## Synapses

[Back to Nervous System]

<table>
<thead>
<tr>
<th>Synapses</th>
<th>Types of synapses</th>
<th>Summation</th>
<th>Why have gaps in nerves?</th>
<th>Neurotransmitters</th>
<th>Drugs and the Nervous System</th>
</tr>
</thead>
</table>

http://www.biologymad.com/NervousSystem/synapses.htm
Information from one neuron flows to another neuron across a **synapse**. The synapse is a small gap separating neurons. The synapse consists of:
- a **presynaptic ending** that contains neurotransmitters, mitochondria and other cell organelles,
- a **postsynaptic ending** that contains receptor sites for neurotransmitters and,
- a **synaptic cleft** or space between the presynaptic and postsynaptic endings. It is about 20nm wide.

An action potential cannot cross the synaptic cleft between neurones. Instead the nerve impulse is carried by chemicals called **neurotransmitters**. These chemicals are made by the cell that is sending the impulse (the **pre-synaptic neurone**) and stored in **synaptic vesicles** at the end of the axon. The cell that is receiving the nerve impulse (the **post-synaptic neurone**) has chemical-gated ion channels in its membrane, called **neuroreceptors**. These have specific binding sites for the neurotransmitters.

### Check Point ➔ Synapse is a small gap separating neurones

- Synapses consist of:
  - **presynaptic ending** (where neurotransmitters are made)
  - **postsynaptic ending** (has neuroreceptors in the membrane)
  - **synaptic cleft**
- Action potentials **cannot** cross the synaptic cleft
- Nerve impulse is carried by **neurotransmitters**
1. At the end of the pre-synaptic neurone there are voltage-gated calcium channels. When an action potential reaches the synapse these channels open, causing calcium ions to flow into the cell.

2. These calcium ions cause the synaptic vesicles to fuse with the cell membrane, releasing their contents (the neurotransmitter chemicals) by exocytosis.

3. The neurotransmitters diffuse across the synaptic cleft.

4. The neurotransmitter binds to the neuroreceptors in the post-synaptic membrane, causing the channels to open. In the example shown these are sodium channels, so sodium ions flow in.

5. This causes a depolarisation of the post-synaptic cell membrane, which may initiate an action potential, if the threshold is reached.

6. The neurotransmitter is broken down by a specific enzyme in the synaptic cleft; for example the enzyme acetylcholinesterase breaks down the neurotransmitter acetylcholine. The breakdown products are absorbed by the pre-synaptic neurone by endocytosis and used to re-synthesise more neurotransmitter, using energy from the mitochondria. This stops the synapse being permanently on.
Different Types of Synapses

The human nervous system uses a number of different neurotransmitter and neuroreceptors, and they don’t all work in the same way. We can group

**Check Point → How the impulse is transmitted across the synaptic cleft**

<table>
<thead>
<tr>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>action potential reaches the presynaptic terminal</td>
</tr>
<tr>
<td>voltage-gated Ca^{2+} channels open</td>
</tr>
<tr>
<td>influx of Ca^{2+}</td>
</tr>
<tr>
<td>synaptic vesicles fuse with membrane (exocytosis)</td>
</tr>
<tr>
<td>neurotransmitters are released into synaptic cleft and diffuse to postsynaptic terminal</td>
</tr>
<tr>
<td>neurotransmitter binds to neuroreceptor on postsynaptic membrane</td>
</tr>
<tr>
<td>causes Na+ channels to open, and Na+ flows into postsynaptic membrane</td>
</tr>
<tr>
<td>if threshold is reached then action potential is initiated</td>
</tr>
<tr>
<td>neurotransmitter is broken down by specific enzymes in the synaptic cleft.</td>
</tr>
</tbody>
</table>
synapses into 5 types:

1. **Excitatory Ion Channel Synapses.**
   These synapses have neuroreceptors that are sodium channels. When the channels open, positive ions flow in, causing a local depolarisation and making an action potential more likely. This was the kind of synapse described above. Typical neurotransmitters are acetylcholine, glutamate or aspartate.

