BMED2402 – Semester 1

Histology of the nervous system

What is: neurohistology and a neuron?

Neurohistology *Study of Neural System*

Neuron *Cells that form interconnected pathways in the NS*

Define the histological spaces within the brain

- Spaces and barriers
    - Function of many cells is to mediate the passage of mobile cells and molecules between spaces
    - **Interstitial/extracellular space** between neuron and glial cells
    - **Intravascular space** within blood vessels
    - **Intraventricular space** within ventricles
    - **Subarachnoid space** between pia and arachnoid
    - Relative barriers between spaces to mobile cells and molecules are formed by the capillary endothelium, glial limitations, ependymal and the arachnoid

Discuss the various ways in which cells of the nervous system including neurons are characterized (classified, described), give examples

1. Function
2. General location (CNS or PNS)
3. Specific location (layer of the cerebral cortex – table 6)
4. General connections (peripheral motor, sensory, central intermediate/integrative – table 5)
5. Polarity
6. Size
7. Shape
8. Axon length
9. Transmitter
10. Electrical behaviour

TABLE 2. CELLS OF THE NERVOUS SYSTEM.

Cell.	CNS (Brain, Spinal Cord).	PNS.
Neuron.	Integrative. Golgi 1 (Projection). Golgi 2 (Interneurons).	Sensory. Motor. Golgi 1 (Projection)
Supportive/Glia.	Astrocytes (Protoplasmic, Fibrous). Oligodendrocytes. Microglia. Ependymal.	Schwann. Satelite. Perineural.
Miscellaneous.	Pia. Arachnoid. Dura. Vessels (including capillaries. pericytes).	Fibroblast. Vessels (including capillaries). Wandering cells eg macrophages, mast cells.

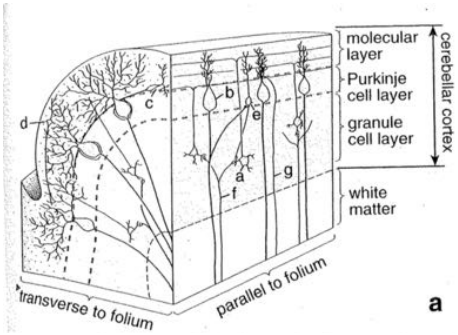
Give an overview of the techniques (microscopes, stains) used to visualize the cells of the nervous system

Stain.	Ease of Use.	Numbers of Neurons.	Cell Body.	Processes, Tracts.	Limitations.	Useful Features.
H & E.	Easy.	Most.	Nucleus, some membranes.	Sometimes proximally.	No processes or tracts.	Ease, grey matter.
Nissl (eg Toluidin Blue).	Easy.	Most.	Nucleus, ER, some membranes.	Some proximal.	Few processes or tracts.	Ease, grey matter.
Reduced Silver.	Moderate.	Most.	Nucleus, membrane.	Processes including axons, tracts.	Dense background.	Tracts and their origins destinations
Golgi.	Can be difficult.	Few.	Outlines, no intracellular structures.	Dendritic trees, some axons.	Preparation, cell selection, not all axons.	Extent of dendritic trees, detailed following of some projections.
Fibre (eg Weigert Stain).	Moderate.		None.	Tracts (axons).	No cell bodies. Doesn't differentiate within tracts.	Tracts.
Degenerating Fibre (eg Marchi Stain).	Moderate.	None unless counterstained	None.	Degenerating tracts.	No cell bodies, experimental aspect.	Particular tracts, extent of tracts.
Microinjection.	Difficult.	Usually one.	Yes.	Yes.	Difficulty. Single cells.	Clarity. Tracing processes. Correlation with electronic behaviour.
Uptake Markers.	Difficult.	Several.	Yes.	Yes.		Tracing processes.
Immunostains and Histochemistry.	Difficult.	Many.	Usually, particular components.	Usually, particular components.		Show specific cell populations
Electron Microscope.	Specialised.	All.	Membranes and intracellular substructure in detail.	Membranes and intracellular substructure in detail.	Preparation, processes rarely traceable, little 3D.	Intracellular structures, membranes relationship of adjacent cells.

