Metabolic pathways

1. ***Understand the concept of metabolic pathway as a sequence of enzyme-controlled reactions; appreciate the roles of enzymes in the control of such pathways, illustrated by oxidoreductases (in respiration) and hydrolases; anabolism (photosynthesis) and catabolism (respiration).***

A metabolic pathway is a sequence of enzyme-controlled reactions, where every step in the pathway is controlled by a specific enzyme.

Starch ***Amylase(hydrolase)*** **Maltose** ***Maltase(hydrolase)*** **Glucose**

Starch is the primary substrate, Maltose is an intermediate compound and glucose is the final product. Every reaction in the pathway is controlled by a specific enzyme. This enables the cell to have more control over metabolic reactions.
E.g. Glycolysis, Kreb' s cycle, Calvin cycle, digestion.

The advantage of enzymes controlling these pathways is that a particular reaction can be **slowed down, speeded up or diverted along another route** by the **amount** or **type** of enzyme present. The **site of the reactions** can also be controlled.

- During aerobic respiration pyruvate is broken down into acetate in the matrix of mitochondria by the enzyme pyruvate dehydrogenases, however, during anaerobic conditions pyruvate is converted into lactate by the enzyme lactate dehydrogenase. Thus we can observe that the route of the reaction has been diverted because of the presence of another enzyme. Thus **the type of enzyme present controls the direction of the metabolic pathway, this allows pathways to branch**.
- The **site of a metabolic pathway is also controlled by enzymes**. The enzymes involved in glycolysis are found only in the cytoplasm, so glycolysis takes place only in the cytoplasm. The enzymes involved in Kreb' s cycle are present only in the matrix of mitochondria, so Kreb' scycle occurs only in the mitochondria. Oxidoreductases are located in the inner mitochondrial membrane, where oxidative phosphorylation occurs. Starch digestion does not occur in the stomach because the enzymes for starch digestion are not present in the stomach.

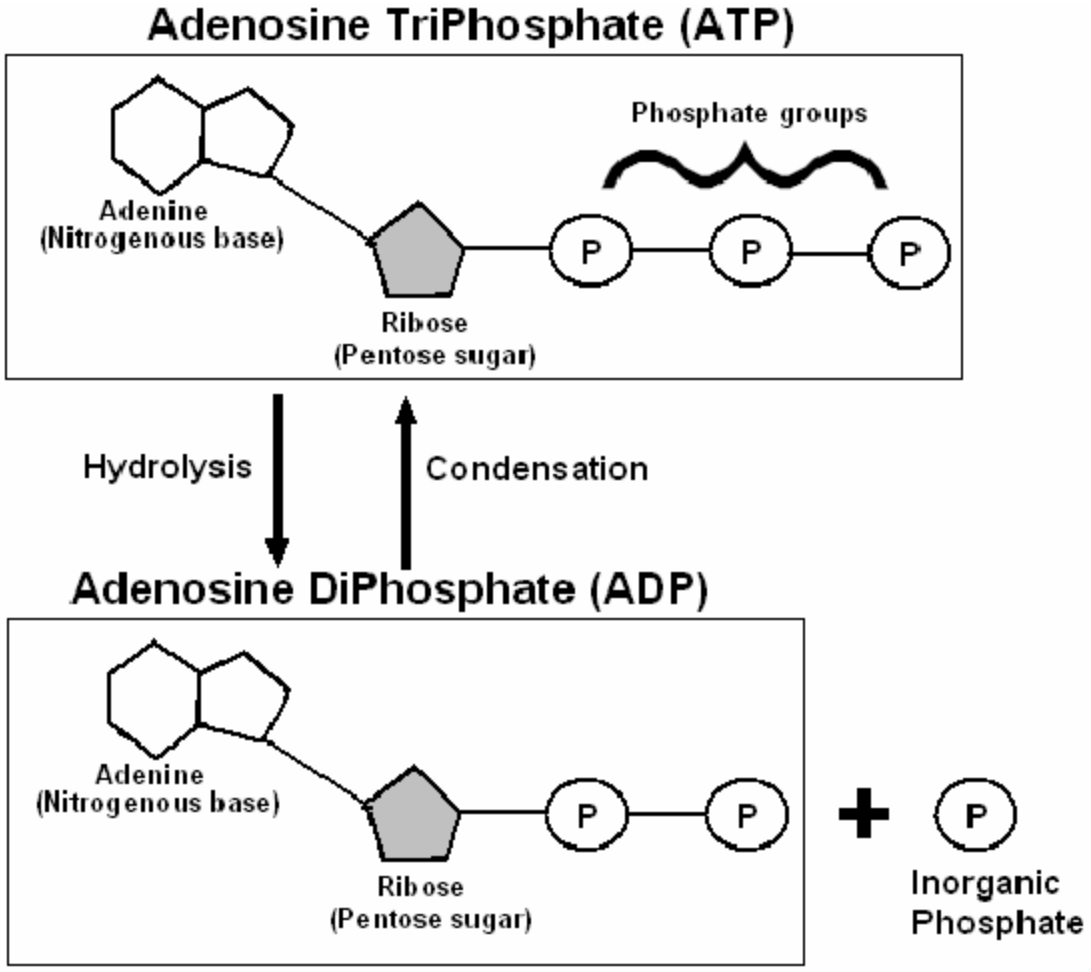
Metabolic reactions can be of two types:

- **Anabolic reactions**: these are reactions which are involves in the building up of organic compounds. Photosynthesis is an example of such a metabolic pathway. Condensation reactions are examples of such reactions.
- **Catabolic reactions**: these are reactions which are involved in the breaking down of organic compounds. Respiration is an example of such a metabolic pathway. Hydrolysis reactions are examples of such reactions.

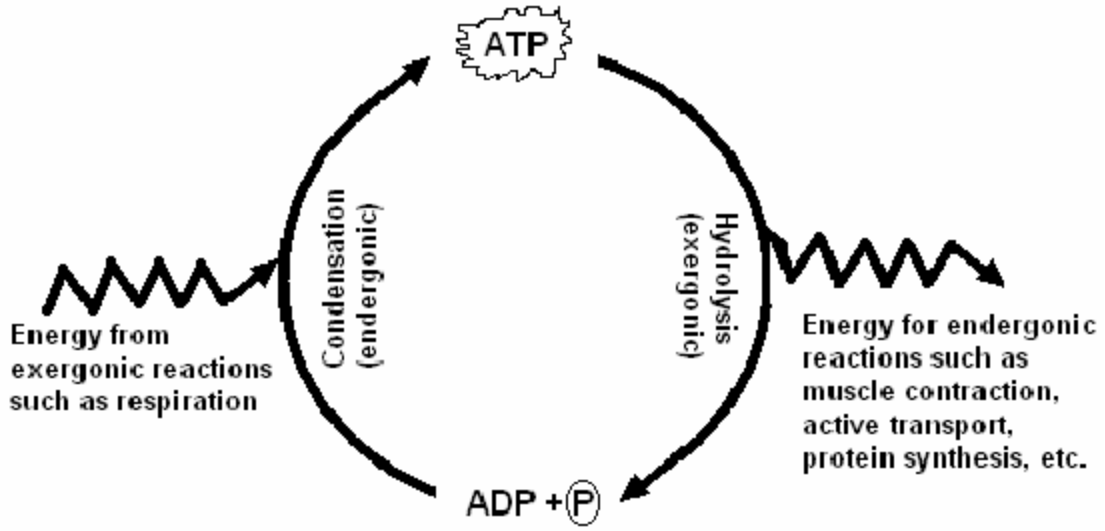
2. ***Understand the significance of ATP in metabolism as the immediate supply of energy for biological processes***

ATP: energy to drive metabolic reactions. ATP is made up of a nitrogenous base (Adenine), a ribose sugar and three phosphate groups. The covalent bond linking the second and third phosphate group is unstable, and is easily broken by **hydrolysis**. When this bond is broken a phosphate group is removed, and **ATP becomes ADP**. 30.6 kJ/mol of energy is released during this reaction. This is an **exergonic** reaction because **energy is released**. The breakdown of ATP releases energy to do work. A contracting muscle cell requires about two million ATP molecules per second. ATP is **not** an energy

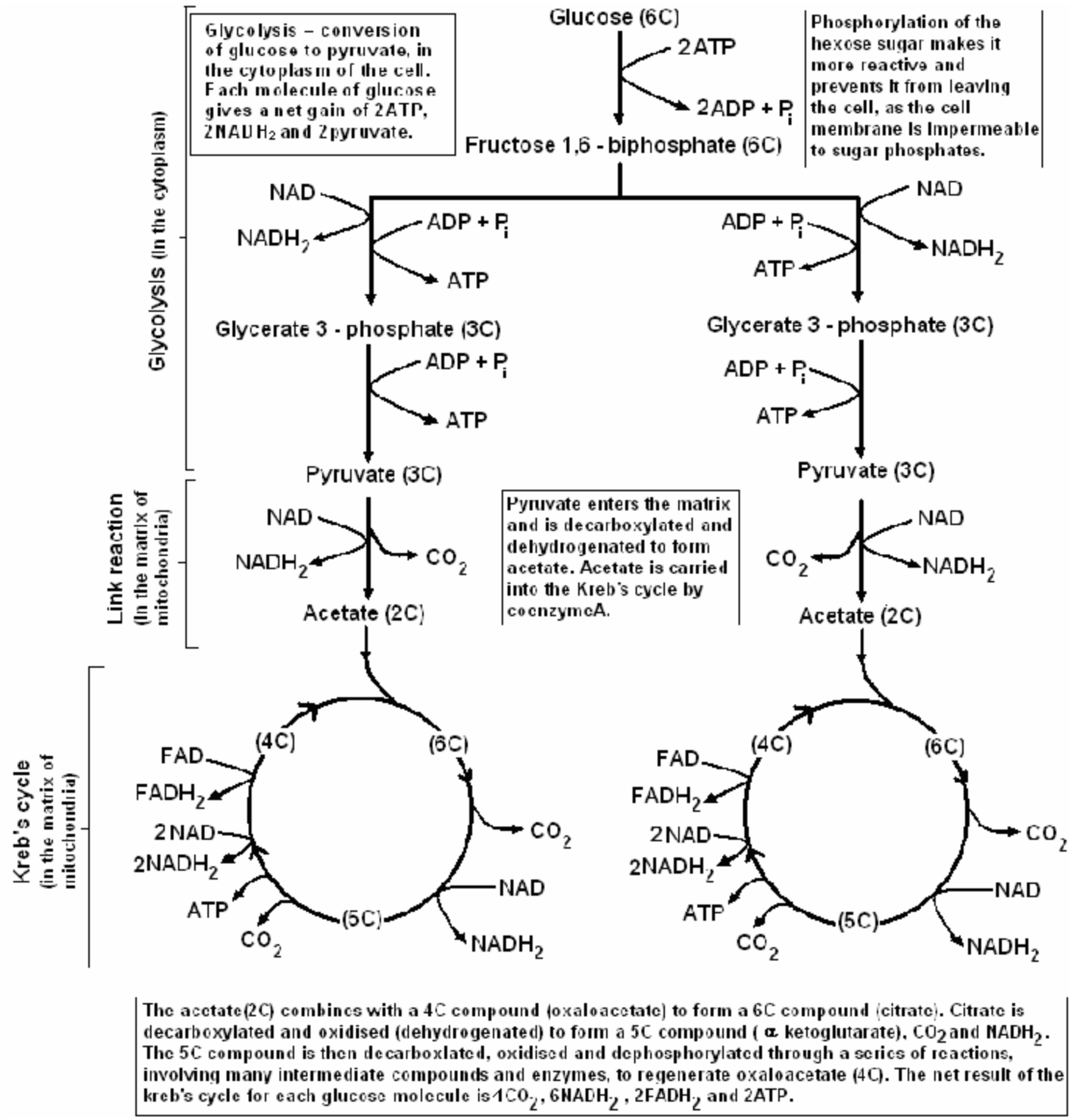
storage molecule, it is used up within one minute after it is produced. All the ATP in our body will be enough to keep us alive only for a few seconds. ATP must be generated continuously to provide energy for metabolic reactions to continue. ATP is regenerated during respiration.



ATP can be resynthesised from ADP and inorganic phosphates by **condensation reactions.** The energy for this reaction comes from **respiration**. The ATP cycle shows the relationship between ATP, ADP and respiration. The condensation of ADP to ATP is an energy-consuming process. **Energy-consuming** processes are called **endergonic**.

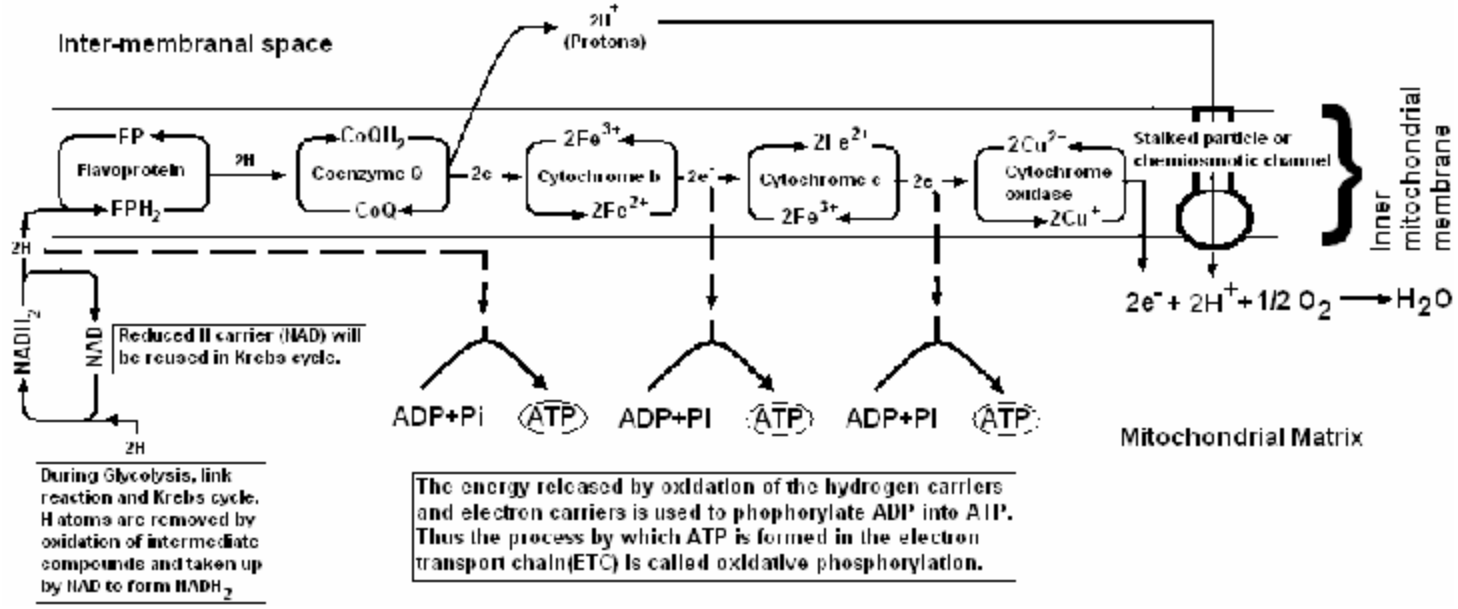


3. ***Describe the conversion of monosaccharides to pyruvate during glycolysis; the phosphorylation of hexose molecules; breakdown to glycerate 3-phosphate (GP); production of reduced coenzyme (NADH + H+) and ATP (details of intermediate compounds and reactions, other than those specified, are not required).***
4. ***Understand that during the complete oxidation of pyruvate the events of the krebs cycle result in the production of carbon dioxide, more reduced coenzyme (NADH + H+) and ATP (detailed knowledge of the intermediate stages in the krebs cycle is not required);***



5. ***Role of ETC in generating ATP (oxidative phosphorylation); understand the role of molecular O_2 as an H acceptor forming water.***

Oxidative phosphorylation: **Phosphorylation of ADP to ATP.**



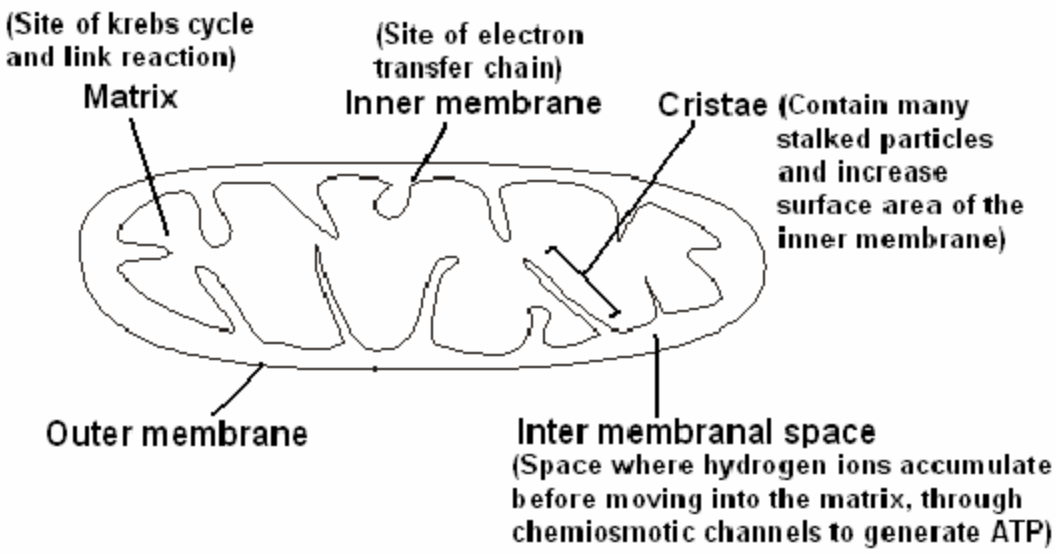
$$4H^+ + 4e^- + O_2 \longrightarrow 2H_2O$$

Oxygen is needed to absorb electrons and H^+ ions so that Electron Transport Chain (ETC) continues to function and NAD^+ (oxidized Hydrogen carriers) can be regenerated for aerobic respiration to continue.

$$\underset{\text{(Reduced Hydrogen carrier)}}{\mathbf{NADH + H^+}} \quad \underset{\text{Reduction (during glycolysis and Krebs cycle)}}{\overset{\text{Oxidation (at the ETC in the inner mitochondrial membrane)}}{\rightleftharpoons}} \quad \underset{\text{(Oxidised Hydrogen carrier)}}{\mathbf{NAD+ + 2H^+ + 2e^-}}$$

- H^+ ions pass into inter-membranal space.
- Electrons pass down Electron Transport Chain.
- ATP is generated from free energy released when H^+ ions move back into mitochondrial matrix, through stalked particles, which contain the enzyme ATPsynthase. These stalked particles are called chemiosmotic channels and the movement of hydrogen ions into the matrix is called chemiosmosis.

