

## Phase analysis

To recap, we have seen the Hodgkin Huxley equation

$$C_m \frac{dV}{dt} = g_\ell(E_\ell - V) + g_{\text{Na}}(E_{\text{Na}} - V) + g_{\text{K}}(E_{\text{K}} - V) + I \quad (1)$$

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

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

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

$$\tau_k \frac{dk}{dt} = k_\infty - k \quad (3)$$

with

$$\tau_k = \frac{1}{\alpha_k + \beta_k} \quad (4)$$

and

$$k_\infty = \frac{\alpha_k}{\alpha_k + \beta_k} \quad (5)$$

Hence the ion channels relax towards some asymptotic value  $n_\infty$ ,  $m_\infty$  and  $h_\infty$  with some time scale  $\tau_n$ ,  $\tau_m$  and  $\tau_h$ ; however all these quantities depend on the voltage so the equations are coupled to the voltage equation.

This is a complicated non-linear equation; in fact, real neurons are likely to be even more complicated. As was mentioned before; the Hodgkin-Huxley equation as described here describes the voltage dynamics of the squid giant axon. The same name is often used to describe the more complex versions of these models

$$C_m \frac{dV}{dt} = \text{lots of different ionic currents} \quad (6)$$

used to describe real neurons. These typically include other channels, often more than one potassium channel which adds other timescales to the dynamics, calcium channels which play some of the same role as the sodium

channels, other sodium channels with more complex dynamics, calcium-gated potassium channels whose open and closing depends not on the voltage but on the concentration of calcium ions, and so on. All of this complexity emphasises the neuron itself as a site of computation, rather than as a node in a network. As such, it is important to understand the dynamics of the neurons models, however, their complexity makes this hard and so we start not by allowing the Hodgkin-Huxley model to become more complex, but by simplifying it.

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

Morris and Lecar [1] developed their model in a direct way as a good model of the dynamics of a muscle fibre in the barnacle. However, 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. Here, however, we will talk about the way this model could approximate the Hodgkin-Huxley model.

The key idea is that  $\tau_m$  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  $\tau$  value governing how closely it succeeds in reaching the equilibrium situation where  $m$  equals  $m_\infty$ . Since  $\tau_m$  tends to be very small, often less than a millisecond, it is reasonable to replace  $m$  by  $m_\infty$ . Next the effect of  $h$  is ignored, or lumped in with  $n$ , in short, from a mathematical point of view stopping the influx of sodium ions and increasing the flow of

potassium is similar to allowing the sodium ions to continue flowing inwards while increasing the potassium flow even more.

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. The sub-gate structure of ion channels gives a very sharp response curve, with gating variables like  $m$  and  $n$  changing rapidly from near zero to near one; however, a similar behaviour can be introduced mathematically by just changing the shape of the asymptotic value.

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 but here we will describe the channel with a positive reversal potential as a calcium channel.

The Morris-Lacer model is

$$\tau_m \frac{dV}{dt} = E_l - V + R_m g_{Ca} m_\infty (E_{Ca} - V) + R_m g_K n (E_K - V) + R_m I \quad (7)$$

and

$$\tau_n \frac{dn}{dt} = n_\infty - n \quad (8)$$

where

$$\begin{aligned} m_\infty &= \frac{1}{2} \left( 1 + \tanh \left[ \frac{V - V_1}{V_2} \right] \right) \\ n_\infty &= \frac{1}{2} \left( 1 + \tanh \left[ \frac{V - V_3}{V_4} \right] \right) \\ \tau_n &= 1 / \left( \phi \cosh \left[ \frac{V - V_3}{2V_4} \right] \right) \end{aligned} \quad (9)$$

Obviously there are lots of parameters here, and changing the parameters changes the behaviour of the model.

Now, to understand how this equation works we will examine the nullclines, the lines where the derivatives are zero:  $dV/dt = dn/dt = 0$ . These nullclines are easily found, they are

$$n = - \frac{E_l - V + R_m g_{Ca} m_\infty (E_{Ca} - V) + R_m I}{R_m g_K (E_K - V)} \quad (10)$$

for the  $v$ -nullcline and

$$n = n_\infty \quad (11)$$

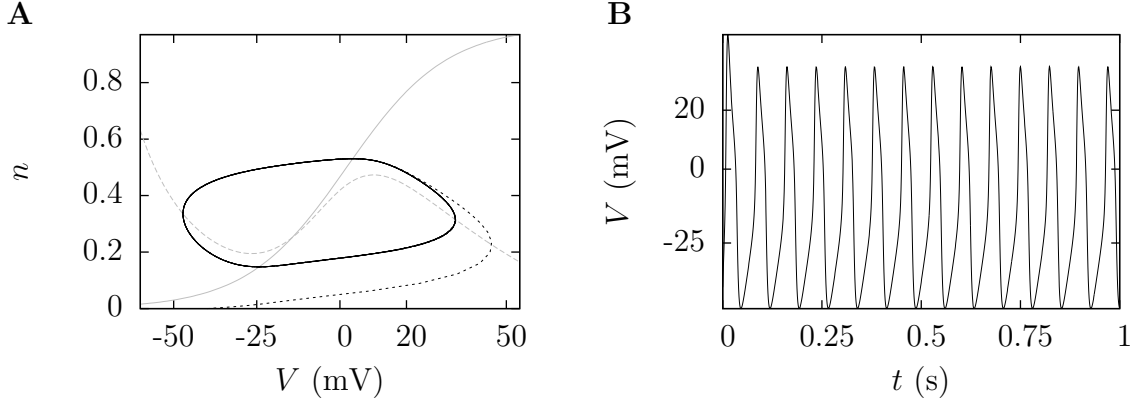


Figure 1: This shows the phase space for the Morris-Lecar equation along with a solution. In **A** the solid grey line is the  $n$ -nullcline, the dotted grey line is the  $V$ -nullcline; the two nullclines cross between the local minimum and maximum of the  $V$ -nullcline, so the equilibrium point is unstable. The dotted black line shows a solution, it starts from  $V = -40$  mV and  $n = 0$  and quickly reaches a stable orbit. The corresponding solution is in **B**. This diagram was produced using `simulation.jl` and all the parameter values can be found there.

for the  $n$ -nullcline. The key point is that the  $V$ -nullcline has a sort of cubic shape which is cut by the  $n$ -nullcline, examples is given in Fig. 1 and Fig. 2.

