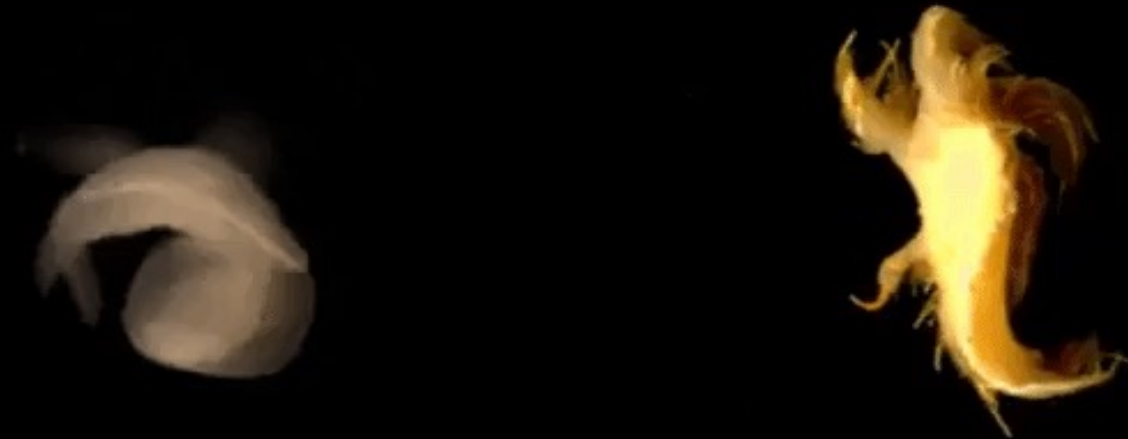


# Long reconstruction saga of rhythm-generation by neural circuits in two sea slugs

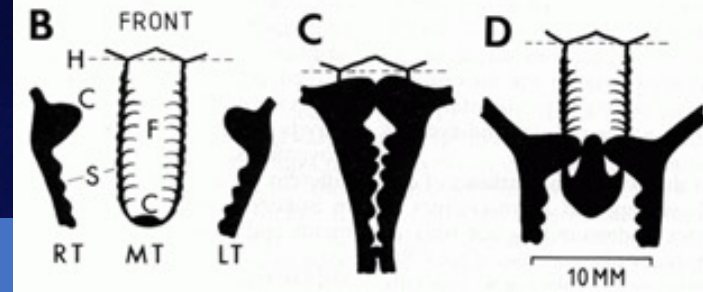
Andrey Shilnikov

Neuroscience Institute & Math Department,  
GSU, Atlanta

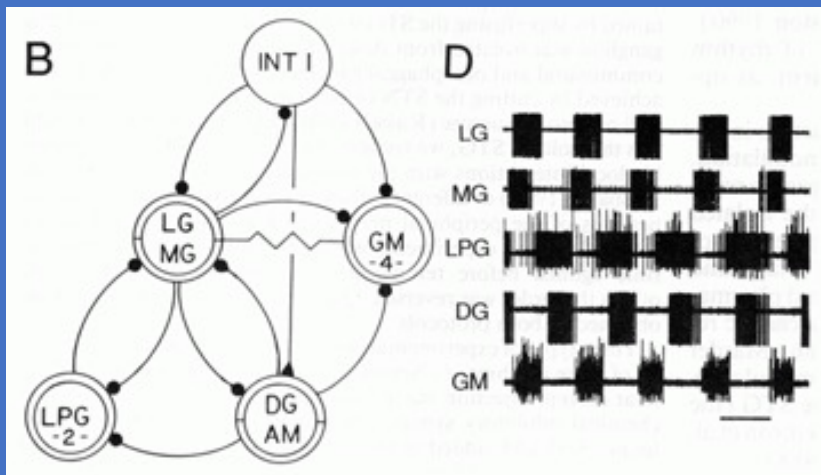


IPAM workshop “Reconstructing Network Dynamics from Data:  
Applications to Neuroscience and Beyond” UCLA 2022

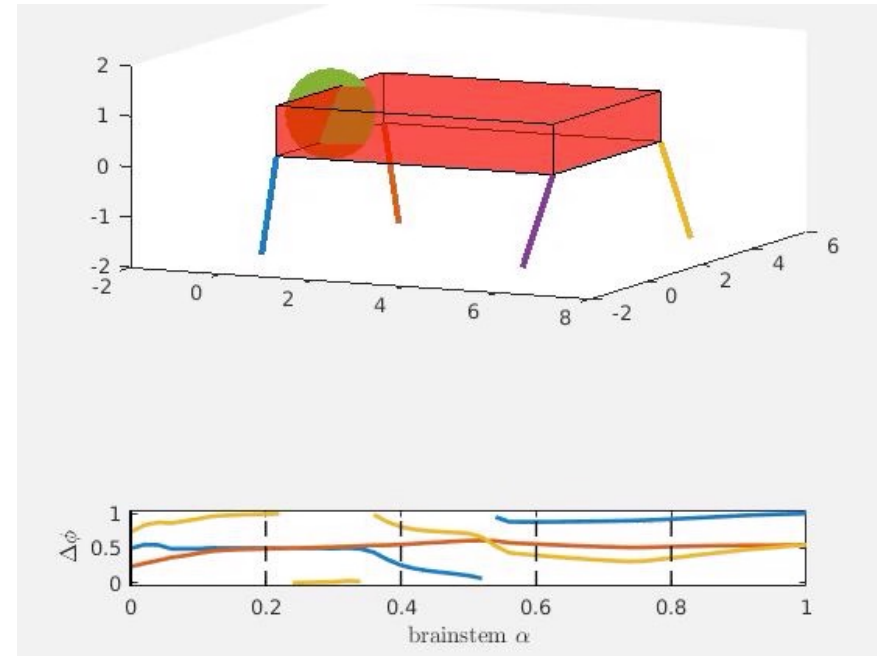
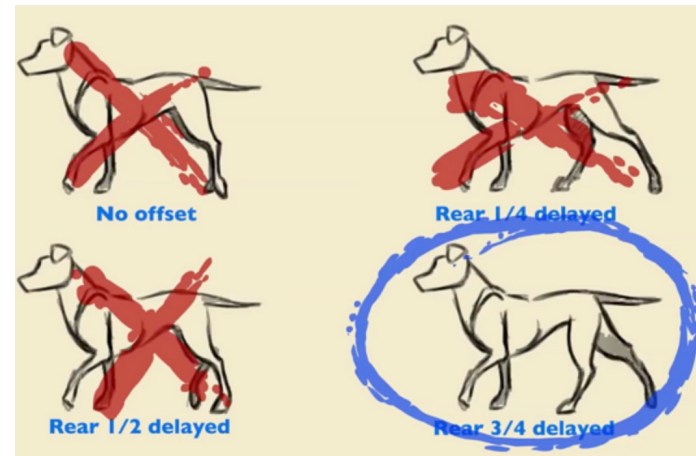
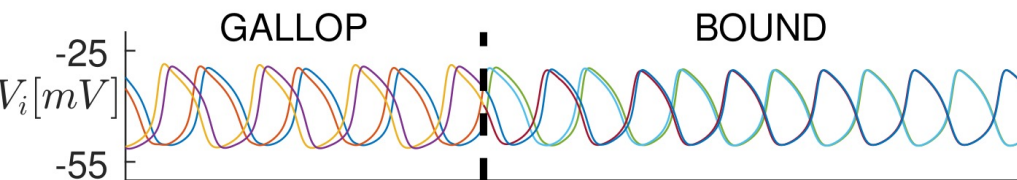
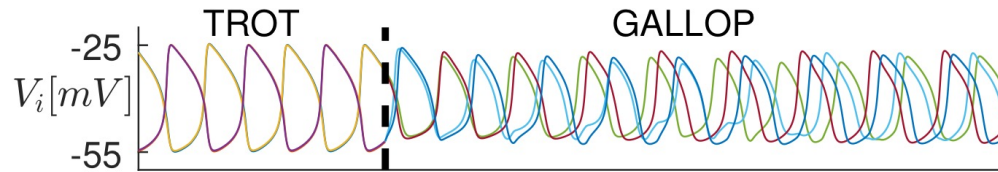
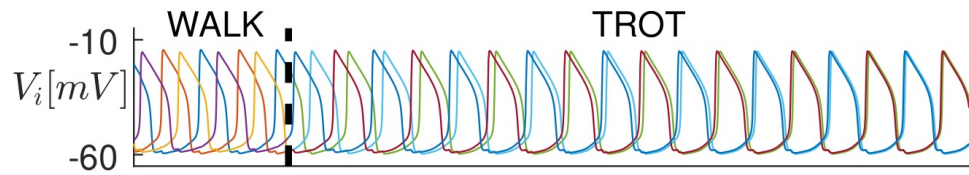
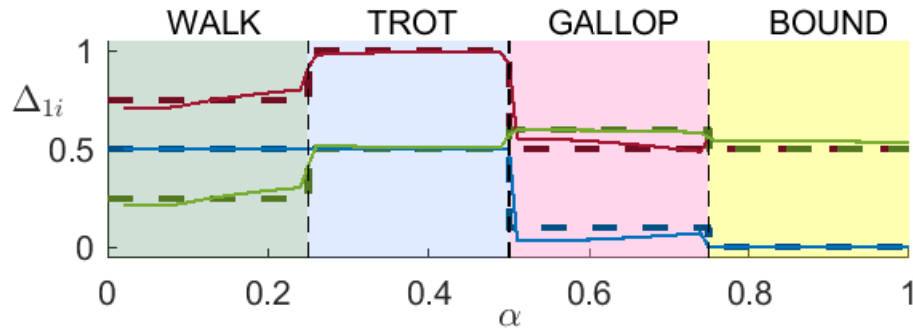
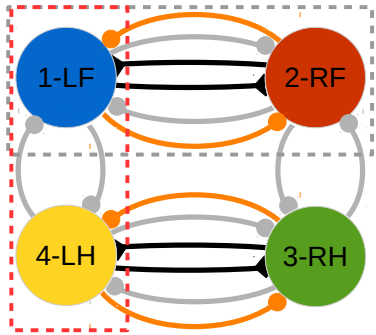
# Gastric mill CPG

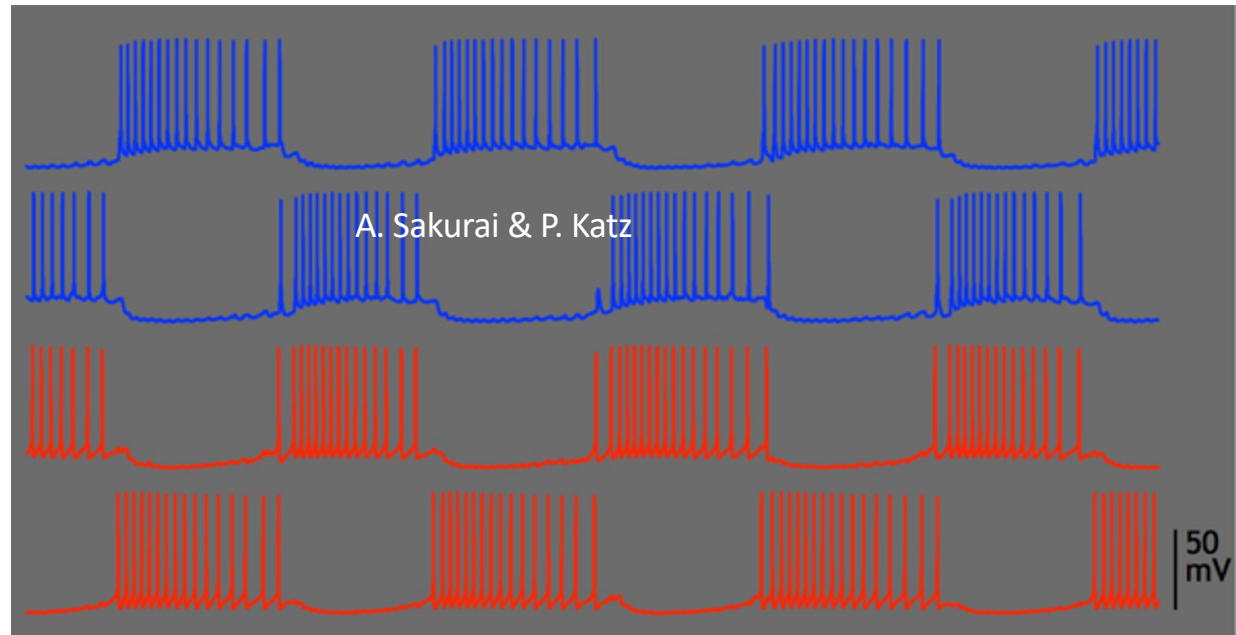
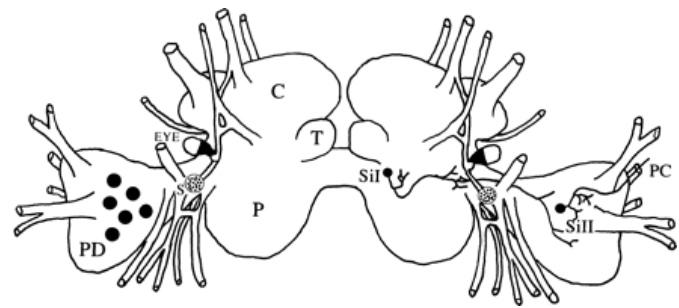
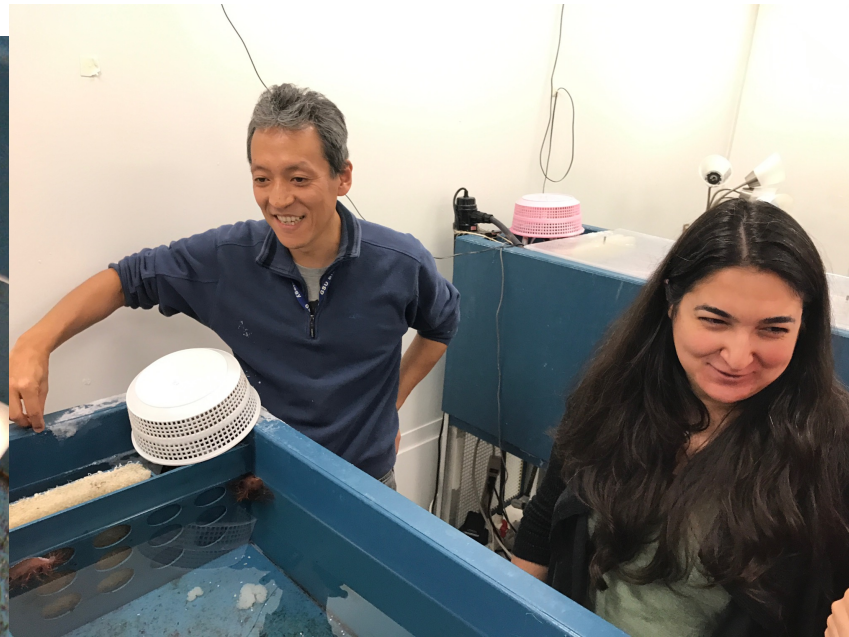


Courtesy A. Selverston

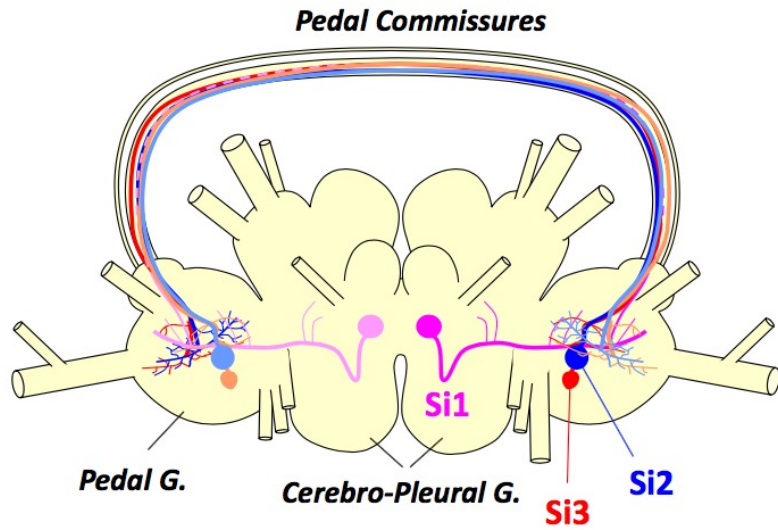
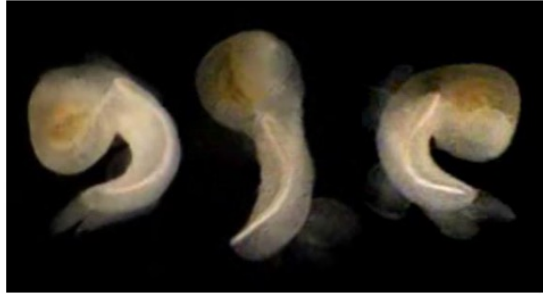


# Toy CPG circuit for quadruped locomotion

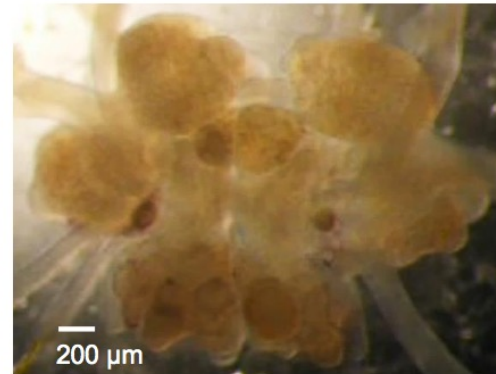
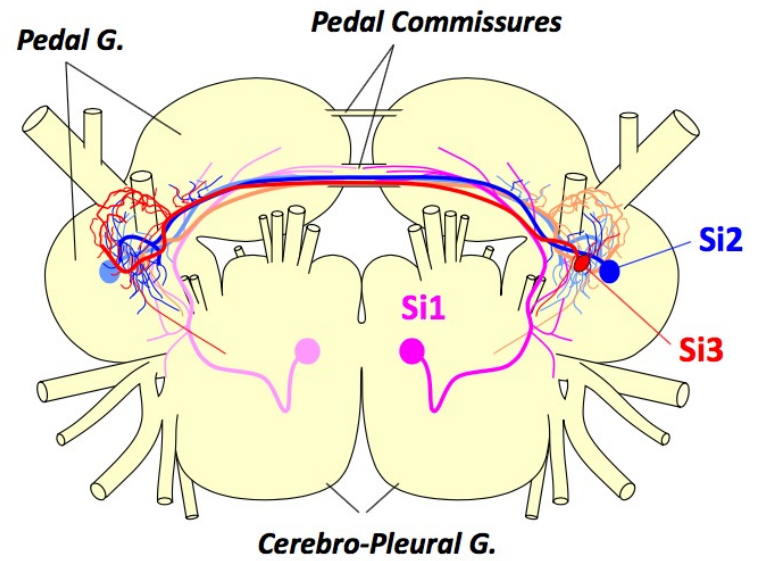




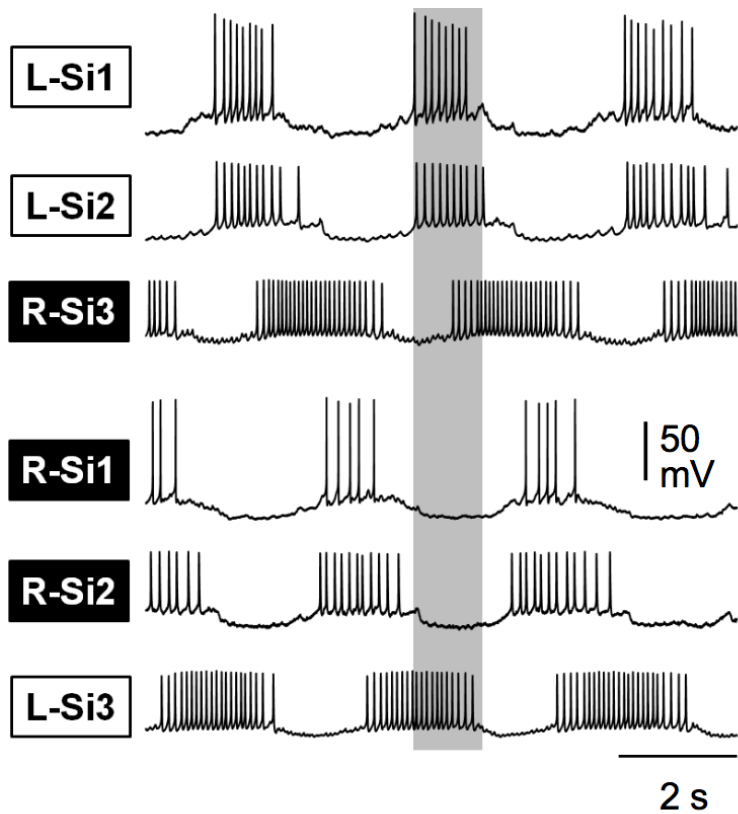
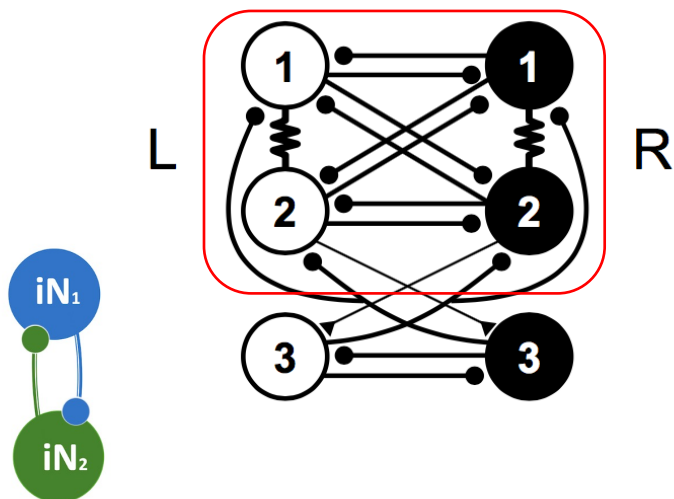
## *Melibe leonina*



