The codimension of pseudo-plateau bursting

Mark Blyth

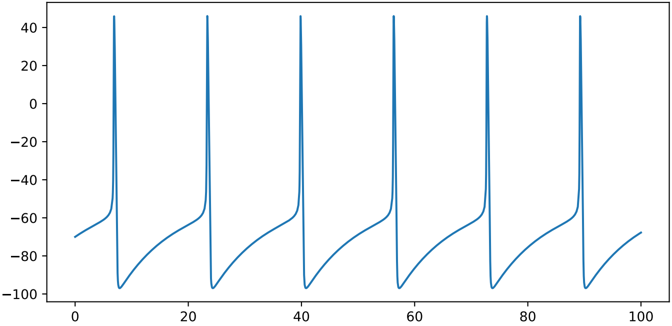
Paper goals

- Determine the codimension-classification of pseudo-plateau bursting
- Propose a normal form for bursting

Plan de jour

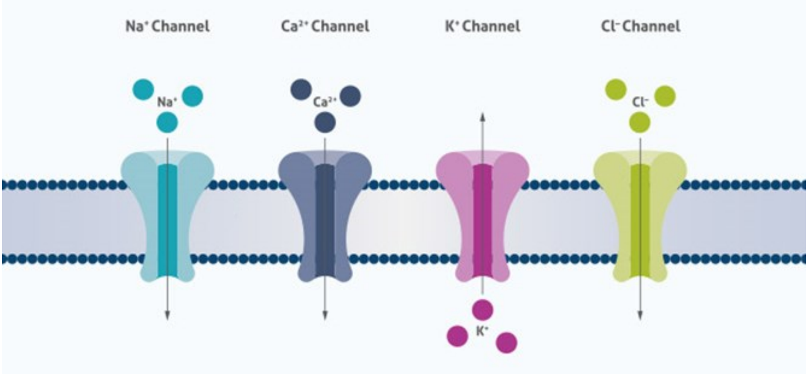
- 30 second intro to neurons
  - What do neurons do?
  - What are bursting neurons?
  - How and why do we categorise them?
- Section 2: Towards a normal form for bursting
- Section 3: Transitions between bursting classes
- Section 4:Codimension-classification of pseudo-plateau bursting
- Section 5: Conclusion

Neurons spike



Neurons encode information in action potentials

Ionic currents



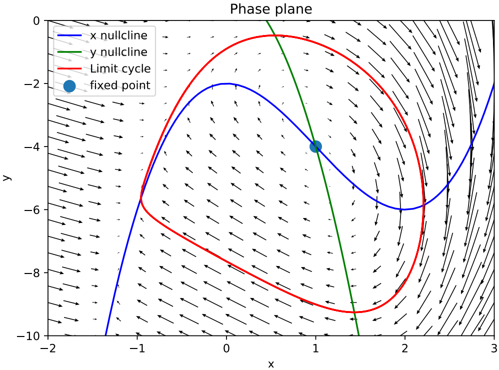
Action potentials happen from ions flowing into and out of the cell

Hodgkin-Huxley

$$\begin{aligned}
\frac{dV}{dt} &= \left[I_{inj} - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K) - g_L (V - V_L)\right]/C \\
\frac{dn}{dt} &= \alpha_n(V)(1-n) - \beta_n(V)n \\
\frac{dm}{dt} &= \alpha_m(V)(1-m) - \beta_m(V)m \\
\frac{dh}{dt} &= \alpha_h(V)(1-h) - \beta_h(V)h
\end{aligned}$$

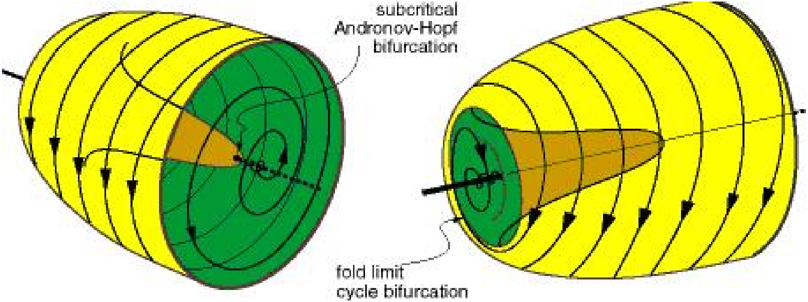
We can understand the causes of spike generation with differential equations

