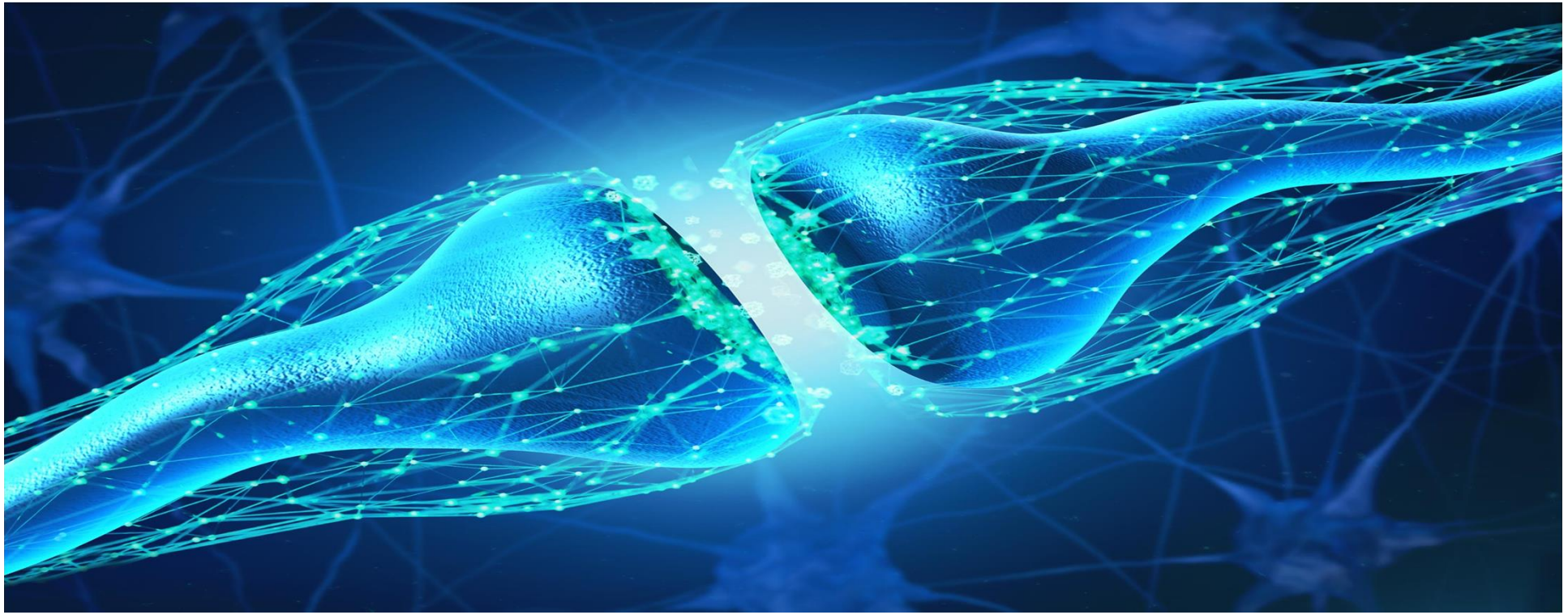
SYNAPSE



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SYNAPSE

COMMUNICATION BETWEEN NEURONS WITH MODIFICATION OF INFORMATION

A synapse is a site where AP travels across 20 -40 nm wide gap separating one neuron from the another

Synapses refer to the points of contact between neurons where information is passed from one neuron to the next.

It is widely accepted that the synapse plays a role in the **formation of memory.**

As neurotransmitters activate receptors across the synaptic cleft, the connection between the two neurons is strengthened when both neurons are active at the same time, as a result of the **receptor's signaling mechanisms**.

The strength of two connected neural pathways is thought to result in the storage of information, resulting in memory.

This process of synaptic strengthening is known as **long-term potentiation.**

Syllabus –

Definition , Classification, Properties , Mechanism

LAQ : Define synapse , Classify synapse. Describe in detail properties of synapse . (10Marks)

Short notes : (5Marks)

1) Properties of synapse
2) Mechanism of synapse

Viva vice :

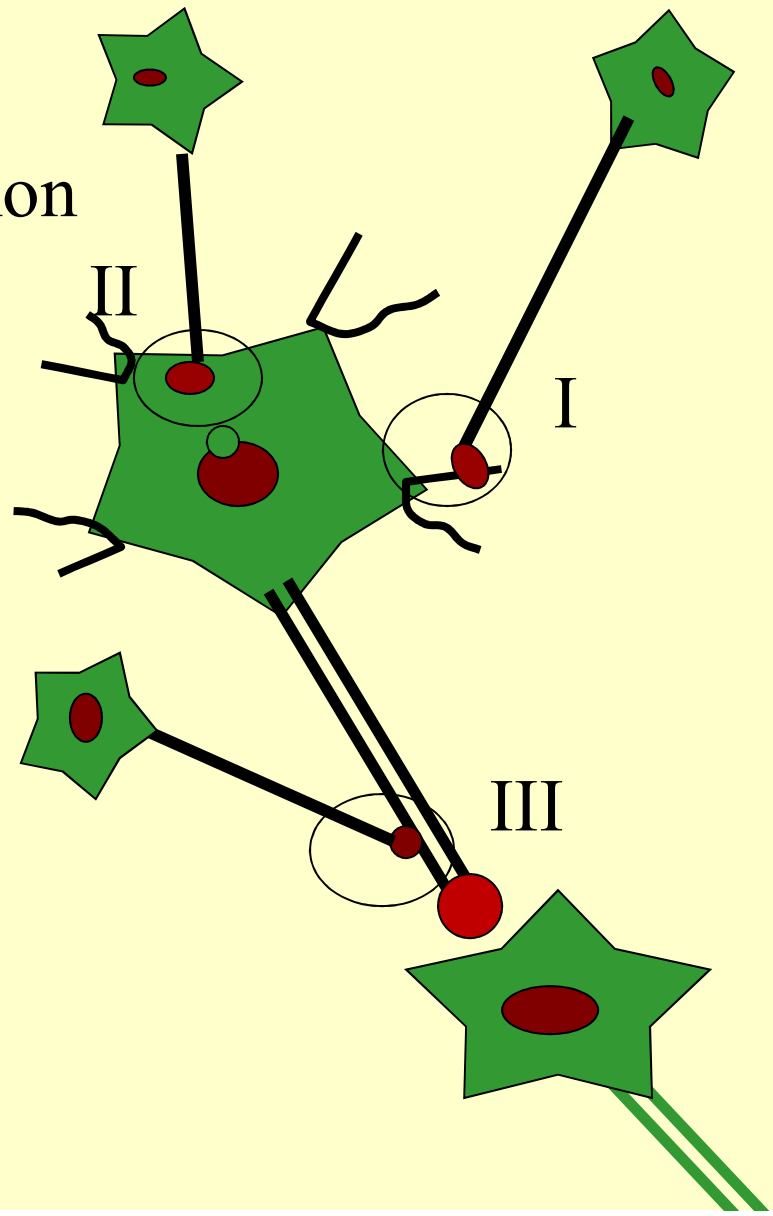
MCQ s

SIGNAL TRANSMISSION

- In nerve fiber – very fast
  - In the form of A. P.
  - Unidirectional
  - All or none response
- From one neuron to another - slow
  - Synapse – chemical
  - Graded response
  - Summated activity
  - Variation in the field of response

CLASSIFICATION OF SYNAPSES

- Anatomical classification
  - I. Axodendritic – most common
  - II. Axosomatic –
  - III. Axoaxonal
- Mechanism of transmission
  - – Electrical
  - – Chemical
  - – - Conjoint (Both)

