ANAT2010

Concepts of Neuroanatomy (I)

S2 2018

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ANAT2010 Lecture 2: The Neuron

- *Composition of the nervous system*

What is a 'nervous system'?

- An organized association of neurons and supporting cells (glia) with its own blood supply (endothelial cells)

1. Neurons
    - Main signaling unit in the nervous system – excitable cells
2. Glia

    10x more gila cells than neurons
    - Macroglial cells – astrocytes and oligodendrocytes – historically thought to have solely a supporting role to neurons, now known to be more than 'helpers'
    - Microglial cells – cells of the immune systems – invades from the bone marrow
3. Endothelial cells
    - Line blood vessels – front line of the blood supply to the nervous system, forming the blood brain barrier.

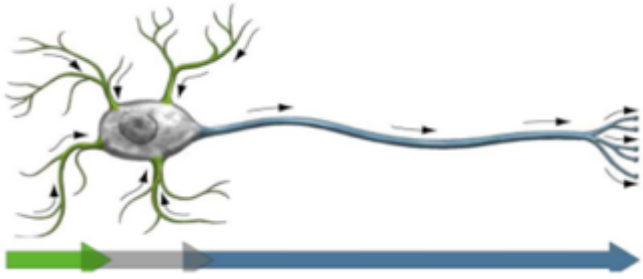
Core knowledge – the 'microanatomy' of a neuron- the cellular composition and morphology

What are neurons?

- The neuron is the structural and function unit responsible for the *transfer of information via electrical (ionic movement)* and *chemical communication.*

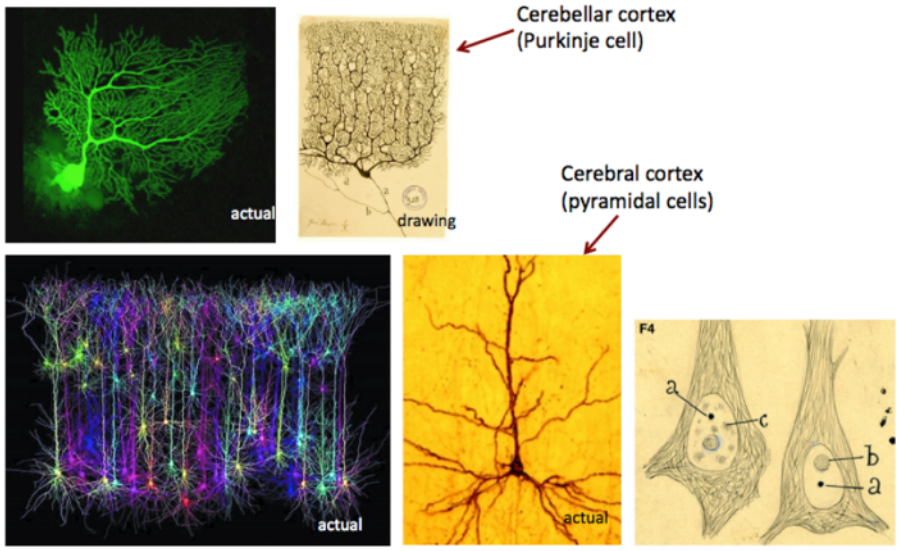
    1. Neurons are *excitable cells* –
    2. Capable of *transmitting* electrical events (action potentials) *to other cells*.

- Transmits signals to other excitable cells, in one direction, via specialized junctions (synapses)



Note: just a diagram, no neuron actually looks like this

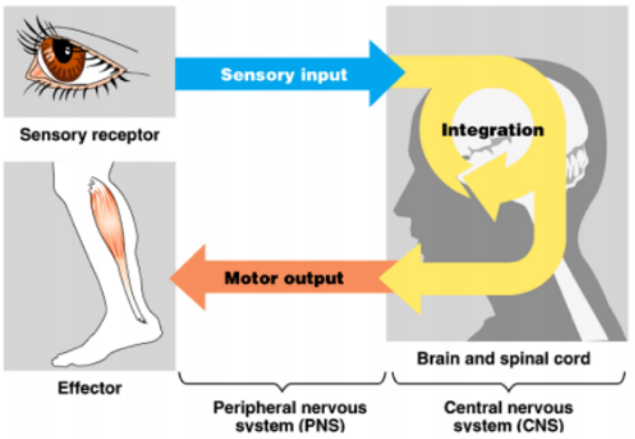
Neuronal shapes – 'morphology'



