

Types of neurons and synapses

This is just a short note to emphasize an important fact about the brain: there are lots of different types of neurons and lots of different types synapses.

Dale's principle

We saw that synapses come in two broad classes, excitatory synapses which make the post-synaptic neuron more likely to fire a spike and inhibitory, which make it less likely. Perhaps surprisingly, a given neuron will only ever have one type of synapse; this is known as *Dale's principle*. It means that neurons are also divided into two main types, *excitatory neurons* whose synapses are all excitatory and *inhibitory neurons* whose synapses are all inhibitory. This division into excitatory and inhibitory neurons appears to be a substantial difference between neurons in the brain and the nodes, a sort of idealized neuron, that make up typical neural networks. It is important to understand that the division relates to the out-going signals, neurons usually receive a mixture of excitatory and inhibitory signals.

In the cortex; the part of the brain which most obviously distinguishes mammals from simpler animals, the inhibitory neurons tend to be small and to have only local connectivity; they are also pretty diverse with lots of different types, basket cells, stellate cells, fast-spiking PV cells. 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 *principle 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 might 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 with the metabotropic receptors actually deviating from our description of how synapses work since they don't directly involve ligand-gated 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 which can change the behaviour of a neuron or synapse; there are a lot of different neuromodulators, but the 'big four' are serotonin, dopamine, acetylcholine and noradrenaline. Neuromodulators are released, at synapses, by specialised cells which 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, 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.