An artificial CPG inspired by a pond snail

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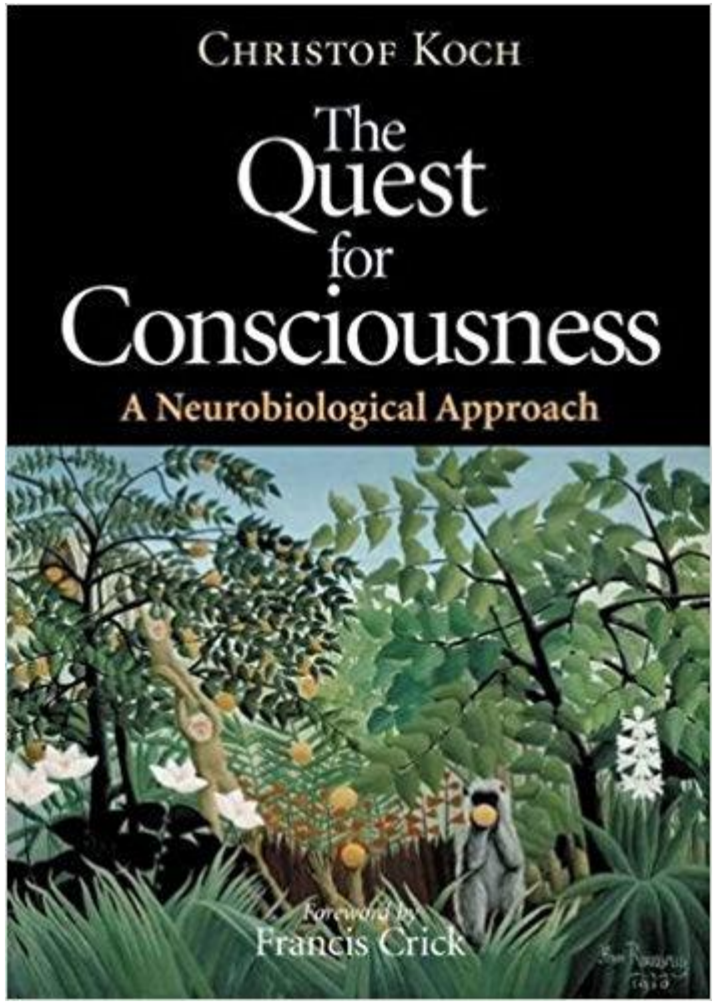
Motivation

- Quest for consciousness and cognition is never ending



People are curious about the origin of consciousness.

“How do the elemental feelings and sensations making up conscious experience, the redness of red and painfulness of pain, arise from the concerted actions of nerve cells and their associated synaptic and molecular processes?”

Benefit from bio-inspiration

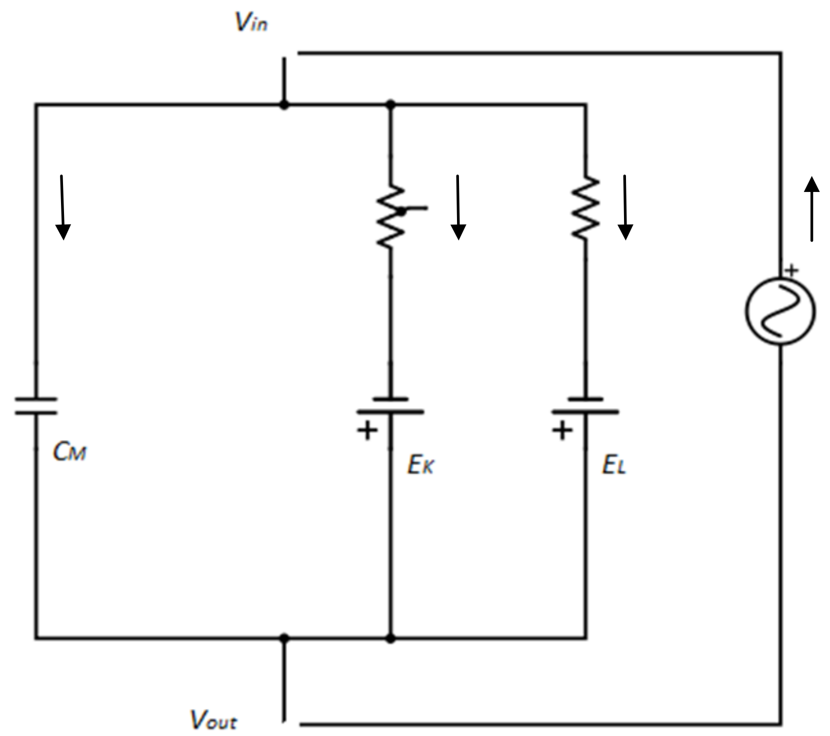
- Artificial Neural Network is a great success in deep learning/machine learning, which is inspired by biological neural networks
- Artificial CPGs can be used in control system, such as robots

Neuron excitability and Hodgkin-Huxley Model

- Human brain is fascinating, it has about 100 billion neurons and many more neuroglia (glial cells)
- Neurons are the basic information processing structures

$$C_M \frac{dV}{dt} + I_{ion} + I_L = I_{ext}$$

$$I_{ion} = \sum_k I_k = \sum_k G_k (V - E_k)$$



Ion channels and gating variable

$$C_M \frac{dV}{dt} + g_{Na} m^3 h(V - E_{Na}) + g_K n^4 (V - E_K) + g_L (V - E_L) = I_{app}$$

$$\frac{dx}{dt} = -\frac{1}{\tau_x(u)}[x - x_\infty(u)], \qquad x \in \{m, h, n\}$$

$$\frac{dx}{dt} = \alpha_x(1 - x) + \beta_x x, \qquad x \in \{m, n, h\}$$

$\alpha(V)$ and $\beta(V)$ are determined by experimental measurement and can be generalized as the form:

$$\frac{A(V - B)}{e^{\left(\frac{V-B}{C}\right)} - D}$$

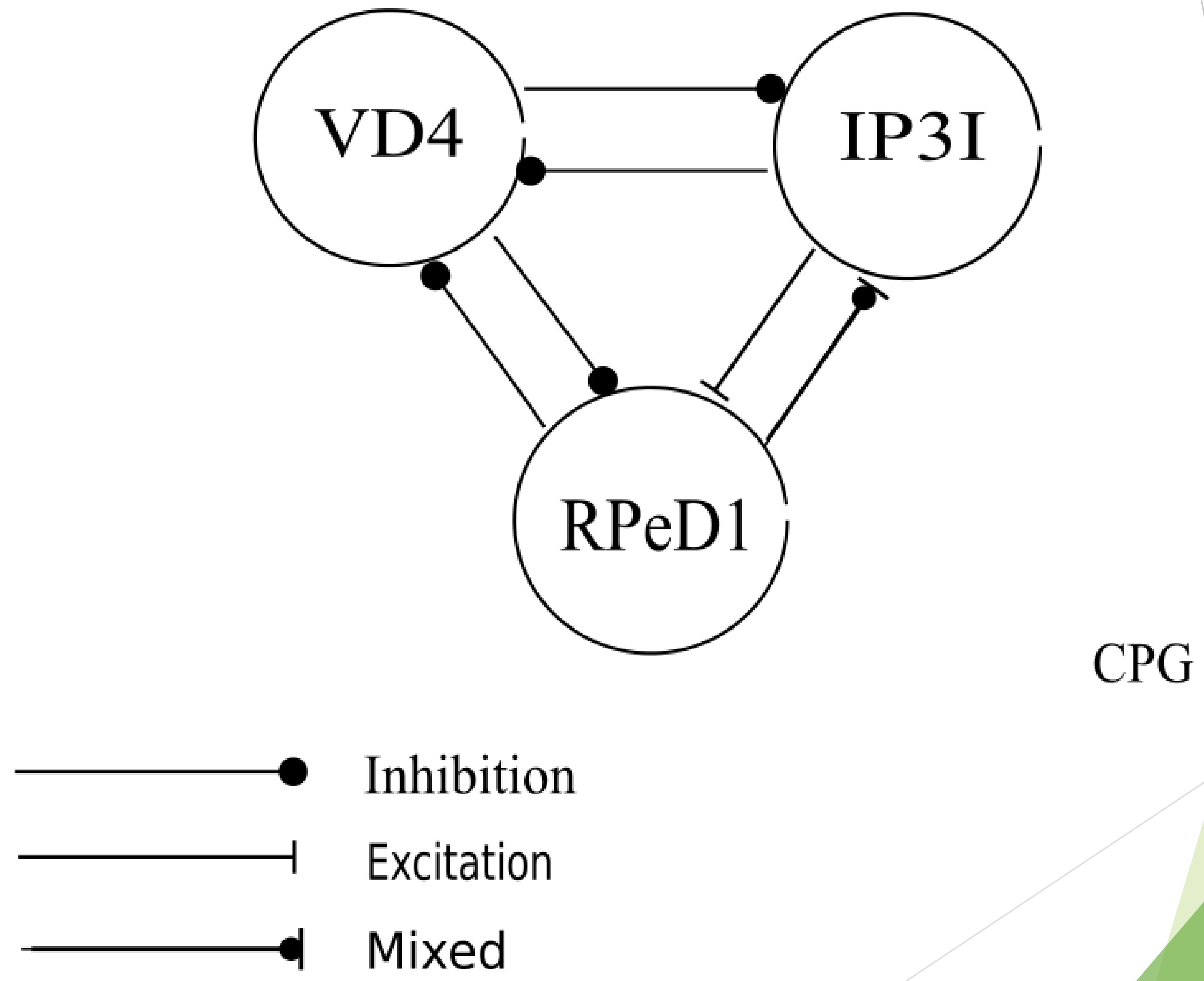
Background

- Trying to reconstruct the respiratory CPG (Central Pattern Generator) of a snail while no enough experimental data available, instead, choose general existing model and approach the behavior of original system by adjusting parameters and adding delay
- The network is assumed to consist of a Half Center Oscillator (HCO)

  VD4 + IP3I

  and a pacemaker neuron

  RPeD1


VD4
IP3I
RPeD1
CPG
Inhibition
Excitation
Mixed

Difficulties

- The internal mechanism remains like black-box without information on ion channels for building a detailed Hodgkin-Huxley type model
- Totally reverse engineering

Behavior of original system

- Individual neuron

A) Neuron VD4 is normally silent when cultured individually but with the injection of depolarizing current, bursts of action potentials are evoked.