6. Structure of a liver mitochondrion; identify the inner, outer and inter membranal space.



7. Desribe and understand the role of mitochondria as the site of krebs cycle and ETC ; understand the location of enzymes and e carriers and the role of oxidoreductases.

The diagram above shows the general simplified structure of a mitochondrion. The sites of Krebs cycle and the electron transfer chain are also indicated. The detailed structure of the electron transport chain is given in the notes for syllabus specification 5, on the previous page.
Note that there are two hydrogen carriers at the beginning of the chain – Flavoprotein and Coenzyme Q. Flavoprotein (FP) accepts hydrogen atoms from Nicotinamide adenine dinucleotide (NAD) and passes it on to Coenzyme Q (CoQ). Thus each carrier becomes oxidized and reduced simultaneously. This is called a redox reaction. These redox reactions are catalysed by **oxidoreductase enzymes** present along with the electron transport chain, in the inner membrane of mitochondria.

Oxidation:

- **Gain of oxygen;**
- **Loss of hydrogen;**
- **Loss of electrons.**

Reduction:

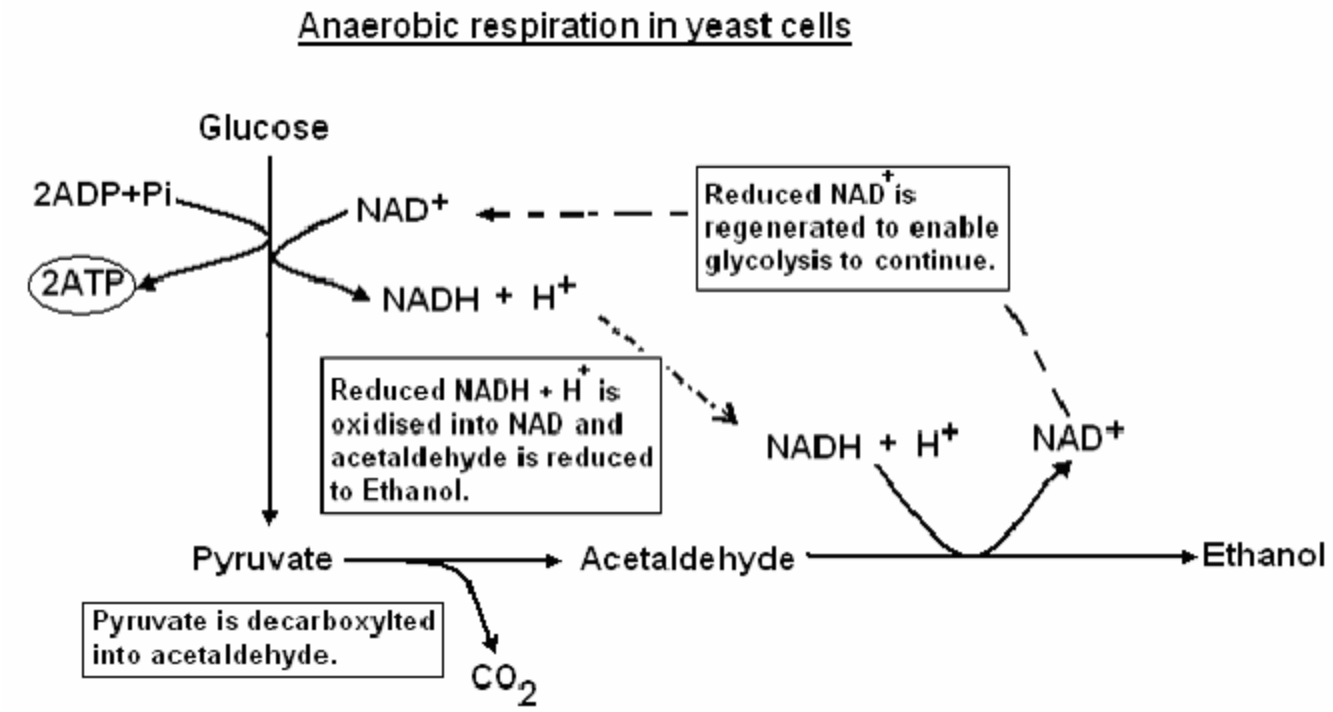
- **Loss of oxygen;**
- **Gain of hydrogen;**
- **Gain of electrons.**

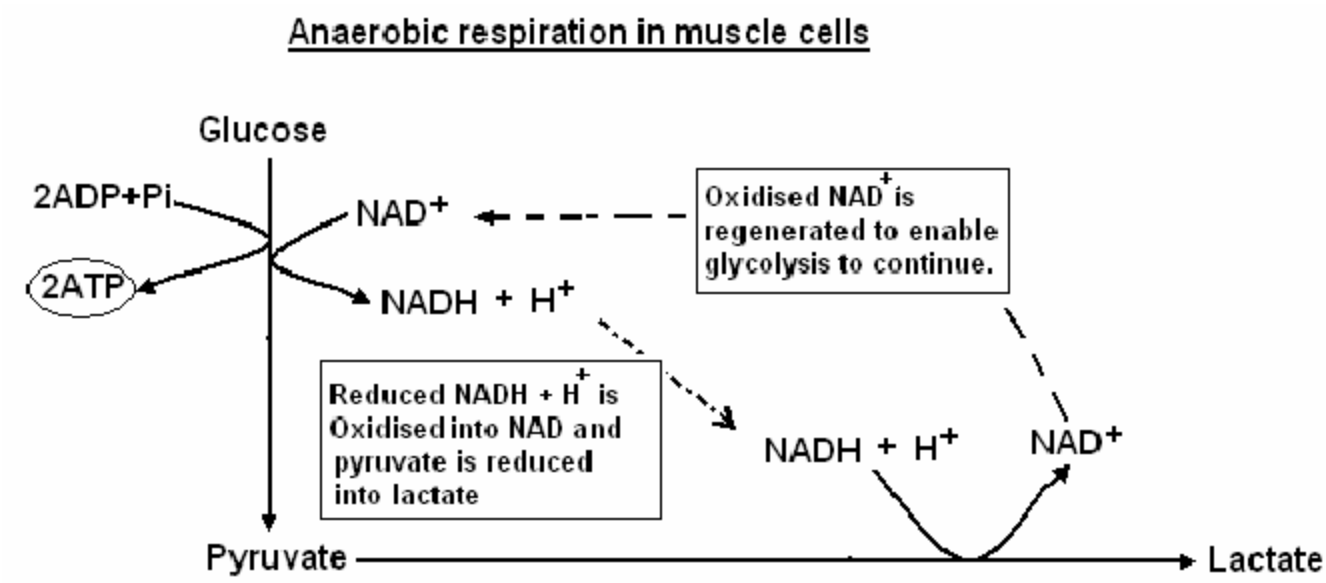
- $NADH_2$ loses Hydrogen atoms to FP. Thus, $NADH_2$ gets oxidized and FP gets reduced.
- Cytocrome b loses electrons to cytochrome c. Thus, cytochrome b gets oxidized and cytochrome c gets reduced.
- Cytochromes b and c contain haem groups (iron containing groups). This gives the mitochondria a reddish appearance. Thus, cells rich in mitochondria appear dark brown or reddish. Cytochrome a contains copper ions.

The hydrogen atoms are then split into Hydrogen ions and electrons (Hydrogen atoms are oxidized – loss of electrons). The Hydrogen ions move into the intermembranal space and the electrons are taken up by Cytochrome b. The electrons are then passed to Cytochrome c.
The electrons then pass from cytochrome c to cytochrome a. Every transfer of electrons from one carrier to the next involves a redox raction, which is controlled by oxidoreductase enzymes. Cytochrome oxidase is an example of an oxidoreductase enzyme which catalyses the transfer of hydrogen to oxygen at the end of the electron transport chain, to form water. Cyanide inhibits this enzyme and cause the ETC to stop functioning, leading to death.

Anaerobic respiration

8. Understand the situations in which the pyruvate formed in glycolysis may not undergo complete oxidation; formation of lactic acid in muscle; formation of ethanol in yeast.





☐ Anaerobic respiration takes place in oxygen deficient conditions. The ATP generated is only from glycolysis, which yields 2 ATP molecules from one glucose molecule.

☐ The respective pathways to yield ethanol and lactate ensure the regeneration of NAD (oxidized H carriers) so that glycolysis can continue.

☐ The electron transport chain does not function, as there is no oxygen to accept electrons at the end of the chain. Thus, the oxidation of $NADH_2$ to NAD is not possible. Since, NAD is not regenerated, Krebs cycle does not operate.

9. ***Compare and explain the differences in the yields of ATP from the complete oxidation of glucose and from the fermentation of glucose to lactic acid or ethanol.***

Yield of ATP during aerobic respiration	
Glycolysis (ATP synthesized by substrate level phosphorylation)	**2ATP**
Krebs cycle (ATP synthesized by substrate level phosphorylation)	**2ATP**
Glycolysis (Each $NADH_2$ from glycolysis will yield two ATP during oxidative phosphorylation, as ATP is used to transfer $NADH_2$ into the matrix.)	**2 $NADH_2$ X 2ATP = 4ATP**
Link reaction (Each $NADH_2$ from link reaction will yield Three ATP during oxidative phosphorylation.)	**2 $NADH_2$ X 3ATP = 6ATP**
Krebs cycle (Each $NADH_2$ from Krebs cycle will yield Three ATP during oxidative phosphorylation.)	**6 $NADH_2$ X 3ATP = 18ATP**
Krebs cycle (Each $FADH_2$ from Krebs cycle will yield two ATP during oxidative phosphorylation as it enters the electron transport chain, later than $NADH_2$, between FP and CoQ)	**2 $FADH_2$ X 2ATP = 4ATP**
Total ATP yield from one molecule of glucose during aerobic respiration =	**36 ATP**

Yield of ATP by anaerobic respiration : (2ATP per molecule of glucose)

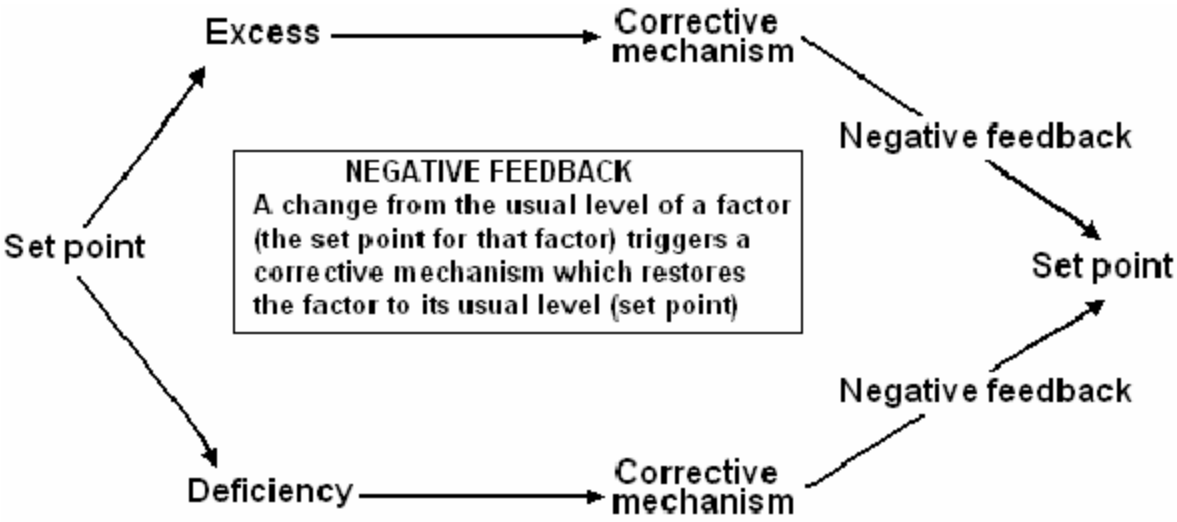
During anaerobic conditions Oxygen is not available to accept hydrogen and electrons from the electron transfer chain. This causes the electron transfer chain to stop functioning. Oxidized hydrogen carriers (NAD^+) cannot be regenerated. Without Oxidized hydrogen carriers (NAD^+),
Krebs cycle cannot operate. Thus, pyruvate cannot be further broken down by respiration.
However, there are certain pathways that can generate enough Oxidized hydrogen carriers (NAD^+) during anaerobic conditions. These Oxidized hydrogen carriers (NAD^+) can be reused for glycolysis to continue. So, during anaerobic respiration only glycolysis is the only source of ATP production. Hence, a single glucose molecule can yield only 2ATP during anaerobic respiration.

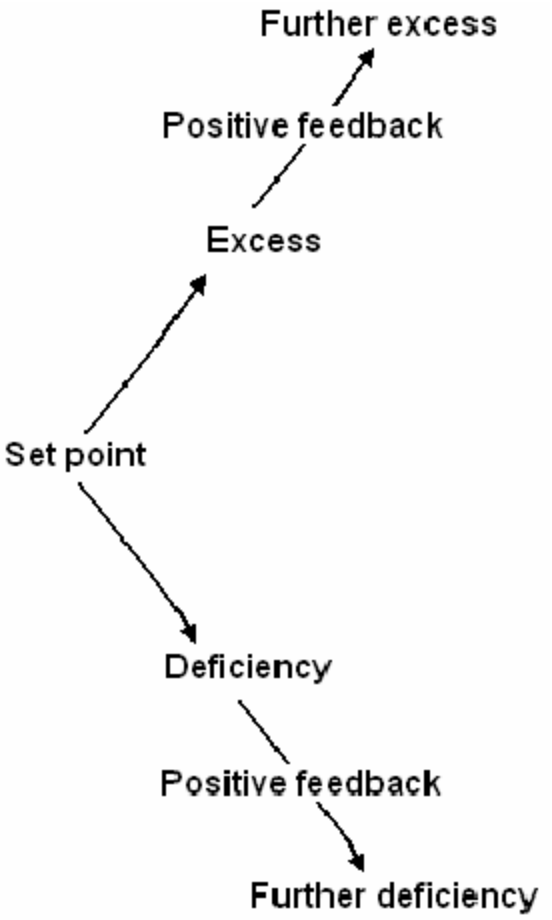
Regulation of internal environment

10. ***Understand the concept of homeostasis and its importance in maintaining the body in a state of dynamic equilibrium; understand that homeostasis allows organisms to be independent of the external environment.***

Homeostasis is the maintenance of a constant internal environment in the cells and tissue fluid, irrespective of changes in the external environment. Homeostasis maintains the body in a state of dynamic equilibrium which means that it works by **making continuous adjustments to compensate for fluctuations** in any factor (under homeostatic control) from its set point or reference point. Some factors under homeostatic control are temperature, glucose concentration and water potential of blood and tissue fluid. Our ability to maintain a constant internal environment enables humans to survive in a greater range of habitats than any other animal on Earth. By using artificial homeostatic devices to support our physiological processes, we are able to go from the depths of the ocean into outer space. Homeostasis is usually achieved by a process called negative feedback. The principle of negative feedback is illustrated in the diagram below.

11. Understand the concept and roles of feedback mechanisms.





Positive feedback mechanism: positive feedback mechanisms do not correct change from the set point. In fact, deviations from the set point are made even larger. A small change in a factor causes a further change in the same direction as shown in the diagram. e.g. increase in the level of oestrogen causes increased secretion of LH from the pituitary gland; the physical and emotional stress associated with labour will stimulate the release of more oxytocin and prostaglandins from the pituitary gland; in nerve cells an initial influx of sodium ions into the neurone will trigger a rapid influx of sodium ions into the neurone to generate an action potential; etc.

