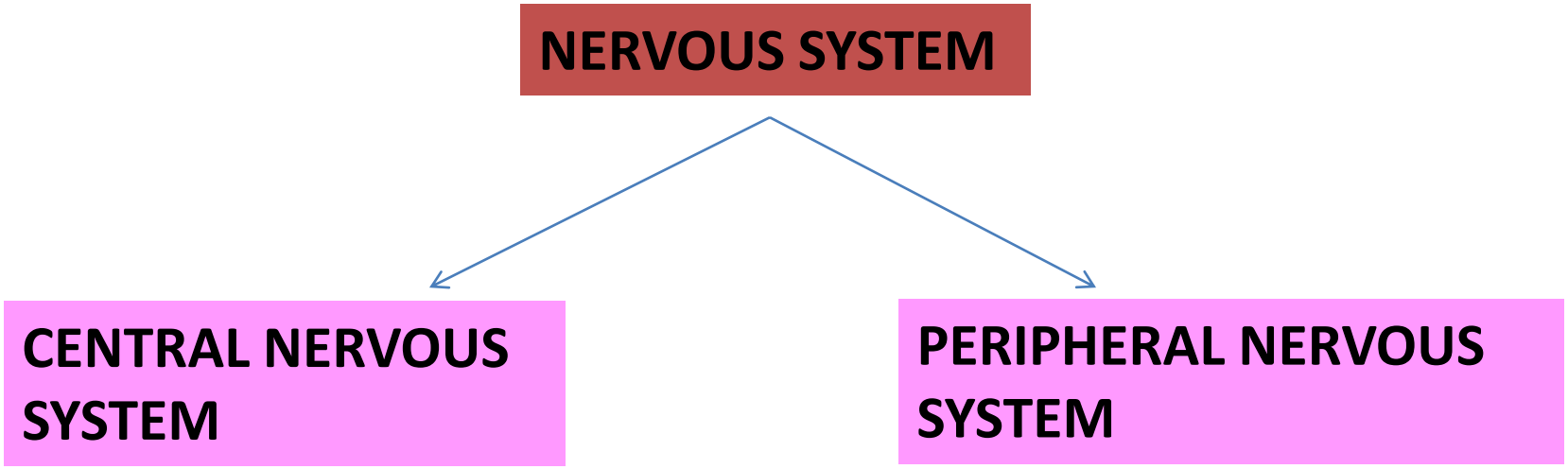
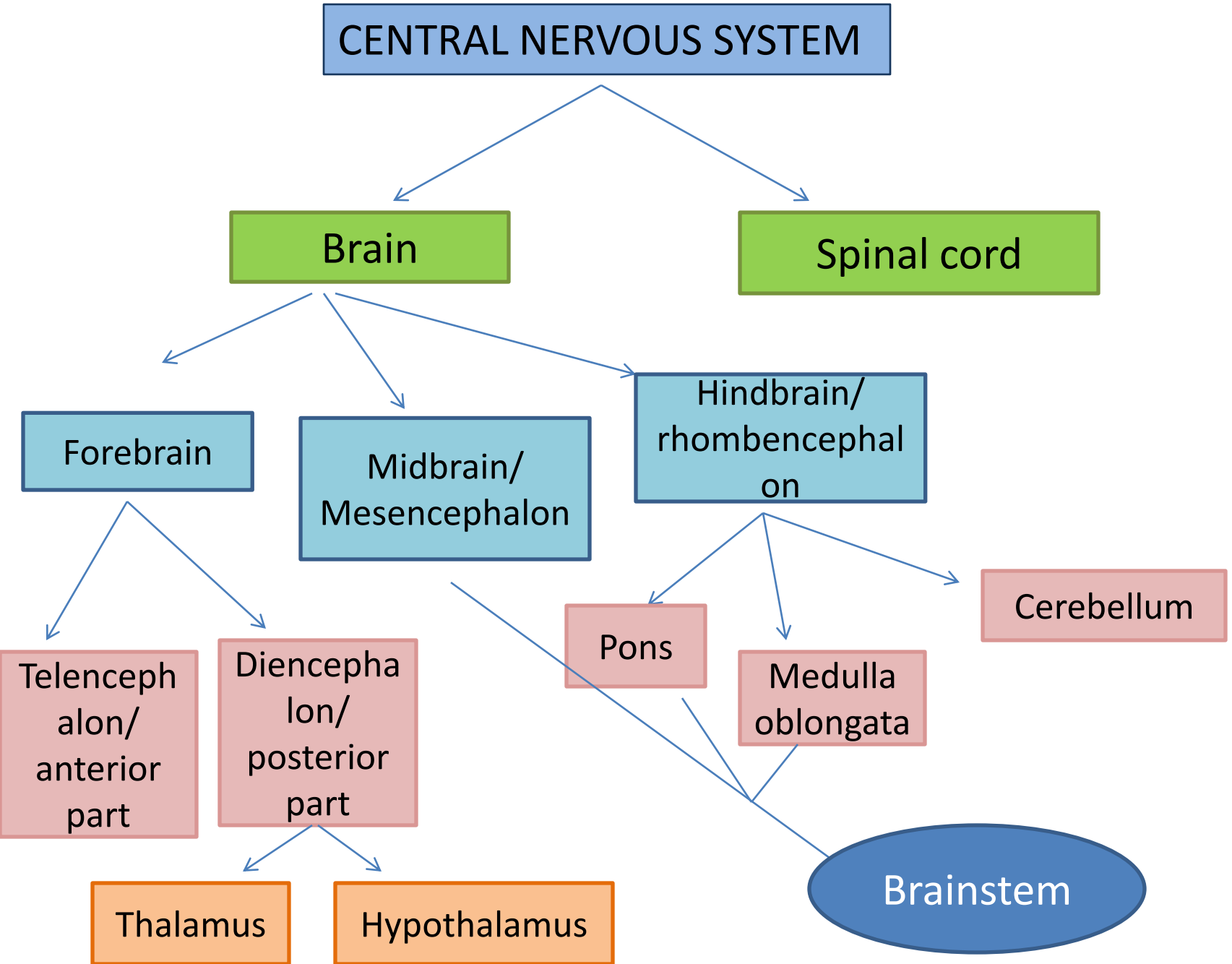
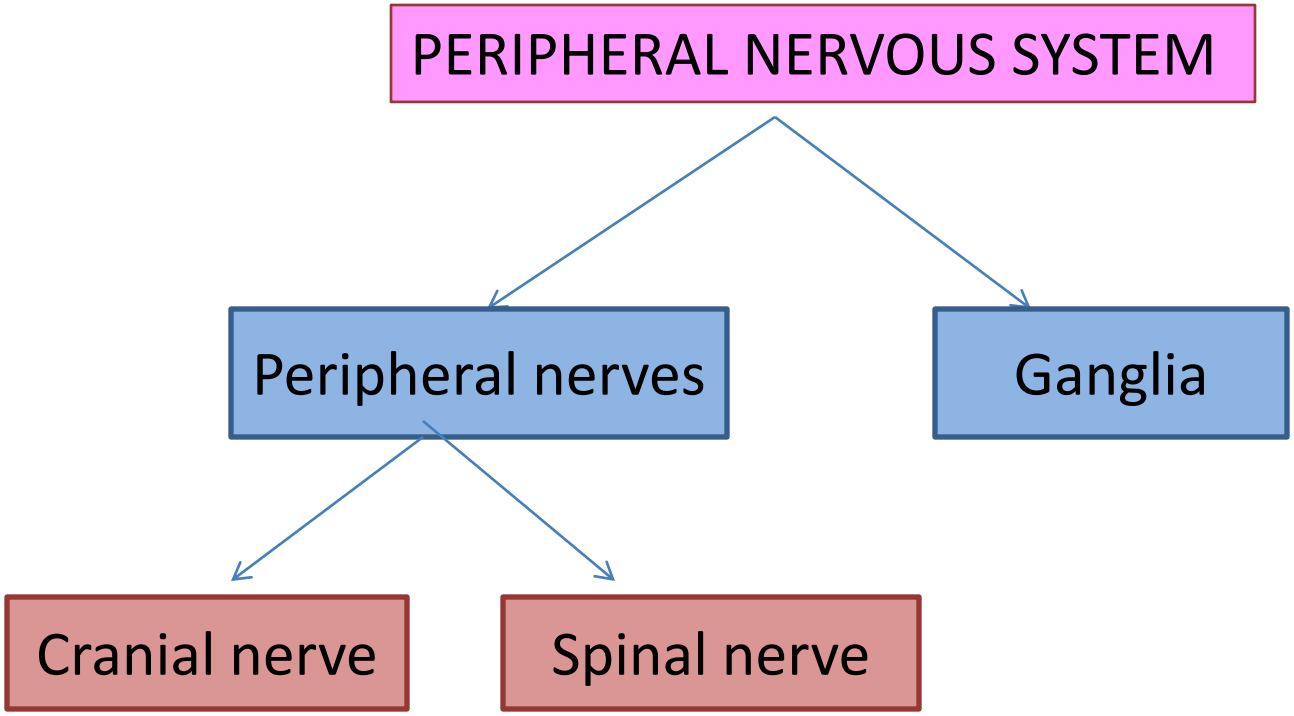
ORGANISATION OF NERVOUS SYSTEM

Dr Renu Raj R

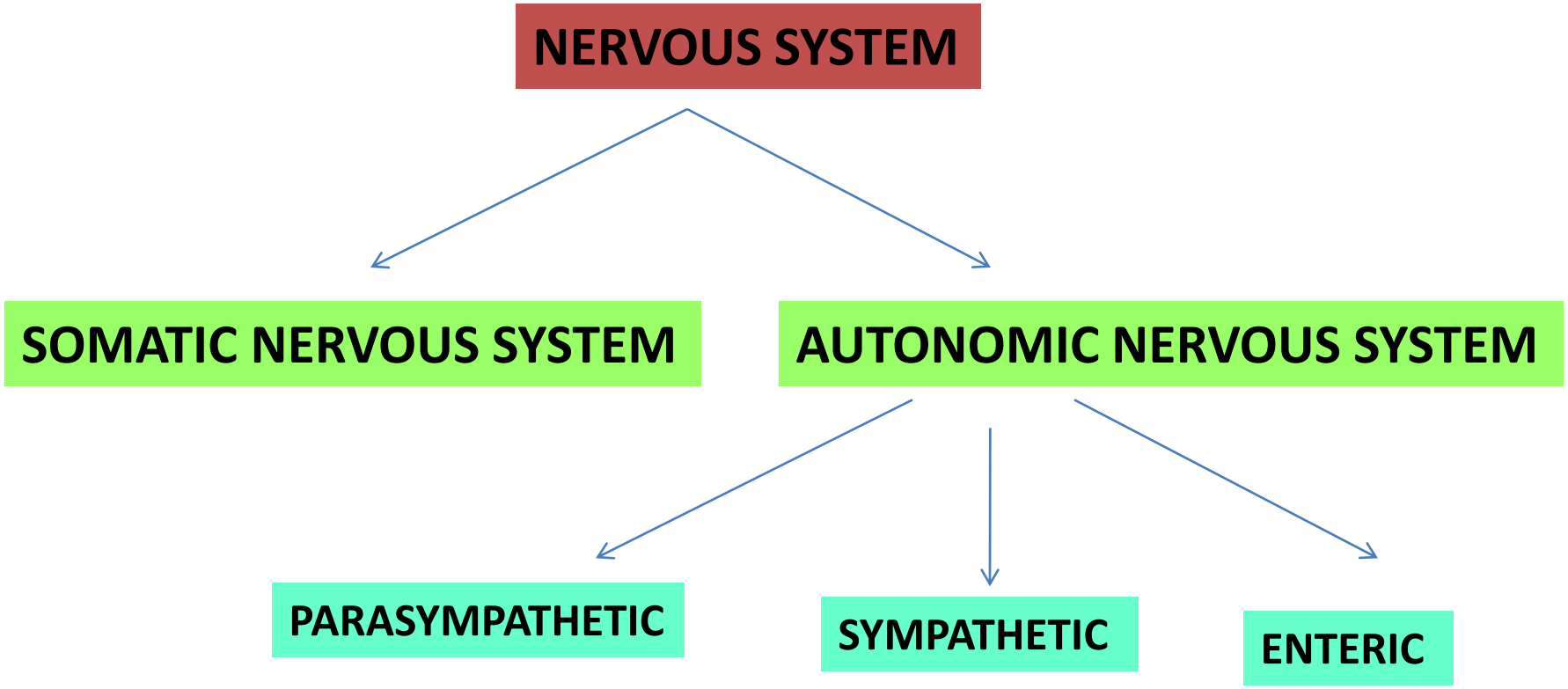
Anatomical classification




CENTRAL NERVOUS SYSTEM
Brain
Spinal cord
Forebrain
Midbrain/ Mesencephalon
Hindbrain/ rhombencephalon
Telencephalon/ anterior part
Diencephalon/ posterior part
Pons
Medulla oblongata
Cerebellum
Thalamus
Hypothalamus
Brainstem