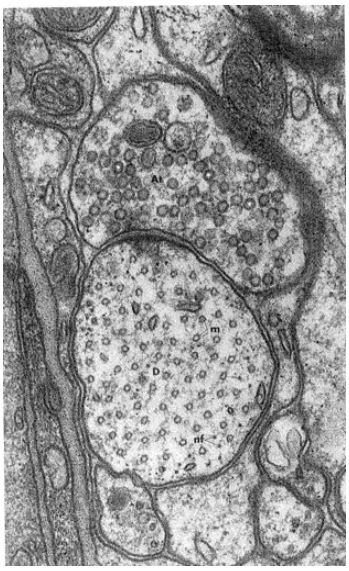
Discuss and give examples of the variation in the structure and function of neurons

Name/Letter*	Polarity	Connections	Axon Length	Size/Shape	Location of Cell Body
Somatic Sensory Neuron G	Unipolar	Sensory	Long	Large Globular	Dorsal Root Ganglion
Lower Motor Neuron D	Multipolar	Motor	Long	Large Fusiform	Ventral Horn Spinal Cord
Pyramidal Cell E	Multipolar	Intermediary	Long Projection	Large Pyramidal	Cerebral Cortex
Granule Cell B	Multipolar	Intermediary	Short Interneuron	Small	Cerebellar Cortex

Discuss and draw the morphological characteristics (internal and external levels) of a typical neuron including the synaptic region and correlate the structure(s) with function



- Has nucleus, nucleolus, ER, ribosomes, mitochondria, Golgi, lysosomes, structural proteins, filaments, tubules and secretory vesicles
- Euchromatic nucleus – dispersed DNA – more of this indicates less active nucleus
- Prominent nucleolus (rRNA)
- Extensive ER (Nissl substance)



Synapse – region for chemical transmission

Discuss in principle the connections of neurons to one another both locally (microcircuits) and at a distance (macrocircuits)

- Microcircuit level (cytoarchitecture) usually within a region of gray matter
- Macrocircuit (as part of a functional system) level (gray matter ----------> grey matter)

Give examples of the histological organization of neurons in gray and white matter eg the cerebral and cerebellar cortex, spinal cord gray matter, and the retina

TABLE 9. LAYERS OF THE CEREBELLAR CORTEX [folded sheet of grey matter]

Layer	Depth	Major Neuronal Cell Type*	Major Connections
Molecular.	Superficial.	Few cells, several types of interneuron.	• Climbing fibres (i) • Granule cell axon (i) • Purkinje dendrite (o)
Purkinje.	Middle.	Purkinje Cell.	To deep nuclei (o)
Granular.	Deep.	Granular Cell.	• Mossy fibres (i) • Axon to molecular (o)

TABLE 10. LAYERS OF THE CEREBRAL NEOCORTEX [sheet of grey matter]

Layer.	Depth.	Major Neuronal Cell Type.	Major Projection Connections.
1 Molecular.	Superficial.	Few.	Within the cortex.
2 External Granular.		Small Pyramidal, Stellate/Granular.	Cortico-cortical (in)
3 External Pyramidal.		Small Pyramidal.	Cortico-Cortical (in and out).
4 Internal Granular.		Stellate/Granule.	Thalamo-Cortical (in).
5 Internal Pyramidal.		Large Pyramidal.	Cortico-Striate /Cerebellum/BS/SC (out).
6 Polymorphic / Multiform.	Deep.	Fusiform.	Cortico-Thalamic (out).

**Cortex contains other interneurons and glia & In (i)/out (o) with respect to the cortical or cortex layer*

Discuss and draw the morphological characteristics of the supporting cells (astrocytes, oligodendrocytes, microglia, ependyma, schwann cells, satellite cells, perineural cells) and other cells (pia, arachnoid, dura, capillaries) of the nervous system and correlate structure and location with function

