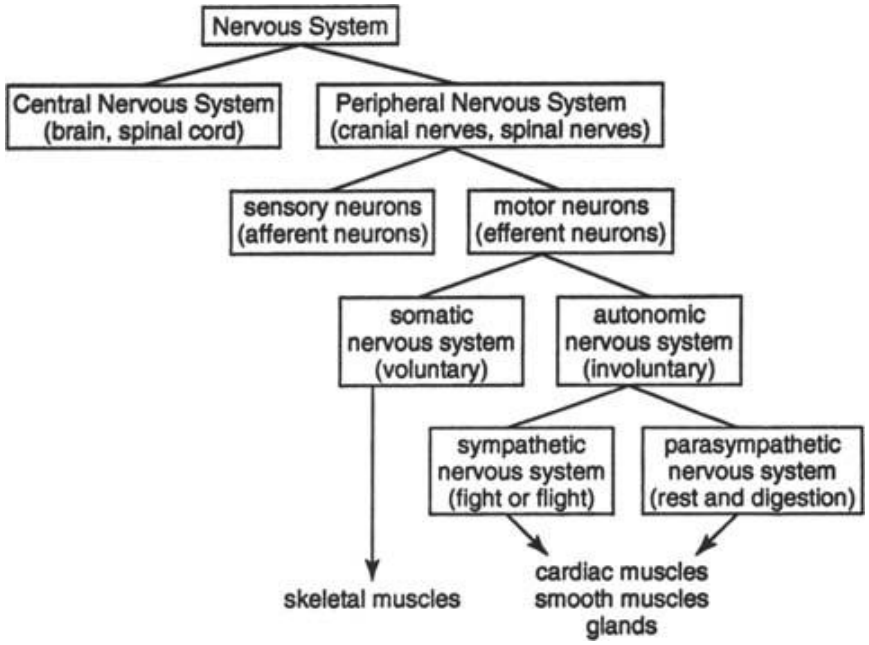
ORGANISATION OF THE HUMAN NERVOUS SYSTEM



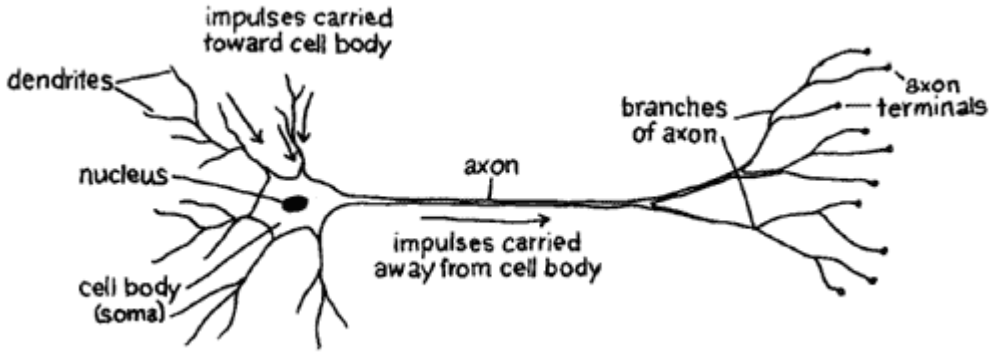
Neurone (nerve cell):
A specialised cell adapted to a transmitting nerve impulses

Definition of ganglion
Structure containing a number of nerve cell bodies, typically linked by synapses, and often forming a swelling on a nerve fiber

CATEGORISATION OF NERVE CELLS (NEURONES)

	(i) Sensory neurone	(ii) Interneuron	(iii) Motor Neurone
Polarity	**Unipolar:** 1 branched process from cell body	**Bipolar**: 1 dendrite, 1 axon	**Multipolar:** Many dendrites, 1 axon
Length	Long dendrites and short axon	Short dendrites, axon length varies	Short dendrites and long axons
Location	Cell body and dendrite are outside spinal cord; the cell body is located in a dorsal root ganglion	Entirely within the CNS	Dendrites and cell body are in spinal cord; axon is outside spinal cord
Function	Conduct impulse to spinal cord	Link sensory to motor nerves	Conduct impulse to effectors

STRUCTURE OF MOTOR (EFFECTOR) NEURONE



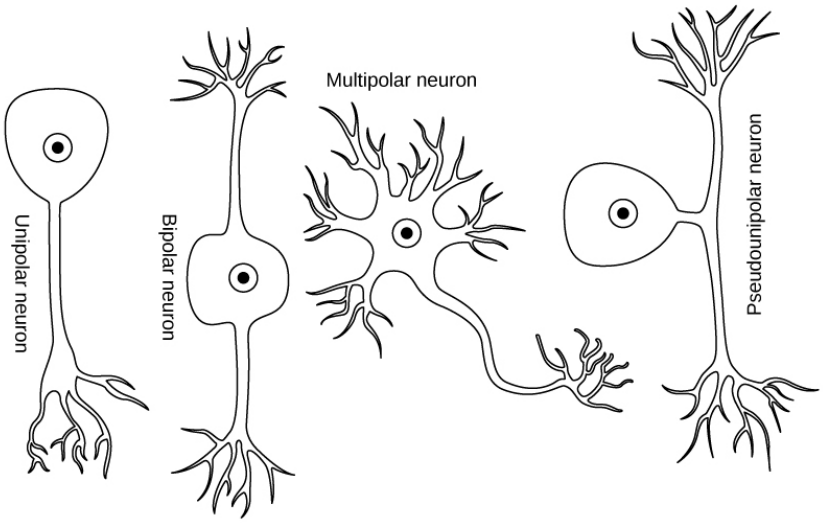
DESCRIPTION OF STRUCTURE OF THE MOTOR NEURONE

- At one end of the axon there is a **cell body**, which contains a relatively large nucleus, mitochondria, ribosomes, numerous rows of rough endoplasmic reticulum called **Nissl's granules**.
- There are short cytoplasmic extensions of the cell body called **dendrons,** which subdivide into smaller branched fibres called **dendrites.**
- A single elongated cytoplasmic extension called **axon** branches off the cell body, with a narrow diameter (about 10µm)
- Many companion cells called **Schwann cells** wrap their cell membrane in intervals, around the axon many times in a spiral to form a thick insulating lipid layer called the **myelin sheath**.
- The part of the axon not covered by the myelin sheath is called the **node of Ranvier**.

HOW THE MOTOR NEURONE IS SUITED FOR FUNCTIONING

- The nucleus is **relatively large** to coordinate the metabolic activities all over the large cytoplasm of the cell.
- There are very many rows of rough endoplasmic reticula (**Nissl's granules**) for massive production of proteins and neurotransmitters.
- The dendrites are **numerously branched** to increase the surface area for synapting with several other neurones.
- Axon is **long** to carry impulses to the target parts.
- The axon membrane is wrapped with a myelin sheath for electrical **insulation.**
- The axon membrane is wrapped with a **thick** myelin sheath for **protection** against damage.
- The axon membrane is wrapped with a myelin sheath at intervals around the axon which **increases speed** of impulse transmission through salutatory conduction.

POLARITY OF NEURONES



WHAT ARE SATELLITE CELLS?

These are cells associated with the nervous system but cannot conduct impulses.

Examples:

- **Schwann cells** which wrap their cell membrane around the axon and carry out **phagocytosis** of cell debris, **increase speed** of impulse transmission, and **protect** the axon against damage.
- **Neuroglia** in the brain and spinal cord form membranes, others are phagocytic while some are thought to be involved in memory.

NB: Neuroglia are more numerous than neurones

DIFFERENCES BETWEEN AXONS AND DENDRITES

Axons	Dendrites
Take information away from the cell body	Bring information to the cell body
Smooth Surface	Rough Surface (dendritic spines)
Generally only 1 axon per cell	Usually many dendrites per cell
No ribosomes	Have ribosomes
Can have myelin	No myelin insulation
Branch further from the cell body	Branch near the cell body

COMPARISON OF NEURONS AND OTHER CELLS IN THE BODY

Similarities:

All:

