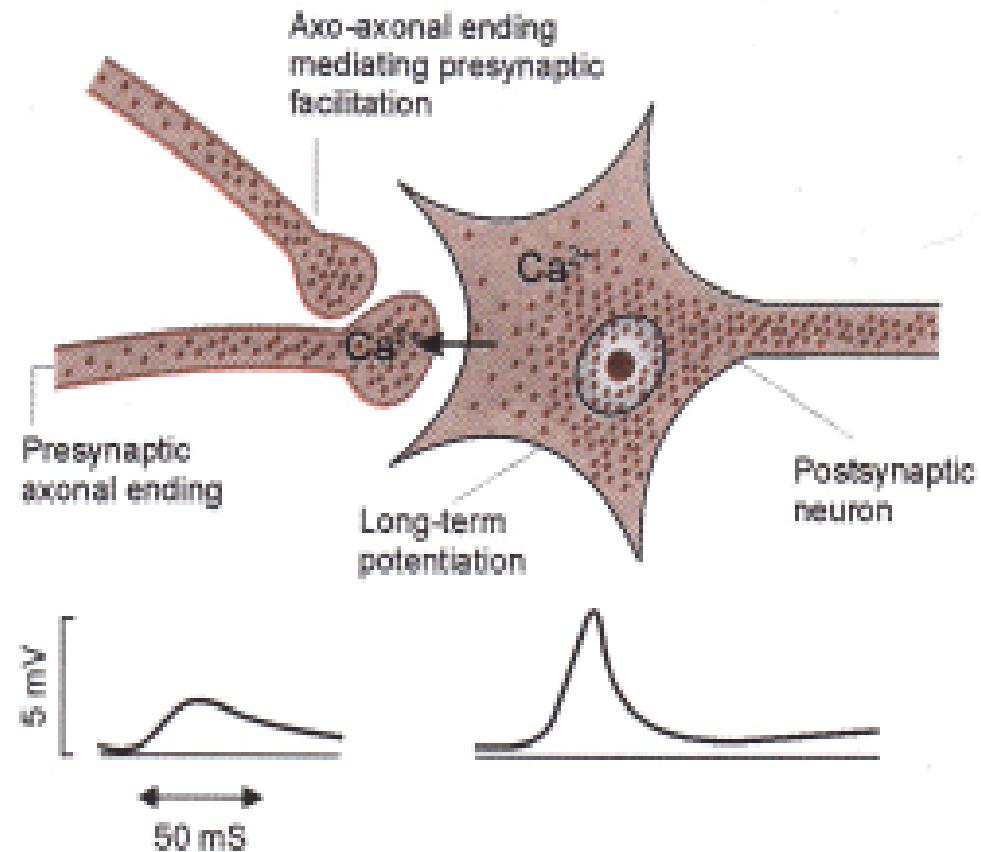


Fig. 10.7-14. Synaptic plasticity: presynaptic and postsynaptic sites producing changes in the strength of synaptic transmission.

Long term depression

- It is opposite to long term potentiation
- It is characterized by decrease in synaptic strength
- It is produced by slower stimulation of presynaptic neurons and is associated with smaller rise in intracellular Ca^{2+}

Neurotransmitter and Neuromodulators

Neurotransmitters

- Neurotransmitters are chemical substances which are responsible for transmission of an impulse through a synapse
- More than 40 important transmitter substances have been discovered so far.
- Some of the best known are acetylcholine, norepinephrine, epinephrine, histamine, gamma-aminobutyric acid (GABA), glycine, serotonin, and glutamate.

Physiological classification

- Physiologically neurotransmitters are divided into 2 groups

1. Excitatory neurotransmitter

- Can cause action potential, contraction (muscle), secretion (gland)
- In CNS, excitatory neurotransmitter produce depolarization of post synaptic neuron (EPSP)
- The most common excitatory neurotransmitter within CNS is glutamate
- Other excitatory neurotransmitter are: Ach, aspartic acid

2. Inhibitory neurotransmitter

- Reduce or block activity of post synaptic cell
- They produce hyperpolarization of the post synaptic membrane (IPSP)
- Most common inhibitory neurotransmitter within CNS is glycine or GABA (gamma aminobutyric acid)
- Other inhibitory neurotransmitter include dopamine

Group	Name	Site of secretion	Action
Amino acids	GABA	Cerebral cortex, cerebellum, basal ganglia, retina and spinal cord	Inhibitory
	Glycine	Forebrain, brainstem, spinal cord and retina	Inhibitory
	Glutamate	Cerebral cortex, brainstem and cerebellum	Excitatory
	Aspartate	Cerebellum, spinal cord and retina	Excitatory
Amines	Noradrenaline	Postganglionic adrenergic sympathetic nerve endings, cerebral cortex, hypothalamus, basal ganglia, brainstem, locus coeruleus and spinal cord	Excitatory and inhibitory
	Adrenaline	Hypothalamus, thalamus and spinal cord	Excitatory and inhibitory
	Dopamine	Basal ganglia, hypothalamus, limbic system, neocortex, retina and sympathetic ganglia	Inhibitory
	Serotonin	Hypothalamus, limbic system, cerebellum, spinal cord, retina, gastrointestinal (GI) tract, lungs and platelets	Inhibitory
	Histamine	Hypothalamus, cerebral cortex, GI tract and mast cells	Excitatory
Others	Nitric oxide	Many parts of CNS, neuromuscular junction and GI tract	Excitatory
	Acetylcholine	Preganglionic parasympathetic nerve endings Postganglionic parasympathetic nerve endings Preganglionic sympathetic nerve endings Postganglionic sympathetic cholinergic nerve endings Neuromuscular junction, cerebral cortex, hypothalamus, basal ganglia, thalamus, hippocampus and amacrine cells of retina	Excitatory

GABA = Gamma-aminobutyric acid, CNS = Central nervous system.

TABLE 141.2: Excitatory and inhibitory neurotransmitters

Excitatory neurotransmitters	Inhibitory neurotransmitters	Neurotransmitters with excitatory and inhibitory actions
1. Acetylcholine 2. Nitric oxide 3. Histamine 4. Glutamate 5. Aspartate	1. Gamma-aminobutyric acid 2. Glycine 3. Dopamine 4. Serotonin	1. Noradrenaline 2. Adrenaline

Neuromodulators

- are chemical messengers that do not cause the formation of EPSPs or IPSPs but rather bring about long-term changes that subtly **modulate; depress or enhance**, the action of the synapse.
- Cholecystokinin (CCK) is an example.
- Neuropeptides act primarily as neuromodulators.

Opioid neuromodulator

Name	Site of secretion	Action
Enkephalins	Many parts of brain, substantia gelatinosa and retina	
Dynorphins	Hypothalamus, posterior pituitary and duodenum	Inhibit pain sensation
β -endorphin	Thalamus, hypothalamus, brainstem and retina	

Name	Site of secretion	Action
Bradykinin	Blood vessels, kidneys	Vasodilator
Substance P	Brain, spinal cord, retina peripheral nerves and intestine	Mediates pain. Regulates anxiety, stress, mood disorders, neurotoxicity, nausea and vomiting. Causes vasodilatation.
Secretin	Cerebral cortex, hypothalamus, thalamus, olfactory bulb, brainstem and small intestine	Inhibits gastric secretion and motility
CCK	Cerebral cortex, hypothalamus, retina and small intestine	Contracts gallbladder Inhibits gastric motility Increases intestinal motility
Gastrin	Hypothalamus, medulla oblongata, posterior pituitary and gastrointestinal (GI) tract	Increases gastric secretion and motility Stimulates islets in pancreas
VIP	Cerebral cortex, hypothalamus, retina and intestine	Causes vasodilatation
Motilin	Cerebral cortex, cerebellum, posterior pituitary and intestine	Stimulates intestinal motility
Neurotensin	Hypothalamus and retina	Inhibits pain sensation Decreases food intake
Vasopressin	Posterior pituitary, medulla oblongata and spinal cord	Causes vasoconstriction
Oxytocin	Posterior pituitary, medulla oblongata and spinal cord	Stimulates milk ejection and uterine contraction
CRH	Hypothalamus	Stimulates release of ACTH

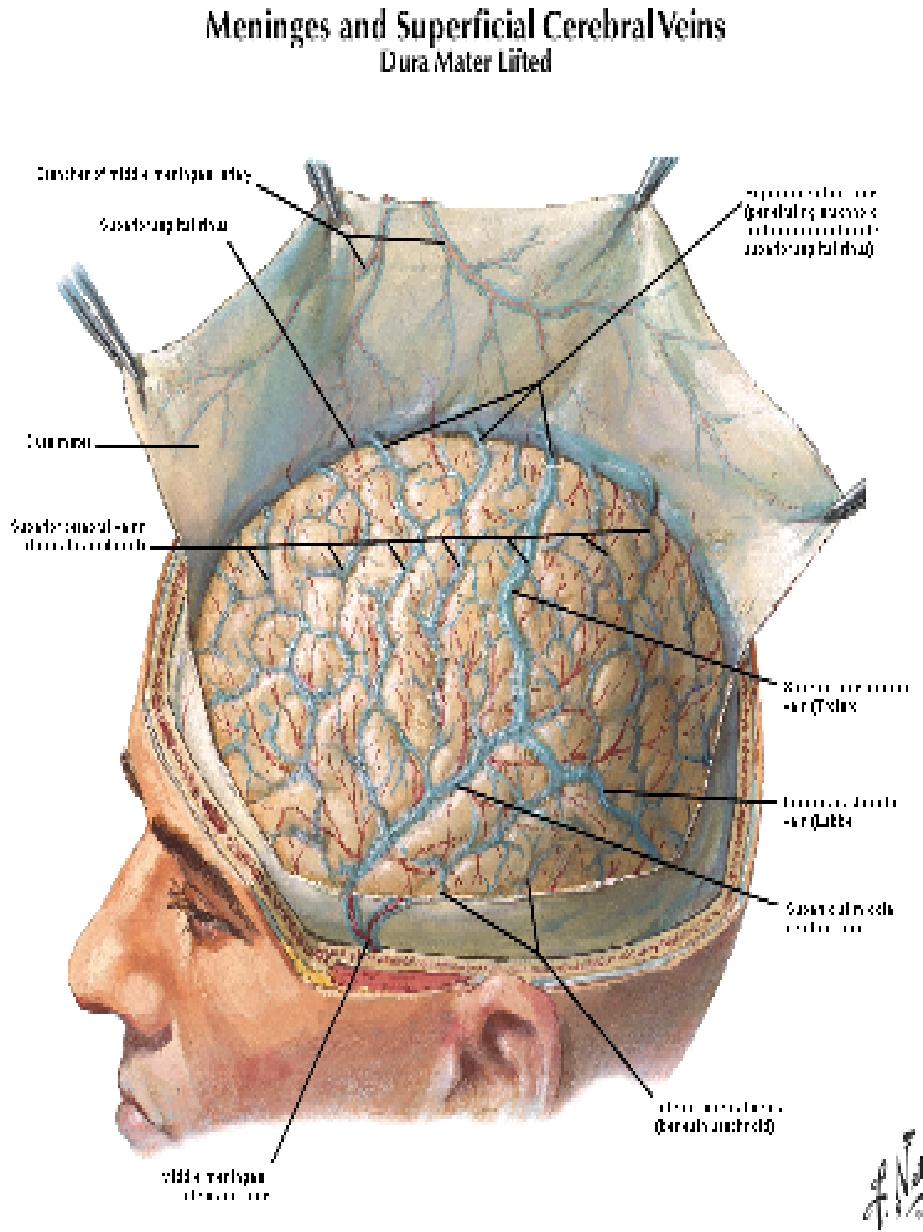
CRH	Hypothalamus	Stimulates release of ACTH
GHRH	Hypothalamus	Stimulates release of growth hormone
GHRP	Hypothalamus	Stimulates release of GHRH
TRH	Hypothalamus, other parts of brain and retina	Stimulates release of thyroid hormones
Somatostatin	Hypothalamus, other parts of brain, substantia gelatinosa and retina	Inhibits growth hormone secretion Decreases food intake
GnRH	Hypothalamus, preganglionic autonomic nerve endings and retina	Inhibits gonadotropin secretion
Endothelin	Posterior pituitary, brainstem and endothelium	Causes vasoconstriction
Angiotensin II	Hypothalamus, brainstem and spinal cord	Causes vasoconstriction
ANP	Hypothalamus, brainstem and heart	Causes vasodilatation Increases sodium excretion
BNP	Hypothalamus and heart	Causes vasodilatation Increases sodium excretion
CNP	Brain, myocardium, endothelium of blood vessels, GI tract and kidneys	Causes vasodilatation Increases sodium excretion
Neuropeptide Y	Medulla, hypothalamus and small intestine	Increases food intake Causes vasoconstriction Increases enteric blood flow
Ghrelin	Hypothalamus, stomach, pituitary, kidney and placenta	Promotes GH release Induces appetite and food intake

TABLE 141.3: Differences between neurotransmitters and neuromodulators

SI No	Neurotransmitters	Neuromodulators
1	Propagate nerve impulse through synapse	Modify and regulate synaptic transmission
2	Packed in small synaptic vesicles	Packed in large synaptic vesicles
3	Found only in axon terminals	Found in all parts of the body
4	Generally, neuron has only one neurotransmitter	Neuron may have one or more neuromodulators
5	Act by changing the electric potential – depolarization or repolarization	Have diverse actions
6	Chemically, neurotransmitters are amino acids, amine or others	Chemically, neuromodulators are only peptides

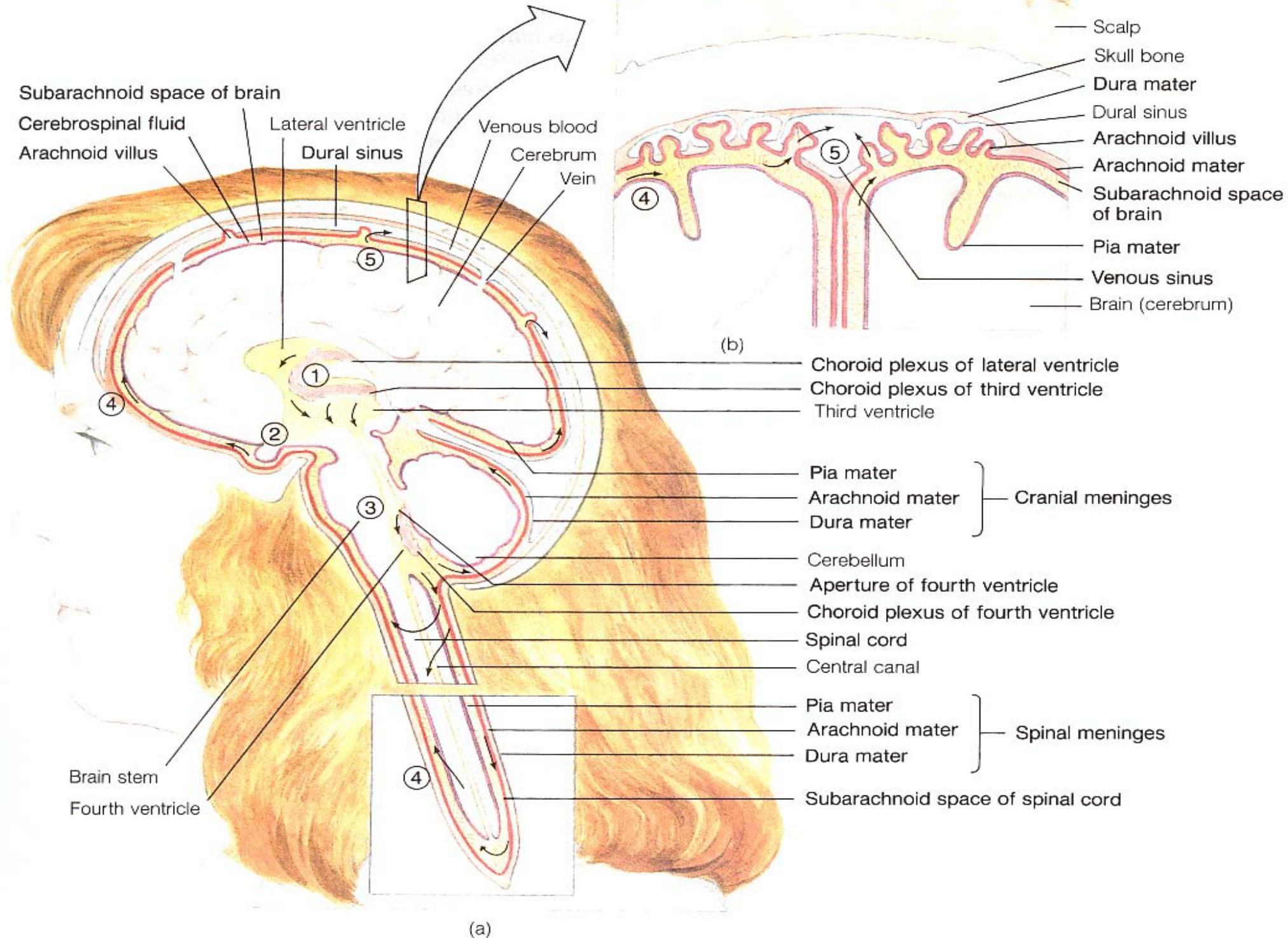
Microenvironment of the Neuron

Microenvironment of the neuron



- Skull
- Duramatter
 - Subdural space
 - Bridging vein
- Arachnoid matter
 - Subarachnoid (CSF, Blood vessels)
 - True space
- Pia matter
 - No space
 - Covers the blood vessels
- Cerebral hemisphere

- Anything that surrounds individual neurons - **neuronal microenvironment**
- Extracellular fluid as well as Cerebrospinal fluid
- Conc. of solute in BECF is fluctuate with neuronal activity, changes in ECF can influence nerve cell behavior



Cerebrospinal fluid (CSF)

- is a clear, colorless, watery liquid that protects the brain and spinal cord from chemical and physical injuries.

Volume: 100-150 ml.

Formation

- Choroid plexus in the ventricle

Secretion

- rate is constant - 0.2 - 0.3 ml/ min & 550 ml/ day.

Pressure

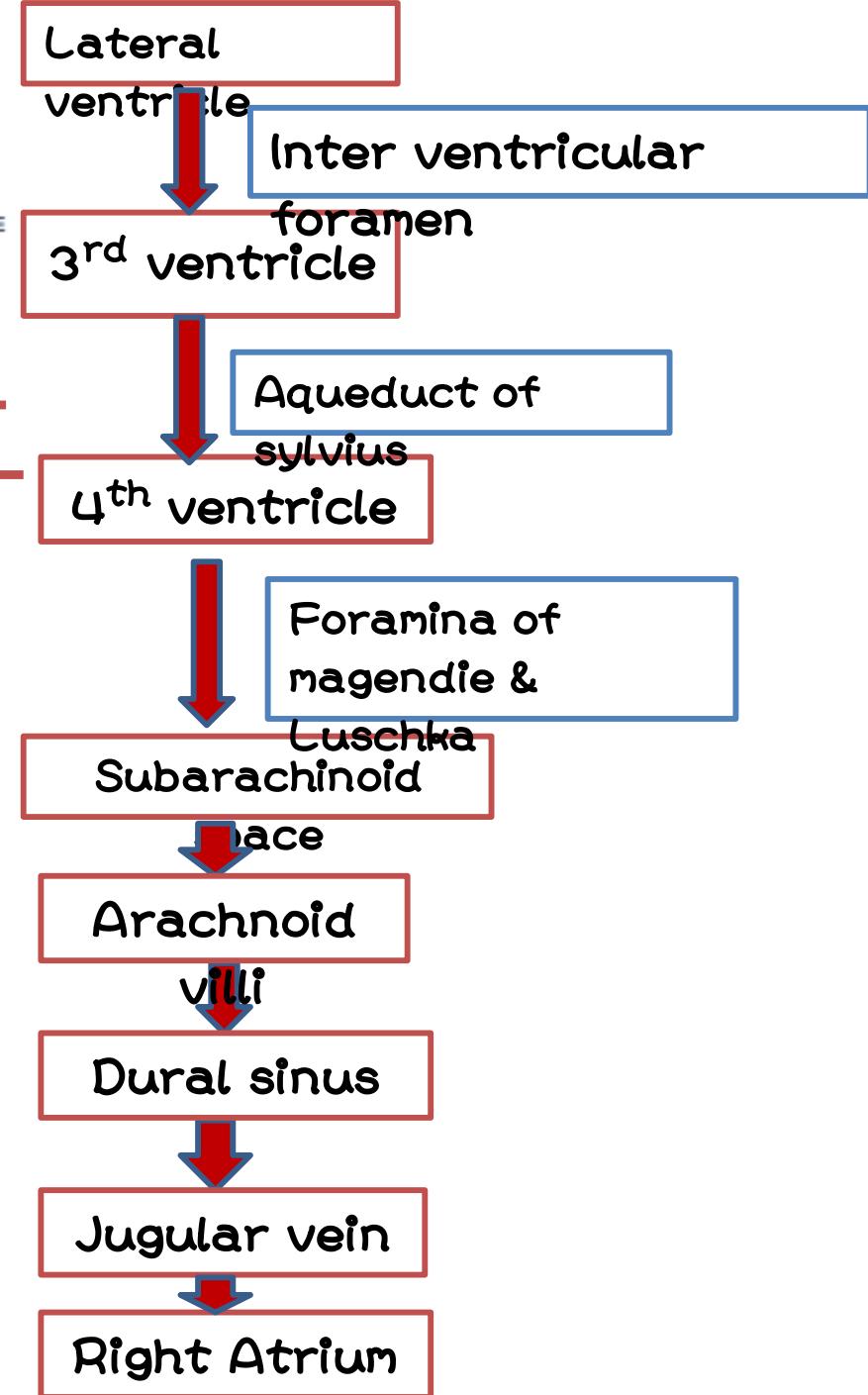
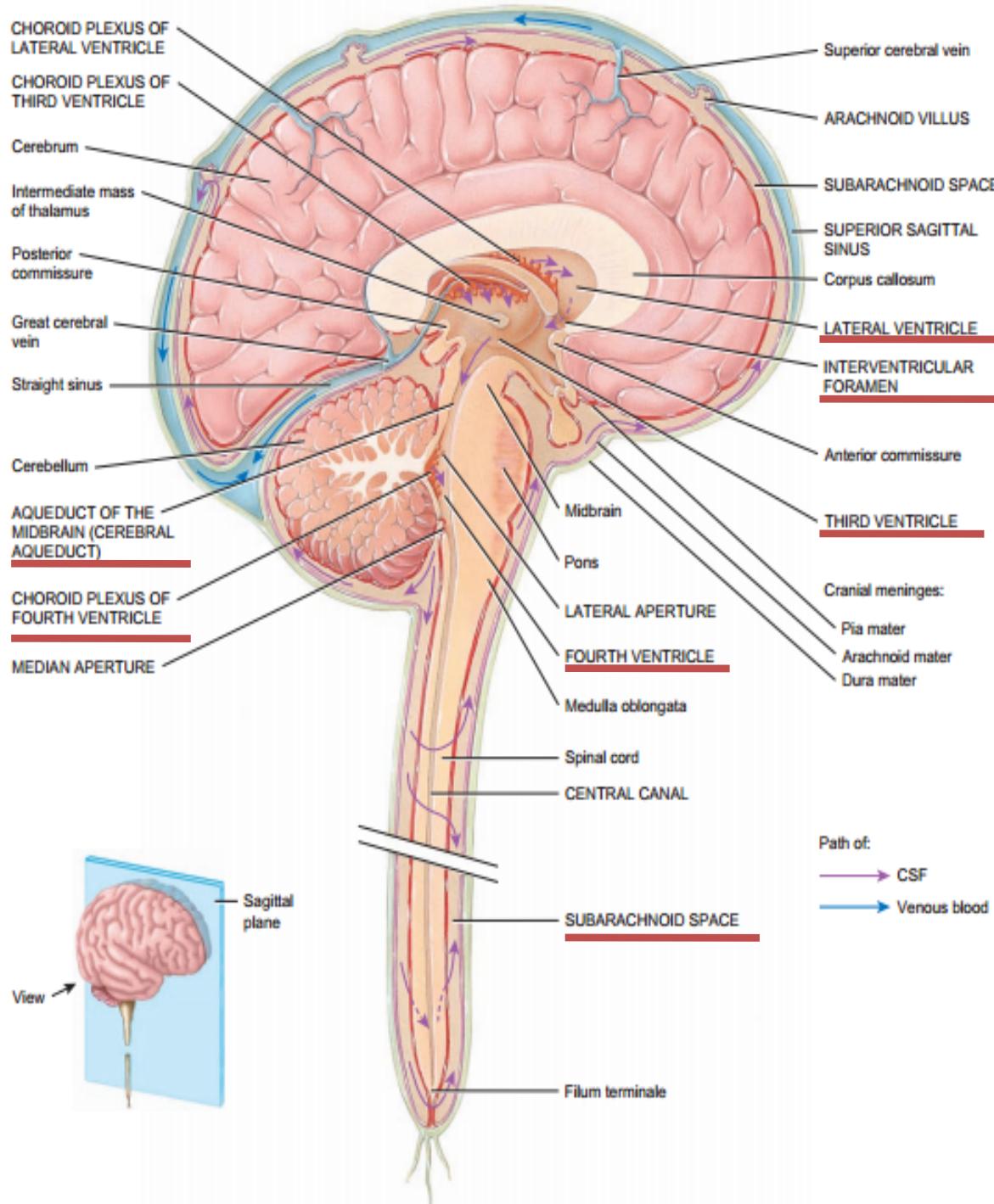
- 70 to 180 mm H₂O

Reabsorption

- into arachnoid villi (dural sinuses)

Rate of CSF formation and reabsorption is equal.

Formation and Circulation of CSF



Functions of CSF

- **Providing optimum environment to neurons**
 - CSF is in contact with blood in one side and IF on other
 - It serve as a fluid buffer thereby provide optimal environment to neuron
- **Removal of proteins**
 - CSF serve as function of lymphatic in CNS
 - In brain, the protein that has leaked out of the capillaries into the interstitial fluid is drained by CSF and return to blood stream
- **Protection**
 - CSF protects brain from injury because brain & CSF have approx. same specific gravity.
- **It acts as a Reservoir to regulate content of cranium**
 - Keeps the total volume of cranial content constant

Monro-Kellie Doctrine

Because brain tissue and CSF are incompressible, the volume of blood, CSF and brain in cranium at any time must be relatively constant

- Brain floats in CSF, which **acts as shock absorber**
- CSF buffer the brain from mechanical injury
- The CSF that surrounds the brain, reduces the effective weight of brain from 1400 g to 50 g; due to specific gravity (brain - 1.040 and CSF - 1.007)

Other uses: - Lumbar Puncture (Adult L3 - 4)

- Introduction of therapeutic agents in subarachnoid space.