B) In similar manner IP3I is silent until the injection of depolarizing current.

C) On the other hand RPeD1 is normally spontaneously active but with the injection of depolarizing current increases its firing frequency.

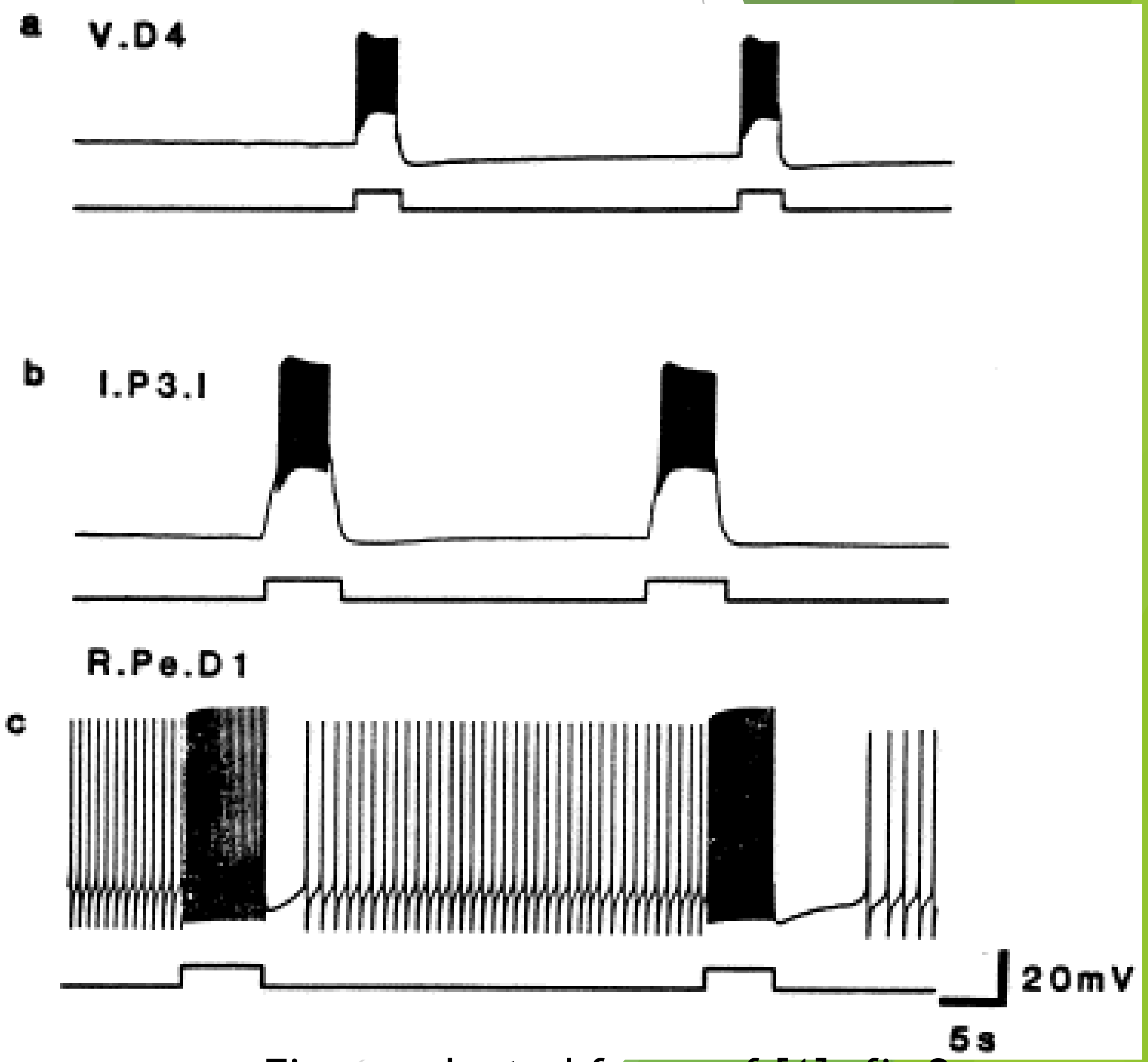
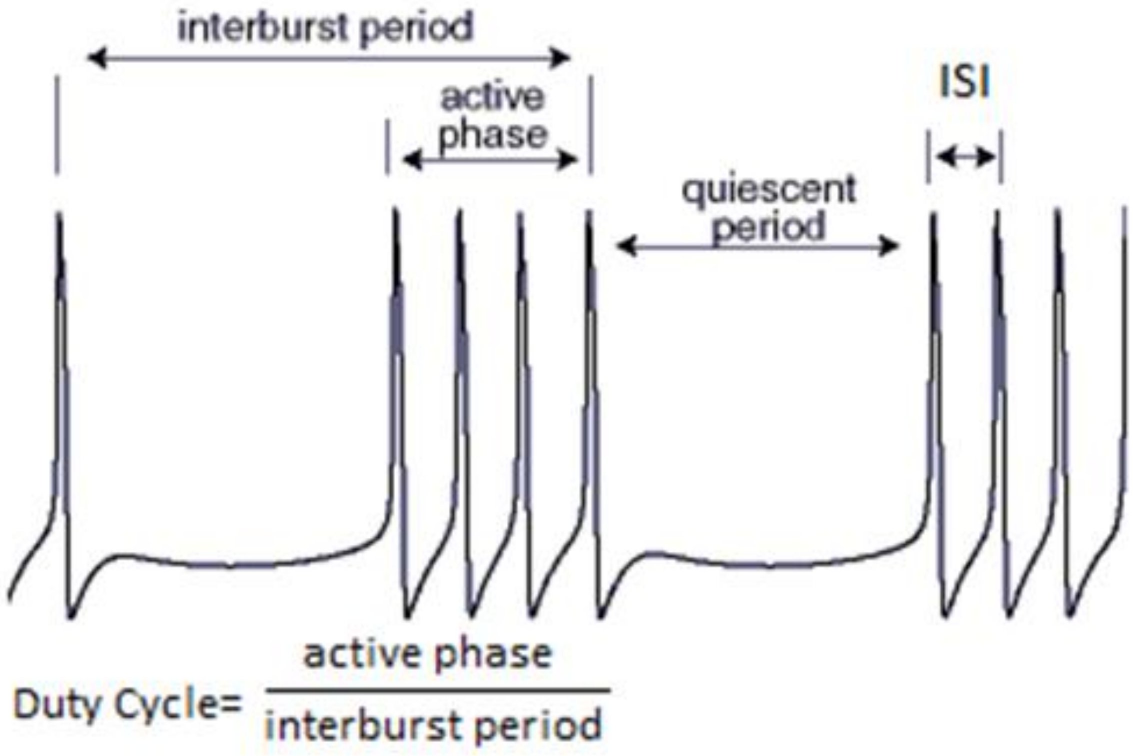


Figure adapted from ref [1], fig 2

Bursting

computational properties commonly used to depict and quantify a burst



- When coupled

A) In vivo recording

B) In virto recording

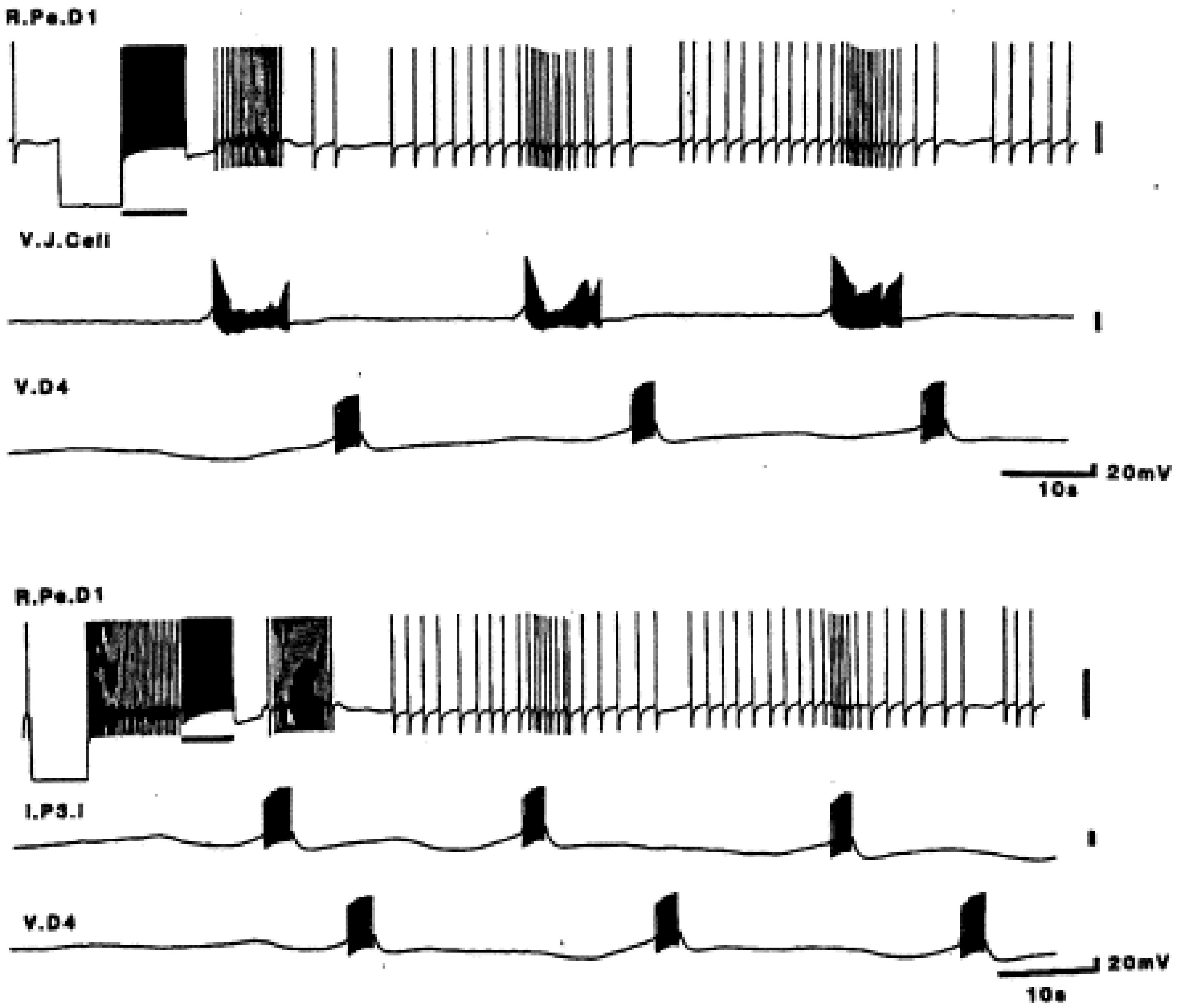


Figure adapted from ref [1], fig 2

Alternating burst of VD4 and IP3I without RPeD1 but phasic dopamine injected

Note: RPeD1 is a giant dopamine neuron, and dopamine can change excitability, which makes the internal mechanism more complicated

