Polyrhythmic motifs in Central Pattern Generator

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Outline

1. Central Pattern generators
2. Dedicated vs Multifunctional CPG
3. Multistability for Multifunctional CPG
4. Half center oscillator
5. Mathematical models of individual and networked neurons
6. Burst regulation
7. Multistability of model for Multi-functionality of CPG motifs
8. Switching between attractor → polyrhythmicity
9. Mixed networks
10. Conclusions
11. Thank you

Central Pattern Generator

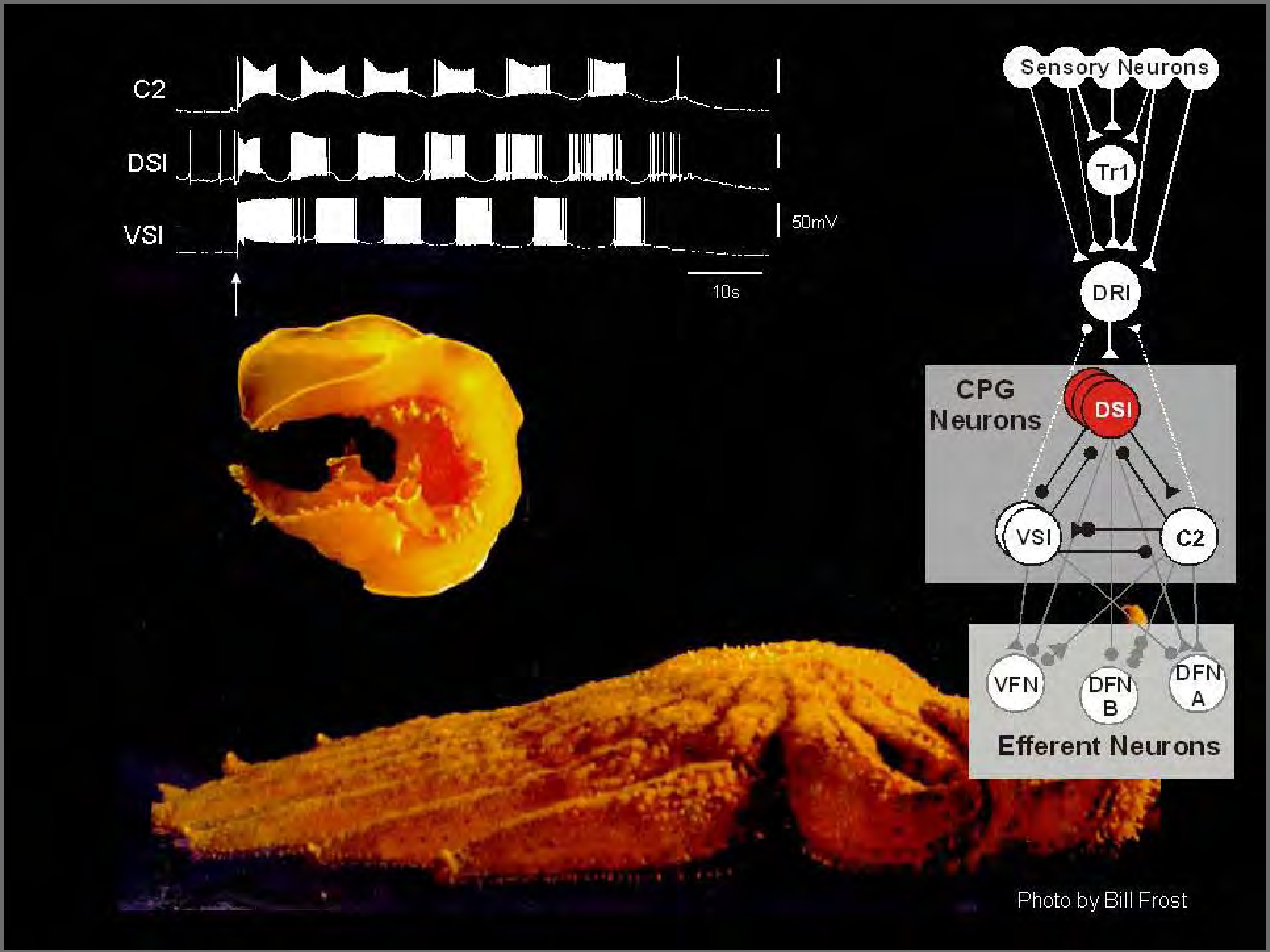
Marder and Calabrese: CPGs are neural networks that can produce endogenously rhythmic outputs without rhythmic sensory, or central input.

Locomotion: walking, crawling, swimming;
Respiration Pattern Generators: pre-Boetzinger complex;
Swallowing Pattern Generators;
Rhythm Generators: leech heartbeat

Kristan 2006: Multifunctional CPG - leech crawling and swimming

Motif – building block of network - CPG

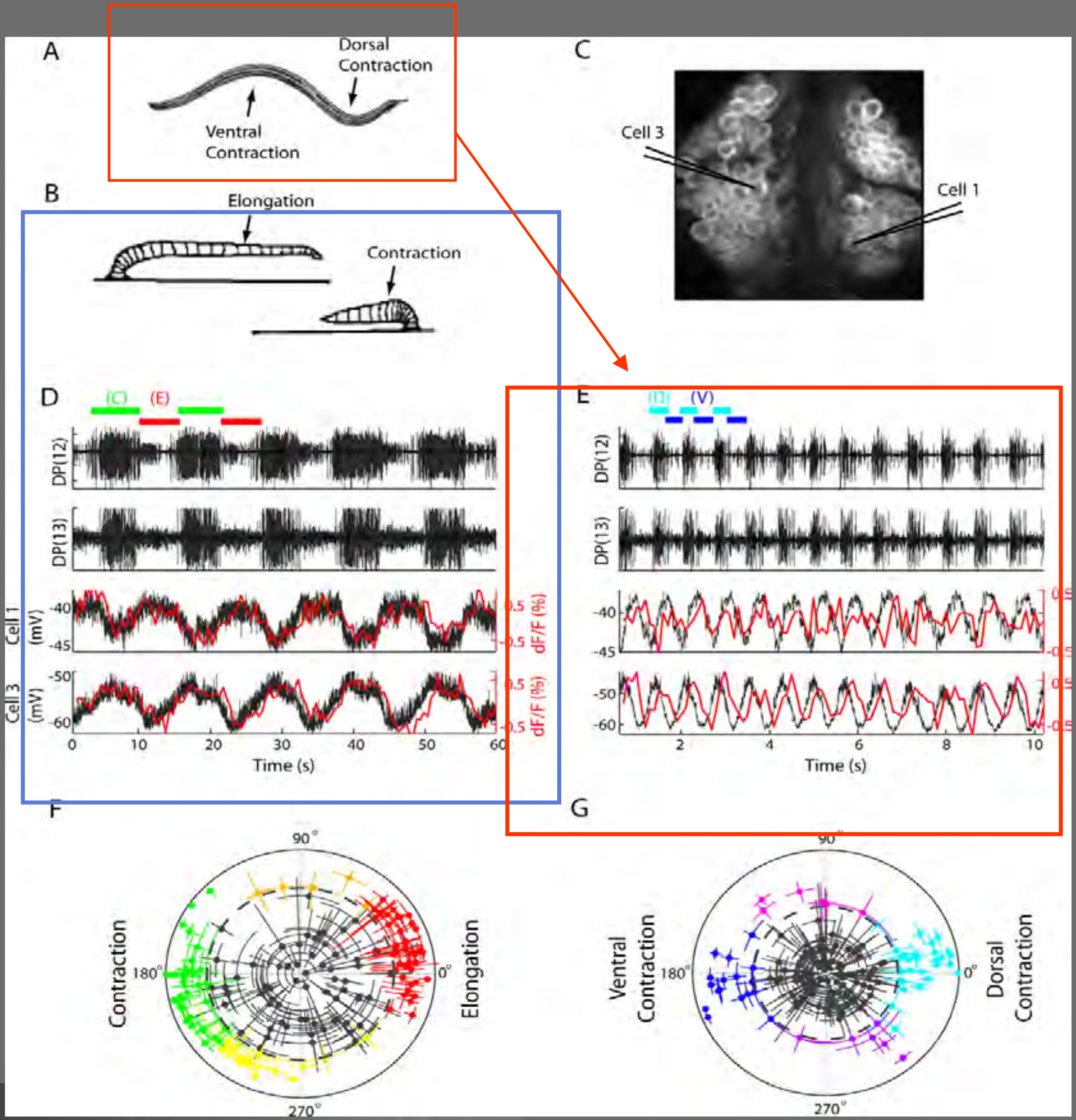
a CPG modulates reflexive withdrawal, escape swimming and crawling



Cerebral Interneuron (C2), Dorsal Swim Interneuron (DSI-A,B,C), and Ventral Swim Interneuron (VSI-B).

from: Paul S. Katz (2007), Scholarpedia, 2(6):3504.

Swimming and Crawling motor patterns in leech nervous system

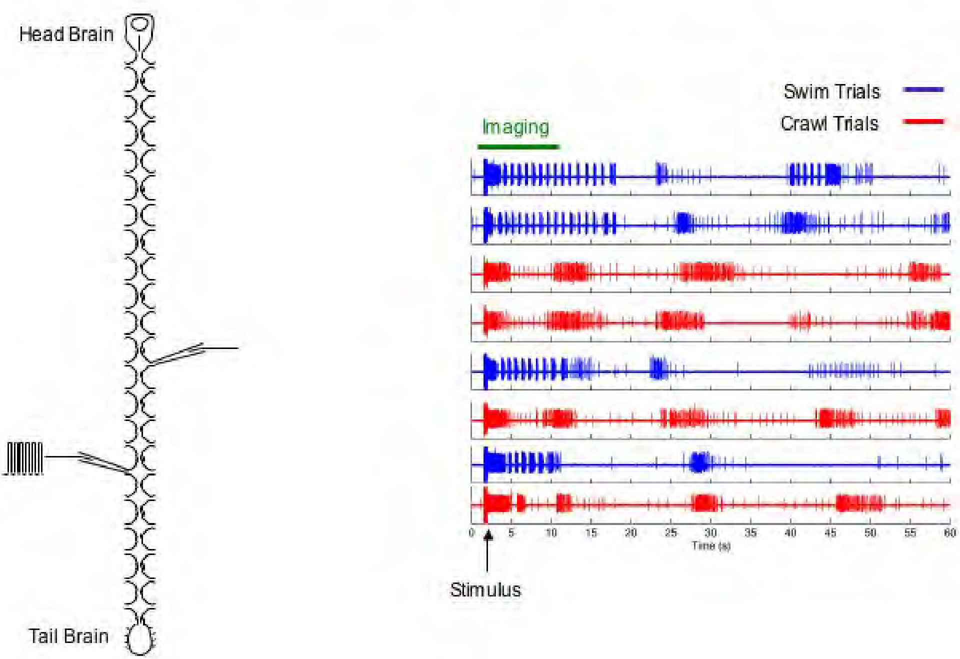


WB. Kristan, RL. Calabrese, WO. Friesen
Neuronal control of leech behavior
Progress in Neurobiology, 76(5), 2005, 279-327

Briggman and Kristan J. Neurosci. 2006;26:10925-10933

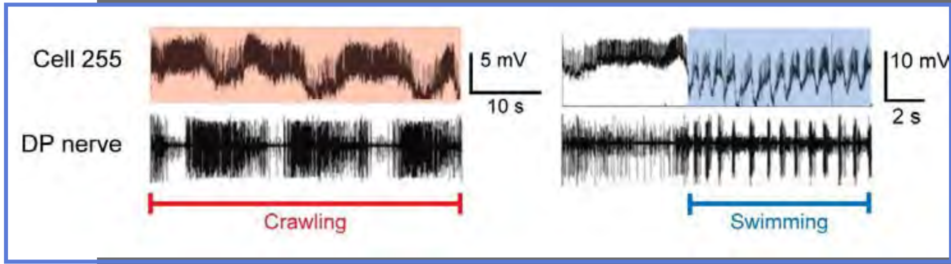
Switching between Swimming and Crawling

The leech CNS chooses whether to swim or to crawl



Briggman, Abarbanel, Kristan, *Science* 2005

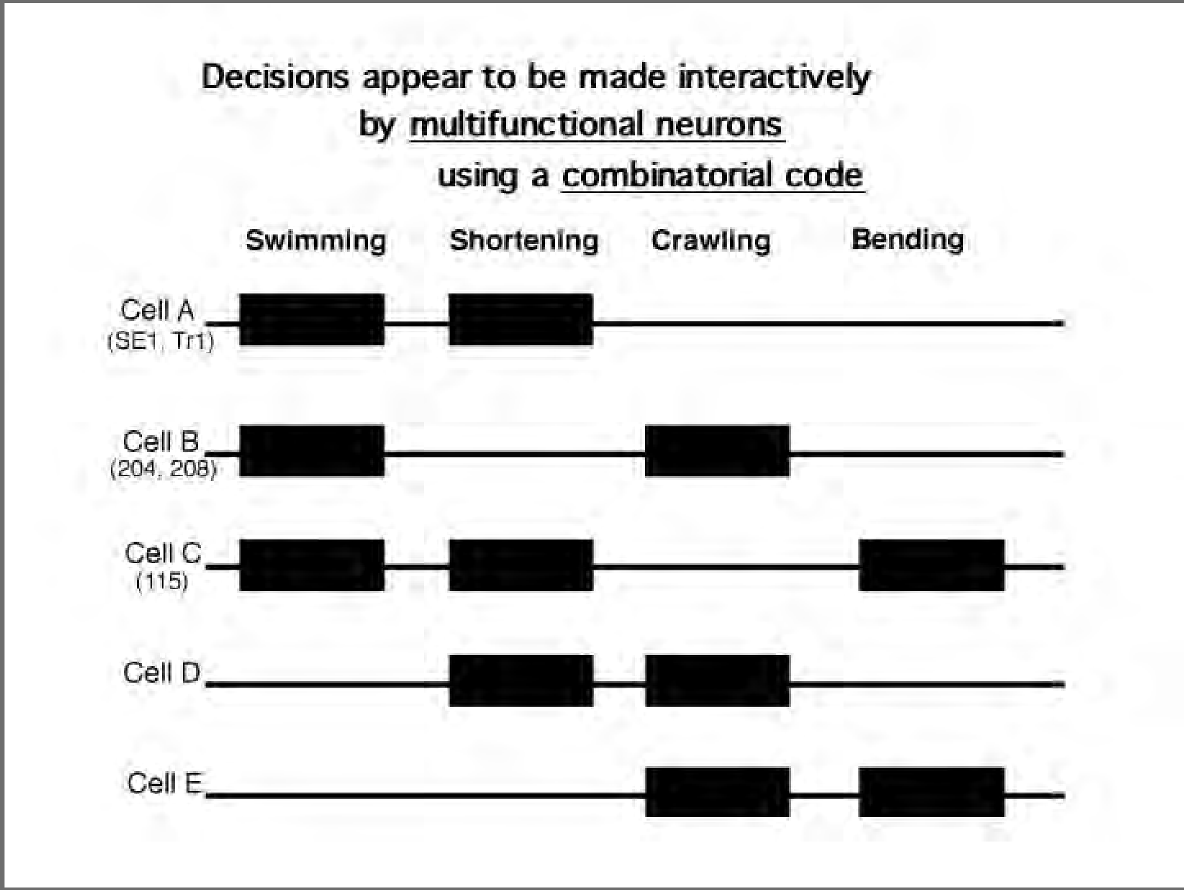
Multifunctional interneuron 255



Briggman and Kristan, J. Neurosci. 2006;26:10925-10933

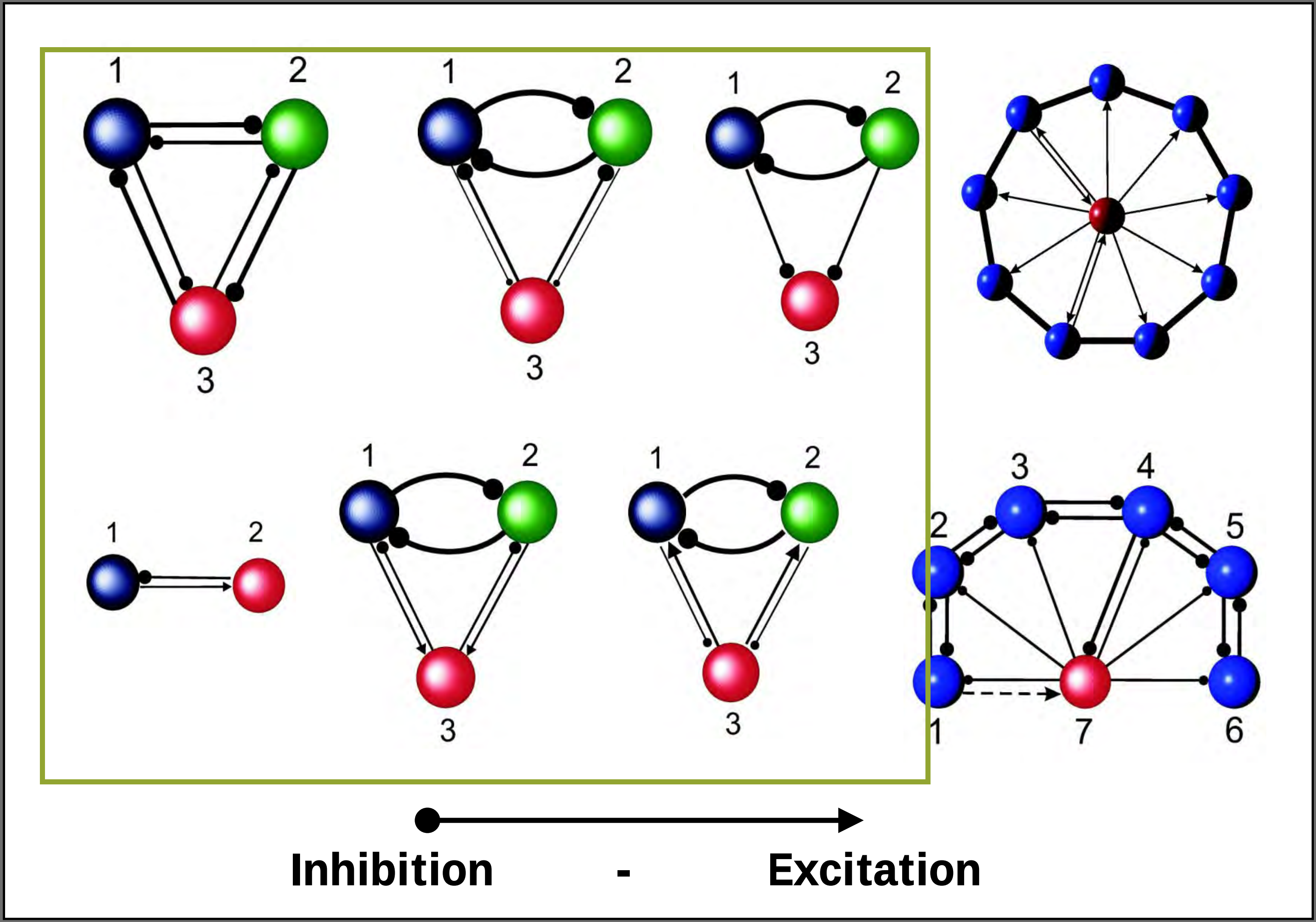
WB. Kristan, RL. Calabrese, WO. Friesen
Neuronal control of leech behavior
Progress in Neurobiology, 76(5), 2005, 279-327

