The Relationship Between Two Fast/Slow Analysis Techniques for Bursting Oscillations

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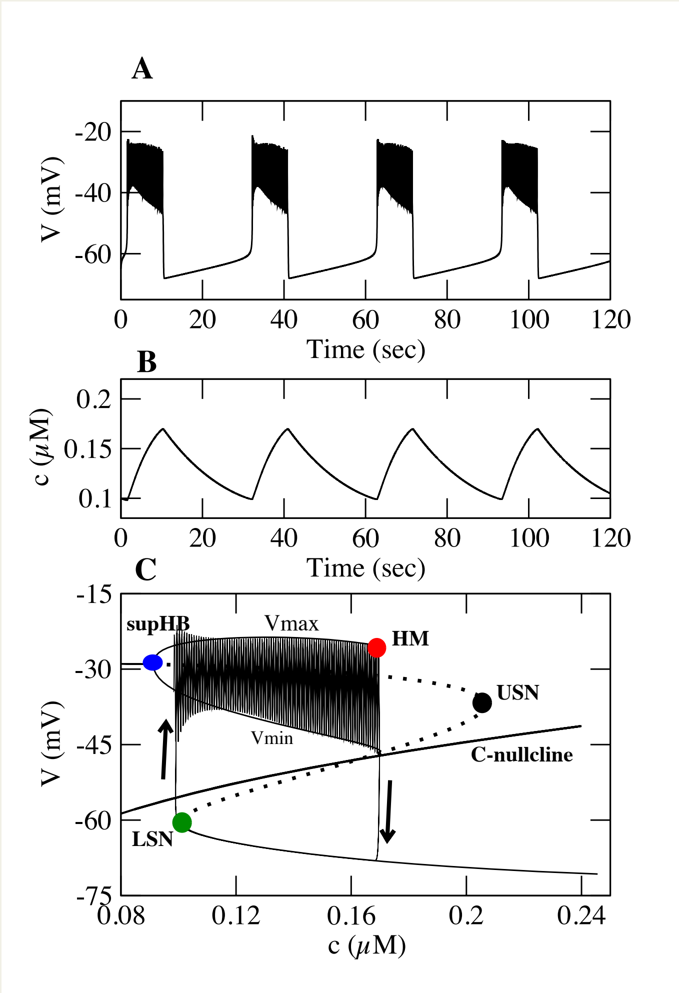
2-Fast/1-Slow Analysis: a Powerful Tool for Understanding Plateau Bursting



$$\dot{V} = f(V,n,c)$$

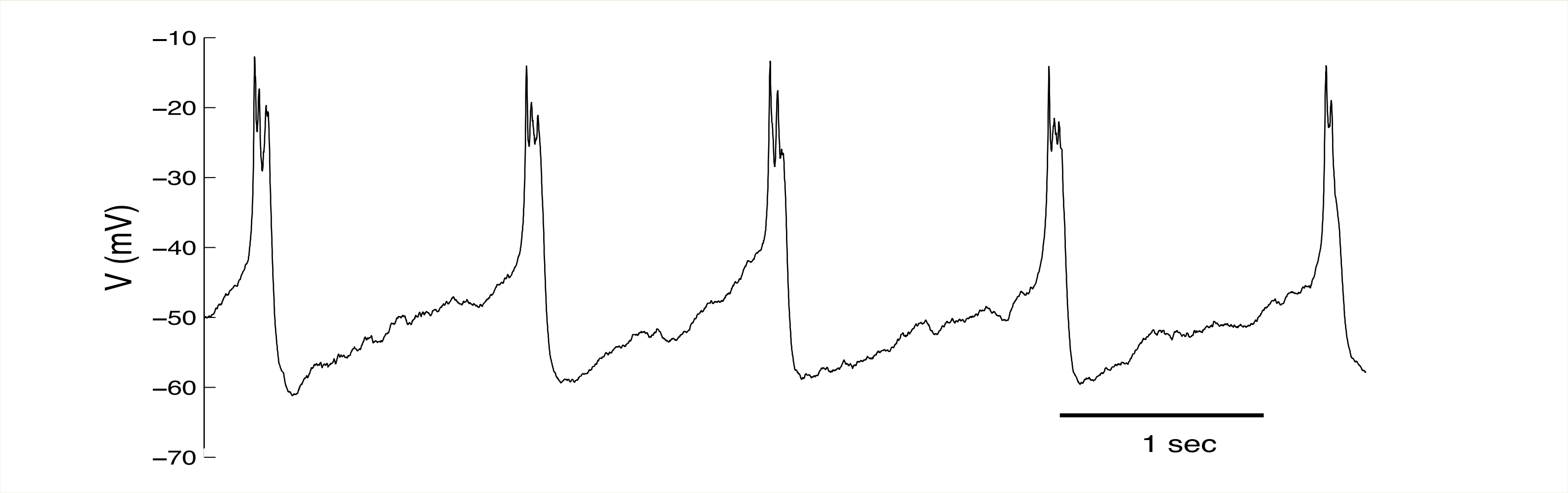
$$\dot{n} = g(V,n)$$

$$\dot{c} = \varepsilon_c h(V,c)$$

Analysis in the limit

$$\varepsilon_c \to 0$$

Pseudo-Plateau Bursting Occurs in Some Pituitary Cells

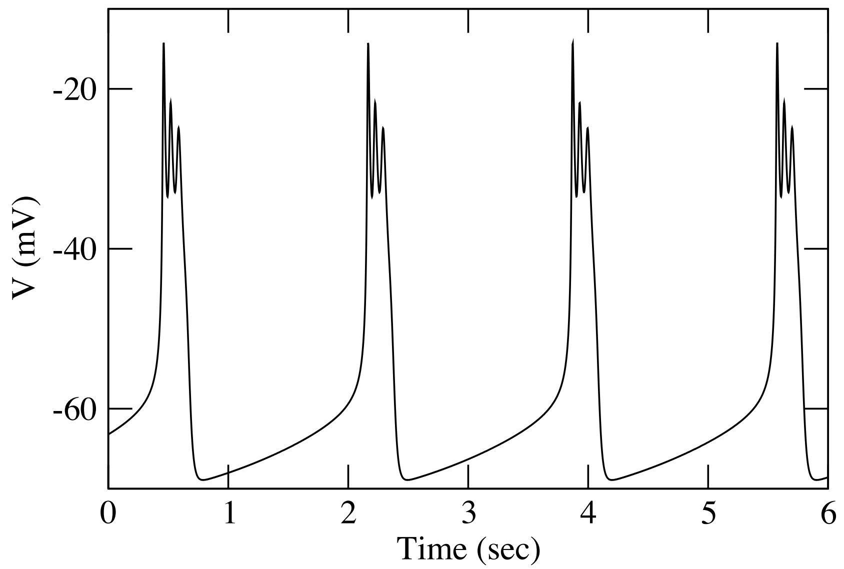


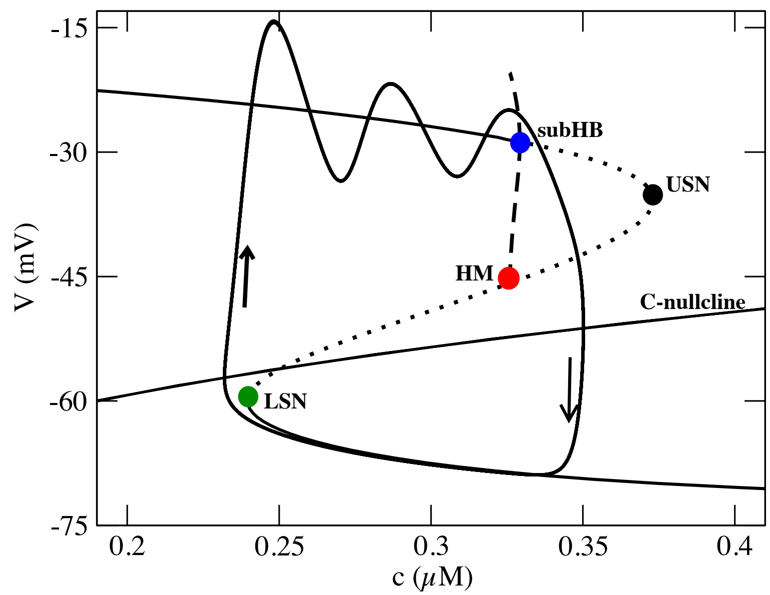
Electrical recording from a GH4 pituitary cell line

Bursts are short and the spikes have very small amplitude.

