

# Dynamical Aspects of Denatured Morris-Lecar Neurons

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# Collaborators



(a) Hammed O. Fatoyinbo



(b) Sishu S. Muni



## A brief survey of computational neuron dynamics models

- ▶ In 1952 Alan Hodgekin and Andrew Huxley developed a conductance-based model of how action potentials in neurons are propagated.

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- ▶ In 1952 Alan Hodgekin and Andrew Huxley developed a conductance-based model of how action potentials in neurons are propagated.
- ▶ This is mathematically modeled using a continuous-time dynamical system (ODEs), characterising the properties of excitable cells like neurons.

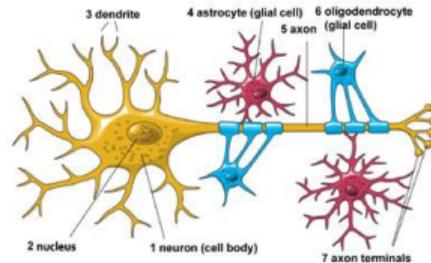


Figure: Schematic of a functional neuron<sup>1</sup>.

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- ▶ Specifically, their model explains the time dynamics of action potential propagation in the *squid giant axon* from experiments.

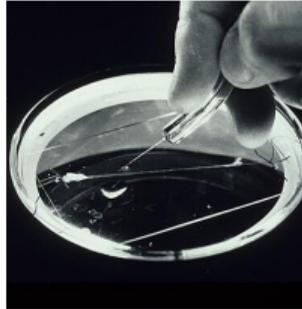


Figure: Squid giant axon<sup>2</sup>.

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<sup>2</sup>Wikipedia (2019)

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- ▶ The Hodgekin-Huxley model uses four state-variables, namely the membrane potential ( $V$ ), and the three uncoupled variables (functions of voltage and time)  $n$ ,  $m$ , and  $h$  for the gated ion (sodium and potassium) channels.

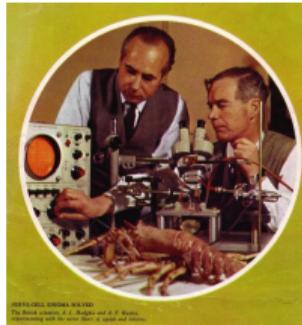


Figure: Hodgekin and Huxley.

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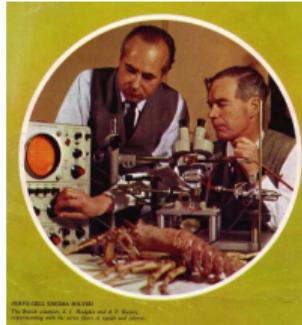


Figure: Hodgekin and Huxley.

- ▶ Hodgkin and Huxley received the 1963 Nobel Prize in Physiology or Medicine for this work<sup>3</sup>.

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- ▶ This model exhibits both Class *I* and *II* excitability.

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## A denatured Morris-Lecar neuron model

- ▶ A simplified variant of the Morris-Lecar neuron was introduced in their book by Schaeffer and Cain, which has been dubbed as the *denatured* Morris-Lecar (dML) model.

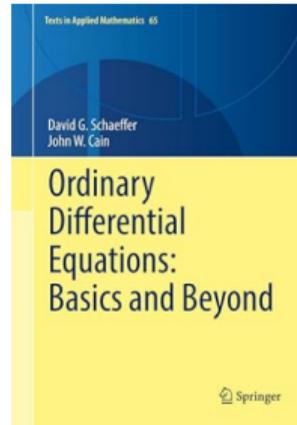


Figure: Book by Scheffer and Cain<sup>5</sup>.

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## A denatured Morris-Lecar neuron model

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- ▶ The exponential term in  $y$  models a negative feedback, corresponding to the dynamics of the refractory period.

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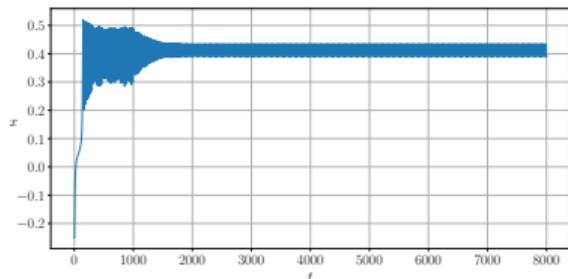
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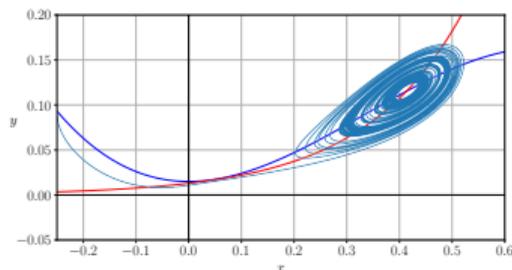
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- ▶ Whereas  $\alpha$  is a control parameter influencing the exponential growth rate of  $y$ .



(a) Time series



(b) Phase portrait

## A denatured Morris-Lecar neuron model

- ▶ The dML model is closely comparable to a FitzHugh-Nagumo type neuron model which can be written as

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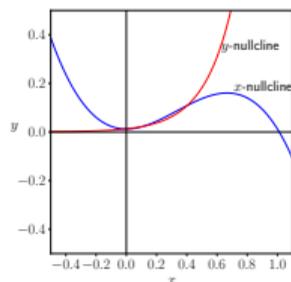
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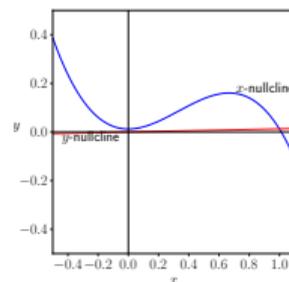
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- ▶ Both models have the same  $x$ -nullclines with differing  $y$ -nullclines. The  $y$ -nullclines curve upward pertaining to the exponential growth term  $Ae^{\alpha x}$ , whereas for FHN the  $y$ -nullclines are straight lines pertaining to the linear term  $Ax$ .



