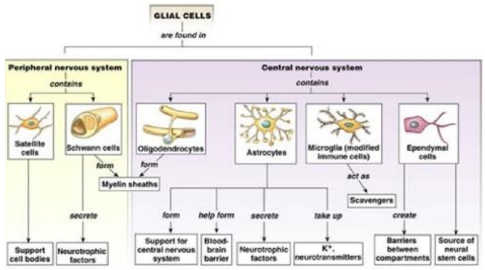
1: Intro to cellular components & neuronal circuits

Neurophysiology: the function of the nervous system

Neurons: excitable cells that are differentiated/characterised by function and phenotype (chemical, functional, structural)

Cell types



'Glia' meaning 'glue'.

- Cover the surface of neurons except the synapse
- Support the CNS
- Contact blood vessels and are an interface between neurons and blood
- Vastly outnumber neurons (was thought to be 10:1)

Glia are present in different types:

- Astrocytes (many functions)
- fibrous (among bundles of myelinated axons)
- protoplasmic (mostly in gray matter)
- Oligodendrocytes (myelination in CNS) and Schwann cells (PNS)
- radial glia (developmental, needed for neural migration)
- ependymal cells (line the ventricles, important for blood-brain barrier)
- microglia (immune cells that defend CNS, involved in injury response)

Astrocytes

- The ratio of astrocytes : neurons increases with increasing complexity of the nervous system.
- Astrocytes are packed around neurons – there's no 'empty space'.
- There can be overlap of astrocytes.
- Ca2+ levels in astrocytes are dynamic - due to changing Ca2+ level in environment.
- Mop up excess release of anything (e.g. K+)
- Gap junctions between astrocytes are formed by connexons - allowing buffering of excess K+ within extracellular space.

ECF ion homeostasis (through Spatial buffering)

- Synaptic activity results in extravasation of K^+
  – under physiological conditions several mM change
- For glia, under physiological conditions, membrane potential is largely determined by K^+
  – small changes in ECF K^+ produce changes in voltage
- Depolarization occurs wherever K^+ concentration changes
  – different from localized nature of synaptic inputs
  – Does not reflect excitation or inhibition, just altered activity.
- Current will flow along a potential gradient. Inward current (due to increased ECF K^+) induces local depolarization that will spread throughout the glial cell and, through gap junctions, to neighbouring glia.
  – At other regions K+ is released to the ECF
- In addition, astrocytes possess Na+/K+ ATPase, an anion pump and a Na+/K+ symporter to assist spatial buffering.
- Neuronal activity also induces considerable changes in ECF pH (increase).
- Astrocytes possess Na^+/H^+ exchanger & Na^+/HCO_3^- cotransporter
- bidirectional, electrogenic pump which is unique to glial cells in the nervous system.
  - Cl-/HCO3- exchanger
  - active H + ion extrusion mechanisms.

Responsive astrocytes

- Astrocytes respond to specific inputs via neurotransmitter receptors, including activation of intracellular calcium via IP3.
- Activation of neighbouring astrocytes occurs via gap junction communication

Blood vessel diameter & neural activity

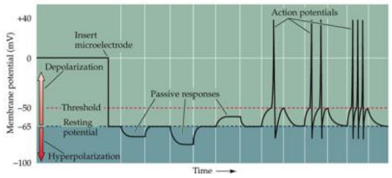
Whisker stimulation in mouse:

- Increase neural activity
- Increase in arterial diameter and blood flow

2: Resting membrane potential

<u>Membrane potential:</u> the electrical potential across the membrane of a cell
Resting membrane potential = -65mV
<u>Hyperpolarisation</u>: membrane potential goes more -ve

- Passive potentials respond to size of input:
  Larger hyperpolarisation = larger size of response



<u>Depolarisation</u>: membrane potential goes more +ve

- Larger depolarisation = larger size of response

Once depolarisation gets to a threshold, causes an <u>action potential</u>

- size of AP doesn't change regardless of depolarisation size (an all or nothing event)
- not size-dependent, but frequency-dependent
- At peak of action potential, it approaches the equilibrium potential for Na+ (due to Na+ channel opening).

Squid and other vertebrates have large axons which can be pinned by electrodes to measure the potential difference across the membrane.
Polarity means that with an ion like Na+ or Cl-, water molecules can form a cloud around it to balance the charge. (e.g. H+ of H2O face the Cl-)

<u>Principle #1:</u> An uneven distribution of ions leads to the development of a <u>concentration gradient</u>. When allowed to move freely within a solution, ions will move along their concentration gradient until equally distributed.
The lipid bilayer represents a barrier to diffusion of polar molecules.
Membrane resistance and capacitance

- Embedded in membranes are proteins that can allow movement of ions across membrane.
- Membrane of cell is so thin that there's still an ability for electrostatic interaction between positive and negative ions, or inhibition between like charges.
- Ions can concentrate themselves on one side of membrane and not the other.

<u>Principle #2:</u> Being charged, ions will also move along an <u>electrical potential gradient</u>.

- Movement of a charge is called <u>current</u> (I) measured in amps.
- Conventionally, positive current is in the direction of positive current flow.
  +ve charge is attracted to the cathode
- Current is dependent upon
  (a) the potential difference – the difference in charge between the positive and negative poles-measured in volts
  (b) the ability of charge to move in a particular substance-conductance (g) measured in siemens.
- Conductance is the movement of charge (the inverse of resistance)

<u>Principle #3:</u> <u>Equilibrium</u> is the point at which the concentration and electrical gradients balance, such that there is no NET movement of an ion.
Neurons have ionic concentration gradients across their membrane.
Mammalian neuron:

- $[K^+]_{inside} > [K^+]_{outside}$
- $[Na^+]_{outside} > [Na^+]_{inside}$
- $[Cl^-]_{outside} > [Cl^-]_{inside}$
- $[Ca^{2+}]_{outside} > [Ca^{2+}]_{inside}$

TABLE 2.1 Extracellular and Intracellular Ion Concentrations

Ion	Concentration (mM) Intracellular	Extracellular
Mammalian neuron		
Potassium (K^+)	140	5
Sodium (Na^+)	5–15	145
Chloride (Cl^-)	4–30	110
Calcium (Ca^{2+})	0.0001	1–2

<u>Ion transporters:</u>

- Actively move ions against concentration gradient
- Create ion concentration gradients

Two main classes:

1. ATPase pumps
2. Ion exchangers

<u>ATPase Pumps:</u> use energy to establish conc gradients across neuronal membrane
Around 70% of energy usage of brain is spent on Na/K+ ATPase

1. Na+ binds on intracellular side
2. ATP phosphorylates the ATPase
3. Conformational change, Na+ goes to other side and opens up bindng potential for K+
4. Dephosphorylation, restoration of original conformation

Electrogenic: 3 Na+ exit and 2 K+ enter, making the inside of the cell more -ve
a subunit: main engine