B. Kristan: multifunctional CPG for crawling and swimming



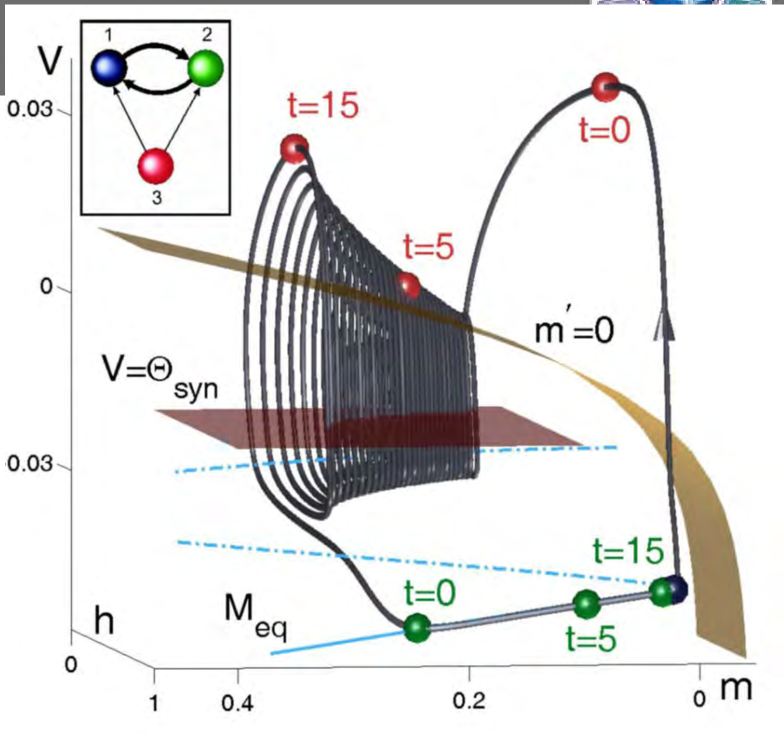
from WB. Kristan, talk at GSU in February, 2009

Mathematical examples of motifs



Reduced model of leech interneuron

$$
\begin{aligned}
C\frac{dV_i{}'}{dt} &= -[I_{\mathrm{Na}} + I_{\mathrm{K2}} + I_{\mathrm{leak}} + I_{\mathrm{pol}} + I_{\mathrm{syn}}],\\
\tau_{\mathrm{Na}}\frac{dh_i}{dt} &= f(500, 0.03391, V_i) - h_i,\\
\tau_{\mathrm{K2}}\frac{dm_i}{dt} &= f(-83, 0.018 + \boxed{V_{\mathrm{K2}}^{\mathrm{shift}}}, V_i) - m_i.
\end{aligned}
$$

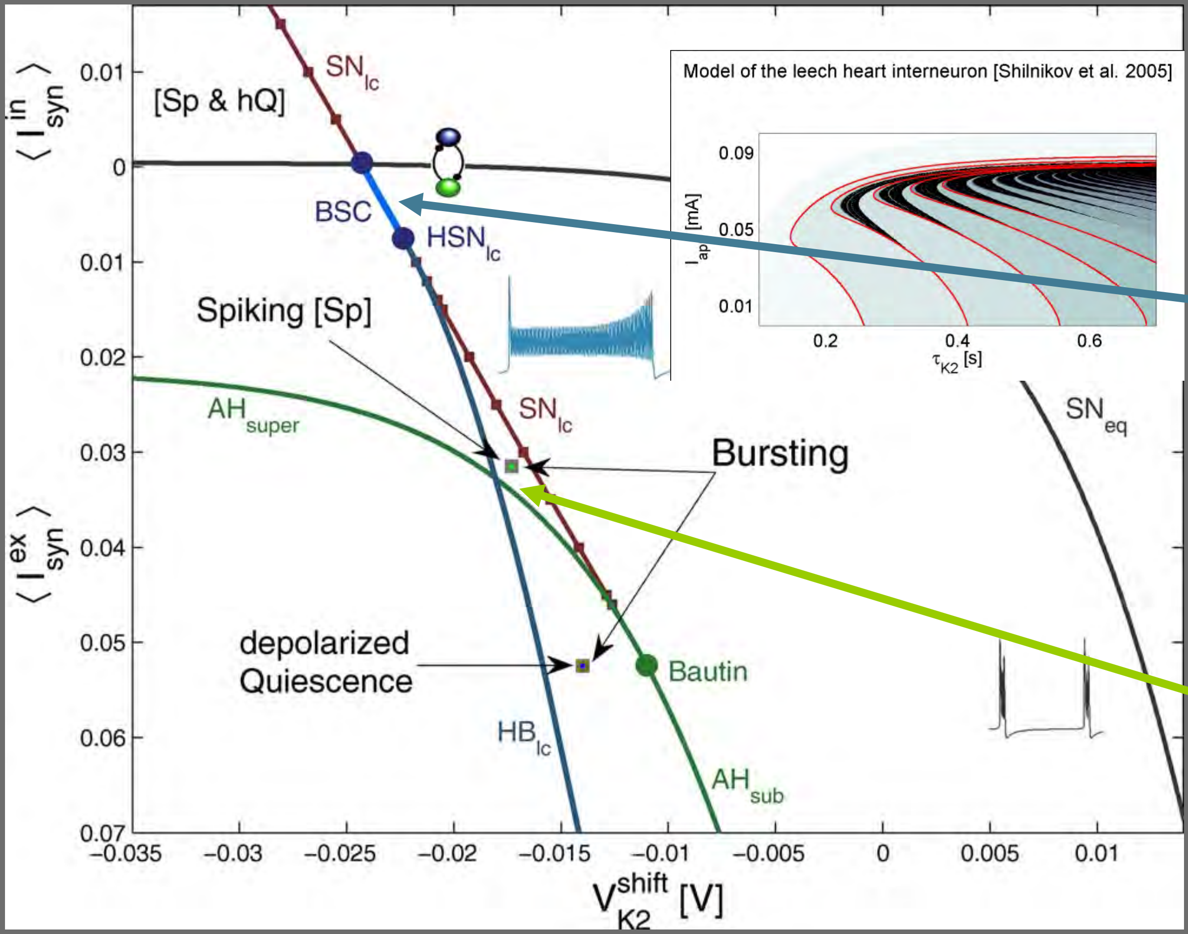


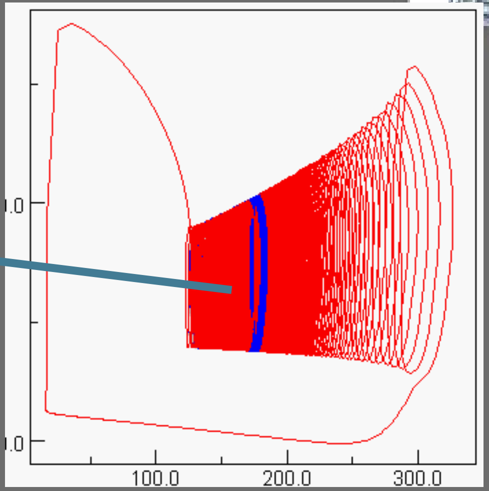
with

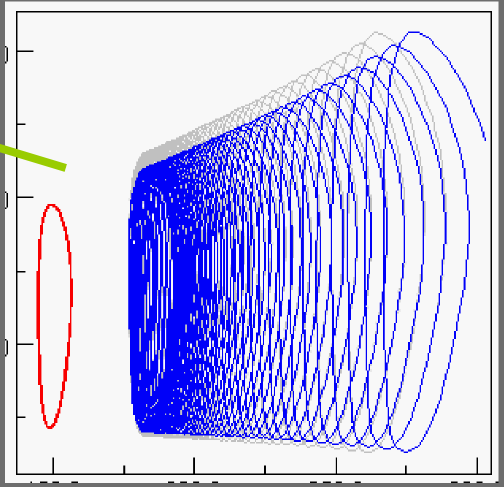
$$
\begin{aligned}
I_{\mathrm{leak}} &= g_{\mathrm{leak}}\,(V_i - E_{\mathrm{leak}}),\\
I_{\mathrm{Na}} &= \bar{g}_{\mathrm{Na}} f(-150, 0.0305, V_i)^3\, h_i\,(V_i - E_{\mathrm{Na}}),\\
I_{\mathrm{K2}} &= \bar{g}_{\mathrm{K2}}\, m_i^2 (V_i - E_{\mathrm{K}}),\\
I_{\mathrm{syn}} &= I_{\mathrm{syn}}^{\mathrm{inh}} + I_{\mathrm{syn}}^{\mathrm{exc}} = -\sum_{j=1}^{n}\left[g_{ij}^{\mathrm{in}}(E_{\mathrm{syn}}^{\mathrm{inh}} - V_i) + g_{ij}^{\mathrm{exc}}(E_{\mathrm{syn}}^{\mathrm{exc}} - V_i)\right]\Gamma(V_j - \Theta_{\mathrm{syn}})
\end{aligned}
$$

where V_i is the membrane potential, $\boxed{m_i}$, and $\boxed{h_i}$ are the gating variables describing the activation of the potassium I_{K2} and inactivation of the sodium current I_{Na} of the i-th cell, respectively. Other parameters are: $C = 0.5$ nF is the membrane capacitance, $\bar{\mathrm{g}}_{\mathrm{K2}} = 30$nS is the maximum conductance of I_{K2}; $\mathrm{E}_{\mathrm{K}} = -0.07$V and $E_{\mathrm{Na}} = 0.045$V are the reversal potentials of K^+ and Na^+, respectively; $\bar{g}_{\mathrm{Na}} = 200$ nS is the maximal conductance of I_{Na};

4 kinds of Multistability: tonic-spiking, bursting, quiescence



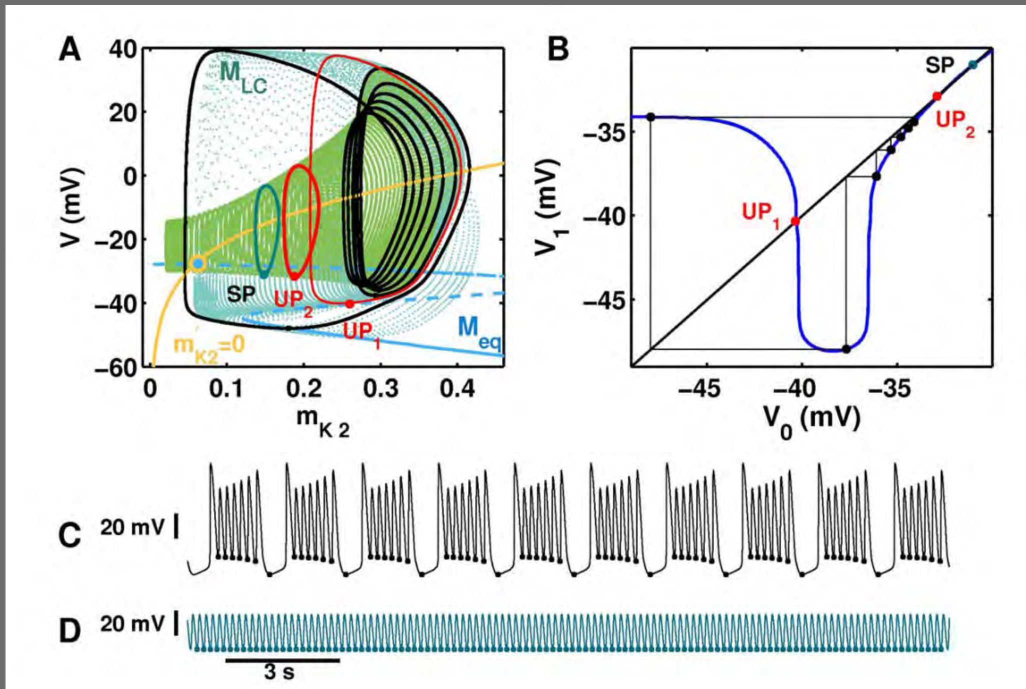


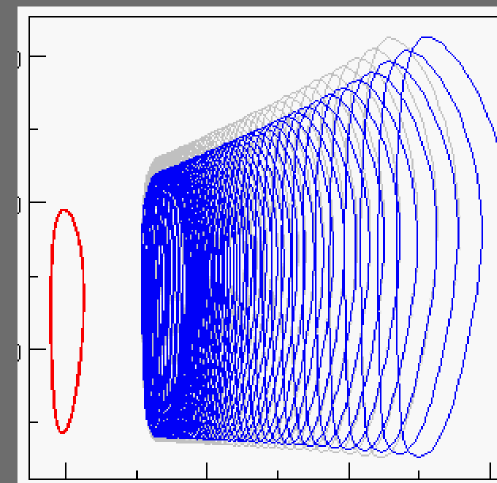


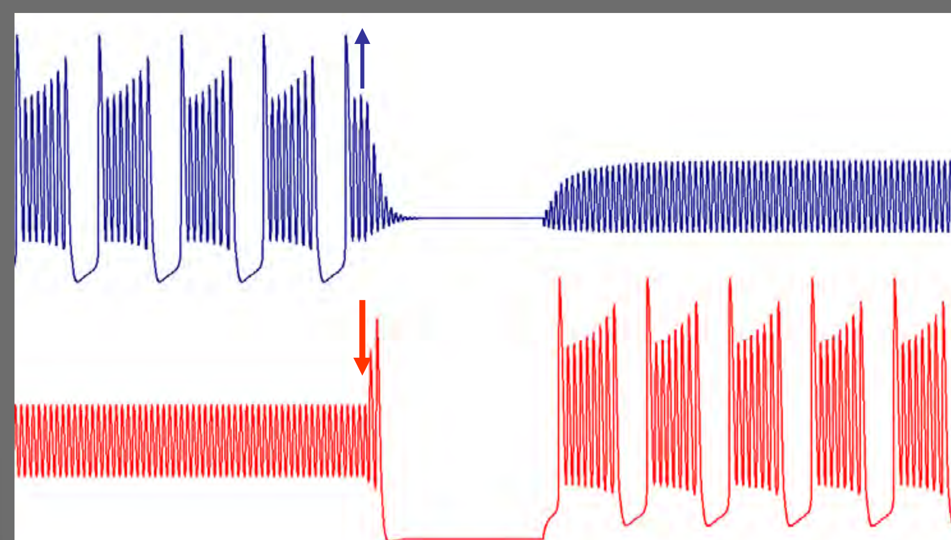
Shilnikov A. and Cymbalyuk G., PRL, 94, 048101, 2005.
Shilnikov A., Calabrese R. and Cymbalyuk G., Phys Review E 71(5), 056214-046221, 2005.
Cymbalyuk G. and Shilnikov A., J. Computational Neuroscience 18 (3), 269-282, 2005.

