2019-12-13 Fri

Experimental Bifurcation Analysis In Neurons Using Control-Based Continuation

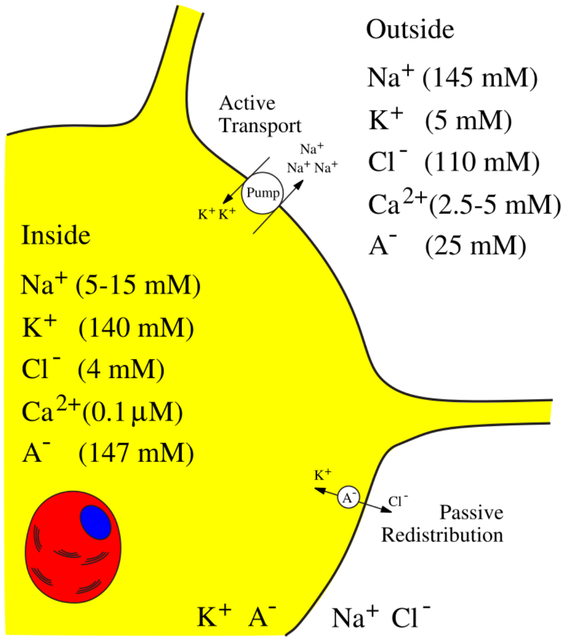
Mark Blyth

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

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

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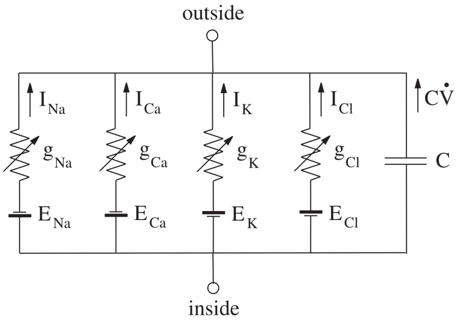
- Slow potassium activation allows the membrane potential to increase fast
- Once it activates, the potassium current pulls the membrane potential back down
- Potassium current takes a while to switch off again, so membrane potential gets pulled down to below the turn-on threshold for the two currents

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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- Biophysically accurate models are high-dimensional
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- Neurons are a stochastic system
- The Hogkin-Huxley model has a chaotic threshold set

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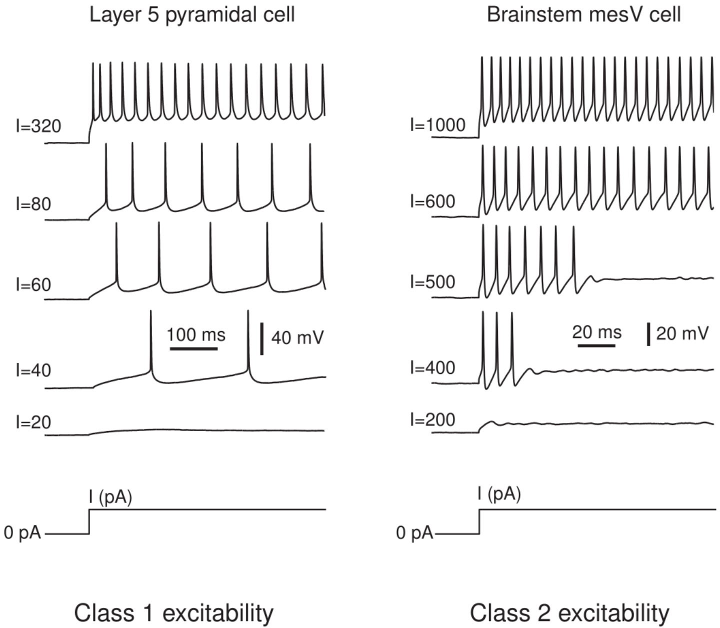
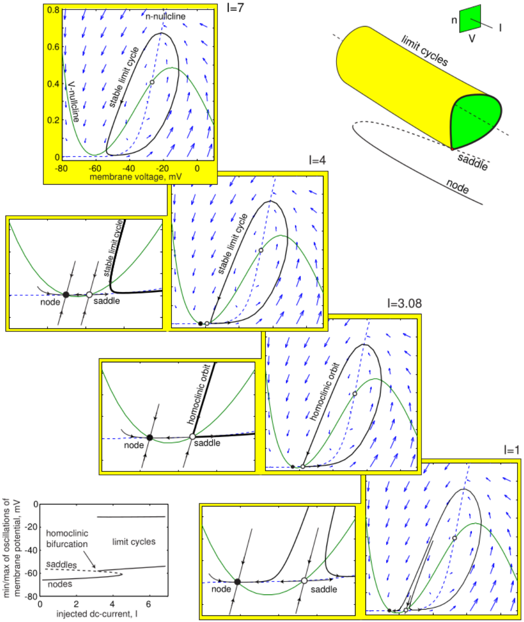
- The current approach is to use numerical continuation to study bifurcations in models of neurons
- My goal: develop a control-based continuation method, to produce a model-free analysis of neuron bifurcations, on living cells


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
stable limit cycle
V-nullcline
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
stable limit cycle
node
saddle
I=3.08
homoclinic orbit
homoclinic orbit
node
saddle
I=1
node
saddle
min/max of oscillations of membrane potential, mV
0
-20
-40
-60
-80
homoclinic bifurcation
limit cycles
saddles
nodes
0
2
4
6
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

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

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?