Nonlinear dynamics



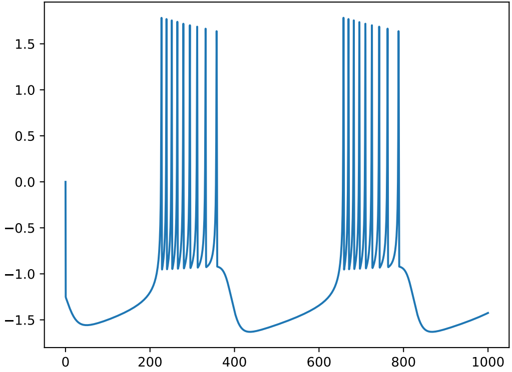
Neuron dynamics rely on limit cycles and equilibria

Bifurcations



Equilibria and limit cycles an appear through bifurcations

KEY POINT: bursting



Ionic currents can appear to drive the neuron over bifurcations – this is bursting!

Why do cells burst?

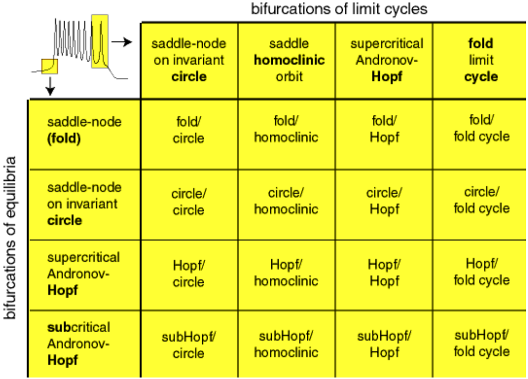
- More reliable for transmitting over synapses
    - Higher signal-to-noise ratio
- Maintain an elevated Ca^{2+} state
    - Promotes neurotransmitter release
    - Promotes hormone release
- Occur in both the brain and elsewhere
    - pre-Botzinger complex bursters control respiration
    - Pituitory somatotroph bursters *[not neurons]* use bursts to release hormones

Why do we categorise them?

Lots of work is done to categorise bursters, but why?

- Complete classification would describe all the ways a cell could be excitable
- Hints at similarities and differences between cells
  - Small parameter changes can sometimes shift cells into different burster categories
  - ‘Close’ cell categories usually perform similar tasks

How do we categorise bursters?



bifurcations of limit cycles

bifurcations of equilibria

	saddle-node on invariant **circle**	saddle **homoclinic** orbit	supercritical Andronov-**Hopf**	**fold** limit **cycle**
saddle-node **(fold)**	fold/ circle	fold/ homoclinic	fold/ Hopf	fold/ fold cycle
saddle-node on invariant **circle**	circle/ circle	circle/ homoclinic	circle/ Hopf	circle/ fold cycle
supercritical Andronov-**Hopf**	Hopf/ circle	Hopf/ homoclinic	Hopf/ Hopf	Hopf/ fold cycle
subcritical Andronov-**Hopf**	subHopf/ circle	subHopf/ homoclinic	subHopf/ Hopf	subHopf/ fold cycle

Under this scheme, there’s 16 planar bursters

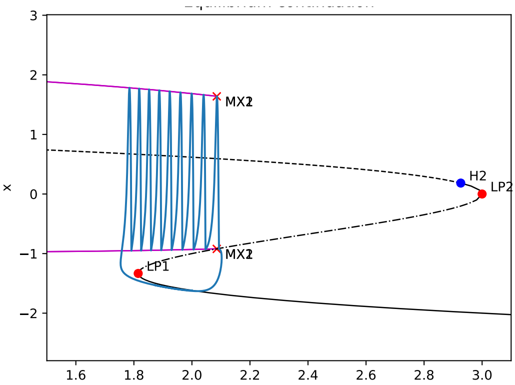
Multiple timescale dynamics

The previous bursting data can be modelled by

$$\dot{x} = f(x, y) \, ,$$
$$\dot{y} = \epsilon g(x, y) \, ,$$
$$|\epsilon| \ll 1 \, .$$

- Assume $\epsilon = 0$
- Spiking is switched off by bifurcations in x
  - y becomes a parameter to cause these bifurcations

How do we categorise bursters?