Shilnikov A.L., Gordon R. and Belykh I.V., Polyrhythmic synchronization in bursting network motifs, J. Chaos, 18, 037120, 2008

Voltage onto Poincare mappings for bistability

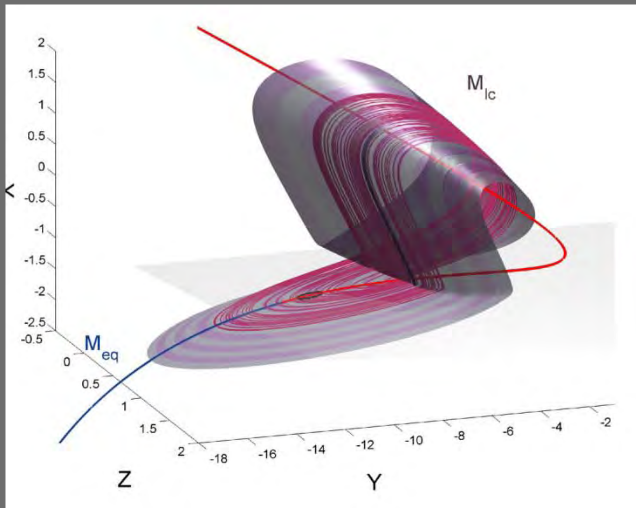


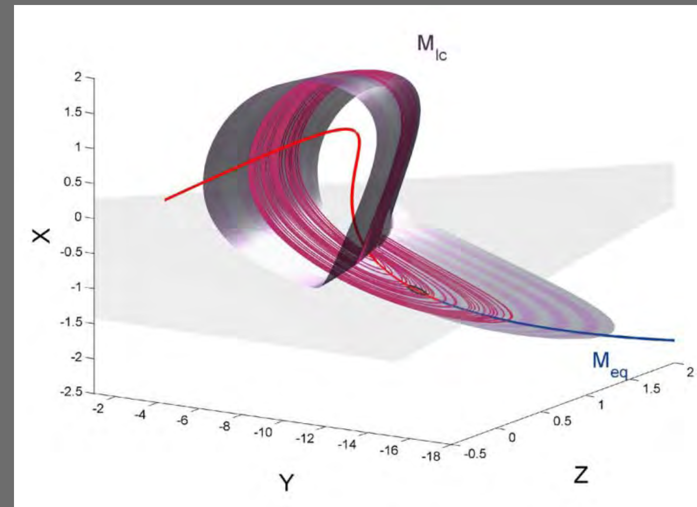




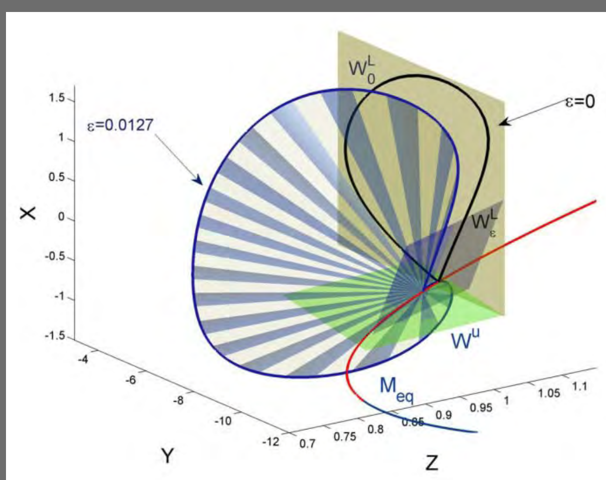
Selecting Bistability: switching between bursting and tonic spiking by applying a pulse of external current, positive or negative

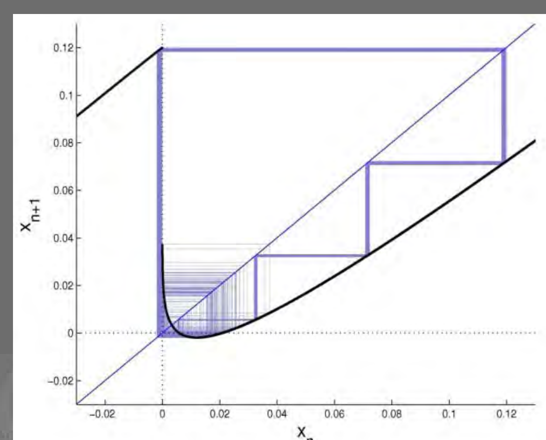
∞ many periodic orbits in a chaotic single cell





Homoclinic orbit-flip & Inclination switch : Shift dynamics –
Smale horseshoe [Terman, 1991]
for square-wave bursters

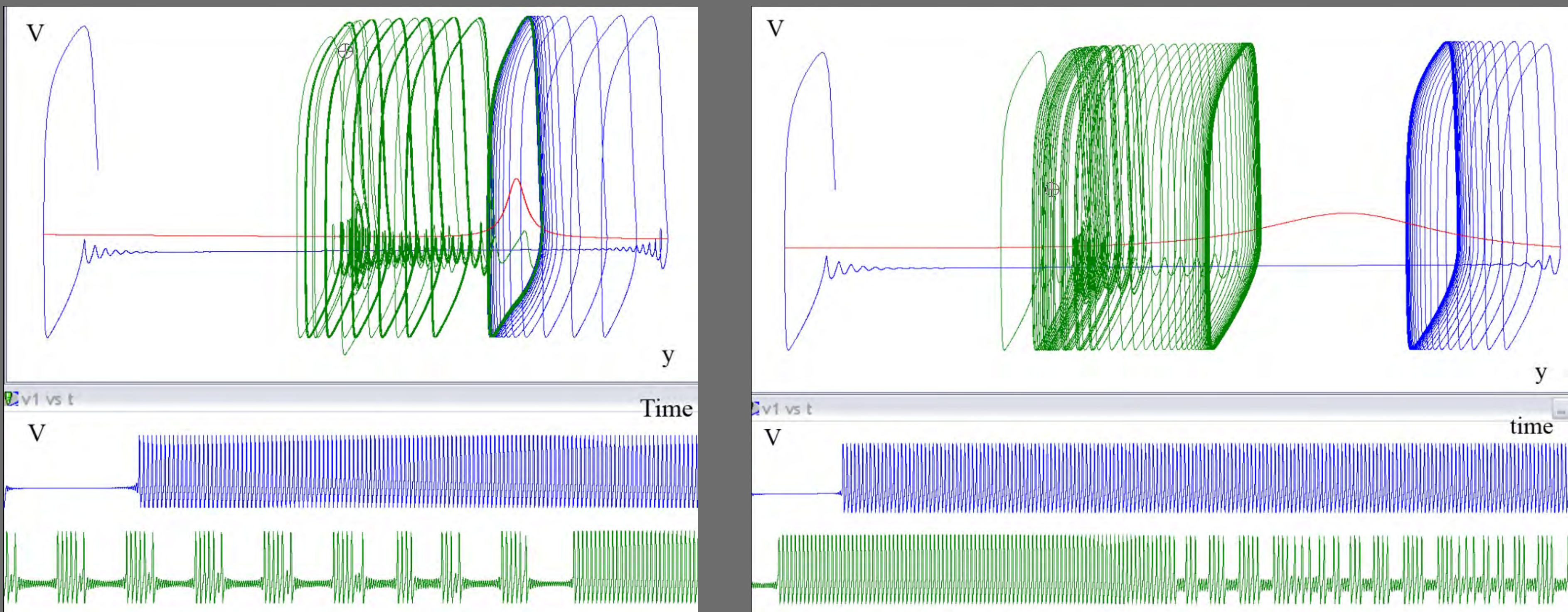




Isolated?
Singed out?
Switching between
Nonwandering orbit
Quasiminimal set

Multistability in individual cells

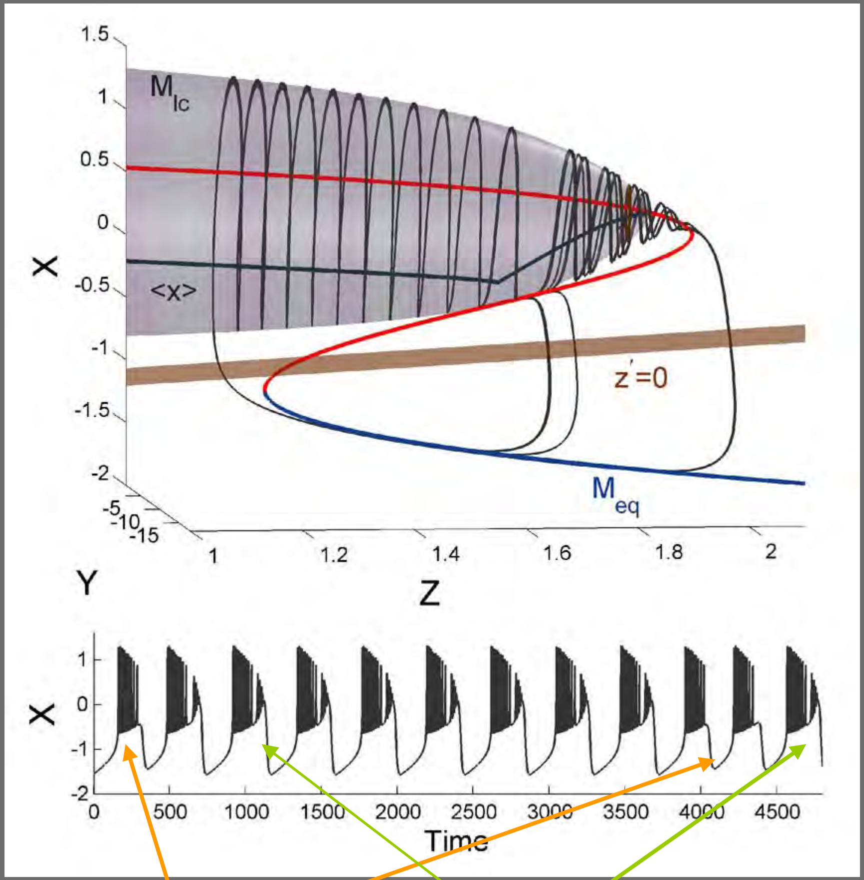
Tonic spiking and bursting in an elliptic burster at the transition edge



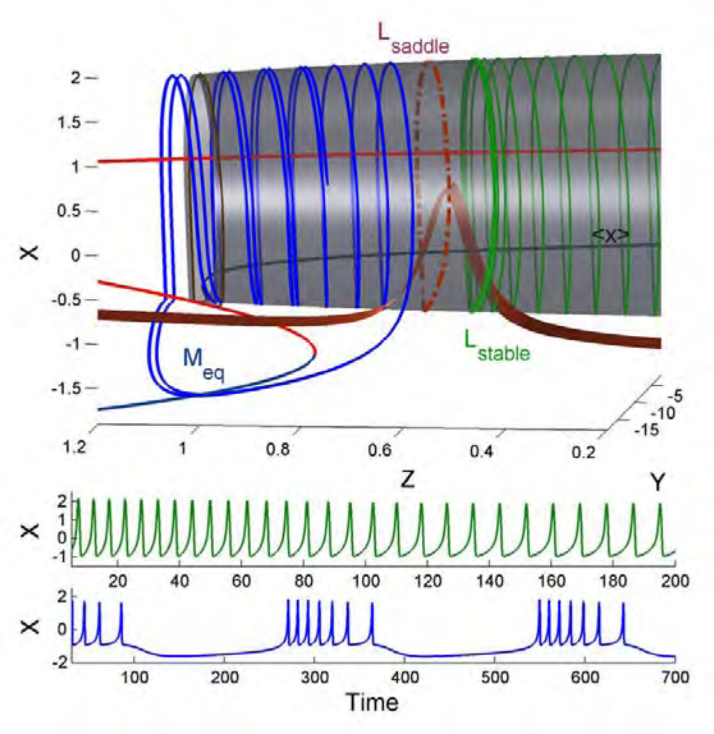
Bistability helps regulating flexibly temporal characteristic of cells by external or synaptic current

Multistability in individual cells

Tonic spiking and bursting in an square-wave burster at the transition edge

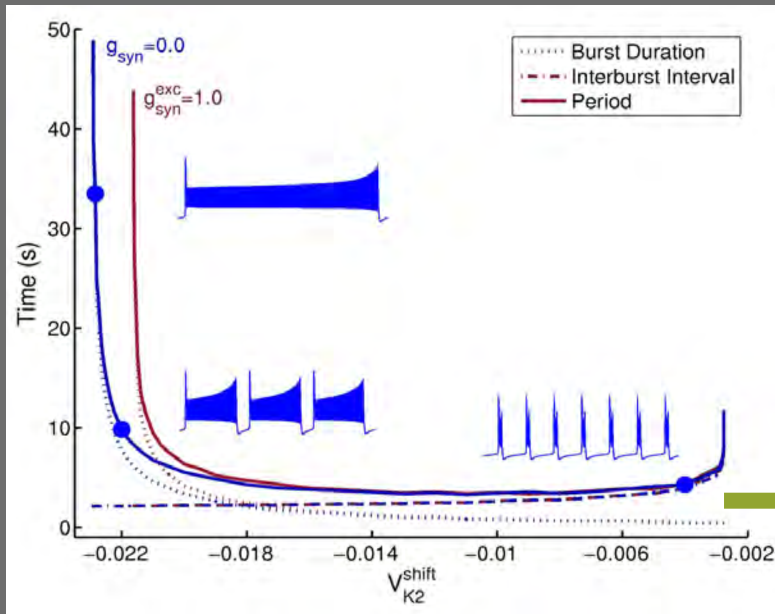


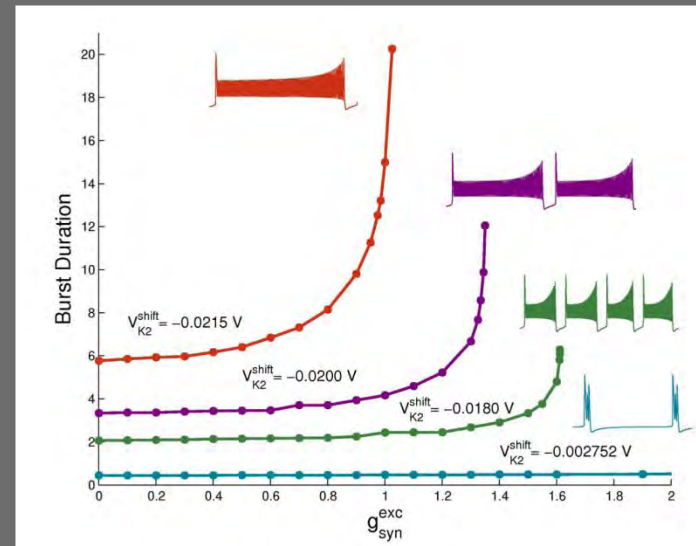
Square-wave vs plateau bursting



Bistability helps regulating flexibly temporal characteristic of cells by external or synaptic current

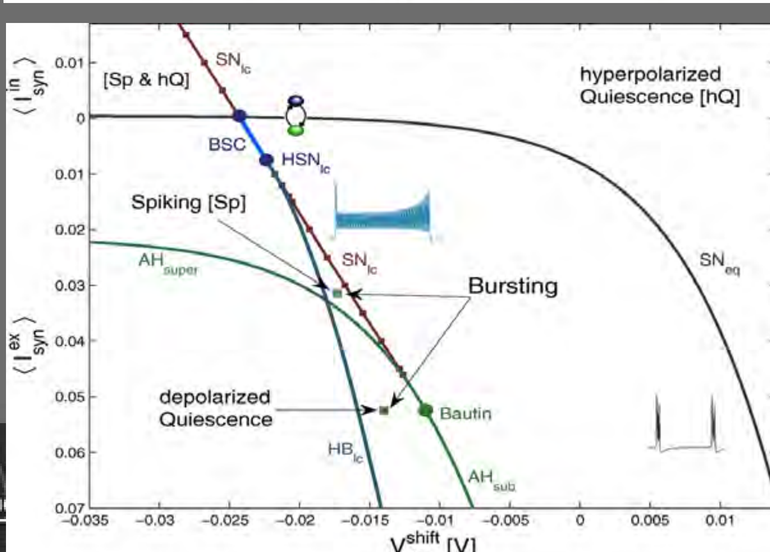
Regulation of temporal characteristics of bursting



