Mind, Brain & Behaviour 1
Behavioural Neuroscience

Neurons, glia and mechanisms of communication within the neuron

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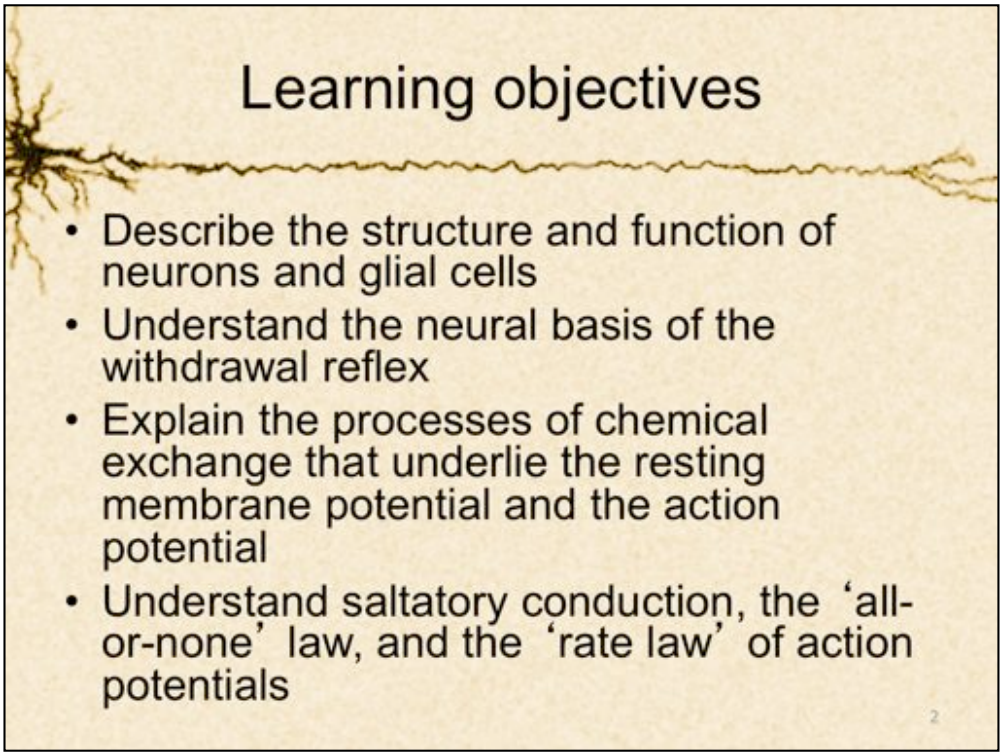
Learning objectives
• Describe the structure and function of neurons and glial cells
• Understand the neural basis of the withdrawal reflex
• Explain the processes of chemical exchange that underlie the resting membrane potential and the action potential
• Understand saltatory conduction, the 'all-or-none' law, and the 'rate law' of action potentials
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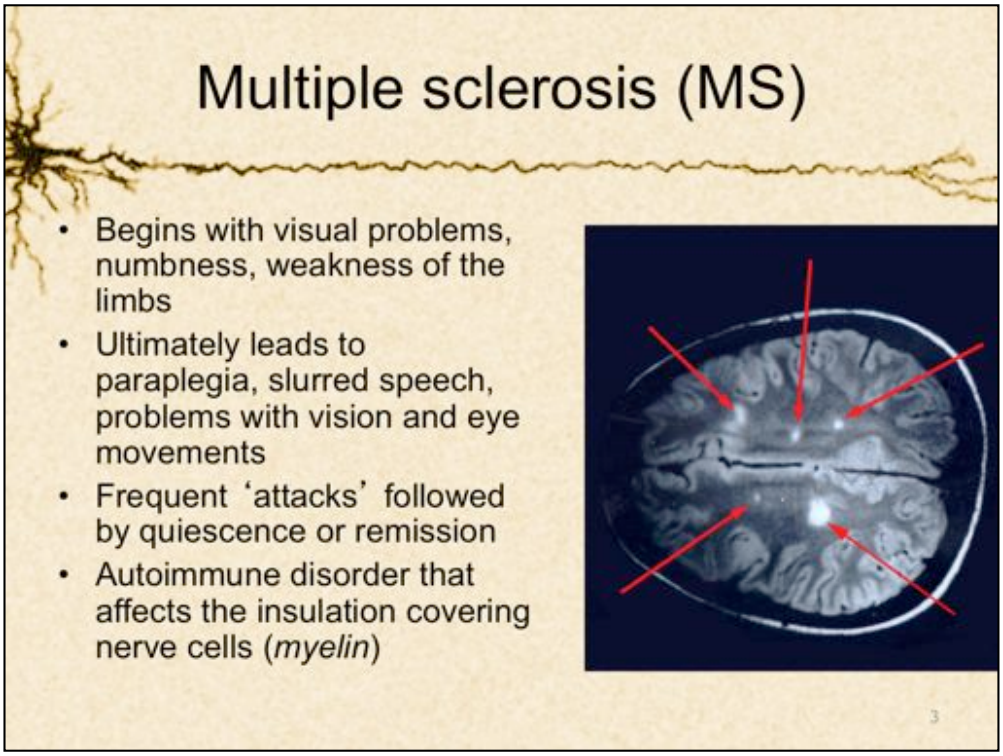
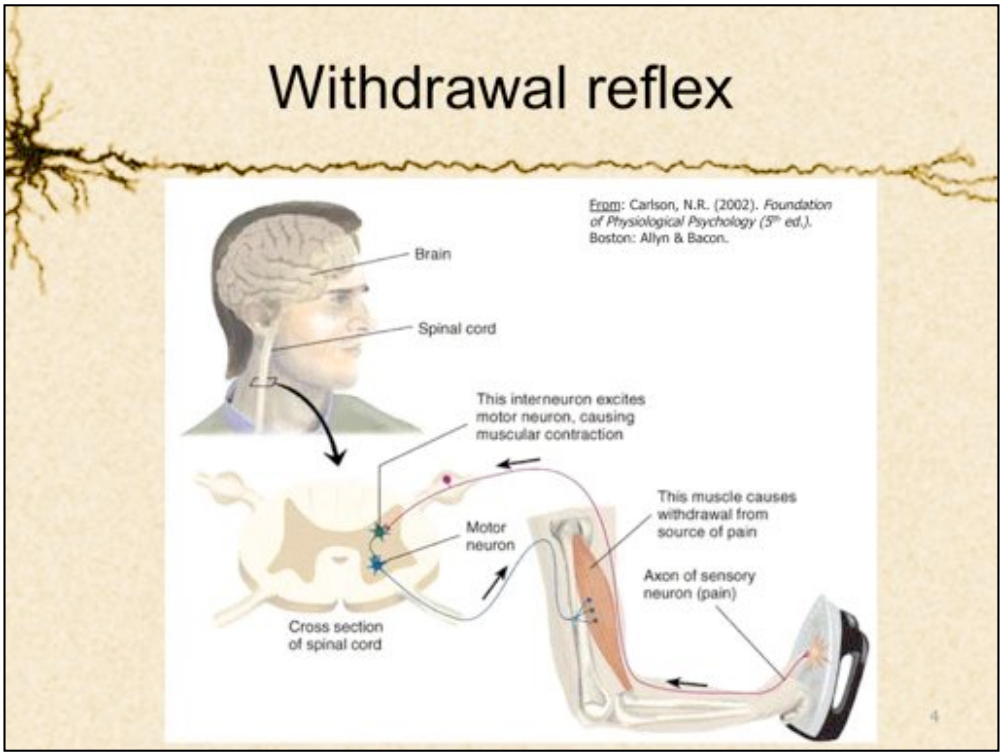


Multiple sclerosis (MS) is an acquired neurological disorder that attacks the insulating sheath (called **myelin**) that surrounds the axons of neurons.

Symptoms include visual impairment, problems with eye movements, numbness, slurred speech, and muscle weakness (eventually leading to paraplegia in many cases).

