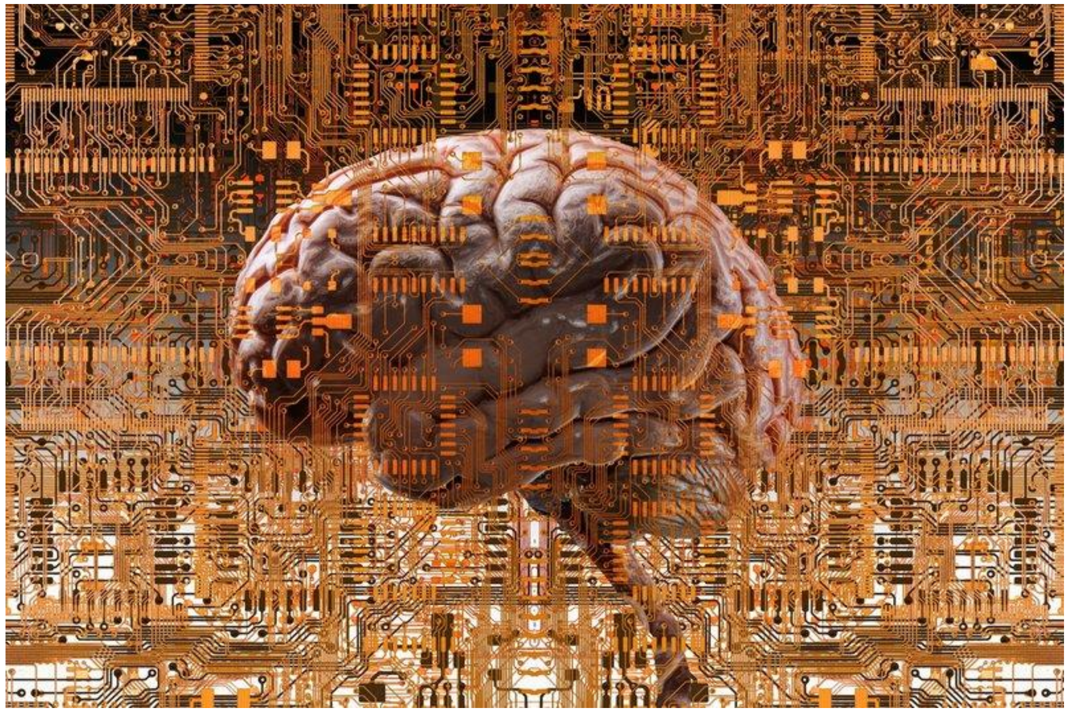
Science of Living System: BS20001

Brain structure and function



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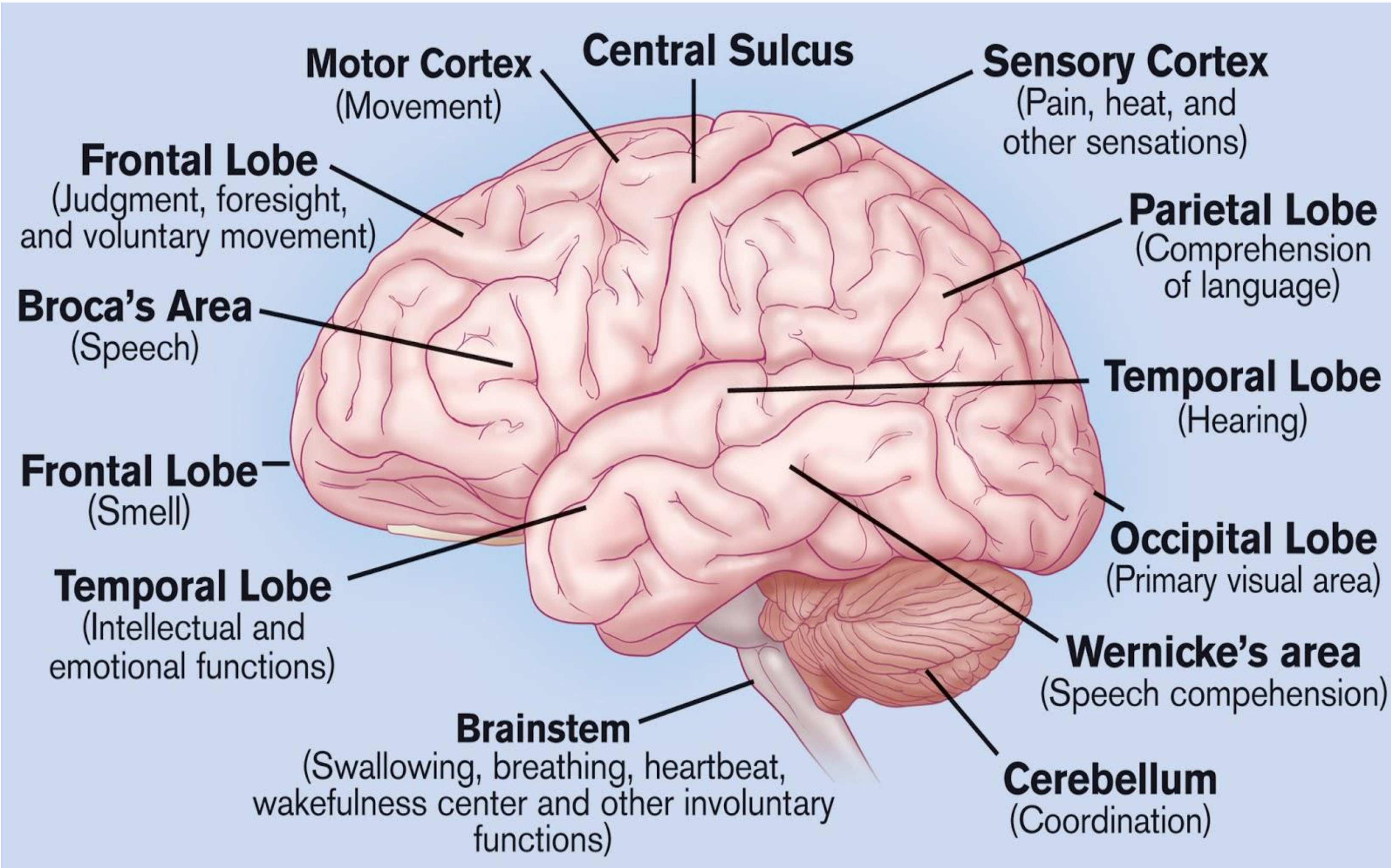
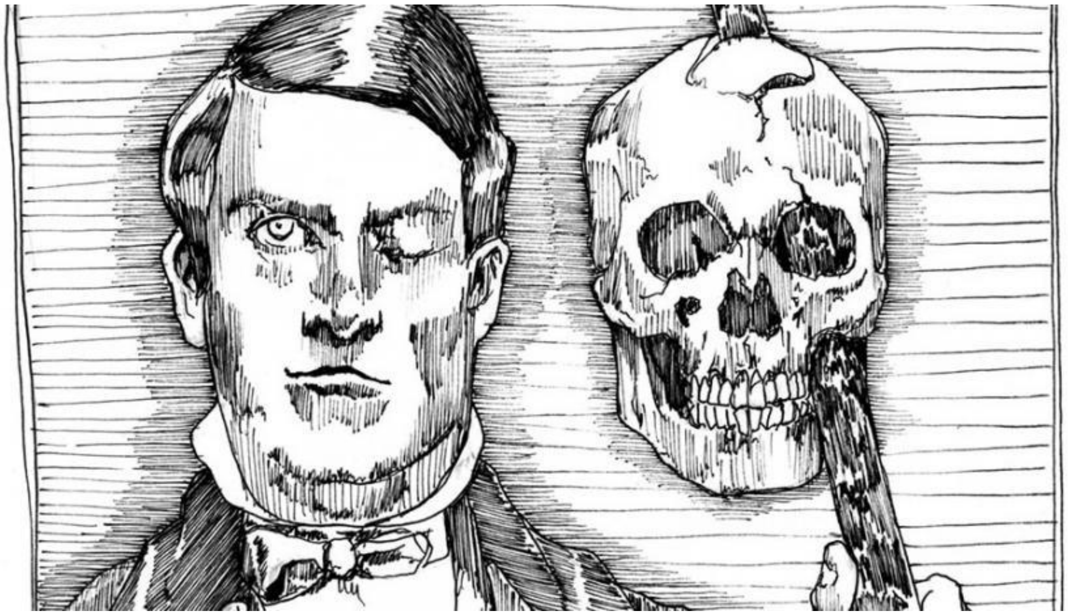
Our brain is the most sophisticated computational machine

- It can change its own components and rewire itself into a new configuration as required for new function.

Anatomy and functional areas of the brain



Accidental injury led to new discoveries in Neuroscience



Phineas Gage (1823–1860) was the victim of a terrible accident in 1848.

A large iron rod was driven completely through his head, destroying much of his brain's left frontal lobe

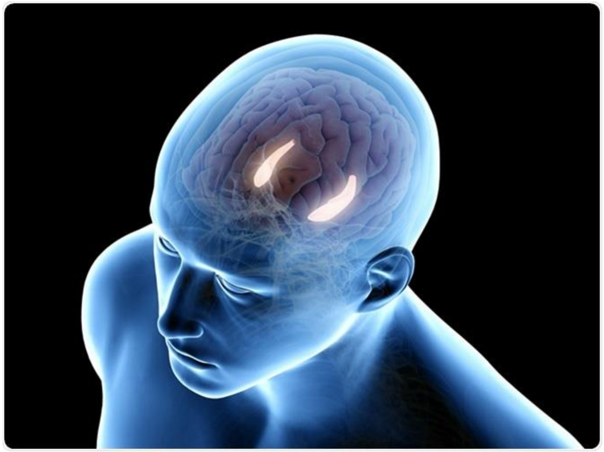
His personality and behavior dramatically changed
over the remaining
12 years of his life

His injuries helped scientists understand more about the brain and human behaviour, particularly role of frontal lobe in personality

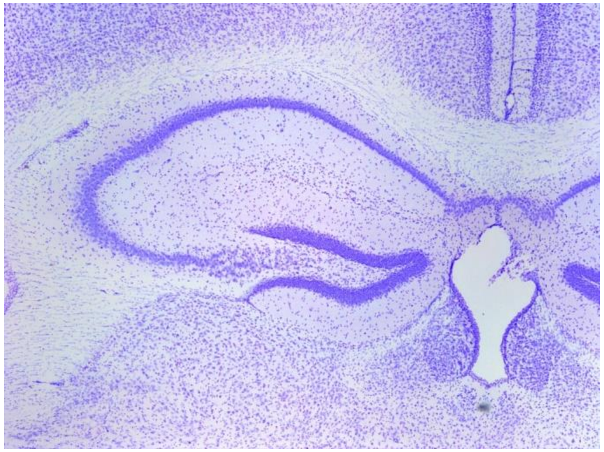
Man with no memory

HM lost the ability to form new memories after surgical removal of the hippocampus and nearby temporal lobe structures to treat intractable epilepsy.

