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Nerves and nerve conduction

By the perioperativeCPD team

It is essential that perioperative practitioners have an understanding of nerve conduction, as many drugs used in the operating theatre have an impact on the nervous system and nerve conduction. The most obvious, but not the only one, being local anaesthetics which prevent pain and other nerve signals reaching the brain, by temporarily blocking nerve conduction.

The human nervous system is incredibly complex and includes the brain, spinal cord, peripheral and autonomic nerves, coordinates all movements, thoughts and sensations that you have. This module examines only a small part of this, specifically how nerve cells communicate by sending signals to each other and various other tissues throughout the body. It is a simplified explanation of a complex topic.

What does the nervous system do?

The nervous system is made up of billions of nerves which:

- Sense your external and internal surroundings (sensations)
- Communicate information between your brain, spinal cord and other tissues and organs
- Coordinate voluntary movements (walking, running)
- Coordinate and regulate involuntary functions like breathing, heart rate, blood pressure and body temperature.

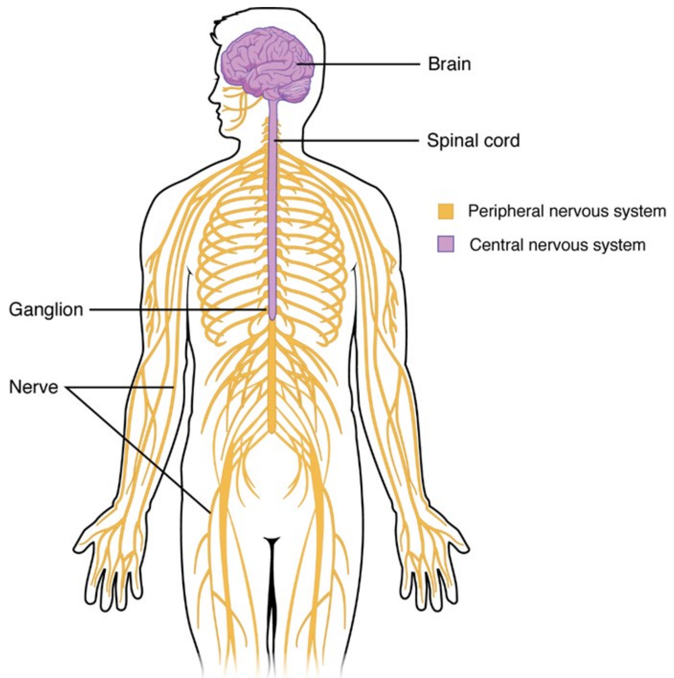
These nerves carry electrochemical signals to and from different areas of the central nervous system as well as between the nervous system and other tissues and organs and are divided into four main classes:

1. **Cranial nerves** connect your sense organs (eyes, ears, nose, mouth) to your brain

2. **Central nerves** connect areas within the brain and spinal cord

3. **Peripheral nerves** connect the spinal cord with your body including your limbs. In the peripheral nervous system there are two main types of nerves, sensory and motor. To put it simply, sensory neurones are for 'feeling' including pain, and motor neurones are for 'doing'.

4. **Autonomic nerves** connect the brain and spinal cord with your organs (heart, stomach, intestines, blood vessels, etc.) and is a system that acts largely unconsciously and regulates bodily functions.



The nervous system

Nerve cell, neurone or neuron?

The brain, spinal cord and nerves consist of more than 100 billion nerve cells, also called **neurones** (In America they miss the 'e' out so spell it neuron/s). Neurones gather and transmit electrochemical signals. They have many of the same characteristics and parts as other cells, but the electrochemical aspect lets them transmit signals over long distances and pass messages to each other.

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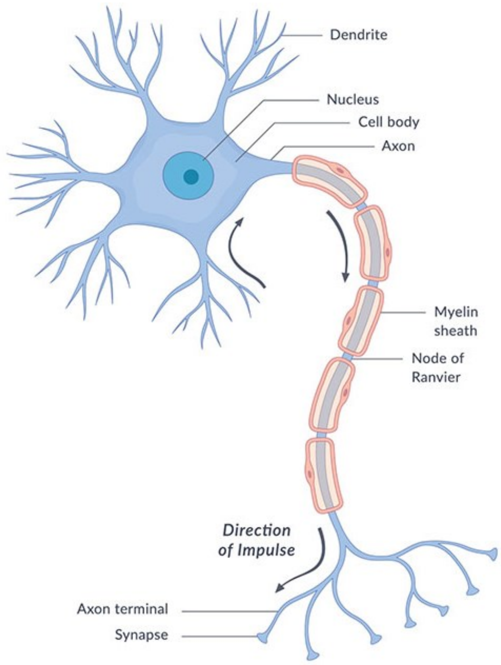
Neurones have three basic parts:

- **Cell body:** This main structure has all of the necessary components of the cell, such as the nucleus (which contains DNA), endoplasmic reticulum (protein production and transportation) and mitochondria (for making energy). If the cell body dies, the neurone dies. Nerve cell bodies are grouped together in clusters called ganglia, which are located in or near the brain and spinal cord.