PERIPHERAL NERVOUS SYSTEM
Peripheral nerves
Ganglia
Cranial nerve
Spinal nerve

Functional classification



SYNAPSE

Synapse

- Term coined by Sherrington
- Described histologically by Ramon y Cajal

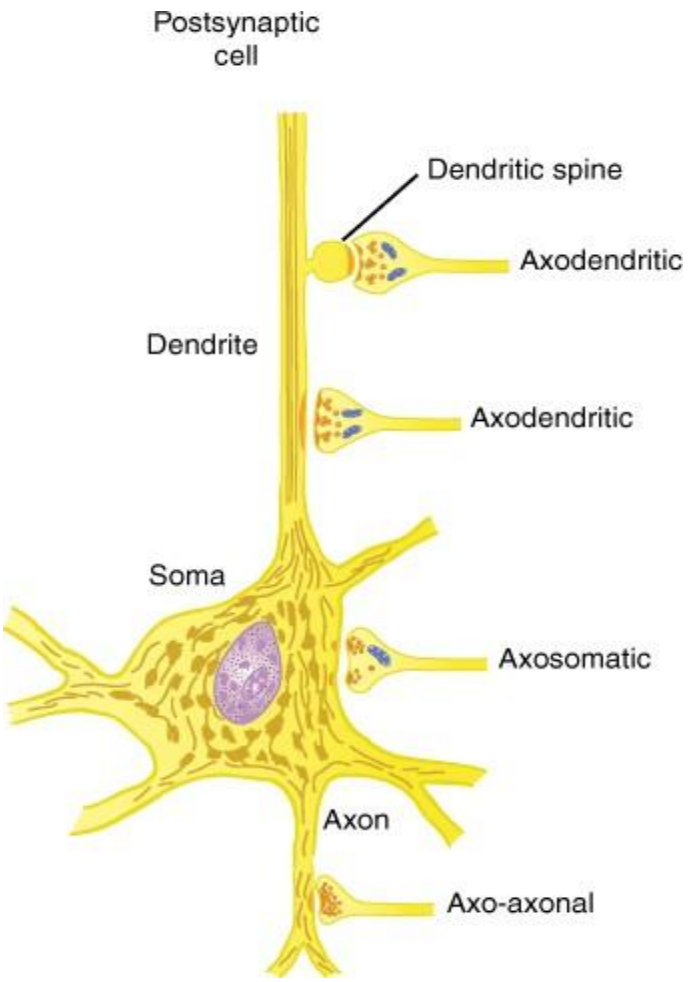
Charles Scott Sherrington

Ramon y Cajal

The Synapse

- Point of communication between two neurons
- Junction between 2 neurons
- It can also be a junction between a **Neuron and a muscle /gland cell /receptor**
- The word “Synapse” from “Synaptein” (syn –together, haptein –to fasten)

Anatomical Types of Synapses



- Axo-dendritic
- Axo-somatic
- Axo-axonal
- Dendro-dendritic

Axo –dendritic

- –Most common type
- – Axon of pre synaptic N.makes contact with dendrite of post synaptic N –on shaft of dendrites or dendritic spines
- – Seen in motor N of SC, excitatory synapses in cerebral cortex, climbing fibers in cerebellum
- – 98% of cerebral cortical & 80% of spinal cord synapses

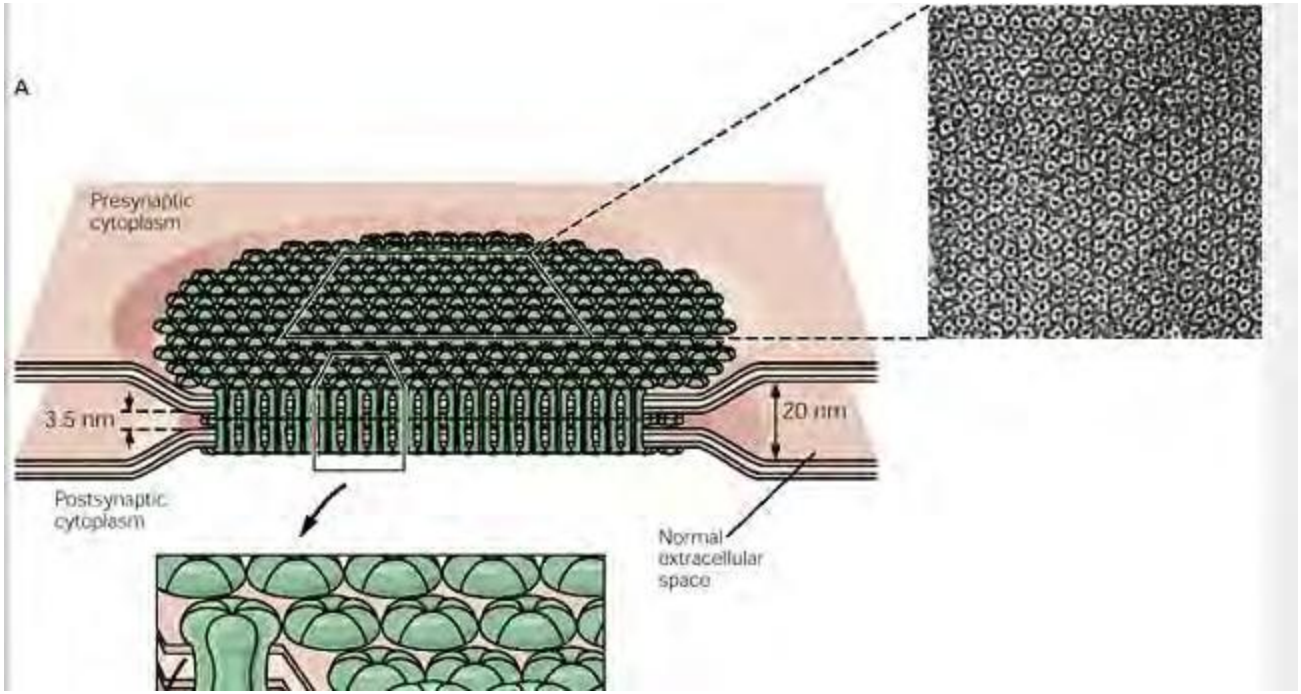
- Axo –somatic
  - Between axon and soma (body) of another neuron
  - 2 % of synapses in cerebral cortex & 20 % in spinal cord
  - Basket cells synapsing with Purkinje cells in cerebellum, autonomic ganglia

- Axo –axonal
  - Axon of 1 neuron with axon of another neuron –eg : in spinal cord
- Dendro –dendritic
  - Rare
  - Dendrite of pre synaptic with dendrite of post synaptic N
  - Eg: synapse between mitral & granule cell in olfactory bulb

Type of Synapses

- Electrical Synapses
- Chemical Synapses
- Conjoint synapse : both electrical and chemical

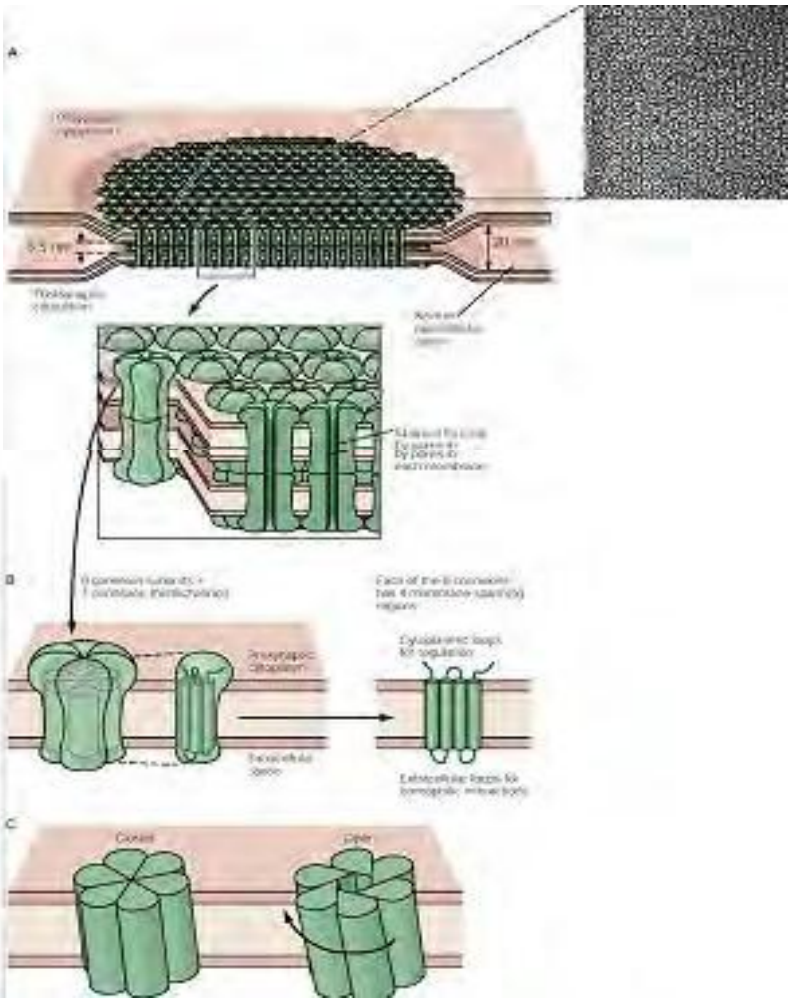
Electrical Synapses



Electrical Synapses

- Membranes of the pre and post synaptic neuron are close together
- Gap junctions form between these cells
- Ion can pass through gap junctions

