Introduction

These notes are about the dynamics of a single neuron, it will cover the Hodgkin Huxley equation, the Integrate and Fire model and the behavior of synapses. I offer an error bounty of between 20p and 2 pounds for mistakes. Contact me at `conor.houghton@bristol.ac.uk` or come up after a lecture.

Electrical properties of a neuron

The potential inside a neuron is lower than the potential on the outside; this difference is created by ion pumps, small molecular machines that use energy to pump ions across the membrane seperating the inside and outside of the cell. One typical ion pump is Na+/K+-ATPase (Sodium-potassium adenosine triphosphatase); this uses energy in the form of ATP, the energy carrying molecule in the body, and through each cycle, it moves three sodium ions out of the cell and two potassium ions into the cell. Since both sodium and potassium ions have a charge of plus one, this leads to a net loss of one atomic charge to the inside of the cell lowering its potential. It also creates an excess of sodium outside the cell and an excess of potassium inside it. We will return to these chemical imbalances later. The potential difference across the membrane is called the **membrane potential**. At rest a typical value of the membrane potential is $E_L = -70\text{mV}$.

There is an interesting argument that explains the voltage scales for the electrodynamics of neurons; it is useful because it touches on themes we will return to in our study of neurons. Basically we will see that neurons work partly due to diffusion, which in turn depends on ions fly around because of their thermal energy. We know the thermal energy of an ion at temperature T, it is k_BT where k_B is the Boltzmann constant. Now, consider the potential difference with that corresponding energy, the energy required to move an ion of charge one across a voltage V_0 is qV_0, so for neurons to work we would expect the scale of the voltages involve to be of the order where the thermal energy was similar to the energy required to overcome the voltage gap, that is, we expect the voltage gap to be able to modulate that flow. Hence $qV_0 \approx k_BT$ or

$$V_0 \approx \frac{k_BT}{q} \approx 27\,\text{mV} \tag{1}$$

at room temperature.

Spikes

So the summary is that **synapses** cause a small increase or decrease in the voltage; **excitatory synapses** cause an increase, **inhibitory synapses** a decrease. This drives the internal voltage dynamics of the cell, these dynamics are what we will learn about here. If the voltage exceeds a threshold, say $V_T = -55$ mV there is a nonlinear cascade which produces a **spike** or **action potential**, a spike in voltage 1-2 ms wide which rises above 0 mV before, in the usual description, falling to a reset value of $V_R = -65$ mV, the cell then remains unable to produce another spike for a **refractory period** which may last about 5 ms.

Buckets of water

In the simplest model of neurons their voltage dynamics is similar to the dynamics of a bucket with a leak. In this analogy a bucket, with straight sides, is filled to a height V, water pours

in the top at a rate I, which might depend on time, so $I(t)$, and water leaks out a hole in the bottom. The amount of water leaking out is GV, V bacause the more water there is, the higher the pressure at the hole and G so that we can specify the size of the hole.

Now, the V is the height of the water not the volume, the confusing use of V is to aid the analogy with neurons where V is the voltage. The volume is VC where C is the cross-sectional area of the bucket. The rate of change of the volume is the water flowing in I, hence

$$\frac{dCV}{dt} = I - GV \tag{2}$$

or

$$\frac{dV}{dt} = \frac{1}{C}(I - GV) \tag{3}$$

Lets solve this equation for constant I before going on to look at neurons. Probably best to do this using an integrating factor, let $\tau = C/G$ and $\tilde{I} = I/G$

$$\tau\frac{dV}{dt} + V = \tilde{I} \tag{4}$$

then we multiply across by $\exp t/tau$

$$\tau e^{t/\tau}\frac{dV}{dt} + e^{t/tau}V = \tilde{I}e^{t/tau} \tag{5}$$

Now we can rewrite the left hand side using the product rule

$$\frac{d}{dx}(uv) = u\frac{dv}{dx} + v\frac{du}{dx} \tag{6}$$

to give

$$\tau\frac{d}{dt}\left(e^{t/\tau}V\right) = \tilde{I}e^{t/tau} \tag{7}$$

Now integrating both sides gives

$$e^{t/\tau}V = \tilde{I}e^{t/tau} + A \tag{8}$$

where A is an integration constant. This gives

$$V = Ae^{-t/\tau} + \tilde{I} \tag{9}$$

and putting $t = 0$ shows $A = V(0) - \tilde{I}$ so

$$V = [V(0) - \tilde{I}]e^{-t/\tau} + \tilde{I} \tag{10}$$

so, basically, the value of V decays exponentially until it equilibriates with $\tilde{I}$.

The bucket-like equation for neurons

We will now try to extend this equation so that it applies to neurons. First off V is now voltage and C will be replaced by c_m, the capacitance of the membrane, the amount of electrical charge that can be stored at the membrane is C_mV, the amount of electrical charge is the analog of the volume of water. The charge leak is a bit more complicated, because of the chemical gradients, that is the effects of the differing levels of ions inside and outside the cell along and

their propensity to diffuse, the voltage at which there is no leaking of charge is not zero, it is $E_L = -70$mV, roughly. G is now G_m, a conductance, the leak current is $G_m(V - E_L)$, as above, we actually divide across by it, and write $R_m = 1/G_m$, the resistance. Finally, we write $\tau_m = C_m/G_m$ to get

$$\tau_m \frac{dV}{dt} = E_L - V + R_m I \tag{11}$$

I might end up being synaptic input, but traditionally we write the equation to match the *in vivo* experiment where I is an injected current from an electrode, so we write I_e, 'e' for electrode.

This leaves out the possibility that there are other non-linear changes in the currents through the membrane as V changes. This is a problem since there are other non-linear changes in the currents through the membrane as V changes. The equation above leaves these out, in fact, the nonlinear effects are strongest for values of V near where a spike is produced, so one approach is to use the linear equation unless V reaches a threshold value and then add a spike 'by hand'. This is the **leaky integrate and fire model**.

- V satisfies
$$\tau_m \frac{dV}{dt} = E_L - V + R_m I_e \tag{12}$$
- If $V \geq V_T$ a spike is recorded and the voltage is set to V_R.

This model is easy to solve; if I_e is constant we have already solved it above up to messing around with constants. If I_e is not constant it may still be possible to solve the equation, but in any case the equation can be solved numerically on a computer. Basically you divide time up into small steps, assume I_e is constant for each small step and use the analytic constant-input equation to get from one time step to another. Alternatively the equation can be solved using a numerical approach to solving differential equations, such as the Euler method, or Runge Kutta.

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

$$g_K = \bar{g}_K n^4 \tag{13}$$

where $\bar{g}_K$ 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

$$\tau_n(V) \frac{dn(t)}{dt} = n_\infty(V) - n(t) \tag{14}$$

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. Before looking at how these play a role in spiking we will look at the sodium gates.