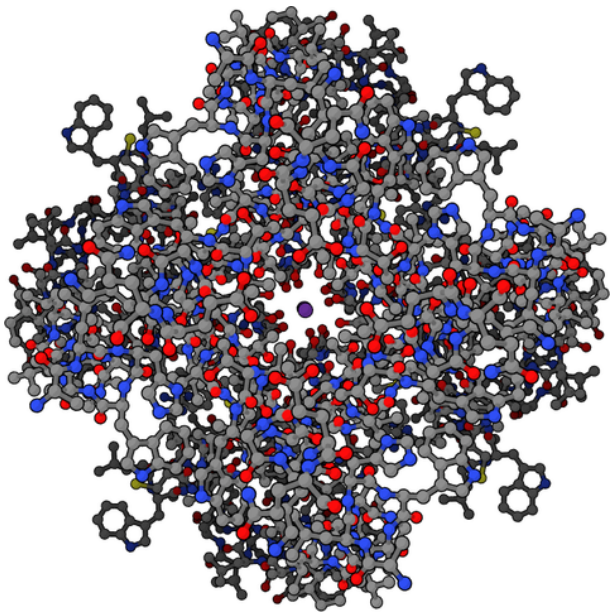


Figure 1: An open potassium channel, picture from wikipedia, which in turn took it from the Protein Data Bank. `http://en.wikipedia.org/wiki/Potassium_channel`

Gated channels

The nonlinear dynamics that neurons rely on to form spikes arise from the **voltage-gated channels**; these are ion channels whose conductance varies as the voltage varies. They are tiny molecular machines which, crucially, are ion selective: only sodium ions can pass through a sodium gate, only potassium ions through a potassium gate. Each individual gate has a number of different gating states. We will briefly examine this, but ultimately each one is either open or closed, the overall smooth, though rapid, variation in these conductances comes from average a large number of individual discrete step-like changes as the individual gates open and close.

The potassium channel is a **persistent** gate; this is actually a little complicated, but roughly speaking it has one type of closed state and one type of open state; the sodium channel, which we will look at after the potassium channel also has one open state, but it has two types of closed states.

The potassium gate is actually composed of four independent subgates, all

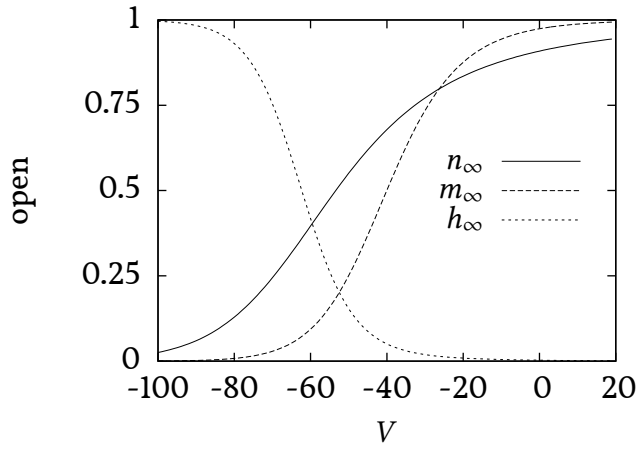


Figure 2: The asymptotic values of the gating probabilities.

these gates must be open to allow potassium ions through, but each has its own independent dynamics. The membrane is usually modelled as having overall potassium conductance

$$g_K = \bar{g}_{\mathrm{K}} n^4 \tag{1}$$

where $\bar{g}_{\mathrm{K}}$ would be conductance if all the channels were open and n is the probability an individual subgate is open so n^4 is the probability an individual gated channel is open. The dynamical equation for n is quite complicated, it is of the standard form

$$\tau_n(v)\dot{n} = n_\infty(v) - n(t) \tag{2}$$

If $\tau_n(v)$ and $n_\infty(v)$ where constant this would be simple, $n(t)$ would decay to n_∞ with a timescale of τ_n, however they aren't constants, they are functions of the membrane potential.

A graph of $n_\infty(v)$ is shown in Fig. 2. We can see that n is small when the voltage is near the resting value but climbs towards one as v increases. Now, n isn't equal to n_∞, rather it decays towards it with a time constant given

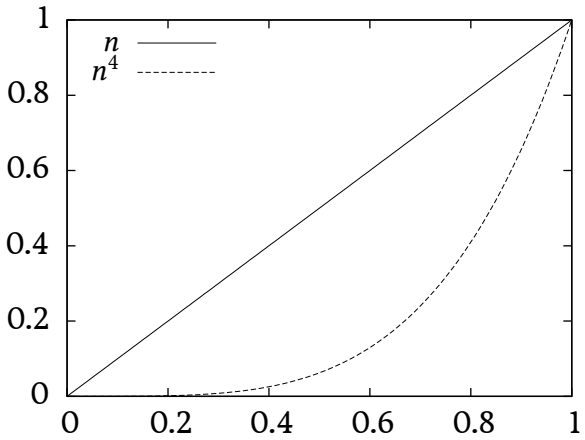


Figure 3: The fourth power gives crisper behavior than n itself would.

by $\tau_n(v)$, but we can see that the potassium channels open as the voltage increases. Before looking at how these play a role in spiking we will look at the sodium gates. It is worth noting though the way having four independent gates makes the dynamics crisper: if n is near zero, n^4 is very small indeed. This is illustrated in Fig. 3.

