Nervous system coordinates and controls the activities of the animals. The nervous system is composed of two principal types of cells: neurons and neuroglia. Neurons are the basic structural and functional units of the nervous system. They are specialized to respond to physical and chemical stimuli, conduct electrochemical impulses and releases chemical regulators. Neuroglia or simply glial cells (glia=glue) supports, nourishes and protects the neurons.

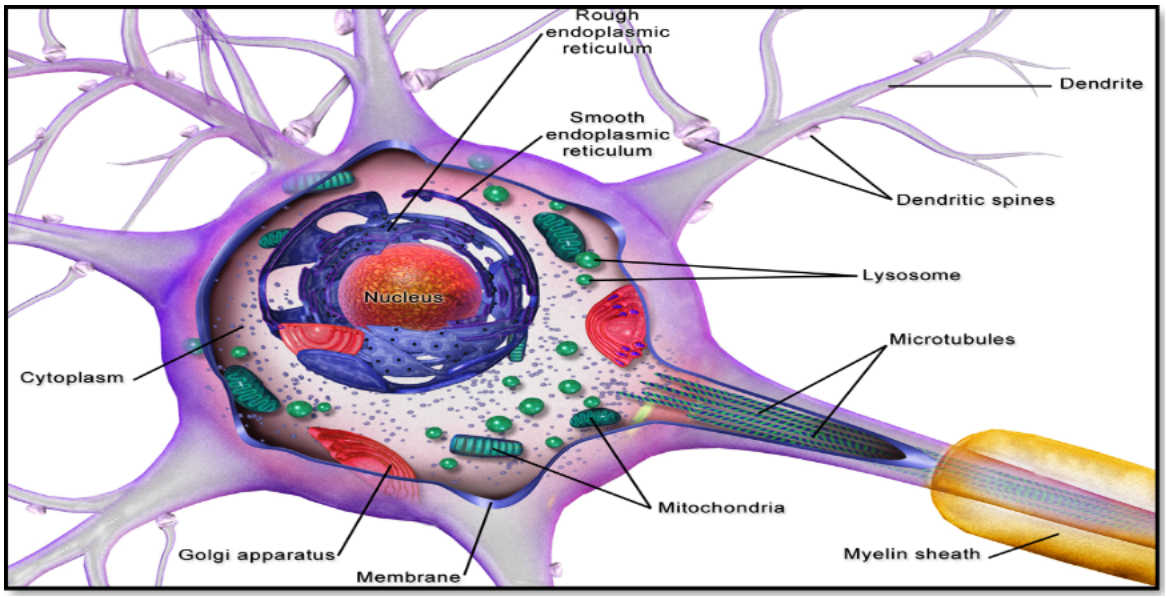
Neurons

Neurons possess electrical excitability, the ability to respond to a stimulus and convert it into action potential. A stimulus is any change in the environment that is strong enough to initiate an action potential. An action potential (nerve impulse) is an electrical signal that propagates (travels) along the surface of the membrane of a neuron.

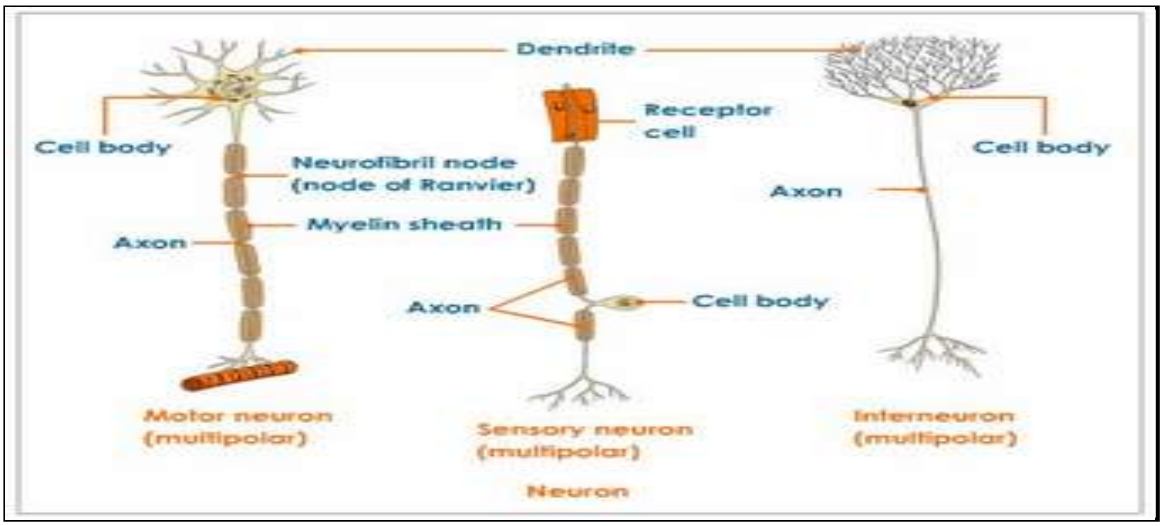
Structure: Most neurons have three parts: a cell body, dendrites and an axon.