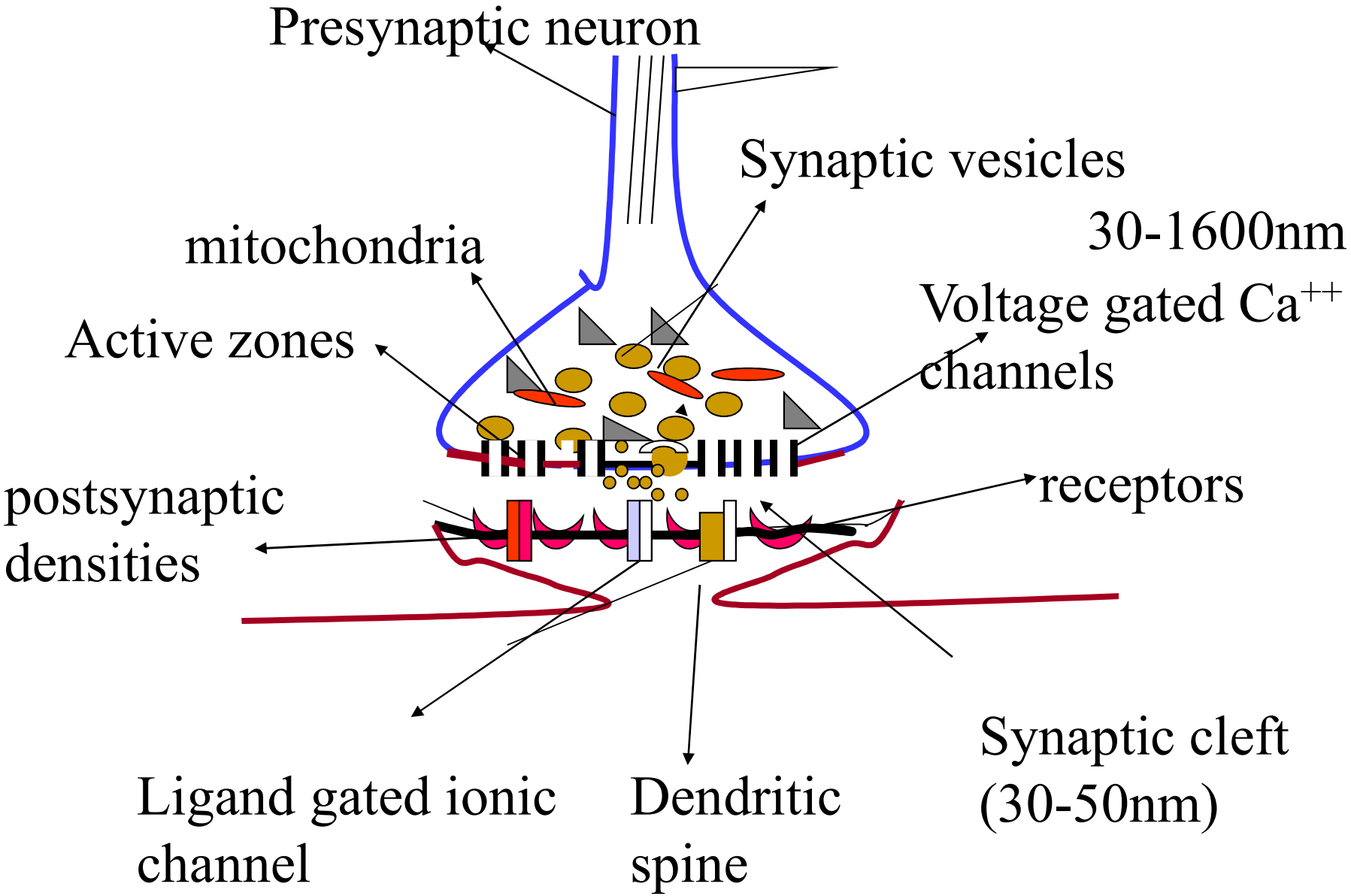


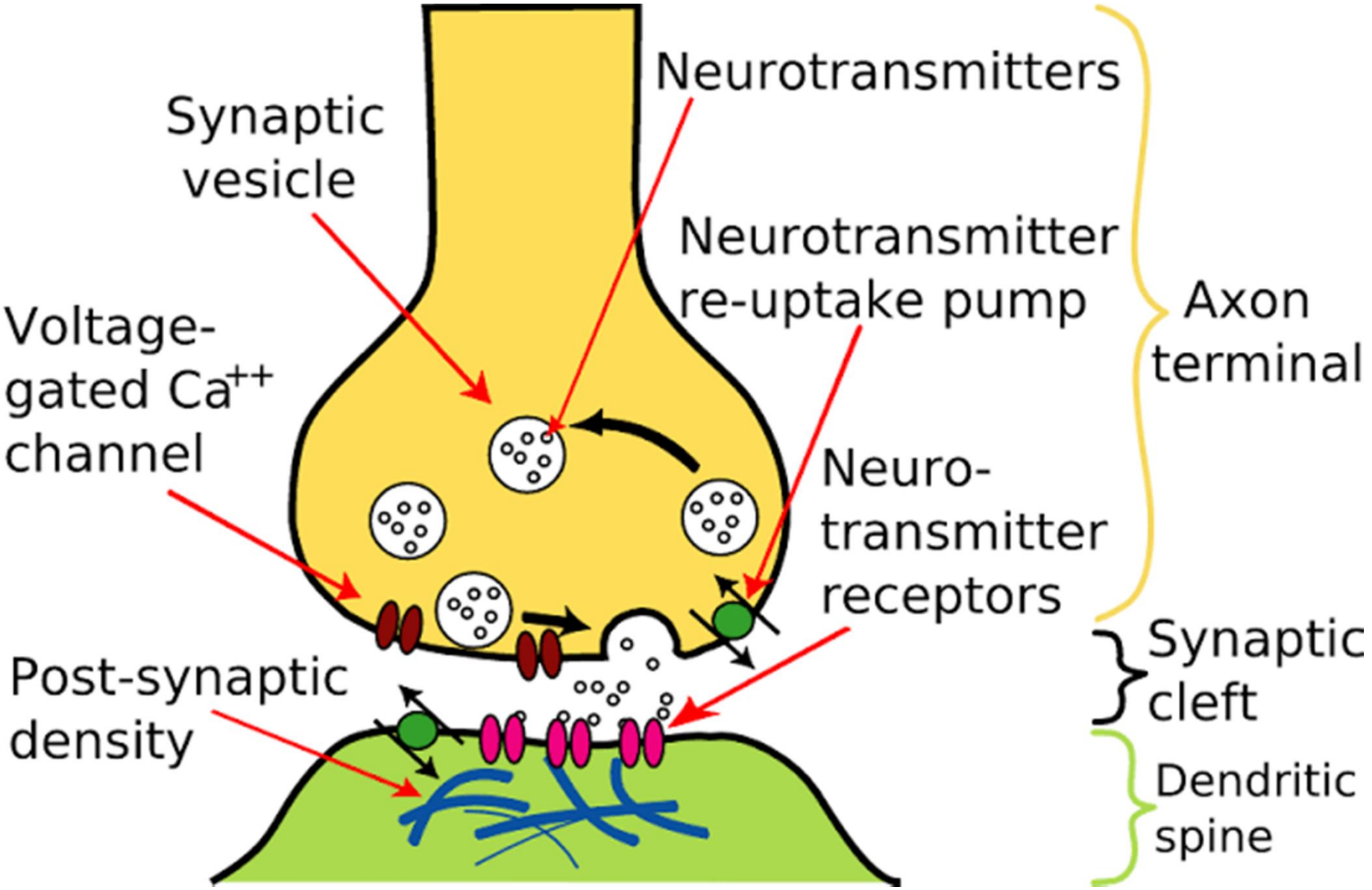
- MAIN PARTS OF SYNAPSE –

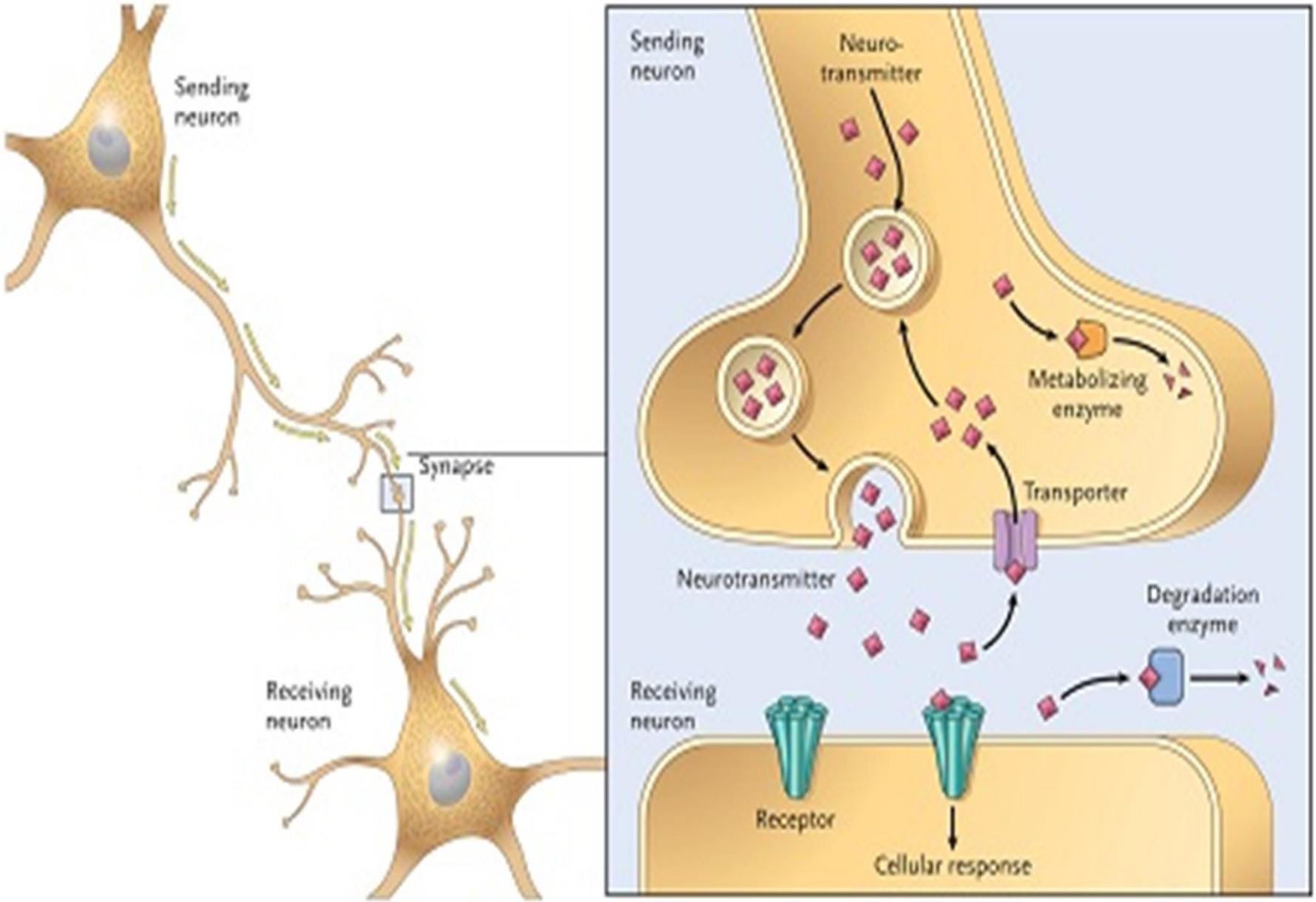
  Presynaptic neuron

  Postsynaptic neuron

  Synaptic cleft


Presynaptic neuron
Synaptic vesicles
30-1600nm
mitochondria
Voltage gated Ca++
channels
Active zones
receptors
postsynaptic
densities
Synaptic cleft
(30-50nm)
Ligand gated ionic
channel
Dendritic
spine


Synaptic vesicle
Neurotransmitters
Neurotransmitter re-uptake pump
Voltage-gated Ca++ channel
Neuro-transmitter receptors
Post-synaptic density
Axon terminal
Synaptic cleft
Dendritic spine


Sending neuron
Synapse
Receiving neuron
Sending neuron
Neuro-transmitter
Metabolizing enzyme
Transporter
Neurotransmitter
Degradation enzyme
Receiving neuron
Receptor
Cellular response

Chemical synapses – Modification of signals through release of neurotransmitter

Depolarization of terminal knob & presynaptic memb.

↓

Entry of Ca^{++} & Release of N.T.

↓

Diffusion

↓

Attachment to receptors on postsynaptic membrane

↓

Opening of ionic channels

↓

Flow of ions

↓

PSP (Post synaptic Potential) in postsynaptic membrane

↓

A.P. at first node of Ranvier

Structure of synapse