Characteristic of bursting in pituitary lactotrophs and somatotrophs

Pseudo-Plateau Bursting Presents New Challenges





Trajectory does not follow the z-curve, and
there is no periodic spiking branch!

The spikes go away as ε_c is decreased to 0

An Alternate Approach

$$\boxed{\varepsilon_V}\dot{V} = f(V,n,c)$$

$$\dot{n} = g(V,n)$$

$$\dot{c} = \varepsilon_c h(V,c)$$

Analyze the reduced system obtained in the limit $\varepsilon_V = C_m \to 0$

Voltage V is in a state of quasi-equilibrium with *n* and *c*

The Critical Manifold

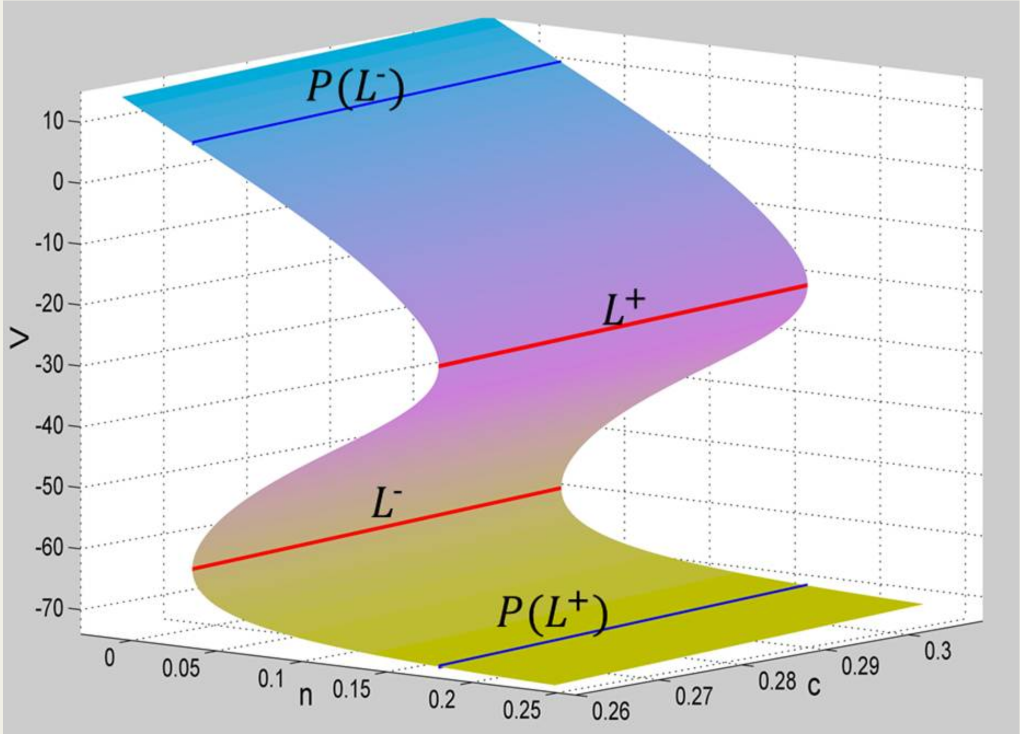
Surface in 3-space where V is at quasi-equilibrium

RHS of V-ODE: $f(V,n,c) \equiv -(I_{Ca} + I_K + I_{SK} + I_{BK})$

Critical manifold: $S \equiv \left\{(V,n,c) \in \Re^3 : f(V,n,c) = 0\right\}$

Top and bottom sheets are attracting

Middle sheet is repelling



The Flow on the Critical Manifold

RHS of V-ODE: $f(V,n,c) \equiv -(I_{Ca} + I_K + I_{SK} + I_{BK})$

Critical manifold: $S \equiv \left\{ (V,n,c) \in \Re^3 : f(V,n,c) = 0 \right\}$

Dynamics on S: $\dfrac{d}{dt} f(V,n,c) = \dfrac{d}{dt} 0$

Reduced system:

$$\underbrace{-\frac{\partial f}{\partial V}}_{=0 \text{ on folds}} \frac{dV}{dt} = \overbrace{g(V,n)}^{\frac{dn}{dt}} \frac{\partial f}{\partial n} + \overbrace{\varepsilon_c h(V,c)}^{\frac{dc}{dt}} \frac{\partial f}{\partial c}$$

$$\frac{dc}{dt} = \varepsilon_c h(V,c)$$

With *n* satisfying

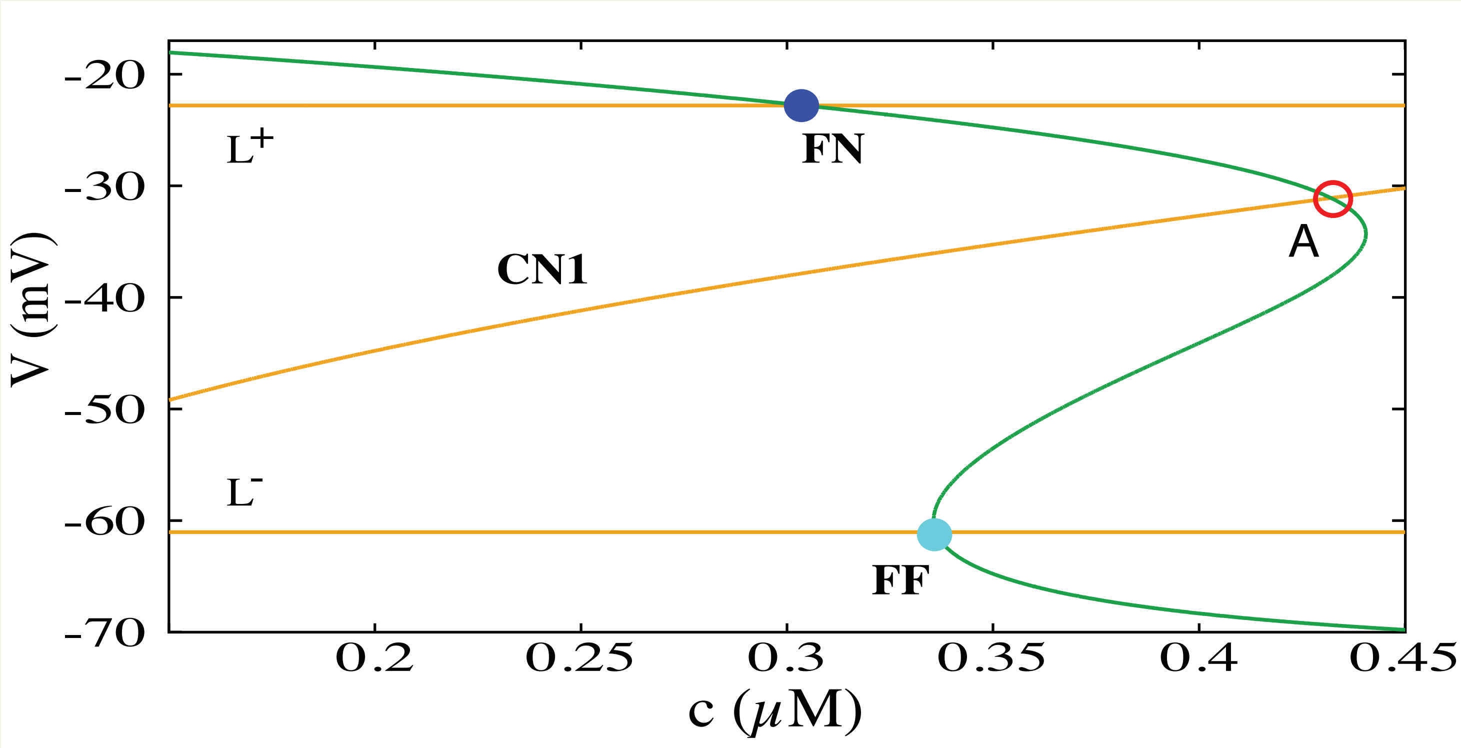
$$f(V,n,c) = 0$$

Desingularized system:

$$\boxed{\begin{aligned} \frac{dV}{d\tau} &= g(V,n)\frac{\partial f}{\partial n} + \varepsilon_c h(V,c)\frac{\partial f}{\partial c} \equiv F(V,c) \\ \frac{dc}{d\tau} &= -\varepsilon_c h(V,c)\frac{\partial f}{\partial V} \end{aligned}}$$

with $\tau \equiv -\left(\dfrac{\partial f}{\partial V} \right)^{-1} t$

Nullclines of the Desingularized System



Green: V-nullcline
Orange: c-nullclines

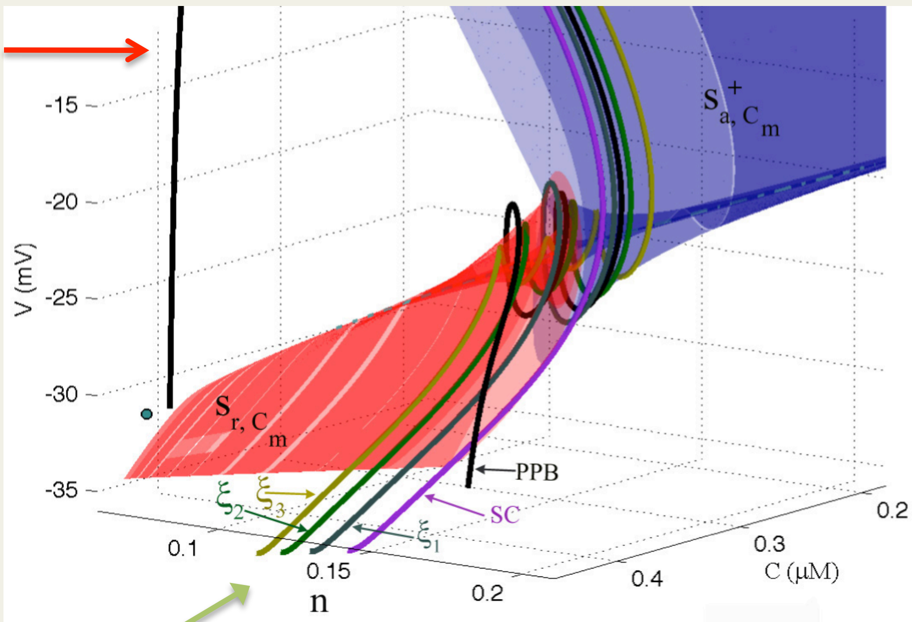
L^+ is upper fold curve
L^- is lower fold curve
CN1 is c-nullcline of full system

FN is folded node
FF is folded focus
A is ordinary equilibrium (saddle point)

The Folded Node Produces Rotations in the Nonsingular System

The sheets of the critical manifold perturb smoothly to form the slow manifold for ε_V>0 (Fenichel theory). This is not true in the neighborhood of the folded node, where the perturbed sheets become twisted to preserve uniqueness of solutions.

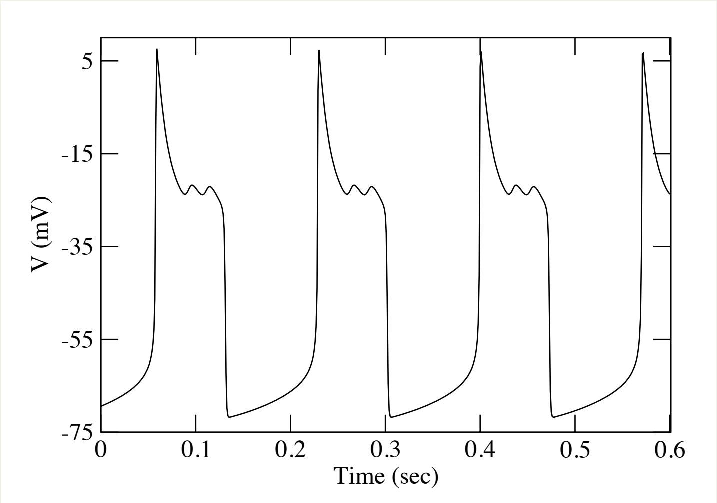
Bursting orbit



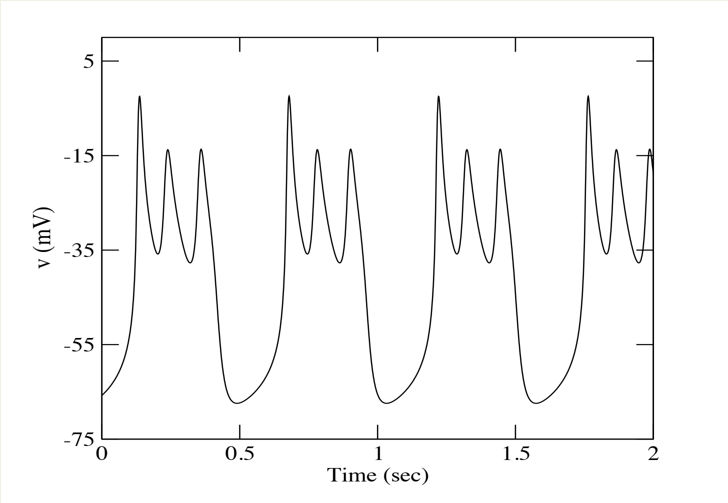
Secondary canards

Pseudo-Plateau Bursting

The small oscillations that emerge in the vicinity of the folded node (for $\varepsilon_V>0$) are small-amplitude voltage spikes. These, combined with the large jumps between upper and lower sheets, form mixed-mode oscillations, which in this context, are called pseudo-plateau bursting.

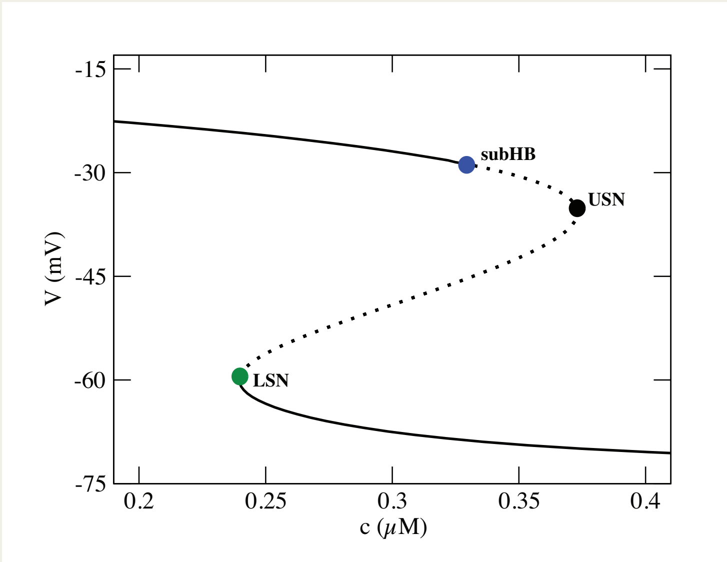


C_m=0.5 pF



C_m=10 pF

How are the traditional 2-fast/1-slow analysis



Limit $\varepsilon_c \rightarrow 0$

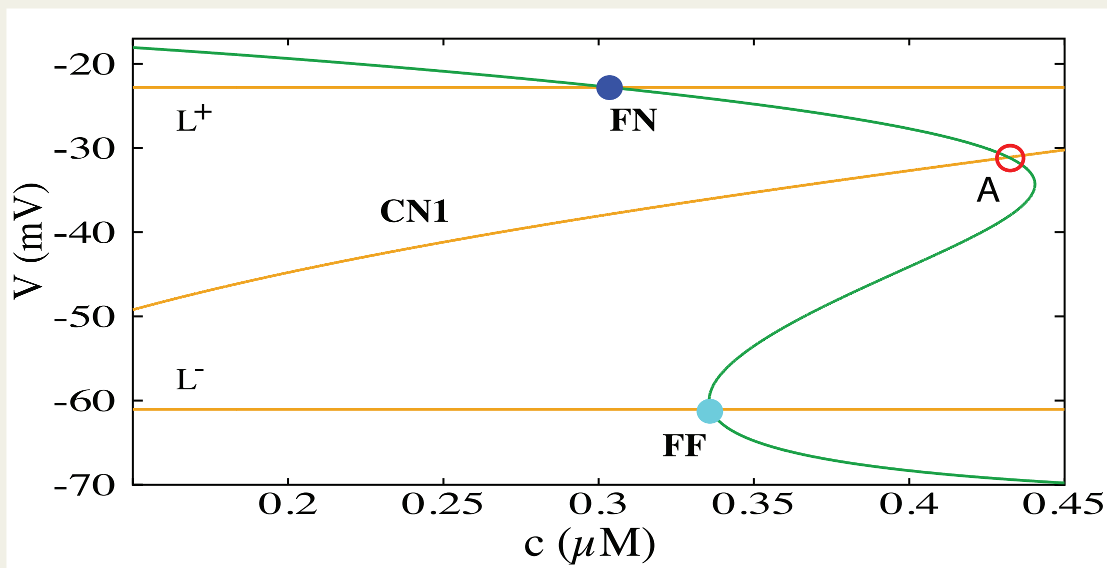
$$\varepsilon_V \dot{V} = f(V,n,c)$$
$$\dot{n} = g(V,n)$$
$$\dot{c} = \varepsilon_c h(V,c)$$

