1.4

Synapses

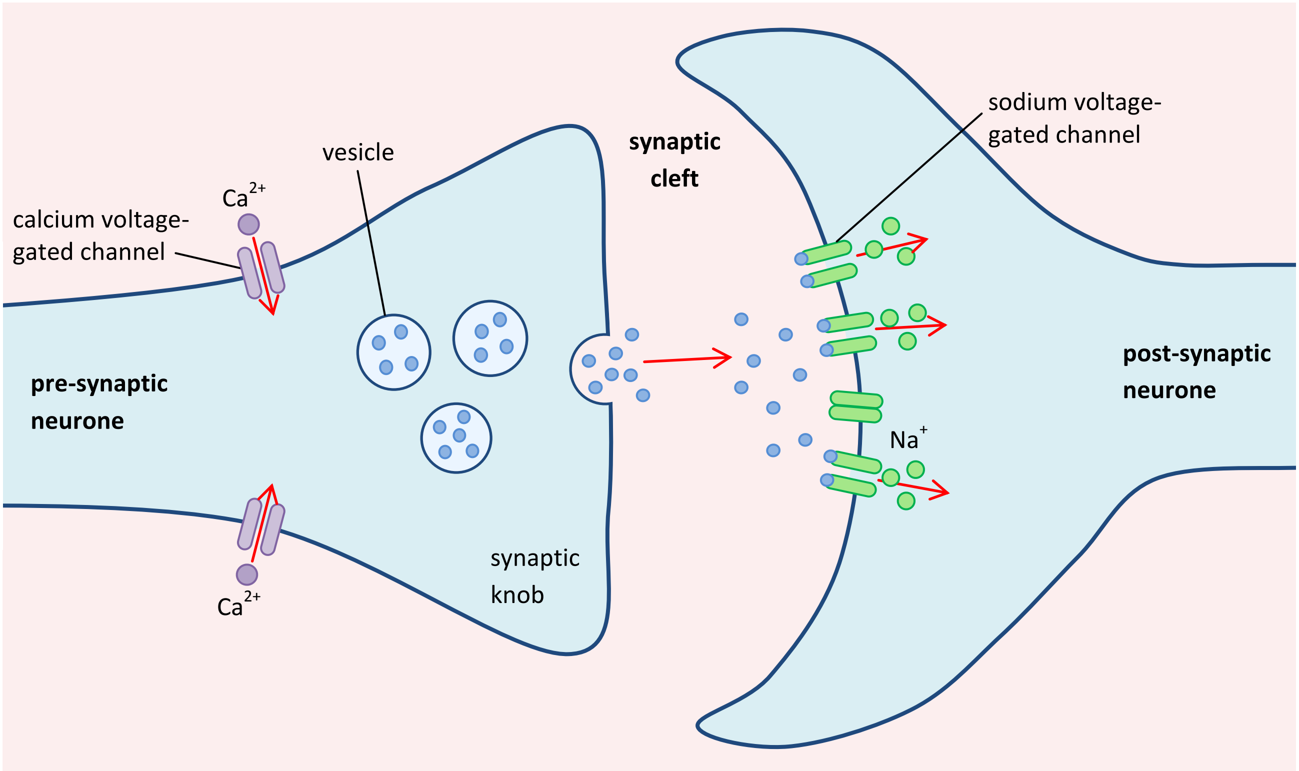
The transmission of an action potential across a synaptic nerve junction

Nerve junctions

A nerve junction occurs between two neurones. This is called a **synapse** and using specialised processes will allow two or more neurones to communicate and send signals to one another. At a synaptic junction you will find the **synaptic knob** on the neurone sending the signal (the **pre-synaptic neurone**), which communicates with the **post-synaptic neurone**.