(a) dML



(b) FHN

Figure: For parameter values  $A = 0.0041$ ,  $\alpha = 5.276$ ,  $\gamma = 0.315$ , and  $I = 0.012347$ .

## Qualitative analysis

- ▶ The equilibrium can be computed from the transcendental equations<sup>6</sup>

$$x^2(1 - x) - y + I = 0,$$

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by solving for  $x$ .

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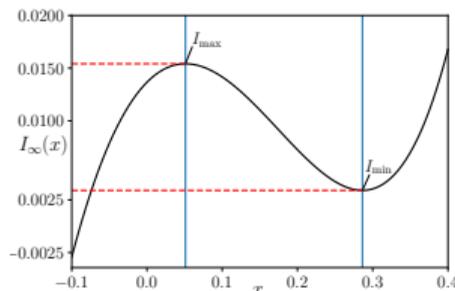
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- ▶ We can write  $I$  as a function of  $x, y$ :

$$I_{\infty}(x) = \frac{A}{\gamma} e^{\alpha x} - x^2(1-x).$$



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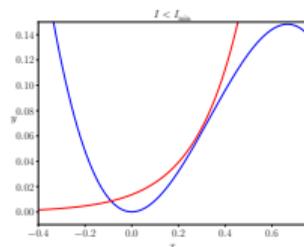
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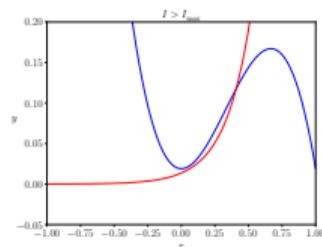
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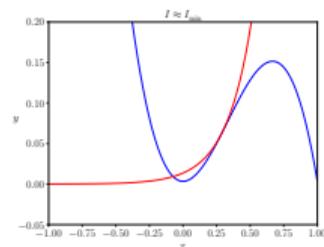
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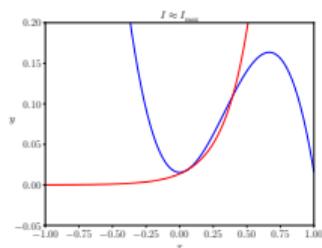
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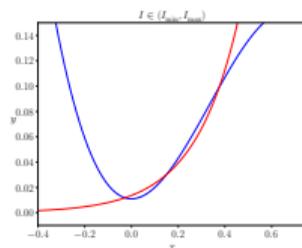
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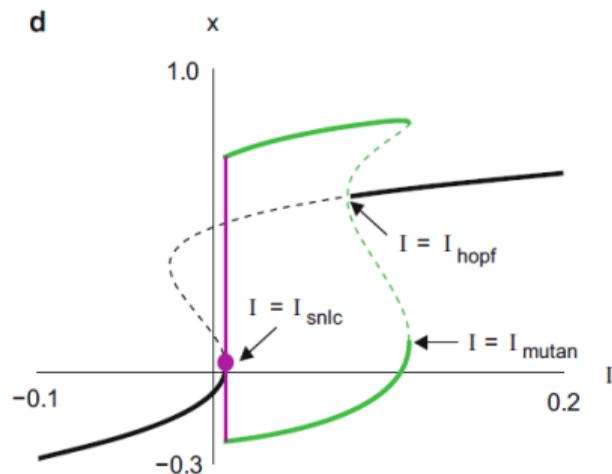
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- ▶ These codimension-one bifurcation computations require hand calculations and might not always be analytically tractable.

# Numerical Bifurcation Analysis



**Figure:** (a) SNLC: Saddle Node Limit Cycle, (b)  $I_{mutan}$ : a mutual annihilation bifurcation occurs at  $I = I_{mutan}$ . See D. Schaeffer and J. Cain, (Springer, 2018).

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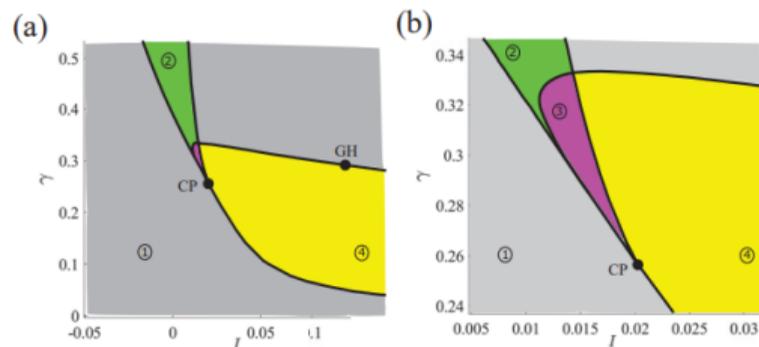


Figure: A codimension-two bifurcation diagram of the dML model in the  $(I, \gamma)$ -plane<sup>7</sup>.

<sup>7</sup>H.O. Fatoyinbo, *et al.* "Numerical bifurcation analysis of improved denatured morris-lecar neuron model". In 2022 international conference on decision aid sciences and applications (DASA) (pp. 55-60). IEEE (2022).

## Effect of Electromagnetic Flux

- ▶ The dML model is perturbed where the membrane potential  $x$  is subjected to an electromagnetic flux term  $\phi$ .

