Phase analysis

To recap, we have seen the Hodgkin Huxley equation

$$C_m \frac{dV}{dt} = g_{\mathrm{l}}(E_{\mathrm{l}} - V) + g_{\mathrm{Na}}(E_{\mathrm{Na}} - V) + g_{\mathrm{K}}(E_{\mathrm{K}} - V) + I \tag{1}$$

where the sodium and potassium conductances, g_{Na} and g_{K} have complicated non-linear dynamics. In fact, the Hodgkin-Huxley equation is really four equation, an equation for V along with equations for the three gating variables n, m and h, each of the form

$$\frac{dk}{dt} = \alpha_k(1-k) - \beta_k k \tag{2}$$

with k standing in for n, m or h and $\alpha_k(V)$ and $\beta_k(V)$ being the probability of going from closed to open and open to closed. By moving stuff around this can be easily rewritten in a familiar form

$$\tau_k \frac{dk}{dt} = k_\infty - k \tag{3}$$

with

$$\tau_k = \frac{1}{\alpha_k + \beta_k} \tag{4}$$

and

$$k_\infty = \frac{\alpha}{\alpha_k + \beta_k} \tag{5}$$

Hence the ion channels relax towards some asymptotic value n_∞, m_∞ and h_∞ with some time scale τ_n, τ_m and τ_h; however all these quantities depend on the voltage so the equations are coupled to the voltage equation.

When it is recognized as a system of four non-linear differential equation it is clear that it may prove hard to analyse the Hodgkin-Huxley equation; for example, the phase space is four-dimensional for a start, making it hard to picture. For this reason it is common to simplify the Hodgkin-Huxley equation in the hope of getting some insight into its behaviour, this is important, for example, if you are interested in getting an intuitive understanding of how different neuronal models can support the different behaviours of observed in neurons: some neurons spike continuously, some don't; some burst, that is, switch back and forth between high spiking and low spiking states.

The goal then is look at models that approximate the Hodgkin-Huxley equation and simplify while keeping it complex enough so that it is still a rich enough to model spiking.

The Morris-Lecar model

The key idea behind the Morris-Lecar model [1] is that τ_m is very small. When we looked at the behaviour of equations like the equation for m we saw that the functions track their asymptotic value, with the τ value governing how closely it succeeds in reaching the equilibrium situation where m equals m_∞. Thus in the Morris-Lecar model m^3 is replaced by an asymptotic value. Next the effect of h is ignored, or lumped in with n. Altogether this gives a two-dimensional model of the neuron which is much easier to think about. The model is simplified further by ignoring the indices on the gating variables, so the single gating variable appears with a single power.

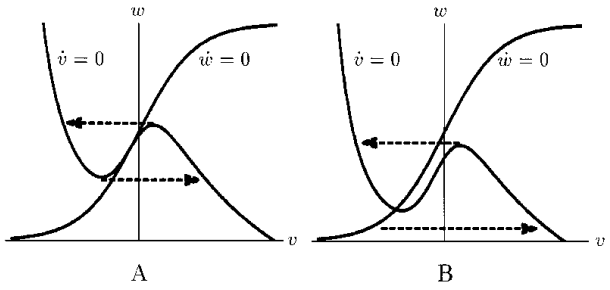

Figure 1: This shows the phase space for the Morris-Lecar equation, it is a temporary figure taken from DOI10.1007/s002850050157 which uses a lower case v for V and uses w where we use n.

Just as the Hodgkin-Huxley model is a model of a specific axon, the squid giant axon, that is adapted to wider use, the Morris-Lecar is a model of a muscle fibre in the barnacle. Like Hodgkin and Huxley, they wrote down an equation of the form they expected to work and then adjust parameters to fit the actual data. In the barnacle the main ion responsible for depolarization is calcium rather than by sodium, so the model has calcium rather than sodium, in applying the model to other neurons this could be changed.

The Morris-Lacer model is

$$\tau_m \frac{dV}{dt} = E_\mathrm{l} - V + R_m g_\mathrm{Ca} m_\infty (E_\mathrm{Ca} - V) + R_m g_\mathrm{K} n (E_\mathrm{K} - V) + R_m I \tag{6}$$

and

$$\tau_n \frac{dn}{dt} = n_\infty - n \tag{7}$$

where

$$\begin{aligned} m_\infty &= \frac{1}{2}\left(1 + \tanh\left[\frac{V - V_1}{V_2}\right]\right) \\ n_\infty &= \frac{1}{2}\left(1 + \tanh\left[\frac{V - V_3}{V_4}\right]\right) \\ \tau_n &= 1/\left(\phi \cosh\left[\frac{V - V_3}{2V_4}\right]\right) \end{aligned} \tag{8}$$

Obviously there are lots of parameters here, and changing the parameters changes the behaviour of the model; a set of typical values would be $\tau_m = 10\,\mathrm{ms}$, $R_m g_\mathrm{Ca} = 2$, $E_\mathrm{Ca} = 120\,\mathrm{mV}$, $R_m g_\mathrm{K} = 8$, $E_\mathrm{K} = -84\,\mathrm{mV}$,$V_1 = -1.2\,\mathrm{mV}$,$V_2 = 18\,\mathrm{mV}$,$V_3 = 2\,\mathrm{mV}$,$V_4 = 30\,\mathrm{mV}$,$\phi = 0.04\,\mathrm{kHz}$.

