CNS revision (Part 1)

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Physiology of sensory receptors

Sensory Receptors

Def: specialized microscopic structures located **at the peripheral terminations of the afferent nerves**.

Functions of receptors:

They **detect** the stimuli and **transduce** (convert) these stimuli into nerve impulses which are then conducted along the afferent nerves to the sensory centers in central nervous system i.e. the receptors act as **"detectors and transducers".**

Physiological classification of receptors

I. According to the location of the receptors: They are classified into:

A. External receptors: on the body surface mainly in skin.

B. Internal receptors: in deeper structures & viscera.

II. According to nature of the stimulus: They are classified into:

A. Mechanoreceptors

B. Chemoreceptors

C. Thermal receptors

D. Pain receptors (Nociceptors)

E. Photoreceptors or electromagnetic receptors

Physiological classification of receptors

A. Mechanoreceptors

They are stimulated by the mechanical forms of energy, they include:

- **Touch receptors in the skin.**
- **Proprioceptors in the muscles e.g. muscle spindle & Golgi tendon organs.**
- **Pressure receptors e.g. pacinian corpuscles.**
- **Baroreceptors in the aortic arch & carotid sinus that detect the changes in arterial blood pressure.**
- **Sound receptors.**
- **Vestibular receptors that detect the changes in the equilibrium.**
- **Stretch receptors as in alveoli, urinary bladder & right atrium.**

Physiological classification of receptors

B. Chemoreceptors :

They respond to the chemical stimuli e.g.

a. **Peripheral chemoreceptors in the aortic and carotid bodies.**

b. **Central chemoreceptors in the brain stem.**

c. **Taste & smell receptors.**

C. Thermal receptors:

They respond to changes in temperature.

- **They include cold receptors which respond to the drop of temperature & warm receptors which respond to the increase in temperature.**

Physiological classification of receptors

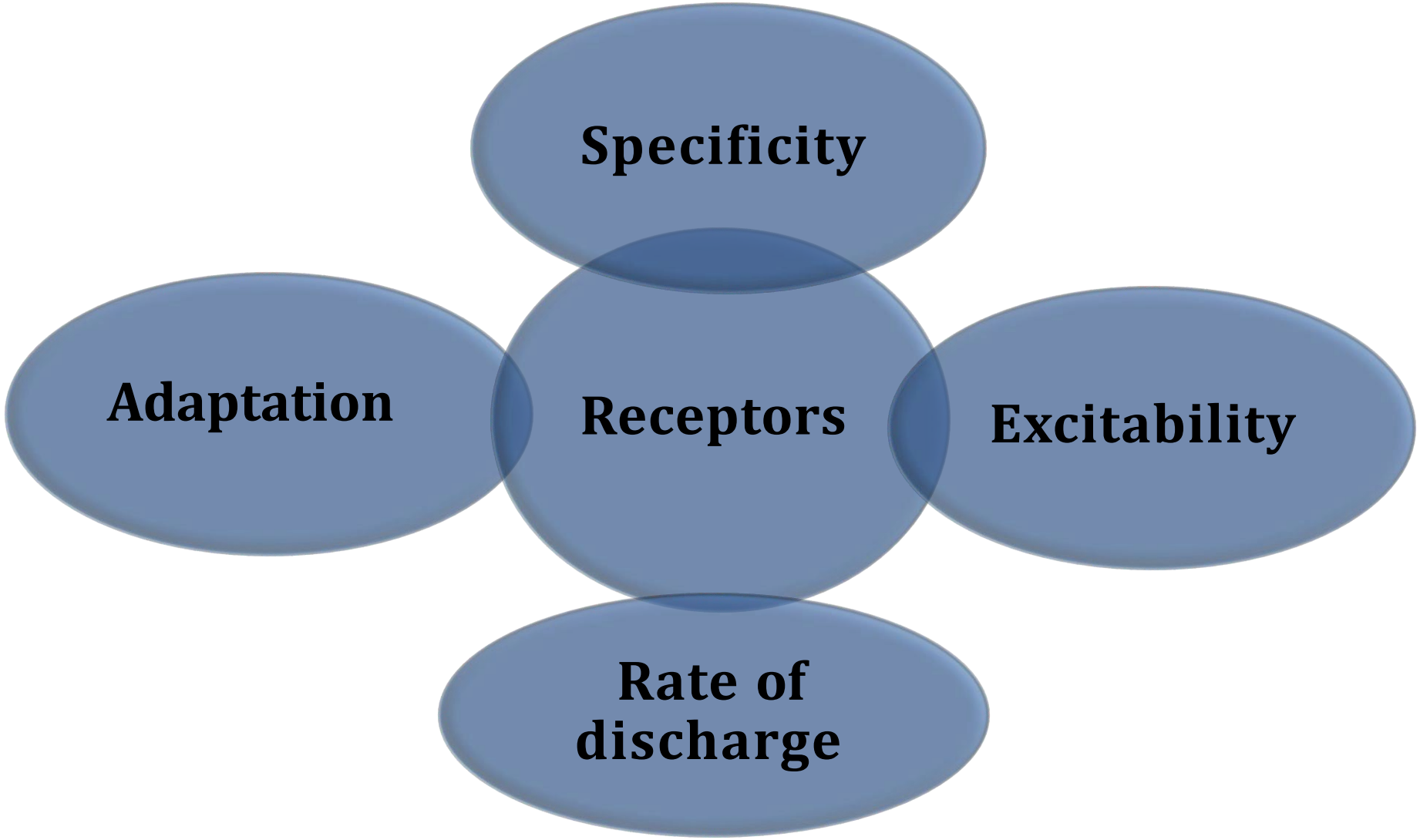
D. Pain receptors (Nociceptors):

They respond to the injurious or painful stimuli.

E. Photoreceptors or electromagnetic receptors:

They respond to the electromagnetic waves of light in the retina.

Properties of Receptors



1- Specificity (Muller's law)

- **Each type** of receptor is **most sensitive** to a particular stimulus called the **adequate stimulus**
- **Each type** of receptor when stimulated gives **one type** of
  - **sensation**
- **Examples:**

1. **Rods and cones** → more **sensitive** to light waves
2. **Auditory receptors** → more sensitive to sound

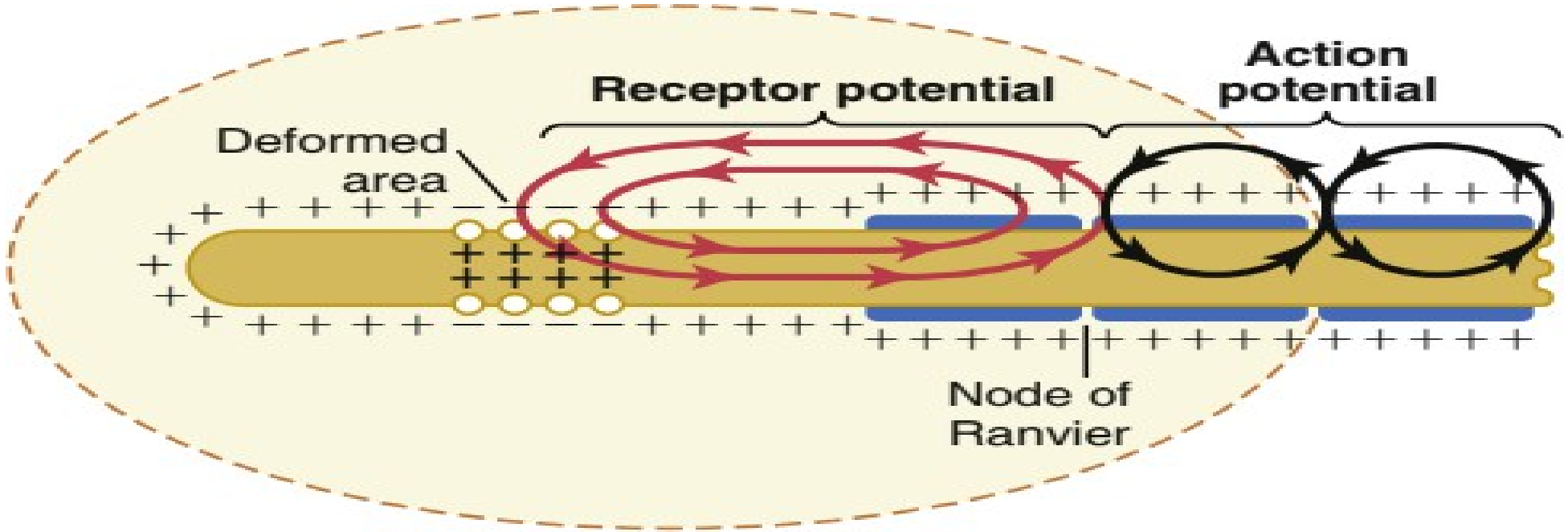
1- Specificity (Muller's law)

- **However,** the receptors can respond to stimuli **other than adequate ones,** provided that these **stimuli** are **very strong**; but still **the response is the same modality** to which the receptor is specialized e.g. **heavy blow to the eye give flash of light (visual sensations)**

2- Excitability

Def.

- The ability of the receptors to **respond to** their **adequate stimuli** and convert these stimuli into **receptor potential**



Receptor potential (RP)

Def.

- **It** is a **potential changes** that occur in the receptors on adequate stimulation
- Usually in the form of **partial depolarization** **and may be hyperpolarization** **in visual receptors (Rods & Cones).**

Receptor potential (RP)

Mechanism

- Each type of receptors has a specific mechanism to produce RP as follow;

i) <u>In mechanoreceptors:</u>

- The stimulus deforms the nerve terminal i.e. stretch its membrane → open ionic channels for Na → depolarization.

ii) <u>In chemoreceptor:</u>

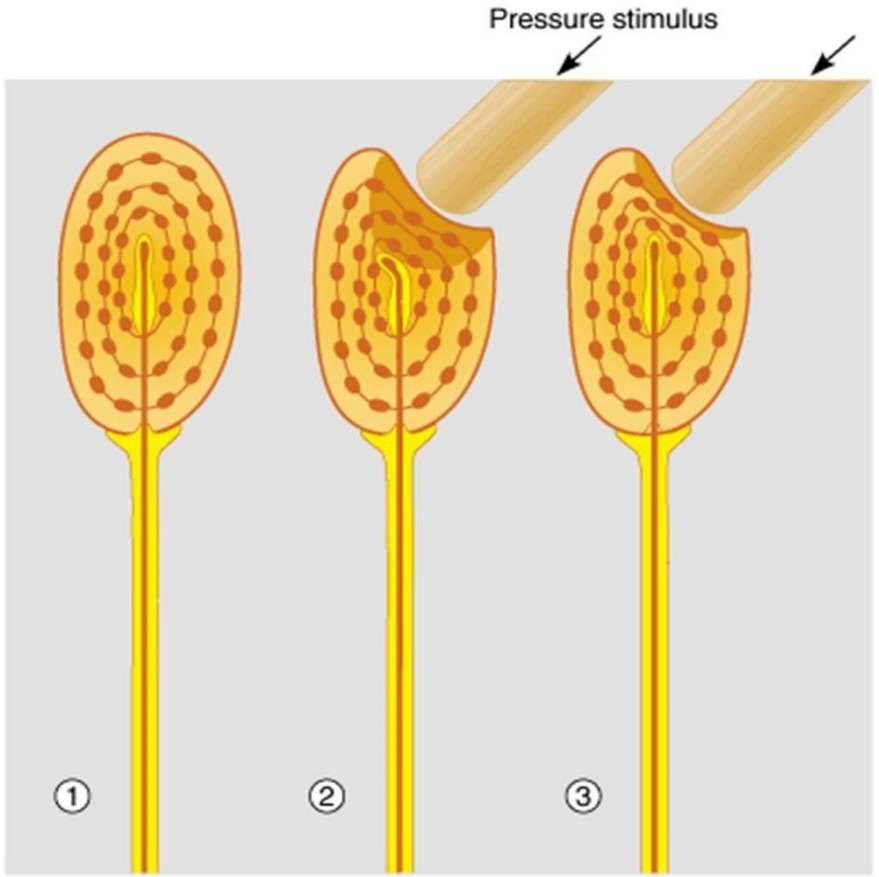
- When the chemical agent binds to its chemoreceptor, it opens its ionic channels →↑ Na influx → depolarization.

<u>iii) In Photoreceptors:</u> →light closes Na channels → ↓Na influx → hyperpolarization.

Receptor potential (RP)

Mechanism:

- In **mechanoreceptors** is caused by deformation of receptor → open ion channels
- Better studied in **Pacinian corpuscles** due to;
  a. **Easily stimulated by microglass rods**
  b. **Large in size and easily dissected.**

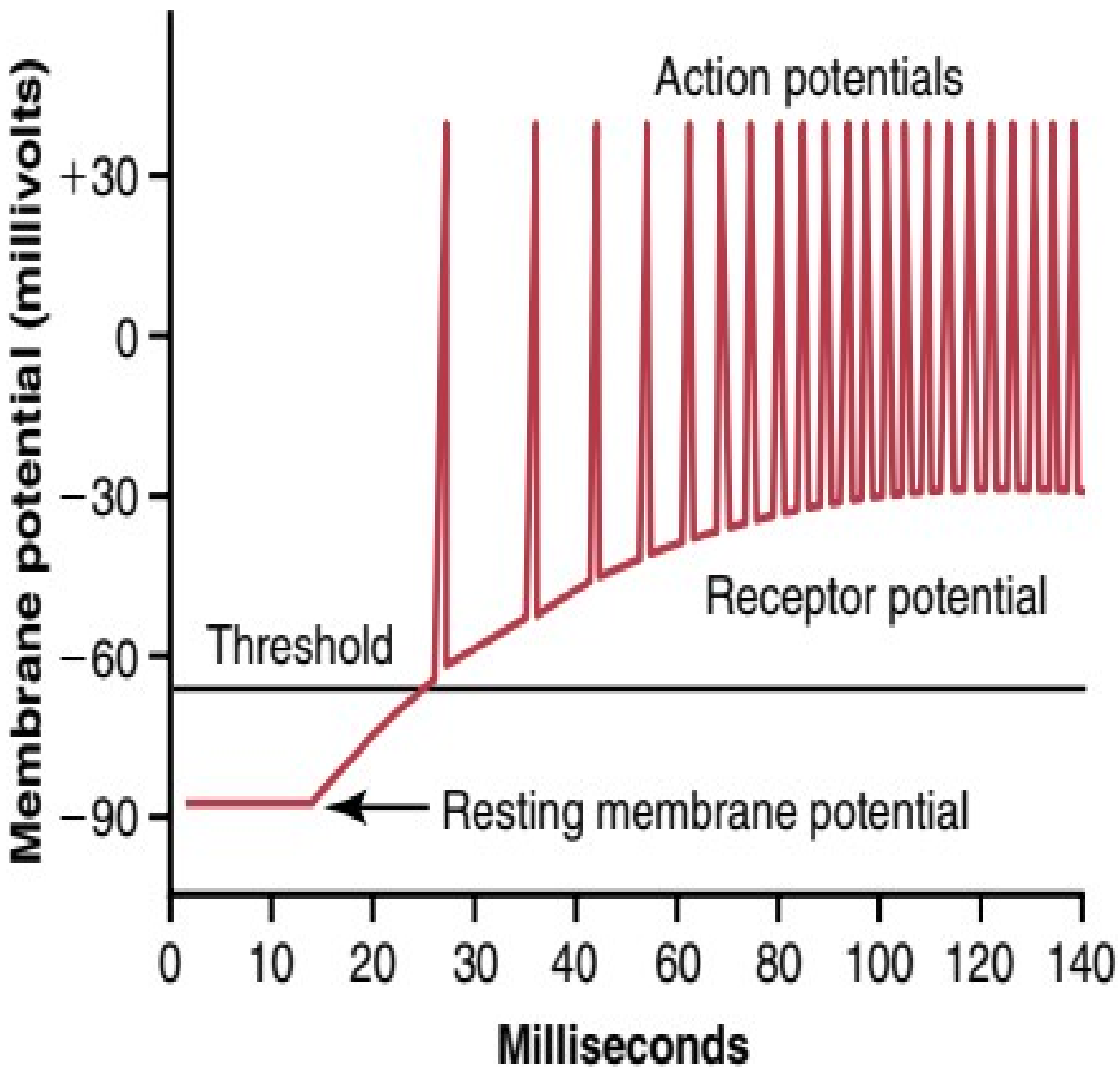


Mechanism of Receptor potential (RP)

- When the pressure is applied to the corpuscle → it **compresses** the concentric lamellae → **deformation** of the nerve terminal → **opening of Na+ channels** → increasing Na+ influx → **partial state of depolarization** in the nerve terminal known as **"RP".**
- The **maximal amplitude** of RP around **100 mv** that occurs when maximal opening of Na+ channels in the receptor membrane.
- When the **RP** reaches certain **threshold**, it generates **local electrotonic current** which flows to the first node of Ranvier → gradual depolarization till the **firing level is reached** & **action potential** (AP) is **generated** → AP is **propagated** along the afferent nerves to the CNS.

Mechanism of Receptor potential (RP)

- The amplitude of **electrotonic current** is determined by the **amplitude of the RP** which by its turn depends upon the **intensity of the stimulus**.
- As long as the amplitude of the **electrotonic current** is strong, ➔ the **1st node of Ranvier** can be depolarized in short time ➔ this increases the rate of discharge.



Properties of the RP

1. **Graded amplitude:** i.e. its amplitude is directly related to the intensity of the stimulus i.e. does not obey the all or none rule.

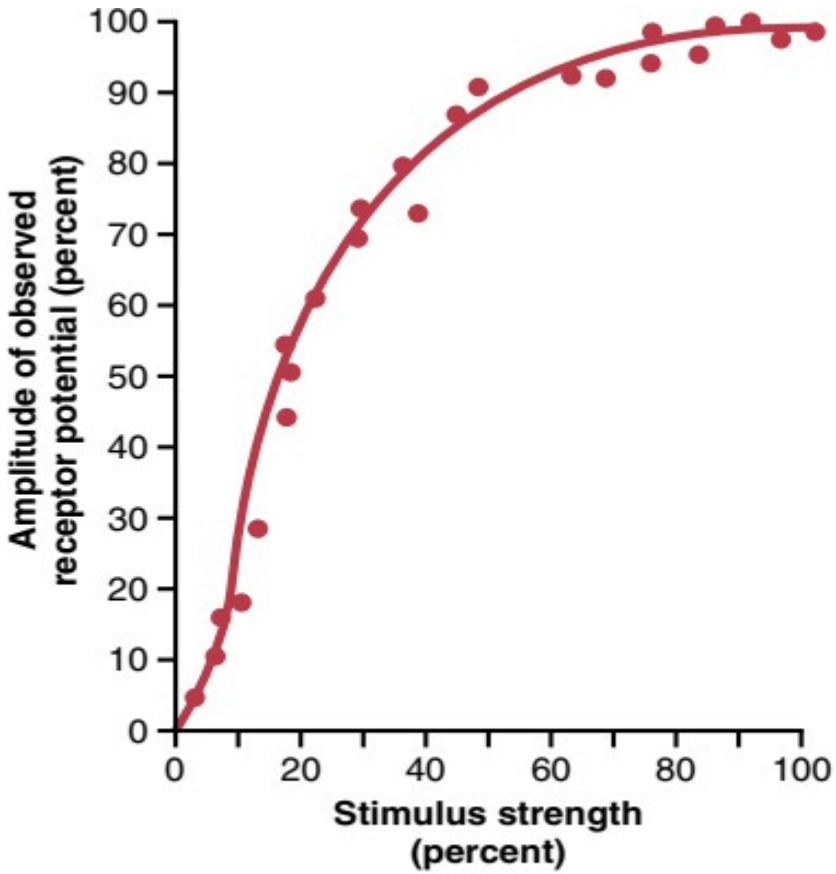
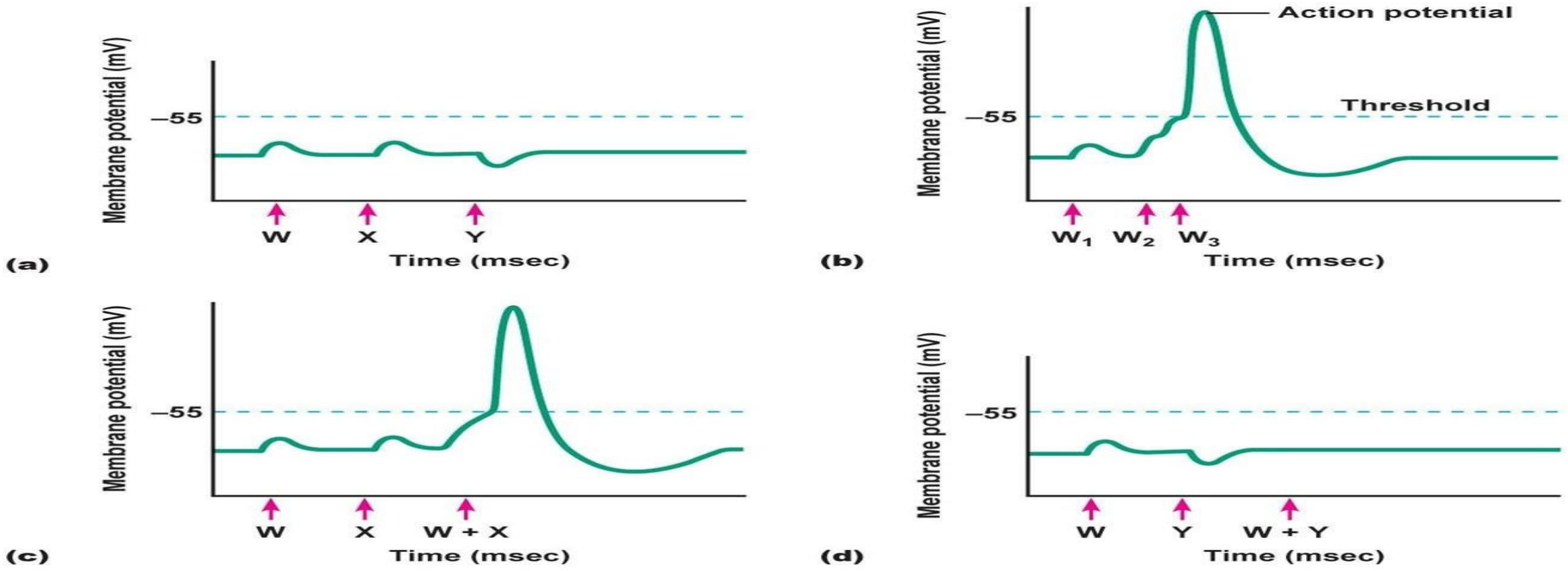


Figure 47-4 Relation of amplitude of receptor potential to strength of a mechanical stimulus applied to a Pacinian corpuscle. *(Data from Loëwenstein WR: Excitation and inactivation in a receptor membrane.*

Properties of the RP

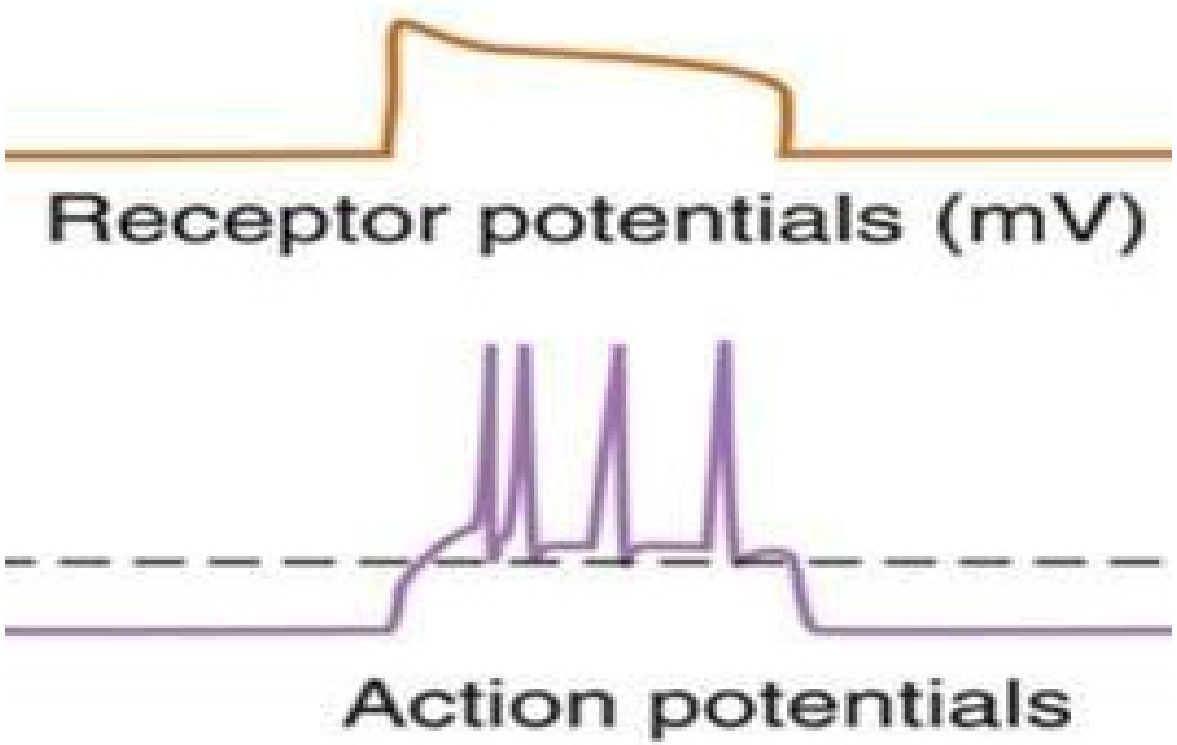
2. Can be summated: multiple RPs can be summated with each other by temporal (time) and spatial (space) summation.



Properties of the RP

3. Passive localized spread.

4. It has a short duration (5 msec).

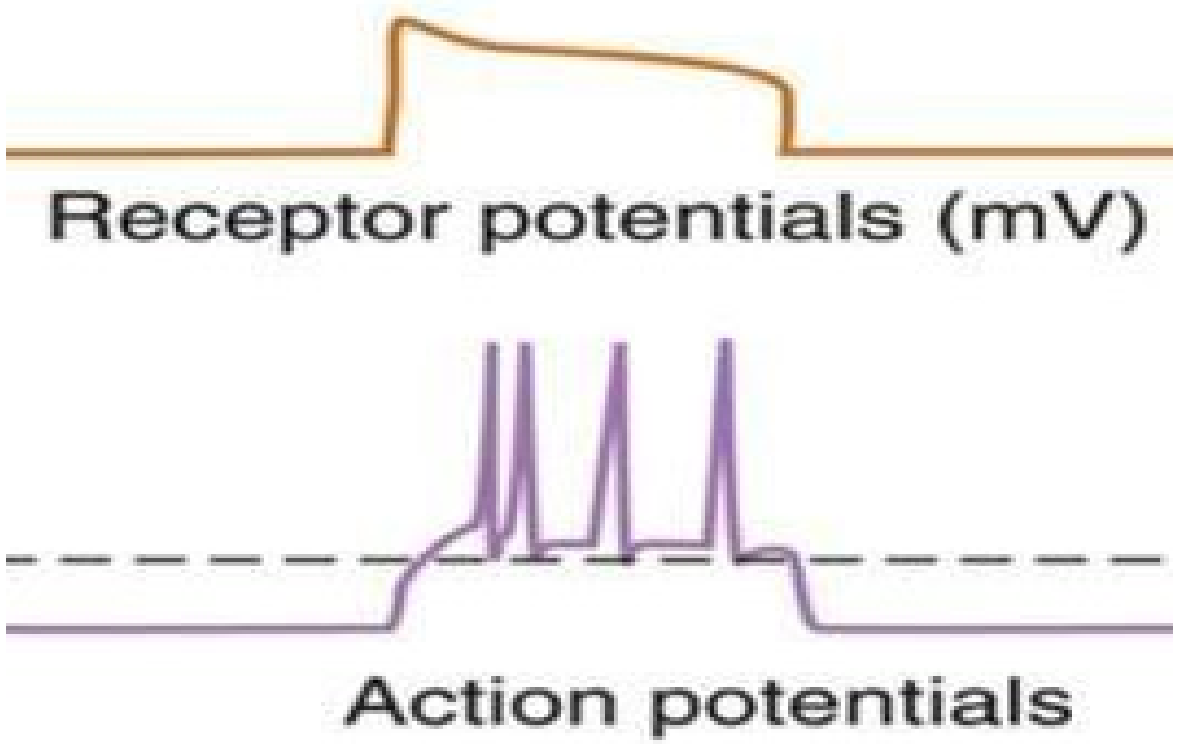


Properties of the RP

3. Passive localized spread.

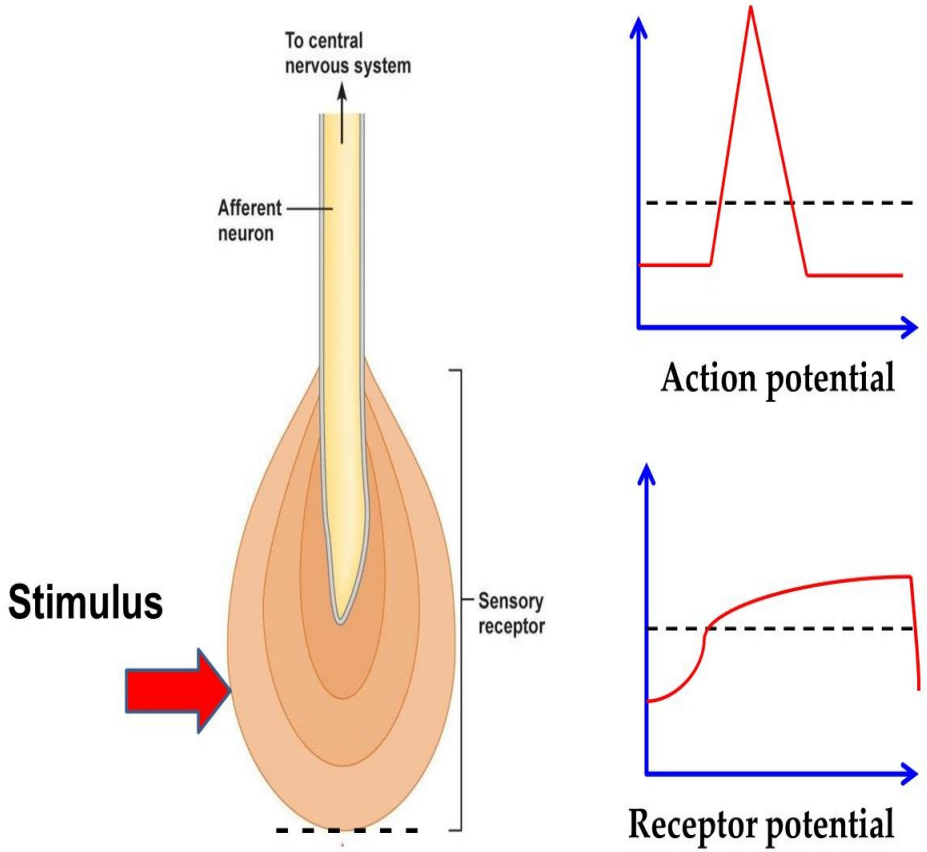
4. It has a short duration (5 msec).