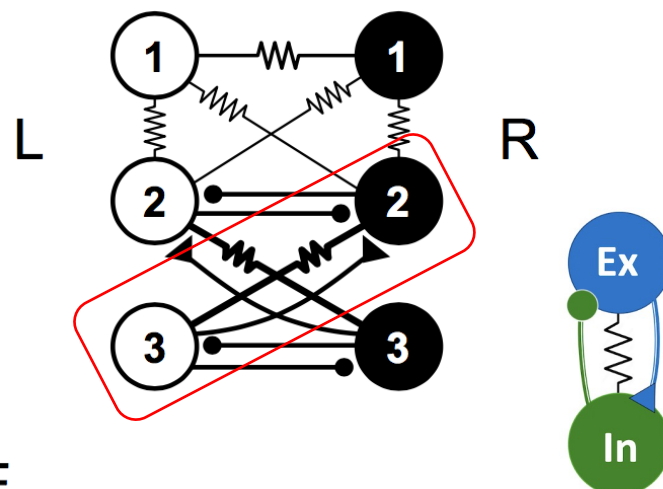
## *Dendronotus iris*



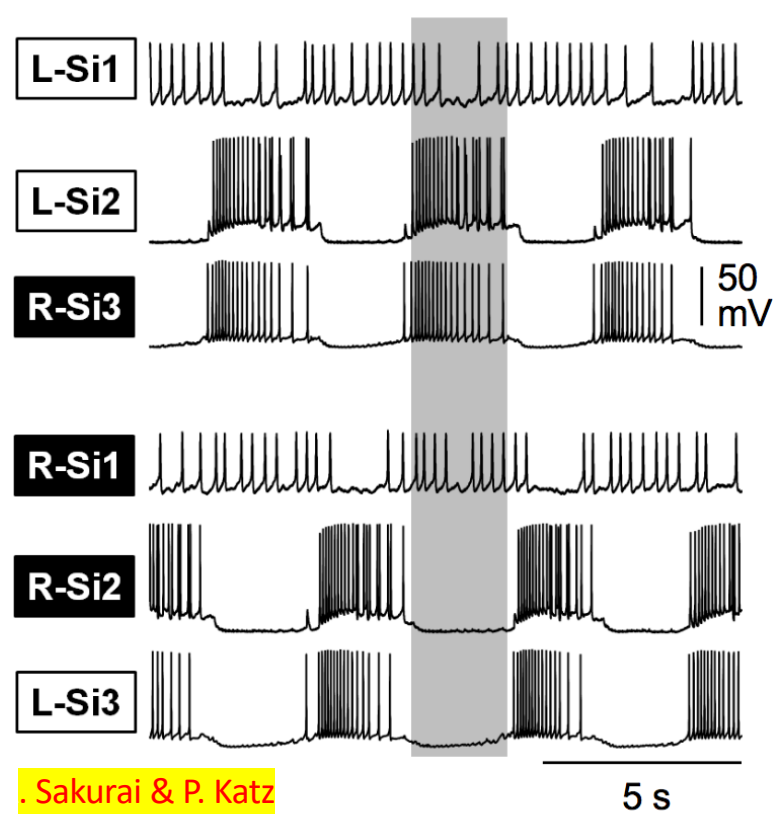
B

*Melibe*

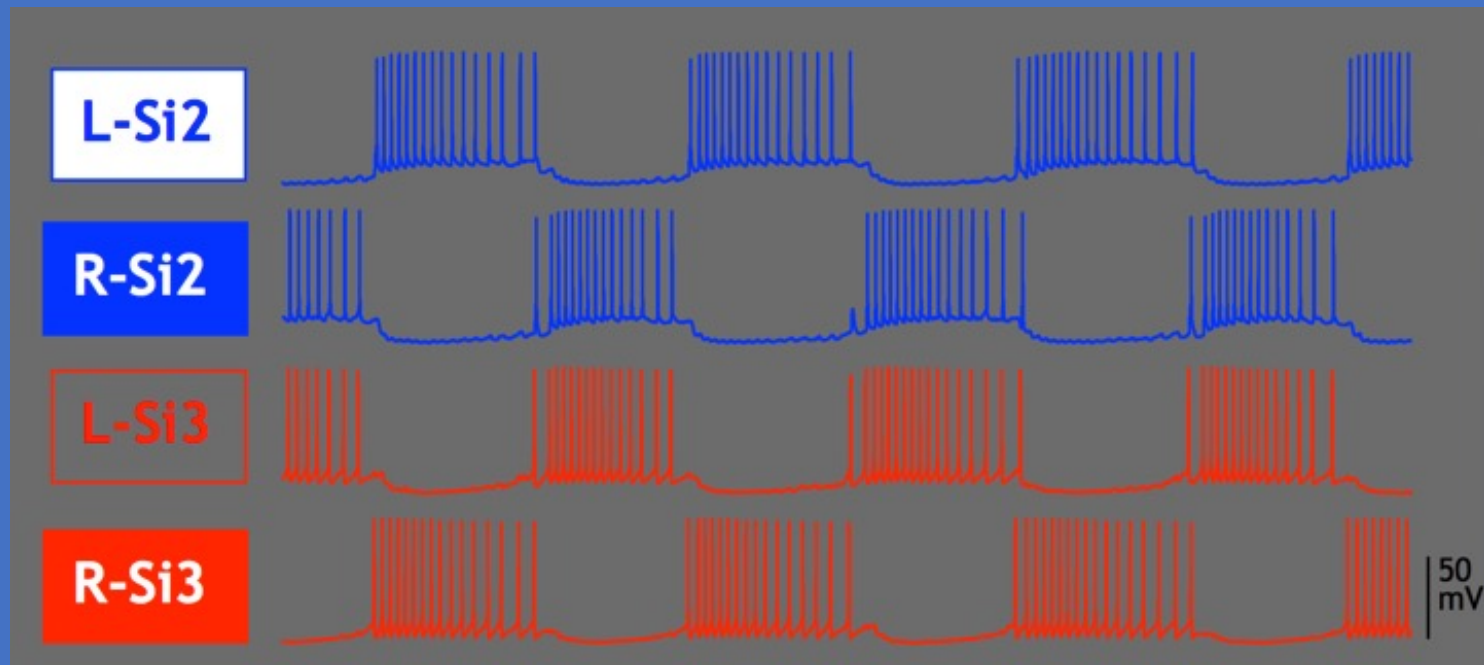
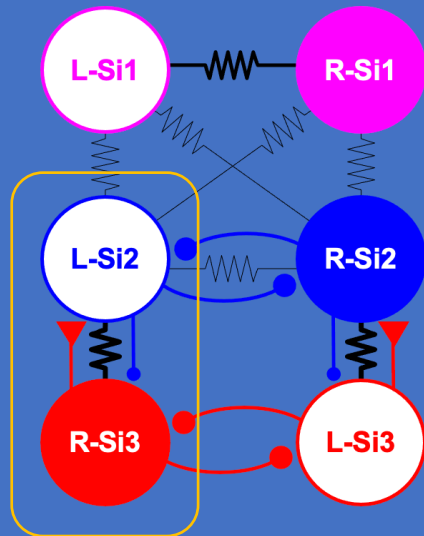
D

*Dendronotus*

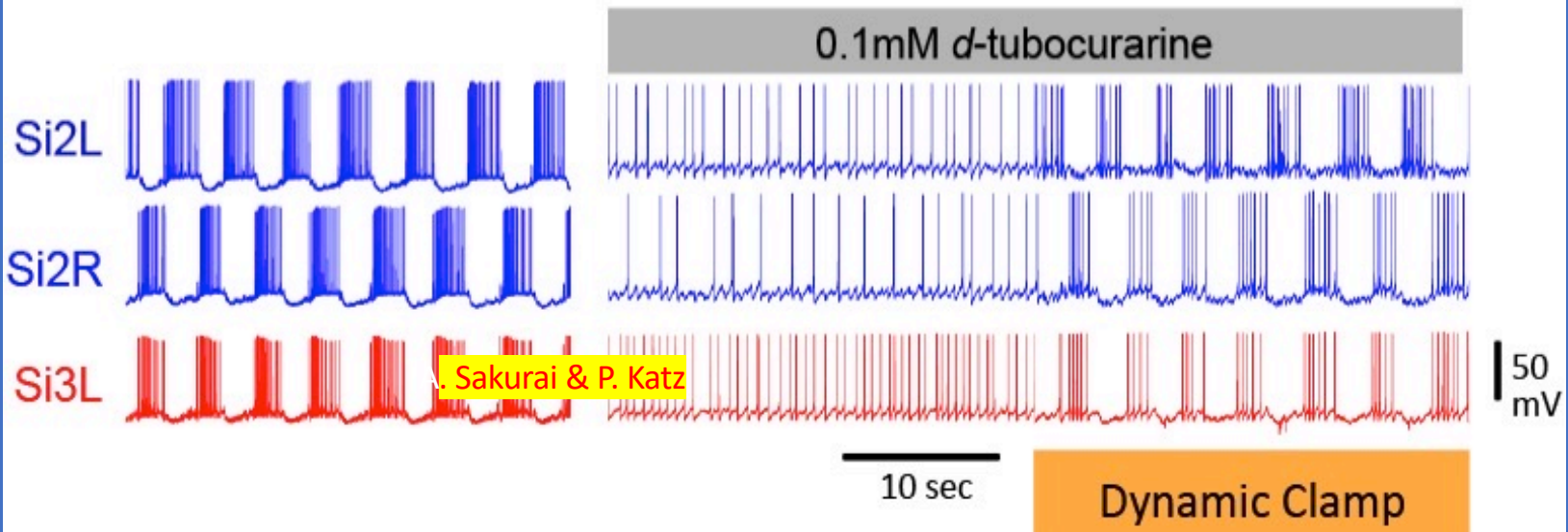
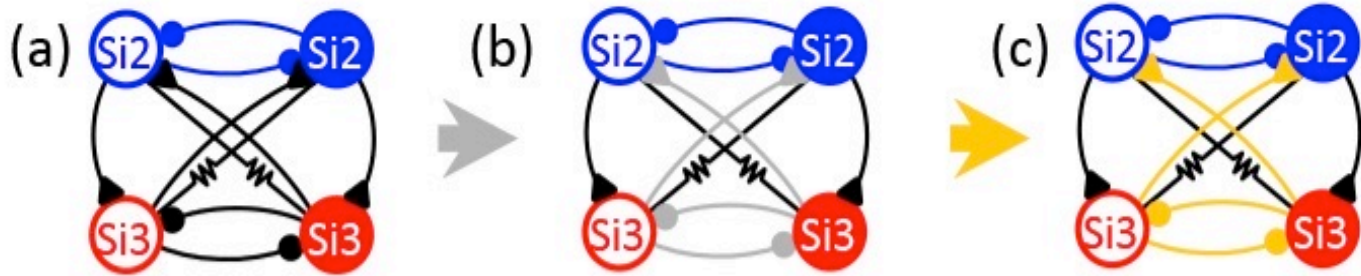
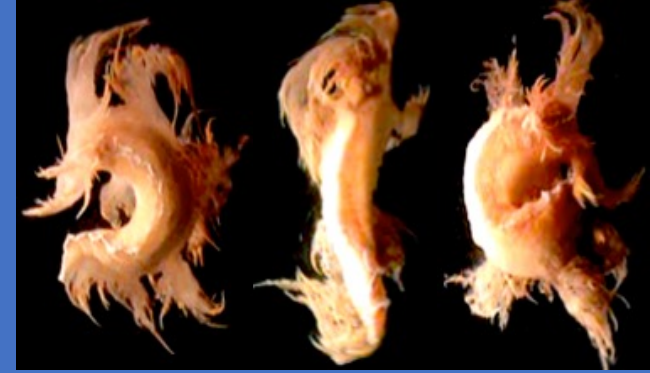
E



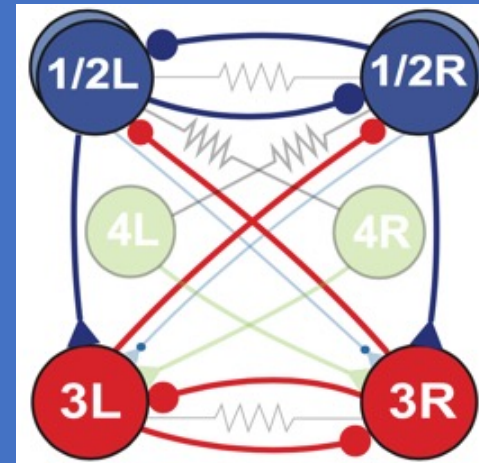
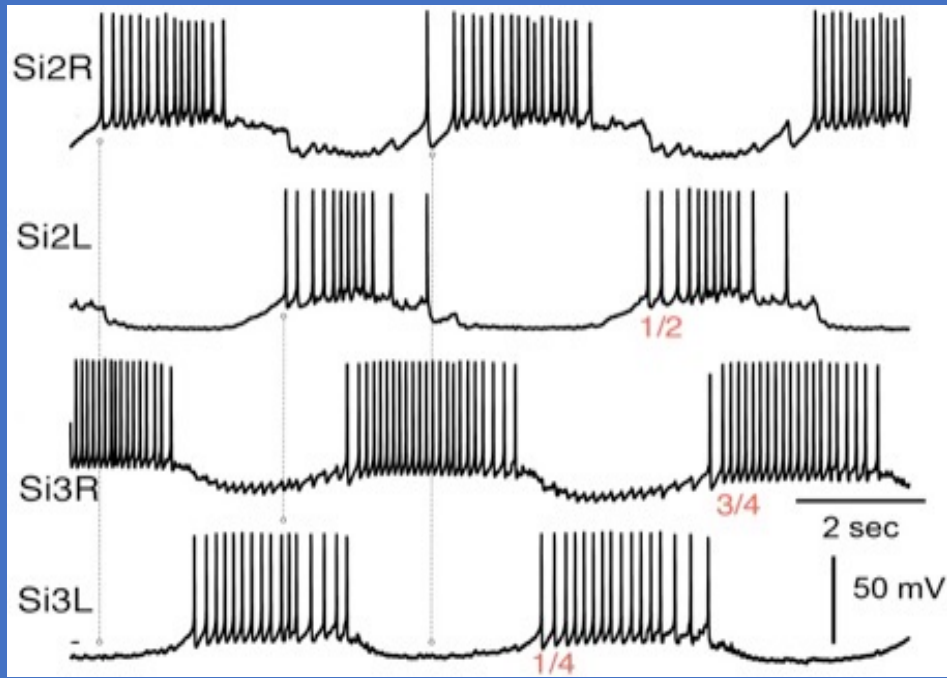
# *Dendronotus Iris* swim CPG



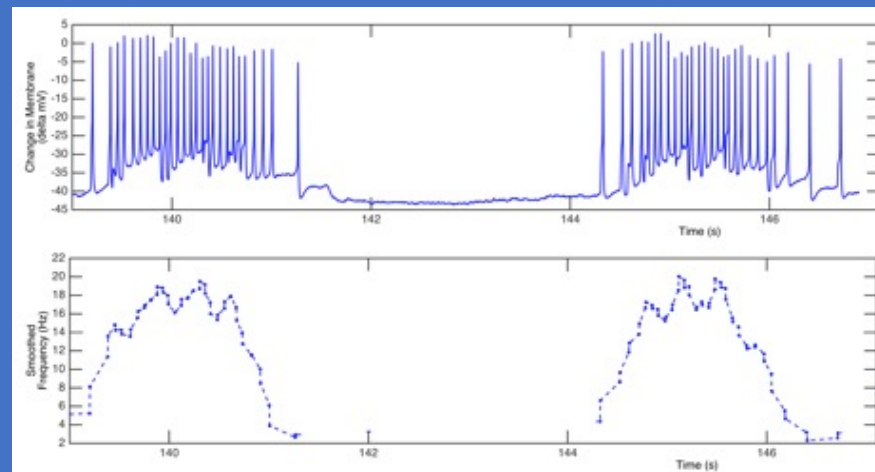
# Swim CPG of *Dendronotus iris*

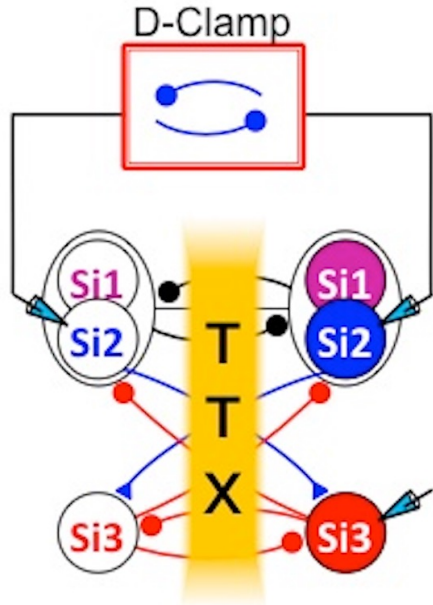


# Swim CPG of *Melibe Leonida*

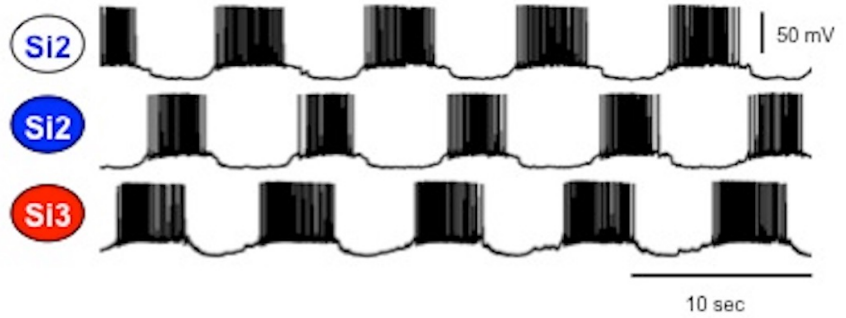


Courtesy: Akira Sakurai and Paul Katz





### Control

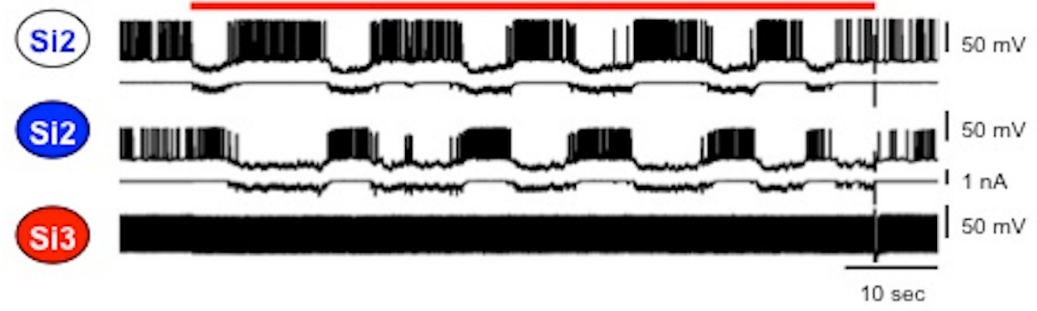


### TTX

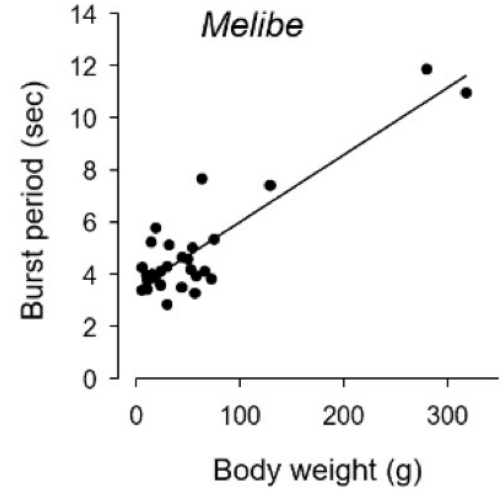
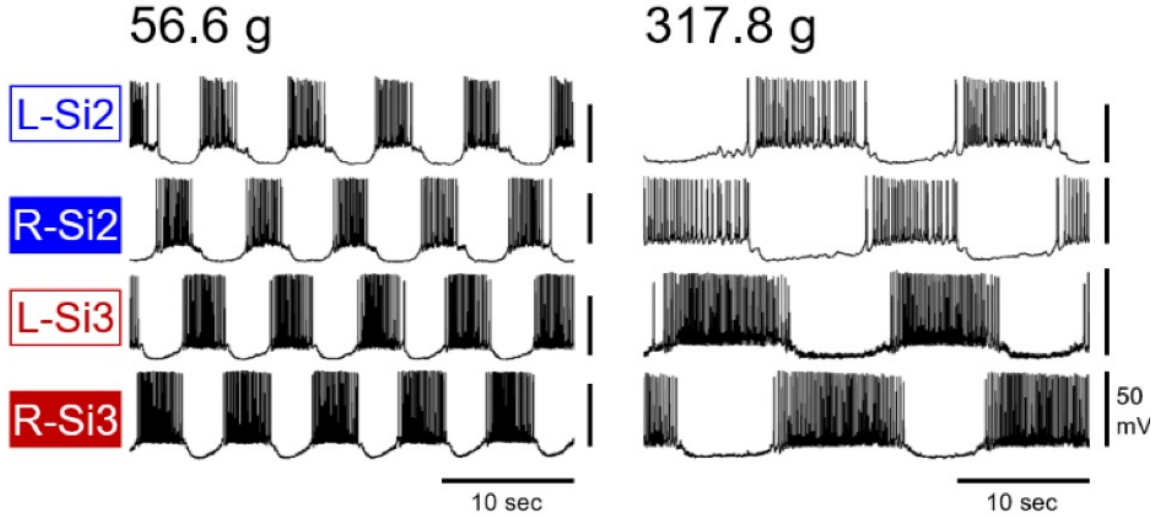


$g_{Syn} = 20 \text{ nS}$

### Dynamic clamp



# Body growth



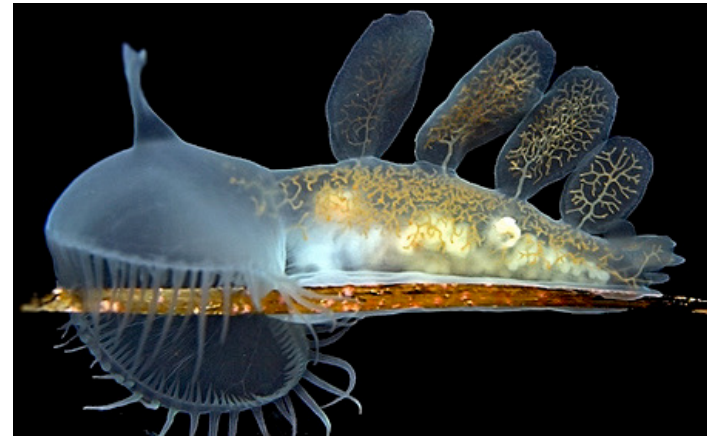
Courtesy: Akira Sakurai and Paul Katz



1-2 sec

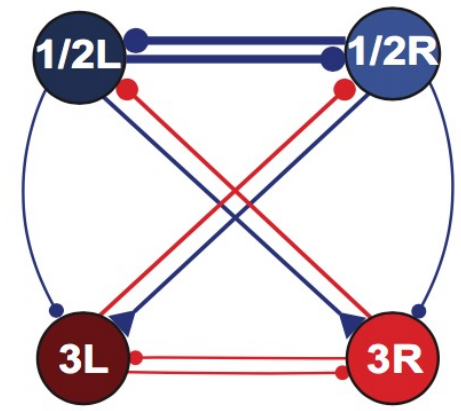
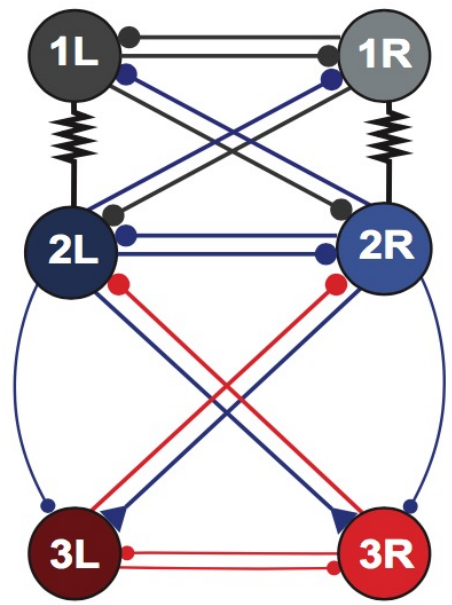
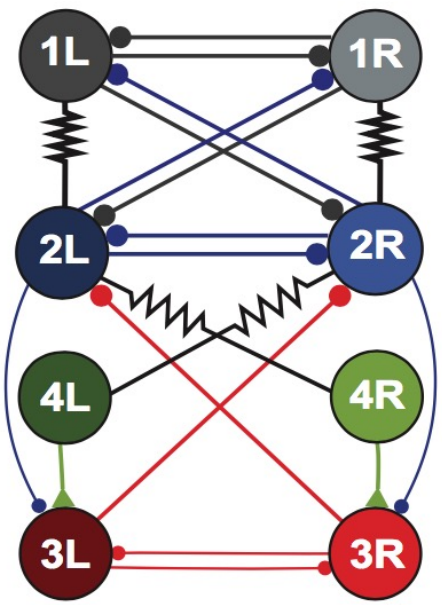
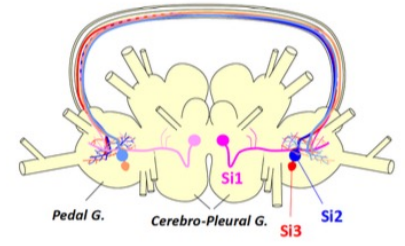
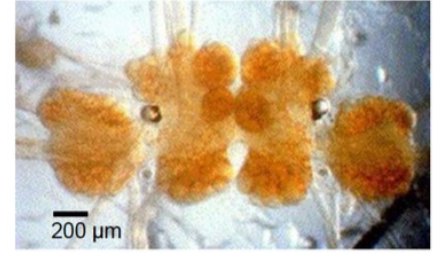