- **Axons:** These long, thin, cable-like projections of the cell carry electrochemical messages (nerve impulses or action potentials) along the length of the cell. Depending upon the type of neurone, axons can be covered with a thin layer of myelin, like an insulated electrical wire. Myelin is made of fat, and it helps to speed transmission of a nerve impulse down a long axon. Myelinated neurones are typically found in the peripheral nerves (sensory and motor neurones), while non-myelinated neurones are found within the brain and spinal cord. How myelinated nerves speed conduction is covered at the end of the module.

- **Dendrites** or **nerve endings:** These small, branchlike projections of the cell make connections to other cells and allow the neurone to talk with other cells or perceive the environment. Dendrites can be located on one or both ends of the cell.

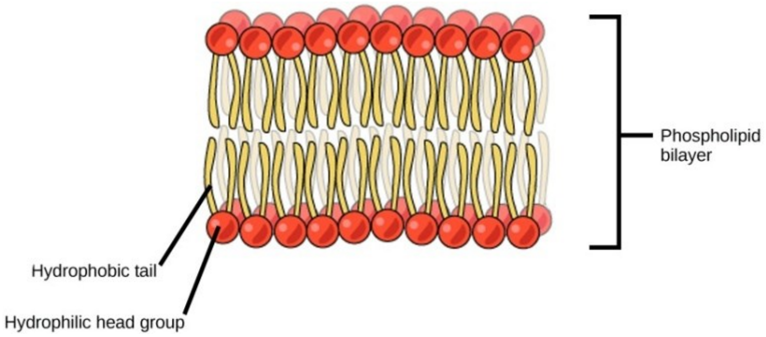


Parts of a nerve cell/neurone

Why is a nerve cell structure important to nerve conduction?

We have talked about nerve signals and mentioned that they are electrochemical in nature, but what does that mean? To understand how neurones transmit signals, we must first look at the structure of the **cell membrane**. The cell membrane surrounds, separates and protects the interior of all cells from the outside environment (the extracellular space).

The cell membrane is made of fats or lipids called phospholipids. Each phospholipid has an electrically charged head that sticks near water and two polar tails that avoid water.



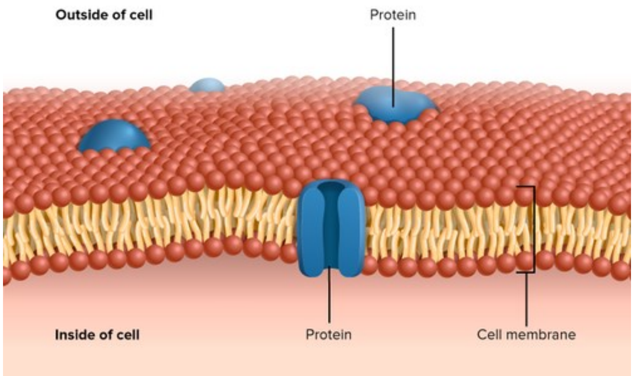
Phospholipid layer

In this configuration, they form a barrier that separates the inside of the cell from the outside and do not permit water-soluble or charged particles (like ions) to move through it. Small, nonpolar molecules, such as oxygen and carbon dioxide, can pass directly through the phospholipid bilayer of the membrane.

So how do charged particles get into cells?

Ion Channels

As ions are charged and water-soluble, they must move through small tunnels or channels made from proteins that span the cell membrane. There are different channels for sodium ions, potassium ions, calcium ions and chloride ions. These channels make the cell membrane selectively permeable or open to various ions and other substances, like glucose. This selective permeability of the cell membrane allows the inside of the cell to have a different composition than the outside.

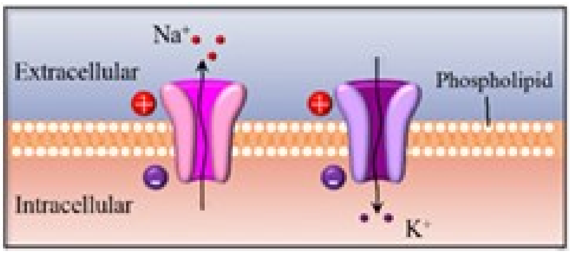


Cell membrane

For the purposes of nerve signals, we are interested in the following characteristics:

- The fluid outside the cell (extracellular) is rich in sodium (Na^+), a concentration about 10 times higher than the inside fluid
- The fluid inside the cell (intracellular) is rich in potassium (K^+), a concentration about 20 times higher inside the cell than outside.
- There are large negatively charged proteins inside the cell that are too big to move across the membrane. They give the inside of the cell a negative electrical charge compared to the outside. The charge is about -70 to -80 millivolts (mV) -- 1 mV is 1/1000th of a volt. For comparison, the charge in your house is about 230 V, about 3 million times more.

