

Characterization of the sequential nature of neuronal dynamics: Experimental recordings, computational models and novel stimulation neurotechnologies

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Universidad Autónoma de Madrid

Alicia Garrido Peña. PhD thesis Seminar
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Universidad Autónoma
de Madrid



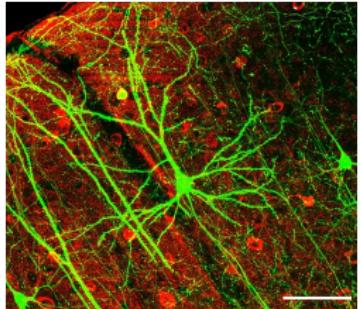
Escuela
Politécnica Superior

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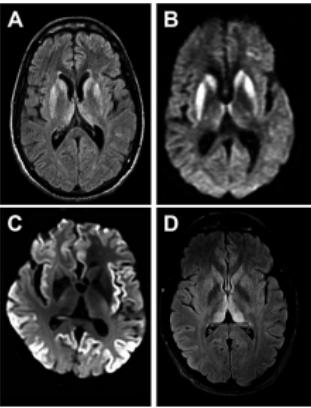
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- 2 Motivation and Objectives
- 3 Sequential constrains in CPG circuits: Dynamical invariants
- 4 CW-NIR laser as an effective neuromodulation technique
- 5 Conclusion

Introduction

Neuroscience



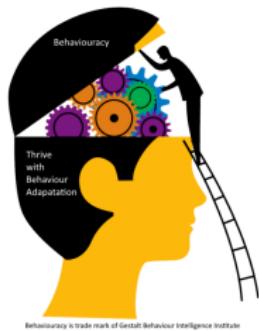
Neurobiology



Clinical Neuroscience



Neurotechnology

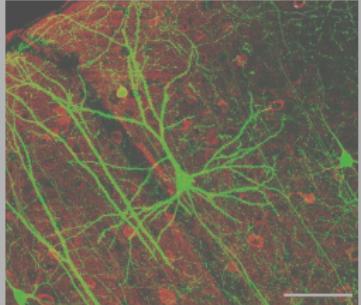


Cognitive Neuroscience

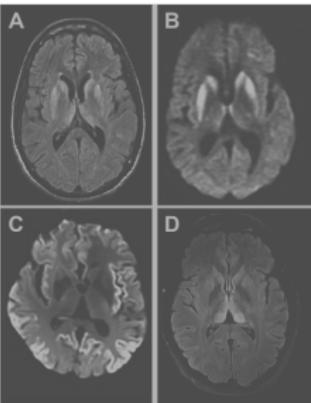


Computational Neuroscience

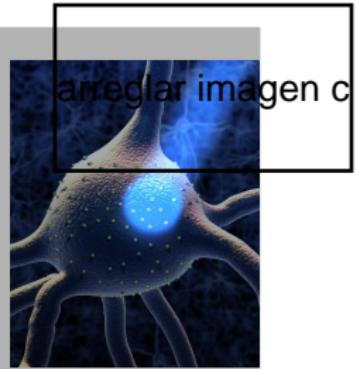
Neuroscience



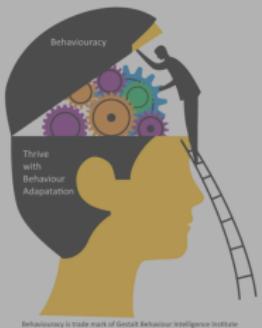
Neurobiology



Clinical Neuroscience



Neurotechnology



Cognitive Neuroscience



Computational Neuroscience

Approach

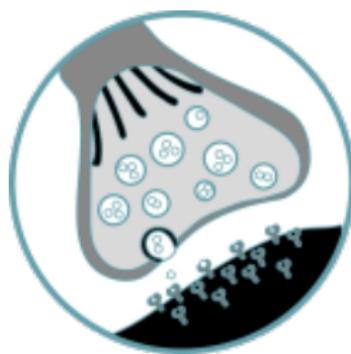
○ Neurocomputational Perspective

Approach

- Neurocomputational Perspective
- Bottom-up approach

Approach

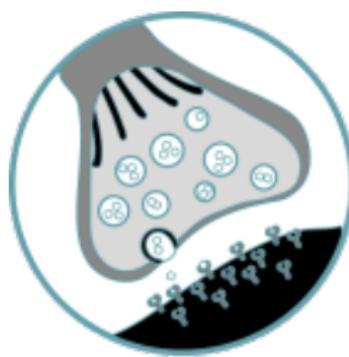
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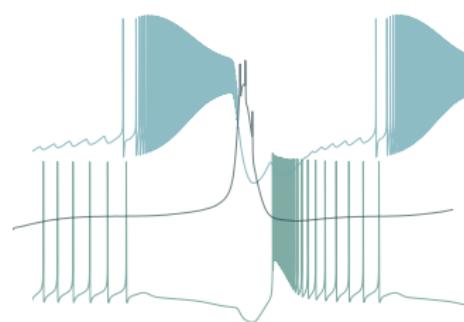
From ionic channels

Approach

- Neurocomputational Perspective
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From ionic channels



To minimal circuits

Approach

- Neurocomputational Perspective
- Bottom-up approach
- Combining electrophysiology

Approach

- Neurocomputational Perspective
- Bottom-up approach
- Combining electrophysiology and computational work

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Neuronal and Networks Dynamics

Neuronal electrical activity is often described in terms of the evolution of membrane voltage caused by the flow of ionic channels between the inside and outside of the cell.