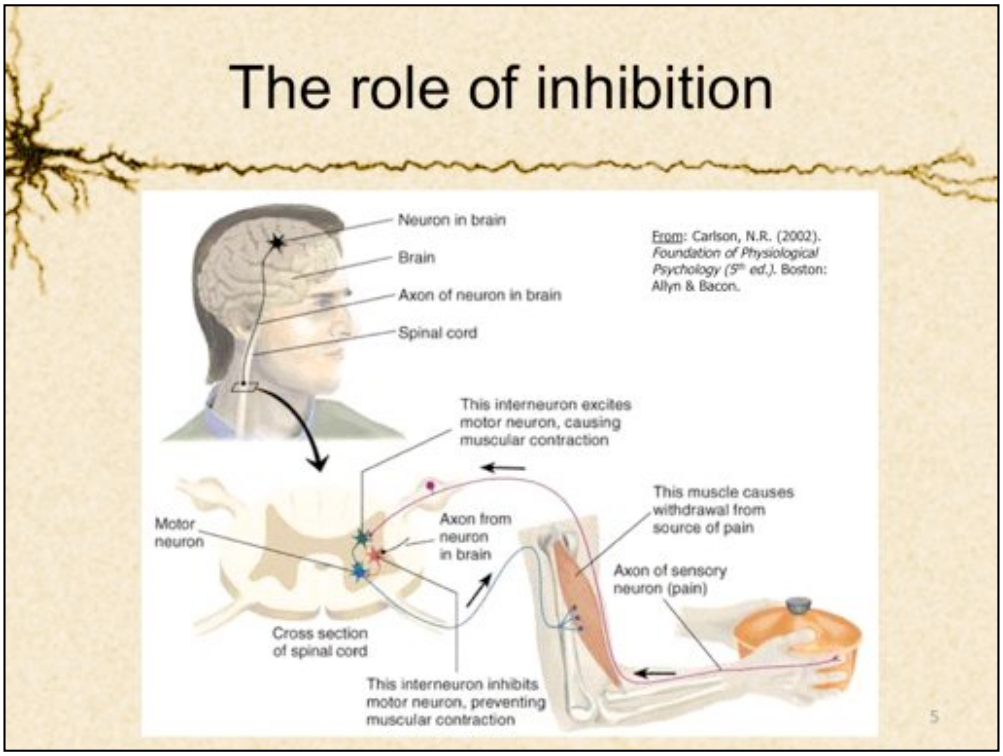
MS is characterised by occasional attacks (on average one every couple of years), in which symptoms worsen, punctuated by periods where the symptoms disappear or are less severe.

MS is an autoimmune disorder – the body's immune system selectively attacks the myelin surrounding the axons of neurons. The cause of MS is unknown, though some believe it is due to a virus contracted around the time of birth or during early childhood. It is more common in females than in males, and typically appears in people in their late 20s or 30s.



To understand the basics of neural communication, consider a simple reflex action: in this case the **withdrawal reflex** that occurs when we touch something that is very hot or otherwise painful.

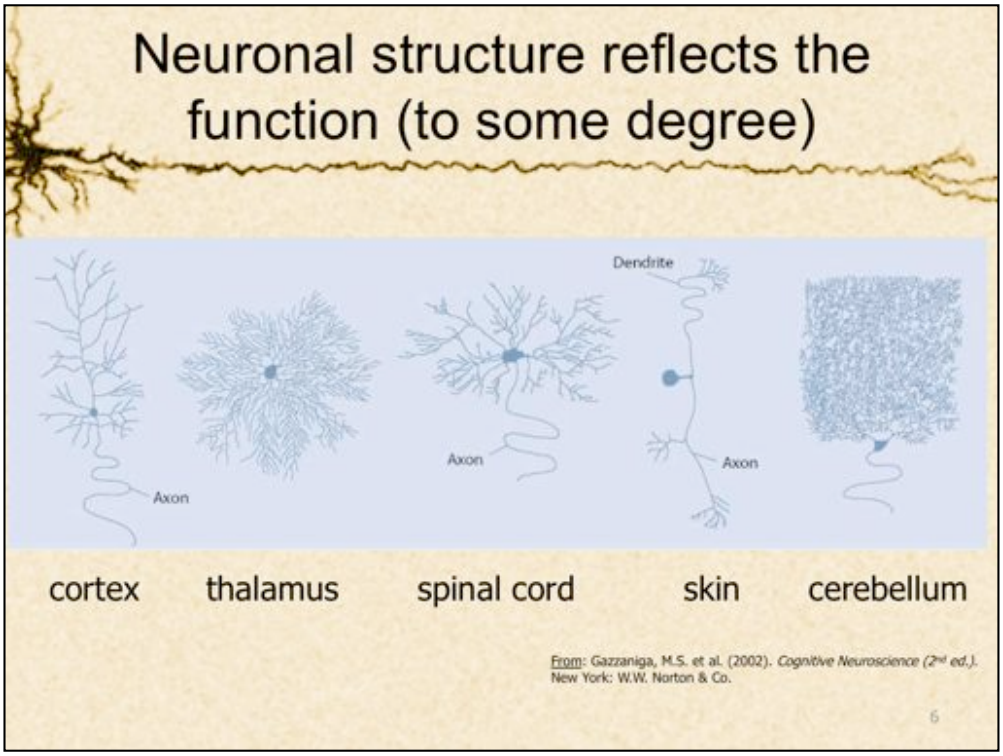
The dendrites of a sensory neuron (in this example located in the skin of the hand) respond to a noxious stimulus in the environment (a hot iron) → this signal is sent back along the axon to the terminal buttons, which are located in the spinal cord → here the terminal buttons release a neurotransmitter into the synapse, and this excites an interneuron, which resides within the spinal cord itself → the interneuron then sends a message down its axon, which in turn releases a neurotransmitter to excite the motor neuron → the axon of the motor neuron joins a nerve (a bundle of motor neurons) and travels to a muscle in the arm, causing the muscle to contract and pulling the hand away from the hot surface.



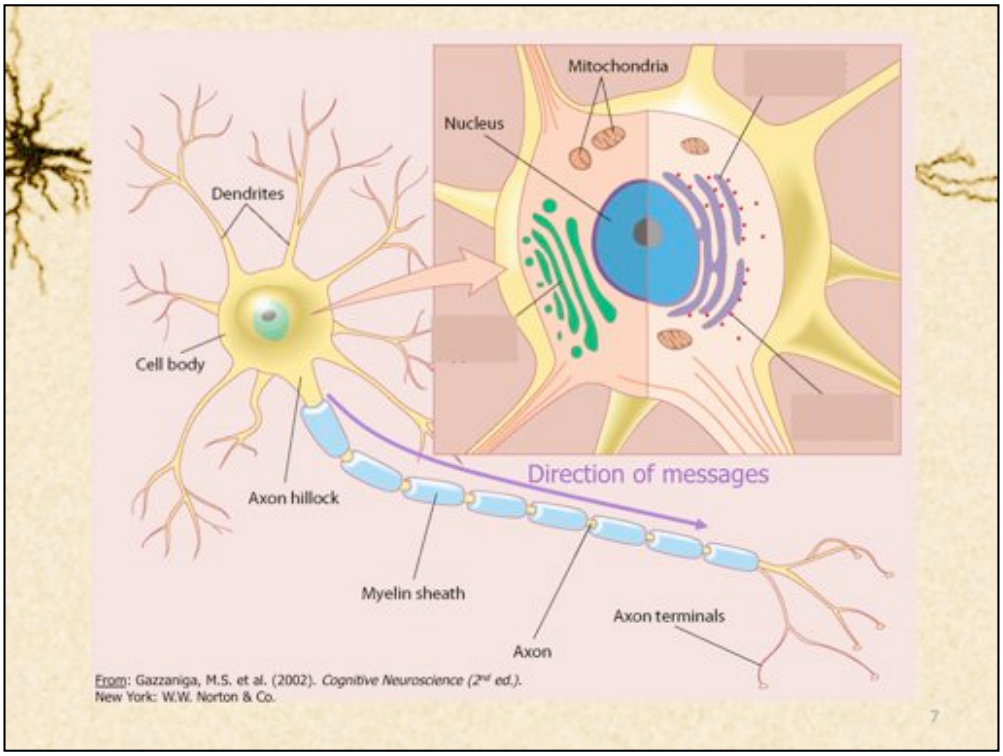
In the previous example, all the synaptic connections had **excitatory** effects. What is the role of **inhibition**? This can be illustrated by imagining that the noxious stimulus is produced by the surface of your mother's favourite casserole dish, which you have just removed from the oven. Now the heat makes you want to drop the dish, but you don't want to break it so you hang on and rush toward the table. How have you overcome the withdrawal reflex?