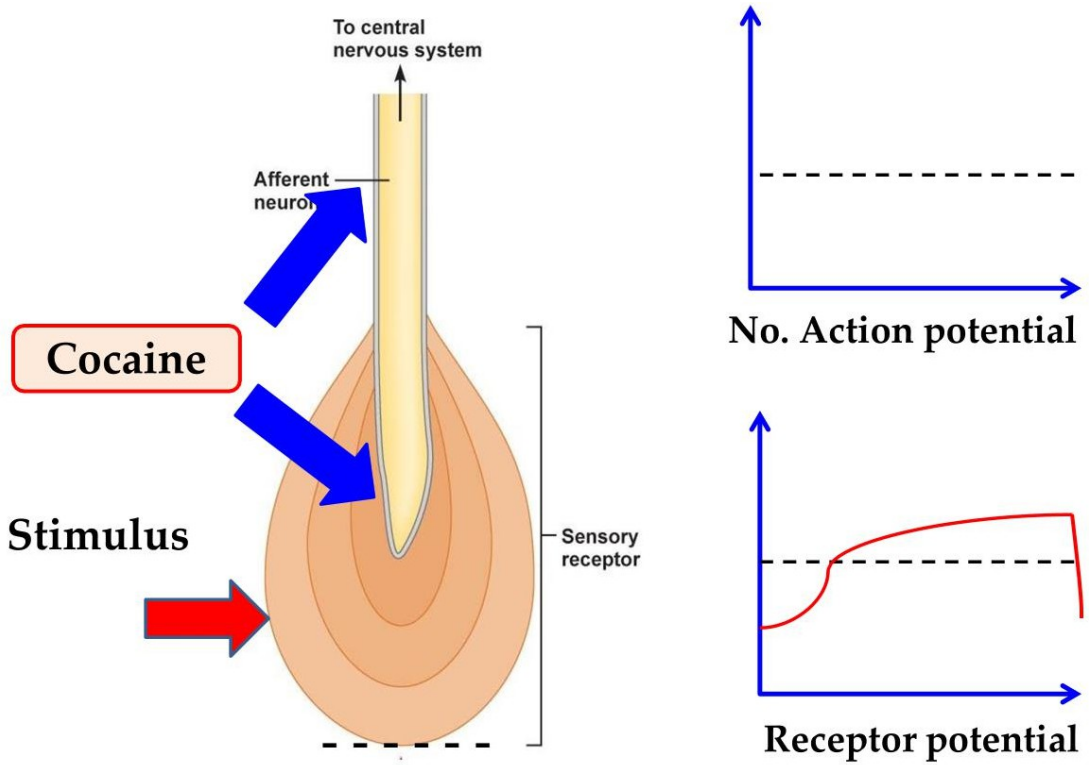
5. It can initiate repeated action potentials at the 1st node of Ranvier.



Properties of the RP

6. It is not blocked by local anesthetics.





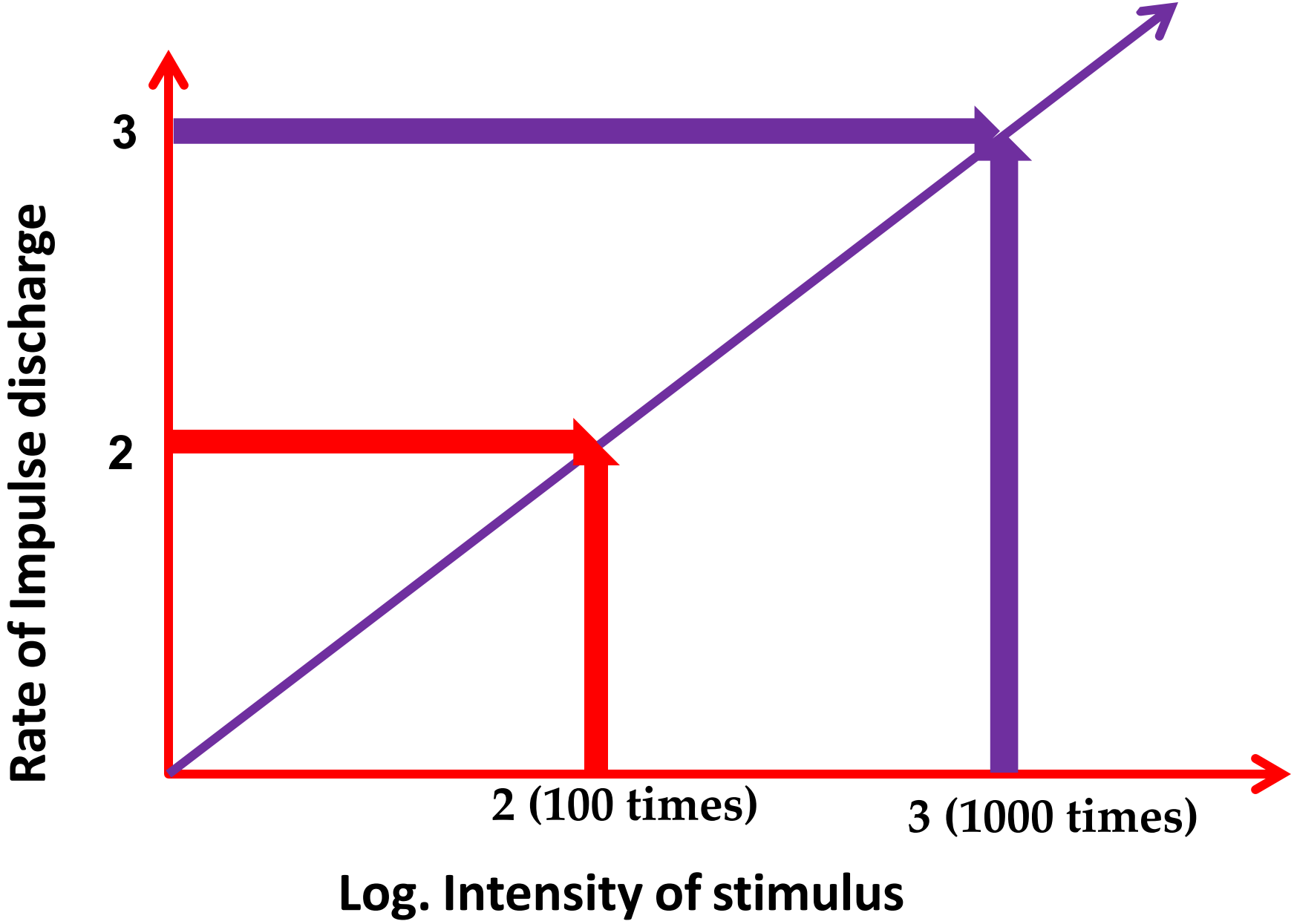
3- Rate of discharge from receptors

Weber-Fechner Law:

- The **rate of impulse** discharged from a receptor is **directly proportional** with the **log intensity** of the stimulus
- **R = log S x K**

(Where R = rate of discharge, S = strength of stimulus, K = constant).

Weber-Fechner Law



3- Rate of discharge from receptors

- So, **To increase the rate of discharge twice, you must increase the intensity of the stimulus 100 times.**
- **So,** receptors compress marked changes in stimulus intensity into smaller changes in frequency of action potential **(Compression function of receptor)**

➢ **Increasing the intensity of the stimulus increases the rate of discharge by:**

a. **By increasing rate of discharge** from each receptor

b. **By increasing the number of excited receptors (Recruitment of receptors**)

4- Adaptation of receptors:

- **Def:** Decrease in the rate of discharge from the receptors in spite of continuous constant stimulation.
- **According to the speed of decline in the rate of discharge from receptors "Rate of adaptation", receptors are classified into:**

a) **Rapidly adapting receptors (Phasic receptors).**
b) **Slowly adapting receptors (Tonic receptors).**

	Rapidly adapting receptors = Phasic receptors	Slowly adapting receptors = Tonic receptors
1- Def.:	They **first** discharge at **high rate**, then the rate ↓ **rapidly** to **zero after 1 or 2 seconds** in spite of continuous stimulation	They **continue to discharge** at a lower rate as long as the stimulus is applied.
2- Examples:	i- Pacinian corpuscle. ii- Meissner 's corpuscle. iii- Hair follicle receptors. iv- Some joint receptors.	i- Muscle spindle ii-Golgi tendon organ. iii-Pain receptors. iv-Cold receptors.

	Rapidly adapting receptors = Phasic receptors	Slowly adapting receptors = Tonic receptors
3-Pattern of discharge:	- They discharge **only at**: i- **onset** of stimulation ii- **termination** of stimulation iii- **change in strength** of stimulation *So, they are called **phasic** receptors.*	-They discharge **continuously** to CNS as long as the stimulus is applied. *So, they are called **tonic** receptors.*

	Rapidly adapting receptors = Phasic receptors	Slowly adapting receptors = Tonic receptors
Importance :	- CNS only needs **to** receive impulse at the ***start, termination & change in strength*** of stimulation. - **Continuous impulses** from these receptors **is not necessary, otherwise** they **would be distracting. (e.g.** no need to continuously inform CNS about contact of clothes).	- Impulses from **muscle spindle & GTO** maintain **posture & equilibrium**. - Impulses from **baroreceptors & chemoreceptors** maintain **ABP & HR.** - **Pain & cold receptors** inform CNS about **harmful** stimuli & initiate **protective reflexes.**

Coding of sensory information

- **Def:** It is the ability of higher centers of the brain **to identify:**
  - **Type** of the stimulus (modality discrimination)
  - **Intensity** of the stimulus (intensity discrimination)
  - **Locality** of stimulus (locality discrimination) **although action potential is the same in all nerves**

Modality discrimination

- **Def:** It's the ability of the CNS to **discriminate the type** of a sensation (e.g touch, pain ,sound, …)
- **It depends on:**
  a) **Peripheral mechanism.**
  b) **Central mechanism.**

a) Peripheral mechanism:

- Occurs at the **level of receptors** and depends on **Muller's law**.
- According to **Muller's law**: each type of receptor gives one type of sensation when stimulated by its adequate stimulus.
- **e.g.** stimulation of retinal receptors gives rise to light sensation.
- So, **specificity** of receptors represents **the first step** in the coding of different modalities (types) of stimuli.

b) Central mechanism:

- **Depends on *"labelled line principle"* which is an extension to Muller 's law.**
- **Labelled line principle states that:**

"There's **a specific anatomical connections (**pathways) for each sensation which begins at a **specific receptor** then through a **specific tract** to terminate at a **specific center (area)** in the cerebral cortex".

- Stimulation of this pathway at any point gives rise to a **specific sensation** **e.g** stimulation of the visual pathway at any point gives rise to visual sensation.

- This **means that** there are **specific pathways** for transmission of different modalities and that **each pathway carries only one sensory modality**.

Intensity discrimination

- **Def:** It's the ability of the CNS to **discriminate the intensity** of a sensation.
- **It depends on:**
  a) **Peripheral mechanism.**
  b) **Central mechanism.**

1- Peripheral mechanism: which **depends on:**

a. ***Rate of impulse discharge from each receptor:*** the **higher the** rate of discharge, the **stronger is** the stimulus.

b. ***The number of stimulated receptors (recruitment of receptors):*** the **more the number** of stimulated receptors, the **stronger is** the stimulus.

2- Central mechanism: which depends on:

The *number of afferents reaching CNS:* the more **the number** of **afferents** reaching CNS the **stronger is** the stimulus.

Locality discrimination

- **Def:** It's the ability of CNS to **discriminate the site** of a sensation.
- **It depends on:**

Somatotopic map:

- Each area in the body e.g hand or leg is **represented** in a specific area in the cerebral cortex with **accurate anatomical pathways** from the receptor to the center in the cerebral cortex.
- So when the impulse reaches specific area in the cerebral cortex, the sensation isn't felt in the cortical neuron but it is **referred (projected)** to its **original site** in the body this principle is called **law of projection**.

Pain sensation

Pain sensation

❑Def of pain:

Unpleasant sensory and emotional experience caused by actual tissue damage.

❑Significance of pain:

It is a **protective** sense, where it directs the person to get rid of the injurious agents.

❑Pain receptors (Nociceptors)

- **Nature:** They are **free nerve endings**.
- **Functional classification of pain receptors according to their sensitivity (Subtypes of pain receptors):**

1- Mechanical pain receptors: Respond only to the **mechanical** trauma **e.g.** heavy pressure.

2- Chemical pain receptors: Respond to tissue damage produced by **chemical** agents **e.g.** concentrated H_2SO_4 or concentrated HCl in esophagus.

3-Thermal pain receptors: Respond to tissue damage produced by **thermal** stimuli **(temperatures > 45 C^{o} & < 10 C^{o})**.

4-Polymodal pain receptors: Respond to the tissue damage produced by a wide variety of painful stimuli **(combination of the above stimuli).**

- **Adaptation of pain receptors:**
  - They are **slowly adapting** or even non adapting receptors.
  - **Importance:** directs the subject to get rid of the injurious agent.
- **Threshold of pain receptors:**
  - They are of **high threshold**: the pain receptors need sufficient degree of tissue damage to be stimulated.
  - The lowest intensity of injurious agent needed to stimulate the pain receptors and produces pain sensation is known as **Pain Threshold.**

- **Distribution:**

- **More in:** *Skin. *Periosteum. * Arteries. * Dura.
- **Less in:** *Deep tissues. *Viscera.
- **Absent in:** Parenchymatous organs **e.g.** liver, brain & lung alveoli.
- **Thus, diseases affecting the parenchyma may not cause pain early. However, later on they cause severe pain when they invade the serous covering e.g. peritoneum and pleura which is richly supplied by pain receptors.**

- **Mechanism of stimulation of pain receptors:**

Tissue damage

↓

Release of chemical agents called pain producing compounds which are of 2 types:

Sensitizers

↓

sensitizing the receptor membrane by lowering its threshold e.g. substance- P and PGE2.

Direct stimulators

↓

includes: K^+, serotonin, histamine, bradykinins, acids and proteolytic enzymes.

Cutaneous pain

- **Def:** **Pain sensation results from the stimulation of pain receptors in the skin**

- **Types of cutaneous pain**

	Pricking (fast) pain	Burning (slow) pain
Nature (Quality)	Pricking	Burning
Localization	Well localized	Diffuse
Onset	Felt **immediately after** injury (0.1sec)	felt **shortly after** injury (1 sec. or more)
Duration	short (less than 1 sec.) " Fast "	Long (several minutes). "slow"

	Pricking (fast) pain	Burning (slow) pain
Pathway	Transmitted by **rapidly** conducting **A delta** " fibers (**6 - 30** meter/sec). **(Neospinothalamic tract**).	Transmitted by the **slowly** conducting **C fibers** (**0.5-2** meter/sec). **(Paleospinothalamic tract**).
Center	Cerebral cortex	Thalamus (so still can be felt after the damage of the cerebral cortex.)
Initiate	Somatic protective reflexes	Autonomic and somatic reflexes
Lost by	**hypoxia or pressure**	**local anesthesia**

➢ Reactions to cutaneous pain

1. Somatic reactions: skeletal muscle contraction **e.g.** flexion withdrawal reflex

2. Autonomic reactions:

i) **Mild to moderate cutaneous pain** is associated with **pressor (sympathetic)** effects as ↑ heart rate, ↑ arterial blood pressure.

ii) **However, severe cutaneous pain** is associated with **depressor (parasympathetic)** effects as ↓ heart rate, ↓ arterial blood pressure, nausea and vomiting.

3. Emotional and psychic reactions: **e.g** anxiety & depression.

4. Hyperalgesia

Cutaneous hyperalgesia

- **Def:** increased pain sensibility in the skin area surrounding the 1ry site of injury.
- **Types:**

	1ry hyperalgesia (Allodynia)	2ry hyperalgesia
Def	**Increased** pain sensitivity in the **red inflamed area (flare)** surrounding the site of injury	**Increased** pain **sensitivity** in the **normal healthy** skin area surrounding the red (flare) area
Character	**non painful** stimuli e.g. touch **produce pain**	**mild painful** stimuli produce **severe pain**

	1ry hyperalgesia (Allodynia)	2ry hyperalgesia
Onset & duration	it develops **30 to 60 minutes** following skin injury **&** lasts for several hours or days	Its duration is **shorter** than the 1ry hyperalgesia
Pain Threshold	Lowered	Not lowered

Deep pain

- **Def:**

A type of pain produced by stimulation of pain receptors in the deep tissues **e.g.** muscles, tendons, joints & ligaments.

- **Causes:**

1. ***Injury*** of deep tissues.
2. ***Inflammation*** e.g arthritis and myositis.
3. ***Ischemia*** (ischemic pain).

- **Characters:**

1- Nature (Quality): **Dull aching or throbbing.**

2- Localization: **Diffuse and poorly localized.**

3- Pathway: Transmitted via the **C-non myelinated nerve fibers.**

4- Associated with:

a) Depressor (parasymp.) effects: as ↓HR & ↓ABP

b) Reflex spasm of the nearby muscles ➔ reduce movements of injured part ➔ minimize tissue damage.

Visceral pain

- **Def:** Pain sensation results from stimulation of pain receptors in viscera
- **Causes of visceral pain:**
  1. ***Ischemia:*** **:➔** accumulation of metabolites as lactic acid ➔ stimulation of pain receptors. **Ischemia results from:**

a) Thrombosis as in superior mesenteric artery or coronary artery.

b) Spasm of the smooth muscles in the wall of the viscus (**Colic**)➔ compression of the blood vessels.

c) Overdistension of hollow organs **e.g.:** Stomach, uterus & urinary bladder➔ collapse of the blood vessels that pass in its wall.

2. ***Trauma***

3. ***Inflammation:*** e.g cholecystitis, appendicitis.

4. ***Chemical irritation:*** e.g. irritation by HCl (heart burn)

- **Characters of visceral pain:**

1- Nature (Quality): colicky, burning, or dull aching.

2- Localization: Diffuse& poorly localized.

N.B: when the disease reaches the **parietal layer** of the serous membranes, pain become **sharply localized** & felt in its origin.

3- Transmission:

The visceral pain pathway reaches the C.N.S by **2 separate routes:**

	Parietal pathway	Visceral pathway
Arise from	parietal layers of serous membranes & some retroperitoneal organs as kidney.	viscera itself & visceral layers of serous membranes.
Transmitted by	A-δ & C- nerve fibers	C- nerve fibers
Join	somatic nerves	autonomic nerves

4- Associated with:

a) **Somatic reactions** in the form of contraction of the overlying muscles (**Guarding response**) to protect the underlying inflamed viscus.

b) **Depressor (parasympathetic) effects** as ↓ in H.R, ↓ in A.B.P., nausea & vomiting.

5- It is usually **referred**.

Referred pain

- **Def:** Viscera pain is **poorly localized** and **is not felt in the affected viscera**, but in the **skin area or somatic tissue** (dermatome) supplied by the same spinal dorsal roots which innervate the diseased viscus **i.e.** ***pain arises frm a viscus & is felt in a related somatic structure***.
- **NB:** Both the viscus and somatic structure originated from the **same embryonic segment or dermatome**.

❑ Examples of referred pain:

Type of pain	Referred to:
Cardiac pain:	- Inner side of left arm & forearm or little finger. - Left shoulder. - Retrosternal region. - Base of the neck. - Epigastric pain.
Esophageal pain	-Pharynx. -Lower neck. -Midline chest region
Gastric pain	-Epigastric region
Biliary & gall bladder pain	-Epigastric region to the right. -Right shoulder, if diaphragm is irritated.

Type of pain	Referred to:
Renal & ureteric pain	- Inguinal region. - Testicle & scrotum
Appendicular pain	-Skin area around umbilicus. **- N.B.** later on localized to the **right iliac fossa** when the **peritoneal covering** is irritated.
Uterine pain	Suprapubic - perineum - lower back

Convergence projection theory

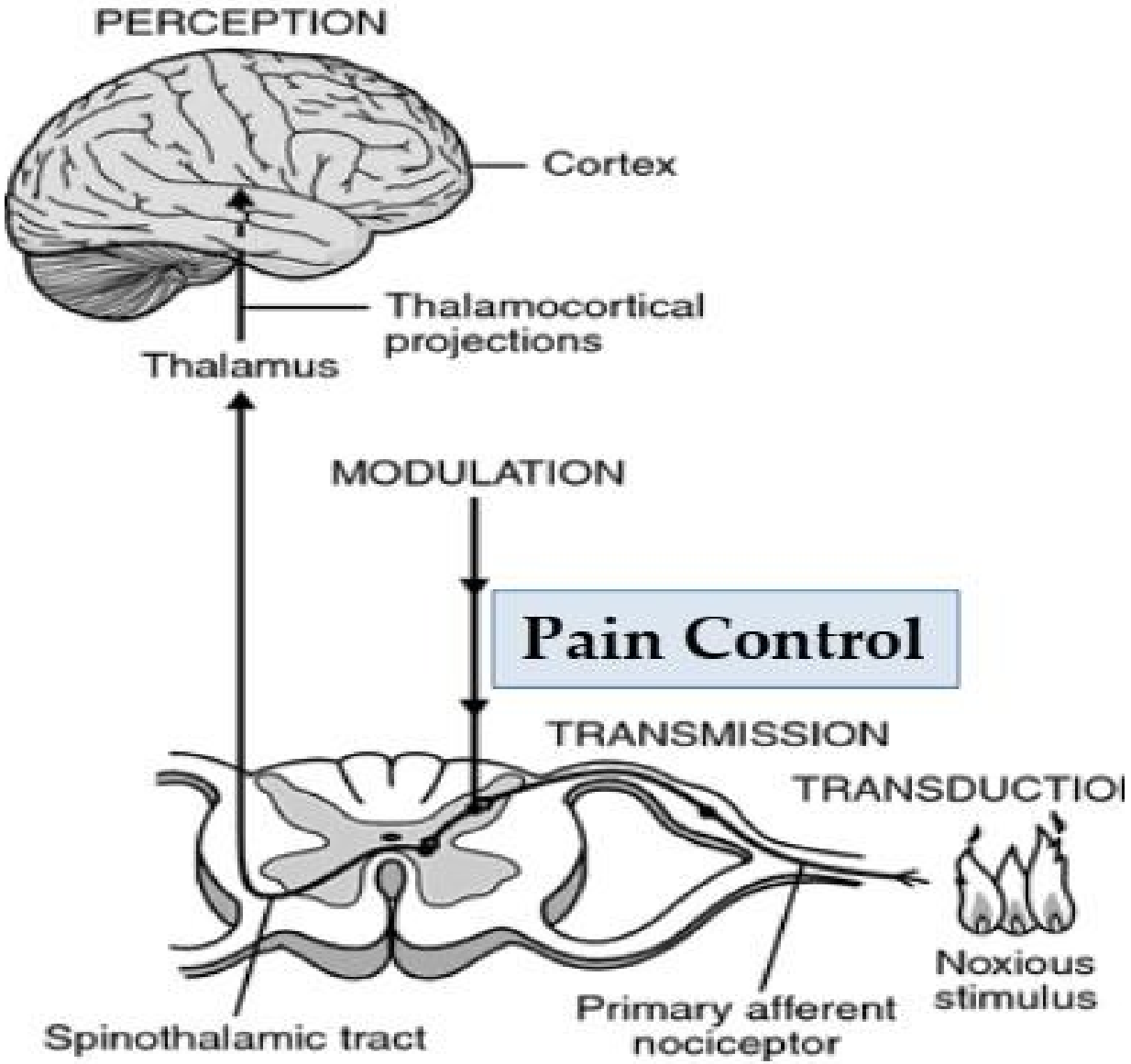
- Pain carrying fibers from the diseased viscus & from the related somatic structures converge on the **same SGR** cells "Dorsal horn cells" and ascend to the **same cortical neurons**.
- Since the cortical sensory areas **accustomed to receive pain impulses from the somatic structure**.
- So, when **the viscus** is injured or diseased the impulses from it perceived by the cortex as if coming from **the somatic structure,** so the pain sensation is projected to somatic structure.

Pain Control System

1) Definition:

- System which control pain transmission in CNS or inhibit pain transmission i.e. **endogenous analgesia system**

- The activity of this system differs from one person to another and from time to time in the same person

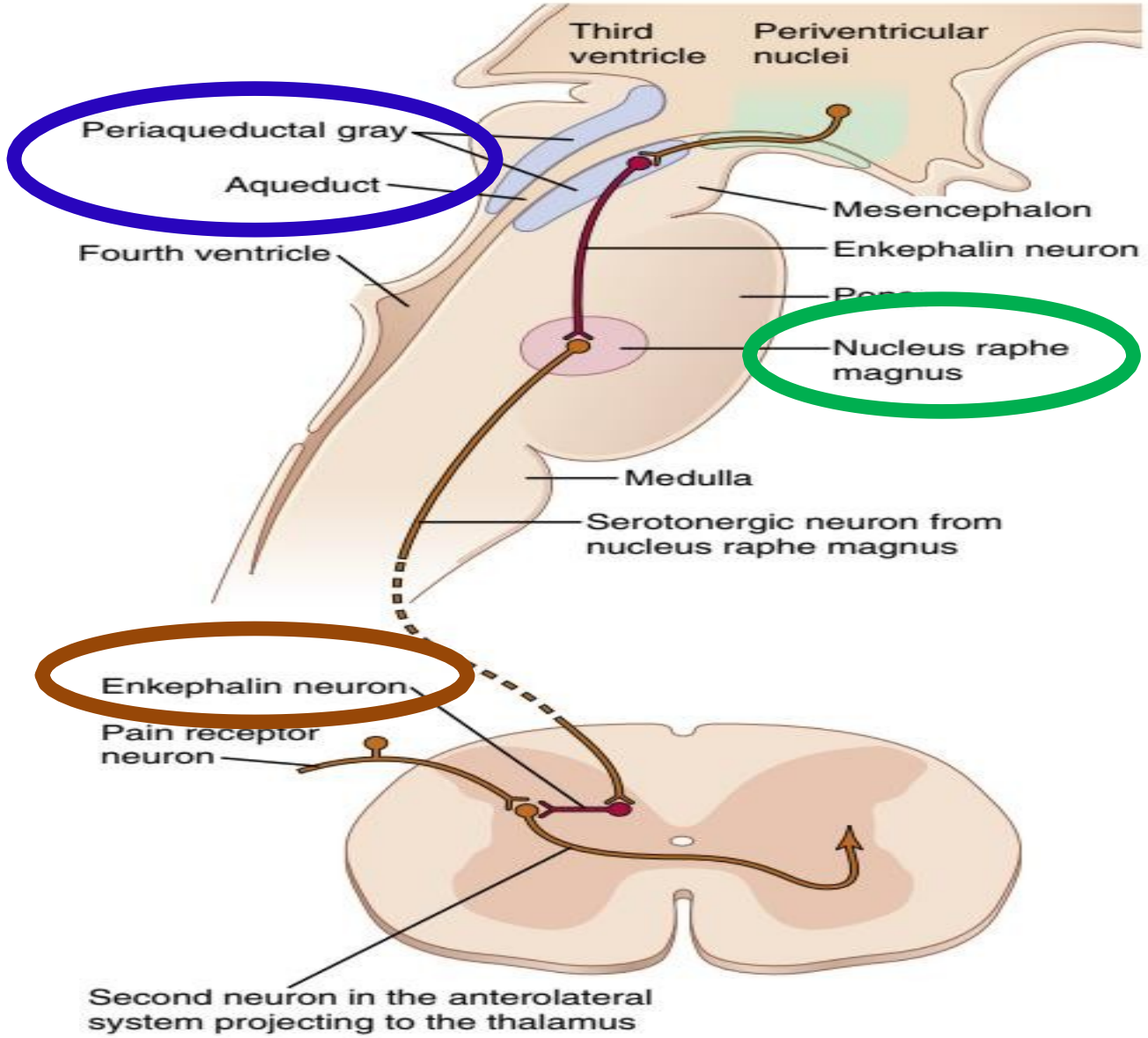


Pain Control System

2) Components of pain analgesia system:

3 major components:

1. **Peri-aquiductal gray area (PAG)** in midbrain and pons.
2. **Raphe magnus nuclei (RMN) and nucleus reticularis para giagantocellularis (NRPG)** in medulla oblongata.
3. **Pain inhibitory complex** located in the dorsal horn of the spinal cord.