Supporting Cell	Cell Size	Location	Function
Astrocytes	Small to medium spherical cells	• Fibrous (in white matter) • Protoplasmic (in grey matter)	• Regulates ion and transmitter content • Maintains BBB (as metabolically active) • Forms scar tissue
Oligodendrites	Small to medium cells	Mainly in white matter near proximal end of axon projection	• Wraps around axons to form myelin sheaths → increase transmission speed • Single one can myelinate numerously
Microglia	Small cells with elongated nuclei	Migratory in CNS and pass though cerebral capillary junction to leave and enter CNS freely	Functions as a phagocytic and immunologic cell
Ependymal cells	Small cells with villi and cilia on surface	Forms cuboidal cell layer lining ventricle + spinal cord	Assists choroid plexus in secretion/absorption of CSF → villi
Satellite cells	Small cells	Surround neuronal bodies	Surround somatic sensory neurons and autonomic ganglia neurons
Schwann cells *(oligodendrocytes of PNS)*	Elongated rounded cell with large nuclei	Wraps around section one **myelinated** axon or embedded in unmyelinated axon	Improve impulse conduction speed by limiting leakage from axonal membrane
Perineural Cells	Flattened cells arrange in multiple layers	• Surround groups of axons • Cells joined by tight junctions	• Produce collagen

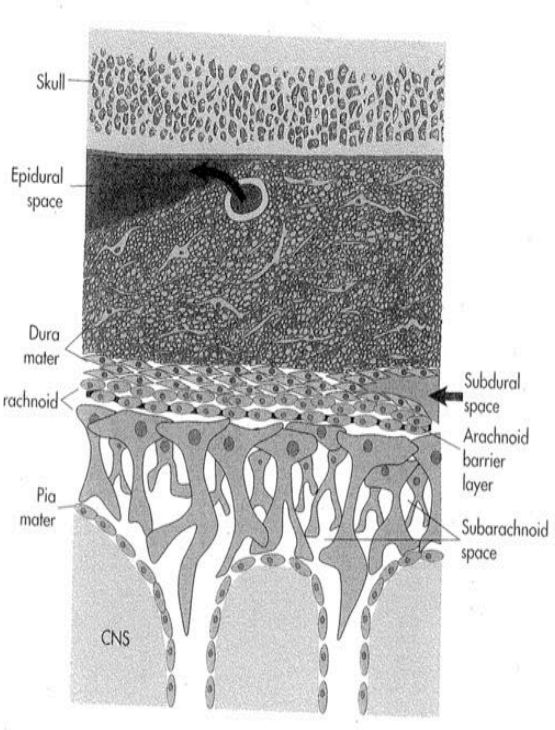
Discuss and draw the histological structure seen in a cross section of a typical peripheral nerve + Correlate with function

Nerve fibres with 4 levels of wrapping,

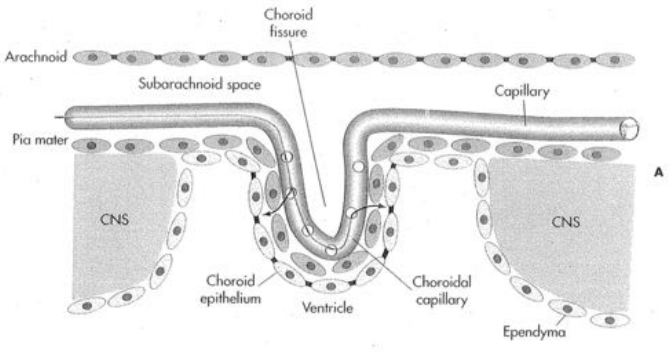
1. **Schwann cell** — Axon or process surrounded by or embedded in a Schwann cell, bound together by endoneurium
2. **Endoneurium** — connective tissue, fibroblasts, capillaries
3. **Perineurium** — surrounded by perineural cells to form fascicles
4. **Epineurium** *(wavy pattern)* — connective tissue, fibroblasts, adipose cells, small arteries, wandering cells → protect neural fibres from damage

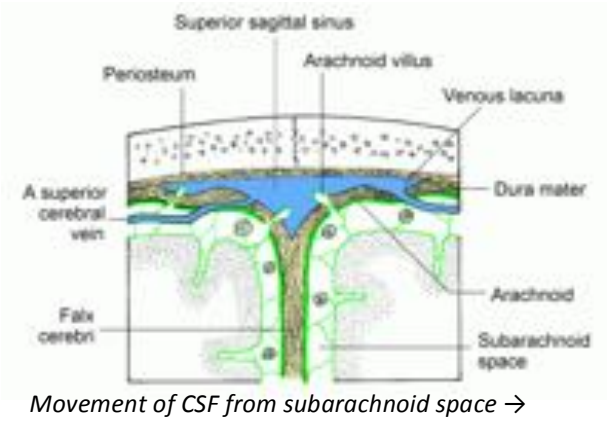
Discuss and draw the organization of cells in the meninges, glia limitans, choroid plexus, arachnoid villi and blood brain barrier and correlate the structure with function.