CLINICAL SIGNIFICANCE

Hydrocephalus

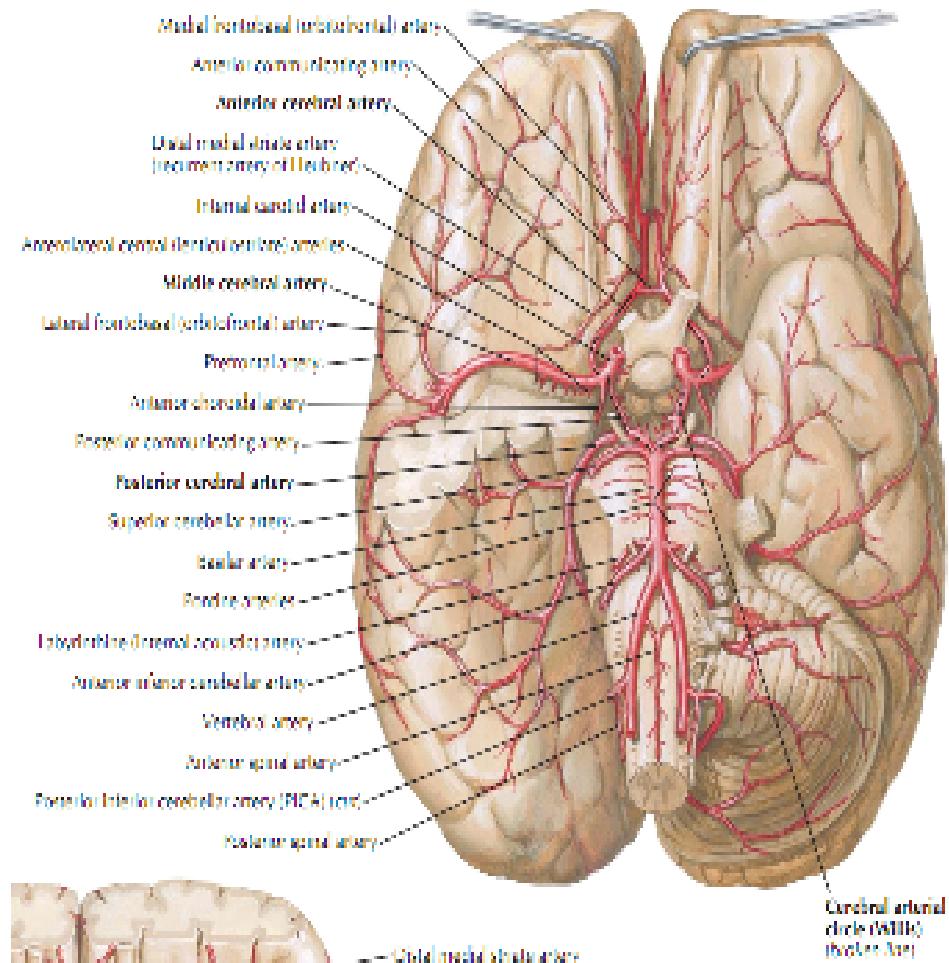
Causes: - Decreased absorption as in Obstruction

- Increased formation as in inflammation.

Cerebral circulation

- In an adult
 - the brain represents only **2%** (1400 gm) of total body weight (70 kg); 60% white matter and 40% Grey matter
 - Blood flow: 750 ml/ min (15% of CO), 55-60ml/ 100gm of tissue/min
 - O₂ consumption: 3.3ml/100g/min or 45 ml/min i.e. 20% of whole body at rest
 - Brain is extremely **sensitive to hypoxia**
 - an interruption in blood flow for **1 or 2 minutes** impairs neuronal function
 - total deprivation of oxygen for about **4 minutes** causes permanent injury.
 - **Glucose** is the main source of energy for brain
 - If blood entering the brain has a **low level of glucose**, mental confusion, dizziness, convulsions, and loss of consciousness may occur

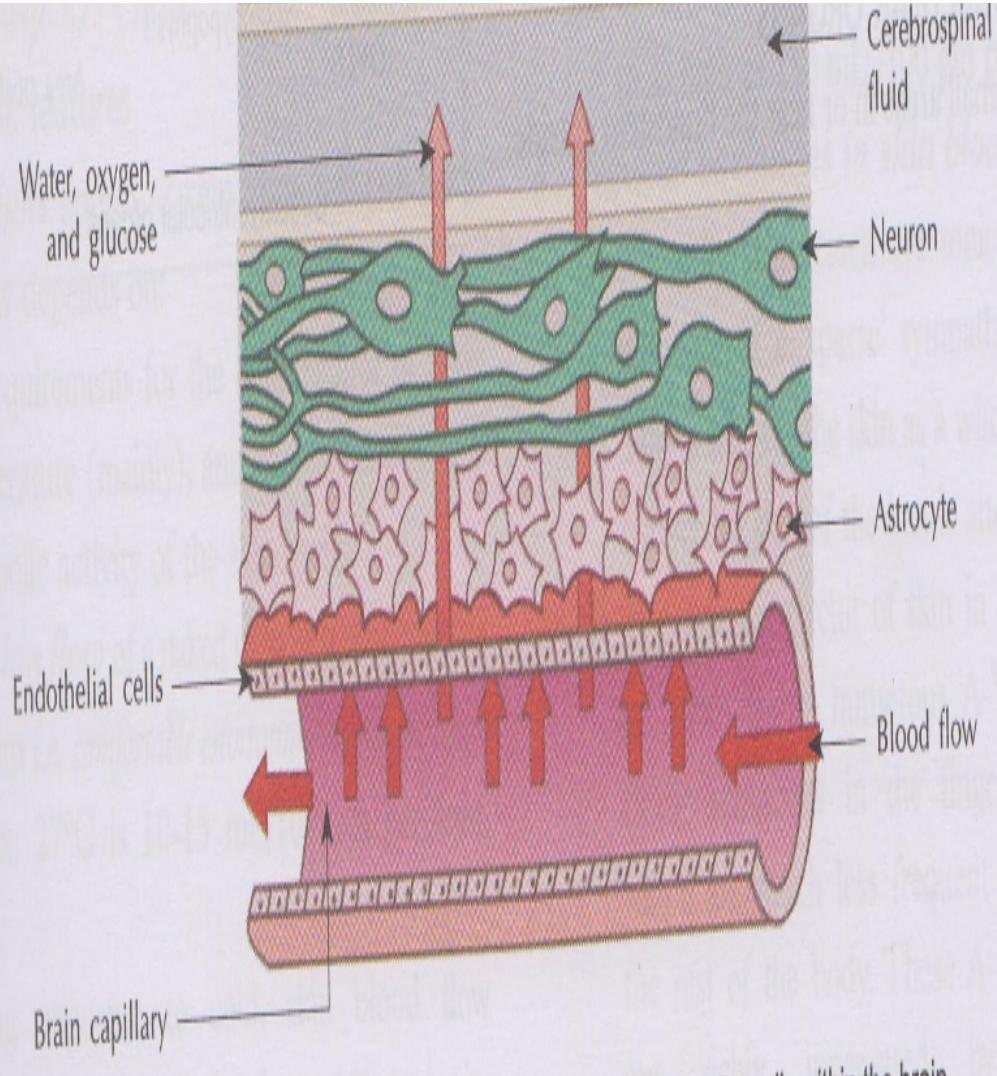
Cerebral Circulation



- Anterior circulation
 - Comes from internal carotid artery
 - Posterior circulation
 - Vertebral artery

Regulation of Cerebral circulation

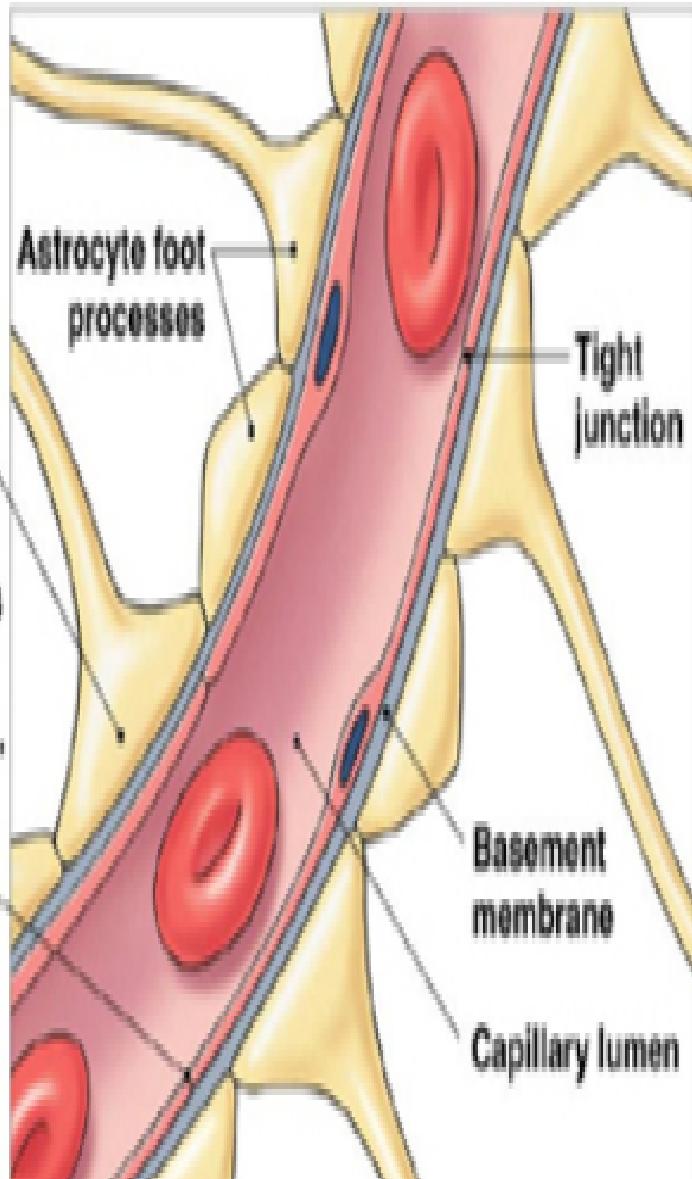
- Perfusion Pressure
- Intracranial Pressure: Monro-Kellie Doctrine
- Autoregulation: Myogenic Mechanism
- Neural
- Chemical
 - K^+ , H^+ , (CO_2 , lactic acid, pyruvic acid), Adenosine → Vasodilatation
 - Cerebral blood flow increases linearly with rise in arterial pCO_2
 - Hypoxia ($\downarrow pO_2$): Vasodilatation (Oppos. to Pulmonary hypoxia)



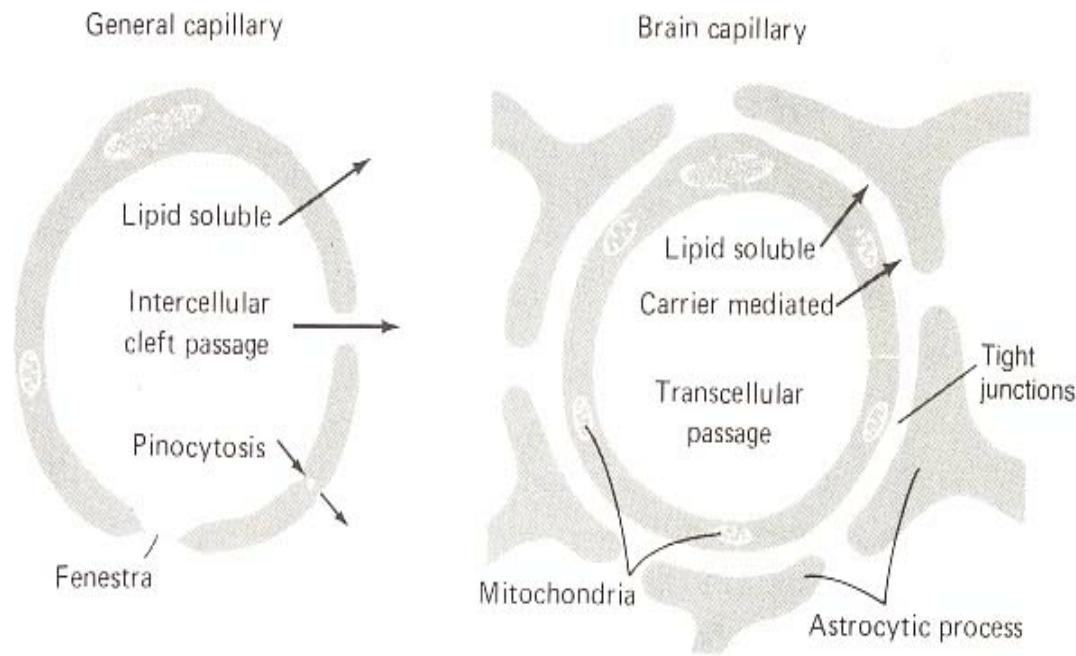
- Barrier between blood and brain tissue
- Two types of barrier in Brain
- **Blood CSF barrier**
 - b/n choroid plexus and CSF fluid
- **Blood Brain barrier**
 - Located b/n CSF & brain capillaries elsewhere than choroidal plexus

Astrocyte foot processes secrete paracardines that promote tight junction formation.

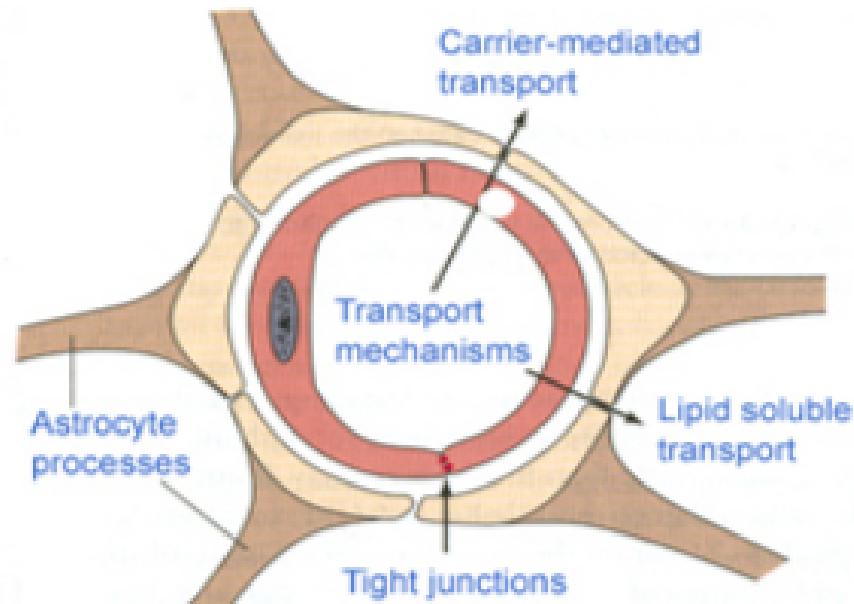
Tight junction prevents solute movement between endothelial cells.



- Is composed of capillaries
- non fenestrated capillaries
 - tight junction in endothelium
 - surrounded by end feet of astrocytes



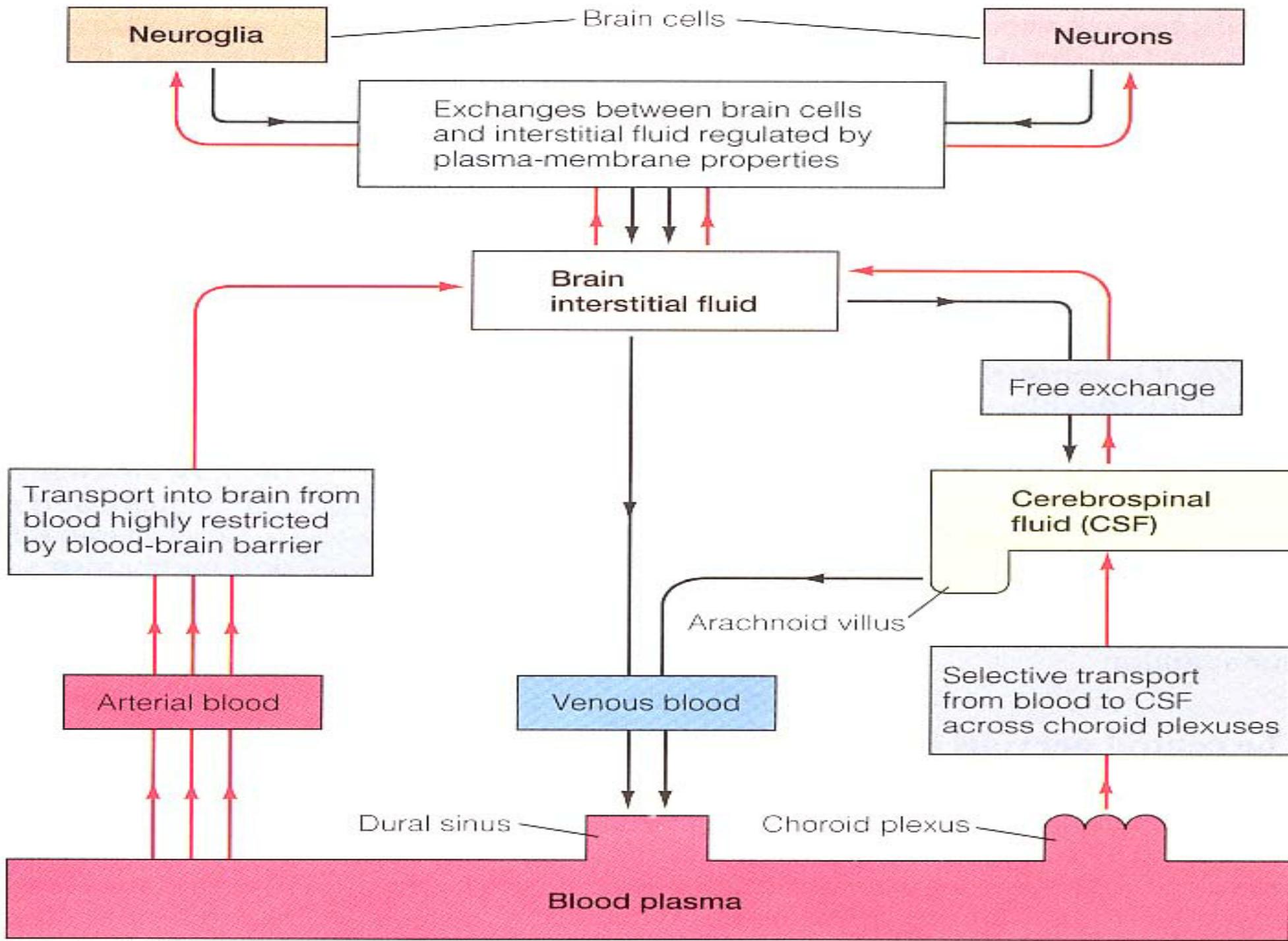
Blood Brain Barrier



- **General Properties of the BBB**
 1. **Highly permeable** to water, O_2 , CO_2 , erythromycin
 2. **Slightly permeable** to electrolytes (H^+ , Na^+ , K^+ , HCO_3^- , glucose, some drugs such as penicillin, tetracyclin)
 3. **Almost impermeable** to urea, catecholamine, protein and bile salt

Therefore:

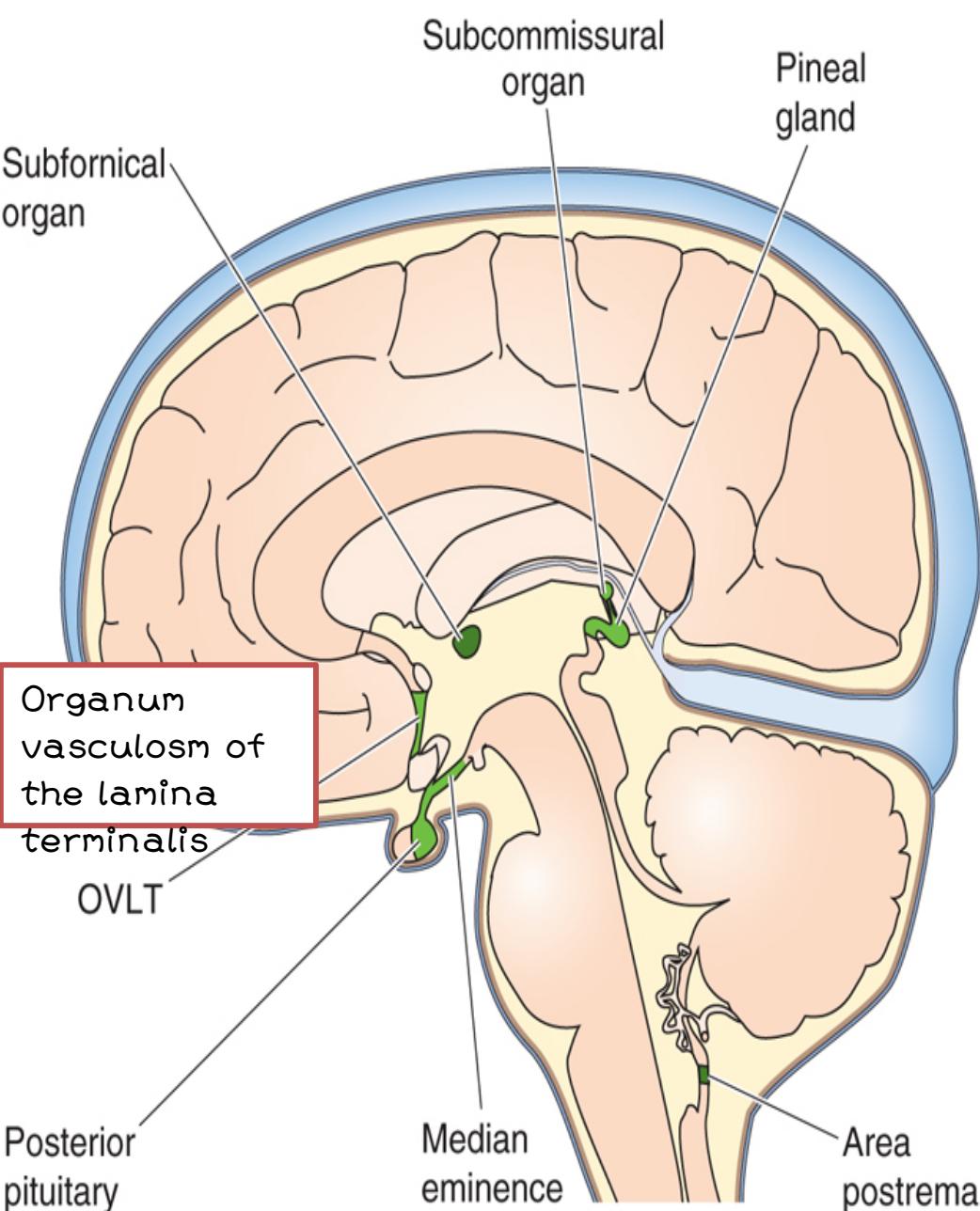
- The BBB is selectively permeable to :Oxygen, Carbon dioxide and glucose
- The BBB is not permeable to hydrogen ions



Deficit blood brain barrier

- Circumventricular organs
- Infancy
- Brain tumor
- Infection of brain or meninges

Circumventricular organs



- No significant BBB exists in some region of the brain
- **Area postrema**
 - Chemoreceptor trigger zone
 - initiates vomiting in response to chemical change in plasma
- Subfornical organ: Ang II
- OVLT: osmoreceptor controlling vasopressin secretion
- Pituitary gland
- pineal gland

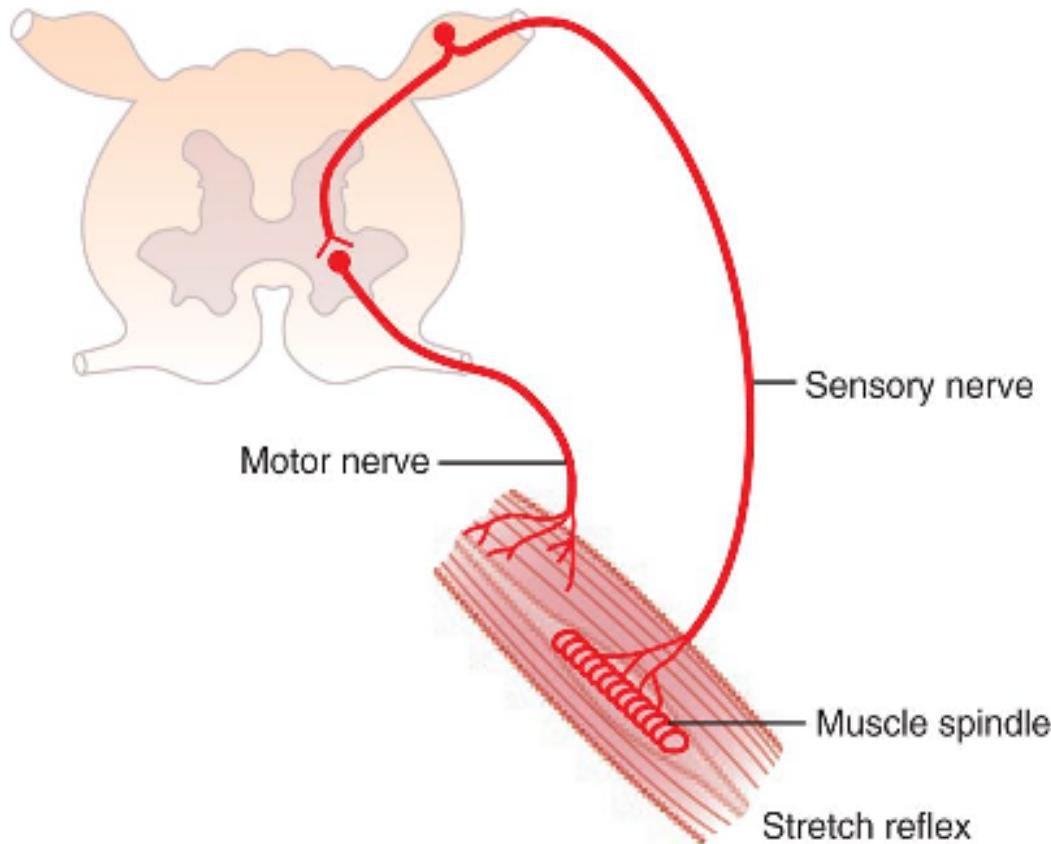
Infancy

- Blood brain barrier is weak during infancy
- If an infant has jaundice, bilirubin may enter nervous system (kernicterus)
- Region most often damaged by bilirubin are
 - Nuclear masses in basal ganglia
 - Brainstem
 - Cerebellum

Brain tumor

- BBB is deficit in brain tumor
- Useful in diagnosis
- If a brain tumor is suspected in a patient; radioiodinated serum albumin is injected in blood stream.....
CT scan.....radioactivity appears only in the region of tumor

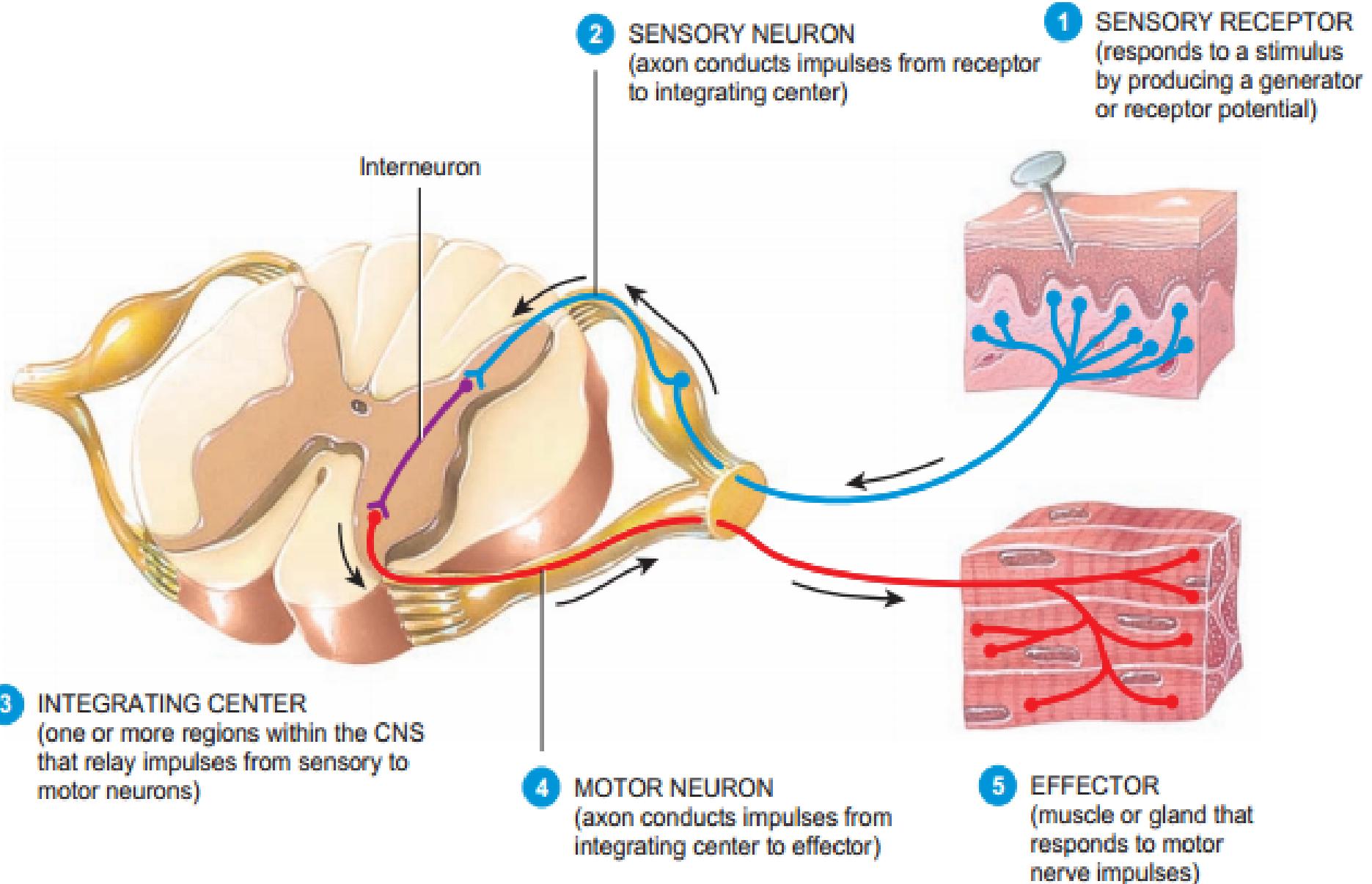
Reflexes



Reflex

- A reflex is a spontaneous, involuntary, repetitive, purpose serving response for afferent stimulation
- It is a protective mechanism
- Eg. When the hand is placed on a hot object, it is immediately withdrawn reflexly