Pain Control System

- **How and when this system is activated?**

This system is activated by impulses from many areas in cases of severe **stresses and strong emotions** e.g. during severe exercise, battles, fear …etc.

Areas that excite pain control system include:

1 Limbic system and hypothalamus during stress and emotions.

2 Cerebral cortex.

3. Reticular formation.

4. Ascending pain pathways via collaterals (-ve feedback).

Pain Control System

Ascending pathway

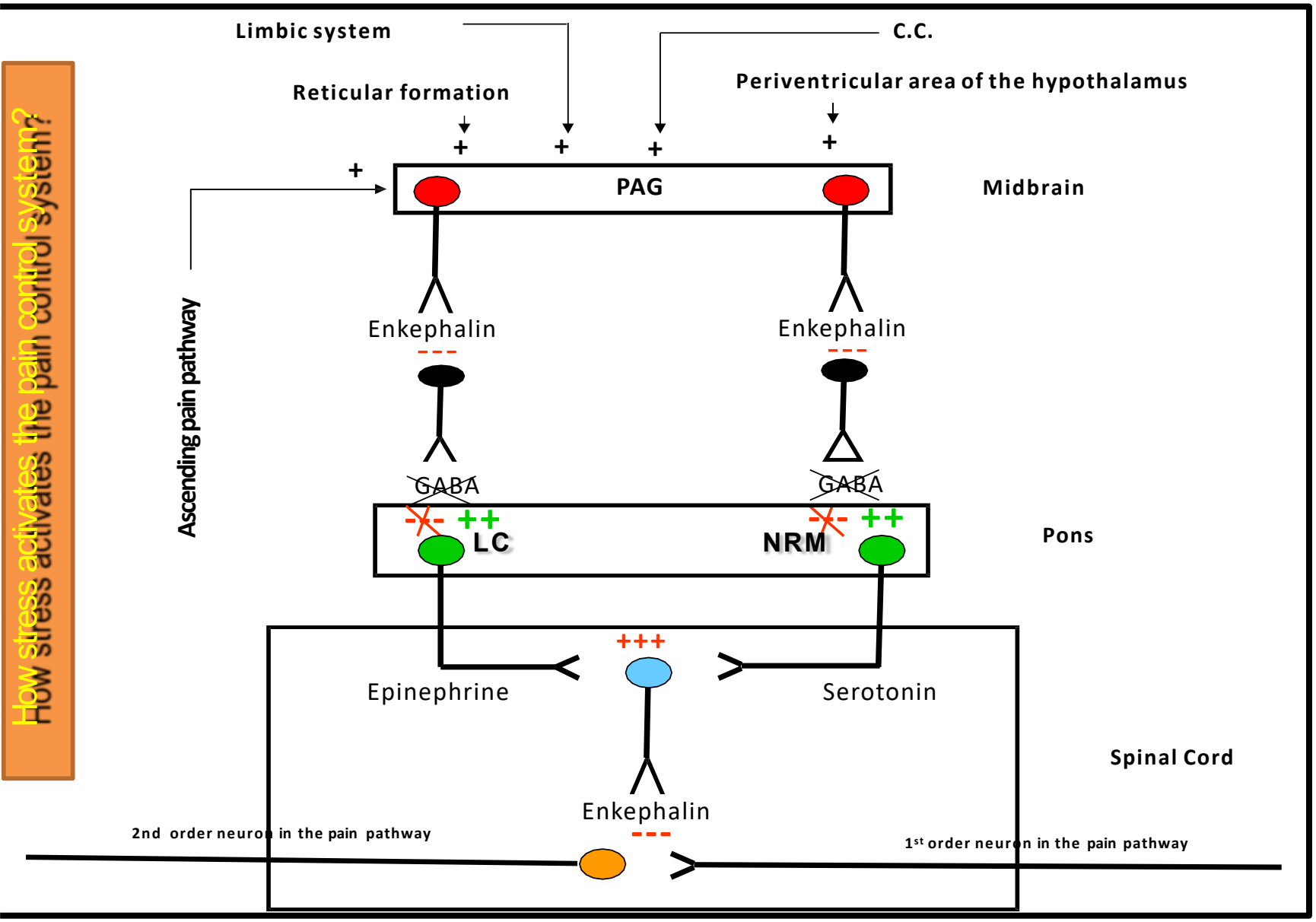
Substance P

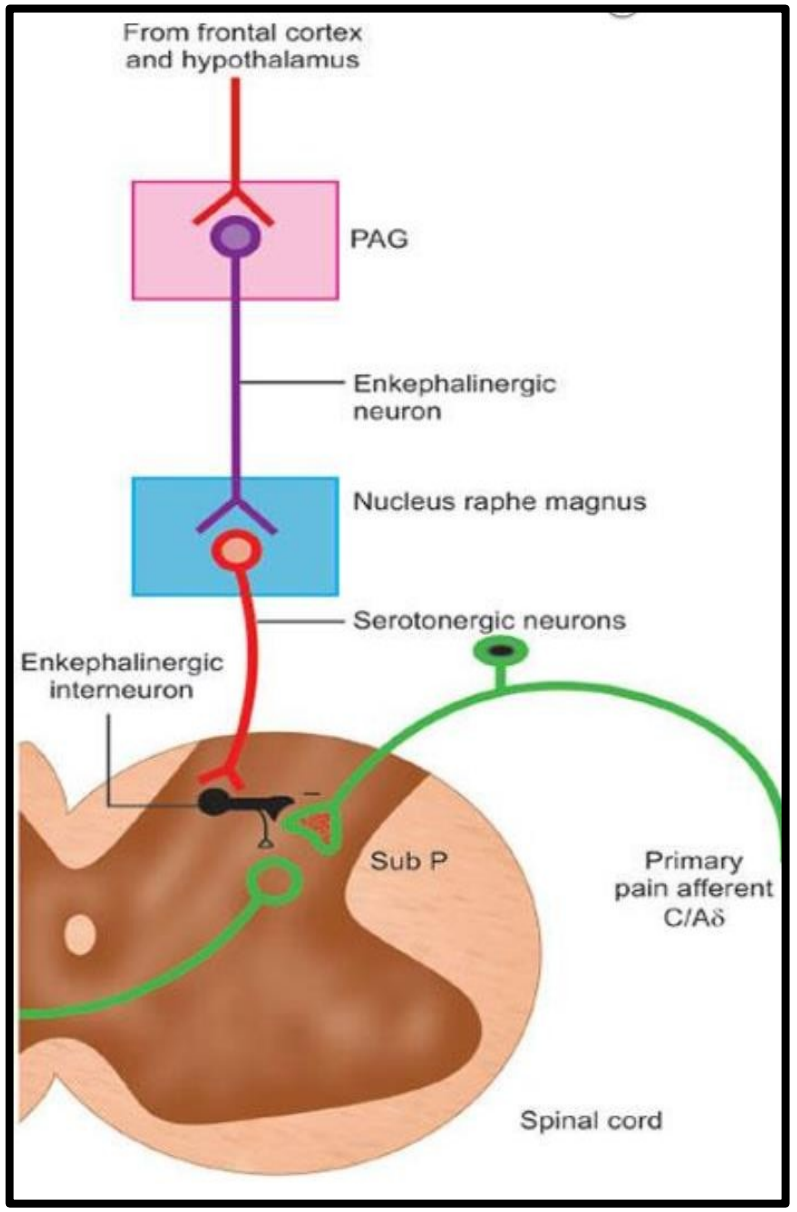
1st order neuron of pain

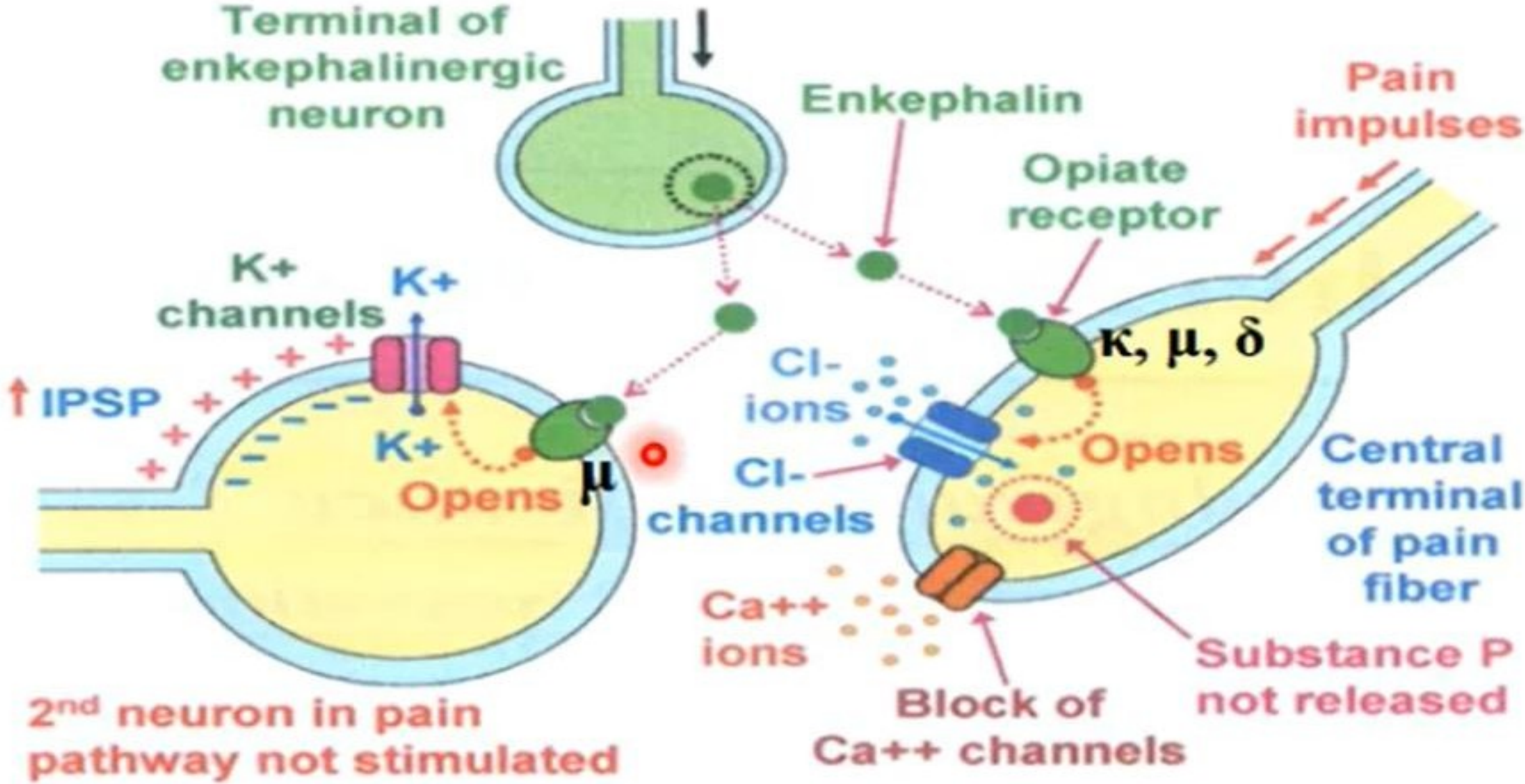
Posterior Horn of Spinal Cord (SGR)

Pain Control System

How stress activates the pain control system?






Terminal of enkephalinergic neuron
Enkephalin
Pain impulses
Opiate receptor
K+ channels
K+
IPSP
K+
Opens
μ
κ, μ, δ
Cl- ions
Cl- channels
Opens
Central terminal of pain fiber
Ca++ ions
Substance P not released
Block of Ca++ channels
2nd neuron in pain pathway not stimulated

Hypothalamus	During stress and emotions, sends stimulatory input to PAG.
PAG	Fibers from PAG release **enkephalins** → inhibit GABA-ergic neurons (which inhibits RMN & NRPG) → activation of RMN and NRPG.
RMN & NRPG	The activated RMN (serotonergic neurons) and NRPG (noradrenergic neurons) release **serotonin & noradrenaline** at their terminals in the dorsal horn of spinal cord.
Dorsal horn (PIC)	Serotonin and noradrenaline stimulate inhibitory interneuron in the dorsal horn → release **enkephalins** (inhibitory transmitter)
Presynaptic inhibition	Enkephalins bind to opioid receptors on the terminals of afferent pain fibers. ↓ Opening of Cl- channels leading to hyperpolarization & closure of Ca2+ channels (presynaptic inhibition) ↓ inhibit release of substance-P & glutamate ↓ inhibit pain transmission & no impulses reach brain (ANALGESIA)

Neurochemistry of pain control system

(Endogenous opioids)

Def: Natural peptide substances produced inside the body & have the ability to bind opioid (morphine) receptors producing pain analgesia.

Classes:

	1. Enkephalin	2. Endorphin
Derived from	**proenkephalin**	**Pre-opio-melanocortin (POMC)**
Present in	**brain stem & spinal cord**	**Anterior pituitary & hypothalamus**
Main types	**leu-enkephalin & met enkephalin**	**β-endorphins**

- **3. Dynorphin**
  - Derived from **pre-dynorphin.**
  - Present in **brain stem**.

Opioids receptors:

- Respond to opiates (exogenous opioids e.g morphine) and endogenous opioids.

Types:

Receptor	responds to
1. Delta (δ)	*enkephalins.*
2. Mu (μ)	*endorphins.*
3. Kappa (K)	*dynorphins*
4. Sigma (σ)	*dynorphins.*

-**Morphine (exogenous opioid) binds to and stimulates** most opioid receptors & produces profound analgesia.

-**Naloxone blocks** opioid receptors and act as **morphine antagonist**.

Gate theory of pain control

States that, the sites of synapses along the pain pathway are considered as gates through which pain transmission can be; **Facilitated** (if the gate is open) or **Blocked** (if the gate is closed).

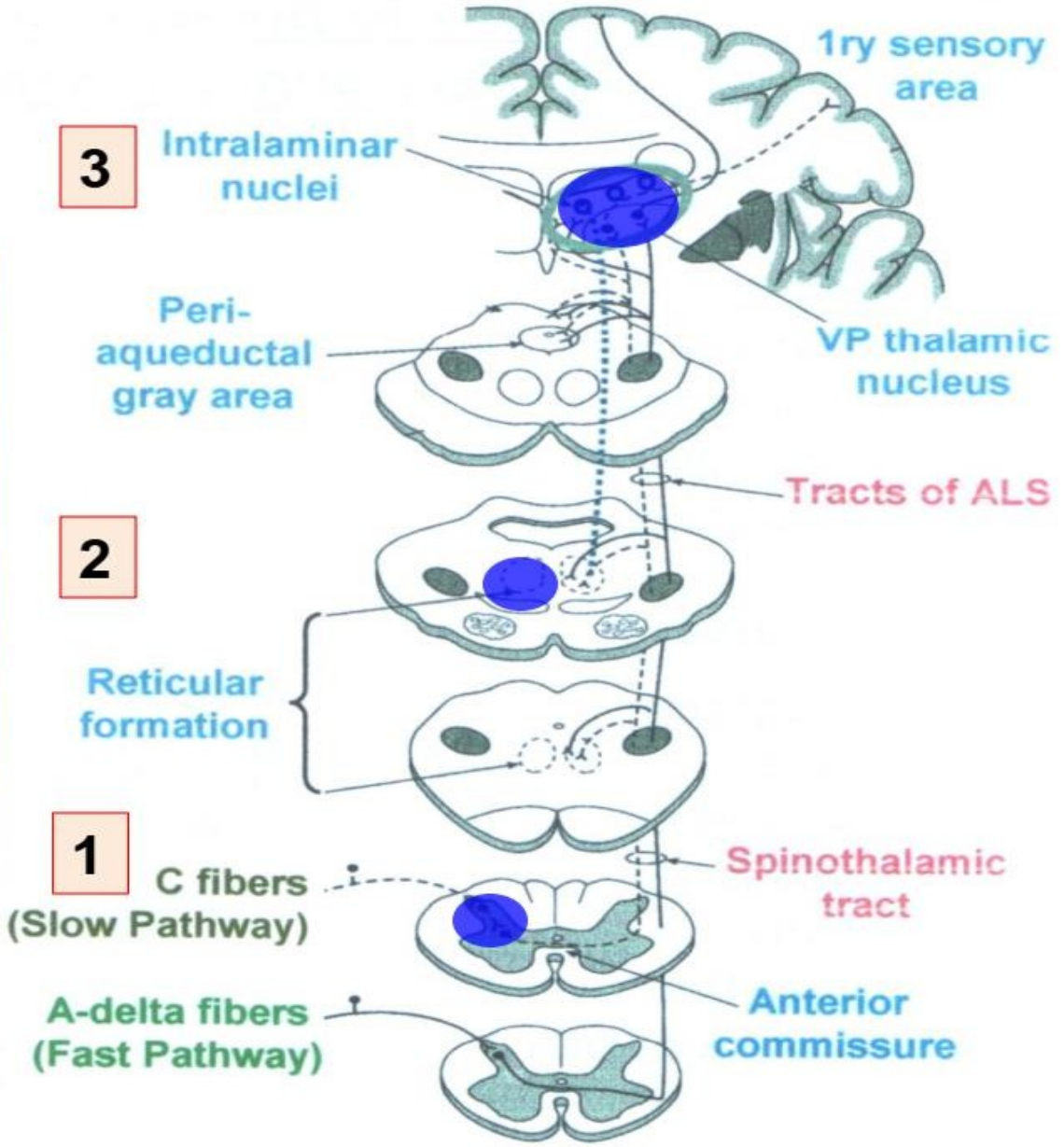
Sites:

The main pain gates are:

1 **Spinal gate**: at the **SGR**.

2 **Brain stem gate**: at the nuclei of reticular formation.

3 **Thalamic gate**: At neurons of PVNT & intalaminar thalamic nuclei.



Control of Pain at Spinal Gate (SGR)

At spinal gate pain transmission is **blocked by;**

1. **Supraspinal pathway** through the pain control system activating enkephalin-secreting interneuron

2. **Spinal inhibition through Stimulation of**

- A delta fibers by acupuncture
- A beta fibers by rubbing of the skin

3. **Cortico-fugal fibers** (as during thinking)

Somatic Sensory Cortex

Def:

-It is the part of the cerebral cortex concerned with the perception and interpretation of the sensory information.

It is divided into 3 areas:

A) Primary sensory cortex , SI (Broadman areas 3,1,2):

Site: postcentral gyrus in Broadman areas 3,1,2

B) Secondary somatic sensory cortex, SII (Broadman area 40):

Site: behind and lateral to face representation area in SI.

C) Somatic sensory association cortex (Broadman areas 5 & 7):

Site: behind the upper most part of SI.

Primary somatic sensory area (SI area)	Secondary somatic sensory area (S II area)	Somatic sensory association area
Brodmann's classification: Areas 3,1, and 2	Area 40	Areas 5 and 7
Location: In the postcentral gyrus of the parietal lobe.	Lateral & posterior to face representation in SI area	Behind the upper most part of SI.
Receive signals from: Ventral posterior nucleus of thalamus (VPNT)	• VPNT • SI area.	• VPNT • Other thalamic nuclei • SI area. • Visual cortex and auditory cortex.

Primary somatic sensory area (SI area)	Secondary somatic sensory area (S II area)	Somatic sensory association area
Body representation **1 Contralateral (crossed):** receive sensation from opposite side of body. **2 Inverted:** face is represented downward & the leg upward. **3 The area of representation depends on the number of receptors in the organ (not its size):** so, peripheral parts of the body (as fingers) have wider area of representation than thighs.	• **Bilateral representation**. (in a horizontal manner) ✓ **Head** ➔ anteriorly. ✓ **Leg** ➔ posterioly. ✓ **Arm** ➔ in between	• **Contralateral** • **Inverted** • **peripheral parts are widely represented**.

Primary somatic sensory area (SI area)	Secondary somatic sensory area (S II area)	Somatic sensory association area
Functions: **1 Perception of somatic sensation** as touch, pressure, vibration, stereognosis & kinesthetic sensations. **2 Identify** the **shape & form** of objects **(stereognosis)** **3 Localize the site of sensation.** **4 Discriminate** different **intensities**.	Potentiate functions of SI	**1. Interpretation** of somatic sensory information to find their **meaning (stereognosis)**. 2. Provide **brain motor centers** by **pre-analyzed proprioceptive** information for control & coordination of movements.

Primary somatic sensory area (SI area)	Secondary somatic sensory area (S II area)	Somatic sensory association area
Effect of lesion: 1. **Inability to localize** site of different stimuli. 2. **Inability to discriminate different intensities** of sensory stimuli. 3. **Astereognosis** i.e. inability to recognize the shapes or forms or texture of materials.	**Defect in learning based on tactile discrimination.**	1. **Astereognosis:** The patient cannot interpret sensory information. 2. **Parietal lobe neglect (amorphosynthesis):** - The sensory information from opposite side of body are ignored and neglected - The brain forgets other ½ of body & forgets to use it during motor activity.

Synaptic transmission

Synapses

- **Def:** areas of contact between neurons
- **Types:**

1- Electrical synapses

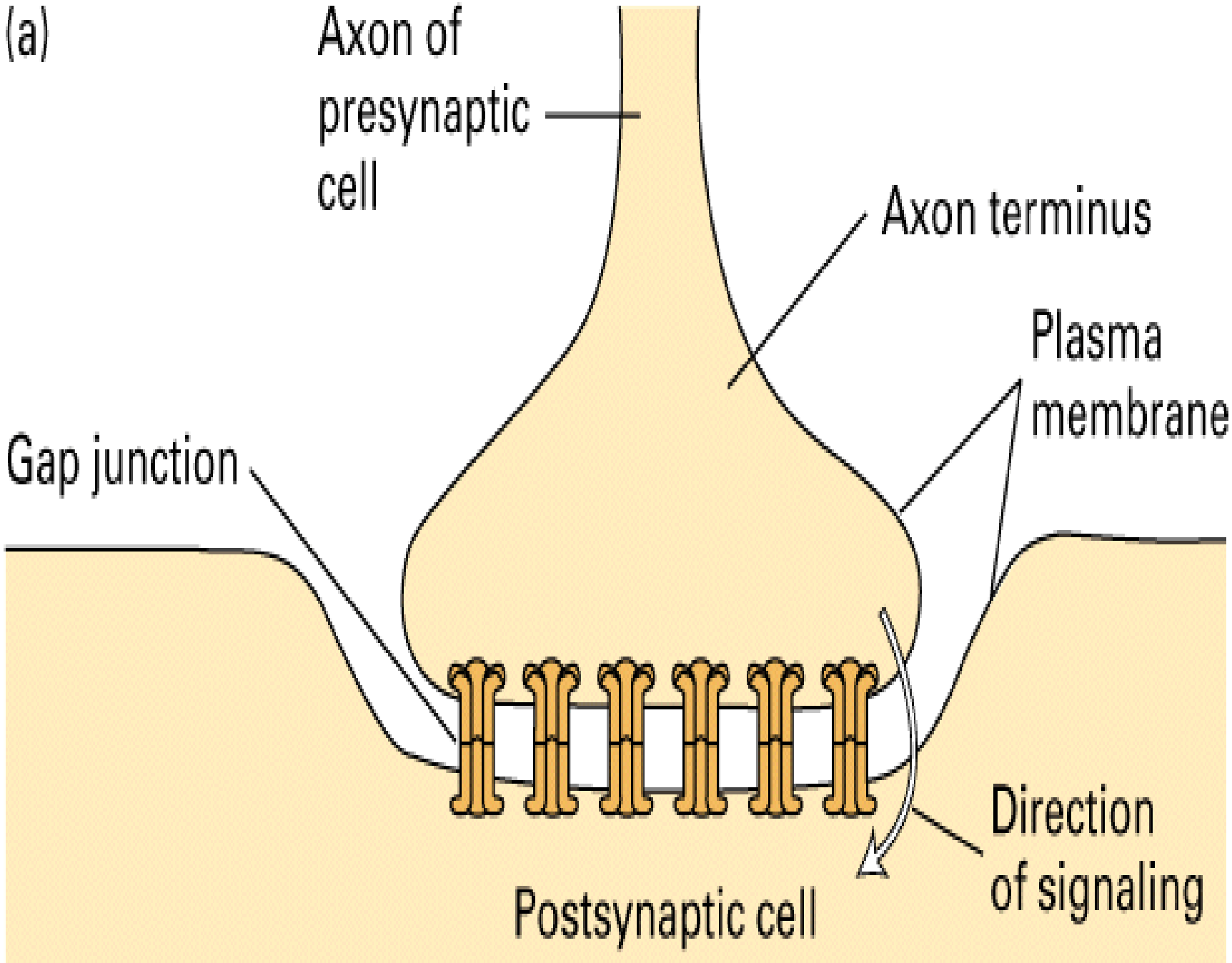
2- Chemical synapses

1-Electrical synapses

- **Site:**
  - They are extremely **rare**.
  - Present in **hippocampus** and **retina.**
- **Structure:**
  - They are in the form of ***Gap junctions*** between the membranes of presynaptic and postsynaptic neurons.

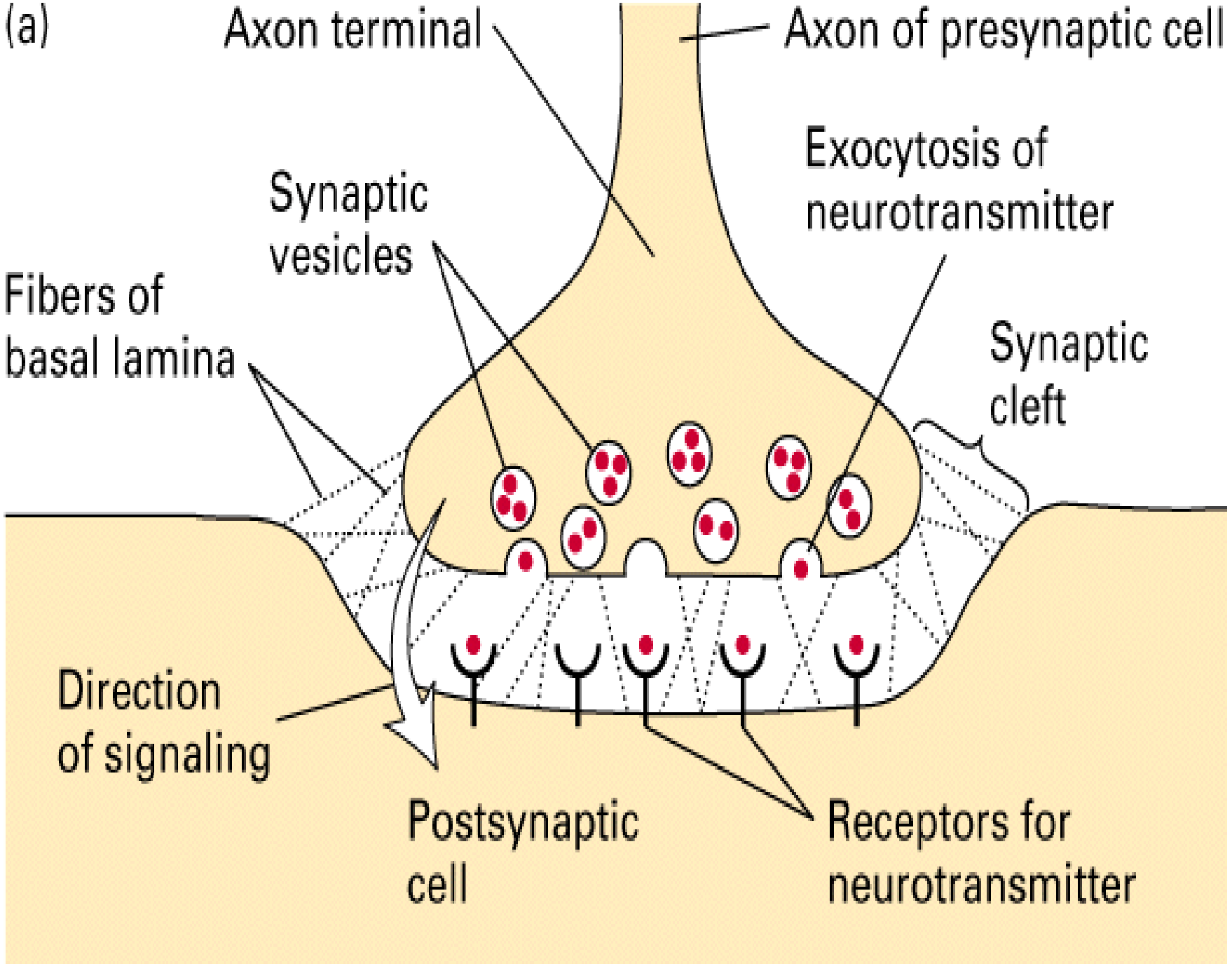
- These junctions are composed of proteins called ***"connexons"*** which are **highly permeable to ions**, ➔ so allow **ease transmission** of potential changes from one neuron to next.