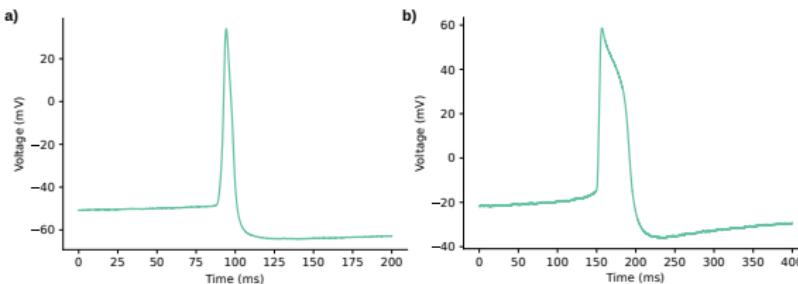
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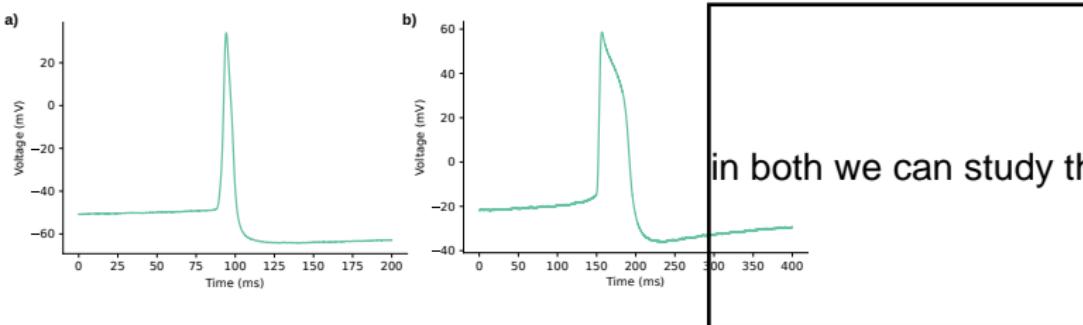
In terms of the spike waveform:



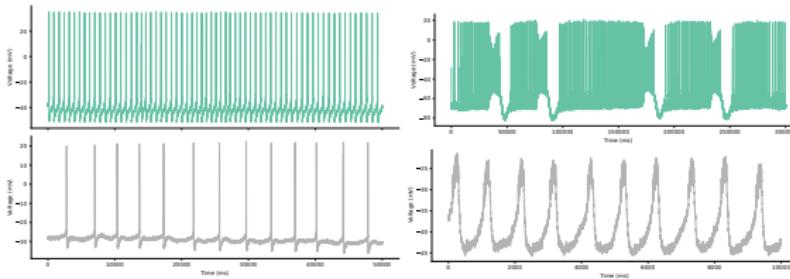
Neuronal and Networks Dynamics

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In terms of the spike waveform:



And the type of spiking activity: tonic firing, bursting, etc.

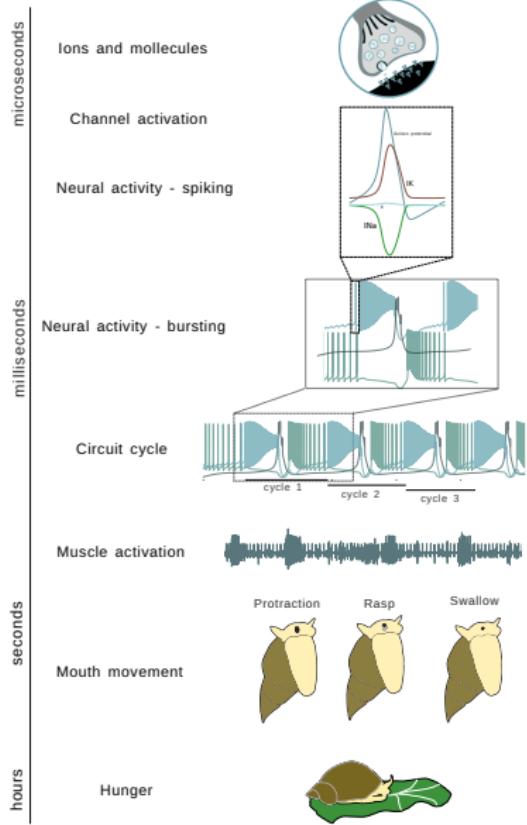


The sequential nature of neural dynamics

- There are sequential processes at different time-scales.