As illustrated in the previous slide, the tendency to want to drop the dish comes from excitatory synapses on motor neurons in the spinal cord. But this excitation can be counteracted by inhibition arising from another source: the brain. The brain contains complex circuits of neurons that represent the consequences of dropping the dish (embarrassment, expense, the loss of a good meal, your mother's anger, etc.); these circuits send information to the spinal cord to prevent you dropping the dish.

The relevant neuron in the brain sends a message along its axon to the spinal cord. Here it excites an **inhibitory interneuron**, which in turn releases an **inhibitory neurotransmitter**. This decreases the activity of the motor neuron, thus blocking the withdrawal reflex.



The shape and size of a neuron is related to its function. Neurons of similar architecture tend to be clustered together in the CNS, reflecting the functioning of that particular region.



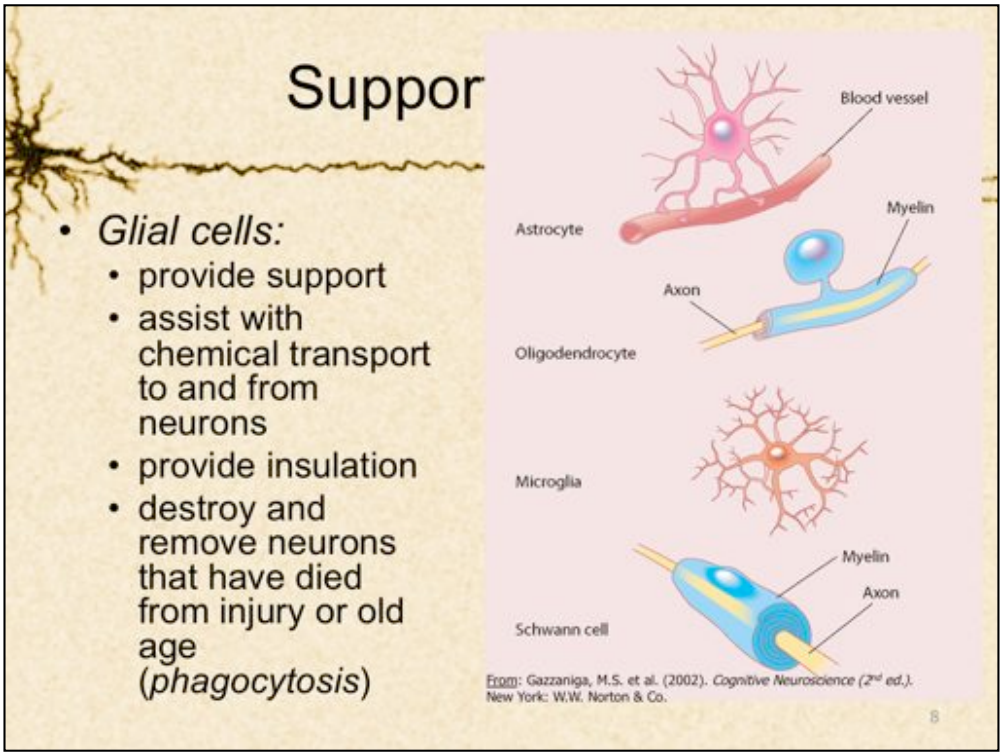
The **neuron** is the basic information-processing and information receiving unit of the nervous system. Neurons form complex networks within the nervous system, but they are not directly connected with one another; they are separated by a tiny gaps called **synapses**, across which chemicals called **neurotransmitters** are passed.

Neurons come in many different shapes and sizes. Almost all have four basic structures or regions:

1) **Cell body**– contains the nucleus (genetic material) and internal organelles necessary for cell maintenance.

2) **Dendrites** – the tree-like branches that allow neurons to communicate with one another. Dendrites receive information from other neurons.

3) **Axon** – a long, slender fibre that carries signals from the cell body. The signal carried by an axon is an **action potential**, which as we shall see later is a wave of electrical potential that begins at the cell body and travels down the axon to the terminal buttons.

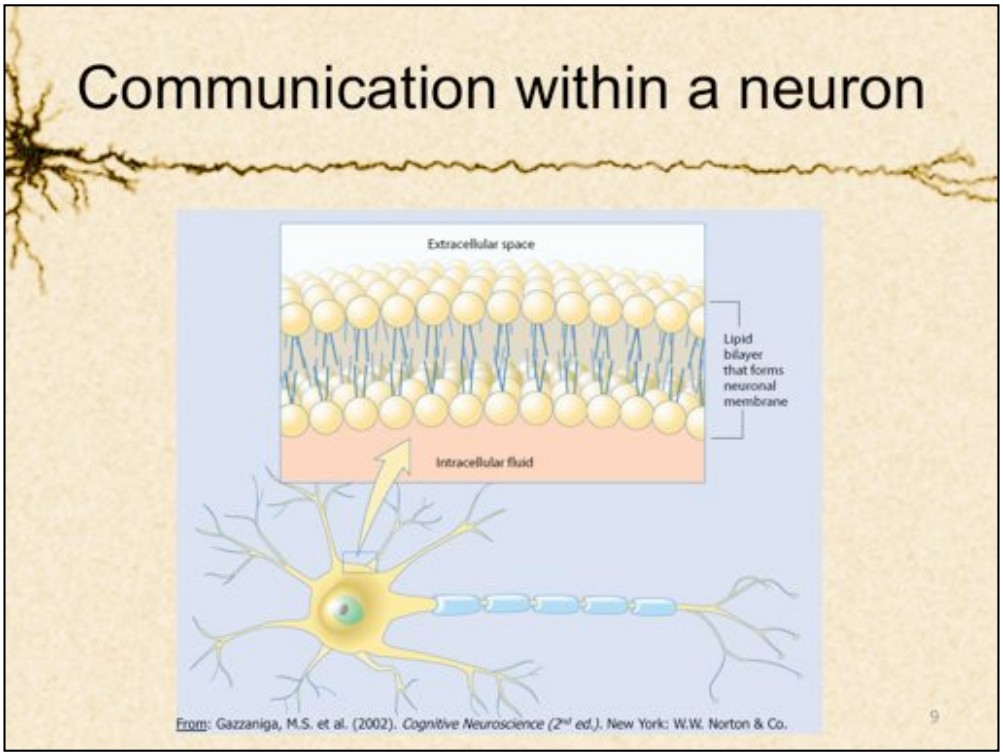


Neurons constitute only half the volume of the CNS; the other half is made up of various other cells, collectively known as **glial cells** (or **glia**), that play an important role in providing physical support for neurons and in supplying them with oxygen and nutrients.

