CBCS THIRD SEM GENERAL

;

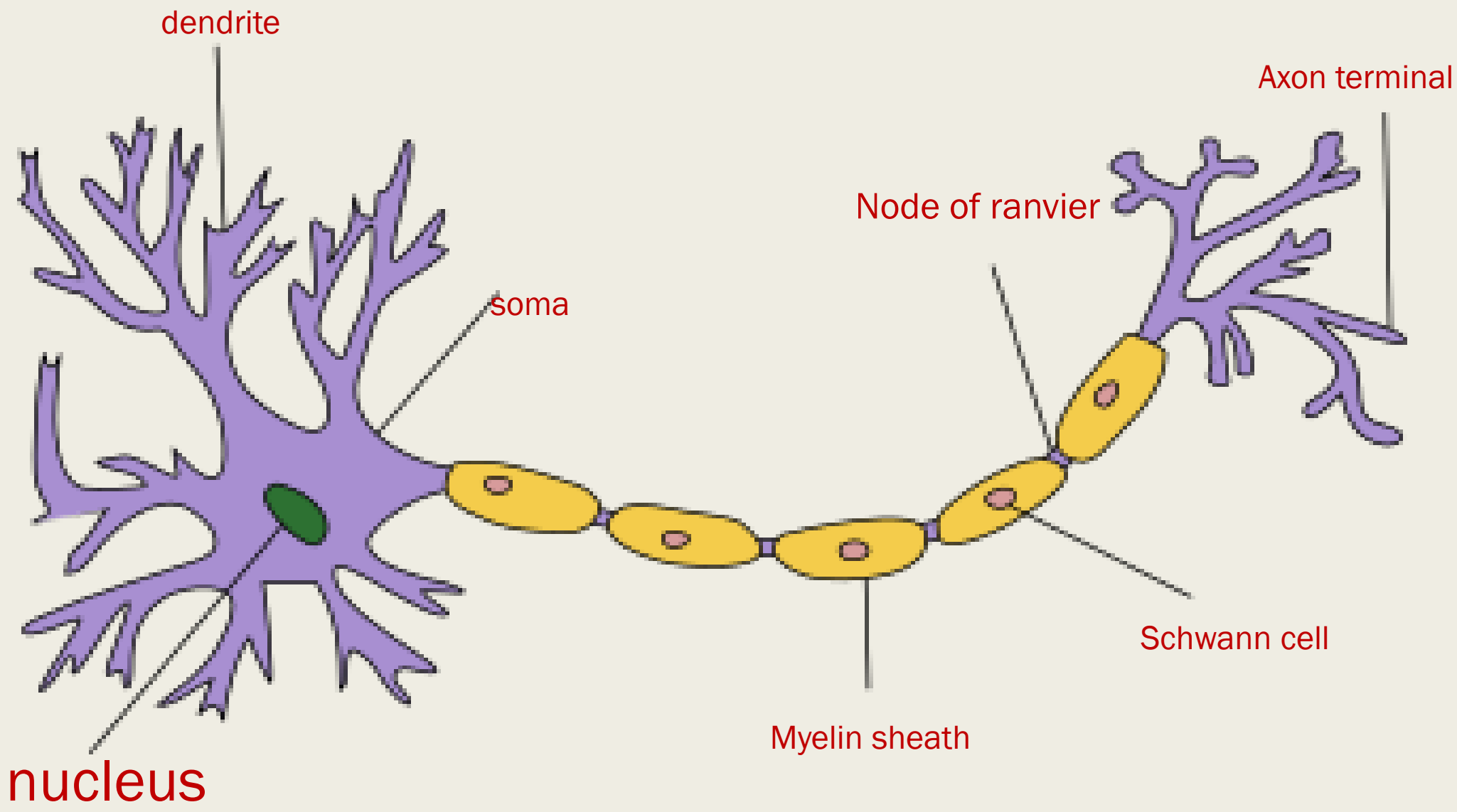
UNIT1:NERVE AND MUSCLE:

STRUCTURE OF A NEURON ,RESTING MEMBRANE POTENTIAL,GRADED POTENTIAL,ORIGIN OF ACTION POTENTIAL AND ITS PROPAGATION IN MYELINATED AND NON MYLINATED NERVE FIBER, ULTRA STRUCTURE OF SKELETAL MUSCLE, MOLECULAR AND CHEMICAL BASIS OF MUSCLE CONTRACTION

BY: DR. LUNA PHUKAN

The neuron is the basic working unit of the brain, a specialized cell designed to transmit information to other nerve cells, muscle, or gland cells.

Neurons are cells within the nervous system that transmit information to other nerve cells, muscle, or gland cells. Most neurons have a cell body, an axon, and dendrites.


dendrite
Axon terminal
Node of ranvier
soma
Schwann cell
Myelin sheath
nucleus

NEURON STRUCTURE AND CLASSIFICATION

Neurons have four specialized structures that allow for the sending and receiving of information: the cell body (soma), dendrites, axon and axon terminals .

Cell body or soma: The cell body is the portion of the cell that surrounds the nucleus and plays a major role in synthesizing proteins.

Dendrites: Dendrites are short, branched processes that extend from the cell body. Dendrites function to receive information, and do so through numerous receptors located in their membranes that bind to chemicals, called neurotransmitters.

Axon: An axon is a large process that extends from the cell body at a point of origin-called the axon hillock-and functions to send information. In contrast to the shorter dendrites, the axon can extend for more than a meter. Because of this length, the axon contains microtubules and is surrounded by myelin. Microtubules are arranged inside the axon as parallel arrays of long strands that act as highways for the movement of materials to and from the soma. potential propagation.

Specialized motor proteins "walk" along the microtubules, carrying material away from the soma (anterograde transport) or back to the soma (retrograde transport). This system can move materials down the axon at rates of 400mm/day (see lowest figure).

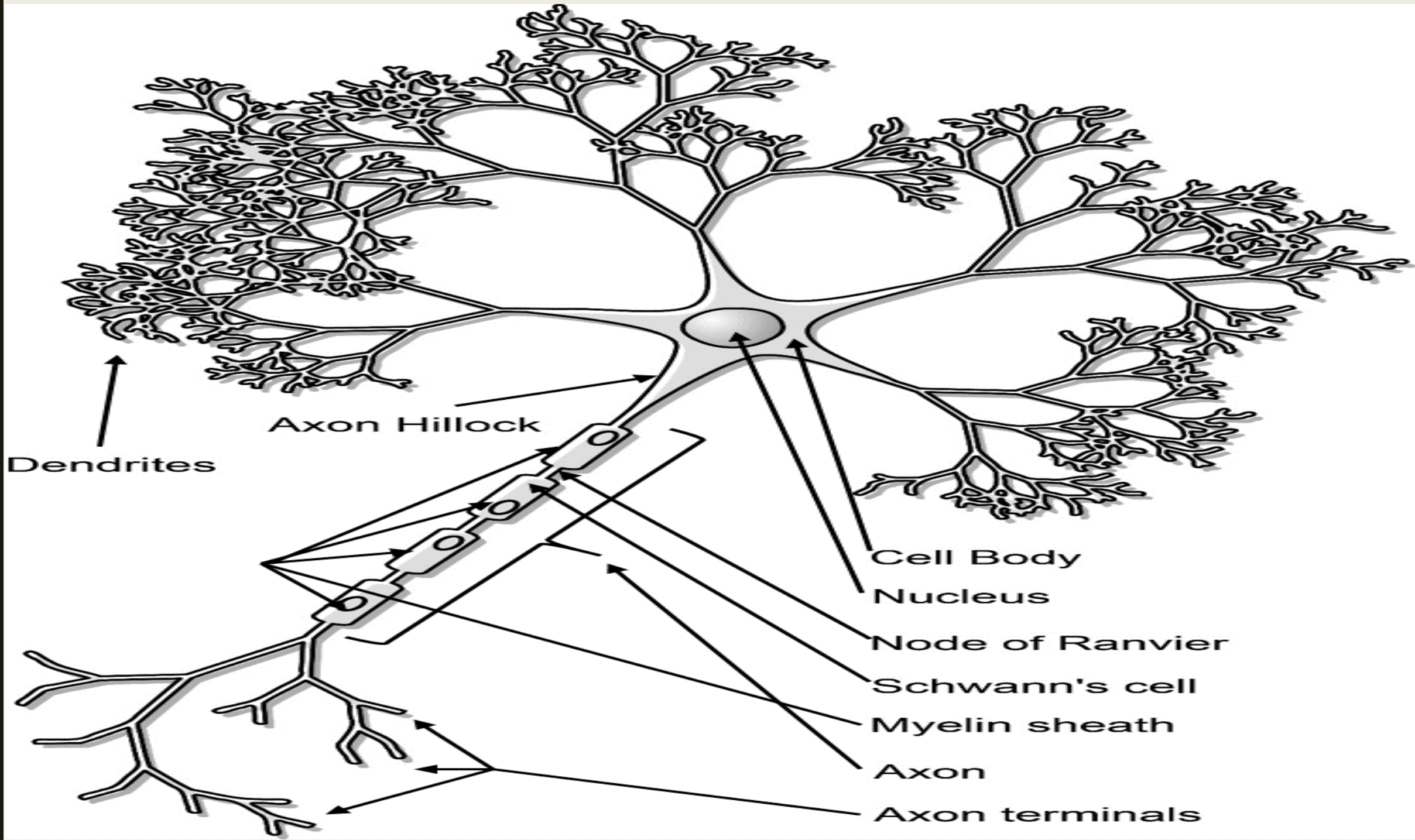
Myelin consists of totally separate cells that coil and wrap their membranes around the outside of the axon. These are essential for electrical insulation and to speed up action potential propagation.