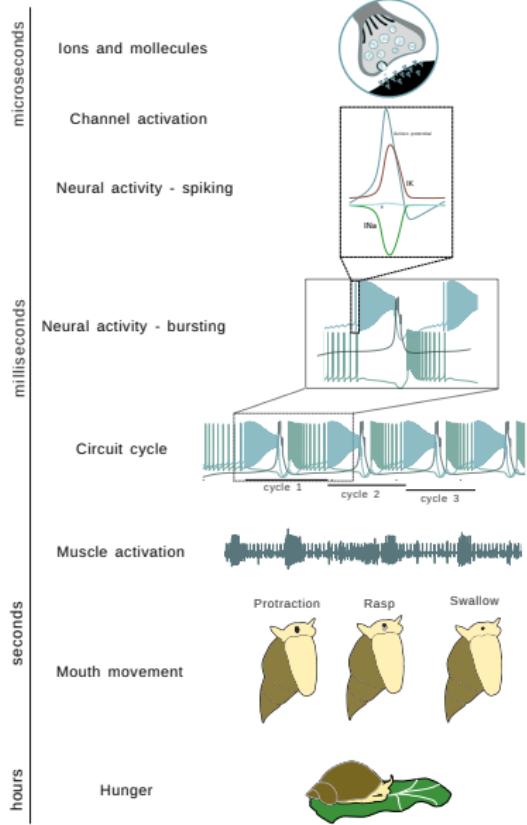
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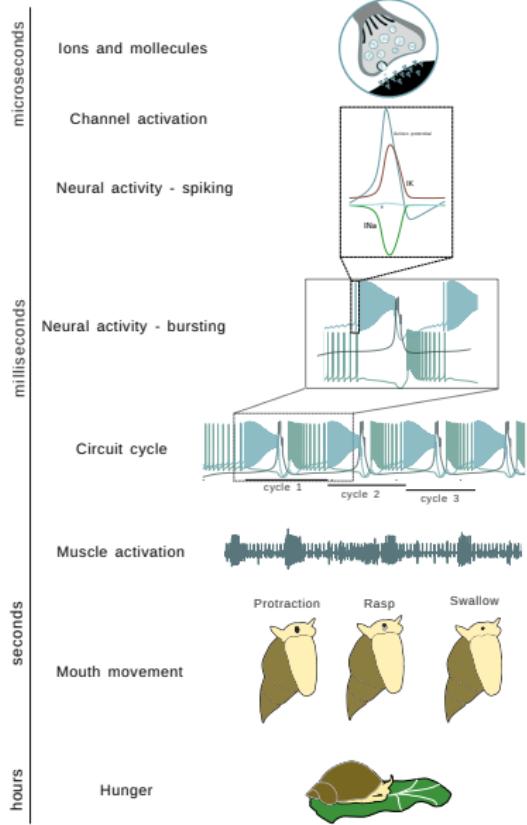
The sequential nature of neural dynamics

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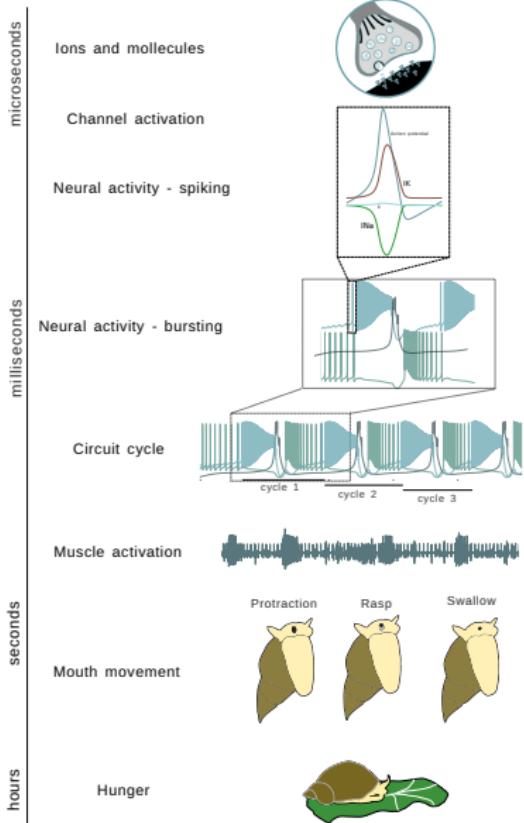
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The sequential nature of neural dynamics

- There are sequential processes at different time-scales.
- Many behaviors and actions are governed by sequential processes
- Motor control, speech, decision making, etc.
- Sequential dynamical invariants might have a crucial role in neural coordination to autonomously establish a balance between the robustness and flexibility required for effective function.



Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics

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Conductance-based models

Studying neural dynamics in computational models

Conductance-based models

Voltage equation	$C \frac{dV}{dt} = I - g_K n^4(V - E_K) - g_{Na} m^3 h(V - E_{Na}) - g_L(V - E_L)$		
	Activation variables	Inactivation variable	
gating variables	$\frac{dm(t)}{dt} = \frac{m_\infty(V(t)) - m(t)}{\tau_m(V(t))}$	$\frac{dn(t)}{dt} = \frac{n_\infty(V(t)) - n(t)}{\tau_n(V(t))}$	$\frac{dh(t)}{dt} = \frac{h_\infty(V(t)) - h(t)}{\tau_h(V(t))}$

Studying neural dynamics in computational models

Conductance-based models

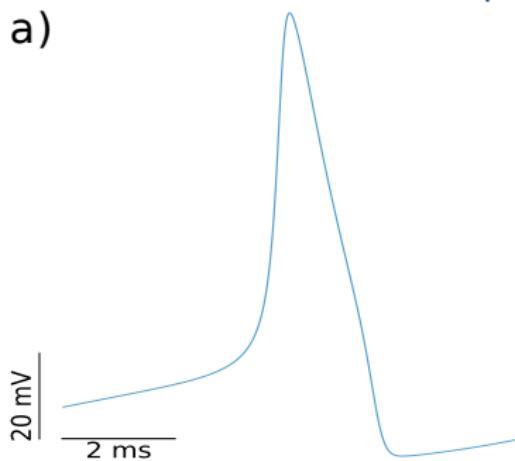
By different combinations of ionic channels we can achieve different activities and waveform shapes

Studying neural dynamics in computational models

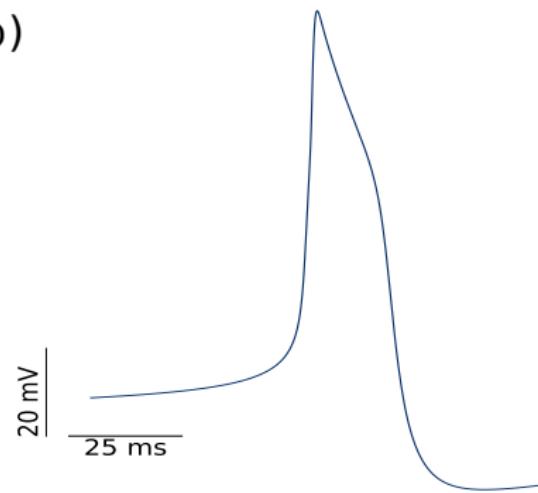
Conductance-based models

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a)



b)



Studying neural dynamics in computational models

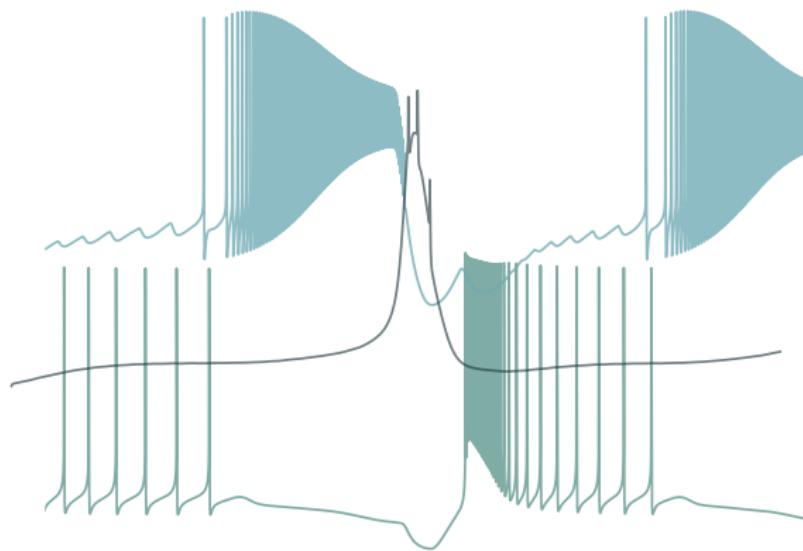
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By modeling synapses we can model whole circuits by connecting single modeled neurons.

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 - Ease of breeding and reproduction.
 - Full description of their systems.

Vertebrate and invertebrate animal studies



- In this thesis we work with the neural system of *Lymanea stagnalis*.

Vertebrate and invertebrate animal studies



- A pond snail whose system is well studied and described.

Neural stimulation

When studying neural systems, we need neuromodulatory technics.

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When studying neural systems, we need neuromodulatory technics.

- To study different conditions.
- Test their robustness.
- Simulate external inputs.

Neural stimulation

We can classify them based on:

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive
- The source of the stimulation:

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive
- The source of the stimulation:
 - Chemical

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive
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 - Chemical
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Neural stimulation

We can classify them based on:

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 - Optical

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Motivation and Objectives

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4. To illustrate the possible functionality of sequential dynamical invariants in biohybrid robotics.

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2. To study the possible biophysical candidates underlying the CW-NIR effect in model simulations.
3. To design and implement a new technique for CW-NIR stimulation in closed-loop.

