Nervous System

Need for 2 communication systems

- Nervous system: Rapid detection and reaction especially towards dangerous situations due to fast speed at which nerve impulses are generated and transmitted
- Endocrine system: Ensures constant internal environment but is relatively slower as transmission of information is via chemical signals (hormones)

Resting Membrane Potential

- -70mV when not stimulated and maintained by:
  1. K^+ and Na^+ ion channels
     - More K^+ inside neuron, more Na^+ outside neuron
     - Ions able to move across membrane of the nerve cells by facilitated diffusion down the electrical chemical/concentration gradient through leak channels
     - More K^+ leak channels than Na^+ leak channels
       - Net +ve charge leaving the cell ⇒ Contributes to -ve electrical charge inside cell
  2. Na^+-K^+ pump
     - Ions actively transported against concentration gradient with the expenditure of ATP
     - 3 Na^+ pumped out for every 2 K^+ pumped in
  3. Fixed anions in cytoplasm of cell
     - Large negatively charged organic anions that cannot diffuse out of the cell due to their size (immobile)

Action Potential

- Characteristics
  - **<u>All or none</u>** event - Only triggered when threshold potential is reached
  - <u>Identical in magnitude and duration</u> independent of strength of stimulus
  - Does not diminish in strength down the axon
  - <u>Individual</u> events - Cannot add or interfere with one another due to refractory period
  - <u>Stronger stimulus</u> results in action potential being generated at a <u>higher frequency</u>
  - Generated only at <u>nodes of Ranvier</u> in myelinated neurons where voltage-gated Na^+ and K^+ channels are clustered
- Generation
  1. Resting State
     - Membrane at resting membrane potential, <u>-70mV</u>, in absence of stimulus
     - All voltage-gated Na^+ and K^+ channels are closed

2. Depolarisation
    - Action potential generated when stimulus arriving at first node of Ranvier is above threshold potential, -55mV
    - Causes opening of voltage-gated Na^+ channels
    - Influx of Na^+ into neuron, leading to further depolarisation of membrane for generation of action potential
3. Repolarisation
    - At the peak of action potential, +40mV, voltage-gated Na^+ channels will close while voltage-gated K^+ channels will open
    - Efflux of K^+ leads to repolarisation and restoration of resting membrane potential
4. Hyperpolarisation
    - When resting membrane potential is reached, K^+ ions continue to leave the axon as voltage-gated K^+ channels are slow to close, causing hyperpolarisation of membrane
    - Action potential undergoes refractory period where another action potential cannot be initiated as voltage-gated Na^+ channels need time to be reset following depolarisation of the membrane

