Types of neurons and synapses

This short note emphasises an important fact about the brain: there are many different types of neurons and synapses.

Dale's principle

In lecture notes 01.2 "Synapses", we noted that synapses come in (roughly) two broad classes: excitatory synapses that make the post-synaptic neuron more likely to fire a spike, and inhibitory, which make it less likely. (Some neurotransmitters have effects that can be described as *modulatory*; We touch upon this in the last subsection of these notes). Typically, a single neuron will receive a mixture of excitatory, inhibitory, and modulatory inputs from many different sources. Perhaps surprisingly, the picture is usually simpler when it comes to the chemical signals that a neuron *emits* onward to other cells: Most neurons release the same set of chemicals from all terminal boutons on their axon, regardless of the identity of cell receiving these synaptic connections. This is known as *Dale's principle*

According to Dale's principle, the majority of neurons can be roughly classed as *excitatory neurons* whose outgoing synapses are all excitatory, or *inhibitory neurons* whose outgoing synapses are all inhibitory. It is important to understand that the division relates to the outgoing signals, neurons usually receive a mixture of excitatory and inhibitory signals.

In cortex, inhibitory neurons tend to be small and to have only local connectivity; they are also diverse with many different types: basket cells, stellate cells, fast-spiking PV cells, and many others. The excitatory neurons are usually larger, they tend to have local and distal connections and come in varieties of one main type: the pyramidal cell. It is tempting to think of the pyramidal cells as doing 'the work' and the inhibitory cells as helping modulate and sculpt the activity of the pyramidal cells. It remains to be seen if that is a useful way of thinking of what happens. In other parts of the brain there are circuits where the *principal cells*, the ones tasked with signalling outside of the region, are inhibitory.

More types of synapses

Synapses are also classified by the sort of neurotransmitter they produce. For excitatory synapses this is almost always *glutamate*, a small amino acid. This does not end the classification; there are different receptor types for glutamate, the main ones are called *NMDA* and *AMPA*; the acronyms are short for complicated chemical names and we are, here, straying into more detail than we need. The main point is that NMDA and AMPA receptors have different behaviours, both in short-term in the time course of their binding to the transmitter, and in the longer term, in how they change in number and strength in response to what is happening at the synapse. A glutamate synapse will usually have a mixture of ligand-gated channels with NMDA and AMPA receptors.

For inhibitory synapses the most common neurotransmitter is called *GABA*, again, the acronym is short for a complicated chemical name. There are also two types of receptor here, but these are classes of receptors rather than distinct receptors as in the case of glutamate. The story for inhibitory synapses is more complex even than the story of excitatory synapses: the two classes are *ionotropic* receptors and *metabotropic* receptors. Metabotropic receptors trigger biochemical signals, rather than modulating voltage dynamics via the conductance's of ligand-gated ion channels.

Again, we risk straying into the massive complexity of synapses; the main point of this short subsection is to note that there is a complicated story and to, perhaps, suggest that the complexity of synapses and the huge range of behaviours in terms of the temporal behaviour and the different PSP profiles this produces is an interesting element of any attempt to compare learning in the brain and in computers.

Neuromodulation

We have concentrated so far on electrical signalling; the part of neuronal computation that involves neurons sending spikes to each other. There is another system in the brain that is important for computation: neuromodulation. Neuromodulators are chemicals that can change the behaviour of a neuron or synapse; there are a lot of different neuromodulators, but the 'big five' are serotonin, dopamine, acetylcoline, histamine, and noradreneline (also called norepinephrine). Many other small molecules and peptides have been identified as having neuromodulatory functions.

Neuromodulators are released at synapses by specialised cells that are usually found in specific brain regions but with axons that spread over the whole brain. Sometimes the neuromodulator is released to one post-synaptic cell, but often they are released into the extracellular fluid so that they affect a group of cells.

There are a large number of different receptors for the neuromodulators and these can have complicated affects, changing the excitability of a neuron for example, or prompting a synapse to change strength.

It is common to think of neuromodulation as adjusting the computational circuit, like a series of knobs and levers which can up- or down-regulate the computational dynamics and they do so over different timescales. These neuromodulators are very interesting because they seem to link the quite low-level details of how circuits work, they are produced by neurons in response to signals to those neurons, and high-level behaviours. Changes in neuromodulation can be linked to different decision-making strategies and can, it is thought, be experienced as mood.