Chemical synapses

Spikes—the voltage pulses that carry signals from neuron to neuron—are notably stereotypical; there aren't big spikes and small spikes, to a good approximation, there are just spikes. However, the effect one neuron has on the other can vary considerably, not just from neuron to neuron, but from time to time. This variability can occur because of chemical synapses, the complicated biochemical machinery responsible for connect the axon of one neuron to the dendrite of another.

Chemical synapses are not the only synapses, there are also **gap junctions**. If an axon is connected to a dendrite by a gap junction there is a small hole directly connecting the inside of one neuron through to the inside of the other, usually this means that the axon of one neuron is connected to the dendrite of the other, though axon to axon gap junctions are also found. For an axon to dendrite gap junction this means that when a spike travelling along the axon reaches the gap junction some of the charged ions diffuse through the gap changing the charge in the dendrite. In some simple animals like jelly fish most or all of the synapses are gap junctions. There are gap junctions in the mammalian brain, for example gap junctions are thought to be responsible for the dynamics which supports very rapid oscillations in the hippocampus, however, most of the synapses in the mammalian brain are chemical synapses. We will see that this allows a more variable effect of a pre-synaptic spike on the voltage of the post-synaptic dendrite.

In a chemical synapse the pre-synaptic spike does not affect the post-synaptic voltage directly, instead it causes a cascade of bio-electrodynamics events which ultimately causes a transient change in conductance of the post-synaptic membrane.

Roughly, the synapse consists of a protuberance in the axon called the **terminal bouton**, the terminal bouton is held by astrocytes, supporting non-neuronal brain cells, so that it is separated by a tiny gap, called the **synaptic cleft** from a protuberance in the dendrite called the **dendritic spine**; depending on the neurons involved this protuberance might be a small bump, or a substantial spine. Figure 1 indicates the range of spine shapes. The shape of the spine is thought to be important in the modulation of synaptic signalling; this isn't an aspect of synapses we will consider here.

The terminal bouton is filled with tiny bags or bubbles called **vesicles**, these

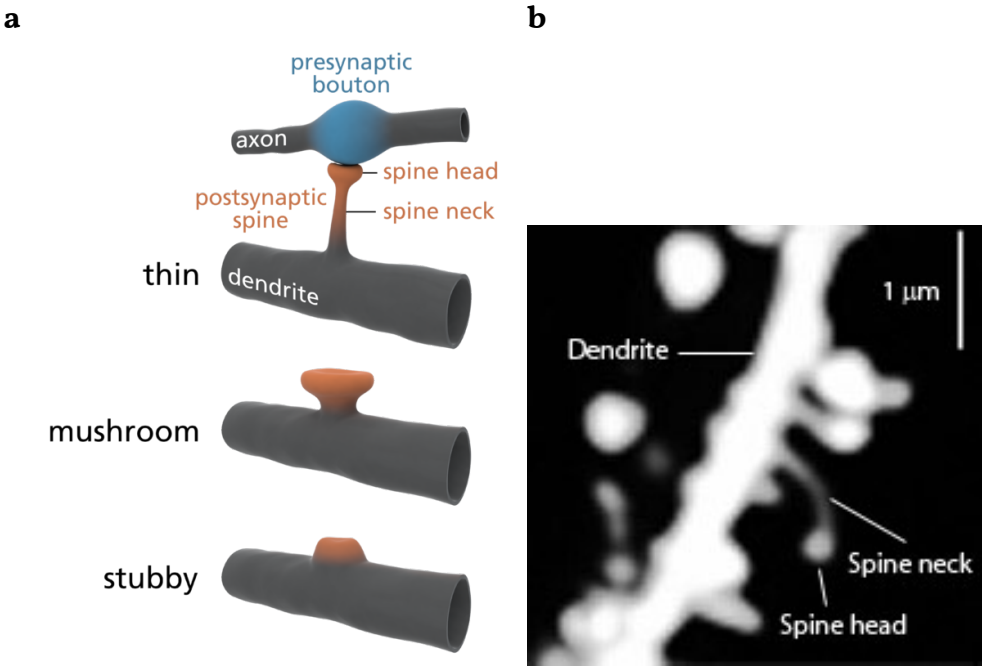

Figure 1: Types of dendritic spines: **a** shows a set of different spine types, **b** shows a photograph of a spiny dendrite of a striatal medium spiny neuron. [Both pictures from `https://en.wikipedia.org/wiki/Dendritic_spine`]