Axon terminals: Once an axon reaches a target, it terminates into multiple endings, called axon terminals. The axon terminal is designed to convert the electrical signal into a chemical signal in a process called synaptic transmission (further explained in the section "Physiology of the Neuron").

Most neurons are amitotic or lose their ability to divide. Exceptions to this rule are found in olfactory neurons (those associated with smell) and hippocampal regions of the brain. Fortunately, lifespans of amitotic neurons is near 100 years. Still, if a neuron is damaged or lost, it is not easily replaced. For this reason, there is usually limited recovery from serious brain or spinal cord injuries.

Perhaps the slow recovery rate or lack of regeneration is to ensure that learned behavior and memories are preserved throughout life. Neurons also have exceptionally high metabolic rates and subsequently require high levels of glucose and oxygen.

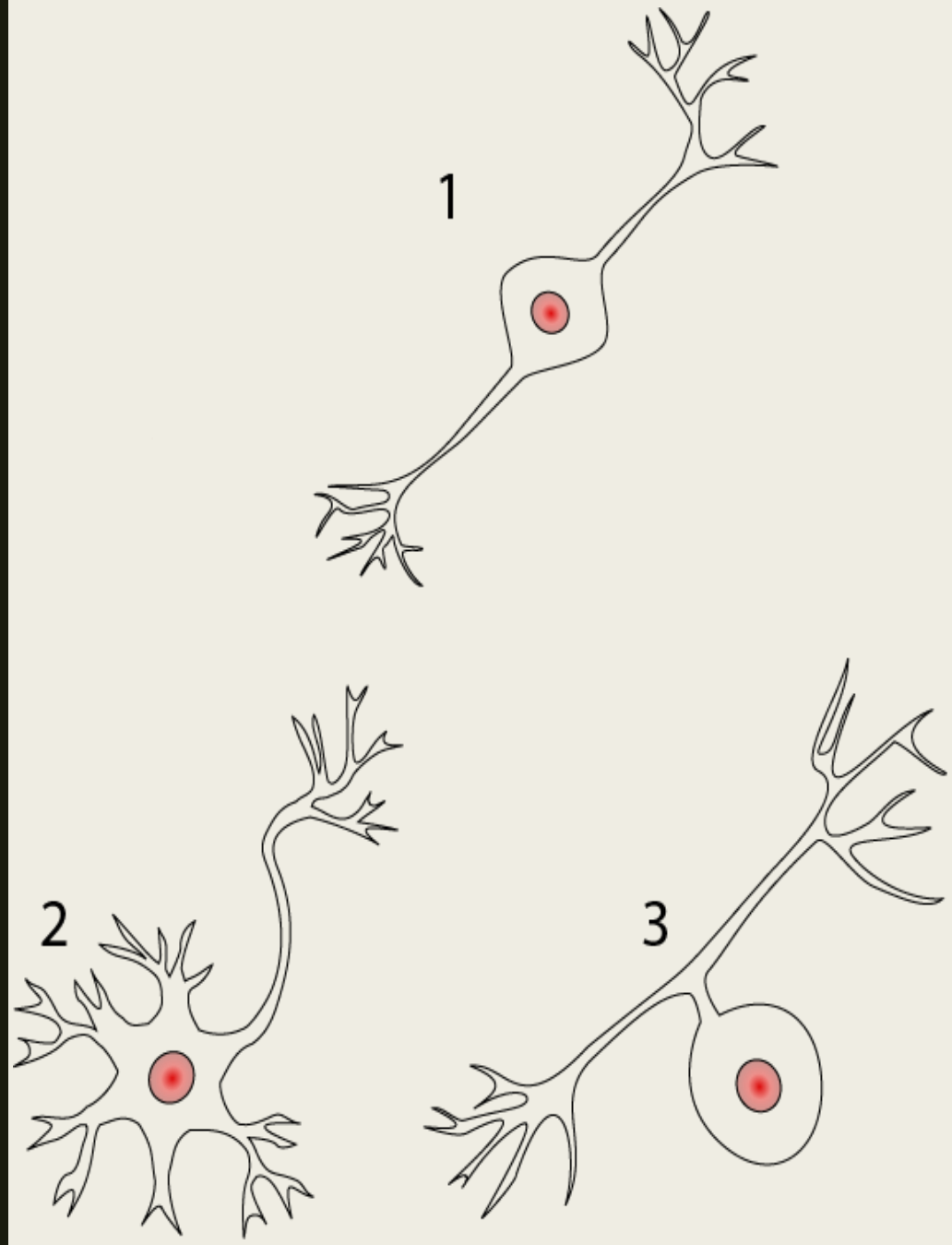
The body will go to great lengths to ensure that neurons are adequately fed; in fact, if for some reason the brain detects that it is not receiving adequate amounts of nutrition, the body will shut down immediately (i.e., faint).


Dendrites
Axon Hillock
Cell Body
Nucleus
Node of Ranvier
Schwann's cell
Myelin sheath
Axon
Axon terminals

Classification of Neurons

Structural classification of neurons is based upon the number of processes that extend out from the cell body. Three major groups arise from this classification: multipolar, bipolar, and unipolar neurons.

Multipolar neurons are defined as having three or more processes that extend out from the cell body. They comprise of more than 99% of the neurons in humans, and are the major neuron type found in the CNS and the efferent division of the PNS



Title: Neurons uni bi multi pseudouni.svg; Author: Pseudounipolar_bipolar_neurons.svg: Juoj8 derivative work: Jonathan Haas; Site: https://commons.wikimedia.org/wiki/File:Neurons_uni_bi_multi_pseudouni.svg; License: This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license.

Structural classification of neurons.

1) Bipolar; 2) Multipolar and 3) Unipolar.

Bipolar neurons have only two processes that extend in opposite directions from the cell body. One process is called a dendrite, and another process is called the axon. Although rare, these are found in the retina of the eye and the olfactory system.

Unipolar neurons have a single, short process that extends from the cell body and then branches into two more processes that extend in opposite directions. The process that extends peripherally is known as the peripheral process and is associated with sensory reception. The process that extends toward the CNS is the central process. Unipolar neurons are found primarily in the afferent division of the PNS.

Functional Classification of Neurons

Neurons are classified functionally according to the direction in which the signal travels, in relation to the CNS. This classification also results in three different types of neurons: sensory neurons, motor neurons, and interneurons.

Sensory neurons, or afferent neurons transmit information from sensory receptors in the skin, or the internal organs toward the CNS for processing. Almost all sensory neurons are unipolar.

Motor, or efferent neurons transmit information away from the CNS toward some type of effector. Motor neurons are typically multipolar.

Interneurons are located between motor and sensory pathways and are highly involved in signal integration. The vast majority of interneurons are confined within the CNS.

RESTING MEMBRANE POTENTIAL,

Resting membrane potentials are maintained by two different types of ion channels: the sodium-potassium pump and the sodium and potassium leak channels. Firstly, there is a higher concentration of thepotassium ions inside the cell in comparison to the outside of the cell.

The resting membrane potential of a neurone is the electrical potential, or voltage, across the plasma membrane of an unstimulated nerve cell

It occurs when the net flow of ions across the plasma membrane equals zero. In humans this is said to be around -70 Mv

This means that the inside of the cell is negatively charged in comparison to the outside.

Resting membrane potentials are maintained by two different types of ion channels: the sodium-potassium pump and the sodium and potassium leak channels

Firstly, there is a higher concentration of thepotassium ions inside the cell in comparison to the outside of the cell.