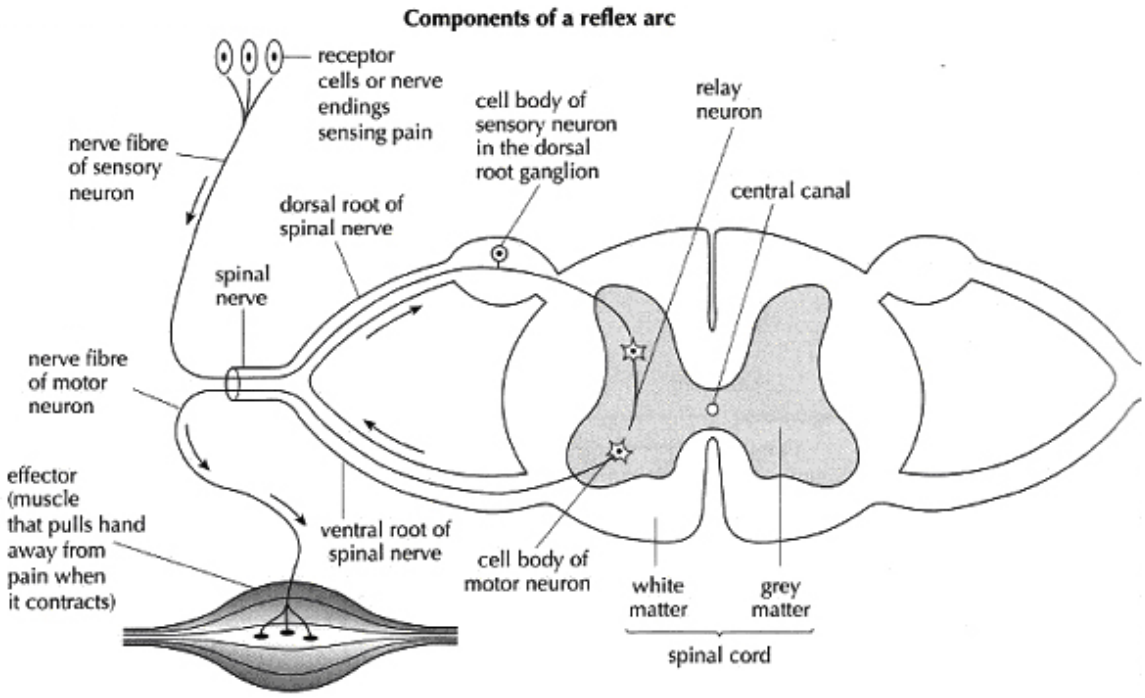
(1) are surrounded by a cell membrane
(2) have a nucleus that contains genes
(3) contain cytoplasm, mitochondria and other organelles
(4) carry out basic cellular processes such as protein synthesis and energy production.

Differences:

Neurons	Other cells in the body
Have specialised extensions called dendrites and axons.	Lack dendrites and axons
Communicate with each other through an electrochemical process.	No such electrochemical communication
Contain some specialized structures (for example, synapses) and chemicals (for example, neurotransmitters).	No neurotransmitters

REFLEX ARC

The neural pathway over which impulses travel to produce a reflex action, consisting of at least one afferent (receptor) and one efferent (effector) neuron



CATEGORISATION OF REFLEX ARCS

1. Monosynaptic reflex arc: A reflex arc consisting of only a single chemical synapse between one sensory neuron, and one motor neuron e.g. Patellar reflex, Achilles reflex, Muscle spindle reflex

2. Polysynaptic reflex arc: A reflex arc comprising of one or more interneurons connecting the afferent (sensory) and efferent (motor) neurones

NB: All but the simplest reflexes are polysynaptic, allowing processing or inhibition of polysynaptic reflexes within the brain

FUNCTIONING OF NEURONS

Neurones are electrically excitable cells i.e. they can change their membrane potential and are capable of transmitting electrical nerve impulses. The impulses are due to events in the cell membrane.

THE RESTING MEMBRANE POTENTIAL

- This is the difference in potential across the membrane of a cell when it is at rest, i.e. fully repolarized. In the heart, this occurs during electrical diastole in **pacemaker cells** and continuously in **non-pacemaker cells**.
- **The membrane potential** (***V***m) = ***V***in – ***V***out; (***V***in = potential inside membrane, ***V***out = potential outside)

NOTE: By convention, the potential outside the cell is defined as **zero (0 mV)**, therefore the resting potential (***V***r) is equal to ***V***in, and is usually between -60mV to -70mV **(indicating that the inside of the cell is 70 millivolts less than the outside of the cell)**

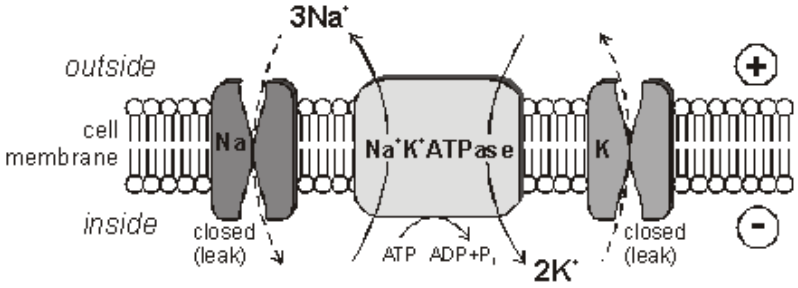
TYPICAL EXAM QUESTION: Describe how the resting membrane potential is created and maintained

How the resting membrane potential is created

- The protein pump called the sodium-potassium pump **(Na^+K^+ATPase)** in all animal cell membranes actively pumps **simultaneously** 3 Na^+ out of the cell and 2 K^+ in, causing a higher concentration of Na^+ outside the membrane than in the cytoplasm, and more K^+ in the cytoplasm than outside thus creating a chemical gradient.
- Although Na^+ and K^+ later leak by diffusion along their gradients, the axon membrane is 100 times more permeable to potassium ions which therefore leak out of the cytoplasm faster than the sodium ions leak in because most of the potassium gates are open while most of those of sodium are closed, resulting in a potential difference (difference in charge) between the negative inside of the neurone and the positive outside, called the **resting membrane potential.**

How the resting membrane potential is maintained

- Further outward movement of potassium ions causes the axon membrane outside to become positively charged and hinders further outward movement of potassium ions due to a great attraction by the negatively charged inside which compels them to move into the axon and the repulsion by the positively charged outside which prevents them from moving out of the axon.
- An equilibrium is established in which the chemical and electrical gradients are balanced and there is no net movement of ions.



Distribution of the major ions inside and outside the neuronal membrane at rest of the squid giant axon and mammal (cat)

Ion	Concentration in cytoplasm / mmol dm^{-3}		Concentration outside cell / mmol dm^{-3}		Comment on ion movement down their concentration gradient
	Squid	***Cat***	***Squid***	***Cat***	
K+	400	140	20	5	K+ ions do not move out of the neurone down their concentration gradient due to a build up of positive charges outside the membrane. This repels the movement of any more K+ ions out of the cell.
Na+	50	10	440	145	
Cl-	52	10	560	125	The chloride ions do not move into the cytoplasm as the negatively charged protein molecules that cannot cross the surface membrane repel them.
A^- (organic anions)	385	----------	----------	----------	Organic anions are primarily amino acids and protein, which are synthesized inside the cytoplasm and their outward flow is restricted by the plasma membrane due to large size.

NOTE:

1. The Na^+K^+ATPase presumably evolved as an osmoregulator to keep the internal water potential high and so stop water entering animal cells and bursting them. Plant cells don't need this due to their strong cells walls that prevent bursting.

2. Had it not been for the sodium and potassium **ion 'leak' channels** in the membrane to check the Na^+K^+ATPase pump, a situation would result when there would be no sodium or potassium ions left to pump.

3. The Na^+ and K^+ channels are voltage-gated, i.e. they can open and close depending on the voltage across the membrane.

THE ACTION POTENTIAL

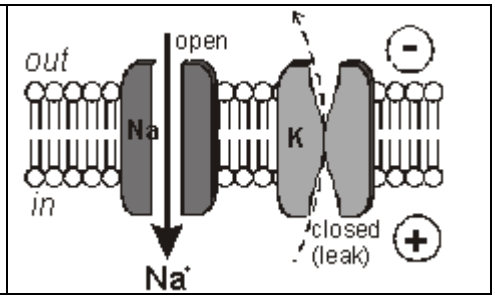
This is a rapid change in the membrane potential of an excitable cell, caused by stimulus-triggered, selective opening and closing of voltage sensitive gates in sodium and potassium ion channels.

- The action potential is generated at the **axon hillock**, where the density of voltage-gated sodium channels is greatest.
- The action potential begins when signals from the dendrites and cell body reach the axon hillock and cause the membrane potential there to become more positive, a process called depolarization

Question*: *Describe how a nerve impulse is initiated and propagated in a neurone

1. Depolarisation:

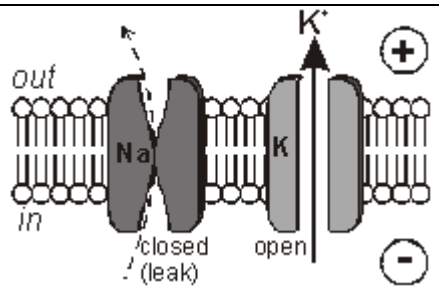
- A stimulus from sensory cell or another neurone can cause the membrane potential of a target neurone to change a little.
- The voltage-gated ion channels can detect this change, and when stimulated past threshold (about –30mV in humans), the sodium channels open for 0.5ms.
- This causes Na^+ to rush in, making the inside of the cell more positive.
- This phase is referred to as a **depolarisation** since the normal voltage polarity (negative inside) is reversed (becomes positive inside).