Fundamental concept and basics

- The nervous system can be broken down into three key functions –

Sensory input → Integration → Motor output (effectors)



Unidirectional signal of neurons

- Sensory systems (afferent – towards the brain)
    - Direction of signal is from the periphery (e.g. skin, joints) towards the nervous system (i.e. to central nervous system for interpretation/integration)
    - Trigger may be from outside the body e.g. visual world, or internal e.g. visceral receptors
    - **Transduced** *(turning signal into action potential)* by special sense organ/structure e.g. pressure receptor in skins, photoreceptor in retina

- Motor systems (efferent – away from the brain)
    - Direction of signal is towards the periphery, away from the nervous system i.e. towards:
        - Voluntary e.g. skeletal muscle
        - Involuntary signals e.g. to smooth muscle contraction, glandular action

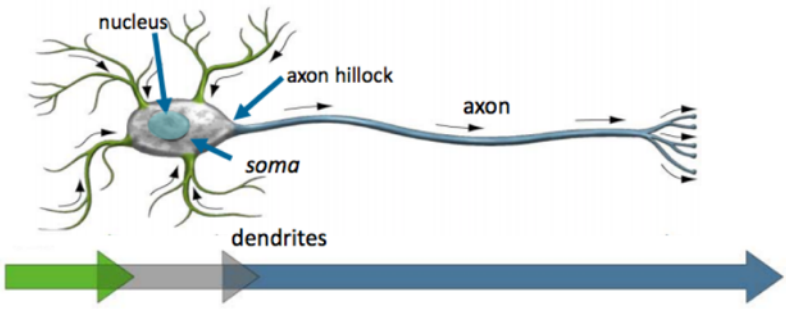
Direction of signal passage through a neuron is always the same; this is due to the microanatomy of the neuron:

Dendrite → Cell body → Axon

<u>The parts of a cell – with special reference to the neuron</u>

The neuronal microanatomy

1. Cell body (also called soma)
2. Dendrites – typically many shorter fibers extending from the cell body
3. Axon hillock – junction between soma and axon
4. Axon – typically a single long fiber extending from the cell body, may branch at terminals



Dendrites collect electrical signals (input)	Soma contains nucleus and organelles	Axon passes the signal on to dendrites of another neuron or to an effector such as a muscle cell

Note: We also use the terms 'fibre' or 'process' to refer to dendrites and axon. Generally used for other ramified (i.e. branched) cells like astrocytes and microglia.
The neuronal soma

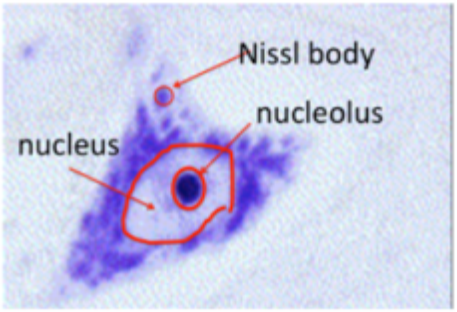
A typical neuron has 15-20µm diameter soma but can be as large as 50µm
Width of human hair approx. 20µm

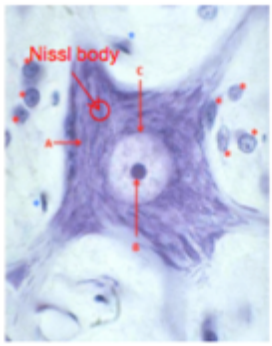
- A **nucleus,** containing **DNA** and **nucleolus,** an organelle actively engaged in ribosome synthesis, rich in RNA.

- Abundant **free ribosomes** and prominent **rough endoplasmic reticulum** (rER)
    - rER in neurons called '**Nissl bodies'**

- **Golgi apparatus** – for processing and packaging proteins into vesicles
- Abundant **mitochondria** – site of oxidative metabolism

Note: neurons have massive protein production and very high metabolic activity (high amounts of oxygen and blood flow).