This is a fold-homoclinic burster

A better classification

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- A burster will sit in the unfolding of some singularity
  - More unfolding parameters = more complexity
  - More unfolding parameters = higher codimension

A better classification

Classify in terms of. . .

- Singularity codimension
  - Measures the complexity of the burster
- Bifurcations to turn spikes on and off
  - Describes the dynamics of the burster

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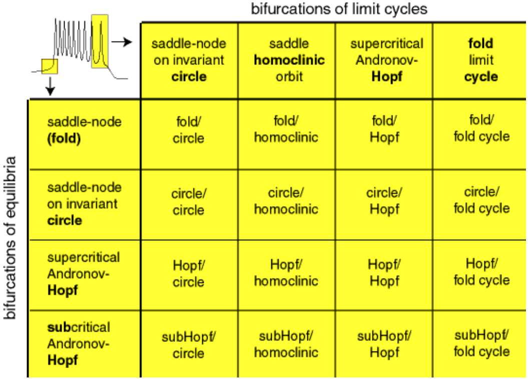
  - *'Same thing'* usually means same bifurcation structure
- A normal form is a simple model that shows prototypical example behaviours
- A burster normal form is a simple model that can describe the bifurcation structure of any bursting neuron

Normal form requirements



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A burster normal form must be able to operate as all of these classes

Model form

- The proposed model has $f(x, y)$ with a complex bifurcation structure...

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

- ...and a simple $g(x, y)$ to drive f over some bifurcations

$$y(t) = A \sin(\omega t)$$

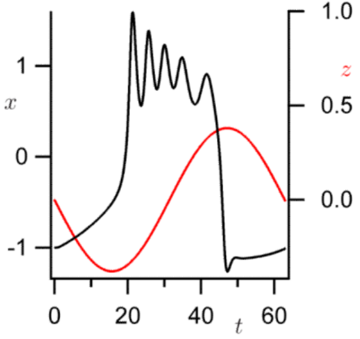
Appropriate models

- Golubitsky found a lot of bursters near the codimension-3 degenerate Bogdanov-Takens singularity:

$$f(x, y) = \begin{pmatrix} y \\ -y + \mu x - x^3 + y(\nu + 3x + x^2) \end{pmatrix}$$

- Has a rich enough bifurcation structure to show most bursting types

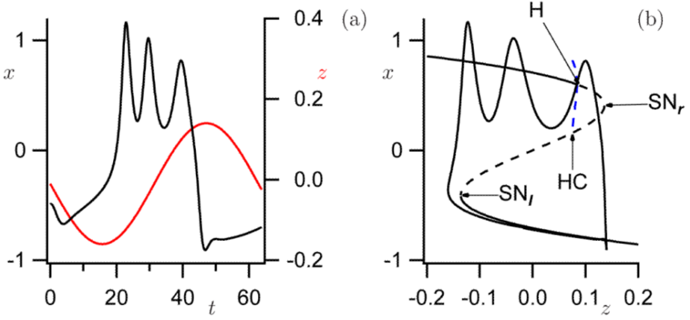
How about this?



- Pituitory cells can also burst
- Looks similar to previous bursters
- No stable limit cycle!
  - *How do we categorise this?*

This is pseudo-plateau bursting

The codimension of pseudo-plateau bursting



- Pseudo-plateau bursting has a similar bifurcation structure to the others
- It doesn't seem to appear near a degenerate Bogdanov-Takens singularity!

Singularity choices

- The original paper goal was to classify the pseudo-plateau burster
- The burster doesn't seem to appear in codim-3 degenerate Bodganov-Takens unfolding
  - The singularity must not be able to exhibit all known bursting types
  - It can't be a normal form!