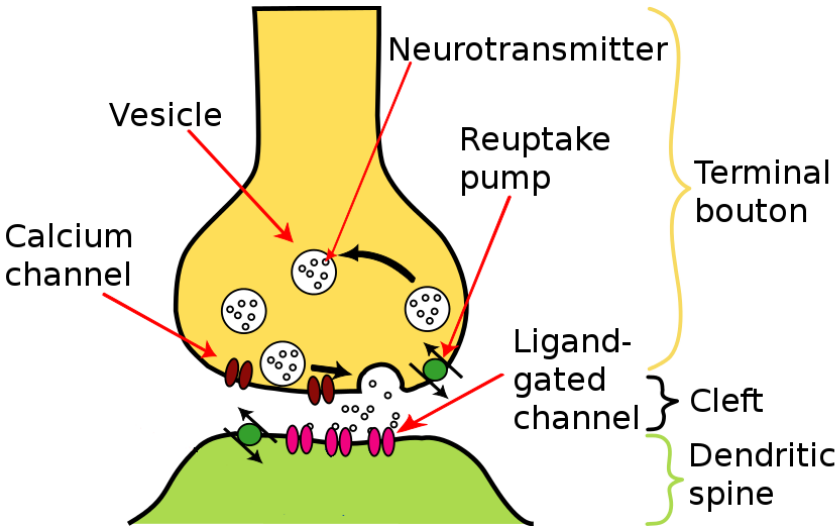

Figure 2: The major parts of the synapse; this shows a vesicle bursting, releasing neurotransmitter into the cleft, this will bind with the ligand-gated channels to allow a current across the membrane of the dendrite. Reuptake pumps are shown in the bouton and the spine, there are also pumps in the astrocyte that surrounds the cleft but isn't shown here. Some is also lost to diffusion. [Diagram modified from one in wikipedia.]

contain special molecules called **neurotransmitters**. When a spike arrives at the terminal bouton it causes calcium gates to open in the cellular membrane, the resulting influx of calcium ions causes some of the vesicles to migrate to the membrane separating the bouton from the synaptic cleft, they burst releasing neurotransmitter into the cleft.

The membrane of the dendritic is pieced by gated ion channels; these are **ligand gated** channels. This means that they contain a receptor site which binds with a particular type of molecule, like a key designed for the receptor site's lock. When the receptor has a molecule bound to it, the gate is open and so ions can pass through the channel, like the other channels we have seen the channel is ion specific, so only one type of ion can pass through it. In the case of the ligand-gated channels in the dendritic spine, the neurotransmitter binds with the receptor, opening the gate. Hence, after a spike arrives at the synapse the cleft is filled with neurotransmitter and some of that neurotransmitter binds to the gated channels, causing them to open. This in turn

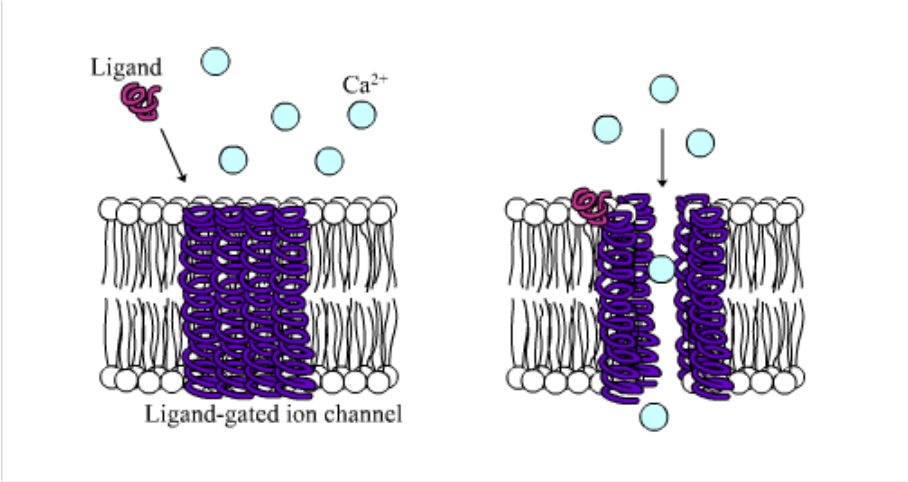

Figure 3: Sketch of a ligand-gated channel; when the neurotransmitter, the ligand, binds to the gate it opens allowing the ions to pass through. This is a Calcium channel, calcium, like sodium, is found in higher concentrations outside the cell so the chemical gradient, as well as the voltage gradient, means these ions flow into the cell from outside, increasing its potential. This is therefore part of an excitatory synapse. Inhibitory synapses have ligand-gated potassium and chlorine channels, potassium, as we have discussed, is at a higher concentration inside the cell and so will flow out, depending on the voltage gradient, lowering the potential inside the cell. Chlorine is at a higher concentration outside the cell but is a negative ion, so when it flows in it also lowers the potential. [Diagram modified from wikipedia.]

allows a flow of ions in or out of the dendrite, changing the voltage there. A cartoon of a ligand-gated channel is given in Fig. 3.