We also need to discuss reversal potentials. You would expect the flow of potassium to be determined by $g_K v$, but it isn't. Because there are more potassium ions inside the cell than outside they would flow out even if $v = 0$. In fact, as we discussed when looking at the integrate and flow model, we assume this doesn't change Ohm's law, the relationship between potential difference and current, rather, it just changes the zero point:

$$i_K = g_K(E_K - v) \tag{3}$$

where $E_K = -70$ mV, approximately, is called the reversal potential and can be calculated using an equation called the Nernst equation.

The sodium channel is called a transient channel because it has two closed states and one open one; generally its dynamics during the spike is

$$\text{closed I} \rightarrow \text{open} \rightarrow \text{closed II} \tag{4}$$

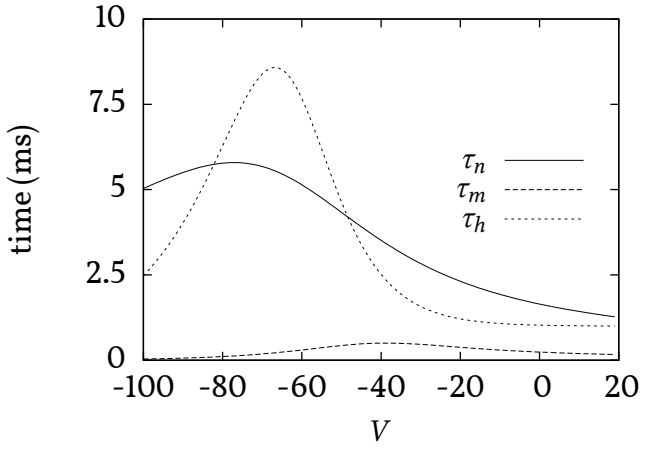


Figure 4: The time constants for the gating probabilities.

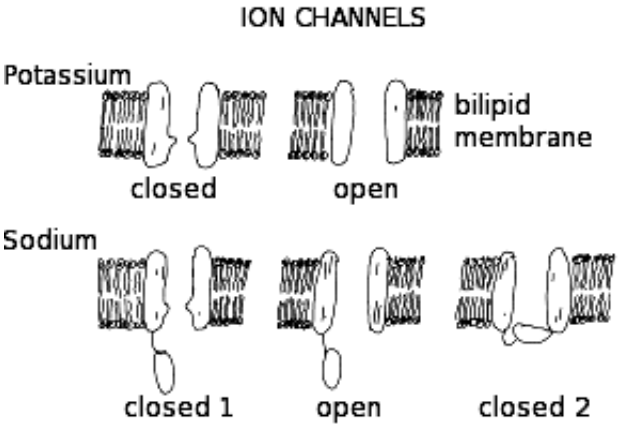


Figure 5: A cartoon of the two types of voltage gated channel we are discussing; the persistent potassium channels open as the voltage rise, the transient sodium channel opens and then closes again.

After that there is a slower process of resetting. The part of the gate that is closed to give the initial closed state is very like the potassium gate, but with three sub-gates; the probability of these sub-gates being open is usually called m; the other part, the gate that closes to give the second closed state is different in that it is not made of sub-gates, its probability of being open is usually called h and its asymptotic value, h_∞, is near one for lower V and near zero for larger. A cartoon of all this is given in Fig. 5. Fig. 2 includes graphs of $m_\infty(V)$ and $h_\infty(V)$. Finally, the reversal potential for sodium is $E_{\text{Na}} = 50$ mV. The sodium current is therefore