Cell Organisation	Structure/Cell Size	Location	Function
Meninges	**Tri-layered membrane**	surround brain and spinal cord	Protect and stabilize CNS (i.e. brain and spinal cord)
Pia mater	Single layer of **flattened cells**	Rest on basal lamina	Adhere to the surface of the CNS
Arachnoid	Multiple layers of **flattened cells** with **tight junctions**	Superficial to pia separated by subarachnoid space	Contains CSF
Dura Mater	**Inner region** has layers of **flattened cells** and a **thicker outer layer** of **connective tissue**	Outermost layer of brain	BBB → selective barrier for cells and molecules between intravascular and interstitial space
Arachnoid villi	Arachnoid invaginates through holes in the dura	In superior sagittal sinus formed from dura and endothelial lining	Site of most absorption of CSF back into the intravascular space (*i.e. venous system*)
Glial limitans	Tightly packed astrocyte end feet	Layer between pia matter and the cerebral hemispheres	Physical and immunological barrier between CNS interstitial and subarachnoid space
Choroid plexus	3 layers 1. **F. Capillary endothelium** 2. **Pial cells** 3. **Ependyma cells**	Found in the **lateral** ventricles (roofs of 3rd and 4th ventricles) of the brain	CSF made here: • Inside or outside brain Behind cerebellum



***Note**: BBB is mostly fenestrated capillary endothelium where ependymal cells have tight cell junctions which are regulated by astrocytes (glial cells) and pericytes*





Movement of CSF from subarachnoid space → arachnoid villus → superior sagittal sinus (2 layers)

Discuss the macroscopic formation of the sympathetic trunk and splanchnic nerves

Sympathetic trunk (autonomic ganglia)

Location:	• Base of skull to sacral region • Trunk contains **ganglia** (but not all preganglionic fibres synapse) → some in prevertebral ganglia – located around aorta and its larger branches
Input	• Spinal cord segments T1-L2 → via spinal nerves **and** their white rami communicantes
Output	• Grey rami communicantes (join peripheral nerves to innervate smooth muscle in BV, sweat glands in limb and body wall) • Splanchnic nerves (C, T, L, S) → extend out to form autonomic plexuses

Discuss and compare how the sympathetic and parasympathetic fibres of the visceral motor (autonomic) system are distributed

Component.	Structure	Location of cell body	Sympathetic Fibres	Parasympathetic Fibres
Preganglionic (GANGLIA)	• Multipolar • Smallish • Large cell body • Central Euchromatic nucleus • Prominent nucleolus	Lateral part of GM on DH and VH of SC or in CN nucleus	**Short** *Thoracic* segments of SC (*T1- L2)*	**Long** *Sacral segments of SC (S 2, 3, 4)*
Postganglionic (EFFECTOR)		Peripheral ganglia	**Long** *(spinal nerves)* *Sympathetic trunk or pre-vertebral ganglia*	**Short** *(splanchnic nerves)* *Ganglion near viscera or walls of viscera*
		Function:	Arousal	Vegetative

Discuss transduction

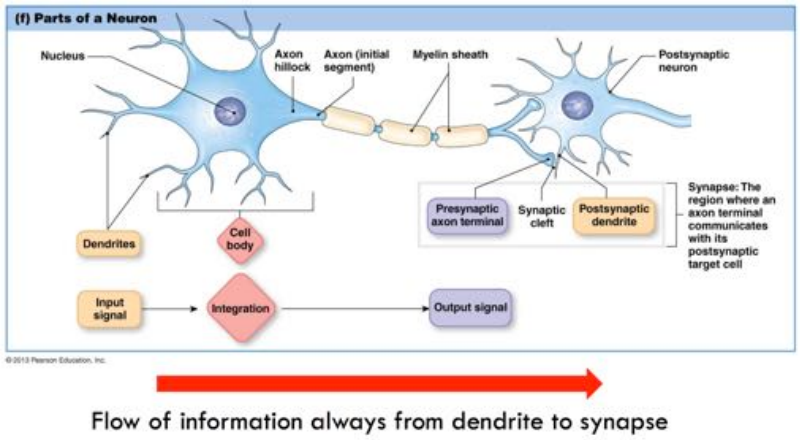
***Transduction** = Process by which a stimulus in the environment → electrical energy in the body = AP*