Rough endoplasmic reticulum (rER) – aka. Nissl bodies

- Most abundant organelle in the neuronal soma; useful in identifying neurons
- Reflects the very high level of protein synthesis in neurons
  e.g. Enzymes for neurotransmitters

Neuronal cytoskeleton

Protein composition:

- Neurofilament: intermediate filament class; supports the shape of neurons
- Microtubules: composed of tubulin subunits
- Actin filaments: 'microfilaments'

General function –

- Provide structural support, support movement of proteins and organelles along axons, contractile properties such as in growth cone extension and dendritic spine formation.

Axon Hillock

- Plays essential role in integration and transmission of signals

The action potential is usually generated at the axon hillock; *'decision point'*. Transmembrane protein barriers – actin filaments – block free diffusion of proteins from soma to axon.

Axon

Function:

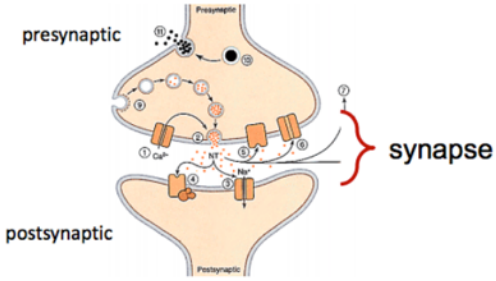
- Cytoplasmic extension of neuron
- Carries information from the soma to another neuron or effector cell

Features –

- Very thin, approx. 1 µm in most humans*
- May be very long, can be >1m in humans

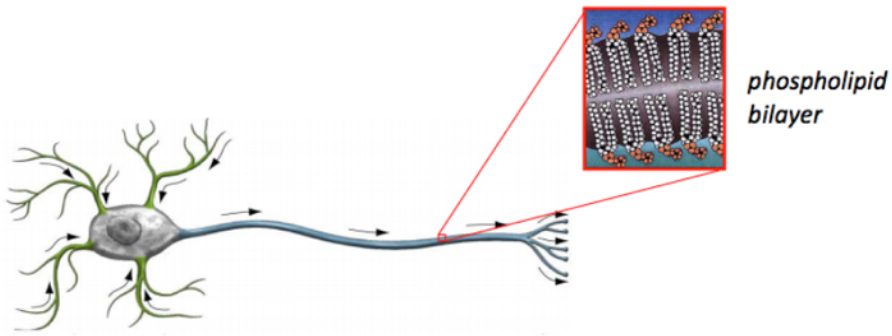
Synapse

- Specialized junctions between neurons
- Sites where neurons communication through chemical messengers called – neurotransmitters



Concept: *How do the structural components of the neuron support neuronal excitability, cell-cell communication and morphologic (structural) stability?*

<u>The neuronal membrane – supporting the action potential</u>

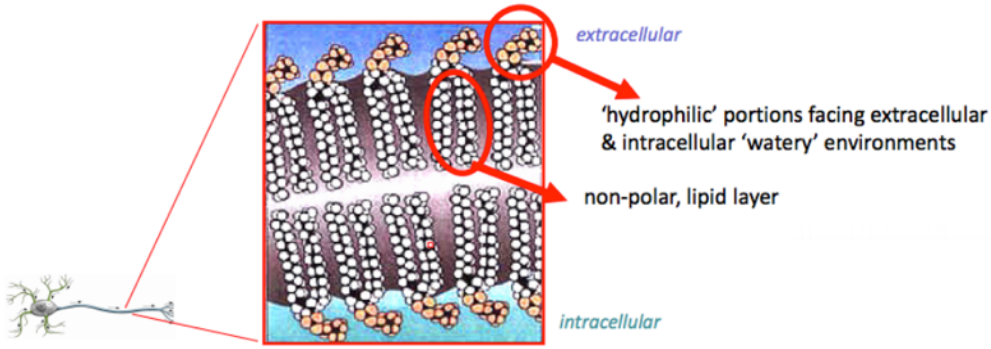


Composition: phospholipid bilayer and special embedded proteins like any other cell

- Ion channels and carrier protein ('pumps')
- i.e. controls what moves across the neuronal membrane, if not there, then there is no neuron transmission and therefore no life.