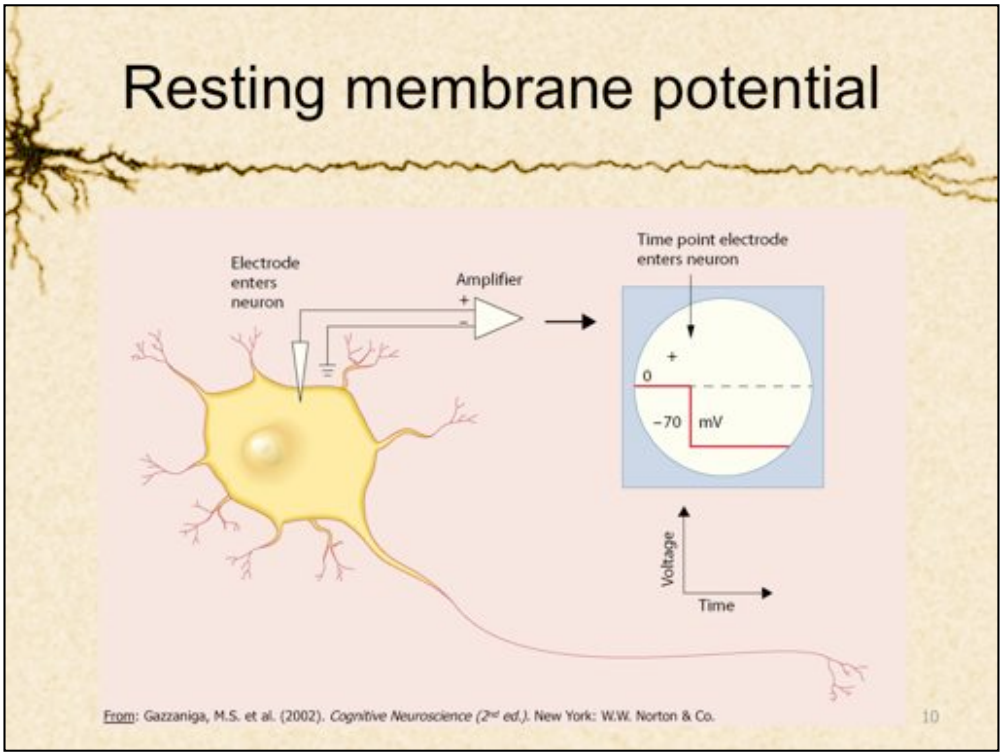
There are several types of glial cell:

Astrocytes provide physical support for neurons and also do housekeeping jobs (cleaning up waste, providing nutrients to neurons, maintaining the correct chemical composition of the **extracellular fluid** that surrounds neurons). Some astrocytes literally crawl around the CNS, cleaning away the debris from dead neurons, a process called **phagocytosis**. After removal of the dead neurons, other astrocytes will take their place, thus maintaining a supportive structure for nearby cells.

Oligodendrocytes also provide physical support to neurons, but most importantly they provide the insulating **myelin sheath** that surrounds the axon. This prevents unwanted cross-talk between neighbouring axons. Most, but not all, axons are myelinated.



The cell membrane of a neuron is composed of a double layer of lipid (fat) molecules, and contains complex protein molecules that regulate the entrance and exit of chemicals from the neuron. It keeps the fluid outside the cell (extracellular fluid) separated from that inside the cell (**intracellular fluid**). The cell membrane is critical for the transmission of information along the axon.

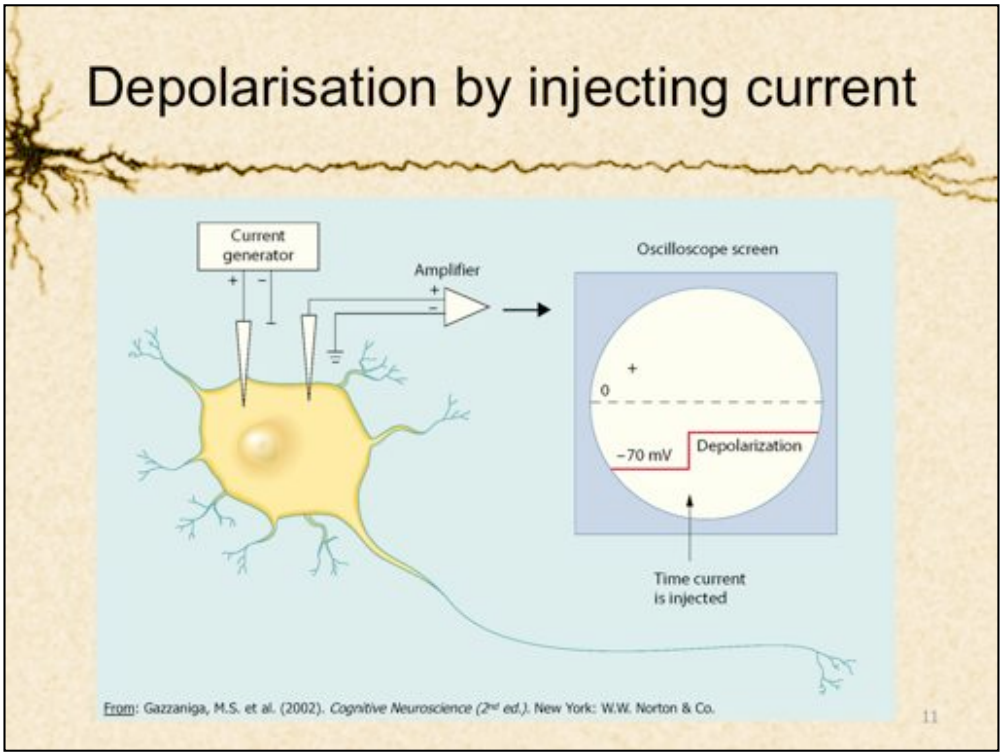


What is the nature of the signal transmitted by a neuron?

Basically it is an **electrical process** which involves movement across the axon membrane of electrically charged molecules called **ions**.

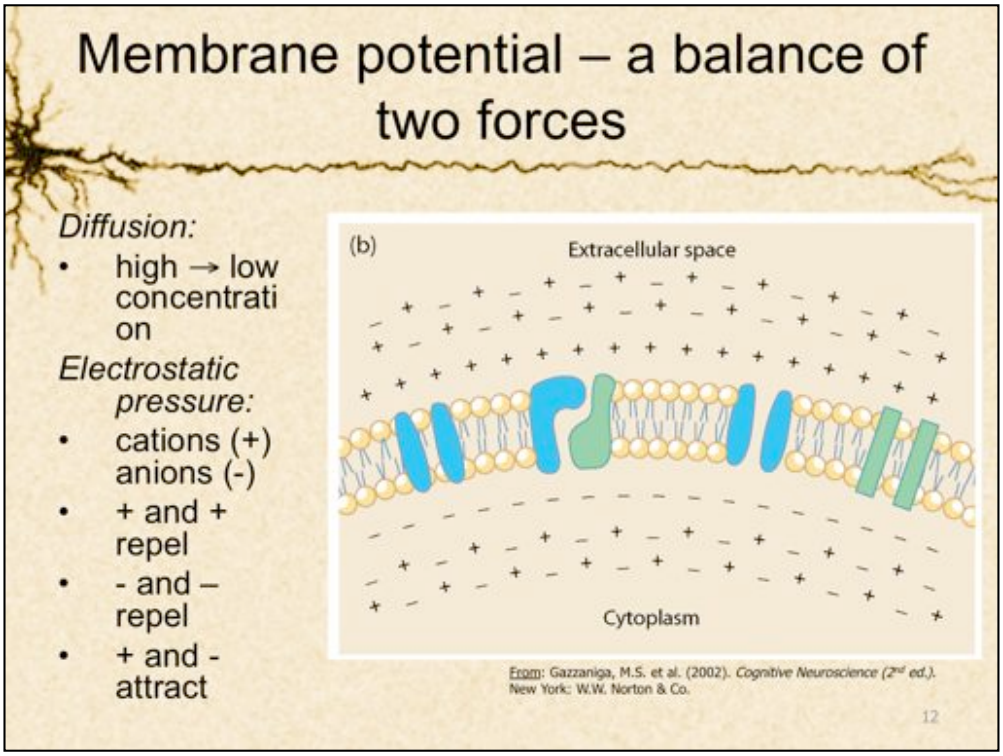
By inserting a very fine microelectrode (less than 1/1000th of a mm in diameter) into a neuron and recording the difference in electrical potential between the intracellular and extracellular fluid, it has been found that the inside of an axon is more **negatively charged** than the outside. This difference, known as the **resting membrane potential**, is about -70 millivolts (mV, a thousandth of a volt).

The message that is conducted down an axon involves a brief change in the membrane potential that sweeps rapidly along the axon from the cell body toward the terminal buttons.



It is possible to disturb the resting potential of a neuron by passing a current into it, via another electrode placed into the cell body. The inside of the neuron is negatively charged, so adding a positive electrical current through the electrode causes **depolarisation**.

A very rapid reversal (depolarisation) of the membrane potential of an axon is called an **action potential**. The action potential constitutes the basic message that is transmitted down an axon from the cell body to the terminal buttons.



How does an action potential arise naturally?