"z-curve"
subcritical Hopf

and the 1-fast/2-slow analysis related?

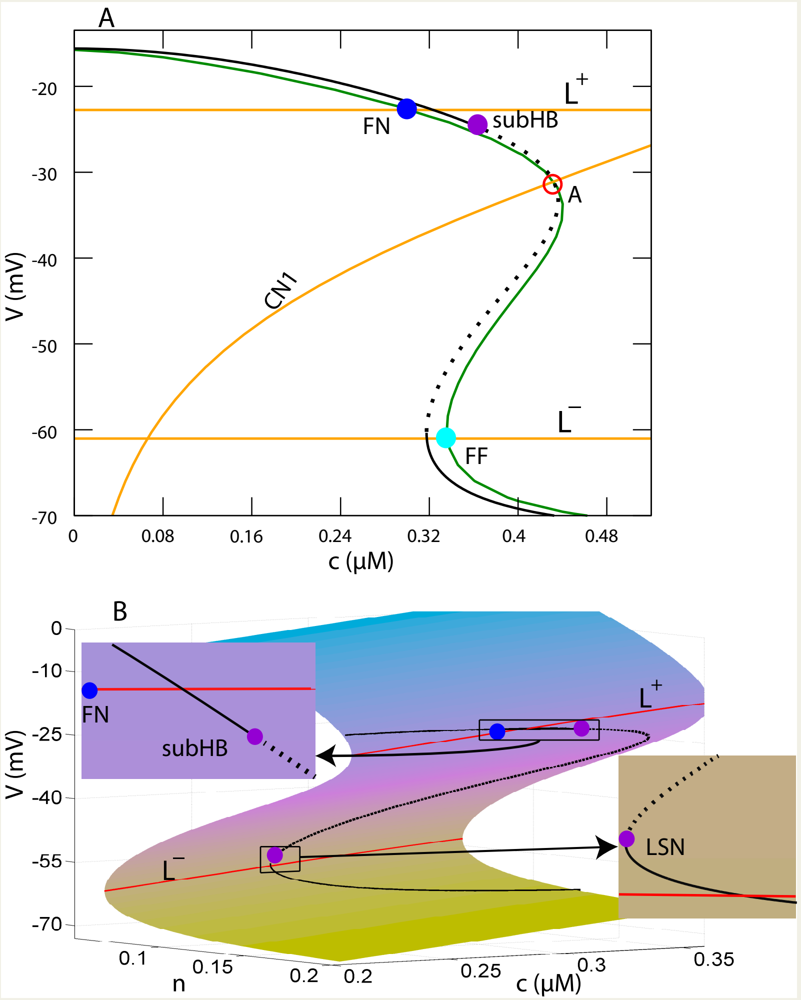
Limit $\varepsilon_V \rightarrow 0$

nullclines
folded node



Z-Curve and V-Nullcline are Suspiciously Similar

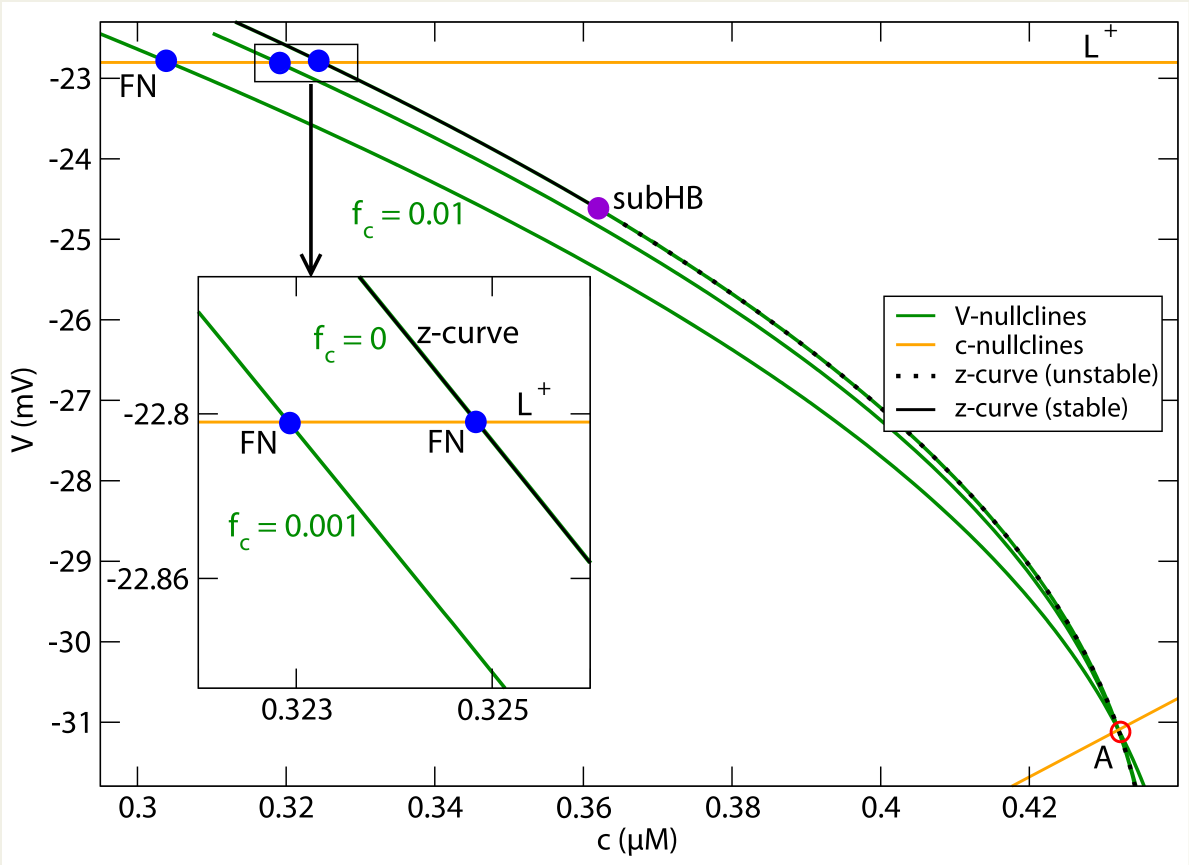
- FN and subHB not the same
- Point A is on both the z-curve and the V-nullcline
- subHB is on the middle sheet of the critical manifold



V-Nullcline Converges to the Z-Curve in the Limit $\varepsilon_c \to 0$

$$0 = g(V,n)\frac{\partial f}{\partial n} + \varepsilon_c h(V,c)\frac{\partial f}{\partial c} \equiv F(V,c)$$