Modality.	Transducer cell.	Location.	Stimulus.	Cranial Nerve.
Olfaction.	Olfactory Cells.	Nasal Mucosa.	Chemical.	1 Olfactory.
Vision.	Rods and Cones.	Retina.	Light.	2 Optic.
Hearing.	Hair Cells.	Inner Ear	Sound, air-fluid movement	8 Cochlea
Balance, Movement, Gravity.	Hair Cells.	Inner Ear.	Movement, static force/gravity.	8 Vestibular
Taste.	Neuroepithelial Cells.	Mostly Tongue.	Chemical.	7, 9, 10.

- In somatic NS peripheral nerve endings of somatic sensory neurons contain ion channel which respond to tissue damage, temp or mechanical deformity with the production of an action potential
- Some nerve endings have specialised structures to facilitate this process
    - Slow/non adaptors = receptors which respond to and ongoing stimulus
    - Fast adaptors = receptors which respond to a change in a stimulus
- Intensity = frequency of the AP
- Visceral sensory nerve transducers similar to that of the somatic system
- More complex process in special sense neurons

Action potential generation & propagation

Draw and label the main anatomical features of a neuron and describe their basic functions

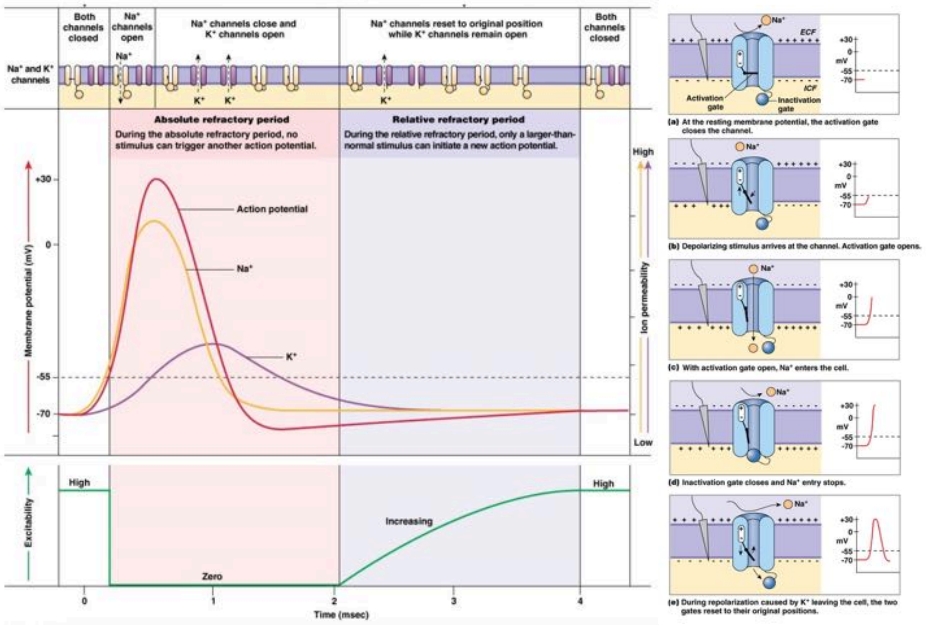


- Cells of excitable tissues can alter the permeability of their membranes to particular ions to generate **fluctuations in membrane potential** → creates APs

Define the terms threshold, depolarisation, repolarisation and hyperpolarisation, and understand the relationship between these terms and the activity of voltage-gated channels