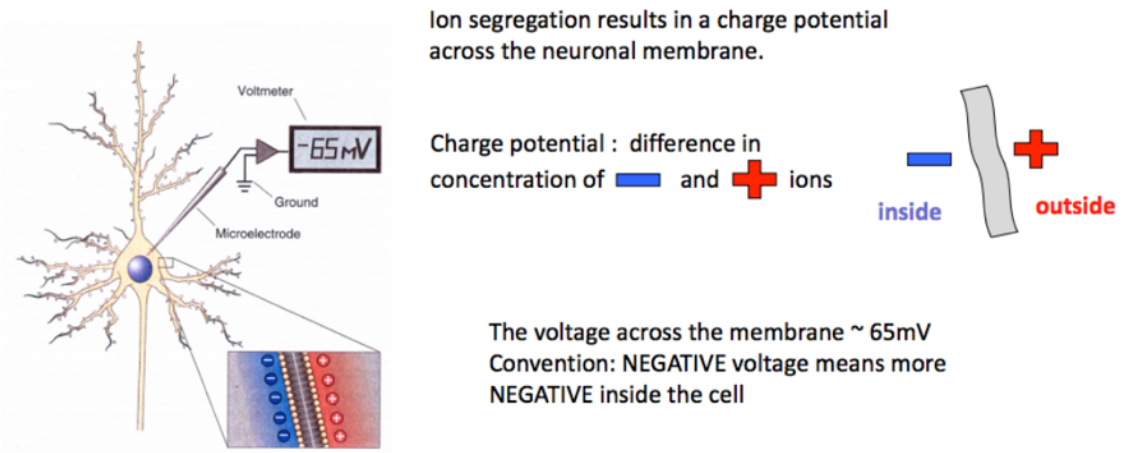
Function: preserves the highly-controlled internal environment necessary for **excitation (action potential)** and for transmission of the signal from the presynaptic to the postsynaptic neuron or muscle cell

Phospholipid bilayer – contains phosphate head and lipid tail

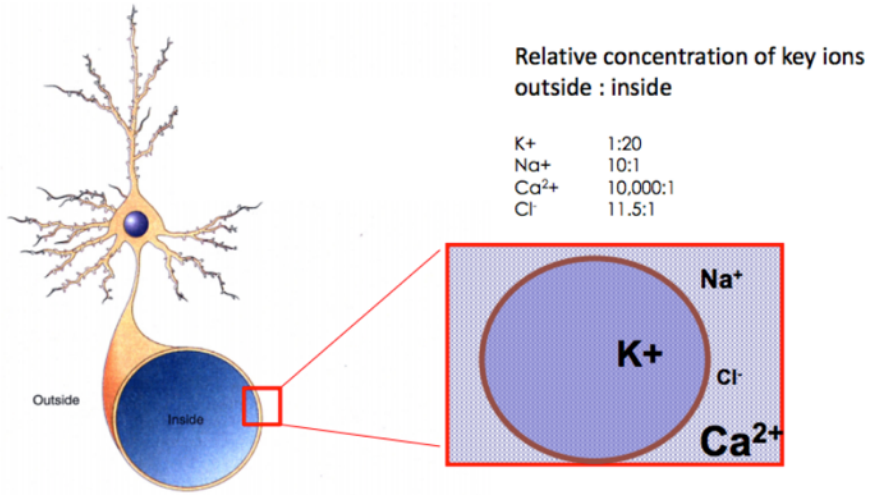


The neuronal membrane supports ion segregation

- ion segregation is essential for neuronal transmission i.e. keeps a certain concentration of ions inside and outside the cell – known as the membrane or charge potential.



Note: think of types of ion concentrations as sea water (i.e. remember the types of ions on each side of membrane).



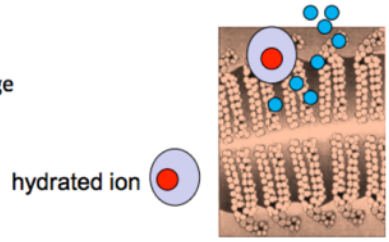
How does neuronal membrane segregate ions?

Note: passively = requires no energy in regulating ions

1. Passively – **lipid solubility.** Ions do no diffuse through the membrane

O, N, CO_2 & alcohols are lipid soluble - freely diffuse through the cell membrane.
H_2O is NOT lipid soluble, but diffuses through – it is small & has high kinetic energy

Ions *do not diffuse through the cell membrane*:
- ions become hydrated in the watery environment & become too large.
- polarities of the phosphate head repel the ion charge

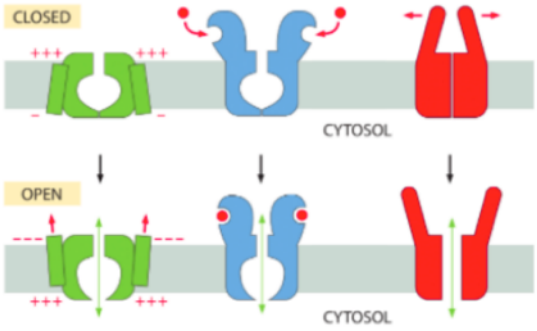


2. Passively – **ion channels***

Note: does require energy for production, removal, maintenance and insertion into the membrane.