The cell body /perikaryon/soma contains a nucleus surrounded by cytoplasm that includes typical cellular organelles, such as lysosomes, mitochondria and a golgi complex . neuronal cell bodies also contain free ribosomes and prominent cluster of Rough endoplasmic reticulum termed Nissl bodies. cell bodies in the PNS (Peripheral nervous system) usually occur in clusters called ganglia.

A nerve fibre is a general term for any neuronal process or extension that emerge from the cell body of the neuron. Most neurons have two kinds of processes: multiple dendrites and a single axon. Dendrites are the receiving or input portion of neurons. They usually are short, tapering and highly branched. The single axon of a neuron propagates nerve impulse towards another neuron, a muscle fibre, or a gland cell. An axon is a long, thin, cylindrical projection that often joins the cell body at a cone-shaped elevation called the axon hillock. Axons vary in length from only a millimetre long to up to a metre or more. Axon sometimes is covered by a fatty substance form by phosphlipids which is known as myelin sheath. This sheath can classify the neuron into myelinated and non myelinated.



Myelinated sheath is not a continuous sheath over the axolemma, rather it is exposed to the extracellular space by some regions known as node of Ranvier.



An axon contains mitochondria, microtubules ,and neurofibrils . Because rough endoplasmic reticulum is not present, protein synthesis does not occur in the axon. The cytoplasm of an axon, called axoplasm, is surrounded by a plasma membrane known as the axolemma (lemma= sheath of husk). Along the length of a axon side branches called axon collaterals may branch off, typically at a right angle to the axon. The axon and its collaterals end by dividing into many processes called axon terminals (telodendria).

Types of Synapse:

There are innumerable synapses in the nervous system (the total number is said to be about 2×10^{14} roughly). These synapses are of different types and have various names. Synapses are usually classified as follows :

A. According to the part of the neurons involved.

1. Axodendric : Axon with Dendrite

2. Axosomatic: Axon with Soma or cell body.

3. Axoaxonic: Axon with axon

4. Dendrodendritic: Dendrite with dendrite

These synapse are not always an end to end affair and may be basket like or intertwining type etc.

B. According to the nature of transmission:

1. Chemical synapse: through neurotransmitter.

2. Electrical synapse: through GAP junction.

3. Conjoint synapse: partly electrical partly chemical

C. According to the number of neurones involved:

1. one neurone ends on another.
2. Multiple neurones ending on a single neurone.
3. One neurones end on a multiple neurones.

Neuromuscular junction:

A neuromuscular junction (or myoneural junction) is a chemical synapse formed by the contact between a motor neuron and a muscle fiber. It is at the neuromuscular junction that a motor neuron is able to transmit a signal to the muscle fiber, causing muscle contraction.

Muscles require innervation to function—and even just to maintain muscle tone, avoiding atrophy. In the neuromuscular system nerves from the central nervous system and the peripheral nervous system are linked and work together with muscles.