Henry Molaison, widely known as "HM,"



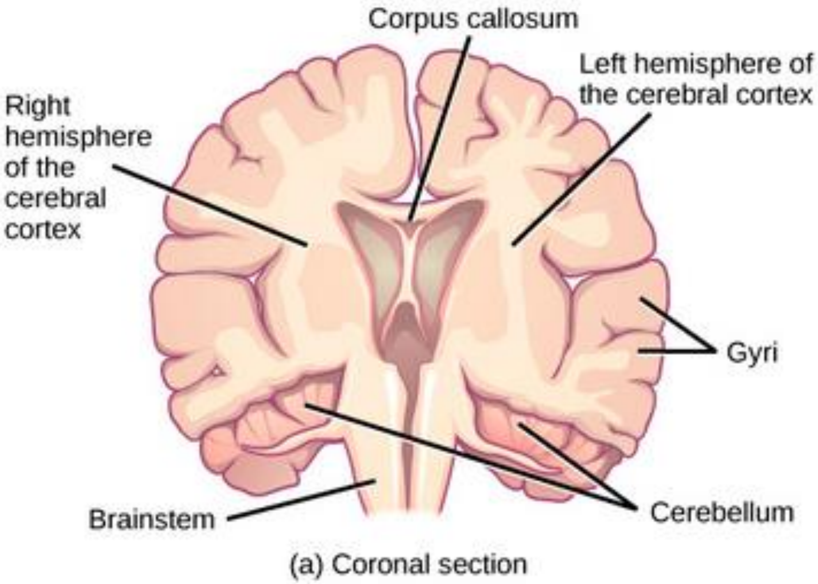
3D image of hippocampus



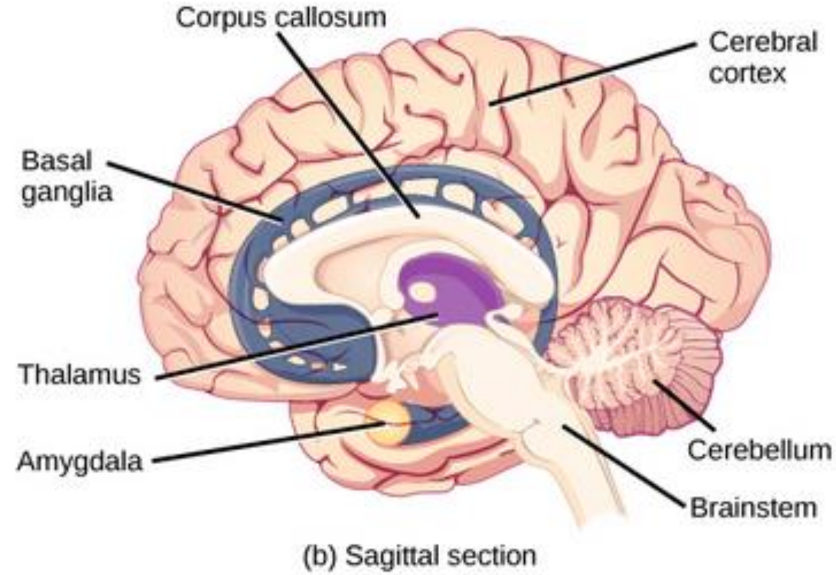
Architecture of hippocampus

Hippocampus is essential for making memories, and that if we lose both of them, we will suffer a global loss of memory

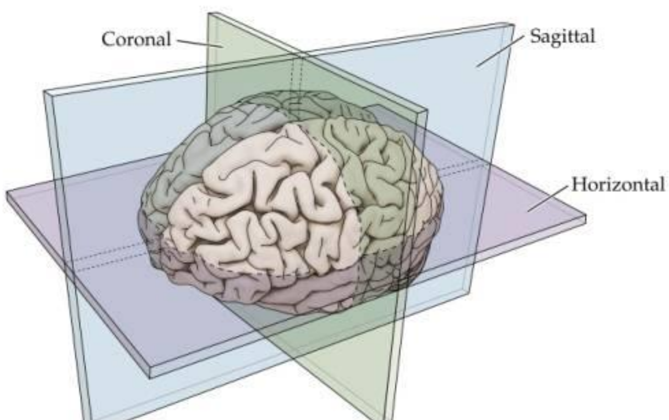
Internal structure of the brain

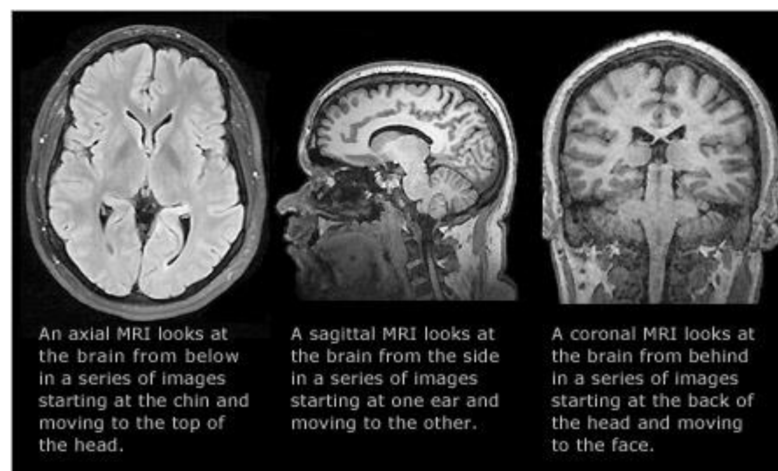


(a) Coronal section



(b) Sagittal section

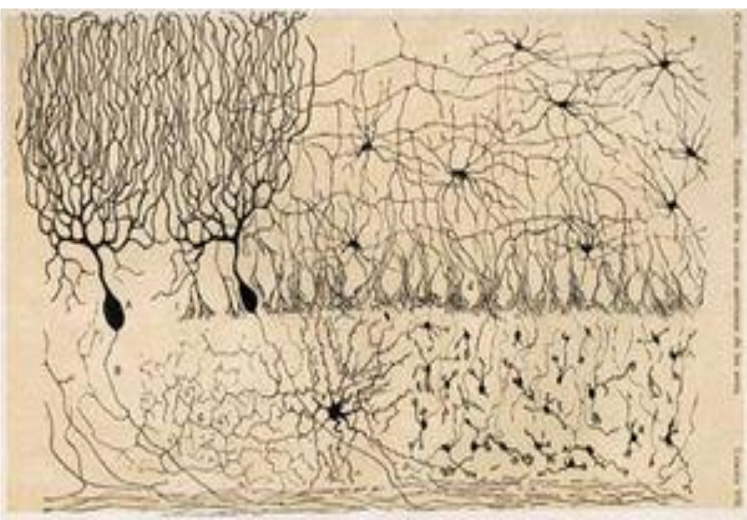




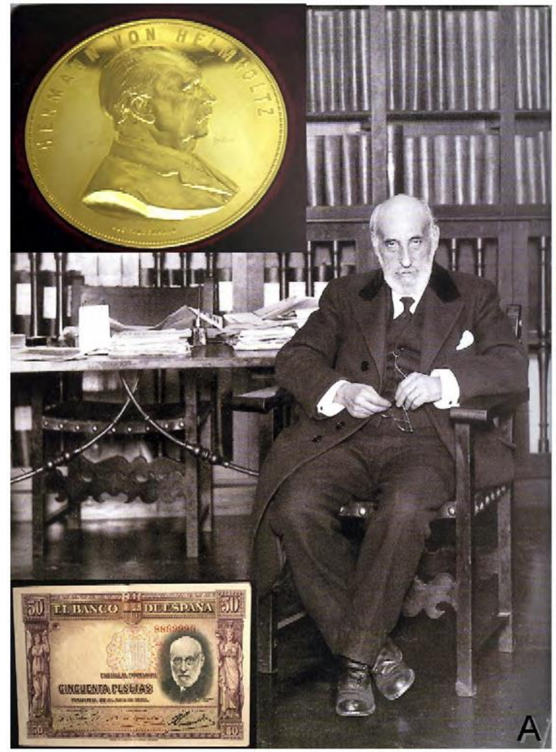
MRI scan of human brain

The neuron doctrine

- Neurons are structural and functional units of nervous system
- They are electrically excitable cells of the brain



Hand drawing of Ramon Cajal

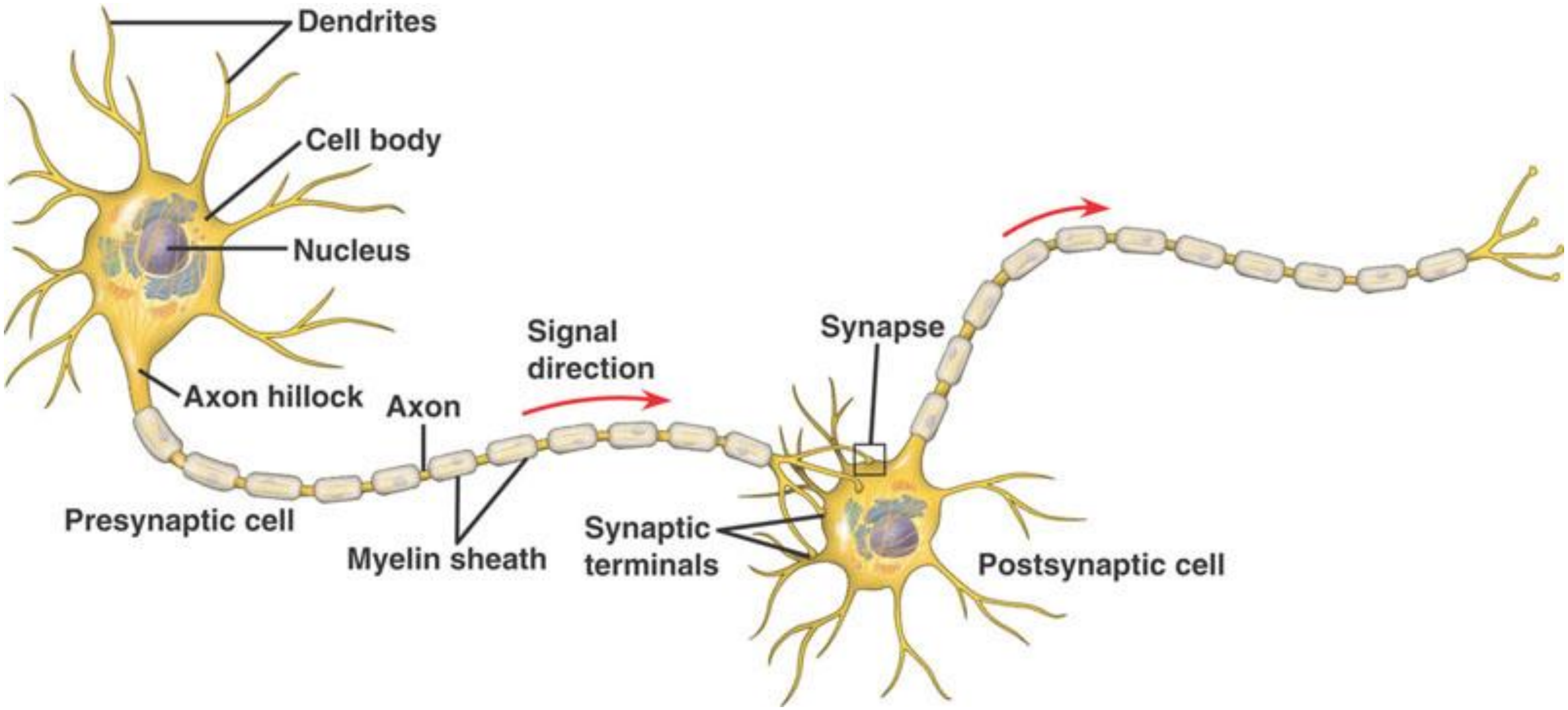


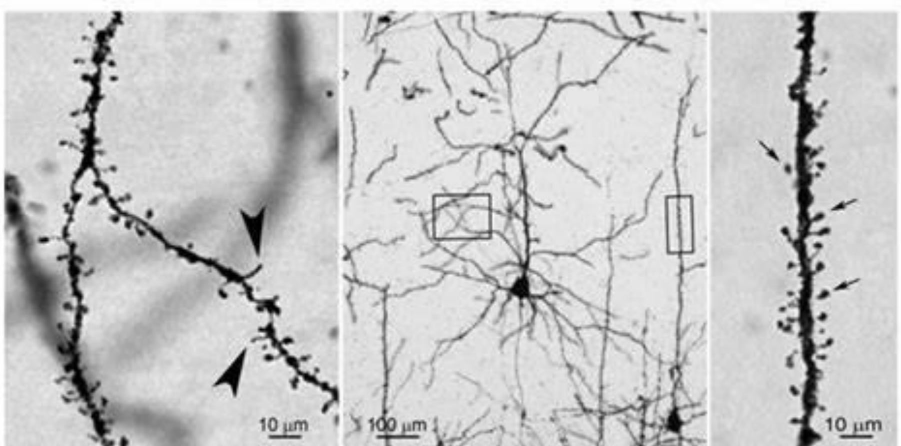
Santiago Ramón y Cajal

Camillo Golgi

The 1906 Nobel Prize in Physiology or Medicine was awarded to both of them for revealing the inner beauty of the nervous system