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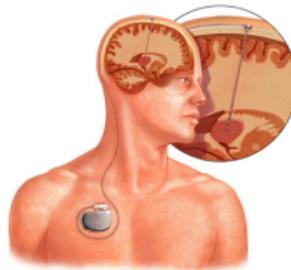
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- ▶ DBS involves putting an electrode deep inside the brain and treating people with mobility conditions.



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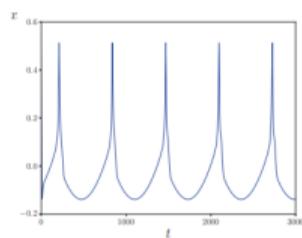
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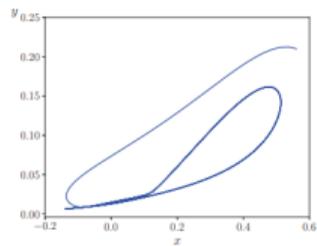
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- ▶ The external current can be modeled as a periodic function  $I = I_0 \sin(\omega t)$ , with  $I_0$  as the current amplitude and  $\omega$  is the angular frequency.

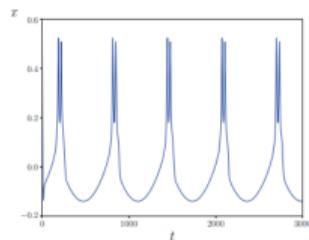
# Effect of Electromagnetic Flux



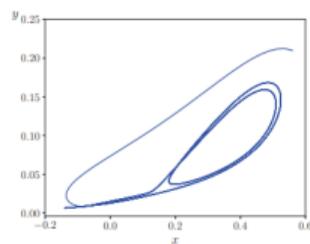
(e)



(f)



(g)



(h)

Figure: Time series and Phase portrait with increasing  $I_0$

## Effect of Electromagnetic Flux

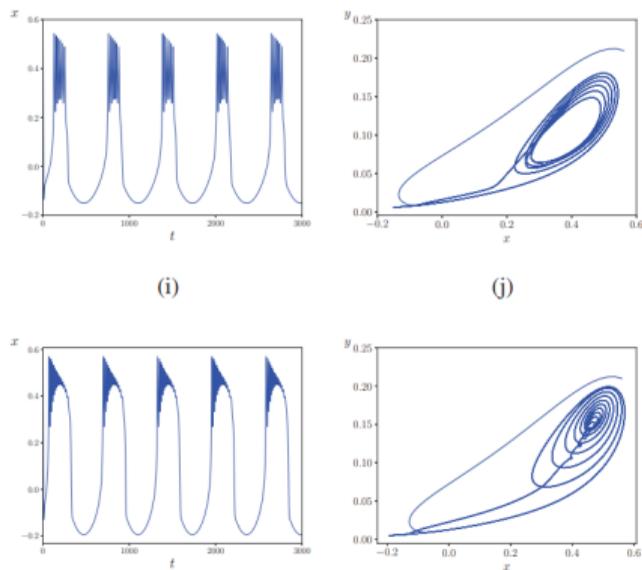


Figure: Time series and Phase portrait with increasing  $I_0$

- The external periodic current produces multiple-mode bursting activities.

## A slow-fast variant

- ▶ The slow-fast version of the dML also introduced by Schaeffer and Cain is given by

$$\dot{x} = x^2(1 - x) - y + I,$$

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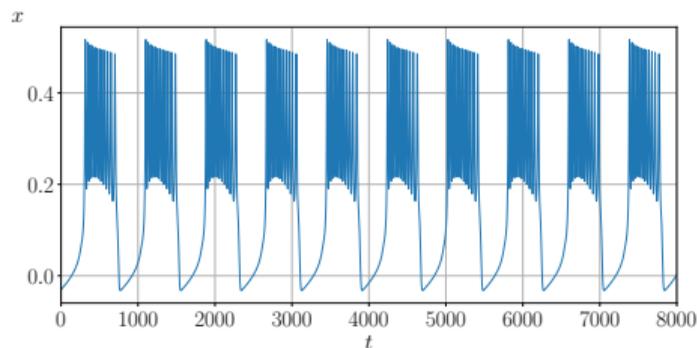
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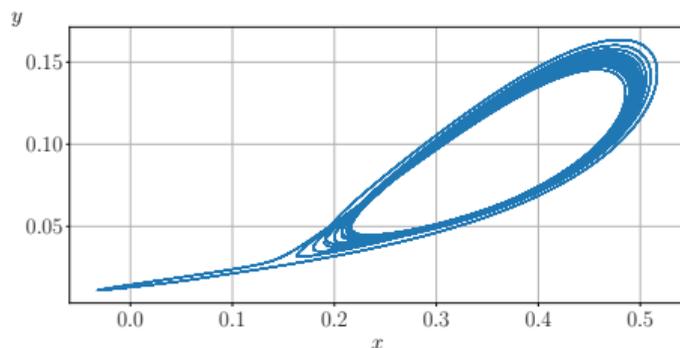
is the smoothed-out version of a step function.

- ▶ the parameter  $\varepsilon$  is a small perturbation parameter that separates the time scales and is sometimes referred to as the *time-scale parameter*.

## A slow-fast variant



(a) Time series



(b) Phase portrait

**Figure:** We observe a periodic bursting behavior. Here  $A = 0.0041$ ,  $\alpha = 5.276$ ,  $\gamma = 0.315$ , and  $\varepsilon = 0.001$ . The initial condition  $x(0)$  is sampled uniformly from the range  $[-1, 1]$ . Furthermore  $(y(0), I(0)) = (0.1, 0.012347)$ .

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- ▶ Neurons manifest repeated rapid bursting with quiet intervals.