The FN and the subHB are still different



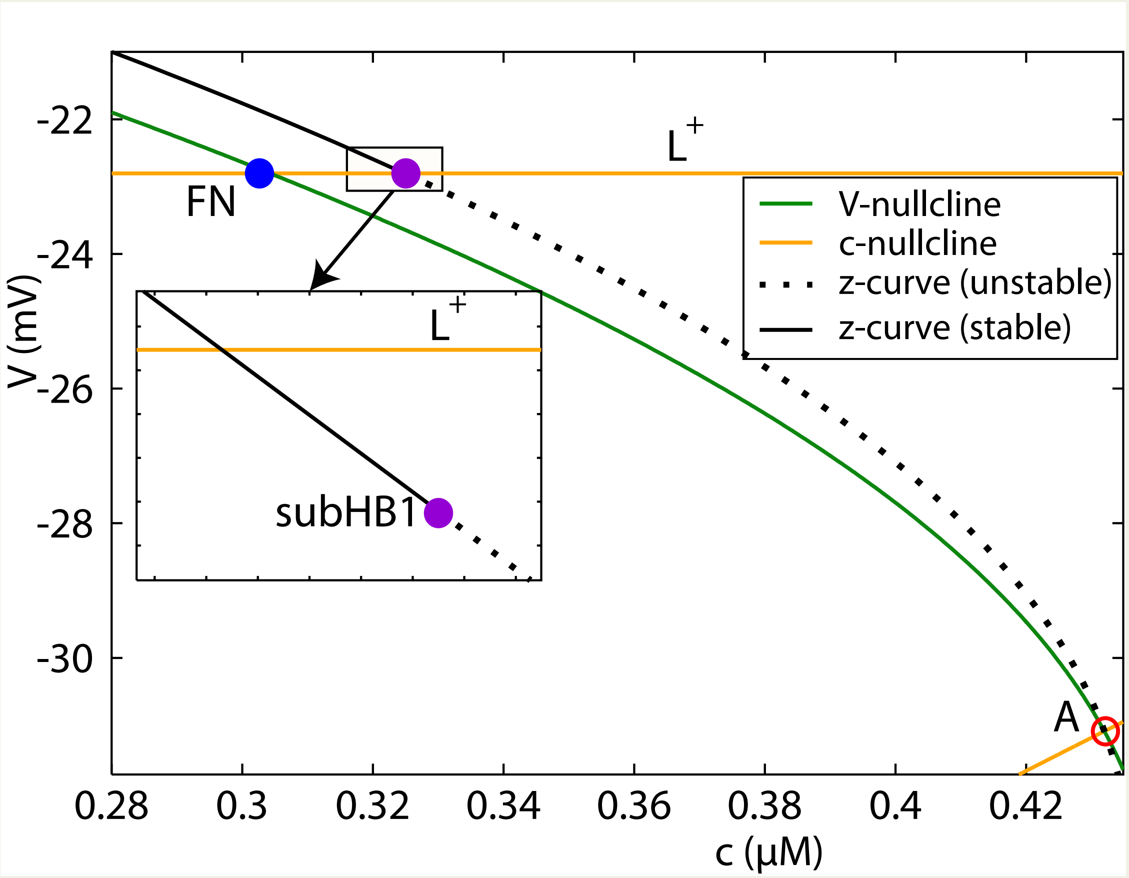
The subHB Moves to the Upper Fold Curve L⁺ in the Limit $\varepsilon_V \to 0$

Steady states of:

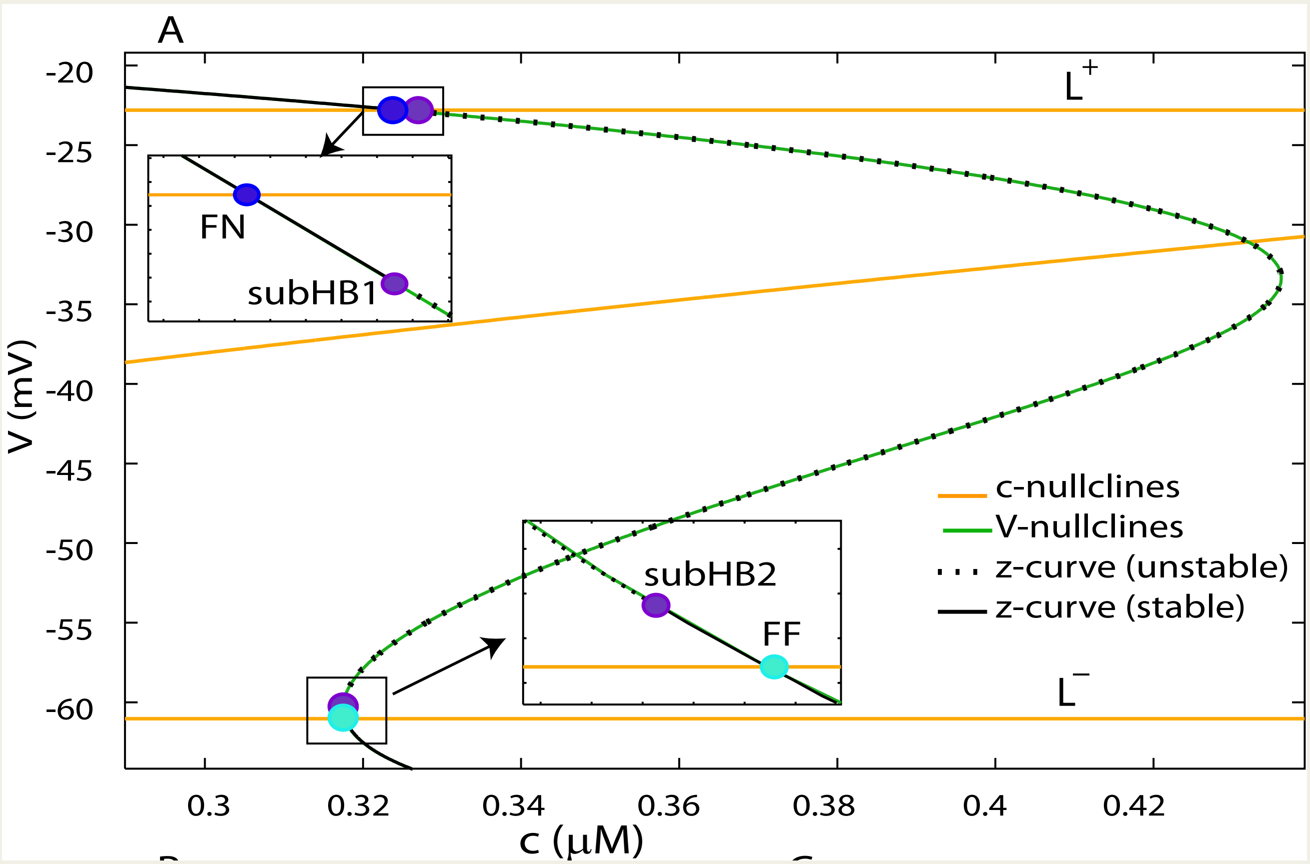
$$\varepsilon_V \dot{V} = f(V,n,c)$$

$$\dot{n} = g(V,n)$$

The FN and the subHB are still different, but both are on L⁺



The subHB Converges to the FN in the Double Limit $\varepsilon_c, \varepsilon_V \to 0$