Structure of the neuron





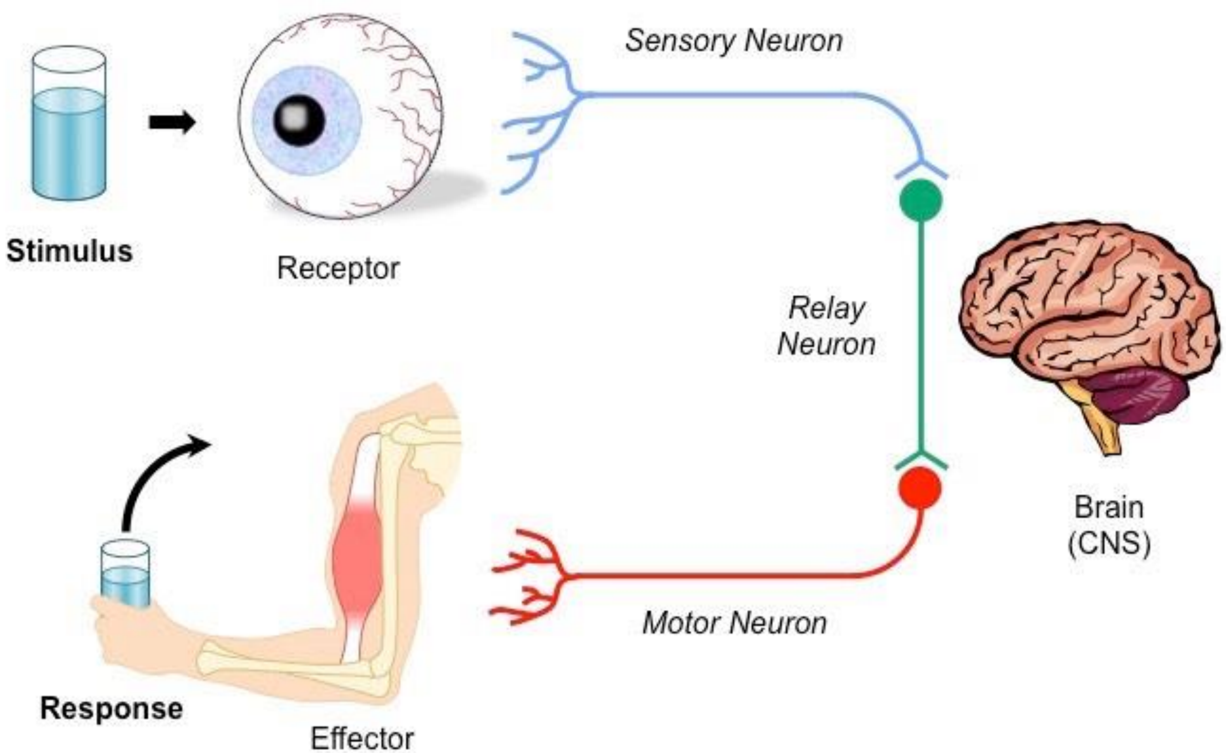
Golgi staining

Arrow points to the **dendritic spines**, connecting site with other neuron called synapse

Electrical activity of neurons:

Nerve Impulse or Action Potential

Our brain function depends on Stimulus-Response Pathway



1. Environmental Stimulus activates Receptors on Sensory neurons
2. Sensory neurons are **excited** (**nerve impulse** generated)
3. Impulse transmitted to Central Nervous System (site for decision making)

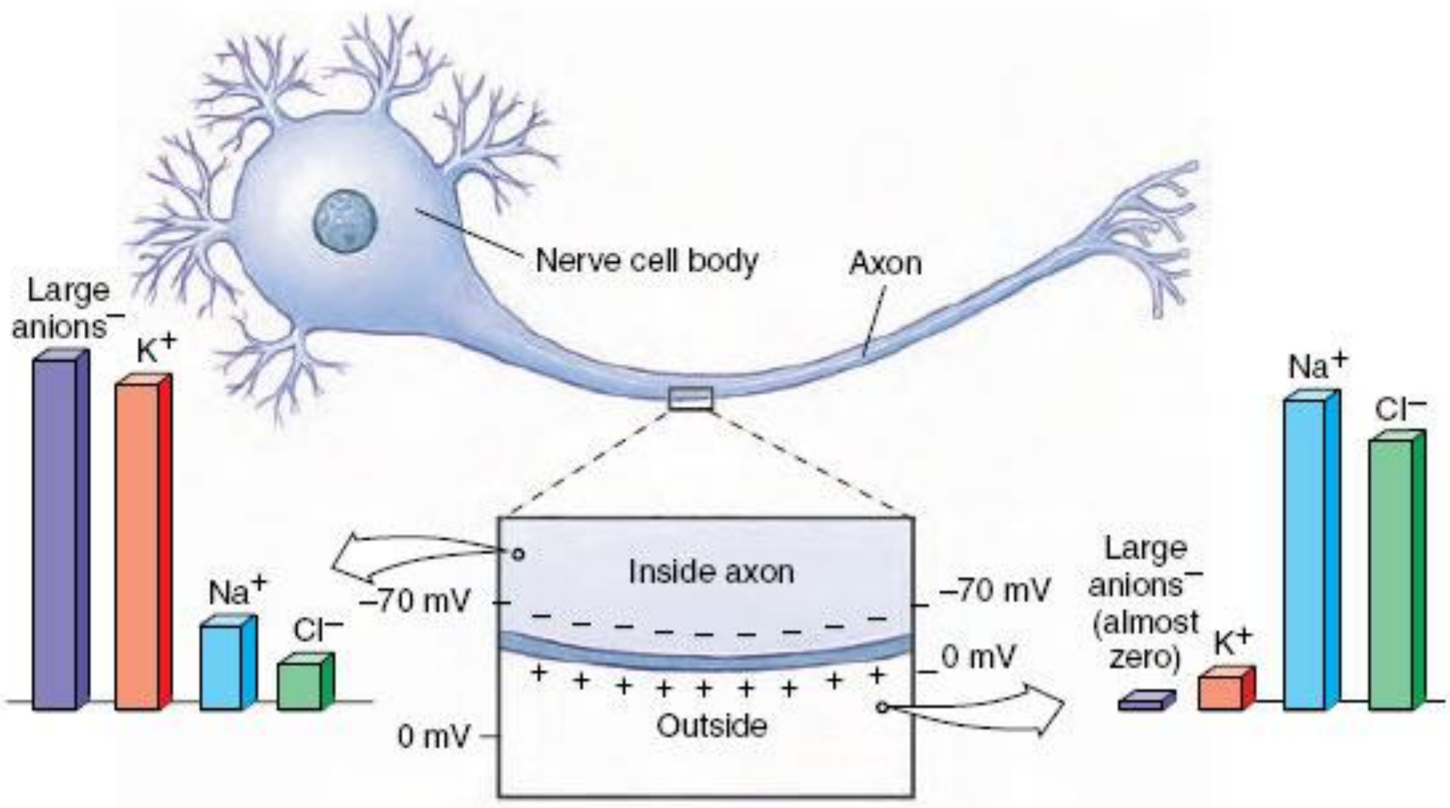
4. Response signal transmitted via Motor Neurons to Effector (Muscle)

5. Muscle contracts to take necessary action

How is nerve impulse generated?

1. Resting membrane potential (RMP):

- A electrical potential difference across the cell membrane
- Neurons have resting membrane potential like all other cells (varies from -60 to -70mv)



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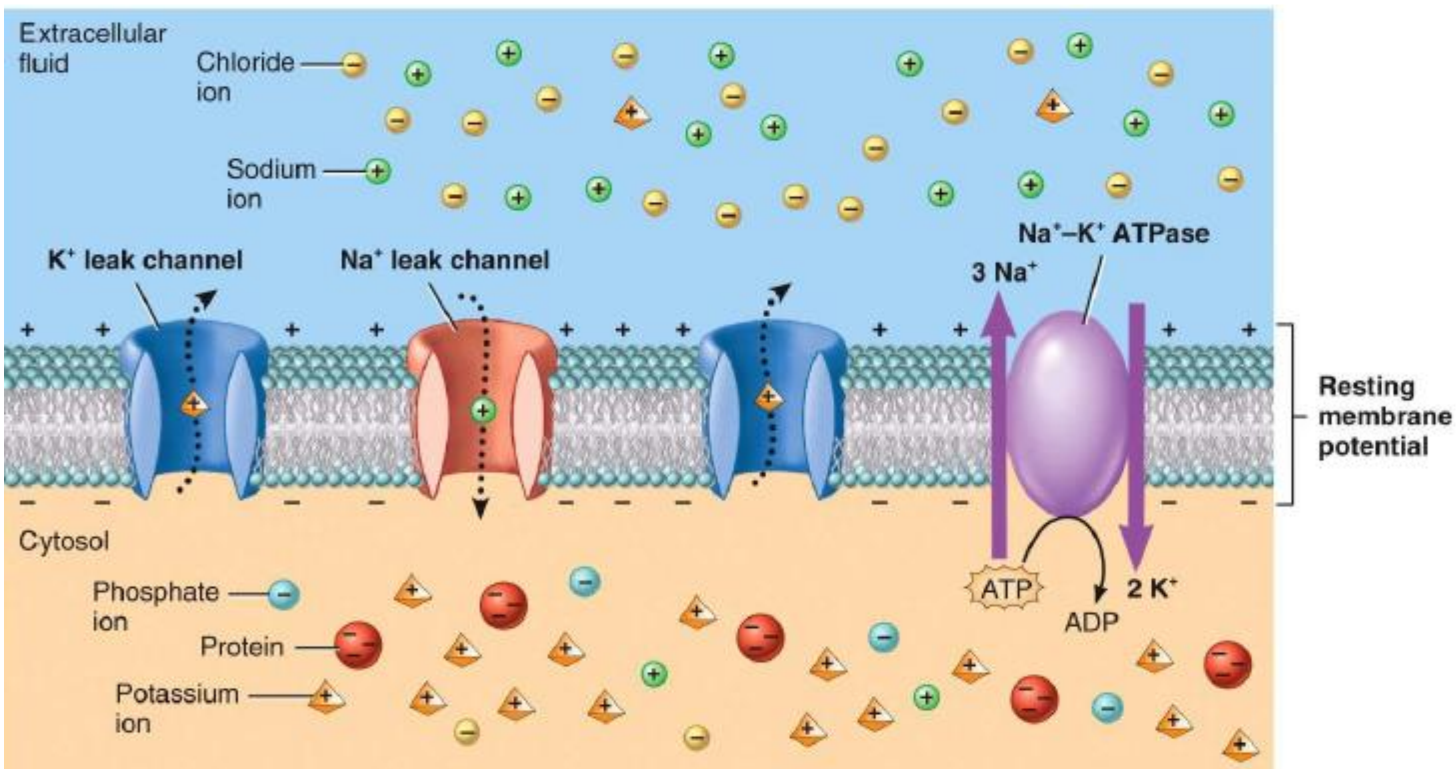
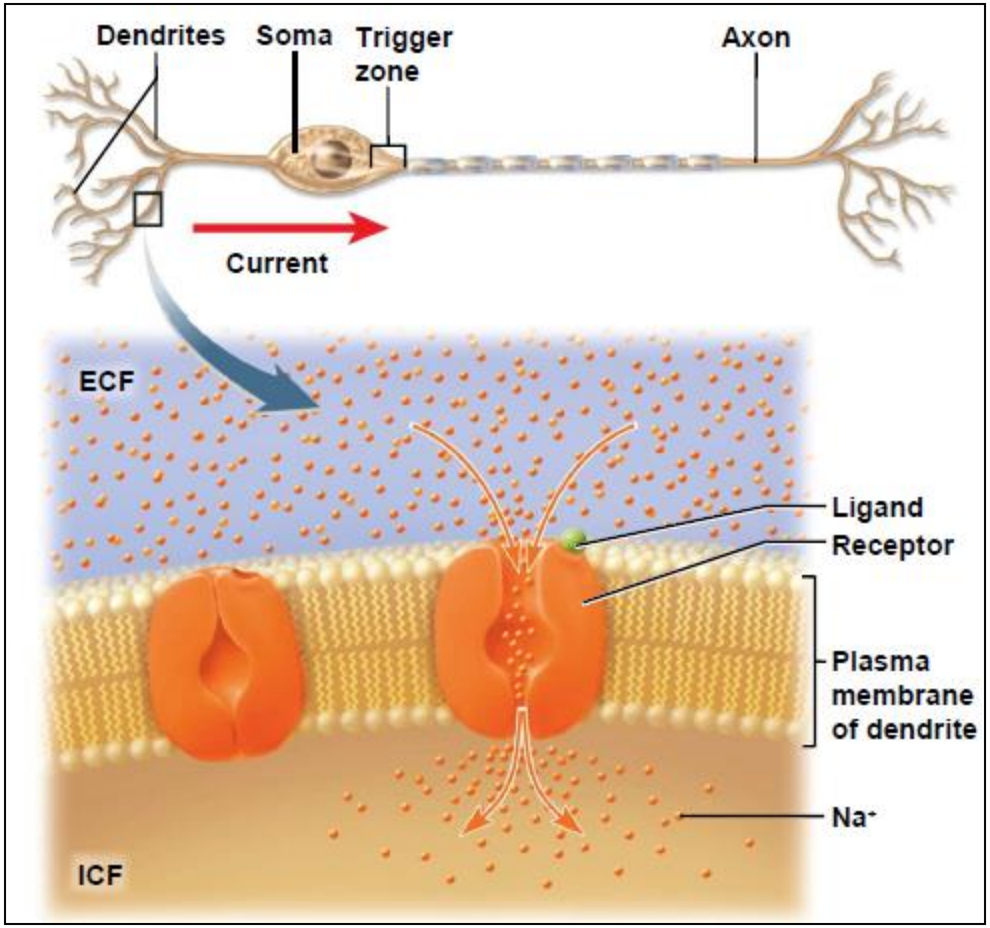


How is nerve impulse generated?