Working Mechanism: Synaptic transmission at the neuromuscular junction begins when an action potential reaches the presynaptic terminal of a motor neuron, which activates voltage-gated calcium channels to allow calcium ions to enter the neuron. Calcium ions bind to sensor proteins (synaptotagmin) on synaptic vesicles, triggering vesicle fusion with the cell membrane and subsequent neurotransmitter release from the motor neuron into the synaptic cleft. In vertebrates, motor neurons release acetylcholine (ACh), a small molecule neurotransmitter, which diffuses across the synaptic cleft and binds to nicotinic acetylcholine receptors (nAChRs) on the cell membrane of the muscle fiber, also known as the sarcolemma. nAChRs are ionotropic receptors, meaning they serve as ligand-gated ion channels. The binding of ACh to the receptor can depolarize the muscle fiber, causing a cascade that eventually results in muscle contraction.

Neuromuscular junction diseases can be of genetic and autoimmune origin. Genetic disorders, such as Duchenne muscular dystrophy, can arise from mutated structural proteins that comprise the neuromuscular junction, whereas autoimmune diseases, such as myasthenia gravis, occur when antibodies are produced against nicotinic acetylcholine receptors on the sarcolemma.

Origin and propagation of Action potential :

In nerve cells (neurons), the resting potential (membrane potential in resting state) is about -70mV, with the inside of the cell at a negative potential relative to the external medium. A nerve cell that exhibit a resting membrane potential is said to be polarized. Changes in membrane potentials are brought about by a changes in ion movement across the membrane. For example, if the net inward flow of positively charged ion increases compared to the resting state (such as more Na^+ moves in), the membrane depolarizes (become less negative inside). By contrast if the net outward flow of positively charged ions increases compared to the resting state (such as more K+ moves out), the membrane hyperpolarizes (become more negative inside).

A rapid and large changes in membrane potential of excitable cells (such as nerve cells) during which the potential actually reverses so that the inside of the excitable cell transiently becomes more positive than the outside is termed as action potential. An action potential in a muscle fiber is called a muscle action potential. When an action potential occurs in a nerve cell, it is called a nerve action potential (nerve impulse).

Ion channels may be either leaky channels or gated channels. Leaky channels, which are open all the time, permit unregulated leakage of specific ion across the membrane. Gated channels, in contrast , have gates that can be open or closed, permitting ion passage through the channels when open and preventing ion passage through the channels when closed. Movement of K^+ through K^+ leaky channels makes the greatest contribution to the establishment of the resting potential.

During an action potential, rapid fluxes of Na^+ occur through voltage gated Na^+ channels down their electrochemical gradients. This voltage-gated Na^+ can exist in three conformations: 1. closed but capable of opening; 2. open or activated and ; 3. closed and not capable of opening or inactivated.

- At resting potential (about -70mV), Na^+ voltage-gated channels are closed. Therefore Na^+ cannot pass through these voltage-gated channels at resting potential. A stimulus that causes sufficient depolarization promptly causes voltage-gated Na^+ channels to open, allowing a small amount of Na^+ to enter the cell down its electrochemical gradient. The influx of positive charge depolarizes the membrane further, thereby opening more Na^+ channels, which admit more Na^+ ions, causing still further depolarization. This changes the membrane potential value of about -70mV to about +30mV within a fraction of a second.

- The Na^+ channels have an automatic inactivating mechanism, which causes the channels to reclose rapidly even through the membrane is still depolarized. The Na^+ channels remain in this inactivated state, unable to reopen, until a few milliseconds after the membrane potential returns to its initial negative value.

- Another channels operate to help bring the activated plasma membrane more rapidly back toward its original negative potential. It is voltage-gated K^+ channels. The opening and consequent efflux of K^+ quickly drives the membrane back toward the K^+ equilibrium potential. This process is called repolarization. Voltage-gated K^+ channels respond to changes in membrane potential in much the same way as the Na^+ channels do, but with slightly slower kinetics; for this reason they are sometimes called delayed K^+ Channels. Unlike voltage-gated Na^+ channels, most voltage-gated K^+ channels do not exhibit an inactivated state. Instead, they alternate between closed and open states.