2. **Inhibitory Ion Channel Synapses.**
   These synapses have neuroreceptors that are chloride channels. When the channels open, negative ions flow in causing a local hyperpolarisation and making an action potential less likely. So with these synapses an impulse in one neurone can inhibit an impulse in the next. Typical neurotransmitters are glycine or GABA.

3. **Non Channel Synapses.**
   These synapses have neuroreceptors that are not channels at all, but instead are membrane-bound enzymes. When activated by the neurotransmitter, they catalyse the production of a "messenger chemical" inside the cell, which in turn can affect many aspects of the cell's metabolism. In particular they can alter the number and sensitivity of the ion channel receptors in the same cell. These synapses are involved in slow and long-lasting responses like learning and memory. Typical neurotransmitters are adrenaline, noradrenaline (NB adrenaline is called epinephrine in America), dopamine, serotonin, endorphin, angiotensin, and acetylcholine.

4. **Neuromuscular Junctions.**
   These are the synapses formed between motor neurones and muscle cells. They always use the neurotransmitter acetylcholine, and are always excitatory. We shall look at these when we do muscles. Motor neurones also form specialised synapses with secretory cells.

5. **Electrical Synapses.**
   In these synapses the membranes of the two cells actually touch, and they share proteins. This allows the action potential to pass directly from one membrane to the next. They are very fast, but are quite rare, found only in the heart and the eye.

---

**Check Point**

**Different types of synapses**

- **Excitatory ion channel synapses** - neuroreceptors are Na⁺ channels. When Na⁺ channels open, local depolarisation occurs, if threshold is reached then action potential is initiated.

- **Inhibitory ion channels** - neuroreceptors are Cl⁻ channels. When Cl⁻ channels open, hyperpolarisation occurs.
One neurone can have thousands of synapses on its body and dendrons. So it has many inputs, but only one output. The output through the axon is called the **Grand Postsynaptic Potential (GPP)** and is the sum of all the excitatory and inhibitory potentials from all that cell's synapses. If there are more occurrences, making action potential less likely.

**Non channel synapses** - neuroreceptors are membrane-bound enzymes. When activated, they catalyse the 'messenger chemical', which in turn can affect the sensitivity of the ion channel receptors in the cell.

**Neuromuscular junctions** - synapses formed between motor neurones and muscle cells. Always use the neurotransmitter acetylcholine, and are always excitatory.

**Electrical synapses** - the membranes of the two cells actually touch and they share proteins. The action potential can pass directly from one membrane to the next.

---

**Summation**

When one postsynaptic neuron is excited/inhibited by more than one presynaptic neuron. Thus several neurons converge and release their neurotransmitters towards one neuron.

One neurone can have thousands of synapses on its body and dendrons. So it has many inputs, but only one output. The output through the axon is called the **Grand Postsynaptic Potential (GPP)** and is the sum of all the excitatory and inhibitory potentials from all that cell's synapses. If there are more occurrences, making action potential less likely.
excitatory potentials than inhibitory ones then there will be a GPP, and the neurone will “fire”, but if there are more inhibitory potentials than excitatory ones then there will not be a GPP and the neurone will not fire.

This summation is the basis of the processing power in the nervous system. Neurones (especially interneurones) are a bit like logic gates in a computer, where the output depends on the state of one or more inputs. By connecting enough logic gates together you can make a computer, and by connecting enough neurones together to can make a nervous system, including a human brain.

**So why bother? Why have gaps in the nerves?**

1. They make sure that the flow of impulses is in one direction only. This is because the vesicles containing the transmitter are only in the presynaptic membrane and the receptor molecules are only on the postsynaptic membrane.

2. They allow integration, e.g. an impulse travelling down a neurone may reach a synapse which has several post synaptic neurones, all going to different locations. The impulse can thus be dispersed. This can also work in reverse, where several impulses can converge at a synapse.