Let's free up a parameter:

$$\dot{x} = \begin{pmatrix} y \\ -y + \mu_2 x - x^3 + y(\nu + bx - x^2) \end{pmatrix}$$

A new model

We have

$$
\begin{aligned}
\dot{x_1} &= y \\
\dot{x_2} &= y + \mu_2 x - x^3 + y(\nu + bx - x^2) \\
y &= A \sin(\omega t)
\end{aligned}
$$

- This is the unfolding of a doubly-degenerate Takens-Bogdanov singularity
- It contains more dynamical richness – enough to show pseudo-plateau bursting
- How do we analyse it?

Model analysis

We can't plot 4-dimensional bifurcation diagrams, so we need to get creative…

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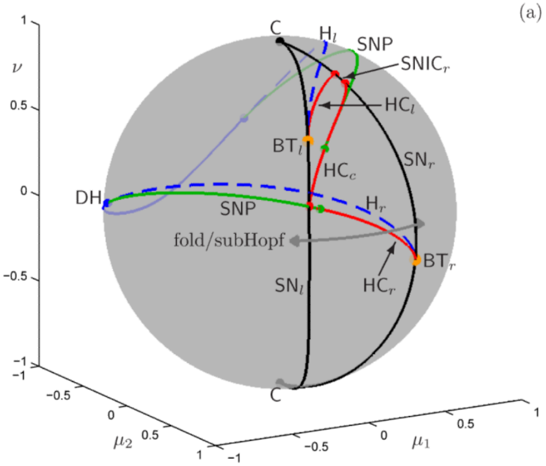
  - Find the surface of a ball around the chosen b
  - We now have a 2d parameter space!

Bifurcation structure



- This parameter subspace contains the pseudo-plateau burster
- The model is a good normal form candidate

Section 2 summary

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  - The known unfoldings don't contain pseudo-plateau bursters
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- A doubly-degenerate Bogdanov-Takens singularity *does* contain pseudo-plateau bursters
  - It is as close as we can currently get to a normal form

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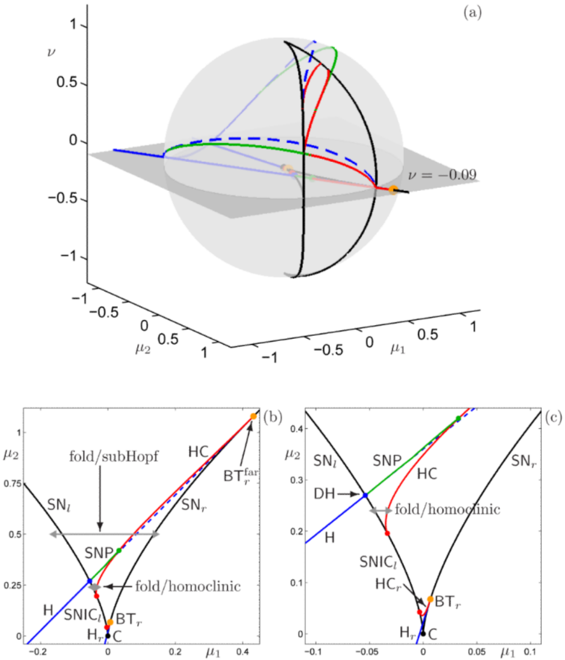
  - This parameter is analogous to Calcium current activation
- Similar cells have similar bifurcation structures
- Biological robustness: we can mess around with parameters and still see similar behaviour


(a)
ν
1
0.5
0
−0.5
−1
ν = −0.09
−1
−0.5
0
0.5
1
μ2
−1
−0.5
0
0.5
1
μ1
(b)
μ2
1
0.75
0.5
0.25
0
-0.2
0
0.2
0.4
μ1
fold/subHopf
HC
BT_r^far
SN_l
SN_r
SNP
fold/homoclinic
H
SNIC_l
BT_r
H_r
C
(c)
μ2
0.4
0.3
0.2
0.1
0
-0.1
-0.05
0
0.05
0.1
μ1
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SNP
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C

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Section 4

- The pseudo-plateau burster appears in a codimension-4 unfolding
  - It must be at most a codim-4 -category system
- There's different forms the unfolding could take; this section justifies why they aren't used

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  - The singularity unfolding can act as a burster normal form
- Cells can easily transition between bursting classes, in biologically meaningful ways