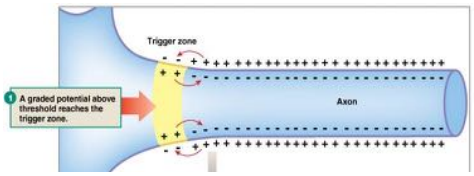
Terms	**Definition**
Depolarisation	increasing polarity → more +ve (Na^+ enters cell)
Repolarisation	returns membrane potential to a negative value just after the depolarization phase
Hyperpolarisation	makes cell more negative than what it initially started at → more -ve membrane potential (K^+ leaves cell)
Threshold	minimum amount required to generate a response

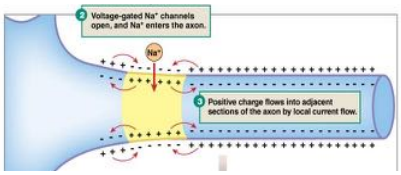
Explain the refractory period and its impact on action potential generation

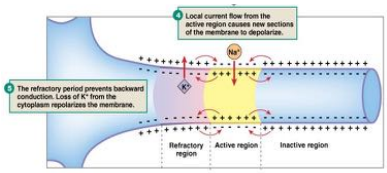


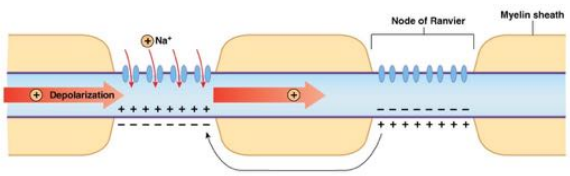
Refractory period	• Period when neuron does not respond normally to depolarising stimulus • Ensures AP move in **one-direction only**
Absolute refractory period:	• All Na^+ channels are open or inactivated • Action potential **CANNOT** fire
Relative refractory period:	• Na^+ channels begin to resume resting state • Action potential **CAN** fire but requires larger-than-normal stimulus

Continuous vs. Saltatory propagation







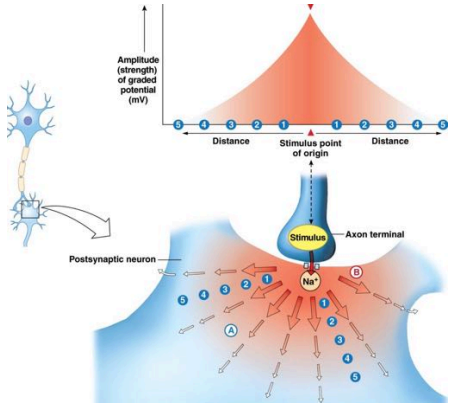
	Axons	AP movement	Speed
Continuous propagation	***Unmyelinated***	• Channels open sequentially • Depolarisation of one region → depolarisation of adjacent region, and so on	Slow (~1 m/s)
Saltatory propagation	***Myelinated*** (Myelin sheath prevents current leak (insulator)	Jump" between Nodes of Ranvier 	Fast (>100 m/s)

Describe the generation of a graded potential and an action potential, and key differences between the two

Action potentials exists because neurons are excitable cells that can generate signals by a change in membrane potential

Note: ***Threshold*** *= depolarisation large enough to trigger opening of voltage-gated Na^+ channels (≈-60 to -55mV)*

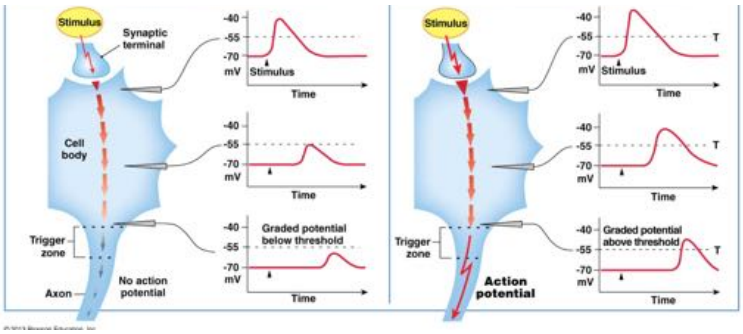
Graded Potential (GP)	**Action Potential (AP)**
Depolarising or Hyperpolarising	**Always** depolarising
Produced by any stimulus that opens a gated channel (no threshold)	Produced only if threshold is reached/exceeded in the trigger zone (axon hillock & initial segment)
Amplitude of GP → dependent on the stimulus intensity	**All or none principle** → any stimuli that exceeds threshold will produce identical AP (same strength)
Passive spread but does not spread far from stimulation site	APs on one site depolarises adjacent sites to threshold
Effect on membrane potential decreases with increased distance from stimulation site	**Propagated** along the length of the axon, resulting in depolarisation of synaptic terminals
No refractory Period (i.e. no regeneration)	Refractory period occurs
In most plasma membranes	Only in excitable membranes of specialised cells (e.g. neurons and muscle cells)