Presynaptic neuron

- synaptic knob – terminal button
  - synaptic vesicles
  - voltage gated Ca^{++} channels
  - Active zone
  - mitochondria

Synaptic cleft - 20 - 40 nm

Postsynaptic neuron – postsynaptic density

ionic channels and receptors

Mechanism of synaptic transmission

- basic steps

-**Calcium entry** depends upon- ?

-repetition of A.P.

-Size and shape of A.P.

- Same neurotransmitter at all terminals of a neuron

- pre & post synaptic densities

- release of neuromodulator -neuropeptides

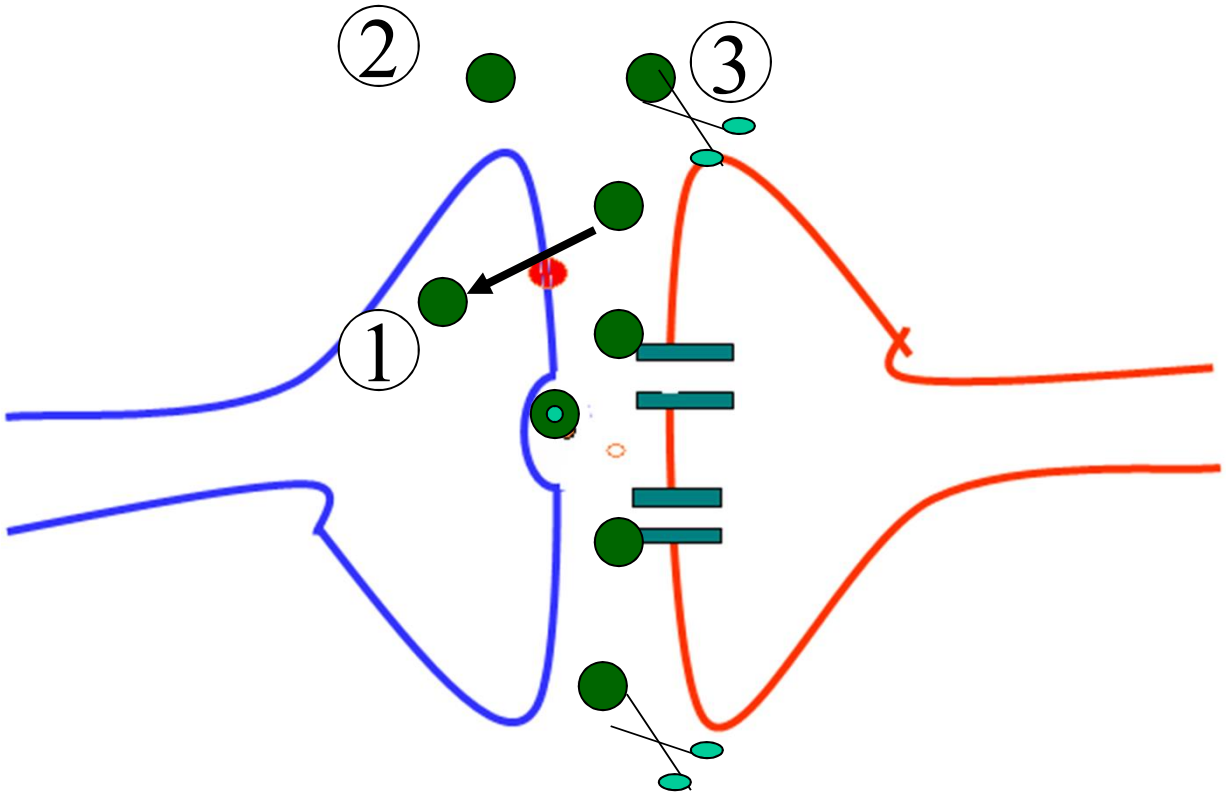
Fate of NT

PRESYNAPTIC EVENTS

- A.P. reaching synaptic knob
- Opening of voltage gated Ca^{++} channels located at active zone
- Entry of Ca^{++} from ECF causing fusion of vesicles to presynaptic membrane
- Exocytosis of NT along with neuromodulators
- Decreased Ca^{++} due to Ca^{++} pump
- Recycling of membrane

Fate of Neurotransmitter –

1) reuptake – by same neuron or glial cells
2) diffusion
3) enzymatic degradation



POSTYNAPTIC EVENTS

- Attachment of NT to receptors on postsynaptic membrane
- Opening of ligand gated ionic channels
- Entry or exit of ions along electrochemical gradient
- Depolarization or hyperpolarization