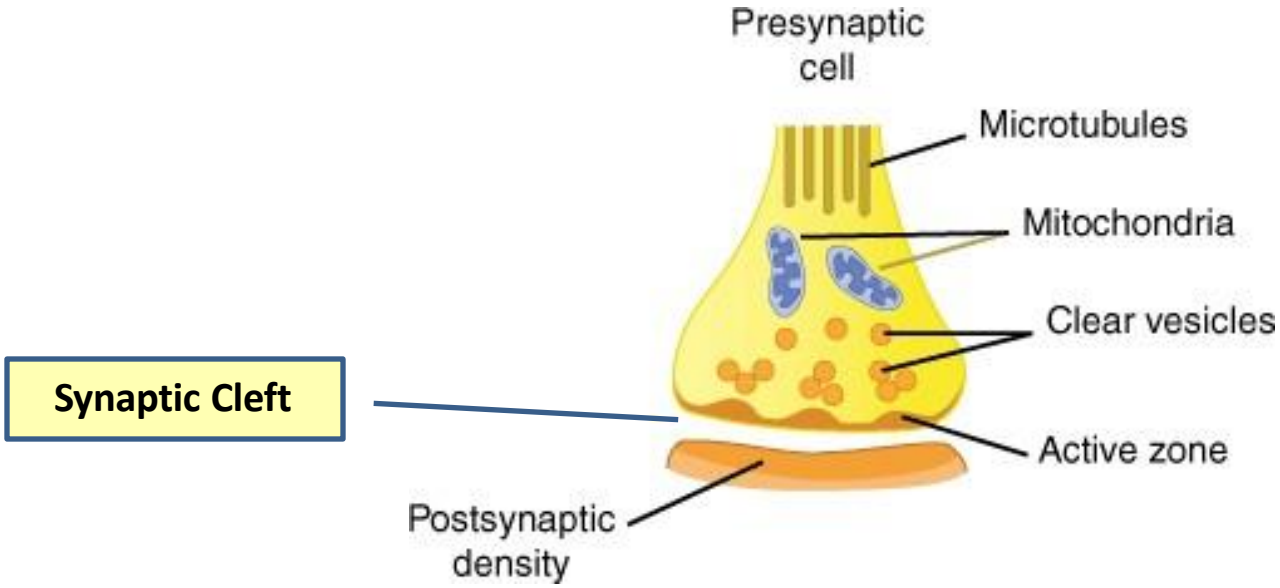
Electrical Synapses



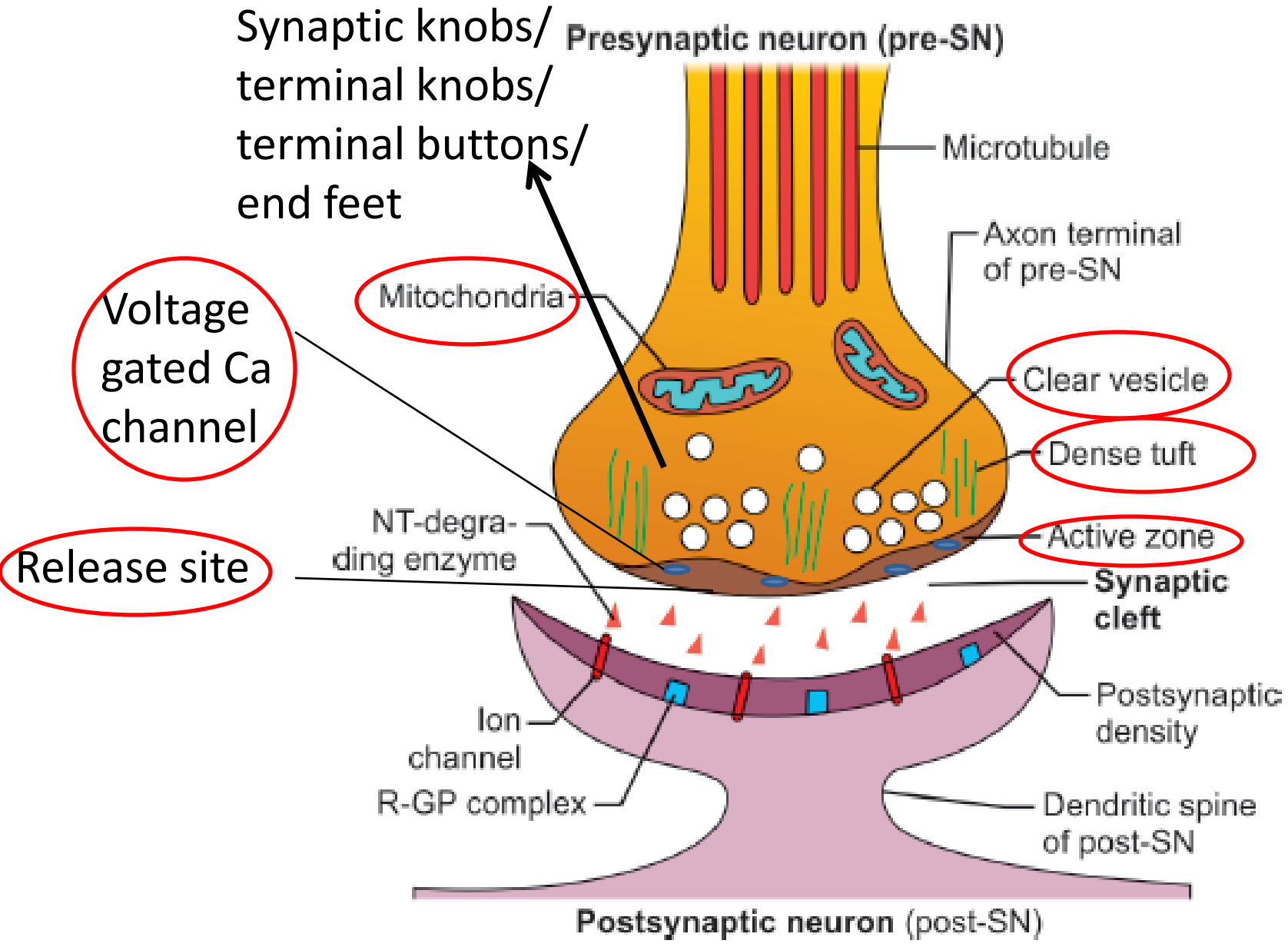
- Gap junctions contain connexins
- These are hemi channels
- Electrical synapses permit fast transmission of the action potential
- Eg in the heart for coordinated contraction

Chemical synapse

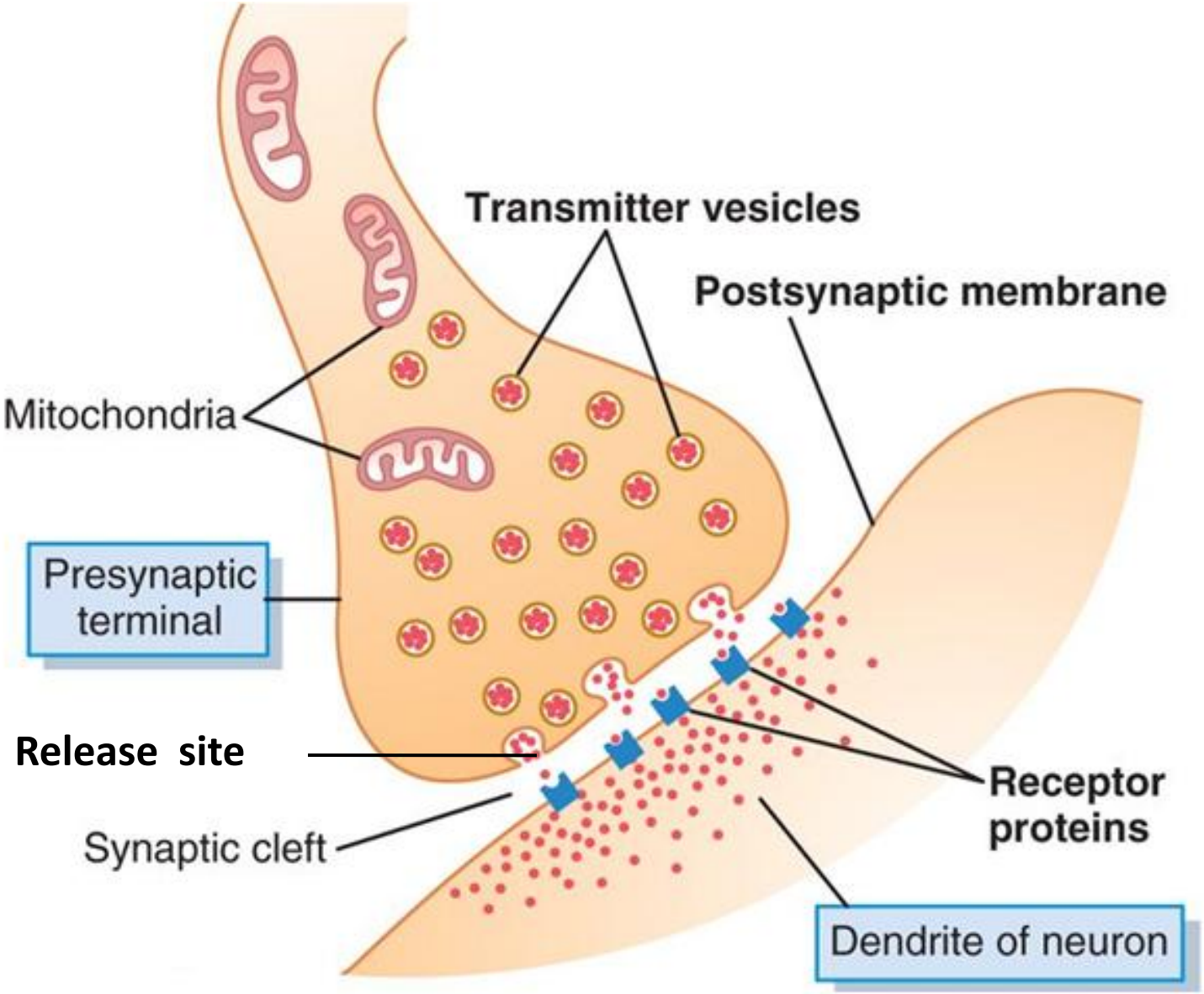
- Pre and post synaptic neuron separated by a space called the synaptic cleft



Functional anatomy of chemical



Synapse


Transmitter vesicles
Postsynaptic membrane
Mitochondria
Presynaptic terminal
Release site
Receptor proteins
Synaptic cleft
Dendrite of neuron

Functional anatomy of chemical synapse

- **Components**
  - Pre synaptic neuron
  - Synaptic cleft
  - Post synaptic neuron

Pre synaptic neuron

- Ends enlarged to form small round /oval knobs – **synaptic knobs/ terminal knobs/ terminal buttons/ end feet**
- Inside pre synaptic terminal –many mitochondria & membrane enclosed vesicles which contain neurotransmitter (NT)
- NT when released –can excite / inhibit post synaptic memb. depending on receptor
- Mitochondria provide ATP →supplies energy for synthesis of NT

- Presynaptic membrane thickened near synaptic cleft to form **Active Zone**
- Active zone contains many Voltage Gated Ca^{2+} channels
- Close to channels –many protein molecules on inner surface –**release sites**
- Release of NT vesicles into synaptic cleft occurs through these sites

Dense tuft

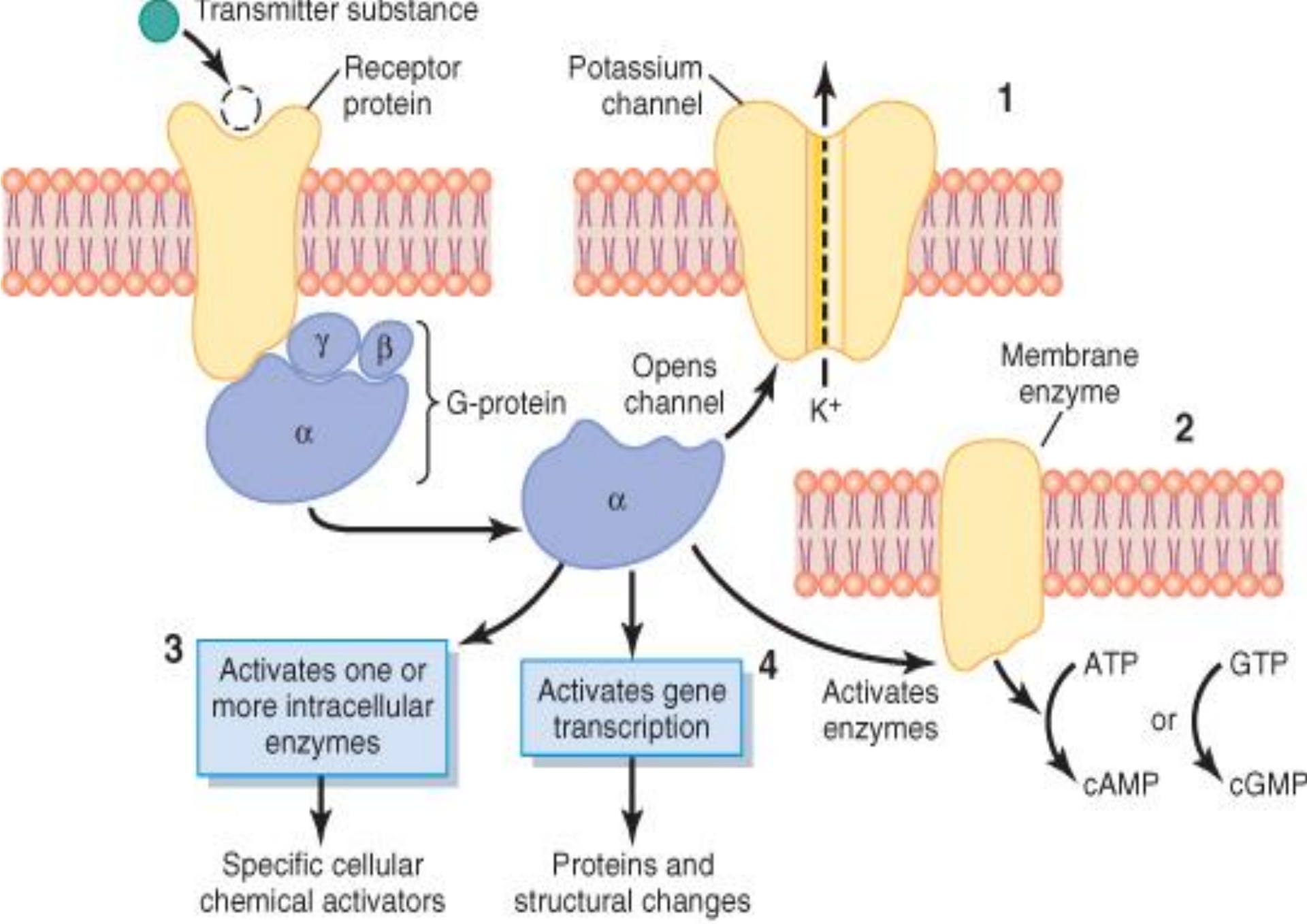
- Filamentous projections present in close contact with vesicles
- Play an important role in exocytosis of vesicle
- Present mainly in active zone