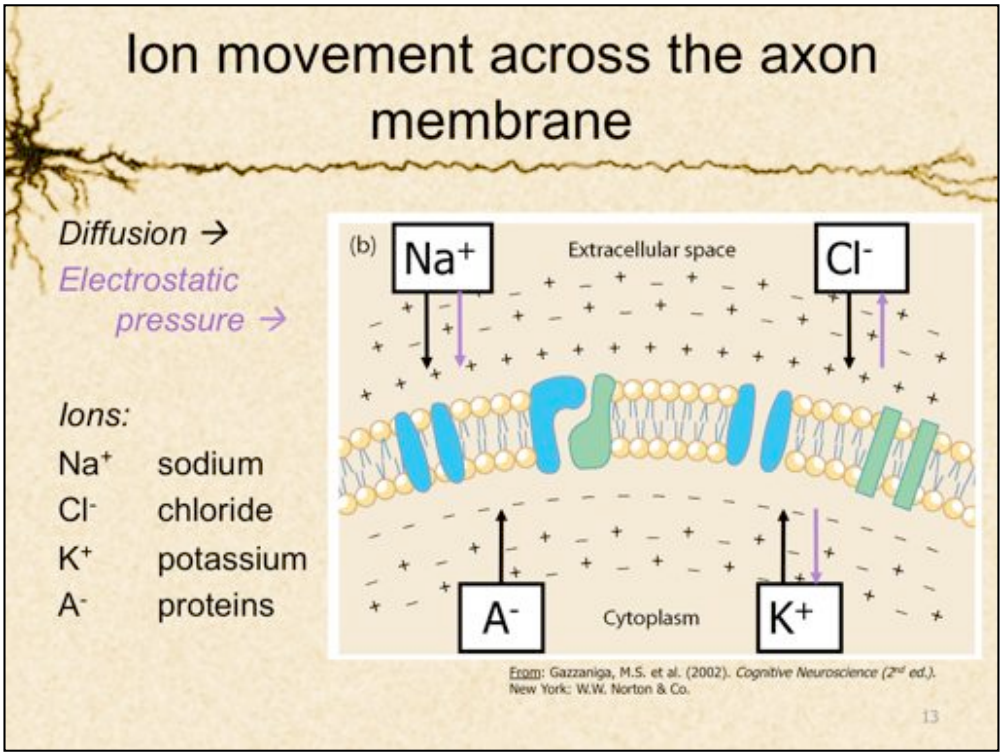
This is determined by the balance of positively and negatively charged ions inside and outside the neuron. There are two forces that are relevant:

1) **Diffusion** – when a soluble substance, such as sugar, is added to water, the molecules dissolve and distribute themselves from regions of high concentration to regions of low concentration. The process by which molecules distribute themselves evenly throughout a medium is called diffusion.

2) **Electrostatic pressure** – when some substances are added to water, they split into two parts, each with an opposing electrical charge. These charged particles are called ions. There are two types of ion:

Anion – negatively charged (a particle that has gained an electron)

Cation – positively charged (a particle that has lost an electron)

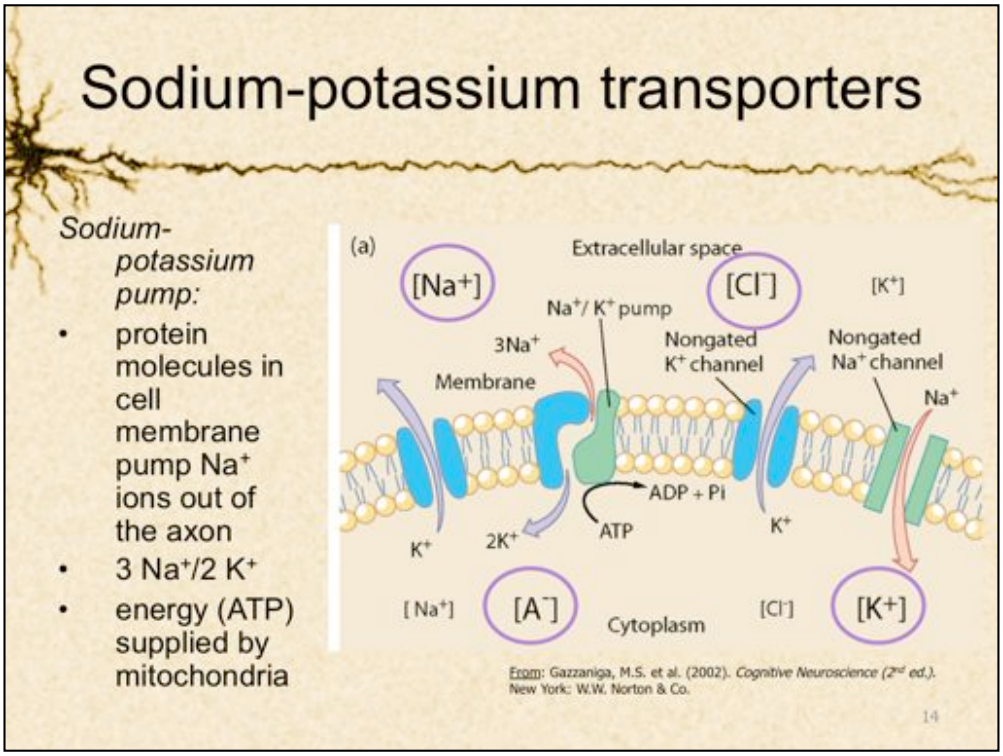


The forces of diffusion and electrostatic pressure determine the resting membrane potential of a neuron.

There are four ions that are crucial to the resting membrane potential, two with a positive charge (cations) and two with a negative charge (anions). These are: (1) **sodium** (Na^+); (2) **chloride** (Cl^-); (3) **potassium** (K^+); (4) **organic anions** (which are proteins, A^-).

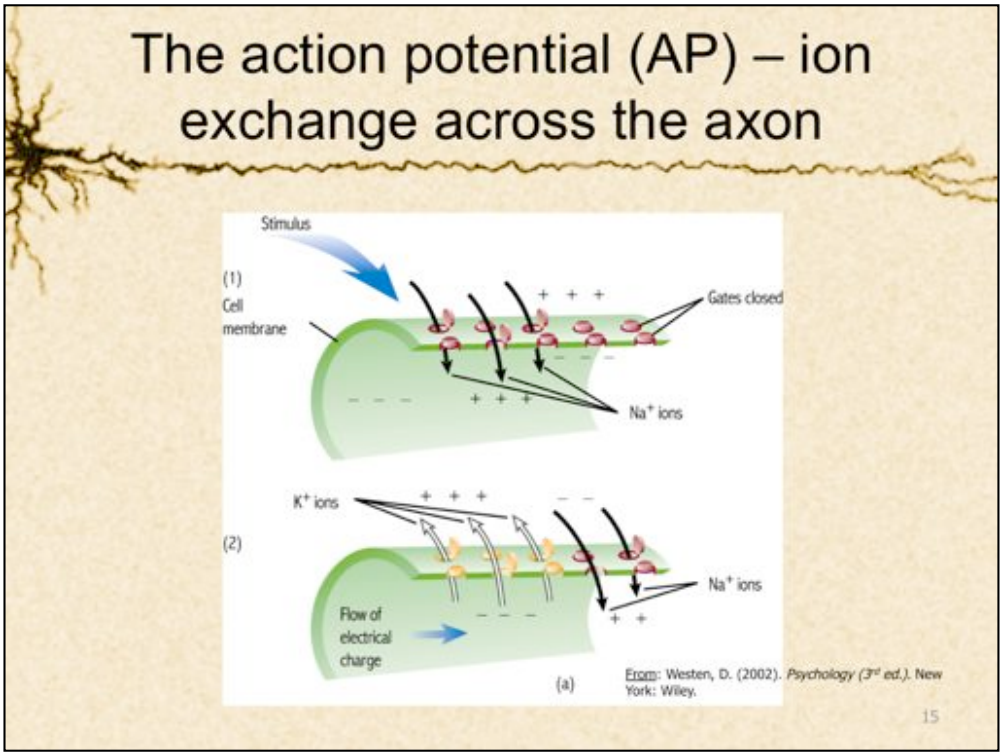
Although organic anions are found only inside the neuron (**intracellular**), the other three ions are found both inside and outside (**extracellular**). Crucially, sodium and chloride are in higher concentration outside the neuron, whereas potassium (and organic anions, as already noted) are in higher concentration inside. An easy way to remember the concentrations of these ions is to realise that the extracellular fluid is salty (NaCl) like seawater; the ancient ancestors of our cells lived in the ocean, so the seawater would literally have been their extracellular fluid.