  Summation and initial spike at axon hillock and initial unmyelinated segment

  A.P. at first node of Ranvier

Post Synaptic Potential - PSP

Excitatory - EPSP

Opening of Na^+ & Ca^{++} ionic channels

↓

Entry of Na^+ & Ca^{++} ions

↓

Depolarization of postsynaptic membrane magnitude 8 mV,

Inhibitory - IPSP

Opening of K^+ & Cl^- channels

↓

Entry of Cl^- or exit of K^+

↓

Hyperpolarization magnitude - -2 mV

opening of ionic channels

indirect or metabotropic

-channel looks inwards

-signal from within cell

-coupled through G-protein in membrane & activate cAMP

-provide amplification, prolongation. Control by cell

e.g. muscarinic receptors, adrenergic receptors

direct or ionotropic

-channel looks outwards

-signal from outside

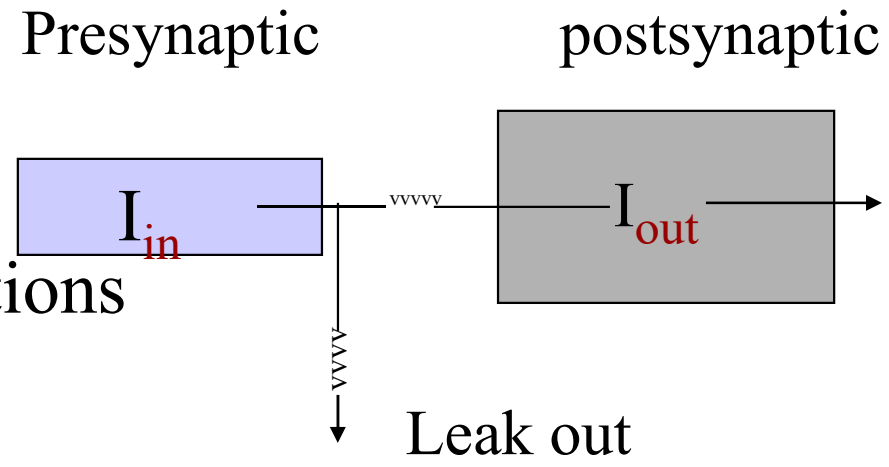
-Receptor forms part of channel protein

-fast & secured action

e.g. nicotinic receptors, GABA & glycine receptors

– Electrical synapses

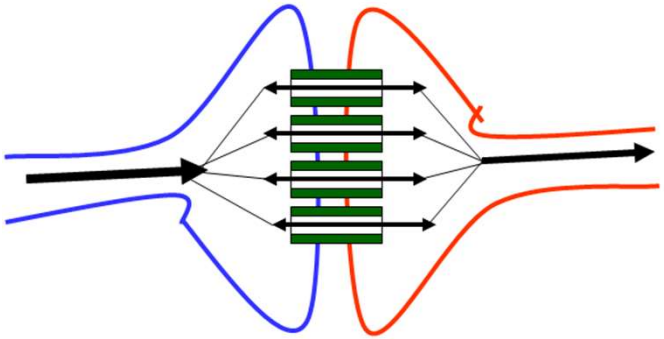
- Gap junctions & tight junctions
- Two way transmission



Mechanism of transmission

- Factors affecting amount of current

•Transmembrane resistance
•Leakage current
•Size of postsynaptic neuron
•Photoreceptors in retina
•Area of contact



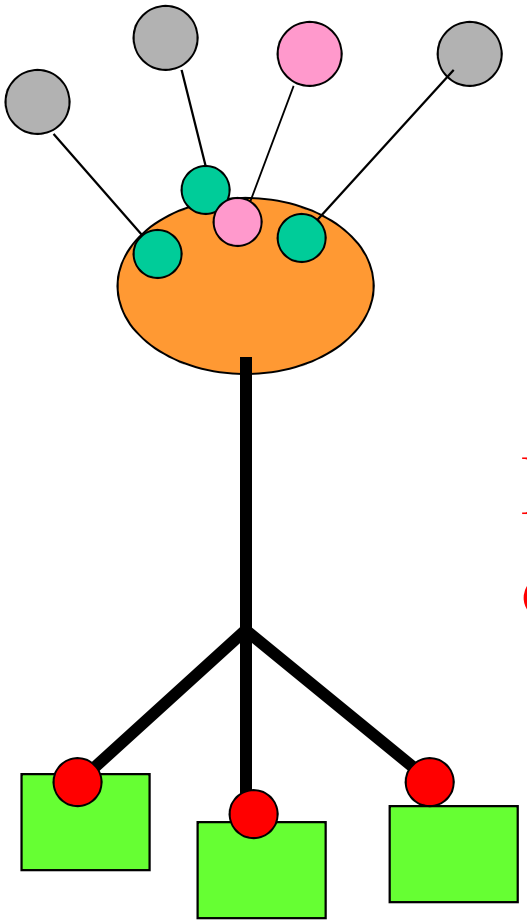
Properties of synapses

1. Convergence and divergence
2. One way conduction
3. Synaptic delay – 0.5 msec.
4. More susceptibility to hypoxia than nerve
5. Site of fatigue
6. Summation of response – synaptic integration
   - Spatial summation
   - Temporal summation
7. Occlusion and facilitation
8. Habituation & sensitization
9. Post tetanic potentiation

PROPERTIES OF SYNAPSE

A neuron Postsynaptic to one synapse can be presynaptic to another synapse .

I Convergence and Divergence



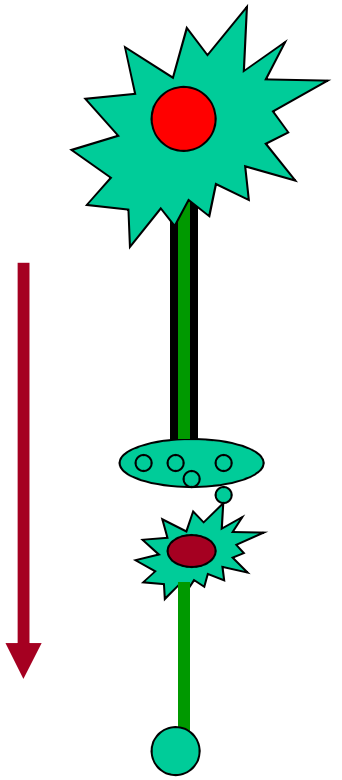
Summated activity at axon

Increases field of activity

Forms basis for facilitation, occlusion and reverberation

II. One way conduction (Law of forward conduction)

Presynaptic neuron ⟶ Postsynaptic neuron



-Helps in orderly neuronal function

III. Synaptic Delay

Minimum – 0.5 msec.

For release of NT

action of NT on receptors

Helps to know no. of synapses in reflex arc.

IV. Susceptibility for hypoxia

more than nerve

V. Site of fatigue –

diminished response on repeated stimulation

causes – Presynaptic

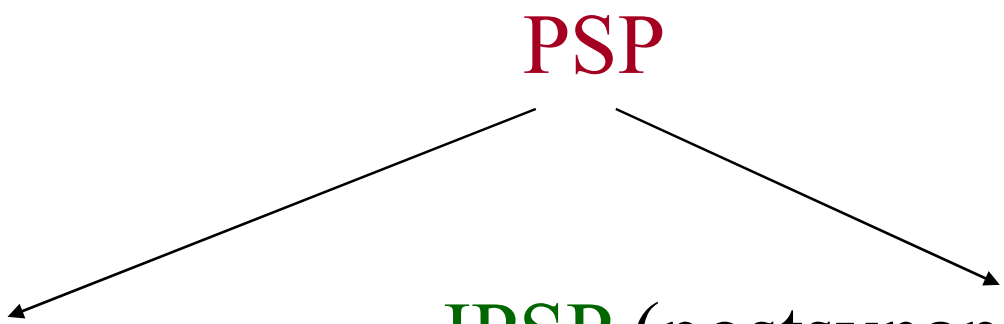
Exhaustion of NT.,

Inactivation of Ca++ channels

VI. Postsynaptic potentials :

Single stimulus –PSP. (but no A.P.)

PSP - starts within 0.5 msec. and peak 1-1.5 msec



EPSP

Opening of Na^+ or Ca^{++} Channels

increased excitability

IPSP (postsynaptic inhibition)

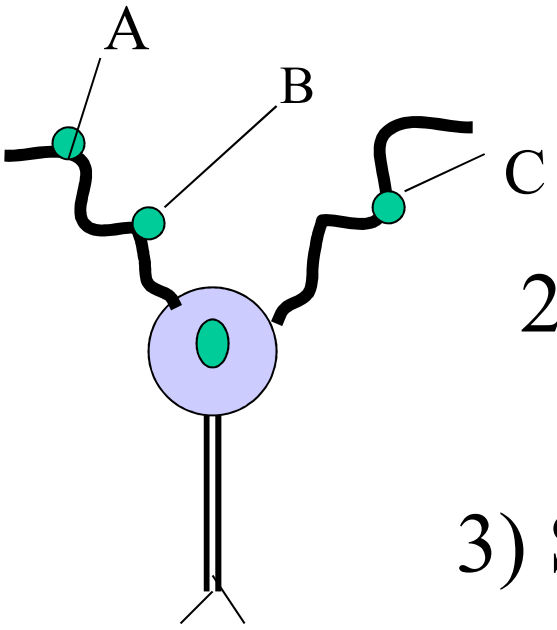
Opening of Cl^- or K^+ channels

Decreased excitability

VII. Summation of response

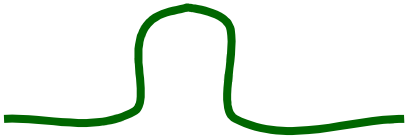
Spatial Summation –PSP separated in space –different sites on soma or dendrites

Temporal Summation – separation in time – subsequent PSP before decay of previous response

