Membrane Potential

↳ The voltage across the membrane caused by the difference in the distribution of Ions between the Two sides of the membrane.

* Ions are effected by Two gradients :-
  1) chemical gradient (concentration)
  2) Electrical gradient (charges)

* Electrochemical Equilibrium :- No net movement of Ions across the membrane because of the chemical and Electrical are equal but in oppsite directions.
* at Equilibrium, the Electrochemical gradient is Zero, but not chemical nor Electrical is Zero.

Equations :-

1) Nernst

* only for 1 Ion
* It is called nernst Potential and Equilibrium Potential for Ions
* The sign is related to the Inner surface of the membrane.

$$E = \frac{RT}{zf} \ln \frac{[c]_{out}}{[c]_{in}}$$

R ⇒ gas constant
T ⇒ Tempreture in k
z ⇒ valence
f ⇒ faraday's constant

Valence :-
$Na^+ \rightarrow z = +1$
$k^+ \rightarrow z = +1$
$Ca^{+2} \rightarrow z = +2$
$Cl^- \rightarrow z = -1$

* جدول للحفظ :-

E	E.P
Ca^{+2}	+130
Cl^-	-80
Na^+	+60
k^+	-95

2) Goldman - Hodgkin - katz

↳ Calculate the membrane potential for more than one Ion
↳ It is calculated in consideration of Permeability
It is determined by the number of activated channels.

$$E = \frac{RT}{F} \ln \left(\frac{P_{Na^+}[Na^+]_{out} + P_{k^+}[k^+]_{out} + P_{Cl^-}[Cl^-]_{in}}{P_{Na^+}[Na^+]_{in} + P_{k^+}[k^+]_{in} + P_{Cl^-}[Cl^-]_{out}} \right)$$

P = Permeability

3) The cord conductance

↳ It is calculated in consideration of conductance (g)
↳ It is derived from ohm's Law

* conductance of an Ion is Propotional to the number of activated channels.
* The current across the membrane is measured using a Technique called patch clamp

$$V = \frac{g_{k^+}}{g_{tot}} E_k + \frac{g_{Na^+}}{g_{tot}} E_{Na^+} + \frac{g_{Cl^-}}{g_{tot}} E_{Cl^-}$$

Permeability :- The ability of any substance to pass Through the membrane.

Conductance :- The ability of charged particles (Ions) to pass through the membrane.

The steps of action potential :-

1) Resting membrane Potential (Polarization)

↳ The voltage across the membrane when it is not stimulated.
↳ for most cells the resting potential is about (-90)
↳ All voltage gated channels are closed

2) Depolarization

↳ The arrival of stimulus causes some Na^+ voltage gated channels to open
↳ If this stimulus are strong enough to make the potential reach a certain number called The Threshold, action potential occures.
If it didn't reach the threshold, The cell go back to the resting state.
* k^+ gated channels start open slowely

3) Rising phase (firing phase)

↳ all Na^+ gated channel open rapidly
↳ membrane Potential becomes more positive until reaching The Peak

Notes
* The phase from The Zero until The Peak is called Overshoot.

4) Repolarization (falling phase)

↳ at the Peak all Na^+ gated channels close very fast
↳ all k^+ gated channels are opened.

5) Hyperpolarization

↳ more negative than resting.
↳ some k^+ gated channels are still opening

Notes
* It will not reach E_{k^+} (-95) due to the contribution of Na^+ Ions
* membrane potential is then returned to resting by Na^+/k^+ pump

Channels :-

Leaky

responses for the resting membrane potential, They are always opened

gated

Voltage

↳ The stimuli is The changes in Ion distribution

chemical

↳ The stimuli is a specific ligand

Na^+ voltage gated channels:

1) opens at the Depolarization.
2) closed and capable for opening at resting stage where an activation gate is closed
3) closed and not capable for opening at The falling phase where The Inactivation gate is closed

* The more negative potential during hyperpolarization causes Na^+ gated channels to be converted from closed and not capable to closed and capable.

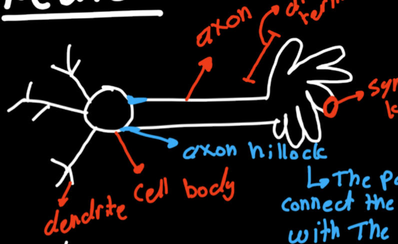
Refractory Period

↳ Period where it is difficult or Impossible to generate new action potential.

absolute :- during rising phase because Na^+ gated channels are opened and the beginning of the falling phase (Impossible)

Relative :- During the end of falling phase and the Hyperpolarization. (difficult)
↳ but could be generated.