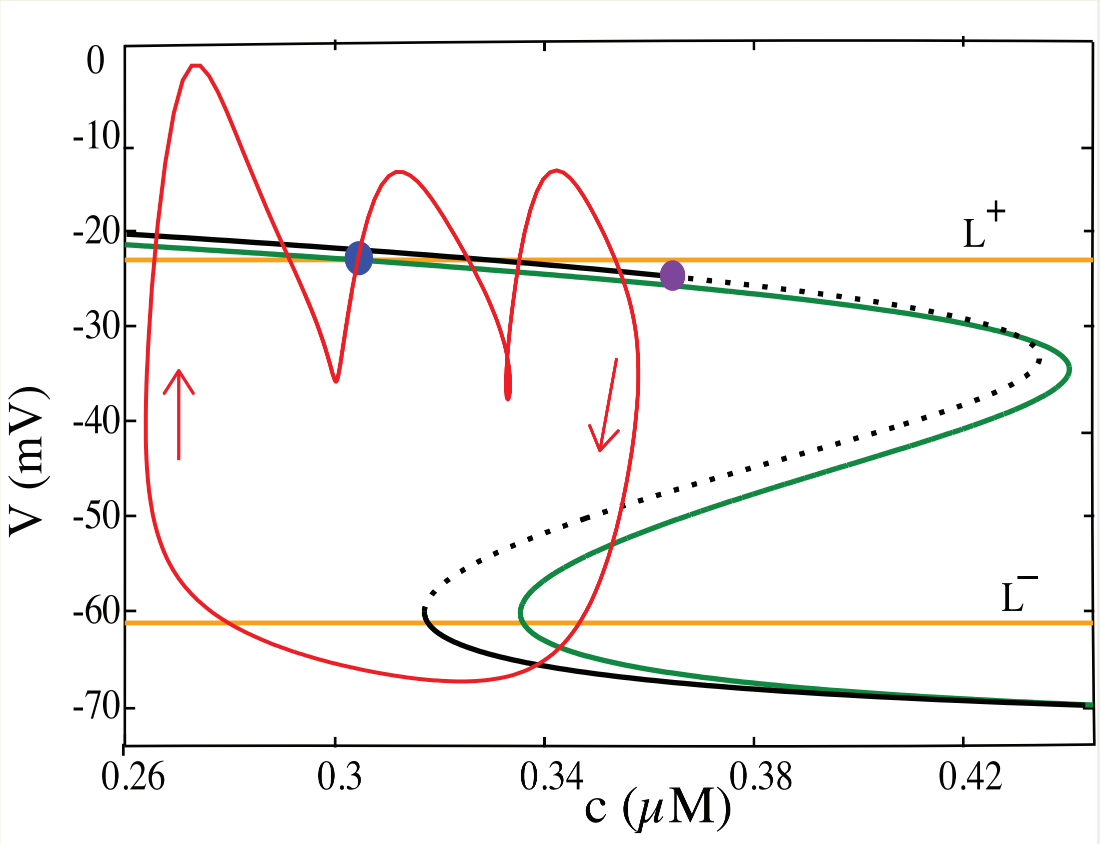


Which Structures Organize the Burst?

Neither of the fast/slow decompositions is very accurate far from the singular limits

$$\varepsilon_V = 10\,pF$$

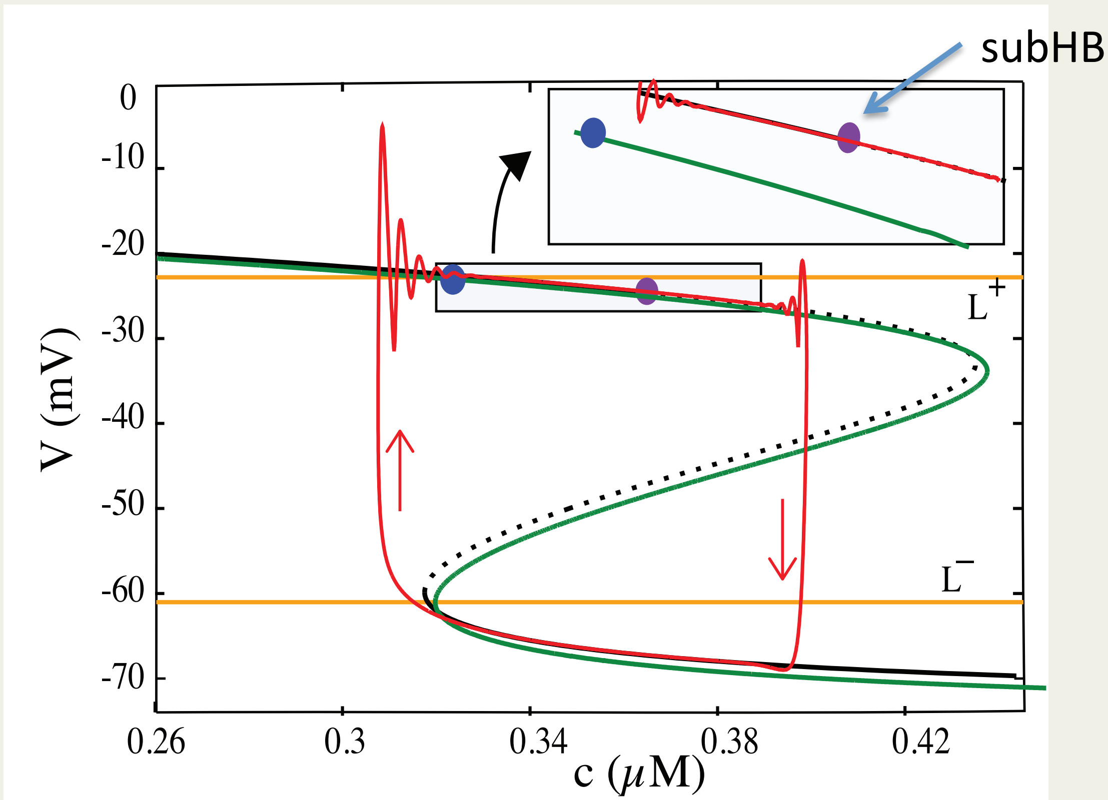
$$\varepsilon_c = 0.01$$



The Orbit Follows the Z-Curve when ε_c is Small

$\varepsilon_V = 10\,pF$

$\varepsilon_c = 0.001$



Orbit moves along top and bottom branches of the z-curve, through the subHB

The Orbit Follows the Z-Curve when ε_c is Small

$$\varepsilon_V = 10\,pF$$

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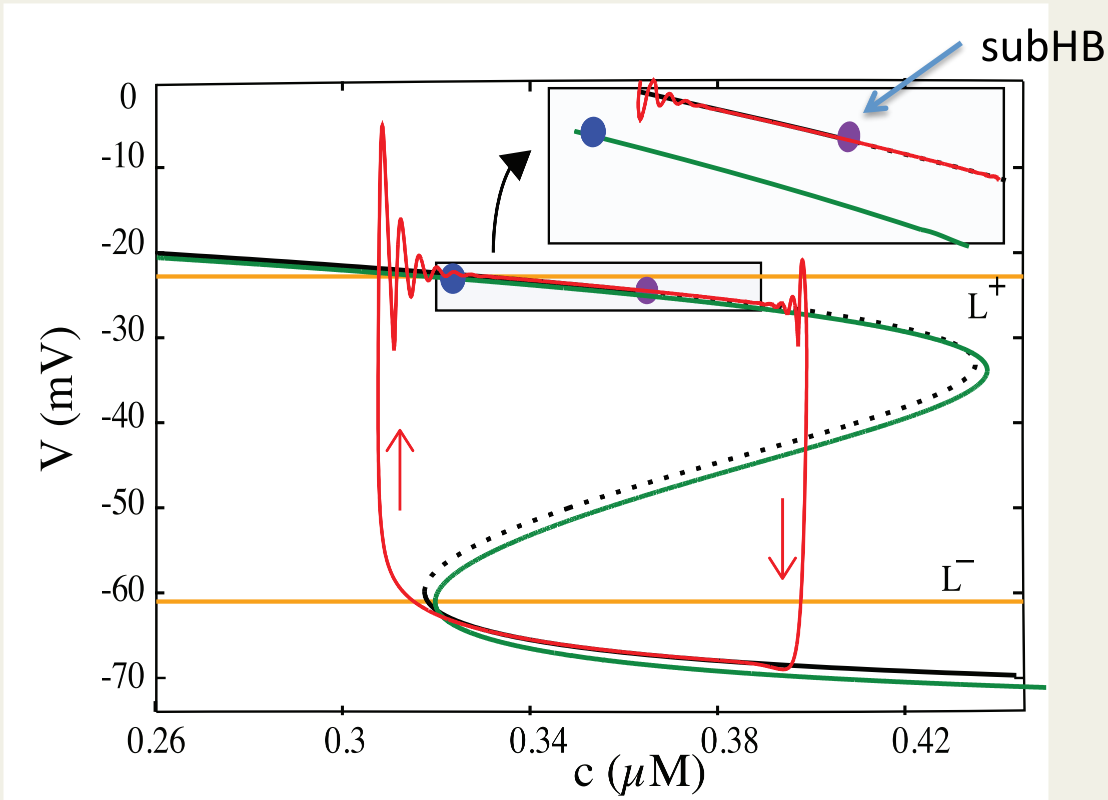
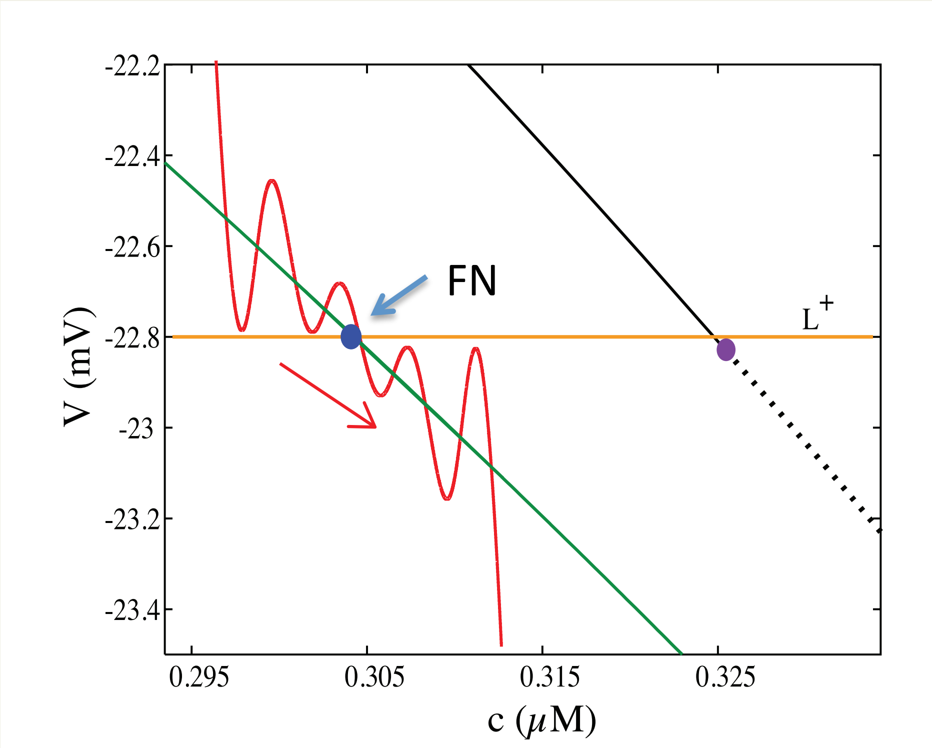