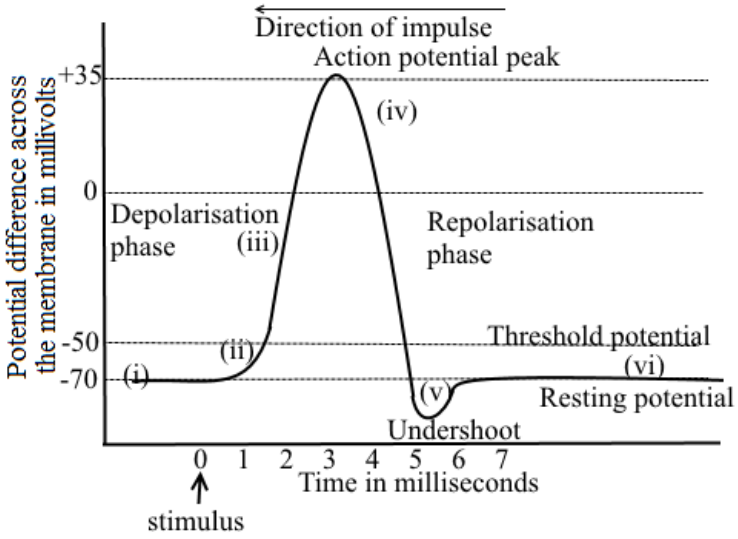
2. Repolarisation:

- The region of positive charge causes nearby voltage gated sodium channels to close.
- Just after the sodium channels close, the potassium channels open wide for 0.5ms, causing potassium ions to rush out, making the inside more negative again, so the charge across the membrane is brought back to its resting potential.
- This is called **repolarisation.** As the polarity becomes restored, there is a slight 'overshoot' in the movement of potassium ions (called **hyperpolarisation**).
- This process continues as a chain-reaction along the axon in one direction.
- The influx of sodium depolarises the axon, and the outflow of potassium **repolarises** the axon.

The resting membrane potential is restored by the Na+K+ATPase pump.



Changes in potential difference across a nerve fibre membrane during the passage of an action potential.



Resting membrane potential

At (i): Both the voltage-gated sodium and potassium channels are closed. The membrane's resting potential is maintained by the Na+/K+ pump and the permeability of the membrane which permits facilitated diffusion of more K+ ions out and less Na+ ions

At (ii): A stimulus triggers the opening of some sodium voltage-gated channels. When the influx of Na+ ions exceeds threshold potential, more sodium voltage-gated channels open

Depolarization phase of the action potential

At (iii): The activation gates of the voltage-gated sodium channels open. There is influx of Na+ ions into the cell and the cell becomes more positive. The voltage-gated potassium channels remain closed.

Repolarization phase of the action potential

At (iv): Inactivation gates close voltage-gated sodium channels. Voltage-gated potassium channels open and K+ ions diffuse out of the cell. The loss of positive K+ ions cause the inside of the cell to become more negative than the outside.

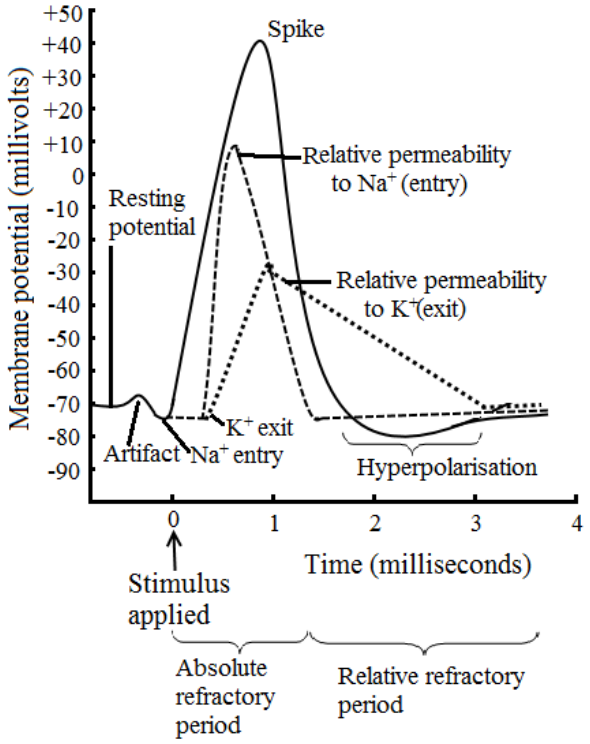
Hyperpolarization / Undershoot

At (v): Both gates of the voltage-gated sodium channels are closed. The voltage-gated potassium channels remain open because their gates close slowly. Within one or two milliseconds, voltage-gated channels close.

Re-establishing resting potential

At (vi): The resting potential is re-established by the Na+/K+ pump and facilitated diffusion through ion channels.

Axon membrane permeability to Na^+ and K^+



Comparison of membrane permeability to Na^+ and K^+

SIMILARITIES

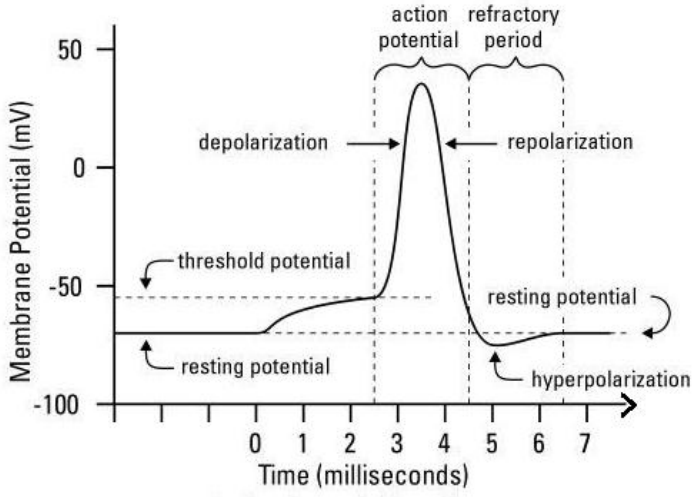
Axon membrane permeability: is **constant** from 0ms to about 0.3ms and 3ms to 3.5ms**; increases** from about 0.3ms to 0.5ms**; equivalent** at about 1ms**; decreases** between 1ms and 1.3ms**;**

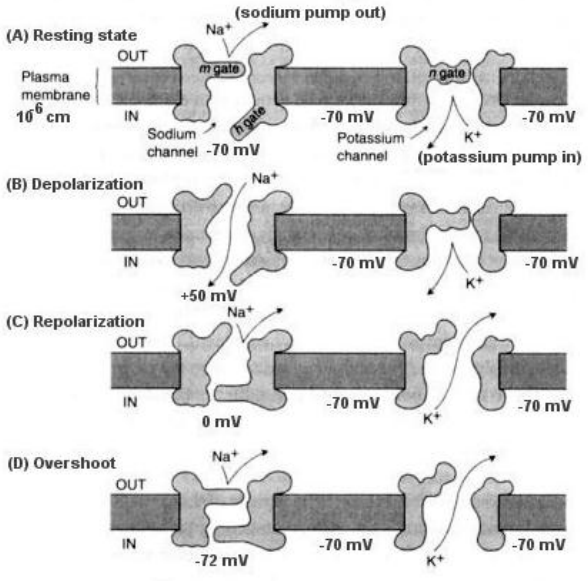
DIFFERENCES

Axon permeability to Na+	**Axon permeability to K+**
Increases rapidly from 0.3ms to about 0.5ms	Increases gradually from 0.3ms to about 0.5ms
Attains much higher peak	Attains much lower peak
Constant from about 1.5ms to 3ms	Decreases from about 1.5ms to 3.5ms

ROLE OF THE NEURONE MEMBRANE IN ESTABLISHMENT OF A RESTING POTENTIAL

1. Membrane is polarised; inside of axon is more -ve than outside
2. A resting potential of -70mV is maintained by:
(i) Negatively charged proteins / large anions inside axon
(ii) Membrane more permeable to K^+ ions than to Na^+ ions / K^+ ions move out faster than Na^+ ions diffuse in
(iii) Sodium/potassium pump / Na^+ ions pumped out faster than K^+ ions pumped in
3. Electrochemical gradient determines movement of ions:
(i) K^+ cannot move down its conc. gradient
(ii) Build-up of positive Na^+ outside membrane repels K^+
4. Imbalance of negative ions causes potential difference/voltage:
(i) Cl- cannot move down its concentration gradient
(ii) Negatively charged proteins in cytoplasm repel Cl-





NEURONE EXCITABILITY DURING AND AFTER AN IMPULSE

Refractory period

1. Represents a time during which the membrane cannot be depolarised again.
(i) Occurs during repolarisation and hyperpolarisation
(ii) Membrane is impermeable to Na^+ ions / sodium ion channels closed
(iii) Sodium ions cannot enter axon
(iv) K^+ ions move out as membrane is more permeable to K^+ ions
(iv) Membrane becomes more negative than resting potential

2. Nerve impulses can only travel in one direction.
(i) Action potential can only depolarise the membrane in front
(ii) Membrane behind is recovering from refractory period (previous action potential)

3. Refractory period limits frequency with which neurones can transmit impulses
(a) Absolute refractory period: is when it is not possible to elicit another action potential despite the size of the stimulus.
Na+ channels are recovering and no matter what stimulus is applied, they cannot activate to allow Na+ in and depolarise the membrane to the threshold of an action potential.
(b) Relative refractory period: is when it is more difficult to elicit an action potential, but still possible if a greater stimulus is used than is needed at rest.
In relative refractory period some of the Na+ channels have re-opened but the threshold is higher than normal making it more difficult for the activated Na+ channels to raise the membrane potential to the threshold of excitation.