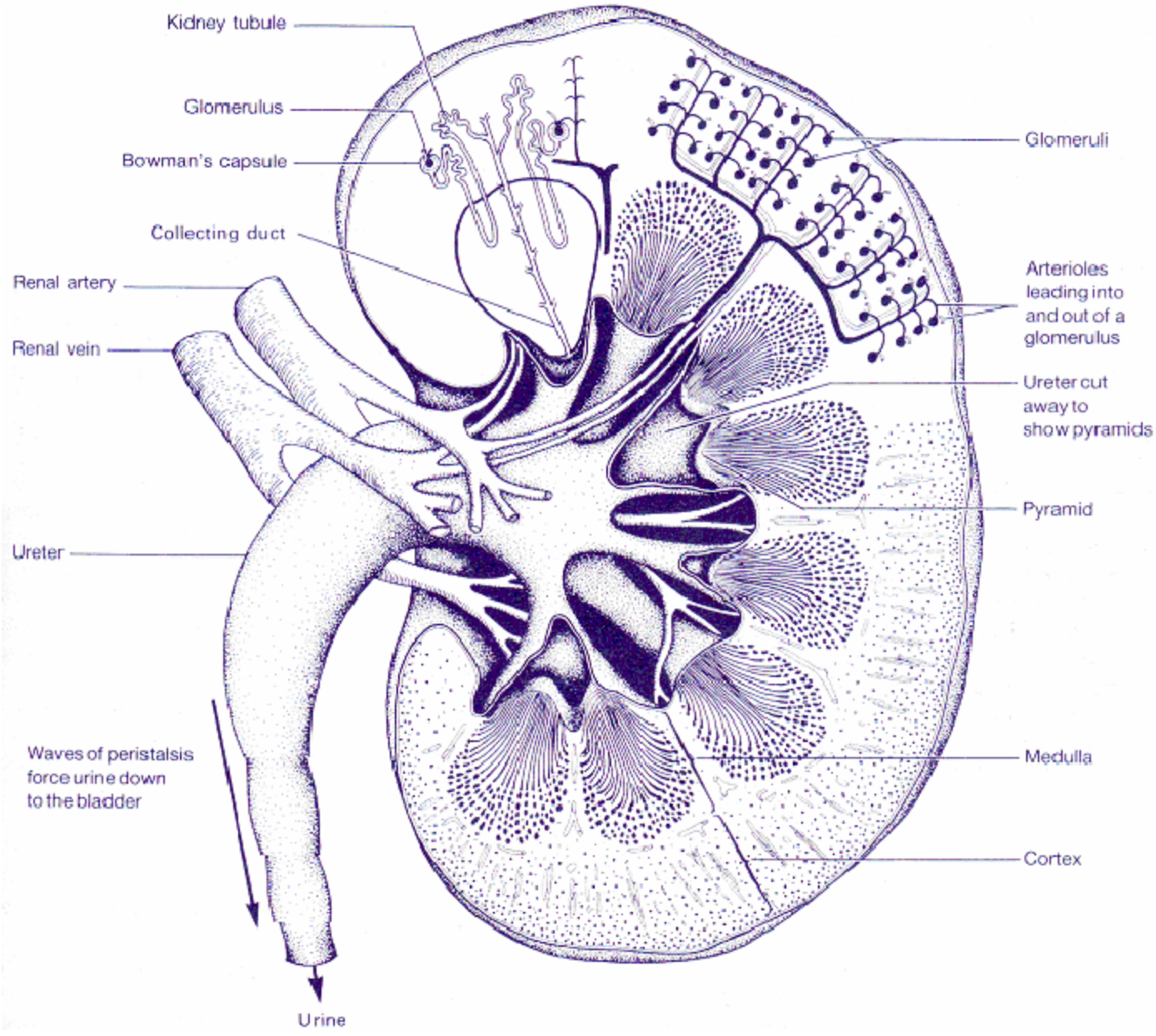
Sometimes positive feedback can be very harmful as it tends to produce unstable conditions. e.g. when negative feedback mechanisms in temperature regulation of mammals breaks down, a rise in body temperature can spiral upwards and threaten death.

12. Role of the mammalian kidney in osmoregulation and nitrogenous excretion; describe the structure of kidney and the function of nephrons.

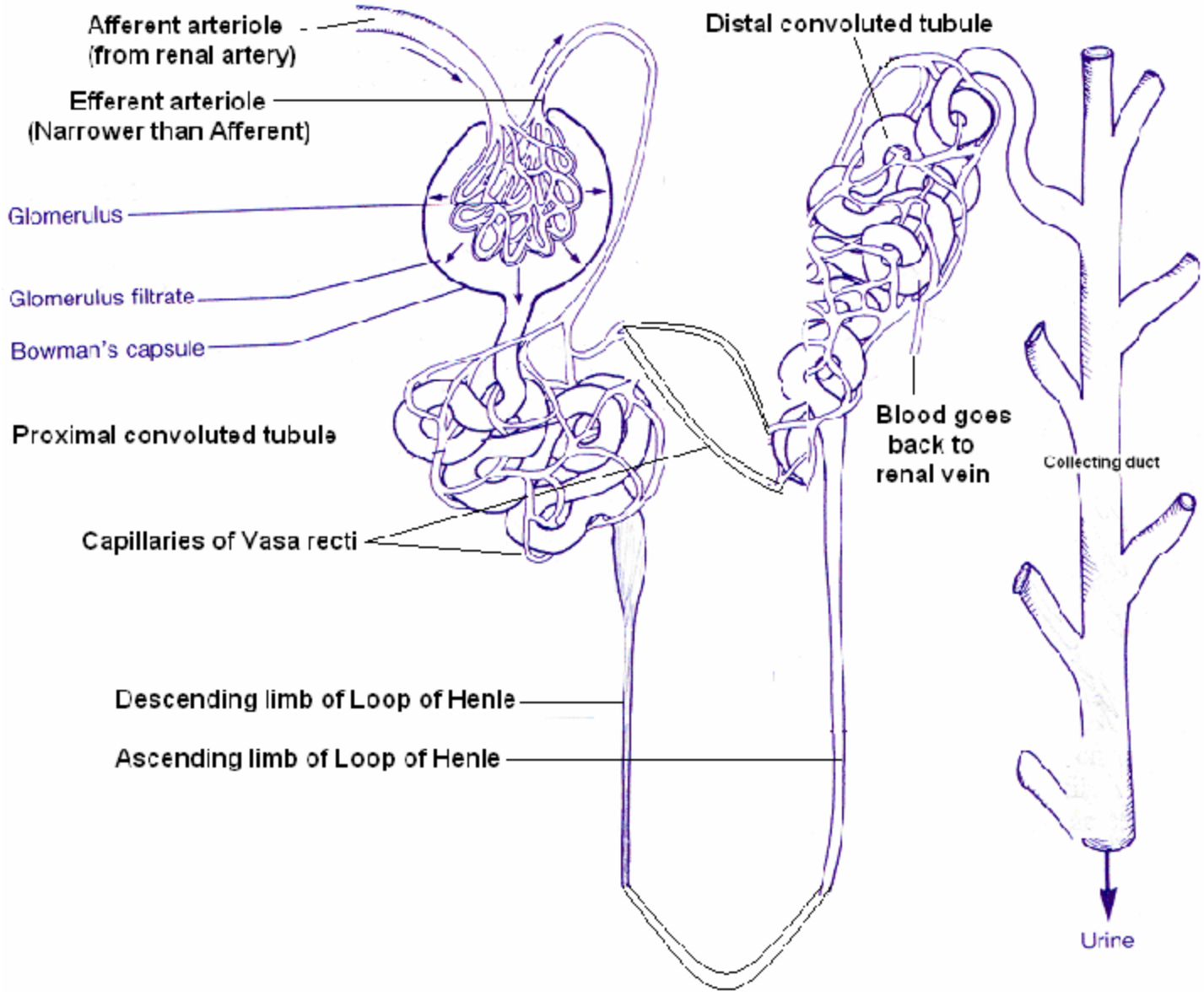
Kidney structure: the mammalian kidneys are located at the back of the abdominal cavity. They are bean seed shaped and are supplied with blood from the renal artery. The renal vein carries blood away from the kidneys. Internally each kidney consists of an **outer cortex** and **inner medulla**. The kidney is composed of nephrons. The glomeruli, Bowman' s capsule and convoluted tubules lie in the cortex. The Loop of Henle, collecting ducts and blood vessels lie in the medulla. The medulla leads into the pelvis, which collects urine and passes it into the ureter.

Functions of the kidney.

- Removal of nitrogenous waste(urea) from the blood.
- Osmoregulation – maintenance of water potential (salt concentration) of blood.



Nephron – the functional unit of kidney.



Nephron structure: the nephron is the functional unit of the kidney. Each nephron consists of the following regions.

The Bowman' s capsule:this part of the renal tubule surrounds a mass of blood capillaries called the glomerulus. Blood enters the glomerulus through the afferent arteriole and leaves from the efferent arteriole. Observe that the afferent arteriole is wider than the efferent arteriole. This helps to maintain a high blood pressure on the walls of the glomerular capillaries, which results in the formation of the glomerular filtrate by **ultrafiltration**. The glomerular filtrate passes into the Bowman' s capsule. Theglomerulus and Bowman' s capsuletogether are called the Malpighian body.

The proximal convoluted tubule: this is a tubular structure which is highly coiled (Convoluted). It is mainly concerned with **selective reabsorption** so that valuable substance such as glucose and amino acids are taken back into the blood and are not lost in the urine.

The loop of Henle: this is a ' U' shaped loop of the renal tubule which passes into the medulla of the kidney. It acts as a **countercurrent** (fluids flowing in opposite direction in both limbs of the loop) exchange mechanism, creating a low water potential (high solute content) in the medulla of the kidney, so that **water can be reabsorbed by osmosis**. Longer loop of Henle means that more water can be reabsorbed and the urine formed will be more concentrated and lesser in volume. This is usually seen in desert animals to reduce water loss from the body.

Distal convoluted tubule: this is the coiled part of the tubule which leads into the collecting duct. Its main function is **osmoregulation**. Varying amounts of water are reabsorbed from the tubule into the blood under the regulation of Anti diuretic hormone (ADH).

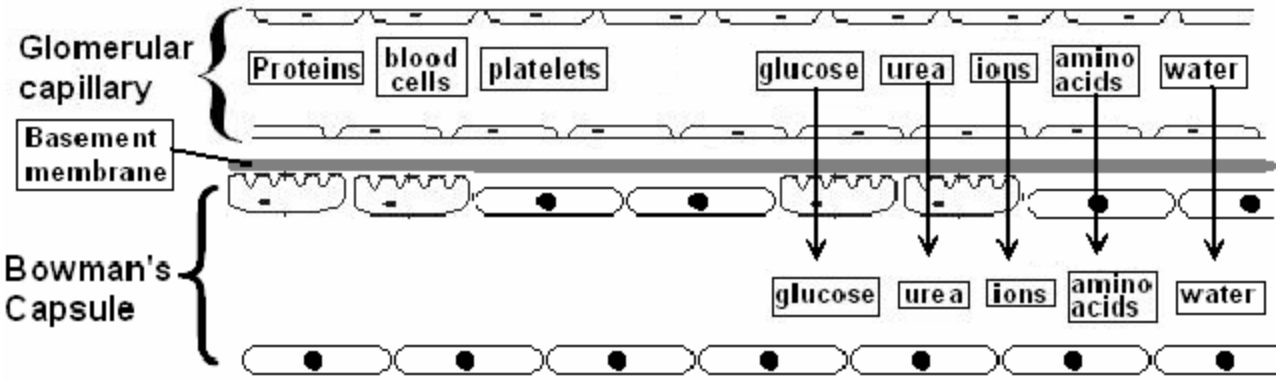
Collecting duct: Apart from collecting urine from the nephrons and passing it to the ureter, the collecting duct also performs the function of osmoregulation.

13. Process of ultrafiltration; selective reabsorption of water and solutes; the counter current multiplier

Ultrafiltration: The separation of large molecules from small ones by a very fine filter (basement membrane). This occurs in glomerulus. The high blood pressure on the walls of glomerulus (due to wider afferent and narrower efferent arteriole) forces water and solutes (having Relative Molecular Mass less than 68000) from the glomerulus into Bowman's capsule. These substances must pass across walls of the capillaries, basement membrane and cells of Bowman's capsule. The fluid entering the Bowman' scapsule is called Glomerular filtrate.

- About 125 cm^3 of glomerular filtrate is formed every minute.

The diagram below shows some of the substances present in blood and some of the substances present is the glomerular filtrate. **Podocytes** are specialized cells in the walls of the Bowman' s capsule which have **foot like processes** that grip onto the basement membrane. These cells do not fit close together, so there are gaps between these cells called **slit pores**, which increase the permeability of the walls. Substances pass into the glomerular filtrate depending on their size, not on their usefulness or any other property. The useful substances are later reabsorbed from the glomerular filtrate.

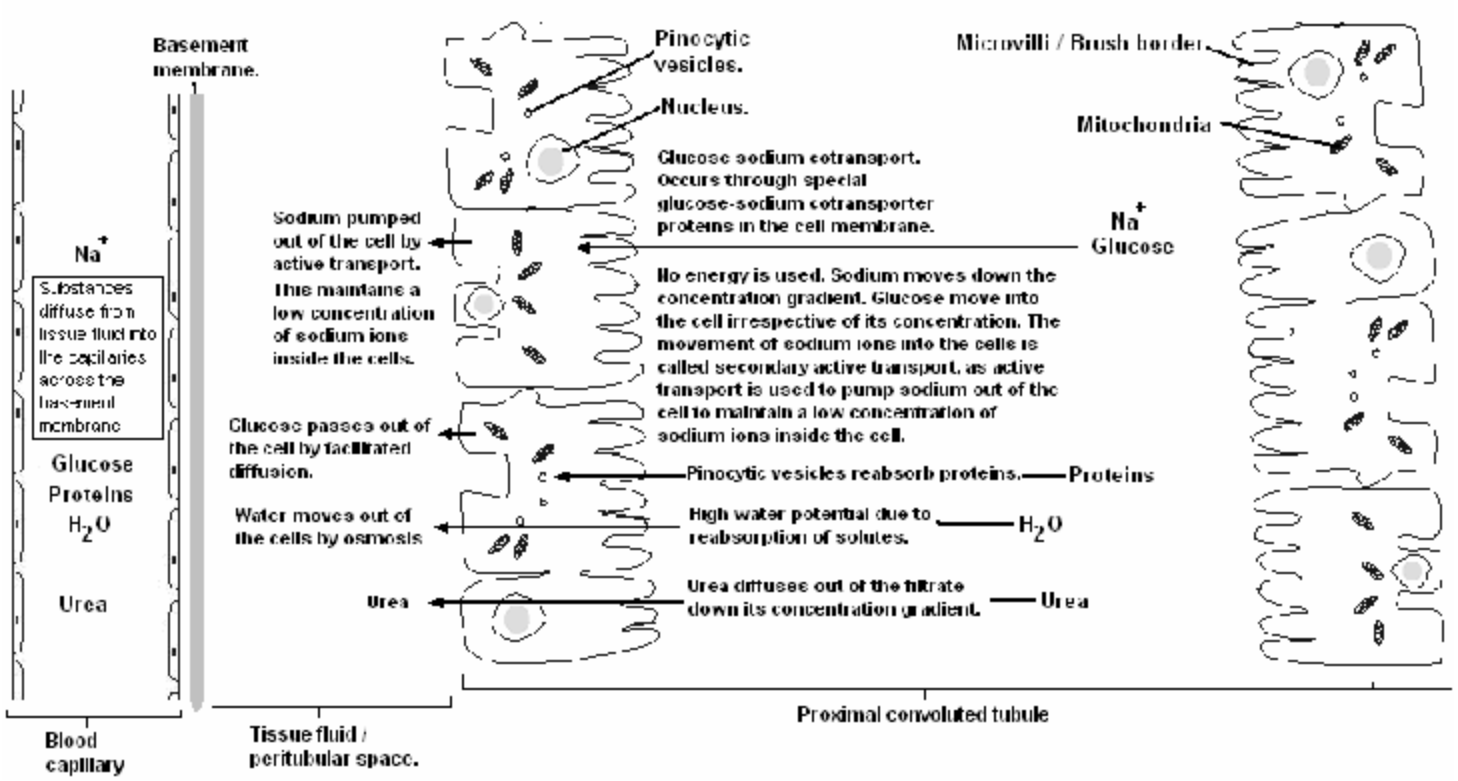


Selective reabsorption (in the Proximal Convoluted Tubule)

- **Glucose** is reabsorbed from the Proximal Convoluted Tubule by secondary active transport. Glucose also moves along with **Na^+ ions** by the glucose-sodium cotransport mechanism. Na^+ ions and glucose molecules are transported through a specific glucose-sodium co-transporter protein

across the cell surface membrane. All the glucose is reabsorbed from the filtrate into the blood. About 70 to 80% of Na^+ ions are reabsorbed.