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- ▶ This bistability ultimately leads to bursting.
- ▶ This would be possible if  $I$  were allowed to vary slowly in time.
- ▶ This kind of bursting is classified as *fold/homoclinic* type<sup>8</sup> where the transition from the resting state to the spiking limit cycle occurs via a saddle-node (fold) bifurcation and from the spiking state to the resting state via a saddle homoclinic orbit bifurcation.

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# Fold/homoclinic burster

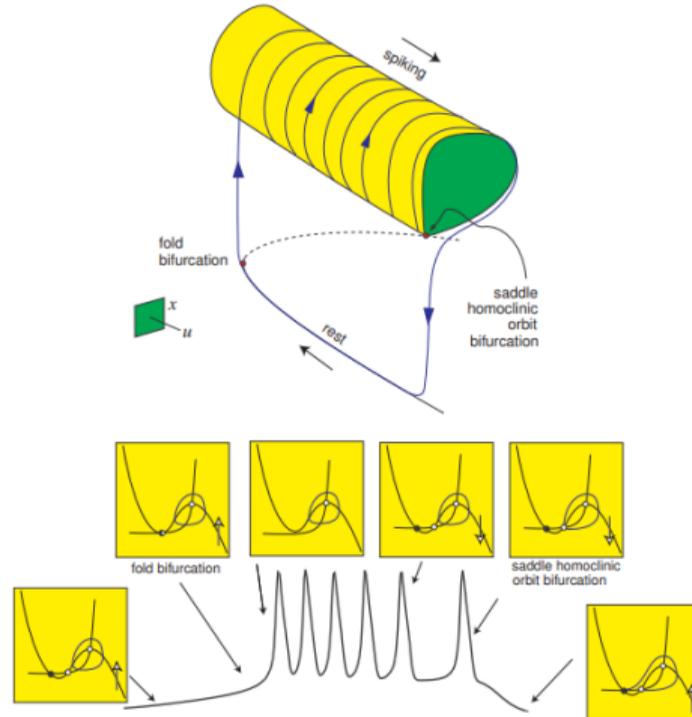


Figure 9.25: “Fold/homoclinic” bursting. The resting state disappears via saddle-node (fold) bifurcation, and the spiking limit cycle disappears via saddle homoclinic orbit bifurcation.

## Qualitative analysis

- ▶ To compute  $X^*$ , the first step requires solving the nonlinear transcendental equation given by,

$$x^{*2} (1 - x^*) - \frac{A}{\gamma} e^{\alpha x^*} + I'(x^*) = 0,$$

which is analytically intractable and can only be solved using a numerical solver.

- ▶ The Jacobian of the system (1) is given by

$$J = \begin{bmatrix} x(2 - 3x) & -1 & 1 \\ \alpha A e^{\alpha x} & -\gamma & 0 \\ \mathcal{L}(x) & 0 & -\varepsilon \end{bmatrix}.$$

## Qualitative analysis

► Here

$$\tau(x) = x(2 - 3x) - \gamma - \varepsilon$$

is the trace of  $J$ ,

$$\sigma(x) = \gamma\varepsilon - (\gamma + \varepsilon)x(2 - 3x) + \alpha Ae^{\alpha x} - \mathcal{L}(x)$$

is the second trace of  $J$ , and

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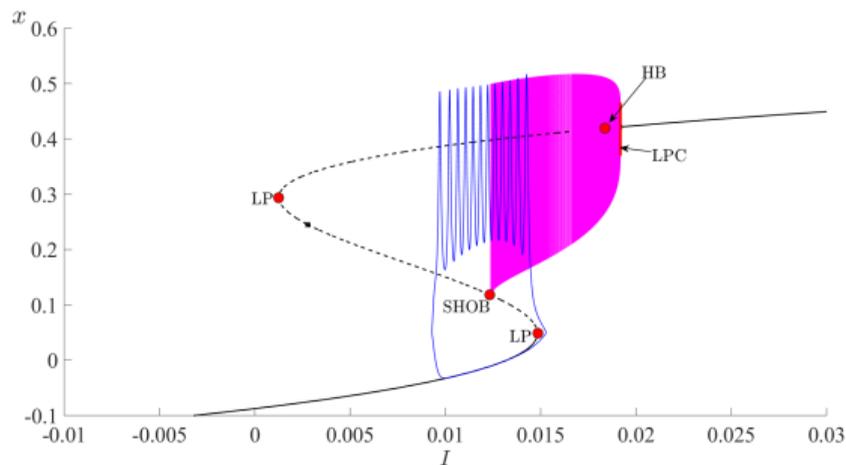
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- ▶ The eigenvalues  $\mu_i$ ,  $i = 1, \dots, 3$  can be evaluated from  $J$  at the equilibrium point by solving the third order characteristic equation  $P_3(\mu) = 0$

## Codimension-one bifurcation diagram



**Figure:** Codimension-one bifurcation diagram of the fast subsystem with superimposition of the periodic bursting of the slow-fast system. Solid [dashed] curves correspond to stable [unstable] solutions and magenta curves are limit cycles. HB, LP, SHOB, and LPC represent Hopf bifurcation, saddle-node bifurcation of an equilibrium, saddle-homoclinic orbit bifurcation and saddle-node bifurcation of cycles respectively. Here  $A = 0.0041$ ,  $\alpha = 5.276$ ,  $\gamma = 0.315$ , and  $\varepsilon = 0.001$  with the initial condition as  $(x(0), y(0), I(0)) = (0.5, 0.1, 0.012347)$ .