All-or-nothing nature of nerve impulses
All-or-nothing law: "The magnitude (size) of the action potential (nerve impulse) is independent of and is not a function of the intensity of the stimulus, provided the stimulus is of threshold value".
(i) Threshold stimulus → impulse that causes an action potential
(ii) Stimulus transmits an impulse at a constant and max strength
(iii) Transmission is independent of any intensity of the stimulus
(iv) High frequency of impulses / more amount of sodium entry / more ATP
(v) Subthreshold stimulus → stimulus weaker than a threshold stimulus
(vi) Summation → series of subthreshold stimuli cumulate to cause an action potential

Diagram illustrating all or nothing law ***[from: MBV Roberts, Biology; A Functional Approach]***

FACTORS THAT AFFECT NERVE CONDUCTION VELOCITY

1. Axon diameter:

(i) Impulses faster in an axon with larger diameter because longitudinal resistance of axoplasm decreases with increasing diameter of axon, which increases the length of the membrane influenced by local circuit as the distance between adjacent depolarisations increases; causing increased conduction velocity.
(ii) Small cells or cells with large surface area : volume ratio or ion leakage weakens membrane.
(iii) Myelin sheath stops ion leakage; therefore large diameter only important for unmyelinated neurons

2. Myelination and saltatory conduction:

(i) Myelination speeds up conduction. In a myelinated neuron, the conduction velocity is directly proportional to the fiber diameter.
(ii) Schwann cells prevent diffusion of ions; flow of current occurs only between adjacent nodes of Ranvier
(iii) Therefore, depolarisation only at nodes of Ranvier because action potential jumps from node to node

3. Temperature:

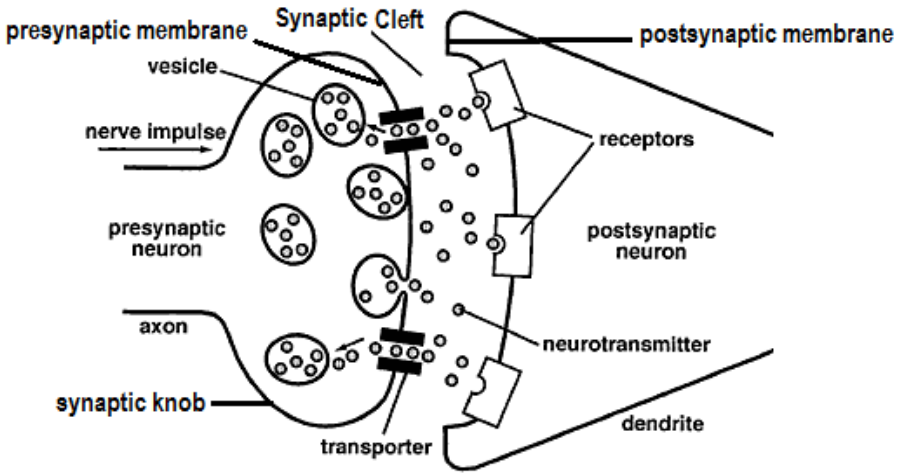
Homoiotherms with steady body temperature have faster impulse propagation than poikilotherms which have fluctuating body temperature.

4. Resting membrane potential: Effect of RMP changes on conduction velocity is quite variable. Usually, any change in the RMP in either direction (hyper polarization or depolarization) slows down the conduction velocity

SYNAPTIC TRANSMISSION

Structure of a synapse

- Synaptic cleft of 20nm separates two neurones at a synapse (junction of 2 neurones)
  -Presynaptic membrane is at the end of first neurone
  -Postsynaptic membrane is at the next neurone in the chain
- Synaptic knob of a presynaptic neurone has many vesicles containing neurotransmitter
- Many mitochondria produce ATP needed for synthesis of neurotransmitter
- There are many calcium ion sacs



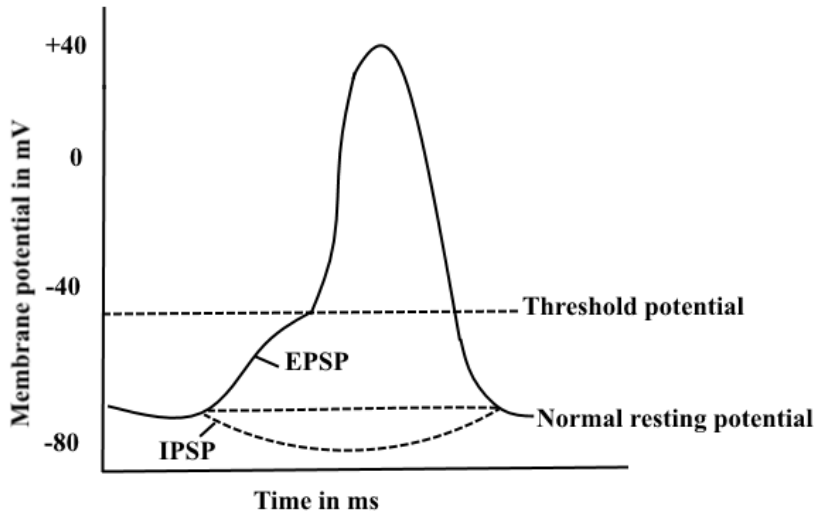
NOTE: Synapses can be:
(1) Inhibitory i.e. neurotransmitter (**e.g. Gamma-Amino butyric Acid – "GABA" and glycine**) opens Cl^- ion or K+ ion-gated channels in the post-synaptic membrane, causing **hyperpolarization** which makes it difficult to generate an action potential
(2) Excitatory i.e. neurotransmitter (**e.g. acetylcholine and glutamate**) opens Na+ channels to cause depolarisation in the post-synaptic membrane.

MECHANISM OF TRANSMISSION AT THE SYNAPSE

1. Nerve impulse reaches synaptic knob/presynaptic membrane/neurone to cause depolarisation.
2. Depolarisation opens Ca^{2+} gates enabling entry of calcium ions.
3. Entry of Ca^{2+} causes vesicles containing neurotransmitter to fuse with presynaptic membrane
4. Release of neurotransmitter into synaptic cleft by exocytosis
5. Neurotransmitter diffuses across synaptic cleft within 0.5 ms
6. Neurotransmitter binds to specific receptors in postsynaptic membrane

7. In **excitable synapses,** Na+ channels open to allow inward diffusion of Na+ ions into postsynaptic neurone
(i) Postsynaptic membrane gets depolarized.
(ii) A new potential known as **excitatory postsynaptic potential (EPSP)** is created, which at threshold levels generates an action potential that is transmitted along postsynaptic membrane.
8. Neurotransmitter are quickly removed from the postsynaptic membrane:
(i) The neurotransmitter e.g. noradrenaline can diffuse actively into the synaptic knob of presynaptic membrane.
(ii) Taken up by presynaptic membrane by endocytosis
(iii) Enzyme **acetylcholinesterase** splits acetylcholine into **choline** and **acetate.** Choline which is absorbed into the synaptic bulb combines with **acetyl coenzyme A** to form **acetylcholine**.
9. In **inhibitory synapses,** the neurotransmitter molecules cause the opening of Cl^- ion and or K+ ion-gated channels.
(i) Facilitated diffusion of Cl^- into the cell and or K+ ions out of the cell causes the postsynaptic membrane to be **hyperpolarized**.
(ii) This is known as **inhibitory postsynaptic potential (IPSP)** and makes it difficult to generate an action potential in the post-synaptic cell.

Differences between the two types of postsynaptic membrane potentials (EPSP and IPSP)
(i) EPSPs are graded potentials that can initiate an AP in the axon, whereas IPSPs produce a graded potential that lessens the chance of an AP in an axon.
(ii) EPSP - small depolarization is created; IPSP - small hyperpolarization is created.
(iii) EPSP - helps bring postsynaptic membrane closer to threshold; IPSP - helps bring postsynaptic membrane further from threshold.
(iv) EPSP - membrane becomes more excited; IPSP - membrane becomes less excited.



Common types of transmitters
(a) **Acetylcholine** released by **cholinergic nerves** like:
(i) Motor neurones on to muscle cells
(ii) Neurones in the parasympathetic division of the ANS (autonomic nervous system)
(b) **Noradrenaline** (**norepinephrine**) is released **adrenergic nerves** in the sympathetic division of the ANS
(c) **Dopamine**
(d) Serotonin, including amino acids **glutamate** and **glycine**

Functional classes of neurotransmitters
1. Excitatory - (e.g., acetylcholine and glutamate) causes depolarization
2. Inhibitory (e.g., Gamma-Amino butyric Acid – "GABA" and glycine) causes hyperpolarization

DRUGS

Chemical substances which causes a change in the natural chemical environment and functioning of the body.