- Hence, an action potential has two main phases: a depolarizing phase and a repolarizing phase. During the depolarizing phase, the negative membrane potential becomes less negative, reaches zero, and then becomes positive. During the repolarizing phase, the membrane potential is restored to the resting state of -70mV. Following the repolarizing phase there may be an after-hyperpolarizing phase, during

which the membrane potential temporarily becomes more negative (about -90mV) than the resting level. The period of time after an action potential begins during which an excitable cell cannot generate another action potential in response to a normal threshold stimulus is called the refractory period. It can be absolute or relative.

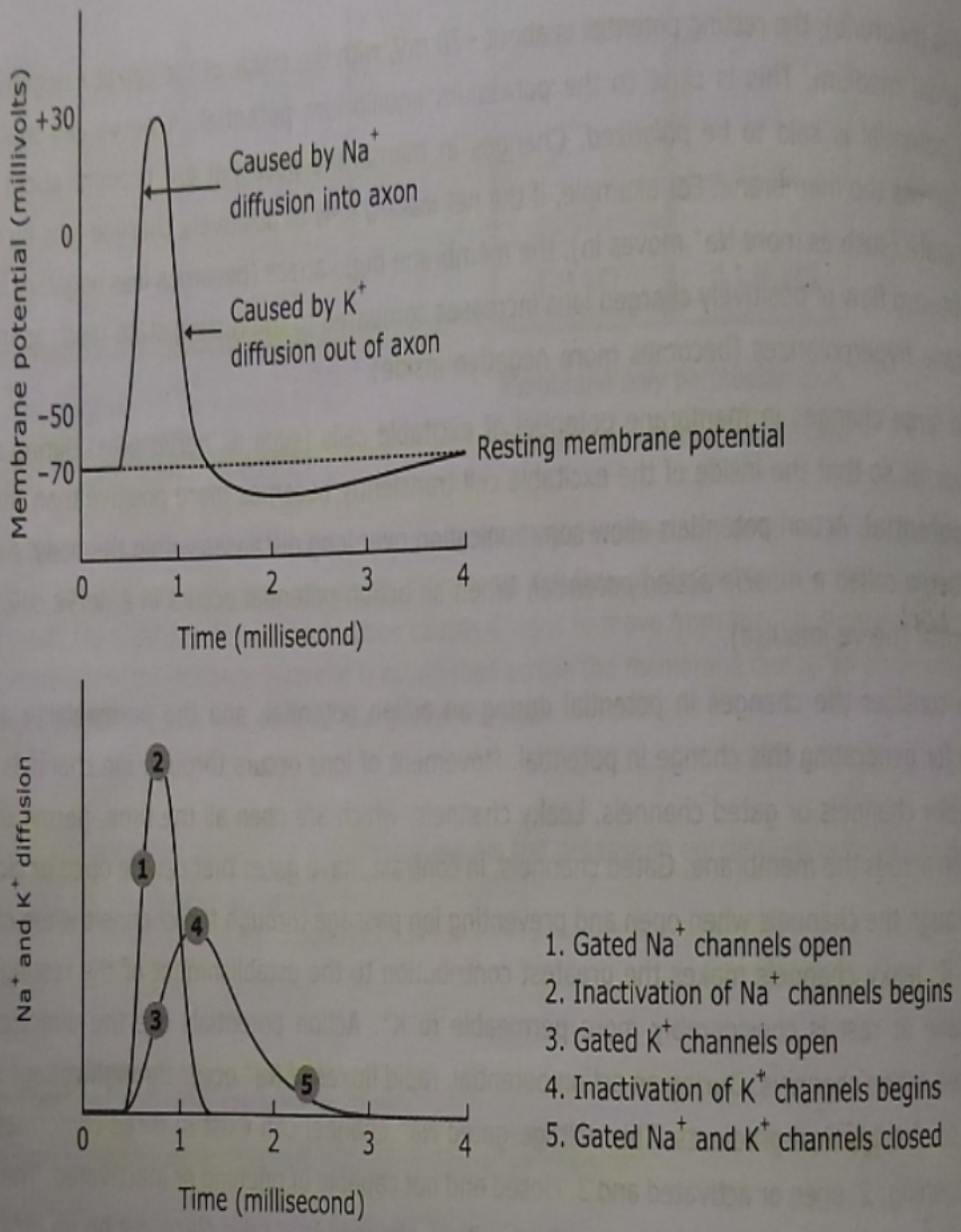


Figure 4.14 : Membrane potential changes and ion movements during an action potential. The top graph depicts an action potential. The bottom graph depicts the net diffusion of Na^+ and K^+ during the action potential. The x-axis for time is the same in both graphs, so that the depolarization, repolarization, and after-hyperpolarization in the top graph can be correlated with events in the Na^+ and K^+ channels and their effects on ion movements in the bottom graph. The inward movement of Na^+ drives the membrane potential toward the Na^+ equilibrium potential during the depolarization (rising) phase of the action potential, whereas the outward movement of K^+ drives the membrane potential toward the potassium equilibrium potential during the repolarization (falling) phase of the action potential.

Transmission of nerve impulse

Nerve impulse propagates (travels) along the surface of the membrane of a neuron at speed ranging from 0.5 to 130 meters per second. There are two types of propagation: continuous coduction and saltatory conduction. The continuous conduction involves step by step depolarization and repolarization of each adjacent segment of the plasma membrane.

In continuous conduction, ions flow through their voltage-gated channels in each adjacent segment of the membrane. It occurs in unmyelinated axons. Saltatory conduction is a special type of axon potential propagation that occurs along myelinated axons. It occurs because of the uneven distribution of voltage-gated channels. Few voltage-gated channels are present in regions where a myelin sheath covers the axolemma (plasma membrane). By contrast at the node of Ranvier (where there is no myelin sheath) the axolemma has many voltage-gated channels.