- Non-gated ion channels (always open)
  - Selective for particular ions based on *charge and size.*

- Gated ion channels
  - Can be voltage-gated, ligand-gated, transaction gated**



Gate channels open and close depending on: charge, ligand binding, transduction

Transduction gates – such as mechanical, hair movement, stretch (e.g. stretch to open the gate and thus we can feel the stretch), light in sensory systems into opening the gate

Gated ion channels

- These are NOT exclusive to the nervous system or to neurons, but neurons use these in a very specific manner

Gating changes means essentially a change in the conformation state of the channel protein; when open, allows specific ions through; when closed, restricts ion movement.

What opens the gate?

- *Voltage gating* – conformational change with change in voltage – ionic difference across the membrane

- *Ligand-gating* – conformational change with binding of effector molecule in the nervous system, the main ligands for signal processing are neurotransmitters

- *Transduction-gating* – as above

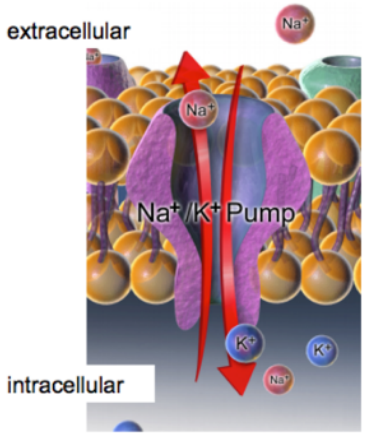
3. Actively: carrier proteins – 'pumps'

Note: Active transport – requires large amount of energy (ATP) – very expensive for the brain.

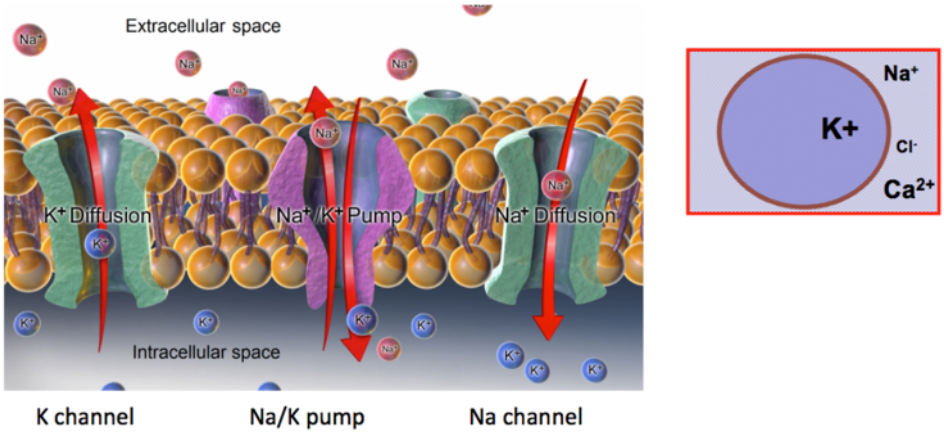
- Transport ions against the gradient – from low to high concentration; ionically uphill

- *Requires ATP:*
    - This segregation of ions creates 'potential' = voltage difference
    - Na+/K+ pump maintains the neuronal resting potential (approx. 65mV) to allow excitability.

  i.e. Maintains the resting potential to permit the action potential.