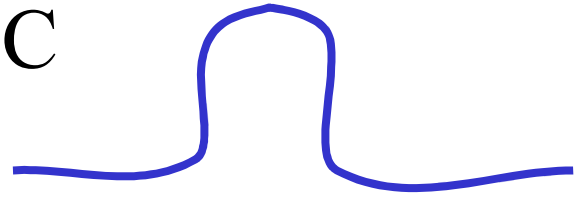


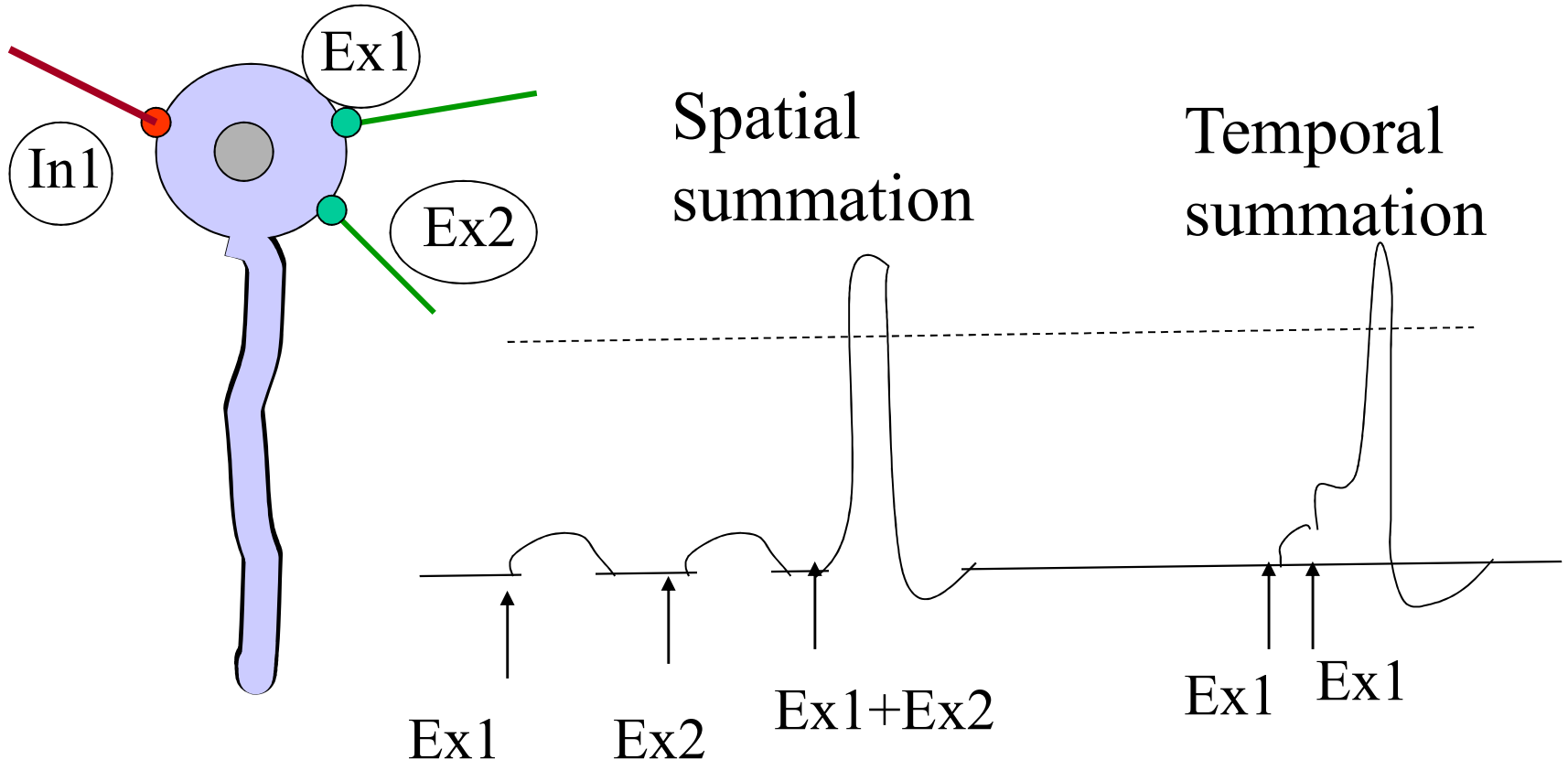
1) Stimulation at A

2) Stimulation at A + B



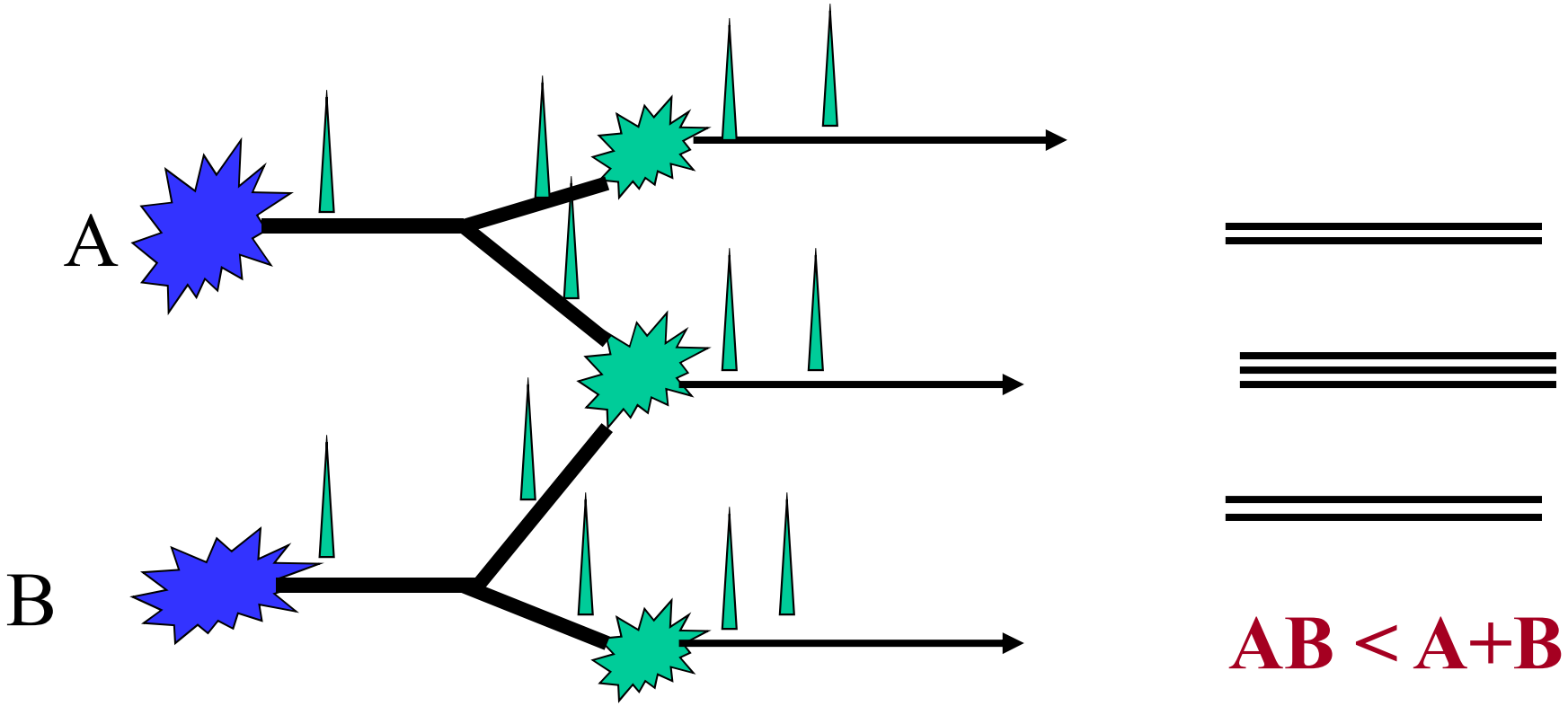
3) Stimulation at A + C




Ex1
In1
Ex2
Spatial
summation
Temporal
summation
Ex1
Ex2
Ex1+Ex2
Ex1
Ex1

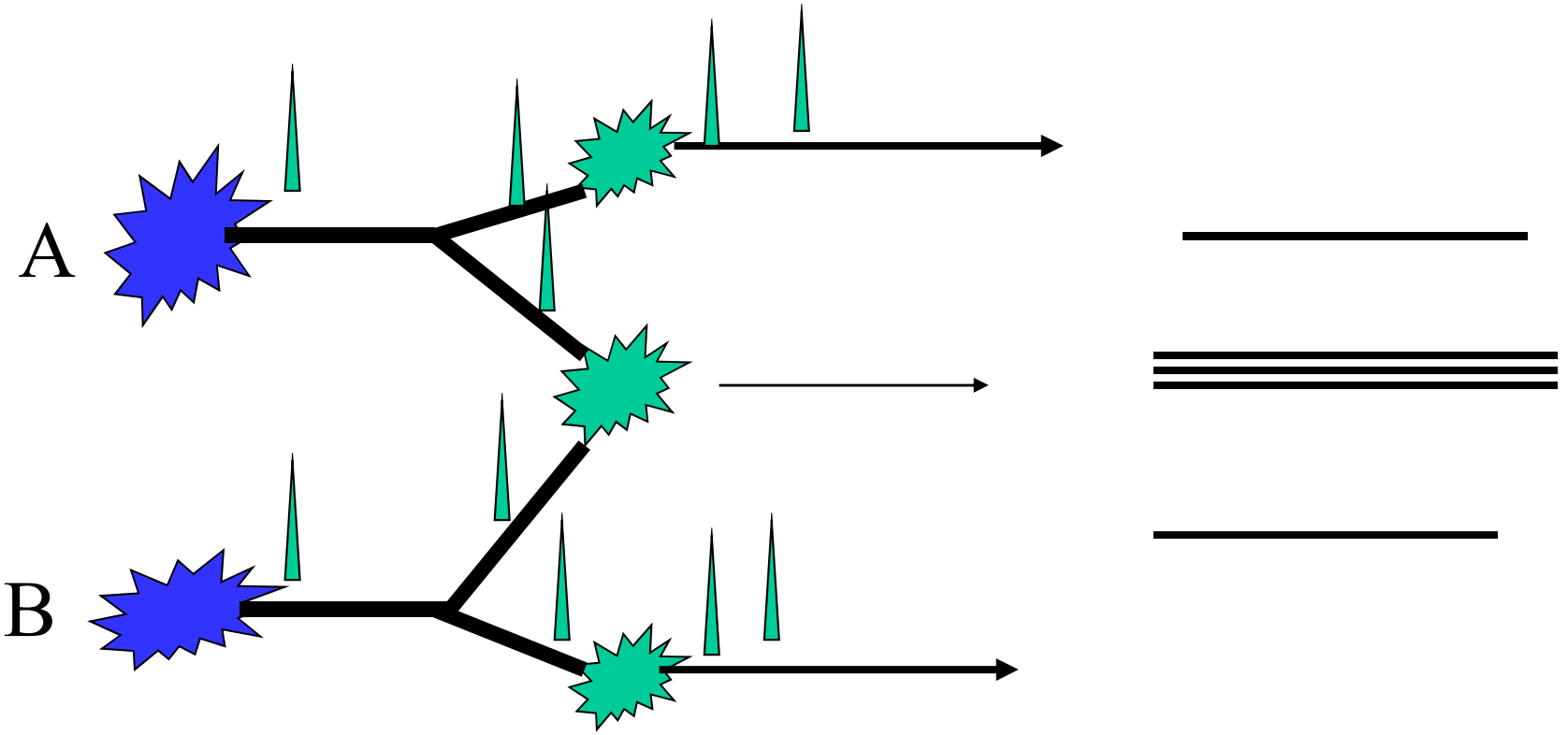
VIII.Occlusion –

Effect of strong stimulation of two afferents on a neuron is less than the sum of effect of individual neuron



IX. Facilitation and subliminal fringe effect

Weak stimulus may cause discharge from some neurons but only increase excitability of other neurons



IX. Synaptic plasticity-

changes in the effectiveness of chemical synapses on the basis of previous experience

1. Post tetanic potentiation - after repeated stimulation of presynaptic neuron ↑PSP for min. to hrs - due to ↑Ca^{++} in presynaptic neuron
2. Long term potentiation – due to ↑ Ca^{++} entry in postsynaptic neuron- hippocampus involved in memory
3. Sensitization – prolonged occurrence of ↑PSP when stimulus is once or more times paired with painful stimulus – presynaptic facilitation

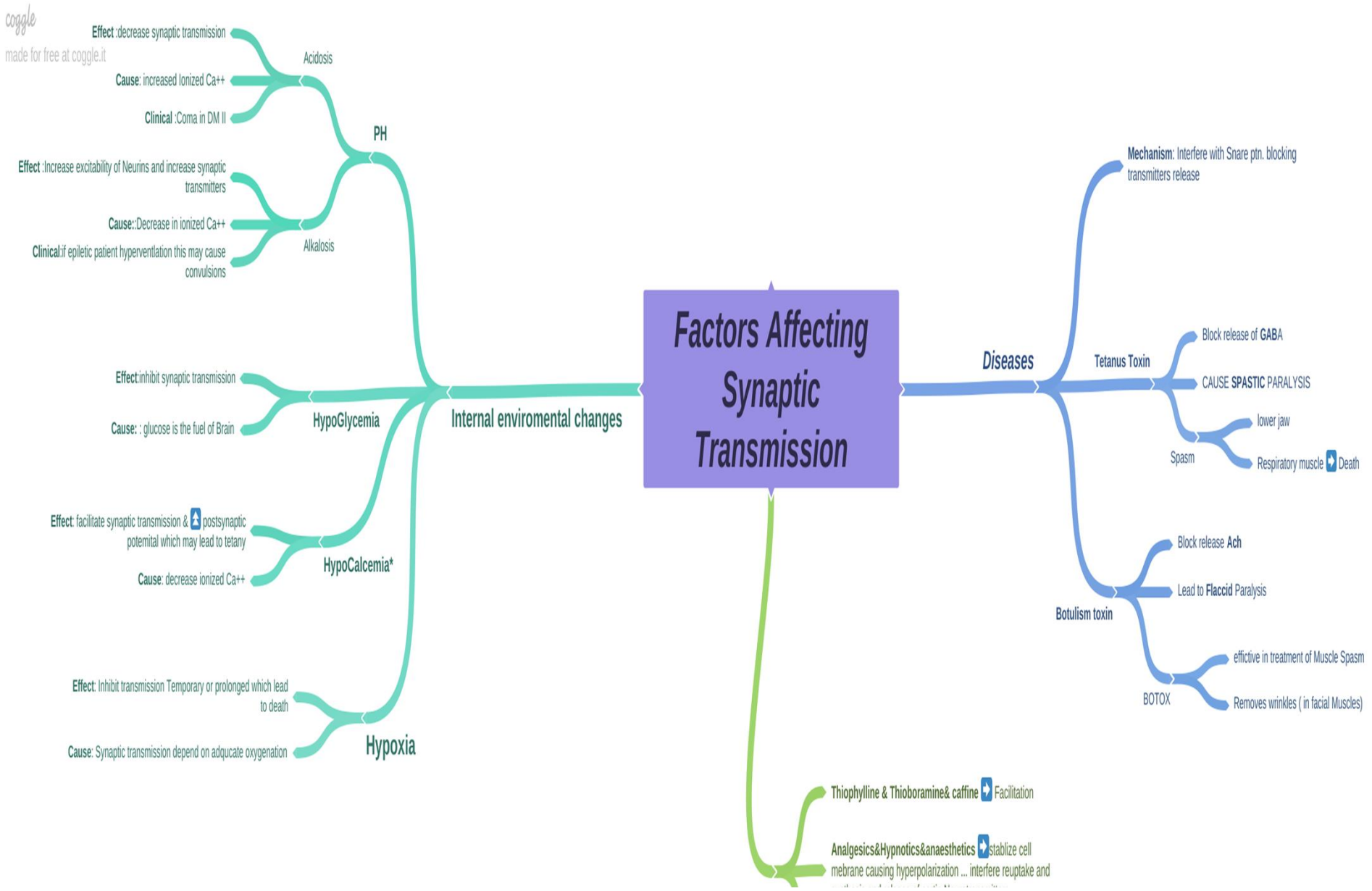
Applied :-

1) Drugs acting by altering synthesis, axonal transport, storage or release of NT-e.g. –tetanus toxin and botulinum toxin

2) They can modify NT-receptor interaction

    1) E.g. cocain blocks reuptake of dopamine and prolongs action of GABA