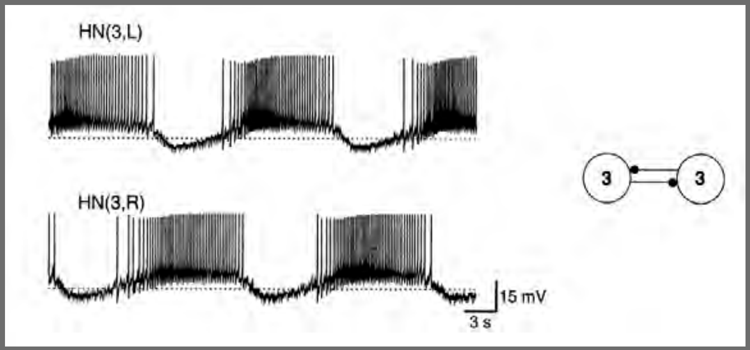


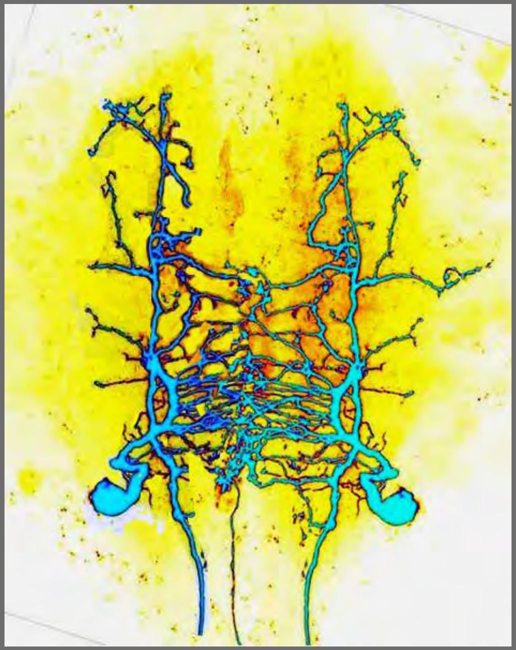
Spiking

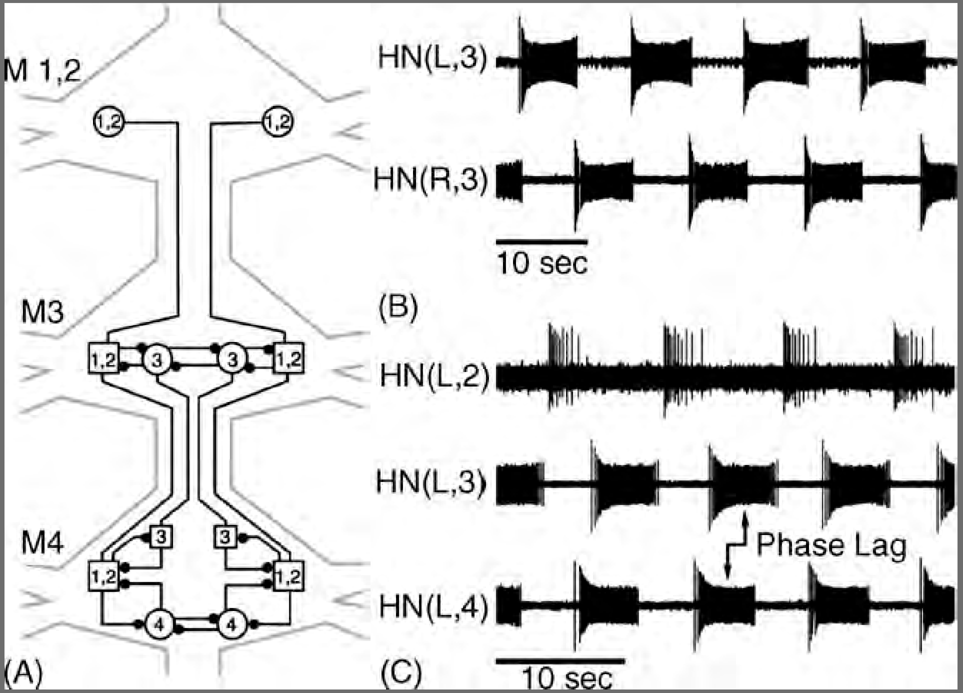
Quiescence



Half Center Oscillator



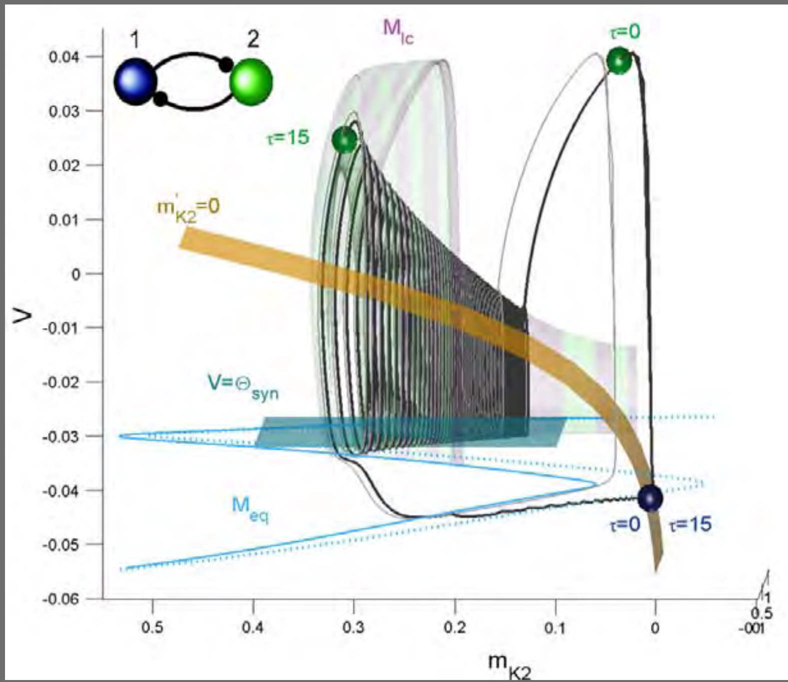


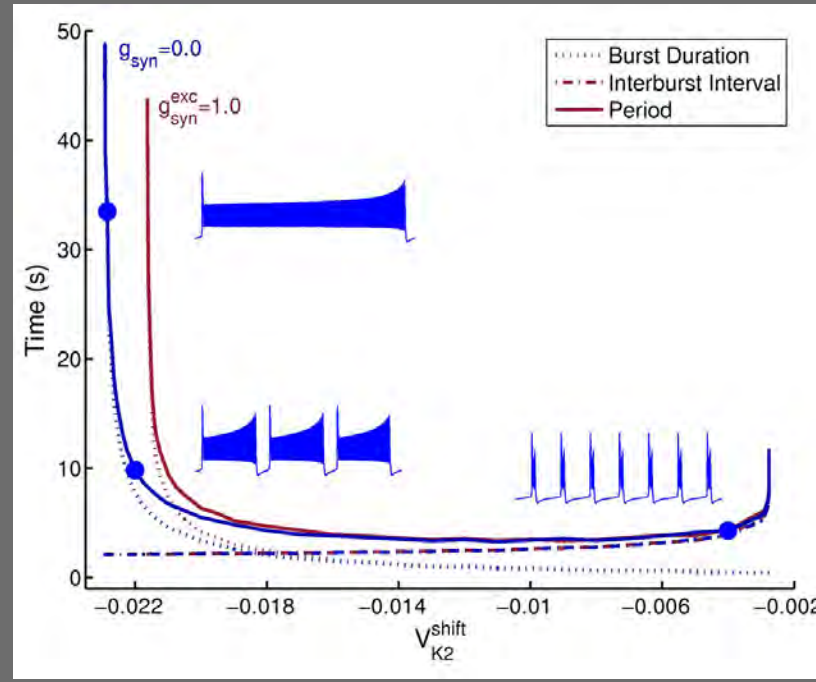


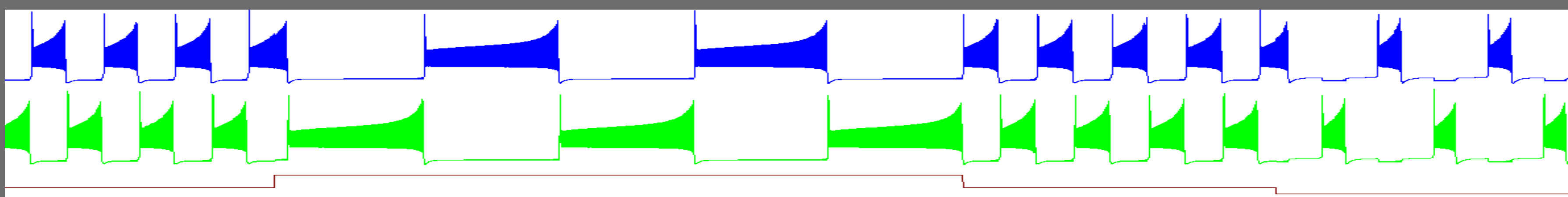
Bursting
is an *oscillatory* activity consisting of
intervals of repetitive spiking
interrupted by intervals of quiescence.

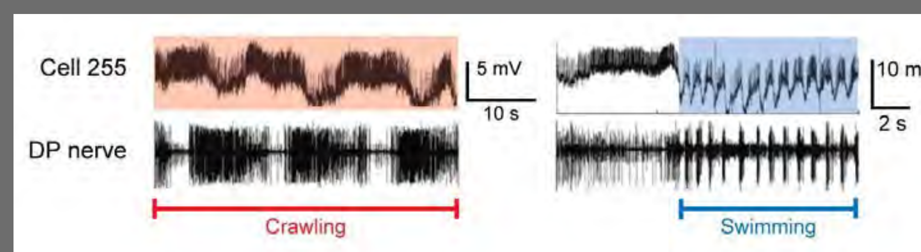
Hill, A. A.V. et al. J Neurophysiol 90: 531-538 2003.

Back to Half Center Oscillator or …

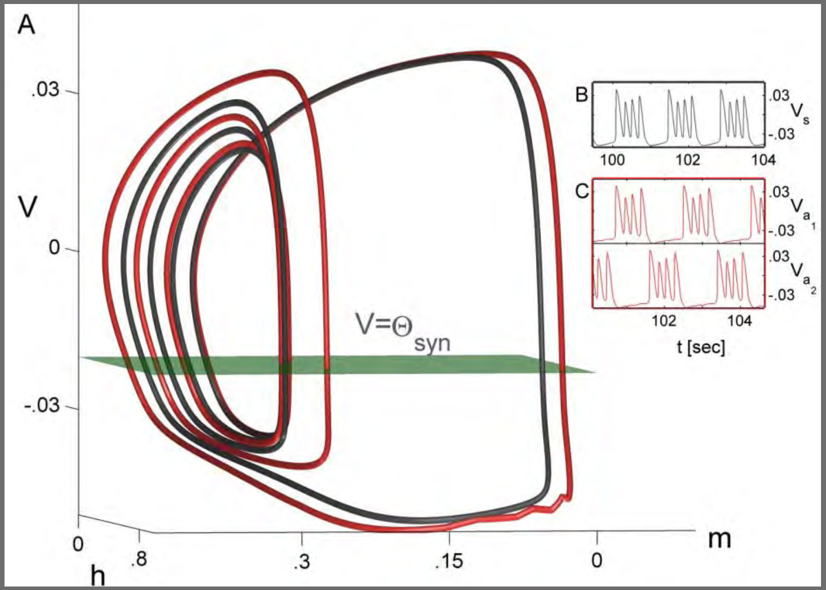


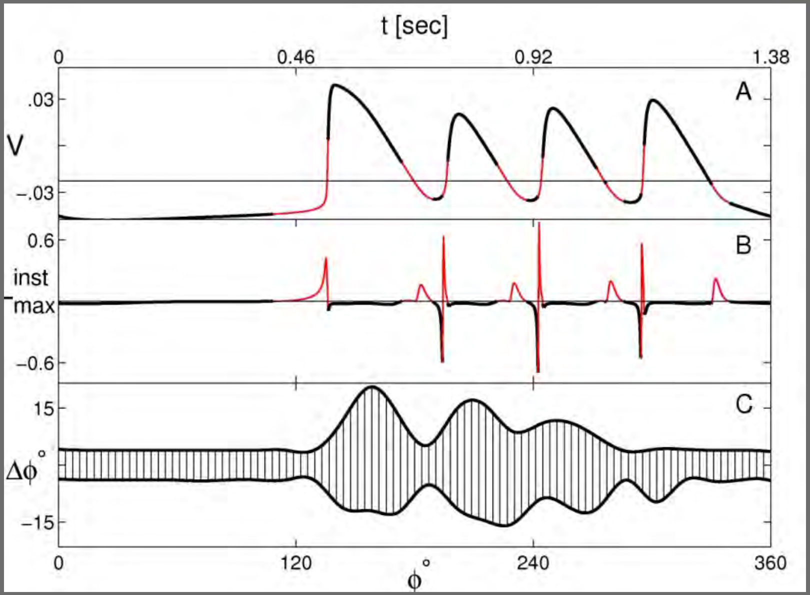


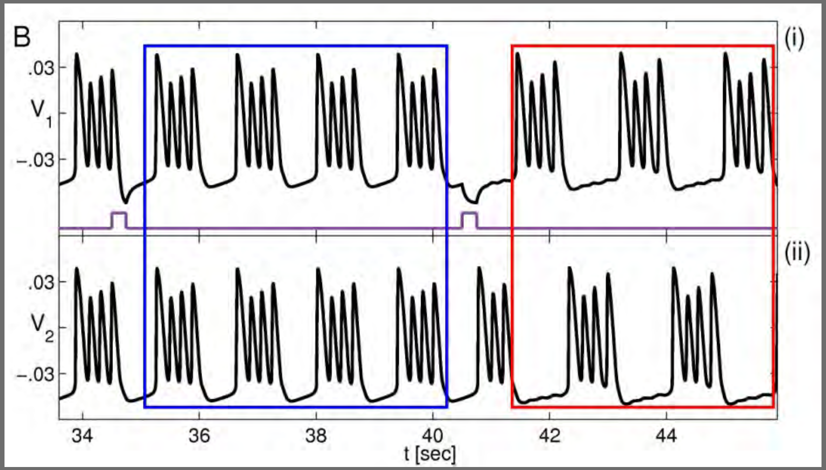


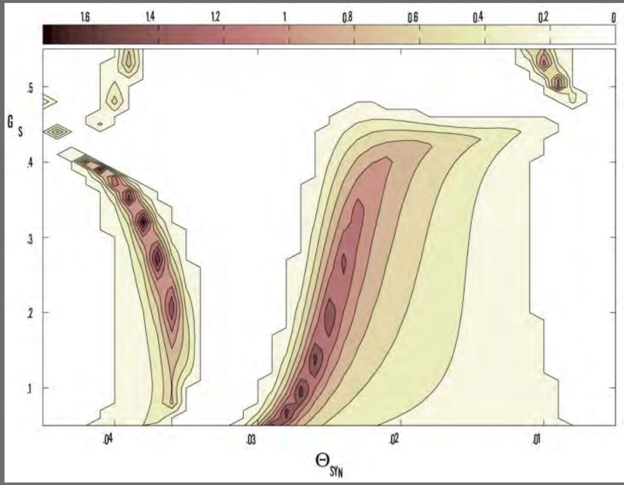


Bistability in Half Center Oscillator

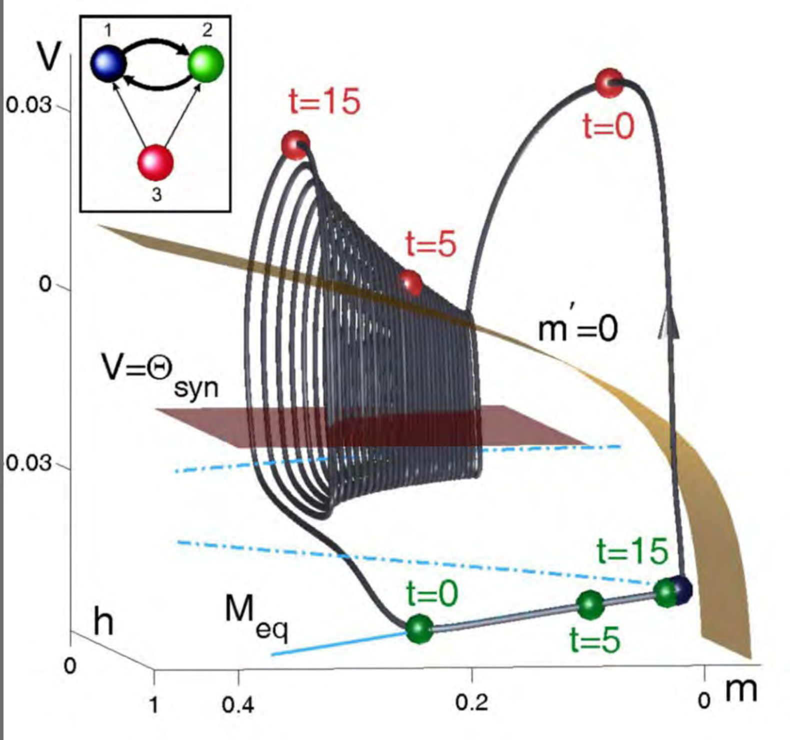


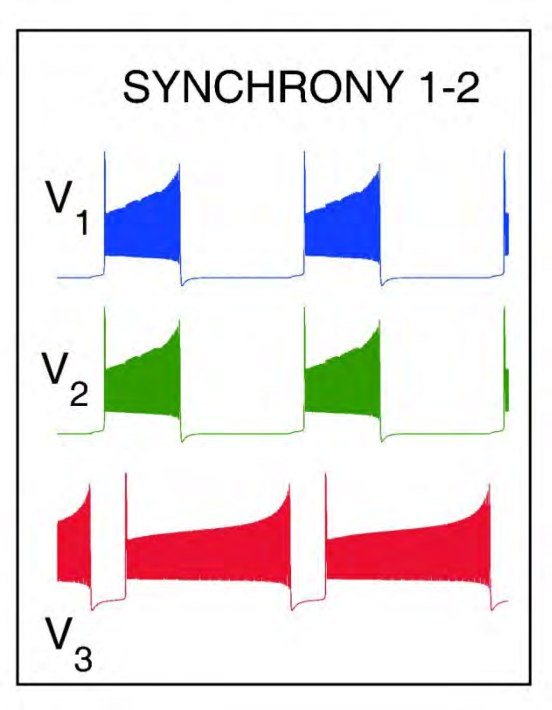


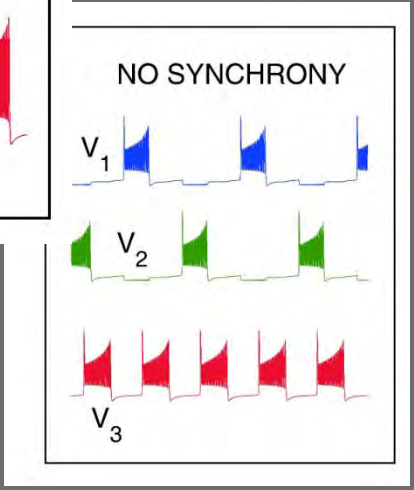




Can weak inhibition synchronize a HCO?