Which ion and which direction, depends on the synapses, we will return to that. For now, though, let us continue describing what happen; after the neurotransmitter floods the cleft it is quickly reabsorbed through neurotransmitter reuptake pumps. Some of the neurotransmitter is absorbed into the bouton, some into the spine and some is absorbed by the astrocyte, the important thing is that the concentration of neurotransmitter in the cleft falls rapidly. Now, the fluid of the cleft has little neurotransmitter, but there is still neurotransmitter bound to the receptors of the ligand gated channels.

This gradually unbinds, this is usually imagined to be a random process, because of the Brownian motion of molecules in the fluid of the cleft and the thermal vibration of the receptor itself, the neurotransmitters unbind as the result of random collisions and thermal variations. As they do so, the channels close again and the conductivity of the dendritic spine's membrane falls back towards zero.

Post-synaptic potential

If we put aside messy nuances such as neuromodulation and co-release of multiple neurotransmitters, the vast majority of neurons the adult brain can be roughly classed as excitatory or inhibitory. Excitatory neurons release neurotransmitters that open sodium or calcium channels in their targets—allowing positive ions to enter the dendrite and increasing membrane voltage. Inhibitory neurons release neurotransmitters that open potassium or chloride channels, which to pull the post-synaptic cell's membrane voltage toward a value below threshold. All of this is a simplification, and many exceptions exist, but it remains a useful simplification.

The post-synaptic change in potential that results from a pre-synaptic spike is called a **post-synaptic potential**; if the synapse is excitatory this is called an **excitatory post-synaptic potential** or EPSP, if it is inhibitory it is called an **inhibitory post-synaptic potential** or IPSP. The profile of PSPs reflects the neurotransmitter dynamics, it rises fast as the neurotransmitter floods the cleft and the ion-channels open, it then decays back to zero following an exponential decay, reflecting the constant rate unbinding process: since any bound molecule has a constant probability of shaking free the number of unbinding events depends on the number of bound molecules, giving an exponential decay.

Often the post-synaptic conductivity is taken to be a what is called an **alpha** function:

$$i_s(t) = g_s s(t)(E_s - v) \tag{1}$$

where $i_s(t)$ is the synpatic current, E_s is the reversal potential of the synapse and $g_s s(t)$ is the conductance, g_s is a constant describing the strength of the synapse and $s(t)$ is

$$s(t) = te^{-t/\tau_s} \tag{2}$$

where τ_s is a time scale, see Fig. 4.

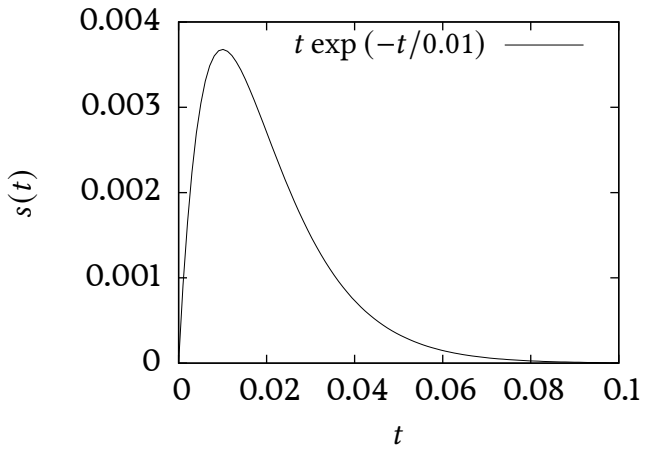

Figure 4: The α-function profile often used to model synaptic conductances, shown here with $\tau_m = 10$ ms.

The rising part of the α function models the period when there is neurotransmitter in the cleft, this is binding to the channels increasing the conductance; the falling part represents the period where the unbound neurotransmitter has been cleared from the cleft and the bound neurotransmitter is unbinding randomly due to the thermal motion of molecules. It is possible to understand these dynamics in terms of the bucket-like equations we have examined before, but this won't be done here. It is also common to leave out the rising part and just model the conductance as

$$\tau_s \dot{s} = -s \tag{3}$$

with

$$s(t) \rightarrow s(t) + 1 \tag{4}$$

whenever there is a spike. This is what is done in the coursework, for example.