    2) Strychnine compete with glycine and produces convulsions


coggle
made for free at coggle.it
Factors Affecting Synaptic Transmission
Internal enviromental changes
PH
Acidosis
Effect :decrease synaptic transmission
Cause: increased Ionized Ca++
Clinical :Coma in DM II
Alkalosis
Effect :Increase excitability of Neurins and increase synaptic transmitters
Cause::Decrease in ionized Ca++
Clinical:if epiletic patient hyperventlation this may cause convulsions
HypoGlycemia
Effect:inhibit synaptic transmission
Cause: : glucose is the fuel of Brain
HypoCalcemia*
Effect: facilitate synaptic transmission & postsynaptic potemital which may lead to tetany
Cause: decrease ionized Ca++
Hypoxia
Effect: Inhibit transmission Temporary or prolonged which lead to death
Cause: Synaptic transmission depend on adqucate oxygenation
Diseases
Tetanus Toxin
Mechanism: Interfere with Snare ptn. blocking transmitters release
Block release of GABA
CAUSE SPASTIC PARALYSIS
Spasm
lower jaw
Respiratory muscle Death
Botulism toxin
Block release Ach
Lead to Flaccid Paralysis
BOTOX
effictive in treatment of Muscle Spasm
Removes wrinkles (in facial Muscles)
Thiophylline & Thioboramine& caffine Facilitation
Analgesics&Hypnotics&anaesthetics stablize cell mebrane causing hyperpolarization ... interfere reuptake and

Synaptic inhibition is **mediated by two basic circuit configurations—Feedback and feed forward**.