Neuron



Supportive cells (Neuroglia)

CNS
- Astrocytes
- microglia
- oligodendroglia cytes
- Ependymal

لـ وردت في ال anatomy

PNS
- Schwan cell
- Satellite cell

responsible of producing myeline sheath

Transmission of action potential :-

1) continuous conduction
There is no myeline sheath, because of that the action potential will move continuously along the axon. (slow)

2) Saltatory conduction :-
There is a myeline sheath, so The action potential will Jump from the node of Ranvier to the next one. (fast)

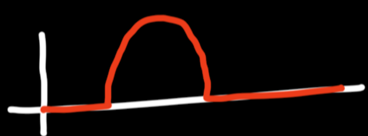
50 times faster than continuous

* ملاحظات مهمة :-
الـ action potential يتحرك باتجاه واحد فقط (من الموجب للسالب) وذلك بسبب ما يسمى ب Refractory Period لذلك يوصف ب unidirectional

* Synaptic delay :- The time needed for signal to travel from one neuron to the other.

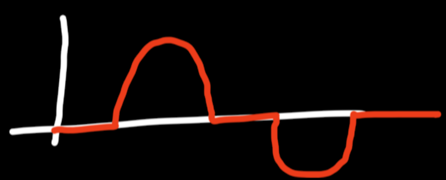
Recording of action potential :-

monophasic A.P
one electrode Inside and the other is outside
{ the result



Diphasic A.P
The Two electrodes placed outside The cell (Two waves obtained)
{ The result

Depolarization
Repolarization



Integration of response In The Postsynaptic membrane:

converging
↳ signal transimission from many axonal terminals from different neurons to one cell body.

Diverging
↳ signal transmission from many axonal terminals from The same neuron to many different neurons.

Neurotransmitters

* Neurotransmitters are stored in vesicles that formed Either by The soma or axon synaptic knob
* When action Potential reaches The axon terminal, Ca^{+2} voltage gated channels will be activated which will send The vesicles outside to the synaptic cleft by Exocytosis, which need Energy (ATP) because of that we need mitochondria in the axon terminals.
* When a Neurotransmitter binds on a receptor at the postsynaptic membrane, There is Two possiblities
  - decrease A.P (IPSP)
  - Increase A.P (EPSP) → also called sub threshold
* after the Neurotransmitters binds to their receptors on the post synaptic membrane, They will Either
  - go back to The presynaptic membrane.
  - diffusion in The synaptic cleft.
* They will be Either undergone Inactivation process in the postsynaptic membrane or without Inactivation

Inactivation
*by an destroying Enzyme bound to the postsynaptic membrane.
{ Example:-
acetylcholine esterase (destroying enzyme) destroys actylcholine Into actyl and choline and they will be transported back to the synaptic knob, where they combine to form actylcholine.

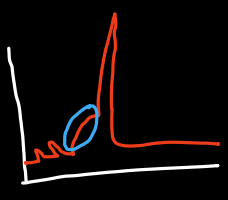
without Inactivation which results in:-
1. alter the activity of the destroying Enzyme
2. Uptake of transmitters by nerve terminals.

or Induce The release of high concentration of transmitters (Presynaptic facilitated) alter the activity of synapse by prolonging The activation of receptors at the postsynaptic membrane.

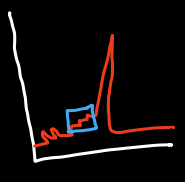
* Some drugs may combine with the receptor to prevent the binding of transmitter to Its receptor. These drugs are called the blockers
  ↳ Ex:- hexamethonium prevents the binding between actylcholine and Its receptor

Summation

Spatial
Two or more responses from Two or more different neurons have been appeared at the same time and same site of Postsynaptic membrane.



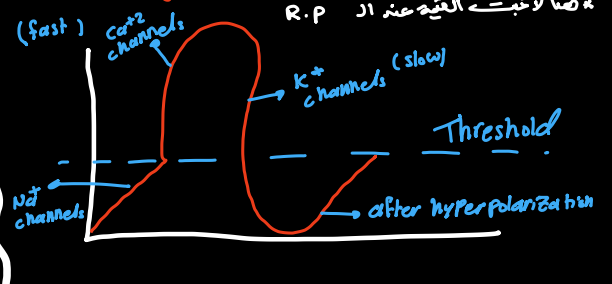
Temporal
Two or more Postsynaptic Potential, which were elicited by Presynaptic neuron at different times.



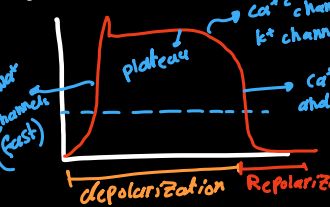
Cardiac Potential:

In the heart, There are Two Types of action Potential:-
1) SA node (sinoatrial)
2) Cardiac muscle

1) SA node
- Pace maker of the heart
- Generates action Potential Every 0.8 Second or 75 action Potential Per minute
- Resting Potential = -60, Threshold = -40.