2. Local or generator potential:

- When a neuron is stimulated by chemicals, light, sound, mechanical disturbance etc. local potential is generated
- Stimulus activates specific receptor and allow Na+ to enter into the cell
- Neuronal membrane depolarizes



Types of receptors:

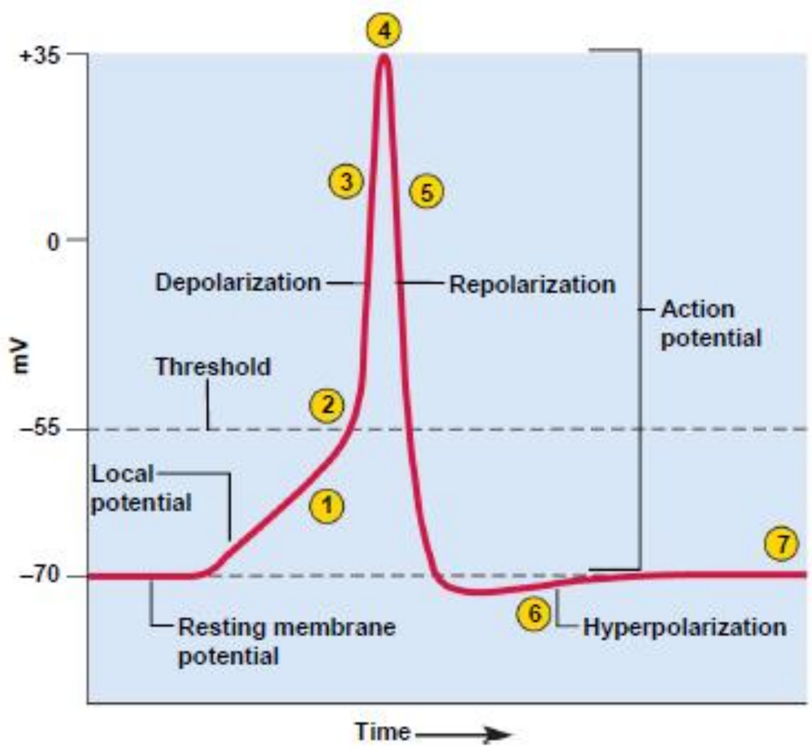
- Photoreceptor (eye)
- Mechanoreceptor (ear)
- Thermoreceptor (skin)
- Chemoreceptor (nose, tongue)

How is nerve impulse generated?

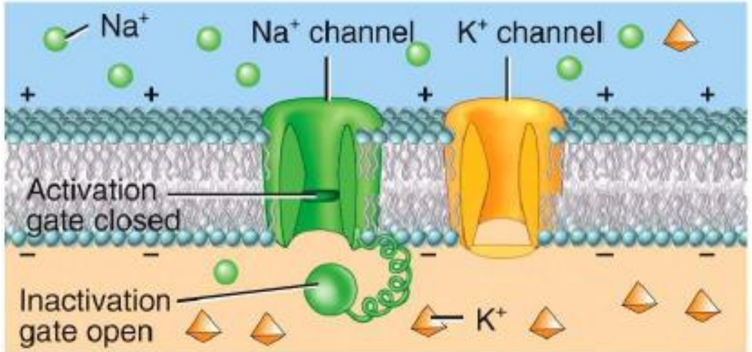
3. Action potential:

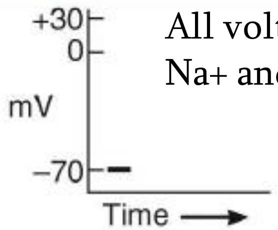
All or none law

- If local potential reaches threshold, neuron fires at its maximum voltage
- If threshold is not reached neuron does not fire



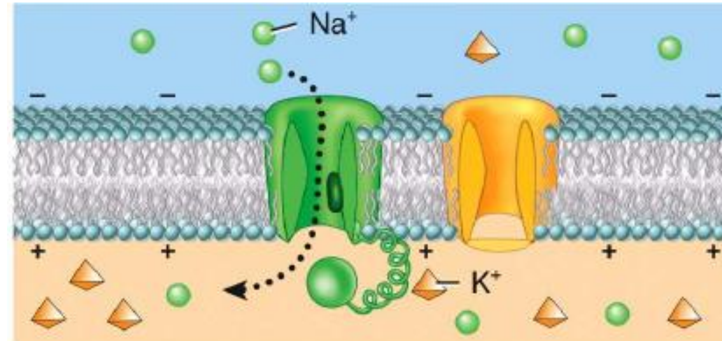
Resting state

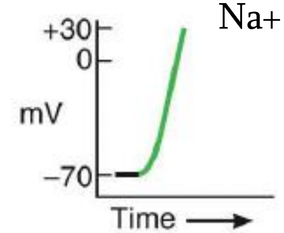




All voltage gated
Na+ and K+ are closed

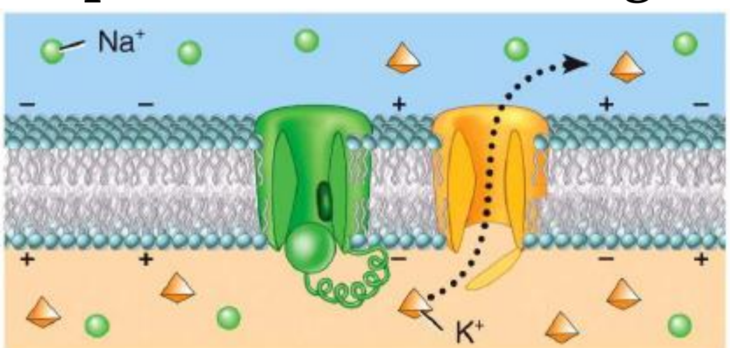
Depolarization state

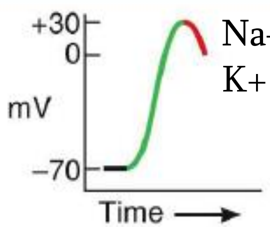




Na+ channels open

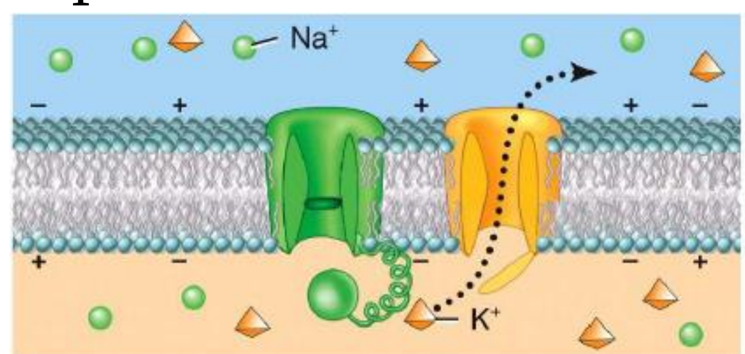
Repolarization state begins

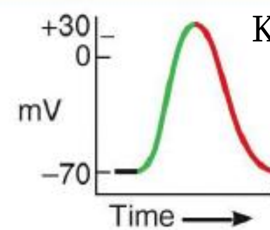




Na+ channels closed
K+ channels open

Repolarization state continues

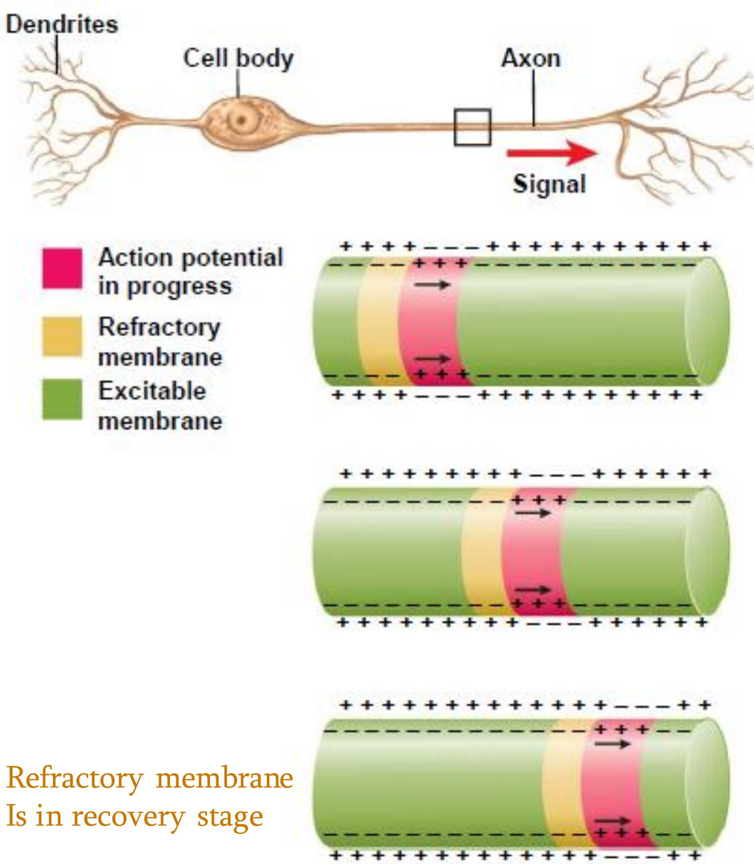




K+ outflow continues

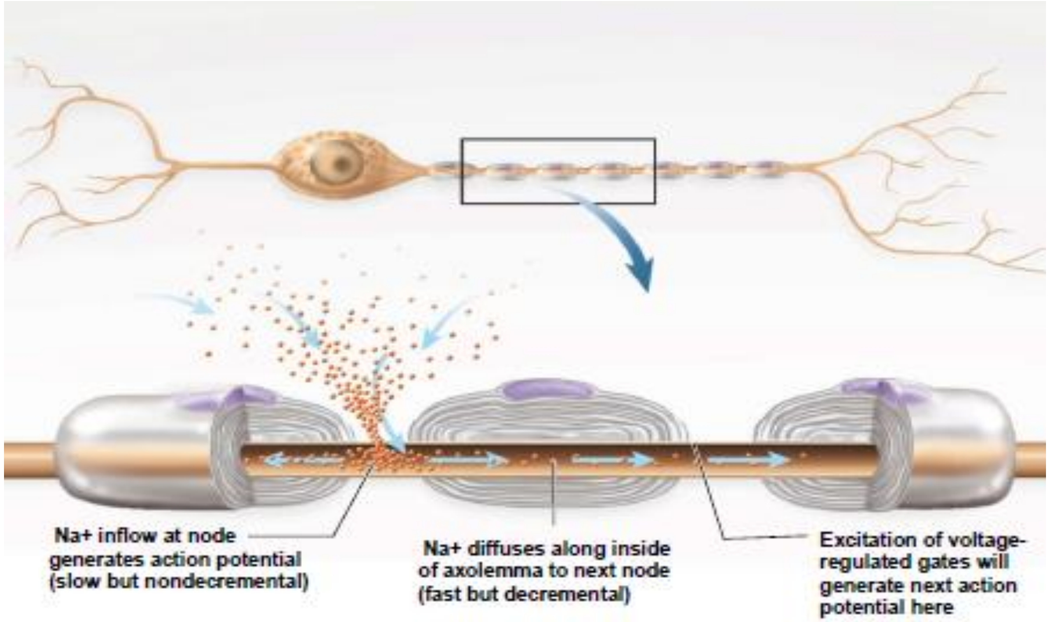
4. Transmission of nerve impulse:

Unmyelinated fiber



Refractory membrane
Is in recovery stage

Myelinated fiber



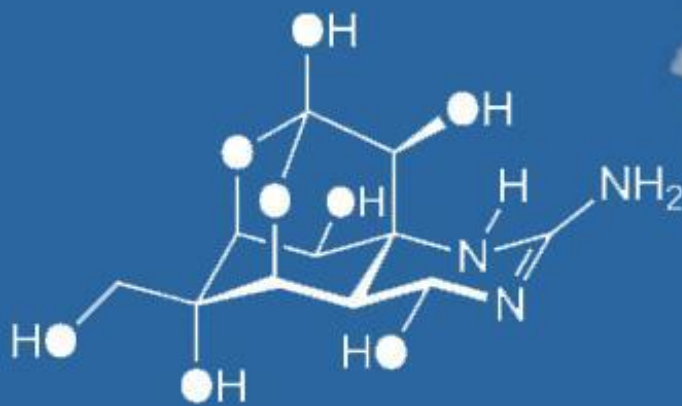
Saltatory conduction (faster speed)

Speed of nerve impulse

- Myelinated neurons: 80-120 miles/sec
- Non-myelinated neurons: 0.5-2 miles/sec
- Nerve impulse speed could be 3 millions times slower than electricity

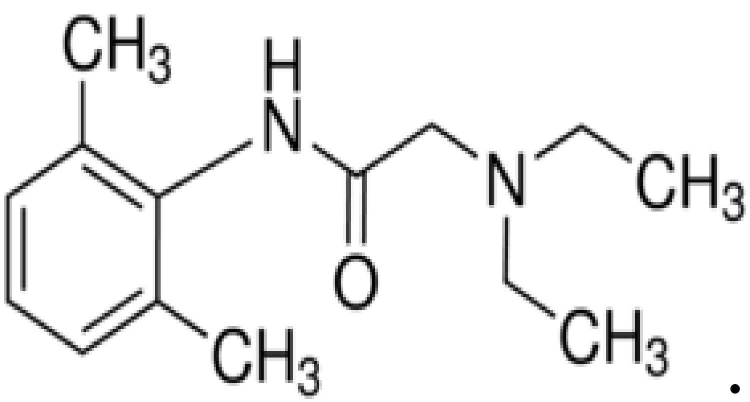
Sodium channel blockers

Tetrodotoxin: in puffer fish



- More poisonous than cyanide.
- Irreversible inhibitor

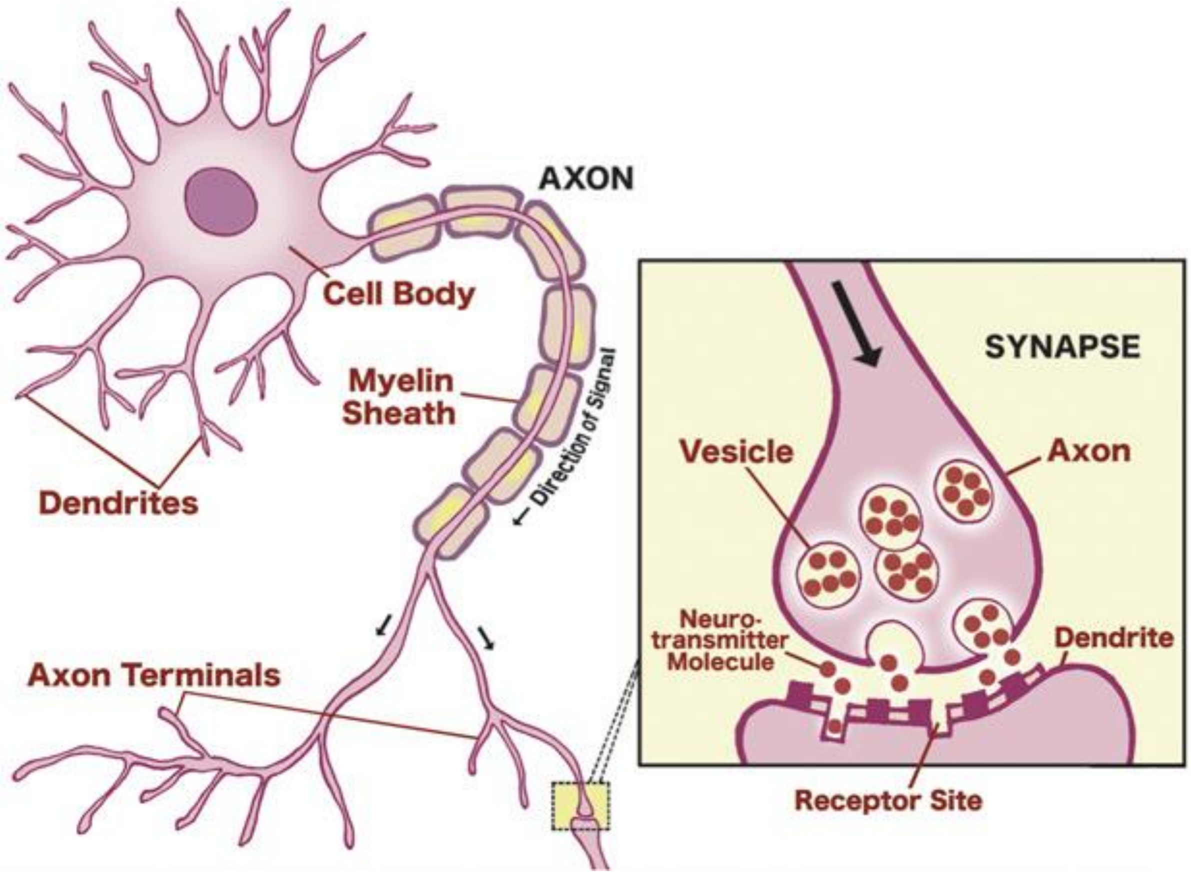
Lidocaine:



- Used as local anaesthetic for dental surgery

- Weak reversible blocker

5. Synaptic transmission: Discovery of the neurotransmitter



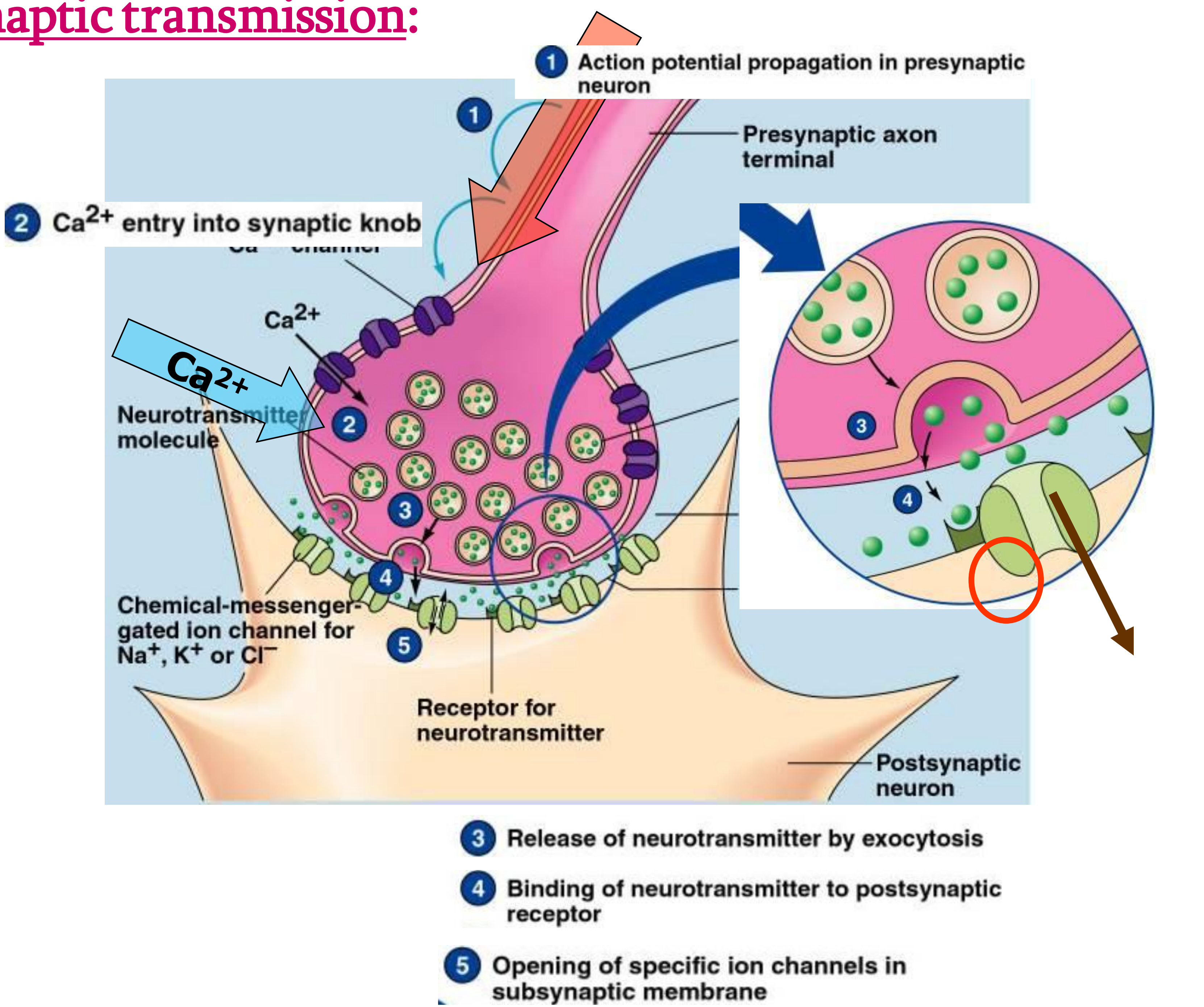
Otto Loewi Sir Henry Dale

Neurotransmitters:

- Acetylcholine
- Dopamine
- Serotonin
- Glutamate
- GABA etc.

The Nobel Prize in Physiology or Medicine 1936 for their discoveries relating to chemical transmission of nerve impulses

5. Synaptic transmission:



5. Synaptic transmission:

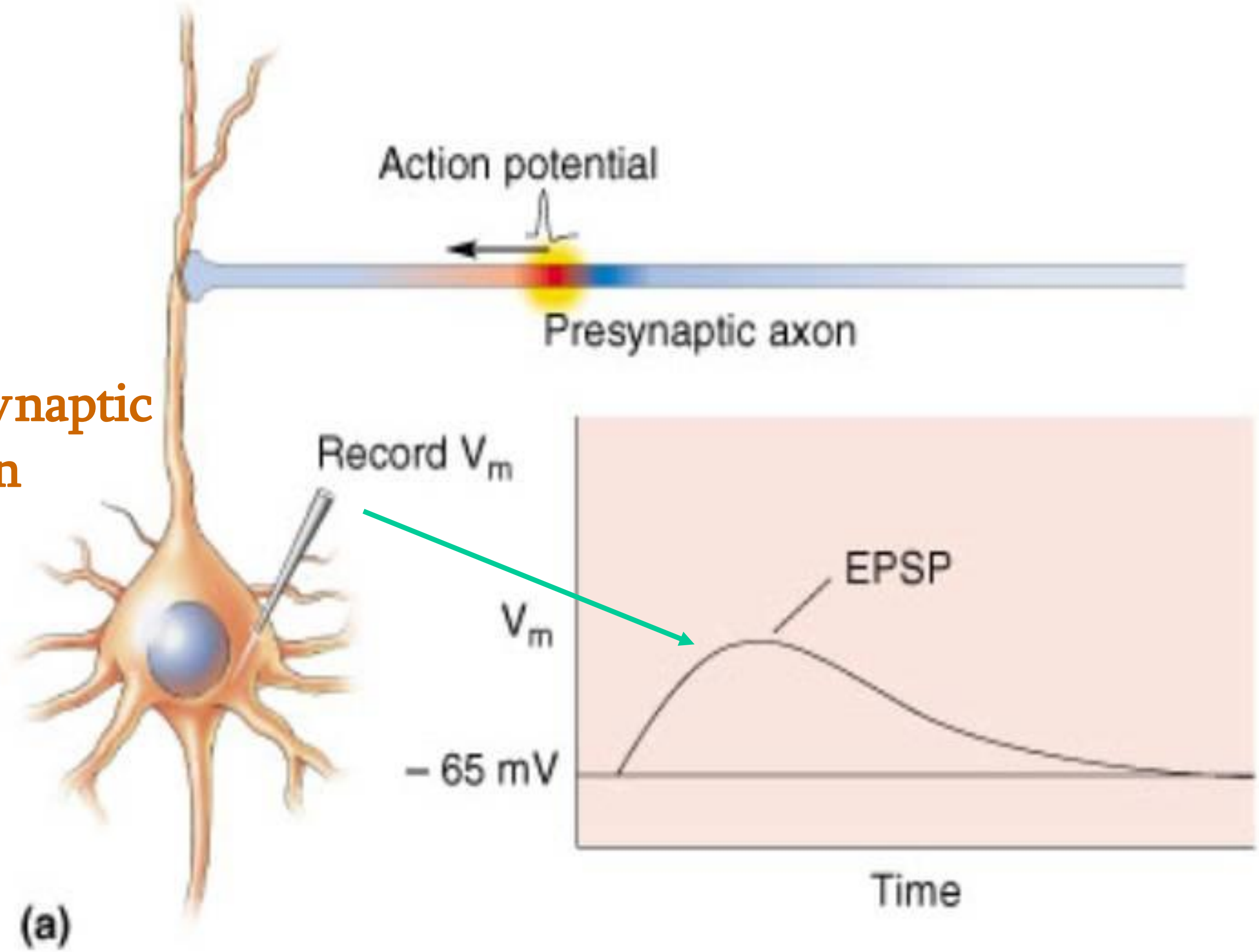
Sequence of events in chemical transmission across a synapse

1. Action potential reaches presynaptic axon ending
2. Presynaptic action potential opens voltage-dependent Ca^{2+} channels
3. Ca^{2+} causes vesicle migration, fusion with presynaptic membrane
4. Neurotransmitter released from vesicles by exocytosis
5. Neurotransmitter diffuses across cleft toward post synaptic membrane
6. Neurotransmitter binds to its receptor in the post synaptic membrane
7. Post synaptic membrane depolarizes

Excitatory post synaptic potential(EPSP)

When the neurotransmitter is glutamate, dopamine, serotonin, acetylcholine etc.