Component of Reflex Arc



Involuntary response to stimulus depends on integrity of reflex arc

1. Receptor

- Is a **modified nerve ending** which receives stimulus
- After getting stimulated, impulses are generated in afferent nerve

2. Afferent neuron

- **Carry sensory input** from the receptor to the center

3. Integrating center

- **Part of CNS** (brain or spinal cord) where afferent neuron either synapse directly with **efferent motor neuron** or establishes connection with efferent motor neuron via interneuron

4. Efferent nerve

- Transmit motor impulse **from center to the effector organ**

5. Effector organs

- **Muscle or gland** which shows response to stimulus

Classification of reflex

1. Monosynaptic Reflex

- Are those which contain only one synapse in the reflex arc

eg. Stretch reflex (biceps, triceps, knee jerk)

2. Polysynaptic reflex

- Characterized by more than one interneuron placed between afferent and efferent neurons

eg. Withdrawal reflex, Flexor reflex, Superficial reflex

Properties of Reflexes

1. Adequate stimulus
2. Delay
3. One way conduction
4. Summation
5. Occlusion
6. Subliminal fringe
7. Irradiation
8. After discharge
9. Fatigue
10. reciprocal innervation

1. Adequate stimulus

- Particular stimulus produce particular response

2. Reaction time and central delay

Reaction time: Refers to time interval between application of stimulus and starting of the response

- For knee jerk reflex: 19 - 24 msec

Central delay: is the time taken for reflex activity to traverse spinal cord

- Since minimum synaptic delay is 0.5 msec
- The central delay for knee jerk is 0.6 - 0.9 ms

3. One way conduction

- During any reflex activity, the impulses are transmitted in only one direction - “Bell magendie law”

4. Summation

- Spatial summation
- Temporal summation

5. Occlusion

- Stimulation of two neighboring nerves simultaneously produce lesser response than sum total of the responses obtained when each nerve is separately stimulated

6. Subliminal fringe

- Simultaneous stimulation of two nerves produce greater response than sum total of the response when each nerve is separately stimulated

7. Irradiation

- When sensory stimulus is too strong, impulse would spread to many neighboring neurons in the center and produces wider response

8. After discharge

- After reflex contraction if the stimulus is discontinued, the muscle does not completely relax at once but it relax gradually
- Because motor neuron stop discharge successively

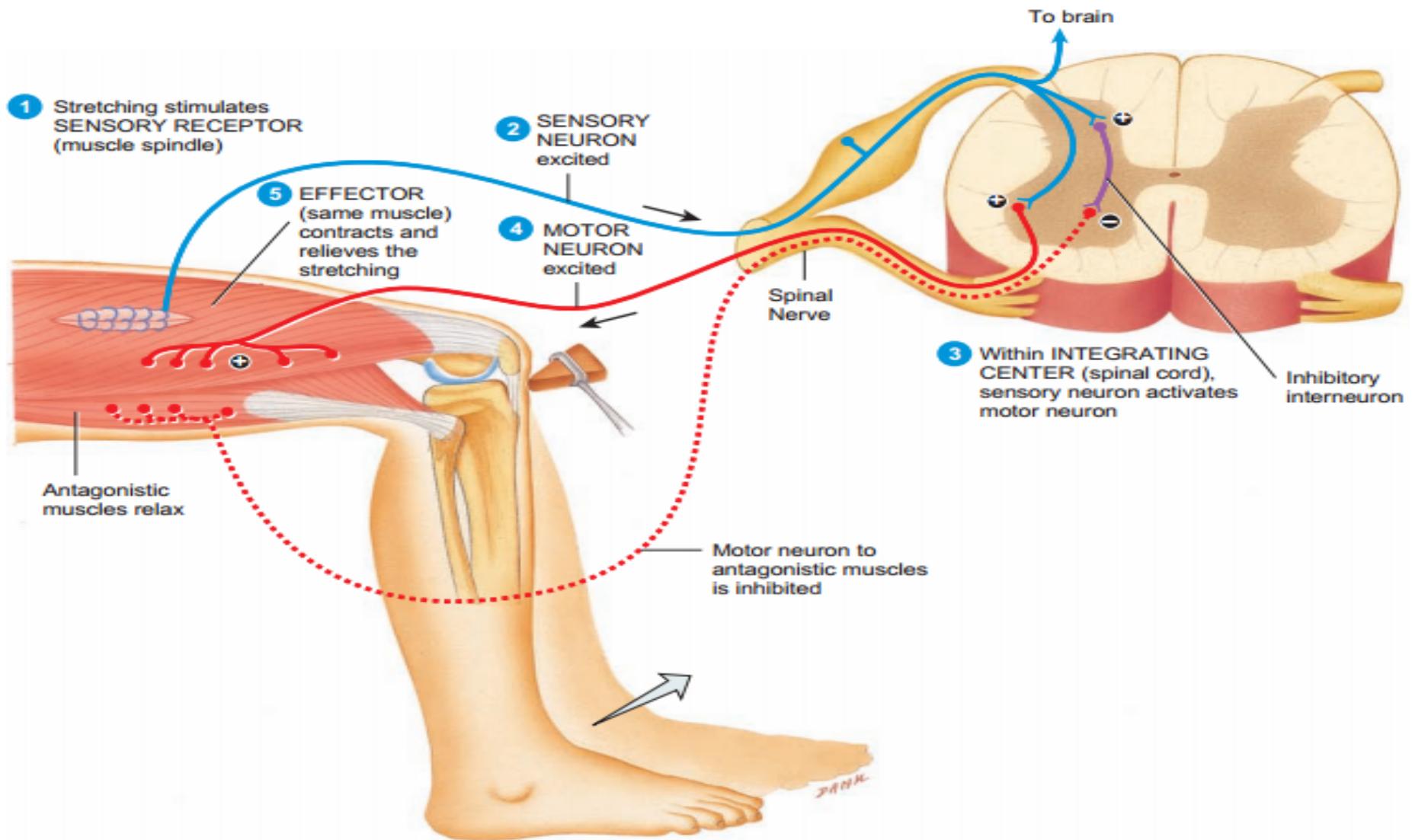
9. Fatigue

- If the reflex is excited repeatedly at frequent intervals the response become gradually weaken and ultimately stop

10. Reciprocal innervation

- excitation of one group of muscle is associated with inhibition of the antagonistic group of muscles on the same side

Stretch reflex



Whenever the muscle is stretched, excitation of spindles cause reflex contraction of muscles

Stimulus: stretch to the muscle

Receptor: muscle spindle

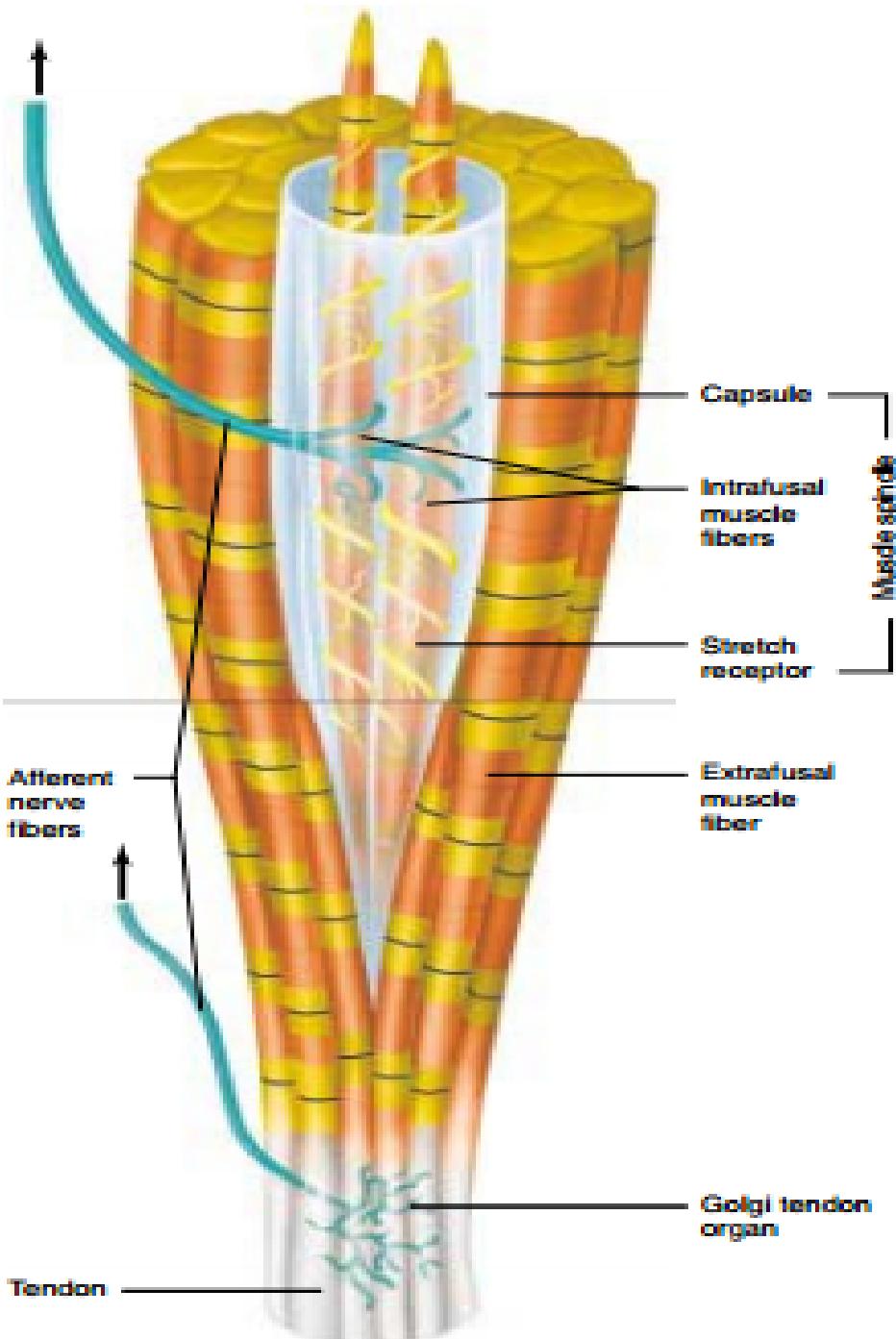
Afferent nerve: group Ia & group II fibers

Center: spinal cord

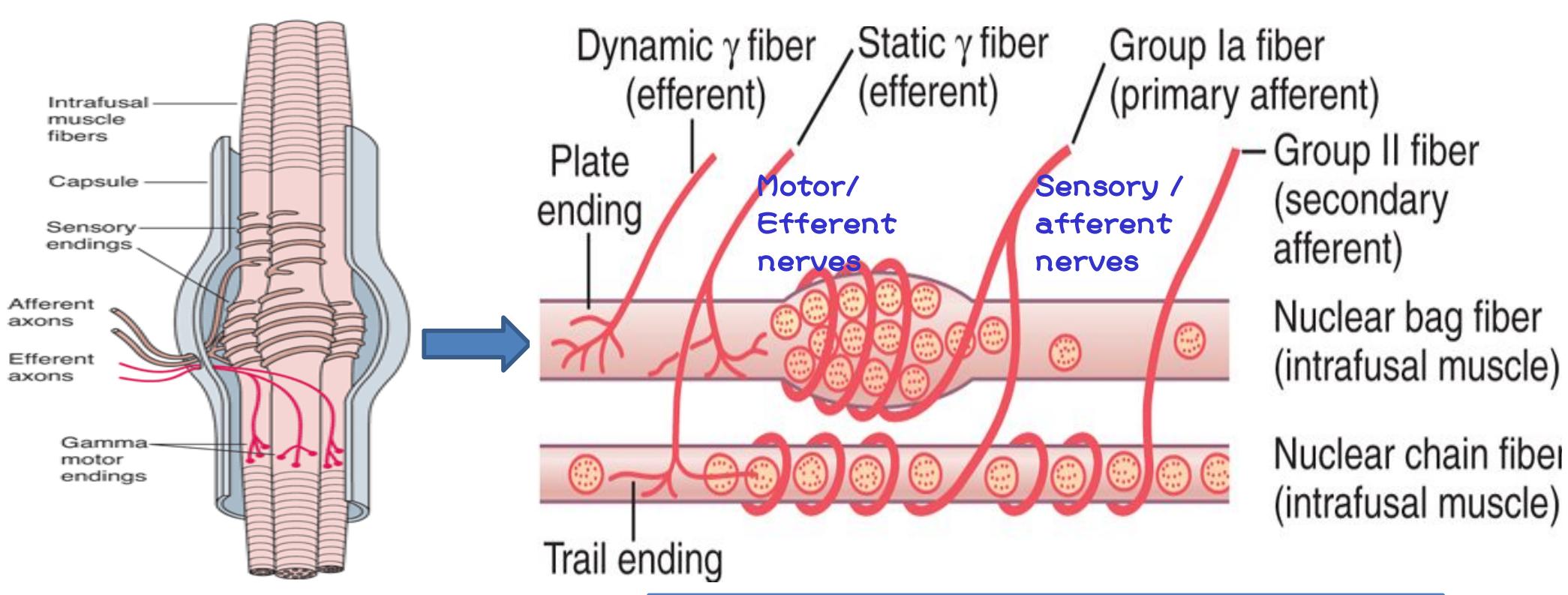
Efferent nerve: α motor neurons

Effector organs: extensor and flexor muscles

Structure of Muscle Spindle



- are distributed among extrafusal muscle fibers
- Arranged parallel with the extrafusal muscle fibers
- Are spindle shaped organs composed of intrafusal muscle fibers
- Innervated by both sensory and motor fibers



Muscle Spindle

- Types of intrafusal muscle fibers
 - 1. Nuclear bag fibers**
 - Larger, their nuclei accumulate in the center
 - 2. Nuclear chain fibers**
 - Smaller, their nuclei are arranged in rows
- Nuclear chain fibers are more plentiful (5 or 6) than nuclear bag fibers (2)

Intrafusal fibers of muscle spindle

Innervation of Muscle Spindles

Sensory innervation

- **group Ia afferent nerve**

- innervates both the nuclear bag fibers and the nuclear chain fibers
- form primary endings in a spiral - shaped terminal around the central region of the nuclear bag and nuclear chain fibers.
- **sense rate of change in length of muscle and actual length**

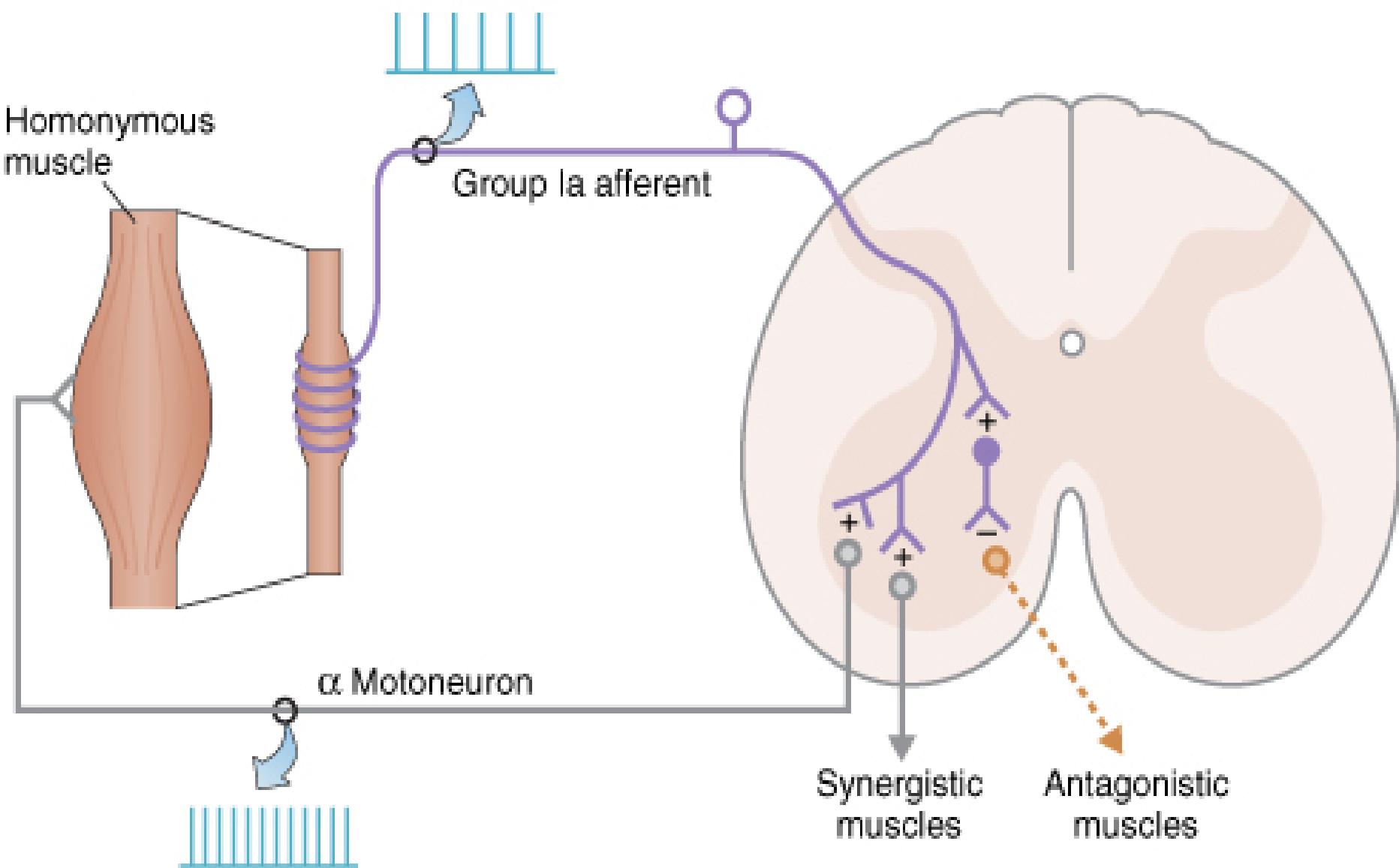
- **group II afferent nerve**

- innervate only the nuclear chain fibers
- form secondary endings on the nuclear chain fibers
- **absolute length**

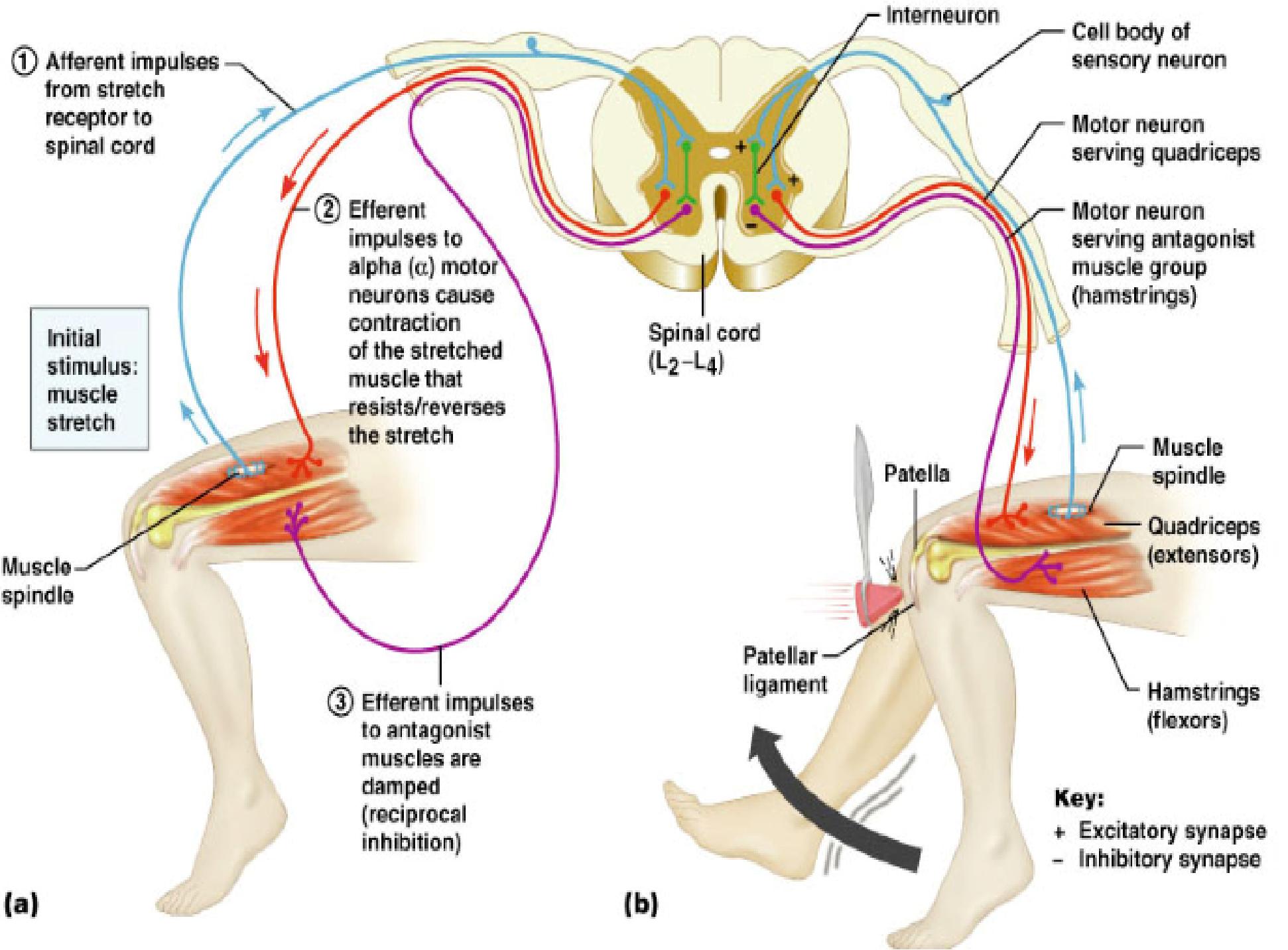
Motor innervation

- γ motoneurons: comes from ventral horn cell in spinal cord
- two types of γ motoneurons: dynamic and static.
- Dynamic γ motoneurons synapse on nuclear bag fibers in "plate endings."
- Static γ motoneurons synapse on nuclear chain fibers in "trail endings."
- **to regulate the sensitivity of the intrafusal muscle fibers**