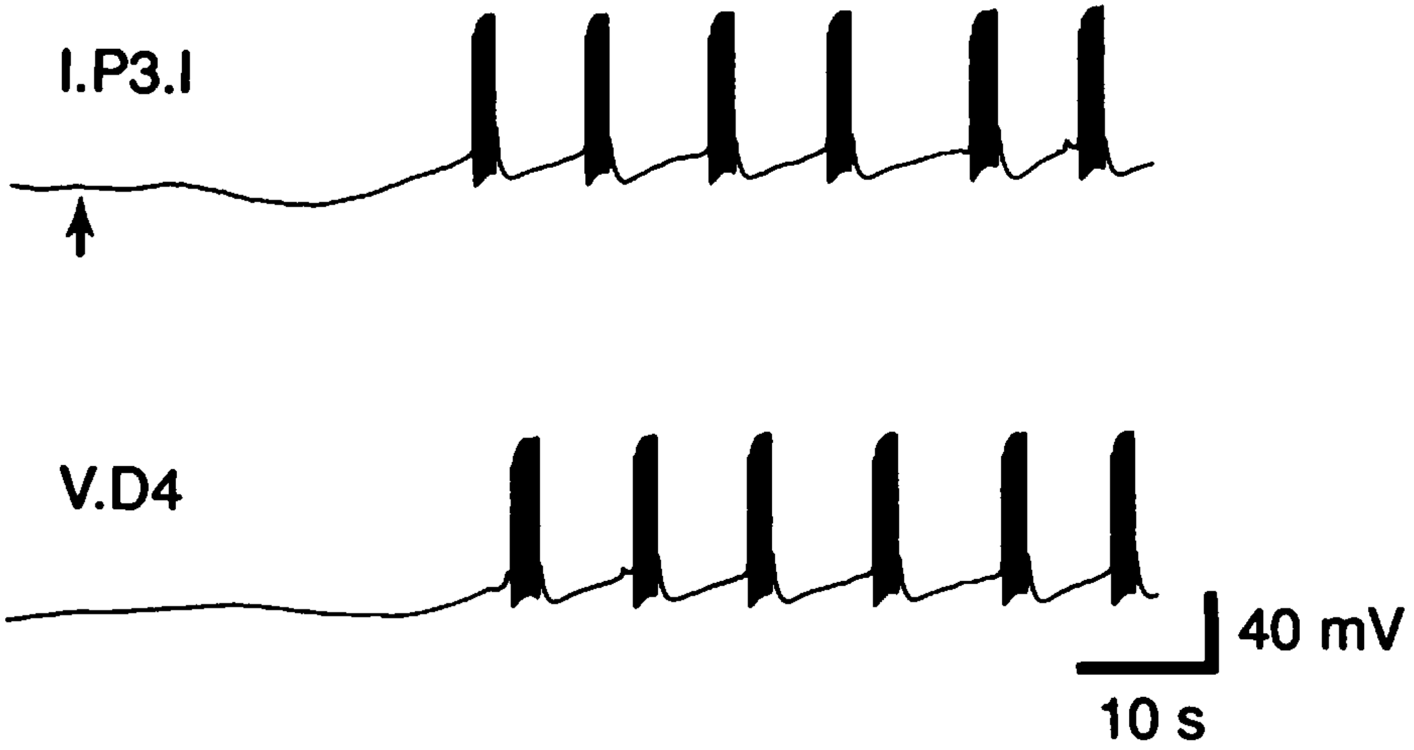


Figure adapted from ref[2], fig 4

Modeling

- Assuming VD4 and IP3I are identical
- All three neurons are based on Morris-Lecar Model, which is 2D but biologically meaningful, corresponds with the idea of balancing complexity and compliance

RPeD1 model

- Morris-Lecar model with parameters corresponds to Type 1 excitability

$$C\frac{dV}{dt} = -g_{Ca}m_\infty(V - V_{Ca}) - g_K w(V - V_K) - g_L(V - V_L) + I_{app}$$

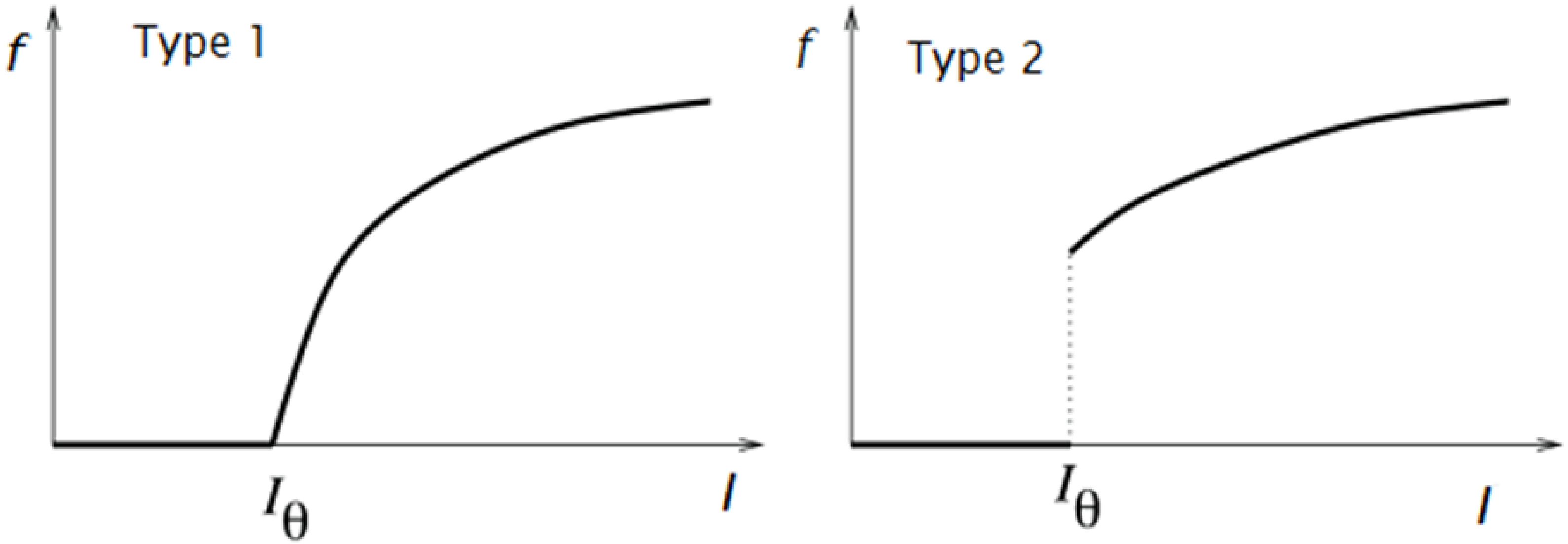
$$\frac{dw}{dt} = \phi\frac{w_\infty - w}{\tau_w}$$