- **Synaptic cleft**
  - Presynaptic terminal is separated from post synaptic structure by synaptic cleft -20 -40nm wide
  - Cleft contains ECF & some enzymes

Post synaptic membrane

- Has a thickening –**post synaptic density** – complex of specific receptors, binding proteins & enzymes
- Receptor protein -2 components
  - **Binding component** that protrudes out from membrane into synaptic cleft –binds the NT
  - **Ionophore component** –passes all the way through post synaptic membrane to the interior

- **Ionophore** is of 2 types
  - –Ion channel –usually ligand gated
    - Cation channel –Na^+, K^+ or Ca^{++}
    - Anion channel –Cl^-
  - –2nd messenger activator
  - – Acts by activating a 2nd messenger
  - – NT attaches to a receptor & brings about the effects


Transmitter substance
Receptor protein
Potassium channel
1
γ
β
α
G-protein
Opens channel
K+
Membrane enzyme
2
α
3
Activates one or more intracellular enzymes
Specific cellular chemical activators
Activates gene transcription
4
Proteins and structural changes
Activates enzymes
ATP
GTP
or
cAMP
cGMP

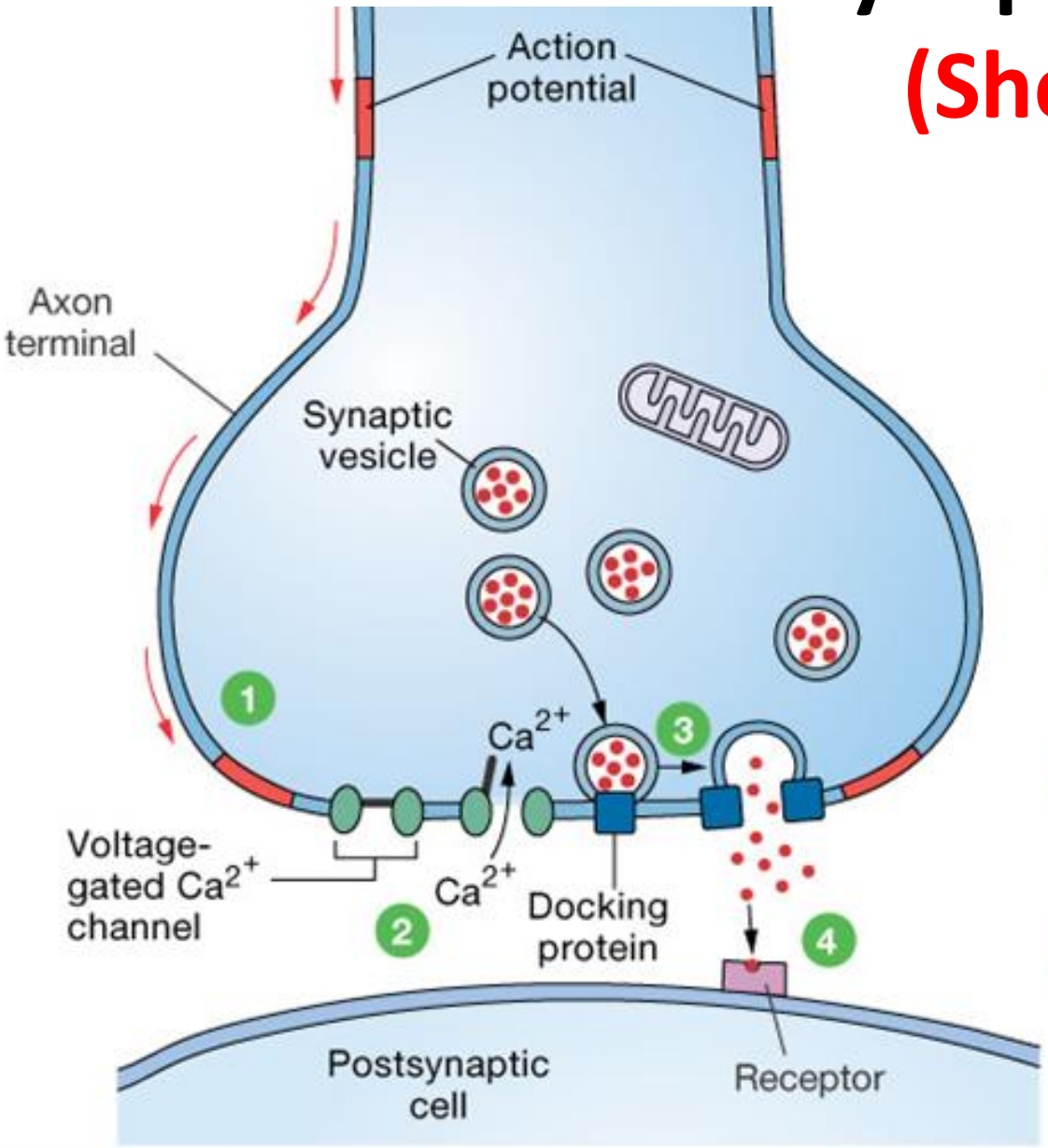
Neurexin

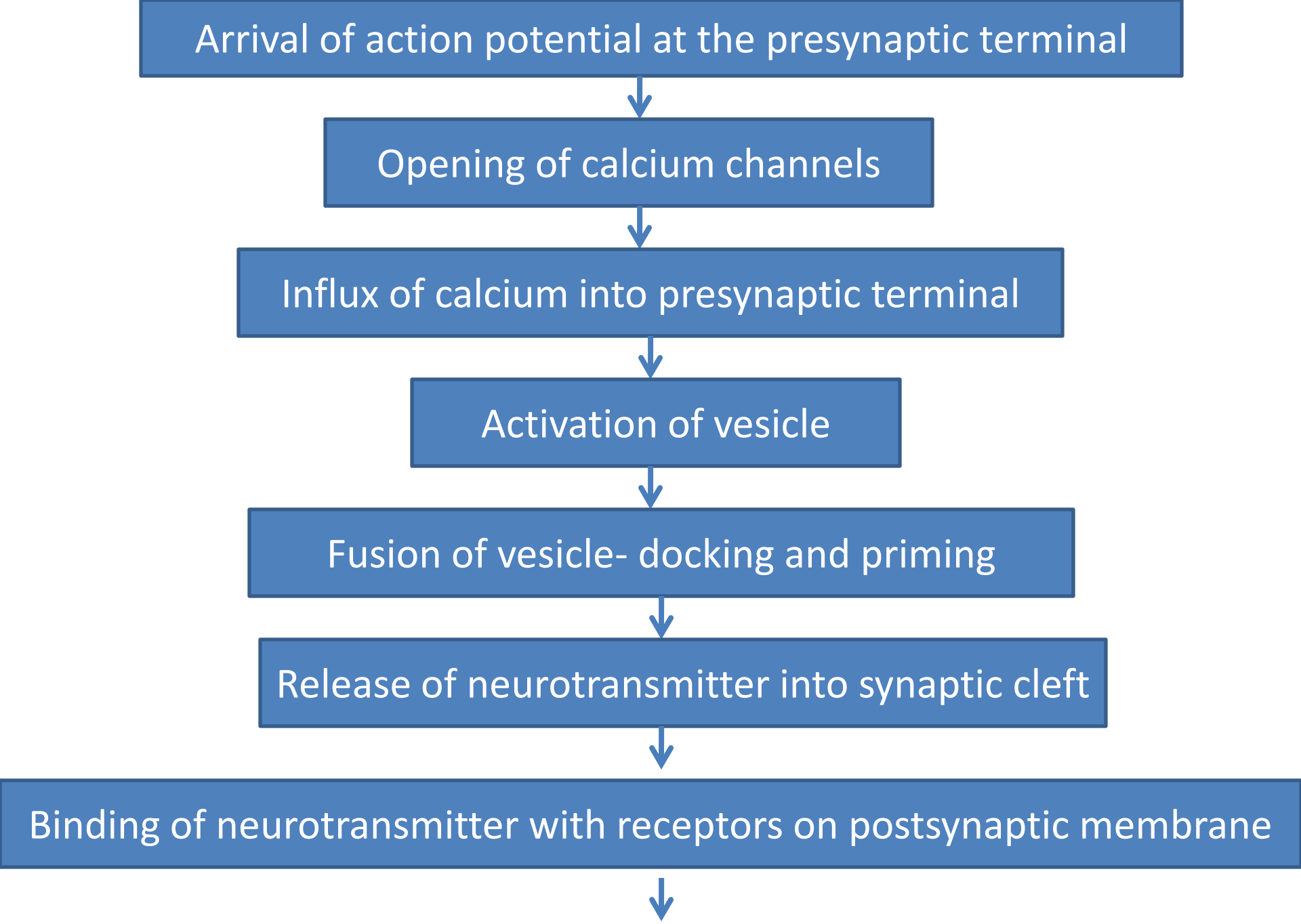
- Proteins attached to the presynaptic membrane
- Neurexin receptors in the post synaptic membrane
- Links the pre and post synaptic membrane
- Provides structural stability to synaptic architecture
- Provide basis for synaptic specificity