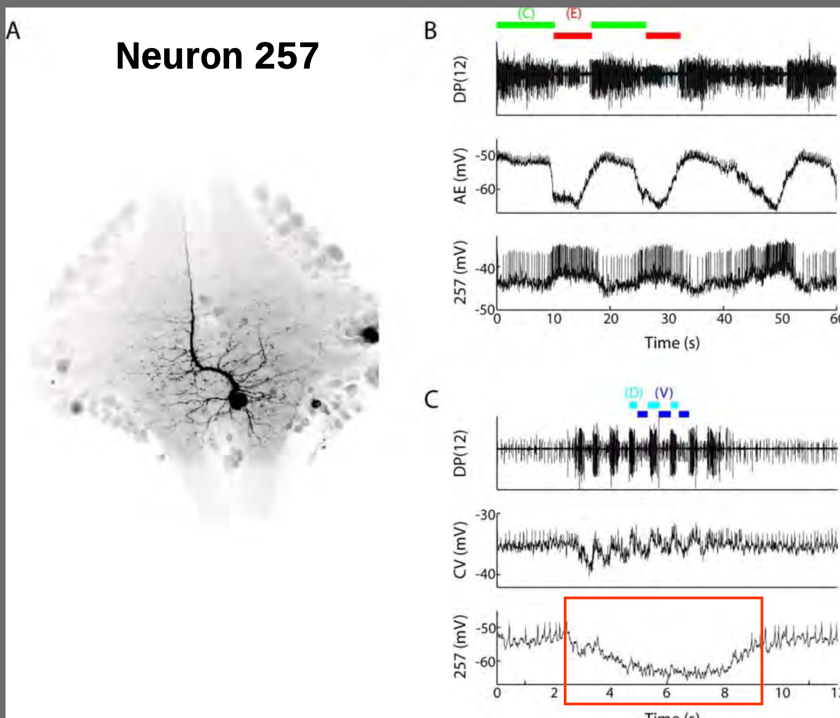
Burst duration vs. interburst period

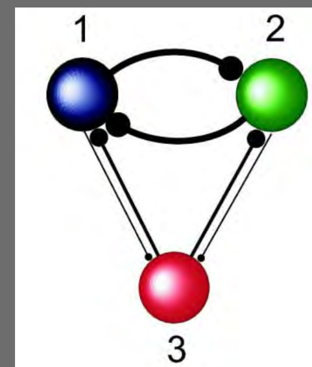
$g_{syn} = 0.025$ (external driving)

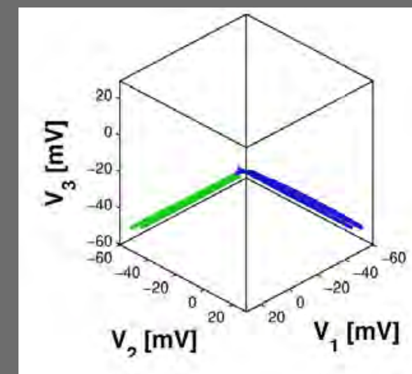
$g_{syn} = 2$ (mutual inhibition)

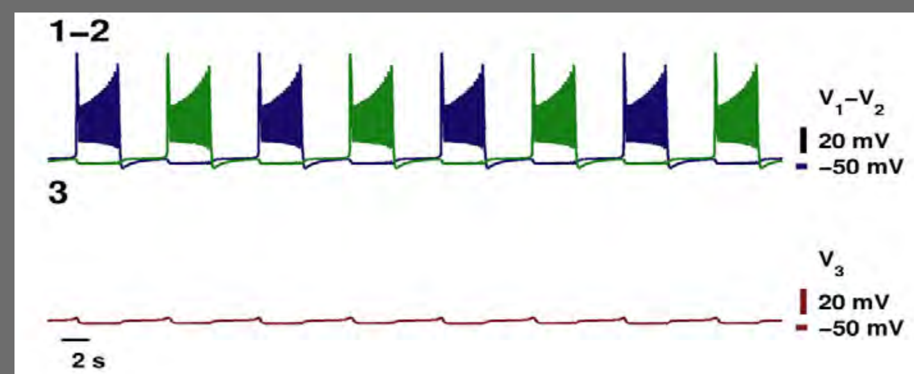
Belykh I.V. and Shilnikov, A.L., *David vs. Goliath*: when weak inhibition synchronizes strongly desynchronizing networks of bursting neurons, Phys. Rev. Letters 101, 078102, 2008

Reciprocally inhibitory motif
Multistability type 1

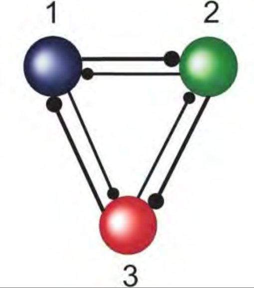


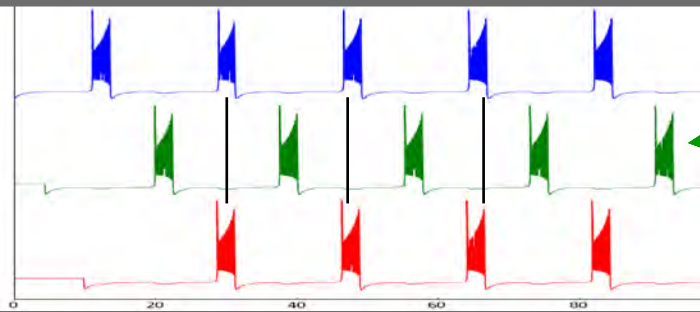


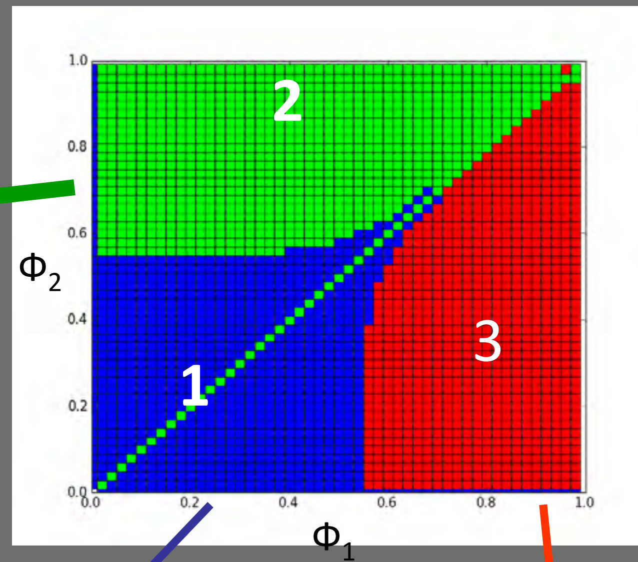




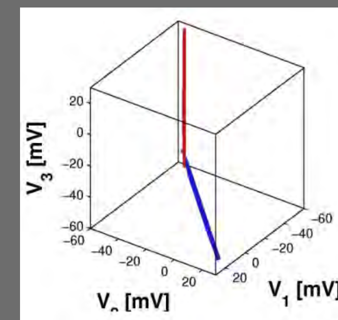
Reciprocally inhibitory motif

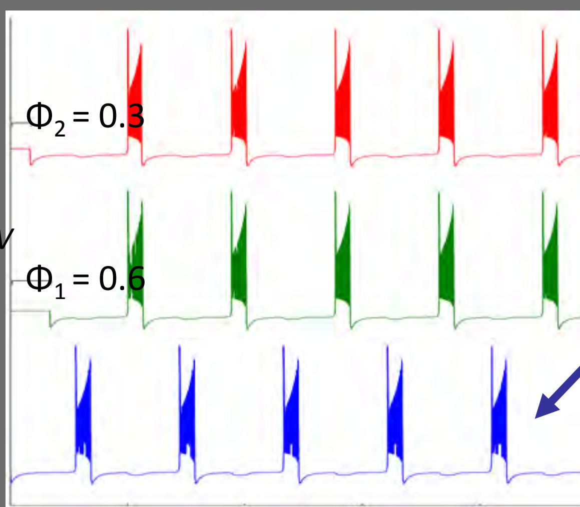






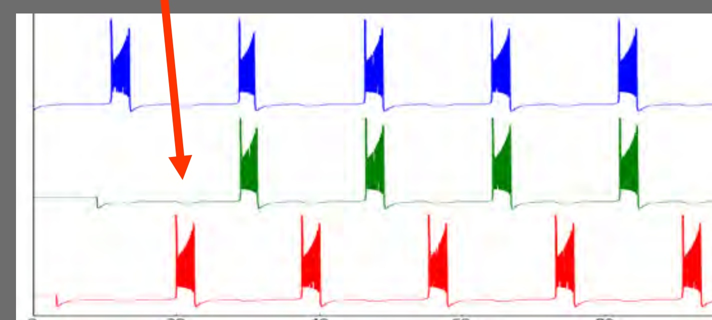
$V_{K2}^{shift} = -0.02;\ g_{ij} = -0.1$





V

t (ms)



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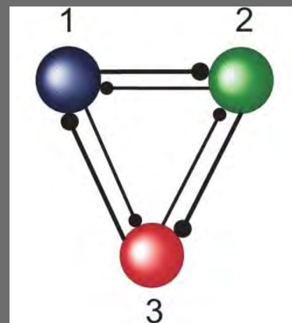
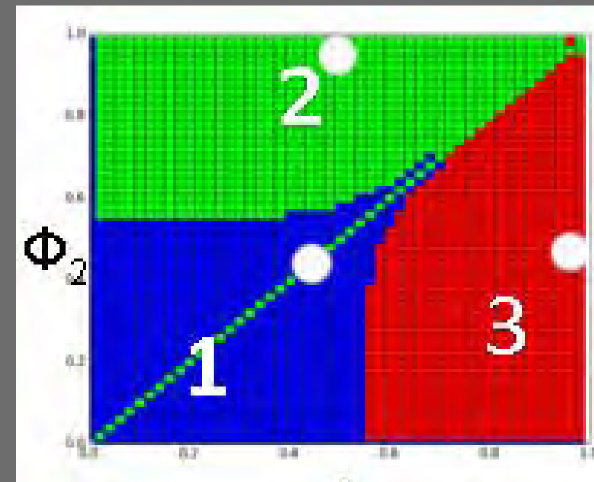
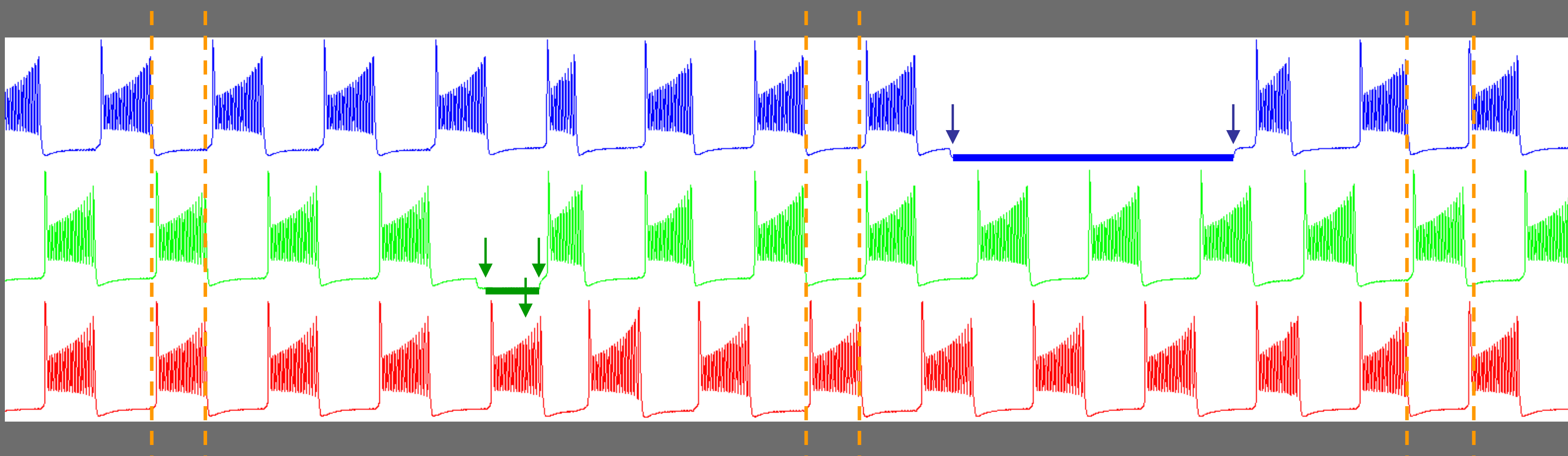
Shilnikov A.L., Gordon R. and Belykh I.V., Polyrhythmic synchronization in bursting network motifs, J. Chaos, 18, 037120, 2008

Controlling multistability switching by external pulse in symmetric motif







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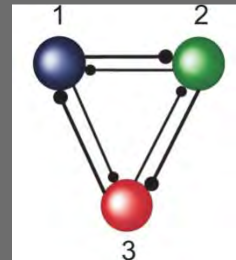
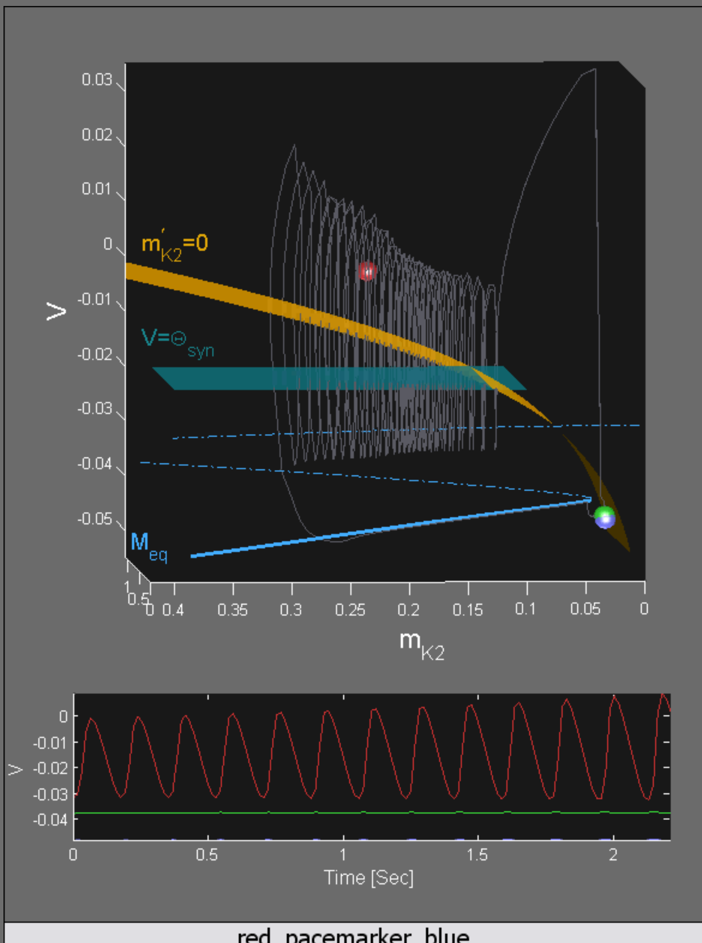
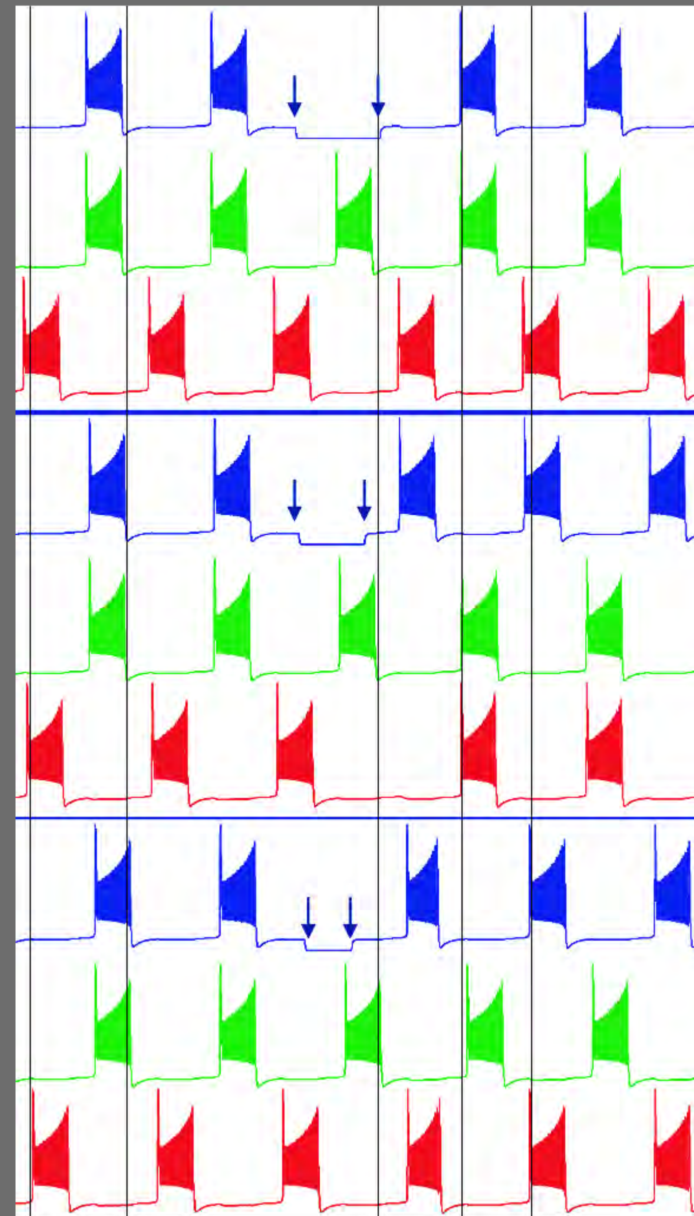
Controlling multistability switching by external pulse