4-6 sec



12-14 sec

# Melibe Swim CPG Circuit



Reduction of *Melibe Leonina* swim CPG from 8 to 4 cells

# 2015 Melibe swim CPG model

DOI: 10.1142/S0218127415400039

## Making a Swim Central Pattern Generator Out of Latent Parabolic Bursters

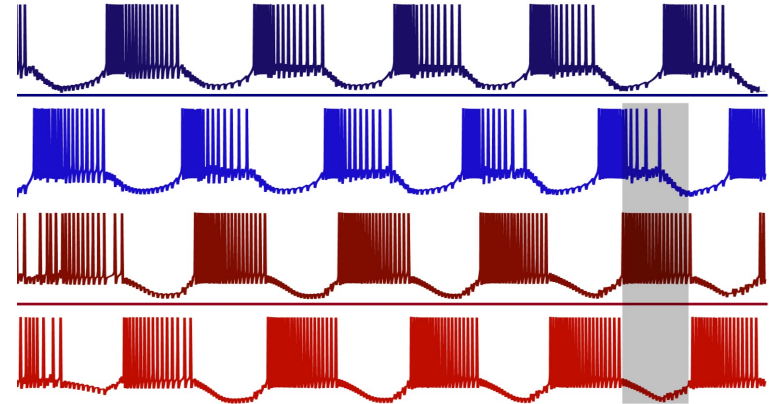
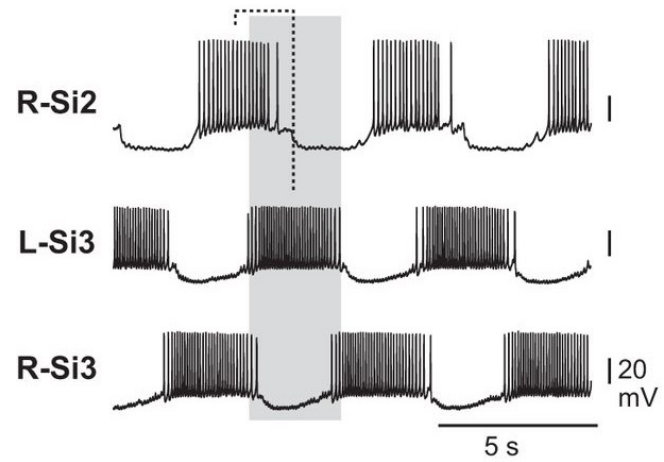
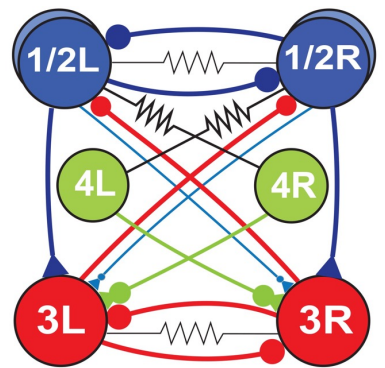
Deniz Alaçam  
Department of Mathematics and Statistics,  
Georgia State University, Atlanta 30303, USA  
dalacam1@student.gsu.edu

Andrey Shilnikov  
Neuroscience Institute and  
Department of Mathematics and Statistics,  
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Institute for Information Technology,  
Mathematics and Mechanics,  
Lobachevsky State University of Nizhni Novgorod,  
Nizhni Novgorod 603950, Russia  
ashilnikov@gsu.edu

Received April 4, 2015

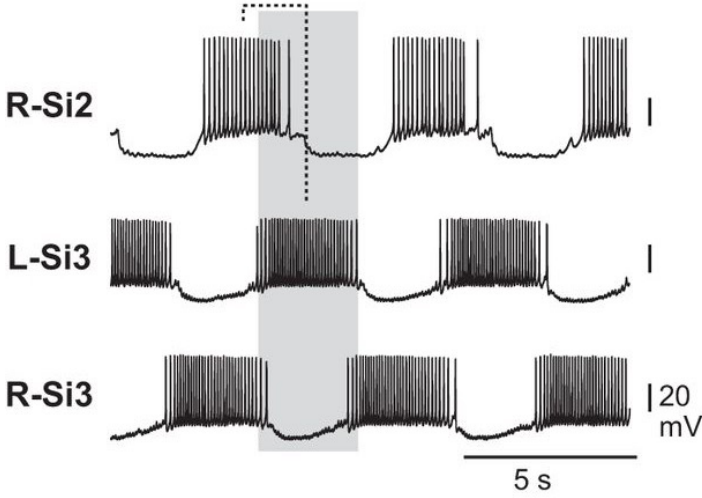
We study the rhythmogenesis of oscillatory patterns emerging in network motifs composed of inhibitory coupled tonic spiking neurons represented by the Plant model of R15 nerve cells. Such motifs are argued to be used as building blocks for a larger central pattern generator network controlling swim locomotion of sea slug *Melibe leonina*.

**Keywords:** Plant model; parabolic bursting; half-center oscillation; central pattern generator; swim locomotion; sea slug.

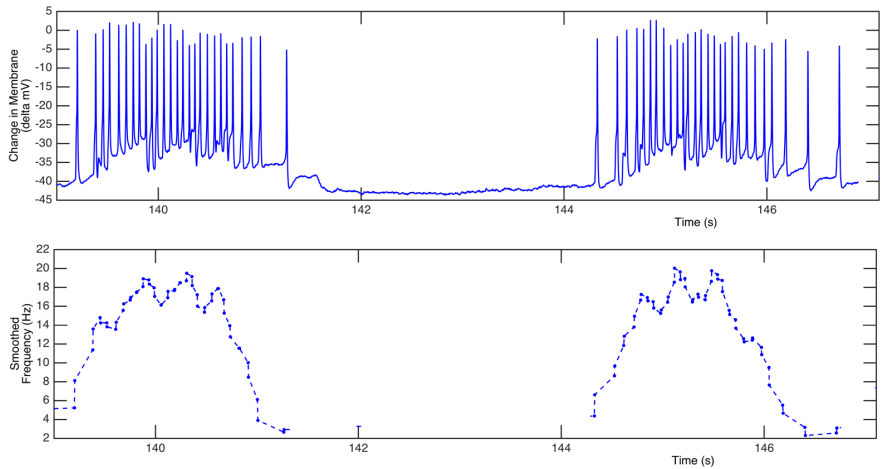


# Single cell dynamics

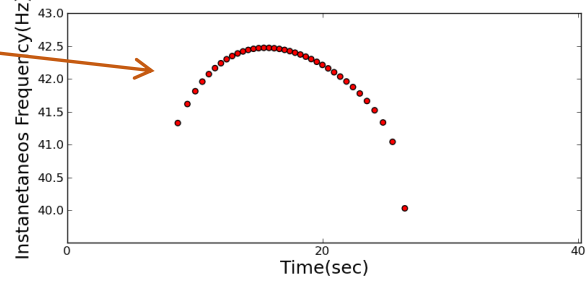
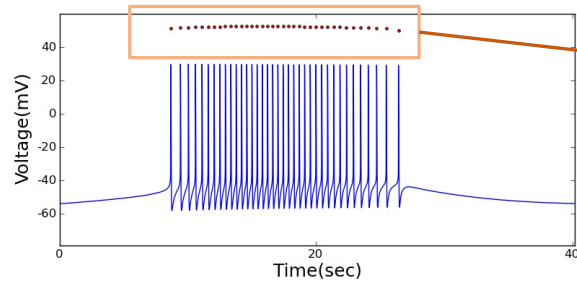
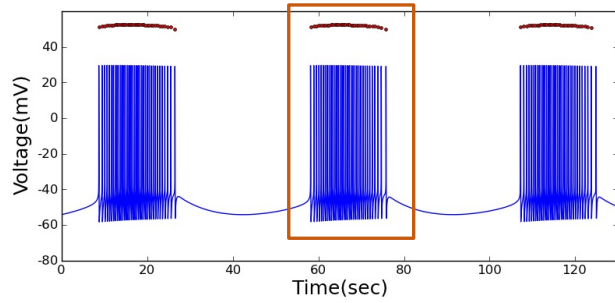
Courtesy: Akira Sakurai and Paul Katz



## Parabolic burster



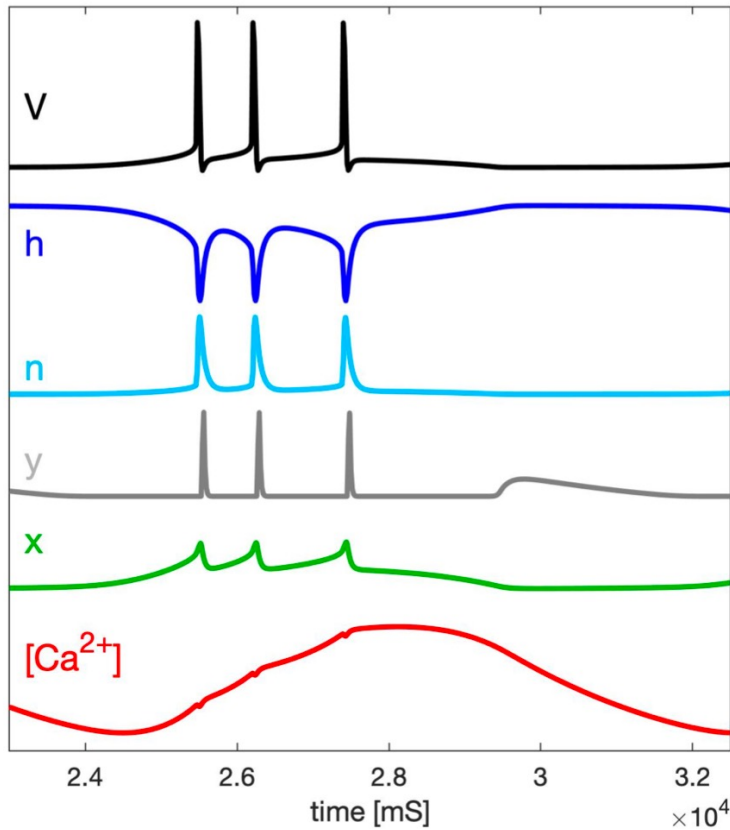
## choice of model - Plant's parabolic buster



# Plant R15 burster - a slow-fast system



*Aplysia* (wiki)



## fast subsystem

$$C_m \dot{V}(t) = -I_{Na} - I_K - I_{leak} - I_h - I_{CaT} - I_{KCa} - I_{syn},$$

$$\dot{h}(t) = \frac{h_{\infty}(V) - h}{\tau_h(V)}, \quad \dot{n}(t) = \frac{n_{\infty}(V) - n}{\tau_n(V)},$$

$$\dot{y}(t) = \frac{1}{2} \left[ \frac{1}{1 + e^{10(V-50)}} - y \right] / \left[ 7.1 + \frac{10.4}{1 + e^{(V+68)/2.2}} \right],$$

$$I_{Na} = g_{Na} h(t) m_{\infty}^3(V) (V - E_{Na}), \quad I_K = g_K n(t)^4 (V - E_K),$$

$$I_h = g_h \frac{y(t) (V - E_h)}{\left(1 + e^{-(V-63)/7.8}\right)^3}.$$

## slow subsystem

$$[\dot{Ca}] = \rho [K_c x (V_{Ca} - V + \Delta_{Ca}) - [Ca]_i],$$

$$\dot{x} = \frac{1}{\tau_x} \left[ \frac{1}{1 + e^{-0.15(V+50-\Delta_x)}} - x \right],$$

$$I_{Ca} = g_{Ca} x (V - E_{Ca}), \quad I_{KCa} = g_{KCa} \frac{[Ca]_i}{0.5 + [Ca]_i} (V - E_K).$$

# Plant R15 burster: slow-fast

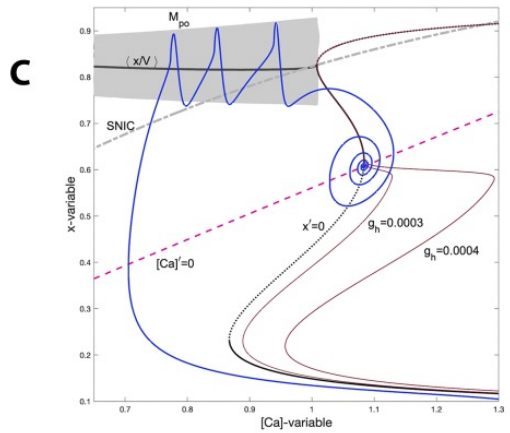
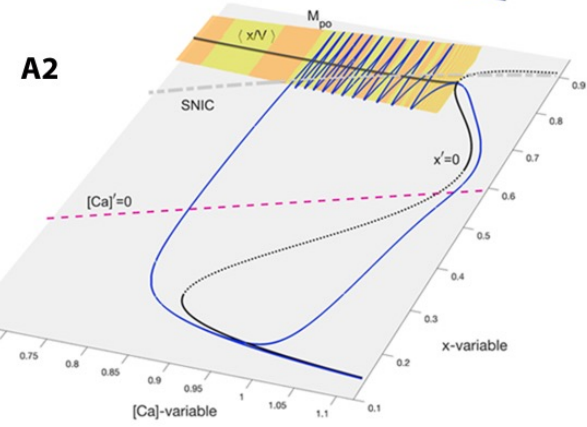
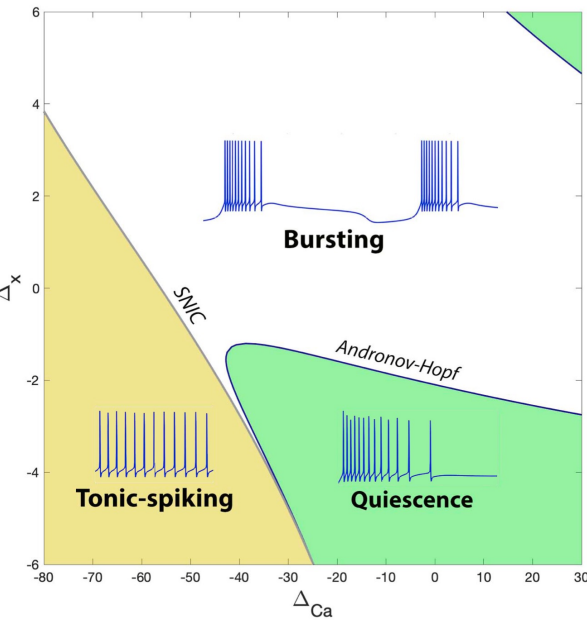
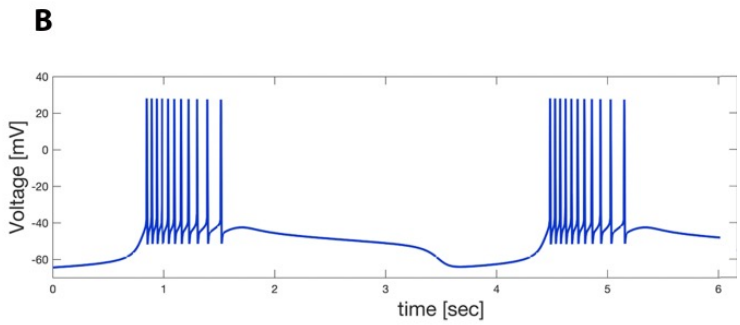
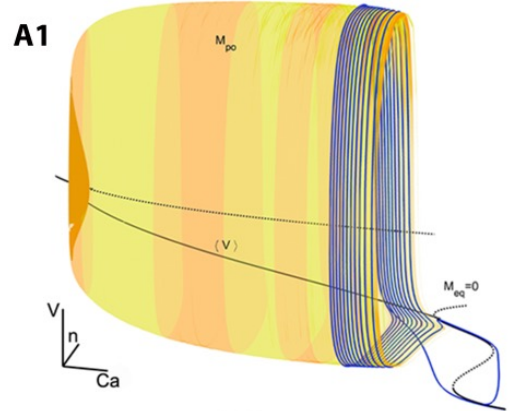
$$C_m \dot{V} = -I_{Na} - I_K - I_{leak} - I_h - I_{CaT} - I_{KCa} - I_{syn},$$

$$\dot{h} = \frac{h_{\infty}(V) - h}{\tau_h(V)}, \quad \dot{n} = \frac{n_{\infty}(V) - n}{\tau_n(V)},$$

$$\dot{y} = \frac{1}{2} \left[ \frac{1}{1 + e^{10(V-50)}} - y \right] / \left[ 7.1 + \frac{10.4}{1 + e^{(V+68)/2.2}} \right].$$

$$[\dot{Ca}] = \rho [K_c x (V_{Ca} - V + \Delta_{Ca}) - [Ca]_i],$$

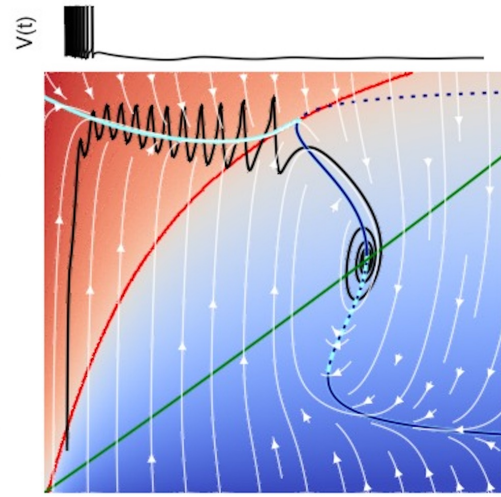
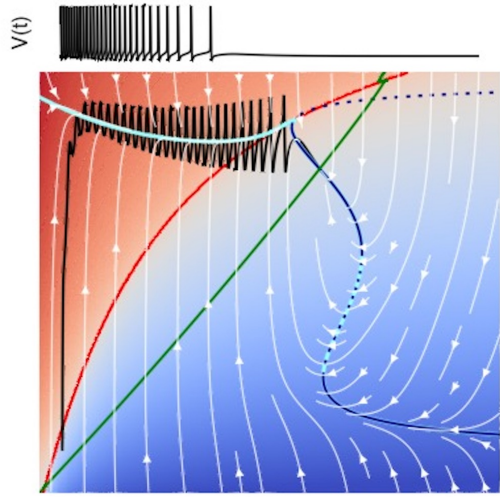
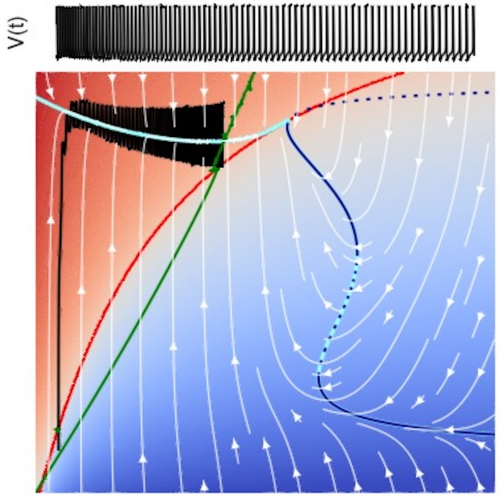
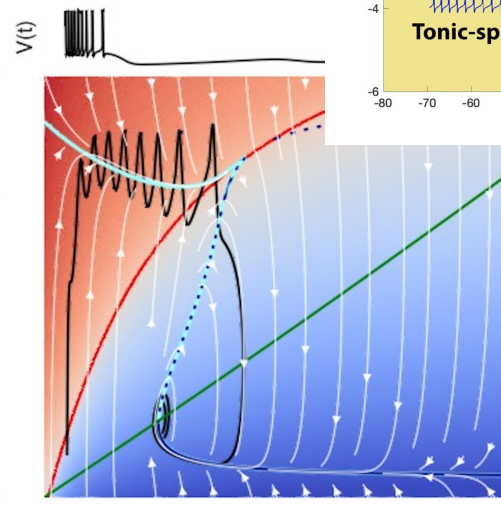
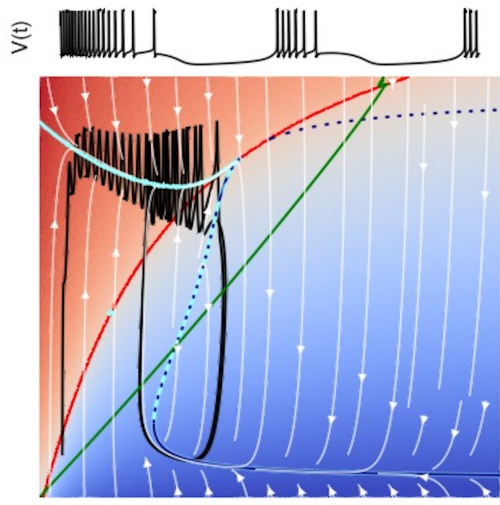
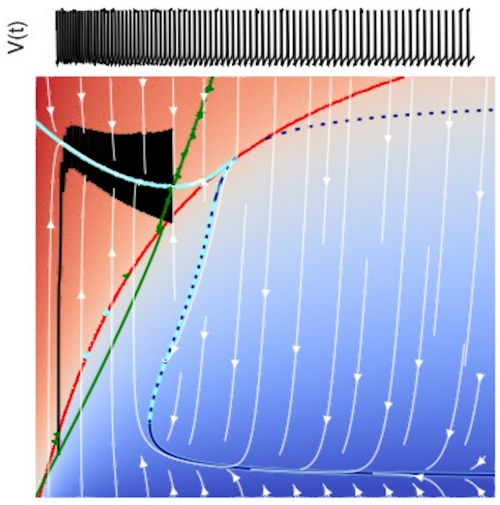
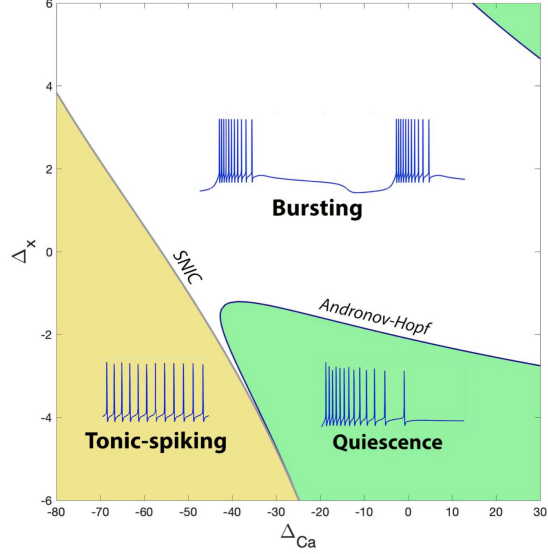
$$\dot{x} = \left[ \frac{1}{e^{0.15(-V-50+\Delta_x)} + 1} - x \right] \frac{1}{\tau_x},$$