- **Chloride ions** and other negative ions move out of the filtrate down an electrochemical gradient formed by the reabsorption of positively charged Na^+ ions from the filtrate.
- **Amino acids** are also reabsorbed by active transport (100% reabsorbed), in the same way as glucose.
- **Water** is reabsorbed by osmosis. The removal of Na^+ ions, glucose, amino acids and other solutes from the filtrate causes the water potential of the filtrate to become higher than the water potential of the blood. This causes water to move out of the filtrate by osmosis. About 70 to 80% of the water is reabsorbed.
- **Urea** is reabsorbed by diffusion. As water is reabsorbed from the filtrate, the concentration of urea in the filtrate becomes higher than the concentration of urea in the blood. This causes urea to diffuse back into the blood. About 50% of the urea is reabsorbed. The remaining 50% remains in the filtrate and passes out in urine.
- **Small proteins** that may be present in the glomerular filtrate are reabsorbed by pinocytosis.

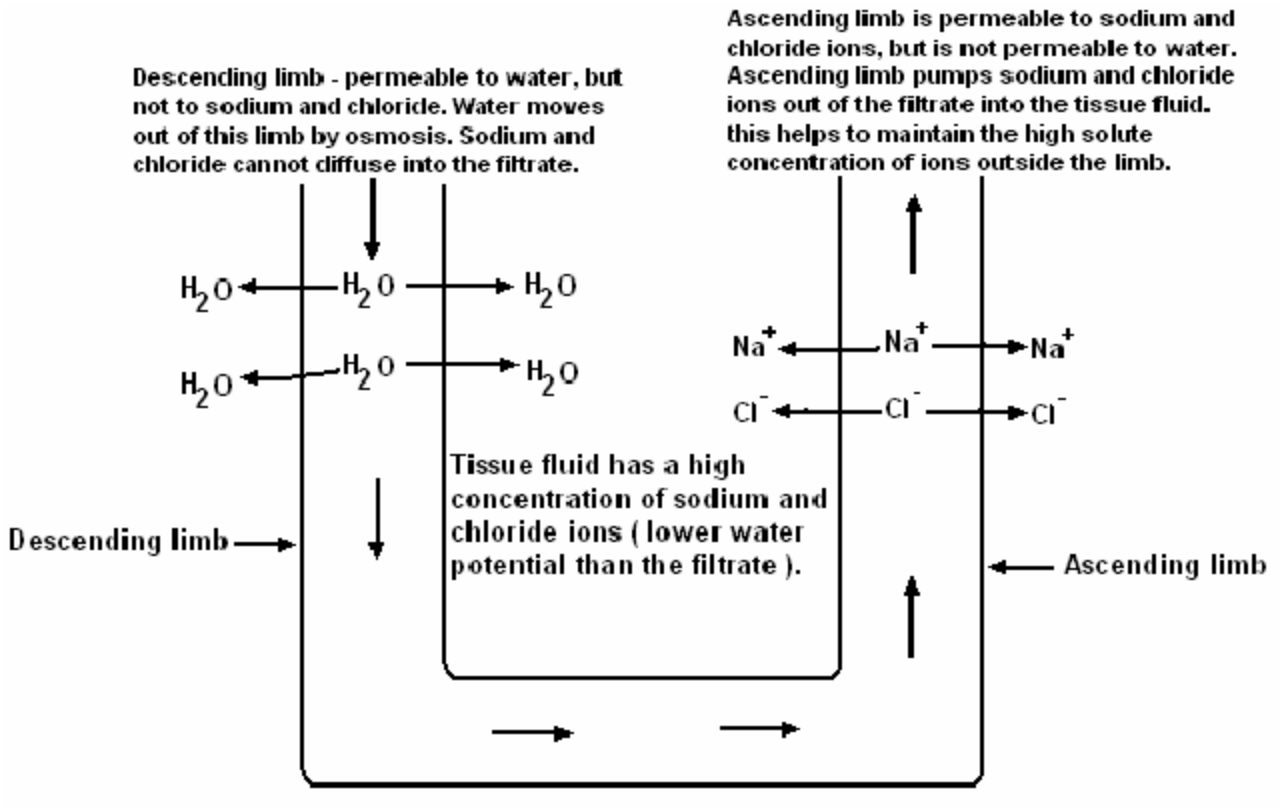


- Brush border / microvilli on the epithelial cells of the Proximal Convoluted Tubule increases the Surface Area for reabsorption of substances.
- Large number of mitochondria provides ATP (energy) for active transport.

Reabsorption of Water, Sodium and chloride in loop of Henle (Counter current multiplier).

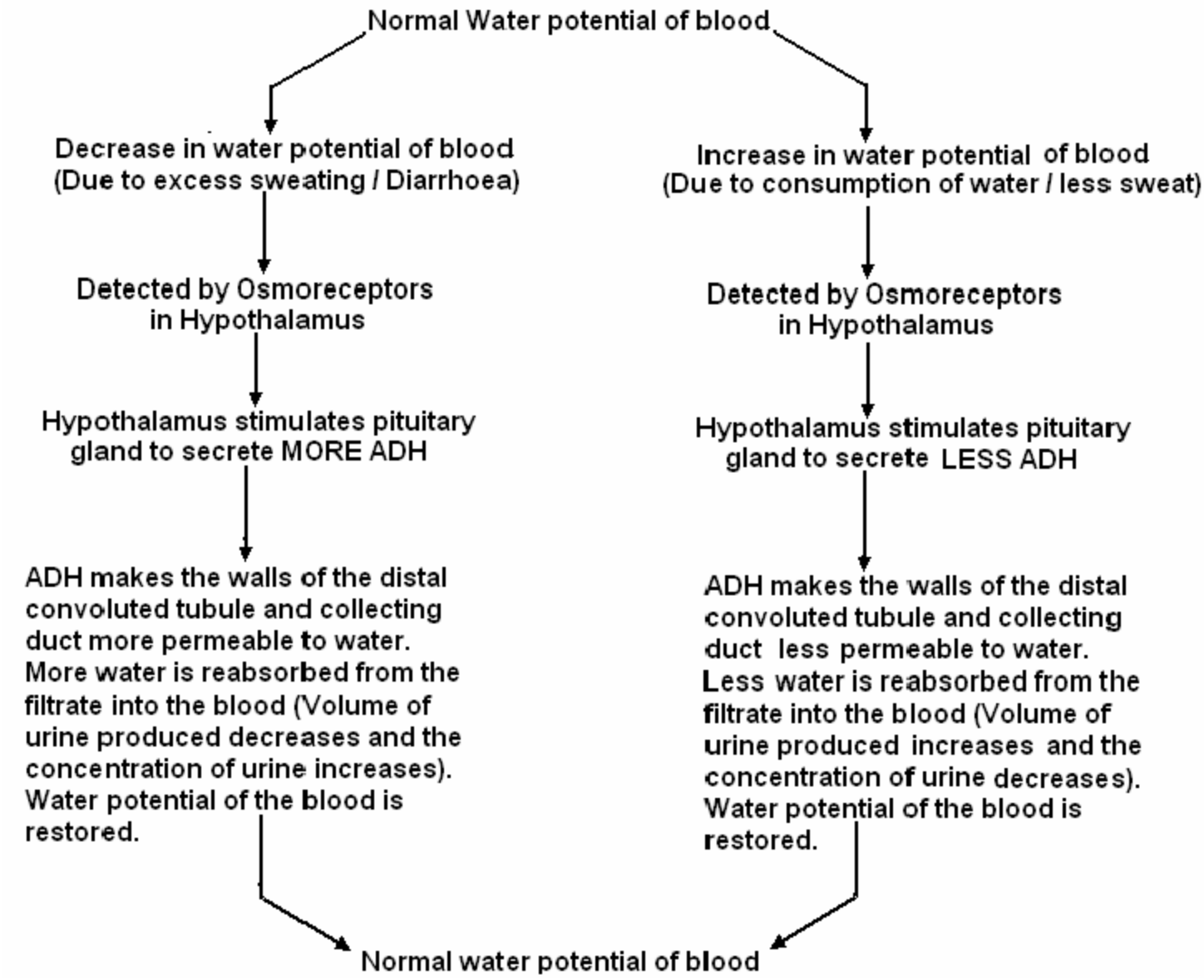
The Descending Limb is permeable to water, water moves from Descending Limb into surrounding tissue fluid and capillaries (vasa recta) by osmosis. At the same time, the Descending Limb is impermeable to sodium and chloride. So sodium and chloride cannot diffuse into the Descending Limb.

- The Ascending Limb pumps Na^+ ions into tissue fluid, so that a low water potential is maintained in the tissue fluid surrounding the loop of Henle. This causes water to be drawn out of the descending limb by osmosis. The ascending limb is impermeable to water.
- This is called the counter current multiplier as the fluids flow in opposite direction (counter current) in both limbs of the loop of Henle. The final result is that the **Urea concentration of the tubular fluid increases** as more water and sodium chloride is reabsorbed from the filtrate.
- Long loop of Henle leads to more concentrated urine as more water is reabsorbed. This is a common feature of desert animals, which produce a small volume of highly concentrated urine.



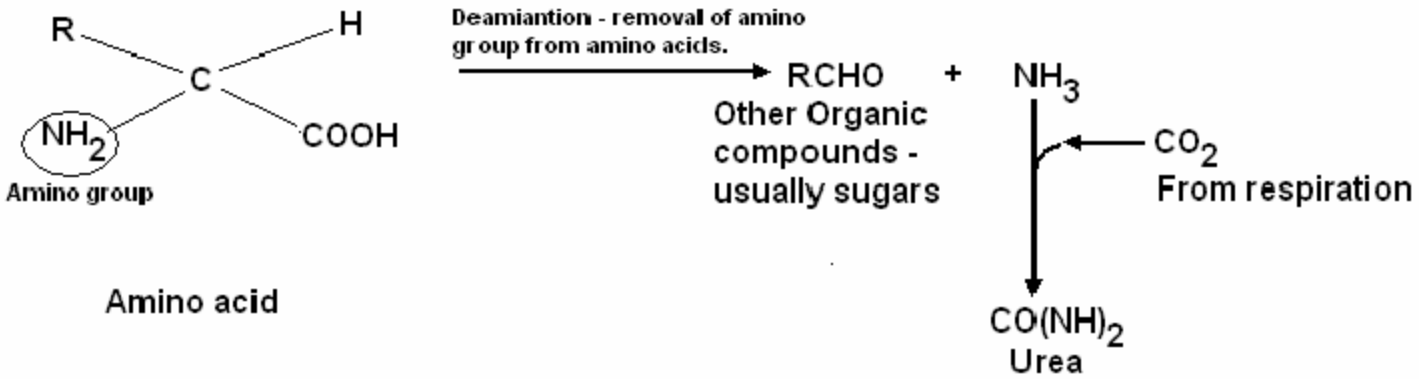
14. How the control of water and solute content of the blood is achieved; role of osmoreceptors in hypothalamus; the pituitary gland; the action of ADH; principle of negative feedback.

Osmoregulation in DCT and collecting duct: Osmoreceptors in the hypothalamus of the brain monitor the water potential of blood. If water potential of blood is higher that normal, less ADH is released from posterior pituitary gland. Collecting duct and Distal Convoluted Tubule become less permeable to water. Less water reabsorbed from the filtrate. So the urine is more dilute and more in volume. The water potential of blood is kept constant by negative feedback, as illustrated in the diagram below:



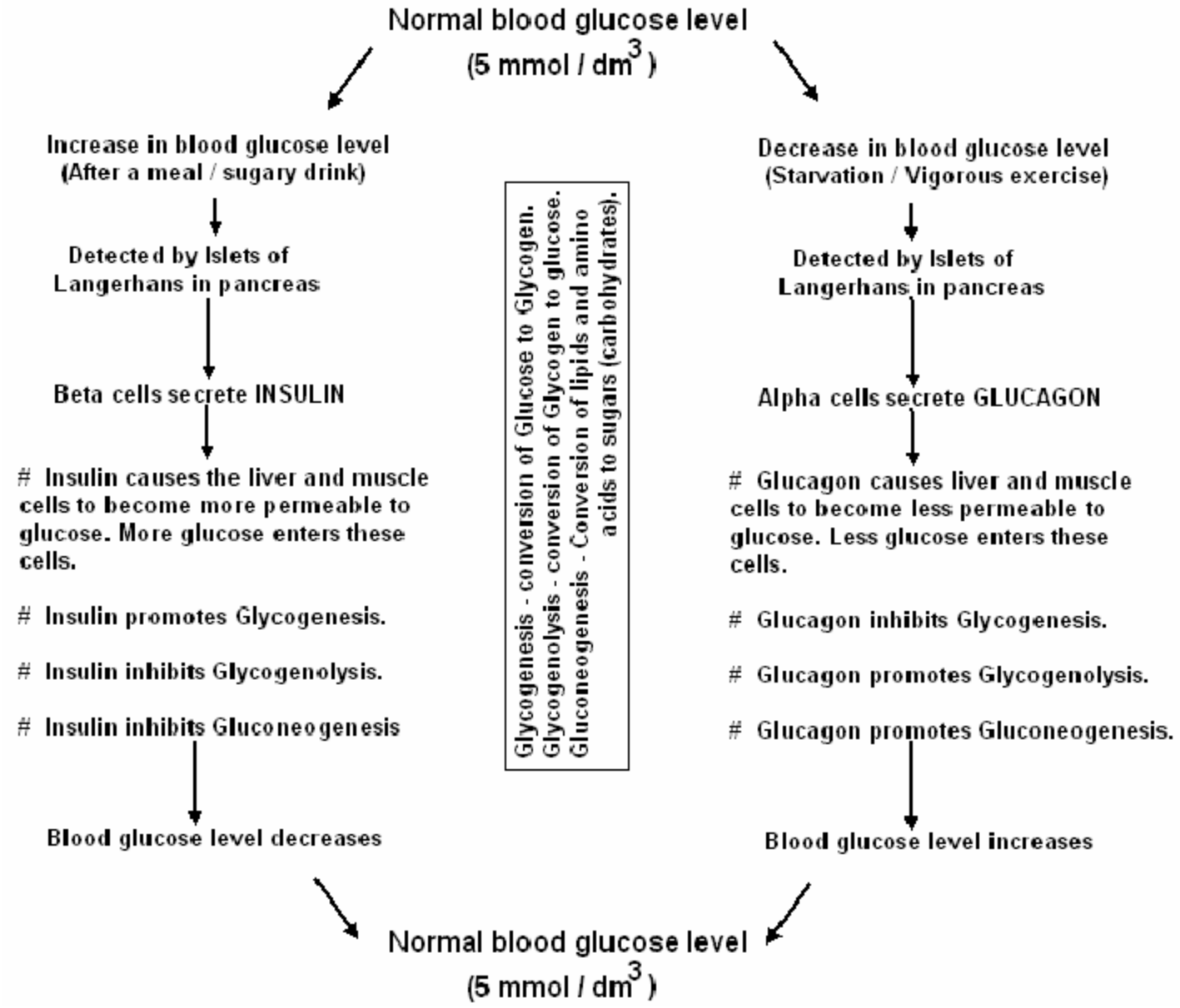
15. Production of urea in liver from excess amino acids.

Excess amino acids are broken down in the liver by a process called **deamination**. The process involves a series of cyclic reactions called the ornithine cycle. The amino group of the amino acids is removed to form ammonia. The ammonia is then combined with carbondioxide from respiration to form urea. Urea is less toxic and can be transported in the blood. It is then removed from the blood by the kidneys.



Regulation of blood glucose

16. Understand the factors, which lead to variation in blood glucose level; the roles of insulin, glucagons and adrenaline in the control of blood glucose level; role of liver in glucose-glycogen metabolism.



Type 1. Insulin dependent diabetes mellitus occurs due to lack of insulin secretion. Beta cells get destroyed due to viral infection / auto immune destruction. This occurs mostly in young people.
Treatment: Insulin injection.

Type 2. Non-insulin dependent diabetes mellitus- Body cells are less receptive to insulin / insulin secreting cells do not respond to changes in blood glucose level.
Treatment: decrease glucose intake / drugs to stimulate insulin secretion.