This creates an unequal distribution of potassium ions, or more accurately, a potassium ion gradient is created.

Therefore, following the concentration gradient, the potassium ions will diffuse from the inside of the cell to outside of the cell via its leaky channels.
As the potassium ions leave the cell, it increases the number of anions trapped inside the cell, hence accumulating the negative charges and the positive charges are accumulated outside of the cell.
Therefore more positively charged ions are being removed from the cell than are entering it making the inside environment of the cell comparatively negative to the outside.

The sodium-potassium pump moves three sodium ions out of the cell for every two potassium ions it moves into the cell continuously. It, therefore, maintains the large potassium ion gradient across the membrane, which in turn provided the basis for resting membrane potential.

The negatively charged macromolecules or ions, usually chloride ions, cannot pass through the plasma membrane as they are too large to be moved in or out of the cell via the chloride channels. This is due to the channels being too large and bulky, hence anions remain trapped inside the cell.

The resting membrane potential can be measured by placing one microelectrode inside the cell and another outside the cell. The values are generated in millivolts (mV). The ratios of the negative charges and positive charges between inside and outside of the cells are compared

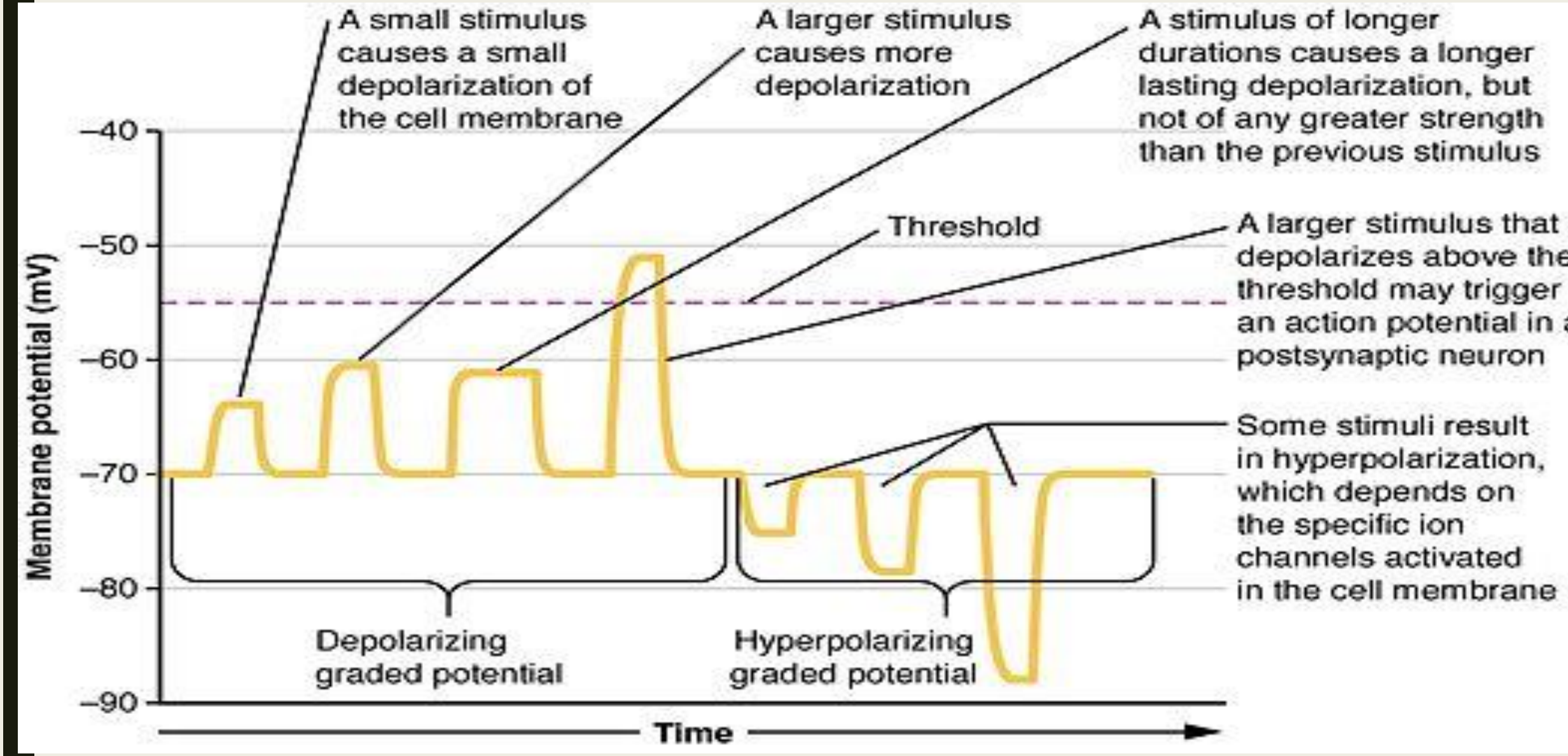
Graded potentials

are brought about by external stimuli (in sensory neurons) or by neurotransmitters released in synapses, where they cause graded potentials in the post-synaptic cell. Action potentials are triggered by membrane depolarization to threshol

Graded potentials are changes in membrane potential that vary in size, as opposed to being all-or-none. They include diverse potentials such as receptor potentials, electrotonic potentials, subthreshold membrane potential oscillations, slow-wave potential, pacemaker potentials, and synaptic potentials, which scale with the magnitude of the stimulus.

They arise from the summation of the individual actions of ligand-gated ion channel proteins, and decrease over time and space. They do not typically involve voltage-gated sodium and potassium channels.These impulses are incremental and may be excitatory or inhibitory.

They occur at the postsynaptic dendrite in response to presynaptic neuron firing and release of neurotransmitter, or may occur in skeletal, smooth, or cardiac muscle in response to nerve input. The magnitude of a graded potential is determined by the strength of the stimulus.



Examples of graded potentials

EPSPs

Graded potentials that make the membrane potential less negative or more positive, thus making the postsynaptic cell more likely to have an action potential, are called excitatory postsynaptic potentials (EPSPs). Depolarizing local potentials sum together, and if the voltage reaches the threshold potential, an action potential occurs in that cell.

EPSPs are caused by the influx of Na+ or Ca2+ from the extracellular space into the neuron or muscle cell. When the presynaptic neuron has an action potential, Ca2+ enters the axon terminal via voltage-dependent calcium channels and causes exocytosis of synaptic vesicles, causing neurotransmitter to be released. The transmitter diffuses across the synaptic cleft and activates ligand-gated ion channels that mediate the EPSP. The amplitude of the EPSP is directly proportional to the number of synaptic vesicles that were released.

If the EPSP is not large enough to trigger an action potential, the membrane subsequently repolarizes to its resting membrane potential. This shows the temporary and reversible nature of graded potentials

IPSPs

Graded potentials that make the membrane potential more negative, and make the postsynaptic cell less likely to have an action potential, are called inhibitory post synaptic potentials (IPSPs). Hyperpolarization of membranes is caused by influx of Cl^- or efflux of K^+. As with EPSPs, the amplitude of the IPSP is directly proportional to the number of synaptic vesicles that were released.

Summary

The resting membrane potential is usually around –70 mV. The typical neuron has a threshold potential ranging from –40 mV to –55 mV. Temporal summation occurs when graded potentials within the postsynaptic cell occur so rapidly that they build on each other before the previous ones fade.

Spatial summation occurs when postsynaptic potentials from adjacent synapses on the cell occur simultaneously and add together. An action potential occurs when the summated EPSPs, minus the summated IPSPs, in an area of membrane reach the cell's threshold potential.

What is action potential

An action potential (AP) is the mode through which a neuron transports electrical signals. It is defined as a brief change in the voltage across the membrane due to the flow of certain ions into and out of the neuron,

Origin of action potential

An action potential begins at the axon hillock as a result of depolarisation. During depolarisation voltage gated sodium ion channels open due to an electrical stimulus. As the sodium rushes back into the cell the positive sodium ions raise the charge inside the cell from negative to positive.

In physiology, an action potential (AP) occurs when the membrane potential of a specific cell location rapidly rises and falls:this depolarization then causes adjacent locations to similarly depolarize. Action potentials occur in several types of animal cells, called excitable cells, which include neurons, muscle cells, endocrine cells, glomus cells, and in some plant cells.

The Resting Membrane Potential

The resting membrane potential of cells varies depending on the cell type, the resting potential for neurons typically sits between -50 and -75mV. This value depends on the types of ion channels that are open and the concentrations of different ions in the intracellular and extracellular fluids.