# Plant R15 burster: slow-fast

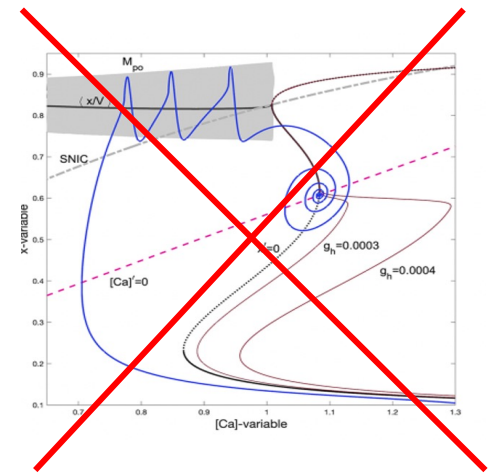
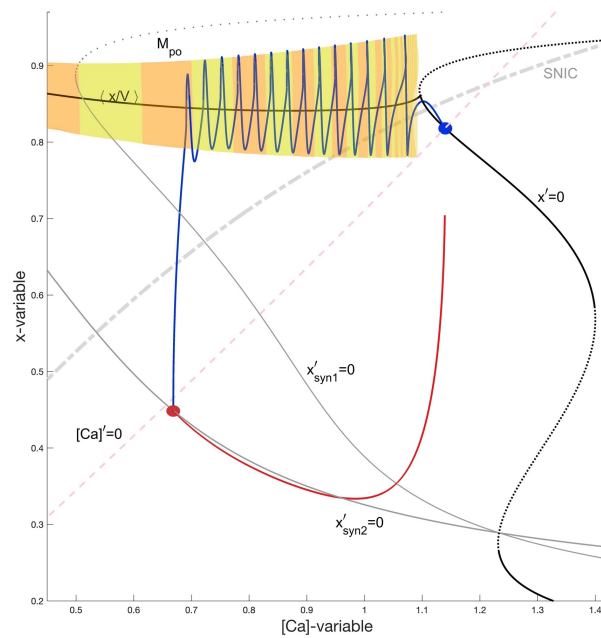
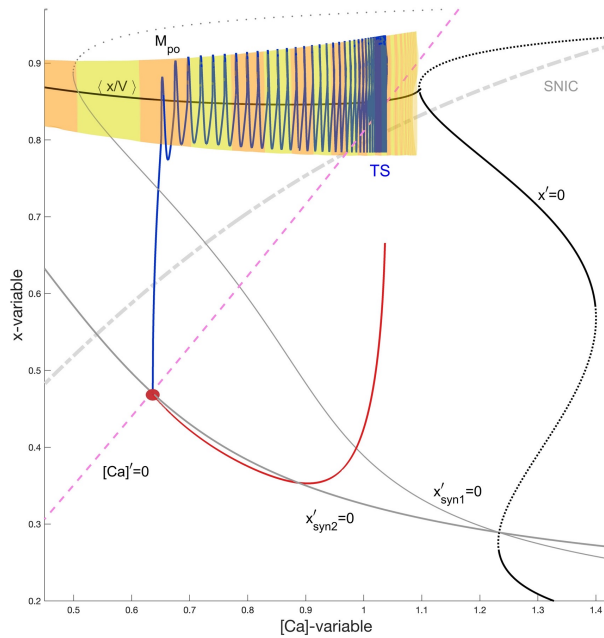
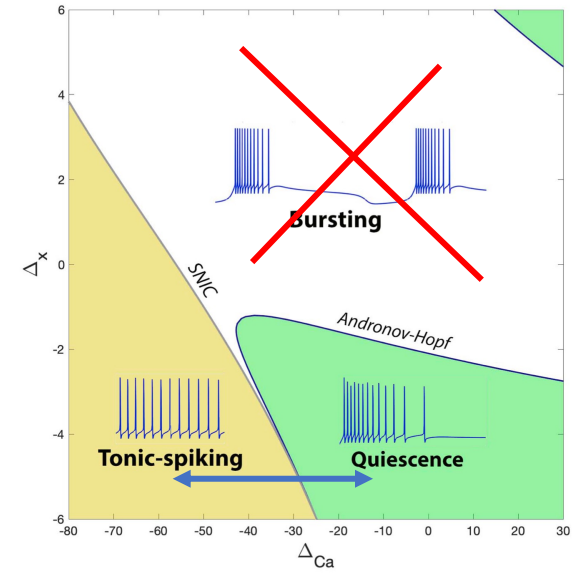
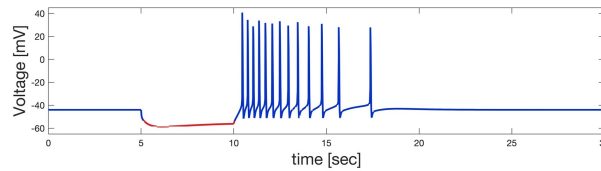
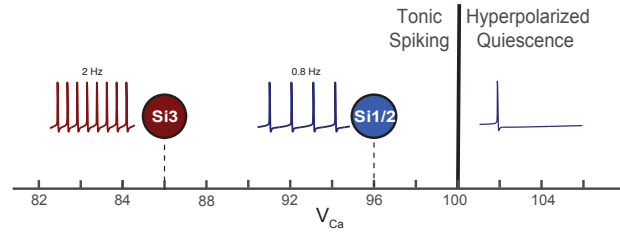
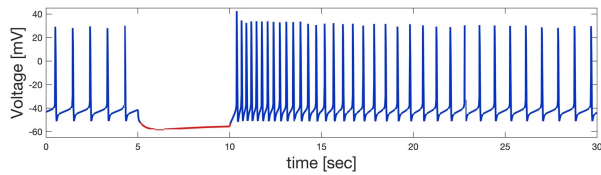
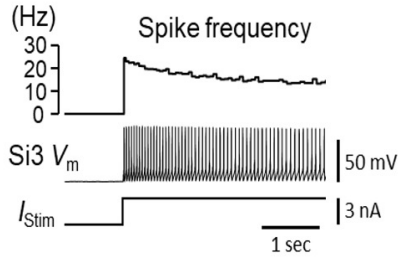
$$[\dot{Ca}] = \rho [K_c x (V_{Ca} - V + \Delta_{Ca}) - [Ca]_i],$$

$$\dot{x} = \left[ \frac{1}{e^{0.15(-V-50+\Delta_x)} + 1} - x \right] \frac{1}{\tau_x},$$



# Membrane properties

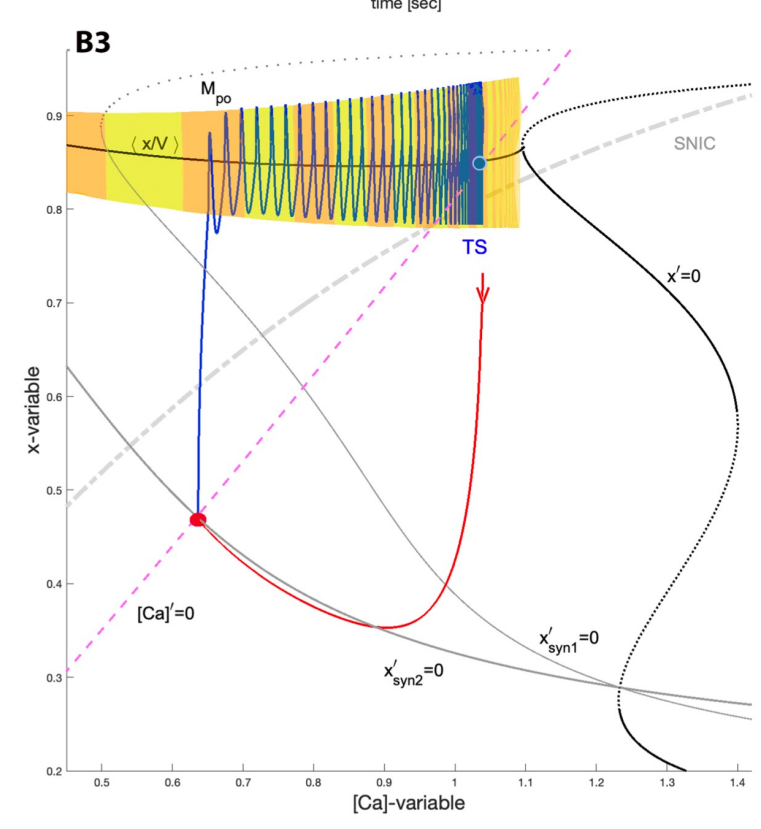
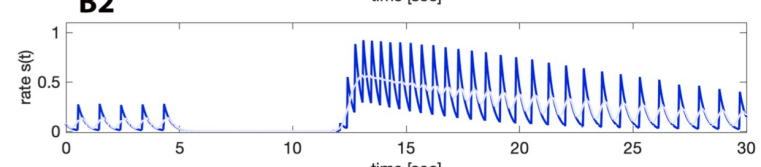
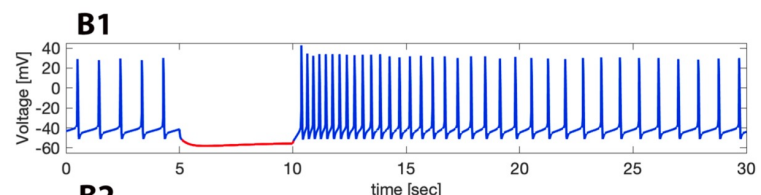
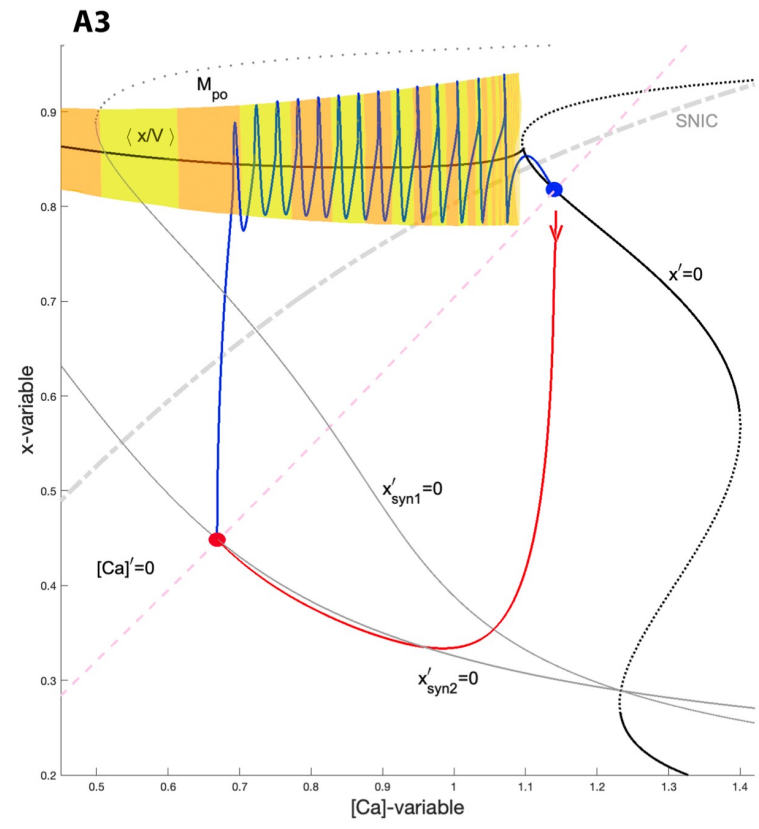
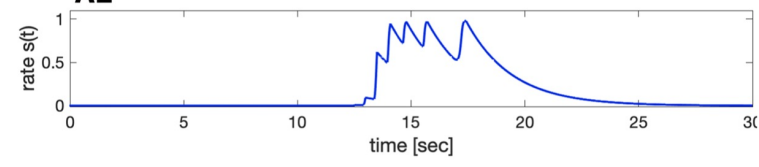
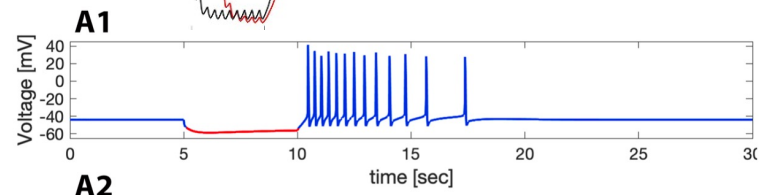
- spiking  $\longleftrightarrow$  quiescent
- post inhibitory rebound
- spike frequency adaptation



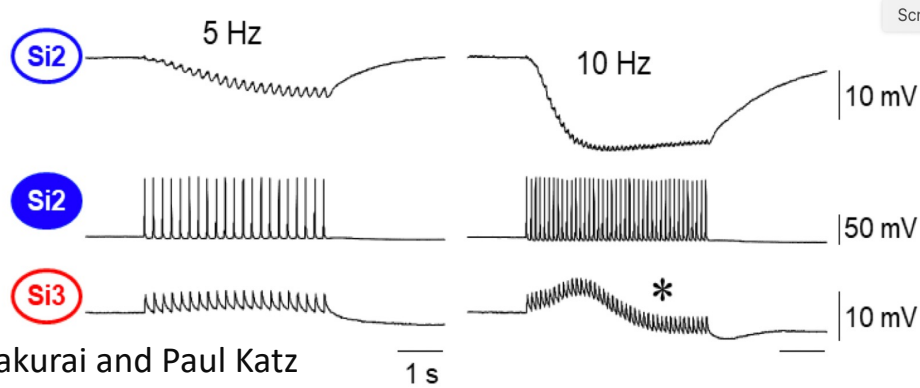
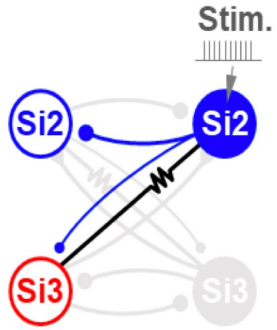
# Membrane properties: perturbed vs. unperturbed:

$$I_{syn} = g_{syn} S(V_{pre}(t)) (V_{post}(t) - V_{rev})$$

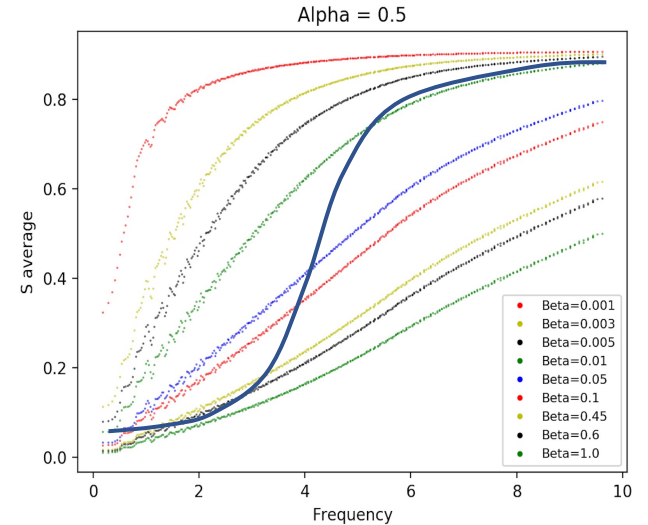
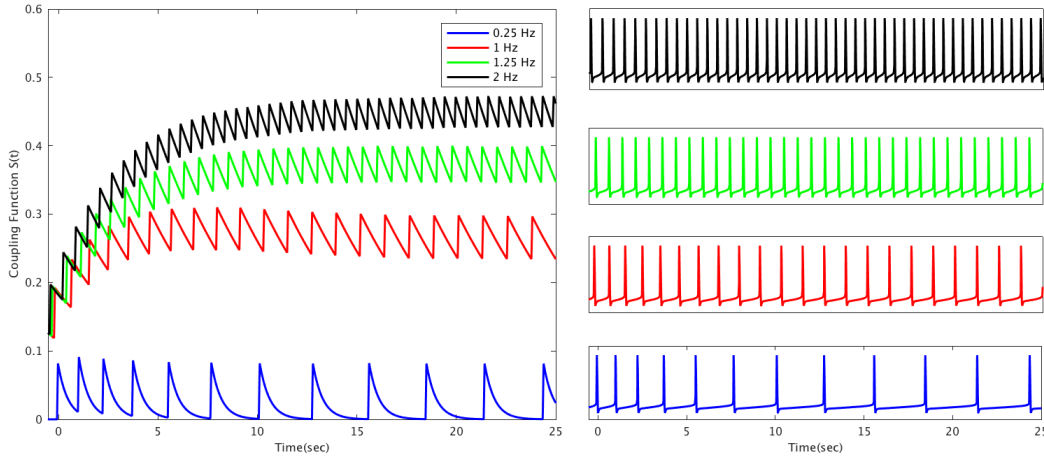
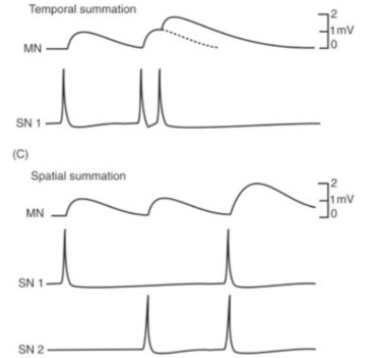
synaptic current pulse



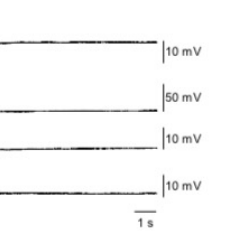
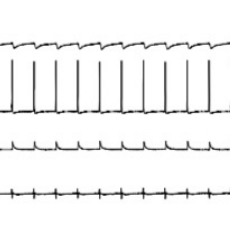
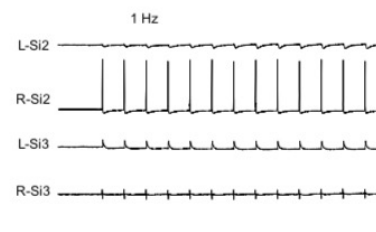
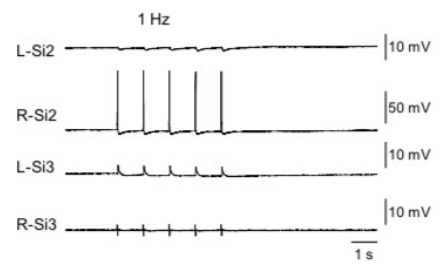
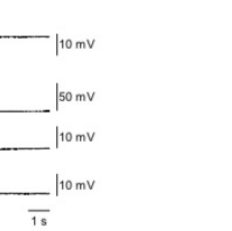
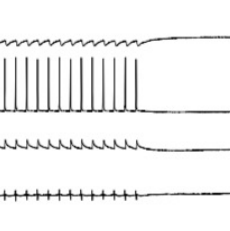
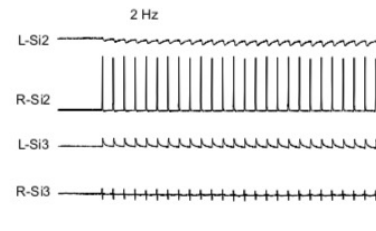
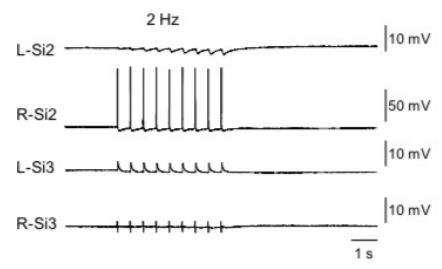
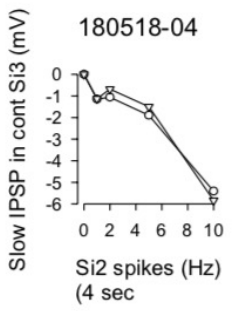
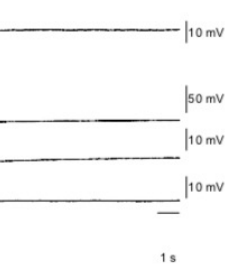
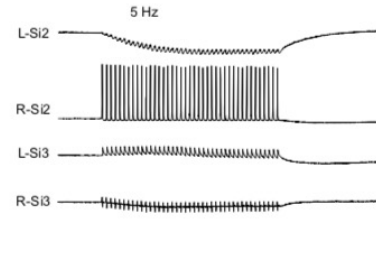
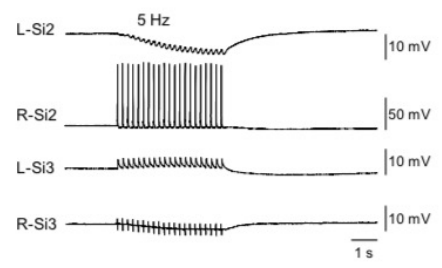
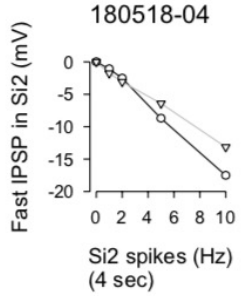
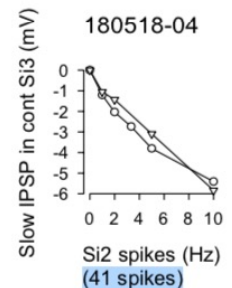
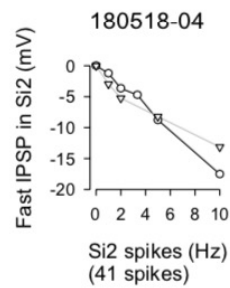
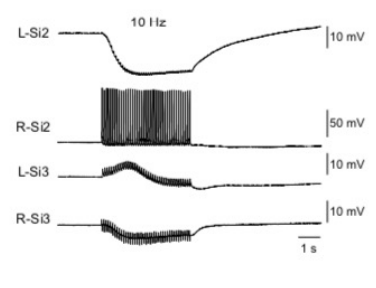
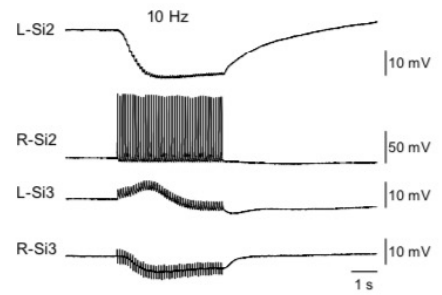
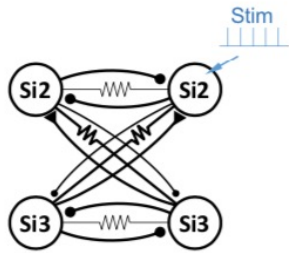
# Synaptic dynamics : slow = accumulation & potentiation