Synaptic transmission

The junction between two neuron is called a synapse. Typically, a synapse involves a junction between a action terminal of one neuron, known as the presynaptic neuron, and the dendrites or cell body of second neuron known as the postsynaptic neuron. The space between the pre & postsynaptic neuron is called synaptic cleft. Synapses are merely gaps, but are functional links between the two neurons. Synapse can be either chemical or electrical.

At electrical synapse, action potentials (Impulses) conduct directly between adjacent cells through structure called gap junctions. Gap junctions allow rapid communication between cells. No neurotransmitters are involved in an electrical synapse. As ions flow from one cell to the next through the gap junctions, the action potential spreads from cell to cell. In contrast two chemical synapses, electrical synapses transmit signals in both directions and have two main advantages: Faster communication & Synchronization.

In chemical synapse, the axon terminal of the presynaptic neuron, which conduct its action potentials toward the synapse, ends in a slight swelling, the Synaptic Knob. The Synaptic Knob contains synaptic vesicles, which store a specific chemical messenger, a neurotransmitter that has been synthesized and packaged b y the pre synaptic neuron. There are many kinds of neurotransmitters, the base studied examples being acetylcholine. Most chemical synapses operates in one direction only: That is the presynaptic neuron brings about changes in membrane potential of the post synaptic neuron. Neurotransmitters are usually small molecular weight paracrine signal molecule, such as, amino acids, amines, purines and neuropeptides. These molecules are synthesized in the presynaptic terminals of neurons and released on stimulation.

Neurotransmitter	Functional class
Ester	
Acetylcholine (Nicotinic)	Excitatory
Acetylcholine (Muscarinic)	Inhibitory
Biogenic amines	

Nor epinephrine Dopamine Serotonin (5-hydroxy tryptamine)	Excitatory or Inhibitory
	Generally excitatory, may be inhibitory at some sites
	Generally inhibitory
Amino acids	
GABA (Gamma aminobutyric acid) Glycine Glutamate Aspartate	Inhibitory
	Inhibitory
	Excitatory
	Excitatory
Neuropeptides	
Substance P Met-enkephalin	Excitatory
	Generally Inhibitory