- **Fatigue:** They **resist** fatigue.
- **Direction:** Conduction occurs in **both** directions.
- **Velocity: Faster**


(a)
Axon of presynaptic cell
Axon terminus
Plasma membrane
Gap junction
Direction of signaling
Postsynaptic cell

2-Chemical synapses

- **Site:** They represent **almost all synapses** in C.N.S.
- **Structure:** These synapses consist of 2 neurons, one **releasing** the chemical transmitter called **(presynaptic neuron)** and one **receiving** the signal called **(postsynaptic neuron).**


(a)
Axon terminal
Axon of presynaptic cell
Exocytosis of neurotransmitter
Synaptic vesicles
Fibers of basal lamina
Synaptic cleft
Direction of signaling
Postsynaptic cell
Receptors for neurotransmitter

- **Fatigue:** They **show** fatigue.
- **Direction: One-way** conduction only
- **Velocity: Slower**

Physiological anatomy of chemical synapses

- **It consists of:**
  1) Presynaptic Terminal.
  2) Postsynaptic membrane.
  3) Synaptic cleft (20-30 nm).
- The presynaptic terminals are dilated forming certain swelling called **presynaptic knobs** that contain the neurotransmitter vesicles.

- **These presynaptic terminals (knobs) may synapse on:**

✓ **Dendrites** of postsynaptic neuron (**Axo-dendritic synapse**) (**most common**).

✓ **Soma** (**Axo-Somatic Synapse**).

✓ **Axon** (**Axo-Axonic Synapse**).

- **The postsynaptic neuron** contains **receptors** for the chemical transmitter.

Steps of synaptic transmission

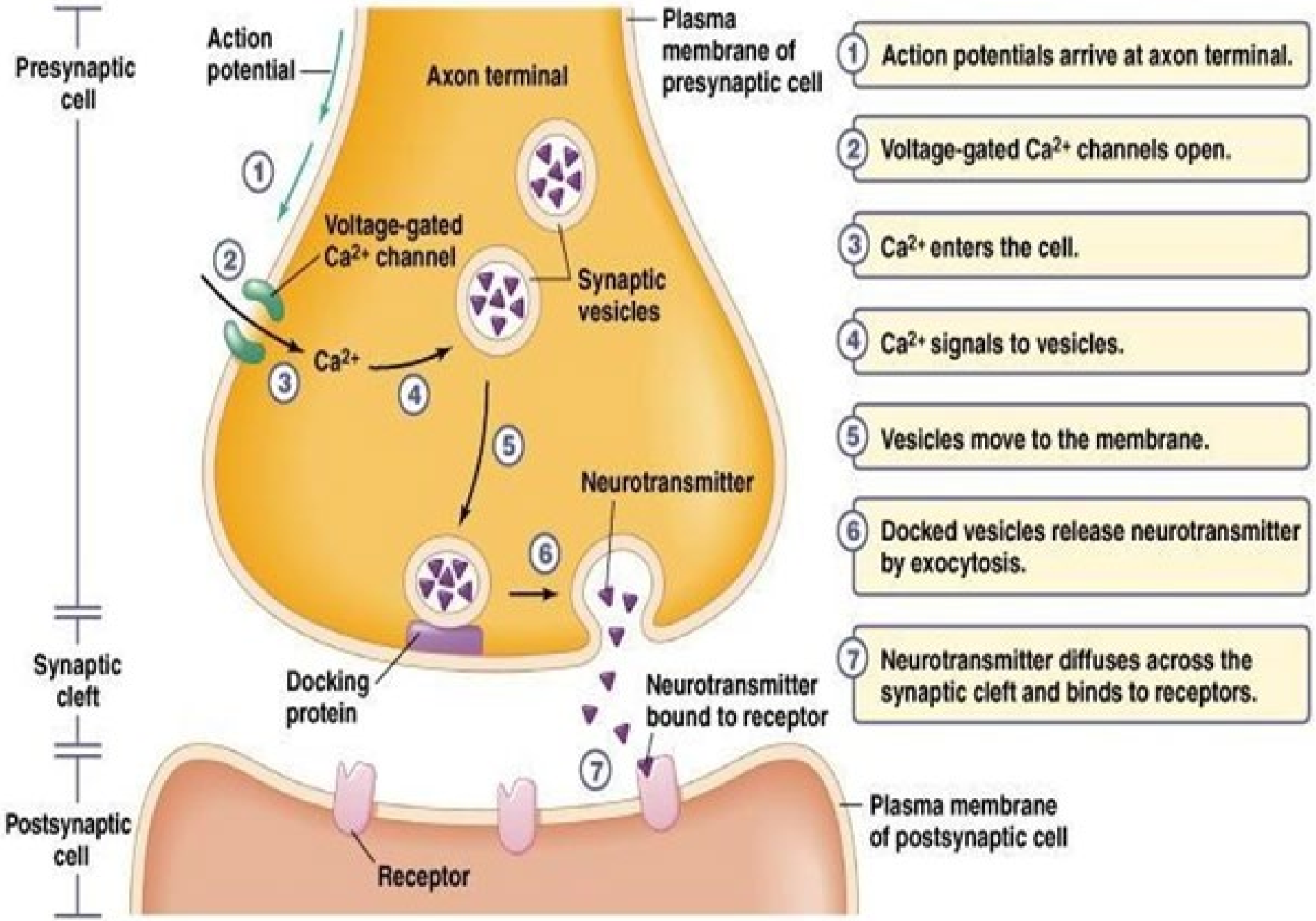
I)**Release** of neurotransmitter into synaptic cleft.

II)**Action** of the neurotransmitter on postsynaptic membrane.

III) **Termination** of synaptic transmission.

1- Release of neurotransmitter into synaptic cleft

- ***During rest***, both the synaptic knobs and the post synaptic membrane are in a ***polarized state*** **i.e.:** R.M.P is about **-70 mV**.
- When the presynaptic neuron is stimulated and an action potential reaches the synaptic knob ➔ transient opening of the ***voltage sensitive Ca^{2+} channels*** ➔ Ca^{2+} entry into the knob ➔ Ca^{2+} will bind the transmitter vesicles with the knob membrane ➔ vesicles open into the synaptic cleft and release the transmitter by ***exocytosis***.


Presynaptic cell
Synaptic cleft
Postsynaptic cell
Action potential
Axon terminal
Plasma membrane of presynaptic cell
Voltage-gated Ca2+ channel
Synaptic vesicles
Ca2+
Neurotransmitter
Docking protein
Neurotransmitter bound to receptor
Receptor
Plasma membrane of postsynaptic cell
1 Action potentials arrive at axon terminal.
2 Voltage-gated Ca2+ channels open.
3 Ca2+ enters the cell.
4 Ca2+ signals to vesicles.
5 Vesicles move to the membrane.
6 Docked vesicles release neurotransmitter by exocytosis.
7 Neurotransmitter diffuses across the synaptic cleft and binds to receptors.

2- Action of neurotransmitter on postsynaptic membrane

- After a chemical transmitter is released into the cleft, it produces its effects through binding with **specific receptors** in post-synaptic membrane.

- ***Types of postsynaptic membrane receptors:***

a) Ligand-gated ionic channels.

b) G-protein coupled receptors.

a) Ligand-gated ion channels

- Binding of these receptors to their specific neurotransmitter ➔ ↑ the channels permeability to ions.
- **Types:**

i- Cation channels:

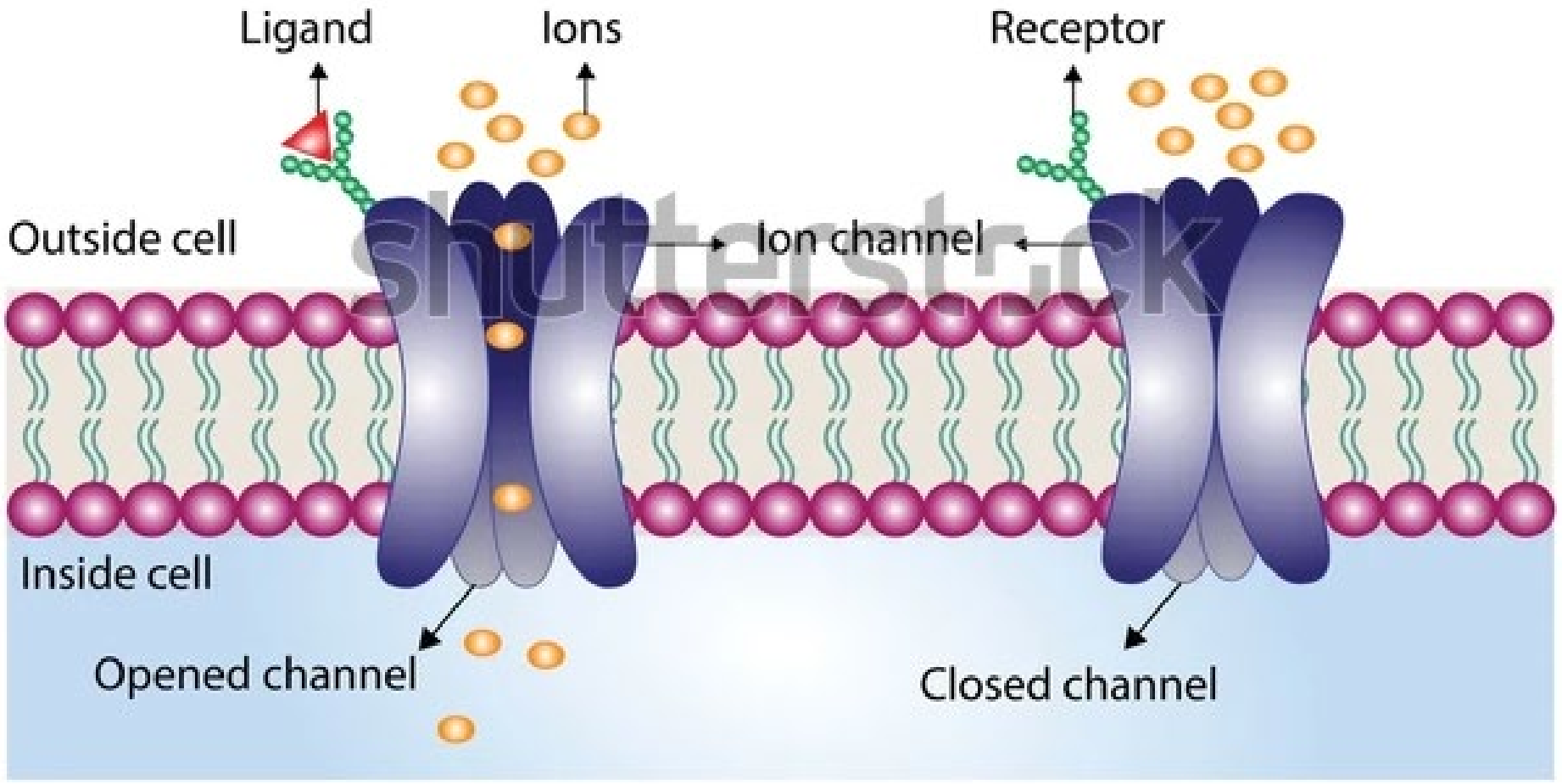
➢ When activated ➔ **Na^+ & Ca^{2+} influx ➔ depolarization** of postsynaptic membrane.

➢ The transmitter which produces this effect is called **excitatory transmitter**.

ii-Anion channels:

- When activated ➔ **Cl^- influx ➔ hyper-polarization** of postsynaptic membrane.
- The transmitter which produces this effect is called **inhibitory transmitter**.

Ligand-gated ion channel receptor



b) G-protein coupled receptors

- Binding of these receptors to their specific neurotransmitter → activation of ***G protein*** molecule (consists of α, β and γ subunits) by replacement of its ***GDP with GTP*** → ***separation of α subunit*** → **perform these functions:**

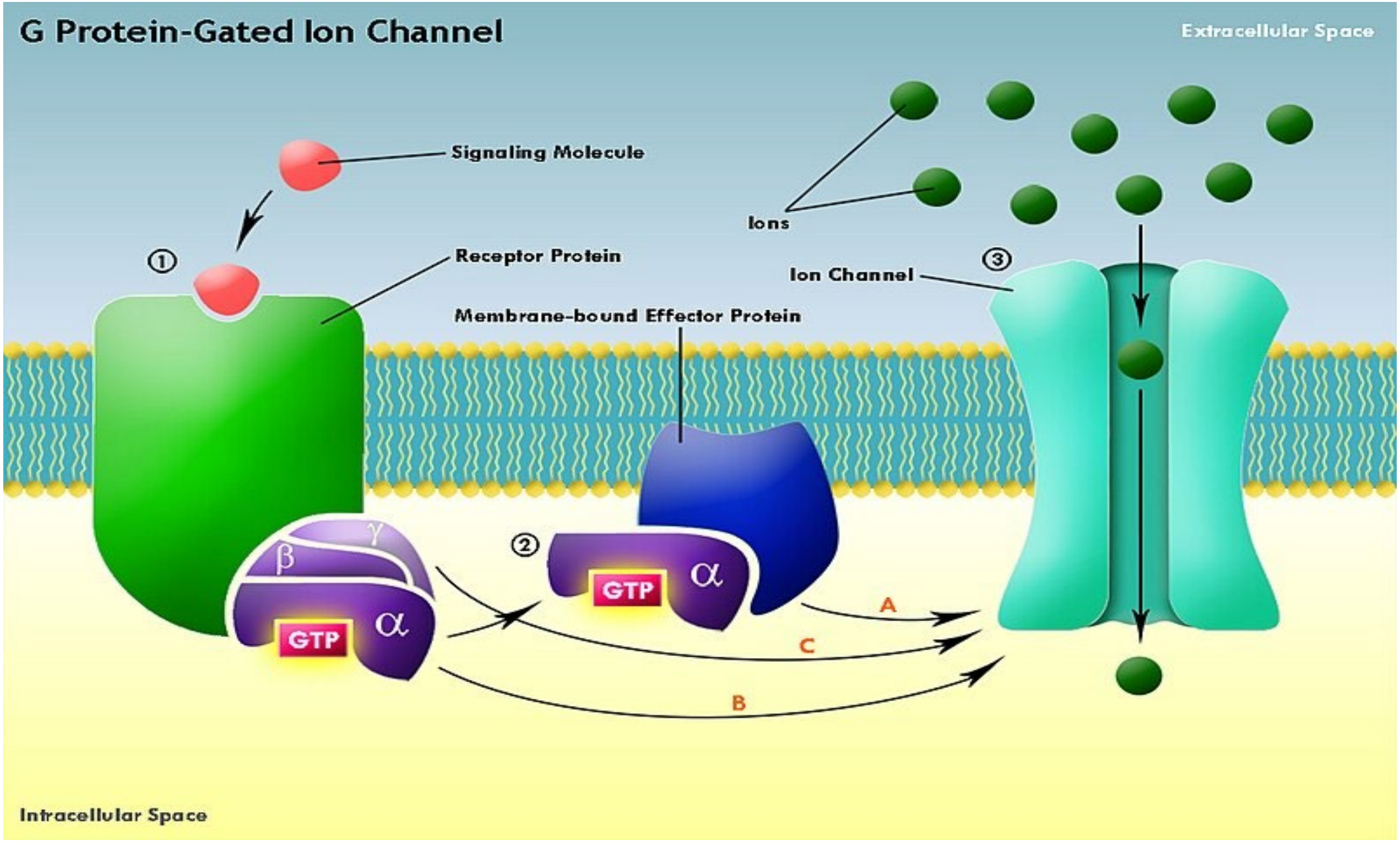
i- Opening specific ion channels as 2nd messenger-gated K^+ channels → ↑ K^+ efflux → **hyperpolarization** of postsynaptic neuron membrane.

ii-Activation of enzymes in cell membrane

➔ catalyze the formation of 2nd messengers as **cAMP** which control **metabolic pathways**.

iii-Regulation of gene transcription ➔

produce **mRNA** molecules ➔ control synthesis of certain **proteins** that act as **receptors** & **enzymes**.


G Protein-Gated Ion Channel
Extracellular Space
Signaling Molecule
Ions
①
Receptor Protein
③
Ion Channel
Membrane-bound Effector Protein
γ
β
α
GTP
②
GTP
α
A
C
B
Intracellular Space

3- Termination of synaptic transmission

- It occurs when **the transmitter is removed** from the synaptic cleft **by:**

i) Active reuptake of the transmitter into the pre-synaptic terminal.

ii) Enzymatic degeneration.

iii) Diffusion to interstitial fluid.

Nature of postsynaptic potentials (PSP)

- The **postsynaptic potentials** are of **2 types:**

1) Excitatory Post-Synaptic Potential (EPSP).

2) Inhibitory Post-Synaptic Potential (IPSP).

Excitatory postsynaptic potentials (EPSP)

- **On stimulation:** presynaptic terminals release ***excitatory neurotransmitter*** which open ***ligand-gated cation channels*** ➔ ↑ Na^+ influx more ➔ ***partial depolarization*** called ***EPSP.***
- **Characterized by:**

1. **↑ excitability** of postsynaptic membrane.
2. **Localized** i.e. not spread.

3.**Short duration** i.e. 15 m.sec.

4.Its **amplitude** is very small (0.5 mv) & cannot reduce the membrane potential to the threshold level, so to produce action potential must be **summated**.

The summation is of 2 types:

a) Spatial: occurs by stimulation of **several presynaptic fibers** that converge on the post synaptic neuron at the **same time**.

b) Temporal: occurs by stimulation of a **single presynaptic neuron** repetitively within **very short duration** (less than 15 m.sec).

Inhibitory postsynaptic potentials (IPSP)

- **On stimulation:** presynaptic knob release ***inhibitory neurotransmitter*** which open ***ligand-gated anion channel*** ➔ ↑ Cl^- influx ***or specific K^+ channels*** with ↑ in K^+ efflux ➔ ***hyper-polarization*** called ***IPSP.***

- **Characterized by:**

1. ↓ **excitability** of postsynaptic membrane.
2. **Localized** i.e. not spread.
3. **Short duration** i.e. 15 m.sec.
4. Its **amplitude** is very small (0.5 mv).

General properties of chemical synaptic transmission

1) One-way conduction:

* At synapses, impulses are conducted only **in one direction** from the presynaptic to the post-synaptic neuron.

* Conduction ***never occurs in the opposite direction*** because no vesicles in the post-synaptic membrane & no receptors in the presynaptic membrane.

2) Synaptic delay:

- **Def:** It is the time that passes between **arrival** of impulse to the **synaptic knob** & appearance of **response** in the **postsynaptic neuron**.
- **It represents the time required for:**

✓ **Release** and **diffusion** of the neurotransmitter

✓ **Activation** of the post synaptic membrane receptors

✓ Altering the membrane **permeability** to ions.

- **Value:** 0.5 msec.

3) Synaptic fatigue:

- **Def:** progressive ↓ and even stoppage of synaptic transmission when a synapse is stimulated rapidly and repeatedly.
- **Cause:** depletion of the neurotransmitters in the presynaptic knobs.
- The **fatigued synapse remains inactive** until the depleted transmitter is **reformed**.

- **Significance:**

✓ Fatigue is a ***protective mechanism*** against ***excessive neuronal activity***.

✓ It could ***suppress the activity of*** reverberating circuits ***during epilepsy*** → **spontaneous ending of the epileptic fit (normal protective mechanism).**

4) Short term potentiation (post-tetanic facilitation) (post-tetanic potentiation):

- **Def:** Rapid repetitive stimulation of presynaptic neuron for a few seconds➔ ↑ excitability of post synaptic neuron.
- **Duration:** seconds or minutes.
- **Cause:** ↑ Ca^{2+} inside the synaptic knob ➔ more & more vesicles release their transmitter ➔ a greater response of post synaptic neuron (↑EPSP)

5) Long-term potentiation (LTP):

- **Def:** Brief repetitive stimulation of presynaptic neuron ➔ rapidly developed, long-term lasting enhancement of synaptic transmission
- **Duration:** several days
- **Cause:** ↑ Ca^{2+} influx in the postsynaptic neuron (where it acts as a 2^{nd} messenger) ➔ ↑EPSP.

6) Effects of hypoxia on synaptic transmission

Marked hypoxia for a short period (few seconds) ➔ **loss of excitability** of many neurons and **stoppage of synaptic transmission**.

7) Effects of pH on synaptic transmission

- **Alkalosis:** increases neuronal excitability ➔ convulsions at pH 8.
- **Acidosis:** depresses neuronal excitability ➔ coma at pH 7.

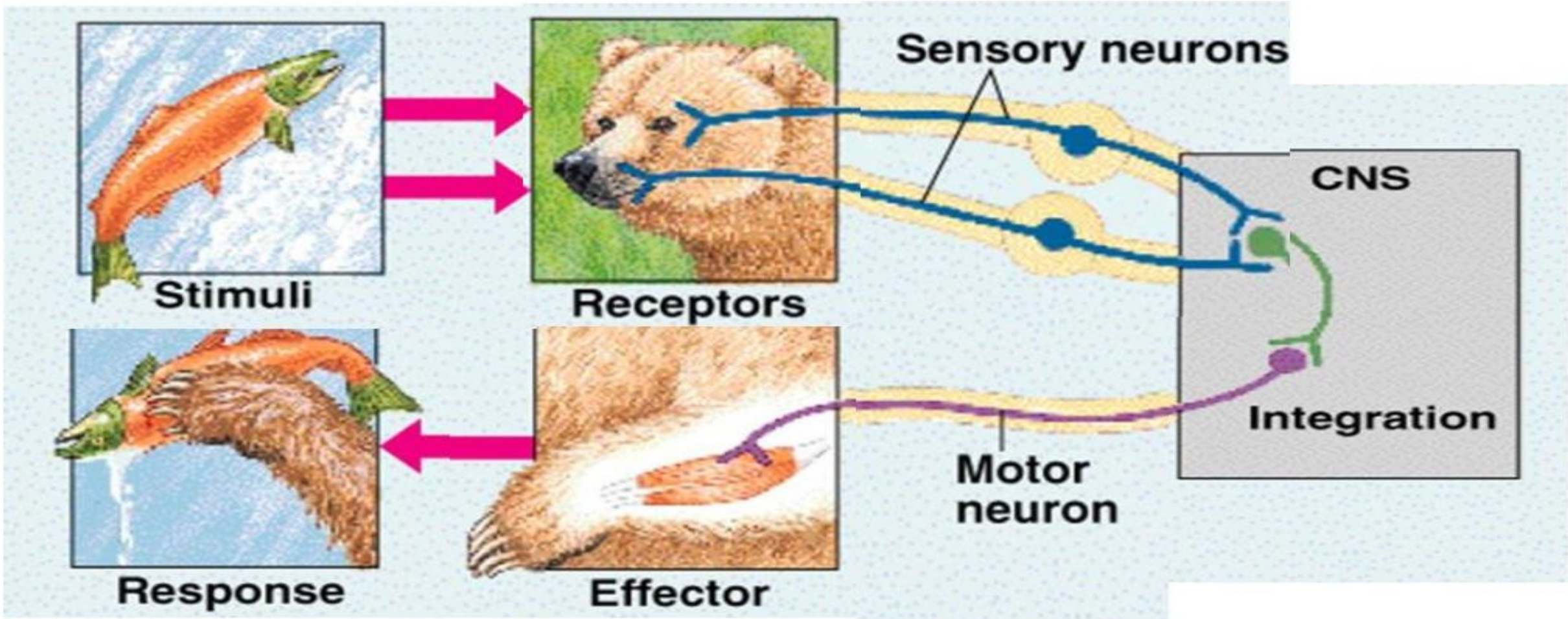
8) Effects of drugs on synaptic transmission

- **Caffeine and theophylline** (in coffee and tea): increase neuronal excitability.
- **Strychnine:** causes hyper-excitability of neurons.
- **Anesthetics and hypnotics:** decrease neuronal activity and thereby decrease synaptic transmission.

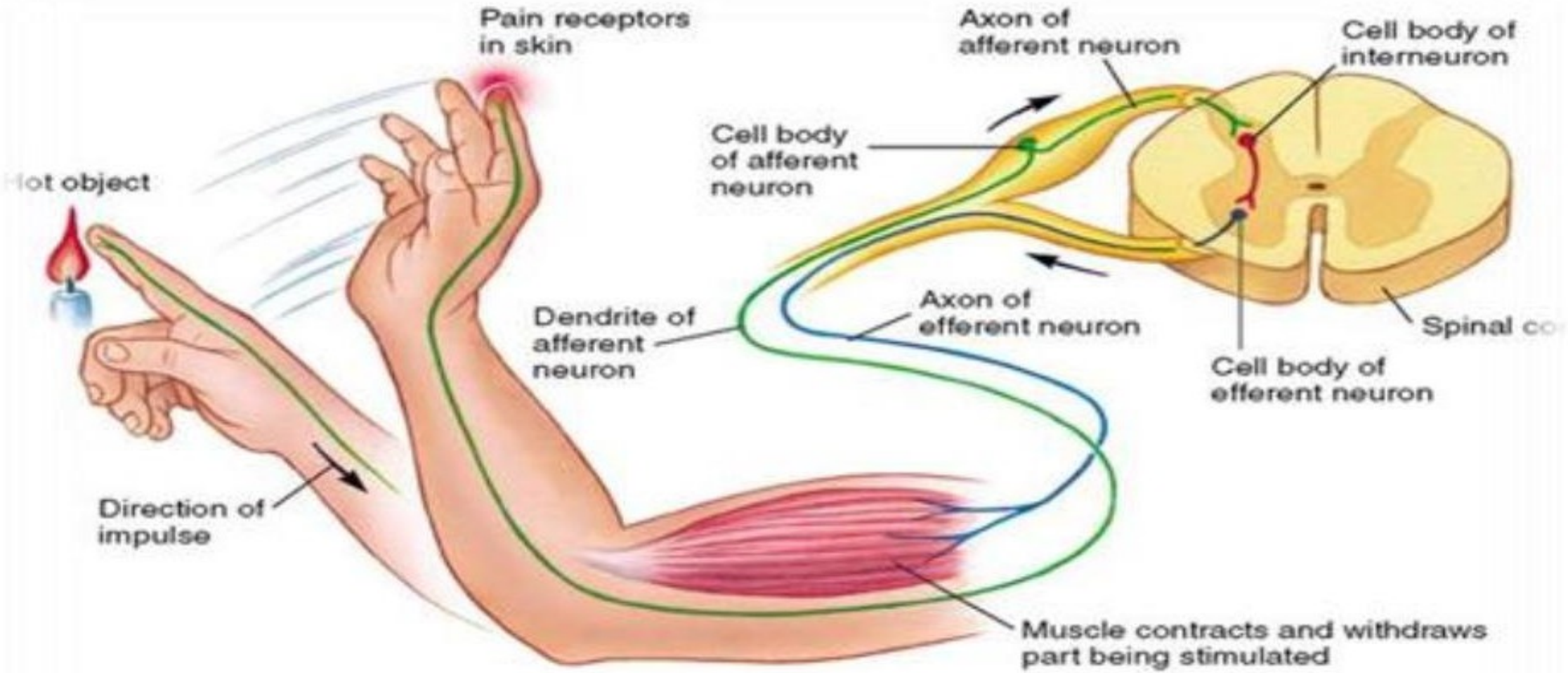
Reflex Action

Def:

- It is an **automatic** (involuntary) **specific response** of an organ caused by an **adequate sensory stimulus**



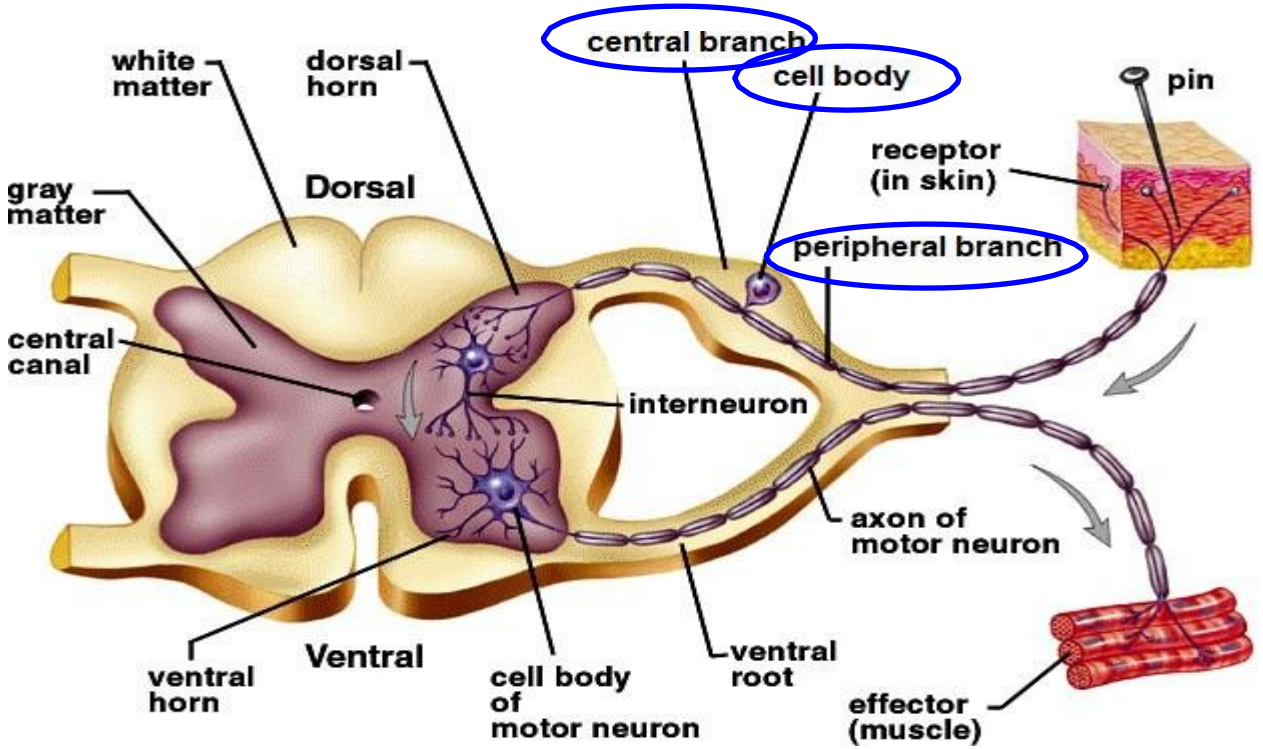
Pathway of Reflex Arc



1) Afferent Neurons

- Are **monopolar neurons** which present in the **DRG**.
- The axon of each neuron divides into **2 branches**;

1. **Peripheral branch** → terminates in sensory receptors
2. **Central branch** → enters into the spinal cord.