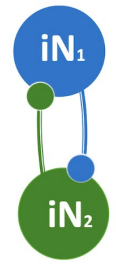
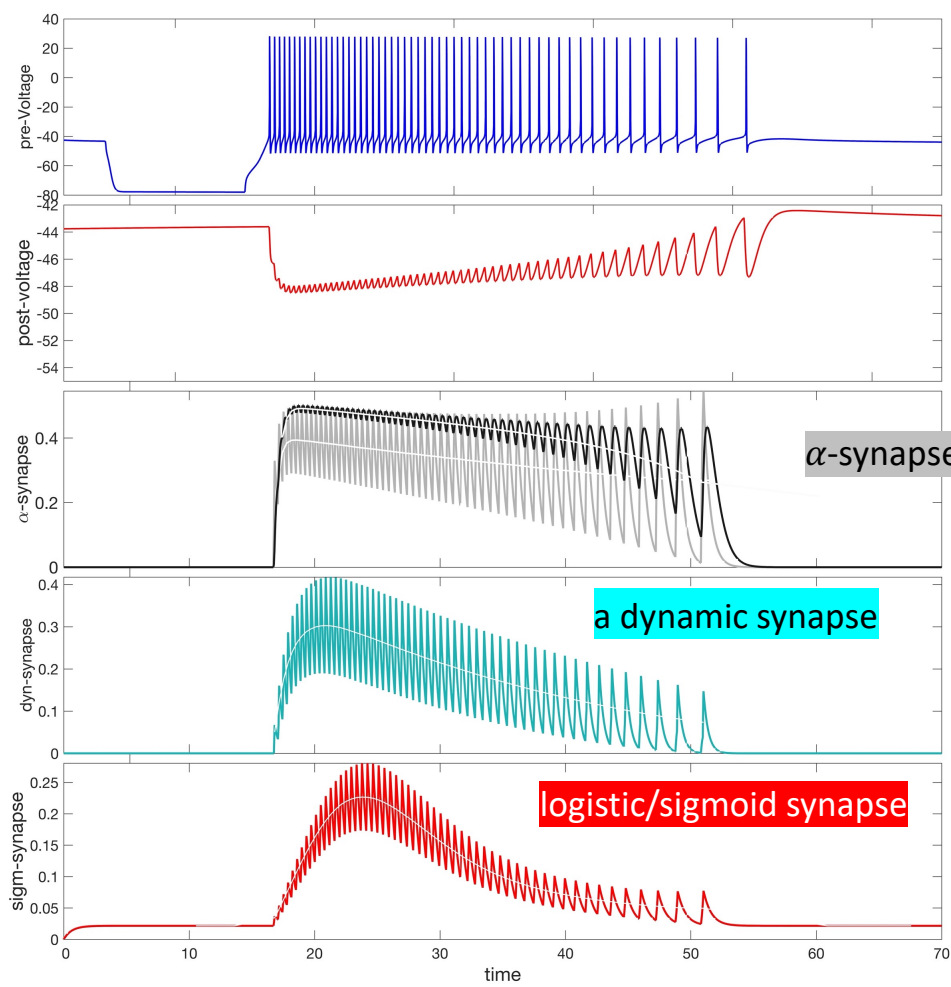


Courtesy: Akira Sakurai and Paul Katz



# Synapses : accumulation & potentiation

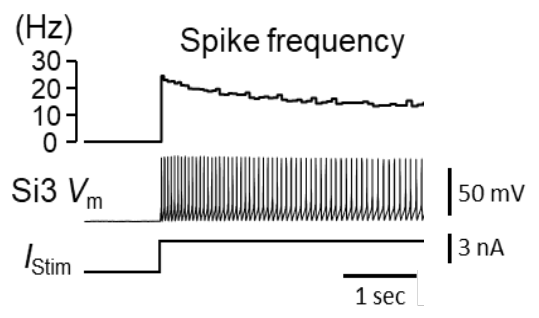
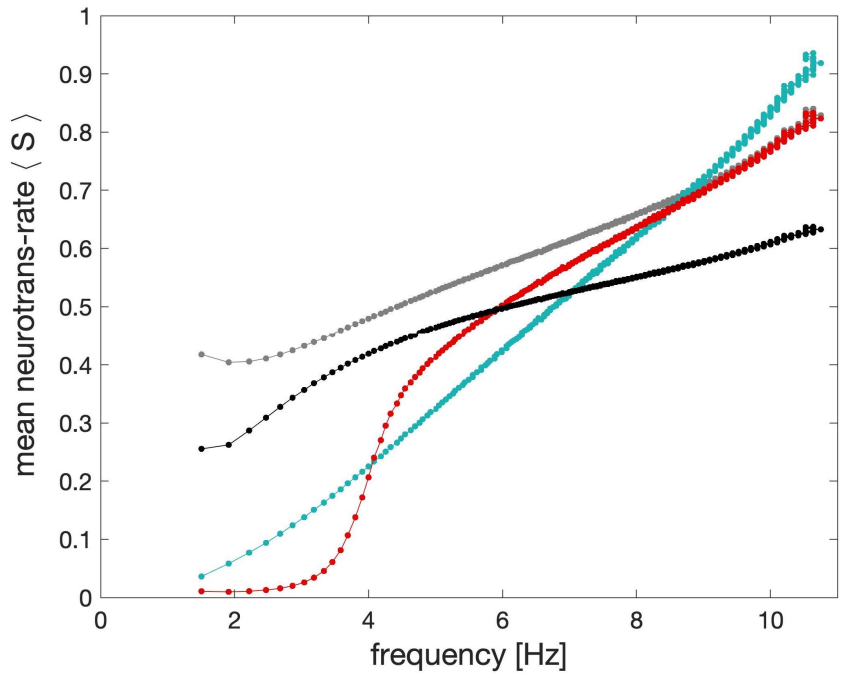




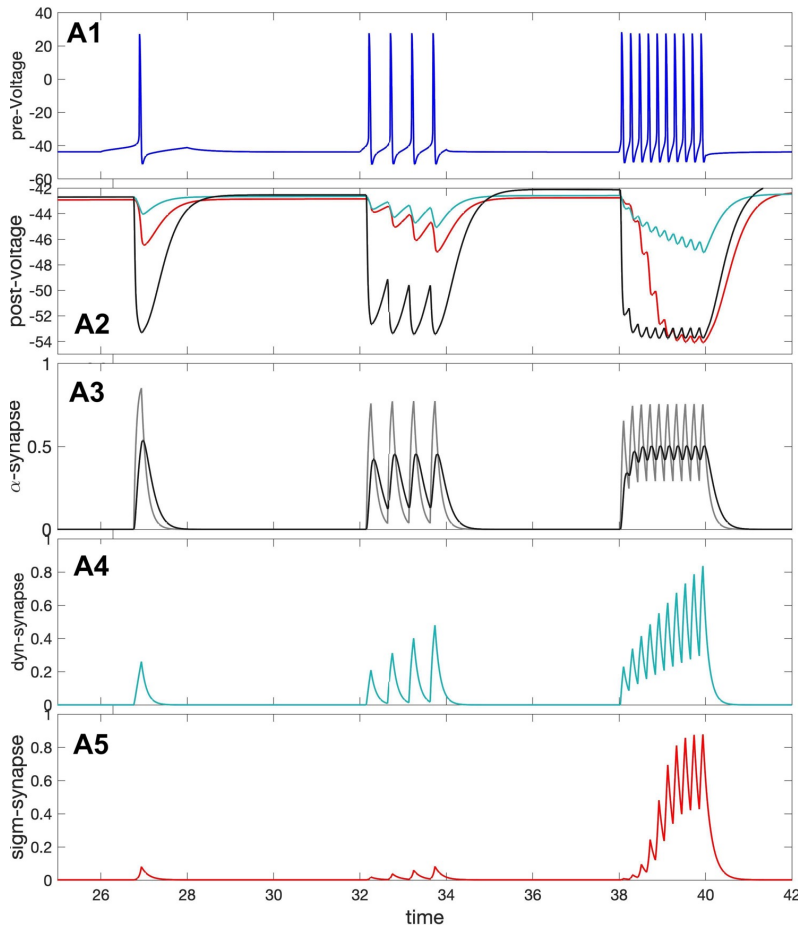
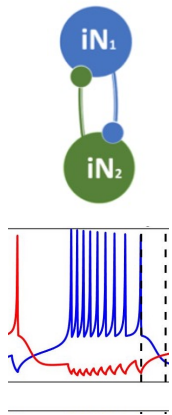
$\alpha$ -synapse: 1<sup>st</sup> and 2<sup>nd</sup> order kinetics

a dynamic synapse

logistic/sigmoid synapse



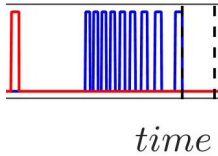
Courtesy: Akira Sakurai and Paul Katz



$$I_{syn} = g_{syn} S(V_{pre}(t)) (V_{post}(t) - V_{rev})$$

Fast Threshold Modulation (FTM)

$$S(V_{pre}) = \frac{1}{1 + e^{-k(V_{pre} - \Theta_{syn})}}$$



$t^p e^{-t}$  **alpha synapse**

$$\dot{S} = \alpha(1 - S) \frac{1}{1 + e^{-k(V - \Theta_{syn})}} - \beta S$$

**alpha synapse: 2<sup>nd</sup> and 3<sup>rd</sup> order kinetics**

$$\dot{S}_1 = \alpha(1 - S_1) \frac{1}{1 + e^{-k(V - \Theta_{syn})}} - \beta S_1,$$

$$\dot{S}_2 = \alpha(1 - S_2) S_1 - \beta S_2,$$

$$\dot{S}_3 = \alpha(1 - S_3) S_2 - \beta S_3, \quad \text{and so on.}$$

**logistic/sigmoid synapse**

$$\dot{S} = \frac{\alpha S (1 - S)}{1 + e^{-k(V - V_{th})}} - \beta(S - S_0),$$

**another dynamic synapse**

$$\dot{S}_1 = \frac{1}{1 + e^{-1000(V - \Theta_{syn})}} - S_1 \quad \text{or} \quad \dot{S}_1 = \frac{\alpha(1 - S_1)}{1 + e^{-k(V - \Theta_{syn})}} - S_1.$$

$$\dot{S}_2 = \frac{S_1 - S_2}{\tau}, \quad \text{with small } \tau = 0.001 - 0.0001;$$

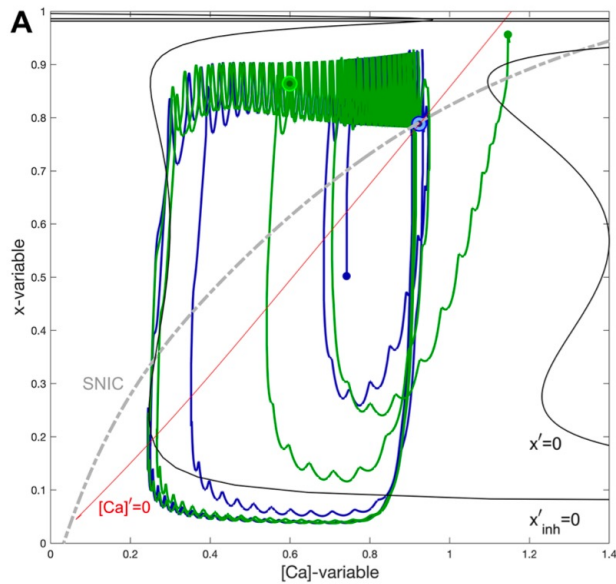
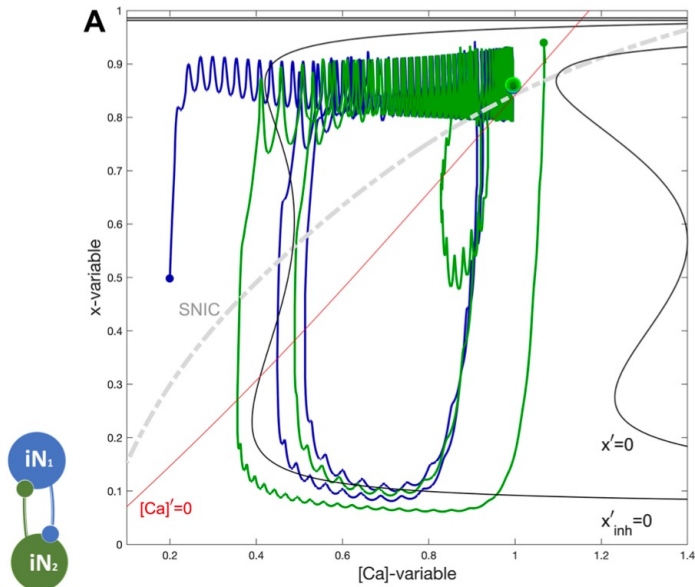
$$\dot{M} = \frac{M_0 + \frac{1 - M_0}{1 + e^{-1000(V - \Theta_{syn1})}} - M}{\tau_M}, \quad \text{with } \tau = 1000 - 3000,$$

$$S = S \cdot M :$$

# Network hysteresis: HCO

- balance of amplitudes or coupling
- balance of phase  $180^\circ$
- bistability

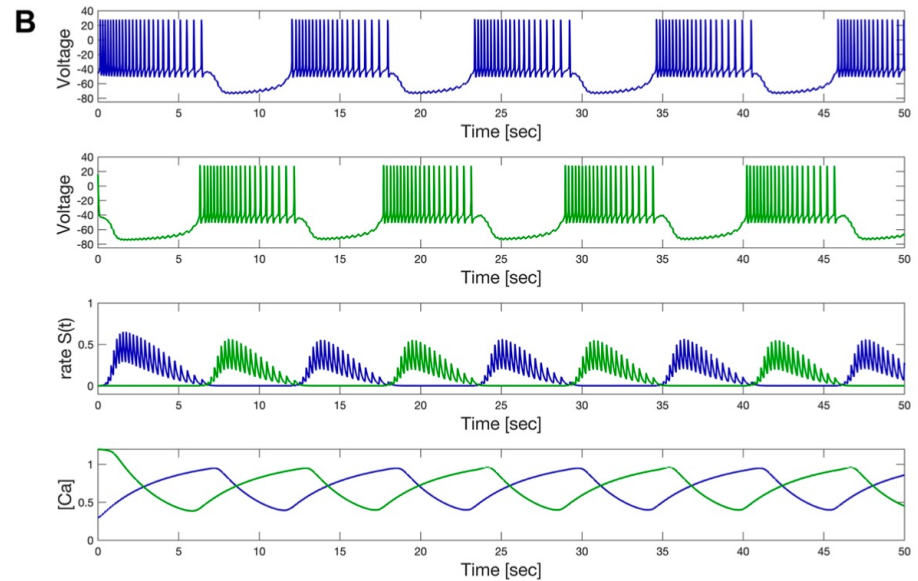
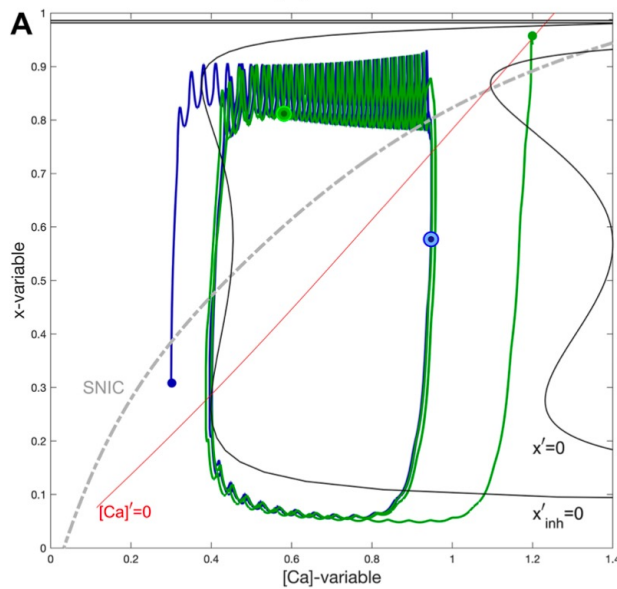
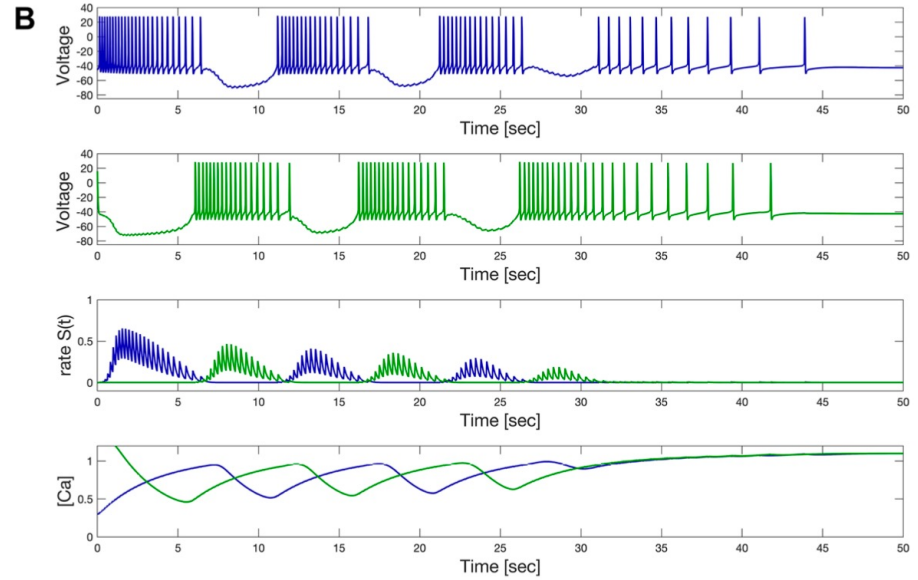
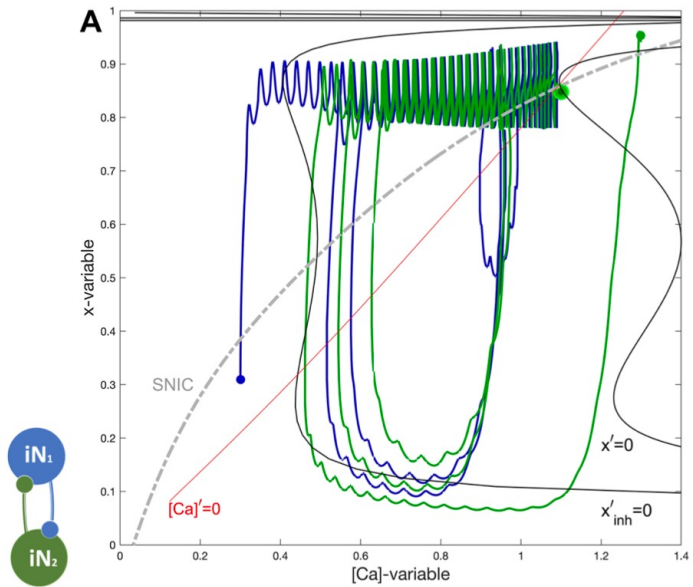
both tonic-spiking neurons



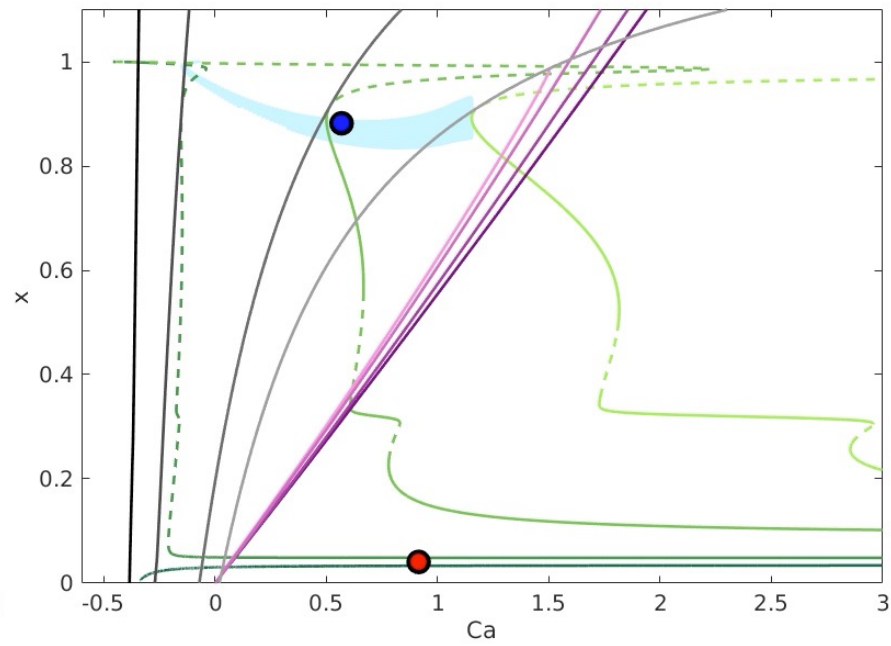
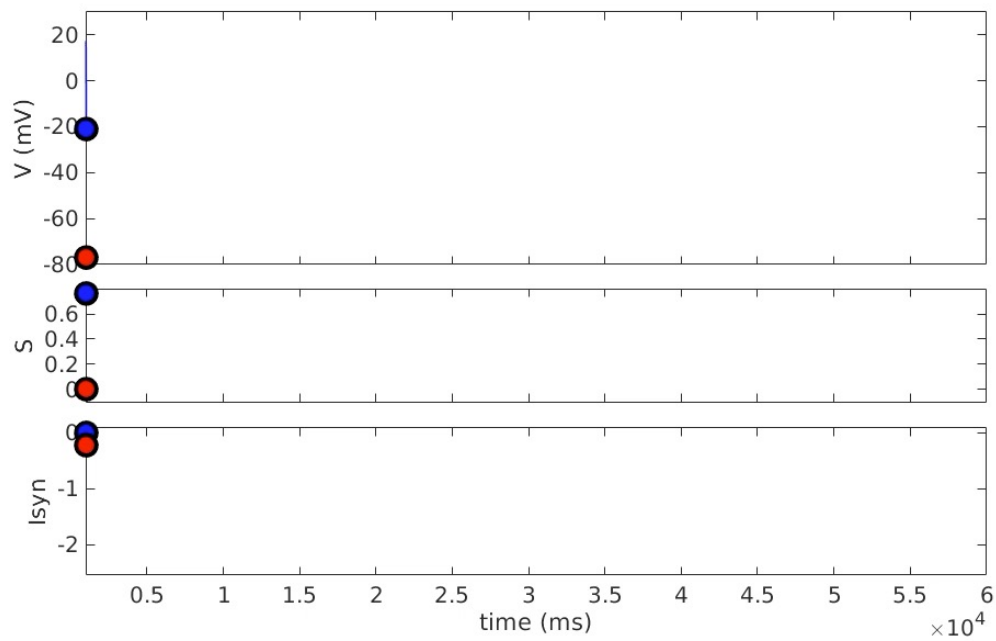
# Network hysteresis: HCO