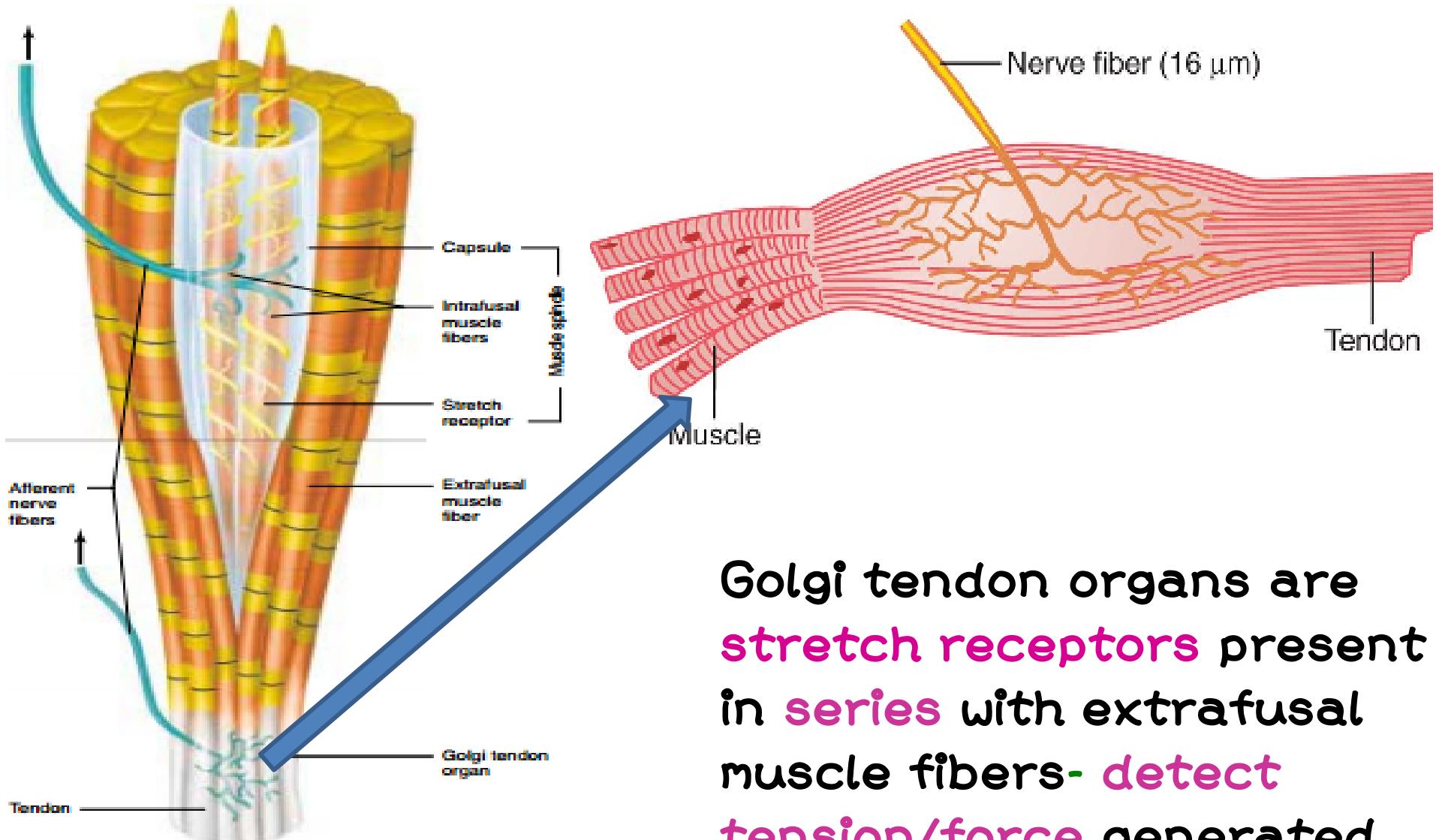
STRETCH REFLEX



Stimulation of Ia fibers causes contraction of relaxed muscle

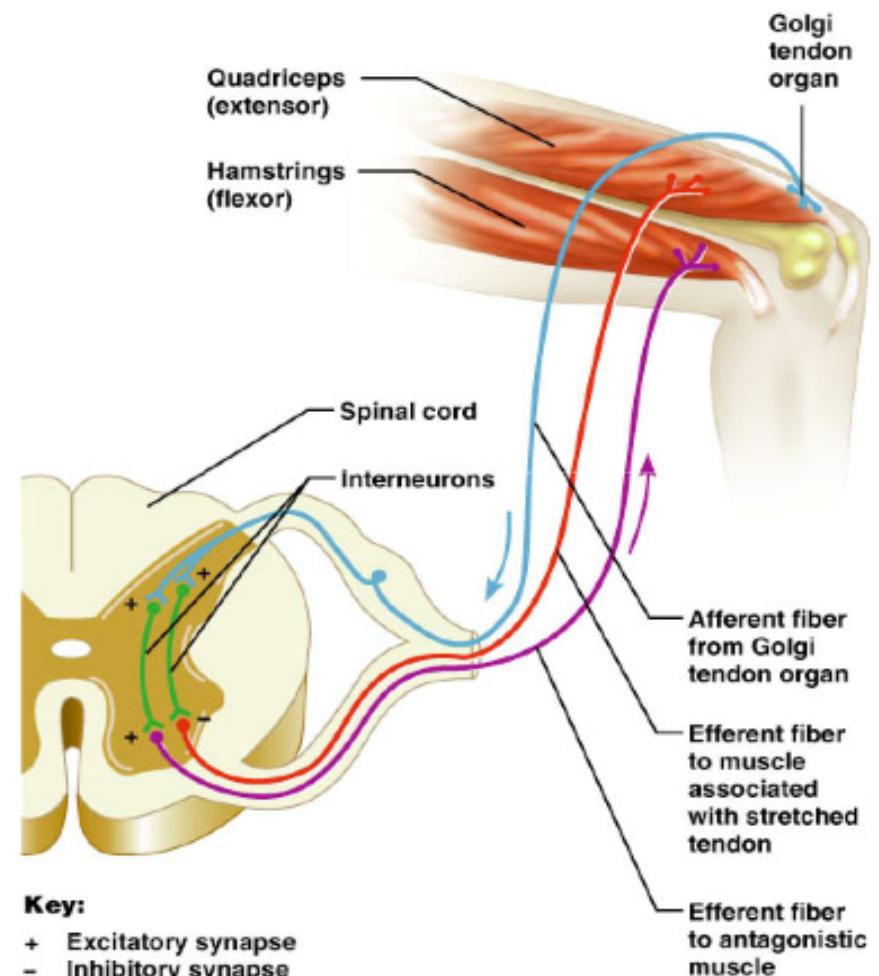
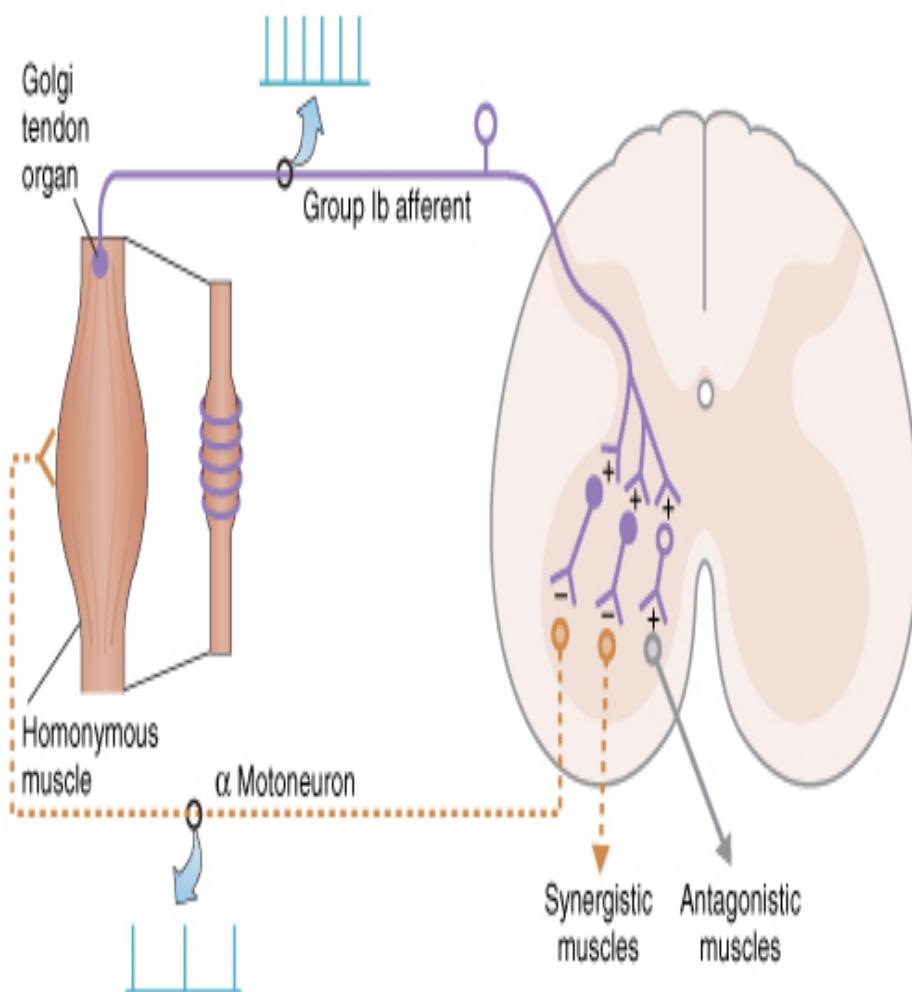


Golgi tendon organ



Golgi tendon organs are stretch receptors present in series with extrafusal muscle fibers- detect tension/force generated by muscle during contraction

Golgi tendon reflex



Golgi tendon organ are stimulated by contraction of the muscle or passive stretch applied to the muscle. When stimulated they inhibit the αMN's of the same muscle from which they arise and thus relax the muscle. They are thus protective in nature and prevent damage of

- There are two types of motoneurons: α motoneurons and γ motoneurons.
- α Motoneurons innervate extrafusal skeletal muscle fibers
- Activation of α motoneurons leads to contraction of extrafusal muscle fibers
- γ Motoneurons innervates intrafusal muscle fibers
- their function is to adjust the sensitivity of the muscle spindles
- α Motoneurons and γ motoneurons are coactivated, so that muscle spindles remain sensitive to changes in muscle length

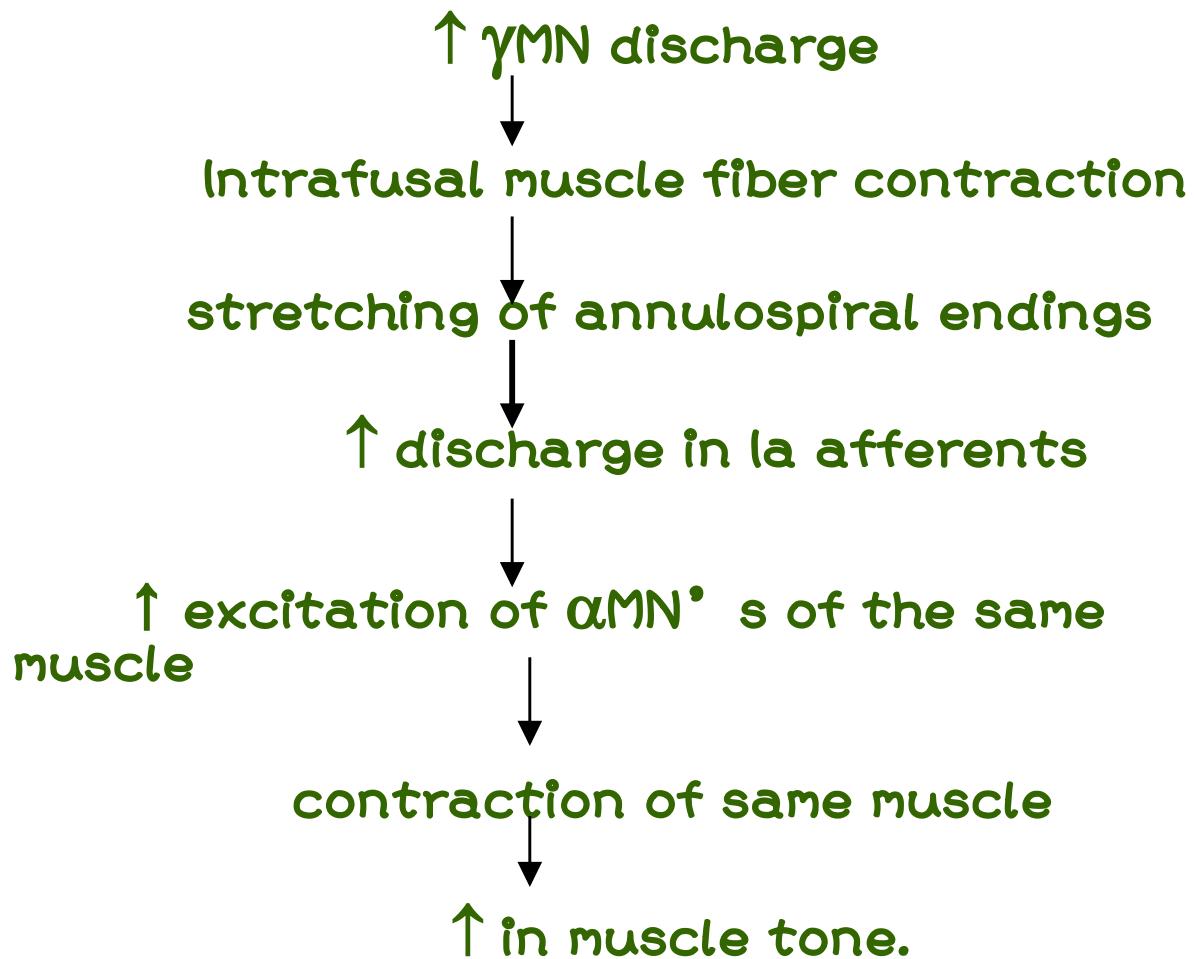
Muscle Tone

- It is a state of partial involuntary contraction of voluntary muscles or extrafusal muscle fibers.

Contraction occurs due to reflex stimulation of αMN via monosynaptic stretch reflex. An intact stretch reflex arc is essential for the maintenance of muscle tone.

Contracting muscles offer resistance to passive stretch which is often referred as its tone. Thus, muscle tone is measured by testing the resistance of the muscle to passive stretch.

Gamma Loop Mechanism in maintenance of tone.



Tone is abolished in a muscle, if there is sectioning of posterior root which carries group Ia afferents, lesion of α MN's or its motor nerve.

Supra Spinal Control of Muscle Tone

- ❖ A vital element in the regulation of muscle tone is controlled by the supra spinal centers. They exert their influences by modulating the excitatory and inhibitory influences either on gamma loop mechanism or directly on α MN's.
- ❖ γ MN's differ from α MN's in that they are spontaneously firing. The excitatory or inhibitory descending tracts excite or inhibit γ MN's, thereby increasing or decreasing reflexly the sensitivity of α MN's and thereby affecting the tone of the muscle.

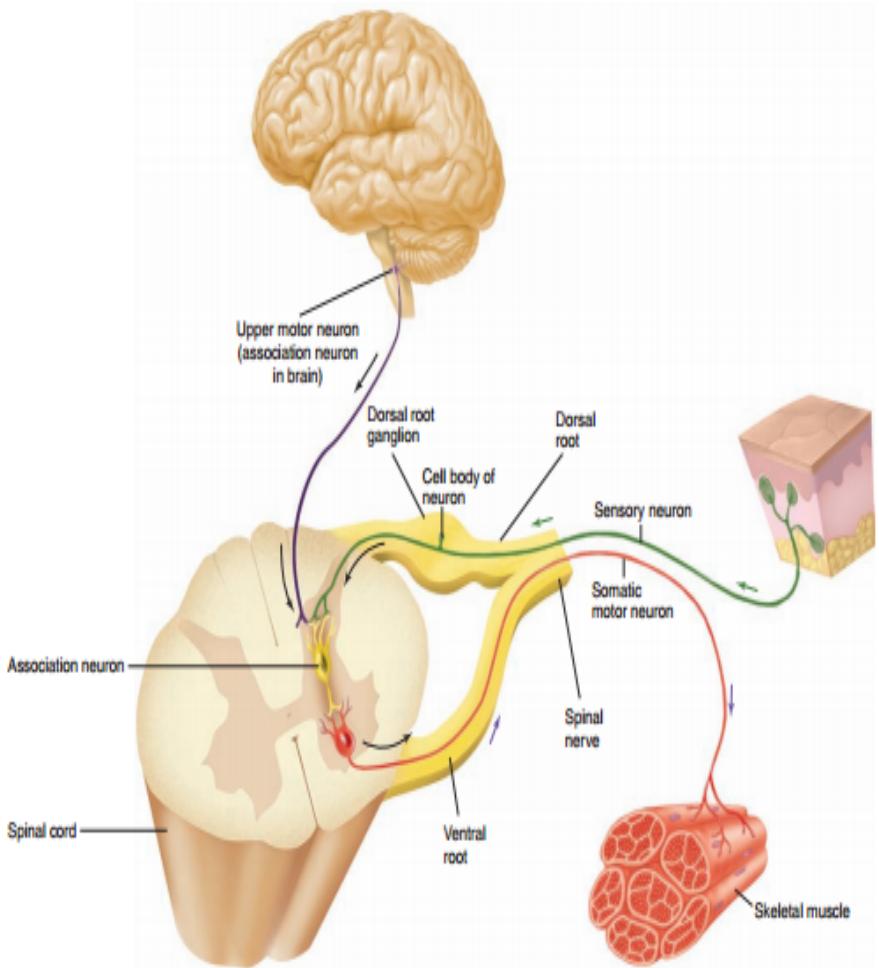


Figure 8.28 Activation of somatic motor neurons. Somatic motor neurons may be stimulated by spinal association neurons, as shown here, or directly by sensory neurons, in a reflex arc that doesn't involve the brain. The spinal association neurons and motor neurons can also be stimulated by association neurons (called upper motor neurons) in the motor areas of the brain. This affords voluntary control of skeletal muscles.

Brain area	Facilitation/ Inhibition
------------	-----------------------------

Cerebral Cortex	+/-
Basal ganglia	+/-
Cerebellum	-
Reticulospinal tracts	+/-
Rubrospinal Tracts	+
Vestibulospinal Tracts	+
Tectospinal tract	+

Since connection between the afferent and efferent neurons is usually present in the CNS. Therefore activity in reflex arc is modified by the multiple inputs converging on the efferent neuron

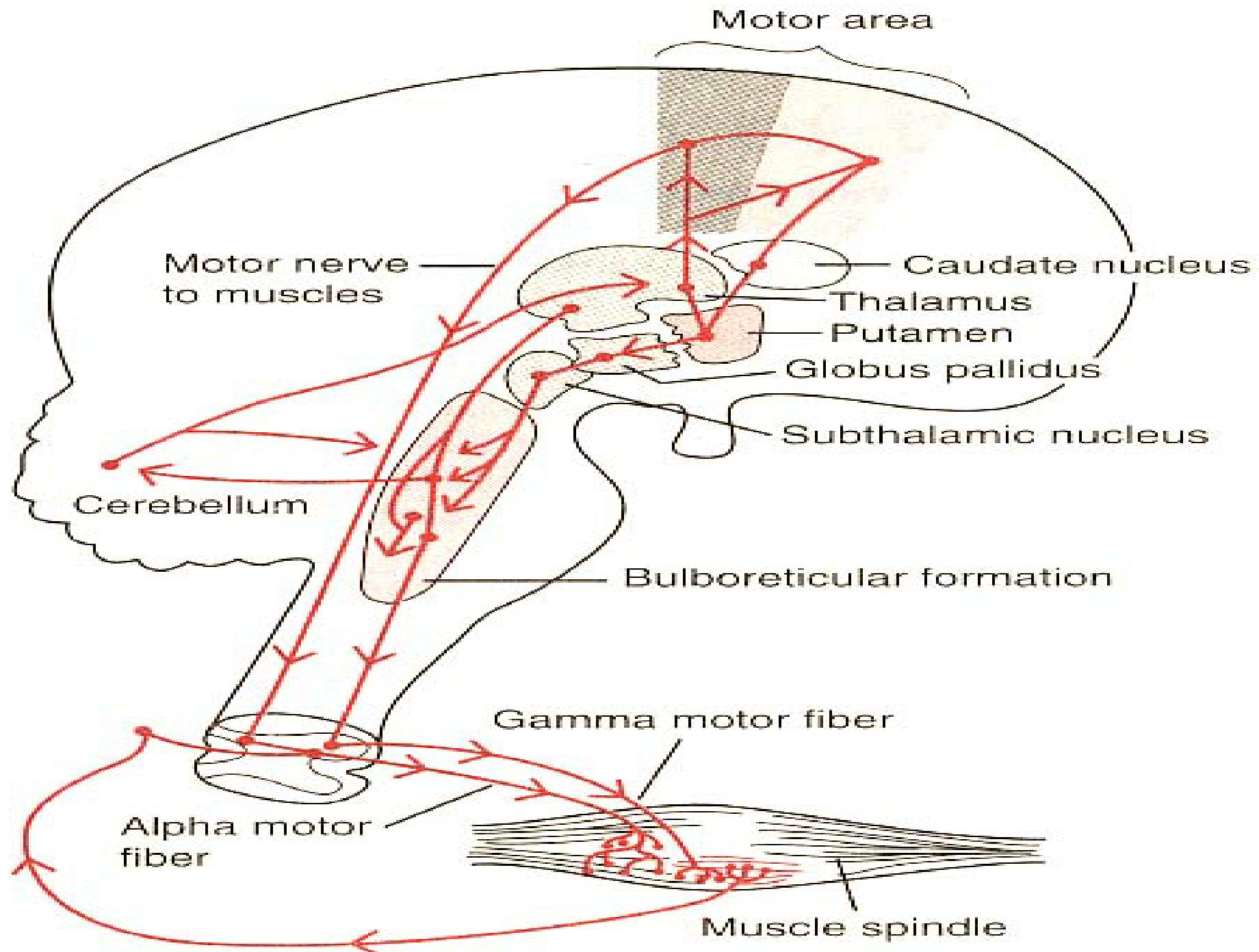


FIGURE 45 – 3

Skeletal motor nerve axis of the nervous system.

The Spinal motoneuron pool functions in an integrated manner

1. αMN's are the final pathway for voluntary contraction and reflexes.
2. γ MN's adjust the sensitivity of muscle spindle afferents; and thus through stretch reflex adjust tone and posture to provide a stable back ground for movement.
3. It co-ordinates the actions of various groups of muscles to make movements smooth and precise.

Alpha motor neurons are stimulated

- i) directly by impulses from higher brain structures
- ii) reflexly due to the stretching of the muscle spindle (mono synaptic stretch reflex)
- iii) Stimulated by other afferents such as pain

Sensory Receptors

Sensory receptors

- Receptor is a **specialized modified sensory nerve-ending** which undergoes depolarization in response to a **specific stimulus** and sends information to the CNS.
- Receptors **convert** various forms of energy in the environment into electric energy in the neuron.
- Stimulus is a sudden change in the external or internal environment **detected** by the body.

Classification of receptors

According to type of stimulus:

- **Mechanoreceptors:** stimulated by mechanical deformation of receptor cell membrane (eg. Touch and pressure receptor)
- **Chemoreceptors:** sense chemicals stimuli in environment or blood ((e.g., the taste buds, olfactory epithelium, and the aortic and carotid bodies)
- **Thermoreceptors:** respond to heat or cold
- **Nociceptors:** responds to extremes of mechanical, thermal & chemical stimuli that produce pain
- **Photoreceptors or electromagnetic receptors:** rod & cones of retina that respond to light stimuli

- According to the type of receptors:
(sherrington's classification)

Telereceptors: that receive stimuli from distance

- Cochlear receptor (hearing)
- Visual receptors (vision)
- Olfactory receptors (smell)

Exteroceptors: receive stimuli from immediate surrounding outside the body

- touch, temperature, pain, pressure

Interoceptors: responds to change within the body

- Proprioceptors (joint & position sense)
- Baroreceptor (blood pressure)
- Chemoreceptors (measures blood gases)

According to type of sensations

- Touch receptors, Cold receptors, Heat receptors, Pain receptors, Taste receptors, Olfactory receptors, Auditory receptors, Light receptors

Depending on the rate of adaptation

- Slow adapting receptors
- Rapidly adapting receptors

Anatomical classification of receptors

- Superficial receptors: eg. Touch, pain, pressure, temperature
- Deep receptors: eg. sensation of joint, muscle and tendon
- Visceral receptors: eg. Pain from visceral structure

Adaptation or desensitization

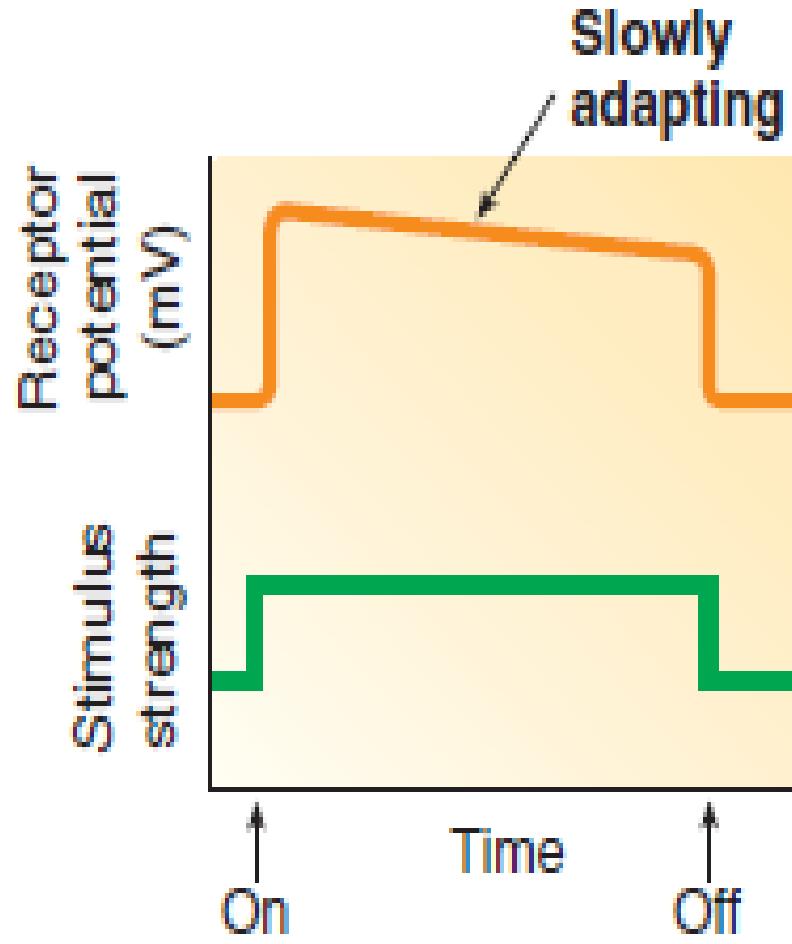
- ↓ in receptor sensitivity results ↓ in AP frequency in AN despite maintenance of stimulus at constant strength

Rapidly adapting (phasic) receptors

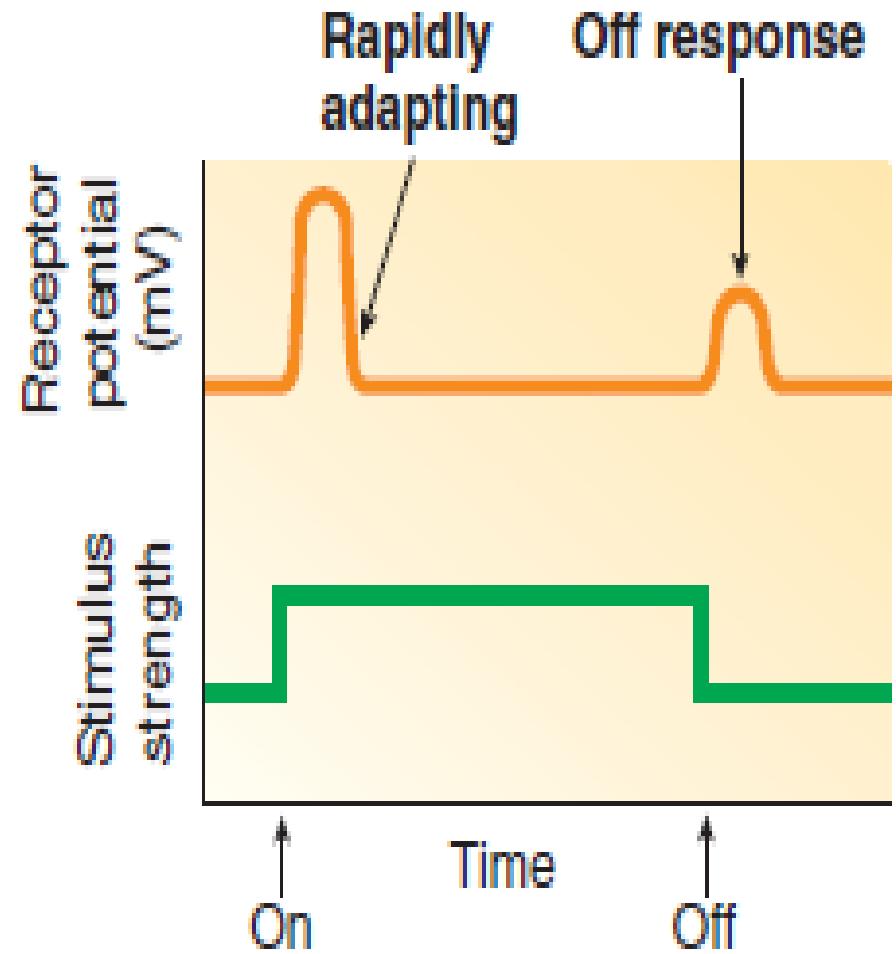
- A phasic receptor **adapts rapidly** to a sustained stimulus and frequently **exhibits an off response when the stimulus is removed.**

Slowly adapting (tonic) receptors

- A tonic receptor **does not adapt at all or adapts slowly** to a sustained stimulus and thus **provides continuous information** about the stimulus

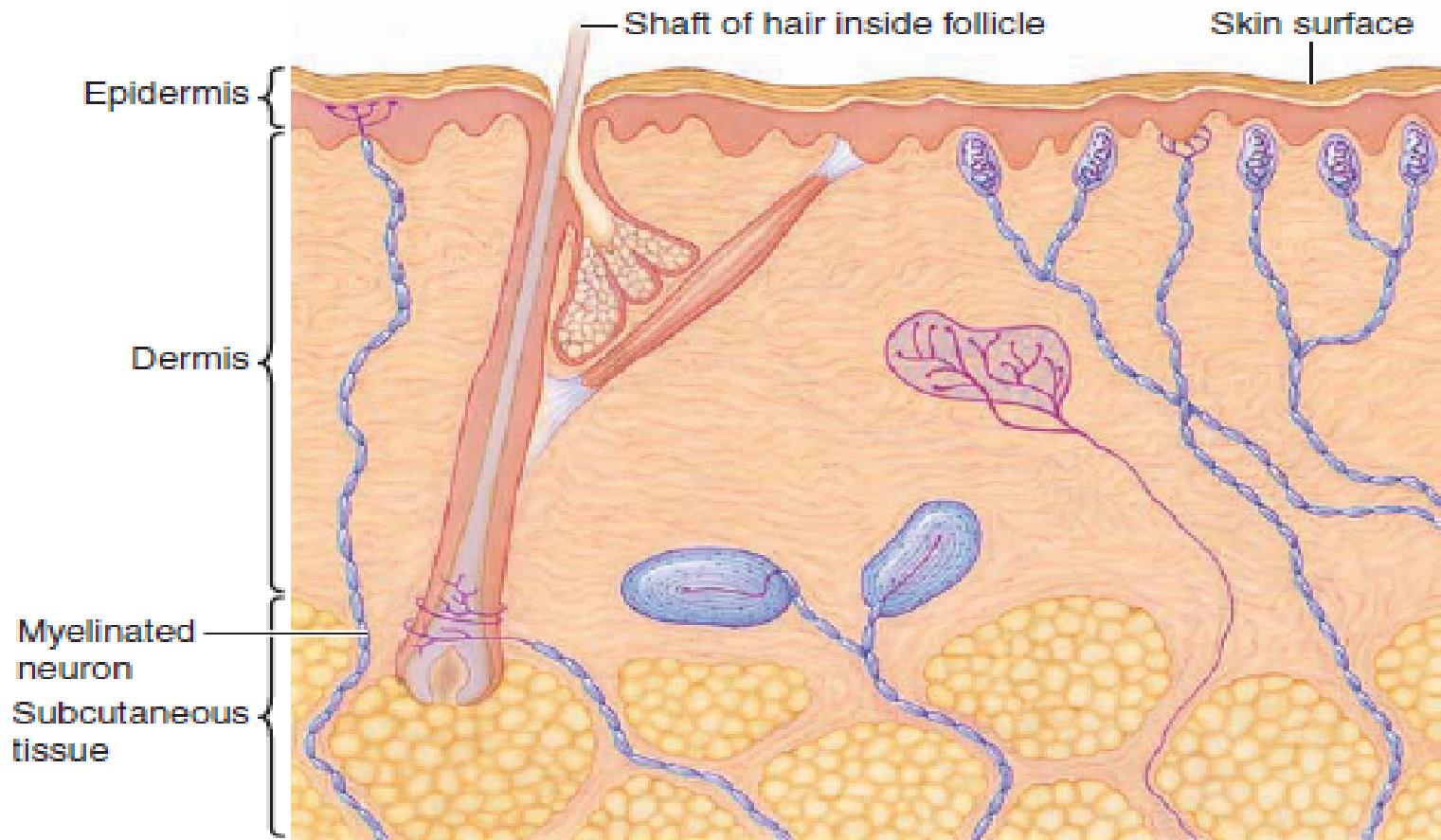


**Slowly adapting
(tonic) receptors**



**Rapidly adapting
(phasic) receptors**

Coetaneous Receptors



Receptors present in the skin that respond to **touch, pressure, pain, temperature and vibration.**