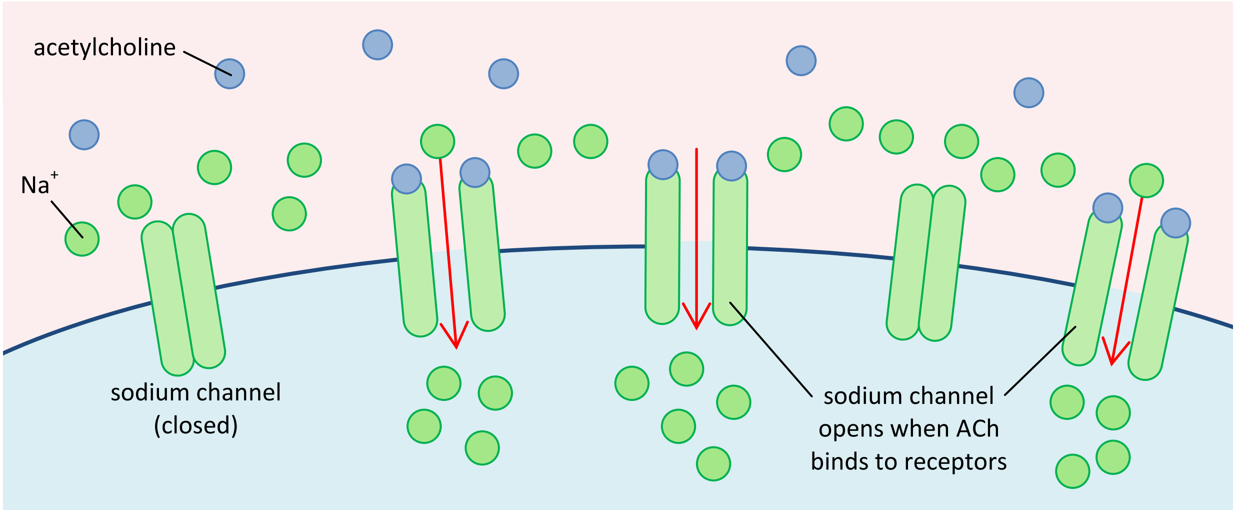
In between the two neurones is a small space called the **synaptic cleft** or synaptic gap. As an action potential cannot travel directly across this cleft, the action potential arriving at the pre-synaptic membrane (in a series of processes) triggers the release of a chemical called a **neurotransmitter**, a chemical communicator, which *can* travel across the gap and produce an action potential on the post-synaptic membrane (effectively continuing the action potential onwards).

There are many variations of the common synapse, but the most ordinary example of a synapse is one which uses the chemical substance **acetylcholine** (ACh) as its neurotransmitter. These synapses are known as *cholinergic synapses*. Other types of synapse will use different neurotransmitters (e.g. dopamine).



The transmission of an impulse across the synapse happens as follows:

1. An action potential arrives at the synaptic knob of the pre-synaptic neurone
2. This triggers voltage-gated calcium ion (Ca^{2+}) channels to open on the pre-synaptic membrane, and so calcium ions diffuse into the cell
3. The influx of calcium ions causes vesicles containing acetylcholine within the neurone to move to the cell surface membrane and fuse with the pre-synaptic membrane
4. Via exocytosis, the vesicles release the neurotransmitter acetylcholine into the synaptic cleft which diffuses across the gap down the concentration gradient to reach the post-synaptic membrane
5. The acetylcholine binds to receptors on sodium channels on the membrane which causes the channels to open, so Na^{+} ions diffuse into the cell
6. Influx of sodium ions triggers an action potential as normal, via the depolarisation of the membrane, on the post-synaptic membrane, which travels along the membrane of this new neurone



The diagram above shows what's going on around the post-synaptic membrane during the final few steps of this transmission process. After the acetylcholine has diffused across the cleft, it binds with the sodium channels on the membrane, which have ACh receptors. This will cause those channels to open, causing an influx of sodium ions. This, in turn, will generate an action potential (provided sufficient ACh was released in order to open enough sodium channels) – see 1.3 Action Potentials to see this process in more detail. Note that these sodium channels are not voltage-gated, but receptor-bound – they require the presence of acetylcholine, not a specific voltage.

Keeping the gradients constant

For obvious reasons, it is essential that acetylcholine is able to be removed from the binding sites on the sodium channels, in order to prevent a continuous signal being transmitted across the synapse. The enzyme **acetylcholinesterase**, which is present within the synaptic cleft, has the important role of breaking down acetylcholine into choline and ethanoic acid, via a *hydrolysis* reaction. These two products are recycled by re-entering the pre-synaptic neurone, where (using ATP) they recombine to form acetylcholine so they can be used again when the next action potential arrives.

Conveniently, all of these processes provide perfect concentration gradients at both ends of the synapse for the processes to function seamlessly. This is because:

- acetylcholine is released in high concentrations at the pre-synaptic membrane, but the concentration of this substance is kept continually low over at the post-synaptic membrane, providing a steep gradient for the transmitter to diffuse down when needed to transmit a signal
- and similarly because the acetylcholine is broken down into choline and ethanoic acid (by acetylcholinesterase) at the post-synaptic membrane, both of which are not present at the pre-synaptic membrane, so again a steep concentration gradient is maintained so that when being recycled, the products can diffuse down the gradient easily

Stopping the synapse

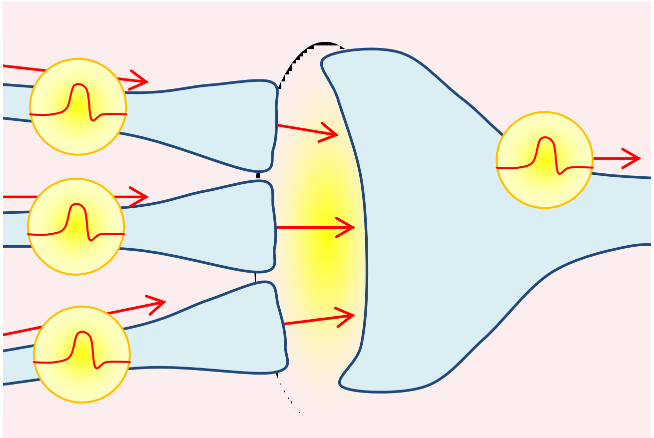
There are a number of illnesses and poisons which can have an impact on synaptic transmission. Prevention of the sending of a signal efficiently (or at all) can happen in a number of ways, for example: inhibition of calcium voltage-gated channels on the pre-synaptic membrane, inhibition of acetylcholine receptor sites on sodium ion channels, and inhibition of the enzyme acetylcholinesterase.