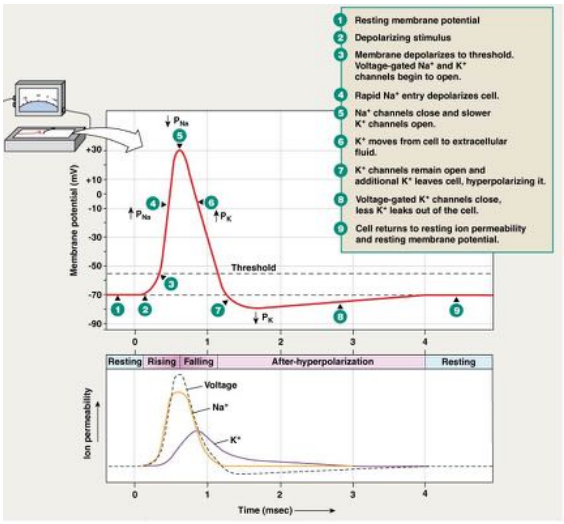


Types of graded potential:

Subthreshold*: GP above threshold at initiation point but decreases to below threshold at trigger zone*

Suprathreshold*: GP above threshold at initiation point and remains above threshold at trigger zone → generation of AP*





1. Depolarisation to threshold
2. Activation of voltage-gated Na^+ channels, rapid depolarisation
3. Inactivation of Na^+ channels, opening of K^+ channels
4. Return to normal permeability

Identify the properties of an axon that can affect action potential conduction velocity

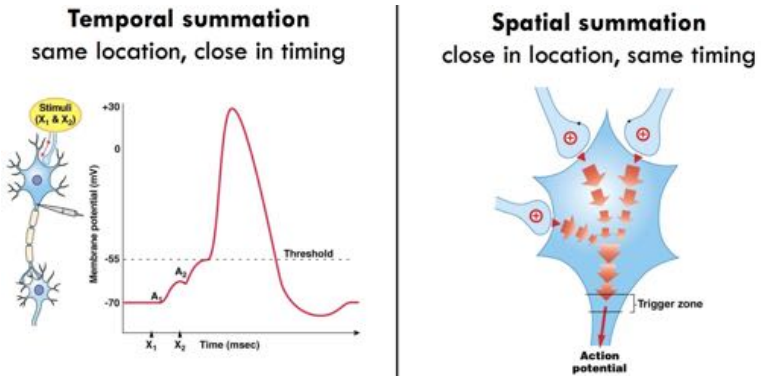
Axon properties that **increase** AP conduction velocity are:

1. **Increasing axon diameter** = less resistance (compromise between speed and space)
2. **Myelination** (but adds bulk)
3. **Higher temperature**

Nerve Fibre Type	Diameter	Myelinated	Conduction Speed	Features
Type A fibres	large diameter (4-20 µm)	**Yes**	Fast (>100 m/s)	Used in sensory and motor signalling essential to survival
Type B fibres	smaller diameter (2-4 µm)	**Yes**	Moderate (≈18 m/s)	
Type C fibres	small diameter (<2 µm)	**No**	Slow (≈1 m/s)	

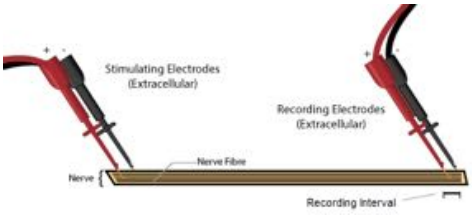
Understand the concept of summation and describe the differences between temporal and spatial summation.