It is possible to understand different spiking regimes from these figure. Remember the nullclines separate areas with different signs for  $dV/dt$  and  $dn/dt$ . Since  $dn/dt$  is proportional to  $n_{\infty} - n$  if  $n > n_{\infty}$  then  $dn/dt < 0$ ; this is the region above the  $n$ -nullcline and because the nullcline is almost vertical, this is the area on the left of the graph in the figure. Similarly with the  $V$ -nullcline,  $V$  decreases above the nullcline and below it, it increases. This is harder to see from the equation, but we do know that the coefficient of  $n$  is negative for  $V > E_K$  so increasing  $n$  should eventually make  $dV/dt$  negative.

In Fig. 1A there is a single equilibrium point where the two lines cross, but it is possible to guess from the arrow directions that this point is unstable. For example, a small perturbation increasing  $V$  moves the neuron to the

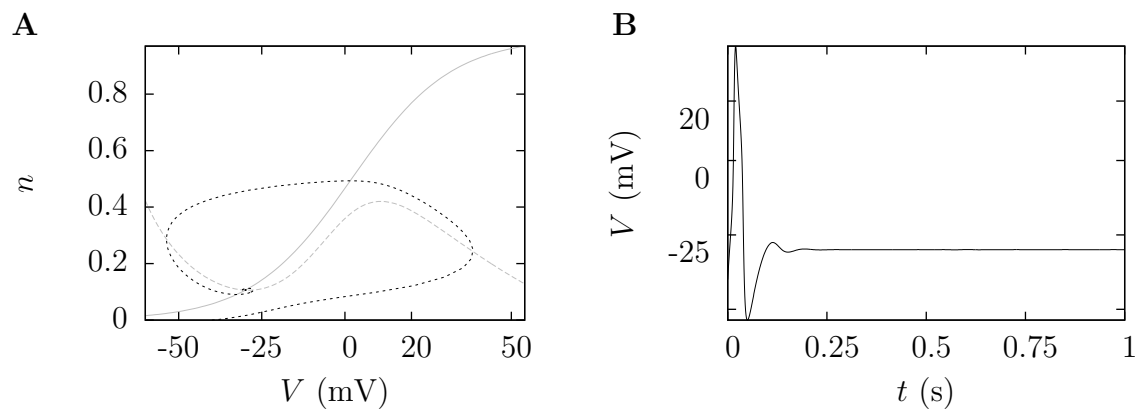


Figure 2: This shows another solution for the Morris-Lecar equation. As before in **A** the solid grey line is the  $n$ -nullcline, the dotted grey line is the  $V$ -nullcline; but here the two nullclines cross to the left of the local minimum and maximum of the  $V$ -nullcline and the equilibrium point is stable. The dotted black line shows a solution, it starts from  $V = -40$  mV and  $n = 0$  and is carried around in a big loop, corresponding to a single spike, before spirals in towards the equilibrium point. The corresponding solution is in **B**.

region below the  $V$ -nullcline so  $V$  increases, moving the neuron further away from the equilibrium point. In fact there is a limit cycle and the equation with this phase diagram exhibits regular spiking, this is shown in Fig. 1B. In Fig. 2A the equilibrium point is stable, for example, if  $V$  increases a tiny bit the neuron is still above the  $V$ -nullcline so that  $V$  decreases again, send the neuron back towards the equilibrium point. 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. 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

$$\begin{aligned}\frac{dv}{dt} &= v - \frac{1}{3}v^3 - w + I \\ \tau \frac{dw}{dt} &= v + a - bw\end{aligned}\tag{12}$$

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

$$w = v - \frac{1}{3}v^3 + I\tag{13}$$

and the  $w$ -nullcline

$$w = \frac{v + a}{b}\tag{14}$$

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

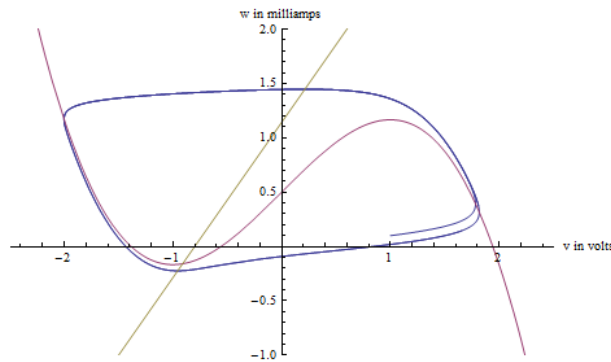


Figure 3: This is a graph of the FitzHugh-Nagumo phase plane with a limit cycle. The parameter values  $I = 0.5$ ,  $a = 0.7$ ,  $b = 0.8$ , and  $\tau = 12.5$  and the figure is taken from Wikipedia.

unstable and therefore shifts the model from spiking to quite. There is nice animation of this available at

[www.scholarpedia.org/article/FitzHugh-Nagumo\\_model](http://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

[coms30127.github.io](https://coms30127.github.io)

- [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.