One example of a poison which affects the central nervous system is **sarin gas**, which has been classified as a biochemical weapon of mass destruction. This substance inhibits acetylcholinesterase, making it impossible for the enzyme to break down ACh. This means that the neurotransmitter has to remain in the sodium channel, keeping it open indefinitely, causing (in effect) endless nerve impulses to be transmitted. This can result in paralysis if the build up of acetylcholine occurs at motor neurones, or eventually death due to asphyxiation. A lethal dose for the average adult human of sarin gas is a mere 0.5mg of the gas.

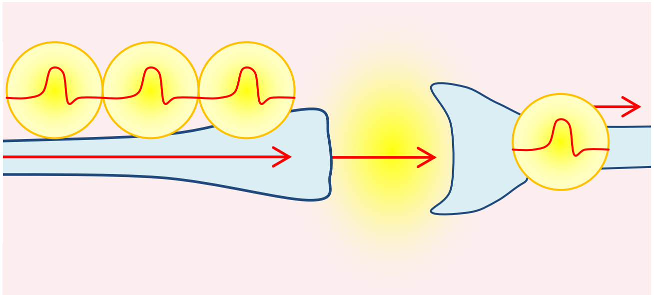
Synaptic summation

Whilst synapses usually send signals from the end of one neurone to the beginning of the next, but within the central nervous system, each individual neurone is connected to a network of other neurones.

For this reason, the process of **summation** occurs where multiple impulses are transmitted to one post-synaptic neurone. There are two types of summation:



- **spatial summation** occurs where multiple neurones can fire impulses to one receiving neurone, where one of those action potentials alone will not be sufficient to produce an action potential on the other side, but if they all fire simultaneously, the impulse will continue along the post-synaptic membrane; however, not all neurones will send **excitatory post-synaptic potentials**, EPSPs (to generate an impulse), some will send **inhibitory post-synaptic potentials**, IPSPs (which inhibit the production of an action potential) – and an IPSP can override incoming EPSP signals from adjacent neurones



- **temporal summation** occurs where one neurone fires multiple impulses from the same place, which with pauses in between will not be sufficient to generate an impulse on the receiving neurone, but when fired within rapid succession of each other, it will be enough to produce an action potential on the post-synaptic membrane

For example, with spatial summation, using the diagram above and calling the top pre-synaptic neurone A, the middle B and the bottom C, if we know that the post-synaptic neurone receives *inhibitory* signals (IPSP) from C, and *excitatory* signals (EPSP) from A and B, it would be the case that:

- if neurone A or B fires an impulse alone, an action potential will *not* be generated on the post-synaptic neurone because it is not sufficient to open enough sodium channels to generate an impulse
- if neurones A and C, or neurones B and C, or neurones A, B and C fire simultaneously, an action potential on the post-synaptic neurone will *not* be generated as the inhibitory signal from C overrides the impulses from A and B
- if neurones A and B fire simultaneously, an action potential *will* be produced on the post-synaptic membrane because sufficient sodium channels will open, depolarising the membrane enough for an action potential

The roles of synapses in the central nervous system

Of course the most basic role of the synapse is to transmit a signal from one neurone to another. This is done between sensory neurones and relay neurones, and between relay neurones and motor neurones. However, they have a number of other functions in the nervous system:

- in some places, several pre-synaptic neurones converge to one post-synaptic neurone so that signals from different parts of the central nervous system can trigger the same response
- in other places, one pre-synaptic neurone might diverge to multiple post-synaptic neurones which allows a signal to be transmitted from one neurone to several areas of the nervous system simultaneously, useful in a reflex arc as one neurone can evoke a response whilst one informs the brain
- synapses keep the movement of a signal in the correct direction, as the neurotransmitter substances are only found at the synaptic knob, so a signal cannot be transmitted from post-synaptic to pre-synaptic neurone
- low-level signals can be amplified using the process of summation (described above)
- the term **acclimatisation** describes how neurones can eventually run out of the vesicles containing the transmitter substances, preventing further responses from a particular stimulus (the neurone is said to be fatigued) – which explains why after some time you get used to a background smell or noise, and it also prevents overstimulation

The frequency of transmissions over a synapse also vary, depending primarily on the intensity of the stimulus detected by the receptor, as obviously a more intense stimulus will produce more action potentials, and so a bigger signal.