- The cell membrane is slightly "leaky" to sodium and potassium ions, so sodium-potassium pumps are located in the membrane. These pumps use energy (ATP) to pump sodium ions from the inside to the outside and potassium ions from the outside to the inside.
- Three sodium ions are pumped out for every two potassium ions pumped in. This results in more positively charged ions outside the cell compared to inside the cell which helps the inside stay negative.
- Because sodium and potassium ions are positively charged, they carry tiny electrical currents when they move across the membrane. If sufficient numbers move across the membrane, you can measure the electrical currents.



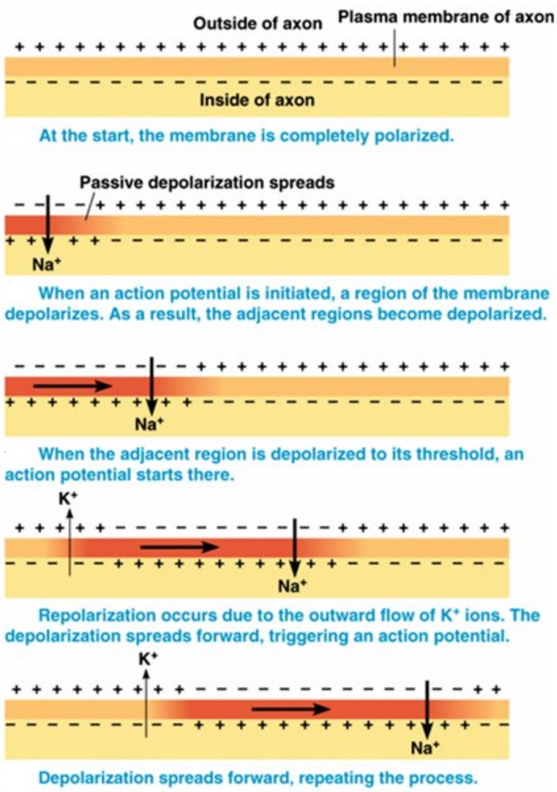
Sodium-potassium ion pump

What is an action potential?

An action potential is a rapid sequence of changes in the voltage across a membrane, action potentials generate nerve signals. Neurones generate and conduct these signals in order to transmit messages to the target tissues. The nerve signal, or action potential, is caused by a coordinated movement of sodium and potassium ions across the nerve cell membrane which is then transmitted down the nerve.

Here's how it works:

1. As discussed, the inside of the cell is slightly negatively charged (resting potential of -70 to -80 mV).
2. If a neurones is triggered by a receptor (mechanical, electrical, or sometimes chemical) this causes the sodium channels in a small portion of the nerve membrane to open.



Nerve signal conduction

3. Sodium ions enter the cell through the open sodium channels. The positive charge that they carry ends up reversing the membrane potential or charge in that area making it positive inside and negative outside. This is called depolarisation.

4. This then stimulates the adjacent sodium channels to open, so the action potential passes along the length of neurone like dominos falling.

5. When the electrical potential reaches +40 mV inside (it takes about 1 millisecond), the sodium channels shut down and let no more sodium ions inside that portion of the membrane.

Action potential

6. This also causes the causes potassium channels to open and potassium ions leave the cell through the open potassium channels. The outward movement of positive potassium ions makes the inside of the membrane negative again and returns the membrane toward the resting state (repolarises the cell).

7. When the membrane potential returns to the resting value, the potassium channels shut down and potassium ions can no longer leave the cell.

8. The sodium-potassium pump, quickly restores the normal ion balance across the membrane and returns the membrane potential to its resting level. It is repolarised

9. Now, this sequence of events occurs in a local area of the membrane. But these changes get passed on to the next area of membrane, then to the next area, and so on down the entire length of the axon. Thus, the action potential (nerve impulse or nerve signal) gets transmitted (propagated) down the nerve cell.

There are a few things to note about the propagation of the action potential.

- When an area has been depolarised and repolarised and the action potential has moved on to the next area, there is a short period of time before that first area can be depolarised again (refractory period). This refractory period prevents the action potential from moving backward and keeps everything moving in one direction.
- The action potential is an "all-or-none" response. Once the membrane reaches a threshold, it will depolarise. In other words, once the events are set in motion, they will continue until the end.
- These ionic events occur in many excitable cells besides neurones (like muscle cells).
- Action potentials are transmitted or propagated rapidly. Typical neurones conduct at 10 to 100 meters per second. Conduction speed varies with the diameter of the axon (larger = faster) and the presence of myelin (myelinated = faster).