Post synaptic neuron



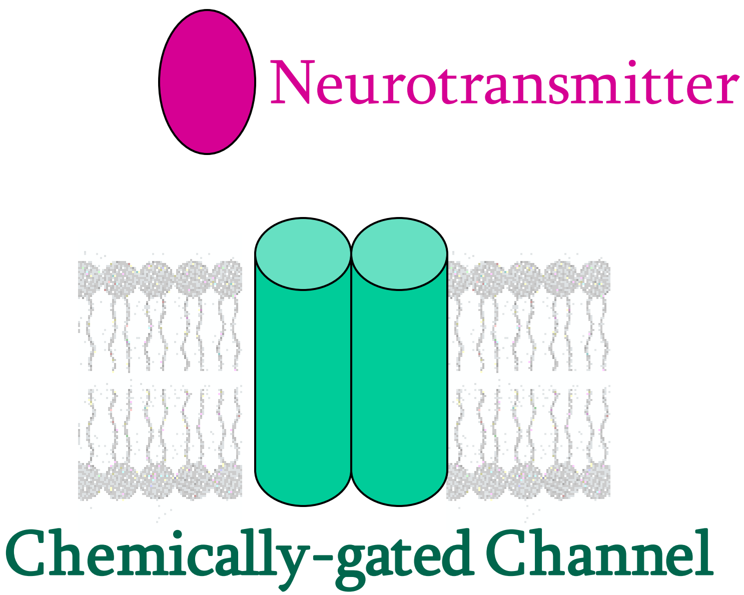
Excitatory Post-Synaptic Potential (EPSP)

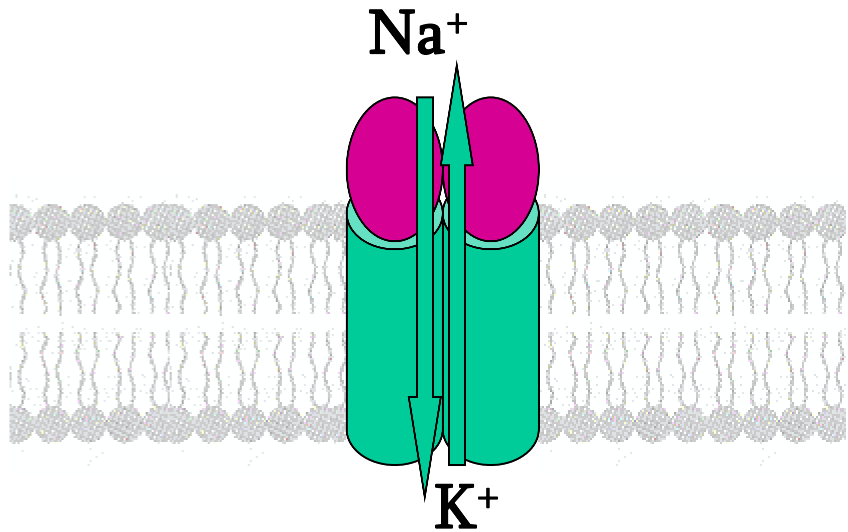
- Release of neurotransmitter from the pre-synaptic terminal

- The transmitter binds to receptors on the membrane of the post-synaptic neuron, opening sodium/potassium ion channels

- Local depolarization of the membrane of the **post-synaptic neuron**

Chemically Gated Ion Channels



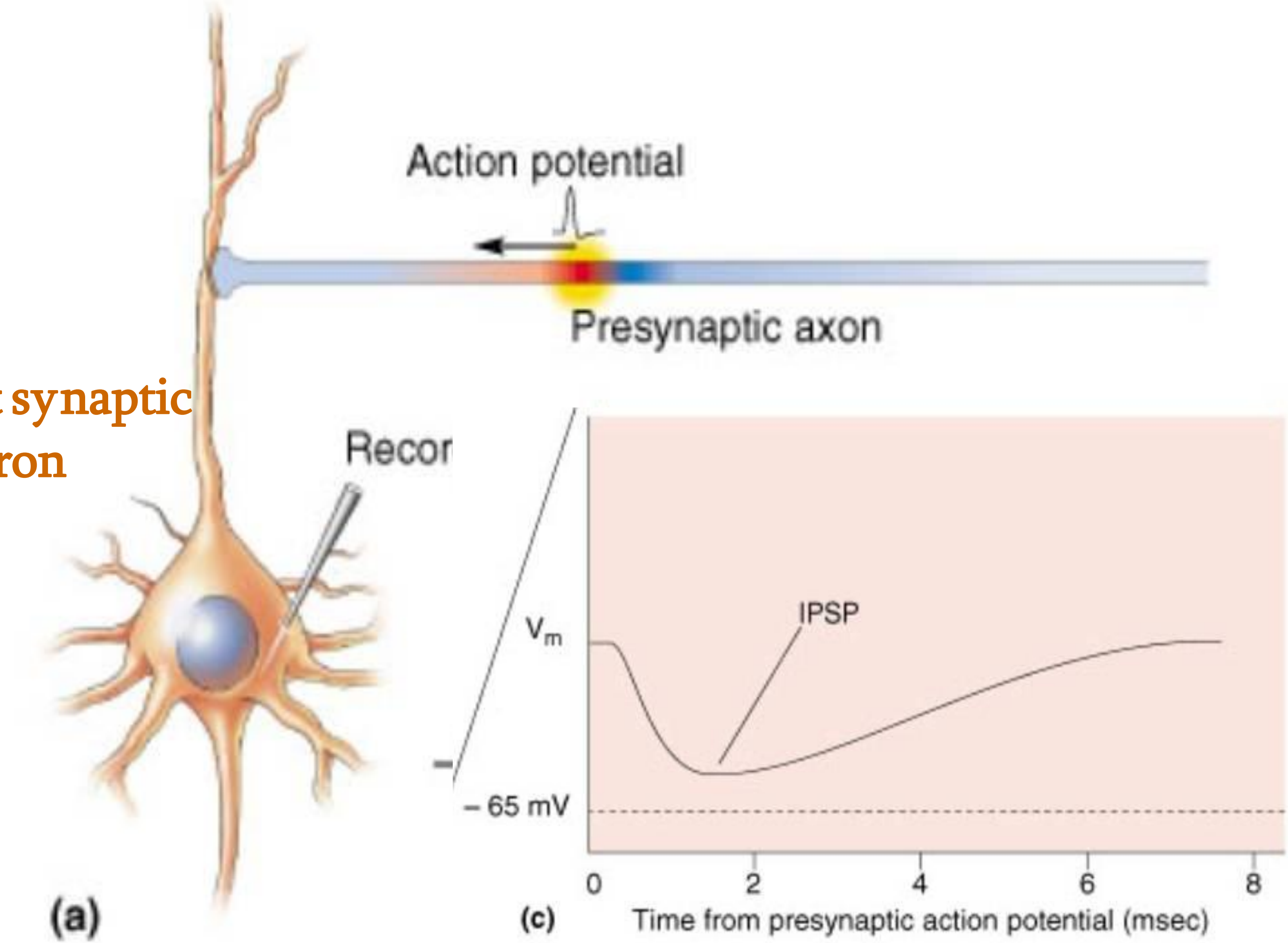


- Causes depolarization of Post-synaptic neuron

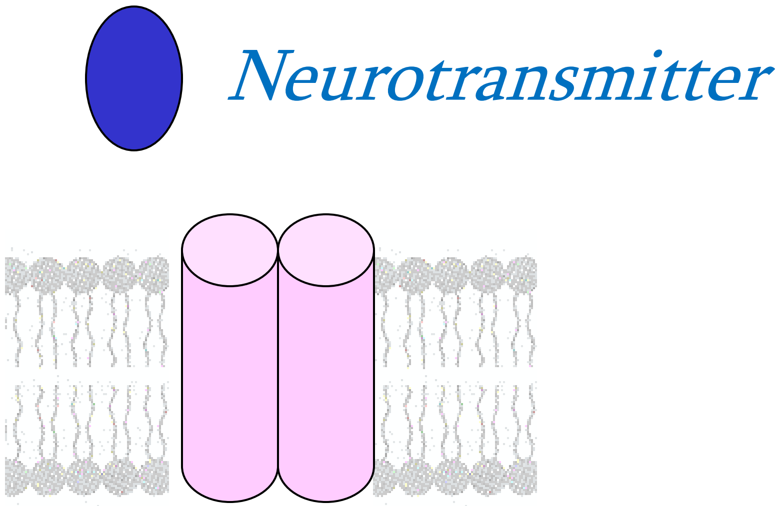
Inhibitory post synaptic potential (IPSP)