- balance of amplitudes or coupling
- balance of phase  $180^\circ$
- bistability

both quiescent neurons

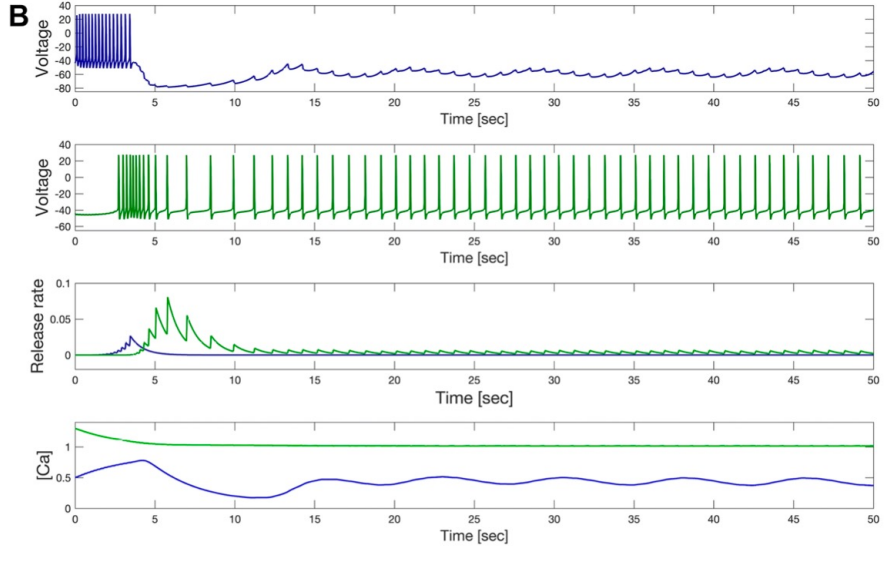
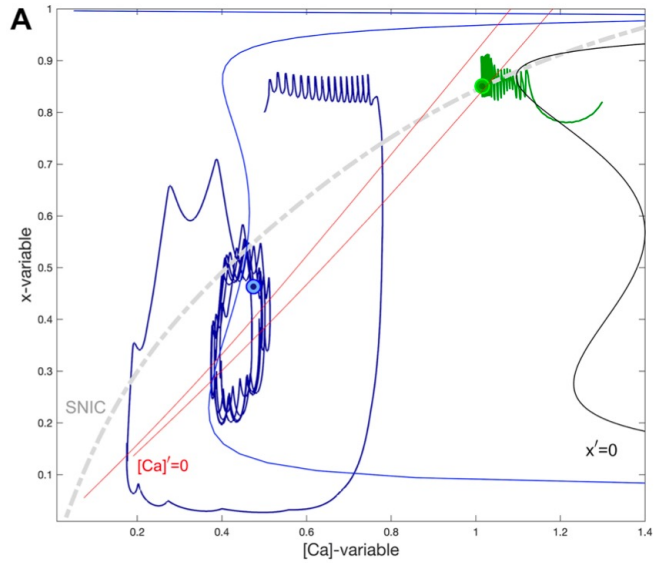
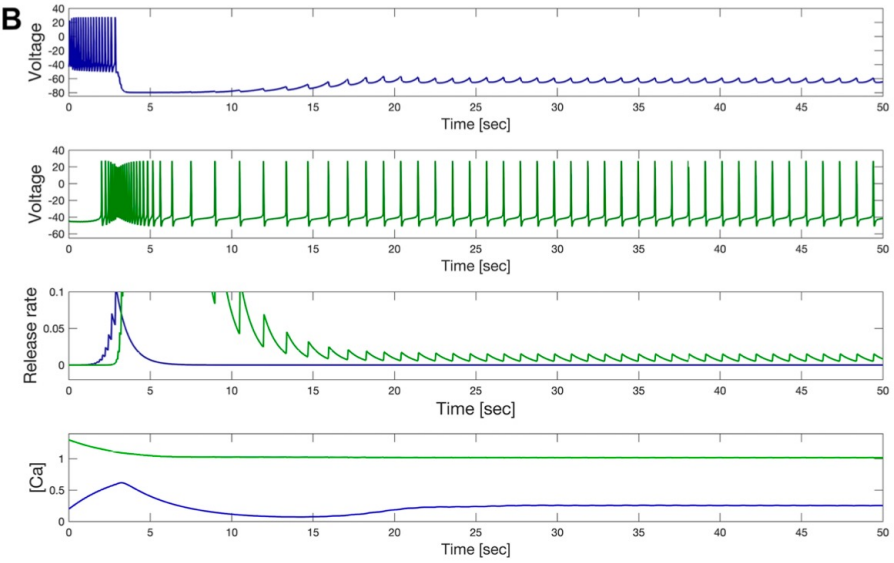
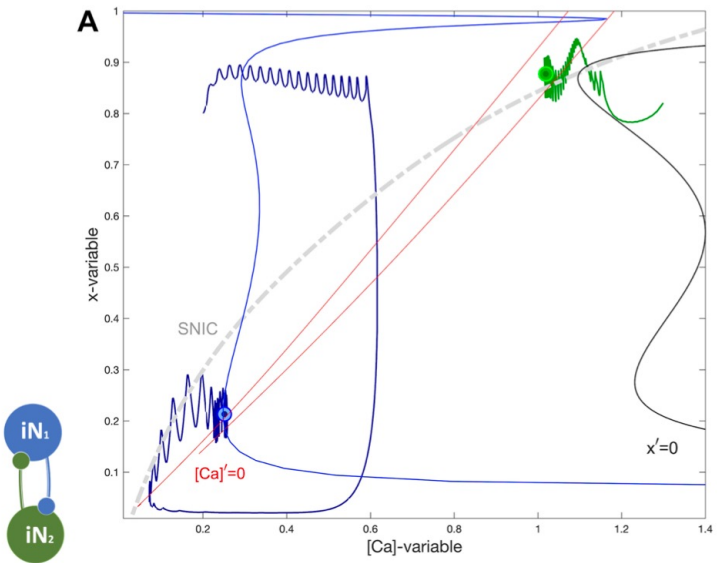


# Network hysteresis: HCO



# HCO: winner takes all

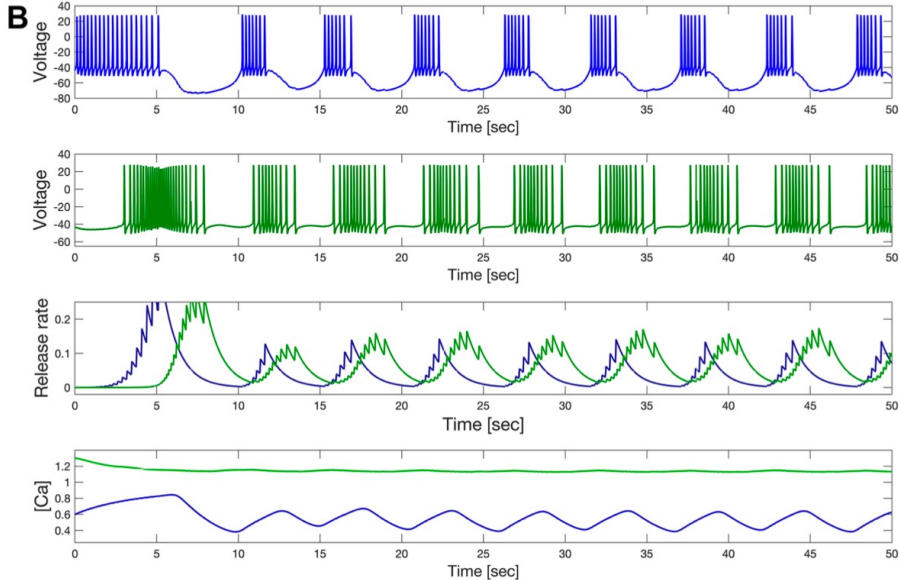
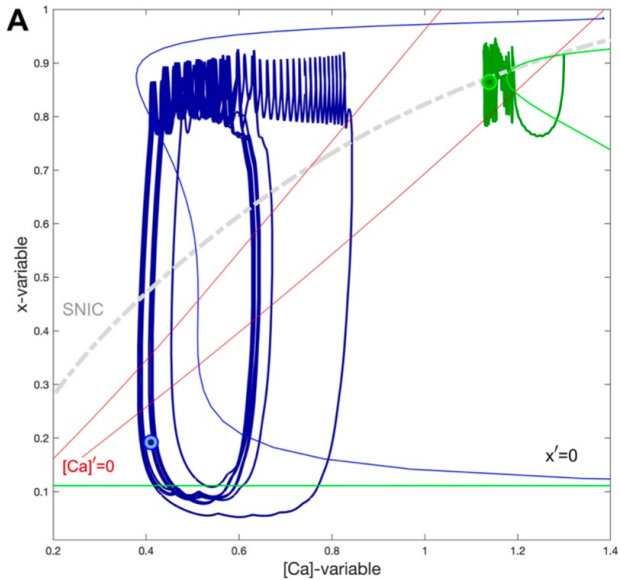
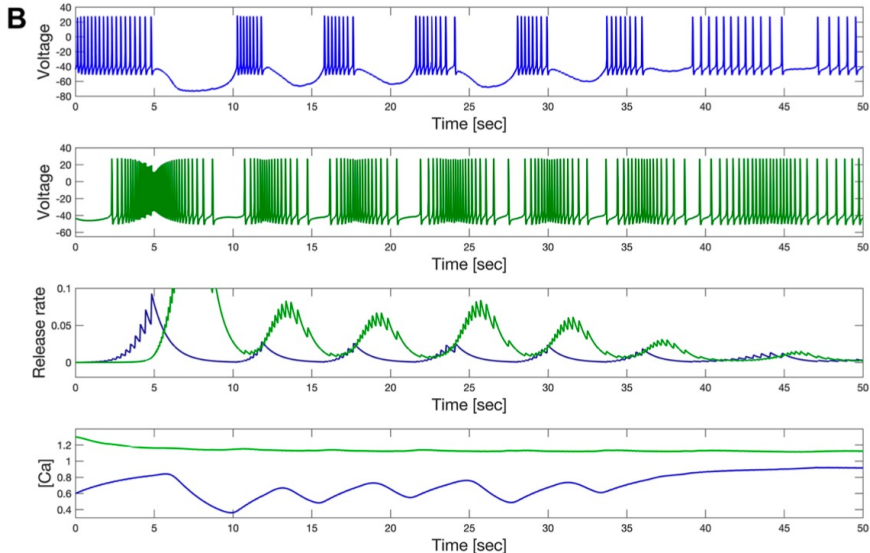
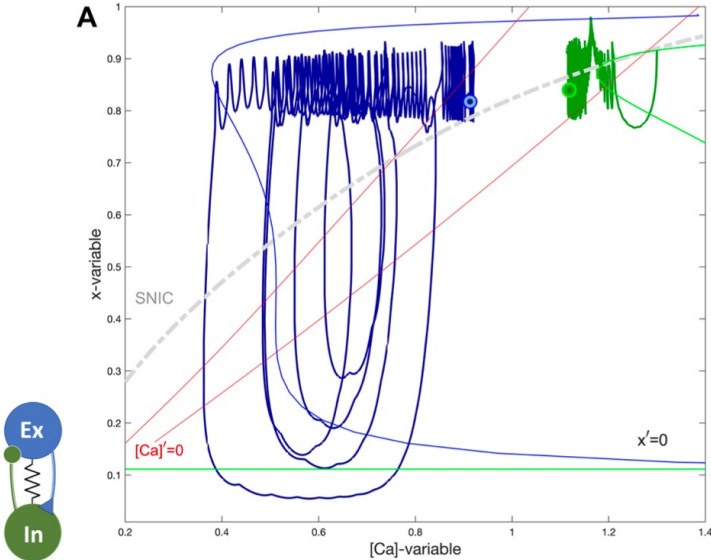
- balance of amplitudes or coupling
- balance of phase 180°
- bistability



# Predator-pray module

Spiking + quiescent neurons

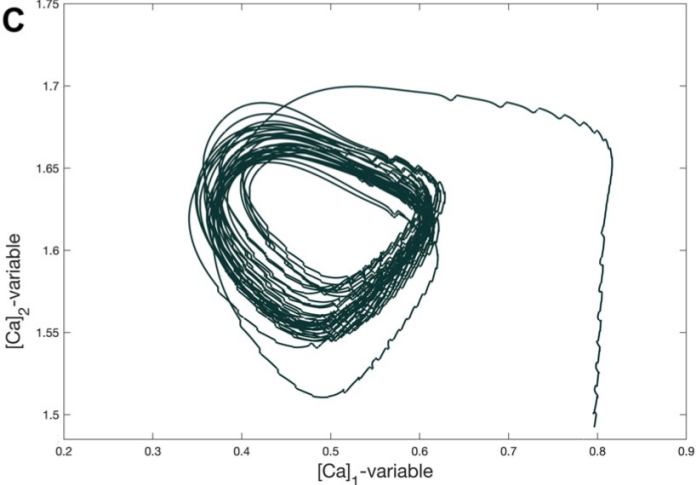
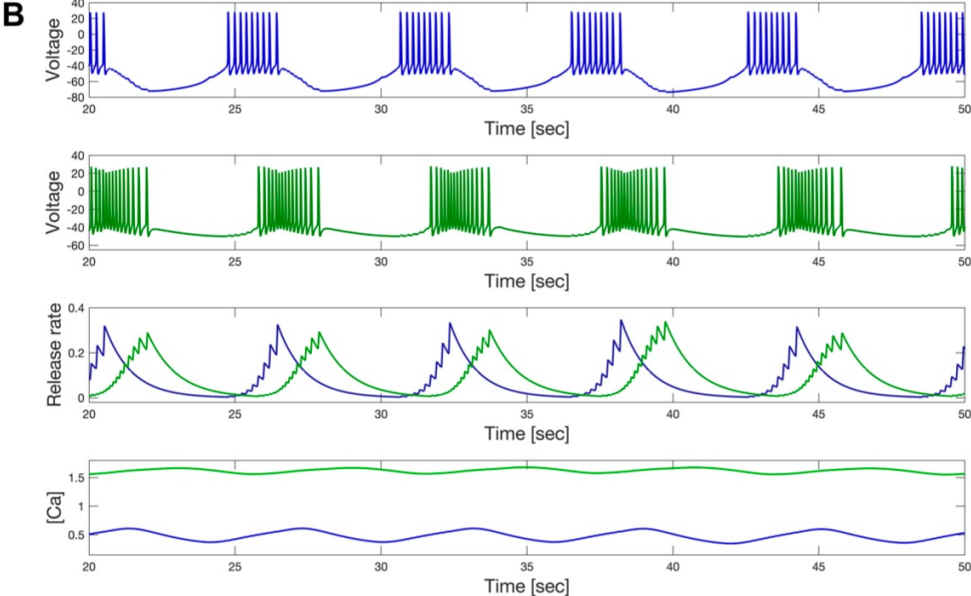
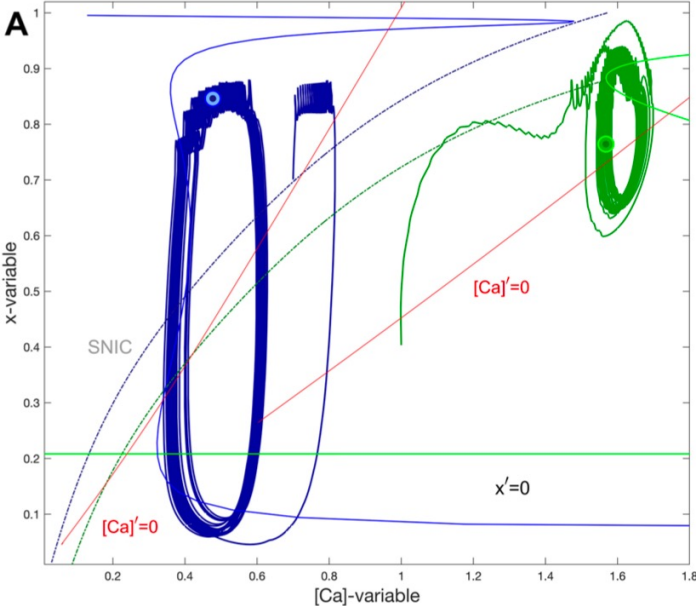
- balance of amplitudes or coupling
- balance of phase  $\frac{1}{4}$  of network period
- bistability



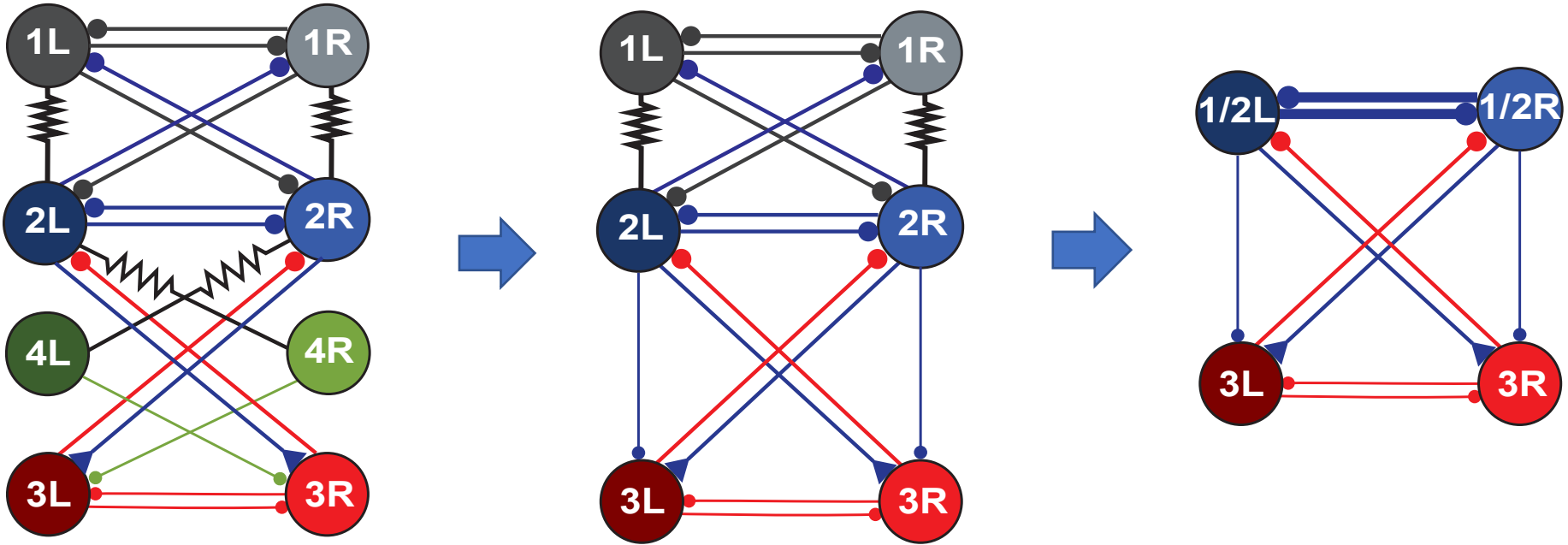
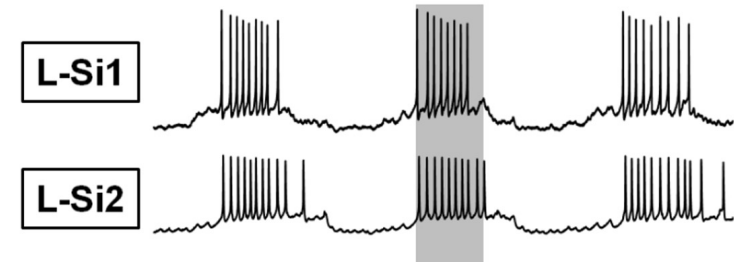
# Predator-pray module

Spiking + quiescent neurons

- balance of amplitudes or coupling
- balance of phase  $\frac{1}{4}$  of network period
- bistability

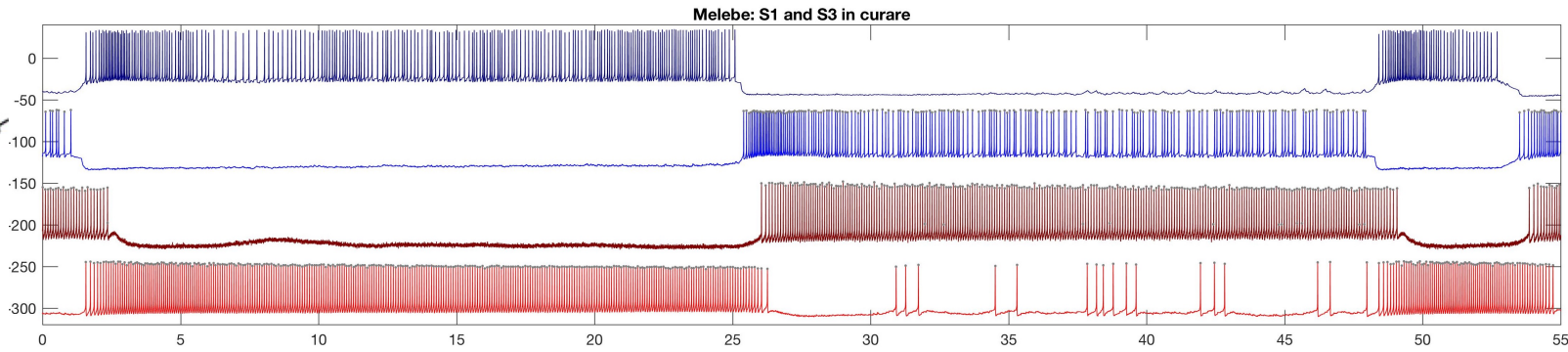
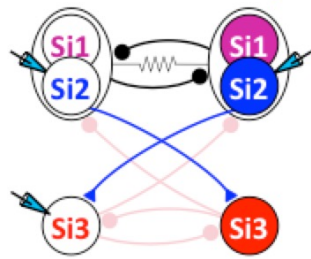
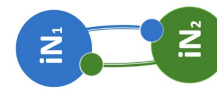