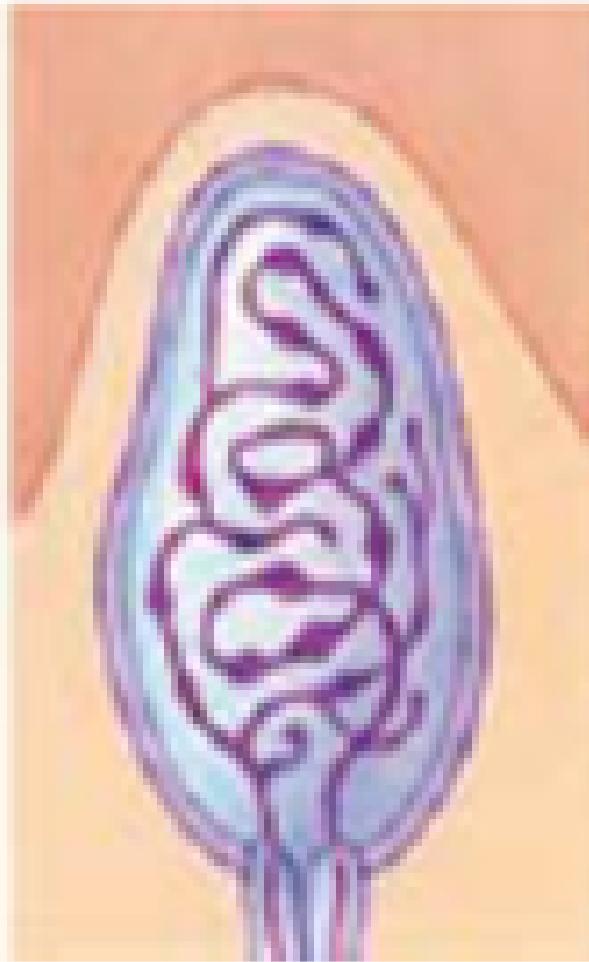
Table 10.2 | Cutaneous Receptors

Receptor	Structure	Sensation	Location
Free nerve endings	Unmyelinated dendrites of sensory neurons	Light touch; hot; cold; nociception (pain)	Around hair follicles; throughout skin
Merkel's discs	Expanded dendritic endings	Sustained touch and pressure	Base of epidermis (stratum basale)
Ruffini corpuscles (endings)	Enlarged dendritic endings with open, elongated capsule	Sustained pressure	Deep in dermis and hypodermis
Meissner's corpuscles	Dendrites encapsulated in connective tissue	Changes in texture; slow vibrations	Upper dermis (papillary layer)
Pacinian corpuscles	Dendrites encapsulated by concentric lamellae of connective tissue structures	Deep pressure; fast vibrations	Deep in dermis

A. Mechanoreceptors

- Concerned with sensation of touch and pressure
- Consists of lamellated connective tissue capsule which surrounds unmyelinated axon
- This includes
 - Merkel's discs
 - Meissner's corpuscles
 - Pacinian corpuscles
 - Ruffini's end organs
 - Krause's end bulbs
 - Naked nerve endings

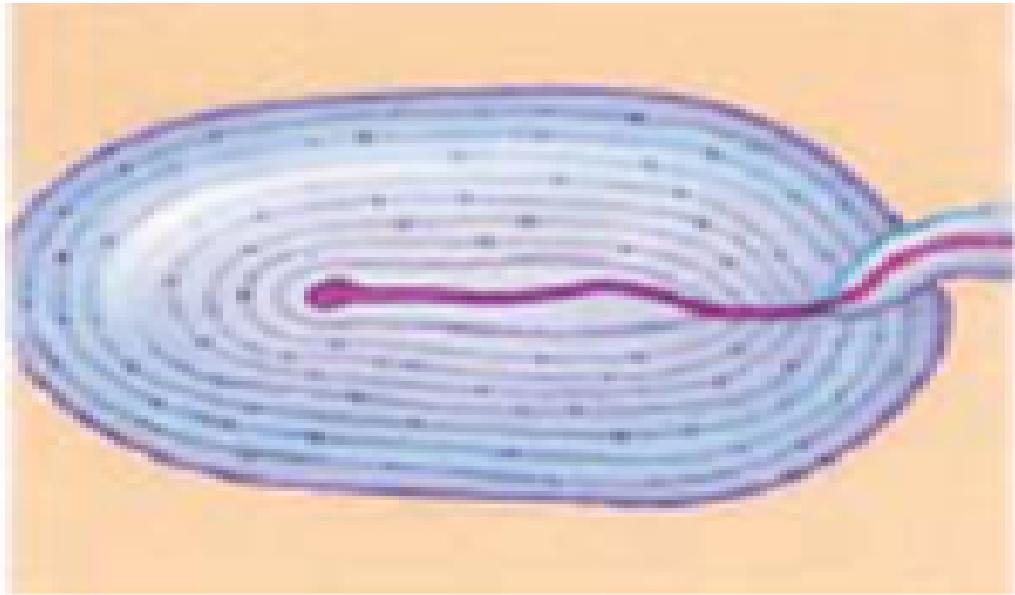
Merkel' s discs and Meissner' s Corpuscle



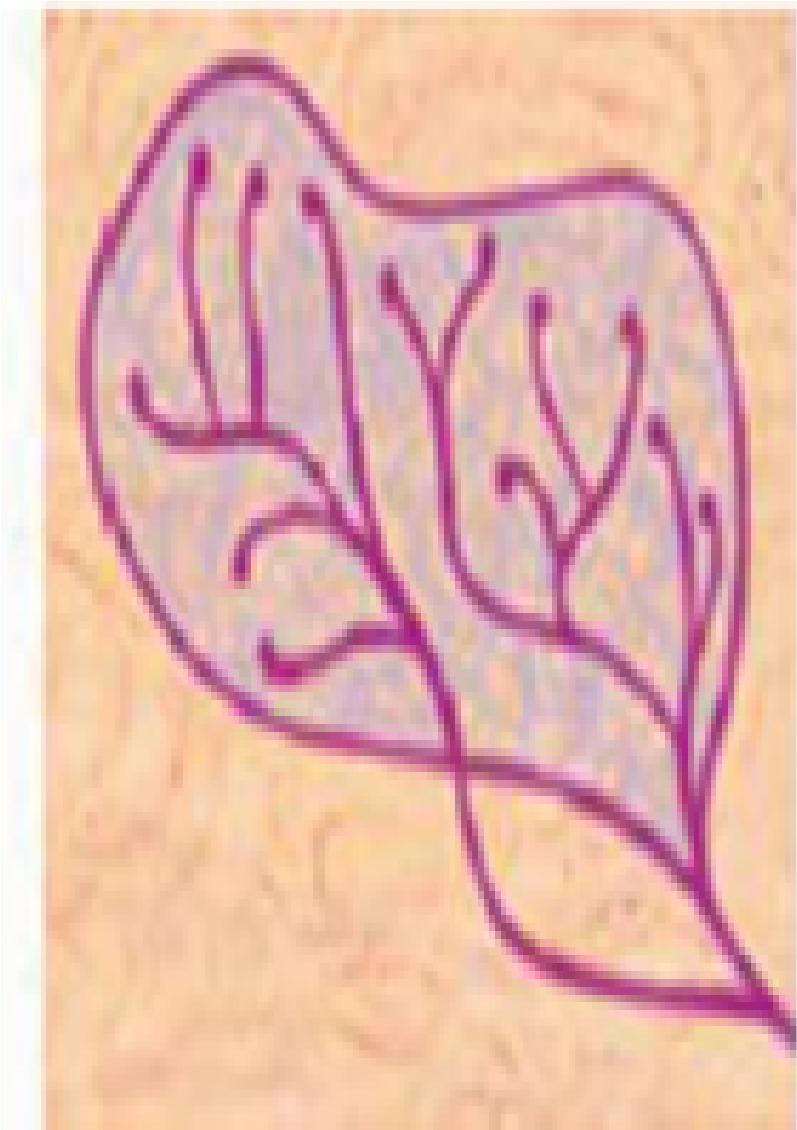
- Concern with perception of touch
- Are encapsulated receptor
- Found in the dermis of nonhairy skin, most prominently on the fingertips, lips, nipples, etc.
- Rapidly adapting receptors

Pacinian Corpuscles

- Perception of pressure and fast vibration
- Large, resemble onion in shape and laminations
- Most rapidly adapting
- Located in skin, subcutaneous tissue & intramuscular tissue

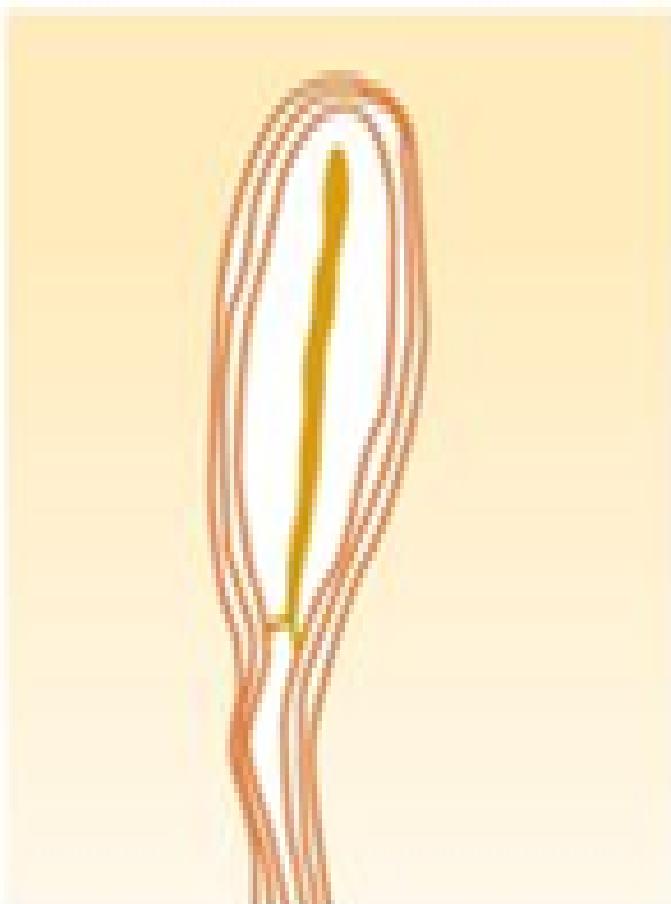


Ruffini end organs



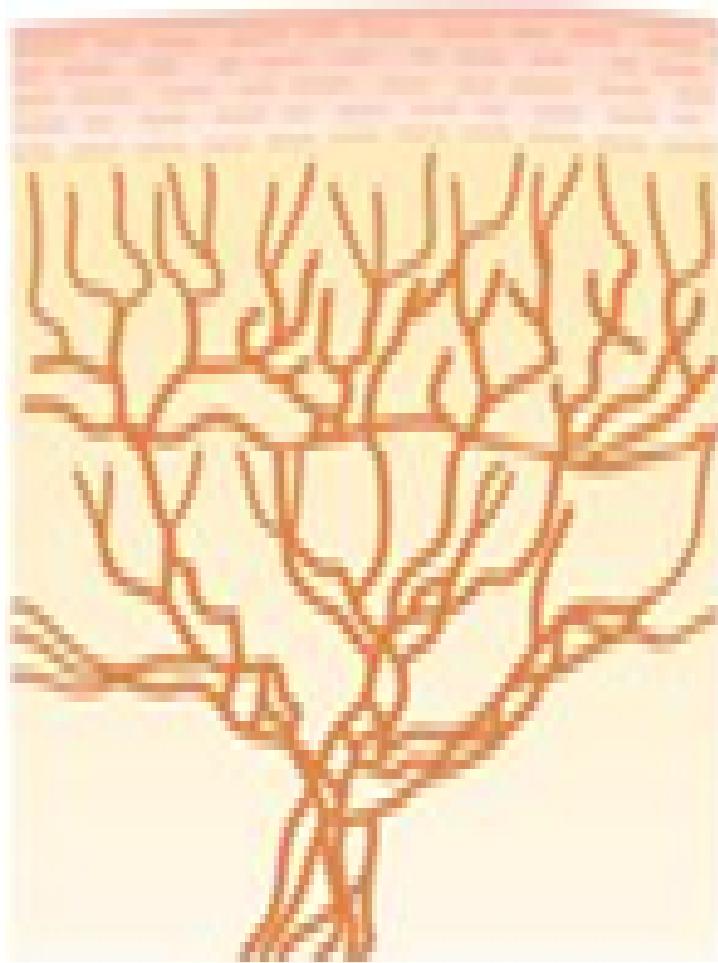
- Perception of warmth
- Are encapsulated expanded ending of A δ and unmyelinated C fibers
- Found in dermis and joints
- Are slowly adapting receptors

Krause' s end Bulbs



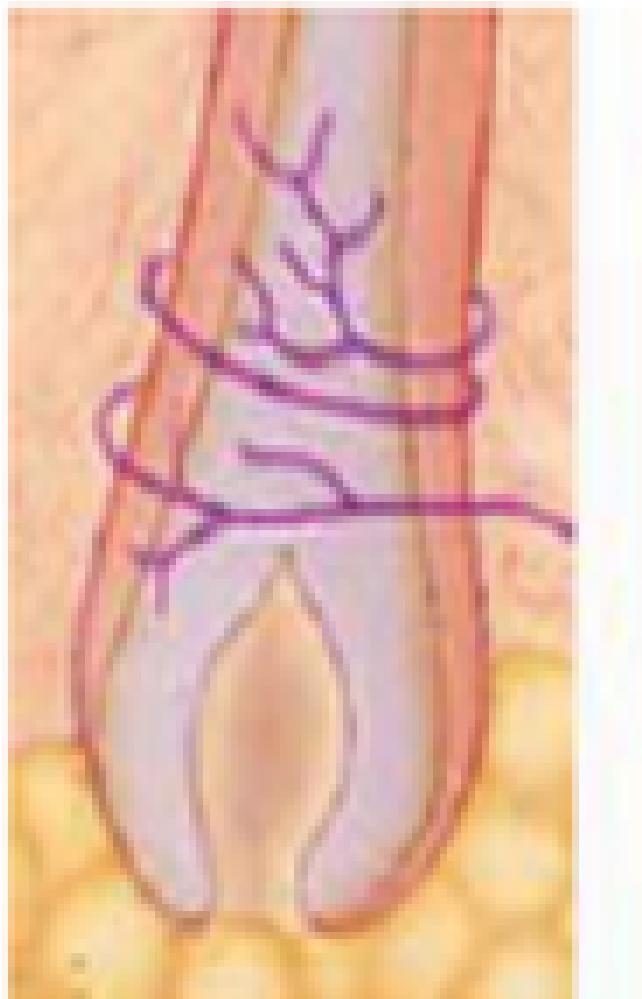
- Are spherical mechanoreceptor and their afferent fiber belong to A δ fiber
- Found in conjunctiva, papillae of lips and tongue, skin of genitalia

Free nerve endings



- Branch of myelinated A δ and unmyelinated c fibers
- Concerned with perception of pain & injurious stimuli

Hair receptor



- Are arrays of nerve fibers surrounding hair follicles in hairy skin
- When the hair is displaced, it excites the hair-follicle receptors.
- Rapidly adapting
- Detect **velocity** and direction of movement across the skin.

Table 3-3 Types of Mechanoreceptors

Type of Mechanoreceptor	Location	Adaptation	Sensation Encoded
Pacinian corpuscle	Subcutaneous; intramuscular	Very rapidly	Vibration, tapping
Meissner's corpuscle	Nonhairy skin	Rapidly	Point discrimination, tapping, flutter
Hair follicles	Hairy skin	Rapidly	Velocity, direction of movement
Ruffini's corpuscle	Hairy skin	Slowly	Stretch, joint rotation
Merkel's receptors	Nonhairy skin	Slowly	Vertical indentation of skin
Tactile discs	Hairy skin	Slowly	Vertical indentation of skin

B. Thermoreceptors

- Are the terminal branches of thin myelinated A_δ and unmyelinated C fibers
- They are found on chest, nose, anterior surface of forearm
- Cold receptors are 4-10x more than warm receptors

Cold Receptors

Fibers are mainly the thin myelinated A_δ fibers

Fire steady discharge at temperature between 10 - 35°

Maximal frequency of discharge is at

Warm Receptors

Fibers are unmyelinated C fibers

Fire with steady discharge at temperature between 35 - 45°

Maximal frequency of steady discharge is at temp.

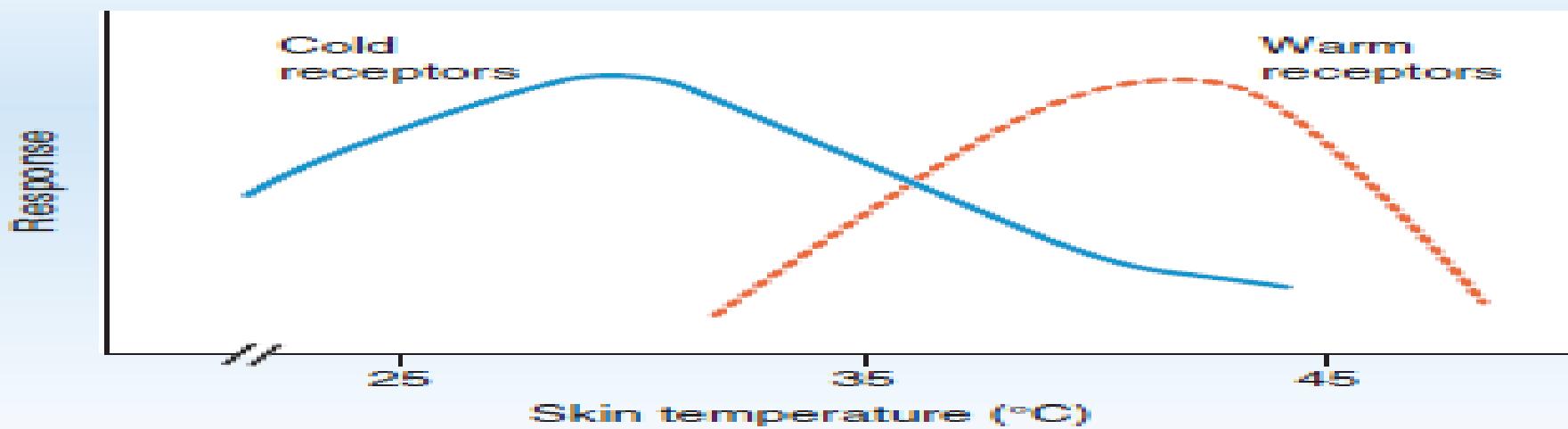


Figure 3-9 The response profiles of skin temperature receptors.

C. Pain Receptors

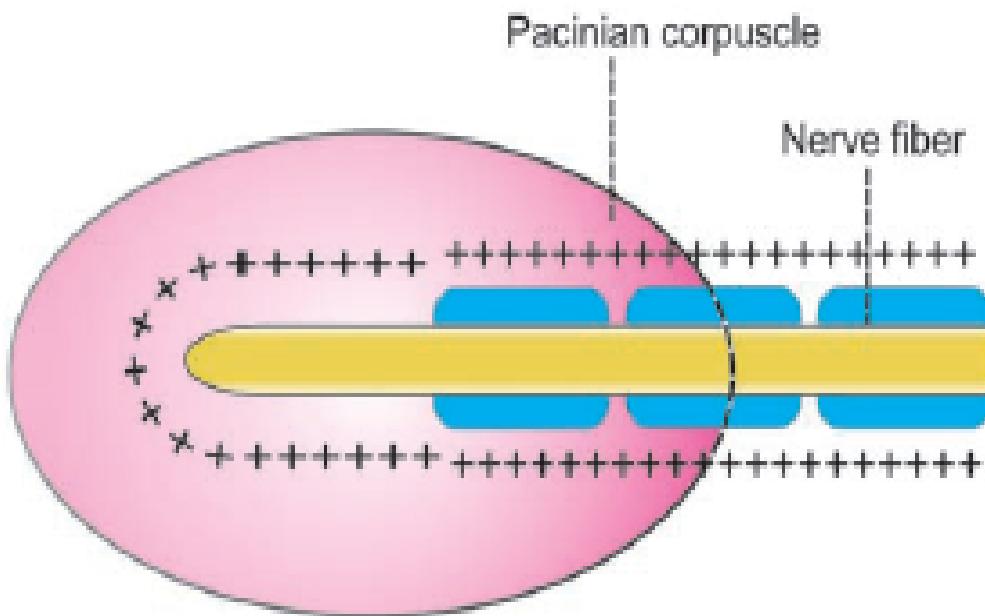
- The receptors which mediate pain are called nociceptors
- Located at end of small unmyelinated C or myelinated A δ afferent neurons

Genesis of Receptor Potential and Properties of Receptors

- Electrical events in receptors can be studied in Pacinian Corpuscles
 - Are relatively large in size
 - Are easily available in mesentry of experimental animal

Pacinian Corpuscle

Consists of



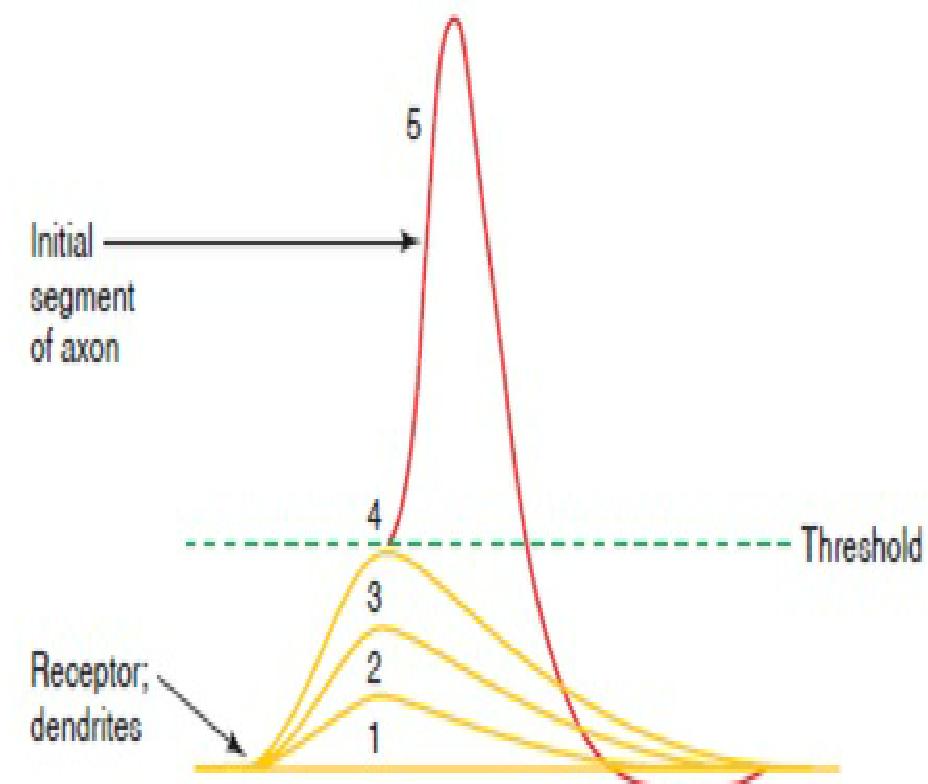
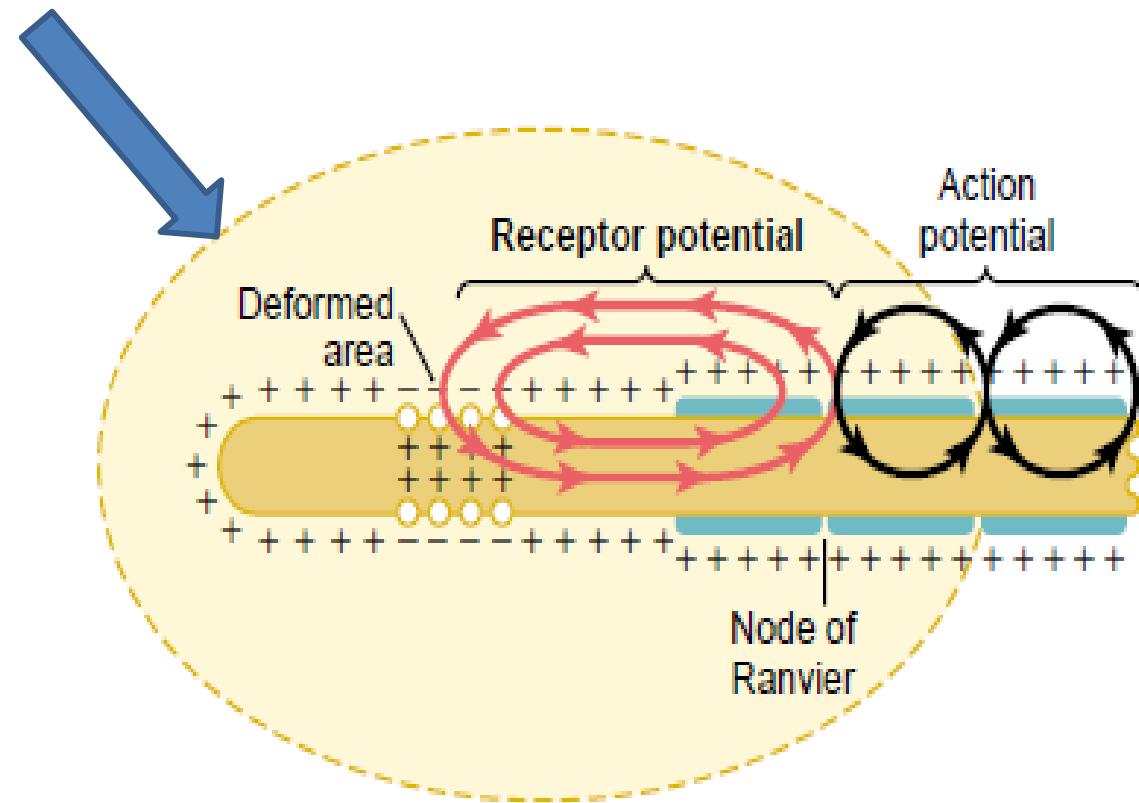
- Straight unmyelinated ending of sensory nerve fiber which is surrounded by **concentric lamellas** of connective tissue
- Myelin sheath **begin inside** the corpuscle
- First node of ranvier is located **inside** and 2nd node of ranvier is located **near the point at which nerve fibers leaves the corpuscle**
- It gives response to **pressure** stimulus