The organic anions A^- cannot pass through the membrane of the axon, and so they remain within.



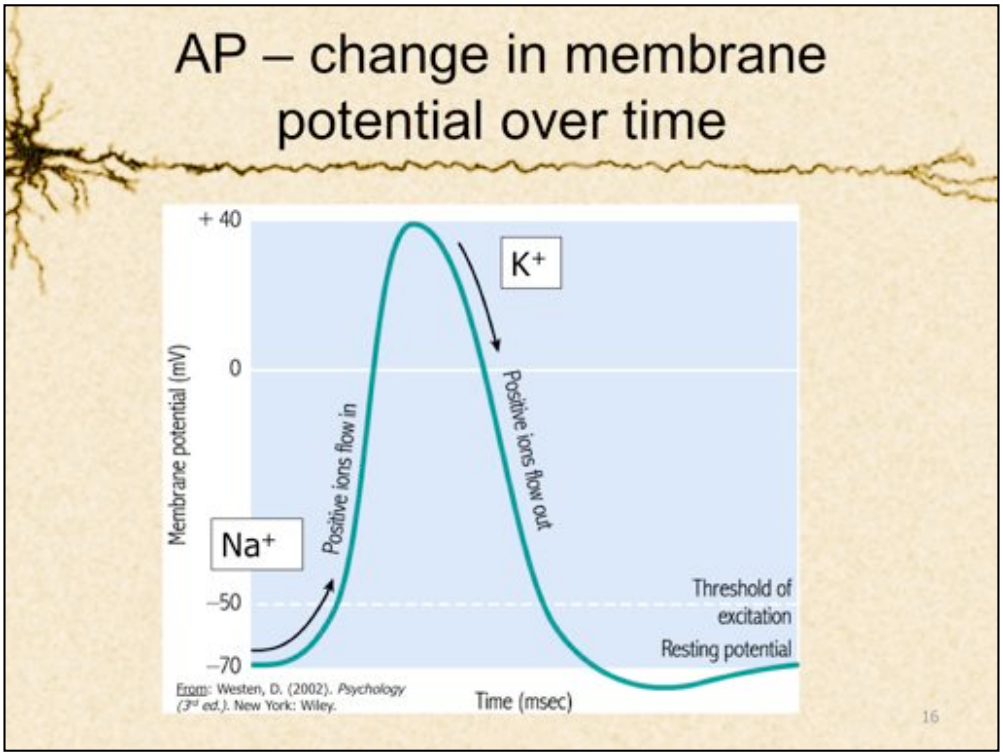
Another force, known as the **sodium-potassium pump**, actively pushes excess sodium Na^+ ions out of the cell. The sodium-potassium pump consists of millions of protein molecules (**sodium-potassium transporters**) embedded in the cell membrane, which use energy (in the form of ATP) provided by the cell's mitochondria to drive out sodium Na^+ ions in exchange for potassium ions K^+, in a ratio of 3:2.

Sodium-potassium transporters are present in neurons and glia (and most other cells of the body); they consume about 40% of a neuron's metabolic resources.



Normally the cell membrane is not very permeable to sodium Na^+. But if the membrane were suddenly to became permeable to sodium Na^+, the forces of diffusion and electrostatic pressure would allow sodium Na^+ ions to rush into the cell, causing a sudden increase in the concentration of positively charged ions and changing the membrane potential. This **change in membrane permeability** is precisely what causes an **action potential**.

Certain protein molecules in the cell membrane, known as **ion channels**, provide an opening through which ions can rapidly enter or leave the cell. When ion channels for sodium Na^+ open, sodium Na^+ ions rush into the cell. Shortly thereafter, ion channels specific to potassium K^+ open, allowing potassium K^+ ions to rush out of the cell.



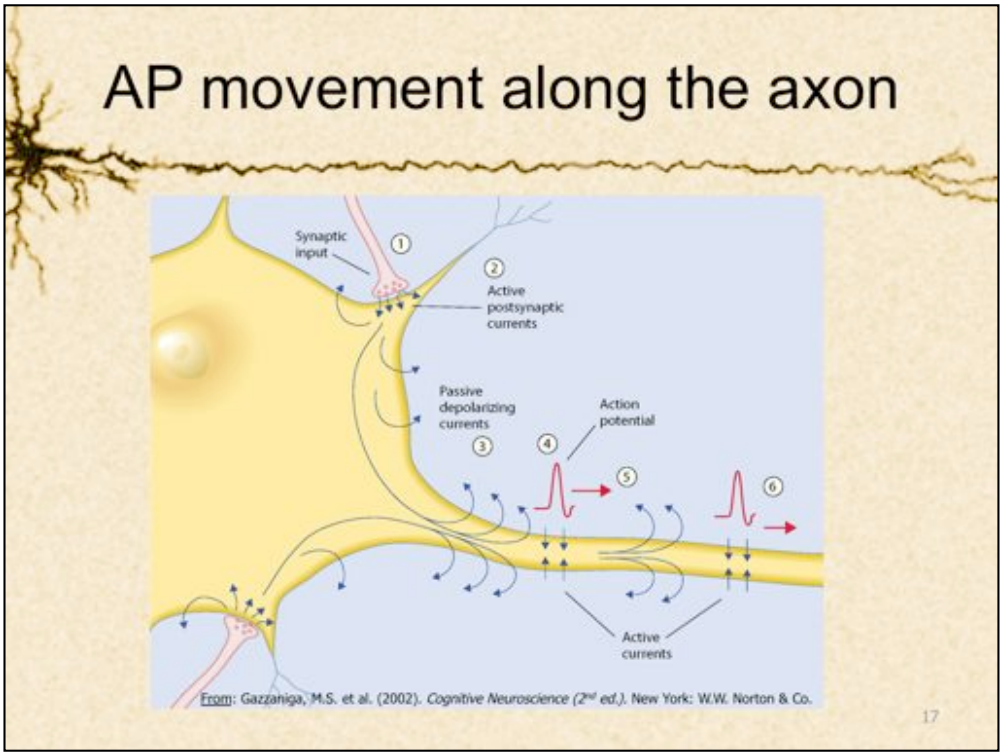
An **action potential** can be described as the following sequence of events:

1) Once a neuron's threshold for excitation is reached, sodium channels in the cell membrane open and there is a rapid influx of positively charged sodium Na^+ ions. This produces a sudden change in the membrane potential, from –70 mV to +40 mV (**depolarisation**).

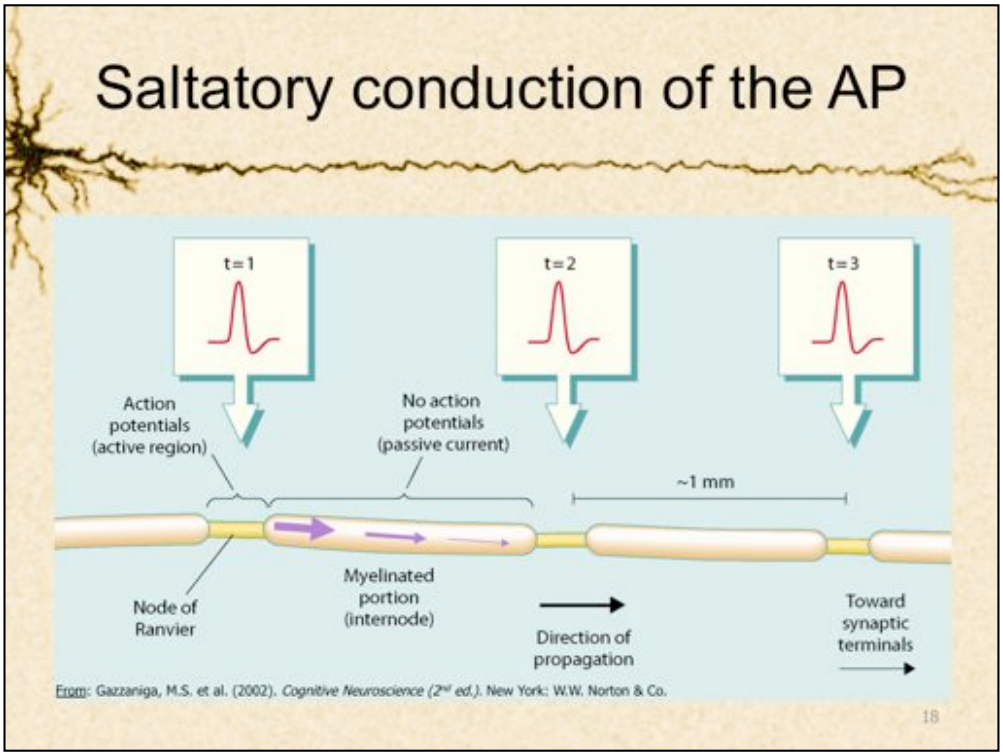
2) Shortly afterwards (less 1 millisecond), the potassium channels also open, allowing positively charged potassium ions to leave the axon (**repolarisation**).