In neurons K^+ and organic anions are typically found at a higher concentration within the cell than outside, whereas Na^+ and Cl^- are typically found in higher concentrations outside the cell.

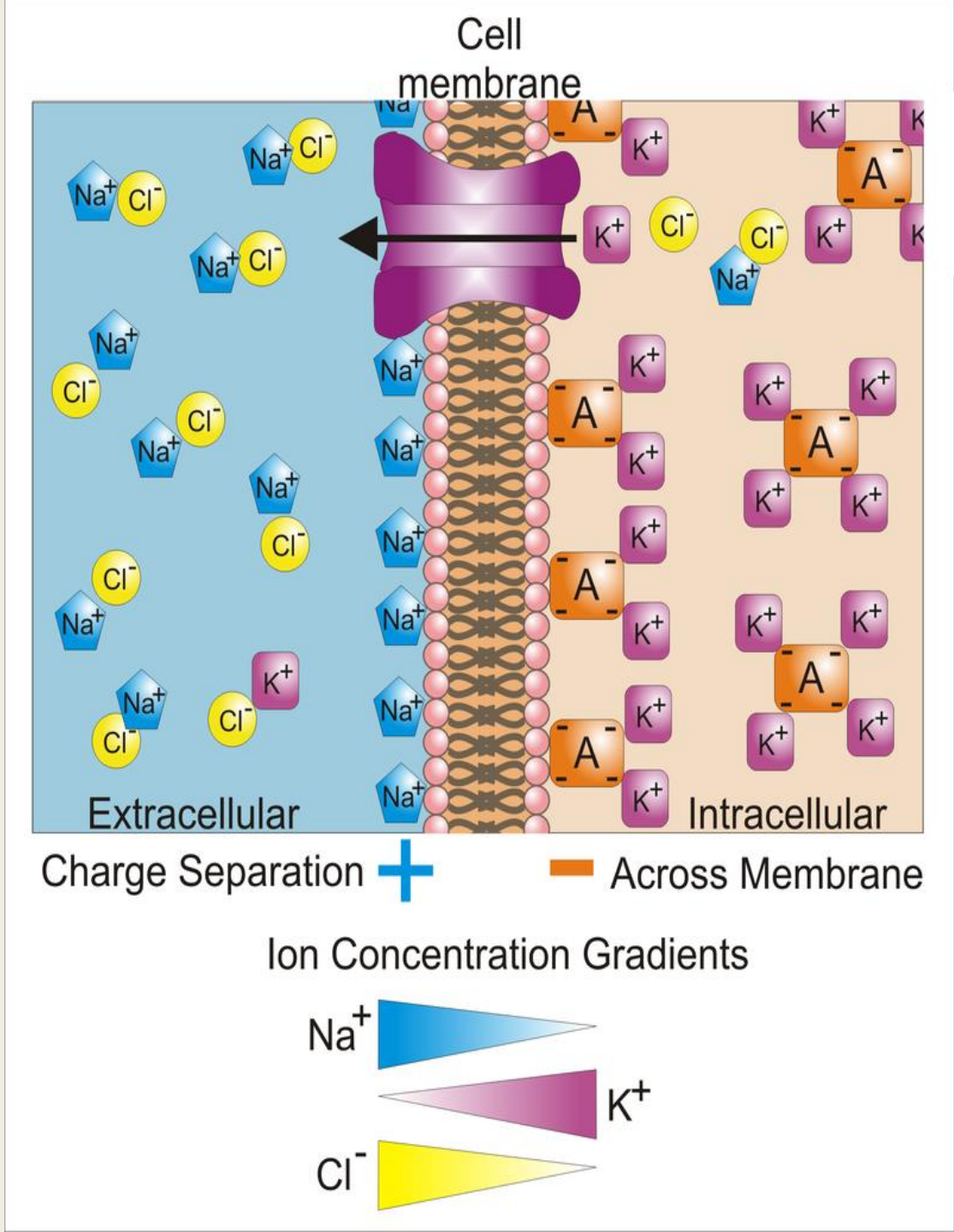
This difference in concentrations provide a concentration gradient for ions to flow down when their channels are open. At rest, most neurons are permeable to K+, Na+ and Cl-, as such they will all readily flow down their concentration gradients, with K+ moving out of the cells and Na+ and Cl- moving in to the cell.

However the cell is most permeable to K+, as such this exerts the greatest influence on the resting membrane potential – and the value is closest to the equilibrium potential of K+ (the membrane potential at which the concentration gradient for an ion is balanced) out of the three ions.

These concentration gradients are maintained by the action of the Na+/K+ ATPase via active transport, which in turn allows the membrane potential to be maintained.

Differences in the concentrations of ions on opposite sides of a cellular membrane lead to a voltage called the membrane potential. Typical values of membrane potential are in the range –40 mV to –70 mV. Many ions have a concentration gradient across the membrane, including potassium (K+), which is at a high concentration inside and a low concentration outside the membrane. Sodium (Na+) and chloride (Cl–) ions are at high concentrations in the extracellular region, and low concentrations in the intracellular regions. These concentration gradients provide the potential energy to drive the formation of the membrane potential.

Membrane potential



Generation of Action Potentials

During the resting state the membrane potential arises because the membrane is selectively permeable to K+. An action potential begins at the axon hillock as a result of depolarisation. During depolarisation voltage gated sodium ion channels open due to an electrical stimulus. As the sodium rushes back into the cell the positive sodium ions raise the charge inside the cell from negative to positive.

If a threshold is reached, then an action potential is produced. Action potentials will only occur if a threshold is reached, as such they are described as “all or nothing“. If the threshold is reached then the maximum response will be elicited.

Once the cell has been depolarised the voltage gated sodium ion channels close. The raised positive charge inside the cell causes potassium channels to open, K+ ions now move down their electrochemical gradient out of the cell. As the K+ moves out of the cell the membrane potential falls and starts to approach the resting potential.

Typically, repolarisation overshoots the resting membrane potential, making the membrane potential more negative. This is known as hyperpolarisation. It is important to note that the Na+/K+ ATPase is not involved in the repolarisation process following an action potential.

Every action potential is followed by a refractory period. This period can be further divided into the absolute refractory period and the relative refractory period. This period occurs as once the sodium channels close after an AP, they enter an inactive state during which they cannot be reopened regardless of the membrane potential. This is known as the absolute refractory period.

Slowly the sodium channels come out of inactivation. This is known as the relative refractory period. During this period the neuron can be excited with stimuli stronger than one normally needed to initial an AP. Early on in the relative refractory period the strength of the stimulus required is very high and gradually it becomes smaller throughout the relative refractory period as more sodium channels recover from inactivation.