2) cardiac muscle



*It takes 0.3 second.
*The presence of plateau is important in prolonging the time of action potential, giving the cell more time to be able to respond to another stimulus because the cell will remain longer in the refractory period.

Nerves system

- Central
  - Brain
  - Spinal cord
- Peripheral
  - Autonomic (Involuntary) (smooth muscle, gland, cardiac)
    - Enteric → Digestive organs only
    - Sympathetic
    - para-sympathetic
  - Somatic (Voluntary) → motor neurons → skeletal muscle

* A widespread collection of axons in CNS is called white matter
* A bundle of axons in CNS ⇝ Tract
  A bundle of axons in PNS ⇝ nerve
* A widespread collection of cell bodies in CNS is called gray matter
* A bundle of cell bodies in CNS ⇝ nucleus
  A bundle of cell bodies in PNS ⇝ ganglion

Synapses

→ The region where communication occurs between Two neurons or between a neuron and effector.
↓
(glands or muscles)

* Information transmitted in the nerve system mainly in a form of action potential is called nerve Impulses. It may be
  - changed into repetitive Impulses
  - blocked
  - Integrated with other Impulses.

Types of synapses

Electrical

The cytoplasm of adjacent cells are directly connected by gap junctions.

Advantages :-
1) Faster communication
2) Synchronization
3) Bidirectional

chemical

The Two cells communicate Through neurotransmitters

In The presynaptic neuron:-
1) transmitter vesicle
2) mitochondria, which provide Energy for Exocytosis.
3) Ca^{+2} gated channels, The quantity of neurotransmitter realed is directly related to the number of Ca^{+2} that enters.

The postsynaptic neuron :-
1) metabotropic (Activating second massenger (prolonged))
2) Ionotropic (gated Ion channels)

Features :-
1) unidirectional
2) delayed.

Neurotransmitter

- Small molecule
  1. It is synthesised in the presynaptic terminal (axon terminal)
  2. The effect is rapid and acute
  3. rapid releases
  4. Stored in vesicles allow for quantal release (fixed amount)
  5. The receptors in postsynaptic neuron could be both metabotropic and Ionotropic
  6. when they are inactive they go back to the presynaptic membrane.
- Neuropeptide
  1. synthesised in the soma
  2. It uses axonal transport to move from the soma to axon terminal
  3. when they are inactivated they will be autolysed.
  4. they are more potent
  5. their receptors are metabotropic (GPCR)
- unclassical

Small molecules.

- GABA (Inhibitory) ⇝ The main "brake" That prevent Epilepsy
- Glycine (Inhibitory) & Secreted mainly in the spinal cord rather than the brain
- Glutimate (Excitatory)
- ACh (Excitatory)
  - motor neuron that innervate the skeletal muscle NMJ ⇝ myasthenia
  - Basal forebrain ⇝ Alzheimer disease
  - Autonomic NS
- Norepinephrine
  - Brainstem (locus ceruleus)
  - sympathetic NS

  low level ⇝ Depression
  low level ⇝ ADHD
- Dopamine
  - nigrostriatal ⇝ Parkinson disease
  - mesocortical ⇝ psychiatric disorder
  - mesolimbic
  - tuberoinfundibular ⇝ control prolactin secretion
    → Dopamine from hypothalamus acts on the anterior pituitary to Reduce milk.
- serotonin → Secreted from Brainstem (raph nucleus)
  low level ⇝ Depression

Neuropeptide

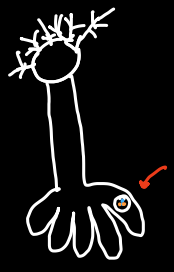
- **Substance P**
  - Sensory neurons, spinal cord and hypothalamus
  - Pain transmission (chronic pain)
  - Inflammation and stress
- **Oxytocin**
  - Produced in hypothalamus and released from posterior pituitary
  - ① control contraction of uterus during labor
  - ② Ejection of milk during lactation
  - ③ Social bonding and Emotional behavior

Nitric oxide

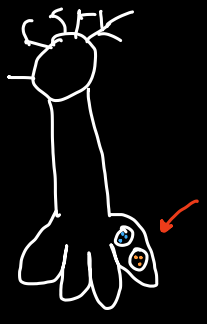
- not prevesicle
- Synthesise in demand (not presynthesised)
- doesn't alter action potential, but changes intracellular metabolic function that modify neuronal excitability.
- Synthesised by nitric oxide synthase (NOS) enzyme.
  - nNOS
    - neuronal
  - iNOS
    - Inducible

Co-transmission

Small molecules and neuropeptide are in the same vesicle



Small molecules and neuropeptide are in different vesicles but same axon terminal and their release may be differently regulated because of different Ca^{+2} sensitivity.



Small molecules and neuropeptide are in different axon terminals.

(Spatial segregation)