3) At the peak of the action potential (about 1 millisecond) the sodium channels close and cannot re-open until the membrane reaches its resting potential again (**refractory period**).

4) As potassium ions are moved out of the axon, the membrane slightly overshoots its resting value (**hyperpolarisation**) before returning to its resting level (–70 mV).



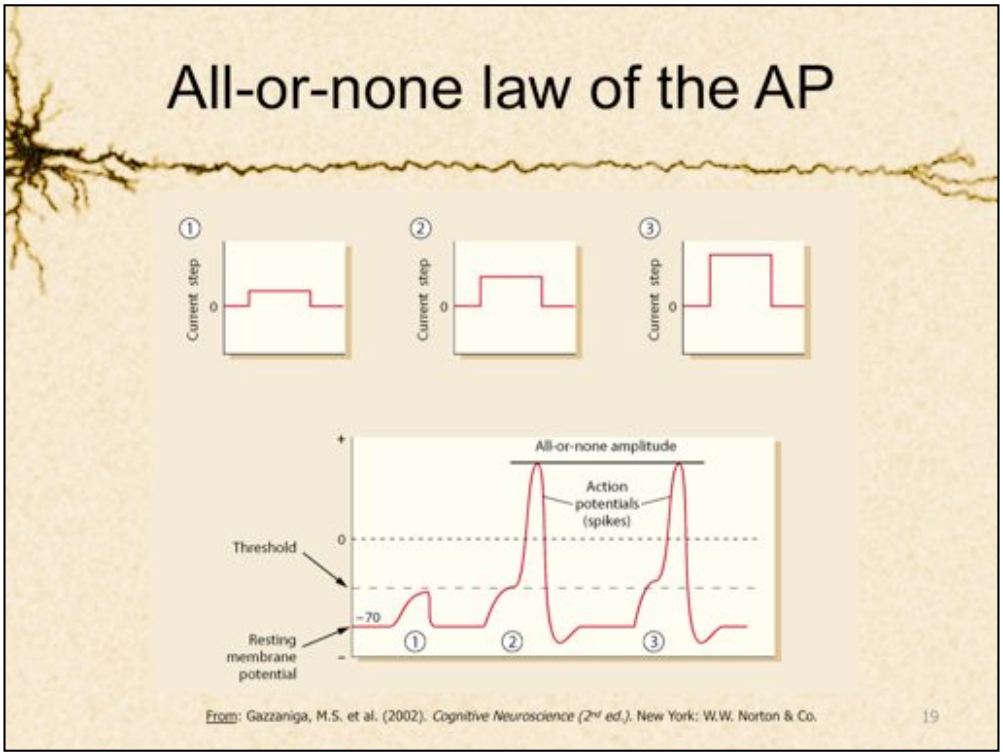
An action potential is triggered when excitatory input is passed from the terminal buttons of a **presynaptic neuron** and received by the dendrites of the **postsynaptic neuron**. This excitatory signal is passed passively toward the axon of the postsynaptic neuron, where it stimulates depolarisation of the membrane if it is above the threshold for excitation.



Rather than moving as a single continuous wave down the axon, action potentials 'jump' into the gaps (**Nodes of Ranvier**) between segments of myelin that are wrapped around the axon (oligodendrocytes and Schwann cells).

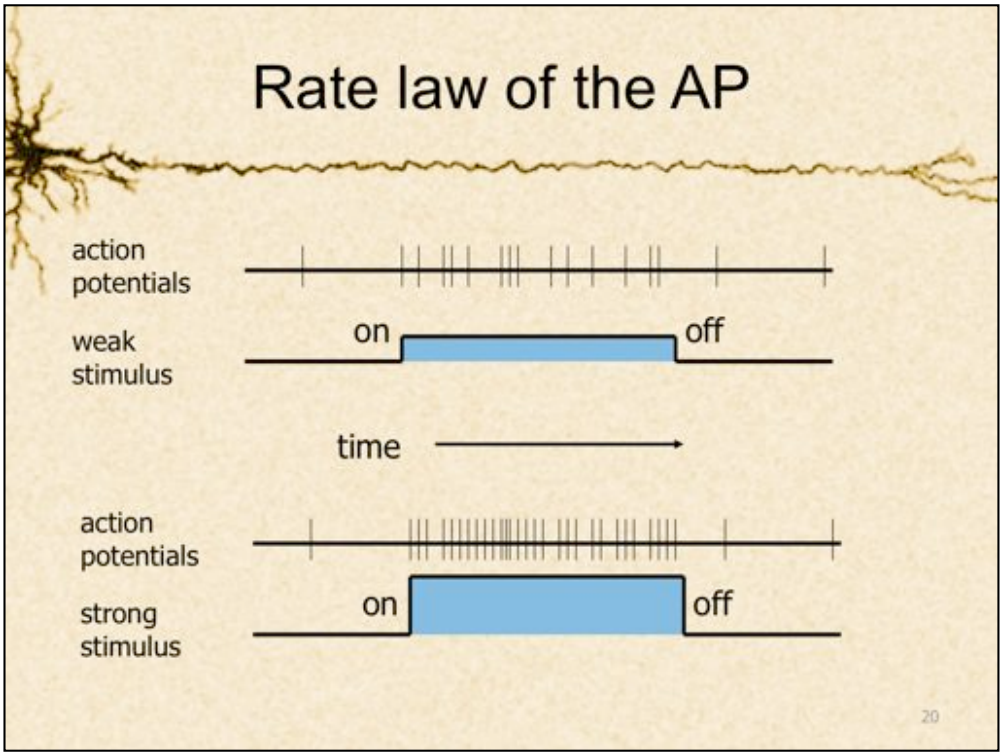
Because an action potential is generated by the rapid influx of sodium Na^+ ions into the cell, this process can only occur where the axon membrane is in direct contact with the extracellular fluid (i.e., at the Nodes of Ranvier). Within the myelinated portion of the axon, the electrical signal is conducted passively (like electricity down a wire) until it gets to the next Node, at which point another action potential is generated. Although the strength of the electrical potential decreases as it moves along myelinated portions of the axon, it is still large enough to trigger a new action potential at the next Node.

This jumping of the action potential along myelinated axons has two advantages. First, it saves energy because sodium-potassium transporters only have to work within the Nodes. Second, it increases the speed of neural signalling, and thus the speed with which we perceive, react and think.



Neurons have a threshold for excitation, above which an action potential will reliably be triggered. In other words, an action potential either occurs or it does not occur – the **all-or-none law**.

Once triggered an action potential remains at the same amplitude (i.e., its membrane reaches the same level of depolarisation), and travels down the axon to its end.