Fig: The major known neurotransmitter

At a chemical synapse a presynaptic neuron converts an electrical signal (Nerve Impulse) into a chemical signal (Neurotransmitter Release). The post synaptic neuron then converts the chemical signal back into an electrical signal (Postsynaptic Potential). Of the many synapses on a neuron, some tend to excite it (excitatory synapse), others to inhibit it (Inhibitory Synapses). Neurotransmitter released at an excitatory synapse causes a small depolarization in the postsynaptic membrane called an excitatory postsynaptic potential (EPSP), while neurotransmitter released at an inhibitory synapse generally causes a small hyperpolerization called an inhibitory postsynaptic potential (IPSP).

Neurotransmitter released from a presynaptic neuron bind to neurotransmitter receptors in the plasma membrane of postsynaptic cell. When a neurotransmitter binds to the correct neurotransmitter receptor, an ion channel opens and a postsynaptic potential (either EPSP or IPSP) forms in the membrane of the postsynaptic cell. Neurotransmitter receptors are classified as either ionotropic receptor or metabotropic receptors based on whether the neurotransmitter binding site and the ion channel are components of the same protein or are components of different protein.

Mechanism of synaptic transmission:

- A nerve impulse arrives at a synaptic end bulb of a presynaptic axon. The change in membrane potential caused by the arrival of action potential.
- This leads to opening of voltage-gated calcium channels in the presynaptic

membrane . Because concentration of calcium ions are more in extracellular fluid, calcium flows inward through the opened channels.

- Increase in the concentration of calcium inside the presynaptic neuron serves as a signal that triggers exocytosis of the synaptic vesicles.
- As vesicle membrane merge with the plasma membrane, neurotransmitter molecules within the vesicles are released into synaptic cleft.
- Each synaptic vesicles contain several thousand molecules of neurotransmitter.
- The neurotransmitter molecule diffuse across the synaptic cleft and bind to the neurotransmitter receptors in the postsynaptic neuron's plasma membrane.
- Binding of neurotransmitter molecule to their receptor on ligand-gated channel opens the channels and allows particular ions to flow across the membrane.
- As ions flow through the opened channels, the voltage across the membrane changes. This change in membrane voltage is a post synaptic potential. Depending on which ions the channels admit, the postsynaptic potential may be a depolarization or a hyperpolarization.
- A single postsynaptic neuron receives input from many presynaptic neurons, some of which releases excitatory neurotransmitters and some of which release inhibitory neurotransmitters.