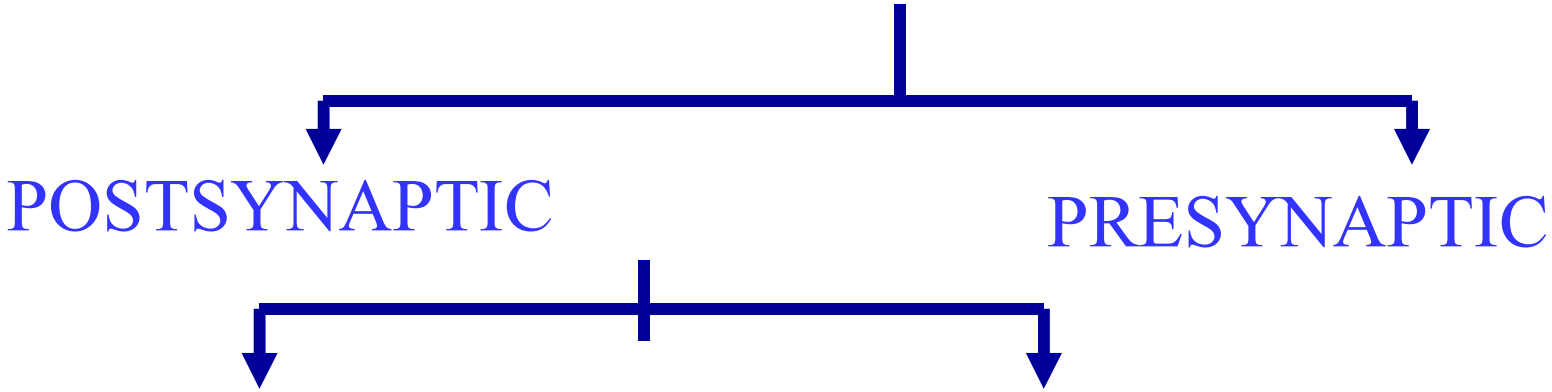
Feedback inhibition occurs when excitatory principal neurons synapse onto inhibitory interneurons, which project back to the principal neurons and inhibit them (negative-feedback loop).

Feedforward inhibition occurs when axons synapse directly onto inhibitory interneurons, inhibiting downstream principal neurons.

Synaptic inhibition

- Advantages of inhibitory synapses-
  - We can have responses like **relaxation** withdrawal
  - Movements of agonists become **smoother** due to relaxation of antagonist
  - **Prevention of explosive action** due to networks having convergence and divergence

SYNAPTIC INHIBITION



1) Golgi bottle neuron

(reciprocal innervation)

Glycine

2) Golgi tendon organ

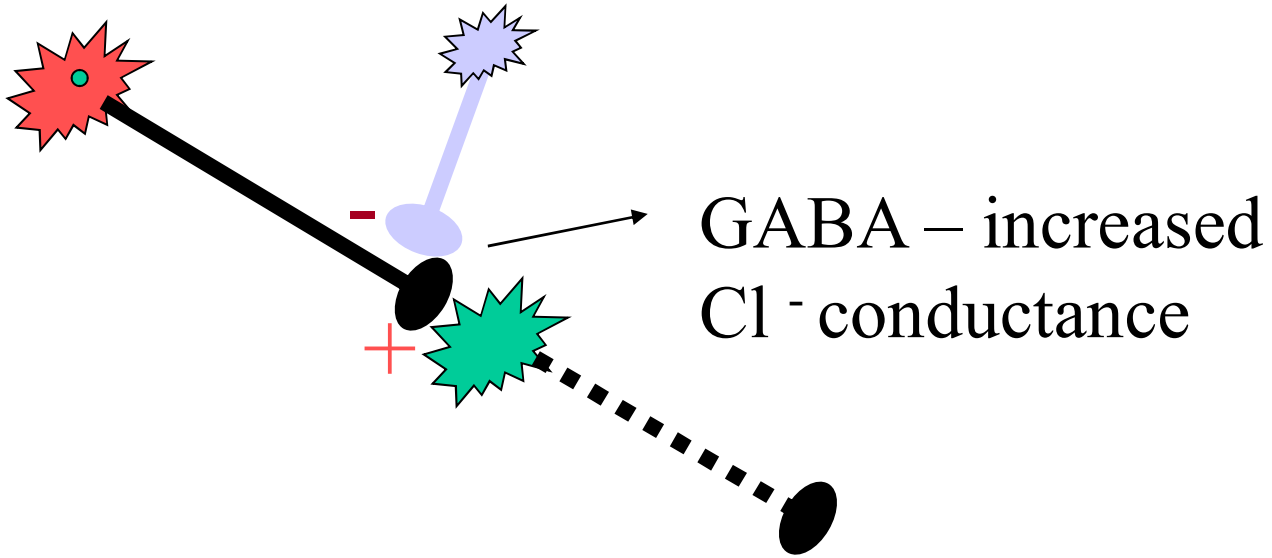
(Inverse stretch reflex)

1)Refractory period

2) Renshaw cell inhibition

Presynaptic inhibition

Inhibition of release of NT by excitatory presynaptic neuron by another neuron which forms axo-axonal synapse with the previous neuron.



Comparison bet.

Presynaptic inhibition

Precise and specific in its action.

Certain inputs are disabled while others left untouched.

Postsynaptic inhibition

generalized action on postsynaptic cell

EPSP likely to produce Action Potential is **+10 mv**

Pathway for direct inhibition is **di-synaptic pathway**

Synapse – introduced by **"Sherrington CS" (1924)**

1. Chemical synapse	2. Electrical Synapse
Synaptic cleft – Present	Absent, Low resistance bridges (Gap junction)
Synaptic delay – Present	Absent
Large number of synapses are involved	Limited numbers only