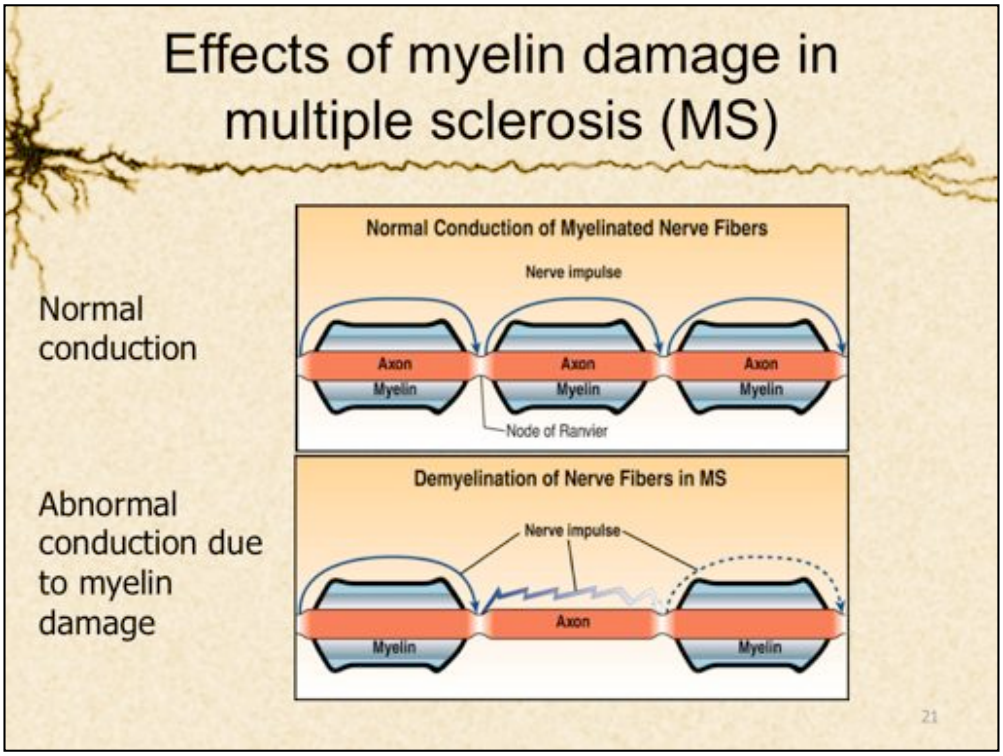


We all know that muscle contractions can be weak or strong, and that sensory stimuli can be weak or intense.

If action potentials are all-or-none in nature, and their amplitude remains constant along the length of the axon, how can they represent information that can vary continuously from weak to strong?

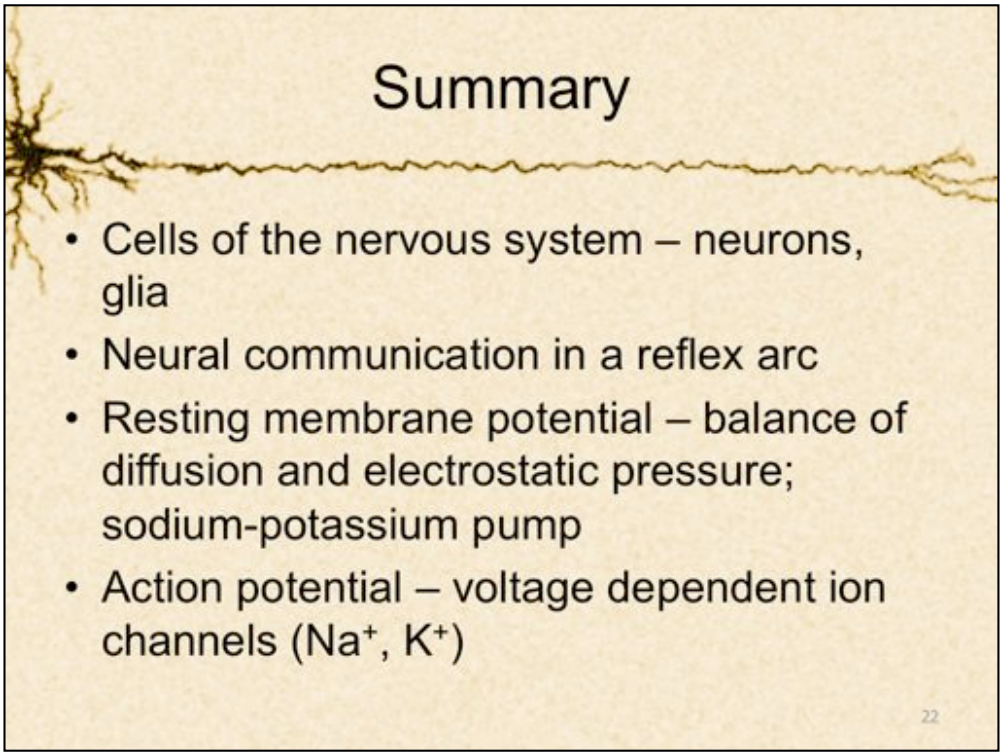
Variable information is signalled by the **number of action potentials** produced by a neuron (i.e., the neuron's **rate of firing**). A strong muscle contraction is caused by a high rate of firing of a motor neuron; similarly, a loud sound is represented by a high rate of firing of an auditory nerve fibre.

Thus, the basic unit of information carried by axons is their rate of firing (known as the **rate law**).



The symptoms of MS are due to disruption of the normal process of transmission of the action potential along the axon. The usual **saltatory conduction** between the **Nodes of Ranvier** is disrupted.

There is no cure for MS. The only form of treatment, a drug called **interferon ß**, modulates the responsiveness of the immune system and reduces the frequency and severity of attacks.


Summary
• Cells of the nervous system – neurons, glia
• Neural communication in a reflex arc
• Resting membrane potential – balance of diffusion and electrostatic pressure; sodium-potassium pump
• Action potential – voltage dependent ion channels (Na^+, K^+)
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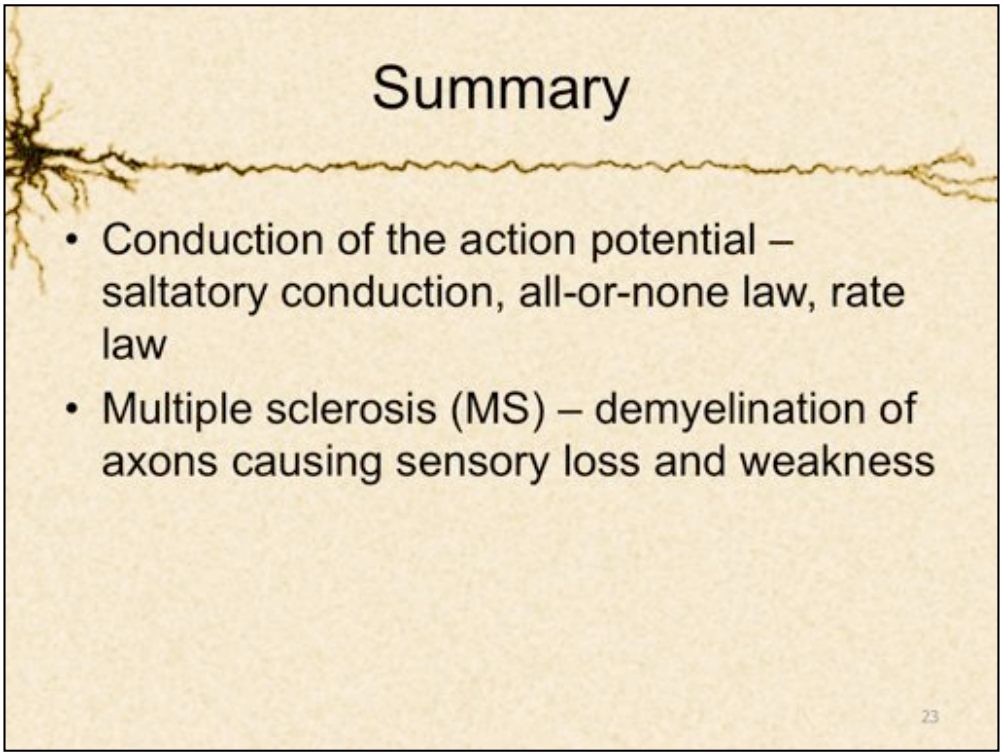
Summary
• Conduction of the action potential – saltatory conduction, all-or-none law, rate law
• Multiple sclerosis (MS) – demyelination of axons causing sensory loss and weakness
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