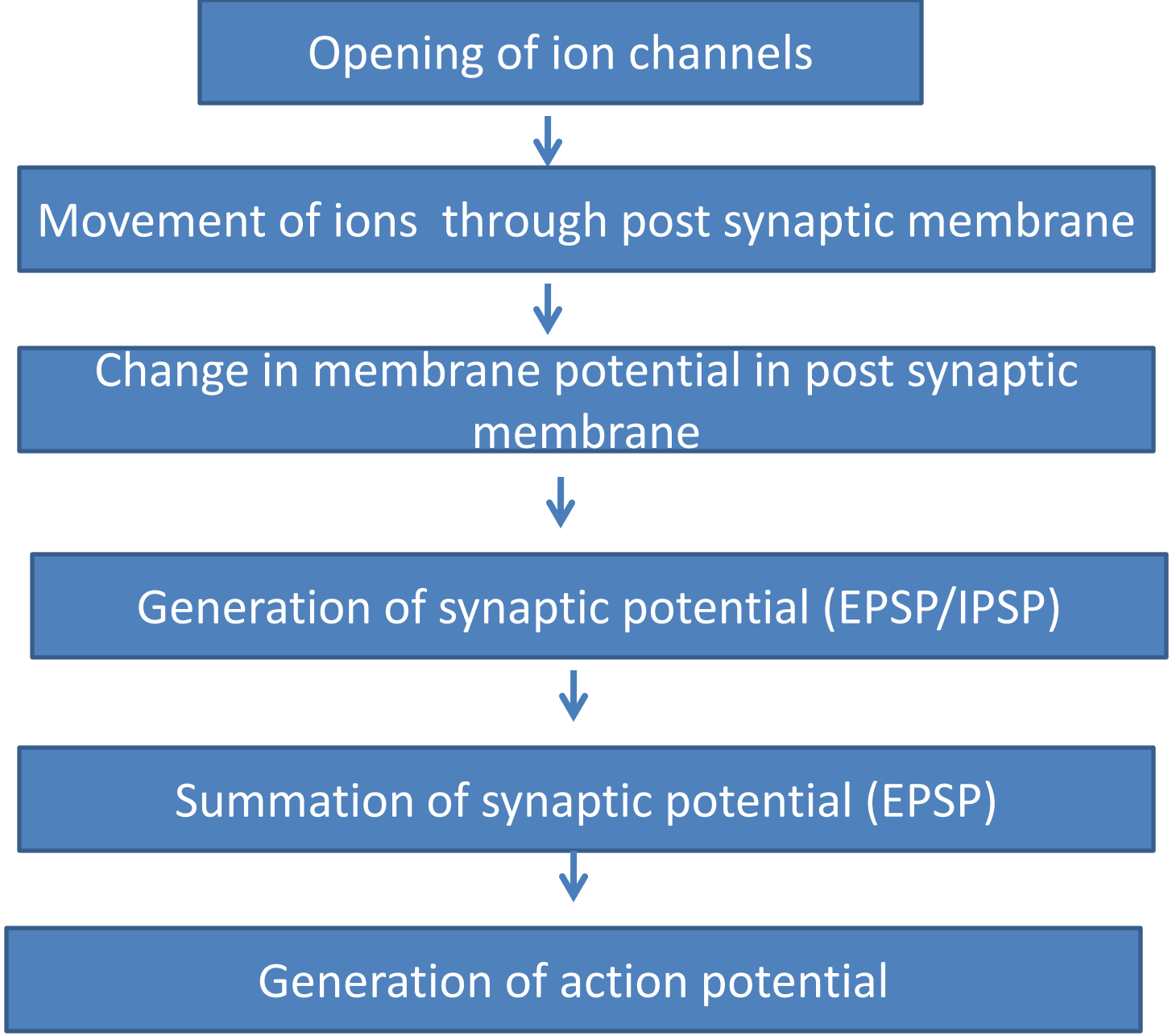
	Chemical synapse	Electrical synapse
Number	More	Very few
Synaptic cleft	20-40 nm	Membranes are close together & form gap junctions
Transmission	Via neurotransmitters	Through gap junctions
Direction	Unidirectional	In either direction
Synaptic delay	Present	Absent
Sensitivity to hypoxia	Sensitive	Insensitive
Fatigue	Present	Absent
No: of synapse per neuron	More	Few

Synaptic transmission

(Short essay)




Arrival of action potential at the presynaptic terminal
Opening of calcium channels
Influx of calcium into presynaptic terminal
Activation of vesicle
Fusion of vesicle- docking and priming
Release of neurotransmitter into synaptic cleft
Binding of neurotransmitter with receptors on postsynaptic membrane


Opening of ion channels
Movement of ions through post synaptic membrane
Change in membrane potential in post synaptic membrane
Generation of synaptic potential (EPSP/IPSP)
Summation of synaptic potential (EPSP)
Generation of action potential

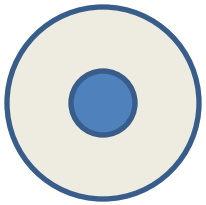
Neurotransmitters

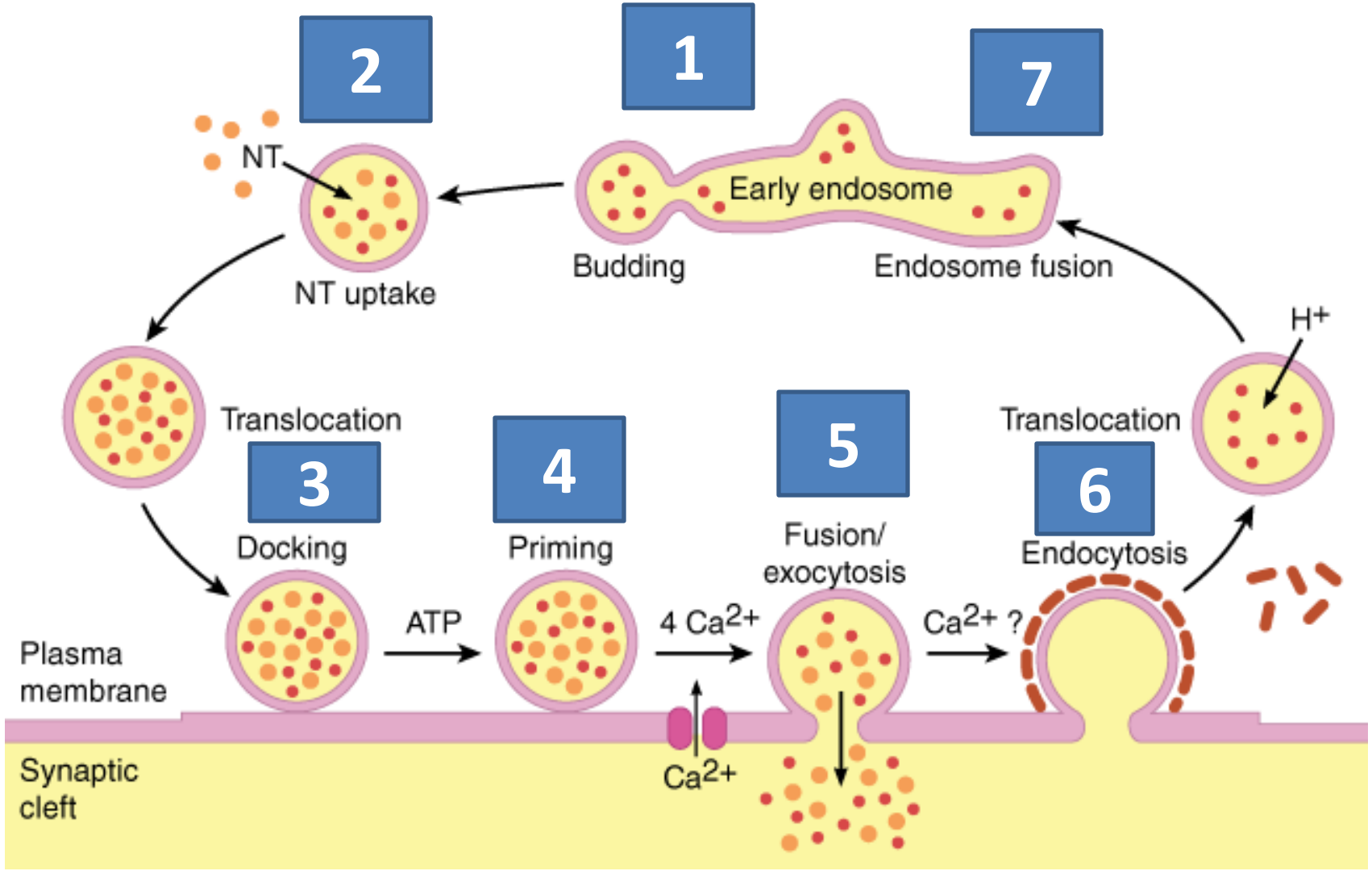
- Can be excitatory or inhibitory
- E.g. of excitatory transmitters : Glutamate, aspartate
- Eg of inhibitory neurotransmitters : GABA and Glycine

Neurotransmitter release

- Vesicles undergo docking and priming
- Docking- vesicle attach to the membrane
- Priming- vesicle become ready to discharge the content in response to stimulus

- Synaptic vesicles are of 3 types
  - **Small clear**
    - Acetyl choline, Glycine, GABA, Glutamate
  - **Small vesicles with dense core**
    - Catecholamines –NE, E, Dopamine
  - **Large vesicles with a dense core** – neuropeptides
    - TRH, GHIF, LHRH, ACTH, TSH, GH, Prolactin, vasopressin, oxytocin,endorphin etc





Recycling of neurotransmitter in presynaptic neuron terminal

- **Small synaptic vesicles cycle in presynaptic nerve terminals.**

1. Vesicles bud off the early endosome
2. Fill with neurotransmitter
3. They then move to the plasma membrane, dock,
4. Become primed
5. Ca^{2+} influx triggers fusion and exocytosis of the granule contents to the synaptic cleft

6. Vesicle wall is then coated with clathrin and taken up by endocytosis.
7. In the cytoplasm, it fuses with the early endosome

- The cycle is repeated.

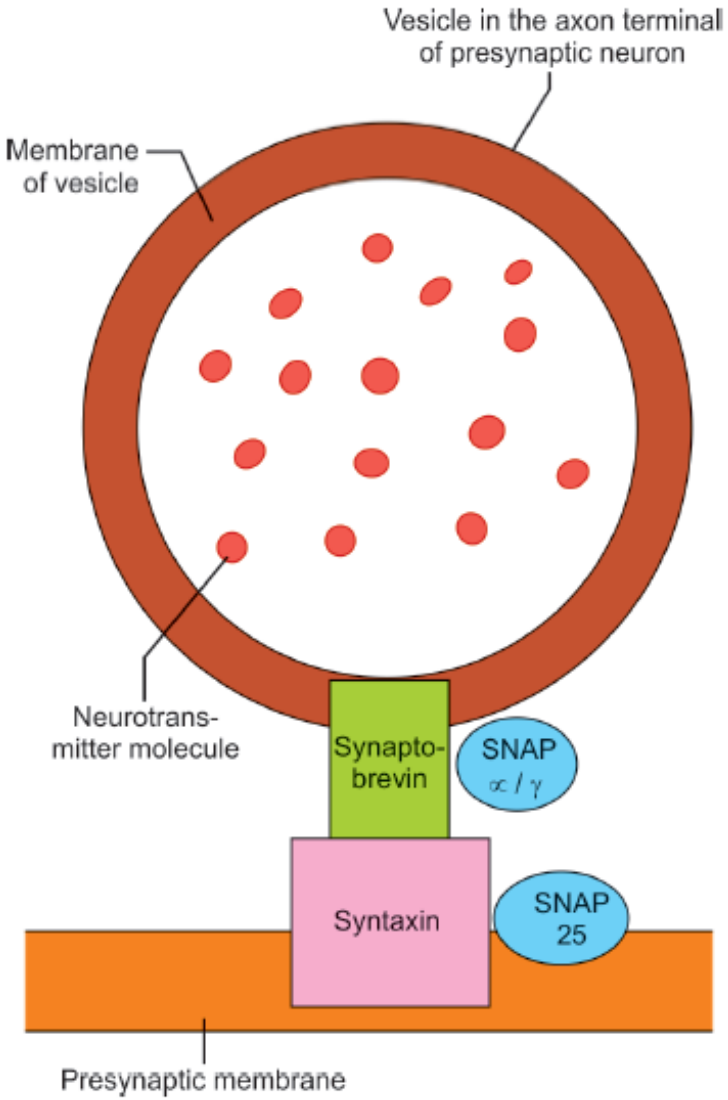
Vesicular discharge

- **Large dense core vesicles** are located throughout presynaptic terminals & release neuropeptide contents from all parts of terminal
- **Small vesicles** discharge their contents at active zones only

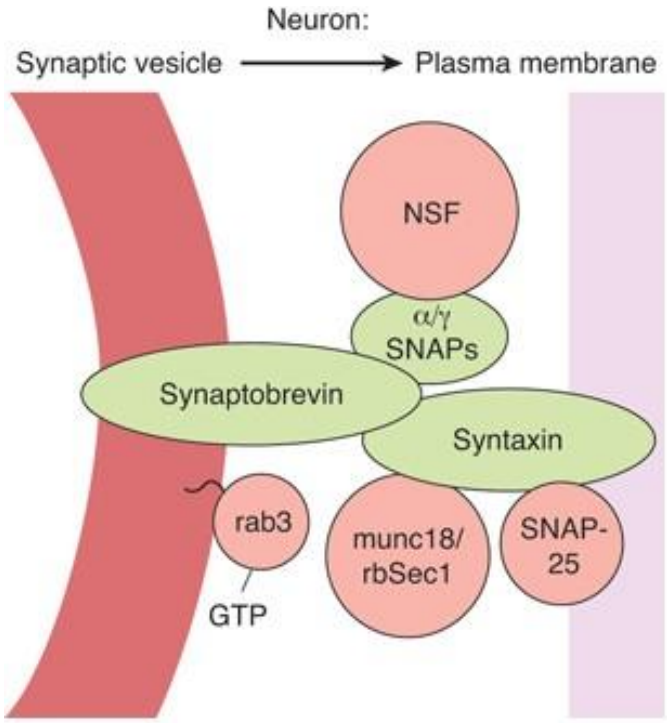
Kiss and run discharge

- Discharge of synaptic vesicular content takes place through small hole in the cell membrane which immediately closes