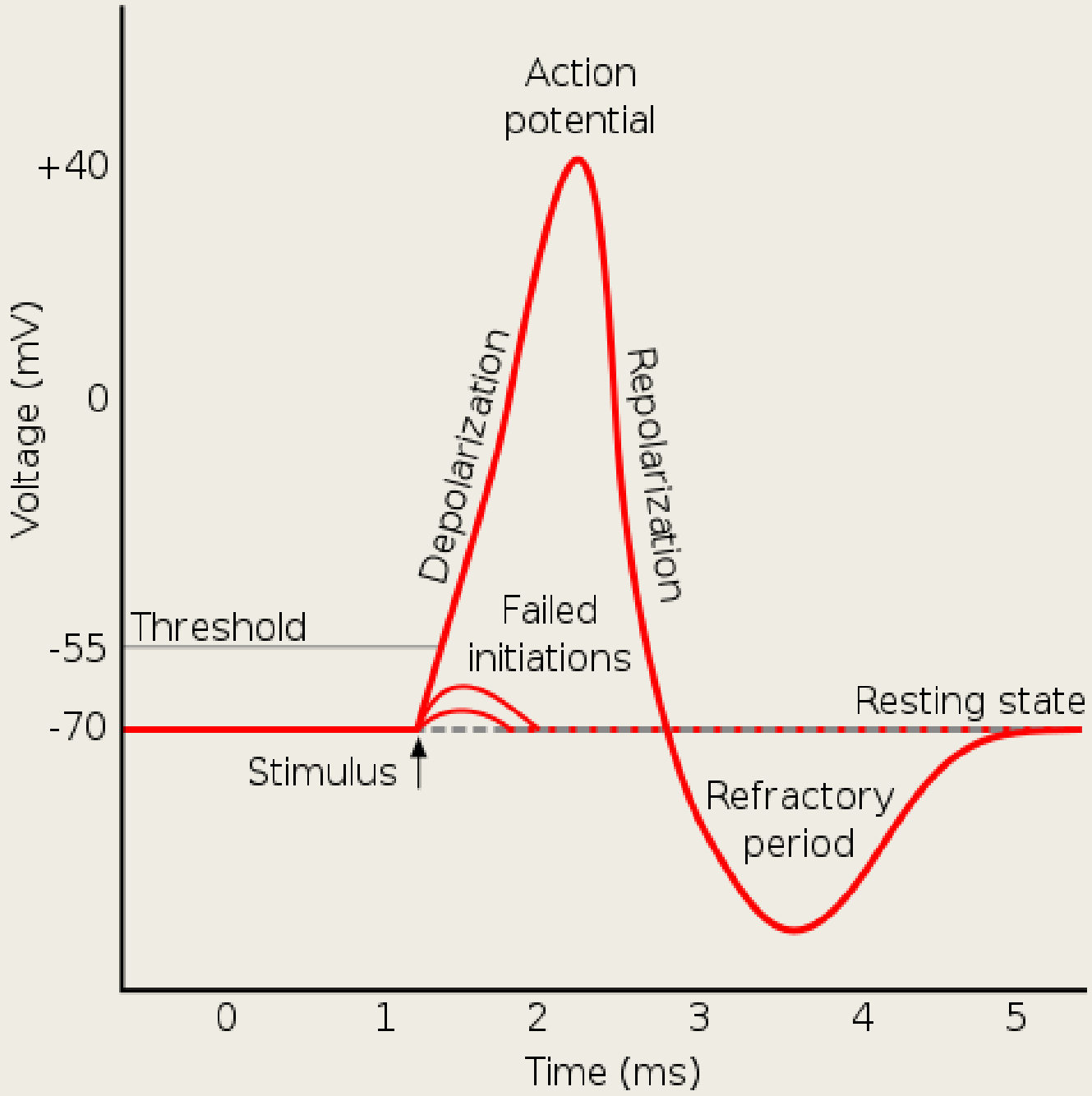


Fig 2 – Diagram showing the phases of an action potential in relation to the membrane voltage over time.

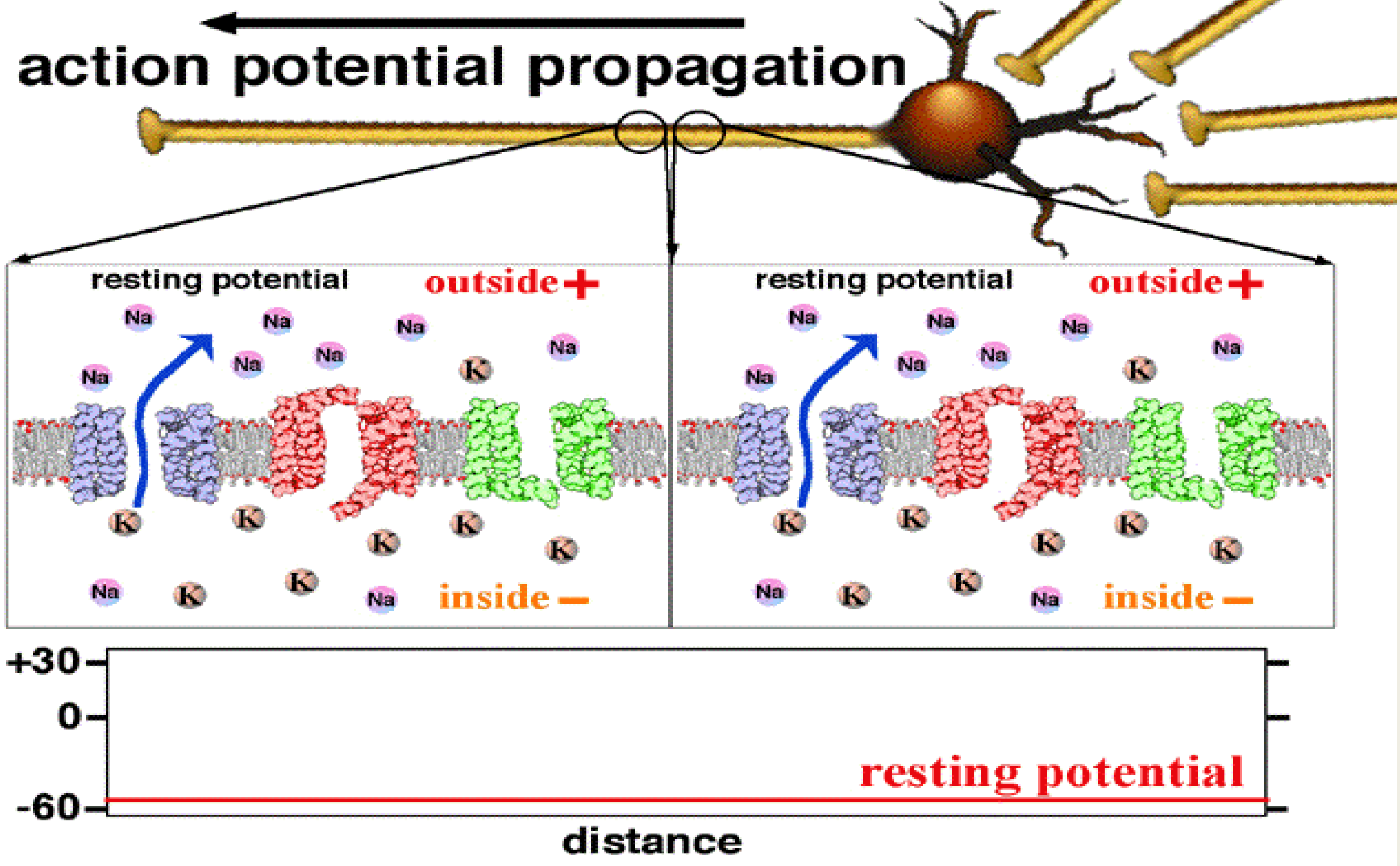
Propagation of Action Potentials

Action potentials are propagated along the axons of neurons via local currents. Local current flow following depolarisation results in depolarisation of the adjacent axonal membrane and where this reaches threshold, further action potentials are generated. The areas of membrane that have recently depolarised will not depolarise again due to the refractory period – meaning that the action potential will only travel in one direction.

These local currents would eventually decrease in charge until threshold is no longer reached. The distance that this would take depends on the membrane capacitance and resistance:

Membrane capacitance – the ability to store charge, lower capacitance results in a greater distance before threshold is no longer reached

Membrane resistance – depends on the number of ion channels open, the lower the number the more channels are open. A higher membrane resistance results in a greater distance before threshold is no longer reached


action potential propagation
resting potential
outside +
Na
K
inside —
resting potential
outside +
inside —
+30
0
-60
resting potential
distance

Myelinated Axons

In order to allow rapid conduction of electrical signals through a neuron and make them more energy efficient certain neuronal axons are covered by a myelin sheath. The myelin sheath surrounds the axon to form an insulating layer. Further information on the myelin sheath can be found here.

Myelination improves conduction by increasing the membrane resistance and decreasing the membrane capacitance.

There are periodic gaps along a myelinate axon where there is no myelin and the axonal membrane is exposed. This gaps are called Nodes of Ranvier. Myelinated sections of the axon lack voltage gated ion channels where as there is a high density of ion channels in the Nodes of Ranvier. For this reason, action potential can only occur at the nodes.