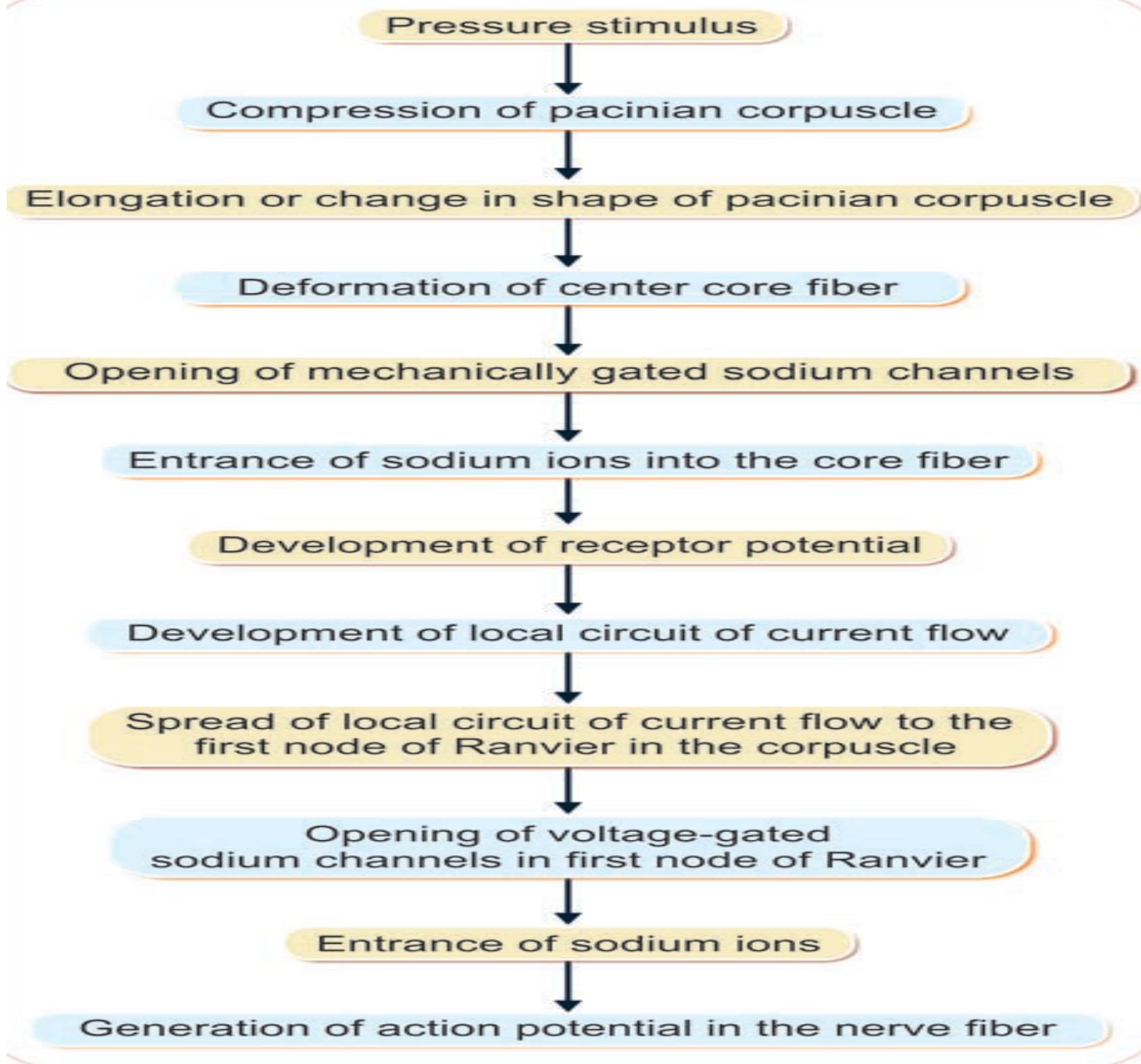
Sensory transduction

- Is a process by which energy in environment (Stimulus) is converted into electrical impulse in nerve fiber

Generation of impulse in cutaneous receptors

Receptor potential in Pacinian Corpuscle in skin



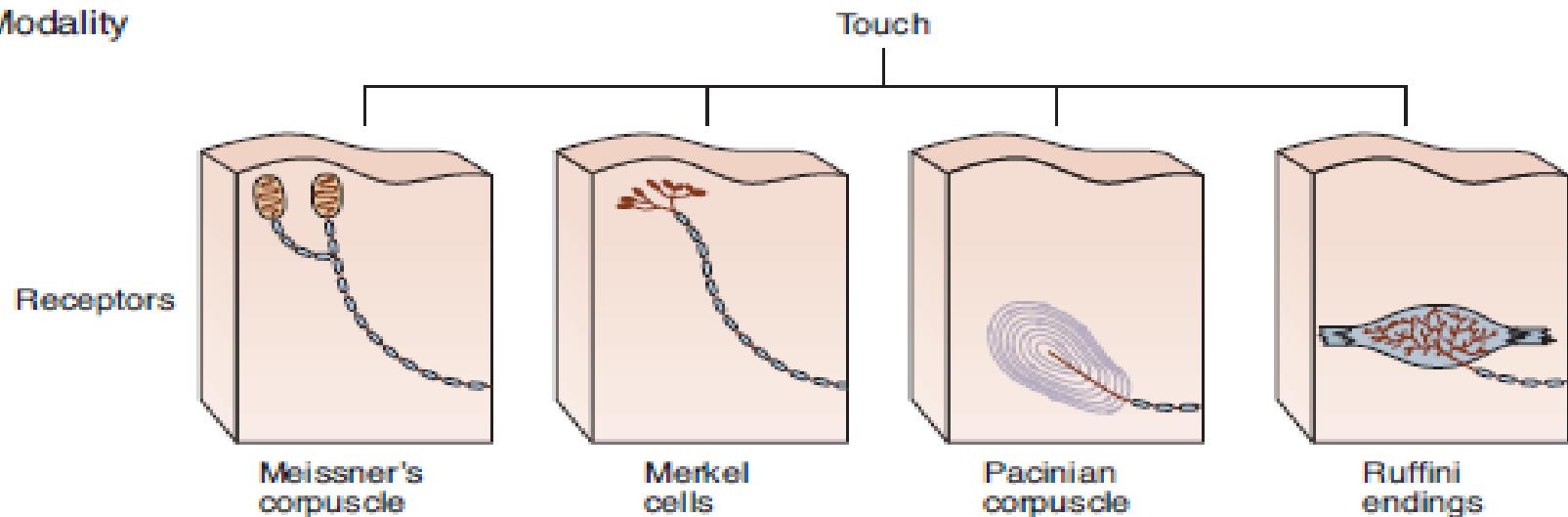


Sensory Coding

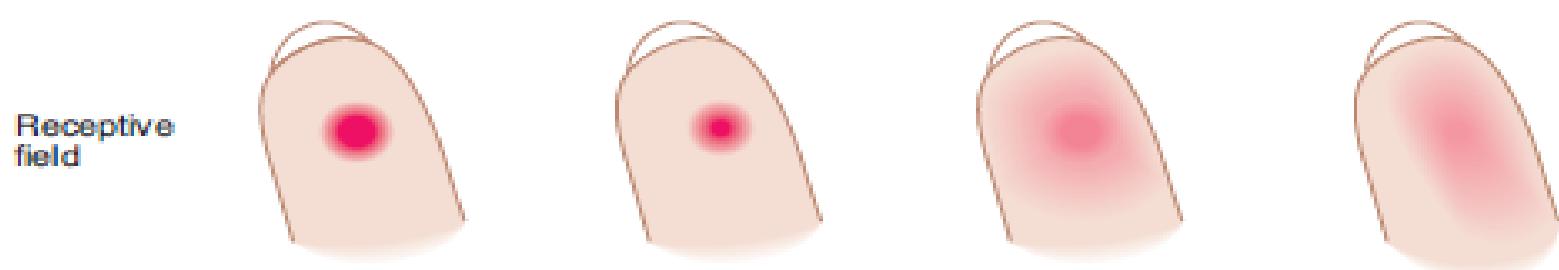
Conversion of GP into a patterns of AP that conveys relevant sensory information to the CNS

- All sensation code for four elementary attributes of a stimulus:
 - **Modality** (type of stimulus energy)
 - **Location** (site on body or space)
 - **Intensity** (signaled by response amplitude/frequency)
 - **Duration** (time from start to end of response)

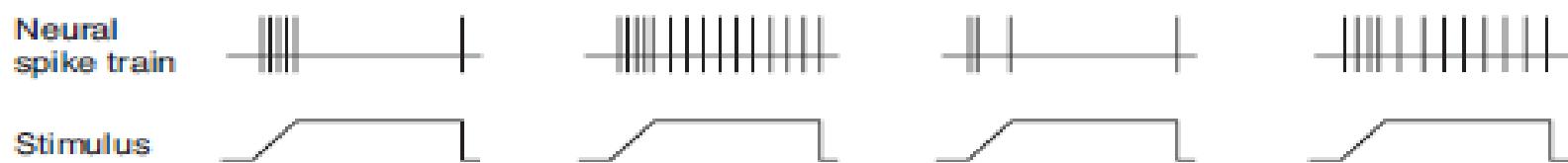
A Modality



B Location



C Intensity and time course



Modality

- Is a **type of energy** transmitted by stimulus
- The particular form of energy to which receptor is most sensitive is called **adequate stimulus**.
- **Each type of receptor responds best only to one particular type of stimulus**
- E.g. receptors in the eye are sensitive to light, receptors in the ear to sound waves (due to difference in sensitivity of receptors, we cannot “see” with our ears or “hear” with our eyes)

Labeled Line Principle

also called Muller's law of specific nerve energies

It states that

Pathways for each sensation, from receptor to cerebral cortex are clear-cut & fixed

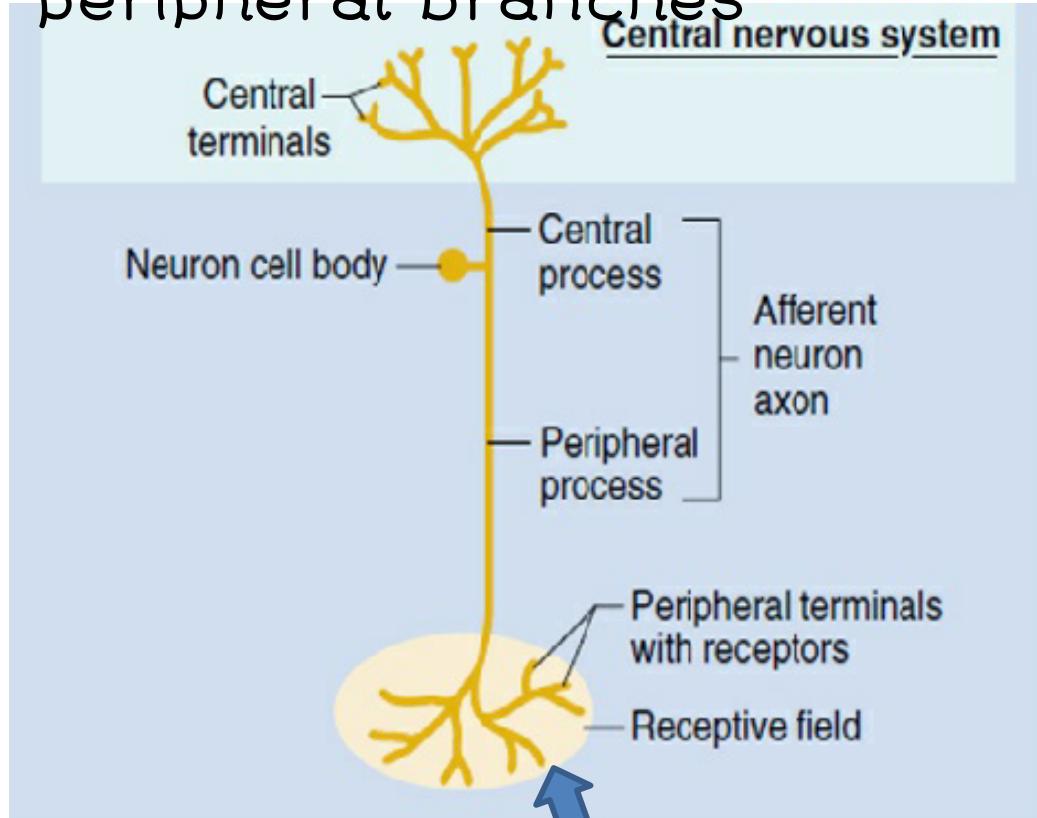
Specificity of nerve fibers for transmitting only one modality of sensation is called the labeled line principle

- When touch stimulus is applied to touch receptors or its pathway is stimulated anywhere along its course, the sensation produced is always touch

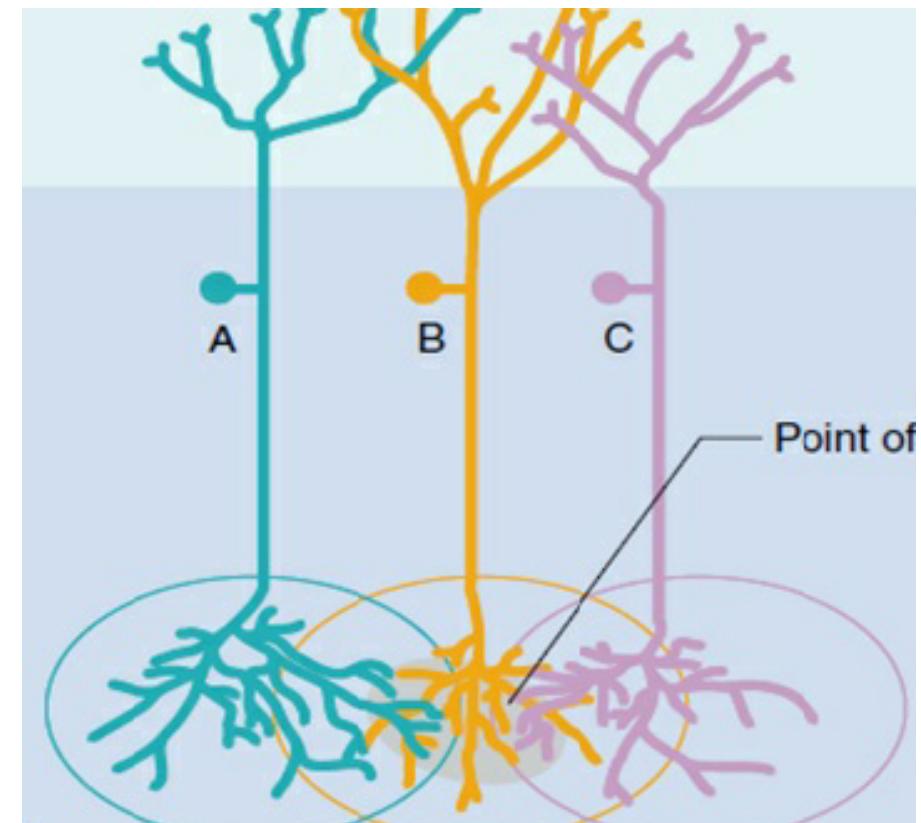
Location

is the site where stimulus is located

Sensory unit: single sensory axon and all of its peripheral branches

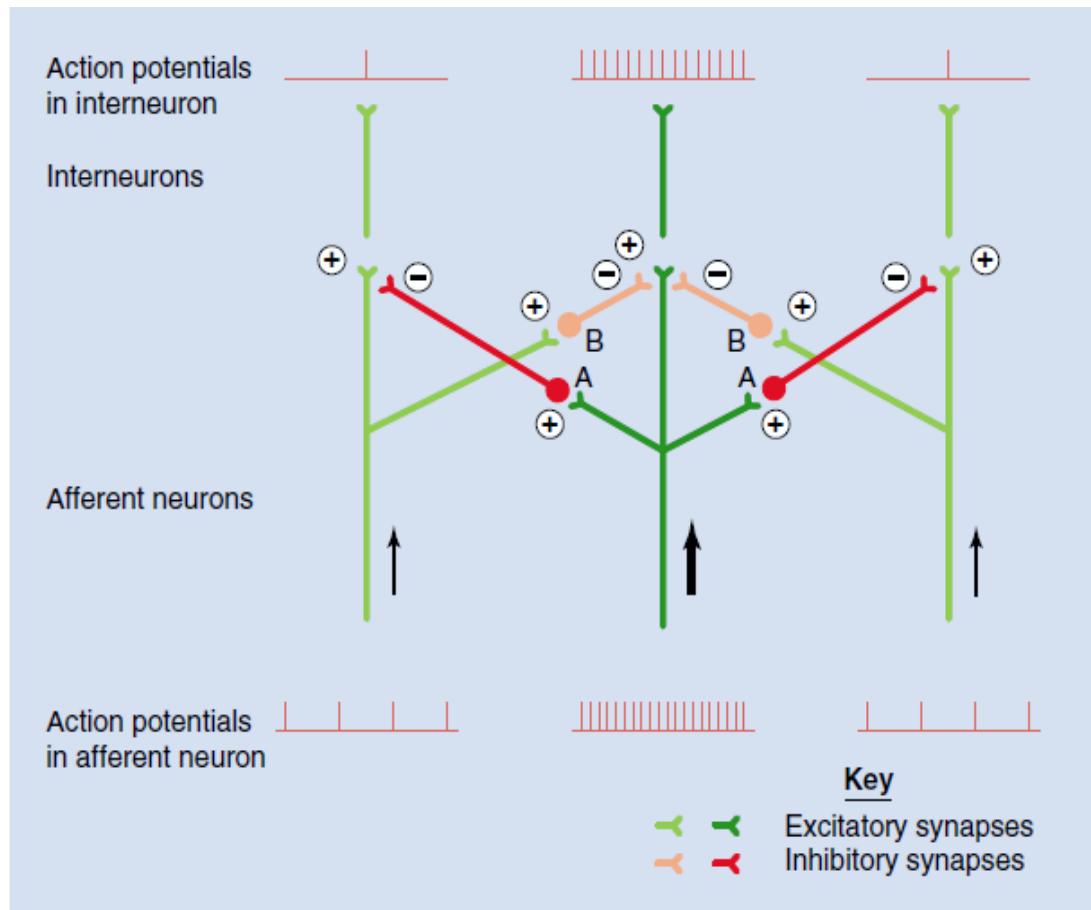


Area in which stimulus produces a response



Area supplied by one unit overlap or interdigitate with area supplied by other

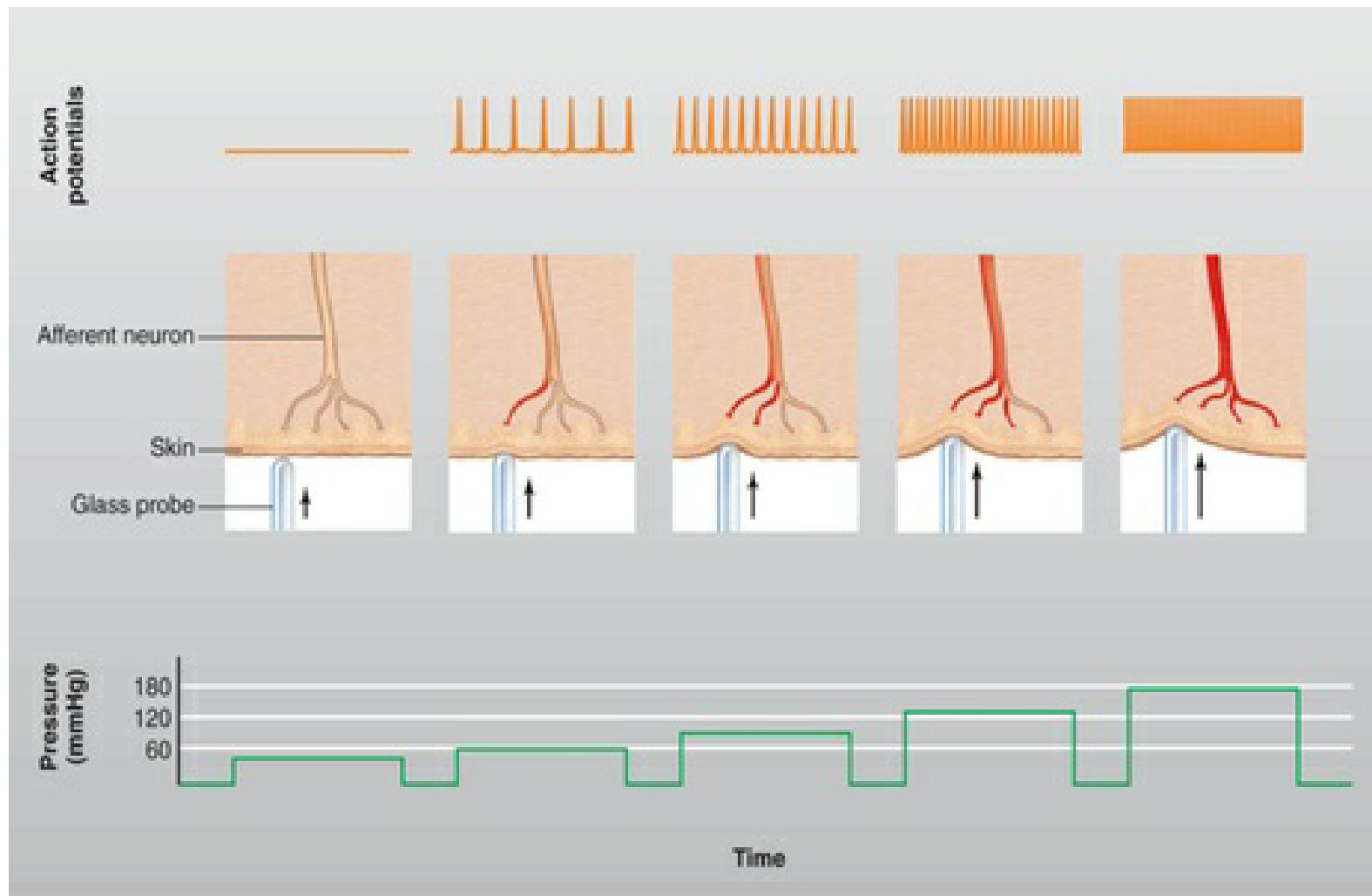
Mechanism that enable localization of a stimulus site is Lateral Inhibition (LI). It enhances the contrast between relevant & irrelevant information.



LI is utilized in pathway providing accurate localization (movements of skin hairs); Retinal processing

Intensity

Stimulus intensity is distinguished both by the frequency of APs generated in the afferent neuron & by the **number of receptors** and thus afferent fibers activated within the area.

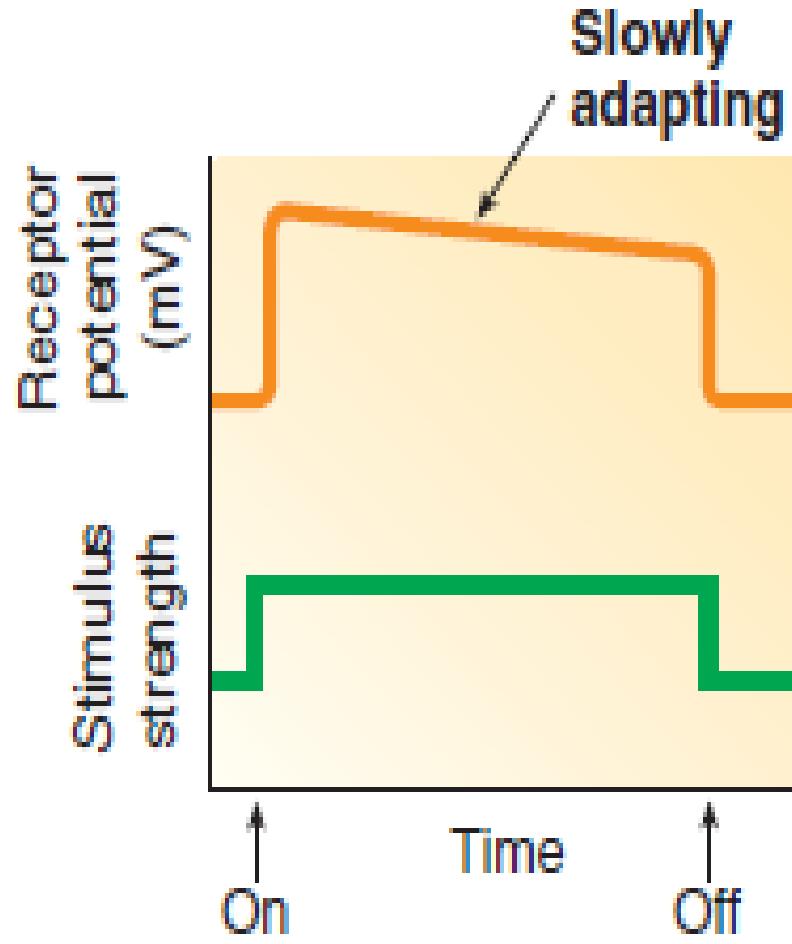


Weber-Fechner Law

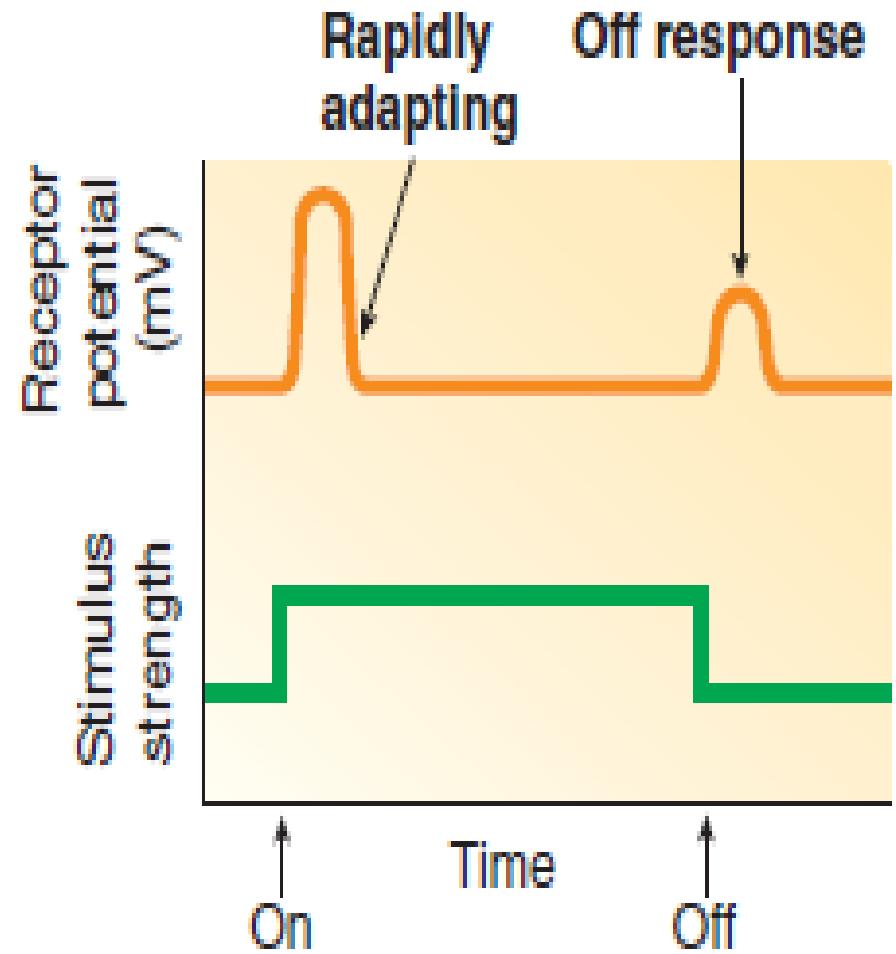
- It states magnitude of sensation felt is proportional to log of intensity of stimulus.

Duration

- Adaptation or desensitization
 - ↓ in receptor sensitivity results ↓ in AP frequency in AN despite maintenance of stimulus at constant strength
- Rapidly adapting (phasic) receptors
 - A phasic receptor **adapts rapidly** to a sustained stimulus and frequently **exhibits an off response when the stimulus is removed.**
- Slowly adapting (tonic) receptors
 - A tonic receptor **does not adapt at all** or adapts slowly to a sustained stimulus and thus **provides continuous information** about the stimulus



**Slowly adapting
(tonic) receptors**



**Rapidly adapting
(phasic) receptors**

Accommodation

site of membrane under stimulation fails to produce action potential

- During depolarization, the opening of the Na^+ channels overwhelms the repolarizing forces but if the depolarization is induced slowly, the opening of K^+ channels balances the gradual opening of Na^+ channels and action potential does not occur.

Properties of Receptors

- **Specificity of response or law of adequate stimulus**
 - Each type of receptor is specialized to respond to one type of stimulus, its **adequate stimulus**.
- **Adaptation**
- **Muller's doctrine of specific nerve energies (Labelled line principle)**
- **Law of projection (Eg: phantom limb)**
 - No matter where a particular sensory pathway is stimulated along its course to cortex the conscious sensation produced is referred to the location of receptor
 - Eg. Limb that has lost by accident or amputation, the pt usually experience intolerable pain & proprioceptive sensation in the limb i.e. no longer there. This is due to irritation of damaged nociceptive and proprioceptive afferents at stump of removed limb
- **Law of intensity discrimination (strength of stimulus): 'Weber-Fechner Law'** -magnitude of sensation felt is directly proportional to the log of intensity of the stimulus.