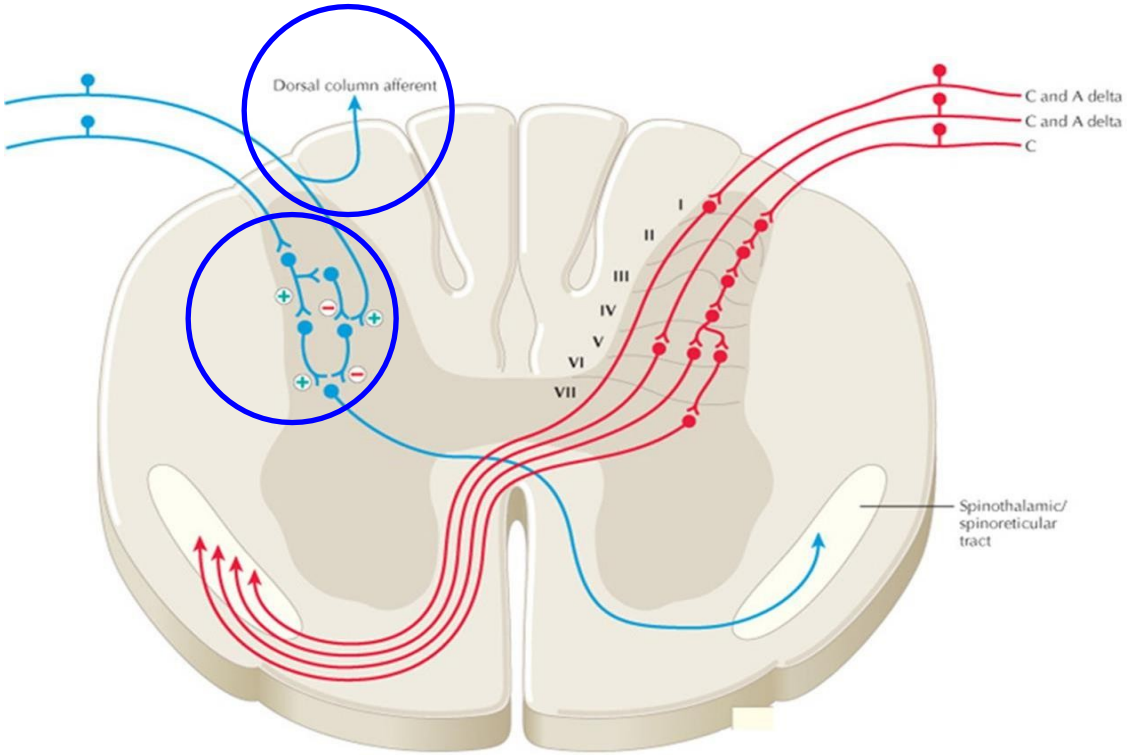


1) Afferent Neurons

- The central branch divides into **several terminals** which ends on;

a. **Gray matter of spinal cord e.g. posterior horn cell** as MSN,SGR ,etc…,**interneurons and anterior horn cells**

b. **Ascend or descend** to higher or lower segments respectively

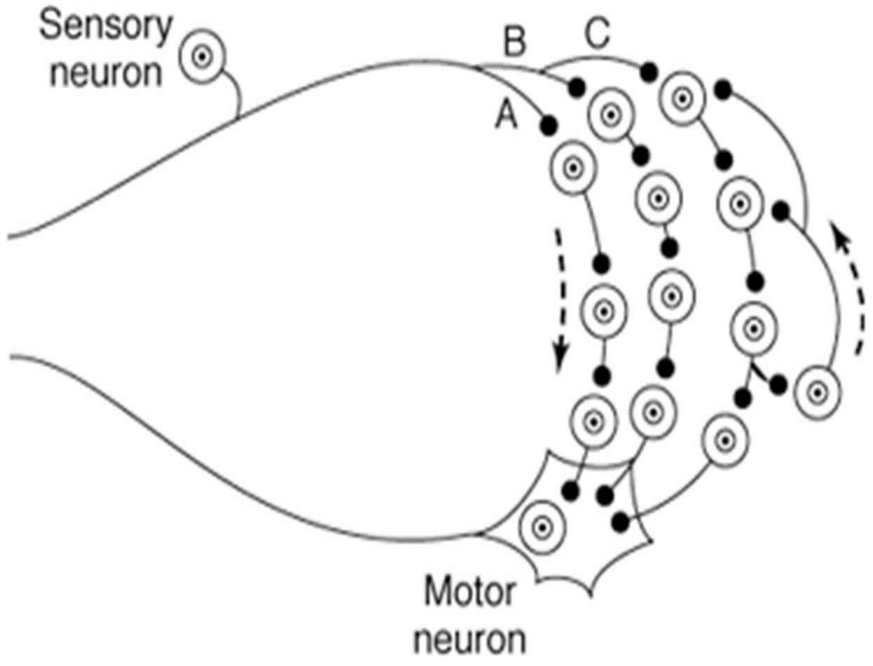


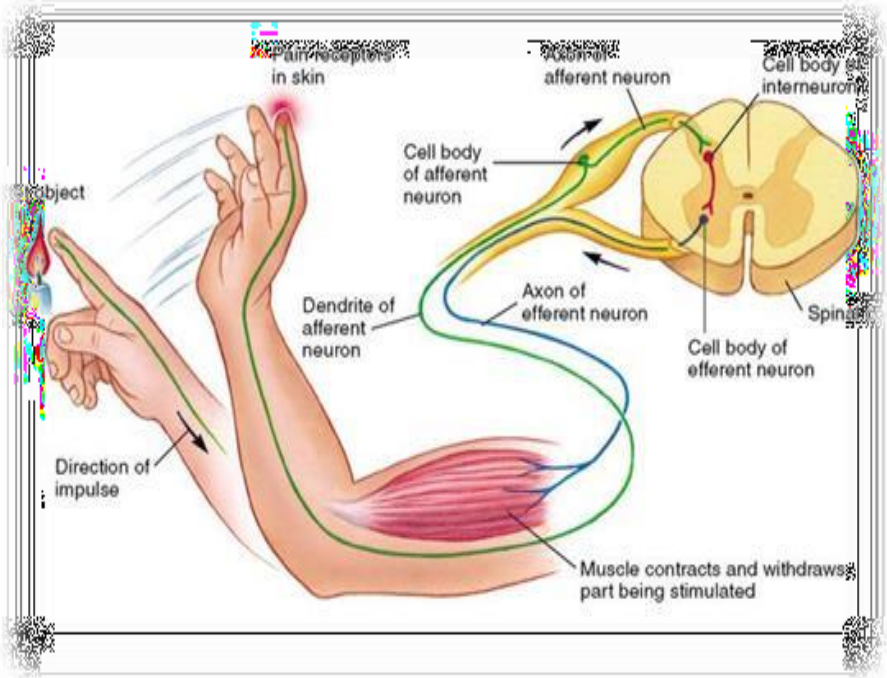
1) Afferent Neurons

Functions:

a) **Conduction** of the sensory signals to the spinal centers to excite the subsequent neurons in the reflex pathways

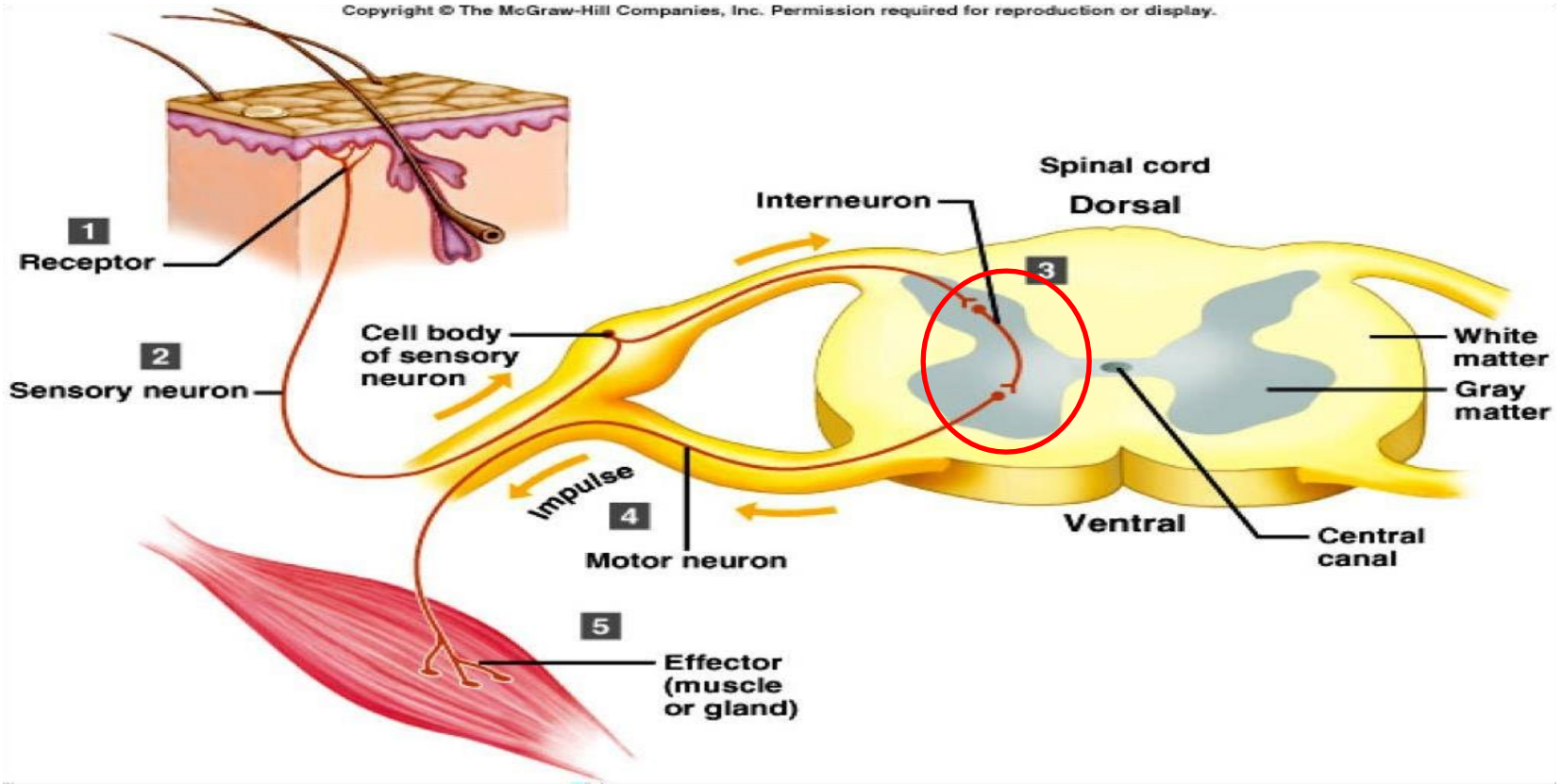
b) **Divergence** of the incoming sensory signals into wider areas in the NS.





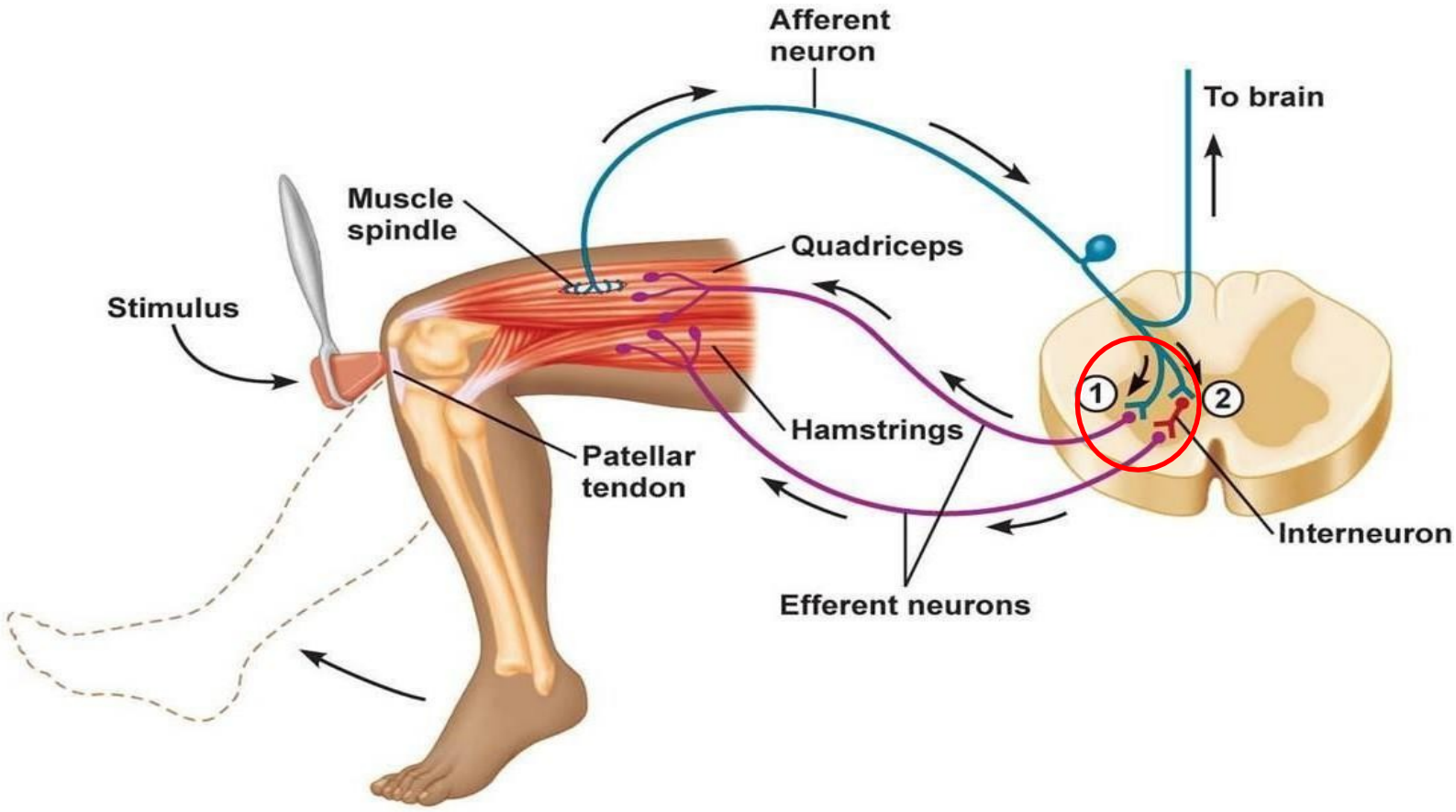
2) Interneurons

- Are **small highly excitable** neurons
- Are located in the **gray matter** between afferent neurons and the efferent neurons.



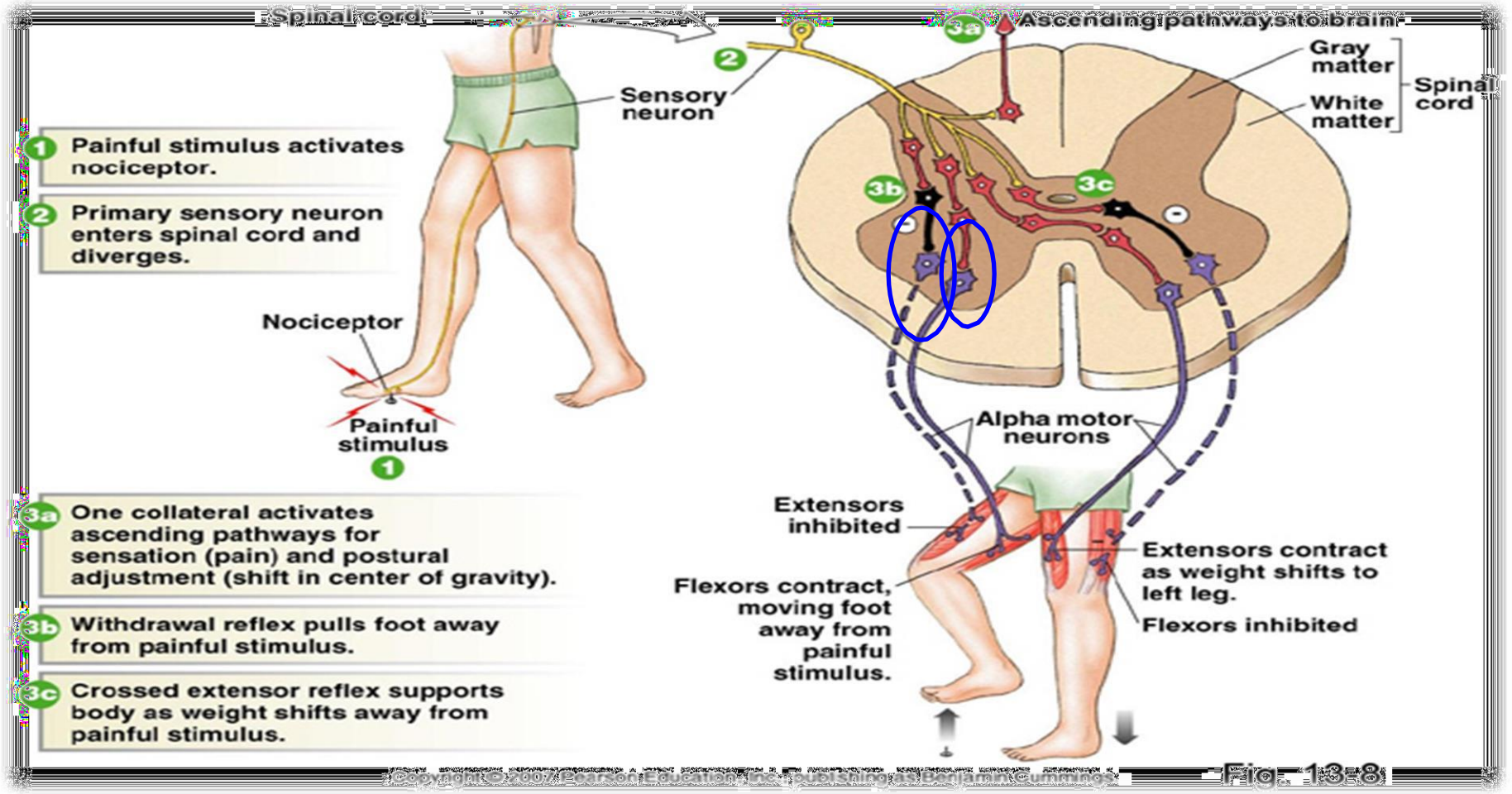
2) Interneurons

- All **reflex arcs** include interneurons **<u>except</u>** the stretch reflex i.e. **monosynaptic i.e. contains no interneurons**



2) Interneurons

- Some of them are **excitatory** and the others are **inhibitory**.

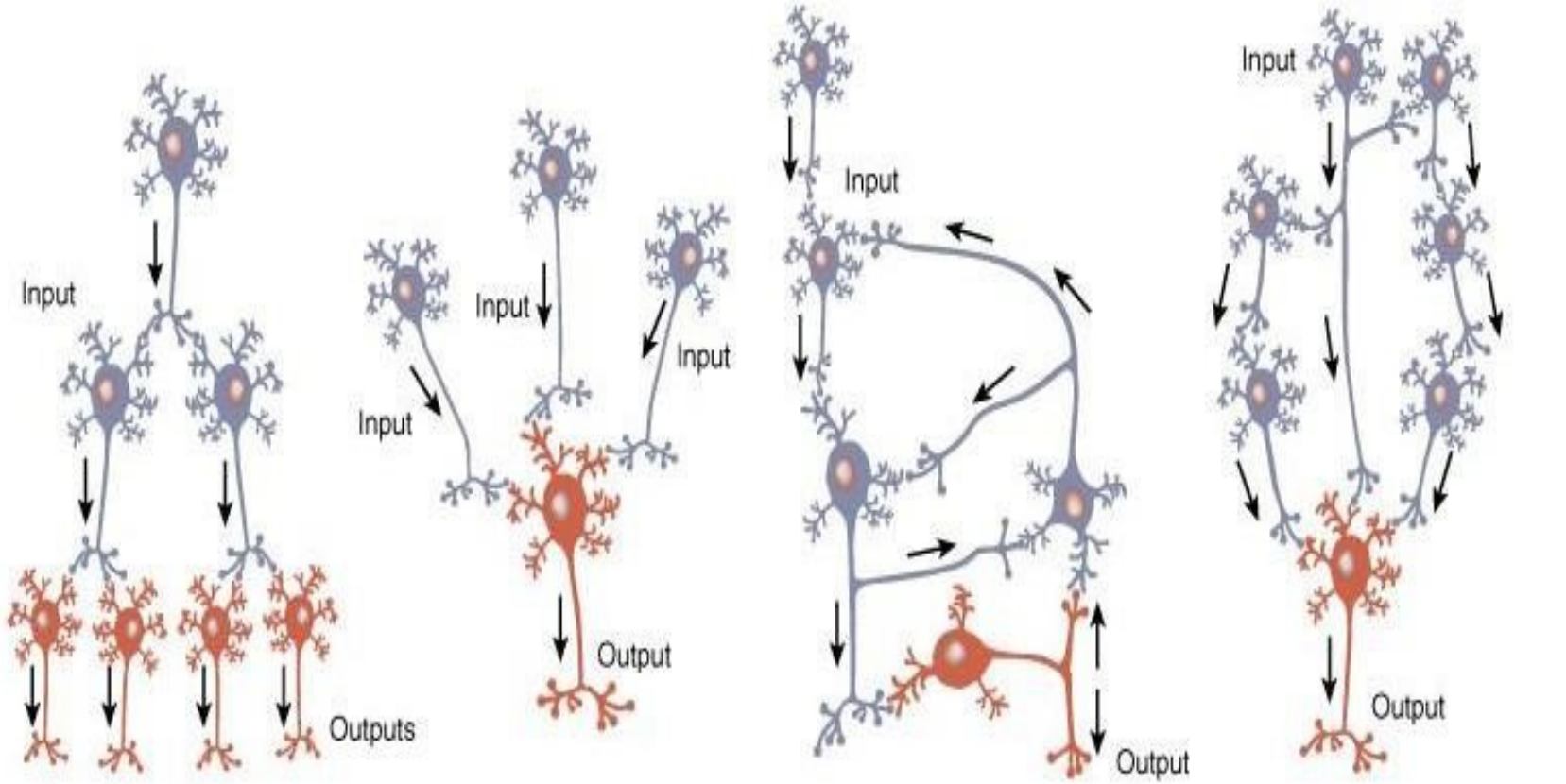


2) Functions of interneurons

- Interneurons form **different types of circuits** that perform the following functions;

1. Divergence circuits
2. Convergence circuits
3. After-discharge circuits
4. Inhibitory circuits

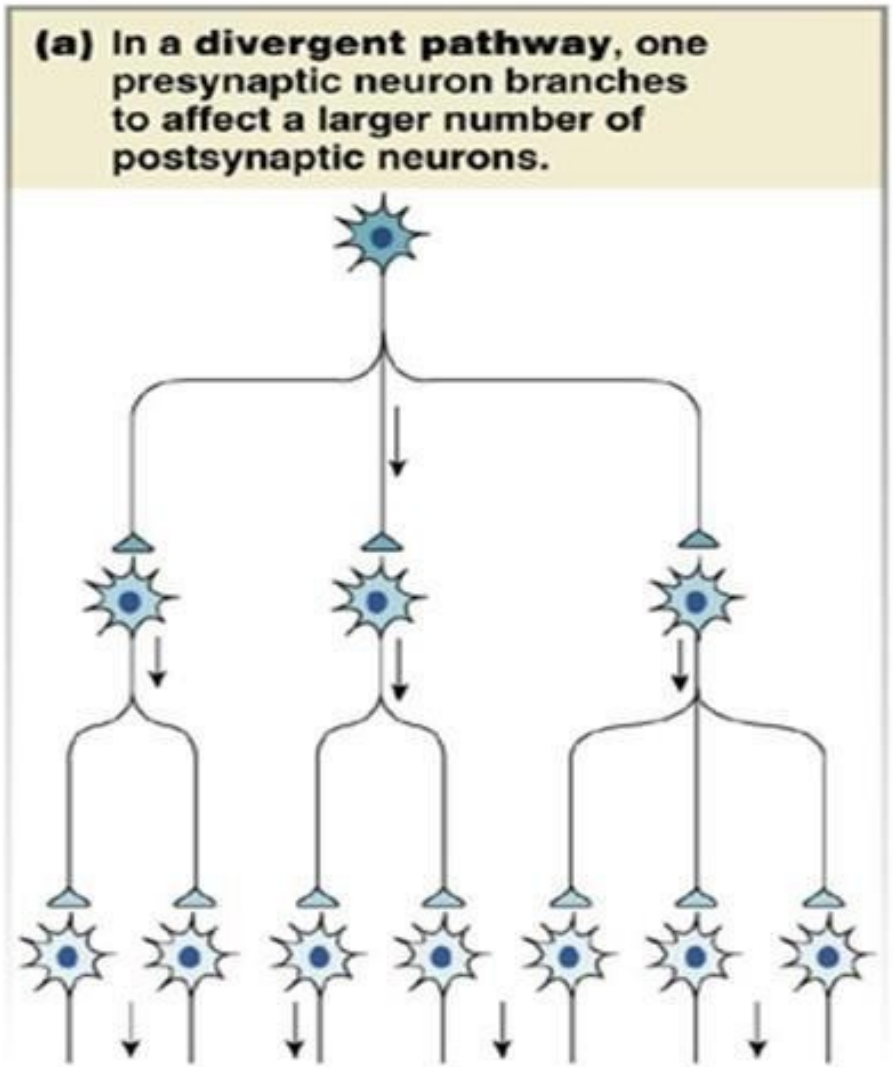
2) Interneurons Circuits



(a) Diverging circuit (b) Converging circuit (c) Reverberating circuit (d) Parallel after-discharge circuit

A) Divergence Circuits

- A **single input** (afferent) neuron or (more commonly) i**nterneuron** divide to give **several collaterals** and reach a **larger number** of efferent neurons

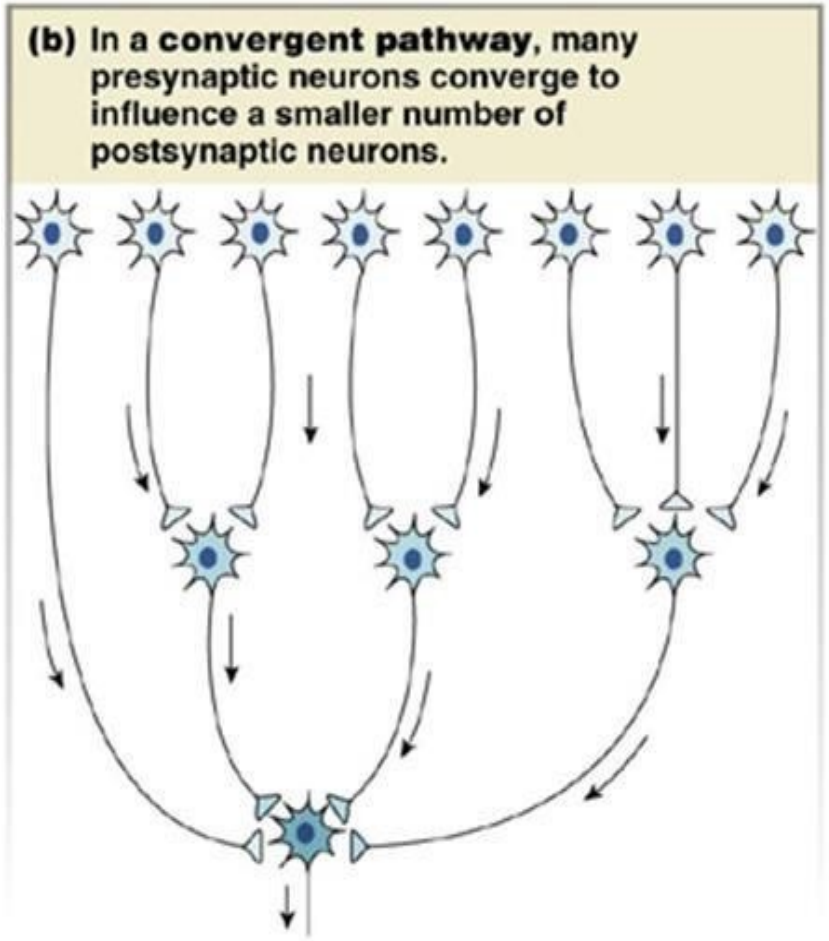


Significance :

- Help in **spread of a single afferent signal** to a **large No.** of **postsynaptic neurons** in the spinal cord .

