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 variablity 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 dentrite of the other, though axon to axon gap junctions are also found. For an axon to dentrite 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 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 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 allows a flow of ions in or out of the dendrite, changing the voltage there.

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

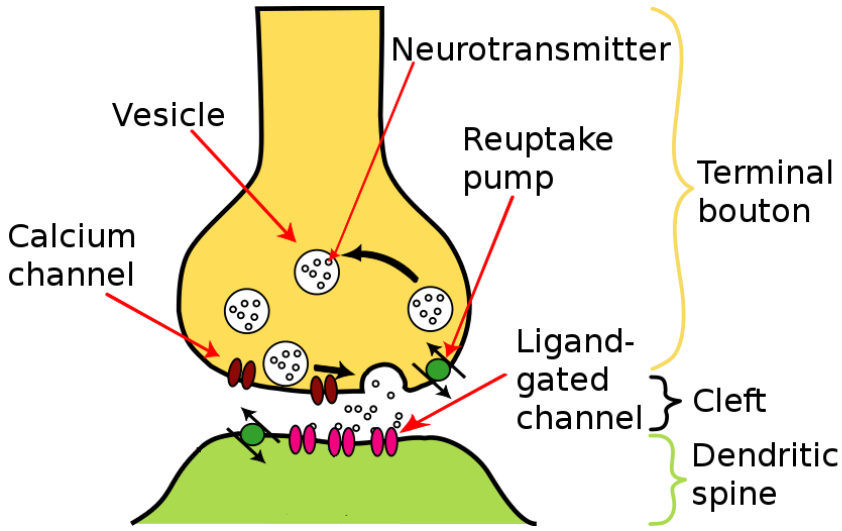

Figure 1: The major parts of the synapse; this shows a vesicle bursting, releasing neurotransmitter into the cleft, this will bind with the ligand-gated channels to allow a current across the membrane of the dendrite. Reuptake pumps are shown in the bouton and the spine, there are also pumps in the astrocyte that surrounds the cleft but isn't shown here. Some is also lost to diffusion. [Diagram modified from one in wikipedia.]

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

One important property of neurons is that a given neuron is either *excitatory* or *inhibitory*. If a neuron is excitatory, this means all its synapses are excitatory, that is, they make the post-synaptic neuron more likely to spike by increasing its voltage. In an excitatory neuron opening the ligand-gated channels causes a positive current into the cell, typically this means that they are sodium or calcium channels, so that when they open positive sodium or calcium ions flow into the dendrite. Conversely, if a neuron is inhibitory all its synapses are inhibitory, they make the post-synaptic cell less likely to fire by decreasing its voltage. In an inhibitory synapse opening the ligand-gated channels causes a positive flow out of the dendrite, lowering the voltage. Typically inhibitory channels are either potassium gates, allowing postive potassium to leave the dendrite, or chlorine gates, allowing negatively charged chlorine to flow in.

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.

From a modeling point of view all this means that there is a current corresponding to the synapse:

$$I_s(t) = g_s(t)(E_s - V) \tag{1}$$

where $g_s(t)$ is the conductance at the synapse and E_s is the reversal potential for whichever ion the synapse conducts, for an excitatory synapse this might be the reversal potential for sodium so that E_s is perhaps 20 mV, for an inhibitory neuron it might be potassium with $E_s = -80$ mV, for example. The next part of the model needs to describe the dynamics of $g_s(t)$. For convenience we often write

$$g_s = \bar{g}_s s(t) \tag{2}$$

where $\bar{g}_s$ is the overall strength and $s(t)$ is the bit that changes with time. The simplest model is probably one that ignores any detail of the rapid process of vesicle release and binding, it also ignores any interaction between spikes, the possibility some channels might already have bound to a neuro-transmitter, or that the calcium in the synapse may have accumulated or that the vesicles may have depleted.

In this simplified situation the synapse model only accounts for the gradual closing of the channels as they unbind from the neurotransmitter and the sudden increase of open channels whenever a spike arrives. In this model the equation is just model the conductance as

$$\tau_s \frac{ds}{dt} = -s \tag{3}$$

with

$$s(t) \to s(t) + p \tag{4}$$

whenever there is a spike, where p is a constant, often taken as one.