(a) **Cocaine** blocks reuptake of neurotransmitter e.g. **dopamine**

(b) **Curare** blocks action of **acetylcholine** by binding to receptors on the post synaptic membrane.

(c) **Organophosphate** insecticides and nerve gases block **acetylcholinesterase**, thus acetylcholine remains active for longer periods.

NOTE:

(i) Being an antagonist of **acetylcholine-receptors** and **adrenaline-receptors** on membrane of muscle cells in heart, **curare** in small doses is used as a general muscle relaxant in patients undergoing major surgery.

(ii) **Curare** is commonly applied on tips of hunting arrows to paralyse animals.

ASPECTS OF SYNAPTIC TRANSMISSION

1. Unidirectionality

(i) Neurotransmitter always travels from pre- to postsynaptic membrane

(ii) Therefore flow in one direction only, action potential only in postsynaptic neurone

2. Summation

(i) Neurotransmitter is releases in low concentrations repeatedly from one neurone or from many neurones.

(ii) Cumulative effect reaches a threshold to depolarise postsynaptic membrane

(iii) E.g. rod cells when they synapse with bipolar neurones in the retina of mammalian eye.

(a) Temporal summation

(i) High frequency stimulation of same neurone via one synapse

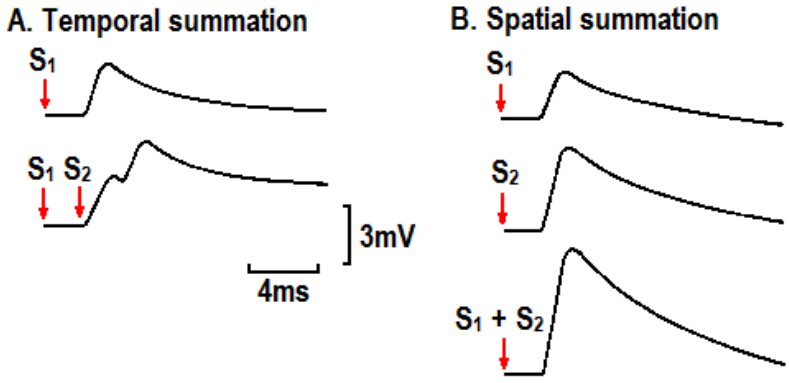
(ii) Neurotransmitter reaches and exceeds threshold to cause an action potential in post synaptic cell.

(b) Spatial summation

(i) Several impulses arrive at one neurone via several synapses

(ii) Cause sufficient depolarisation / open sufficient sodium ion channels

(iii) For threshold to be reached



3. Response latency

This is the time lag between the time a stimulus is present in the environment and the time a neuron responds, due to synaptic transmission.

4. Inhibition

(i) There are more inhibitory postsynaptic potentials (IPSPs) than excitatory postsynaptic potentials (EPSPs)

(ii) Inhibition reduces membrane potential / makes it more negative

(iii) Involves **hyperpolarisation** of postsynaptic membrane

(iv) Cancels effect of action potential when several synapses

Functions of synapses

(i) They transmit information between neurones.

(ii) They filter out low frequency impulses.

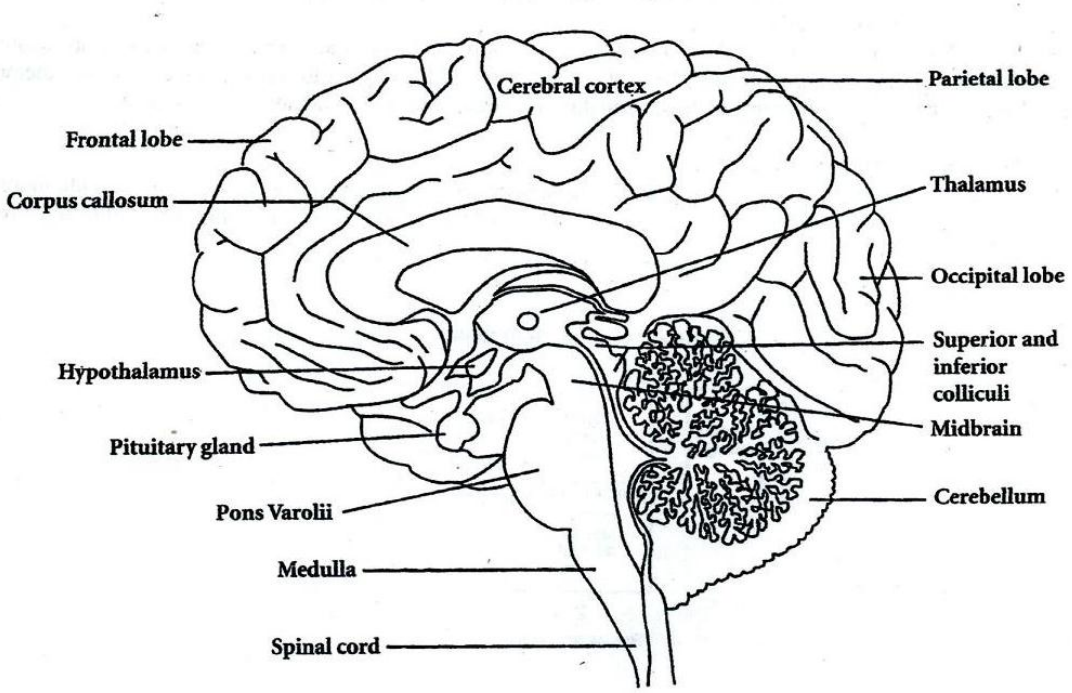
(iii) They act as valves to ensure that impulses pass across them in one direction only.

(iv) They also act as junctions allowing impulses to be divided up along many neurones or merge into one.

(v) To protect effectors from damage by overstimulation.

(vi) Synapses may be involved in memory and the learning process.

STRUCTURE AND FUNCTIONS OF THE BRAIN



THE BRAIN

(a) Is enclosed by the skull bone, surrounded by **meninges,** which consists of three protective membranes:
(i) Outer – Dura mater; fibrous (ii) Middle – Arachnoid; serous (iii) Inner - Pia; vascular

(b) Is made up of:
(i) **Grey matter**: consists of cell bodies of neurons
(ii) **White matter**: consists of mainly nerve fibres (axons). Neuroglial cells support and protect the brain
(c) **Ventricles** are cavities in the brain, richly supplied with capillaries
(d) **Cerebrospinal fluid:** fills spaces within the brain and also between outer two membranes of the meninges.
(i) It cushions against mechanical disturbances.
(ii) Supplies digested food nutrients and oxygen to brain cells.
(iii) Removes wastes from brain cells.

PARTS OF THE BRAIN AND THEIR FUNCTIONS

The brain is divided into three major regions:
(1) Hindbrain, (2) midbrain and (3) forebrain.
Each region is composed of different brain parts that work together to process the information they receive.

HINDBRAIN PARTS

(a) Medulla, (b) cerebellum and (c) pons.
Medulla is where the spinal cord enters the skull. It is responsible for controlling breathing, regulating reflexes, and maintaining an upright posture of the body.
Cerebellum: is responsible for coordinating motor activity (movements of the body), so that extensive damage of the cerebellum can cause failure to even stand up.
Pons:
(i) Serves as the bridge towards the midbrain.
(ii) Responsible for monitoring sleep and arousal by coordinating with the autonomic nervous system.

Brain Stem:
(i) Composed of the hindbrain, plus the midbrain, minus the cerebellum.
(ii) Involved in alertness and in monitoring basic survival functions such as breathing, heartbeat, and blood pressure.

MIDBRAIN
(a) The Midbrain serves to relay information between the hindbrain and the forebrain, particularly information coming from the eyes and the ears.
(b) Composed of:
(i) Reticular formation,
(ii) Cluster of neurons having dopamine, serotonin and norepinephrine receptors.
(c) The **reticular formation** is involved with stereotypical patterns of behavior such as walking, sleeping, and other reflexes.
(i) Usually affected by Parkinson's disease, a degenerative disease of the brain that causes involuntary tremors.

FOREBRAIN
(a) Forebrain is considered as the highest region of the brain because it essentially differentiates us humans from the rest in the animal kingdom.
(b) Composed of:
(i) Limbic system, (ii) Thalamus, (iii) Hypothalamus, (iv) Basal ganglia, (v) Cerebral cortex.

1. Limbic system
(a) Made up of the **amygdala** and the **hippocampus**.
(b) Generally involved in memories and emotions.
Amygdala is responsible for processing emotions; awareness and expression.
(i) Helps us discriminate one object from another hence critical for our survival e.g. damage of the amygdala may cause us humans to eat our own feces, fight the wrong "enemy", or try to mate with a chair.
Hippocampus is presumably involved in memory storage.
(i) Its damage causes inability to store new information.