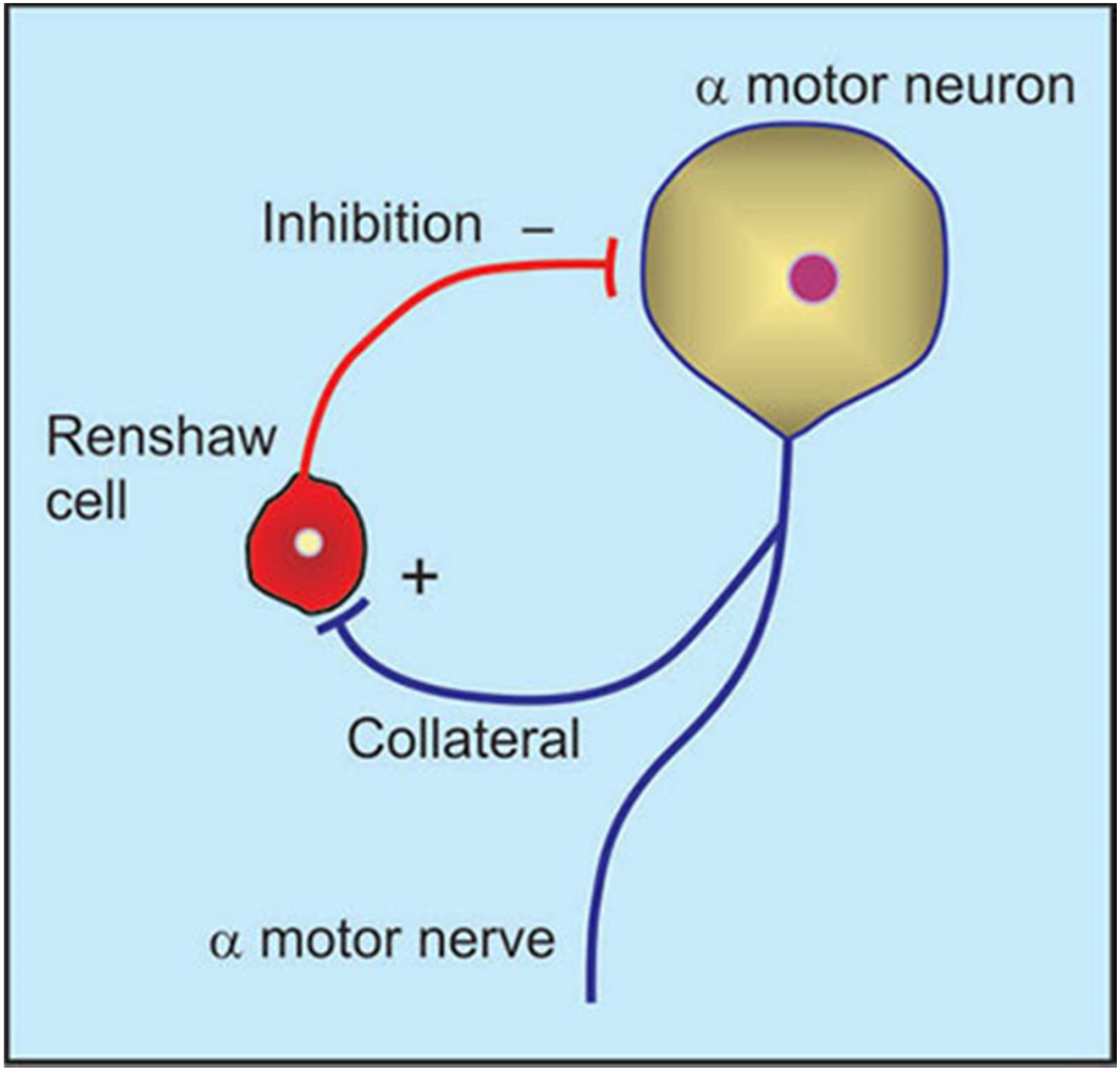
3. Conjoint Synapse

Synaptic Pathways –

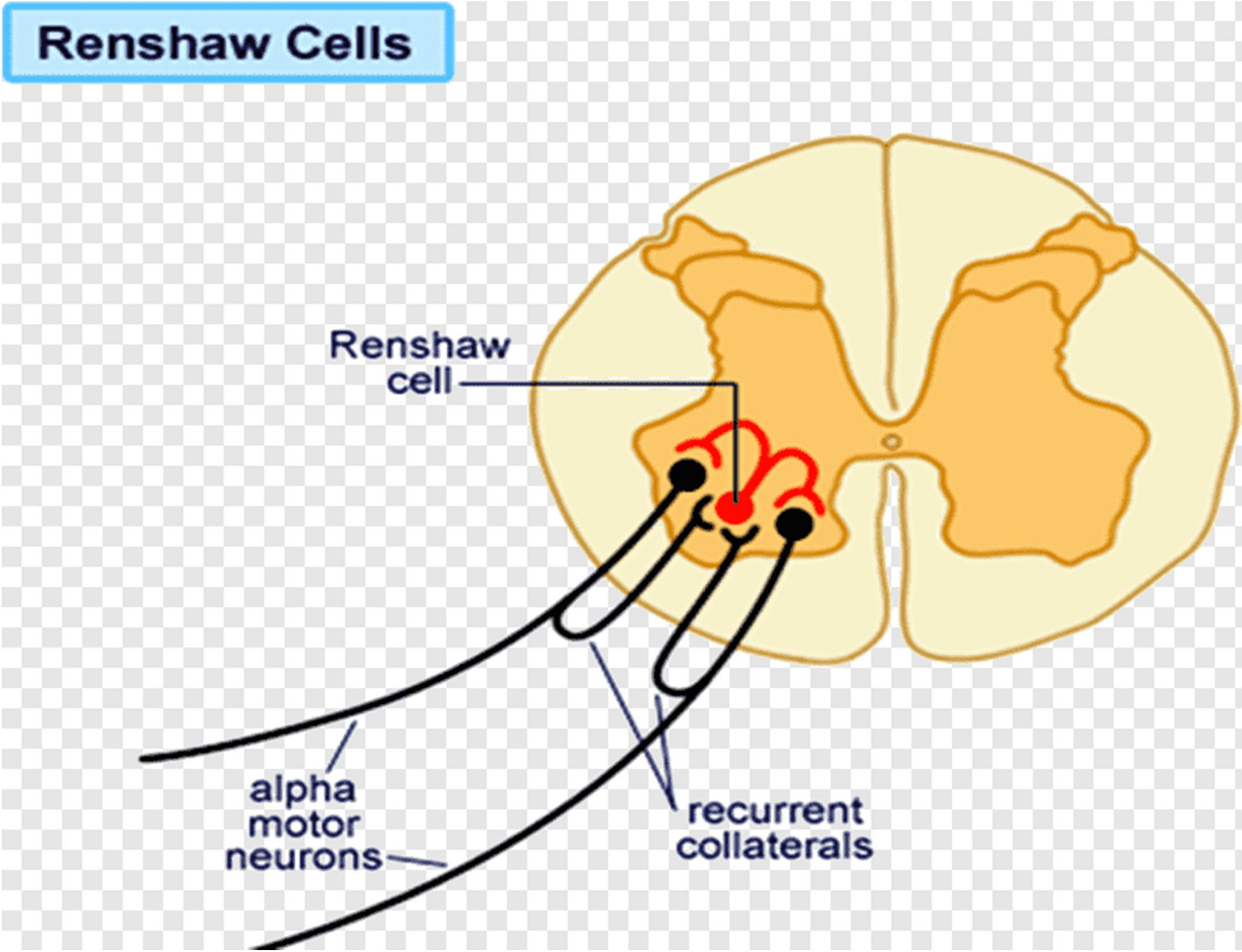
1) Monosynaptic Pathway (Stretch Reflex)
2) Di- synaptic Pathway (Inverse Stretch Reflex)
3) Multi- synaptic Pathway (Withdrawal Reflex)

What is **Renshaw cell?**

Renshaw cells are the **specialized population of spinal inhibitory interneurons that receive the output from motor neurons** (Renshaw, 1946) through excitatory collateral branches


α motor neuron
Inhibition –
Renshaw cell
+
Collateral
α motor nerve

Renshaw Cells



- **Renshaw cells** are **inhibitory interneurons found in the gray matter of the spinal cord**, and are associated in two ways with an **alpha motor neuron.**

- They receive an excitatory collateral from the **alpha neuron's axon** as they emerge from the motor root, and are thus "kept informed" of how vigorously that neuron is firing.

- **Pessimal inhibition:**

This type of inhibition developes in the excitatory synapses as a result of strong depolarization of the postsynaptic membrane under the influence of nerve impulses arriving too frequently.

- What is **feed forward inhibition?**

- Feed-forward inhibition **typically occurs between different brain areas when excitatory neurons excite inhibitory cells, which then inhibit a group of postsynaptic excitatory neurons outside of the initializing excitatory neurons' area**.

NEUROTRANSMITTERS

- Nerve endings act as transducers –

Electrical energy

Chemical energy

Conversion process involves

-Synthesis of transmitter agent

-Storage in synaptic vesicles

-Release into cleft

-Binding with receptors on postsynaptic membrane

-Removal of NT

CLASSIFICATION OF NEUROTRANSMITTERS

I. Acetyl Choline

II. Amines – catecholimines, serotonin

III. Amino acids –excitatory–glutamate, aspartate

inhibitory- glycine, GABA

IV Polypeptides – Sub P, vasopressin, endorphins,

CCK-PZ

V Purins and Pyrimidines – adenosin, APT

VI Gases – NO, CO.

About receptors for NT-

1. One NT can have different types of receptors and their subtypes-
2. Receptors may be located on presynaptic and postsynaptic membrane
3. Structural and functional groups of receptors
    a. Serpentine- acting through G-protein
    b. Part of ion channel

4. Arranged in clusters on postsynaptic membrane
5. Down regulation on prolonged exposure to ligand.

Acetyl Choline

-Acetyl ester of choline

-Small clear vesicles

-Synthesized in nerve terminal

-Hydrolyzed in synaptic cleft by choline esterase

-Receptors- Nicotinic – in muscle memb. &

- autonomic ganglia,rapid action

-Muscarinic- M1-M5-serpentine- action

through G-protein

Norepinephrine & Epinephrine-

Biologic amines,

NE at symp. Postganglionic fibers

Both byadrenal medulla and brain

Secreted in varicosities

Synthesized by tyrosin & phenylalanine

Removal by reuptake, degradation by MAO,COMPT

Receptors- α_1 & α_2 β_1 & β_2

Dopamine

In S.Nigra catecholamine synthesis stops at dopamine

Secreted as NT

Active reuptake of Dopamine

Receptors D1 -D5

Has both inhibitory (in corpus striatum), and excitatory action

Degeneration of S. Nigra - Parkinsonism

Serotonin

Seen in GIT- Myenteric plexus, brain and retina

Formed from tryptophane

Excitatory effect on motor system and inhibitory in sensory system also acts as neuromodulator

Glutamate

Excitatory amino acid

Most abundant in brain and spinal cord

Metabotropic receptors acting through G protein, involved in synaptic plasticity

Action of glutamate on cell body causes cell death due to Ca entry

GABA

Inhibitory amino acid increases Cl or K conductance IPSP

Found in brain, retina and presynaptic inhibition in sp.cord

Diazipam potentiate action of GABA- anxietolytic, muscle relaxant

Glycine

Excitatory in brain but inhibitory in brain stem

and sp. cord

Polypeptides- Substance P -

Found in GIT, Peripheral nerves and CNS- primary afferents carrying slow pain and also involved in axon reflex, and peristalsisne

Opioid peptides- Encephalins in GIT, brain & sub. Gelatinosa in sp. cord

Purins pyrimidins-Neuromodulators, CNS depressants

Gases – NO, CO – smooth muscle relaxants