Key channels and pumps for maintaining the membrane potential: resting and action potentials

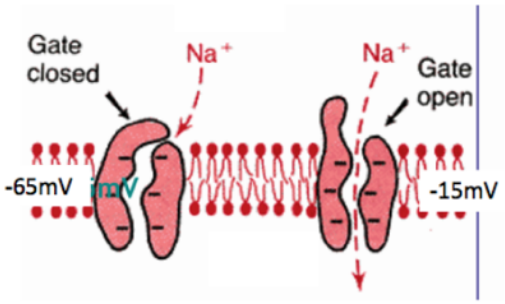


The action potentials: Voltage-gated Na^+ and K^+ channels

Na^+ channel

- Na^+ flows INTO the cell

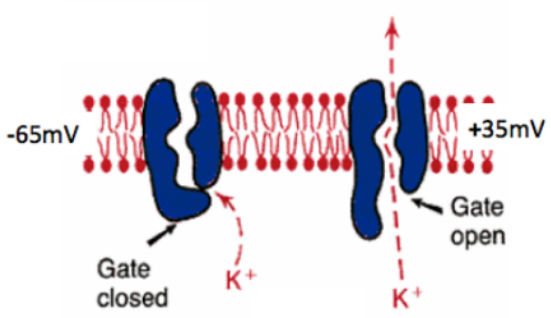
- Closed at resting potential (65mV)
- Begin opening between -65mV and -40mV to pump the sodium ions into the cell. Fully open at -15mV. Closed at +35mV.



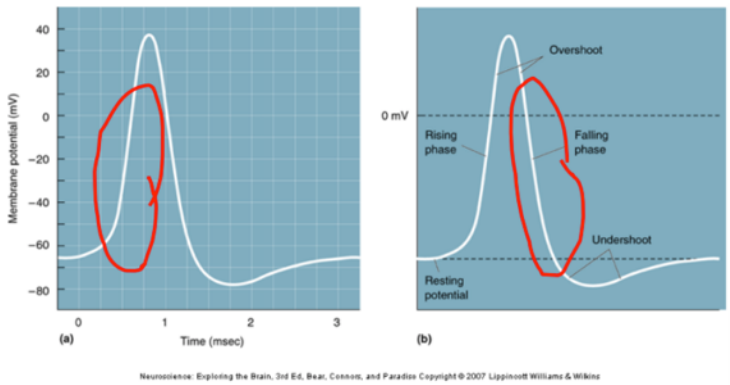
K^+ channel

- K^+ flows OUT of cell.

- Closed at resting potential (65mV). Begin to open at +30 to 35mV to allow potassium ions to flow out of the cell – approx. when the sodium gates shut. Close at resting potential (-65mV).



Gated ion channels & the action potential



Rising phase: Na+ channels open

inside of cell becomes more positive

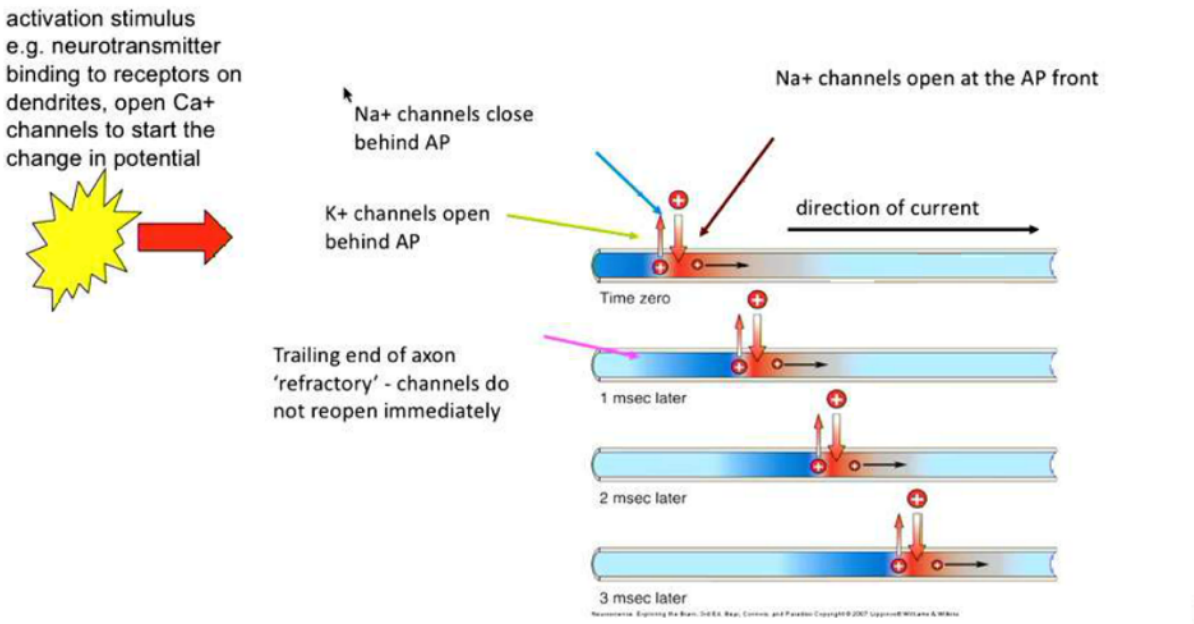
Falling phase: K+ channels open

inside of cell becomes less positive, returns to negative

Neuroscience. Exploring the Brain:

***Concept**: How does the arrangement of structural components in the neuron (the neuronal microanatomy) maintain the neuronal membrane potential & support the action potential?*

<u>Unidirectional signal – the action potential</u>



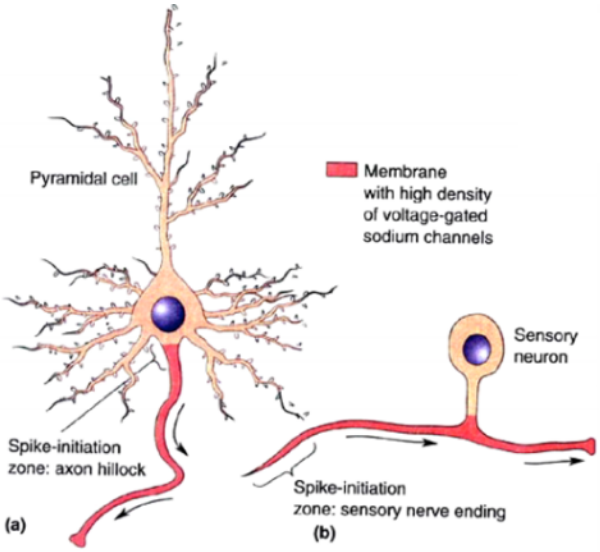
Note: stimulus causing Ca2+ channels to change the potential, making it more and more positive. Na+ channels will open to pump ions into the cell until it reaches threshold and snaps shut. Then the K+ channels open and pump ions out of the cell, again until the threshold is reach – continuing down the axon.

How does the microanatomy of the neuron support the unidirectional signal?

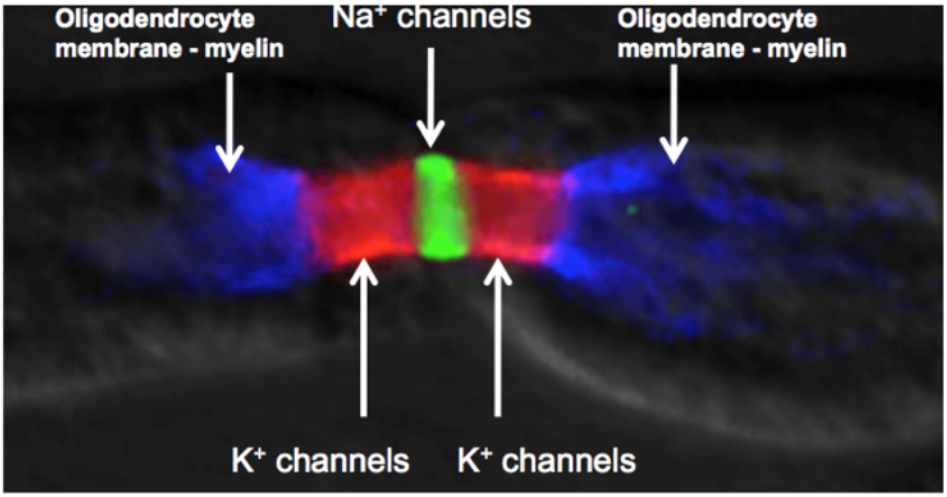
Different regions of the neuronal cell have different densities of the voltage- and ligand-gated channels.

- There is a high density of ligand-channels at the 'input' end of the cells (dendrites) – which respond to ligand - chemical input – neurotransmitters
- At the axon hillock and axon, there is a high density of voltage-gated ion channels – generating and conducting the action potential.

Different types of neurons have difference in location and density of channels expressed in their membranes.



e.g. sensory neurons for sour are just hydrogen ions flowing into the neurons, kick starting the action potential.



Note: 'nodes' to increase the speed of transmission of the action potential along the axon