2. The thalamus
(a) Sorts and relays incoming information to the different parts of the forebrain e.g. information coming from the cerebellum is oftentimes relayed to the motor cortex in the cerebral cortex.
(b) The thalamus also works with the reticular formation on regulating states of sleep and wakefulness.

3. Hypothalamus
(i) It monitors pleasurable activities such as eating, drinking and sex.
(ii) It influences the endocrine system, particularly the pituitary gland, in secreting hormones in response to different emotions, stress and rewarding feelings.

4. Basal ganglia
(i) It works with the cerebral cortex and the cerebellum for coordinating voluntary movements, particularly in forming habitual behaviors, such as bicycle riding and typing.

5. Cerebral cortex
(i) The most recently developed (or evolved) part of the brain.
(ii) Also the largest part of the human brain, making up to 80% of the brain's volume.
(iii) It is where high-level processing takes place.

THE CEREBRAL CORTEX
(a) Divided into two (2) hemispheres:
(i) Left hemisphere is associated with verbal processing, such as speech and grammar, and mathematics;
(ii) Right hemisphere is involved with nonverbal processing, such as spatial perception, visual recognition and emotion.
(a) The left hemisphere processes information coming from the right side of the body, while the right hemisphere processes information coming from the left side of the body.

(b) The two hemispheres of the brain are connected with each other by a bundle of axons called the **corpus callosum.** This connection allows the left and the right hemispheres to communicate and integrate information with each other.
(c) Logical thinking is predominantly on left brain activity, creative activities are more associated with right brain activity.
(d) The cerebral cortex is also divided into lobes - occipital, temporal, parietal and frontal; cortices and association cortices - visual, auditory, motor and sensory.

1. **Occipital Lobe**
(a) Located at the back of the head
(b) Involved in processing visual information, such as color, shape and motion hence the visual cortex and visual association cortex are located in this lobe.
(c) Damage to the occipital lobe may cause cross-eyeing and blindness partly or entirely of the visual field. The
2. **Temporal Lobe**
(a) Located just above the ears and is involved in hearing, language processing and memory (due to its connection with the limbic system).
(b) It is the location of auditory cortex, auditory association cortex, and part of the visual association cortex.
(c) Damage to the temporal lobe leads to failure to store new information.
3. **Parietal Lobe**
(a) Located at the top of the head and towards the rear.
(b) It is involved in attention and motor control, in processing spatial location, and in perceiving pain, touch and temperature.
It is said that Albert Einstein's parietal lobe is 15% larger than average, probably the reason why he oftentimes imagined objects in space while formulating his theories. The sensory association cortex is located in this lobe.
4. **Frontal Lobe**
(a) Located just behind the forehead and towards the top of the head.
(b) Constitutes 30% of the cerebral cortex in humans, 17% in chimps, 3.5% in cats, and it barely exists in rats.
(c) Involved in the control of voluntary muscles, intelligence and personality.
(d) The most important portion of the frontal lobe is the prefrontal cortex, which is involved in planning, reasoning, and monitoring and organizing thinking.
(e) Damage to the frontal lobe causes failure to follow basic directions, distraction from irrelevant stimuli, and personality change.

AUTONOMIC NERVOUS SYSTEM (ANS)
(a) Contains only motor nerves
(b) Regulates activities of internal glands, cardiac muscles and smooth muscles.
(c) Contains the **antagonistic** sympathetic and parasympathetic systems.
(d) Most organs innervated by **ANS** receive both sympathetic and parasympathetic nerves.

An outline of the functions of parasympathetic and sympathetic divisions of the ANS

Target Organ/Tissue Effect on organ: Motor neurone releases:	**Parasympathetic Stimulation** Inhibitory effect / relaxation Acetylcholine (ACh)	**Sympathetic Stimulation** Excitatory effect / stress Norepinephrine (noradrenaline)
Iris of eyes	Constricts pupil	Dilates pupil
Bronchi, bronchioles	Constricts tubes	Dilates tubes
Blood vessels	- Dilates blood vessel - Lowers blood pressure	- Constricts blood vessels - Raises blood pressure
Heart	- Lowers heart rate - Lowers stroke volume	- Raises heart rate - Raises stroke volume
Intercostal muscles	Lowers breathing rate	Raises breathing rate
Salivary glands	Stimulates secretion of salvia	Inhibits secretion of salvia
Gut	Stimulates peristalsis	Inhibits peristalsis
Sweat glands	No effect	Increases sweat production

HUMAN CHEMICAL COORDINATION

1. Chemical signals: chemical substances that can alter cell metabolism or the behaviour of an individual

Types of chemical signalling

(a) Local signalling:

(i) In **Paracrine signalling**, a secretory cell secretes local regulator molecules (e.g. **prostaglandins**) that diffuse through extracellular fluid to act on nearby target cells.

Prostaglandins are physiologically active lipid compounds having diverse hormone-like effects like capillary permeability, smooth muscle tone, clumping of platelets, and pain process of inflammation.

(ii) In **Synaptic signalling,** a neurone releases neurotransmitter molecule (e.g. Acetylcholine) which diffuses through the synaptic cleft and to act on adjacent neurones.

(b) Long distance signalling:

Specialised endocrine cells secrete hormones into body fluids (mainly blood) and carried to target organs.

(c) Signalling between individuals of a species:

Chemical substances (e.g. **pheromones)** are emitted to influence the reproductive behaviour of some mammals and insects.

2. Receptors for chemical messengers:

Proteins with specific binding sites either in the cytoplasm, or nucleoplasm or plasma membrane of target cell.

3. Target cells:

Cells that can recognise and respond to specific chemical signals.

4. Hormones: Chemicals secreted by endocrine glands into blood and bring about specific physiological action (excitatory or inhibitory) away in target organs.

5. A neurosecretion: a chemical messenger that is synthesised, stored and released into blood by **neurosecretory cells (**nerve cells in the brain) and brings about specific physiological action (excitatory or inhibitory) away in target organs.

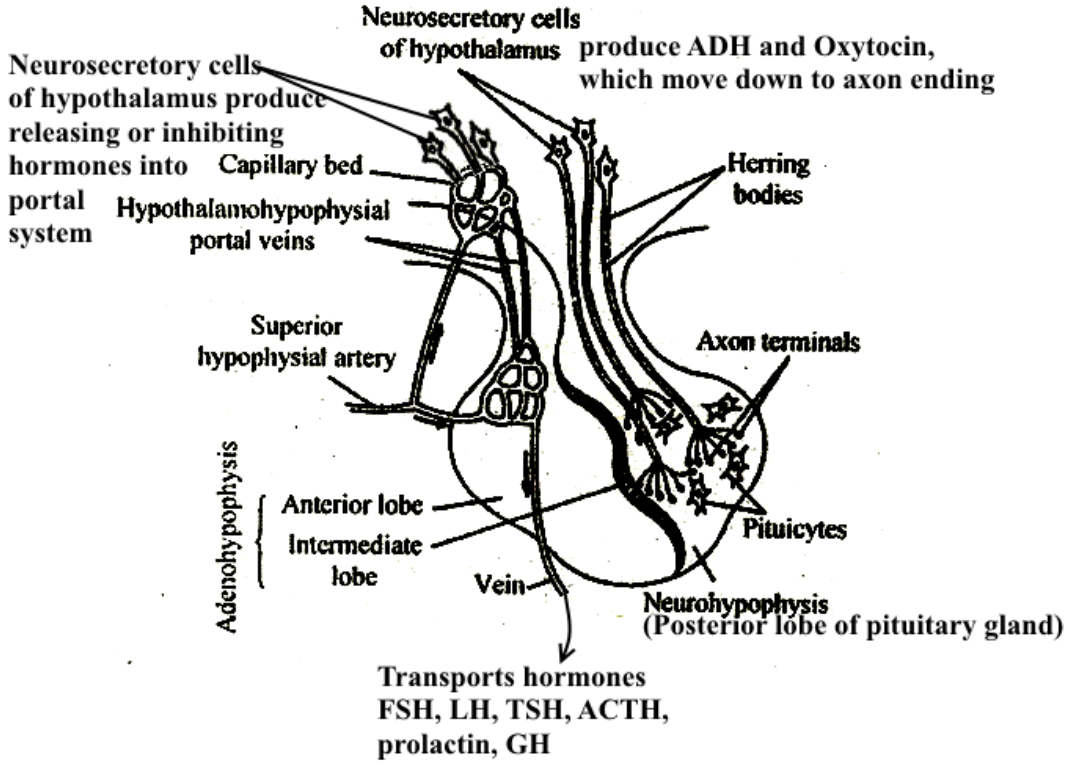
Properties of hormones

(i) Are secreted by endocrine gland.
(ii) Their secretions is released directly into blood (except local hormones *e.g.* gastrin).
(iii) Are carried to specific organs, called **target organs**.
(iv) Have specific physiological action (excitatory or inhibitory).
(v) They co-ordinate different physical, mental and metabolic activities and maintain homeostasis.
(vi) The hormones have low molecular weight *e.g.* ADH has a molecular weight of 600–2000 daltons.
(vii) They act in very low concentration *e.g.* around10^{-10} molar.
(viii) Hormones are non-antigenic.
(ix) Are mostly short-lived, so have a no cumulative effect.
(x) Some hormones are quick acting *e.g.* adrenalin, while some acting slowly *e.g.* oestrogen of ovary.
(xi) Some hormones are secreted in inactive form called **Prohormone** *e.g.* Pro-insulin.
(xii) Hormones are specific. They are carriers of specific information to their specific target organ.