Role of membrane proteins in synaptic transmission



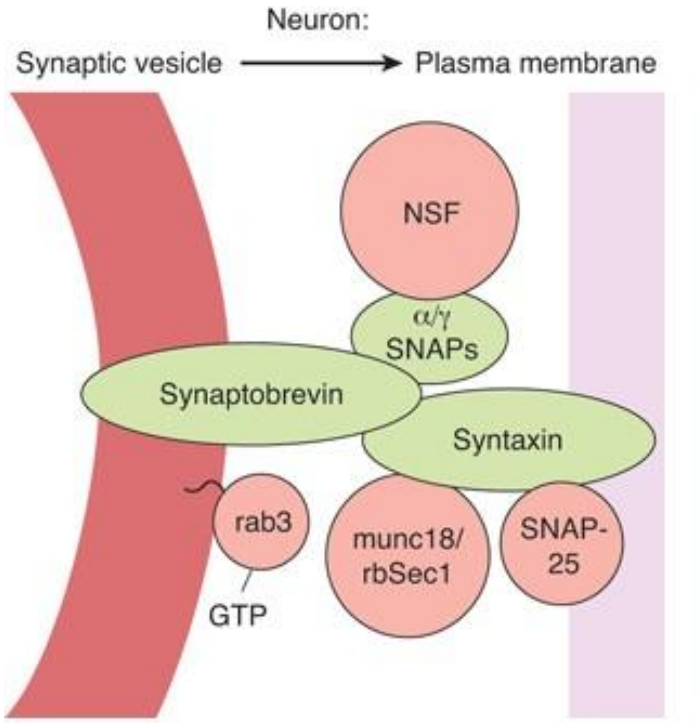
Role of membrane proteins in synaptic transmission



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

- Synaptobrevin : present on the vesicle (v-snare protein)
- Syntaxin : present on the membrane (t-snare protein)

Tetanus toxin



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

- Acts on synaptobrevin
- Causes a spastic paralysis

Botulin toxin

10/2005 Prior to treatment 3/2006 After Botox and Restylane

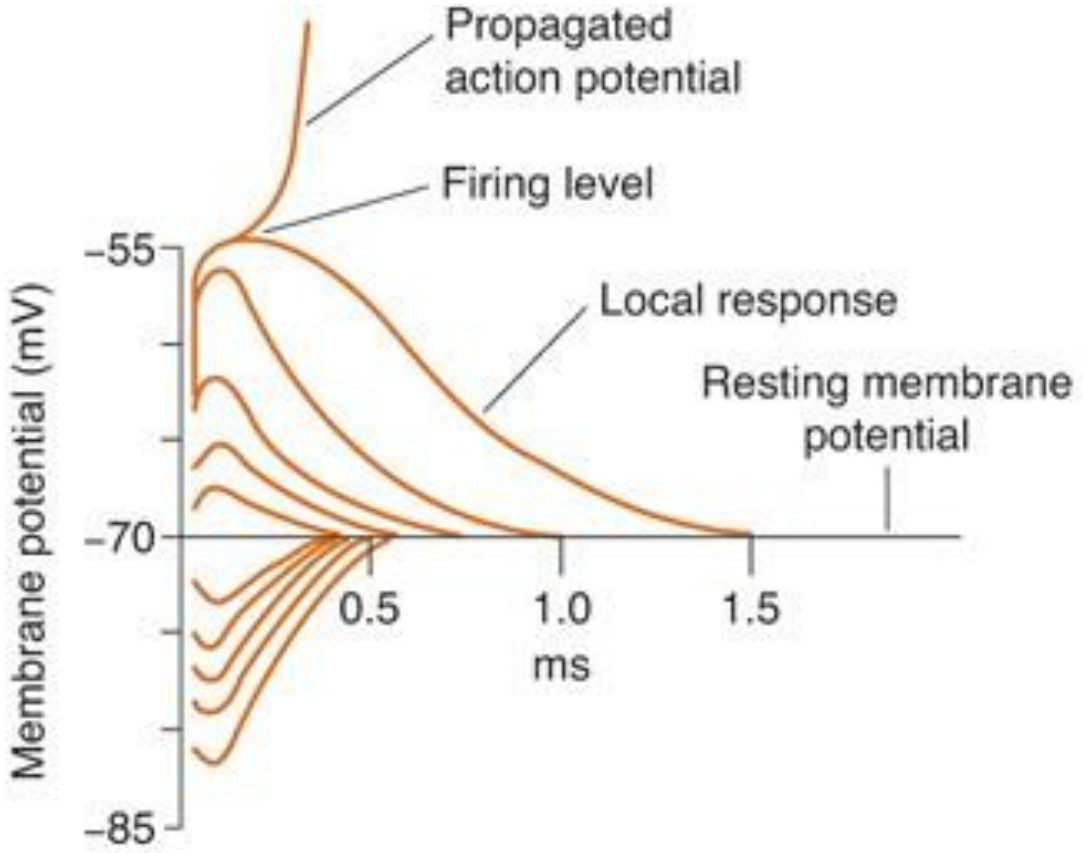
- Some act on syntaxin and some on synaptobrevin
- Causes a flaccid paralysis
- BOTOX injections now used therapeutically
- Local injection to lower esophagus relieves achalasia cardia
- Inj. into facial muscles – remove wrinkles

How is the action of a neurotransmitter stopped?

- Reuptake
- Breakdown

Electrical events in post synaptic neuron

Electrotonic Potentials (Write briefly)



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

Electrical events in post synaptic neuron

- A single stimulus applied to a Presynaptic neuron does not usually lead to formation of a propagated AP in the Post synaptic N
- It produces either a **transient partial depolarisation (EPSP)** or a **transient hyperpolarisation (IPSP)**
- There are also slow post synaptic potentials – **slow EPSP & slow IPSP**

Electrotonic or graded potentials

1. They are local potentials
2. They are either inhibitory or excitatory
3. They can be summated
4. If they reach the threshold an AP develops
5. They are not all or none
6. They do not propagate
7. They decrease in amplitude over distance

EPSP

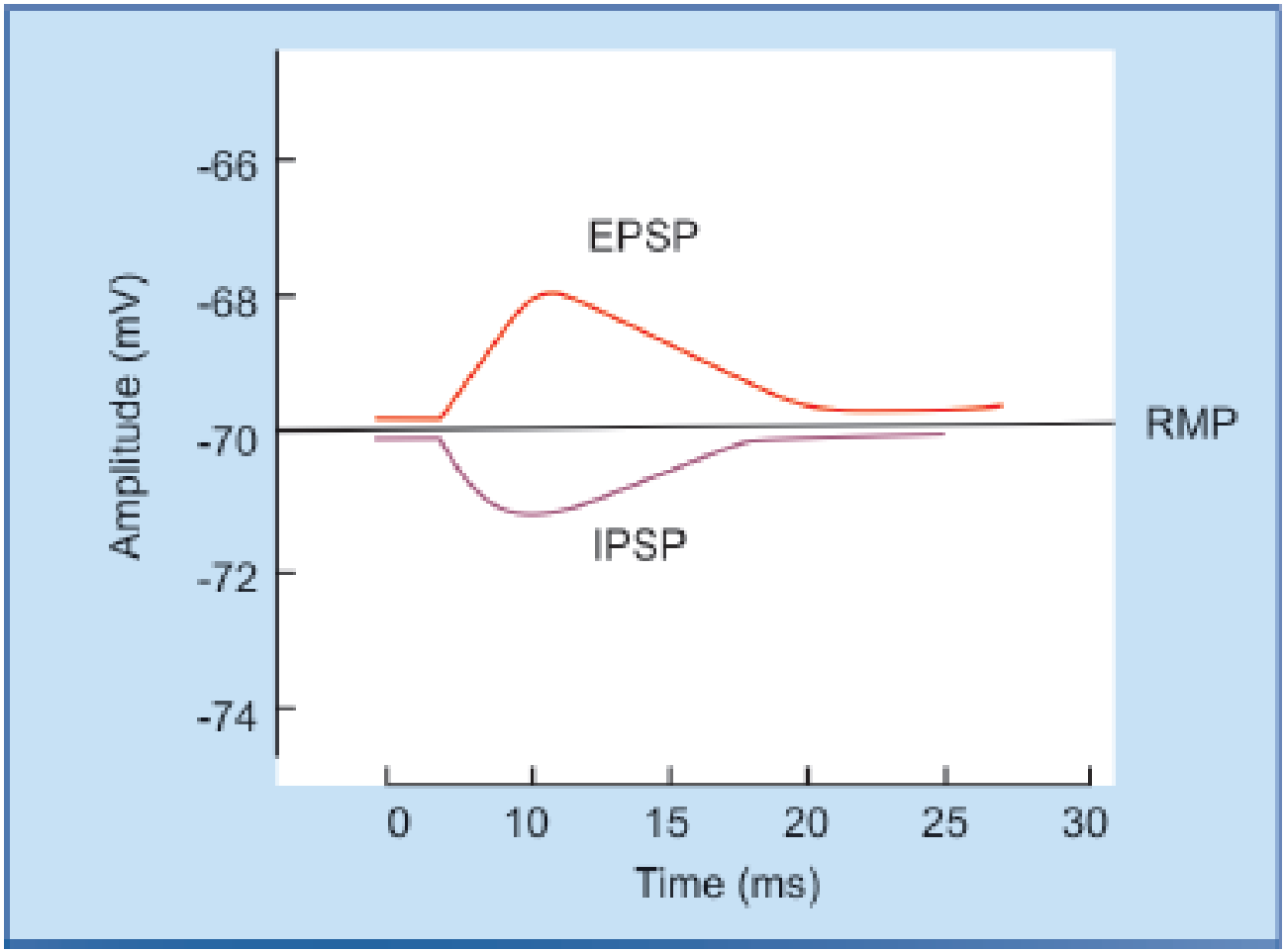


Fig. 116.5: Excitatory (EPSP) and inhibitory (EPSP) postsynaptic potentials.