# Melibe CPG reduction

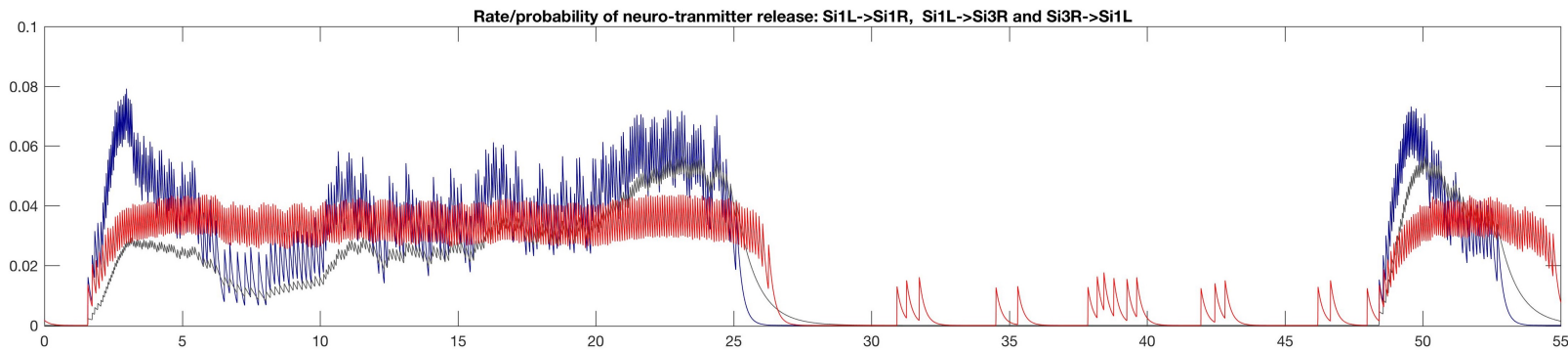
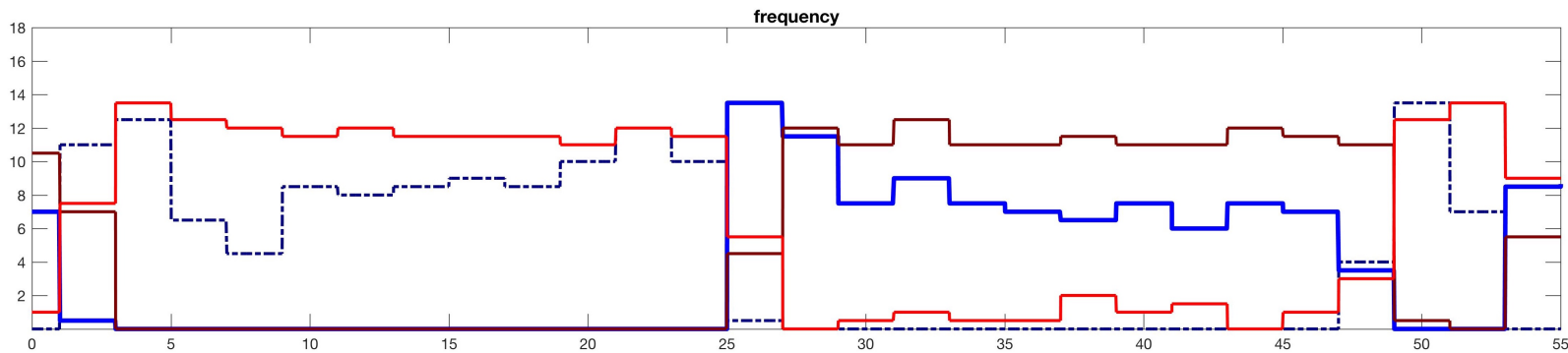


- Delay caused by Si4s are implemented by slow dynamic synapses
- Si1s and Si2s are merged due to strong electrical coupling between them

# Melibe CPG in curare - isolated HCO

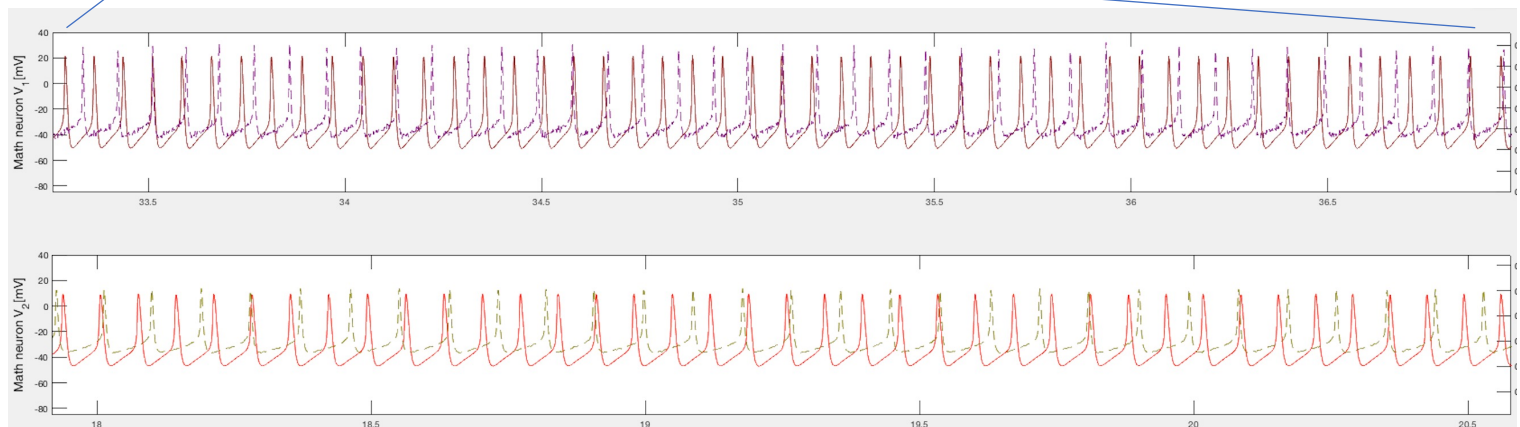
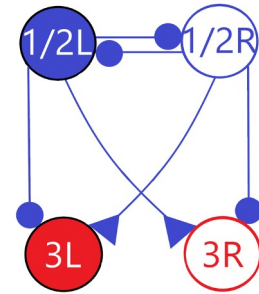
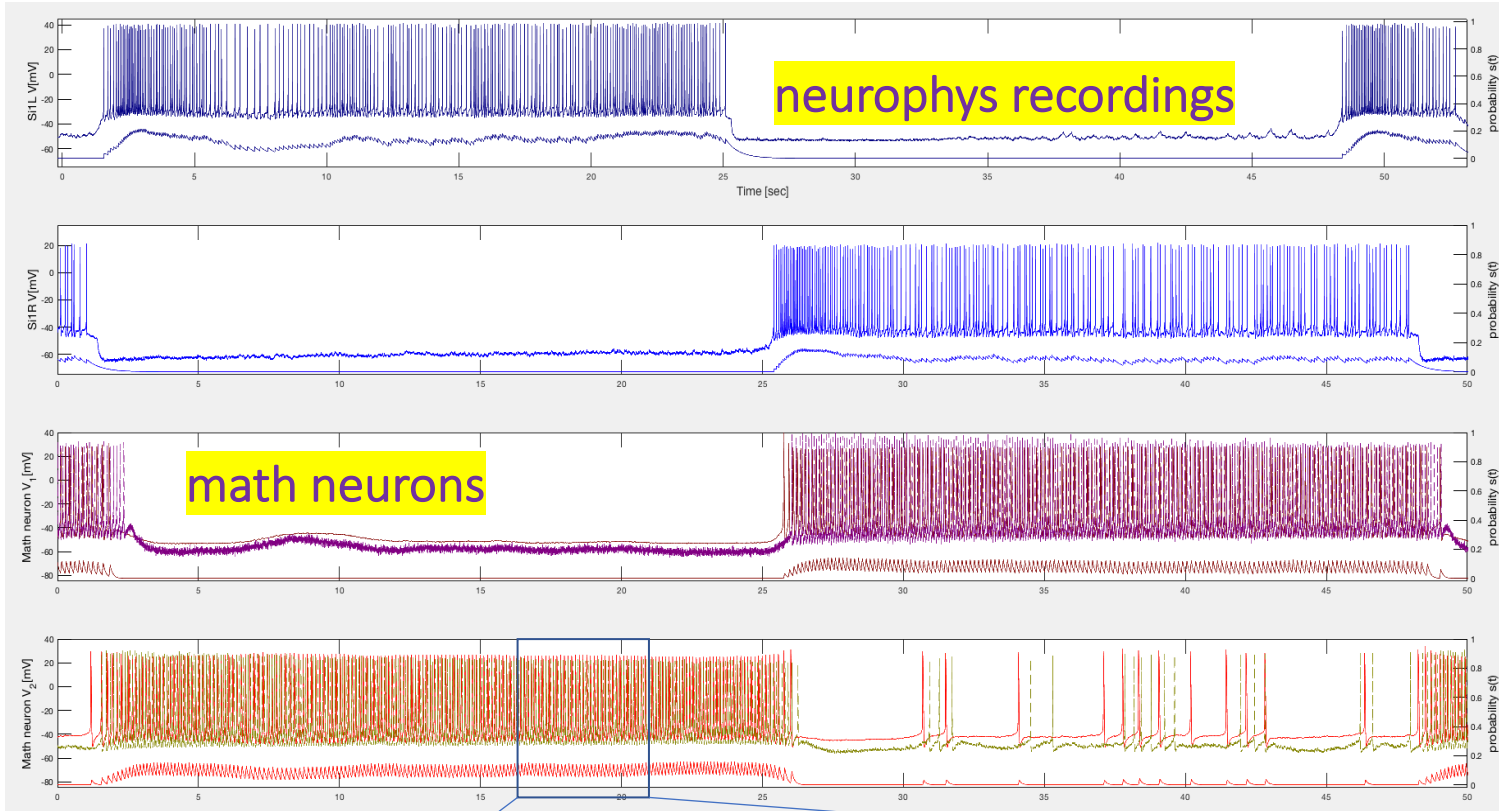


Courtesy: Akira Sakurai and Paul Katz

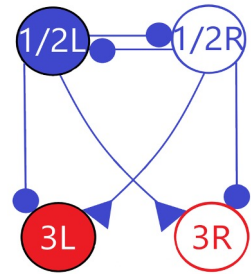
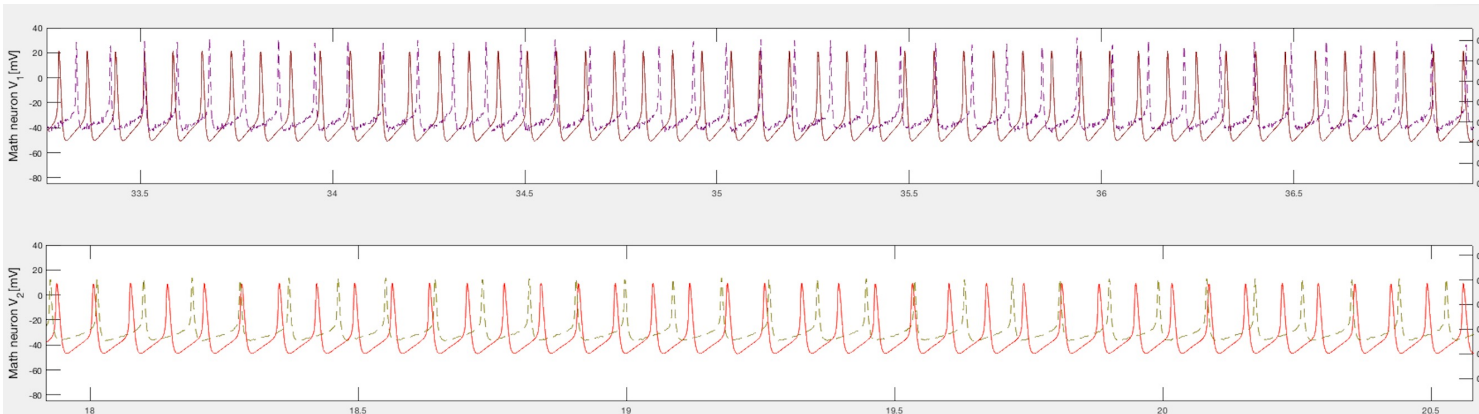
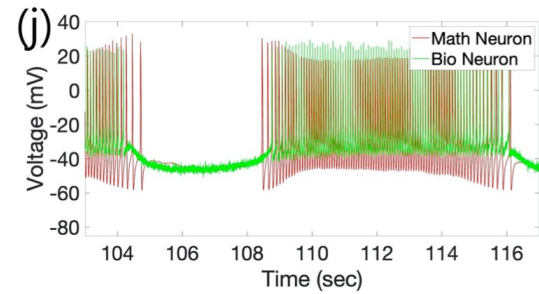
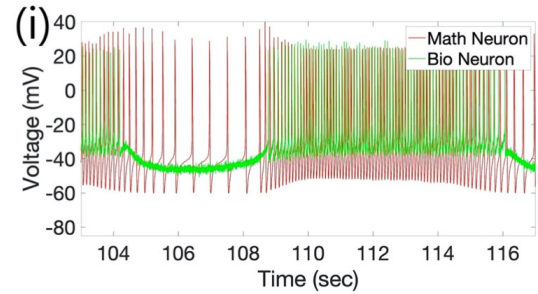
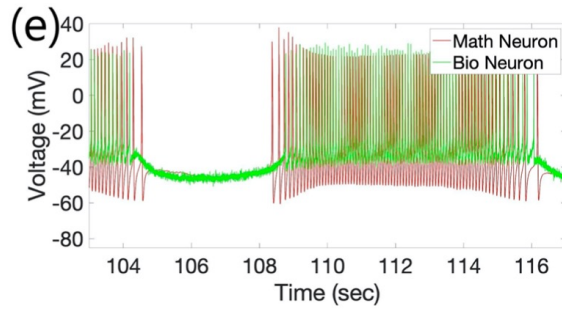
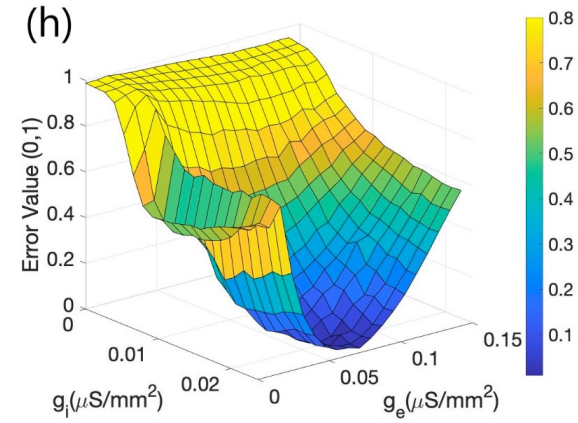
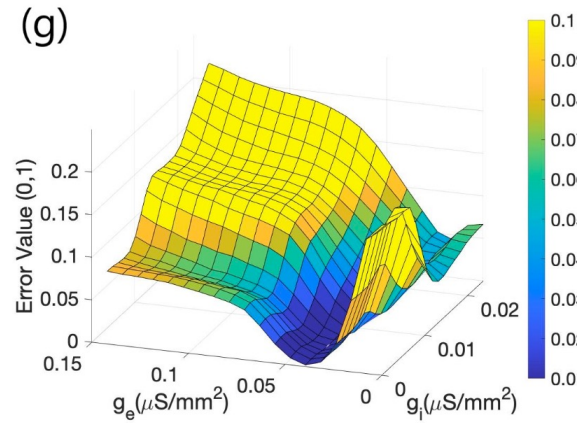
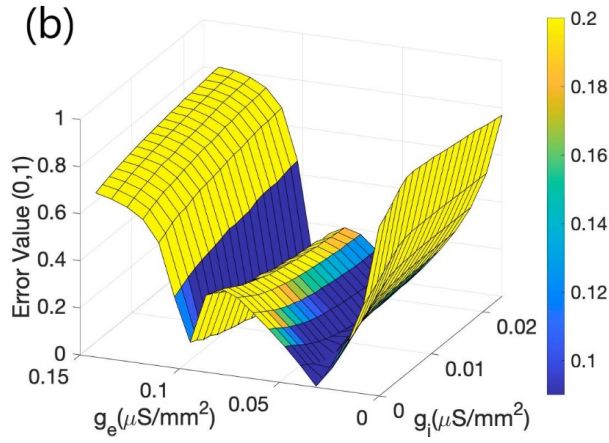


# Hybrid training: math neurons + neurophysiology

in curare

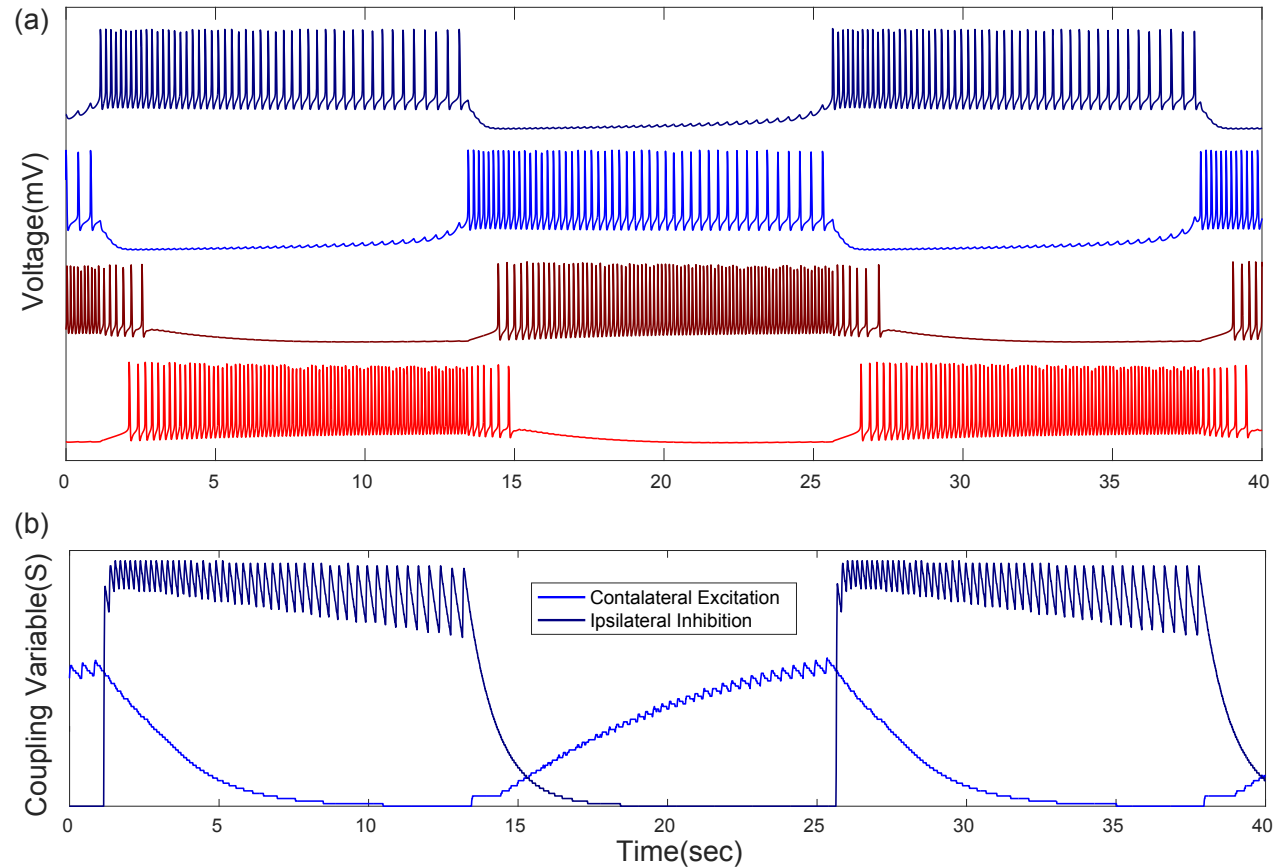
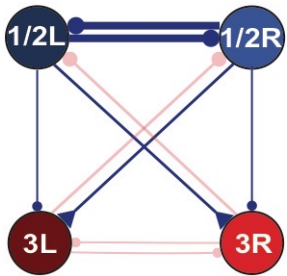


# Training math neurons with neurophys: **machine learning**

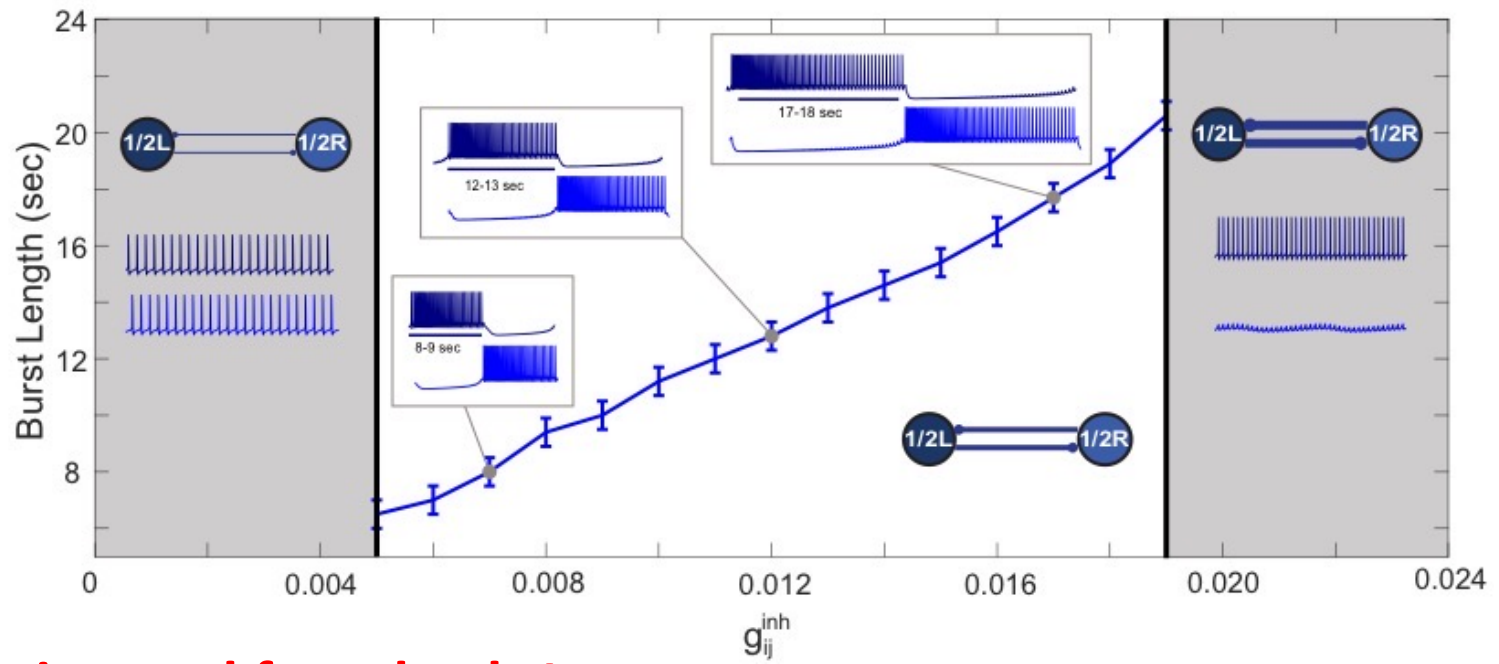


# Curare network model and its calibration

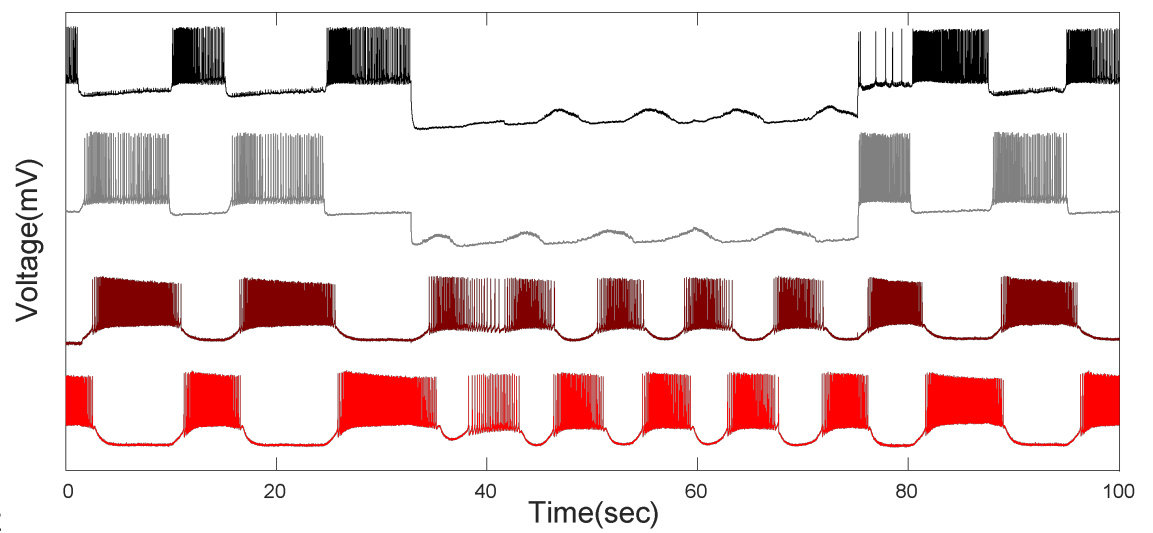
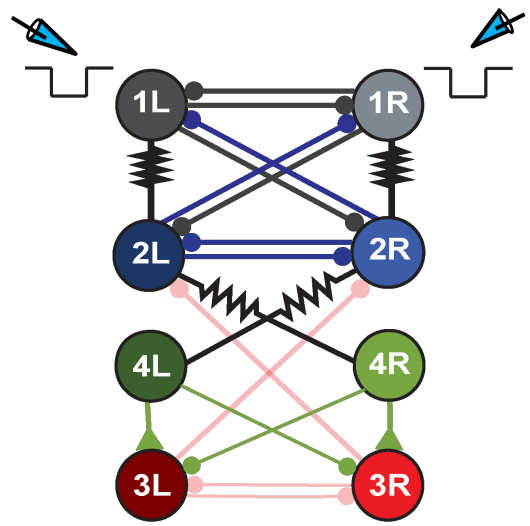
- Delay and tail are controlled by the interplay of contralateral excitation and ipsilateral inhibition.
- At the burst initiation inhibition overrules excitation while the opposite happens at the end of the