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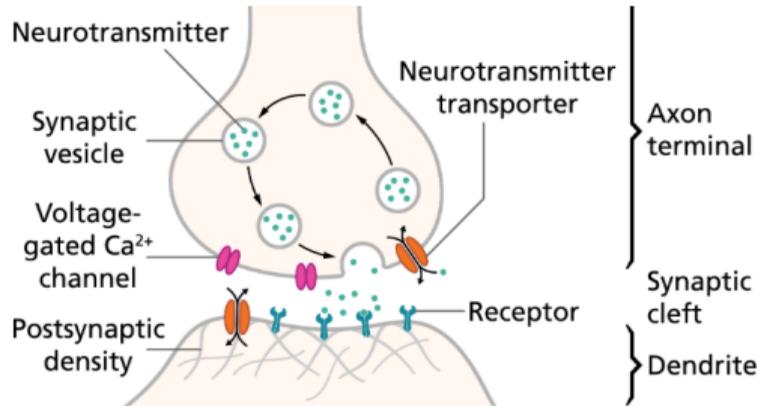
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<sup>9</sup>Source: [https:](https://qbi.uq.edu.au/brain-basics/brain/brain-physiology/action-potentials-and-synapses)

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# Neuron Synapse

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- ▶ Synapses convert an electrical signal propagated by a neuron into a chemical signal in the form of neurotransmitter release.
- ▶ The neurotransmitter can either excite or inhibit the second neuron from firing its own action potential<sup>9</sup>.



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## Two-coupled dML neurons

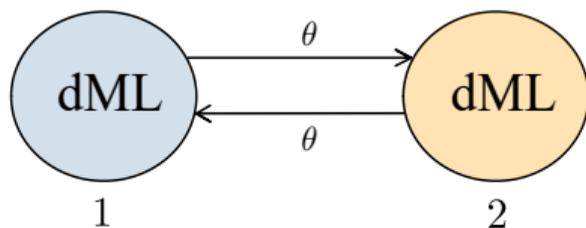
- ▶ Two connected neurons can be mathematically modeled using a directional coupling strategy.

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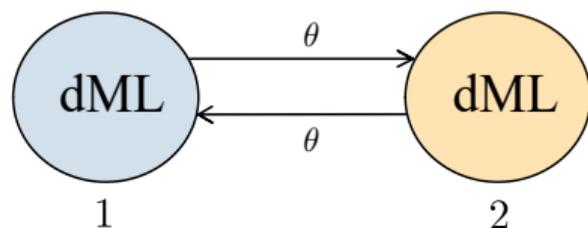


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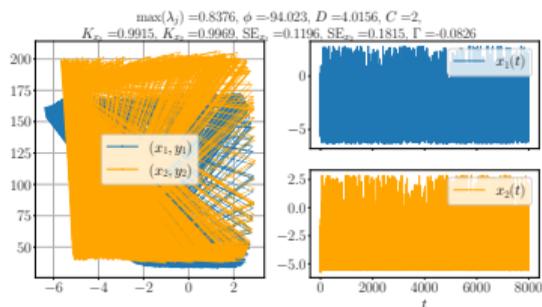
- ▶ The model equations are

$$\begin{aligned} \dot{x}_1 &= x_1^2(1 - x_1) - y_1 + I_1 + \theta(x_2 - x_1), & \dot{y}_1 &= Ae^{\alpha x_1} - \gamma y_1, & \dot{I}_1 &= \varepsilon(I'(x_1) - I_1), \\ \dot{x}_2 &= x_2^2(1 - x_2) - y_2 + I_2 + \theta(x_1 - x_2), & \dot{y}_2 &= Ae^{\alpha x_2} - \gamma y_2, & \dot{I}_2 &= \varepsilon(I'(x_2) - I_2). \end{aligned}$$

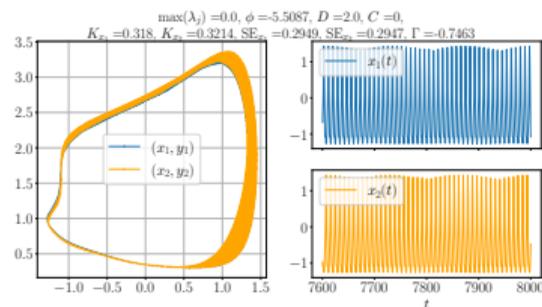
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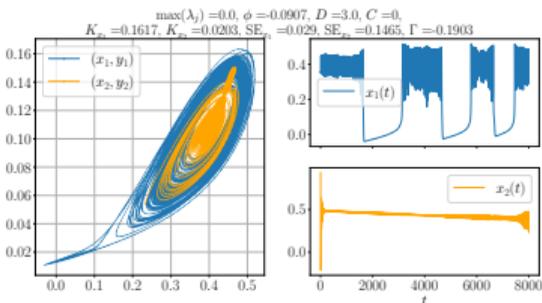
# Time series & phase portraits



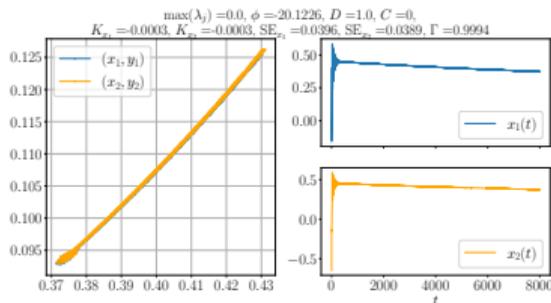
(a)  $\theta = -15$ ,  $\varepsilon = 0.0002$ : Hyperchaotic