B) Convergence Circuits

- **Multiple collaterals** from input (**afferent**) neurons or more **commonly interneurons converge** (collect) on a relatively fewer number of output (efferent) neurons



Significance:

- **Help spatial summation of EPSPs** → discharge of impulses on the postsynaptic neurons.

C) After-discharge Circuits

Def.

- It is a **prolonged** (continuous) discharge from an **efferent neuron** even **after stoppage** of stimulation of the afferent nerves

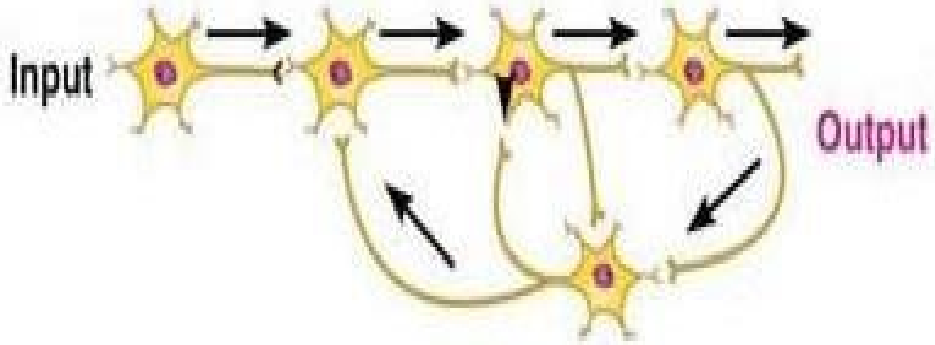
Mechanism:

- Because the afferent impulses **do not reach** efferent directly but **through interneurons** circuits
- There are **2 types** of these **circuits**;

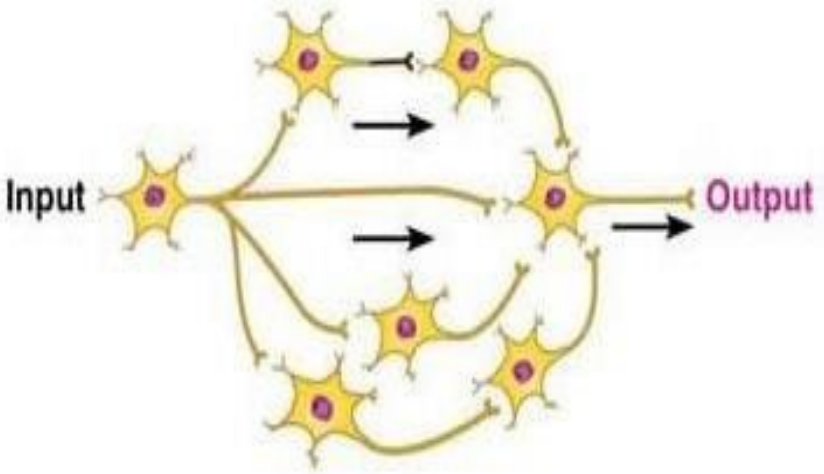
a) **Open interneuron** circuits

b) **Closed interneuron** circuits.

C) After-discharge Circuits



(e) Reverberating circuit

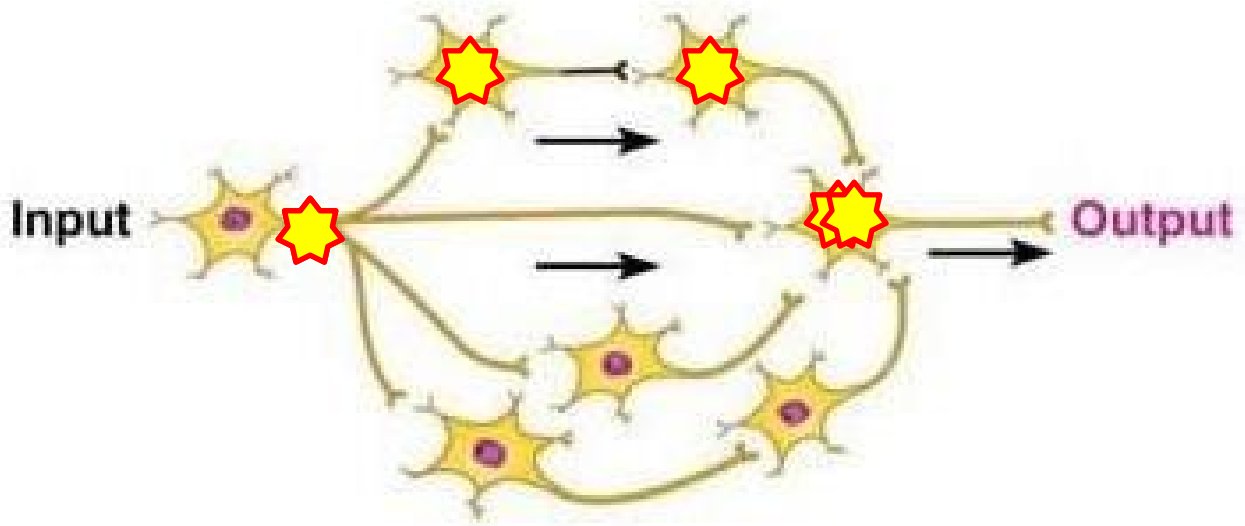


(f) Parallel after-discharge circuit

C) After-discharge Circuits

i) Parallel (Open) Chain Circuits:

- In this circuit an **afferent neuron stimulates** an **efferent neuron** both **directly** and **indirectly through an interneuron** which is **anatomically arranged in parallel** with the afferent neuron.

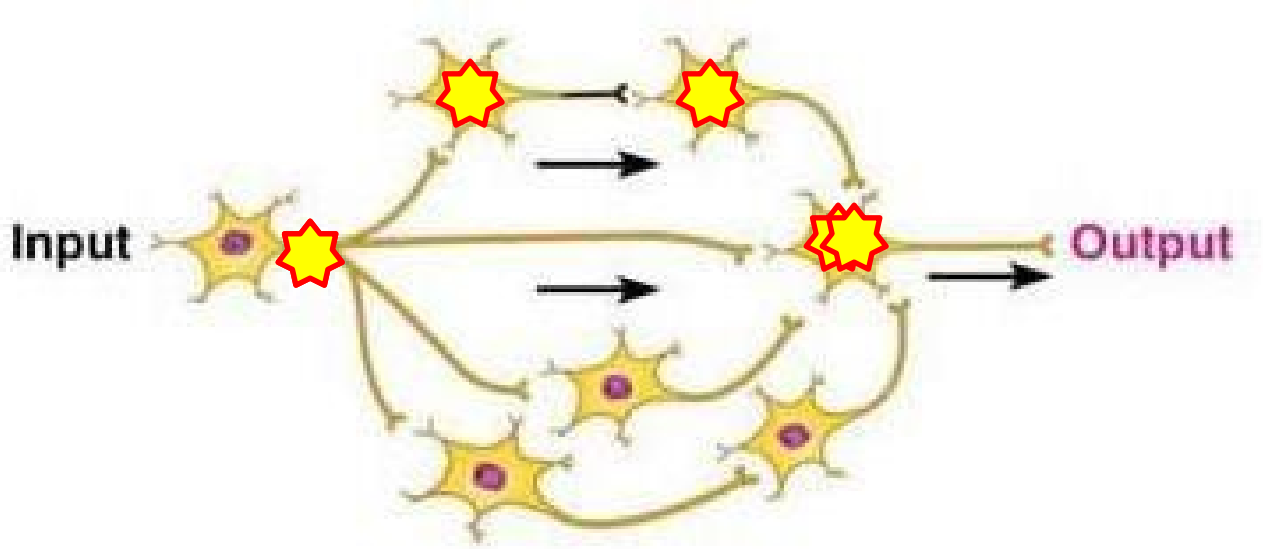


(f) Parallel after-discharge circuit

C) After-discharge Circuits

i) Parallel (Open) Chain Circuits:

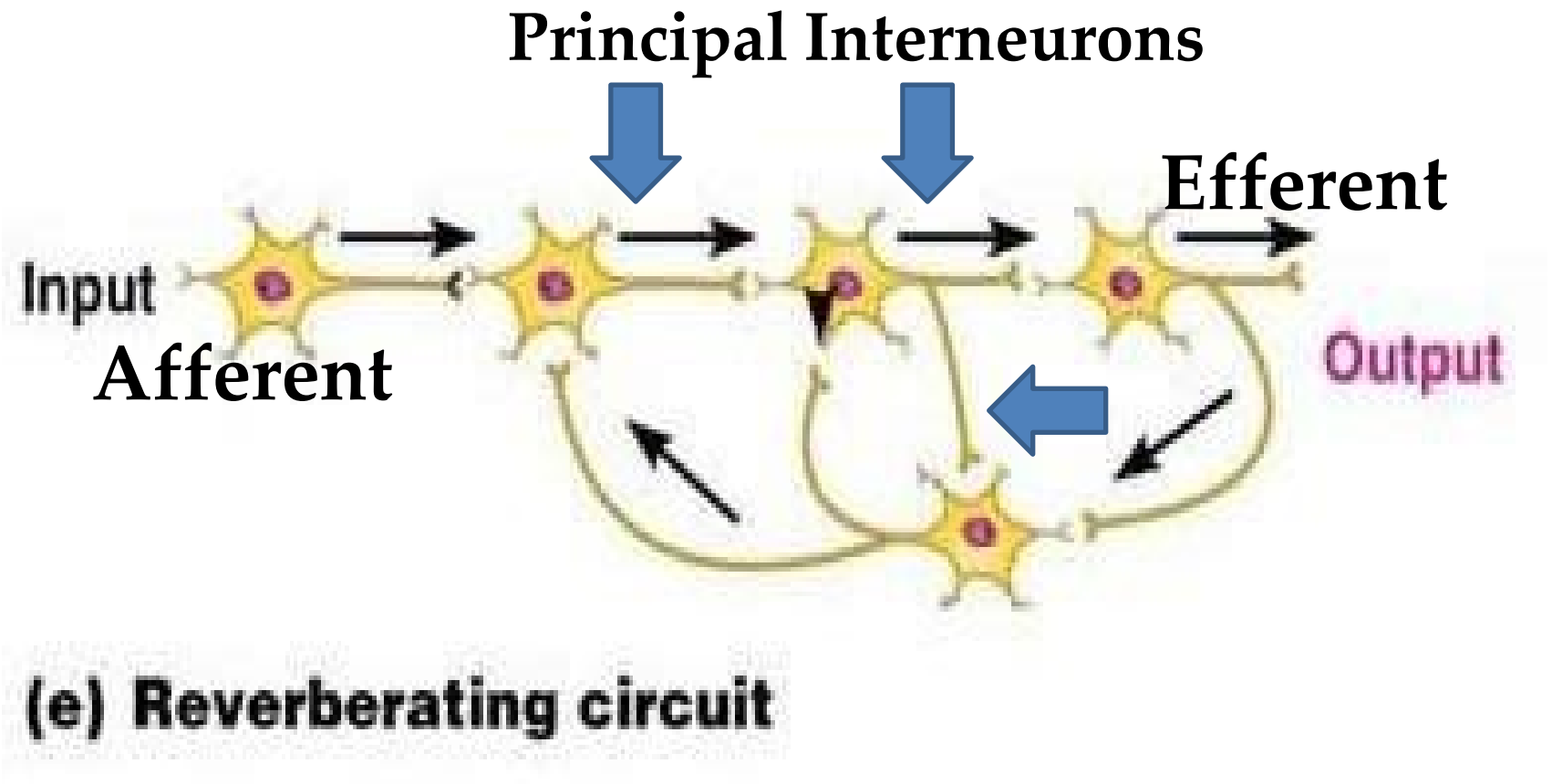
- Impulses from inputs not reach to output at the same time due to **delay 0.5 ms** at each synapse
- **Duration** of discharge depends upon the **No. of interneurons**



(f) Parallel after-discharge circuit

C) After-discharge Circuits

ii) Closed-chain (Reverberating) Circuits:

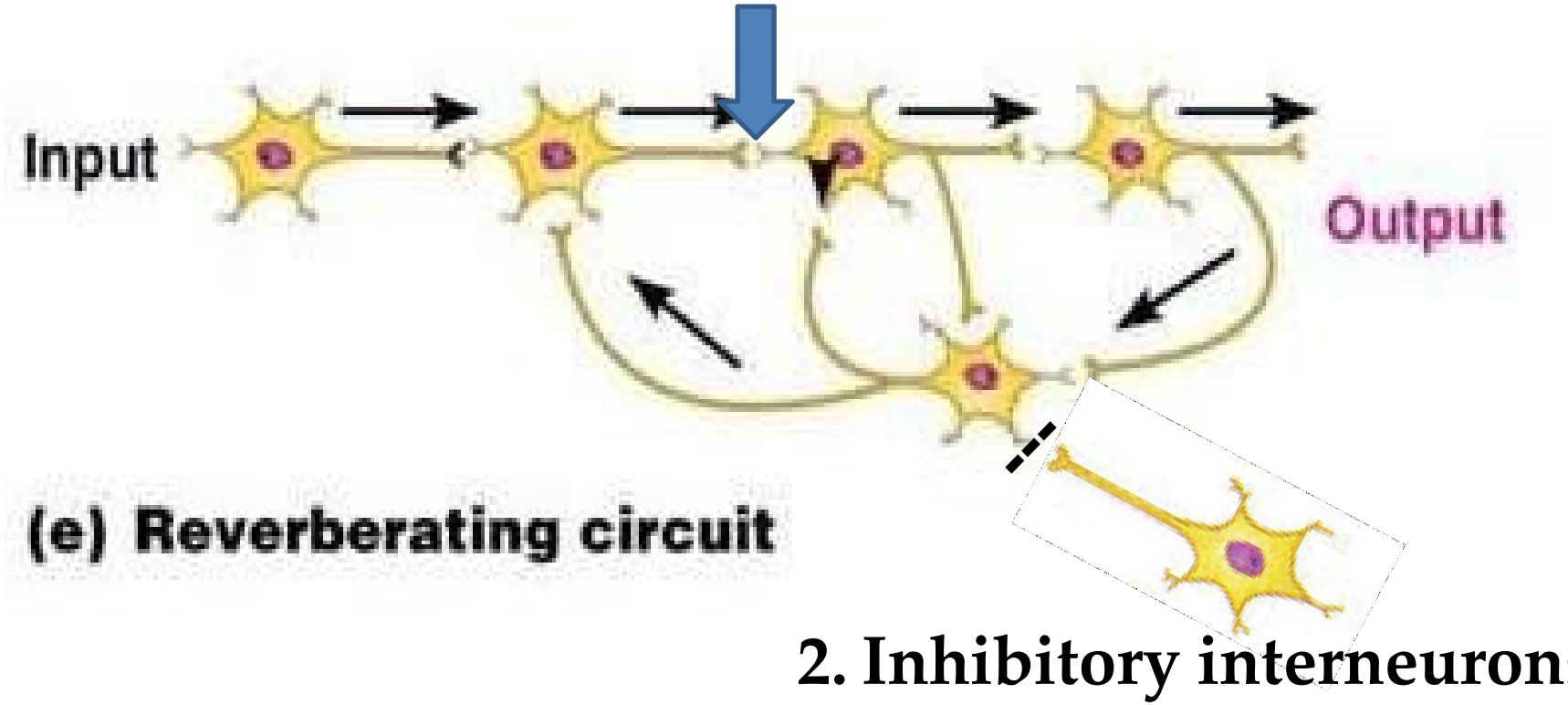


C) After-discharge Circuits

ii) Closed-chain (Reverberating) Circuits:

- The activity of these circuits stop by either;

1. Fatigue of synapse



2. Inhibitory interneurons

C) After-discharge Circuits

ii) Closed-chain (Reverberating) Circuits:

Examples : Reticular activating system (RAS)

- **Wakefulness** depends upon the activity of **RAS (**contains many **reverberating circuits**)
- **Single sensory** stimulation causes **activation of RAS for long time** (16-18 hours), which in turn stimulate the **cerebral cortex** which by its turn **re-stimulate it** & so on.
- RAS activity **continues till fatigue** of the **synaptic transmission** occurs and then **sleep occurs**.

D) Inhibitory Circuits

- In this circuit, an **excitatory input** is converted into an **inhibitory output**.

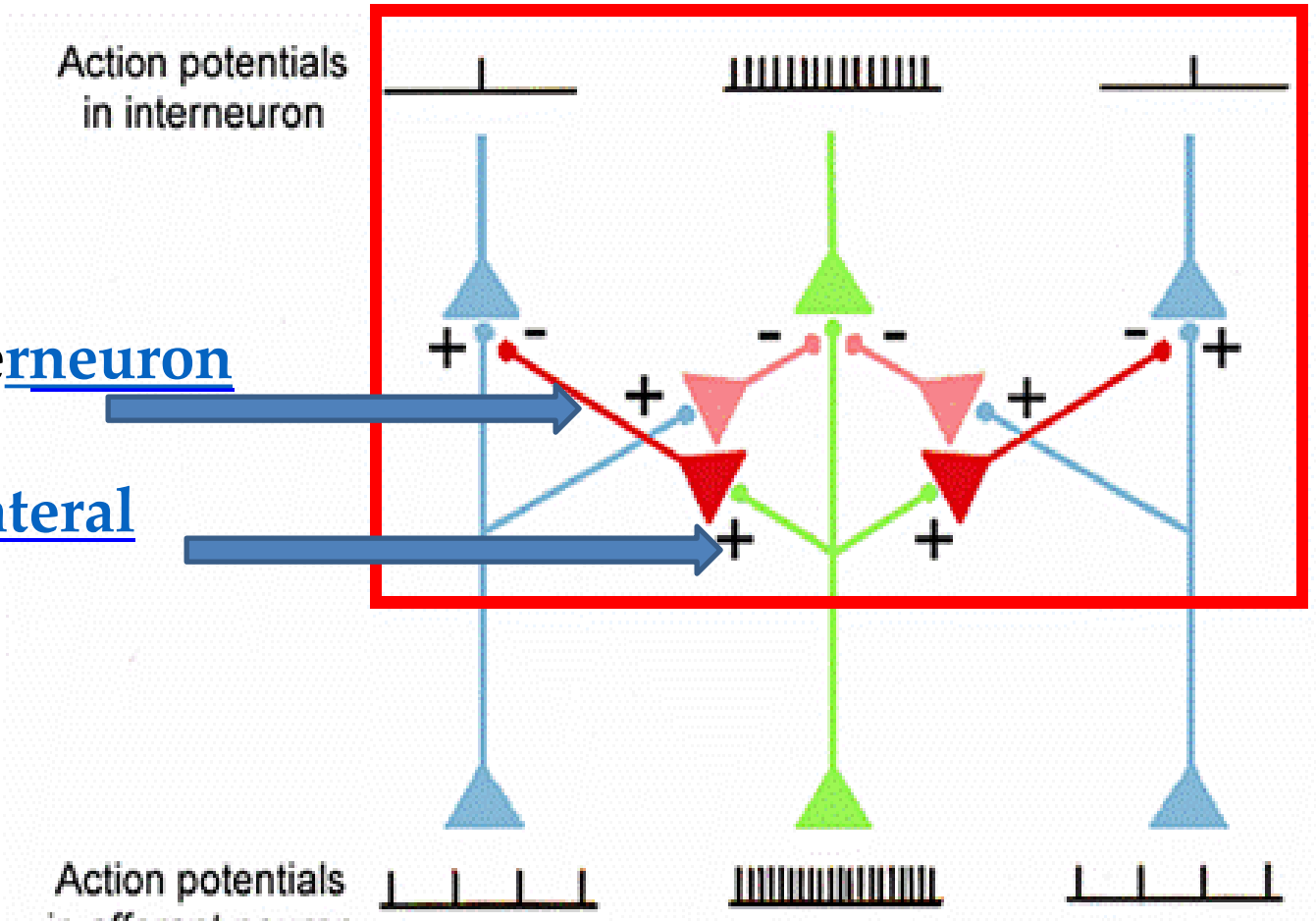
Types:

- 2 types of these circuits;

1. **Lateral inhibitory circuits**
2. **Recurrent inhibitory circuits**

D) Inhibitory Circuits

i) Lateral inhibitory circuits:



Inhibitory interneuron

Collateral

less active neurons

More active neurons

D) Inhibitory Circuits

i) Lateral inhibitory circuits:

- In this circuit the **afferent neuron** activates an **inhibitory interneuron** which **in turn inhibit** the adjacent efferent neurons.

Site:

- Ascending sensory pathways

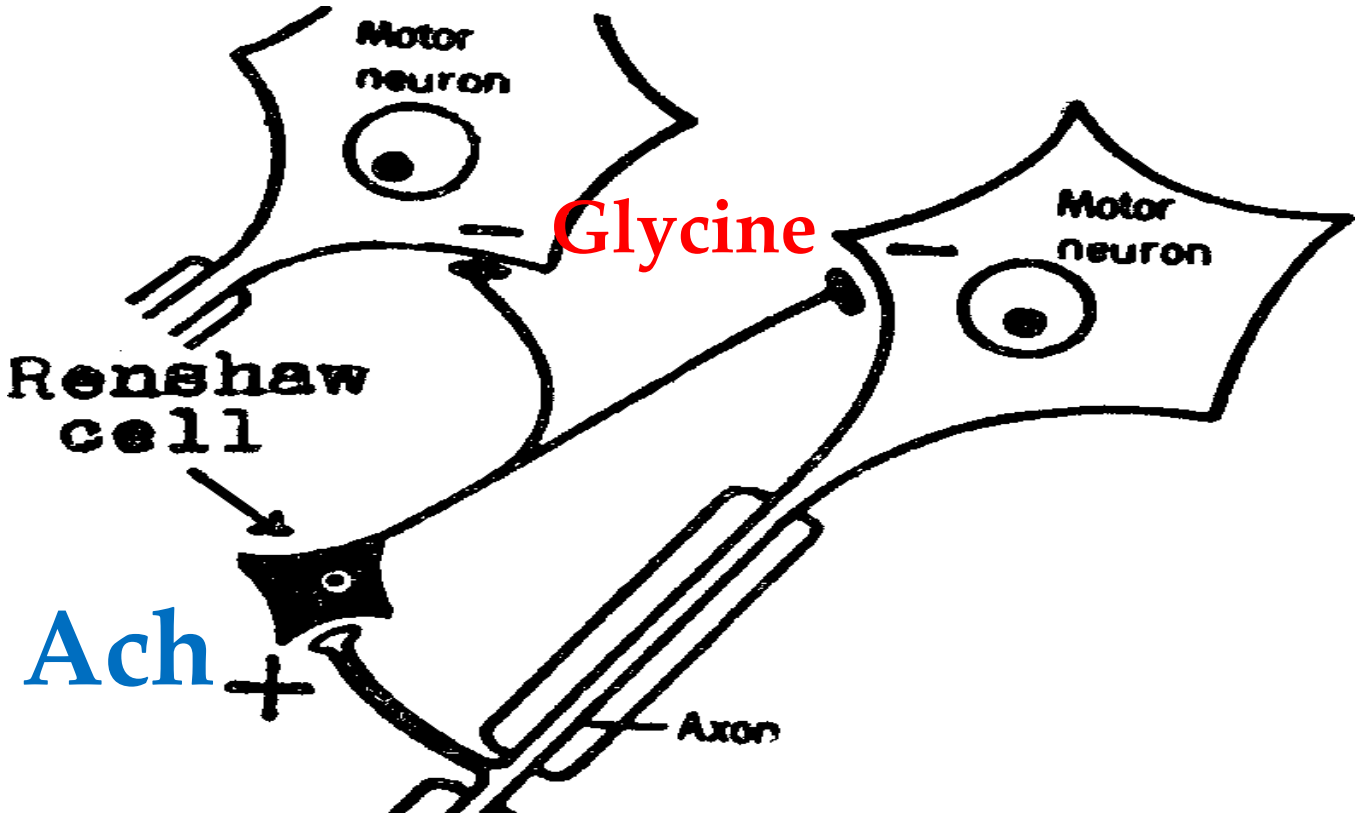
Importance:

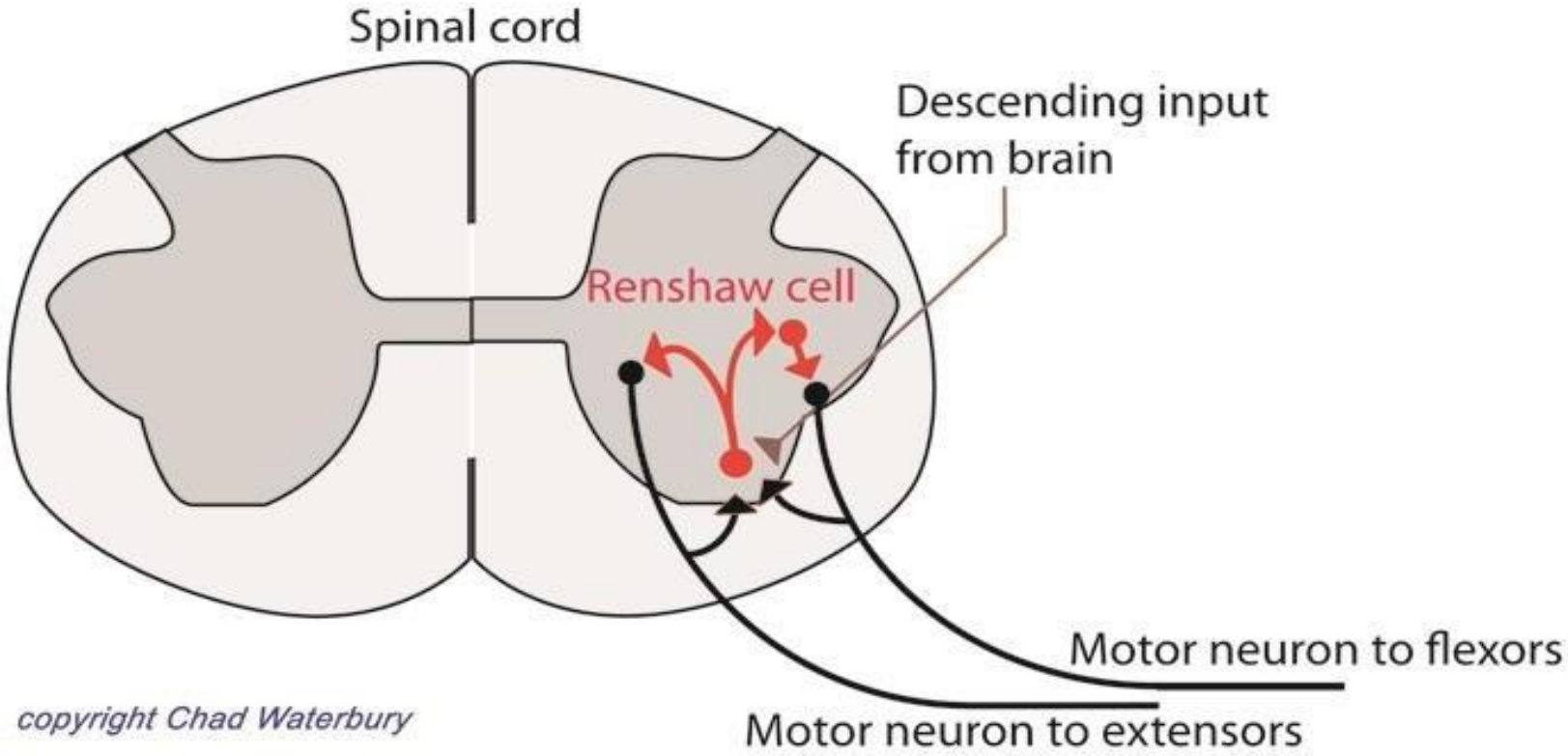
- These circuits are important in **focusing** on or **sharpening** of the most **important sensation**.