SOME HORMONES, THEIR CHEMICAL NATURE AND FUNCTIONS

Endocrine gland	**Hormone & chemical nature**	**Functions**
(1) Pineal in the brain	Melatonin-derivative of amino acid tyrosine	(1) Antagonist to FSH / LH (2) Regulates biological / circadian rhythms.
(2) Thyroid gland (amine hormone)	(a) Thyroxine, iodinated amino acid called tyrosine	(a) Controls basal metabolic rate (BMR). All organs / systems of body respond to thyroxine.
	(b) Thyrocalcitonin (Peptide)	(b) Facilitates Ca^{+2} absorption
(3) Parathyroid gland	Parathormane, Peptide	Ca^{+2} and PO^{-4} metabolism.
(4) Thymus	Thymosine (polypeptide)	Anti-FSH and LH; delays puberty
(5) Islets of Langerhans (Pancreas) (i) alpha-cells (ii) beta-cells (iii) d-cells	(i) Glucagon (ii) Insulin (iii) Secretin } Polypeptide	(i) Gluconeogenesis / Glycogenolysis (ii) Glycogenesis (iii) Gastric functions
(6) Adrenal gland (a) Adrenal medulla	(a) Epinephrine (adrenaline) Norepinephrine (noradrenaline), peptide	(a) Stresses = emergency = Fright, Fight and Flight Hormone (3F) increases heart beat and muscle activity, etc.
(b) Adrenal cortex	(b) Mineralcorticoids and glucocorticoids derived from cholesterol.	(b) Electrolyte and carbohydrate metabolism.
(7) Ovary (a) Ganulosa cells	Oestrogen (estradiol) -Steroid	(a) Secondary sexual characteristics, primary action on uterine endometrium mitogenic.
(b) Corpus luteum	Oestrogen and Progesterone (Steroid)	(a) Secreted during luteal phase of human menstrual cycle. Prepares endometrium for implantation. Also progesterone is anti-FSH and anti-LH
(c) **Placenta**, a temporary endocrine gland during pregnancy	(a) Oestrogen and progesterone - Steroids (b) Relaxin - Polypeptide	(a) Maintenance of pregnancy, prevents lactogenesis, folliculogenesis, and Ovulation. (b) Enlarges the birth canal to facilitate birth.
(8) **Testis** Sertoli (sustentacular) cells	Inhibin – Polypeptide	Inhibits FHS action and weakens spermatogenesis
(ii) Leydig cells (=Interstitial cells)	(ii) Testosterone) Steroid	(i) Pubertal changes in male (ii) Secondary sexual characters in male (iii) Sex drives (iv) Spermatogenesis
(9) Gastro-intestinal hormones (secreted by cells of mucosa of stomach and intestine)	Gastrin, polypeptide	Stimulates gastric juices secretion from gastric gland, movement of sphincters of stomach and increased movement of stomach
	(i) Secretin (ii) Cholecystokinin (CCK) (iii) Enterogastrone	(i) Stimulates secretion of succus entericus (ii) Bile released from gall bladder (iii) Inhibits gastric secretin

RELATIONSHIP BETWEEN HYPOTHALAMUS AND PITUITARY



HYPOTHALAMUS

(i) It is connected with **anterior pituitary lobe** by blood capillaries of **hypophyseal portal system** and with the **posterior pituitary lobe** by **axons** of its **neurons**, both passing through the **pituitary stalk**.

(ii) Hypothalamus is a considered as the "Master controller" or "Master gland"

Hormones of hypothalamus

Neurosecretory cells of hypothalamus secrete proteinous **neurohormones** called **releasing factors (RF) or inhibiting factors (IF)**, which are carried by hypophyseal portal system to anterior pituitary lobe (adenohypophysis) (primary target organ) and stimulate or inhibit the release of trophic hormones from adenohypophysis.

PITUITARY GLAND (HYPOPHYSIS)

Divided into: (i) Adenohypophysis (Anterior lobe) (ii) Neurohypophysis (Posterior lobe)

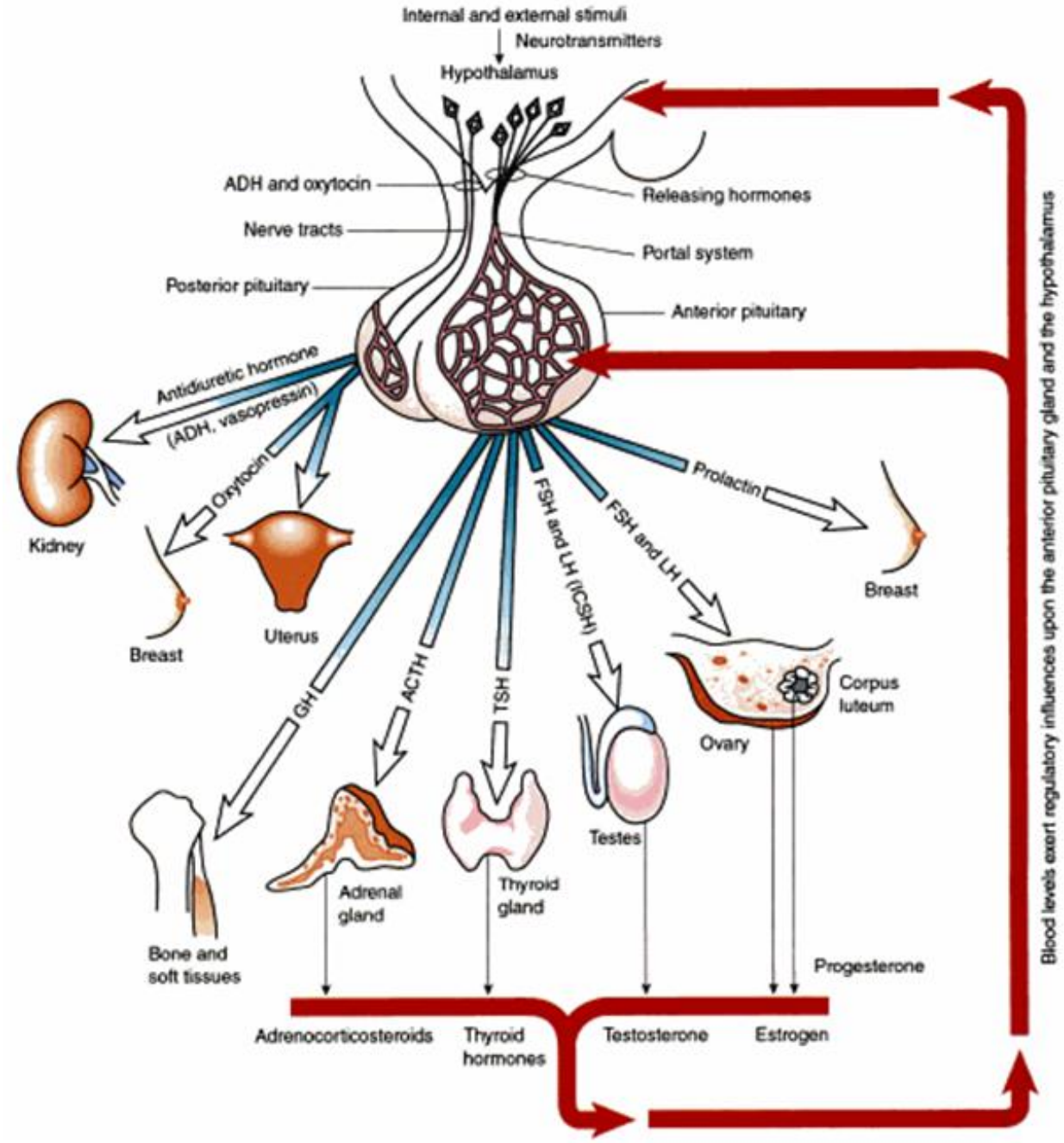
Pituitary Hormones

The hormones secreted by Pituitary are either secreted by the Hypothalamus or are stimulated by the hormones secreted by Hypothalamus e.g. **Thyrotropin releasing hormone** which stimulates release of **TSH**.

Hormones Secreted by Pituitary:

Anterior Pituitary	Middle lobe of Pituitary	Posterior Pituitary
(i) Adrenocorticotropic hormone (ACTH) (ii) Thyroid Stimulating Hormone (TSH) (iii) Follicle Stimulating Hormone (FSH) (iv) Lutenizing Hormone (LH) (v) Growth Hormone (GH) (vi) Prolactin	(i) Melanocyte Stimulating Hormone or Intermedins	(i) Oxytocin (OT) (ii) Antidiuretic Hormone or Vasopressin (ADH)

Note:
Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) are called as Gonadotrophic Hormones as they influence and act on the gonads (reproductive organs).