Two or more *sub-threshold* graded potentials can combine to generate an action potential - **summation**

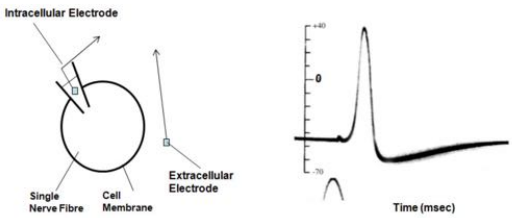


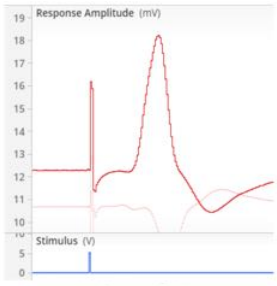
Draw a representative action potential trace

Extracellular recording – measures summed electrical activity in whole nerve (*compound action potential*)

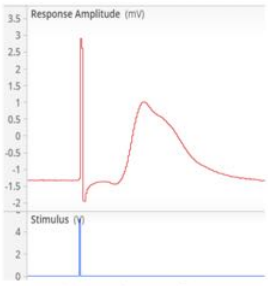


Intracellular recording – measures transmembrane potential for an AP of a single axon at a particular location





Biphasic CAP



Monophasic CAP

List the cells and cell groups found in the CNS and PNS and relate structure to function

Cell.	Classification.	Location.	Shape/Structure	Function.
Alpha (lower) **Motor Neuron.**	Neuron.	PNS, body in the ventral horn of the spinal cord.		**Motor**: activates skeletal muscle.
Somatic Sensory Neuron.	Neuron.	PNS, body in the DRG.		**Sensory** → PTTP
Postganglionic Autonomic Motor Neuron	Neuron.	PNS, body in the autonomic ganglion.		**Motor**: smooth muscle, cardiac muscle, glands.
Preganglionic Autonomic Motor Neuron	Neuron	PNS, body in the intermediate grey of parts of the spinal cord.		**Activates** the postganglionic atonomic motor neuron.
Interneuron.+	Neuron.	CNS, gray matter.		**Mediates** between neurons.
Projection Neuron.+	Neuron.	CNS, gray matter.		**Transfer information**.
Schwann Cell (oligodendrocytes of PNS)	Supporting	PNS, surrounds peripheral axons.	Elongated rounded cell with large curved nuclei	**Myelination** → improve conduction speed Single one can myelinate numerous axons
Satellite Cell.	Supporting	PNS, surrounds neuronal bodies in autonomic ganglia and somatic sensory	Small cells	**Mechanical**, metabolic.
Perineural Cell.	Supporting	PNS, forms the perineurium.	Flattened cells arrange in multiple layers	**Mechanical protection** Form perineurium in fascicle
Astroglia (astrocytes)	Supporting/ Glia	CNS, Fibrous (white matter) Mostly Protoplasmic (in grey matter)	Small to medium spherical cells	**Mechanical** protection → BBB Metabolic active → maintain homeostasis in ECF Scar tissue **repair**
Oligodendroglia.	Supporting/ Glia	CNS, mostly white matter near proximal end of axon projection	Small to medium cells	**Myelination**.
Microglia (derived from mononuclear cells)	Supporting/ Glia	Migratory in CNS and pass though cerebral capillary junction to leave and enter CNS freely	Small cells with elongated nuclei	**Macrophage**→ phagocytic and immunologic cell
Ependymal.	Supporting	CNS, ventricles, spinal canal, choroid plexus.	Small cuboidal cells with villi and cilia on apical surface	Lines the ventricles, helps **produce CSF**.
Meninges.	Misc/Other.	Surrounds brain and spinal cord.	**Tri-layered membrane** *(dura→arachnoid → pia)*	**Mechanical** protection and stabilize CNS (i.e. brain and spinal cord)
Pia mater	Misc/Other	Rest on basal lamina Inner fine shiny layer	Single layer of **flattened cells**	Adheres loosely to the surface of the CNS
Arachnoid	Misc/Other	Superficial to pia separated by subarachnoid space *(Middle semi-opaque layer)*	Multiple layers of **flattened cells** with **tight junctions**	Sub-arachnoid space contains CSF
Arachnoid villi	Misc/ Non-neuronal structure	In superior sagittal sinus formed from dura and endothelial lining	Arachnoid invaginates through holes in the dura	Site of most absorption of CSF back into the intravascular space (*i.e. venous system*)