Sequential constraints in CPG circuits: Dynamical invariants

Central Pattern Generators

- Neural circuits generating robust sequences of neural activity

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- Control motor rhythms in an autonomous manner

Central Pattern Generators

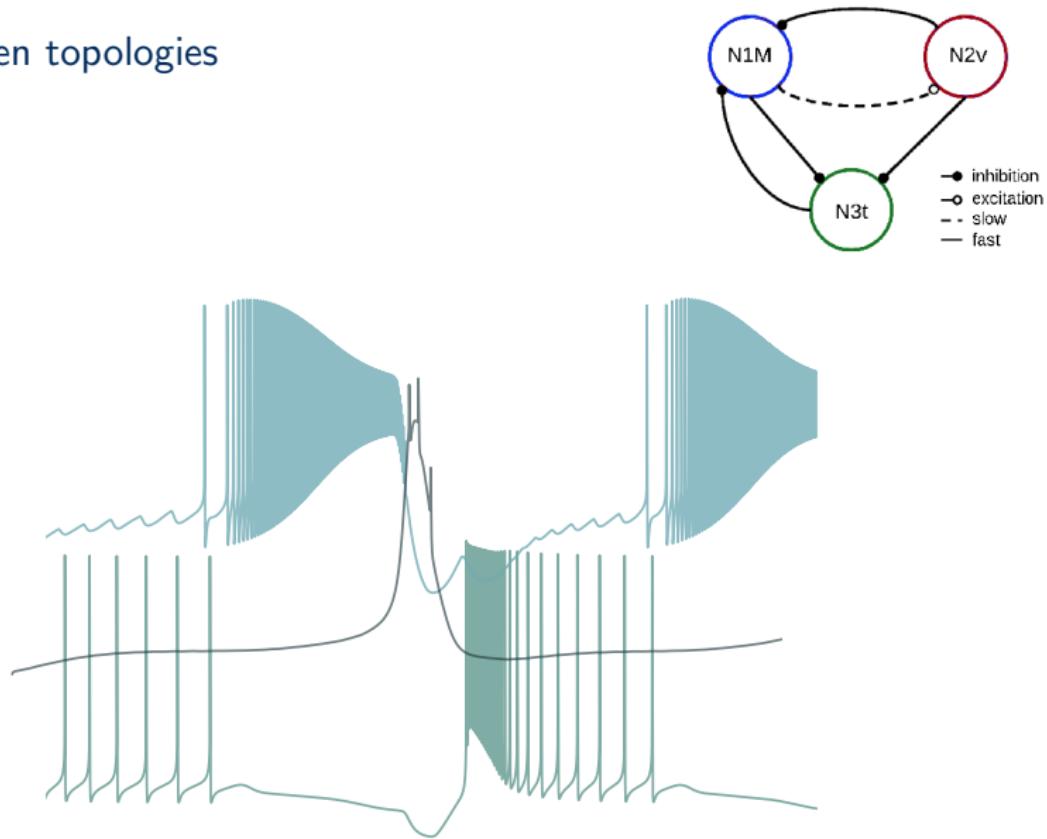
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- Present in vertebrates and invertebrates

Central Pattern Generators

- Neural circuits generating robust sequences of neural activity
- Control motor rhythms in an autonomous manner
- Present in vertebrates and invertebrates
- Flexible enough to adapt the rhythm to the variability keeping a robust sequential activity

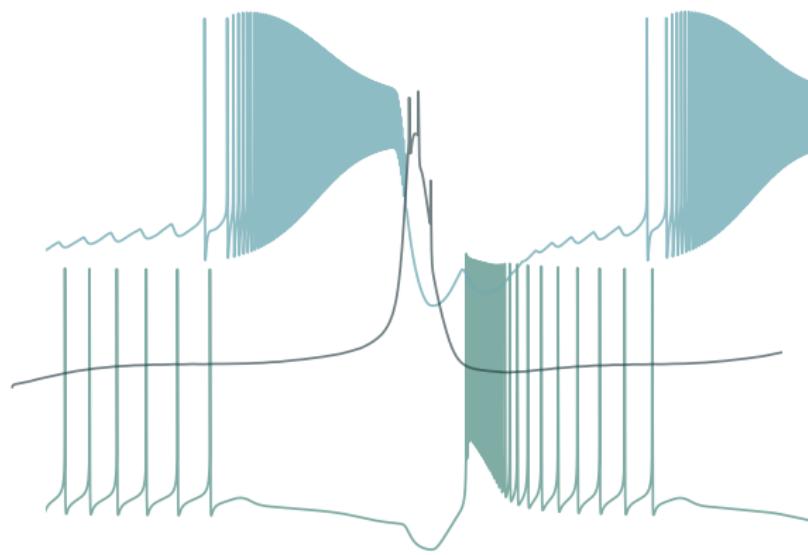
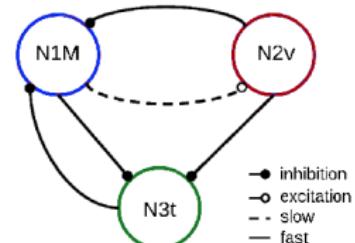
Central Pattern Generators