$$m_\infty = \frac{1 + tanh\frac{V - V_1}{V_2}}{2}$$

$$w_\infty = \frac{1 + tanh\frac{V - V_3}{V_4}}{2}$$

$$\tau_w = \operatorname{sech}\left(\frac{V - V_3}{2V_4}\right)$$

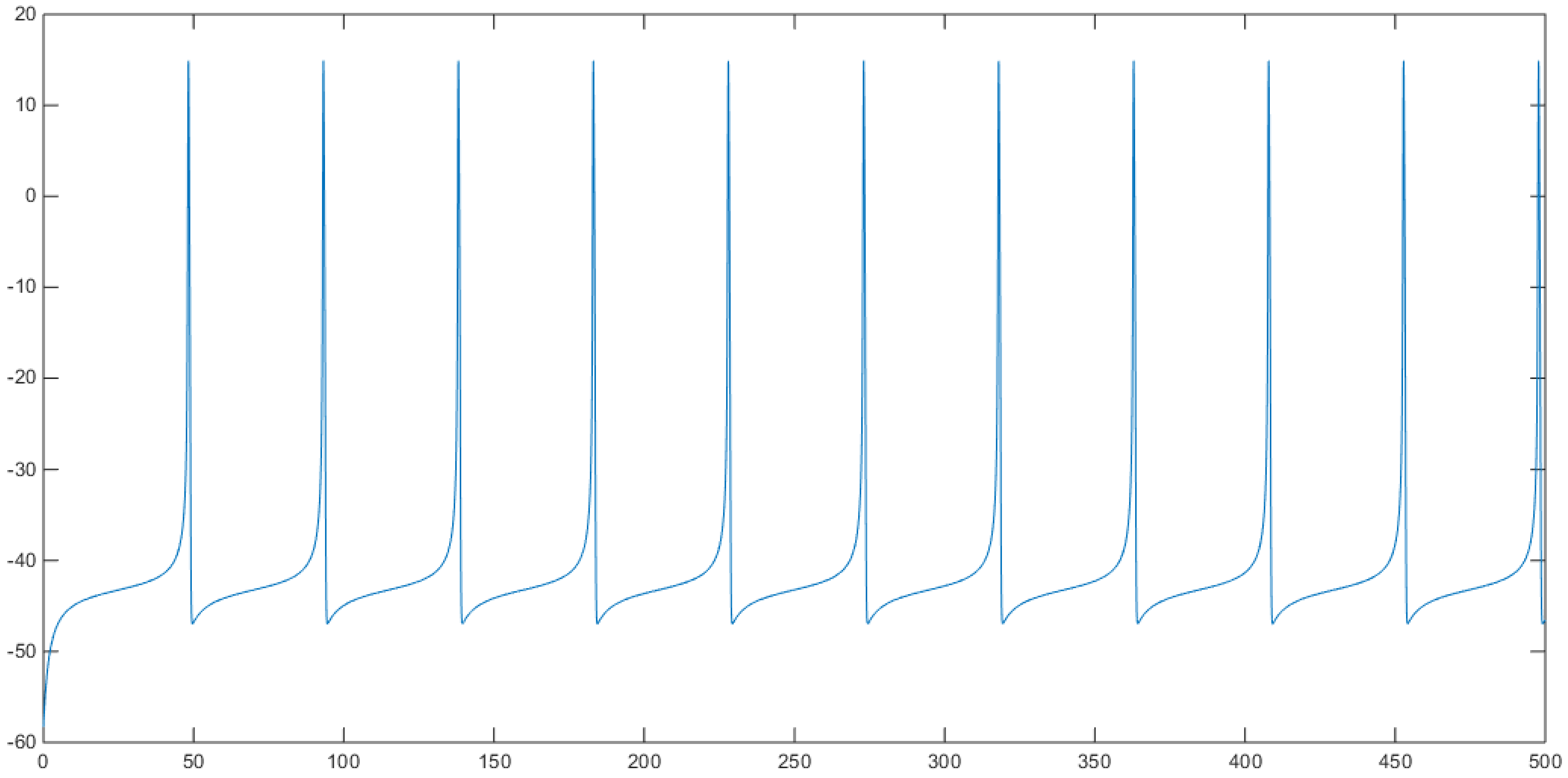
Type 1 and Type 2 excitability



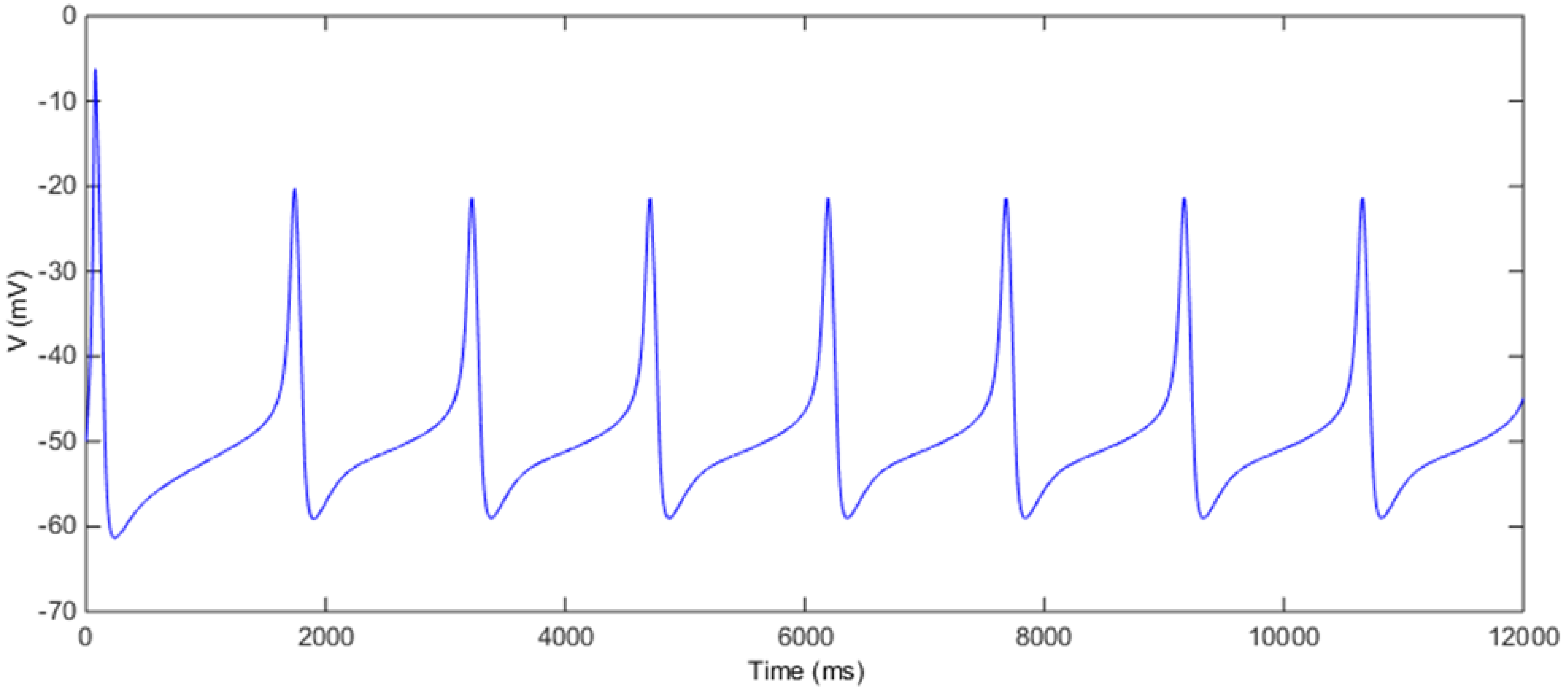
The frequency-current (f-I) curve is continuous for Type 1 neurons, and discontinuous for Type 2 neurons

Tonic spiking with injected current

Simulation in Matlab, with initial condition v(0) = - 58.3, w(0) = 0

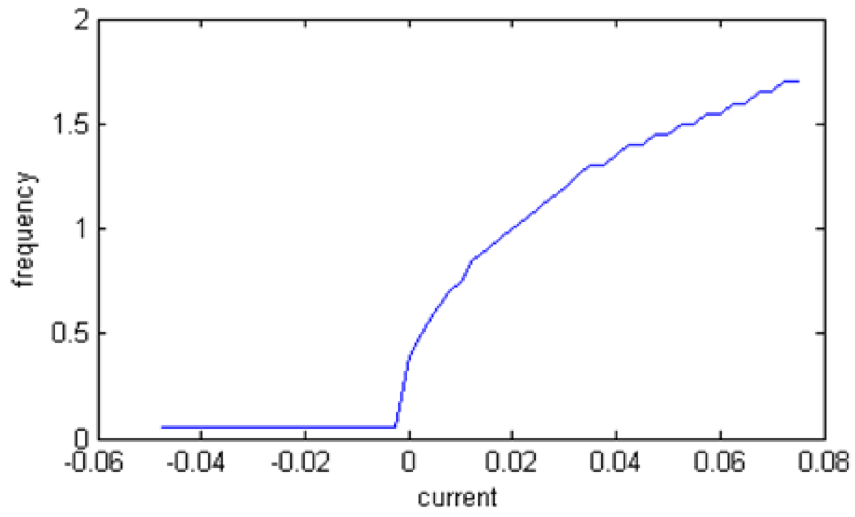


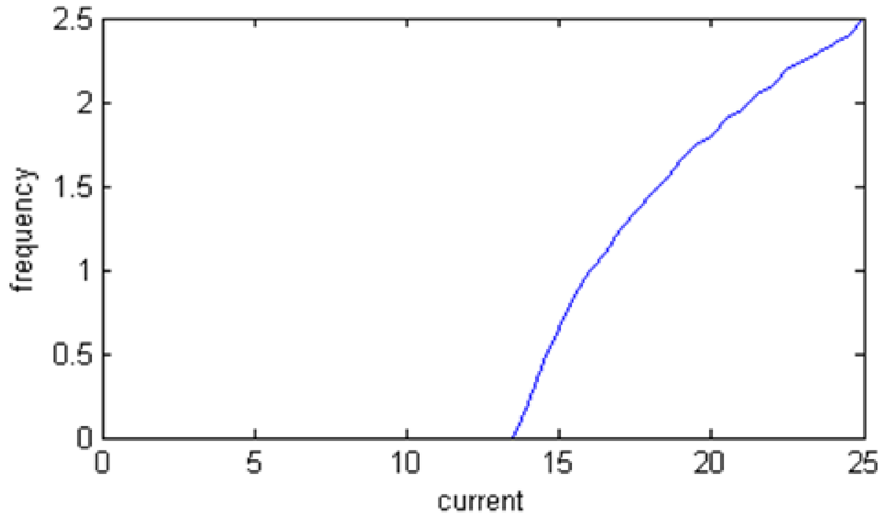
HH-type RPeD1



Tonic spiking of the conductance-based RPeD1 neuron when applied current equals 0, as the RPeD1 neuron in the CPG fires tonic spiking spontaneously, model from *Bungay, S. D., & Campbell, S. A. (2009). Modelling a Respiratory Central Pattern Generator Neuron in Lymnaea stagnalis. CANADIAN APPLIED MATHEMATICS QUARTERLY, 17(2), 283-291.*

Comparison with the HH-type RPeD1





f-I curve of the computational model of RPeD1 neuron

f-I curve of the Morris-Lecar Model based RPeD1 neuron in the artificial CPG

HCO bursting model

- HCO is a pair of neurons with reciprocal inhibitory connection, common building block in CPG
- A low-threshold transient calcium current, the T-current can produce bursting behavior
- Model is Morris-Lecar + T-current, applied current needed,

adapted from *Matveev, V., Bose, A., & Nadim, F. (2007). Capturing the bursting dynamics of a two-cell inhibitory network using a one-dimensional map. Journal of computational neuroscience, 23(2), 169-187.*