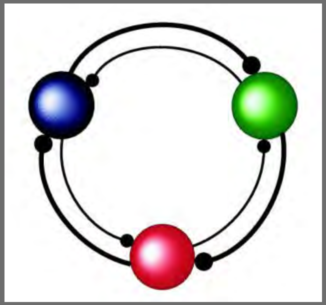


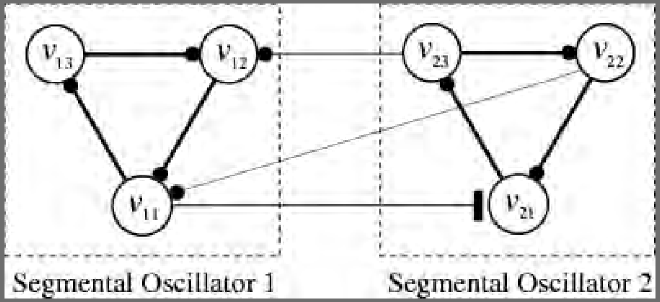


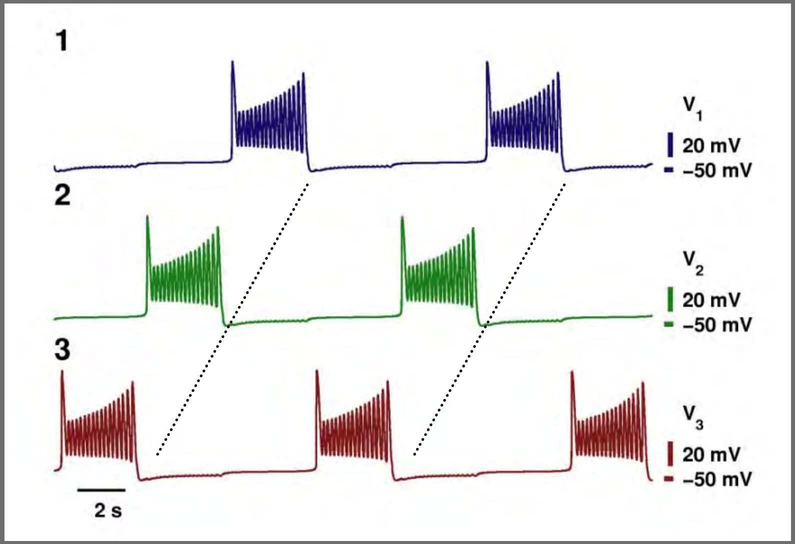


Shilnikov A.L., Gordon R. and Belykh I.V., Polyrhythmic synchronization in bursting network motifs, J. Chaos, 18, 037120, 2008

2π/3 off phase 1: Friesen inhibitory ring

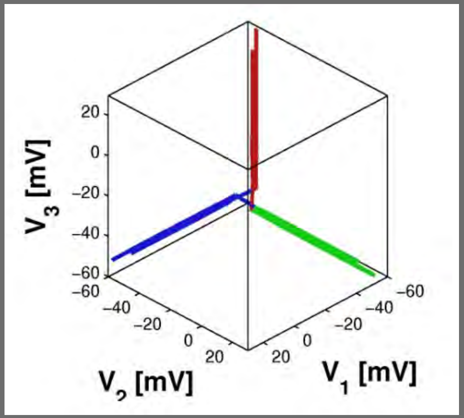




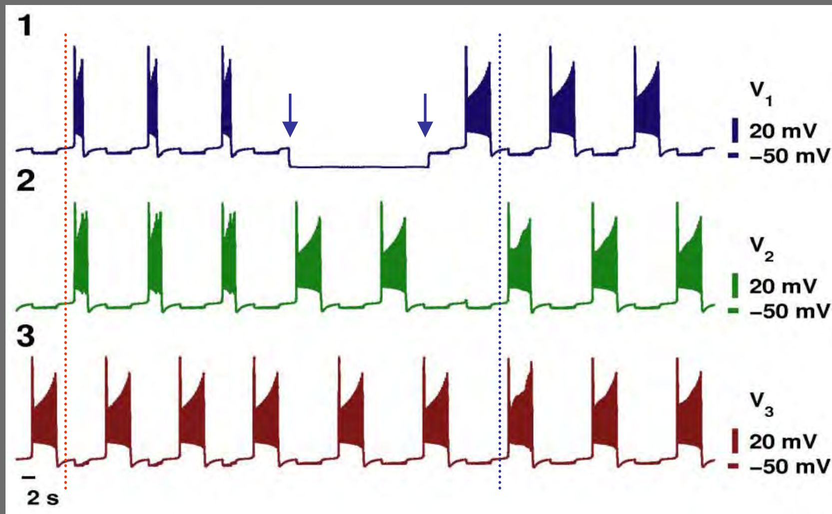


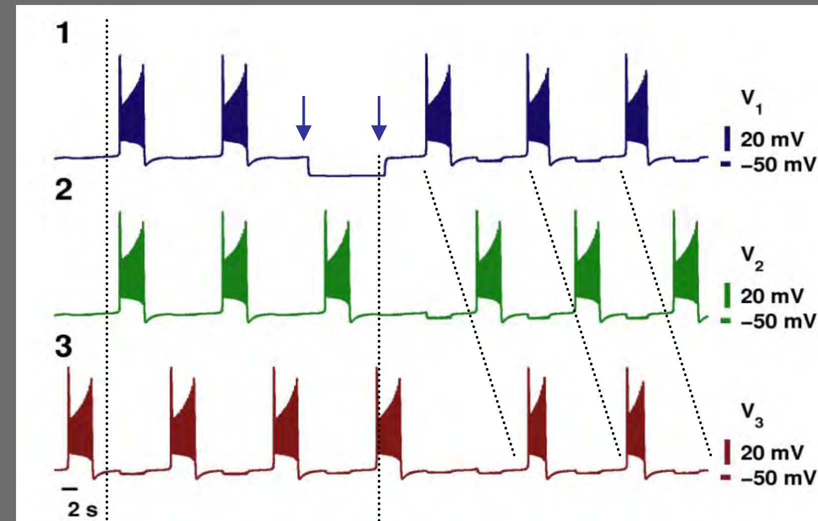
"2π/3" synchronization

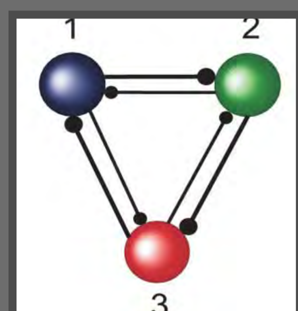
$$0^{\circ} \rightarrow 120^{\circ} \rightarrow 240^{\circ} \rightarrow 0^{\circ} \rightarrow \ldots$$

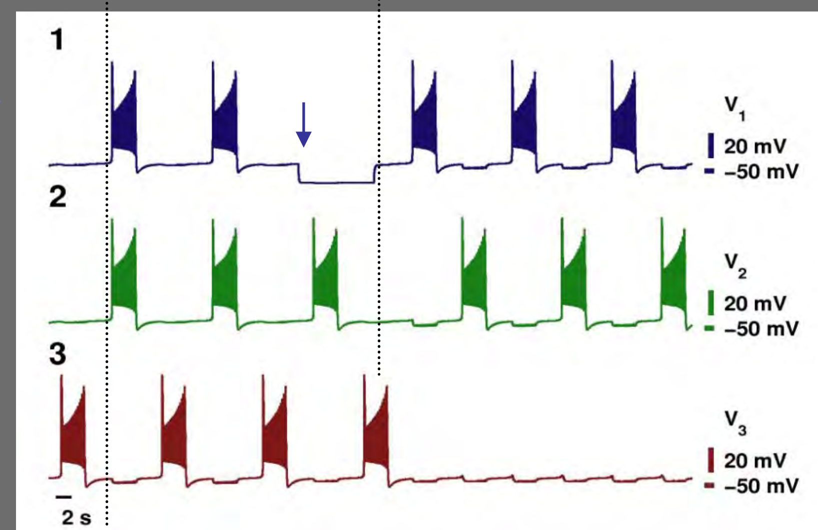


Controlling multistability: switching by hyperpolarizing pulse

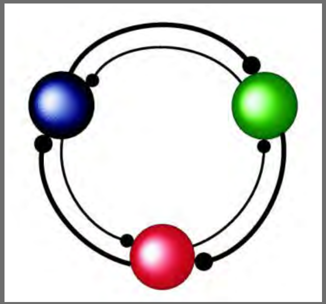






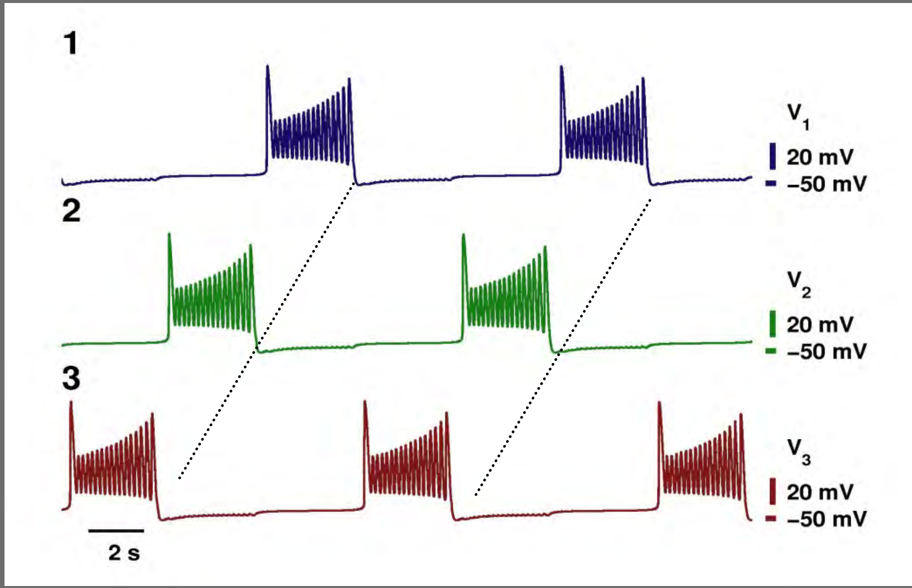


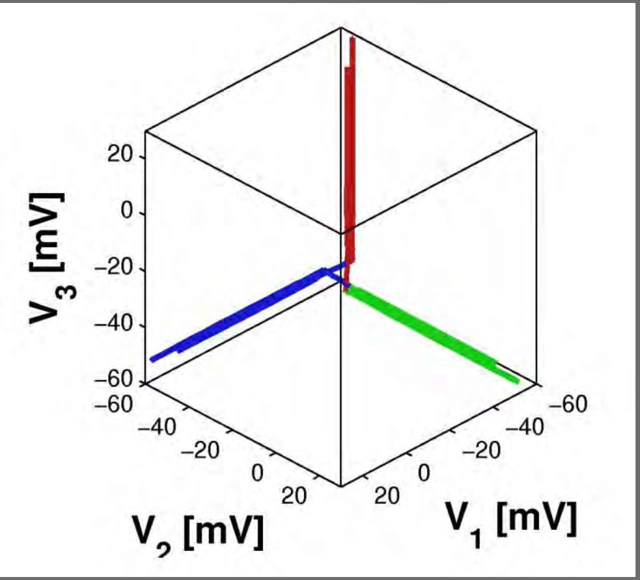
2π/3 off phase 1: Friesen's inhibitory ring



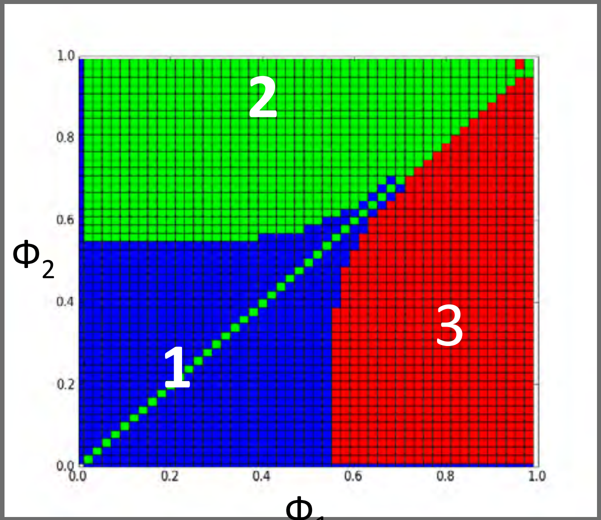
"2π/3" synchronization

$$0^{\circ} \to 120^{\circ} \to 240^{\circ} \to 0^{\circ} \to \ldots$$

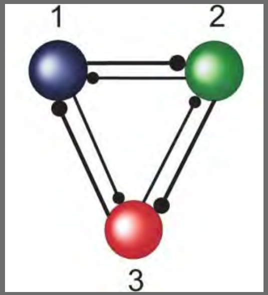




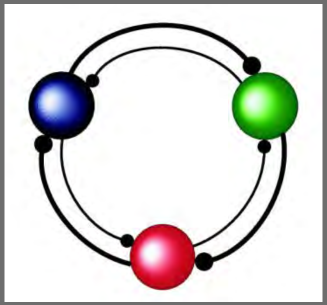
Reciprocally inhibitory motif
Asymmetric strong coupling



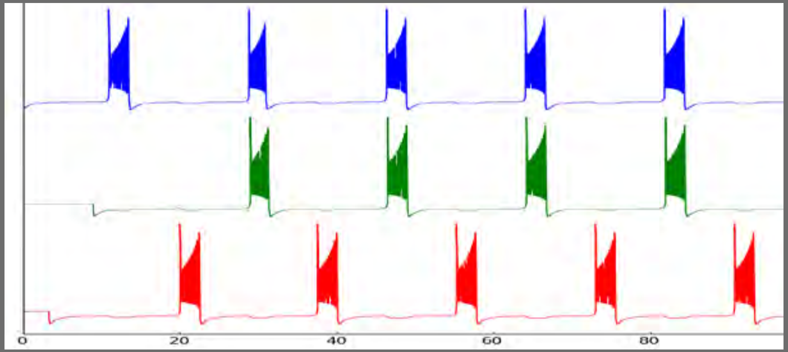
$V_{K2}^{shift} = -0.02;\ g_{ij} = -0.1$

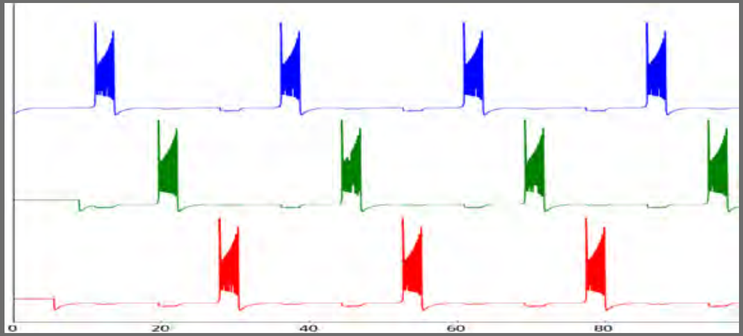


3: $(\Phi_1, \Phi_2) = (0.5, 0.5)$



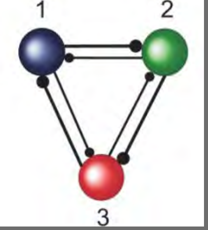
4: $(\Phi_1, \Phi_2) = (0.33, 0.66)$; $g_{ji} = 0.8$

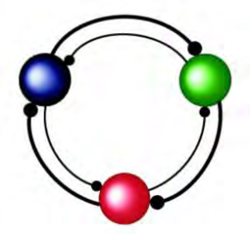


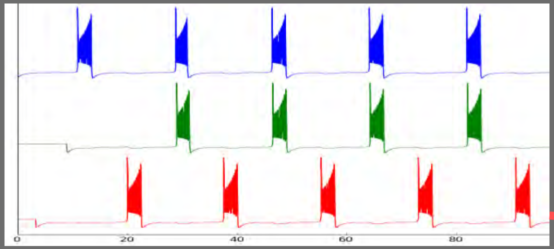


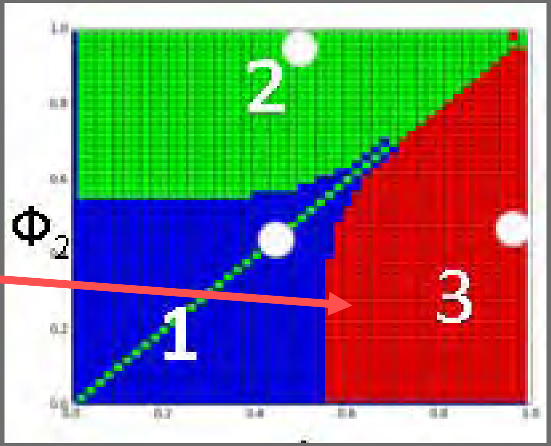
Shilnikov A.L., Gordon R. and Belykh I.V., Polyrhythmic synchronization in bursting network motifs, J. Chaos, 18, 037120, 2008

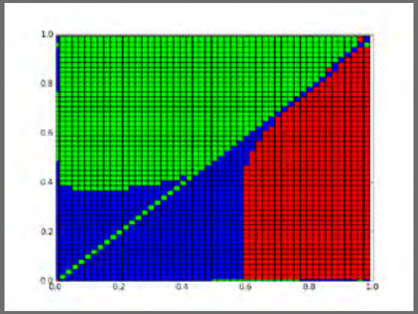
from symmetric to Asymmetric
strong coupling case