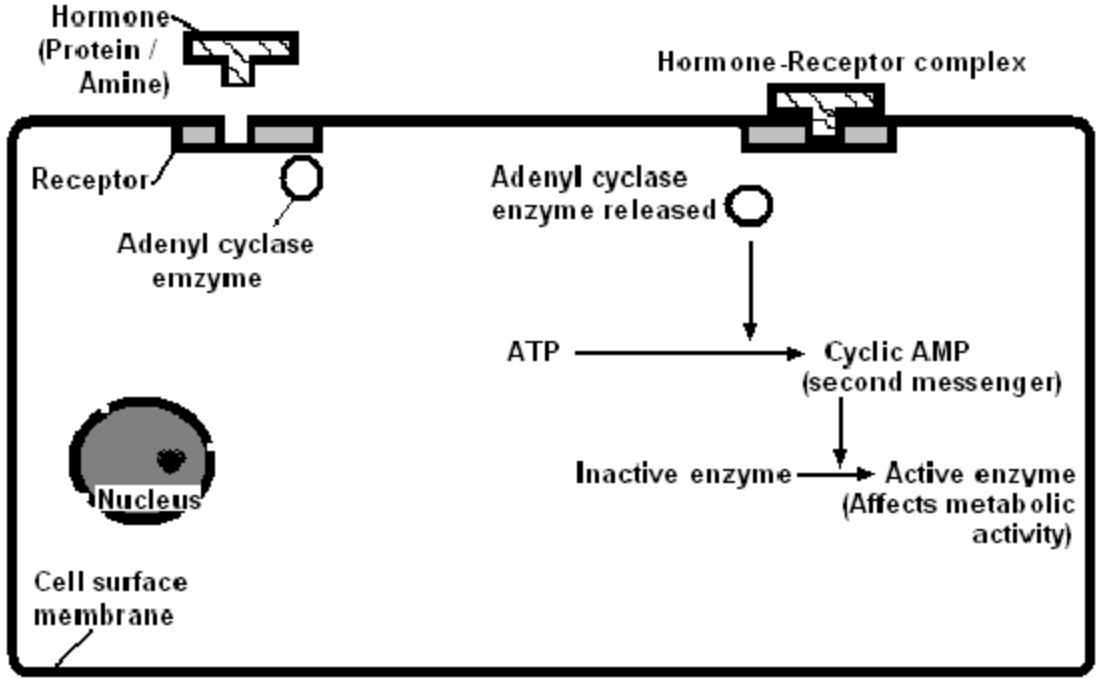
Some terms related to glucose regulation.

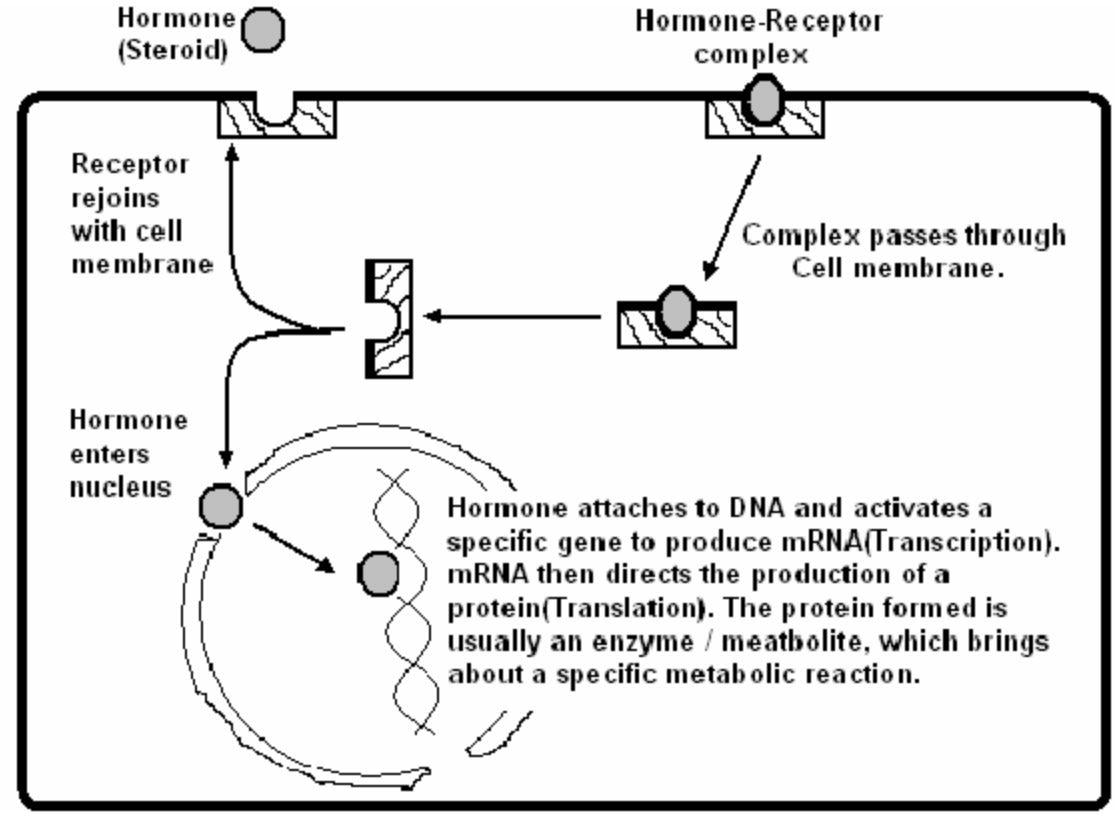
- **Glycosuria** – glucose in the urine. **Hypoglycaemia** – low blood glucose level, usually below 3mmol/ dm^3. **Hyperglycaemia –** high blood glucose level, above 10 mmol/ dm^3.

Mammalian hormones are chemical messengers carried by the blood from endocrine glands to all parts of the body. They affect specific cells, called **target cells**.
Chemically hormones are of three types:

- **Amines**: - Adrenaline / Thyroxine (**Lipid insoluble,** so cannot enter the cell).
- **Peptides/Proteins**: - Insulin / Glucagon (**Lipid insoluble,** so cannot enter the cell).
- **Steroids**: - Oestrogen / Testosterone (Steroids are **lipid soluble** and can enter the cell).

The mechanism of hormone action is shown in the diagrams below:
Note that the mechanism of action is **different for lipid soluble** and **lipid insoluble** hormones.

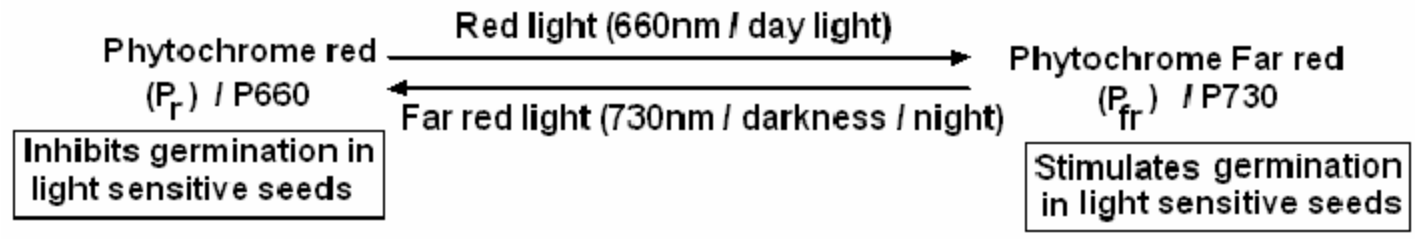




Response to changes in the external environment.

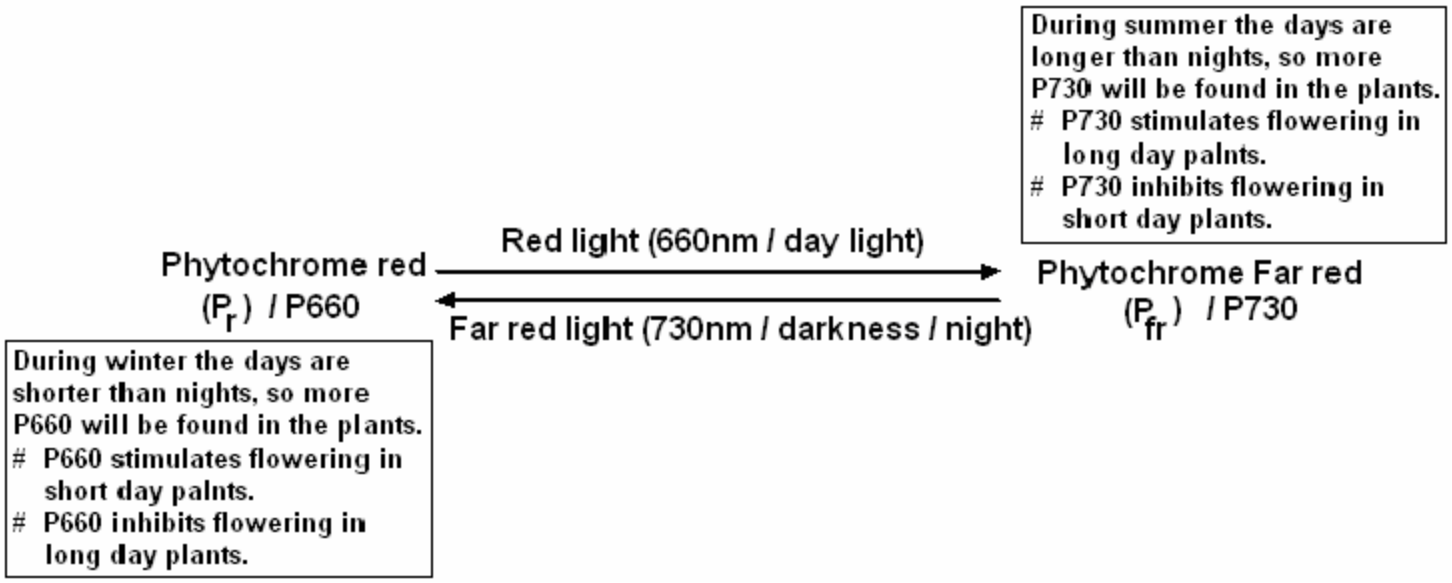
17. Understand the need for the detection of external stimuli; the concept of sensory receptors, illustrated by the detection of light in flowering plants by phytochrome pigments and in animals by the retinal pigments in the eye.

- Phytochrome is a photoreceptor pigment found in plants. It is bluish-green in colour.
- Phytochrome exists in **two inter-convertible forms**: **Phytochrome red (P_r/P660)** and **Phytochrome far red (P_{fr}/P730).**
- Phytochromes affect the germination of seeds.
- P_{fr} stimulates germination. This ensures that seeds germinate only when a lot of light is available. This increases chances of survival of the seedling. Eg: only seeds just below the surface (which receive some light) will germinate, ensuring that they emerge from the soil and start to photosynthesise even before food stored in the cotyledons is used up.
- Seeds falling on forest floor, below the canopy, will not germinate until a large tree falls down. The seeds on forest floor act as a reserve and ensure that some plants survive even if there is a disastrous year in which adult plants cannot produce seeds.



This mechanism is used by seeds to **start germinating in the spring or summer**. During summer the days are longer than in the winter. More P730 accumulates in the seeds and stimulates germination. On the other hand, **seeds do not germinate in winter** because there would be a higher concentration of P660 in the seeds. Remember that P660 inhibits germination. If seeds begin to germinate in winter, there is little chance of the seedling surviving the harsh environmental conditions of winter.

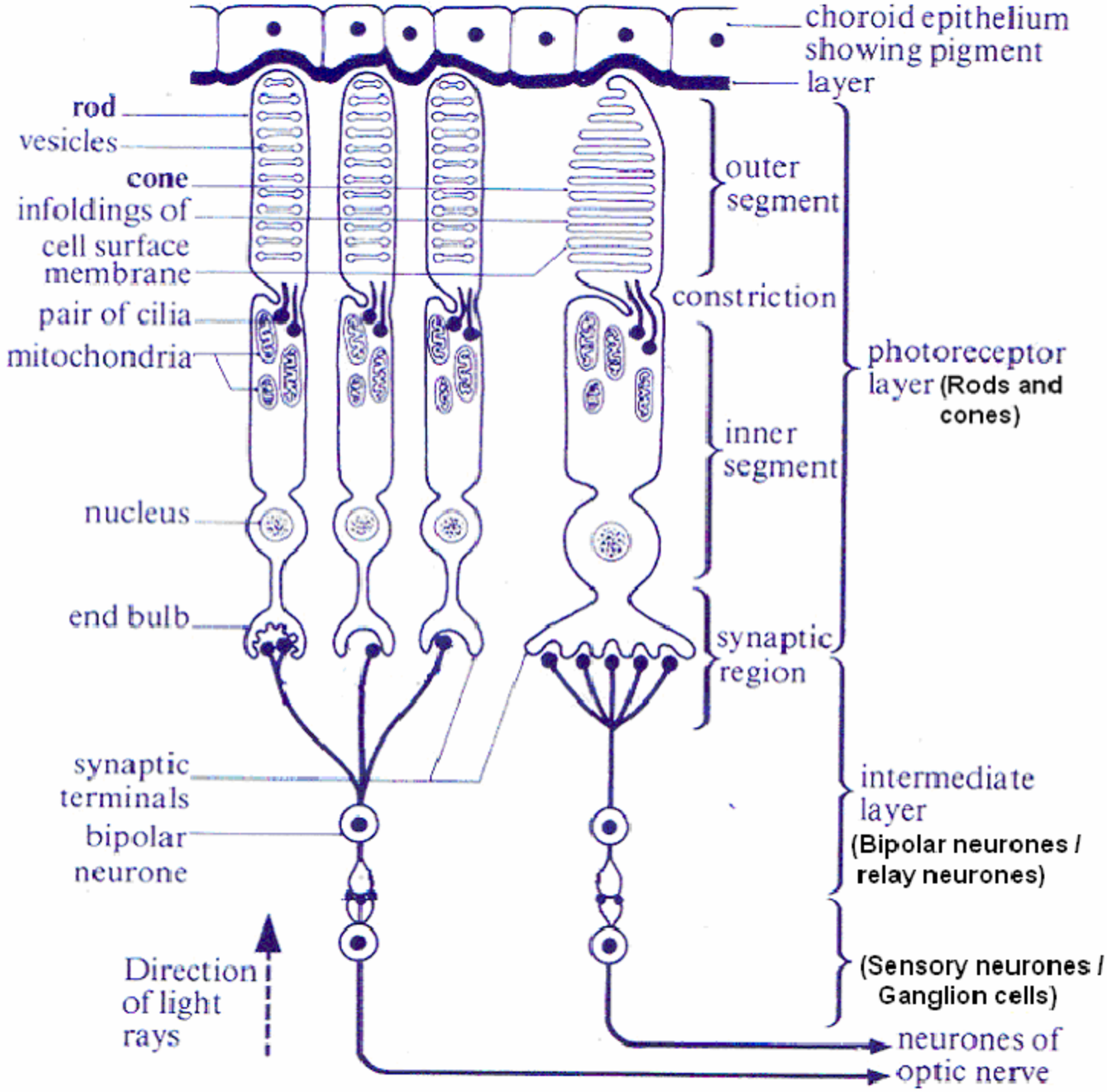
- Phytochromes provide a mechanism to detect the length of daylight or night (photoperiod).



Photosensitive pigments in the eye: The eyes are the most important sense organs. We receive about 80% of information from the surroundings through the eyes. Photosensitive pigments in the eye convert light energy into electrical signals, in the form of nerve impulses. The process by which a stimulus is converted into a nerve impulse is called **Transduction.** These nerve impulses are then sent to the **visual cortex** of the brain for interpretation. An image is then perceived.

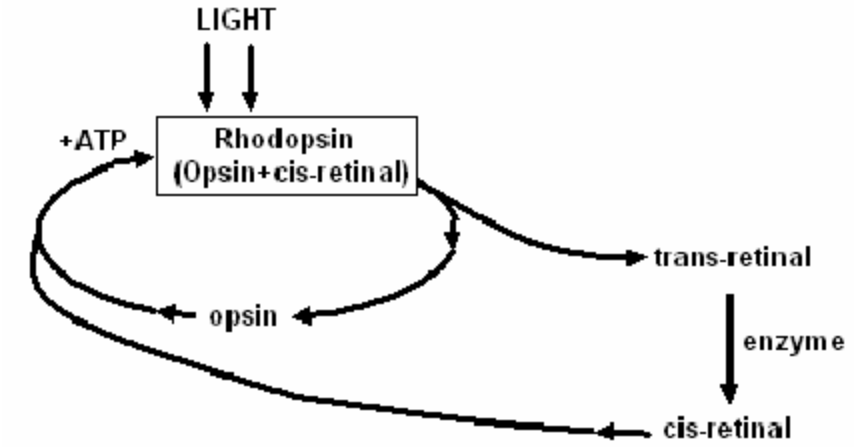
There are two types of photosensitive pigments found in the retina of the eye.

- **Rhodopsin**: this is the photosensitive pigment found in the **rod cells** of the retina. It is sensitive to light of **low intensity / dim light**.
- **Iodopsin**: this is the photosensitive pigment found in the **cone cells** of the retina. It is sensitive to the **wavelength of light / colour vision**.