Orbit moves along top and bottom branches of the z-curve, through the subHB

The Flow is Organized by the Folded Node When ε_V is Small

$$\varepsilon_V = 0.1pF$$
$$\varepsilon_c = 0.01$$

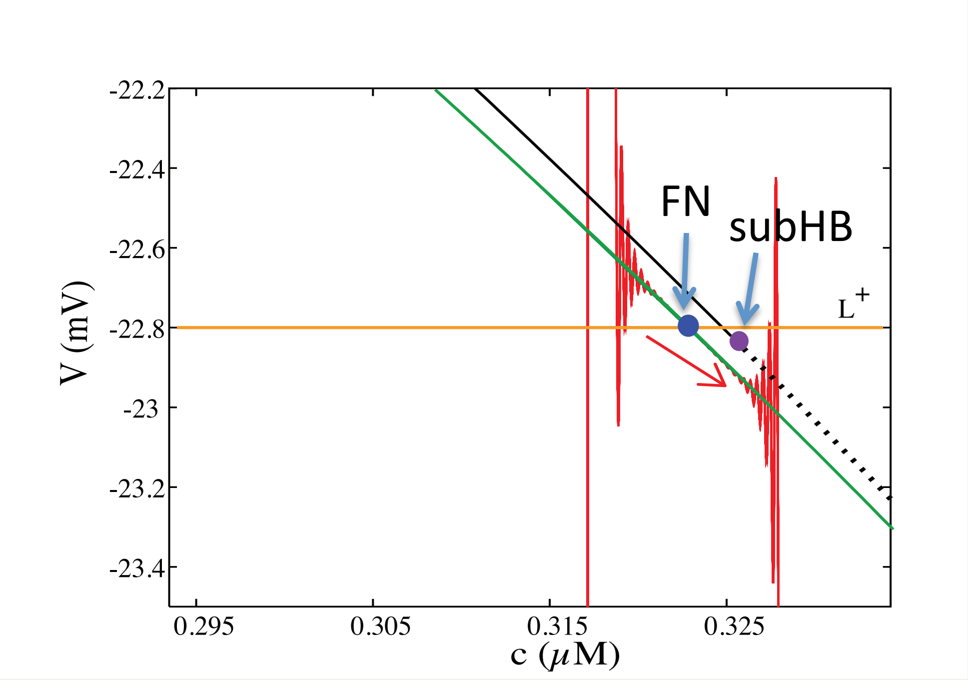


Orbit rotates as it moves along the twisted slow manifold around the folded node singularity

When ε_V and ε_c are Both Small the Orbit Moves Through the Folded Node, Near the Z-curve

$$\varepsilon_V = 0.1pF$$

$$\varepsilon_c = 0.001$$



Orbit rotates as it moves along the twisted slow manifold around the folded node singularity. The V-nullcline is near the z-curve, and the FN is near the subHB.

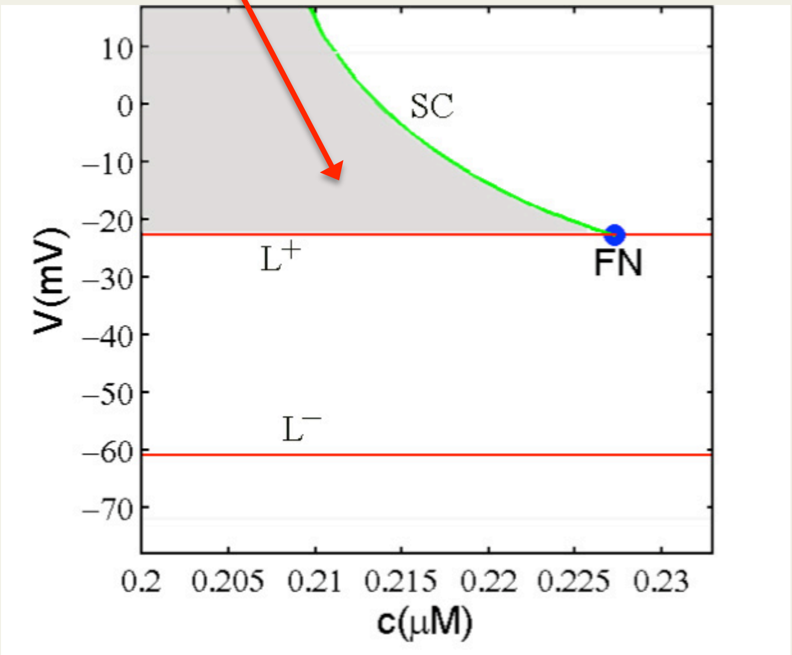
Thank You!

This work has been submitted as "*The Relationship Between Two Fast/Slow Analysis Techniques for Bursting Oscillations*", by Teka, Tabak, and Bertram

Which Structures Organize the Burst

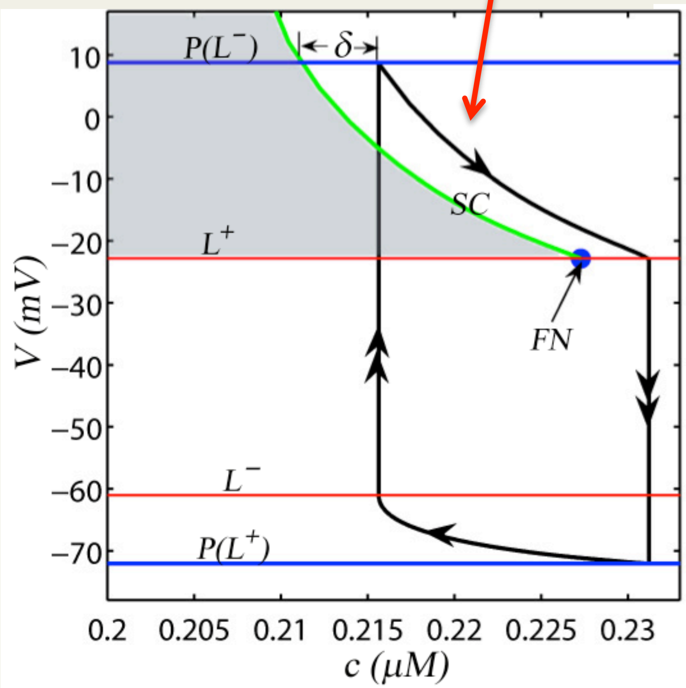
An entire sector of singular canards enter the folded node (FN) from the top (attracting) sheet and travel for some distance along middle (repelling) sheet.