Bursting Neuron model

- T-current

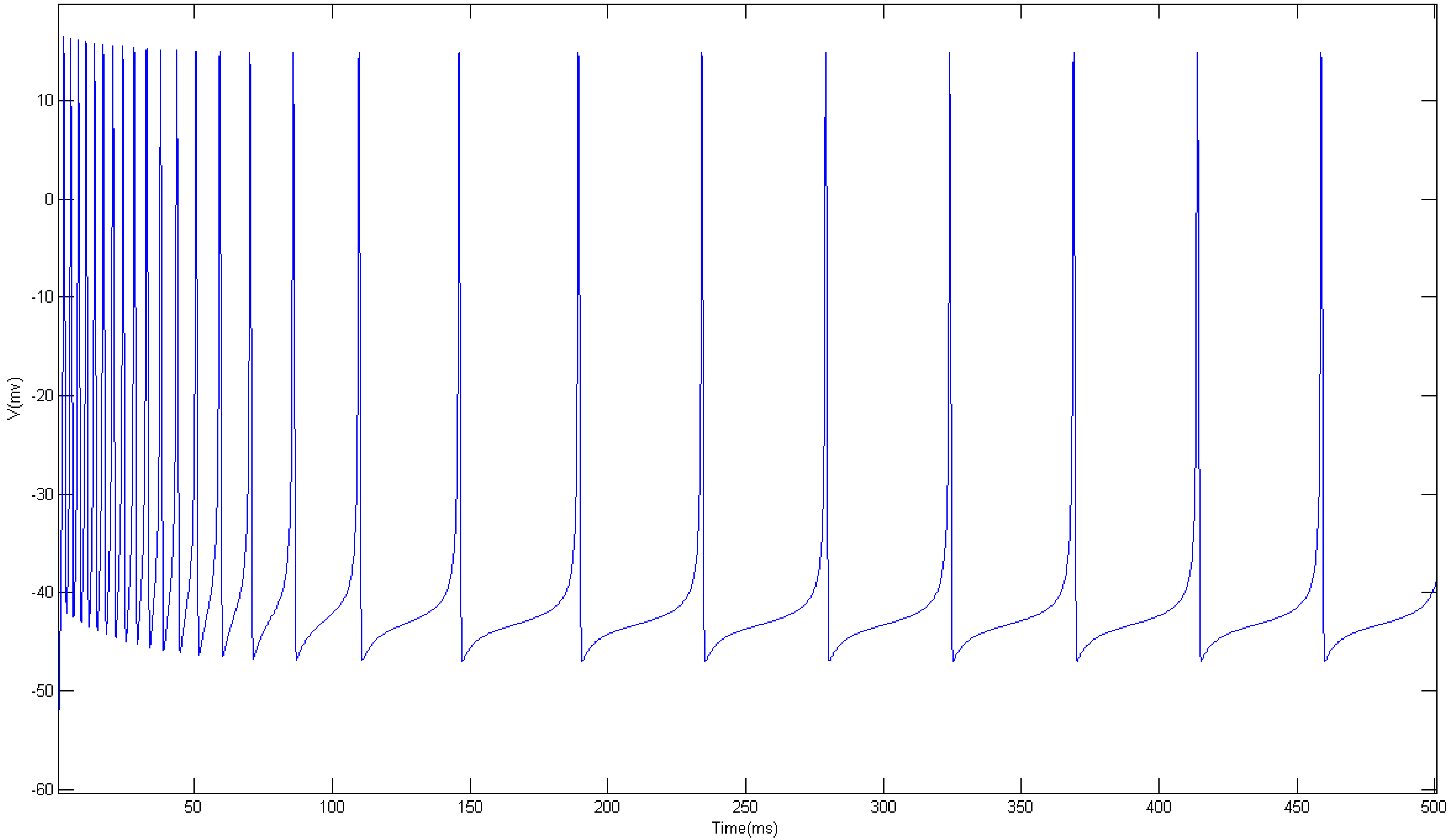
$$I_T = g_T a h (V - V_{Ca})$$

$$a = H(V - V_h) = \begin{cases} 0 & V \leq V_h \\ 1 & V > V_h \end{cases}$$

$$\frac{dh}{dt} = \begin{cases} \dfrac{1 - h}{\tau_{low}} & V \leq V_h \\ -\dfrac{h}{\tau_{hi}} & V > V_h \end{cases}$$

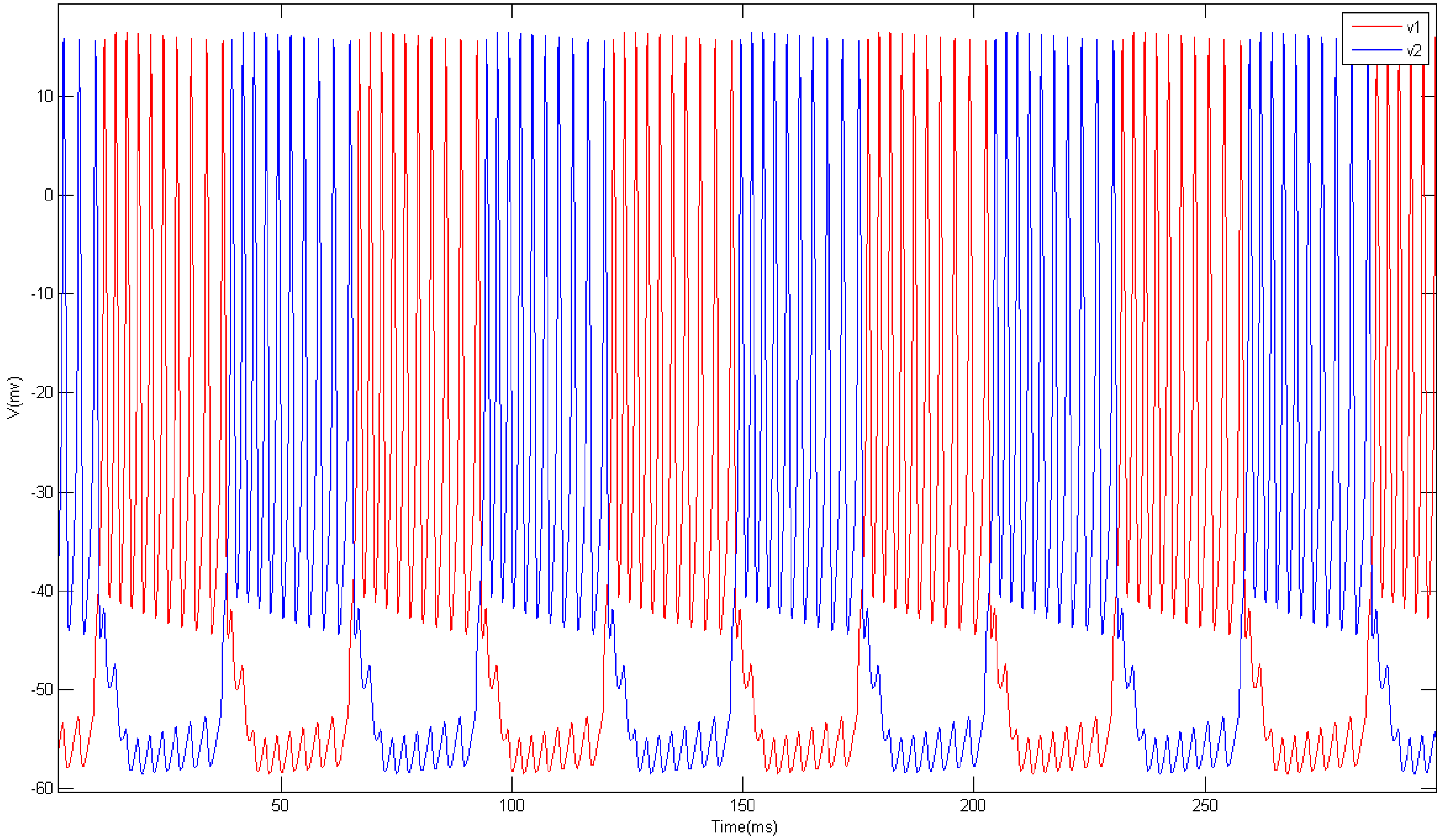
Single Neuron behaviour ML+IT

Initial condition v=-56, w=0, h=0.161,



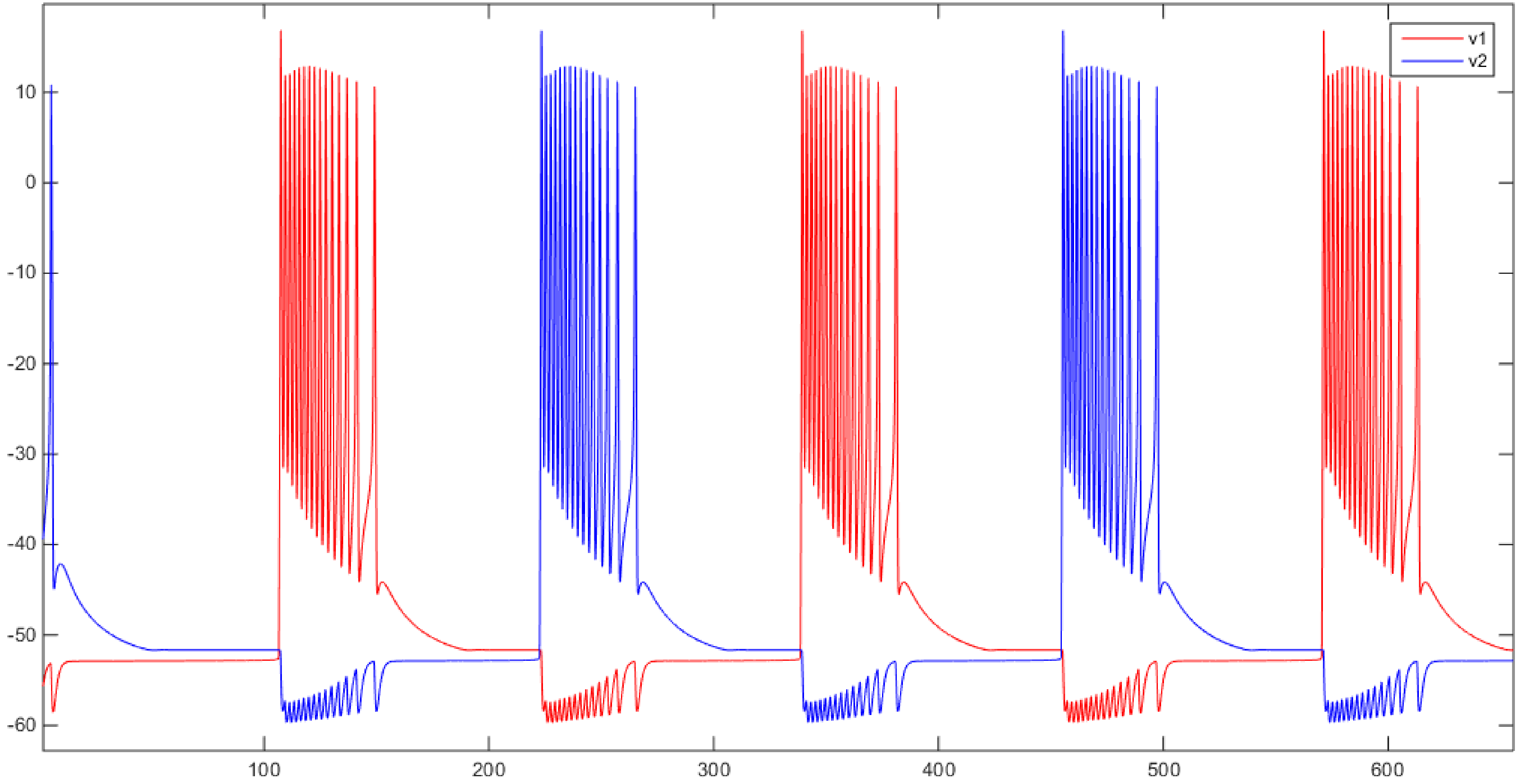
The original HCO model

- An 8-D ODE system, original paper focuses on discovering the relationship between inter-spike interval (ISI) and bursting length