Hormones which stimulate the anterior Pituitary Gland to secrete its hormones

Neurohormones	**Physiological effects**
(1) TSH-RF (Thyroid Stimulating Hormone – Releasing Factor)	Increased ACTH secretion from adenohypophysis.
(2) ACTH-RF (Adrenocorticotrophic Hormone-Releasing Factor)	Increased ACTH secretion from adenohypophysis.
(3) STH-RF (Somatotrophic Hormone-Releasing Factor)	Increased STH secretion from adenohypophysis
(4) SOMATOSTATIN (GROWTH INHIBITING HORMONE)	Decreased STH secretion from adenohypophysis.
(5) GTH-RF (Gonadotrophic Hormone-Releasing Factor)	
(i) FSH-RF (Follicular Stimulating Hormone-Releasing Factor)	Increased FSH secretion from adenohypophysis.
(ii) LH-RH (In female) (Luteinising Hormone – Releasing Factor)	Increased LH secretion from adenohypophysis.
or ICSH-RF (In male) (Interstitial Cells stimulating Hormone-Releasing Factor)	
(6) Prolactin-Releasing hormone (P-RH)	Increased secretion of prolactin or leutotrophic.
(7) Prolactin-Inhibiting hormone (P-IH)	Increased secretion of prolactin or leutotrophic.
(8) MSH-RF (Melanophore Stimulating Hormone-Releasing Factor)	Increased MSH secretion from intermediate pituitary
(9) MIF (Melanophore Inhibiting Factor)	Decreased MSH secretion from intermediate pituitary

NEUROHORMONES OF PITUITARY

1. Thyroid stimulating hormone (TSH) or Thyrotropin:

(a) This hormone which is secreted by the anterior lobe of the pituitary.
(b) TSH acts on the Thyroid gland to release Thyroxine (T4) and Triiodothyronine (T3) which **"Regulate Body Metabolism"**
(c) Hypothalamus secretes Growth Hormone inhibiting hormone (GHIH) to inhibit the secretion of TSH.

2. Growth hormone (GH):

(a) Also called as **(hGH – Human Growth Hormone) or Somatotrophin,** is released by the Anterior Pituitary.
(b) Growth hormone stimulates the Special Liver cells which produce somatomedin-C, which is critical for the growth of all body tissues.
(c) It assists with the movement of amino acids into tissue cells and the transformation of amino acids into proteins that the body requires.
(d) It aids in the release of fatty acids from adipose (fat) tissue so that they can be used for energy.
(e) Regulates blood nutrient levels after eating and during periods of fasting.When sufficient amounts of Growth Hormone has been released the hypothalamus secretes GHIH (Growth Hormone Inhibiting Hormone) which inhibits the further release of growth hormone.

3. Prolactin (PRL):

(a) It is secreted by Anterior lobe of Pituitary.
(b) Prolactin hormone stimulates milk production in women following pregnancy.
(c) Men secrete Prolactin whose function is not known yet.
(d) Stimulates breast milk production and controls menstrual periods following pregnancy.

4. Adenocorticotrophic Hormone (ACTH) or **Corticotropin**:

(a) Secreted by the Anterior lobe of Pituitary.
(b) ACTH Stimulates the adrenal cortex to produce glucocorticoids like Steroid "Cortisol" which play a vital role in metabolizing carbohydrate.
(c) ACTH has melanocyte stimulating properties that can increase skin pigmentation.

5. Follicle Stimulating Hormone (FSH):

Stimulates the growth and secretion of Ovarian Follicles in women and the production of Sperm in men.

6. **Luteinizing Hormone**:
(a) Stimulates Ovulation and formulation of the Corpus luteum in females.
(b) In males LH is called **(Interstitial cell stimulating hormone -ICSH)** which influences the secretion of testosterone and other sex hormones from specialized area in the testes.

7. Melanocyte Stimulating Hormone or Intermedins:
(a) It is secreted by the Middle Lobe of Pituitary.
(b) MSH stimulates the release of melanin (melanogenesis) by melanocytes in the skin and hair.
(c) MSH has certain effects on the Appetite and Sexual Arousal.
(d) MSH is the main cause of color of the skin in Humans.
(e) MSH levels increase in females during Pregnancy.

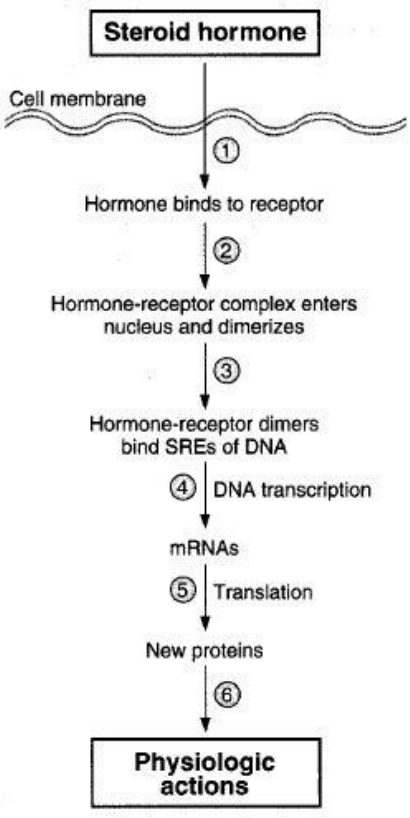
8. Anti-Diuretic Hormone or Vasopressin:
(a) It is a hormone secreted by the Posterior Pituitary.
(b) It is a peptide hormone produced by the magnocellular cells of the hypothalamus.
(c) Increased osmolarity stimulates the secretion of ADH from the posterior pituitary.
(d) ADH acts in increasing blood pressure
(e) ADH increases water resorption

9. Oxytocin:
(a) It is a hormone secreted by Posterior Pituitary.
(b) Causes uterine contractions just before and after birth which acts during the 2nd and 3rd labour stages.
(c) Oxytocin is released during breast feeding in the first few weeks of lactation.
(d) Helps in controlling Social behavior
(e) Oxytocin helps in Wound healing
(f) Prepares the foetus for delivery
(g) Known to be the reason behind Romantic Attachments

CHEMICAL NATURE OF HORMONES
On the basis of their chemical nature, hormones are of 4 types:
(i) Peptide/protein hormone e.g., insulin, glucagon, TSH, LH, FSH
(ii) Steroids e.g., cortisol, testosterone, progesterone, adrenaline
(iii) Iodothyronines e.g., thyroid hormones
(iv) Amino acid derivatives e.g., epinephrine

MECHANISM OF STEROID HORMONAL ACTION via gene activation

(i) Steroid hormones are not water-soluble, so they travel in blood attached to protein carriers.
(ii) On arrival at their target cells, they dissociate from the protein carrier, pass through the plasma membrane of the cell into the cytoplasm.
(iii) In the cytoplasm, some steroid hormones bind to specific receptor proteins and then move as a hormone-receptor complex into the nucleus via nuclear pore. Others travel directly into the nucleus and then bind to specific receptor proteins.
(iv) The hormone-receptor complex is now activated to bind to specific regions of DNA called **hormone response elements.**
(v) The binding of the hormone-receptor complex activates specific genes in the DNA which transcribes messenger RNA (mRNA).
(vi) mRNA passes into the cytoplasm via nuclear pore and functional ribosomes attach to it to allow translation.
(vi) Peptide chains are synthesised, which form specific enzymes required for causing a physiological response.
e.g. if the steroid hormone is oestrogen, it stimulates the repair and thickening of endometrium.



MECHANISM OF NON-STEROID HORMONAL ACTION via activation of cyclic AMP system
Example of non-steroid hormone: Glucagon; ***target cell:*** liver cell (hepatocyte)
(i) A non-steroid hormone, being insoluble in lipids, cannot diffuse through the plasma membrane but acts as **first messenger** and binds to its receptor in the plasma membrane of target cells (e.g. hepatocytes).
(ii) Bound receptor interacts with and, through a set of G proteins, turns on adenylate cyclase enzyme, which is also an integral membrane protein.
(iii) Activated adenylate cyclase enzyme converts ATP to cyclic cyclic adenosine monophosphate (cAMP), hence increasing the intracellular concentration of cAMP.
(iv) cAMP acts as a **second messenger**, which then activates other enzymes.
(v) cAMP in the cytoplasm enables binding of protein kinase A with cAMP to become catalytically active.
(vi) Active protein kinase A adds phosphates to other enzymes in the cell, causing them to become catalytically active.
(vii) This **cascade effect**, where the action of one enzyme in turn activates another enzymatic reaction results in many product molecules.
(viii) For example the hormone glucagon activates the enzyme kinase, which activates glycogen phosphorylase enzyme through cascade effect.
(ix) Glycogen phosphorylase catalyses the hydrolysis of glycogen to glucose phosphate, which on oxidation releases energy.