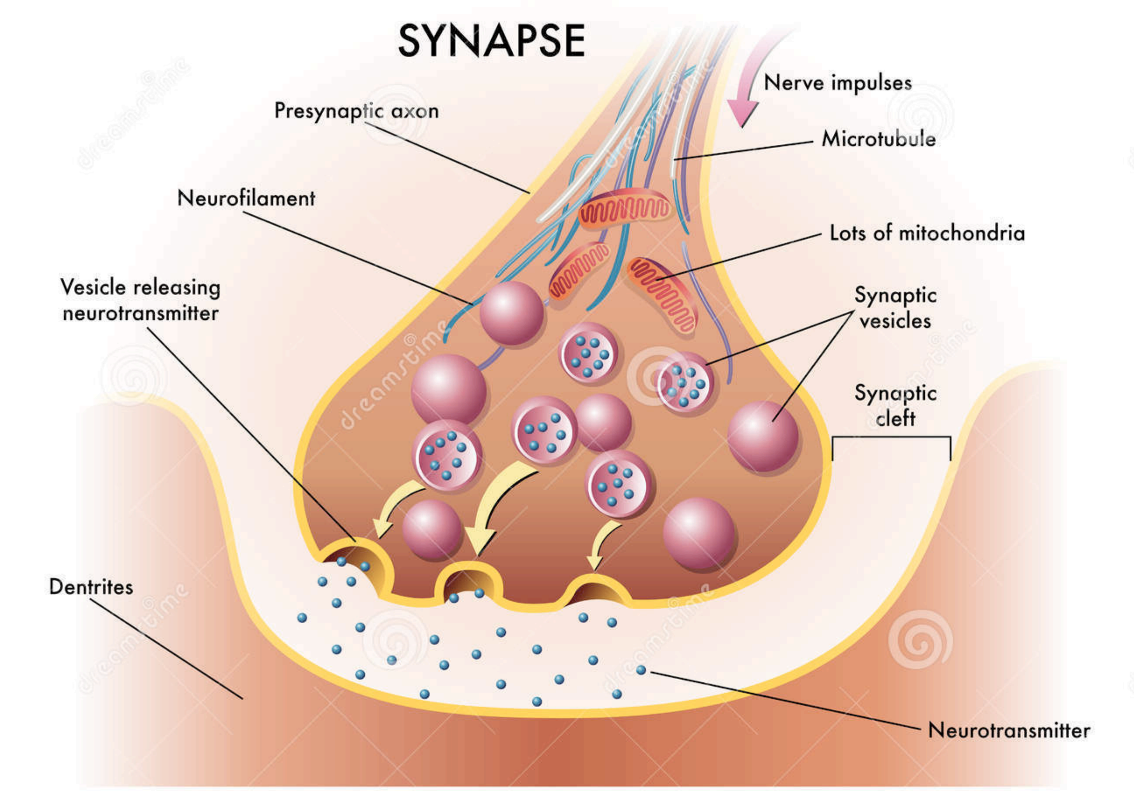
- Transmission along myelinated neuron
    - Influx of Na^+ creates local currents of Na^+ which diffuse sideways within the axoplasm down the electrochemical gradient
    - Diffusion of Na^+ down the axon causes depolarisation of membrane that will be above the threshold potential when it reaches the next node of Ranvier, causing the voltage-gated Na^+ channels in the next node to open and generate an action potential
    - Results in propagation of action potentials along the myelinated axon of the neuron
    - Although local currents of Na+ ions can travel upstream, the voltage-gated Na+ channel in the previous node of Ranvier would have been in the **refractory period** and will not respond to any stimulus
    - Hence, impulse travels only in one direction, down the axon
    - Myelin sheath made up of Schwann cells contains high level of lipids that wrap around the axon to act as an electrical insulator against the movement of Na+ and K+ ions
    - Action potential can only be generated at the nodes of Ranvier where there is a high density of voltage-gated Na+ and K+ channels and exposed to extracellular fluid
    - **Presence of myelin sheath speeds up the transmission of impulse by **saltatory conduction** as action potential jumps from node to node

Explain how decrease in proportion of neuron covered with myelin sheath can result in a decrease in the speed of conduction of nervous impulses

- Loss of myelin sheath ⇒ less insulation ⇒ reduced strength of local circuit reaching the

next node of Ranvier ⇒ Threshold potential not reached
- Reduced/No saltatory conduction
- Impulses must pass through greater amount of membrane, thus more time taken for opening and closing of voltage gated Na+ and K+ channels

Synapses



- Comprises
  - Presynaptic terminal/knob
    - Synaptic vesicles
      - Neurotransmitters (e.g. acetycholine)
    - Mitochondria
    - Microfilament
  - Postsynaptic knob/membrane
    - Specific ligand-gated ion channels
  - Synaptic cleft
- Transmission of synaptic impulse
  - When an action potential arrives, depolarising the presynaptic membrane, voltage-gated Ca^{2+} channels open
  - Influx of Ca^{2+} into **presynaptic knob** down its concentration gradient causes synaptic vesicles containing neurotransmitters to move towards and fuse with