D) Inhibitory Circuits

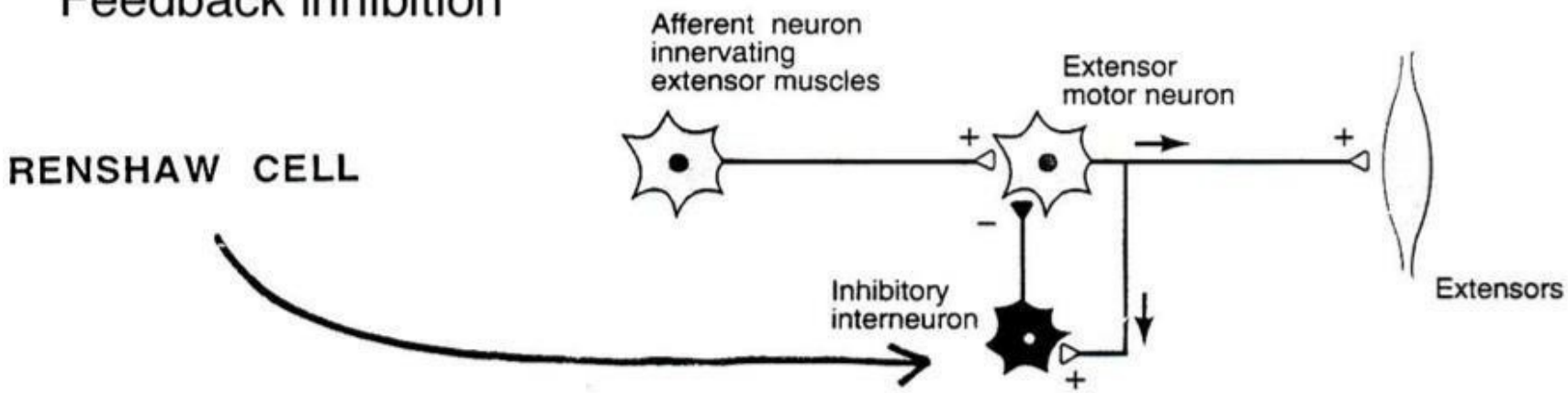
ii) <u>Recurrent inhibitory circuit:</u>

- Nerve fiber gives a collateral branch which **excites (via Ach) an inhibitory** neuron which **in turn, inhibits (via glycine) the original neuron** as well as the **surrounding** neurons.





Feedback inhibition



4.Inhibitory Circuits

Renshaw cells :

- **Small inhibitory interneurons** present in AHCs of the spinal cord
- **Stimulated A.H.C.** gives a recurrent collateral branch which **stimulates the Renshaw cells**.
- **Renshaw cells** in turn **inhibits either**: stimulated or surrounding A.H.C.

Importance:

a) **Focus** the motor activity to the most facilitated motor neurons

b) **Stops** the activity of the stimulated motor neurons.

3) Functions of Efferent Neurons

- In spinal reflexes the **efferent neurons** are of **<u>2 types</u>**;

Autonomic M. Neurons

↓

From LHCs

↓

Mediate autonomic reflexes

Somatic M. Neurons

↓

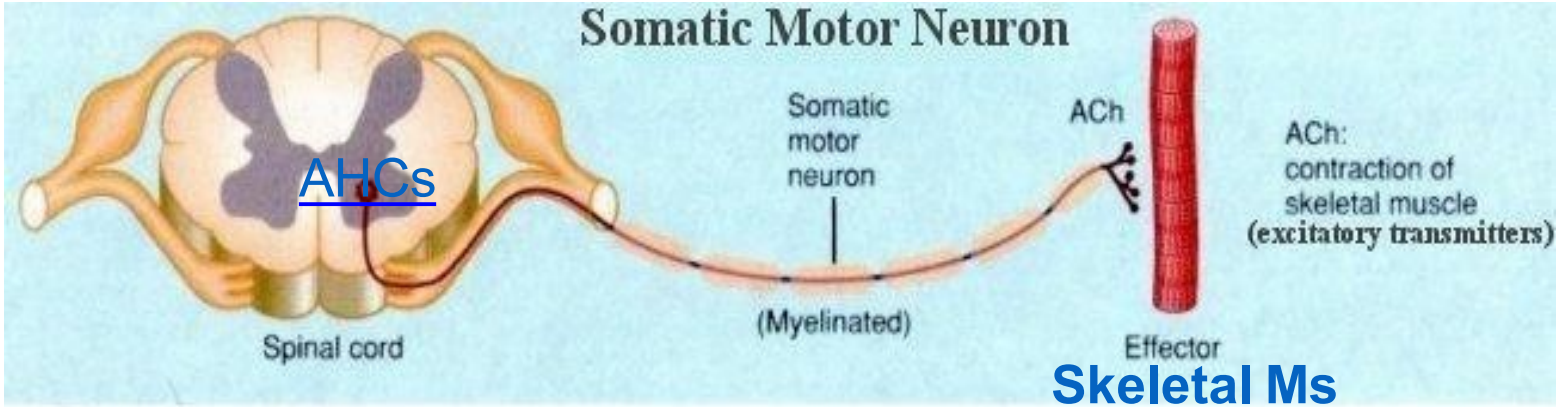
From AHCs

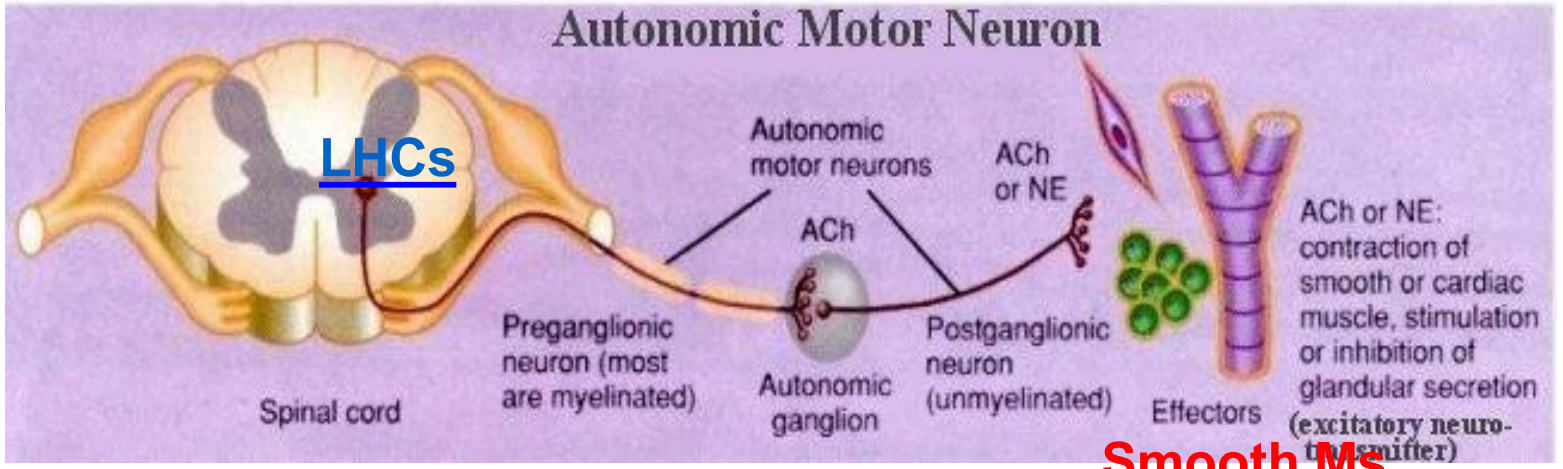
↓

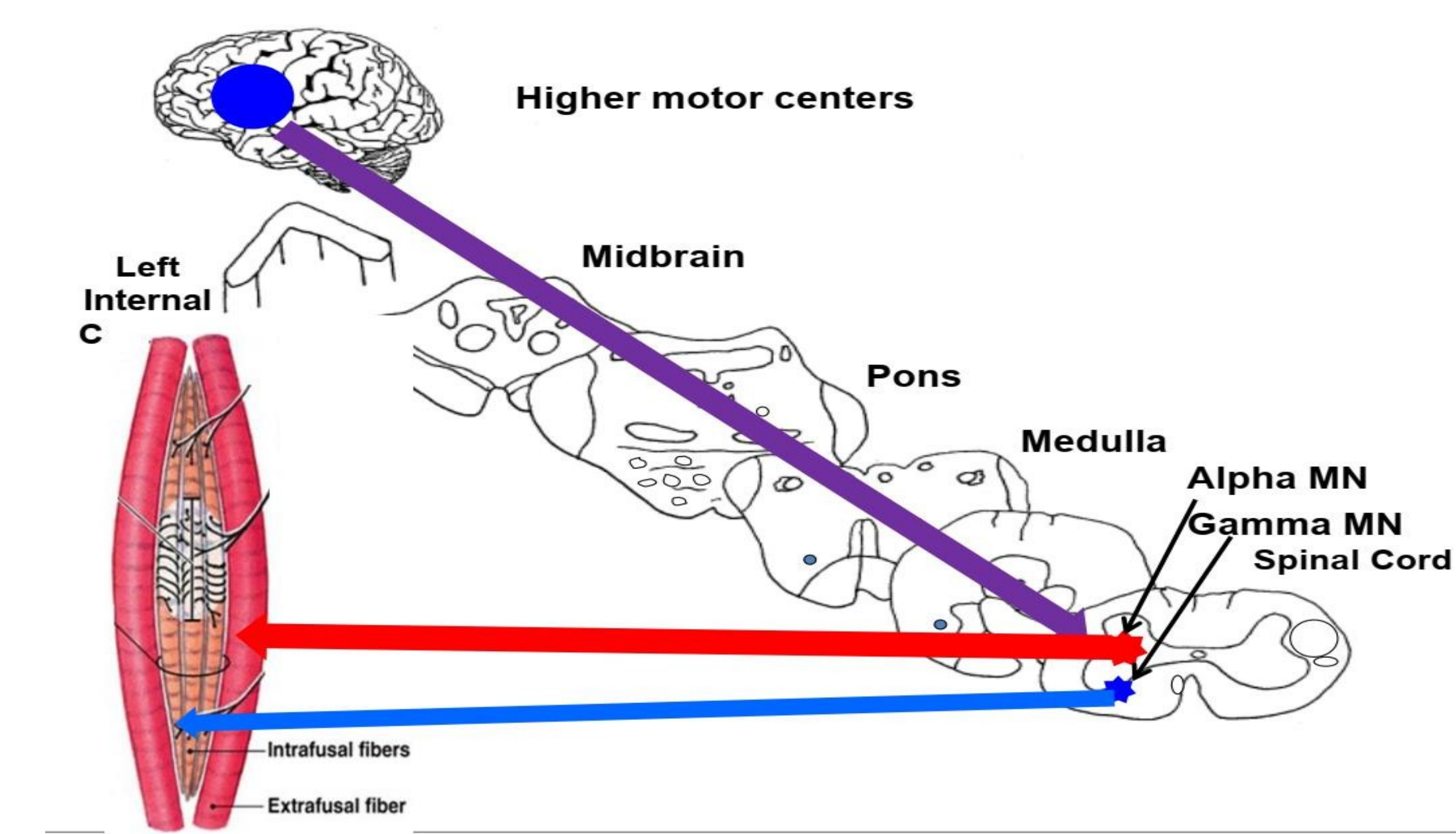
Mediate somatic reflexes

- **Alpha MNs**
- **Gamma MNs**

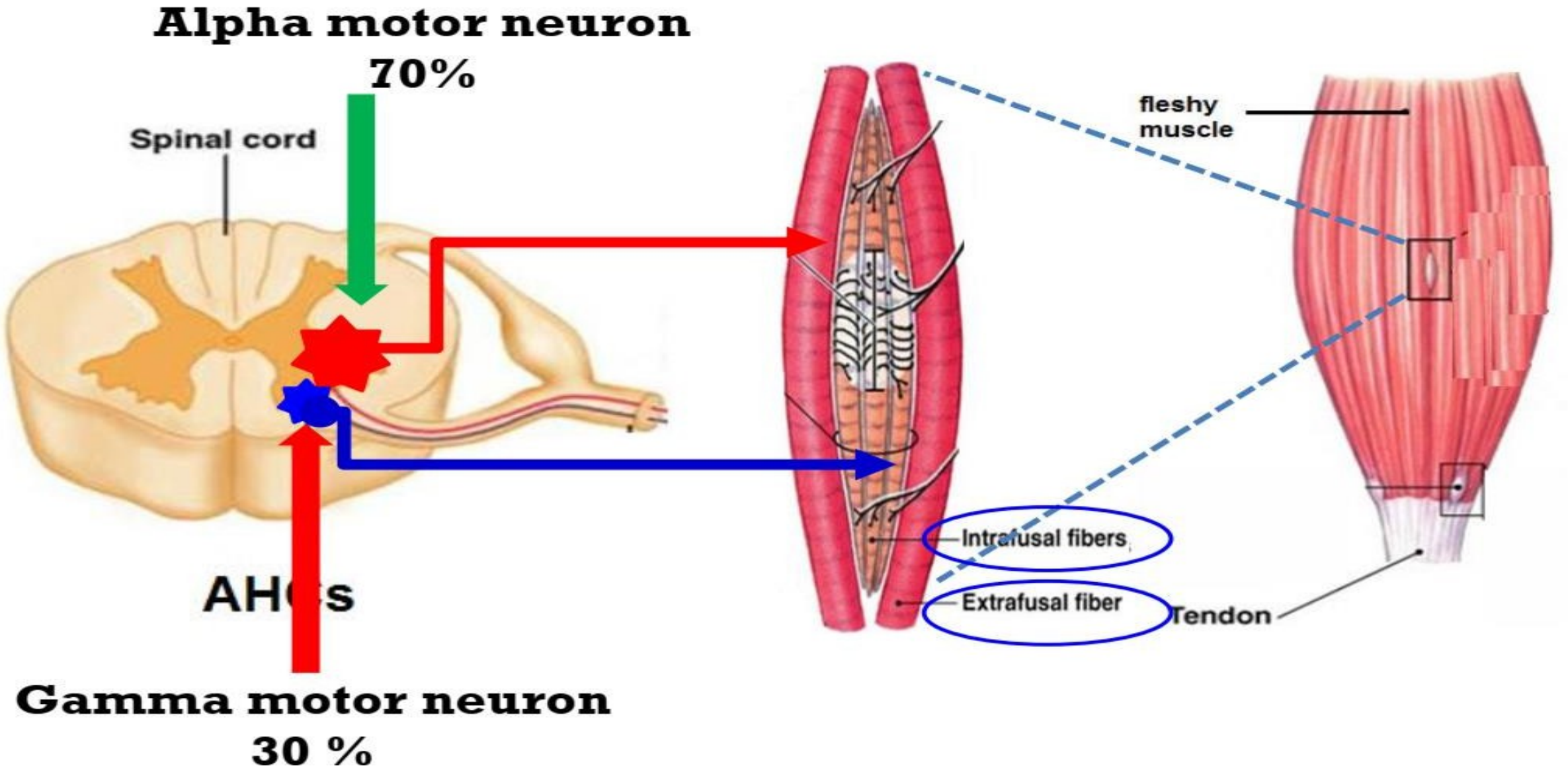
3) Functions of Efferent Neurons

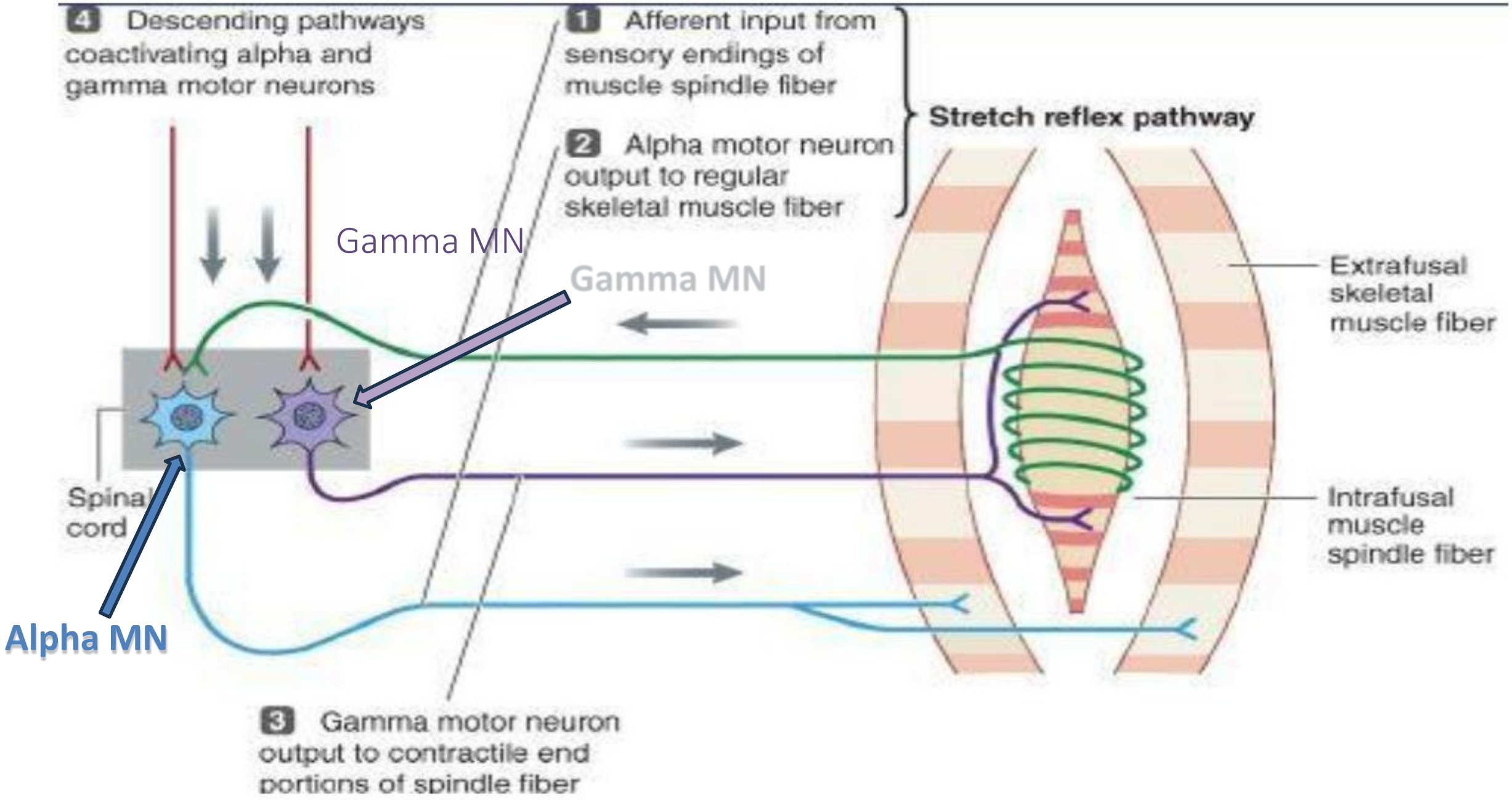





Higher motor centers
Midbrain
Left
Internal
C
Pons
Medulla
Alpha MN
Gamma MN
Spinal Cord
Intrafusal fibers
Extrafusal fiber

Alpha and Gamma motor Neurons




4 Descending pathways coactivating alpha and gamma motor neurons
1 Afferent input from sensory endings of muscle spindle fiber
2 Alpha motor neuron output to regular skeletal muscle fiber
Stretch reflex pathway
Gamma MN
Gamma MN
Extrafusal skeletal muscle fiber
Intrafusal muscle spindle fiber
Spinal cord
Alpha MN
3 Gamma motor neuron output to contractile end portions of spindle fiber

Flexion Withdrawal-Crossed Extensor Reflex

Def

- Applying painful or sometimes touch or pressure stimuli to the skin or subcutaneous tissues of one limb results in;

1. Reflex contraction of **flexor ms** and withdrawal of the stimulated limb

2.Reflex contraction of **extensor ms** and ↑ed extension of the opposite limb.

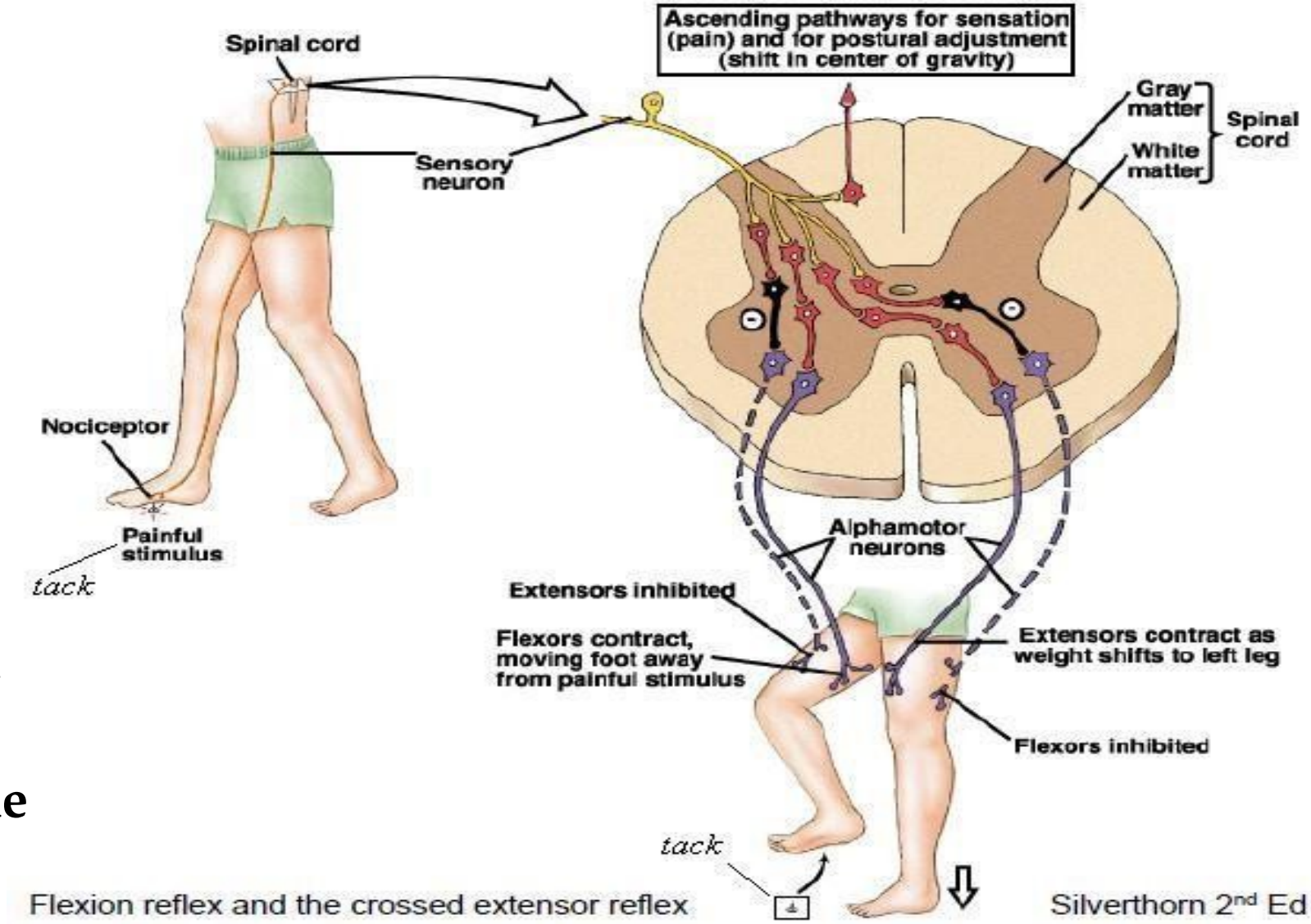
N.B. it is **polysynaptic reflex**

Flexion Withdrawal-Crossed Extensor Reflex

Pathway

1. **Stimulus** → painful or tactile stimuli
2. **Receptors** → free nerve endings
3. **Afferents**→ A delta
4. **Center** → AHCs
5. **Response**

- Flexion of the stimulated limb
- Increased extension of the contralateral limb



Flexion Withdrawal-Crossed Extensor Reflex

Significance

1) Withdrawal reflex:

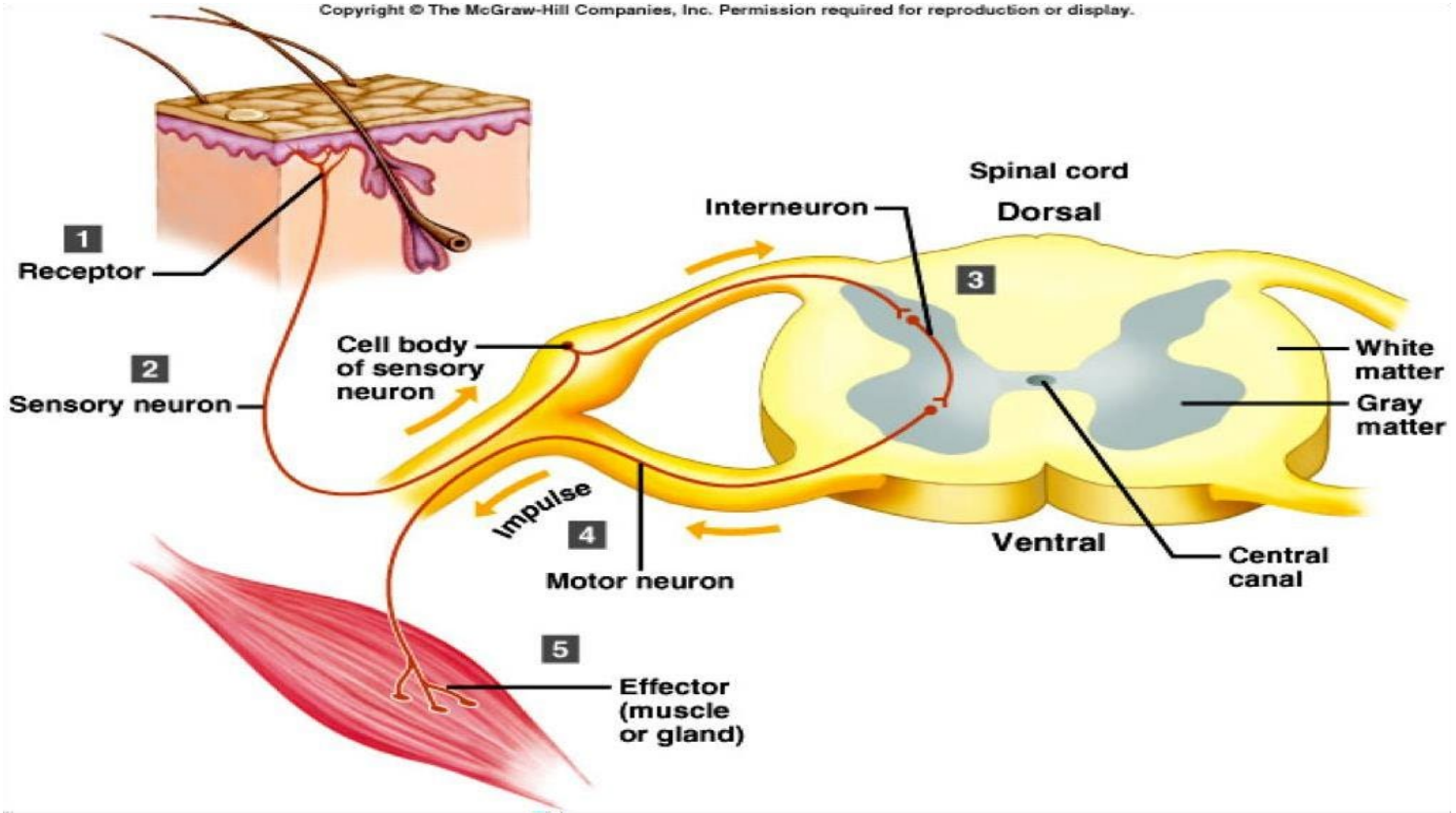
- It is **protective reflex** →help to immediately remove the stimulated part of the body away from sources of painful stimuli.
- It is a **prepotent reflex**; i.e. can suppress any other reflex occurring at the same time.