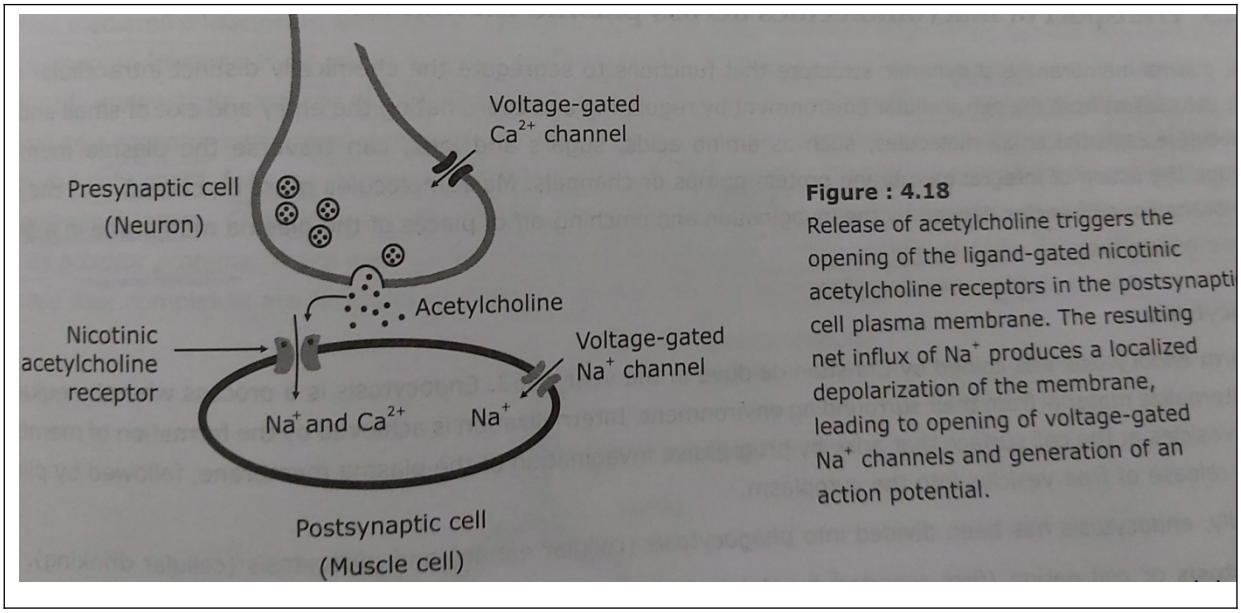
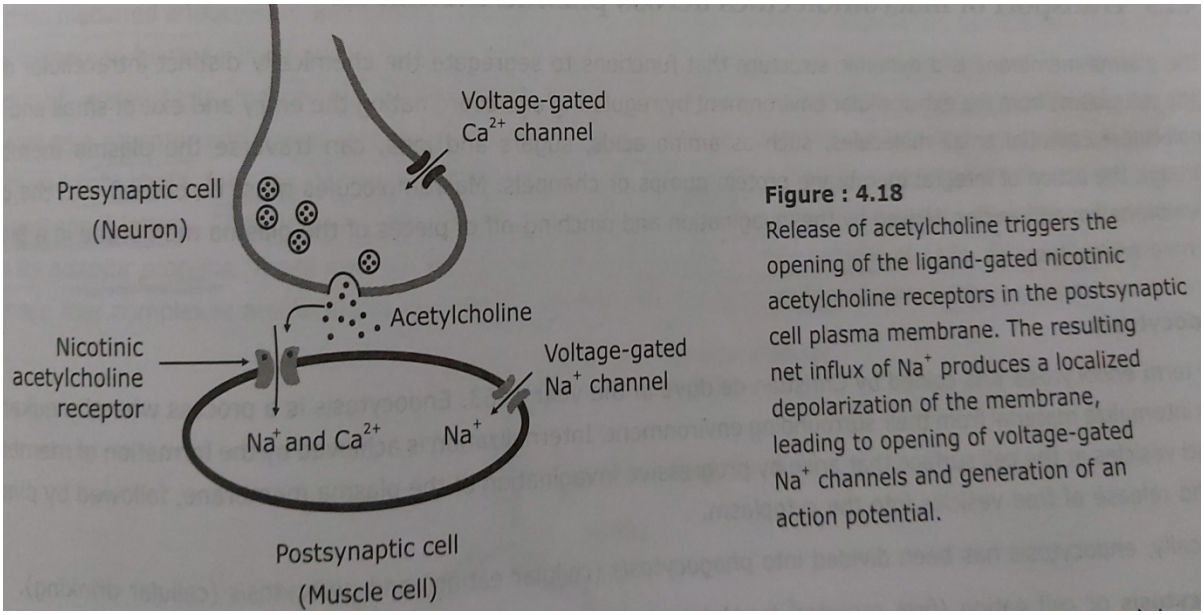


Figure : 4.18
Release of acetylcholine triggers the opening of the ligand-gated nicotinic acetylcholine receptors in the postsynapti cell plasma membrane. The resulting net influx of Na^+ produces a localized depolarization of the membrane, leading to opening of voltage-gated Na^+ channels and generation of an action potential.



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Acetylcholine is a colinergic neurotransmitter synthesized from choline and acetyl co-A by enzyme choline acetyl transferase. It is synthesized in the axonal terminal bulbs. After synthesis,it is released by the process of exocytosis in the synaptic cleft. GPI linked enzyme acetylcholine esterase located on the post-synaptic membrane breaks acetylcholine into choline and acetyl-coA.