(b)  $\theta = -1$ ,  $\varepsilon = 0.0002$ : Quasiperiodic

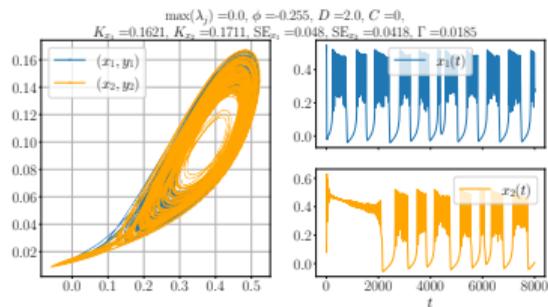


(c)  $\theta = 0$ ,  $\varepsilon = 0.0002$ : irregular bursting

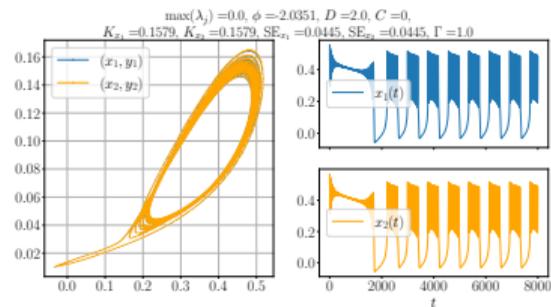


(d)  $\theta = 10$ ,  $\varepsilon = 0.0002$ : Decay oscillations

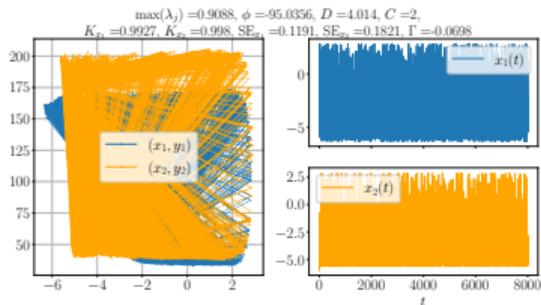
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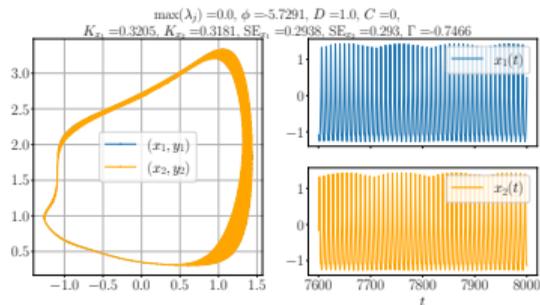
(e)  $\theta = 0, \varepsilon = 0.001$ : Mixed mode



(f)  $\theta = 1, \varepsilon = 0.001$ : Mixed mode

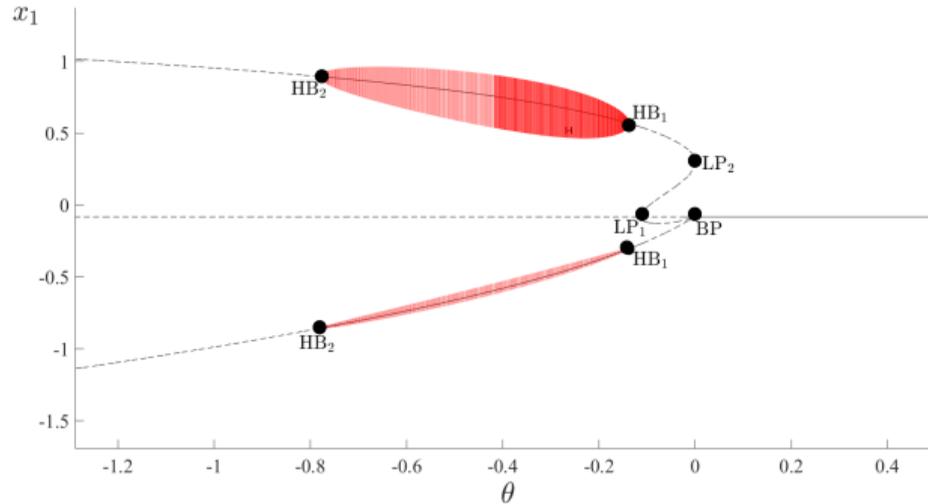


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# Codimension-one bifurcation diagram



**Figure:** Codimension-one bifurcation diagram of the coupled fast subsystem. Solid [dashed] curves correspond to stable [unstable] solutions and red curves are limit cycles. HB, LP, and BP represent Hopf bifurcation, saddle-node bifurcation of an equilibrium and branch point respectively.

## The 0 – 1 test for detecting chaos

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$$p_e(n) = \sum_{k=1}^n x(k) \cos(ek),$$
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- ▶ The  $p_e$  vs.  $q_e$  plot will typically be bounded for regular dynamics or will approximately behave like a two-dimensional diffusive Brownian motion with evolution rate  $\sqrt{n}$  and zero drift for chaos.

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- ▶ This can be inferred from the mean square displacement, given by

$$m_e(n) = \frac{1}{M} \sum_{i=1}^M \left[ \{p_e(i+n) - p_e(i)\}^2 + \{q_e(i+n) - q_e(i)\}^2 \right].$$

