Experimental Bifurcation Analysis In Neurons Using Control-Based Continuation

Mark Blyth

About me

- First year PhD student (started in September)
- Supervised by Lucia and Ludovic
- Studied EngMaths for my undergrad
- Research interests are in dynamical systems theory and applied nonlinear mathematics

Presentation plan

- How do neurons work?

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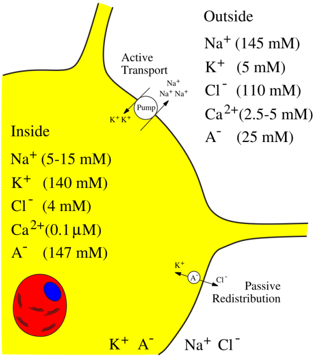
- What is my research topic? Why am I doing what I’m doing?
- What challenges am I trying to solve, and how?

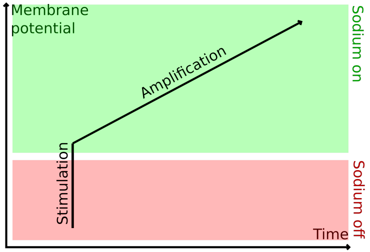
Whistlestop tour of electrophysiology

- Neurons are cells; they and their surrounding media contain charged ions
- Acive transport across the cell membrane means that, at rest, there's a voltage over the membrane
- At rest, this membrane potential is typically around -70 mV



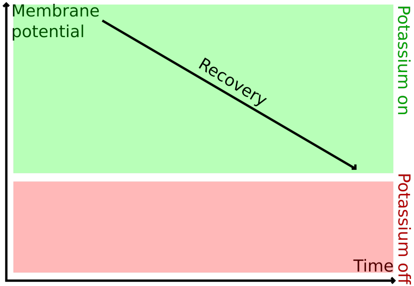
Whistlestop tour of electrophysiology

- Sodium current activates as membrane potential increases
- Simple model: current switches on when membrane potential exceeds a threshold
- It's an inward current, so it brings positive ions into the cell and increases membrane potential
- This causes positive feedback!



Whistlestop tour of electrophysiology

- Potassium currents activate as membrane potential increases
- Potassium forms an outward current - positive ions flow out, returning the membrane potential to its rest value
- The potassium current turns on and off slower than the sodium current



Whistlestop tour of electrophysiology

The interplay of slow potassium and fast sodium currents causes neurons to spike, rather than settling to a steady state

A recipe for spiking

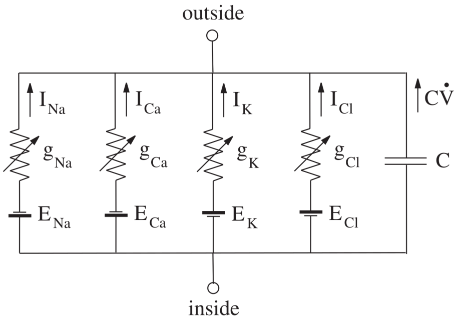
- Sodium currents switch on and off fast
- Potassium currents switch on and off slowly
- Slow potassium activation allows the membrane potential to increase fast
- Once it activates, the potassium current pulls the membrane potential back down
- Potassium current takes a while to switch off again, so membrane potential gets pulled down to below the turn-on threshold for the two currents

Whistlestop tour of electrophysiology

Currents flow through different ion channels; let's consider each one separately. Using current laws,

$$C\dot{V} = I_{Na} + I_{Ca} + I_K + I_{Cl}\ . \qquad (1)$$

The Hodgkin-Huxley model gives each ionic current as a function of membrane potential. This is exciting, as we now have a mathematical model of a neuron, to which we can apply a rigorous analysis.



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- Highly nonlinear
- High-dimensional
- Multi-timescale dynamics
- Stochastic behaviour

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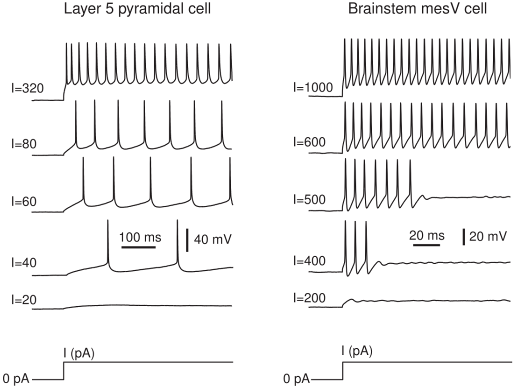
- Many behaviours that seem confusing when explained as ionic currents, have a very natural interpretation in dynamical systems theory
- Dynamical neuroscience is also something of a new field, though, so there’s still a big research gap in experimental bifurcation analysis

Project goal

Goal: develop a method of observing bifurcations in the dynamics of living neurons.