# HCO calibration

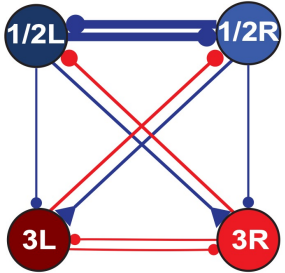
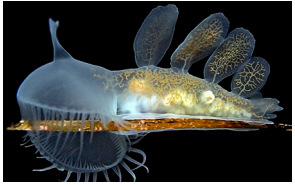


## Experimental fact check 1

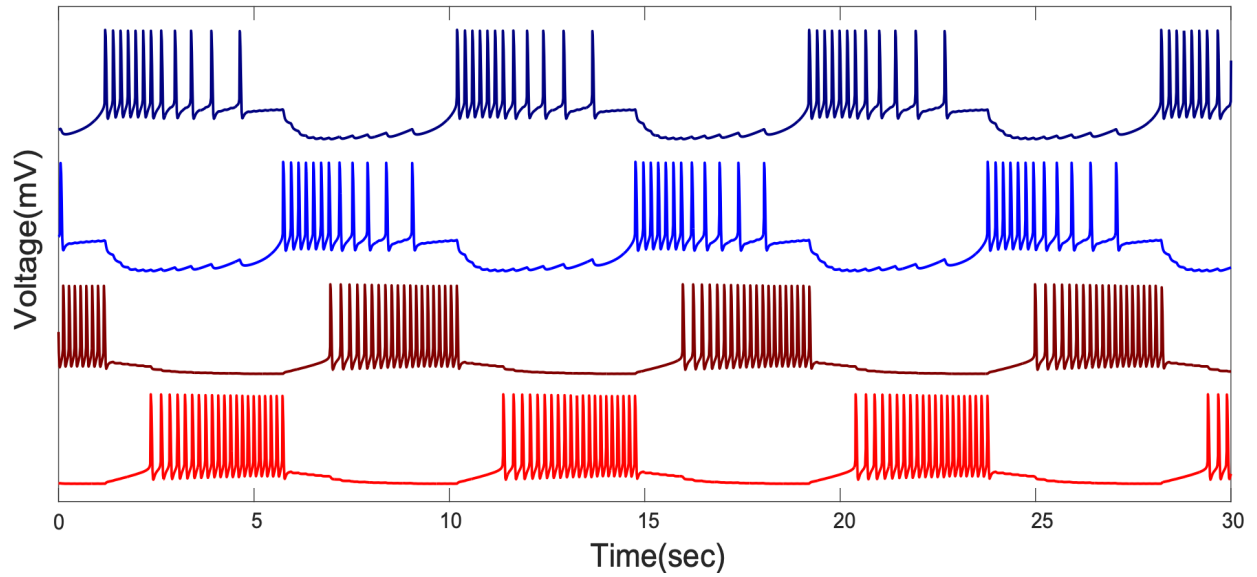


Courtesy: Akira Sakurai and Paul Katz

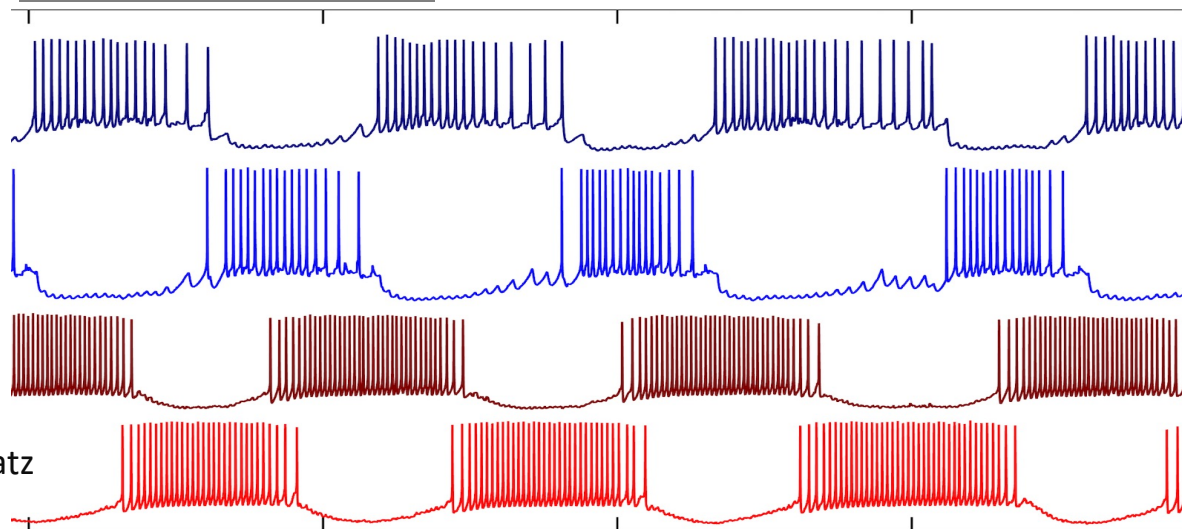
# Control swim cpg: normal saline



math neurons

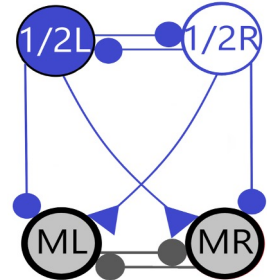


neurophys recordings

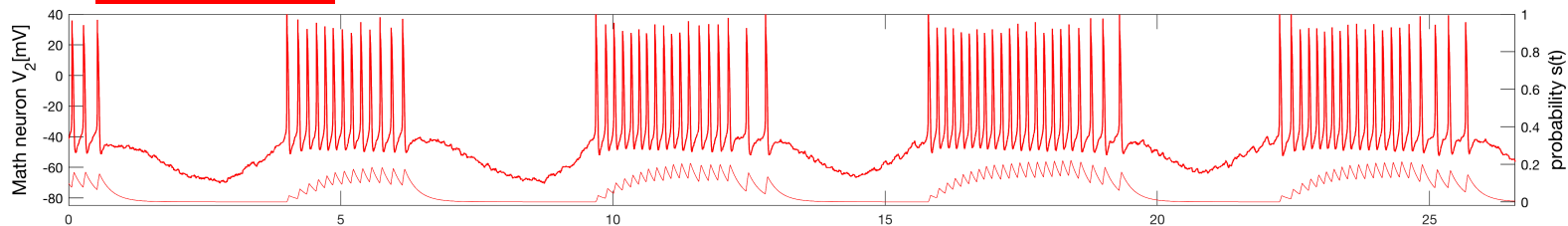
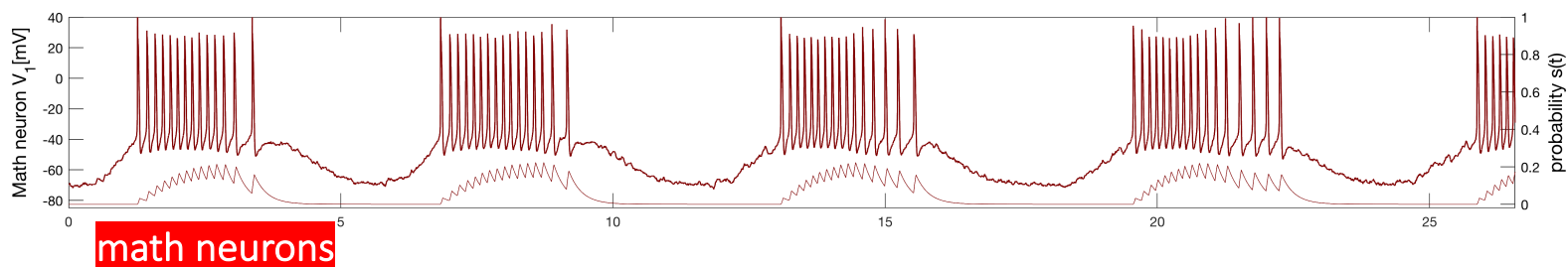
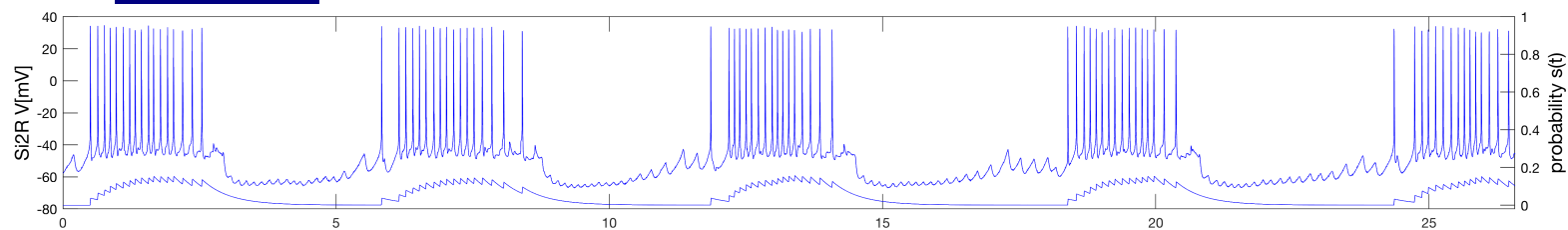
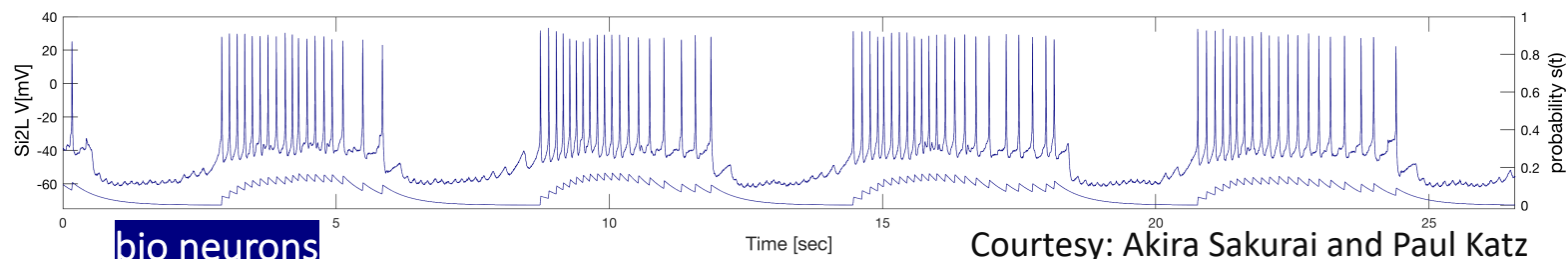


Courtesy: Akira Sakurai and Paul Katz

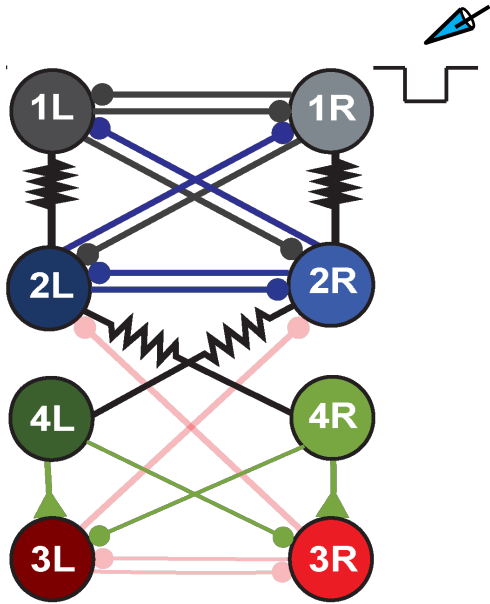
# Hybrid training math neurons with neurophysiology



## control swim

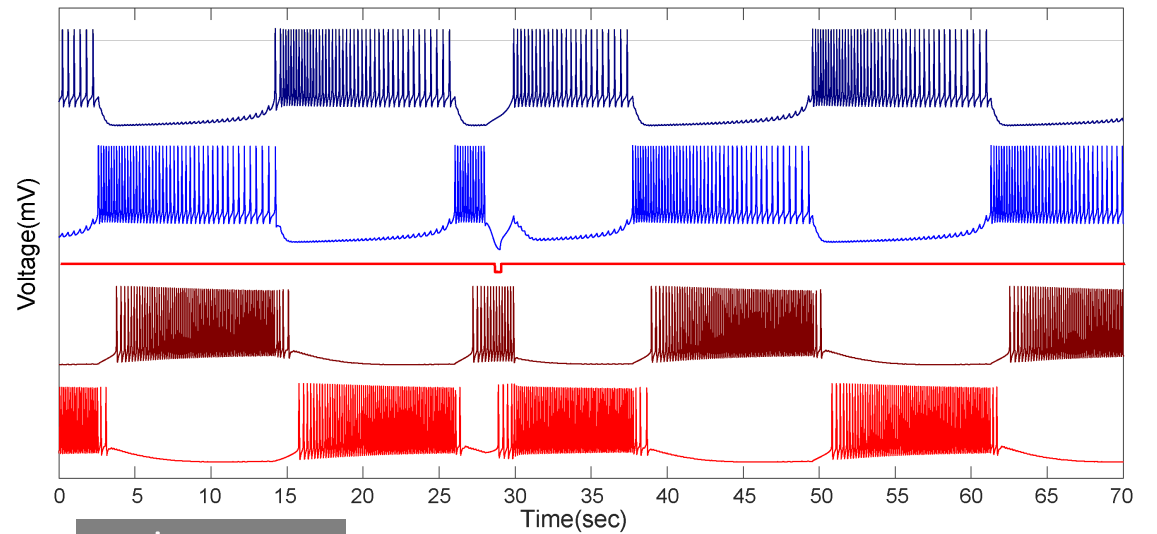
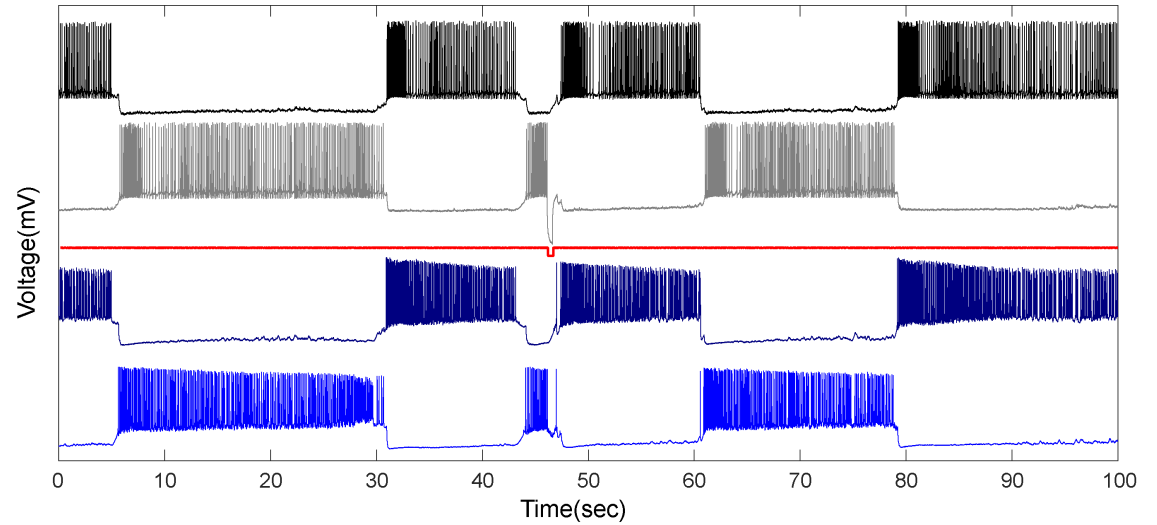


# CPG model fact check 2



neurophys recordings

Courtesy: Akira Sakurai and Paul Katz

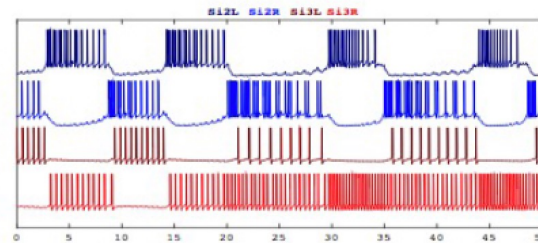
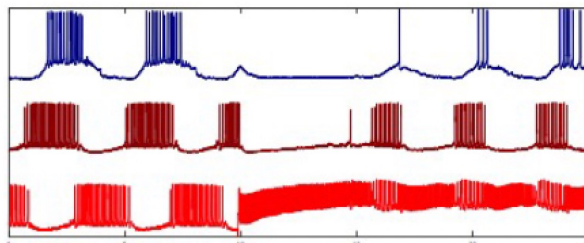
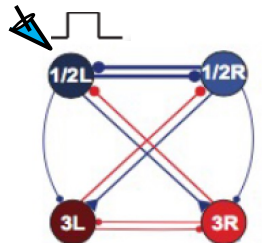
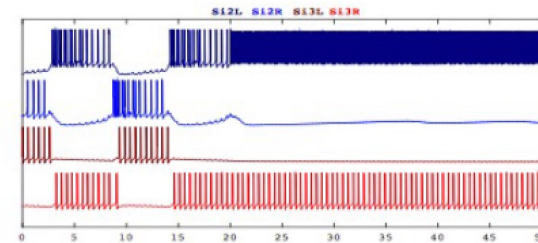
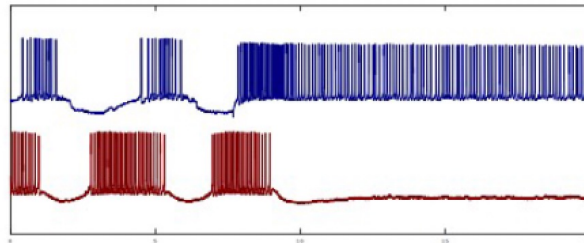
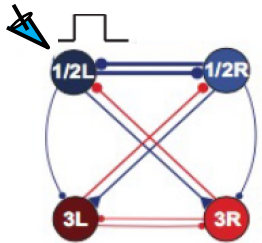
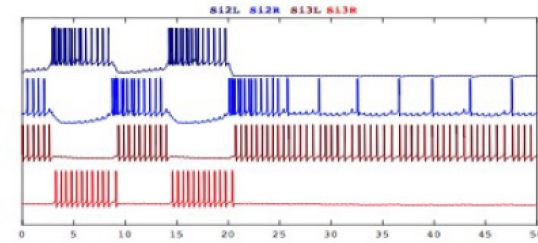
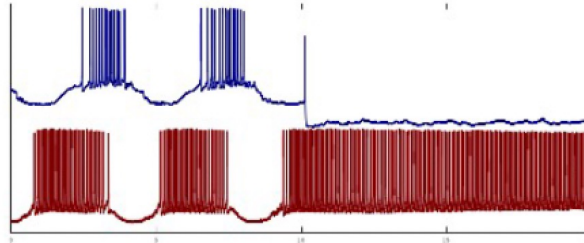
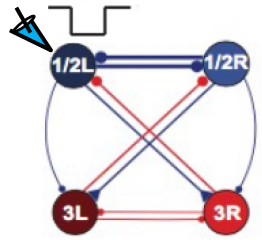


math neurons

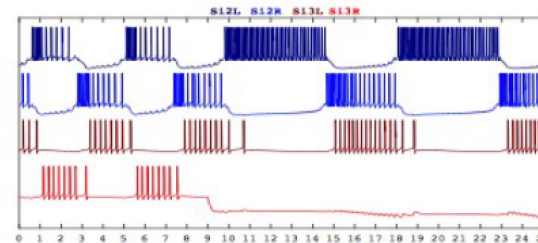
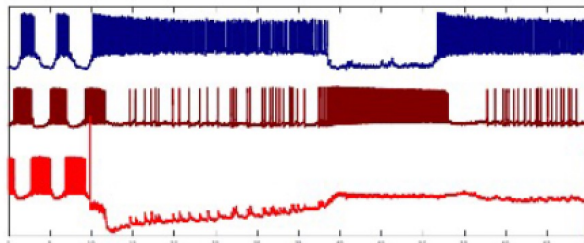
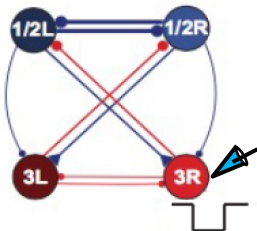
# FACT CHECKS : perturbations

Biological CPG

Mathematical CPG



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# Acknowledgments : NeurDS lab



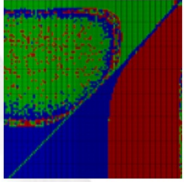
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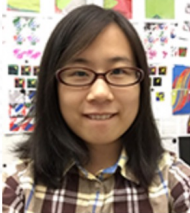
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