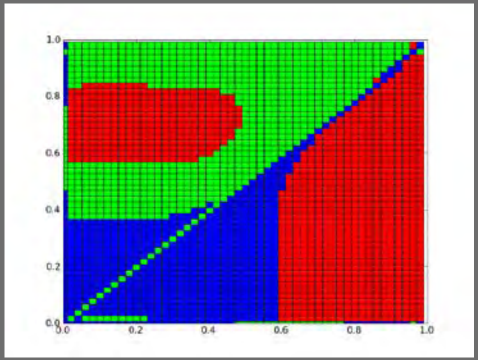


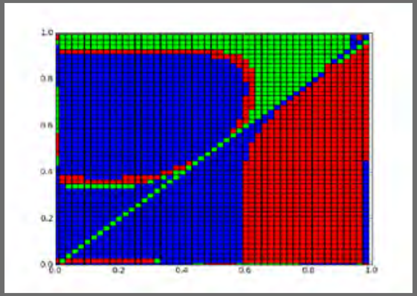


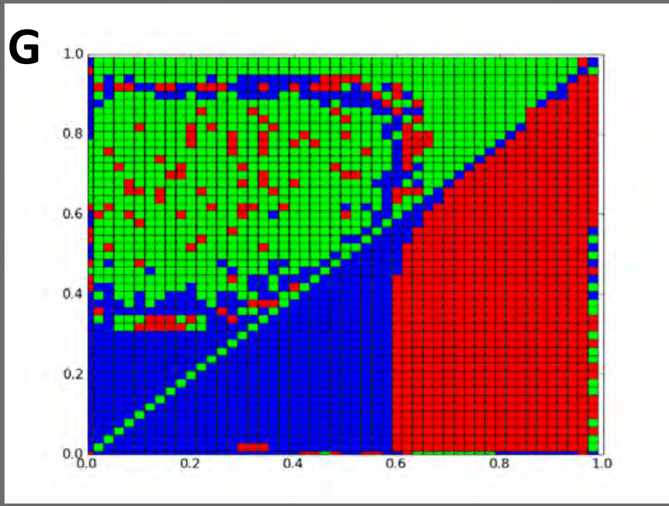


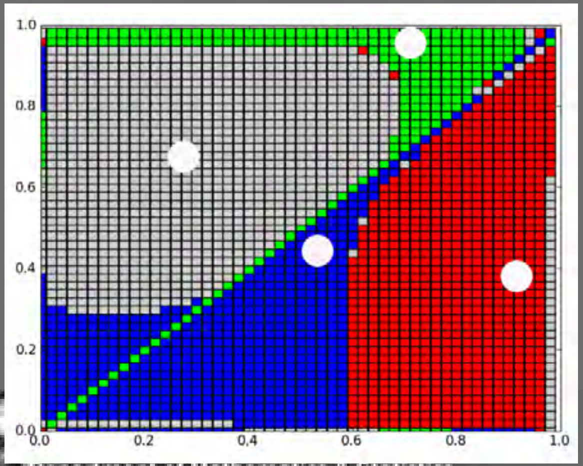


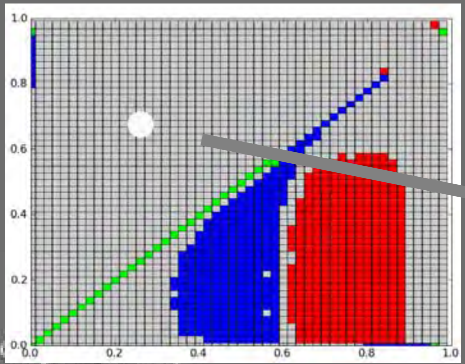


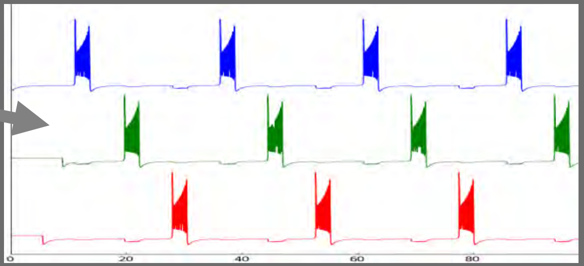






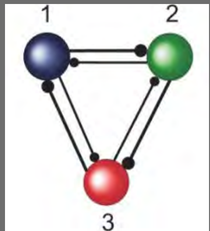


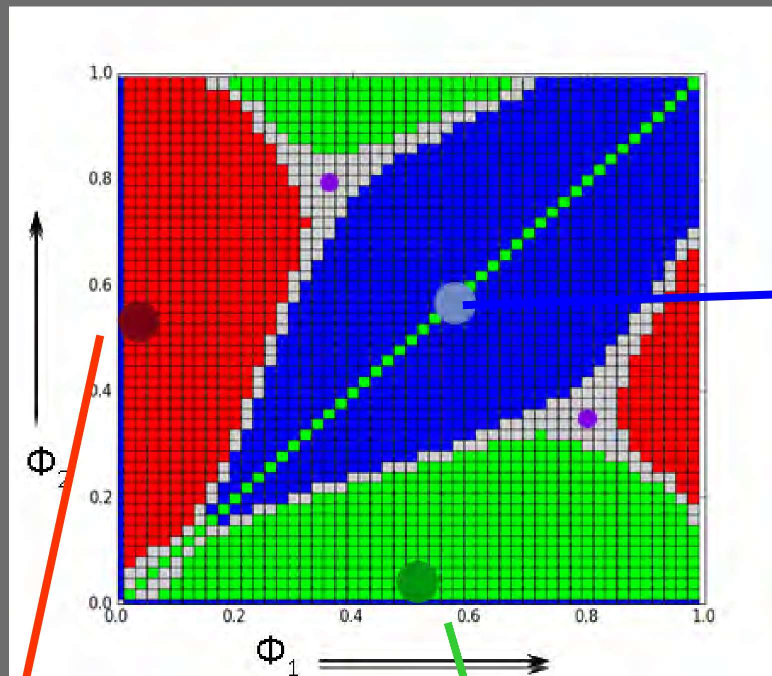


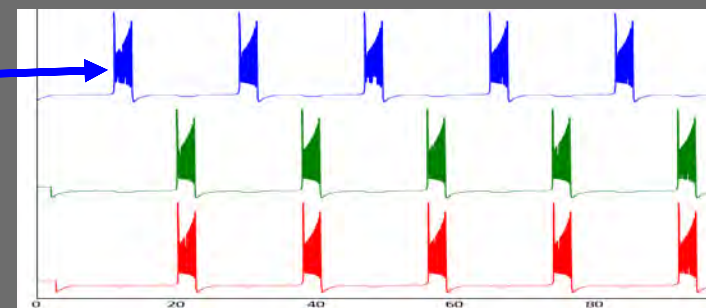


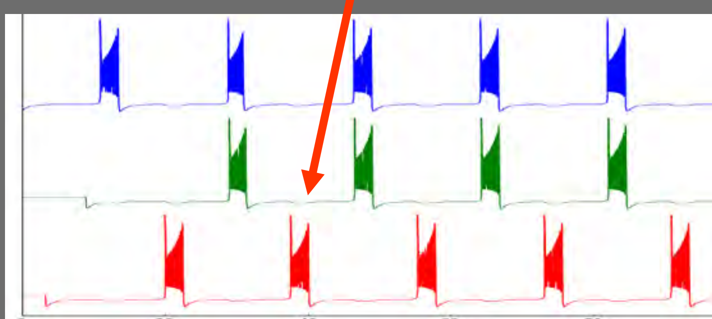
Reciprocally inhibitory motif

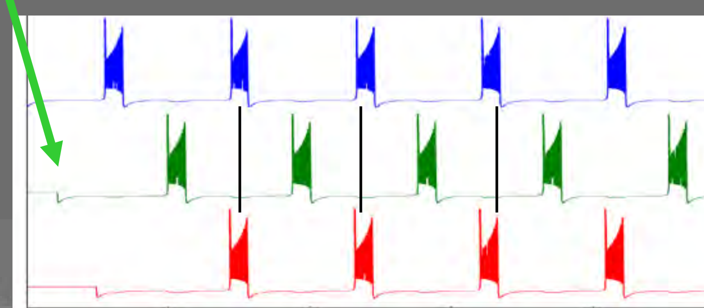
symmetric *weak* coupling



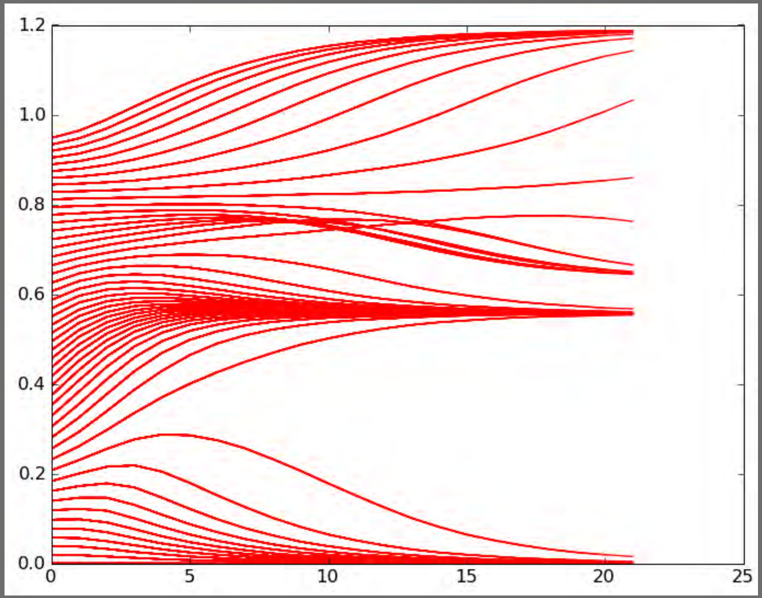


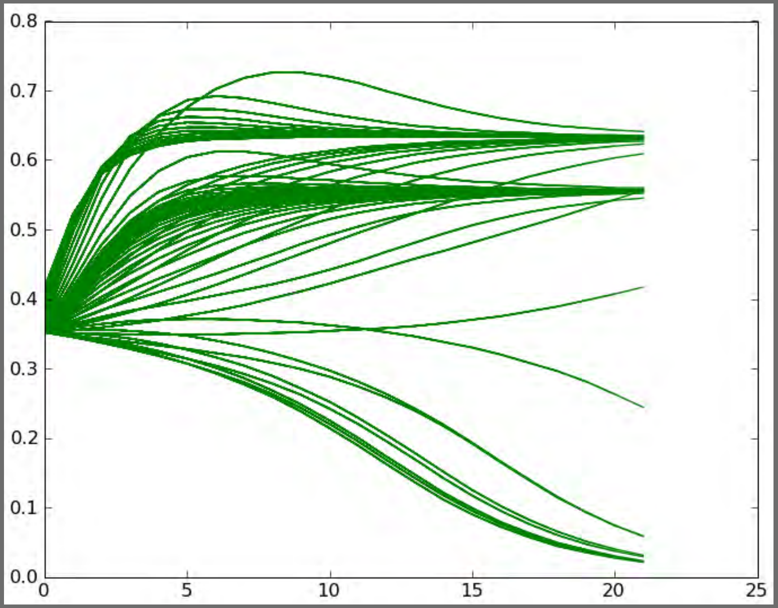


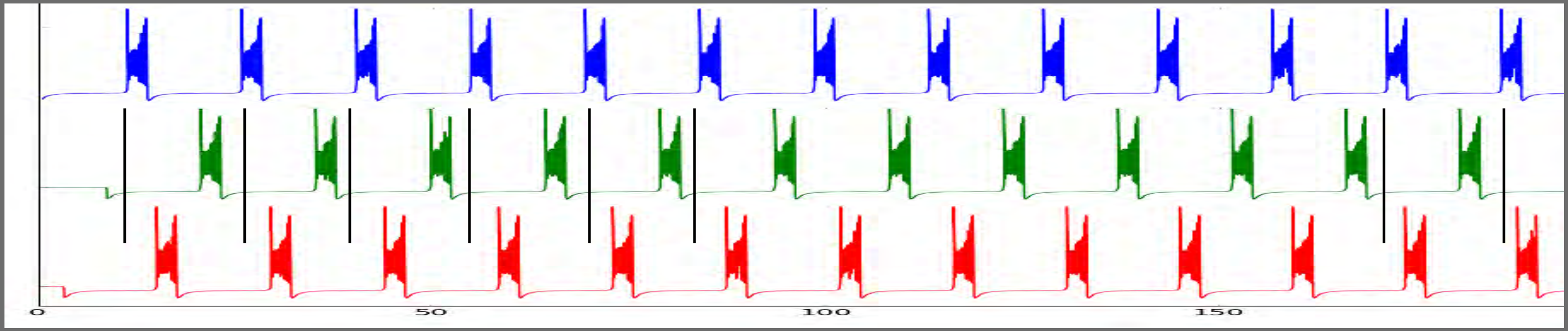




Reciprocally inhibitory motif
weak coupling

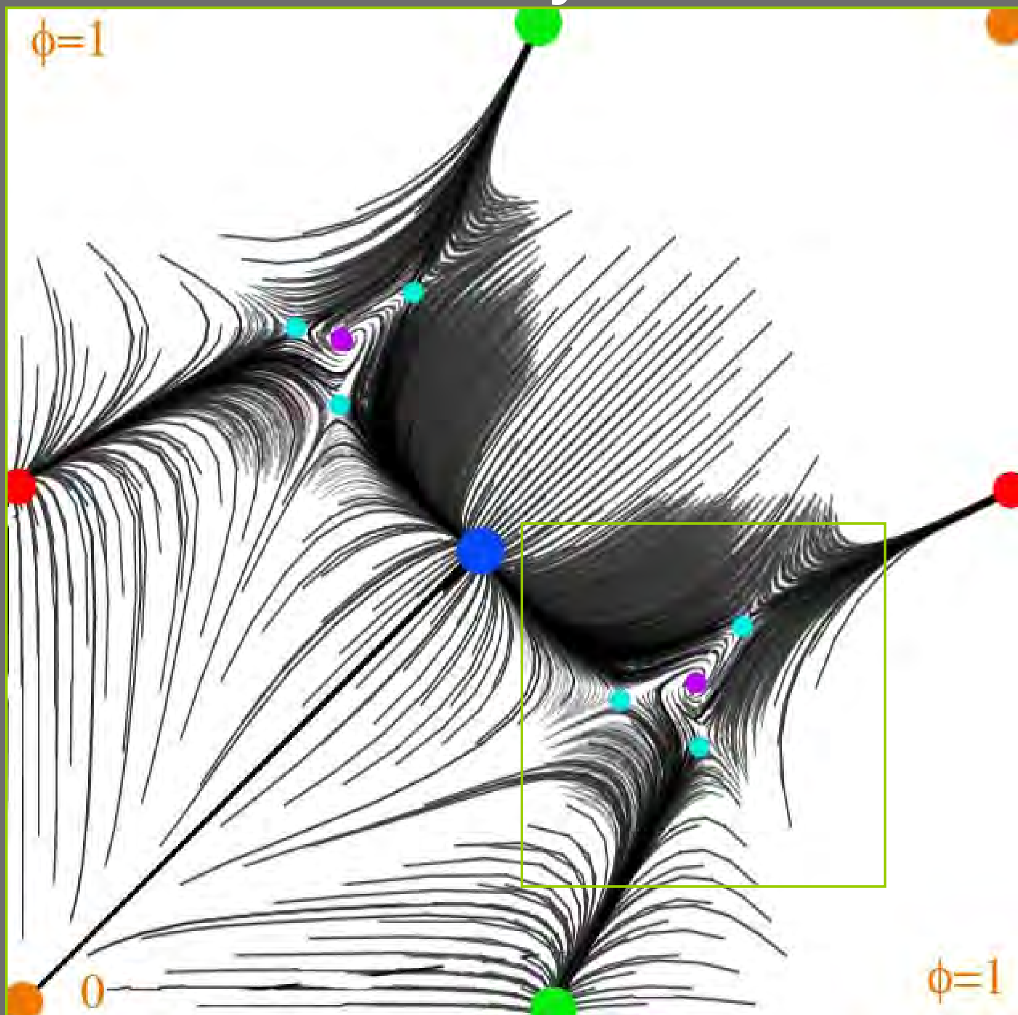


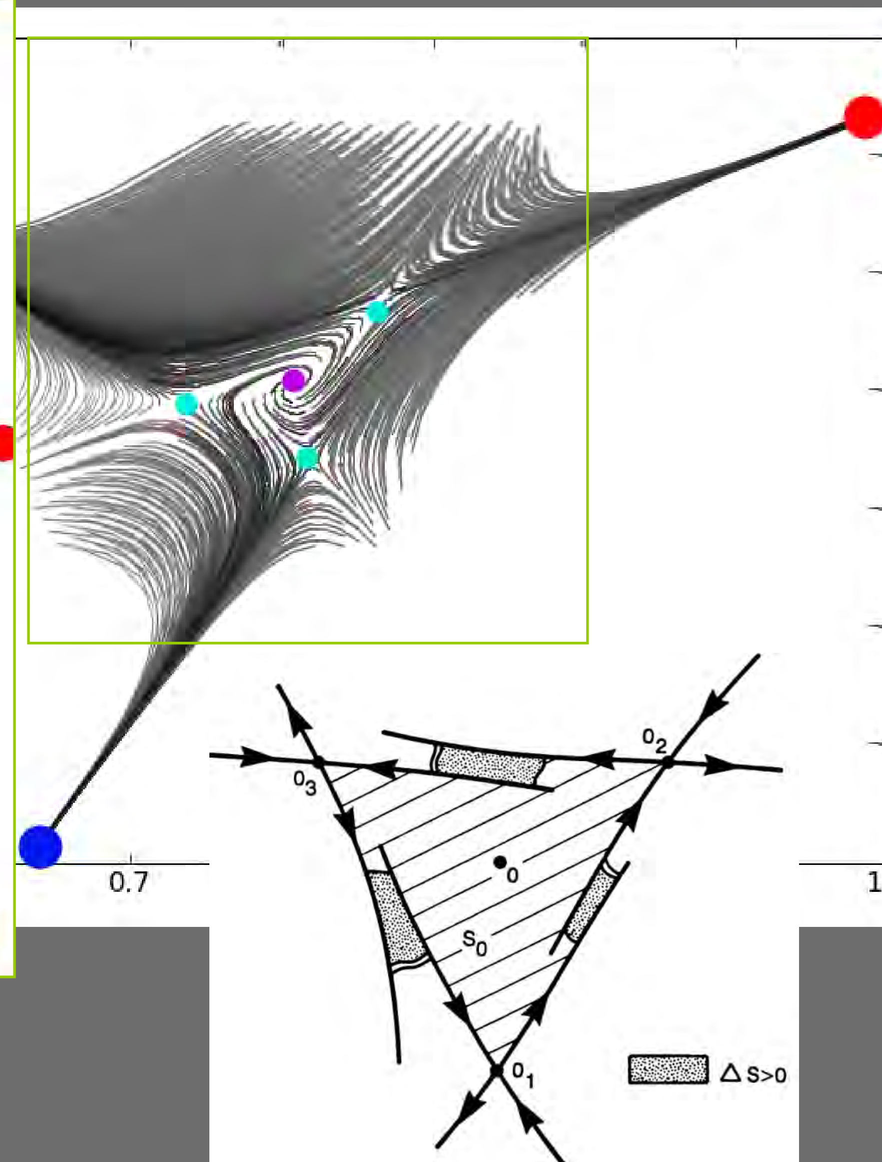




Reciprocally inhibitory motif

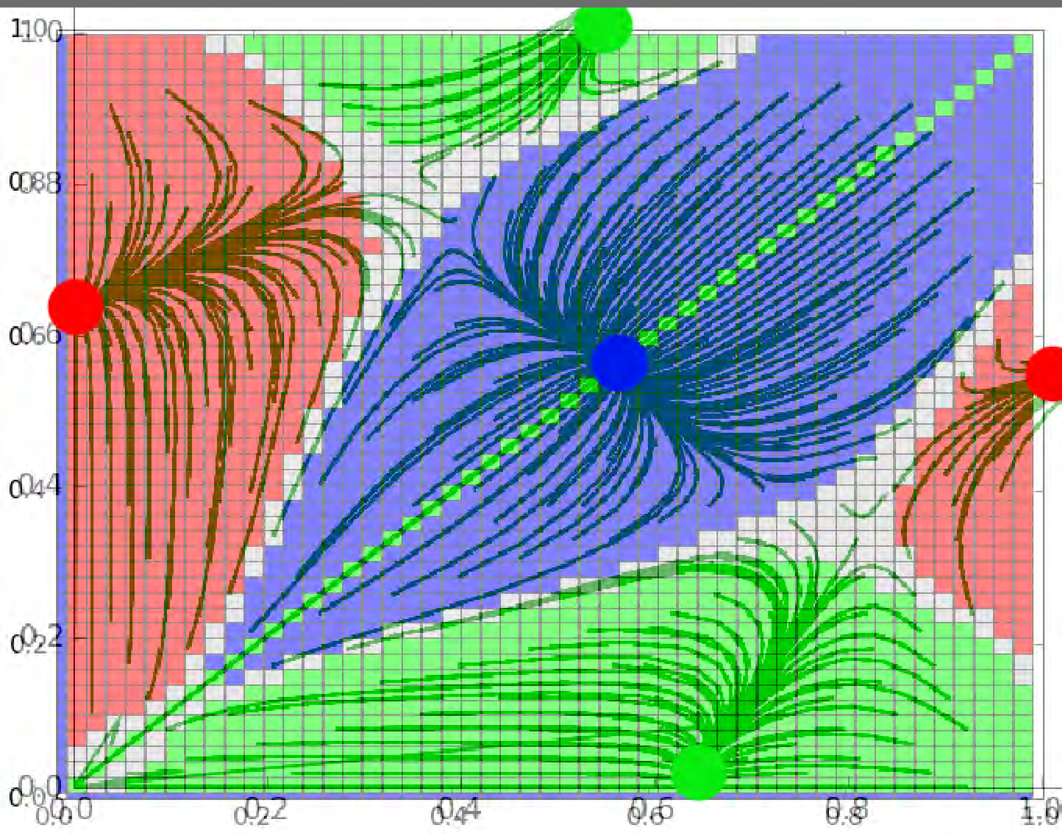
symmetric weak coupling

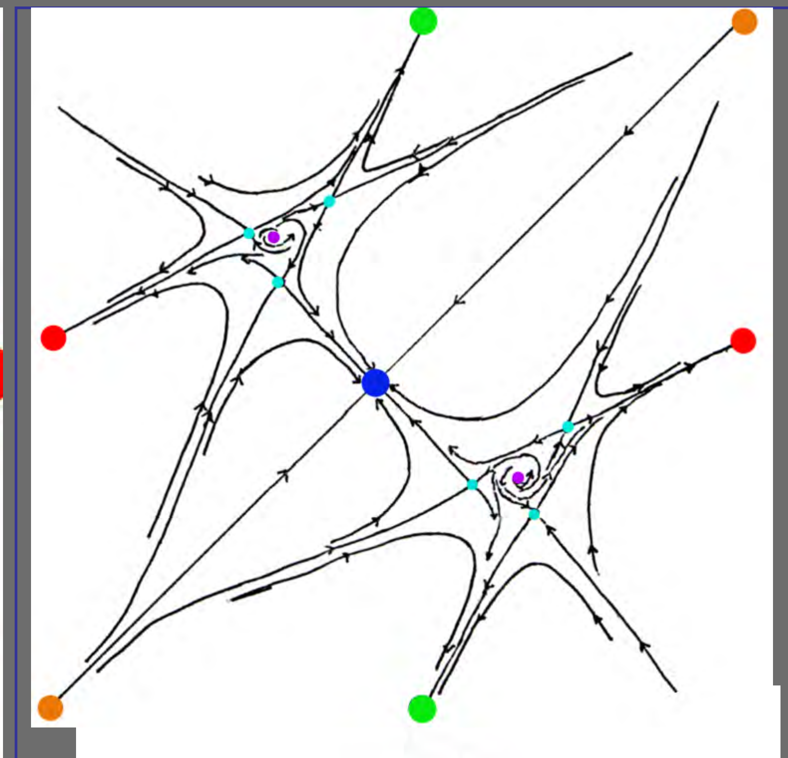


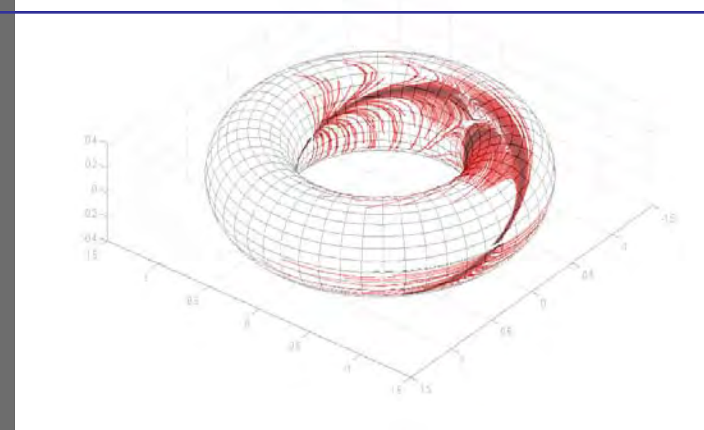


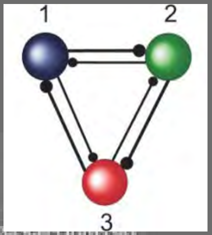