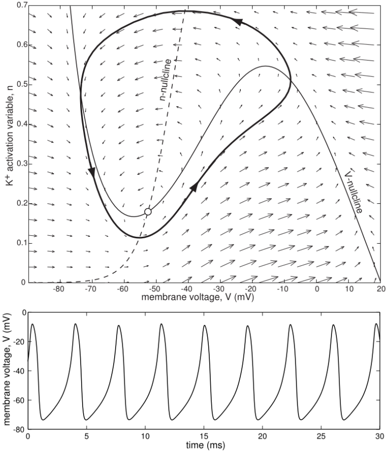
Spike trains and neural computation



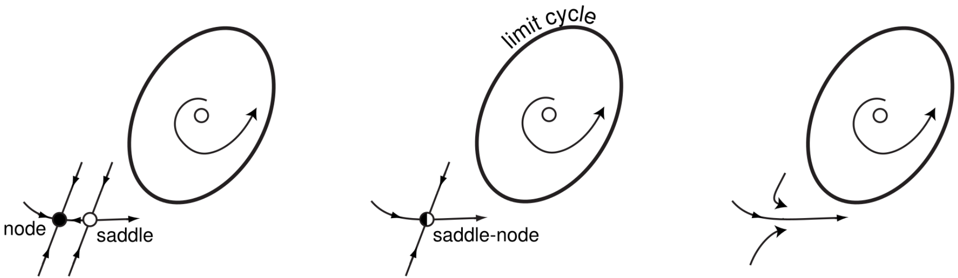
Class 1 excitability

Class 2 excitability

Phase diagrams



Bifurcations



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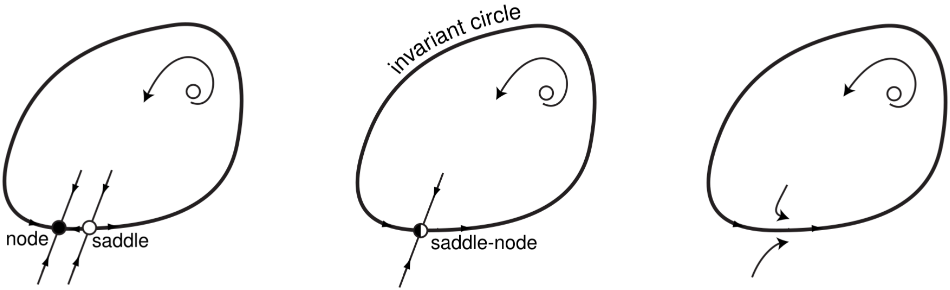

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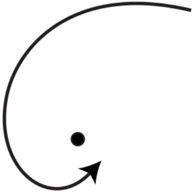

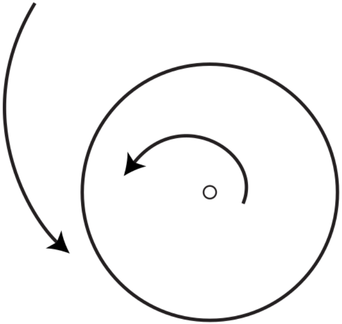

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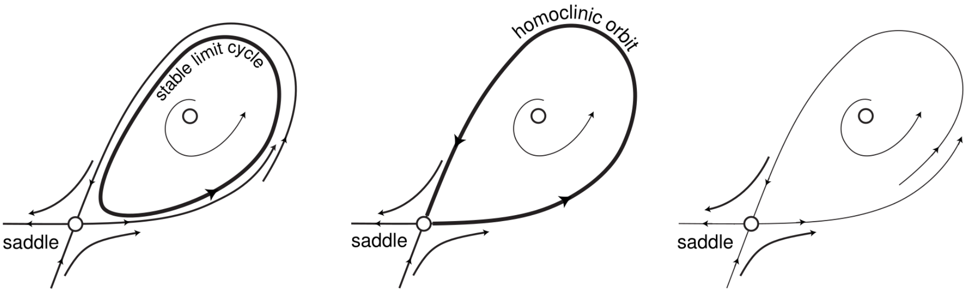

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George Box

All models are wrong, but some are useful

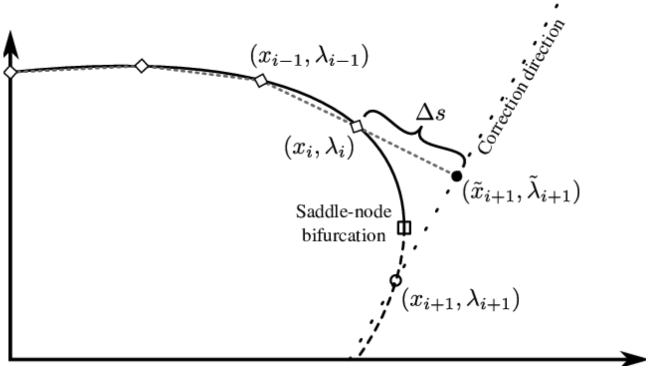
Numerical continuation

Consider $f(x, \lambda) = 0$. Numerical continuation seeks to track x, as λ varies. For ODEs of form

$$\dot{x} = f(x, \lambda) \ ,$$

this can be used to find bifurcations.

Numerical continuation



Control-based continuation

CBC allows us to apply continuation methods on black-box numerical or physical systems, no model needed.

- Use control theory to steer the system onto a (possibly unstable) natural invariant set
- Track that invariant set as the bifurcation parameter changes

This tracking step can be a classical psuedo-arclength continuation, or something more problem-specific.

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- Neurons are inherently stochastic; how do we deal with controlling and analysing this?
- The system has poor observability (eg. can't easily see population ion channel conductance); how do we control a system that we can't observe?
- We have limited control inputs; how can we use them to steer the dynamics effectively?