2) Crossed extensor reflex:

- It is **supportive reflex** i.e. supports the body weight which is shifted to the opposite limb.

Properties of Polysynaptic Reflexes

- All **spinal reflexes** are polysynaptic except **stretch reflex**
- Properties of polysynaptic spinal reflexes are due to the presence of **interneurons** and **synapses** in the reflex arc.



1. Localization

- **The pattern** of the reflex **motor response** is determined by the **site of stimulus** e.g. in a flexion withdrawal reflex, if a painful stimulus is applied to;

a) Medial side of limb → flexion and abduction of the limb.

b) Lateral side of limb → flexion and adduction of the limb.

Mechanism:

1. P**ain fibers** from the **lateral aspect** of the thigh centrally connected with the motor neurons of the **flexors and adductors**
2. **Pain fibers from medial side are connected with flexors and abductors**

2. Irradiation

- The **extent** of the **response** is determined by the **strength** of stimulation, so;

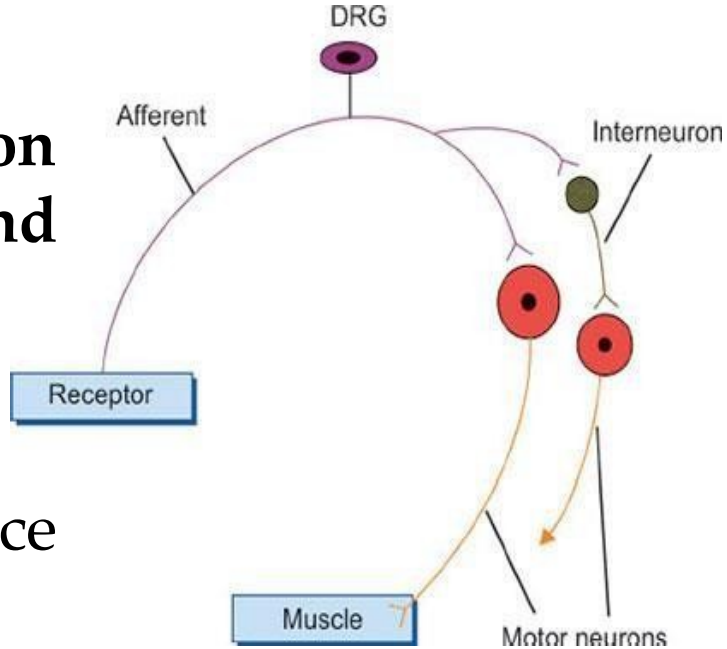
a) **Weak stimuli** produce limited responses

b) **Stronger stimuli** produce more widespread responses

Example: apply pain stimulus to sole of the foot

1. **Mild painful stimulus → dorsiflexion of the ankle** only.
2. **Moderate painful stimulus →dorsiflexion of the ankle and flexion of the knee**.

3. Severe painful stimulus → dorsiflexion of the ankle and flexion of both knee and hip.



Mechanism:

- Due to spread of impulses by divergence functions of afferents and interneurons

3. Total Reflex Time and Central Delay

Total reflex time:

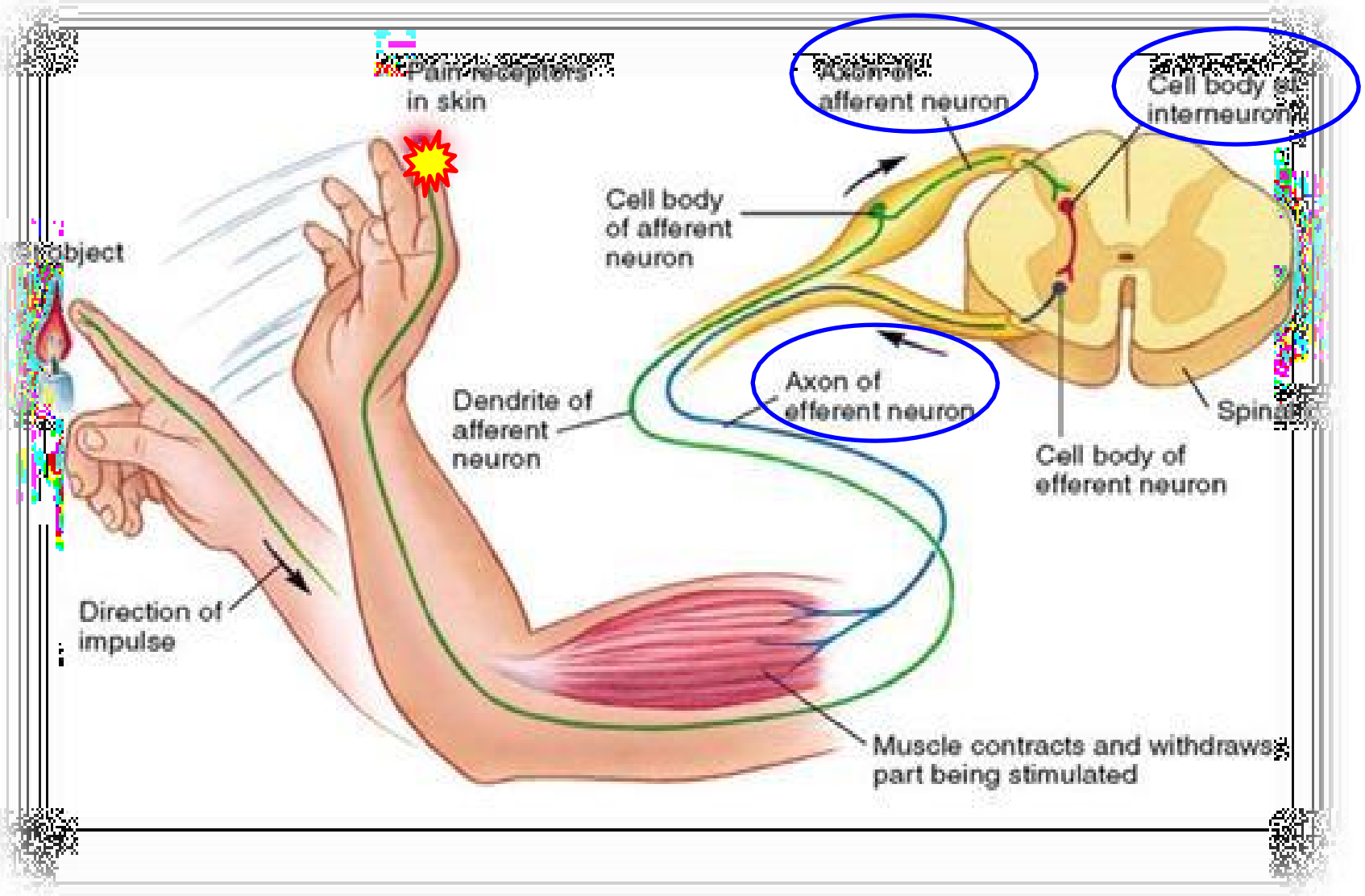
Def.,

- Is the period or **time** that passes between **application** of the stimulus and the **onset** of the reflex **response**.

Causes:

1. Conduction of impulses along the afferent and efferent nerves.
2. The process of neuromuscular transmission.
3. Transmission of impulses through central synapses in the reflex pathway.

Total reflex time



Central Delay

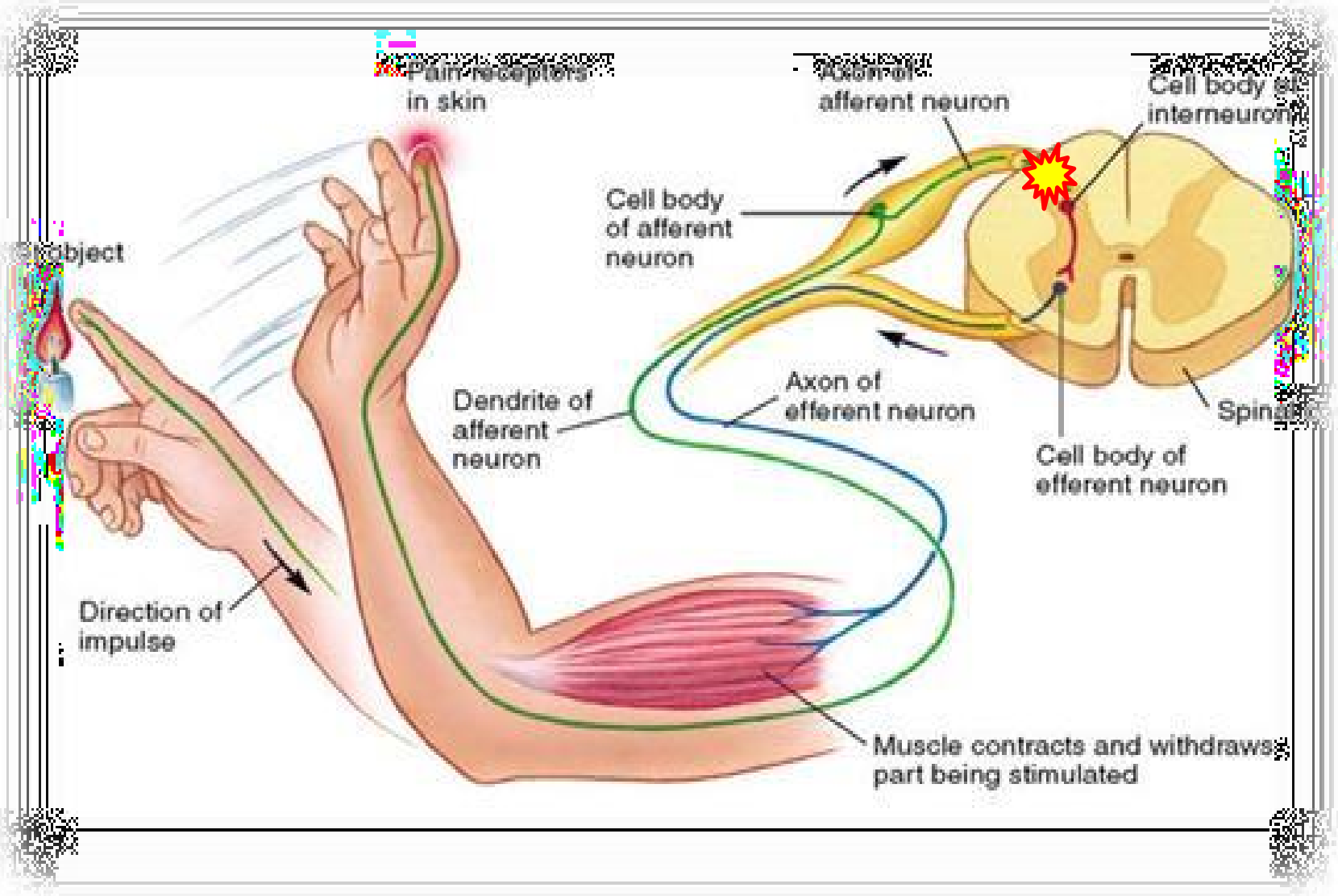
Central Delay :

- It is the **time** needed for t**ransmission** of impulses through **central synapses** in the reflex pathway.
- It depends mainly on the **number of synapses** in reflex pathway.

Importance:

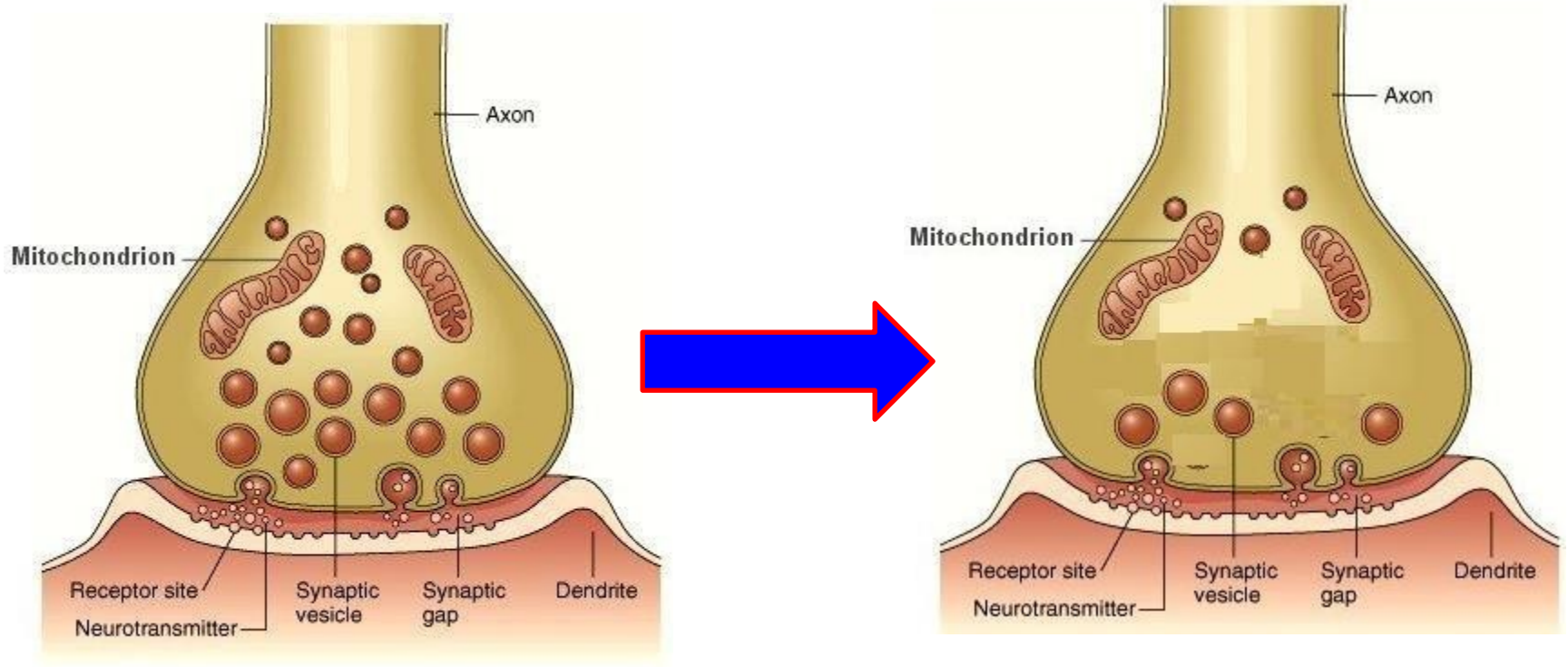
- Can used to calculate number of synapses in a reflex e.g. if central delay in stretch reflex is 0.8 sec and synaptic delay is 0.5 calculate number of synapses = 0.8/0.5 = 1 i.e. monosynaptic reflex

Central delay



4. Synaptic Fatigue

- It is a **gradual decline** in the **reflex response** when its sensory nerve is stimulated for a relatively **prolonged period**.
- It is due to **fatigue of synapses** in the reflex pathway .



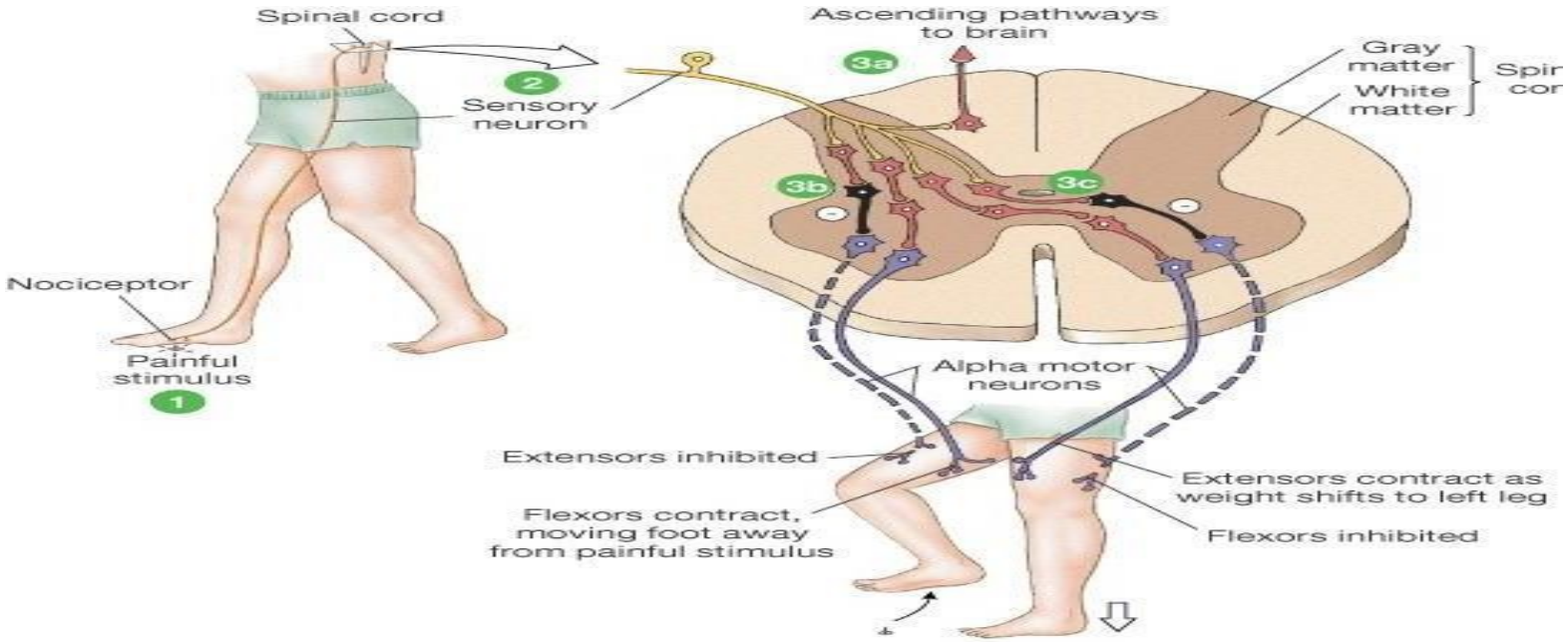
5. Reciprocal Innervations

Def.,

- Reflex **contraction** of a group of ms is usually associated with **inhibition** of the **antagonistic ms**.

Mechanism:

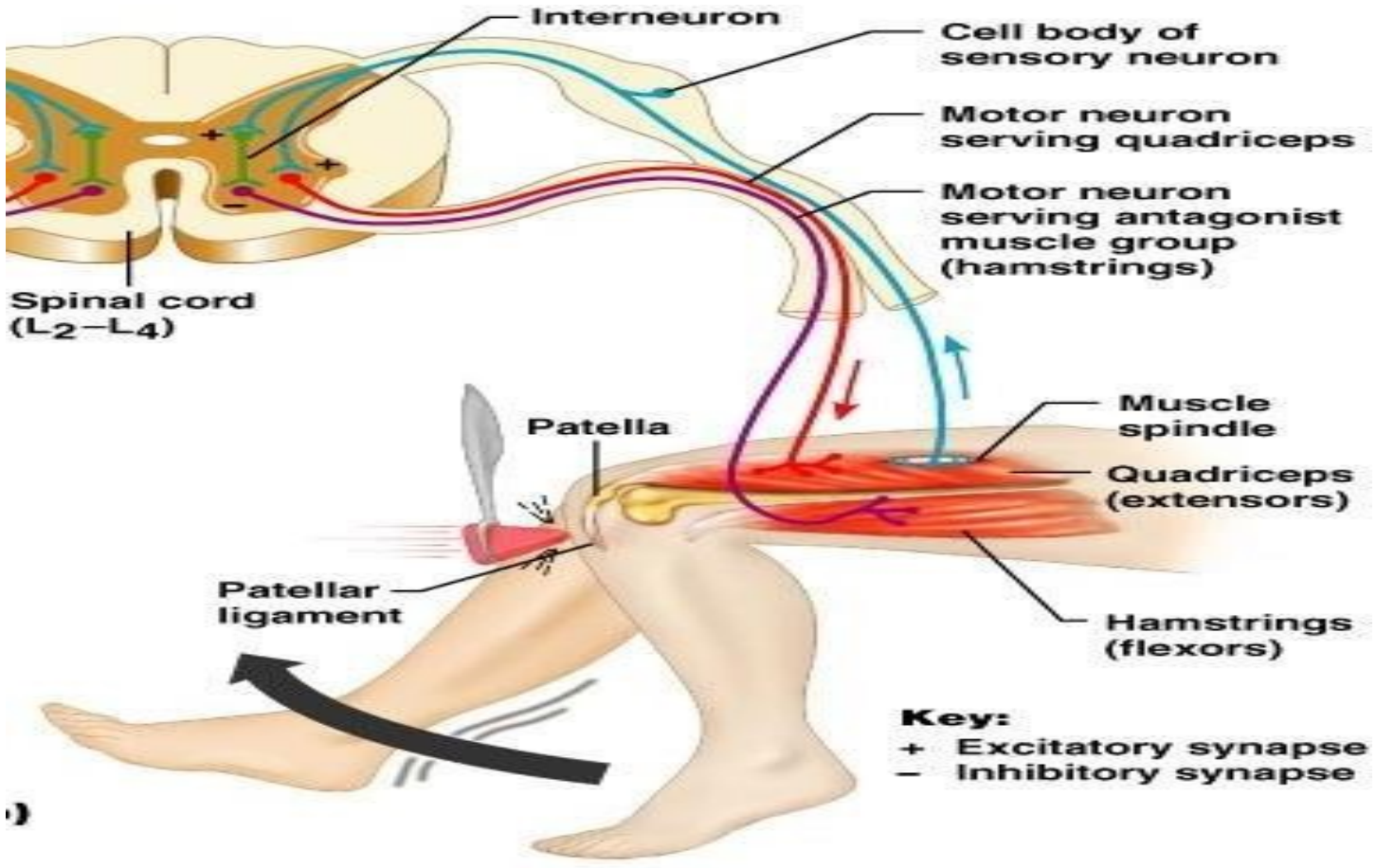
- Afferents give **excitatory inputs** to the **MNs of a ms**, activate at the **same time inhibitory interneurons** ,which inhibit the MNs of **antagonistic ms.**



4. Reciprocal Innervations

Significance:

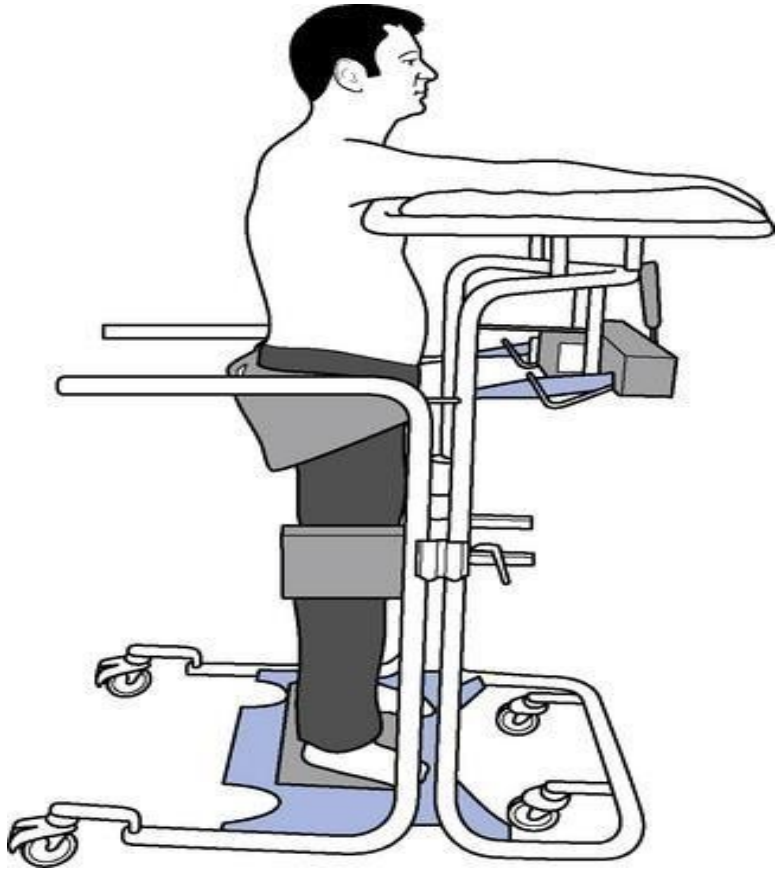
- It provides a **coordinated ms contraction** around the joints and **reduces the resistance** to movements.



5. Reciprocal Innervations

Exception:

- **Positive supporting reaction** in which all groups of ms of lower limbs are contracted at the same time.



Recruitment

Def.,

- It is a gradual ↑ in the **magnitude** of the **reflex response** at the onset of afferent stimulation until the **response reaches its full magnitude**.

Cause:

•**Motor neurons** are said to be gradually **recruited** (activated), one after the other i.e. **not excited** at the same time. Due to;

A. **Different velocities** of nerve impulses due to different thickness of afferent neurons.

B. Presence of **interneurons.**

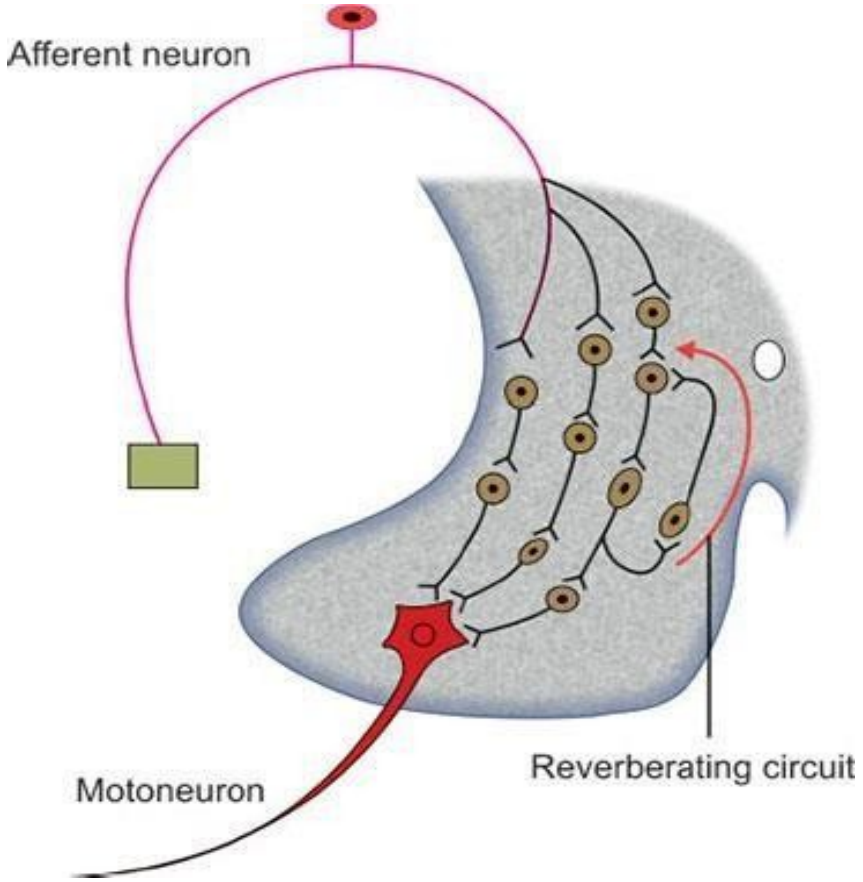
After-discharge

Def.,

- It is the persistence of the reflex response for a period of time after stoppage of sensory stimulation.

Cause:

- Is explained by the repetitive discharge interneuron circuits



	REFLEX TETANUS	**MOTOR TETANUS**
Def:	Continuous contraction of the muscles due to **repetitive** stimulation of the **afferent**.	Continuous contraction of the muscles due to **repetitive** stimulation of the **efferent**.
Latent period:	Much longer. ***It is the time needed for conduction at:*** - Afferent neuron - Synapse - Efferent neuron - MEP.	Shorter ***It is the time needed for conduction at:*** - Efferent neuron. - MEP.
Contraction:	Gradual rise in flexor contraction till reach a peak.	Sudden rise in the flexor contraction.
Relaxation:	Gradual decline in flexor contraction	Sudden decline in the flexor contraction.