Reciprocally inhibitory motif

symmetric weak coupling

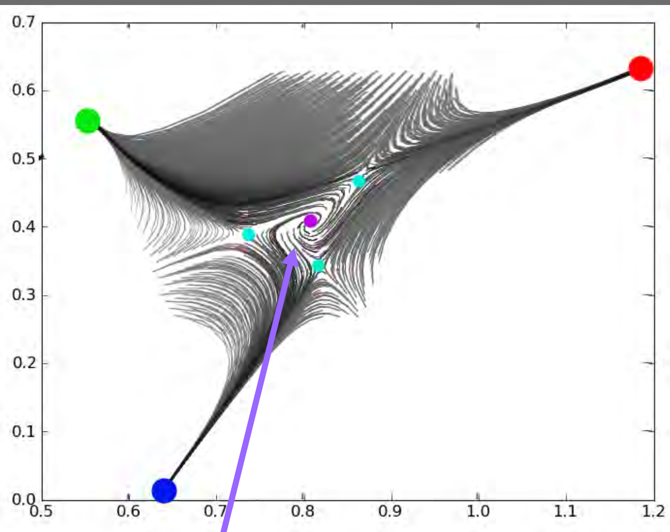


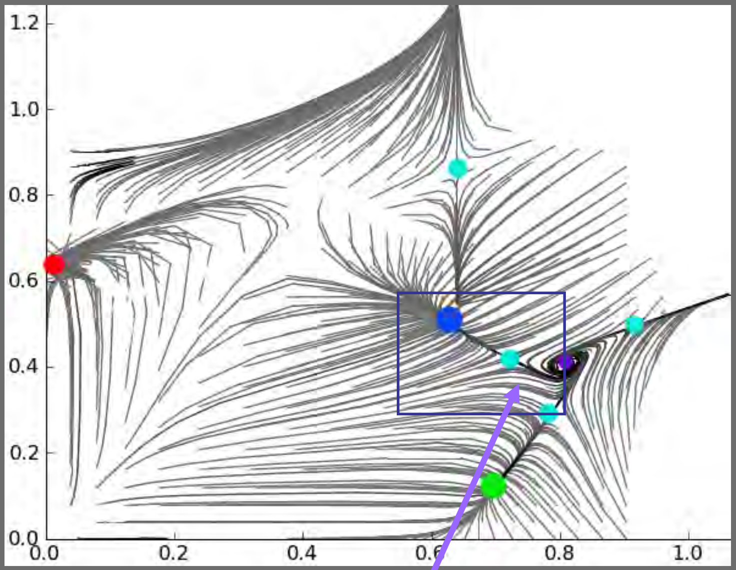


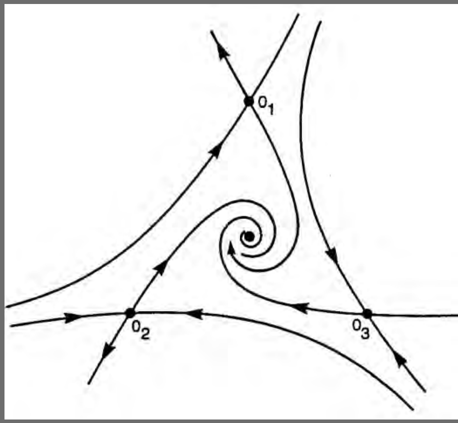




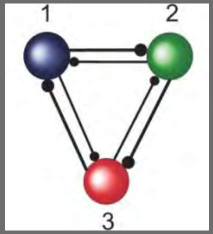
Reciprocally inhibitory motif
Asymmetric weak coupling



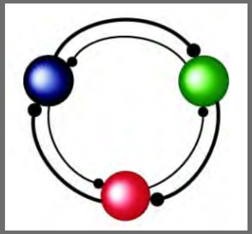


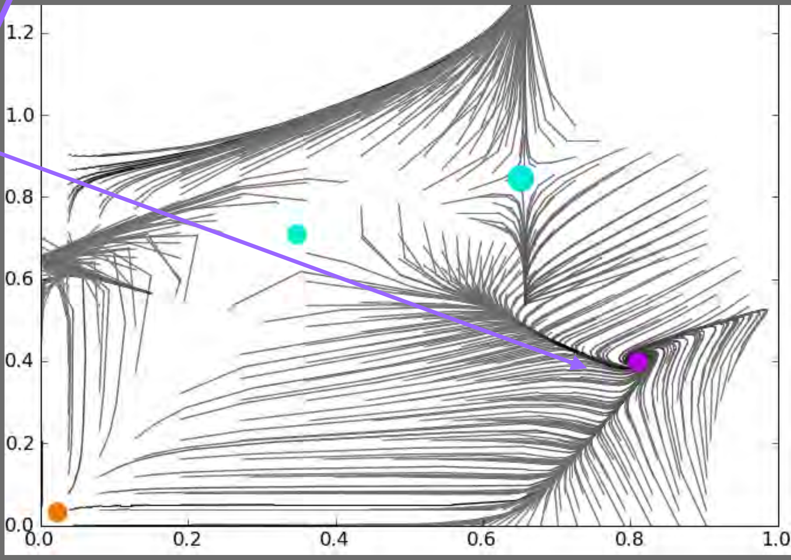


Repeller



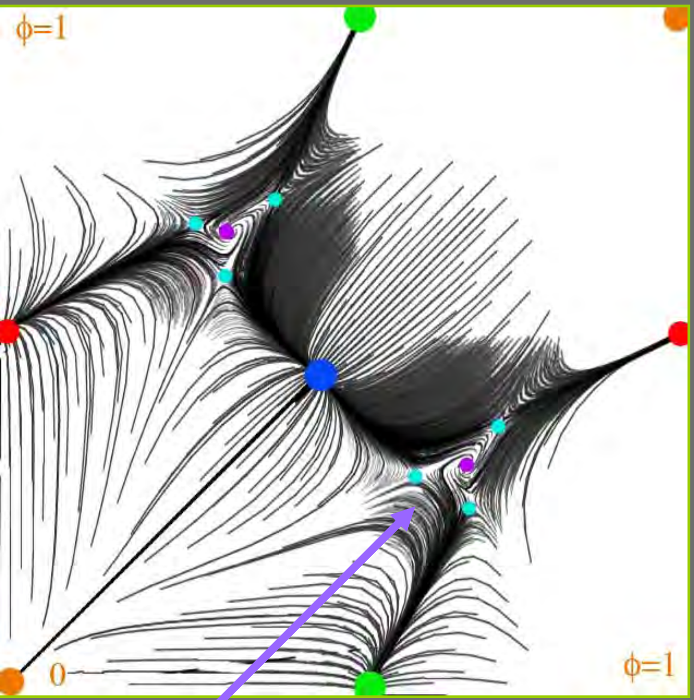
Attractor 2π/3

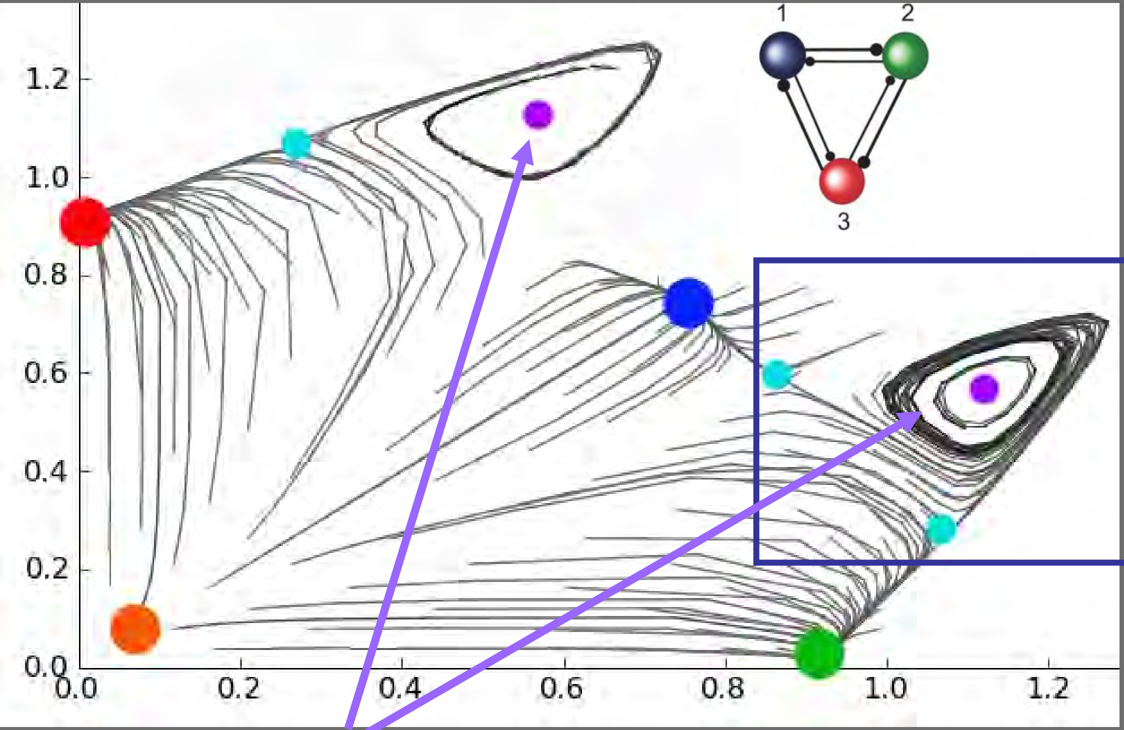




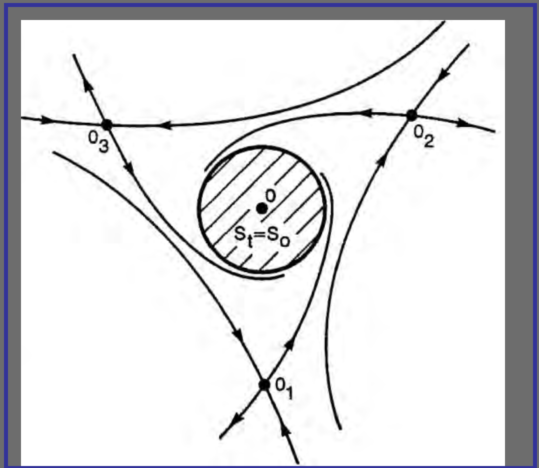
Reciprocally inhibitory motif

symmetric weak coupling – and burst duration





Repeller **or** **?? Attractor 2π/3**



For the future

Math

- Basin of attractions – effective potentials
- Phase relations, intermittency
- Control – switching between the attractors – by external current, inhibitory and/or excitatory

Neuro

- Collaboration with Kristan's lab
- Applications for modeling
- Modeling for applications

Thank you

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Bill Kristan (UC San Diego)