    the presynaptic membrane
  - Neurotransmitters such as acetylcholine are released by **exocytosis** into synaptic cleft
  - Acetylcholine **diffuses** across the cleft and binds to ligand binding site of the ligand-gated Na^{+} channels on the postsynaptic membrane
  - Causing the ligand-gated Na^+ channels to open
  - Influx of Na^+ into the postsynaptic neuron causes the postsynaptic membrane to be depolarised
  - If threshold potential is reached, an action potential will be generated in the postsynaptic neuron
- End of transmission
  - Neurotransmitter is released from the receptors and the channels close
  - Synaptic transmission ends when the neurotransmitters are taken up by the presynaptic terminal/another cell or is degraded by an enzyme
    - e.g. Acetylcholine is degraded by enzyme acetylcholinesterase found within the synaptic cleft to acetic acid and choline
    - Choline is actively taken back into presynaptic terminal where it is combined with acetyl CoA to reform acetylcholine
- Slower than nerve impulse along axon due to:
  - Diffusion of neurotransmitters across synaptic cleft being slower than rapid saltatory conduction
    - Since diffusion of neurotransmitters is driven only by concentration gradient whereas movement of Na^+ is driven by both concentration gradient as well electrostatic attraction within axoplasm
  - Movement of synaptic vesicles towards presynaptic membrane to release neurotransmitters via exocytosis
  - Ca^{2+} influx into presynaptic knob
  - Combined time involved in all above steps

Ca^{2+}

- Low Ca^{2+} concentration in presynaptic terminal compared to extracellular fluid
- When an action potential arrives, depolarising the presynaptic membrane, voltage-gated Ca^{2+} channels open
- Influx of Ca^{2+} into presynaptic knob down its concentration gradient causes synaptic vesicles containing neurotransmitters to move towards and fuse with the presynaptic membrane
- Neurotransmitters such as acetylcholine are released by exocytosis into synaptic cleft
- Acetylcholine diffuses across the cleft and binds to ligand binding site, which it is complementary to, of the ligand-gated Na^+ channels on the postsynaptic membrane
- Causing the Na^+ channels to open
- Influx of Na^+ into the postsynaptic neuron causes the postsynaptic membrane to be depolarised
- Ca^{2+} removed from cytoplasm out of the cell by Ca^{2+} ion pump via active transport to

ensure synaptic transmission is not continuous

Transmission of impulse in one direction

- Refractory Period
  - Transmission of nerve impulse is only down the axon
  - Na^+ influx during generation of an action potential creates local currents of Na^+ which diffuse sideways in both directions within the axoplasm down the electrochemical gradient
  - However, once a region of the nerve fibre has been depolarised, it enters into a refractory period during which it cannot be excited and hence, will not respond to any stimulus
  - On the other hand, the region ahead can be depolarised, thus action potential can only travel in that direction
- Chemical Synapse
  - Synaptic vesicles and Ca^{2+} ion channels only found in the presynaptic knob ⇒ Neurotransmitters only found on presynaptic knob
  - Receptors/ligand-gated ion channel for acetylcholine are only found on the postsynaptic membrane
  - Movement of neurotransmitter in one direction from presynaptic membrane across synaptic cleft to postsynaptic membrane

Point of Comparison	Endocrine System	Nervous System
Nature of information	Chemical signals (hormones) are circulated throughout the body	Electrical signals within neuron and chemical signals (neurotransmitters) across synapses
Mode of transmission	Endocrine glands secrete hormones directly into bloodstream where they are carried to the target organ	Transmission is via a system of neurons that branch throughout the body
Speed of transmission and response time	Slow transmission (mins to days to occur)	Rapid transmission (up to 100m/s)
Duration of response	Long-term changes/responses	Short-term effects

Nature of response	Response is usually widespread/systemic	Response is often very localised
Specificity of pathway	Non-specific hormones are transported by blood throughout body with specific targets	Pathway is specific made up of specific interconnecting neurons
Complexity	Less structurally complex; Effectors are well supported by circulatory system and are regulated separately	More structurally complex; Complicated interconnecting network of neurons that allows for integration of vast amount of information in order to elicit a response