3. They allow ‘summation’ to occur. Synapses require the release of sufficient transmitter into the cleft in order for enough of the transmitter to bind to the postsynaptic receptors and the impulse to be generated in the postsynaptic neurone. In **spatial summation**, several presynaptic neurones converge at a synapse with a single post synaptic neurone. In **temporal summation** there is only one presynaptic and one postsynaptic neurone but the frequency of impulses reaching the synapse is important. Both types of summation allow for ‘grading’ of nervous response – if the stimulation affects too few presynaptic neurones or the frequency of stimulation is too low, the impulse is not transmitted across the cleft.

4. They allow the ‘filtering out’ of continual unnecessary or unimportant background stimuli. If a neurone is constantly stimulated (e.g. clothes touching the skin) the synapse will not be able to renew its supply of transmitter fast enough to continue passing the impulse across the cleft. This ‘fatigue’ places un upper limit on the frequency of depolarisation.

**Neurotransmitters**

You only need to know about two main neurotransmitters:

<table>
<thead>
<tr>
<th>Acetylcholine (Ach)</th>
<th>Noradrenaline</th>
</tr>
</thead>
</table>

http://www.biologymad.com/NervousSystem/synapses.htm
Widely used at synapses in the peripheral nervous system. Released at the terminals of:

- All motor neurones activating **skeletal muscle**
- Many neurones of the **autonomic nervous system** especially those in the **parasympathetic** branch
- Some synapses in the central nervous system

Acetylcholine is removed from the synapse by enzymatic breakdown into inactive fragments. The enzyme used is acetylcholinesterase.

Nerve gases used in warfare (e.g. sarin) and the organophosphate insecticides (e.g. parathion) achieve their effects by inhibiting acetylcholinesterase thus allowing ACh to remain active. In the presence of such inhibitors ACh keeps stimulating the postsynaptic membranes and the nervous system soon goes wild, causing contraction of the muscles in uncontrollable spasms and eventually death. Atropine is used as an antidote because it blocks ACh receptors.

This is another transmitter substance which may be in some synapses instead of acetylcholine, e.g. some human brain synapses and **sympathetic nervous system** synapses.

Synapses result in an appreciable delay, up to one millisec. Therefore slows down the transmission in nervous system.

Synapses are highly susceptible to drugs and fatigue e.g.

- **Curare** (poison used by S. American Indians) and atropine stops Acetylcholine from depolarising the post-synaptic membrane, i.e. become paralysed.
- **Strychnine** and some nerve gases inhibit or destroy acetylcholinesterase formation. Prolongs and enhances any stimulus, i.e. leads to convulsions, contraction of muscles upon the slightest stimulus.
- **Cocaine, morphine, alcohol, ether** and **chloroform** anaesthetise nerve fibres.
- **Mescaline** and **LSD** produce their hallucinatory effect by interfering with nor-adrenaline.

<table>
<thead>
<tr>
<th>Synapses where acetylcholine is the neurotransmitter = cholinergic synapses</th>
<th>Synapses where noradrenaline is the neurotransmitter = adrenergic synapses</th>
</tr>
</thead>
</table>

http://www.biologymad.com/NervousSystem/synapses.htm
Almost all drugs taken by humans (medicinal and recreational) affect the nervous system. From our understanding of the human nervous system we can understand how many common drugs work. Drugs can affect the nervous system in various ways, shown in this table:

<table>
<thead>
<tr>
<th>Drug action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mimic a neurotransmitter</td>
<td>Switch on a synapse</td>
</tr>
<tr>
<td>Stimulate the release of a neurotransmitter</td>
<td>Switch on a synapse</td>
</tr>
<tr>
<td>Open a neuroreceptor channel</td>
<td>Switch on a synapse</td>
</tr>
<tr>
<td>Block a neuroreceptor channel</td>
<td>Switch off a synapse</td>
</tr>
<tr>
<td>Inhibit the breakdown enzyme</td>
<td>Switch on a synapse</td>
</tr>
<tr>
<td>Inhibit the Na⁺K⁺ATPase pump</td>
<td>Stop action potentials</td>
</tr>
<tr>
<td>Block the Na⁺ or K⁺ channels</td>
<td>Stop action potentials</td>
</tr>
</tbody>
</table>

Drugs that stimulate a nervous system are called **agonists**, and those that inhibit a system are called **antagonists**. By designing drugs to affect specific
neurotransmitters or neuroreceptors, drugs can be targeted at different parts of the nervous system. The following paragraph describe the action of some common drugs. You do not need to know any of this, but you should be able to understand how they work. By designing drugs to affect specific neurotransmitters or neuroreceptors, drugs can be targeted at different parts of the nervous system. The following paragraph describe the action of some common drugs. You do not need to know any of this, but you should be able to understand how they work.

