Experimental Bifurcation Analysis In Neurons Using Control-Based Continuation

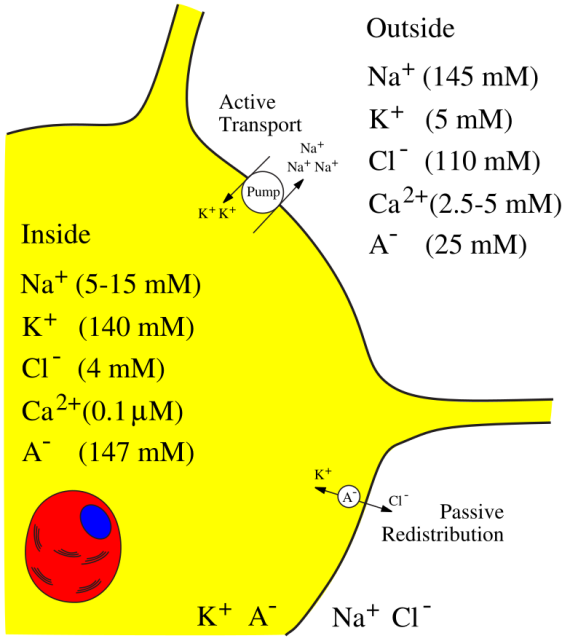
Mark Blyth

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

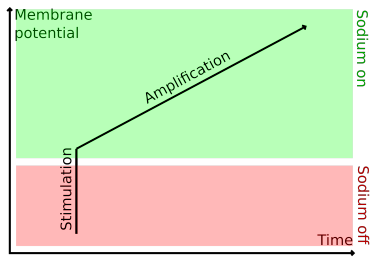
Presentation plan

- How do neurons work?
- Why should mathematicians get excited by neurons?
- What is my research topic? Why am I doing what I'm doing?
- What challenges am I trying to solve, and how?


Outside
Na+ (145 mM)
K+ (5 mM)
Cl- (110 mM)
Ca2+(2.5-5 mM)
A- (25 mM)
Active
Transport
Na+
Na+ Na+
Pump
K+ K+
Inside
Na+ (5-15 mM)
K+ (140 mM)
Cl- (4 mM)
Ca2+(0.1 µM)
A- (147 mM)
K+
A-
Cl-
Passive
Redistribution
K+ A-
Na+ Cl-

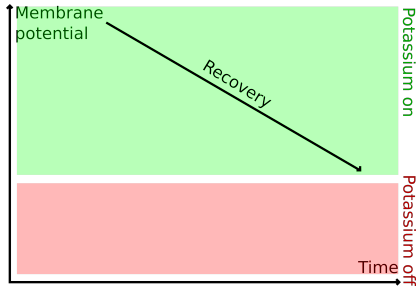
Whistlestop tour of electrophysiology

- 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

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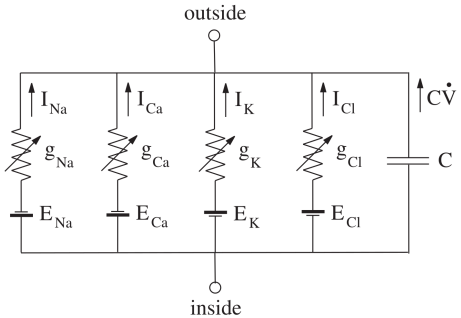
- Slow potassium activation allows the membrane potential to increase fast
- Once it activates, the potassium current pulls the membrane potential back down
- Potassium current takes a while to switch off again, so membrane potential gets pulled down to below the turn-on threshold for the two currents

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

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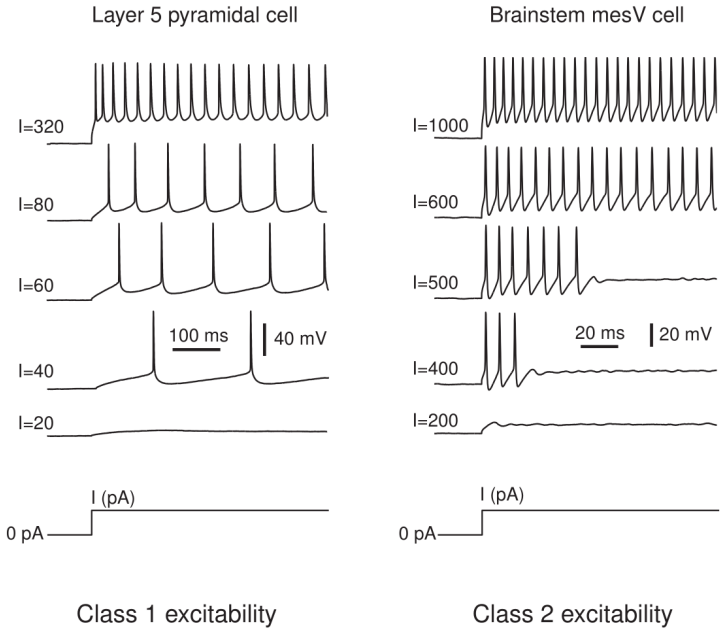
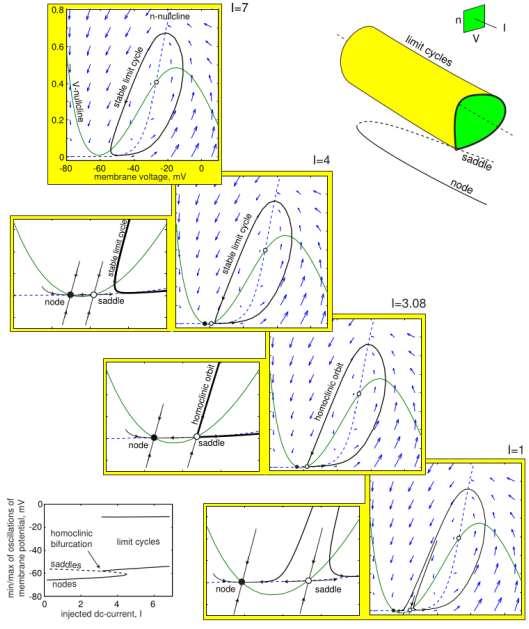

Layer 5 pyramidal cell
Brainstem mesV cell
I=320
I=80
I=60
I=40
I=20
100 ms
40 mV
I=1000
I=600
I=500
I=400
I=200
20 ms
20 mV
I (pA)
0 pA
I (pA)
0 pA
Class 1 excitability
Class 2 excitability


I=7
n-nullcline
V-nullcline
stable limit cycle
0.8
0.6
0.4
0.2
0
-80
-60
-40
-20
0
membrane voltage, mV
n
V
I
limit cycles
saddle
node
I=4
stable limit cycle
node
saddle
I=3.08
homoclinic orbit
node
saddle
I=1
node
saddle
min/max of oscillations of membrane potential, mV
homoclinic bifurcation
limit cycles
saddles
nodes
injected dc-current, I

Project goal

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

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.

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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- We have limited control inputs; how can we use them to steer the dynamics effectively?
- How do we control a highly nonlinear black-box system?
- How can CBC be extended to study global bifurcations?