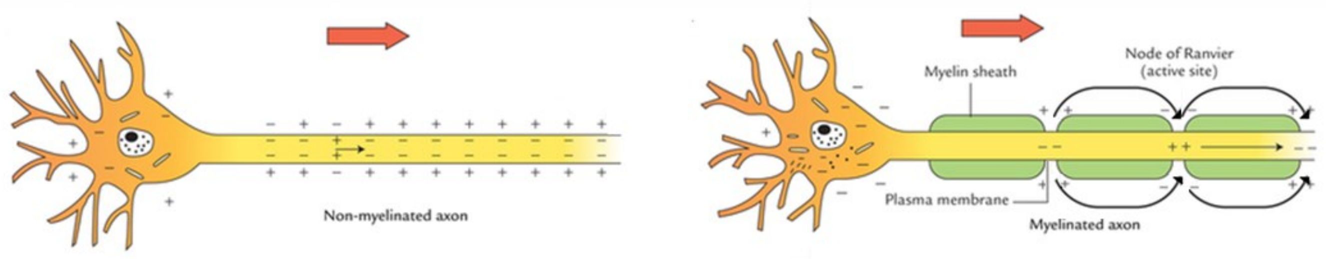
What is saltatory conduction?

Most nerves are wrapped in protective myelin sheaths. A myelin sheath is a sleeve or sheath that's wrapped around a nerve cell and consists of a layer of fat (lipid). The myelin sheath is not continuous but has gaps called the 'nodes of Ranvier'.

Transmission of nerve impulse along a myelinated nerve fibre is 20 times faster than non-myelinated fibre. This is because depolarisation occurs only at nodes, as myelin sheath is impermeable to ions and it acts as insulator, so that the impulses have to jump the myelin sheath to the next node.

This vastly speeds up the conduction process, and this type of conduction is known as saltatory conduction. The majority of neurones in the peripheral nervous system are myelinated although C-fibres which are responsible for conducting dull, throbbing pain are an example of an unmyelinated nerve fibre.

Saltatory is from the Latin saltus meaning 'leap or jump'



saltatory conduction

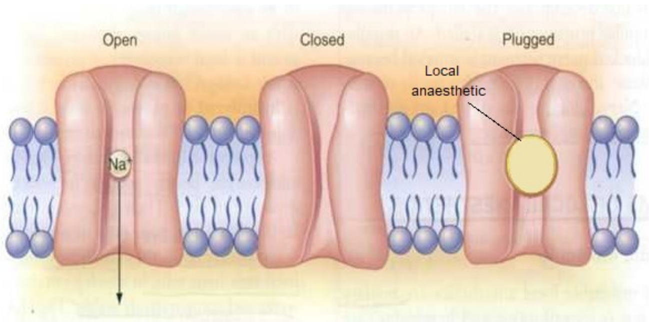
So, if the size of the action potential does not vary, how does an action potential code information?

Information is encoded by the number or frequency of action potentials. A small stimulus will initiate a few action potentials. As the intensity of the stimulus increases, so does the frequency of action potentials.

How do local anaesthetics block the nerve impulses?

When local anaesthetic injected into tissues some infuses into the nerve fibres. This then blocks the nerves sodium (Na+) channels over an area and the nerve impulse cannot be conducted. No nerve impulse means no pain signal can reach the brain and no pain is felt.

Nerve fibres differ in their sensitivity to local anaesthetics. Small nerve fibres are more sensitive than large nerve fibres while myelinated fibres are blocked before non-myelinated fibres of the same diameter. Also a loss of nerve function proceeds as loss of pain, temperature, touch, proprioception (movement), and then skeletal muscle tone. This is why people may still feel touch but not pain when having local anaesthetic.



Sodium channels

The local anaesthetic then slowly gradually diffuses out of the nerve fibre, nerve function returns to normal and impulses can be generated. Once impulses can be generated then pain can again be felt. The smaller pain nerves are also quicker to recover from local anaesthetic, larger motor nerves the slowest.

Why do local anaesthetics often don't work in infected tissue?

Local anaesthetics need to be in an un-ionised state to be absorbed through nerve membranes. A feature of infected tissue is that it tends to be a more acidic environment than usual. As the acidity increases more of the un-ionised local anaesthetic is converted into an ionised state. This lowers the amount that can be absorbed and consequently the effect is delayed and reduced.

Infected tissue may also have an increased blood supply and hence more anaesthetic may be removed from the area before it can affect the neurone.

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