Modification to achieve desired behavior

- Increase the leak channel conductance gL to 3.0, (same parameters and initial conditions) to obtain a quiescent period after active phase



Synapse model

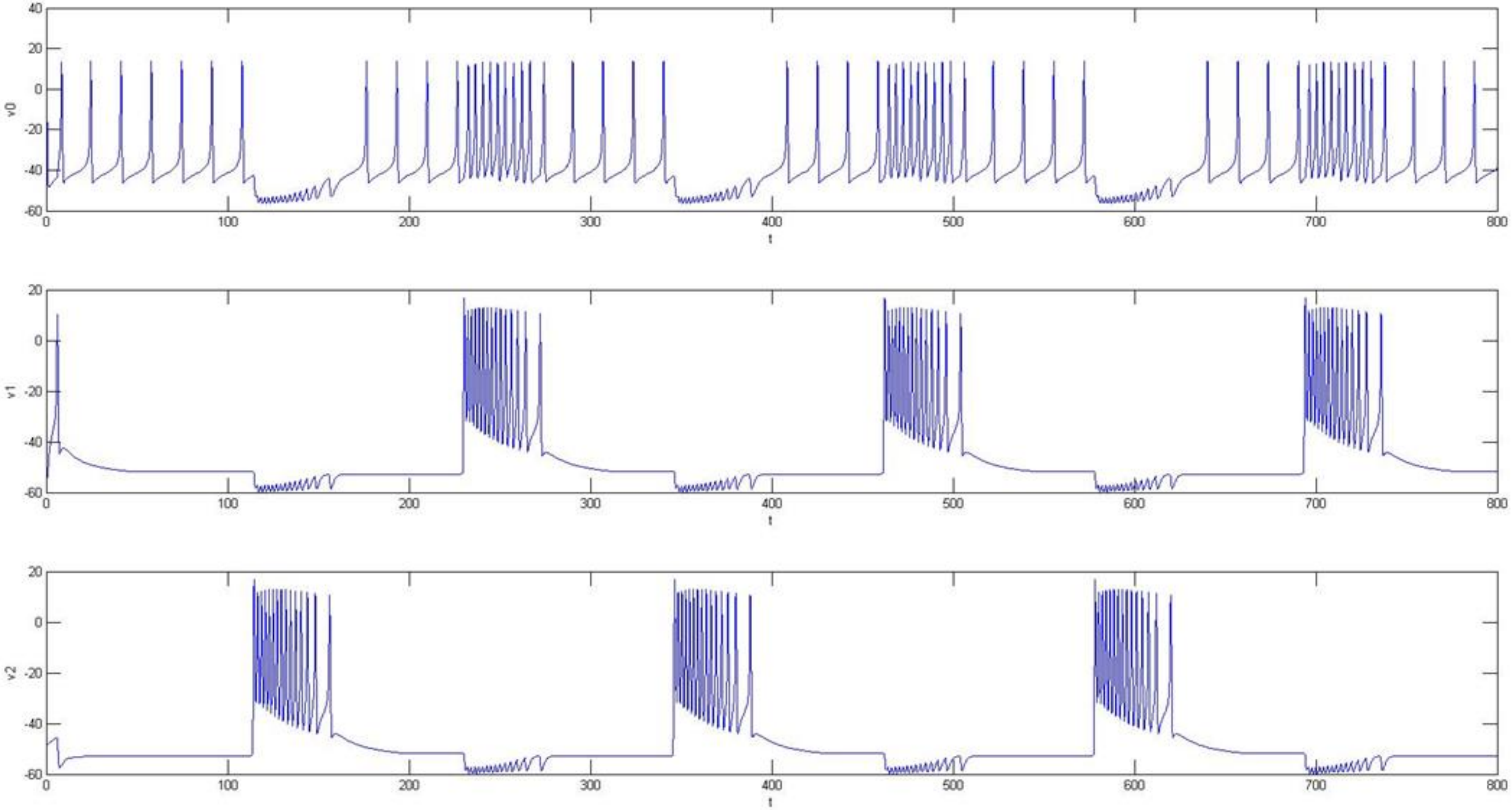
$$I_{syn} = g_{syn} s_{ij} \left(V_j - V_{syn} \right)$$

$$\frac{ds_{ij}}{dt} = \begin{cases} -\dfrac{s_{ij}}{\tau_{syn}}, & V_i \leq V_\theta \\ \dfrac{1 - s_{ij}}{\tau_g}, & V_i > V_\theta \end{cases}$$

Model of network

$$C\frac{dV_0}{dt} = I_{app} - I_L - I_{Ca} - I_K - I_{syn_{10}} - I_{syn_{20}}$$
$$C\frac{dV_1}{dt} = I_{app} - I_L - I_{Ca} - I_K - I_T - I_{syn_{01}} - I_{syn_{21}}$$
$$C\frac{dV_2}{dt} = I_{app} - I_L - I_{Ca} - I_K - I_T - I_{syn_{02}} - I_{syn_{12}}$$

A three-neuron network, a 14-D ODE system



Observations

- When coupled with a third neuron, the period of network is broadened
- The HCO dominates, synaptic interaction from the third tonic spiking neuron isn’t involved when producing a similar scheme as in the CPG

Introduction of delay

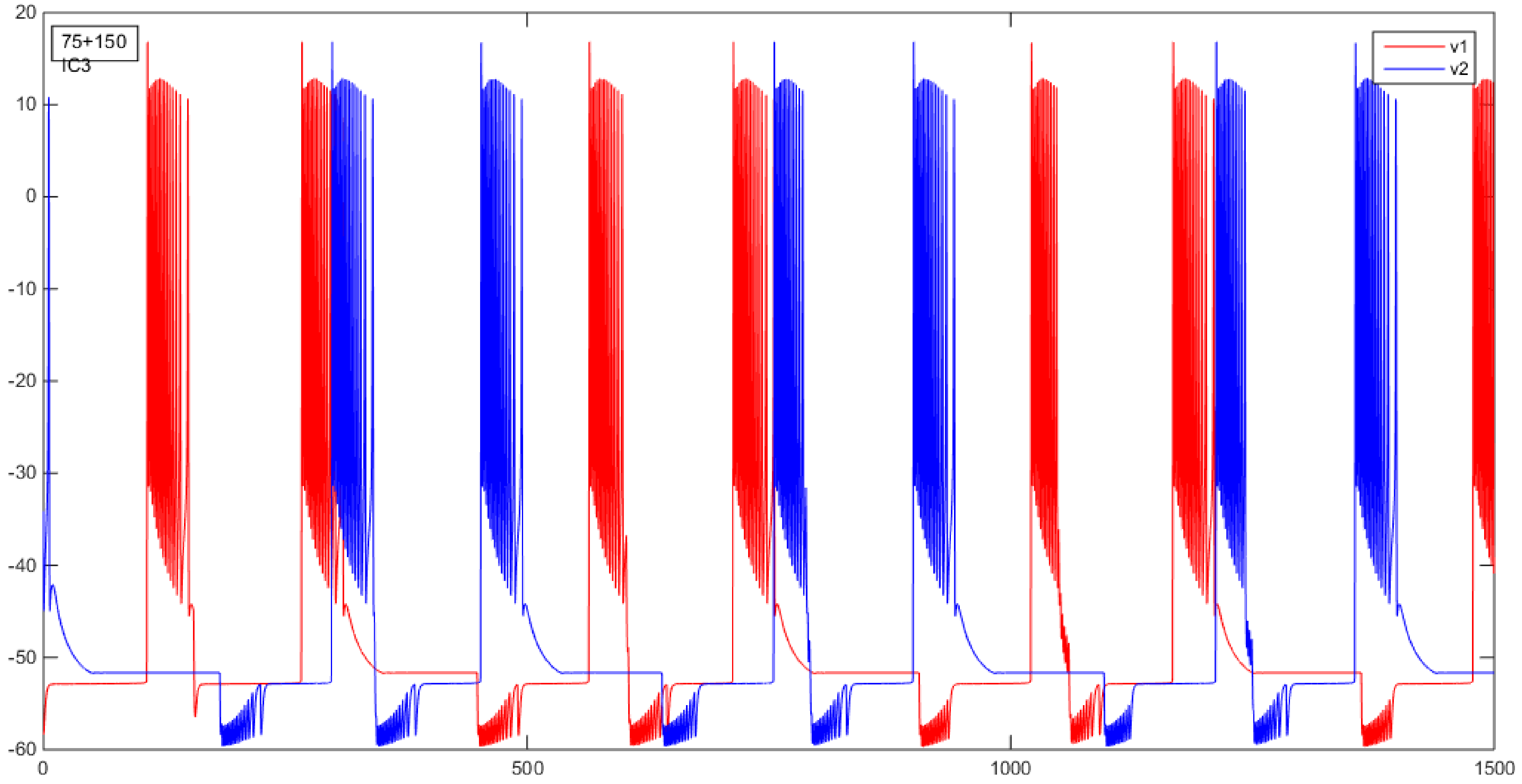
- The synaptic gating variable S_{ij} is dependent of the membrane potential V_i, which can be written as