Now, to understand how this equation works we will examine the nullclines, the lines where the derivatives are zero: $dV/dt = dn/dt = 0$. This is actually quite difficult to work out because the formulas are so complicated, but the key point is that the V-nullcline has a sort of cubic shape which for many parameter values is cut by the n-nullcline, an example is given in Fig. 1.

It is possible to understand different spiking regimes from this figure. Remember the nullclines separate areas with different signs for dV/dt and dn/dt, to the left of the dn/dt nullcline n increases, to the right it decreases, above the dV/dt nullcline V decreases, below it, it increases. In Fig. 1A there is a single equilibrium point where the two lines cross, but it is easy

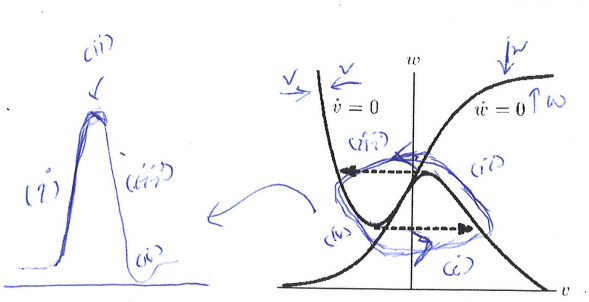

Figure 2: This is a sketch for the Morris-Lecar limit cycle.

to see from the arrow directions that this is unstable, in fact there is a limit cycle and the equation with this phase diagram exhibits regular spiking, this is shown in Fig. 2. In Fig. 1B the equilibrium point is stable so this time the model does not spike regularly, however if the system is moved away from the equilibrium point it sometimes returns there by spiking.

FitzHugh-Nagumo model

One advantage of the FitzHugh-Nagumo model [2, 3] is that it is clear how it derived from the Hodgkin-Huxley equation, though a formal derivation yields slightly different results. However, one disadvantage is that the actual mathematical form of the equations is quite complicated; for example, there is no easy way to solve for the nullclines. Although its origin is quite different one way to think of the FitzHugh-Nagumo model is as a model that has a similar phase plane as the Morris-Lecar, but a much simpler form. The FitzHugh-Nagumo model is

$$\begin{aligned} \frac{dw}{dt} &= v - \frac{1}{3}v^3 - w + I \\ \tau\frac{dw}{dt} &= v + a - bw \end{aligned} \tag{9}$$

where a little-v, v, has been used for the voltage to show these quantities shouldn't be take seriously as biologically relevant, they have been scaled to, for example, get rid of one of the time constants.

In this case we can solve the nullclines easily, the v-nullcline is

$$w = v + \frac{1}{3}v^3 + I \tag{10}$$

and the w-nullcline

$$w = \frac{v + a}{b} \tag{11}$$

We see clearly that the v-nullcline has the same cubic shape as is the case of the Morris-Lecar, the w-nullcline is a straight line now, before it was a sort of sigmoid shape, but it has the same property of crossing the v-nullcline at exactly one place. This gives a similar limit cycle as before: Fig. 3.

In this model we can see the effect of changing I, it shifts the v-nullcline up and down, as it does so it moves the equilibrium point from stable to unstable and therefore shifts the model from spiking to quite. There is nice animation of this available at

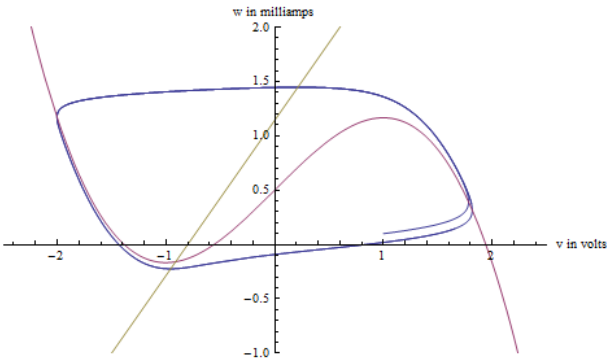

Figure 3: This is a graph of the FitzHugh-Nagumo phase plane with a limit cycle. The parameter values $I = 0.5$, $a = 0.7$, $b = 0.8$, and $\tau = 12.5$ and the figure is taken from Wikipedia.

`www.scholarpedia.org/article/FitzHugh-Nagumo_model`.

One application of this is the study of bursting cells and pattern generation; these are cells that send out regular burst of neurons; these dynamics are important in controlling some fundamental physiological systems where patterns are important, chewing in slugs, struggling in tadpoles and so on. For this to work there is a slow current, for example, a potassium current, whose effect is to reduce I. The slow current sharply increases every time there is a spike and then decays away slowly and these dynamics are considered slow enough that it can be treated separately to the dynamics of v and w. This means that as the neuron spikes I is decreased because of the increase in the potassium current, eventually this cause the equilibrium point to shift from an unstable point to a stable on and spiking stops; it doesn't start again until the potassium current decays away.

References

[1] Morris, C and Lecar, H (1981), Voltage Oscillations in the barnacle giant muscle fibre Biophys. J., 35:93–213

[2] FitzHugh R. (1955) Mathematical models of threshold phenomena in the nerve membrane. Bull. Math. Biophysics, 17:257–278

[3] Nagumo J., Arimoto S., and Yoshizawa S. (1962) An active pulse transmission line simulating nerve axon. Proc. IRE. 50:2061–2070.