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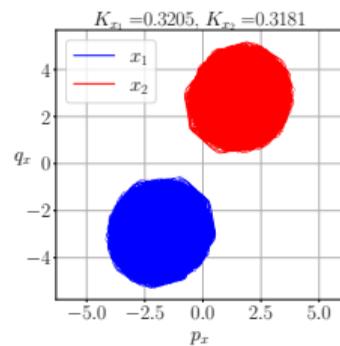
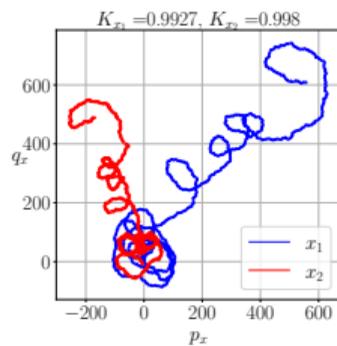
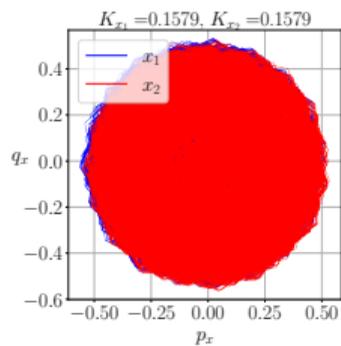
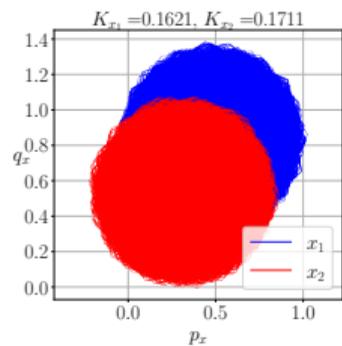
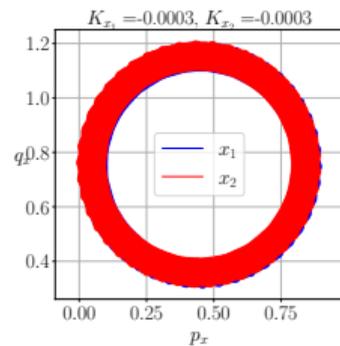
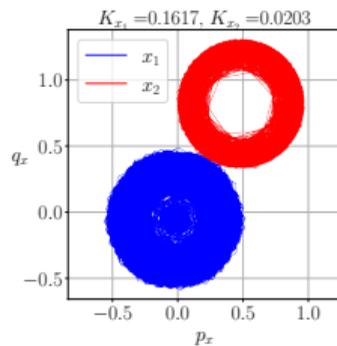
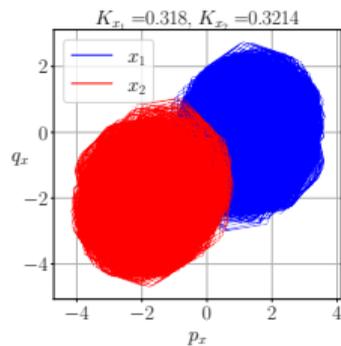
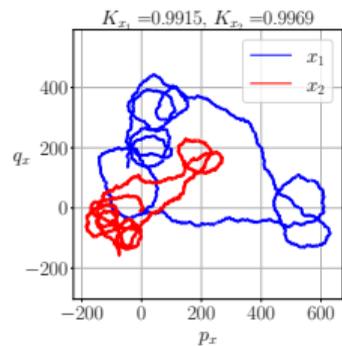
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- ▶  $k_e \sim 1$  indicates chaos and  $k_e \sim 0$  indicates regularity.

# The 0 – 1 test for detecting chaos



## Sample entropy: for measuring complexity

- ▶ The *sample entropy* quantifies the complexity of the time series.

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<sup>12</sup>J. Richman and J. Moorman, Physiological time-series analysis using approximate entropy and sample entropy, Am. J. Physiol. Heart Circ. Physiol. 278 (2000).

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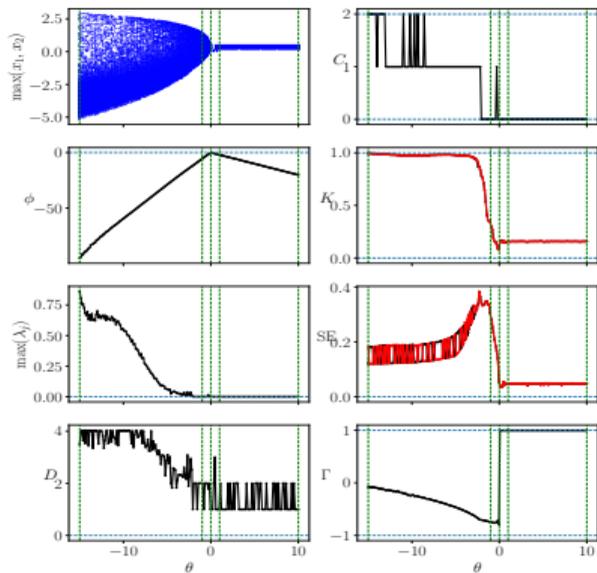
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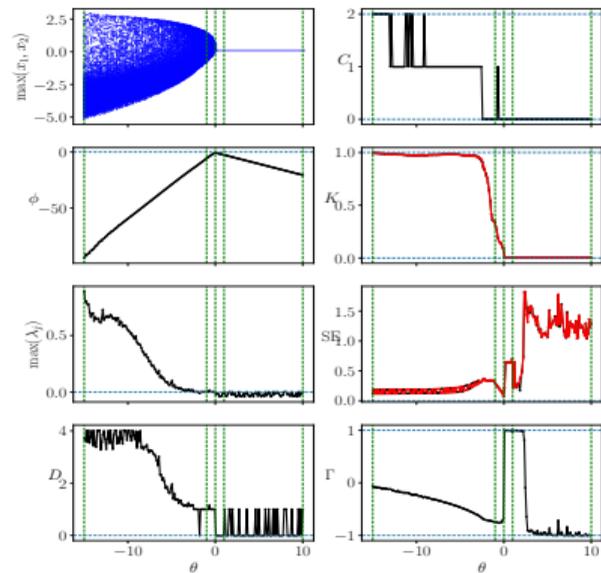
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- ▶ When  $\Gamma = 1$  it means both the nodes are in phase and completely synchronized, whereas  $\Gamma = -1$  represents anti-phase synchrony.

# Numerics



(a)  $\varepsilon = 0.001$



(b)  $\varepsilon = 0.1$

## Fractional order version

- ▶ Now we model the dML neuron as a set of *Caputo-type* fractional order differential equations. Fractional-order systems incorporate memory effects.