EPSP (Excitatory Post Synaptic Potential)

- Produced by an excitatory NT
- Local response
- Produced by depolarisation of Post synaptic memb. immediately under presynaptic ending
- Neuronal potential becomes less negative – **EPSP**
- Single EPSP leads to a change of **0.5-2 mV**
- Initial response begins **0.5ms** after stimulation of Presynaptic membrane
- Reaches its **peak at 11.5ms**
- **Declines exponentially**
- Excitability of neuron to other stimuli ↑

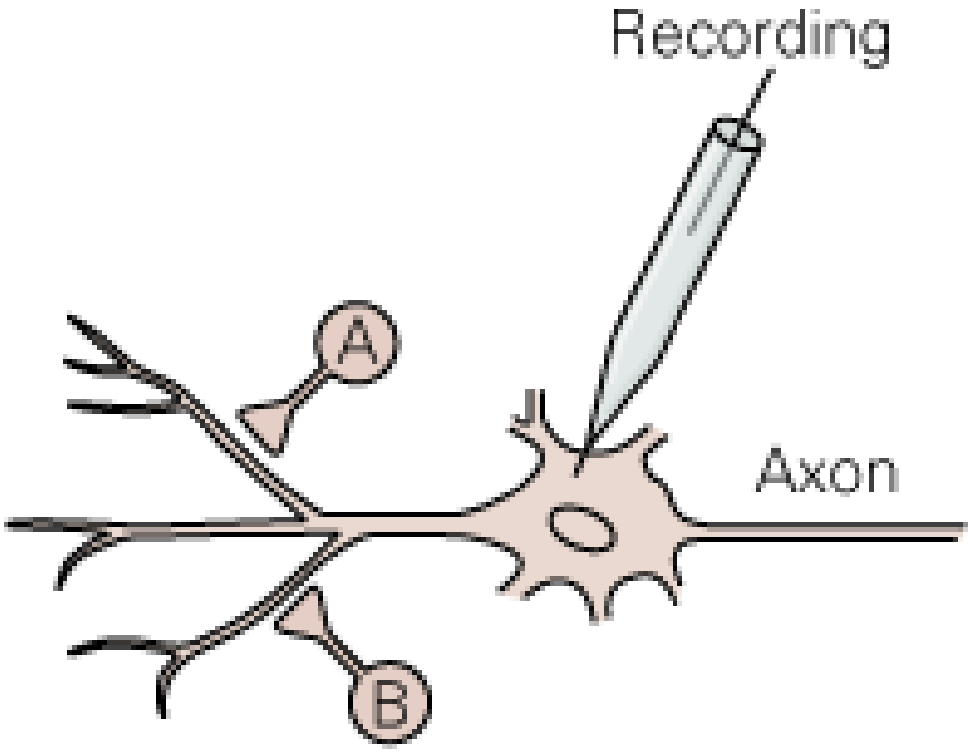
Ionic basis of EPSP

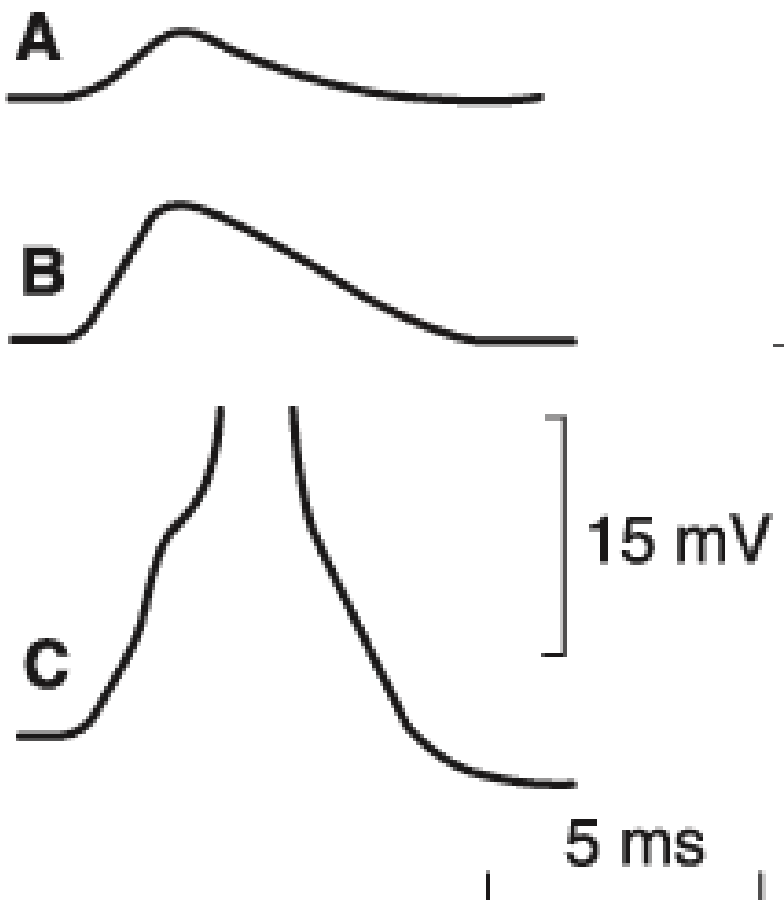
- Opening of Na^+ channels→ ↑ Na^+ influx
- Opening of Ca^{++}channels→ ↑ Ca^{++} influx
- Closing of Cl^- channels →↓ Cl^- influx
- Closing of K^+ channels →↓ K^+ efflux
- Can also change metabolism of Post SN →excite cell activity /↑ no:of excitatory receptors
- **Net ↑ in cations inside post synaptic neuron →local depolarization - EPSP**

Summation

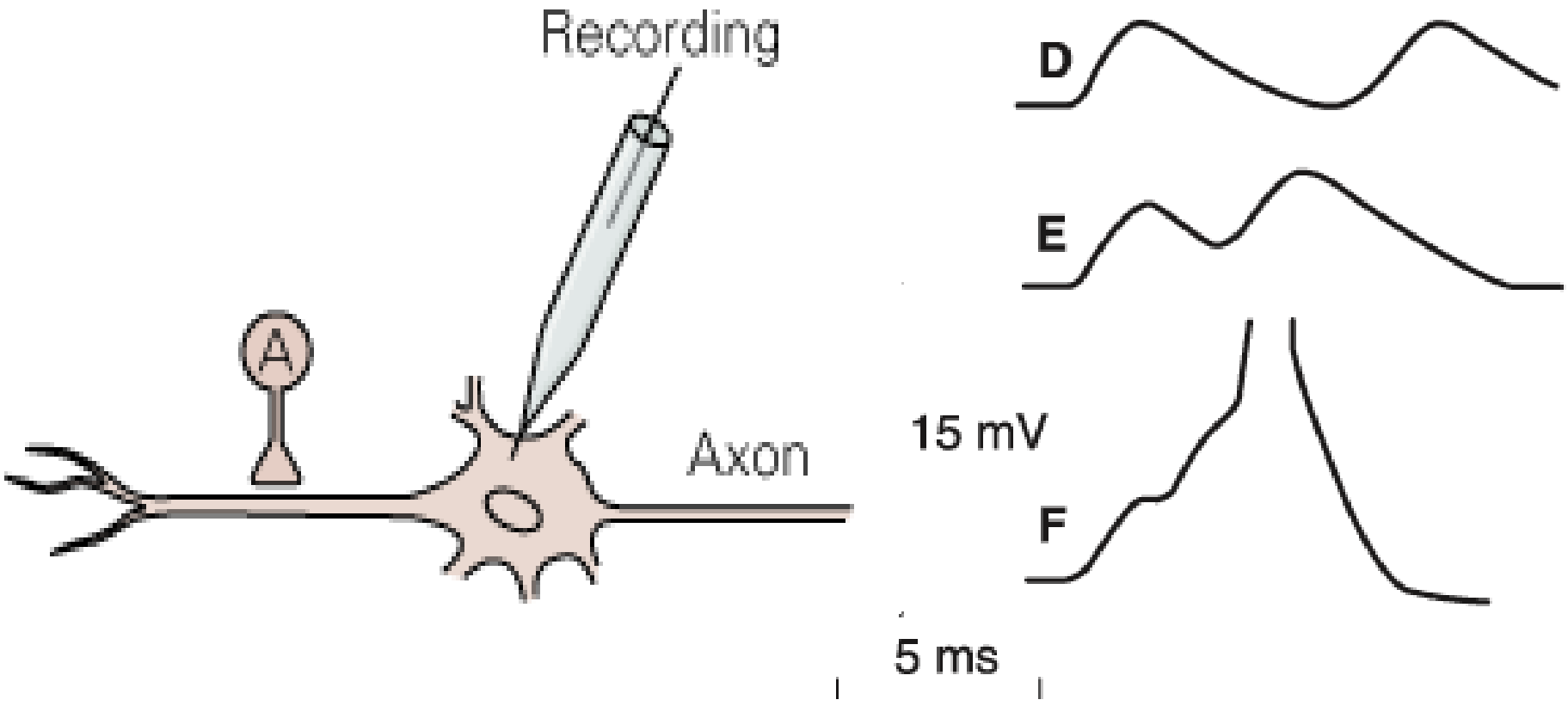
- EPSP due to activity in 1 synaptic knob is small
- But depolarisation produced can be **summated**
- When firing level is reached → AP is produced
- **Summation**
  - Spatial summation
  - Temporal summation

Spatial summation





Temporal summation

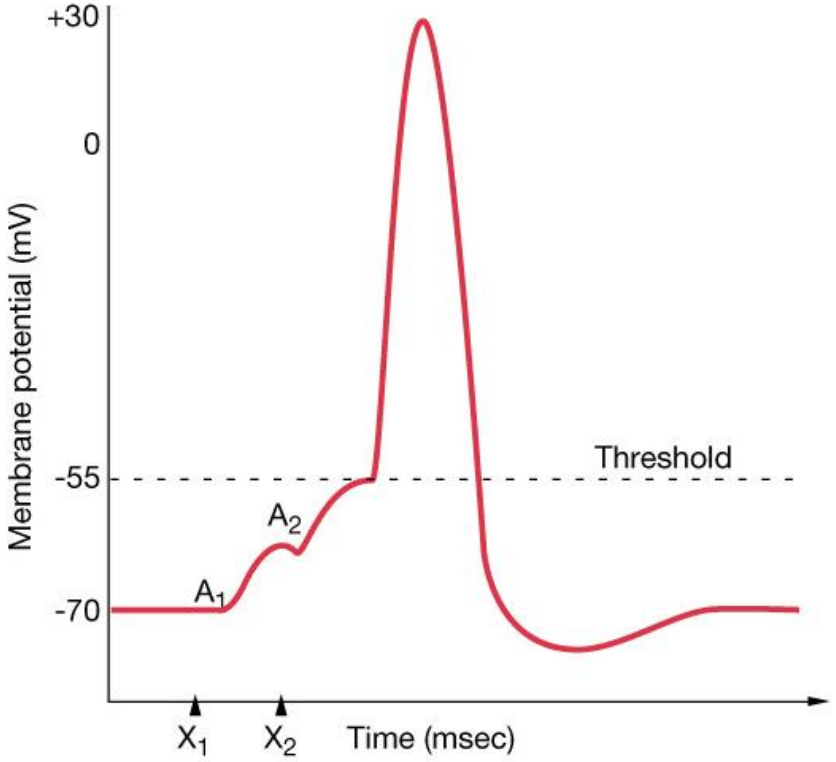


Spatial summation

- When activity is present in more than one synaptic knob at the same time, **spatial summation** occurs
- Activity in one synaptic knob summates with activity in another to approach the firing level
- Activity in 1 synaptic knob facilitates the activity in others to reach firing level

Temporal summation

- Repeated successive stimuli at short intervals –before previous EPSPs have decayed →temporal summation



(b) Summation causing action potential. If two subthreshold potentials arrive at the trigger zone within a short period of time, they may sum and create an action potential.