○ Non-open topologies



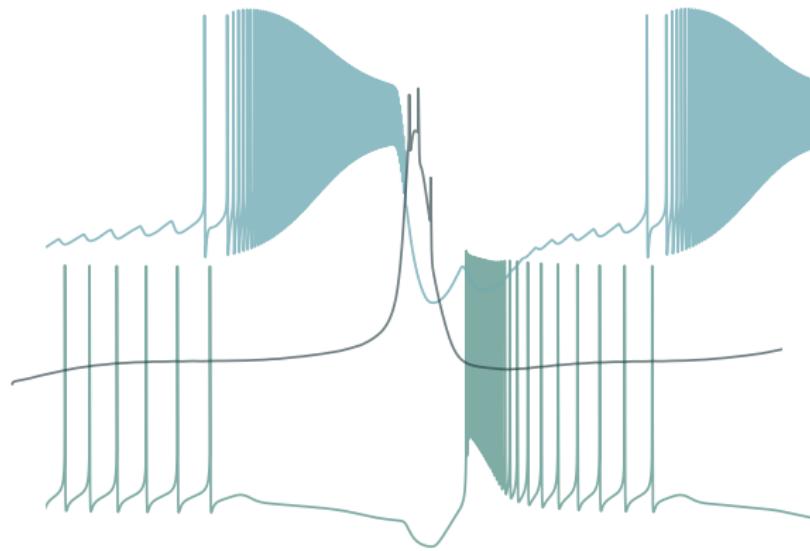
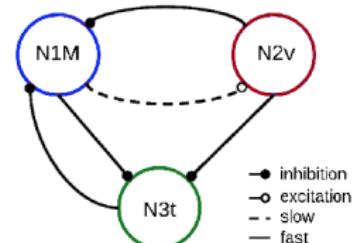
Central Pattern Generators

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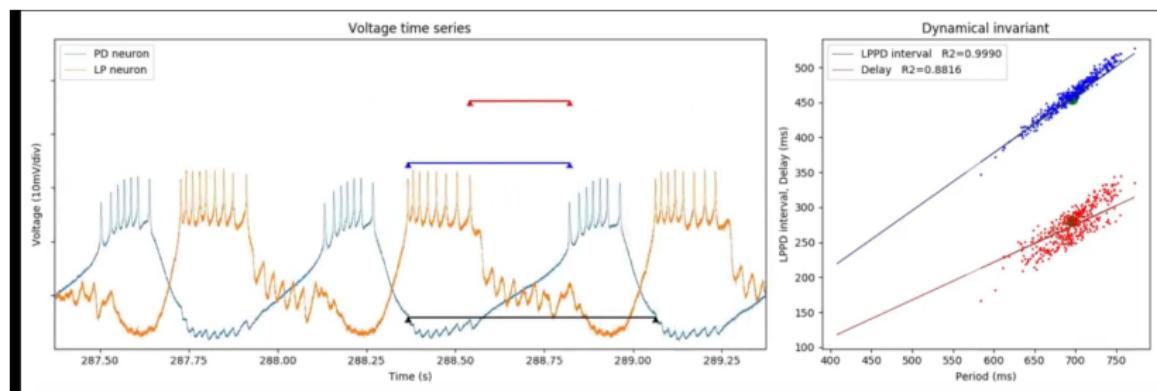
Central Pattern Generators

- Non-open topologies
- Based on mutual inhibition
- Temporal sequences maintained cycle-by-cycle



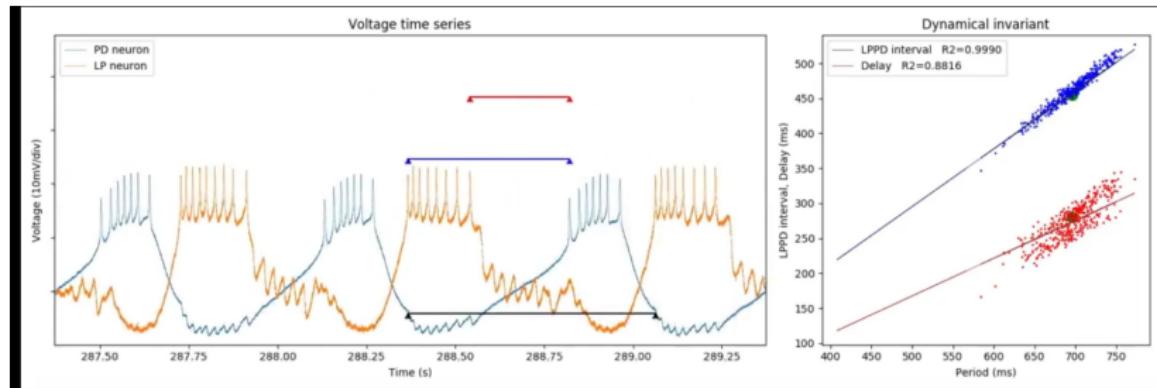
Temporal constraints: Sequential Dynamical invariants

- Recently found in pyloric CPG (experimental study). (Elices et al.)