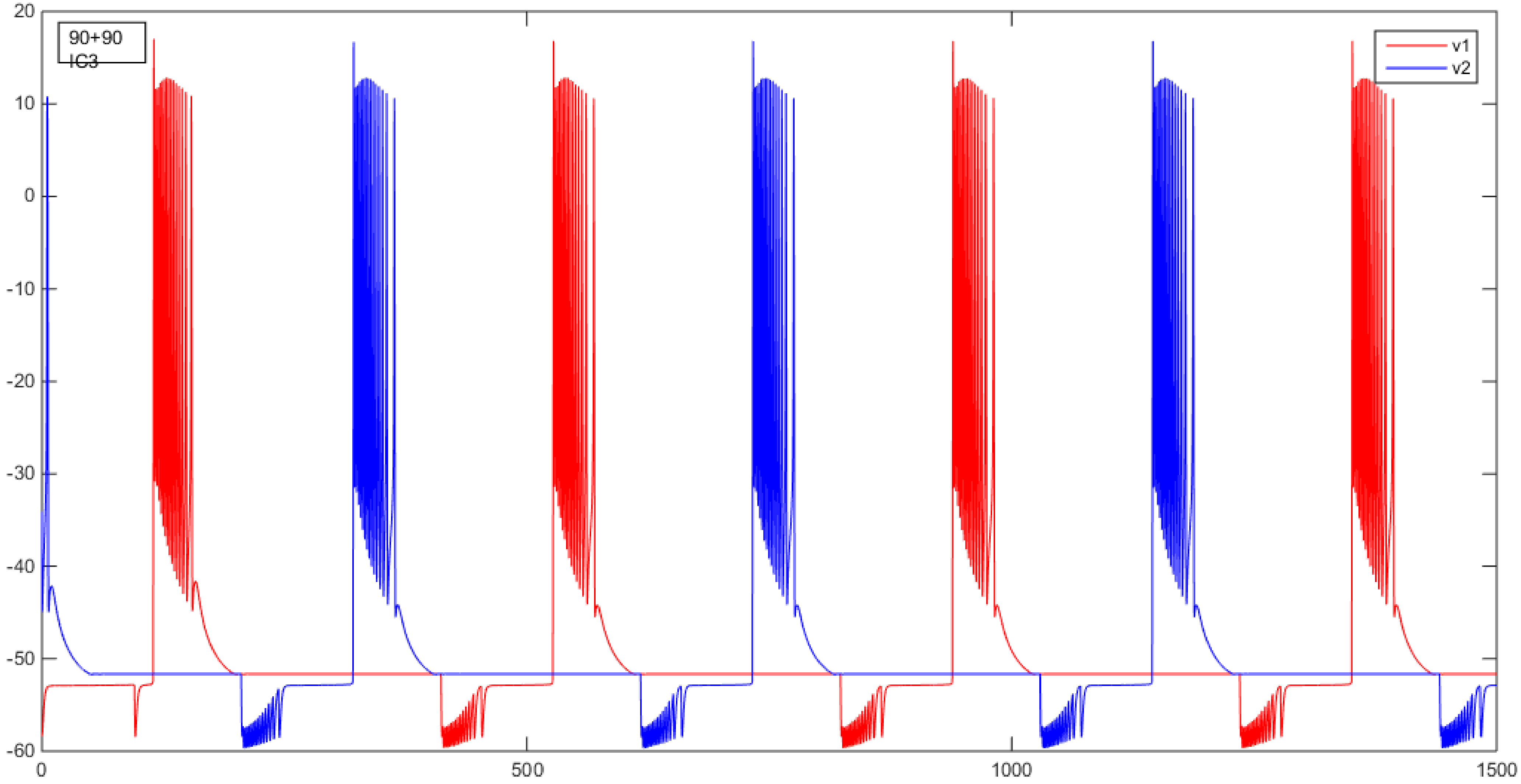
$$\frac{ds_{ij}}{dt} = f\left(V_i(t)\right)$$

- When a delay τ is introduced, the above equation can be written as

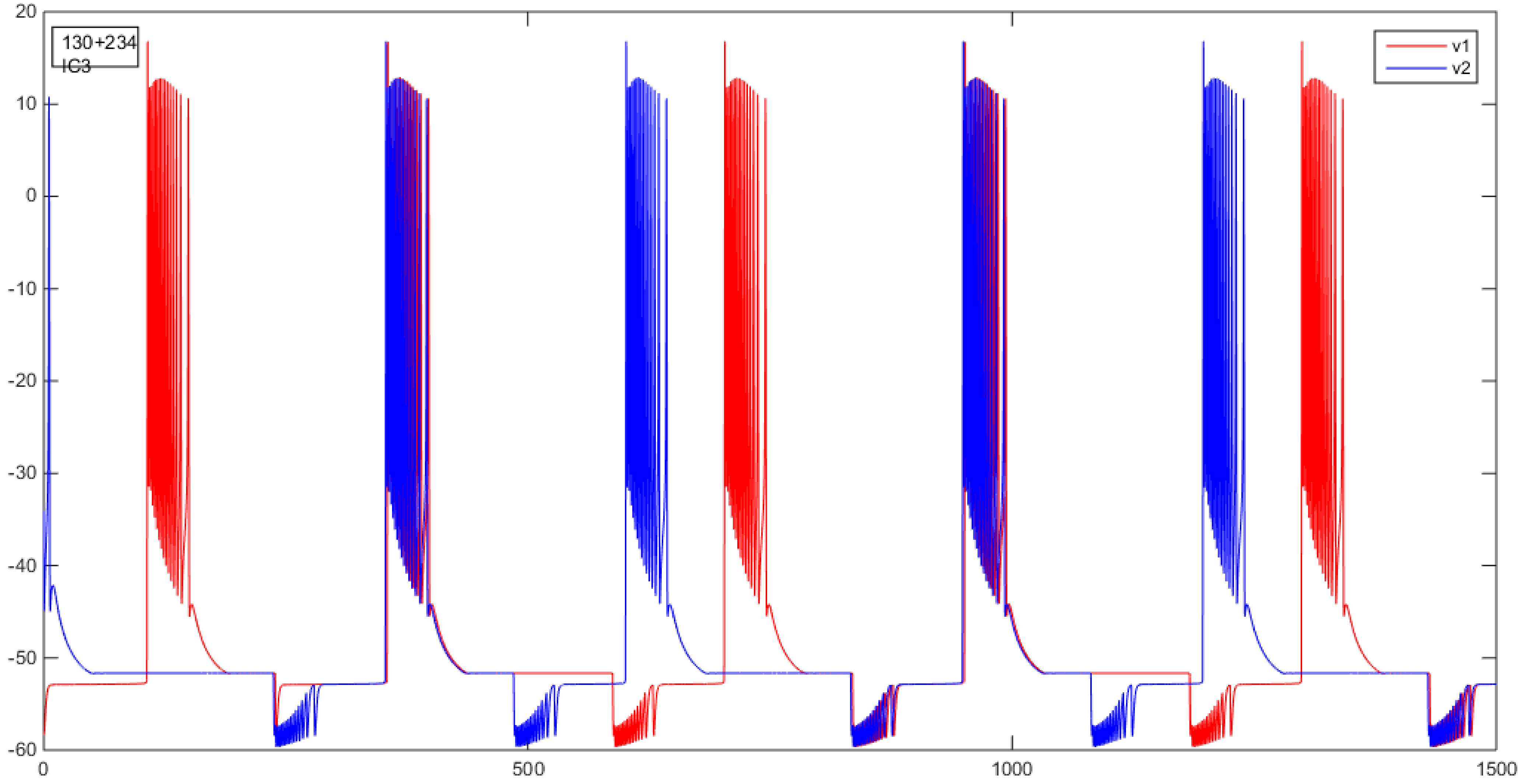
$$\frac{ds_{ij}}{dt} = f\left(V_i(t-\tau)\right)$$