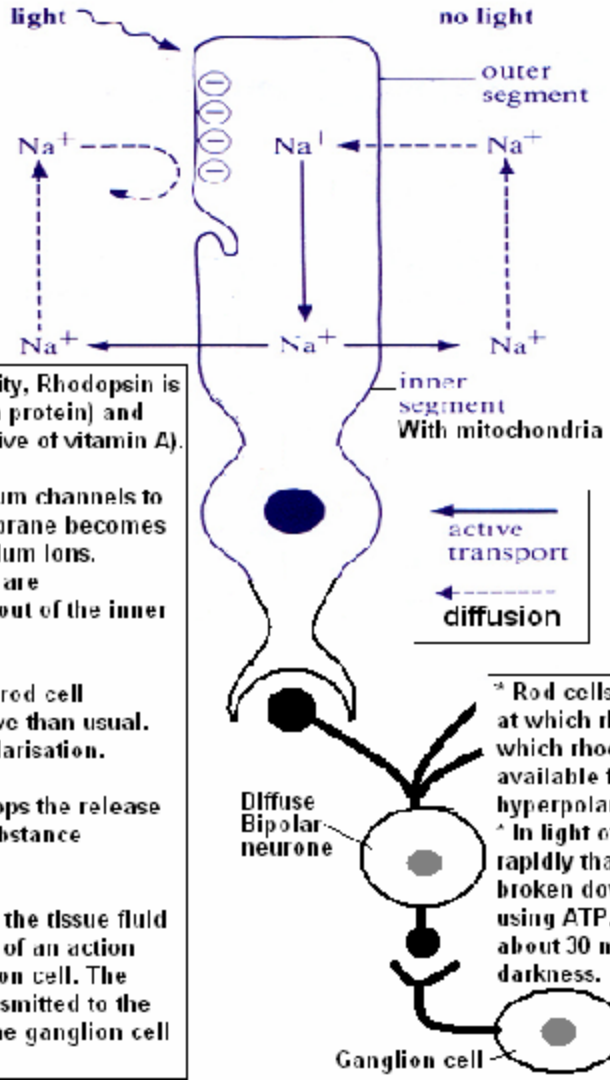


The diagram above shows the arrangement of rods and cones in the retina of the eye. Notice that there are three layers of cells – the layer of rods and cones (towards the choroids); the layer with bipolar neurones and the layer with ganglion cells (towards the vitreous humour).

Vision in Dim light / light of low intensity (Rhodopsin)



Light causes cis-retinal to be converted into trans-retinal, which cannot be bound to the opsin. So it splits into trans-retinal and opsin. Trans-retinal is reconverted into cis-retinal by an enzyme retinal isomerase. The cis-retinal recombines with opsin to form Rhodopsin. ATP is used for this process. Retinal is a derivative of vitamin A. So lack of vitamin A causes night blindness.



In light of low intensity, Rhodopsin is bleached into Opsin (a protein) and trans-retinal (a derivative of vitamin A).

This causes the sodium channels to close. The outer membrane becomes less permeable to sodium ions. However, sodium ions are continuously pumped out of the inner segment.

So, the inside of the rod cell becomes more negative than usual. This is called hyperpolarisation.

Hyperpolarisation stops the release of Neurotransmitter substance (Glutamate).

Lack of glutamate in the tissue fluid causes the generation of an action potential in the ganglion cell. The action potential is transmitted to the brain by the axon of the ganglion cell (in the optic nerve).

In darkness, Rhodopsin is formed faster than it is broken down. So more of it accumulates in the rod cells. This is called the Dark adaptation.

Rhodopsin makes the walls of the outer segment more permeable to sodium ions.

Sodium ions diffuse into the outer segment and reduces the negative charge inside the rod cell. The rod cell is prevented from getting hyperpolarised .

In this state, the outer segment releases a special transmitter substance(glutamate) into the tissue fluid.

Glutamate inhibits the transmission of an action potential in the ganglion cell.

* Rod cells are used for vision in low light intensity. The rate at which rhodopsin is regenerated is higher than the rate at which rhodopsin is bleached. So, rhodopsin will always be available for bleaching to continue and keep the rod cells hyperpolarised to generate action potentials.

* In light of high intensity, the rhodopsin gets bleached more rapidly than it can be regenerated. All the rhodopsin is broken down (light adaptation). This must be regenerated by using ATP, before we can see in dim light again. It takes about 30 minutes for regeneration of rhodopsin in complete darkness.

Cone cells and colour vision.

Cone cells are sensitive to wavelength of light at high light intensity. The photosensitive pigment in cone cells is **Iodopsin**. There are three different forms of iodopsin, each responding to light of a different

wavelength. Each form of iodopsin occurs in a different cone cell. Some cone cells are sensitive to **red light**, some are sensitive to **green light** and others are sensitive to **blue light**.
The relative degree of stimulation of each type of cone cell by **red, blue** or **green** light is combined and interpreted by the brain as different colours. This is called as the **trichromatic theory** as colour vision is stimulated only by three colours (wavelengths of light). The table below shows the colours perceived by the brain when the cones are stimulated by light of different wavelengths (colour).

Type of cone cell stimulated by light			Colour perceived
Red cone cell	Blue cone cell	Green cone cell	
Stimulated	xxxxxxxx	xxxxxxxx	Red
xxxxxxxx	*Stimulated*	xxxxxxxx	Blue
xxxxxxxx	xxxxxxxx	*Stimulated*	Green
Stimulated	*Stimulated*	*Stimulated*	White
Stimulated	*Stimulated*	xxxxxxxx	Magenta
Stimulated	xxxxxxxx	*Stimulated*	Orange / yellow
xxxxxxxx	*Stimulated*	*Stimulated*	Cyan

Synaptic convergence and its effects.
There are about 1.2 x 10^8 rod cells in the retina. The rod cells are evenly distributed in the retina except at the fovea and the blind spot, where there are no rod cells. The rod cells provide black and white vision only and are used mainly for seeing in low light intensities. Rod cells are not tightly packed in the retina and **several rod cells synapse with a single bipolar neurone**. This is called **synaptic convergence** (about 150 rod cells synapse with a single diffuse bipolar neurone). The effect of synaptic convergence is that the rod cells do not give a particularly clear picture (**low visual acuity**). However, synaptic convergence causes the rod cells to be very sensitive to low light intensity and to movements in the field of vision, because several small stimuli in the rod cells can stimulate an action potential in the ganglion cells.

Visual acuity of cone cells.
Cone cells are tightly packed in the fovea. There are about 6 x 10^6 cones. Each cone cell is connected to an individual bipolar neurone. This means that more information is being sent to the brain. This provides a picture of great visual acuity. Since the cones are highly concentrated on the fovea, it is necessary for the image to be focused on the fovea to give a clear image of high visual acuity.

18. Understand the nature of mammalian hormones; the principles of hormonal action and control as illustrated by the action of insulin and glucagons in the regulation of blood glucose level, ADH and reproductive hormones; the principle of Negative feedback.

(Notes in specification 16 of this unit and specification 45 of unit 2).

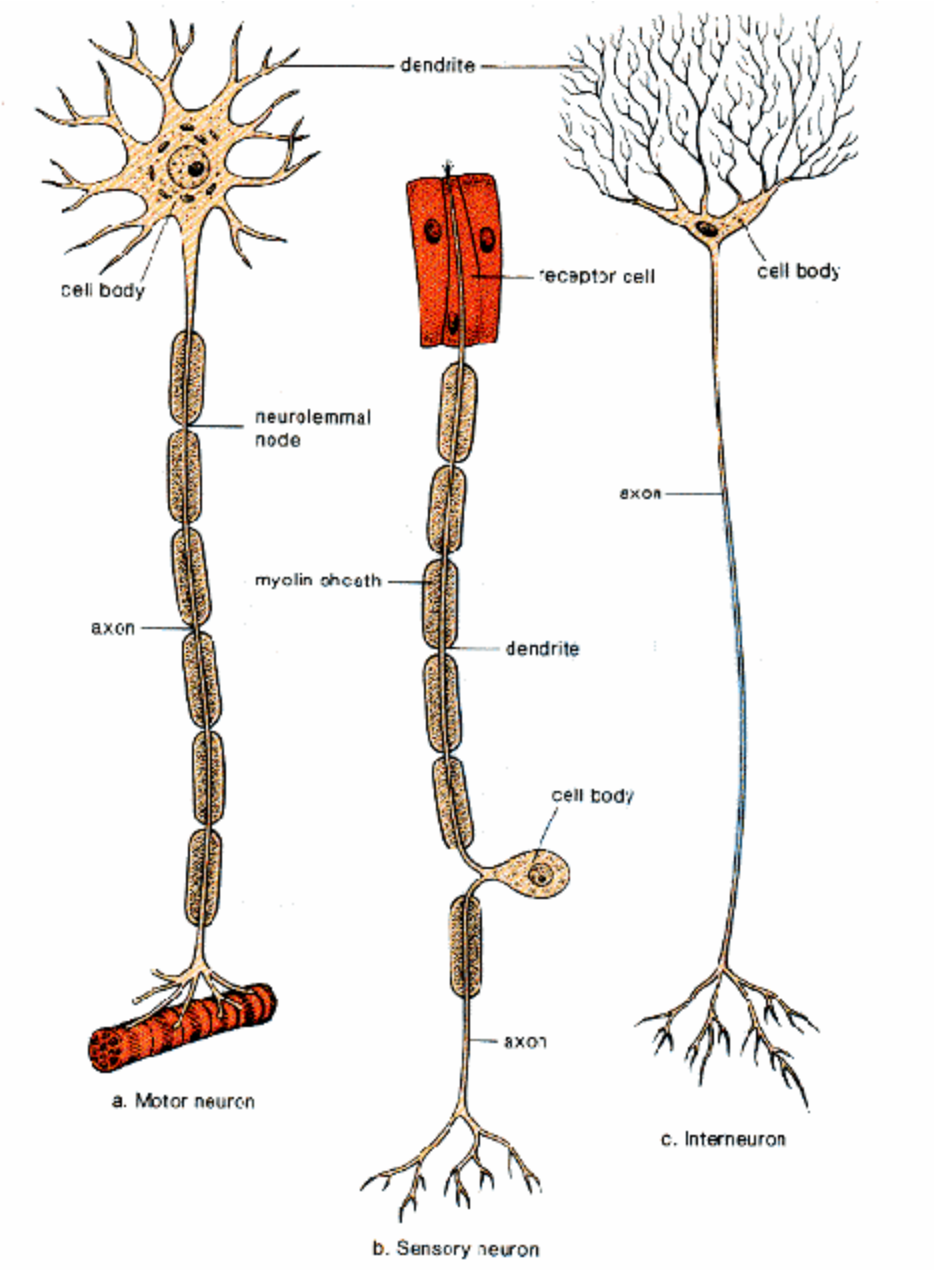
Adrenaline is secreted by the adrenal gland, in response to an emergency. It has a widespread effect on the body, affecting many organs. It increases the blood glucose levels by enhancing glycogenolysis, it increases the heartbeat and breathing rate, it causes the pupils to dilate, it diverts blood from the periphery of the body to vital organs like brain and liver, etc. It is an amine and cannot enter the cell. So it attaches to receptors on the cell membrane of target cells and stimulates the release of adenyl cyclase enzyme to trigger a series of reactions in the target cells.

19. Appreciate the differences between nervous and hormonal coordination.

Nervous control	Hormonal control

Transmitted by electrochemical impulses	Transmitted by chemical messengers (hormones)
Speed of transmission very quick	Speed of transmission much slower
The effect is usually very short lived	The effect is usually long lasting
Transmitted through neurones / nerves	Transmitted through blood
Usually affects a specific organ	Usually has a widespread effect and can affect many organs. Refer to the effect of adrenaline

20. ***Describe the structure and functions of sensory, relay and effector neurons; the role of Schwann cells and myelination.***

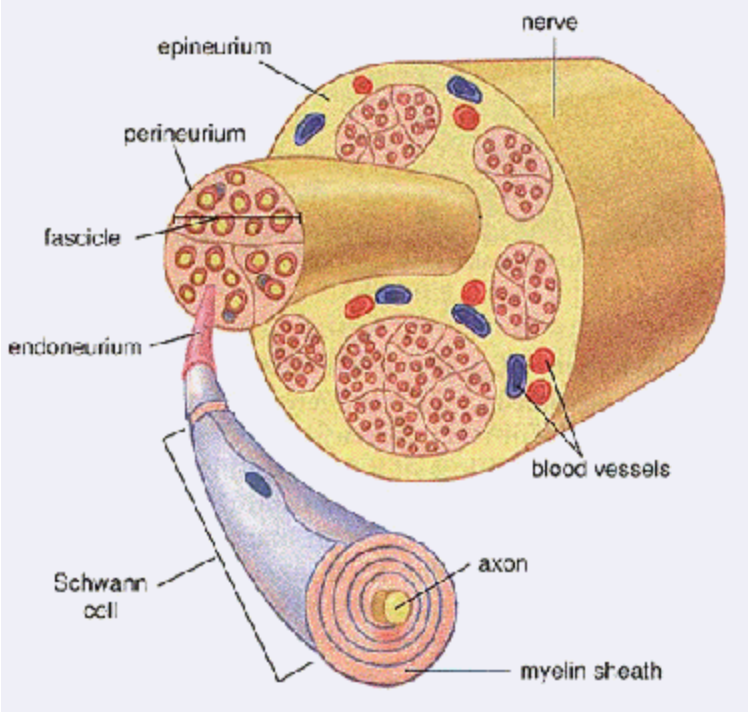


Neurones are nerve cells which carry electrochemical impulses from one part of the body to another. Every neurone consists of three main regions – **dendron; cyton / cell body; axon.** Impulses always travel in one direction along a neurone – **from dendron** to **cyton** to **axon.**

The smaller branches which receive and transmit impulses to the dendron are called dendrites. The **axon endings** usually form **synapses** with the dendrites of other neurones.

The structure and function of the three basic types of neurones are shown in the diagram above and discussed in the notes below.

A. **Sensory neurone:** sensory neurones transmit **impulses from the sense organs to the central nervous system (brain or spinal cord).** The dendron is longer than the axon and is insulated by a **myelin sheath**, formed of **Schwann cells.** The Schwann cells are wrapped around the axon to form many layers of insulating material composed of 70% lipid and 30% proteins. Between adjacent Schwann cells there are gaps called the **Nodes of Ranvier.** These regions are not insulated and can transmit nerve impulses. The nodes of Ranvier speed up the transmission of nerve impulses, as the impulse jumps from one node of Ranvier to the next. This is called the **Saltatory effect**.



B. **Motor neurone:** motor neurones always transmit impulses **form** the **central nervous system** (brain or spinal cord) **to** the **effector organs** (muscles or glands).
There are many dendrons but a single long axon which is myelinated.

C. **Relay neurone:** these are also called connector neurones or intermediate neurones, they are non myelinated. The main function of these neurones is to transmit impulses from one neurone to another. In the brain and spinal cord a single relay neurone connects with many different neurones and helps to analyse information received from many neurones. This is useful in decision making. The connections are made by **synapses**.

Factors affecting speed of nerve impulse

- Diameter of the axon. (Speed is proportional to diameter)
- Myelination - In myelinated axons the action potential travels from one node of Ranvier to the next. This is called the SALTATORY EFFECT, which speeds up transmission of impulses.

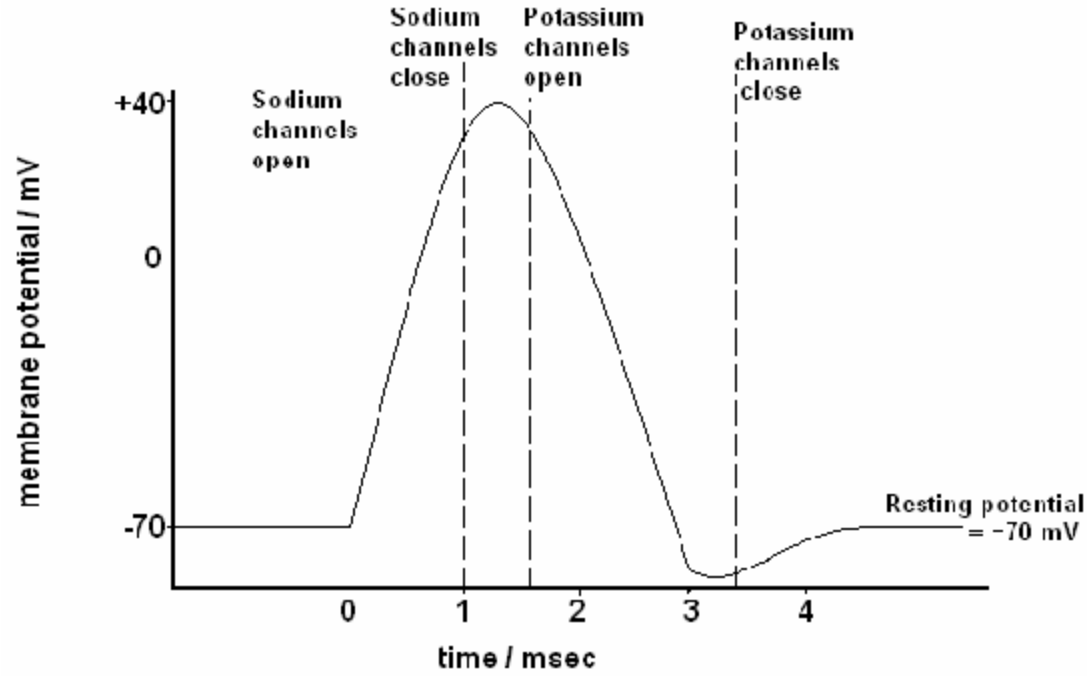
21. Understand the nature of the nerve impulse; describe the propagation of action potential in terms of changes in the permeability of the membrane to Na ions resulting in a wave of depolarization propagating an action potential.