Somatosensory System

Sensation: refers to conscious perception of sensory information reaching the brain.

Sensation is of three types:

1. General sensation

- Touch, pain, temperature

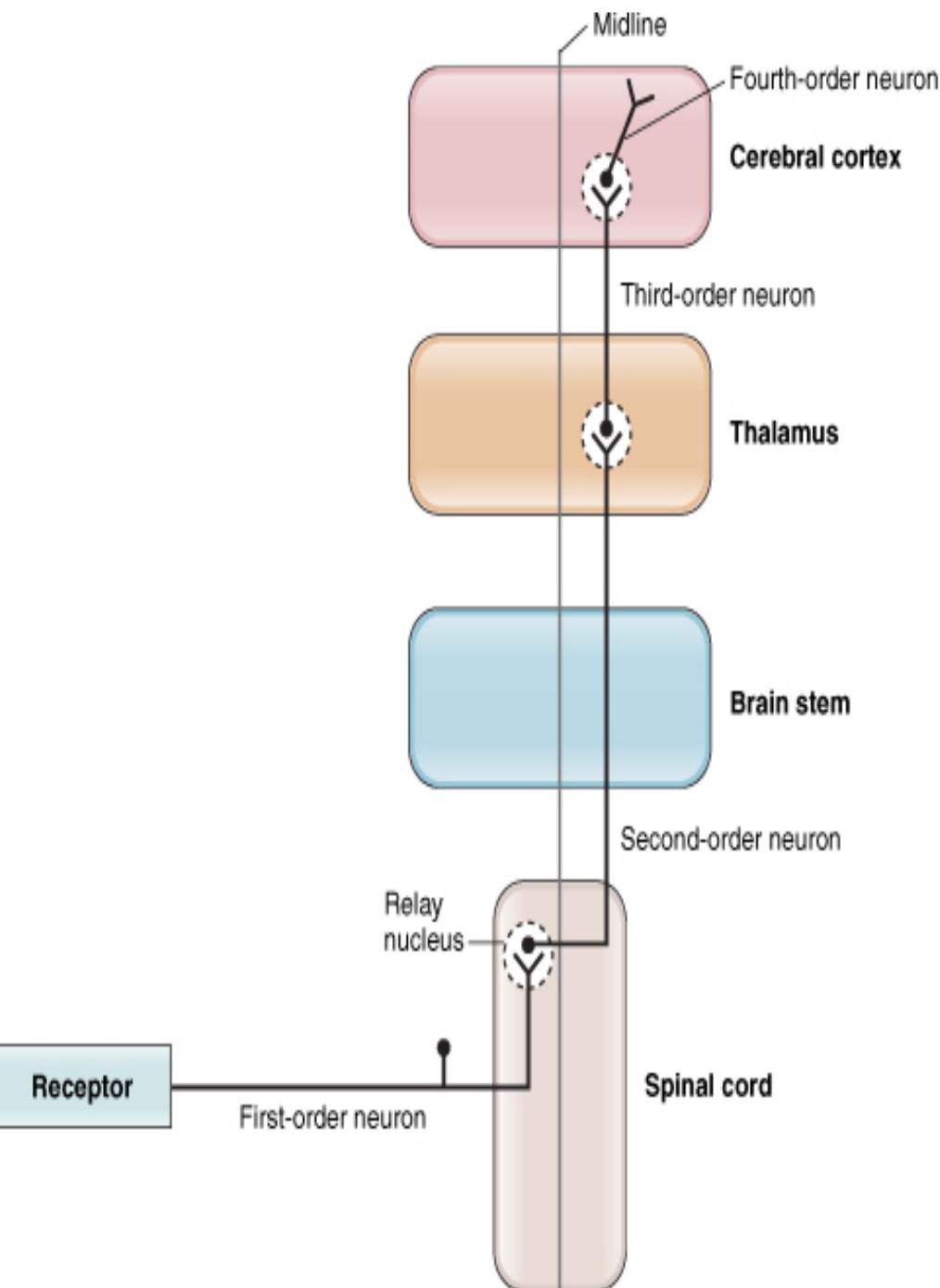
2. Special sensation

- Vision, smell, taste, hearing

3. Visceral sensation

- Distension of stomach

Components of sensory system



- **Sensory receptors**
- **Afferent neuron:** carry **sensory impulses to sensory cortex**
- **Sensory neural pathway consists of**
 - First order neuron**
 - Receive impulses from the receptors
 - Second order neuron**
 - Carry impulses from spinal cord to thalamus.
 - the axon of the second-order neuron crosses the midline
 - Third order neuron**
 - Reside in relay nuclei in thalamus
 - carry the sensory impulses from subcortical areas to cerebral cortex.
 - **Sensory cortex**

Tracts in Spinal Cord

Group of nerve fibers passing through spinal cord are known as tracts or pathway

Spinal tracts are divided into two main groups

- i. **Ascending tracts:** carry sensory impulses from the spinal cord to brain
- ii. **Descending tracts:** carry motor impulses from brain to the spinal cord.

Ascending (Sensory) tracts in the Spinal Cord

Tracts in lateral white column

- Lateral spinothalamic tract
- Dorsal(posterior) spinocerebellar tract
- Ventral(anterior) spinocerebellar tract

Tract in ventral(anterior) white column

- Ventral(anterior) spinothalamic tract

Tracts in dorsal (posterior) white column

- Fasciculus Gracilis
- Fasciculus cuneatus

Principal tracts in the spinal cord

FG= FASCICULUS GRACILIS

FC = FASICULUS CUNEATUS

ASC = ANTERIOR SPINOCEREBELLAR TRACT

PSC =POSTERIOR SPINOCEREBELLAR

LST =LATERAL SPINOthalamic

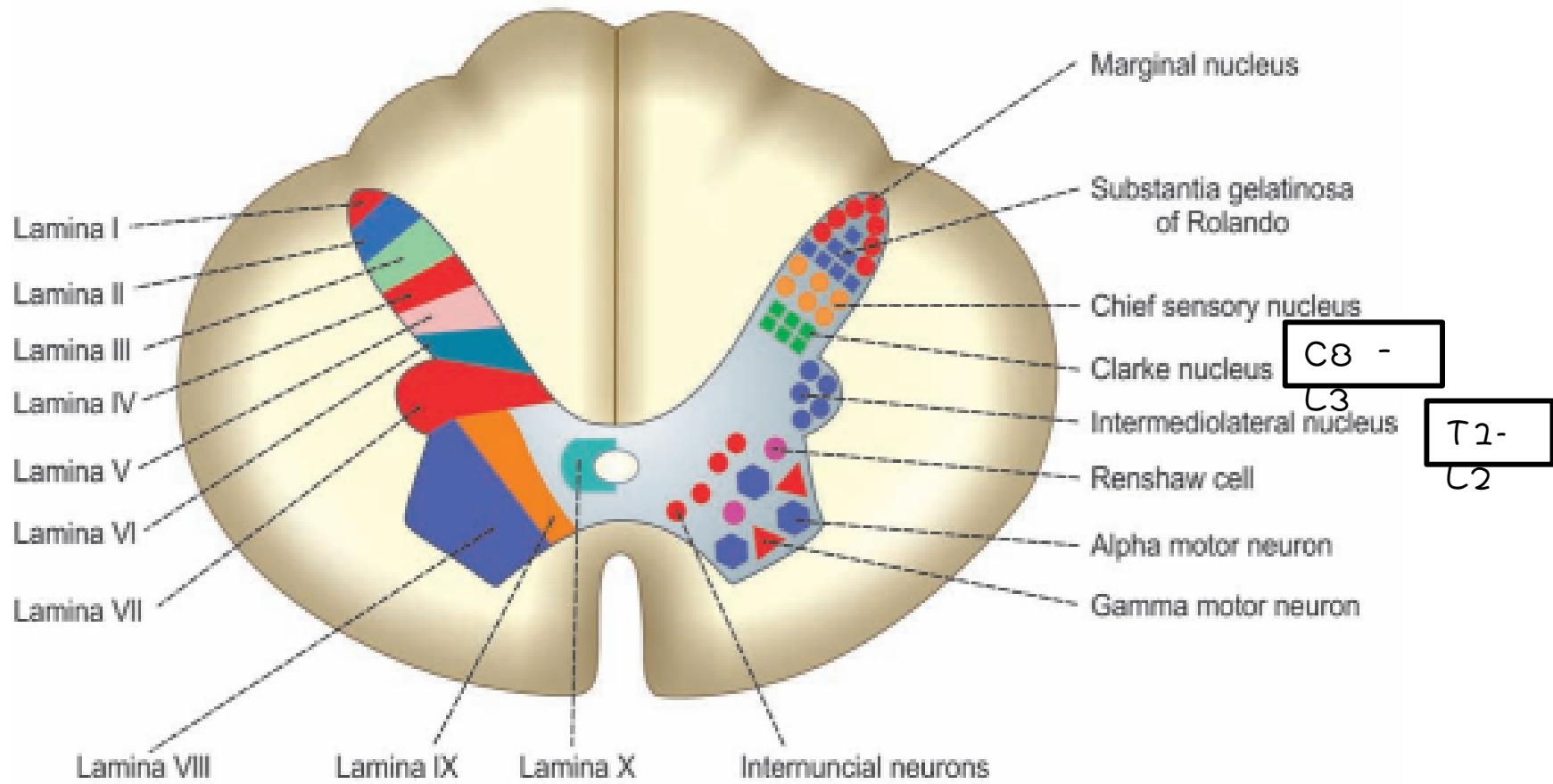
AST =ANTERIOR SPINOthalamic

LCS = LATERAL CORTICOSPINAL

ACS = ANTERIOR CORTICOSPINAL

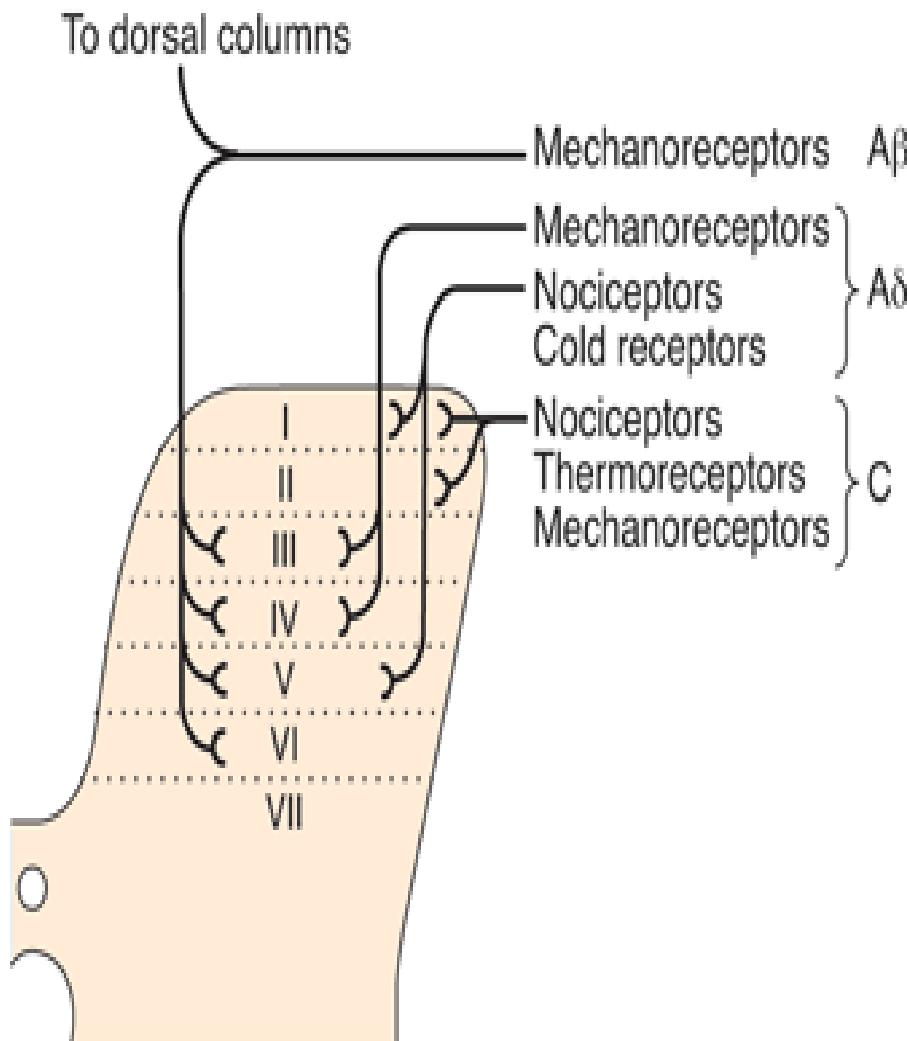
RS = RETICULOSPINAL

VS =VESTIBULOSPINAL



Neurons in grey horn of spinal cord

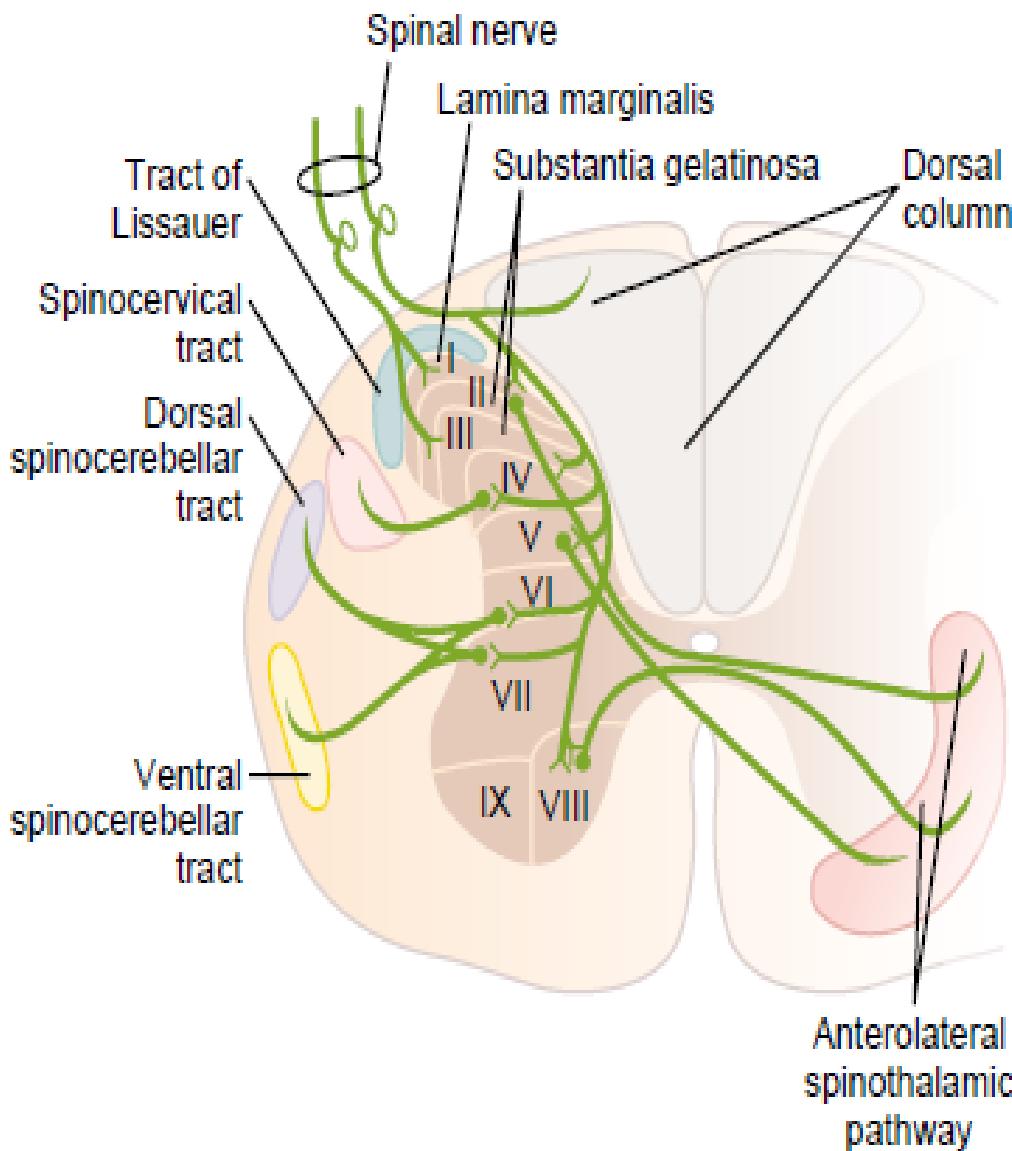
- Neurons of gray matter are distributed in laminae or layers
- These laminae was identified in 1950 by Brian Burke and Rexed, and called Rexed laminae.
- Laminae I to VI constitute the posterior gray horn. These laminae contain nuclei of sensory neurons



- On histological basis, dorsal horn are divided into laminas I - VII
 - lamina I - most superficial
 - lamina VII - deepest
- 3 types of primary afferent fibers mediate cutaneous sensation
- Large myelinated - (A_α & A_β fibers) transmit impulse generated by mechanical stimuli
 - Small A_δ fiber transmit impulse from cold receptor, nociceptor mediate fast pain
 - Small unmyelinated C fiber - concern with pain and temperature

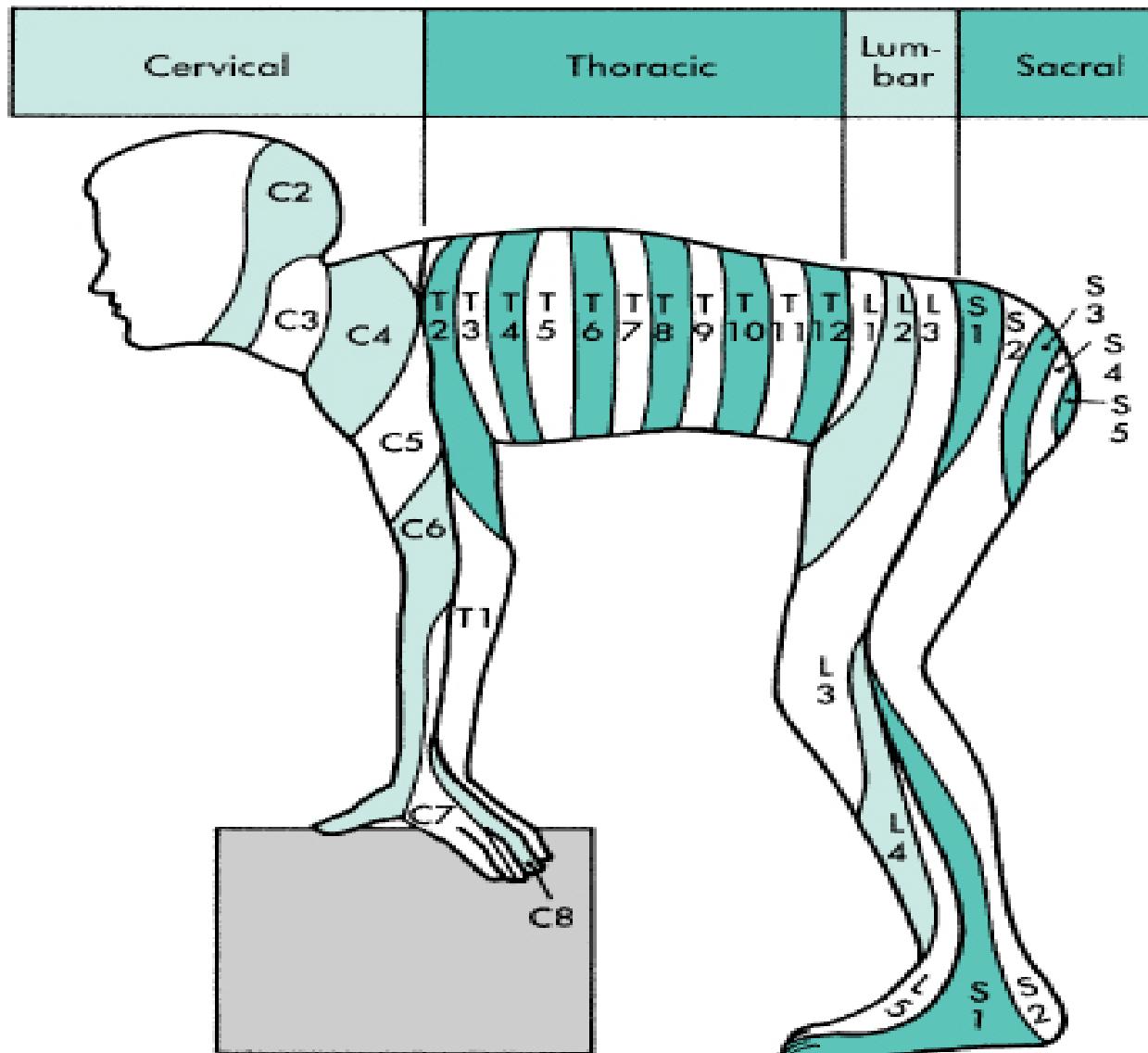
Schematic representation of the terminations of the three types of primary afferent neurons in the various layers of the dorsal horn of the spinal cord.

Dorsal Horn



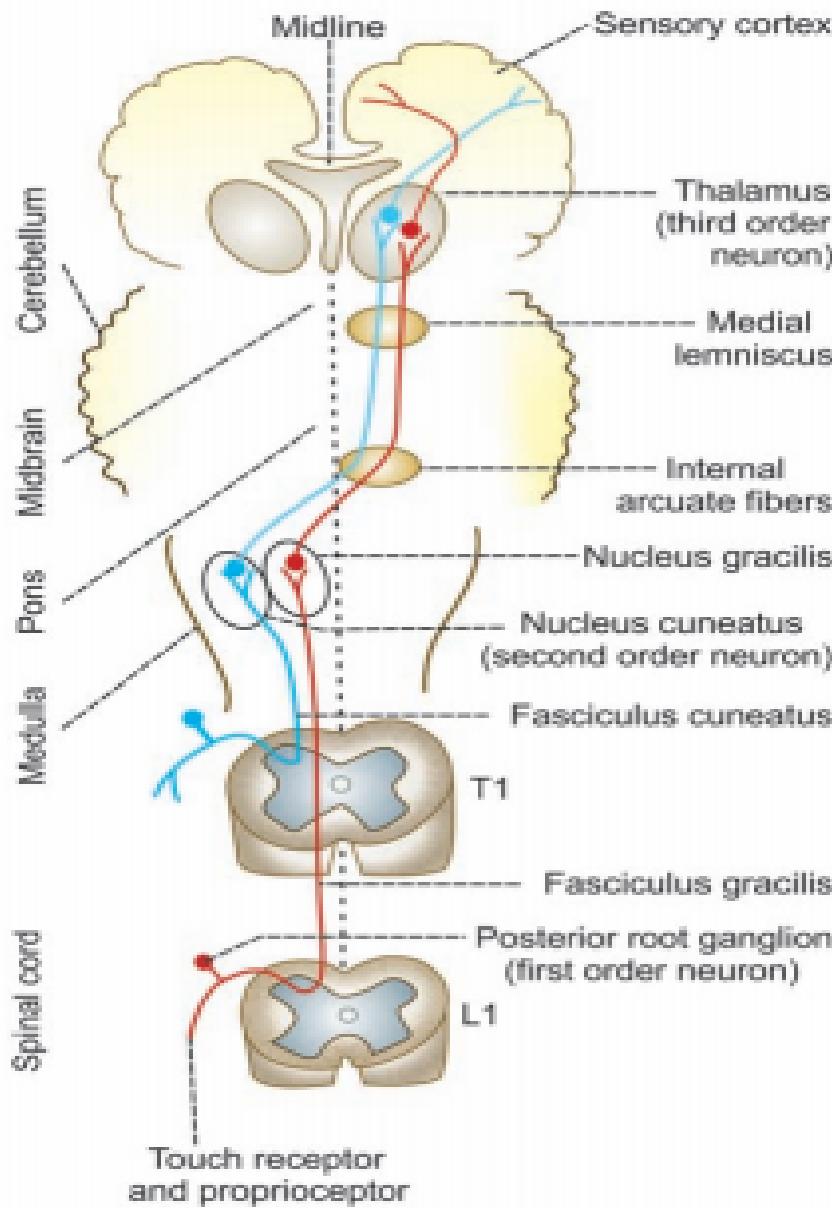
Somatic and visceral neurons converge in **lamina I - VI** of the **ipsilateral** dorsal horn, but **neurons in lamina VII receive afferents from both sides of the body** — a requirement if convergence is to explain referral to the side opposite that of the source of pain

Spinal Roots And Dermatomes



In the adult, a given dorsal root ganglion supplies a specific cutaneous region, which is called a **dermatome**.