1. Drugs acting on the central nervous system

In the reticular activating system (RAS) in the brain stem noradrenaline receptors are excitatory and cause wakefulness, while GABA receptors are inhibitory and cause drowsiness. Caffeine (in coffee, cocoa and cola), theophylline (in tea), amphetamines, ecstasy (MDMA) and cocaine all promote the release of noradrenaline in RAS, so are stimulants. Antidepressant drugs, such as the tricyclics, inhibit the breakdown and absorption of noradrenaline, so extending its effect. Alcohol, benzodiazepines (e.g. mogaon, valium, librium), barbiturates, and marijuana all activate GABA receptors, causing more inhibition of RAS and so are tranquillisers, sedatives and depressants. The narcotics or opioid group of drugs, which include morphine, codeine, opium, methadone and diamorphine (heroin), all block opiate receptors, blocking transmission of pain signals in the brain and spinal chord. The brain’s natural endorphins appear to have a similar action.

The brain neurotransmitter dopamine has a number of roles, including muscle control, pain inhibition and general stimulation. Some psychosis disorders such as schizophrenia and manic depression are caused by an excess of dopamine, and antipsychotic drugs are used to block the dopamine receptors and so reduce its effects. Parkinson’s disease (shaking of head and limbs) is caused by too little dopamine compared to acetylcholine production in the midbrain. The balance can be restored with levodopa, which mimics dopamine, or with anticholinergic drugs (such as procyclidine), which block the muscarinic acetylcholine receptors.

Tetrodotoxin (from the Japanese puffer fish) blocks voltage-gated sodium channels, while tetraethylammonium blocks the voltage-gated potassium channel. Both are powerful nerve poisons. General anaesthetics temporarily inhibit the sodium channels. Strychnine blocks glycine receptors in the brain, causing muscle convulsions and death.

2. Drugs acting on the somatic nervous system

Curare and α-bungarotoxin (both snake venoms) block the nicotinic acetylcholine receptors in the somatic nervous system, and so relax skeletal muscle. Myasthenia gravis (a weakening of the muscles in the face and throat caused by inactive nicotinic acetylcholine receptors) is treated by the drug neostigmine, which inhibits acetylcholinesterase, so increasing the amount of acetylcholine at the neuromuscular junction. Nerve gas and
organophosphate insecticides (DDT) inhibit acetylcholinesterase, so nicotinic acetylcholine receptors are always active, causing muscle spasms and death. Damaged tissues release prostaglandins, which stimulate pain neurones (amongst other things). The non-narcotic analgesics such as aspirin, paracetamol and ibuprofen block prostaglandin production at source of pain, while paracetamol has a similar effect in the brain. Local anaesthetics such as procaine block all sensory and motor synapses at the site of application.

3. Drugs acting on the autonomic nervous system

Sympathetic agonists like salbutamol and isoprenaline, activate the adrenergic receptors in the sympathetic system, encouraging smooth muscle relaxation, and are used as bronchodilators in the treatment of asthma. Sympathetic antagonists like the beta blockers block the noradrenaline receptors in the sympathetic nervous system. They cause dilation of blood vessels in the treatment of high blood pressure and migraines, and reduce heartbeat rate in the treatment of angina and abnormal heart rhythms. Parasympathetic antagonists like atropine (from the deadly nightshade belladonna) inhibit the muscarinic acetylcholine receptors in parasympathetic system, and are used as eye drops to relax the ciliary muscles in the eye.