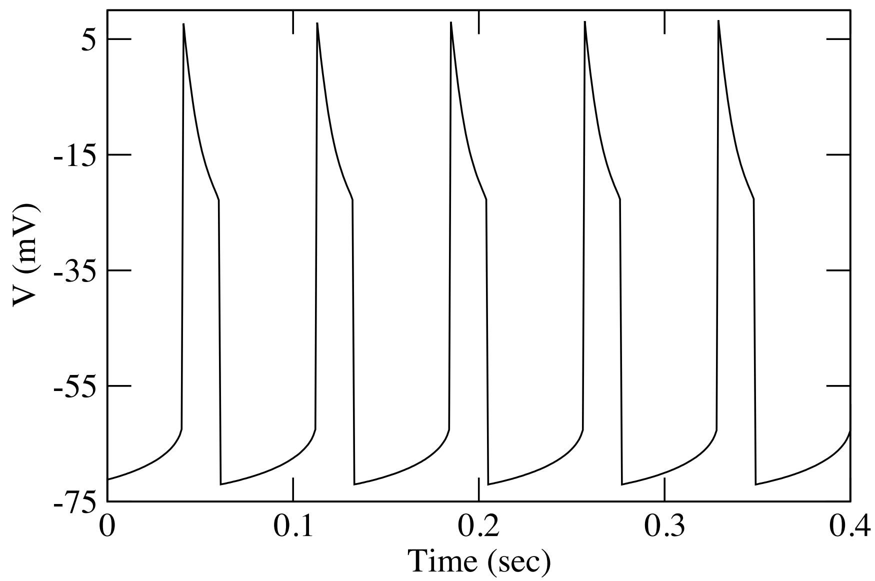
This sector is the Singular Funnel, delimited by the fold curve L^+ and the Strong Canard (SC).



Relaxation Oscillations

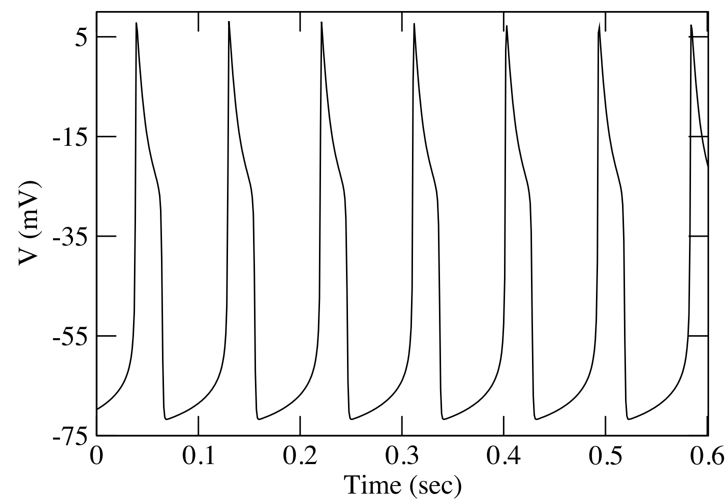
These are periodic solutions that do not enter the singular funnel.





Continuous Spiking

For ε away from 0, the relaxation oscillations transform into a continuous train of impulses.



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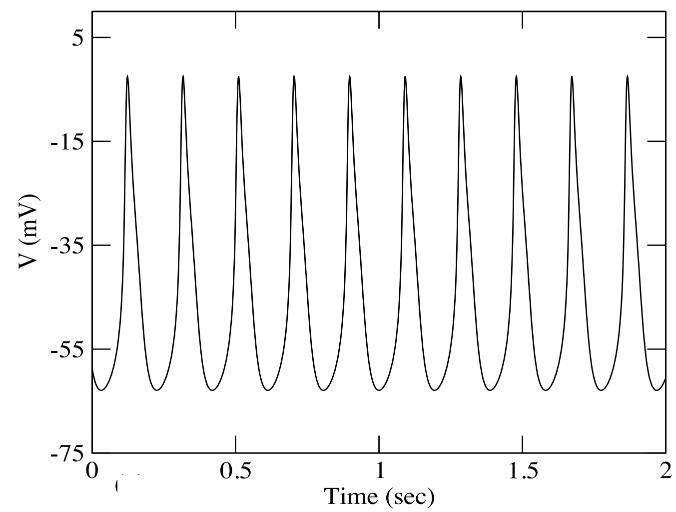
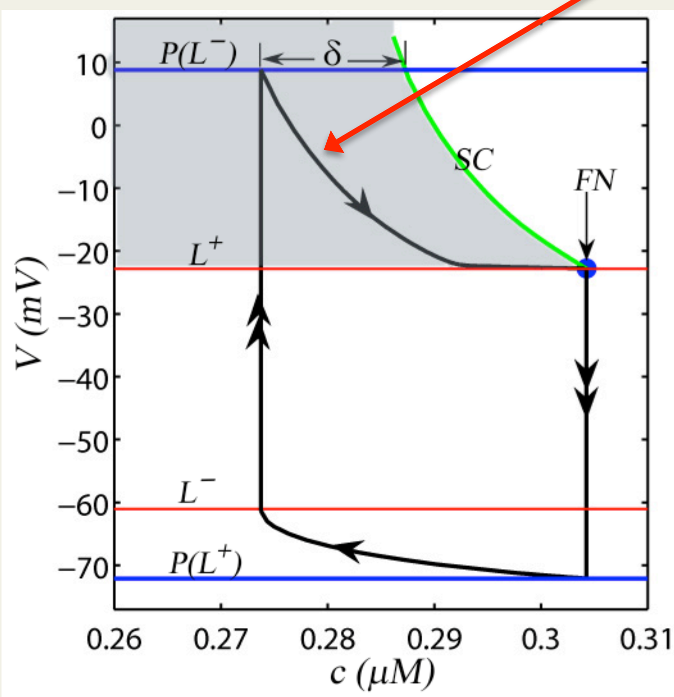


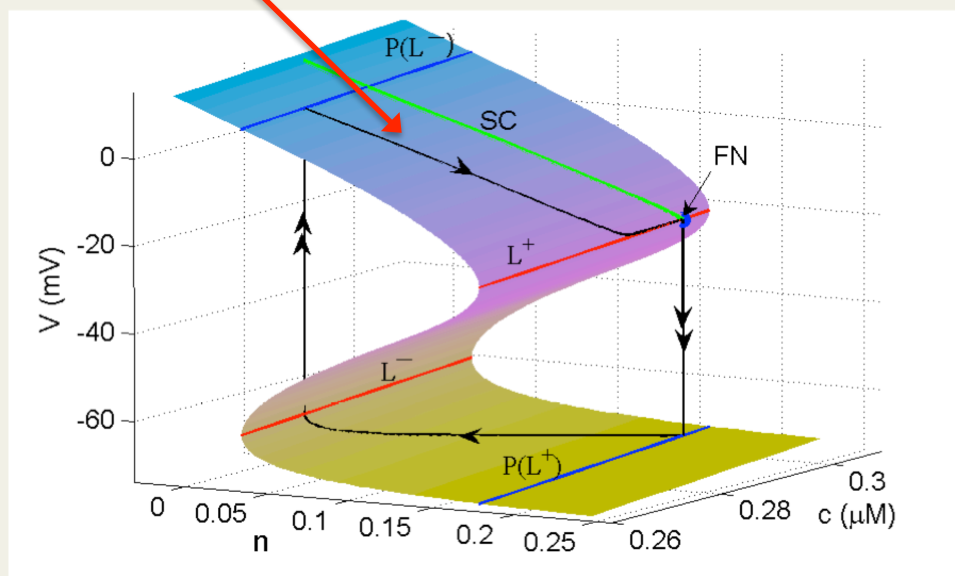
C_m=10 pF

$C_m \approx 5$ pF in lactotrophs/somatotrophs

Mixed Mode Oscillations

These are formed from periodic orbits that enter the singular funnel.





From Singular Orbit to Bursting

Transformation of the periodic orbit as ε (or the membrane capacitance C_m) is increased.