Dorsal column



First order neuron : posterior root ganglia

Fasiculus Gracilis: Lower half of the body (lumbar and sacral)

Fasiculus Cuneatus: upper half of the body (Cervical and thoracic)

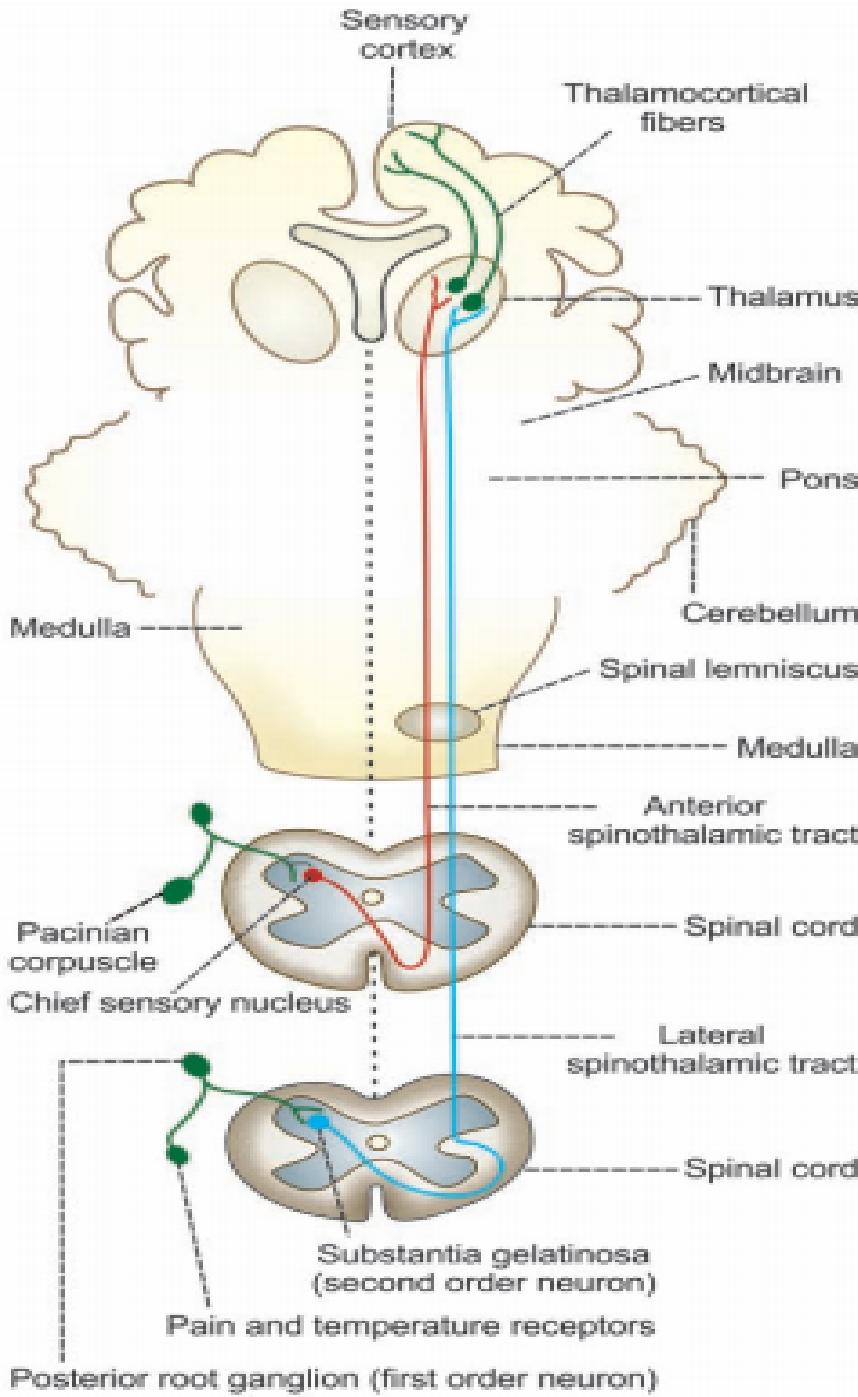
Second order neuron : nucleus gracilis and nucleus cuneatus in Medulla

Third order neuron: thalamus (ventroposterior nucleus)

Functions

Fine touch, Pressure, Vibration, Position & joint sensation, Cortical sensation, Tactile localization, Tactile discrimination, Stereognosis

Lateral Spinothalamic tract



- Carries pain and temperature sensation
- **First order neurons:** Dorsal root ganglia
- **Second order neurons:** fibers of (LST) arise from the neurons of spinal cord
 - i. **Marginal nucleus:** carry impulses of fast pain sensation
 - ii. **Substantia gelatinosa :** carry slow pain and temperature sensations.
- Axons cross to the opposite side and reach the lateral column of same segment.
- All the fibers pass through medulla, pons and midbrain and reach thalamus (VPL)
- Some of the fibers form collaterals to reticular formation of brainstem

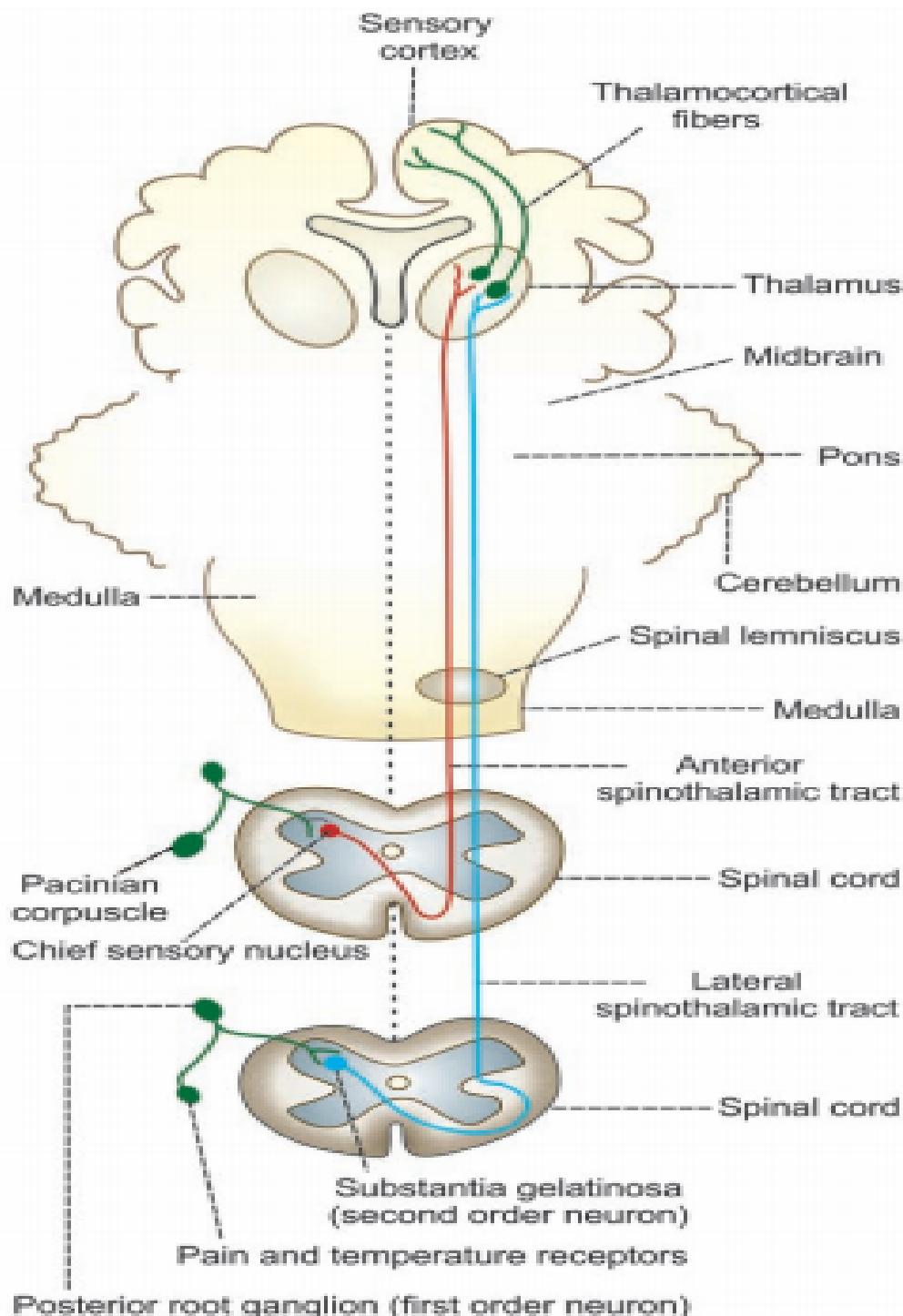
Lesion on Lateral Spinothalamic Tract

Bilateral:

total loss of pain and temperature sensations on both sides below the level of lesion

Unilateral:

loss of pain and temperature below the level of lesion in the opposite side



Anterior Spinothalamic tract

- Carries crude touch

First order neurons: posterior nerve root ganglia and receive crude touch sensation from the pressure receptors

Second order neurons: fibers of (AST) arise from the neurons of chief sensory nucleus of posterior horn

- these **fibers cross obliquely** and enter the anterior white column of opposite side.
- the fibers ascend through other segments of spinal cord and brainstem and reach thalamus (VPL nucleus).

Third order neurons: Neurons of thalamic nucleus form third order neurons

Lesion on Anterior Spinothalamic Tract

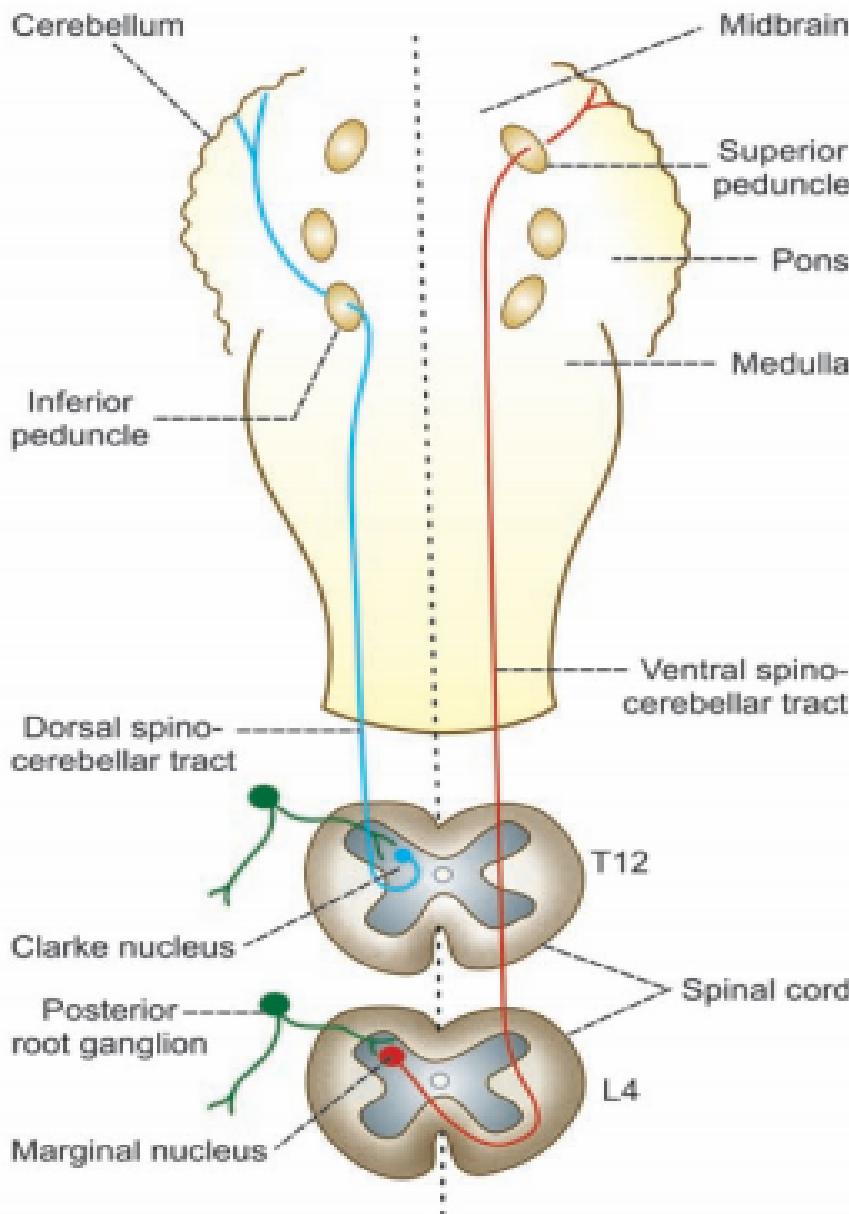
Bilateral lesion

leads to loss of crude touch sensation and loss of sensations like itching and tickling.

Unilateral lesion

Loss of crude touch sensation in opposite side below the level of

Dorsal Spino cerebellar tract



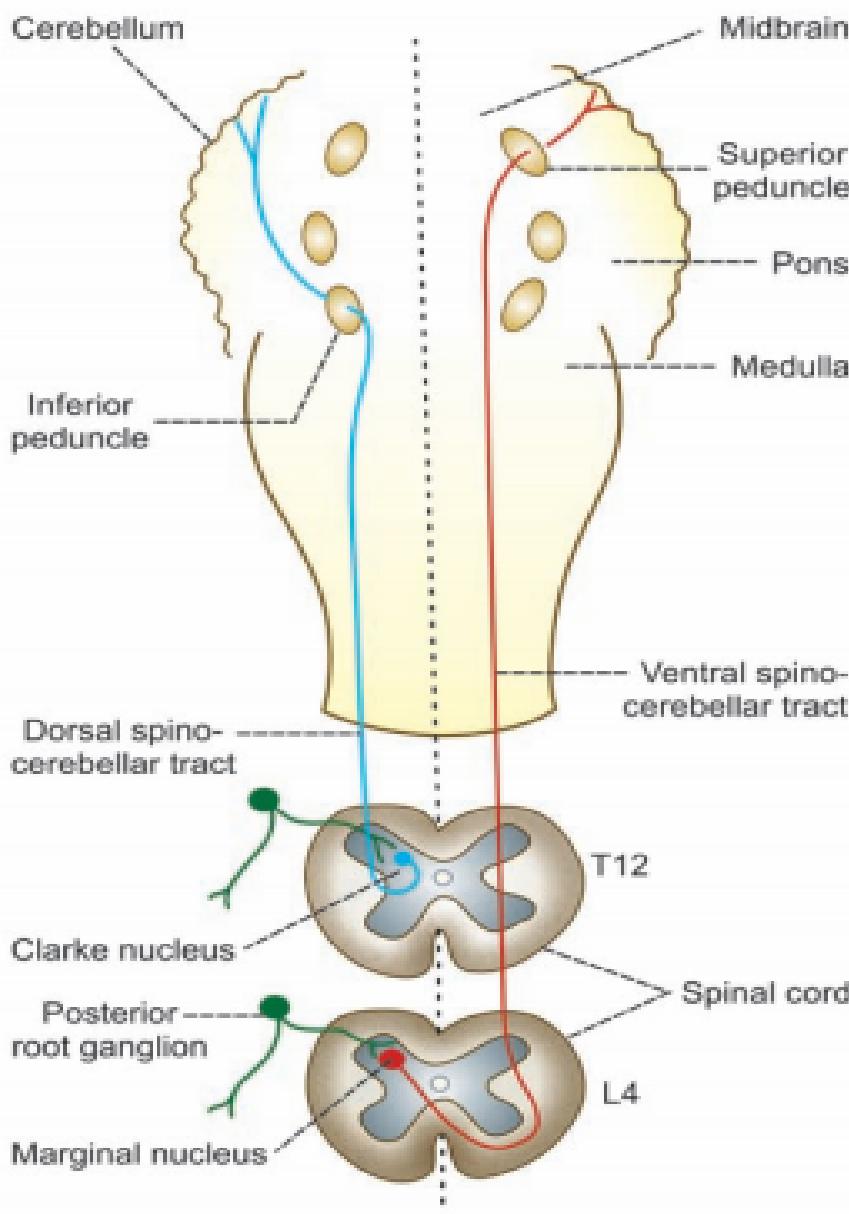
- **First order neurons:** posterior root ganglia
- In the spinal cord, the fiber ends round Clarke's column of cells on the same side
- Dorsal spino cerebellar tract contains uncrossed fibers.
- **Second order neuron:** Axons from neurons in dorsal nucleus of Clarke reach lateral column of spinal cord on same side.
- These nerve fibers ascend through other spinal segments, medulla, and finally, reaches the cerebellum through inferior cerebellar peduncle

Function

- carries the **unconscious kinesthetic sensation** (proprioceptive impulses from muscles, tendons and joints).

Lesion: Ipsilateral loss of the unconscious kinesthetic sensation

Ventral Spinocerebellar tract

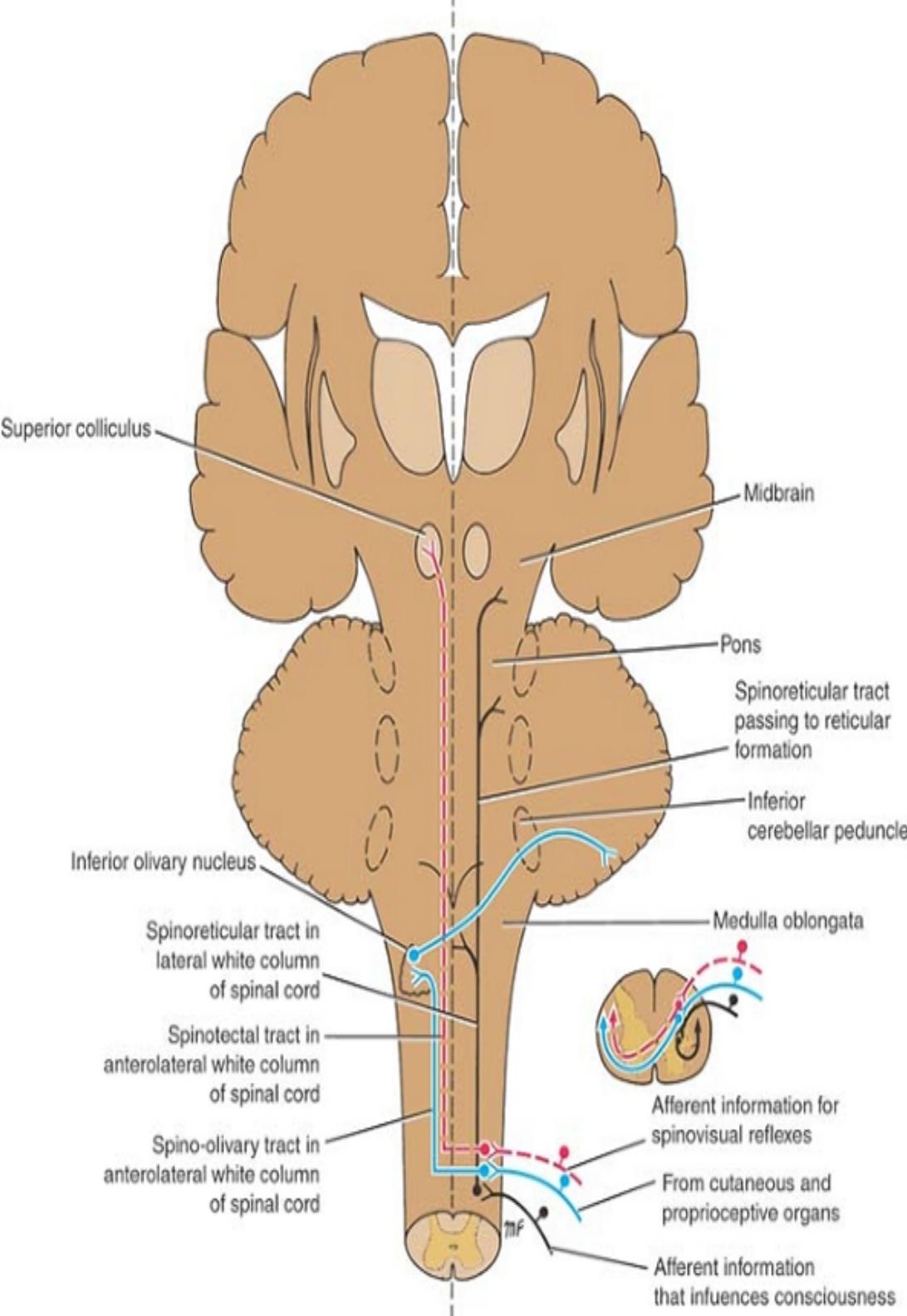


- **First order neurons:** posterior root ganglia
- Fibers from neurons of posterior root ganglia reach the marginal cells.
- Ventral spinocerebellar tract contains both crossed and uncrossed fibers.
- These nerve fibers ascend through other spinal segments, medulla, pons and midbrain and Finally, the fibers reach the cerebellum through the superior cerebellar peduncle

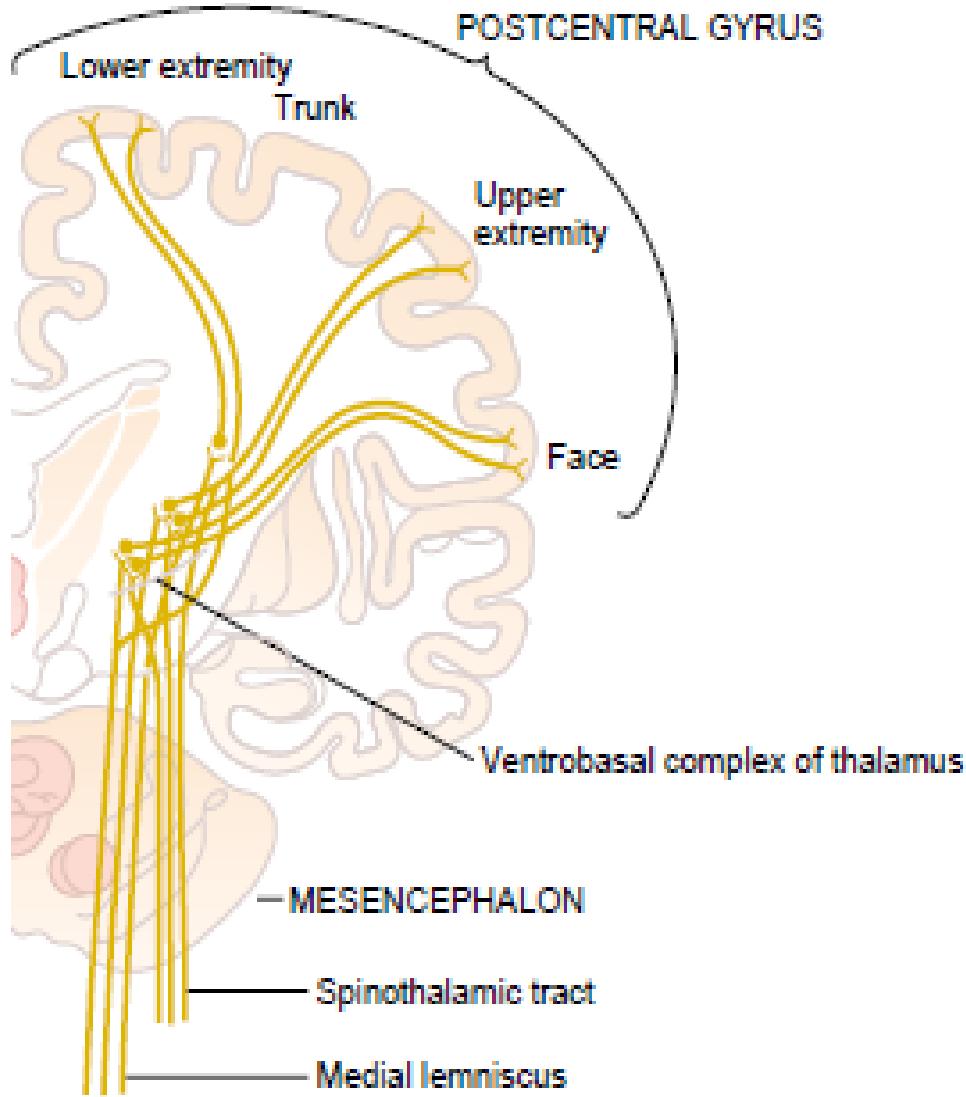
Function

- carries the **unconscious kinesthetic sensation** (proprioceptive impulses from muscles, tendons and joints).

Lesion: contralateral loss of the unconscious kinesthetic sensation



- **Spinotectal tract**
 - Provides spinovisual reflexes and **movements of the eyes and head**
- **Spinoreticular Tract**
 - Send collateral to reticular formation, and **concern with consciousness and awareness**
- **Spino-olivary Tract**
 - Spinal cord to olivary nucleus in medulla
 - **concern to proprioception**



In the thalamus, the medial lemniscal fibers terminate in the thalamic sensory relay area, called **the ventrobasal complex**.

From the ventrobasal complex, third-order nerve fibers project, mainly to **the postcentral gyrus of the cerebral cortex**, which is called **somatic sensory area I**.

These fibers also project to a smaller area **in the lateral parietal cortex called somatic sensory area II**.

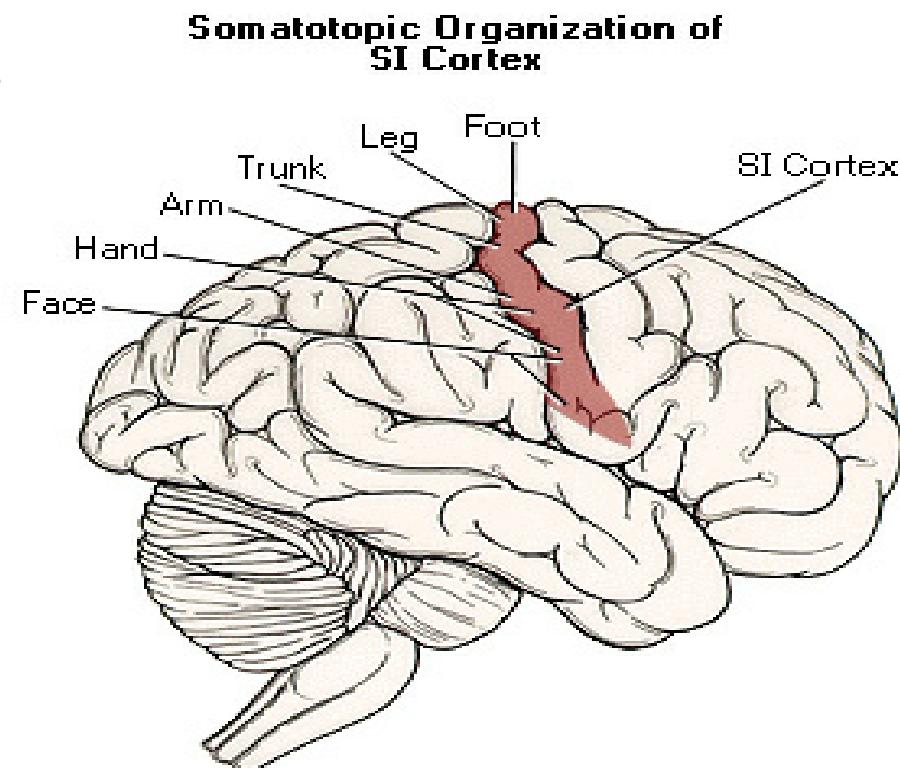
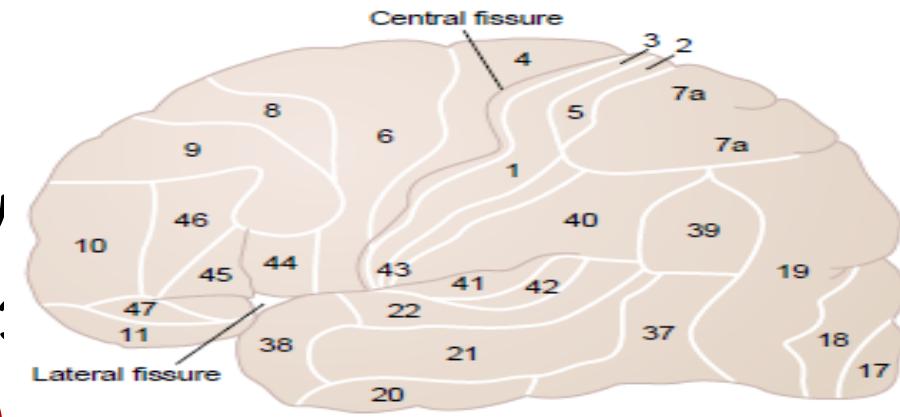
Lesion in VPL or VPM nuclei in thalamus

Destruction of the VPL or VPM nuclei diminishes sensation on the contralateral side of the body or face.

Somatosensory Cortex

Primary sensory area (SI)

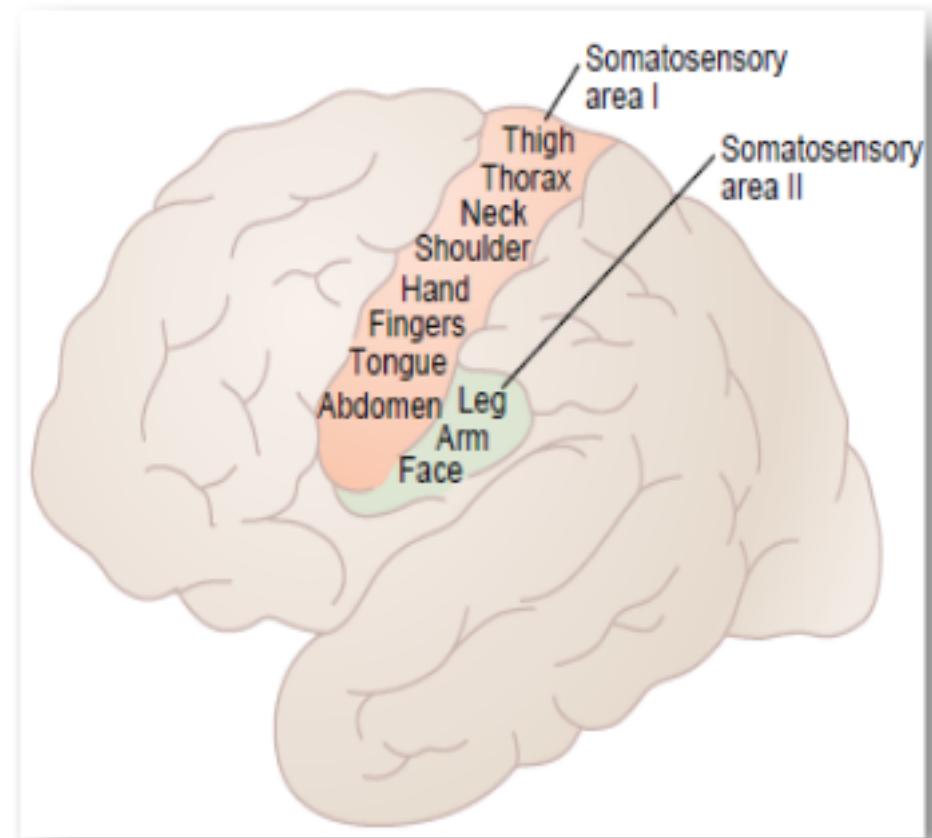
- Located in the postcentral gy containing Brodmann's area :
- Area 3: responds to **light touch**
- Area 1 and 2: **pressure and joint position sense**
- it is supplied by afferents from the **opposite side of body but from same sides of face.**
- Arrangement is such that the represented **upside down**



Lesion: deficit in fine touch, position sense, discrimination power

B. Somatosensory association area (SII)

- it is located **in the parietal cortex**, superior wall of the sylvian fissure
- supplied by afferents from both sides of body
Lesion: tactile discrimination



- The map of the body is called somatosensory homunculus
- The large areas of representation of the body are the face, hands, fingers
- The left half of the body is represented on the right hemisphere of the brain, and the right half of the body is represented on the left hemisphere.