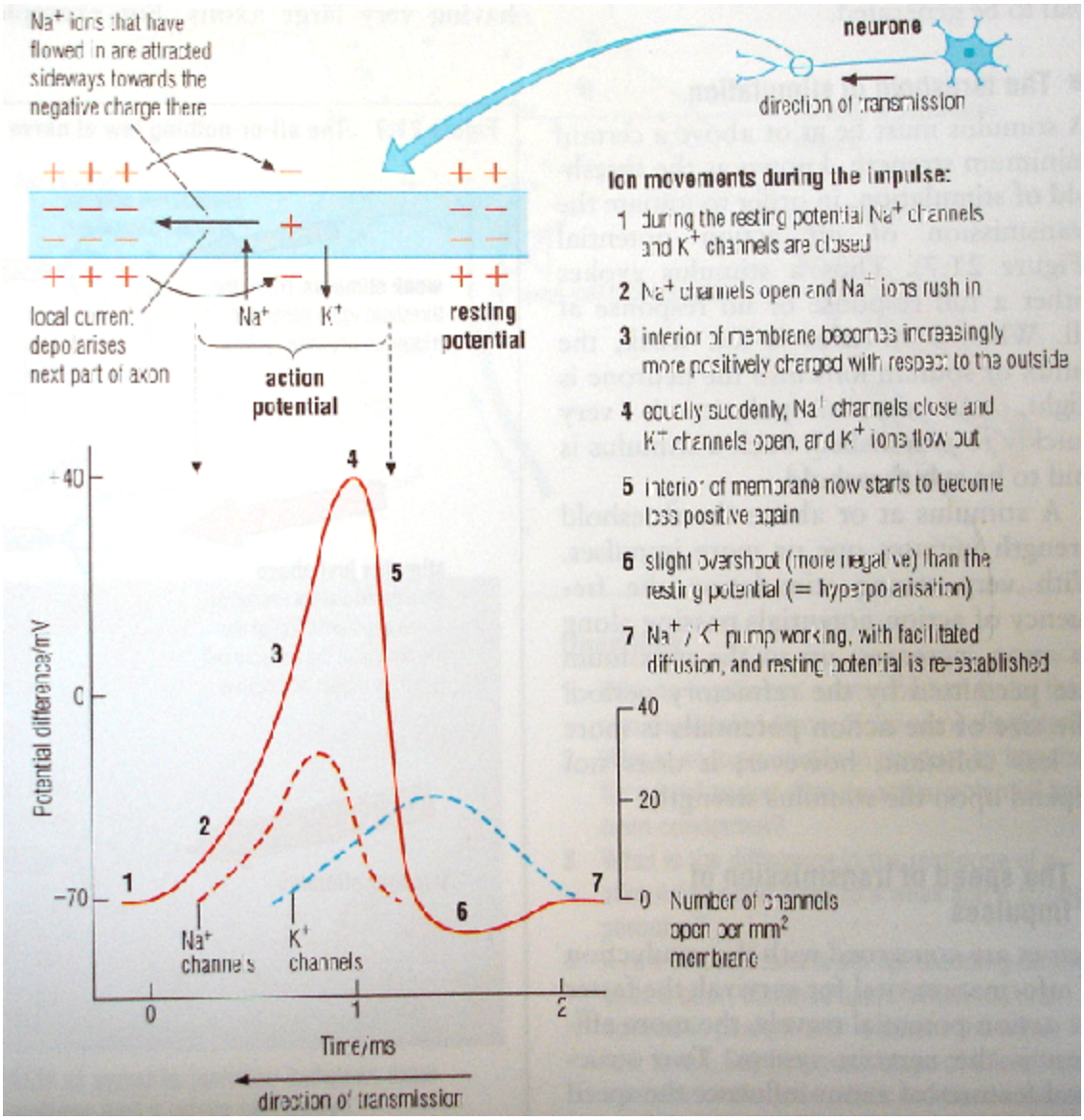
A nerve impulse is the propagation of an action potential (a wave of depolarization) along an axon.

- **Resting potential** (-70 mv): This is the difference in potential between the inside and outside of the neurone membrane. The Na-K pump, pumps $3Na^+$ ions out and $2K^+$ ions into the neurone. The membrane is more permeable to K^+ ions than Na^+ ions. So K^+ ions diffuse out of the neurone. This

causes the inside of the membrane to become more negative than the outside (as positive charges Na^+/K^+ moves out). This is the potential when no impulse is passing along the neurone. *(Even though this is called the resting potential, a lot of energy is used to operate the sodium-potassium pump and maintain a negative potential inside the cell.)*

☐ **Action potential** (+40 mv): This is the potential when a nerve impulse is generated. The Sodium channels in the axon membrane open and allow Na^+ ions to enter into the axon cytoplasm, until the potential reaches +40 mV. Then the Na^+ gates close and K^+ gates open. Na^+ ions cannot move into the cell but K^+ ions move out rapidly causing repolarisation. There is an overshoot of K^+ ions out of the axon, which causes the potential to fall lower than -70 mV. This is called hyperpolarisation. However, closure of the K^+ ion gates and the action of the sodium-potassium pump restores and maintains the resting potential.



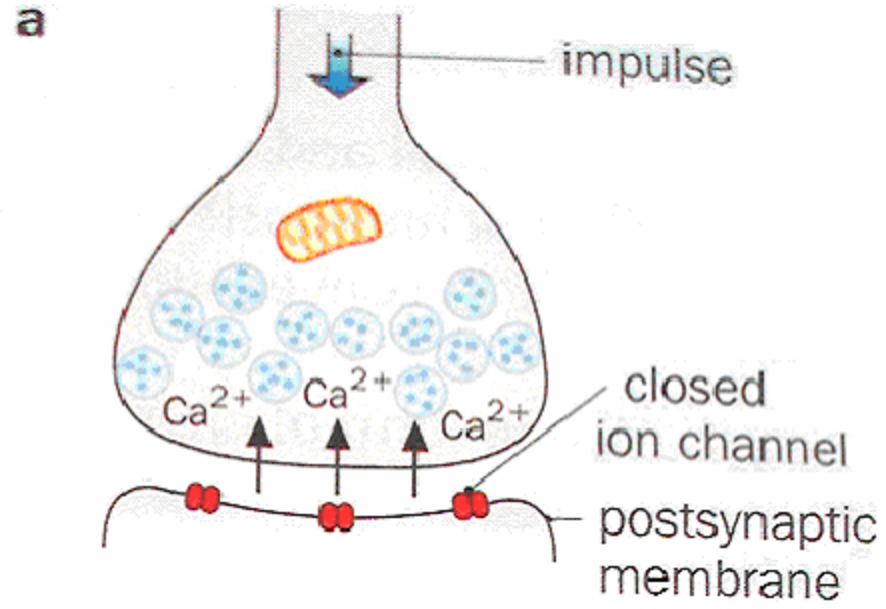


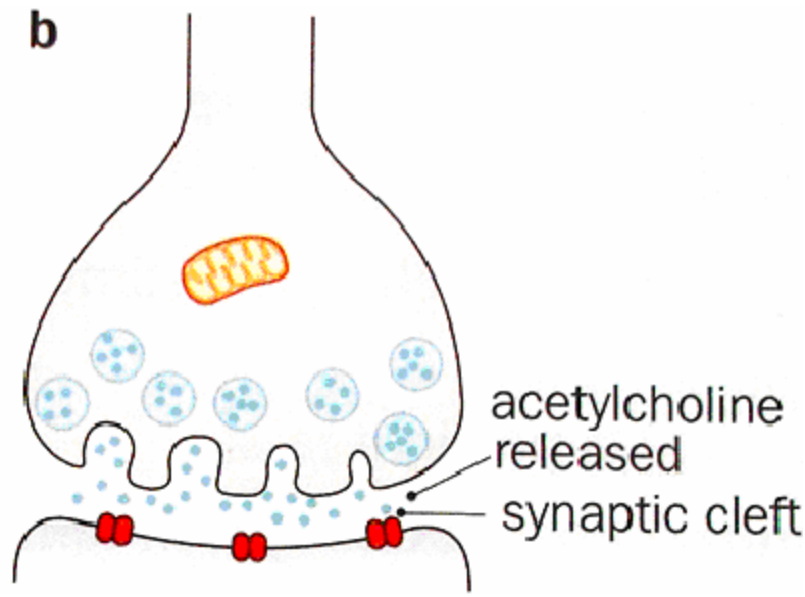
Even though resting potential, action potential, hyperpolarisation and repolarisation are described separately it must be kept in mind that all these processes occur at the same time in a given neurone. The neurone does not become depolarised or repolarised all at once. Instead the impulse moves as a wave of depolarization along the neurone. Refer to the diagram above to understand how a nerve impulse travels along a neurone. Note that local currents drive the action potential from one point of the neurone to the next. The direction of transmission of an impulse is always from a point of action potential away from a point of hyperpolarisation.

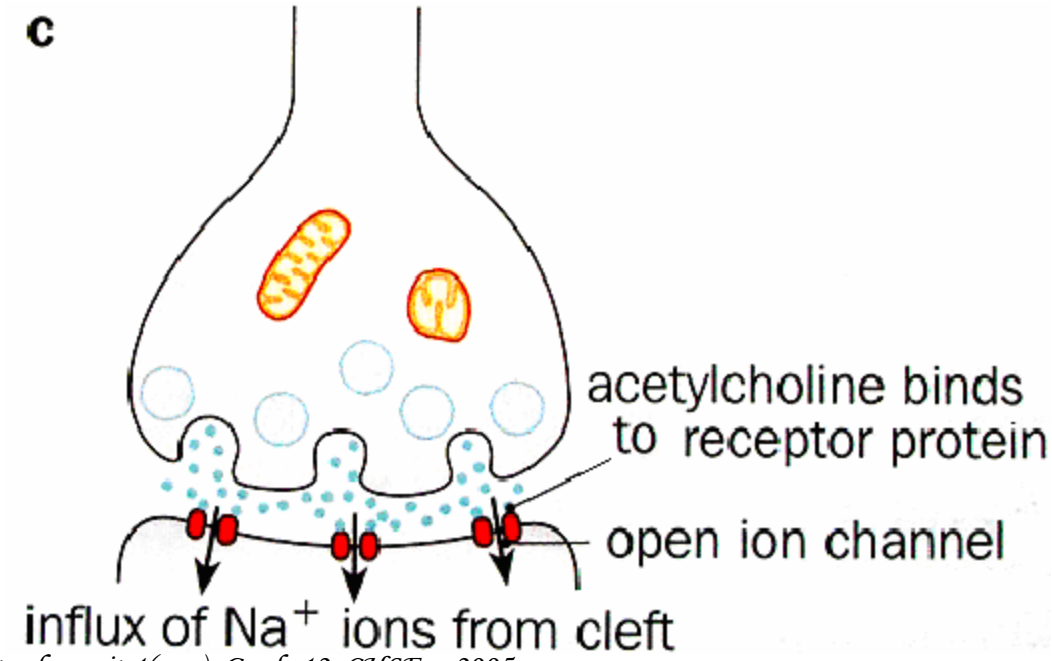
22. Describe the structure and functions of a synapse; understand the role of acetylcholine as a transmitter substance; post-synaptic potentials.

Synapse is a gap between the ends of two neurones. If the gap is less than 2nm then electrical impulses are transmitted from one neurone to the next. But, if the gap (cleft) is larger (upto20nm) then chemical (neurotransmitters) impulses operate.

The sequence of events involved in the transmission of an impulse across a synapse is illustrated in the diagrams below. This synapse involves acetylcholine as a transmitter substance. Hence it is called a ***cholinergic synapse***.

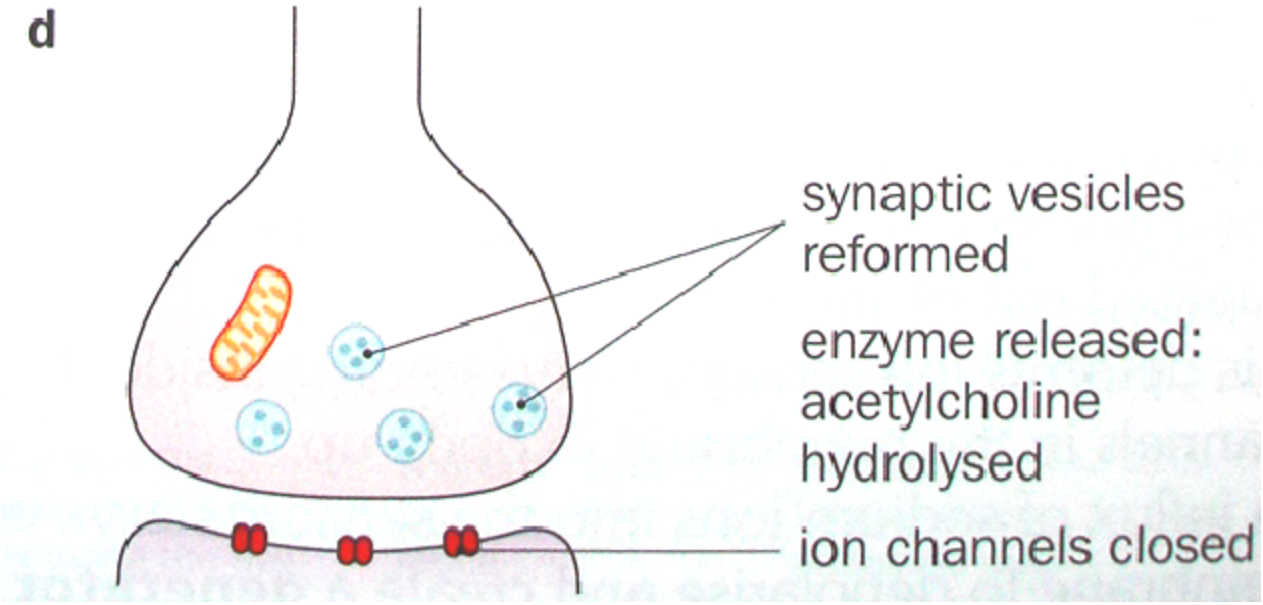






a. Arrival of action potential at the presynaptic knob makes it more permeable to calcium ions, which diffuse into the presynaptic knob from the synaptic cleft.
b. This causes movement of neurotransmitter containing vesicles towards the presynaptic membrane. These vesicles fuse with the presynaptic membrane and release neurotransmitter substances into synaptic cleft by exocytosis.
c. Neurotransmitter (acetylcholine) molecules diffuse across the synaptic cleft and bind with receptors on the postsynaptic membrane.

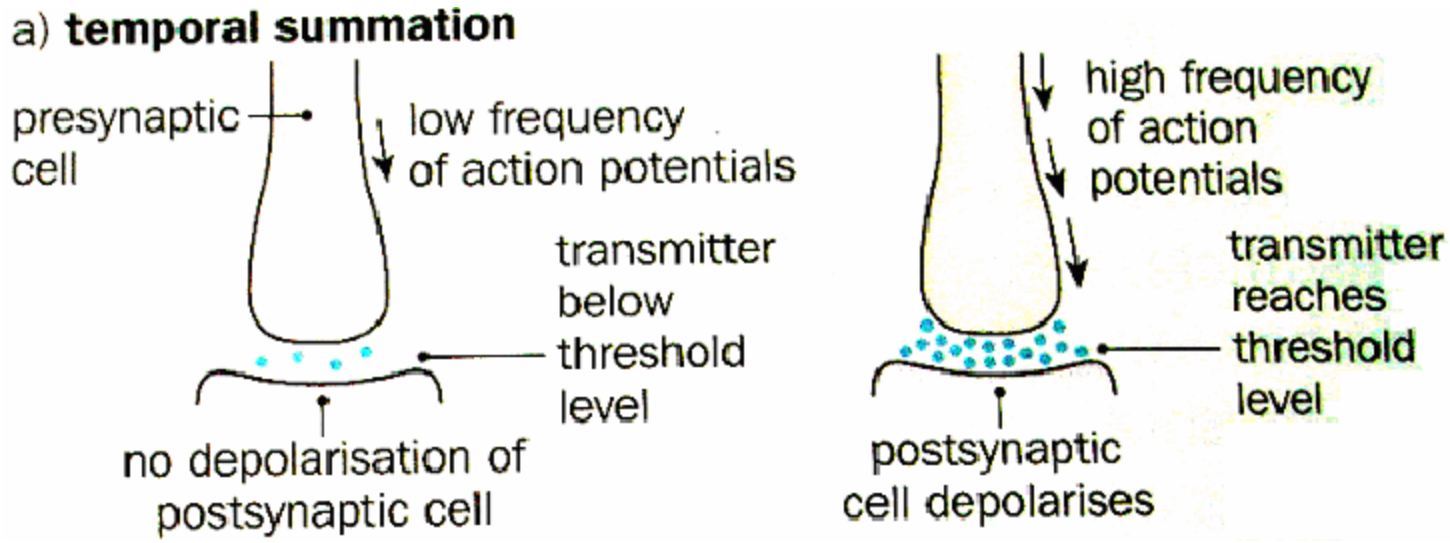
The binding of neurotransmitter (acetylcholine) with the receptors on the postsynaptic membrane cause the membrane to become permeable to sodium ions. The rapid influx of sodium ions causes the generation of an action potential in the postsynaptic neurone. Since acetylcholine causes the generation of an action potential in the postsynaptic neurone it is called an excitatory neurotransmitter, in this example.