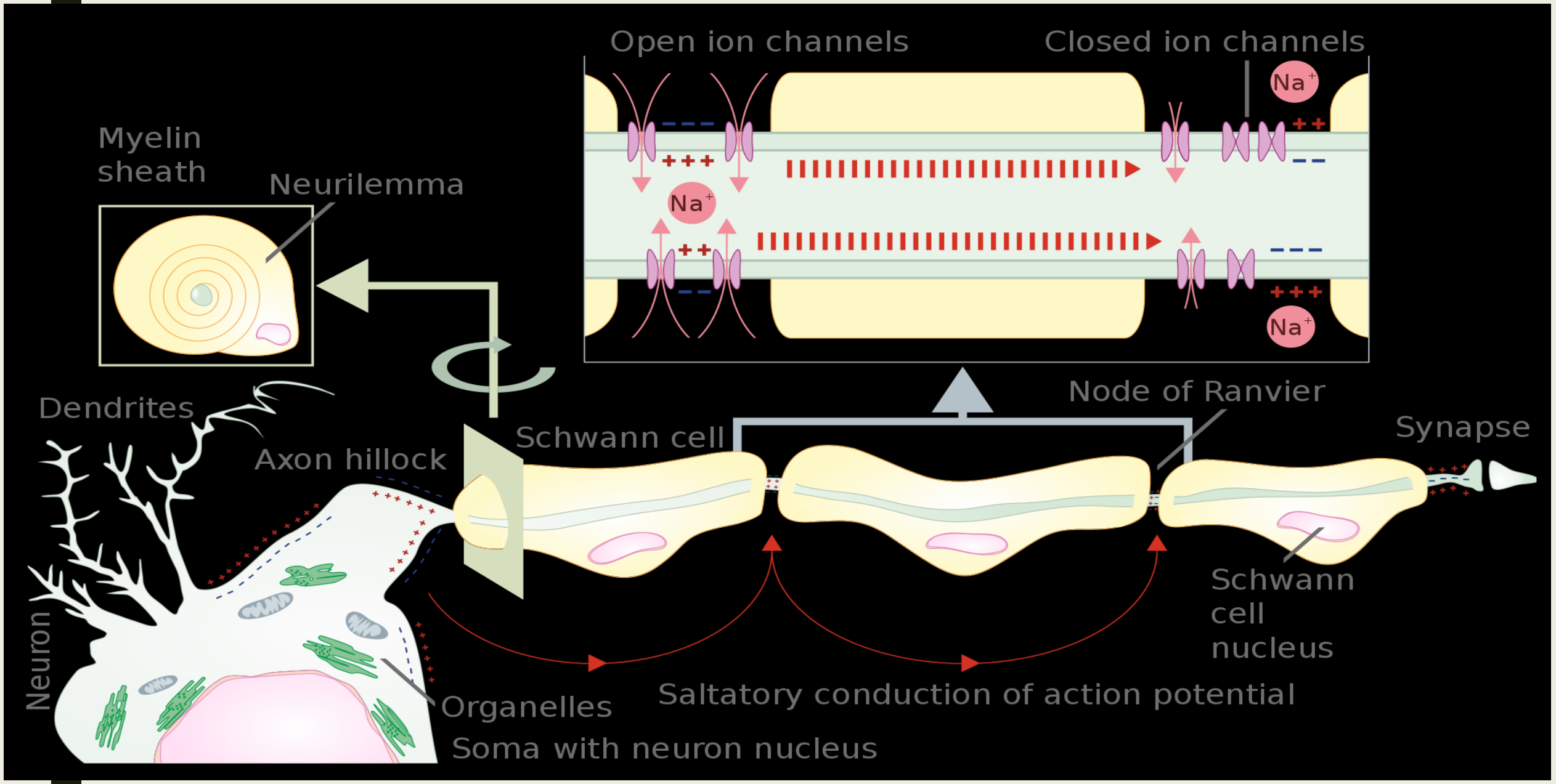
The myelin sheath acts as good insulator so the action potential is able to propagate along the neurone at a higher rate than would be possible in unmyelinated neurons.

The electrical signals are rapidly conducted from one node to the next, where is causes depolarisation of the membrane above the threshold and initiates another action potential which is conducted to the next node. In this manner an action potential is rapidly conducted down a neuron. This is known as saltatory conduction.

Saltatory conduction

(from the Latin saltare, to hop or leap) is the propagation of action potentials along myelinated axons from one node of Ranvier to the next node, increasing the conduction velocity of action potentials.

The uninsulated nodes of Ranvier are the only places along the axon where ions are exchanged across the axon membrane, regenerating the action potential between regions of the axon that are insulated by myelin, unlike electrical conduction in a simple circuit.



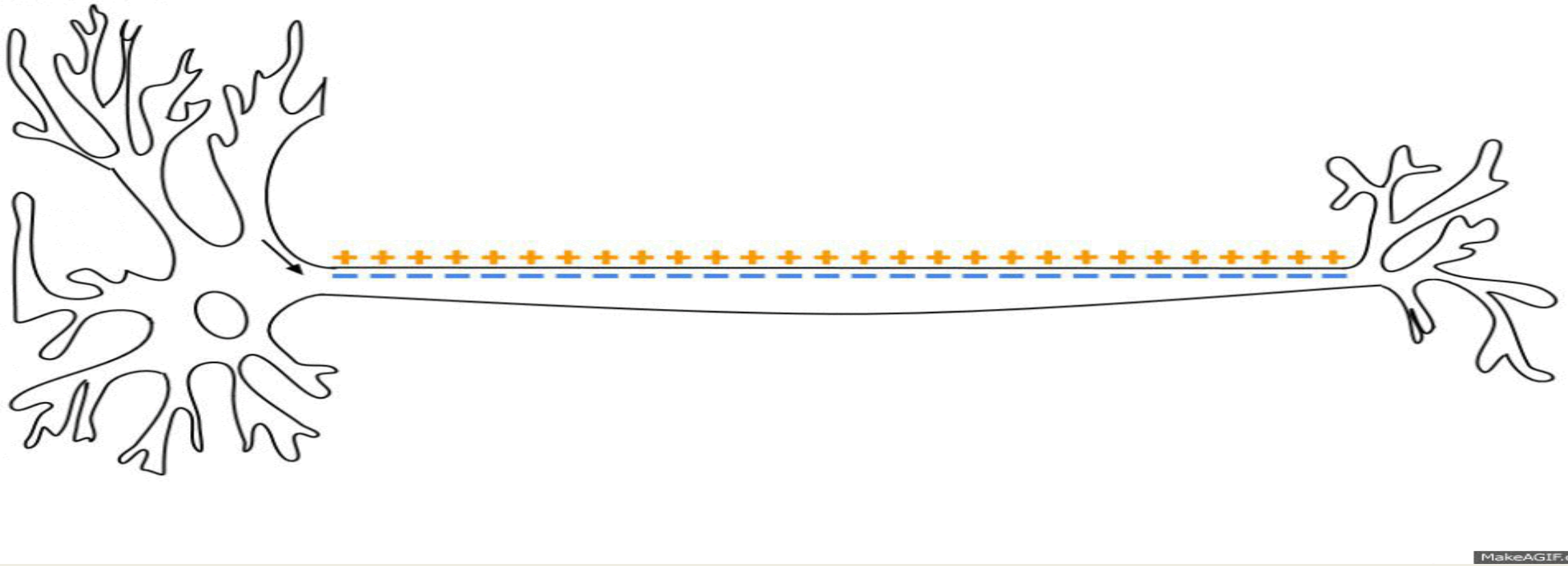
Propagation of action potential along myelinated nerve fiber

Image description: Schematic representation of the action potential propagation through myelinated nerve fiber of peripheral nervous system. From axon hillock of neuron body (soma) action potential propagates from one unmyelinated fiber part to the next one.
The unmyelinated parts of the nerve fiber are nodes of Ranvier. This way of action potential propagation is called saltatory conduction (red arrows in the diagram)
Ion channels open, allow sodium ions to enter the cell leading to membrane depolarization and generation of action potential.

Myelination of nerve fibers in the peripheral nervous system is achieved by Schwann cells wrapping around an axon part (cross section). The nucleus and most of the Schwan cell cytoplasm are contained in the outer most layer called neurilemma.

PROPAGATION OF IMPULSE IN NON MYELINATED NERVE

In neurons, action potentials play a central role in cell-to-cell communication by providing for—or with regard to saltatory conduction, assisting—the propagation of signals along the neuron's axon toward synaptic boutons situated at the ends of an axon; these signals can then connect with other neurons at synapses, or to motor cells or glands. In other types of cells, their main function is to activate intracellular processes.



As an action potential (nerve impulse) travels down an axon there is a change in polarity across the membrane of the axon. In response to a signal from another neuron, sodium- (Na+) and potassium- (K+) gated ion channels open and close as the membrane reaches its threshold potential. Na+ channels open at the beginning of the action potential, and Na+ moves into the axon, causing depolarization. Repolarization occurs when the K+ channels open and K+ moves out of the axon, creating a change in polarity between the outside of the cell and the inside. The impulse travels down the axon in one direction only, to the axon terminal where it signals other neurons.

Action potentials are generated by special types of voltage-gated ion channels embedded in a cell's plasma membrane.

These channels are shut when the membrane potential is near the (negative) resting potential of the cell, but they rapidly begin to open if the membrane potential increases to a precisely defined threshold voltage, depolarising the transmembrane potential.When the channels open, they allow an inward flow of sodium ions, which changes the electrochemical gradient, which in turn produces a further rise in the membrane potential towards zero.

This then causes more channels to open, producing a greater electric current across the cell membrane and so on. The process proceeds explosively until all of the available ion channels are open, resulting in a large upswing in the membrane potential.