When neurotransmitter is GABA or glycine

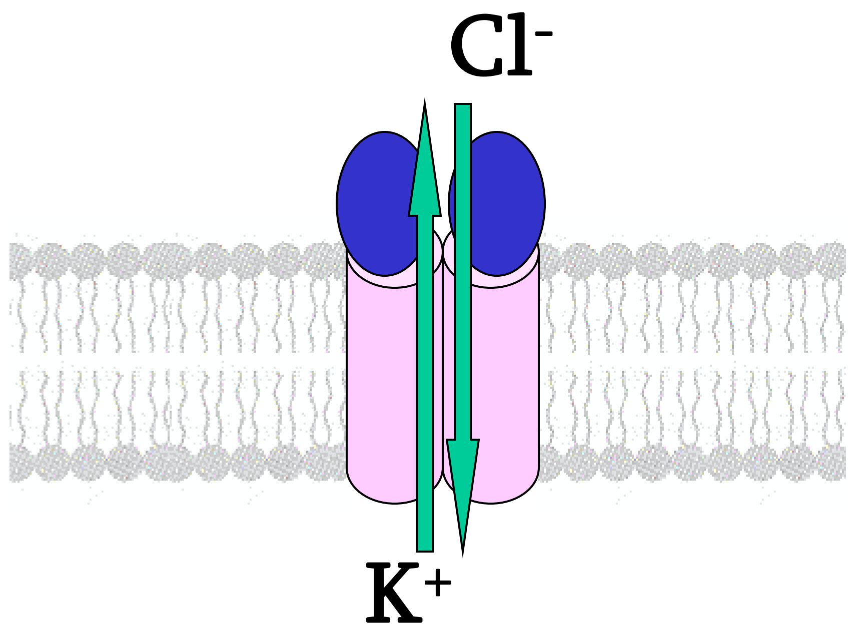
Post synaptic neuron



Chemically Gated Ion Channels



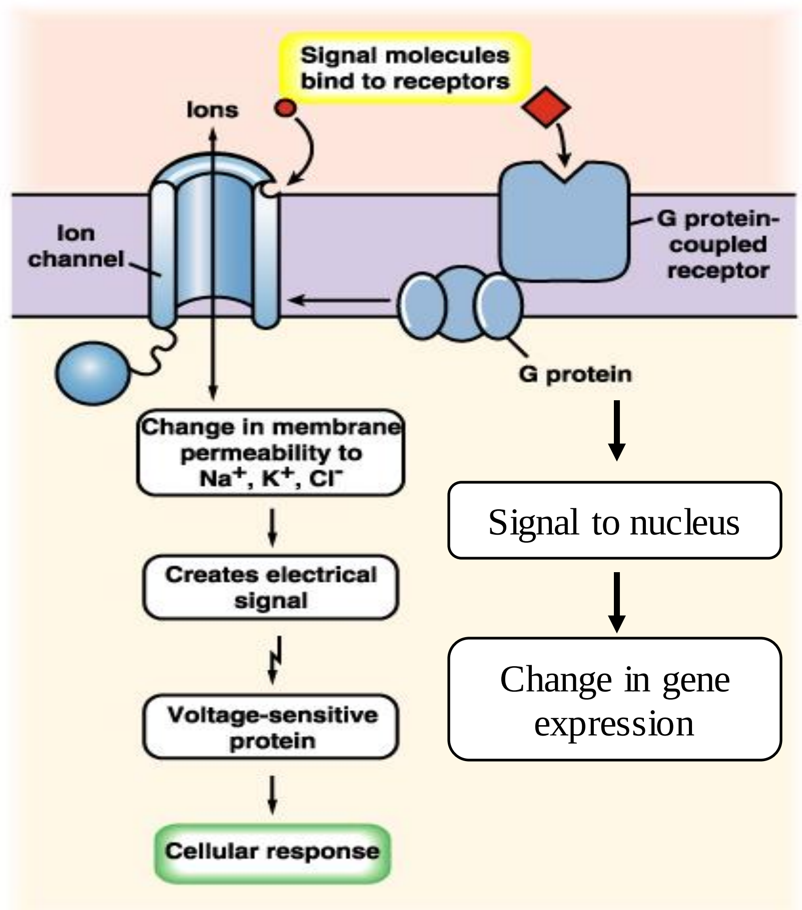
Chemically-gated K^+ Channel



- Causes hyperpolarization of Post-synaptic neuron

Neurotransmitter receptors

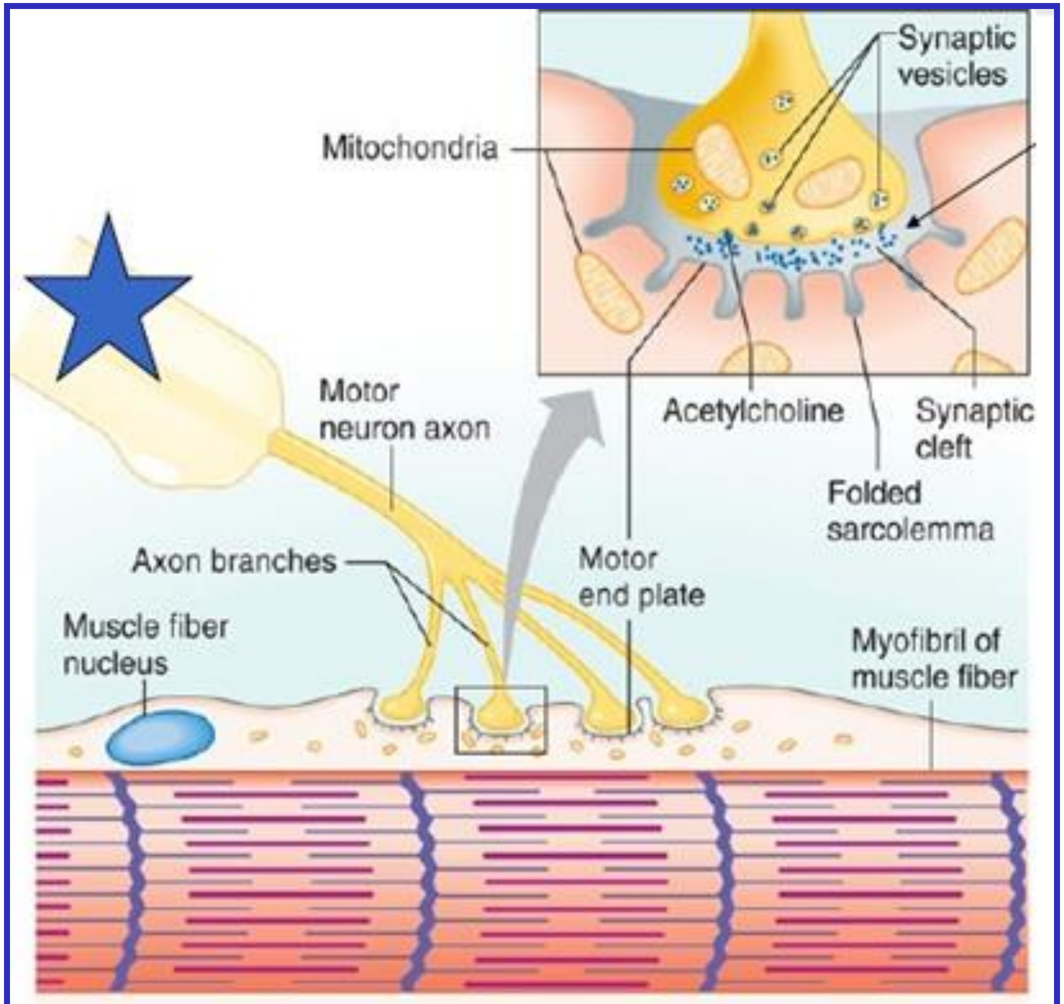
- Ionotropic – ligand gated **channels**
- Metabotropic – ligand gated **G-protein coupled receptor**



All G-protein coupled receptors have 7 transmembrane domains

Transmission at nerve muscle junction

- Neurotransmitter: Acetylcholine



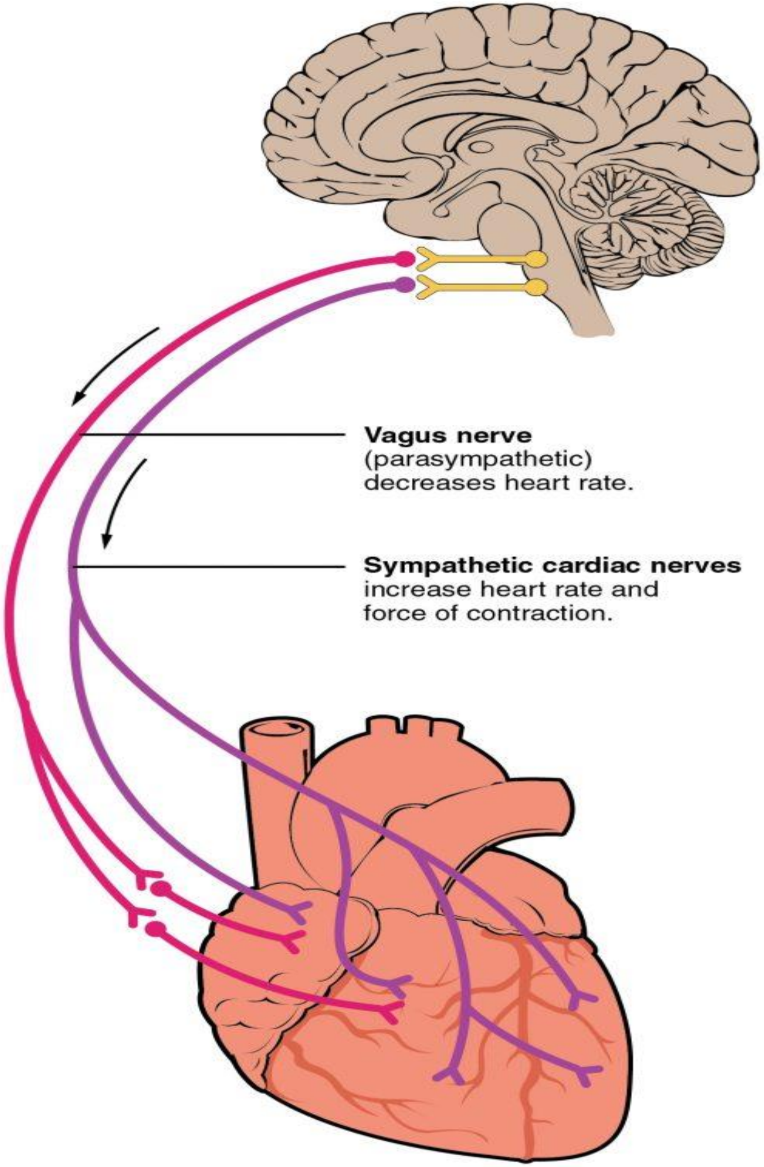
Acetylcholine released from nerve terminals, binds to its receptor in the muscle, generates action potential and muscles contracts.

- Nicotinic type of Acetylcholine receptors are present in the skeletal muscles.
- This is a cation channel

- Kobra snake venum binds with AchR(N)
- Blocks neuromuscular transmission
- Leading to paralysis of muscles

Transmission at nerve muscles junction

- Neurotransmitter: Acetylcholine

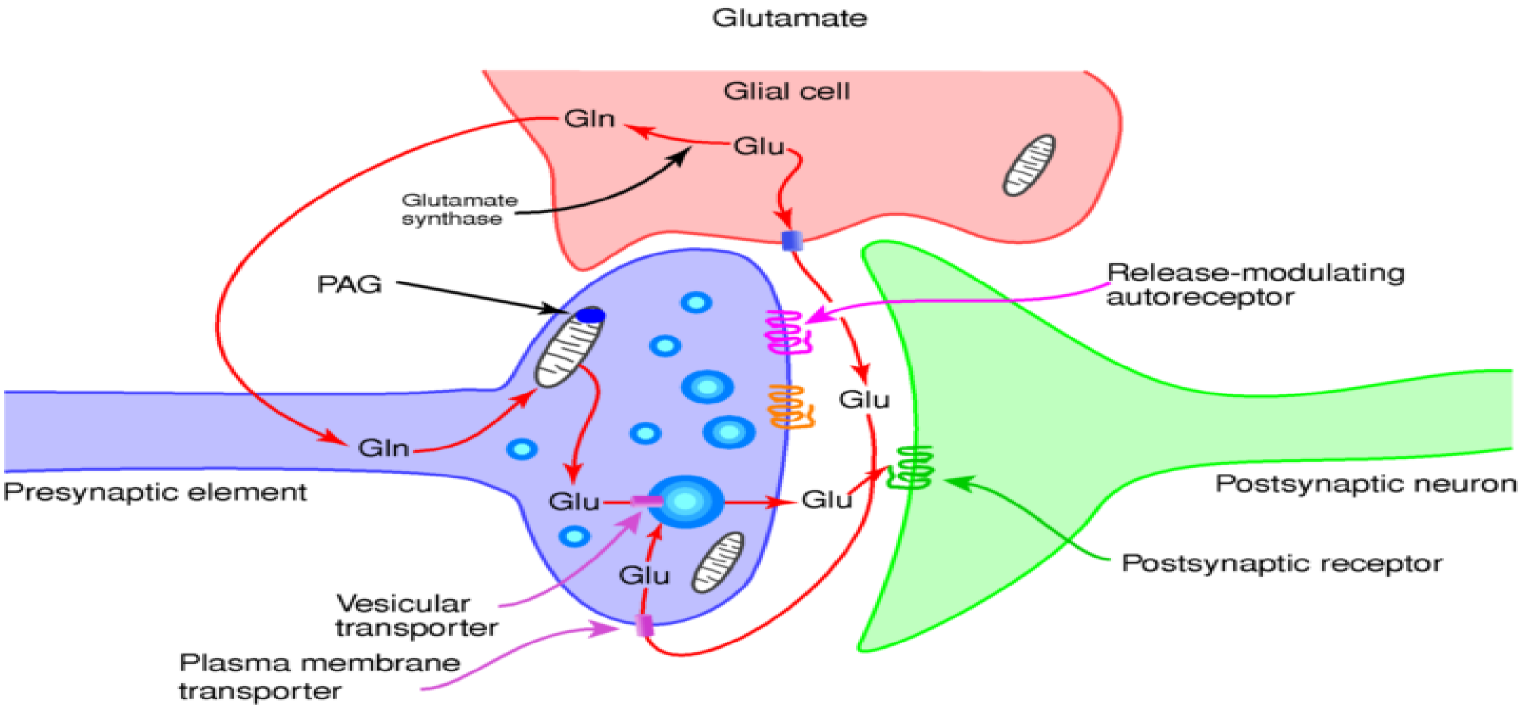


Heart muscles relaxation

- Vagus nerve stimulation releases Acetylcholine that slows heart beat
- Heart muscles have <u>**muscarinic type** of Acetylcholine receptor</u> which is metabotropic in nature