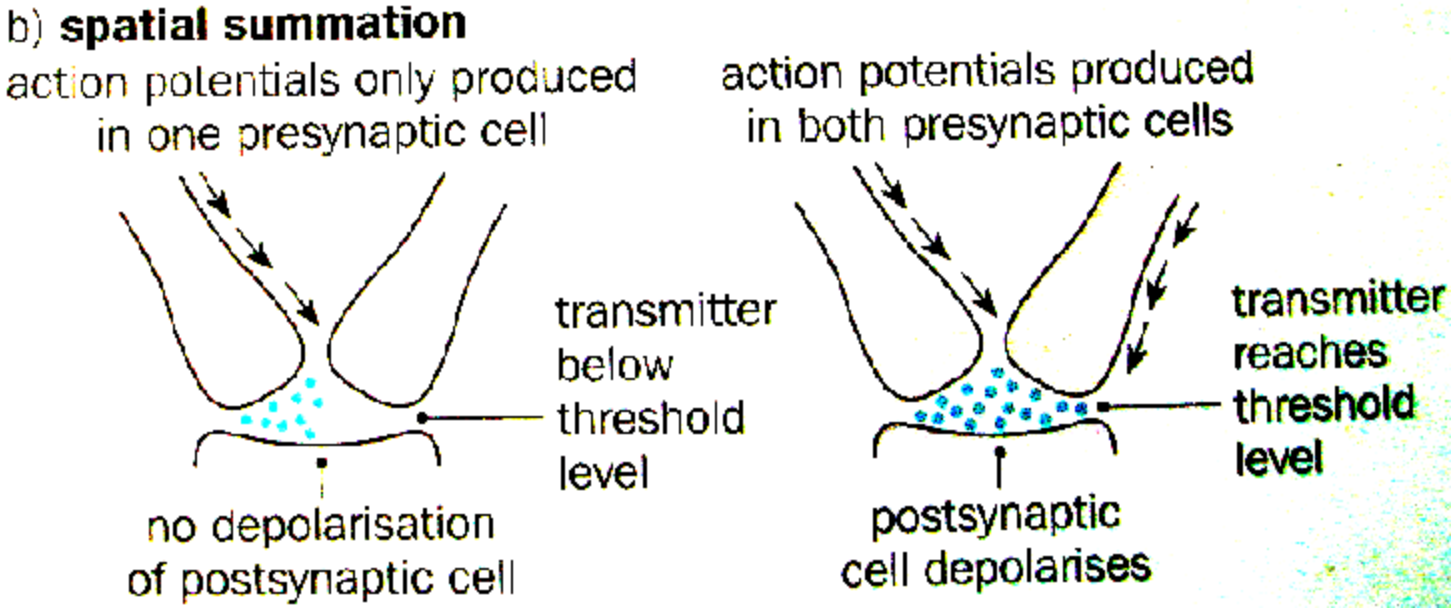
d. The neurotransmitter substance is then removed from the receptors on the post synaptic membrane by enzymes. The enzyme cholinesterase hydrolyses acetylcholine to choline and ethanoic acid, which are inactive as neurotransmitters. This prevents the postsynaptic membrane from ' firing' impulses continuously in the postsynaptic neurone. Choline and ethanoic acid are reabsorbed into the presynaptic neurone and are used to resynthesise acetylcholine. Mitochondria are used to release energy for the synthesis of neurotransmitters.

Post-synaptic potentials.

1. **Summation:** the release of neurotransmitter substance from the presynaptic neurone by a single impulse is not always enough to generate an action potential in the postsynaptic neurone. Normally several vesicles have to be released before there is enough transmitter substance in the synaptic cleft to propagate an action potential. this is possible by multiple impulses. This addition effect is called summation.



Each action potential that arrives at the pre-synaptic membrane will cause a number of vesicles to release their transmitter. A number of action potentials are required before there is enough transmitter to initiate an action potential in the post-synaptic cell. This is called temporal summation.



A number of pre-synaptic neurones may form synapses with one post-synaptic neurone. Action potentials arriving in each pre-synaptic neurone will release transmitter, which build up to the threshold level and triggers a postsynaptic impulse. This is spatial summation.

2. Excitatory and inhibitory synapses.

Excitatory synapses cause depolarization of the postsynaptic membrane. The examples above are **excitatory postsynaptic potentials**.

Inhibitory synapses: the neurotransmitters released from the presynaptic neurone will not cause depolarization of the postsynaptic neurone. Instead they cause the postsynaptic membrane to become more negative than usual (hyperpolarized / -90mV), by opening of chloride ion channels. This makes the neurone less likely to trigger an action potential. This is called the **inhibitory postsynaptic potential.**

Note: The transmitter substances are not inherently excitatory or inhibitory. For example, acetylcholine has an excitatory effect at most neuromuscular junctions and synapses, but has an inhibitory effect on neuromuscular junctions in cardiac muscle and gut muscle. These opposing effects are determined by events occurring at the post synaptic membrane. The molecular properties of the receptor sites determine which ions enter the postsynaptic cell, which in turn determines the nature of the change in postsynaptic potentials.

23. Understand the effects of drugs on synaptic transmission, as illustrated by nicotine.

Nicotine mimics the effect of the neurotransmitter acetylcholine on certain receptors(not all those that acetylcholine binds to). The receptors concerned are called ***nicotinic receptors*** and are found in the receptors of postsynaptic cells. They are found in the sympathetic and parasympathetic nervous system. Activation of the receptors leads to depolarization and therefore excitation of the postsynaptic cell or effector.

Nicotine causes strong sympathetic vasoconstriction in abdominal organs such as gut, and in the limbs. But at the same time parasympathetic effects occur, such as increased gastrointestinal activity and, sometimes, slowing of the heart.

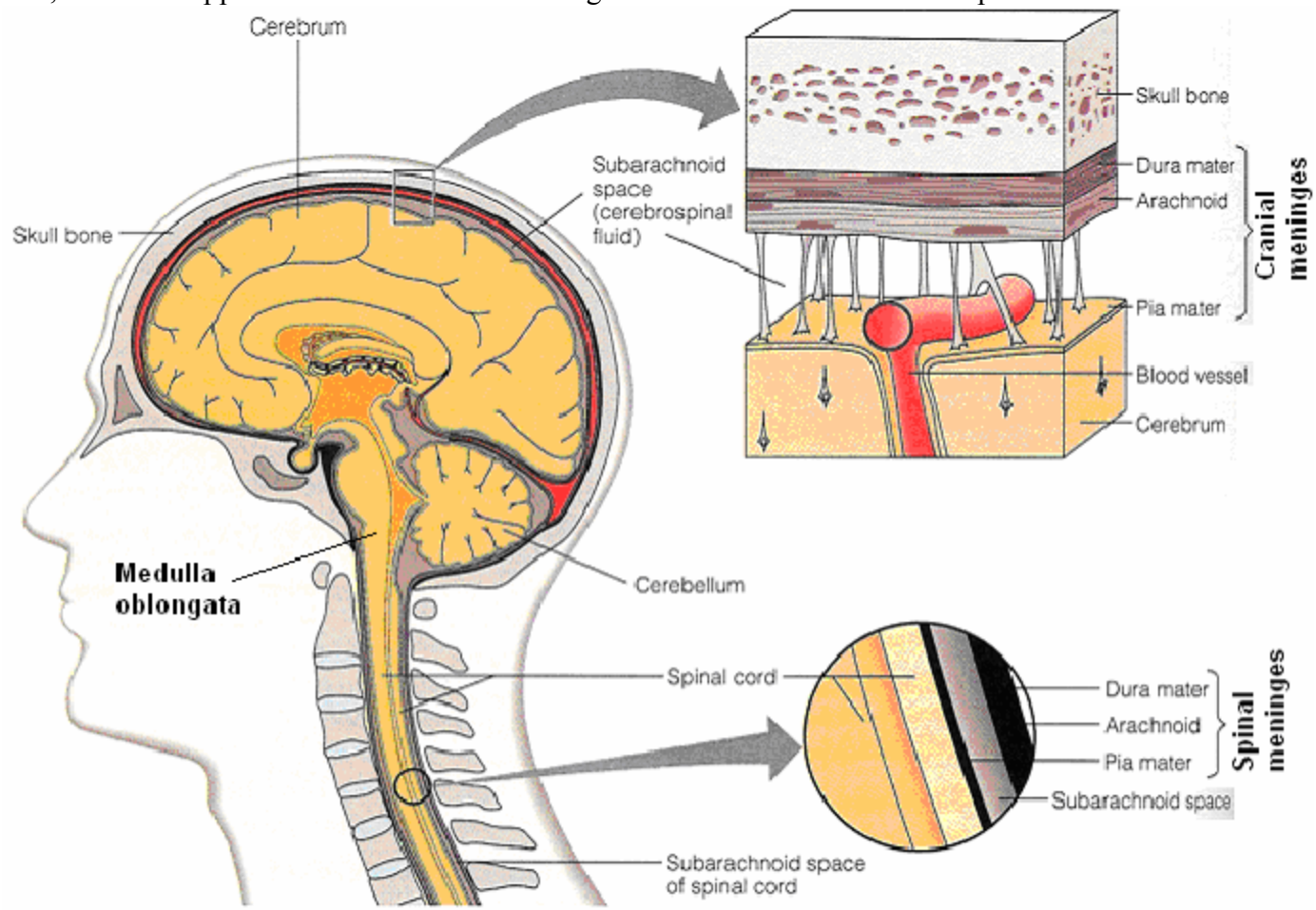
Nicotinic receptors are also found at neuromuscular junctions. If nicotine is applied directly to the junction it makes the muscle contract, mimicking acetylcholine. Nicotinic receptors are found in few regions of the brain, where it stimulates the release of dopamine and therefore stimulate reward and pleasure pathways.

24. Describe the gross structure of the brain and spinal cord.

The brain and spinal cord are made up of **neurones** and **glial** cells **(neuroglia)**. These neurones are interconnected by synapses to for an intricate network. The neuroglia provides physiological and physical support to the neurones.

The cerebrum is the largest part of the brain and consists of about 14 billion neurones. The outer part of the cerebrum consists of gray matter and the internal part consists of white matter. Different regions of the cerebrum control different functions. The cerebrum consists of two hemispheres. The right cerebral hemisphere controls artistic abilities, creative thinking, music and recognition of shapes. The left cerebral hemisphere controls mathematical abilities, logical thinking, speech and writing.

The cerebellum is located posterior and below the cerebrum. It is smaller than the cerebrum and has a tree like, branched appearance. The medulla oblongata connects the brain to the spinal cord.



The meninges and cerebrospinal fluid. The meninges, whether cranial or spinal, consist of three layers: dura mater, arachnoid, and pia mater. Between the arachnoid and the pia mater is the subarachnoid space, in which cerebrospinal fluid circulates. Notice that the CSF is vulnerable to contamination by microbes carried in the blood that are able to penetrate the blood-brain barrier at the walls of the blood vessels.

Cerebrospinal fluid is vulnerable to contamination by microbes that cross the blood-brain barrier.

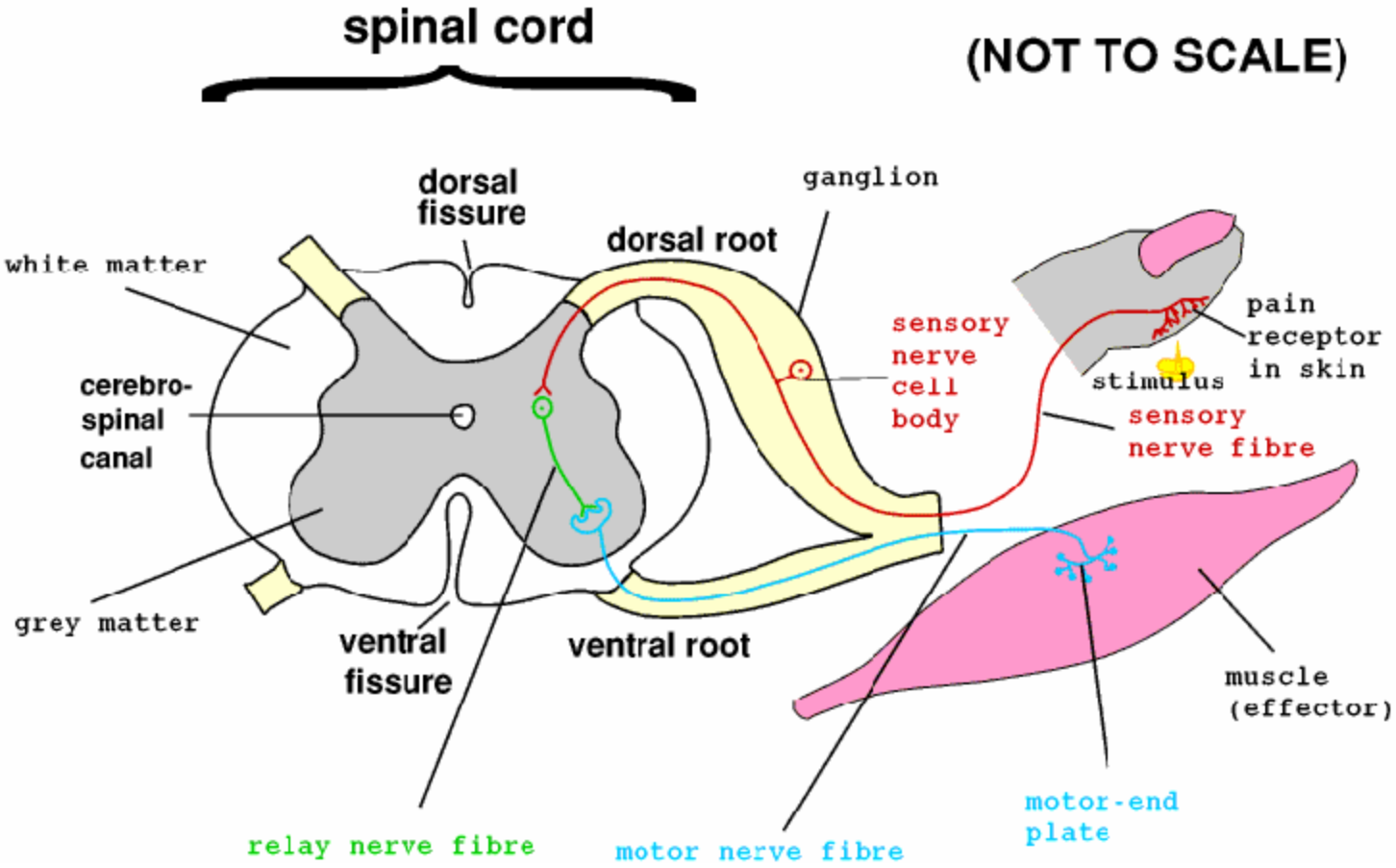
The spinal cord is about 43 cm long and about the thickness of a pencil. The spinal cord is located in the neural canal of the vertebral column. The spinal cord is also made of neurones. But the arrangement of neurones is different from that of the brain - the spinal cord has white matter on the outside and gray matter on the inside.

Both the brain and spinal cord are surrounded by membranes called the meninges, in which cerebrospinal fluid circulates. The diagram above shows the structure of the meninges, brain and spinal cord. The cerebrospinal fluid serves as a medium of transport between the blood and neurones. It provides nourishment to the cells of the brain and spinal cord and to carry away wastes. It also provides lubrication.

25. Describe the location and functions of the medulla, cerebellum, hypothalamus and cerebral hemisphere.

- **Cerebrum**: receives impulses/ controls contraction of voluntary muscles/ controls mental activities like speech, memory, emotions and other conscious activities.
- **Cerebellum**: maintenance of balance and posture of body/ coordination of skeletal muscles.
- **Medulla oblongata**: controls rate of heartbeat, breathing rate, reflexes like coughing, sneezing and vomiting.
- **Hypothalamus**: plays an essential role in osmoregulation, maintaining body temperature and synthesis of hormones of posterior pituitary gland.

26. Describe the functioning of a spinal reflex arc and the types of neurones involved; understand the value of such reflexes in response to changes in the external environment.



The diagram above represents a simple spinal reflex. The path travelled by the impulses to bring about a reflex action is called a reflex arc. If the response is directed by the spinal cord then it is called a spinal reflex. A typical spinal reflex arc passes along the following path:

STIMULUS (CHANGE IN ENVIRONMENT) → RECEPTOR (SENSE ORGAN) → SENSORY NEURONE → RELAY NEURONE → MOTOR NEURONE → EFFECTOR (MUSCLE OR GLAND) → RESPONSE (CHANGE IN BEHAVIOUR / PHYSIOLOGY)

Spinal reflexes are useful to allow animals to respond quickly to danger. The impulse to operate the effector organs is generated by the spinal cord itself. This helps to save valuable time for the organism to respond. This ability to respond quickly to a stimulus increases an organism' schances of survival. This response is usually an unconscious response, without the involvement of the brain. However, the impulse will be sent to the brain later on and the organism becomes conscious of the response.

The diagram below shows the basic design of the human nervous system. The brain and spinal cord, constitute the central nervous system and coordinate activities from different neurones. The nerves are bundles of axons and dendrons which transmit impulses to and from the central nervous system. There are 31 pairs of spinal nerves and 12 pairs of cranial nerves. The spinal nerves and cranial nerves constitute the peripheral nervous system.