The rapid influx of sodium ions causes the polarity of the plasma membrane to reverse, and the ion channels then rapidly inactivate. As the sodium channels close, sodium ions can no longer enter the neuron, and they are then actively transported back out of the plasma membrane.

Potassium channels are then activated, and there is an outward current of potassium ions, returning the electrochemical gradient to the resting state. After an action potential has occurred, there is a transient negative shift, called the afterhyperpolarization.

An action potential propagates along the cell membrane of an axon until it reaches the terminal button. ... Action potentials are propagated faster through the thicker and myelinated axons, rather than through the thin and unmyelinated axons.

Mechanism

As sodium rushes into the node it creates an electrical force which pushes on the ions already inside the axon. This rapid conduction of electrical signal reaches the next node and creates another action potential, thus refreshing the signal.

In this manner, saltatory conduction allows electrical nerve signals to be propagated long distances at high rates without any degradation of the signal. Although the action potential appears to jump along the axon, this phenomenon is actually just the rapid, almost instantaneous, conduction of the signal inside the myelinated portion of the axon.

If the entire surface of an axon were insulated, there would be no place for current to flow out of the axon and action potentials could not be generated

ULTRASTRUCTURE OF SKELETAL MUSCLE

Muscle tissue has a unique histological appearance which enables it to carry out its function. There are three main types of muscle:

Skeletal – striated muscle that is under voluntary control from the somatic nervous system. Identifying features are cylindrical cells and multiple peripheral nuclei.

Cardiac – striated muscle that is found only in the heart. Identifying features are single nuclei and the presence of intercalated discs between the cells.

Smooth – non-striated muscle that is controlled involuntarily by the autonomic nervous system. The identifying feature is the presence of one spindle-shaped central nucleus per cell.

In this article, we will look at the histology of skeletal muscle – its composition, histological appearance and clinical correlations.

Composition of Skeletal Muscle

A muscle cell is very specialised for its purpose. A single cell forms one muscle fibre, and its cell surface membrane is known as the sarcolemma.

T tubules are unique to muscle cells. These are invaginations of the sarcolemma that conduct charge when the cell is depolarised.

Muscle cells also have a specialised endoplasmic reticulum – this is known as the sarcoplasmic reticulum and contains a large store of calcium ions.

Muscles also have an intricate support structure of connective tissue. Each muscle fibre is surrounded by a thin layer of connective tissue known as endomysium.

These fibres are then grouped into bundles known as fascicles, which are surrounded by a layer of connective tissue known as perimysium. Many fascicles make up a muscle, which in turn is surrounded by a thick layer of connective tissue known as the epimysium.

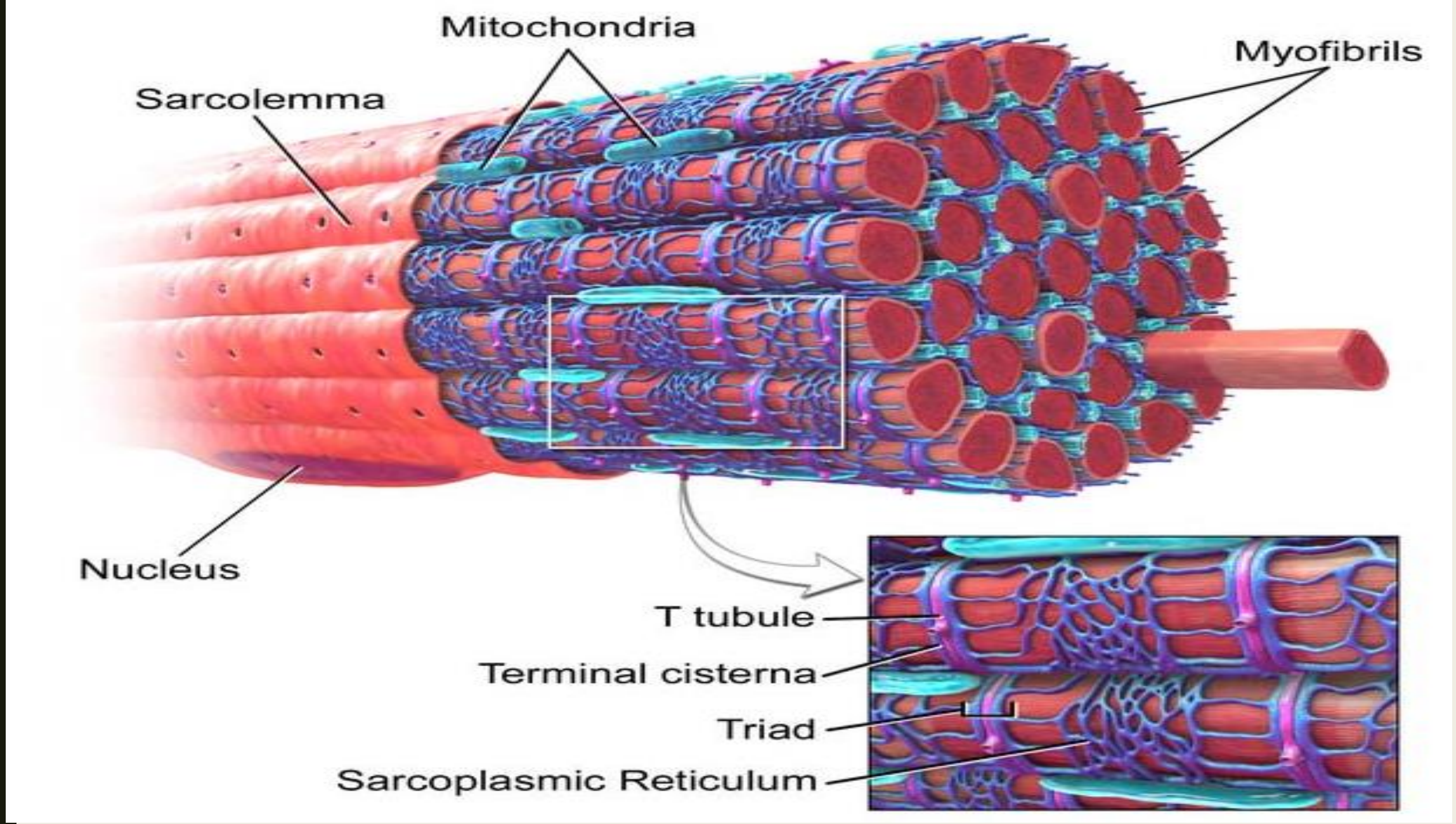


Fig 1 – Ultrastructure of a skeletal muscle fibre

Ultrastructural Appearance of Skeletal Muscle

The striated appearance of skeletal muscle fibres is due to the organisation of two contractile proteins: actin (thin filament) and myosin (thick filament).

The functional unit of contraction in a skeletal muscle fibre is the sarcomere, which runs from Z line to Z line. A sarcomere is broken down into a number of sections:

Z line – where the actin filaments are anchored.

M line – where the myosin filaments are anchored.

I band – contains only actin filaments.

A band – the length of a myosin filament, may contain overlapping actin filaments.

H zone – contains only myosin filaments.

A useful acronym is MHAZI – the M line is inside the H zone which is inside the A band, whilst the Z line is inside the I band.