- Muscarine present in this deadly mushroom binds to and blocks AchR(M)
- Can slow down or stop the heart beat

Glutamatergic synapse



Types of glutamate receptors:

Ionotropic

- NMDA
- AMPA
- KINATE

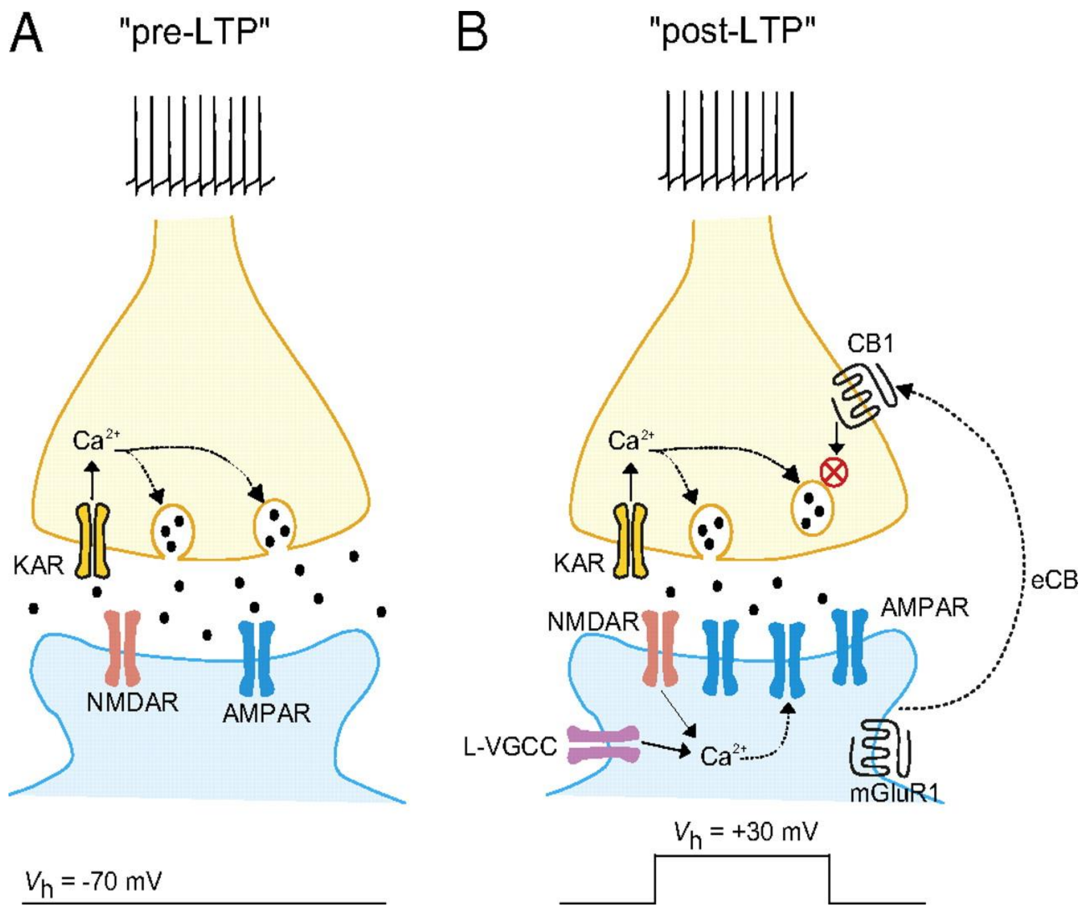
Metabotropic

- mGluRs

Neurotransmitters: Glutamate and aspartate

- Glutamatergic synapse involved in learning and memory formation
- Excessive activity of glutamatergic synapse can lead death of neuron during Epilepsy or Stroke

Glutamate receptor, long term potentiation (LTP) and memory



- LTP is defined as persistent increase in synaptic strength by repeated stimulation of synapse
- LTP causes physical changes in the synapse during memory storage
- LTP is the major cellular mechanism that leads to long term memory

Memory storage and recall

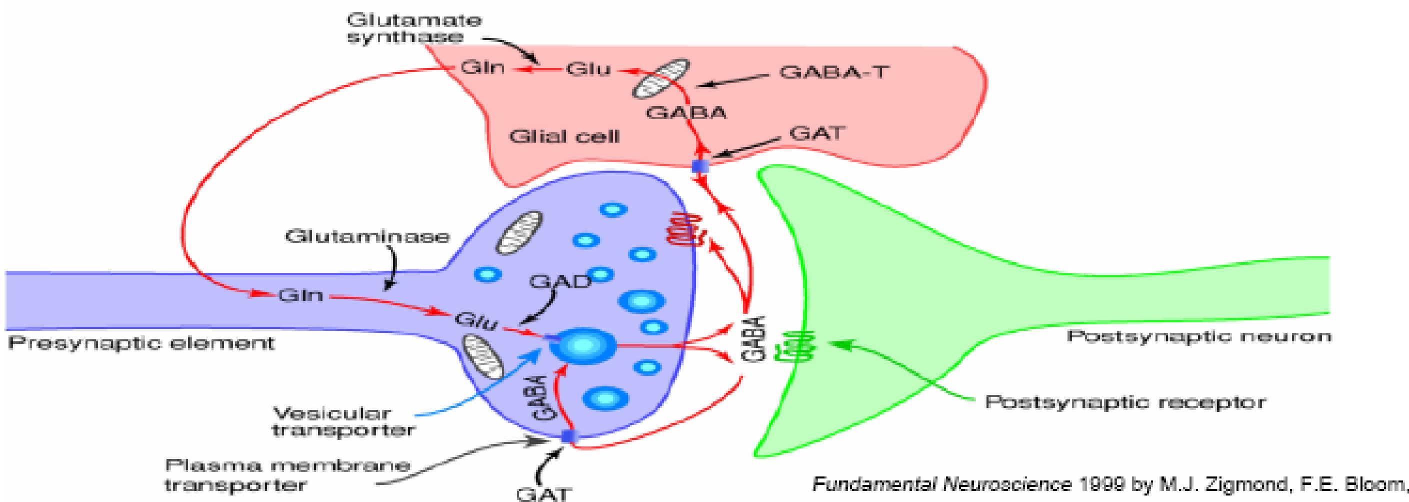
- Memory is encoded in the form of new synapse and circuits

- New proteins are synthesized during memory formation

- The circuits involved in forming memory and recalling memory might be same or different

- Different memories are stored in different interconnected brain regions

GABAergic synapse



Fundamental Neuroscience 1999 by M.J. Zigmond, F.E. Bloom, S.C. Landis, J.L. Roberts & L.R.Squire. Academic Press, San Diego CA, USA. ISBN: 0-12-780870-1

Regulation of inhibition is important:

Too much - **loss of consciousness**

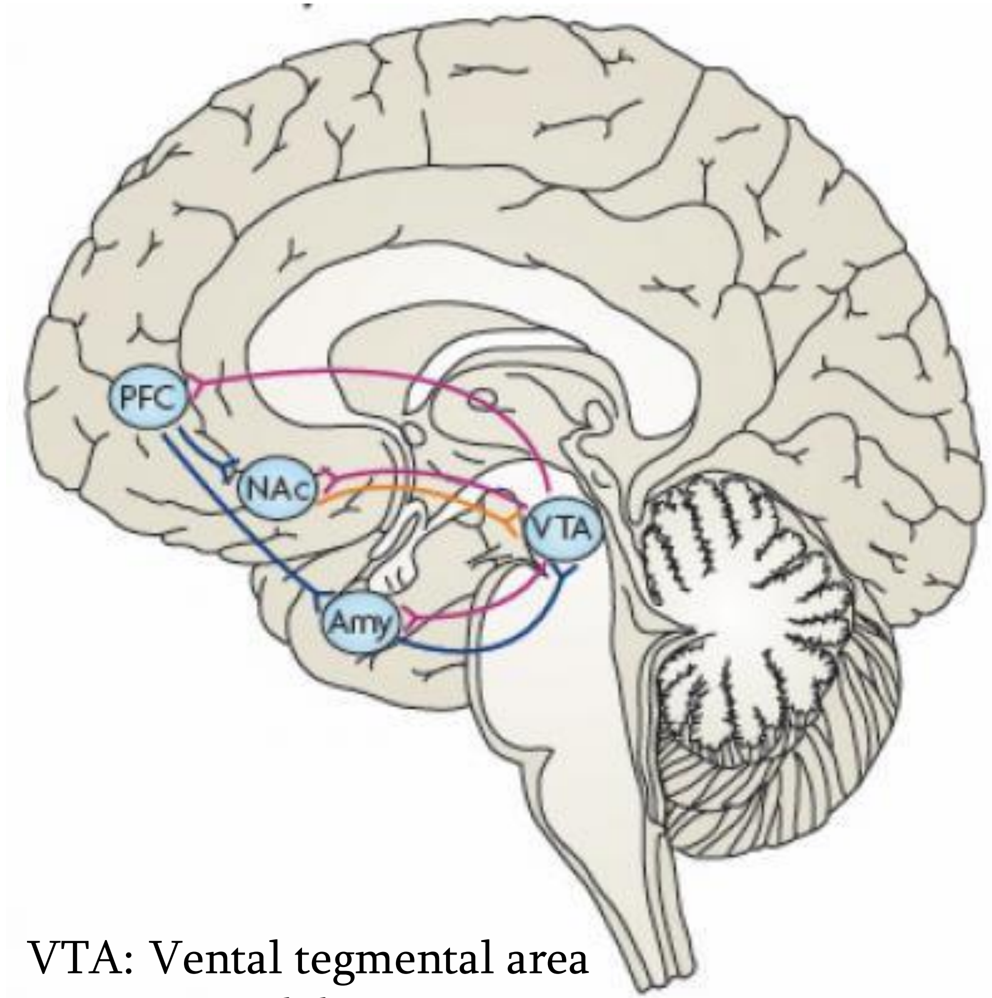
Too little - **seizures may occur**

- Most of the anaesthetics stimulate the function of GABA receptor
- Reduced activity of GABA receptor can cause seizure in epilepsy

Reward circuitry in the brain

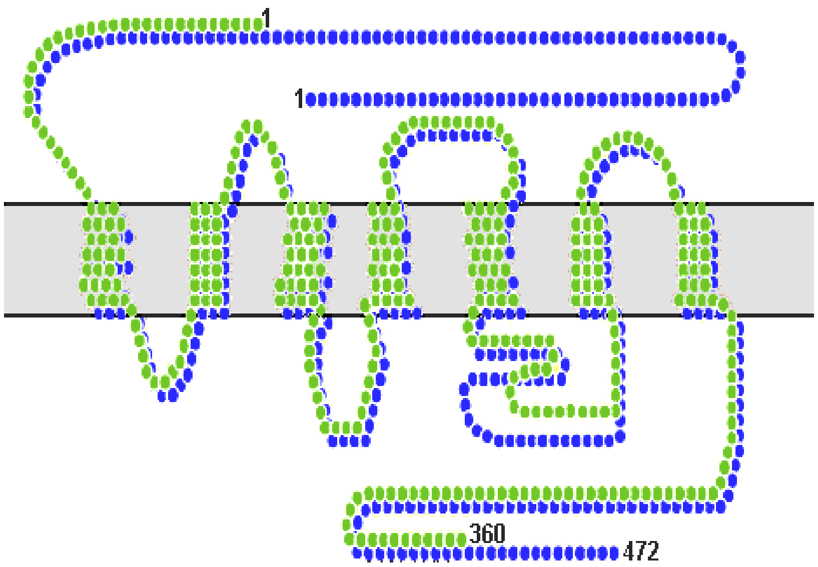
❑ Neurotransmitter: Dopamine

- Reward pathway is responsible for:
  - ➢ reward related memory,
  - ➢ pleasure motivation,
  - ➢ desire etc.
- Most abused drugs activates this pathway, for example:
  - ➢ Cocaine
  - ➢ Amphetamine
  - ➢ Heroine
  - ➢ LSD
  - ➢ Cannabis



VTA: Vental tegmental area
Amy: Amygdala
Nac: Nucleus acumbence
PFC: Prefrontal cortex

Cannabis, Euphoria and pain relief



Struttura dei recettori CB1 • e CB2 •

- Euphoria: intense pleasure or happiness
- Cannabinoid works through cannabinoid receptor (G-protein coupled receptor)
- Cannabinoid receptors widely expressed in all parts of the brain
- Endogenous ligand: Anandamides
- It is produced and released by neurons during laughing, exercise, injury etc.
- Paracetamol activates cannabinoind receptor and induces relief from pain