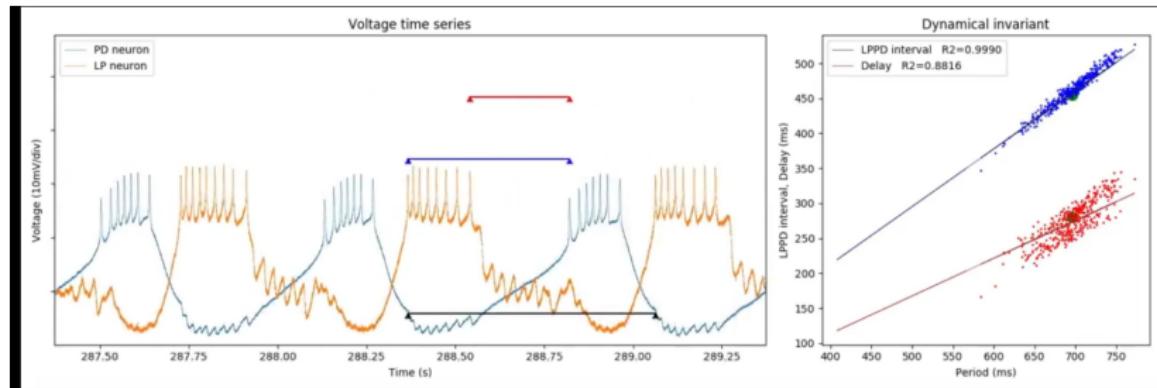
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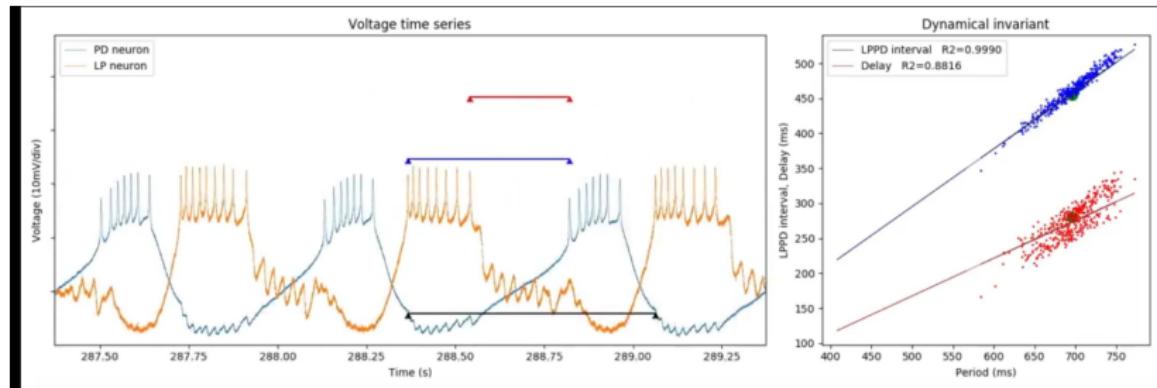
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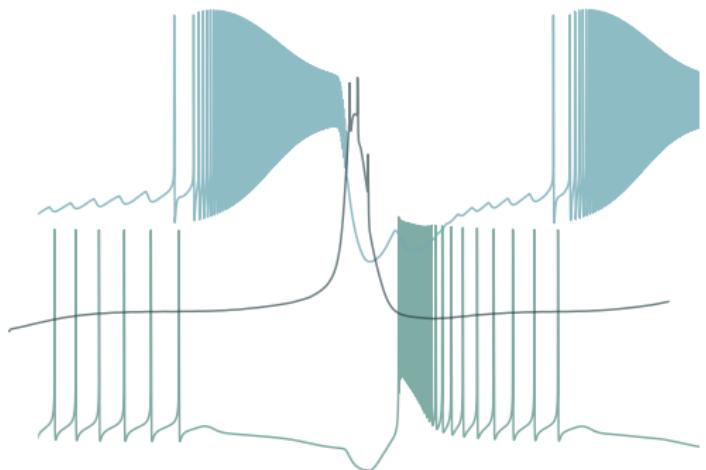
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Feeding CPG of *Lymnaea stagnalis*

Triphasic rhythm:

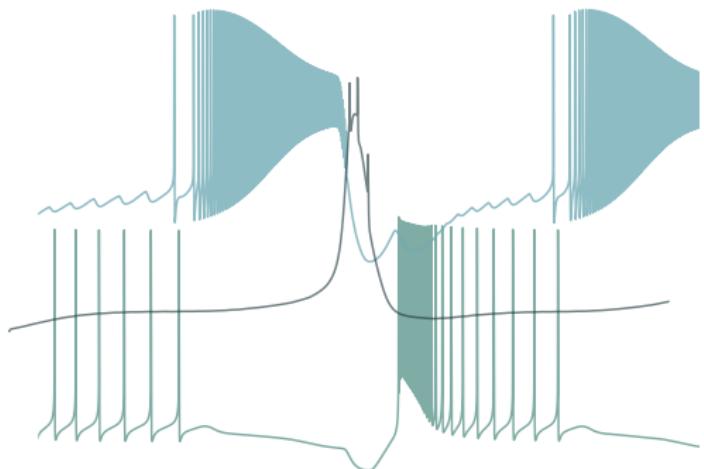
- N1 phase → Protraction



Feeding CPG of *Lymnaea stagnalis*

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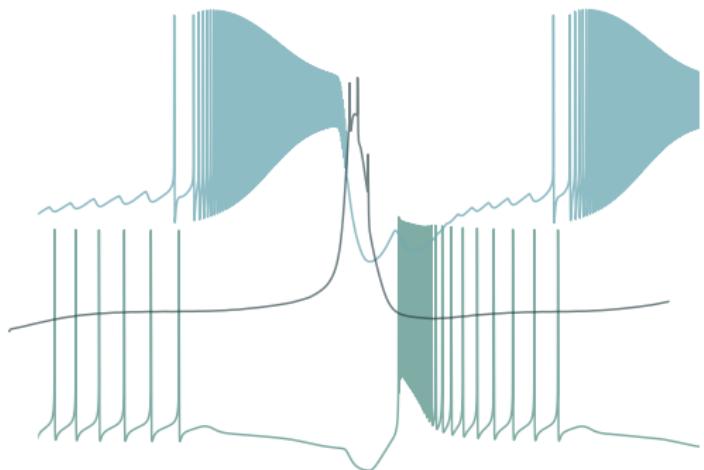
- N1 phase → Protraction
- N2 phase → Rasp