$$i_{\text{Na}} = g_{\text{Na}}(E_{\text{Na}} - v) \tag{5}$$

with

$$g_{\text{Na}} = \bar{g}_{\text{Na}} m^3 h \tag{6}$$

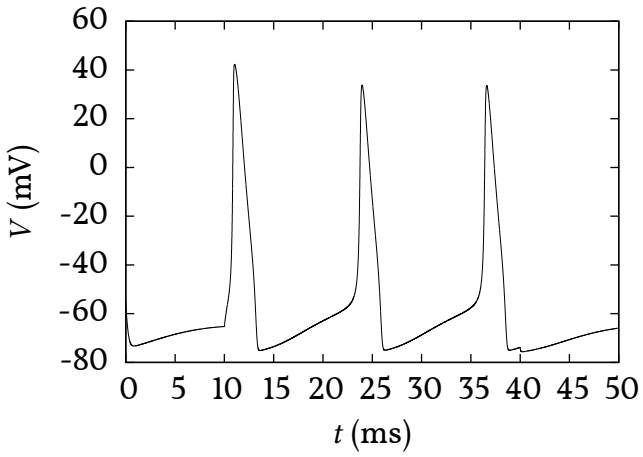
All of this together gives the Hodgkin-Huxley equation, which equates the rate of change of v to a set of currents, the leak current giving the roughly linear behaviour below threshold we saw in the integrate and fire model and the gated channels forming the spike.

$$C_m \dot{v} = \text{currents} \tag{7}$$

We can now give a rough description of how spikes are formed. The time constants τ for the three gating probabilities are given in Fig. 4, these are quite complicated, but the key thing is that τ_m is very small, no matter what the value of V is. This means that m stays very close to its asymptotic value m_∞. As V approaches the threshold of about -55 mV, m increases towards one, with m^3 increasing even more dramatically. Opening the sodium gates allows sodium to flood the cell, increasing the V further and further opening the gates. This gives the rapid upswing in voltage, the rising part of the spike. The other two gating probabilities have slower dynamics and it takes n and h a while to catch up with n_∞ and h_∞. However, as h decreases, it closes the sodium gates again, preventing more sodium getting in to the cell; n increases opens the potassium gates, potassium flows out reducing the V again, back towards -70 mV. This gives the downswing of the spike. Afterwards everything resets. An example spike is shown in Fig. 6.

For a more accurate model further channels, and therefore further currents, can be added, other sodium and potassium channels with different dynamics, or a calcium channel. It is also common to investigate models 'between'

A



B

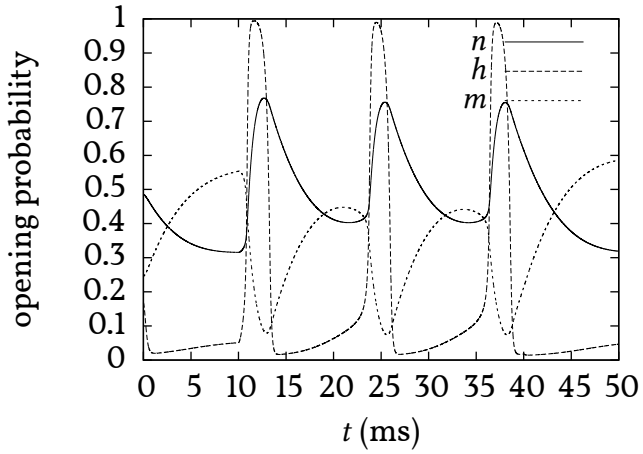


Figure 6: Some spikes in the HH model. **A** shows the spikes produced by a standard HH model in response to a current input. **B** shows how the gating probabilities vary during the spike, in this graph h and m are labelled the wrong way around.

the integrate and fire model and the Hodgkin-Huxley equation which add some of the nonlinearity to the integrate and fire dynamics.

Summary

There are voltage-dependant channels in the cell membrane. These are modelled with the equation

$$\tau_\ell(v)\dot{\ell} = \ell_\infty(v) - \ell \tag{8}$$

where ℓ is standing in for one of the so called gating probabilities. Here we consider the channels found in the giant axon of the squid. This has a potassium channel with conductance:

$$g_{\mathrm{K}} = \bar{g}_{\mathrm{K}} n^4 \tag{9}$$

with gating probability n and a sodium channel with conductance

$$g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} m^3 h \tag{10}$$

with gating probabilities m and h. In the case of the the sodium channel the timescale for m is small so m closely tracks m_∞; this rises towards one as voltage increase beyond the threshold, so, provided h is not close to zero, the sodium channel opens as the voltage crosses zero, since the reversal potential for sodium is high, this means sodium rushes in, causing m to increase still further. However, h does not remain above zero, as the votage increases h_∞ falls to zero and τ_∞ decreases, causing the sodium conductance to fall. At the same time, the potassium conductance increases, since the reversal potential for potassium is low this causes a current out of the cell, pushing the voltage back down. Thus a spike is formed.

References

[1] Hodgkin, AL and Huxley HF (1952) "Propagation of electrical signals along giant nerve fibres." Proceedings of the Royal Society of London. Series B, Biological Sciences 140: 177-183.