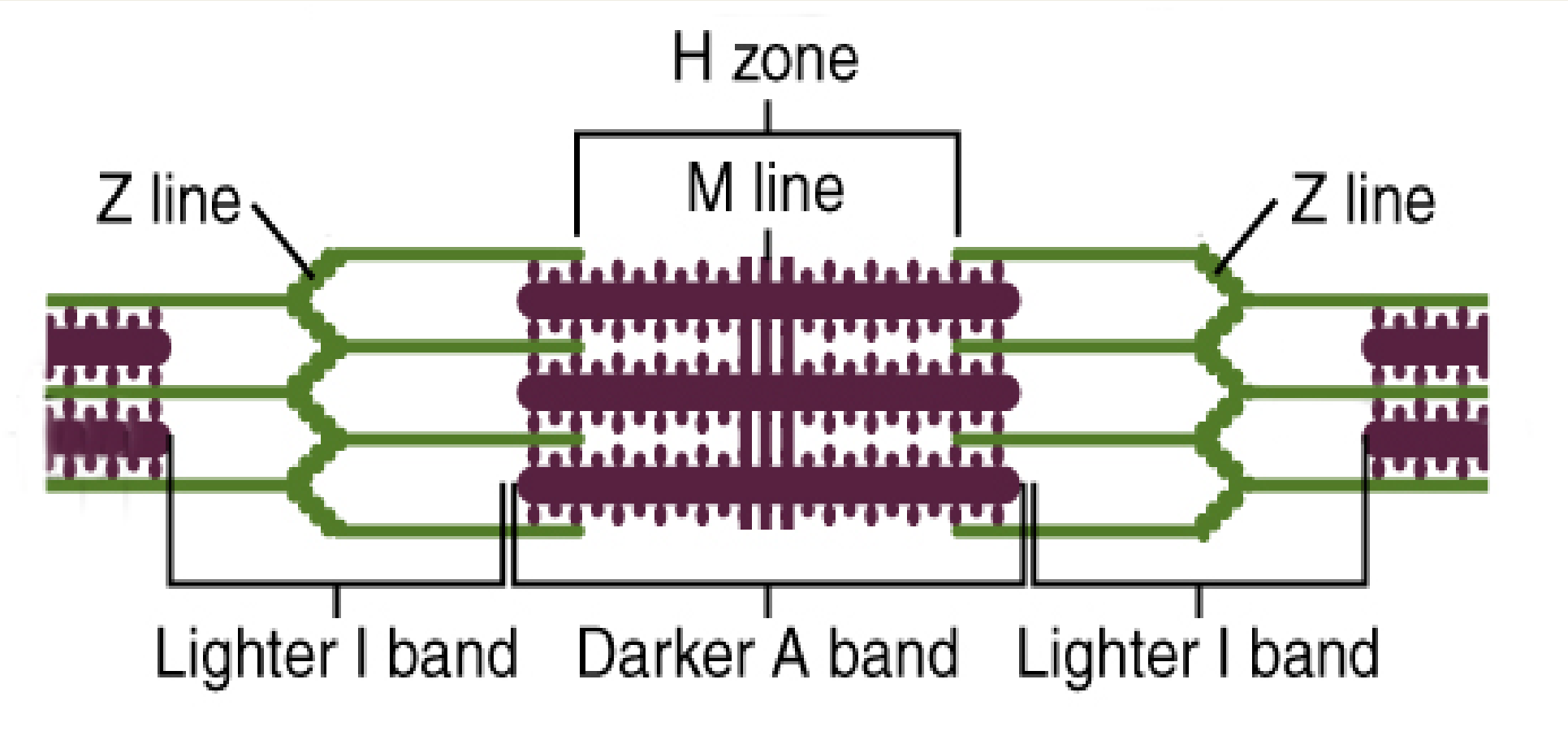


Fig 2 – A sarcomere is measured from Z line to Z line

MOLECULAR AND CHEMICAL BASIS OF MUSCLE CONTRACTION

Sliding Filament Model

The sliding filament model describes the mechanism of skeletal muscle contraction

Actin and Myosin

Muscle fibres are formed from two contractile proteins – actin and myosin. Myosin filaments have many heads, which can bind to sites on the actin filament. Actin filaments are associated with two other regulatory proteins, troponin and tropomyosin. Tropomyosin is a long protein that runs along the actin filament and blocks the myosin head binding sites.

Troponin is a **small protein that binds the tropomyosin to the actin. It is made up of three parts:**

Sliding Filament Model

The sliding filament model describes the mechanism of skeletal muscle contraction

Actin and Myosin

Muscle fibres are formed from two contractile proteins – actin and myosin.

Myosin filaments have many heads, which can bind to sites on the actin filament. Actin filaments are associated with two other regulatory proteins, troponin and tropomyosin. Tropomyosin is a long protein that runs along the actin filament and blocks the myosin head binding sites.

Troponin is a small protein that binds the tropomyosin to the actin. It is made up of three parts:

Troponin I – binds to the actin filament.

Troponin T – binds to tropomyosin.

Troponin C – can bind calcium ions.

Excitation-Contraction Coupling

The unique structure of troponin is the basis of excitation-contraction coupling:

When depolarisation occurs at a neuromuscular junction, this is conducted down the t-tubules, causing a huge influx of calcium ions into the sarcoplasm from the sarcoplasmic reticulum.

This calcium binds to troponin C, causing a change in conformation that moves tropomyosin away from the myosin head binding sites of the actin filaments.

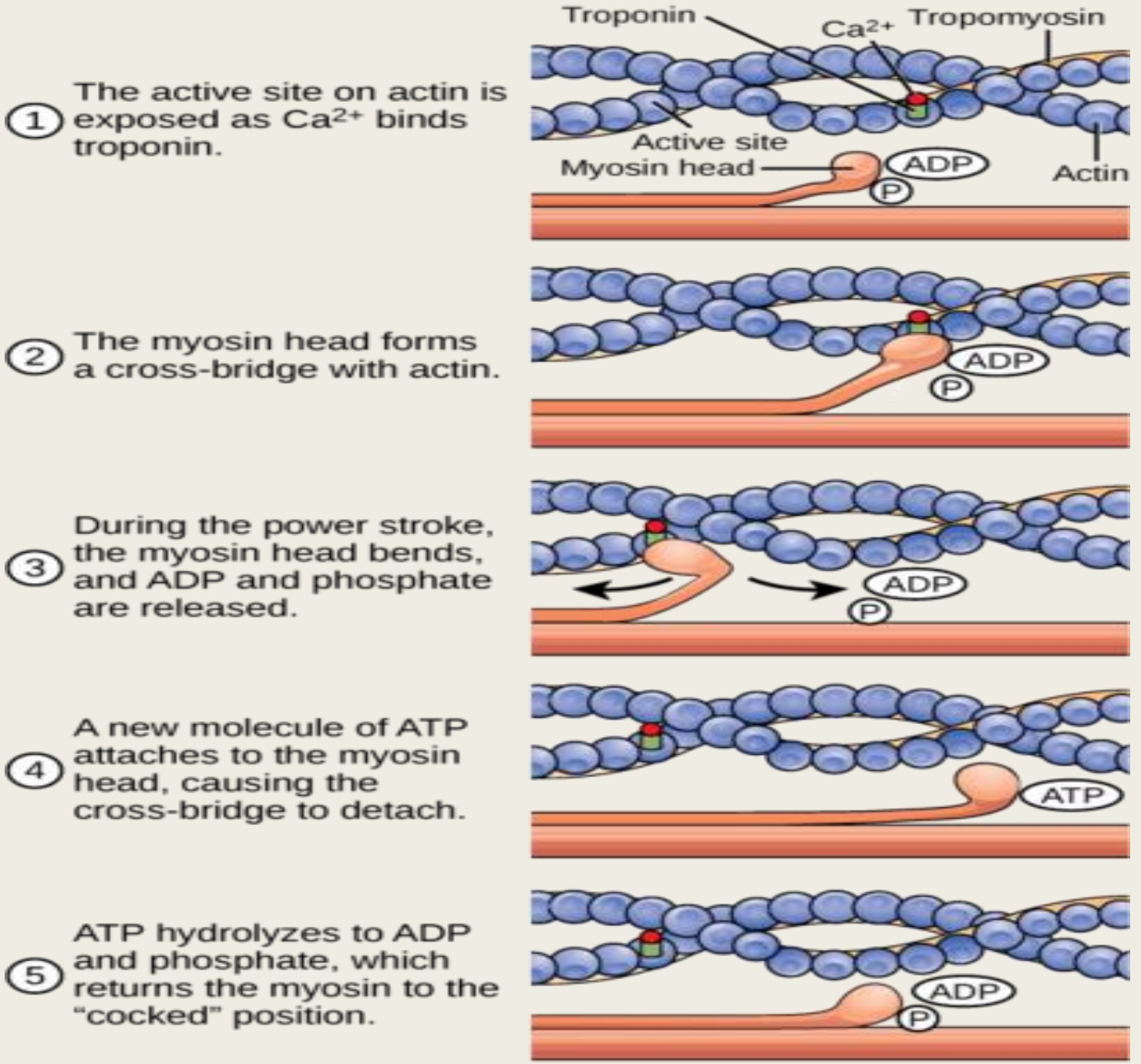
This allows the myosin head to bind to the actin, forming a cross-link. The power stroke then occurs as the myosin heads pivots in a ‘rowing motion’, moving the actin past the myosin towards the M line.

ATP then binds to the myosin head, causing it to uncouple from the actin and allowing the process to repeat.
Hence in contraction, the length of the filaments does not change.

However, the length of the sarcomere decreases due to the actin filaments sliding over the myosin.

The H zone and I band shorten, whilst the A band stays the same length. This brings the Z lines closer together and causes overall length of the sarcomere to decrease.

Fig 3 – The sliding filament model of muscle contraction



THANK YOU