When delayed added to synaptic gating variable s

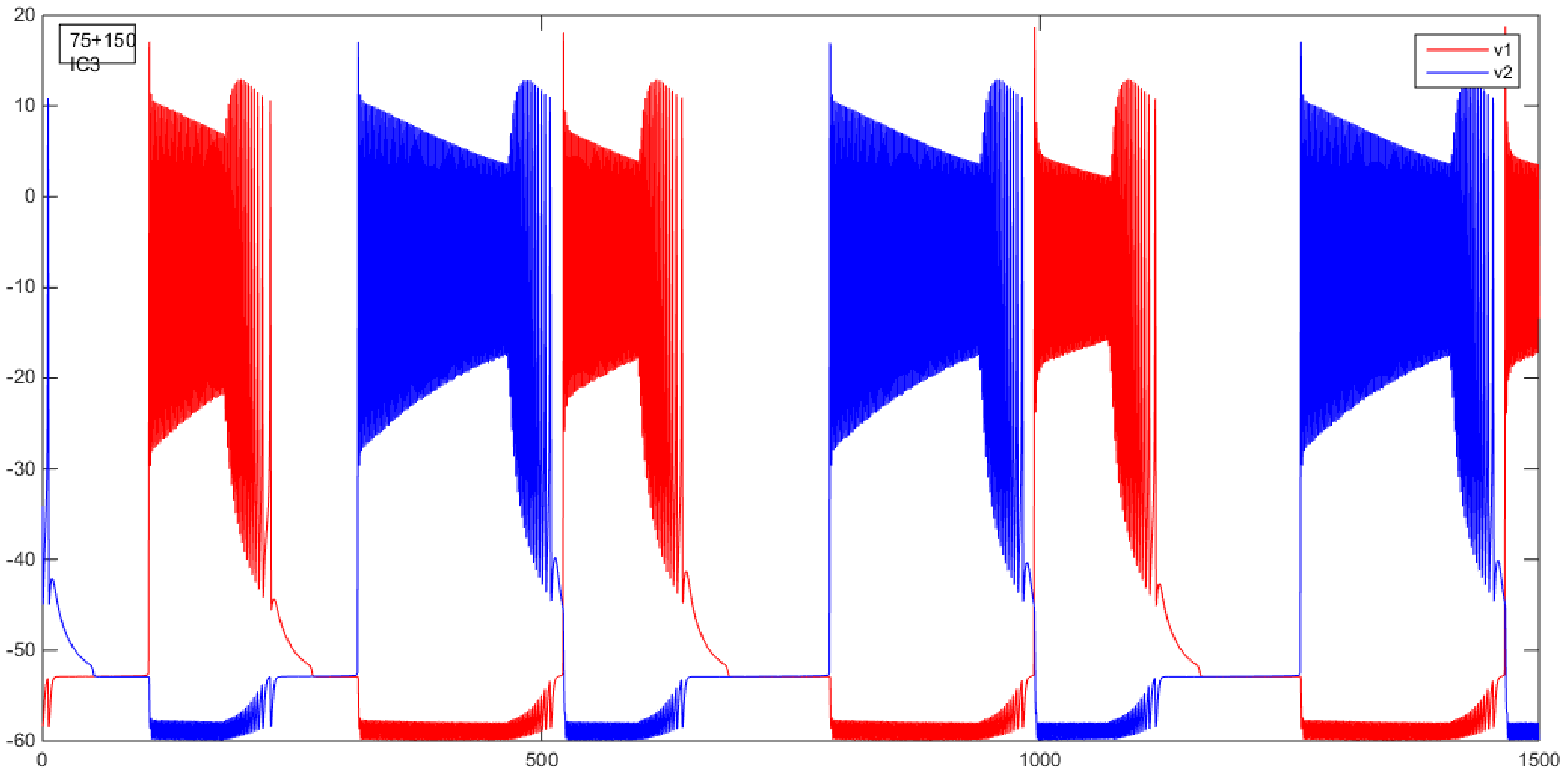




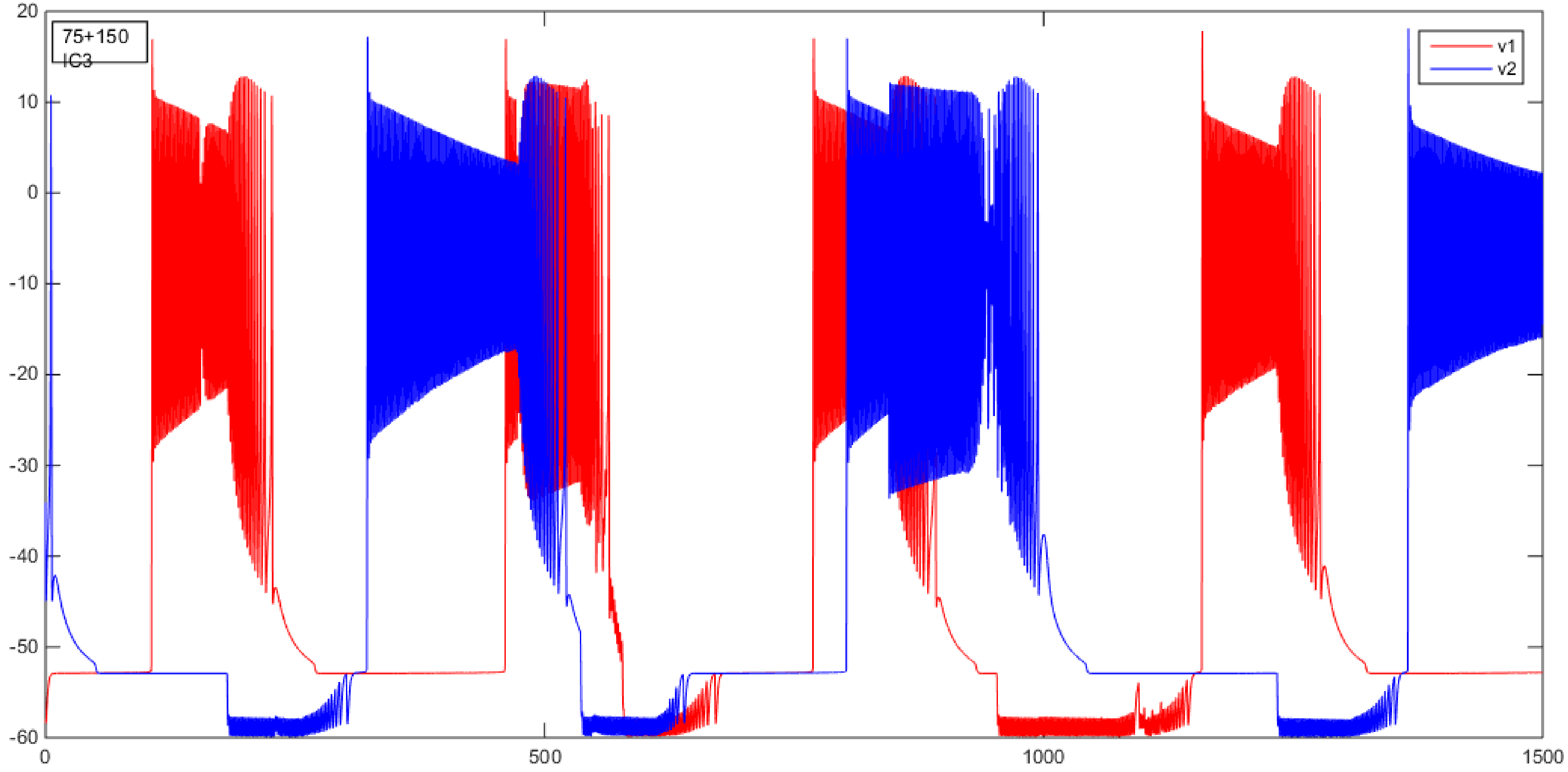
90+90
IC3
v1
v2
20
10
0
-10
-20
-30
-40
-50
-60
0
500
1000
1500


130+234
IC3
v1
v2
20
10
0
-10
-20
-30
-40
-50
-60
0
500
1000
1500

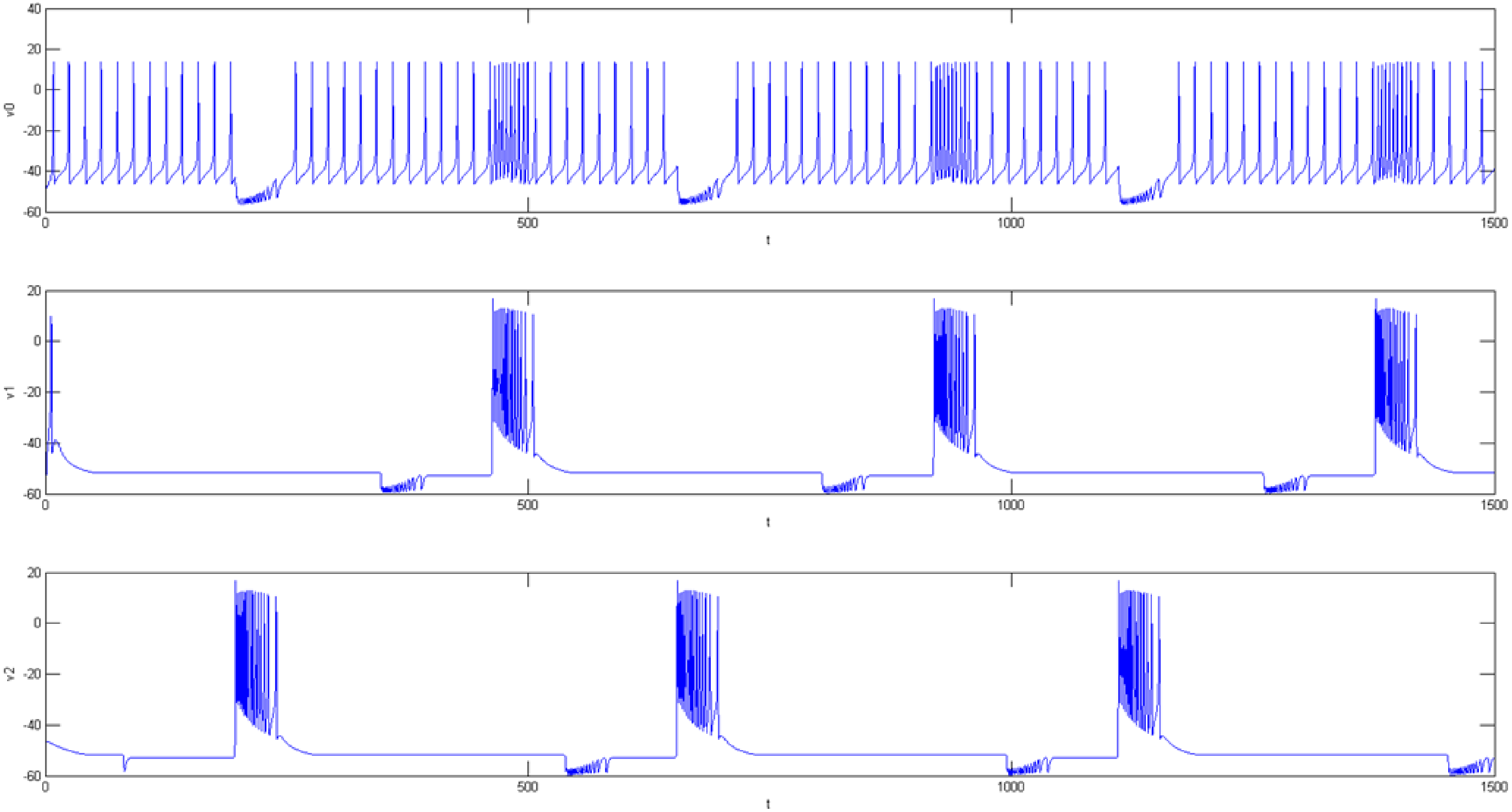
When delay added to the inactivation variable h of the T-current



When delay added to both h and s



A DDE system of the three neuron network



Summary

- Delay is a flexible and effective way of controlling period, and brings a variety of behaviours to a system
- Different delays can break or preserve the symmetry, may also be linked to intrinsic period though need further analysis

Feasibility and Significance

- All models involve certain level of abstraction of the real system
- A neuron is a very complicated biological system consisting of thousands of channels such as voltage-gated, ligand-gated, mechanically gated
- As a bio-inspired CPG, successfully produce rhythmic output resembling the original system

Conclusion

- We explored the electrophysiological fundamentals of action potential generation and the Hodgkin-Huxley mechanism of voltage-gated ion channels.
- We studied and analyzed the respiratory CPG in Lymnaea, then replicated its output by the construction of an artificial CPG with ODE and DDE systems based on the Morris-Lecar model.
- We hope this study could promote interest in computational neuroscience and many other interdisciplinary areas where computer science helps better visualizing the deep and great unknowns of this world.

Ref

- [1] Lukowiak, K., & Syed, N. (1999). Learning, memory and a respiratory central pattern generator. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, *124*(3), 265-274.
- [2] Syed, N. I., Bulloch, A. G., & Lukowiak, K. (1990). In vitro reconstruction of the respiratory central pattern generator of the mollusk Lymnaea. *Science*, *250*(4978), 282-285.
- [3] Matveev, V., Bose, A., & Nadim, F. (2007). Capturing the bursting dynamics of a two-cell inhibitory network using a one-dimensional map. *Journal of computational neuroscience*, *23*(2), 169-187.