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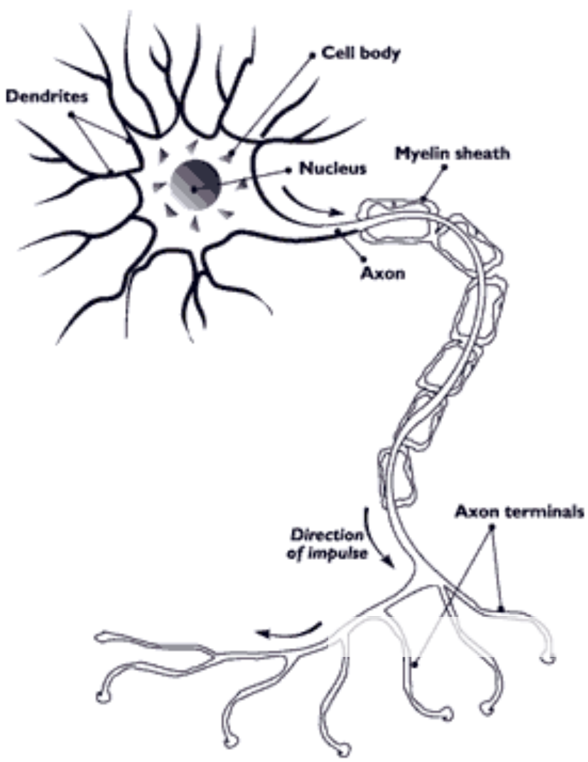
Structure of a Neuron



- Cell body
    - Contains Nucleus
    - Location of metabolic activities (e.g. synthesis of membrane, neurotransmitter)

- Abundance of RER, Golgi apparatus, mitochondria
- Dendri**T**e (**T**o cell body)
  - Receives electrochemical stimulation from other neurons and conduct it towards cell body
  - Highly branched
- **A**xon (**A**way from cell body)
  - Long single projection
  - Conducts impulses away from cell body
  - Axoplasm (fluid in the axon)
  - Terminates at synaptic knobs/axon terminals
  - Capable of propogating action potential (electrical impulses)
- Myelin Sheath
  - Made of Schwann cells
  - High lipid content
    - Acts as an electrical insulation, preventing movement of K^+ and Na^+ ions across the cell membrane along the axon
  - Action potential can only be generated at Nodes of Ranvier where there are high density of voltage-gated K^+ and Na^+ channels and neuron membrane is exposed to the extracellular fluid
  - Action potential jumps from node to node, enabling impulses to spread by saltatory conduction along the axon, speeding up impulse transmission
- Nodes of Ranvier
  - Exposed regions along the axon where myelin sheath is absent

Structure	**Function**
Numerous dendrites	Neuron can communicate with many other neurons
Axon is long	Enables transmission of impulses over long distance
Axon has a wide diameter	Increases the speed of conduction of a nerve impulse
Permeability of plasma membrane of neuron can be altered by a stimulus	Voltage-gated Na^+ channels open in response to stimulus results in depolarisation while opening of voltage-gate K^+ channels results in repolarisation to resting potential. Action potential produced can be propogated along the neuron

Presence of myelin sheath along axon	Increase speed of conduction of impulse along axon. Local circuits produced at one node of Ranvier travels to another node with sufficient stimulus to trigger another action potential. (Saltatory conduction)
Membranes at nodes of Ranvier have numerous voltage-gated ion channels	Allows for regeneration and transmission of an action potential along a myelinated neuron
The membranes at the nodes of Ranvier have sodium potassium pumps	Na-K pumps actively pump the sodium and potassium ions against their respective concentration gradients to restore the unequal ion concentration distribution across the membrane of the neuron so that another action potential can be generated
Presence of synaptic vesicles in synaptic knob	Synaptic vesicles contain neurotransmitters for synaptic transmission
Presence of numerous mitochondria in the axoplasm and at synaptic knobs	ATP produced by mitochondria is needed for impulse transmission along the axon as Na-K pumps require energy. ATP is needed at synaptic knobs to synthesise neurotransmitters, actively pump out Ca^{2+} ions and for exocytosis that release neurotransmitters to synaptic cleft.

Membrane potential = Difference in electrical charge across the plasma membrane of a cell due to the unequal distribution of ions inside and outside the cell (cytoplasmic side wrt extracellular side)

- Maintained by hydrophobic core of the phospholipid bilayer