IPSP

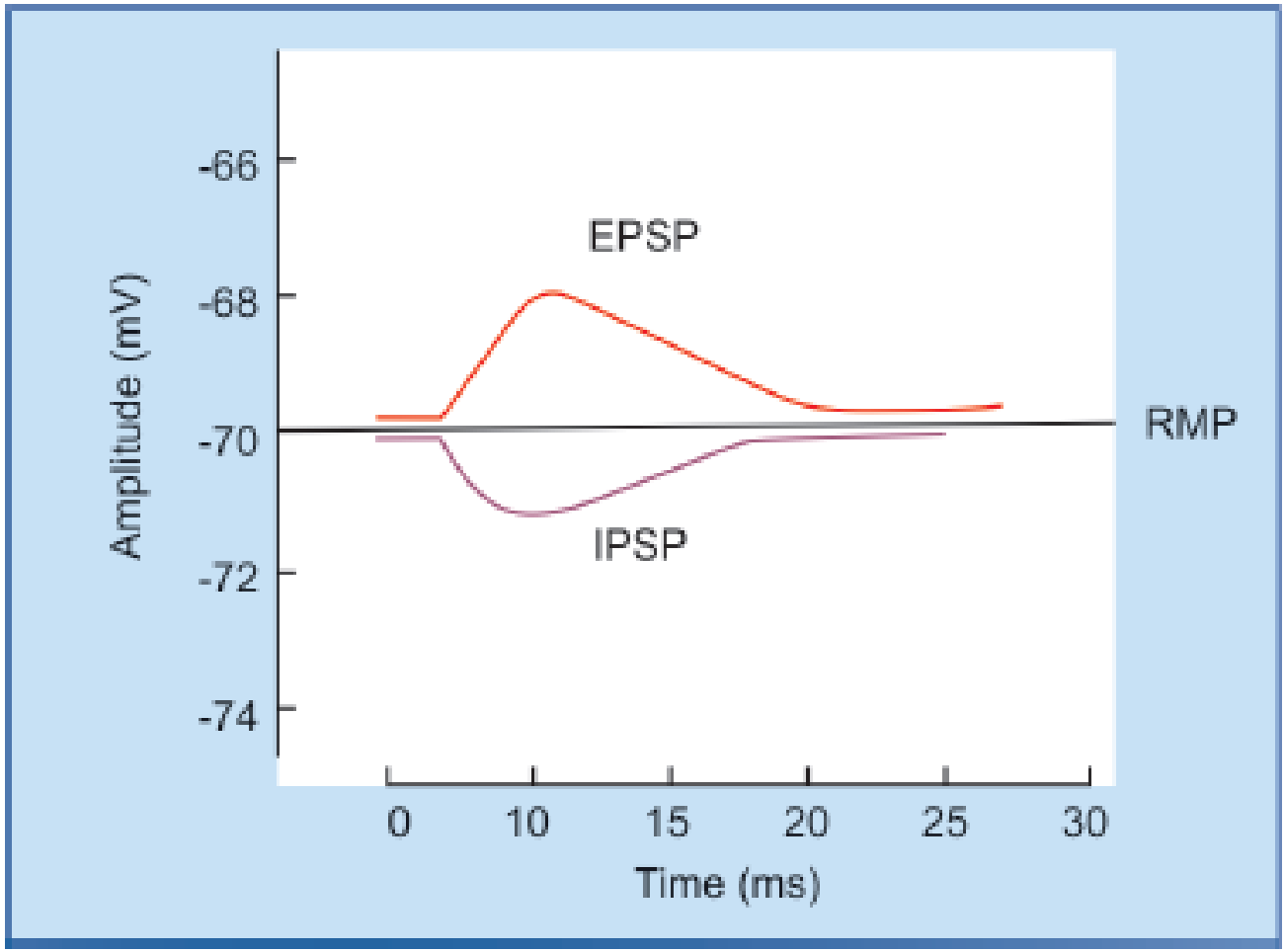


Fig. 116.5: Excitatory (EPSP) and inhibitory (EPSP) postsynaptic potentials.

Inhibitory Post Synaptic Potential (IPSP)

- Caused by release of inhibitory NT
- Peaks 11.5ms after stimulus & ↓ exponentially with time
- Membrane potential becomes more negative – **hyperpolarised**
- Makes **0.5 mV** change
- Excitability of neuron to other stimuli ↓
- More depolarising activity is required to reach firing level
- Both spatial & temporal summation can occur in IPSP also

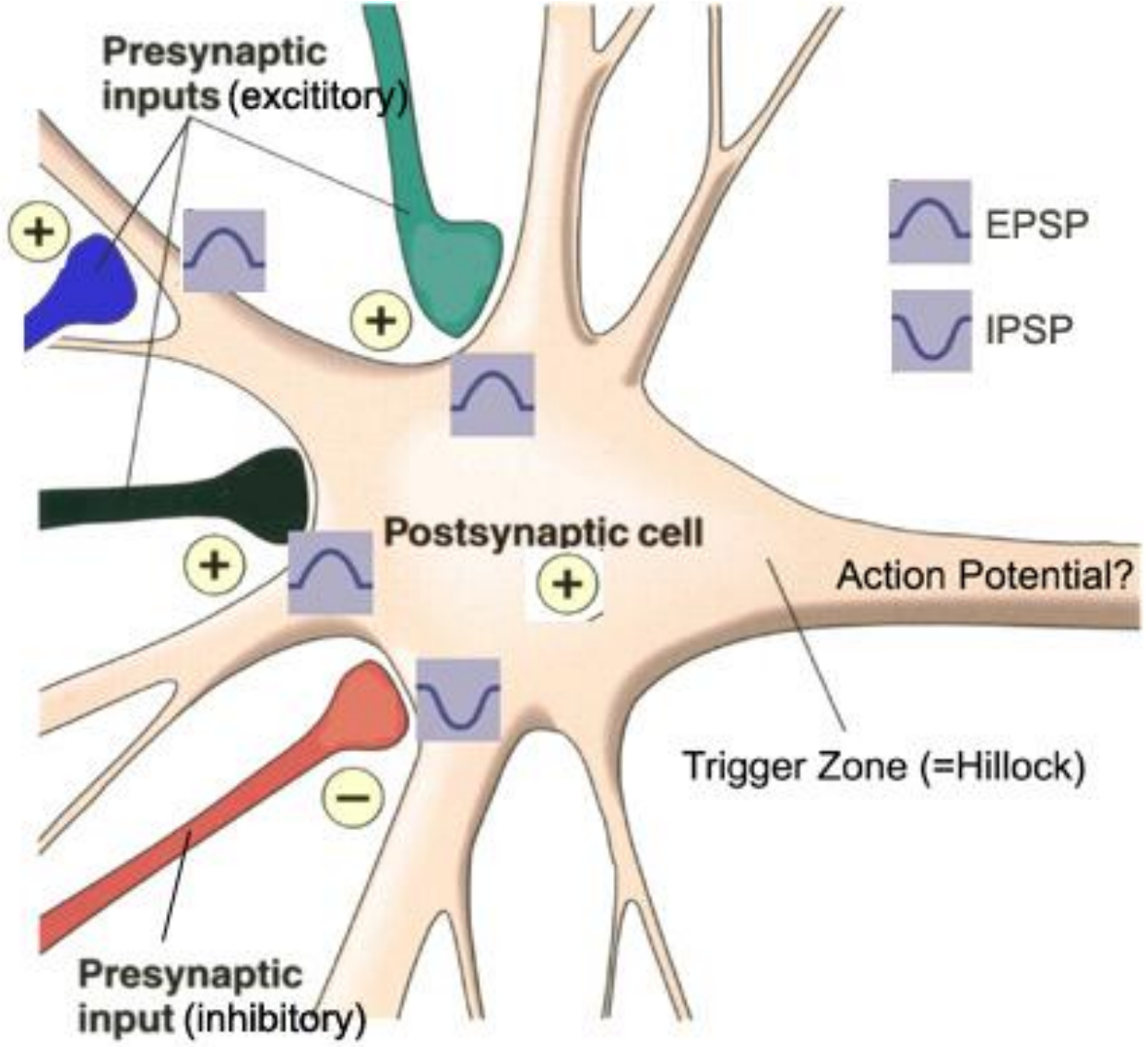
Ionic basis of IPSP

- Opening of Cl^- channels→ ↑ Cl^- influx
- Opening of K^+ channels→ ↑ K^+ efflux
- Closing of Na^+ channels →↓ Na^+ influx
- Closing of Ca^{++} channels →↓ Ca^{++} influx
- Activate enzymes that ↑ no:of inhibitory receptors / ↓ no:of excitatory receptors
- **Net ↑ in anions inside post synaptic neuron → hyper polarization → IPSP**

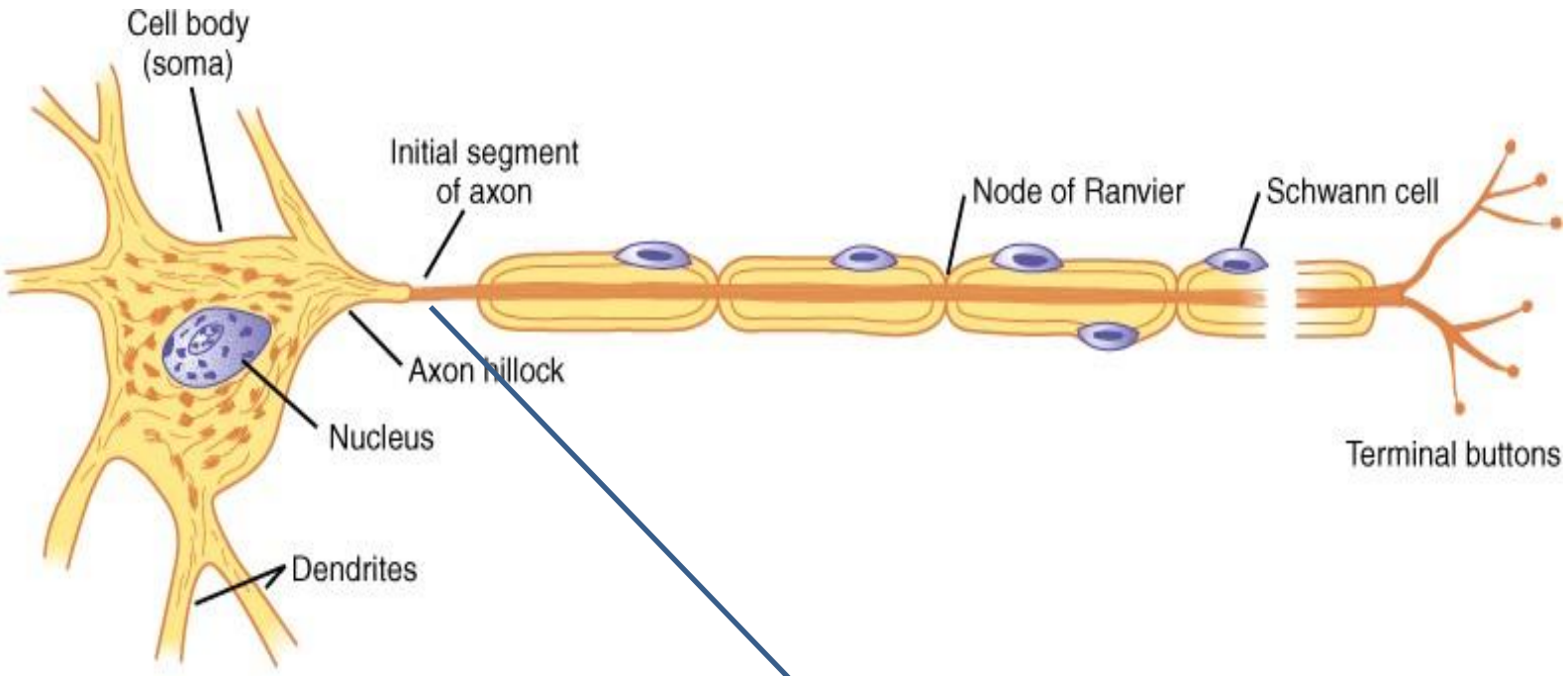
Slow EPSP & IPSP

- Described in autonomic ganglia, Cardiac muscle, Smooth muscle & cortical neurons
- Slow PSP have long latency- 100 to 500 ms & lasts several seconds
- **Slow EPSP** due to **↓ in K^+ conductance**
- **Slow IPSP** due to **↑ in K^+ conductance**
- **Late slow EPSP**
- Latency 1-5 s & lasts 10-30 min.
- Also due to ↓K+ conductance

Genesis of AP in post synaptic N



Where in a neuron is an AP formed?



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

At the initial segment

Genesis of AP

- **Soma acts as an integrator**
- If the net of depolarising & hyperpolarising activities is depolarising & enough to reach firing level (+10 to 15 mv) →**AP occurs**
- The membrane potential is the algebraic sum of all the EPSPs and IPSPs at a given time
- AP does not arise in Post synaptic membrane or soma
- **AP begins in initial segment of axon** (Lowest threshold in this part)

Propagation of AP

- AP is propagated in 2 directions – down the axon (Orthograde propagation)
- And back to soma (retrograde propagation)
- The orthograde conduction helps to conduct the impulse
- Retrograde firing cleans the soma for next postsynaptic activity (“wipes the slate clean”)
- Soma –dendritic tree is quickly restored to RMP

	Action potential	Electronic potential
Stimulus	Threshold stimulus	Subthreshold stimulus
Propagation with decrement	Propagated along entire length of cell without decrement	Can be conducted with decrement for a short distance
Size of potential	Constant throughout the fiber	Decreases with distance
All or none law	Obeys	Does not obey
Refractory period	Present	Absent
Summation	Absent	Can occur