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- ▶ Here  $C$  stands for “Caputo” and  $\beta \in (0, 1]$  is the order of the integral, also known as the *memory index*.

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## Qualitative analysis

### Theorem

*Suppose*

- i)  $x^*(2 - 3x^*) - \gamma > 0$ , and
- ii)  $-\gamma x^*(2 - 3x^*) + \alpha A e^{\alpha x^*} < 2\sqrt{-\gamma - x^*(2 - 3x^*)} \cos(\frac{\beta\pi}{2})$ .

*Then an equilibrium point  $(x^*, y^*)$  of the fractional order system is asymptotically stable.*

### Theorem

*Suppose  $I \in (I_{\min}, I_{\max})$ . Then this branch of equilibrium points is completely unstable.*

- From the above theorem we can directly see that  $\delta(x^*) < 0$  implies one of the two eigenvalues is positive and the other negative, meaning the equilibrium point on this branch is a saddle, irrespective of the fractional order  $\beta \in (0, 1]$ .

### Theorem

*Suppose  $I = I_{\min}$  or  $I = I_{\max}$ . Then the fractional order system has a saddle-node bifurcation.*

## Qualitative analysis

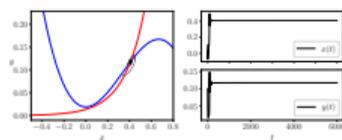
### Theorem

Suppose  $I < I_{\min}$  or  $I > I_{\max}$ . Then

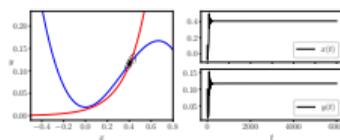
- i) the stability of an equilibrium point of the system depends on the sign of  $\tau(x^*)$ ,
- ii) for  $\tau(x^*) \geq 0$  the equilibrium is asymptotically stable if and only if the order

$$\beta < \beta^* = \frac{2}{\pi} \cos^{-1} \left( \min \left( 1, \frac{-\gamma + x^*(2 - 3x^*)}{2\sqrt{\alpha A e^{\alpha x^*} - \gamma x^*(2 - 3x^*)}} \right) \right).$$

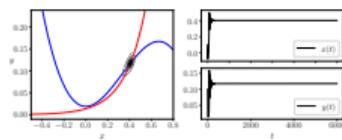
# Phase portraits



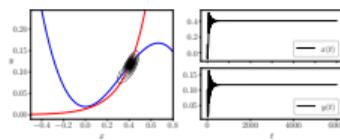
(a)  $\beta = 0.9$



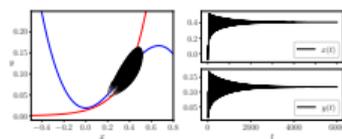
(b)  $\beta = 0.92$



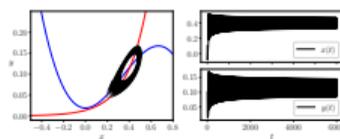
(c)  $\beta = 0.94$



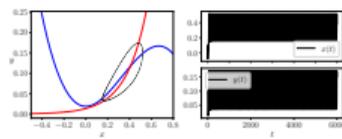
(d)  $\beta = 0.96$



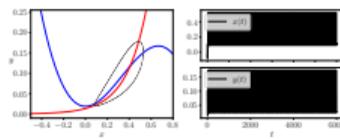
(e)  $\beta = 0.98$



(f)  $\beta = \beta^*$

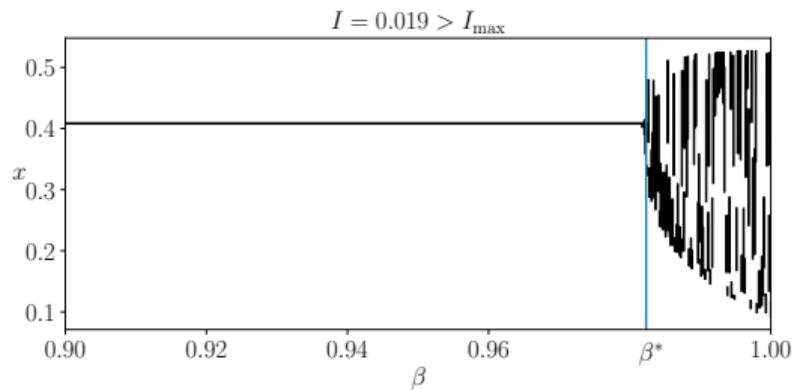


(g)  $\beta = 0.99$

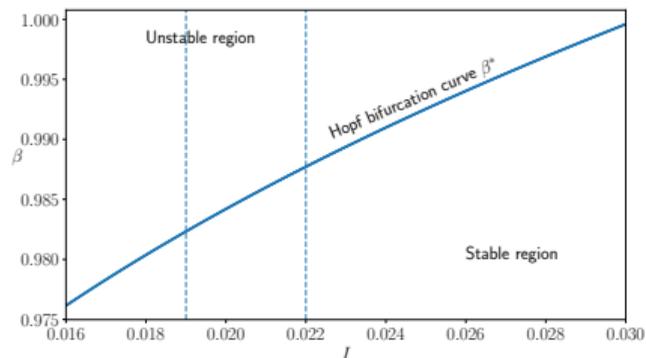


(h)  $\beta = 1$

# A crude bifurcation diagram



(a)  $\beta^* \approx 0.98233$



(b) Hopf bifurcation curve

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- ▶ An adaptive coupling strategy based on the Hebbian learning rule is justifiable.
- ▶ It would be intriguing to investigate the dynamical behaviour of the coupled neurons as a game-theoretic model.

The End

Thank you! Questions?