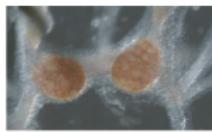
Feeding CPG of *Lymnaea stagnalis*

Triphasic rhythm:

- N1 phase → Protraction
- N2 phase → Rasp
- N3 phase → Swallow



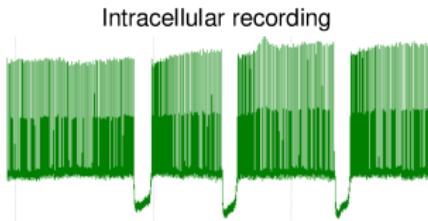
Computational and Experimental approach



Buccal Ganglia of *Lymnaea stagnalis* Microscope Image

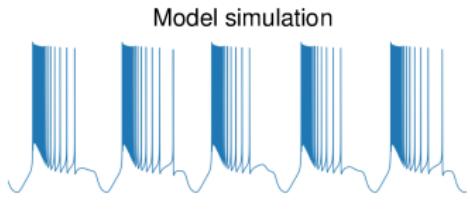


Lymnaea stagnalis



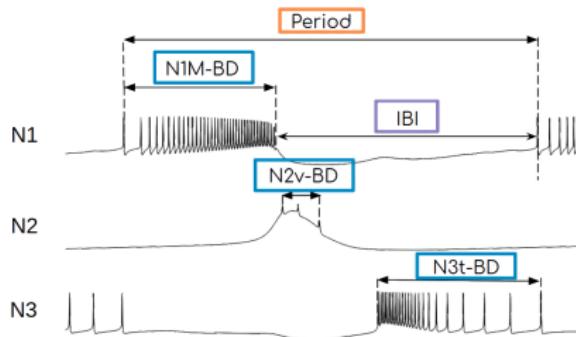
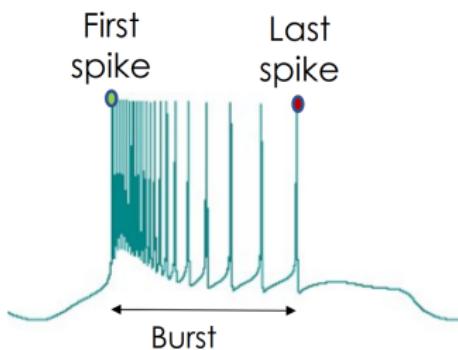
$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_I (V - V_I)$$

$$\begin{aligned} dn/dt &= \alpha_n(1-n) - \beta_n n \\ dm/dt &= \alpha_m(1-m) - \beta_m m \\ dh/dt &= \alpha_h(1-h) - \beta_h h \end{aligned}$$



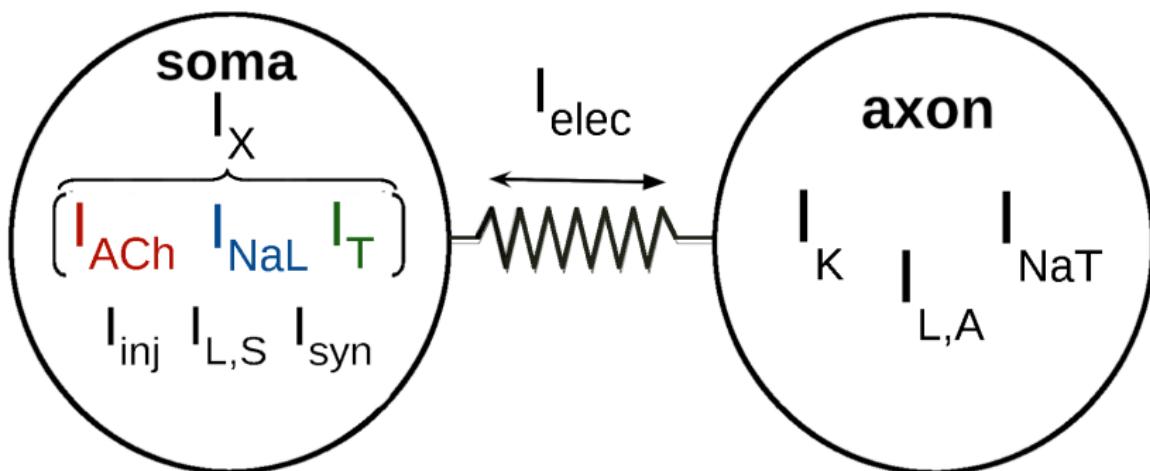
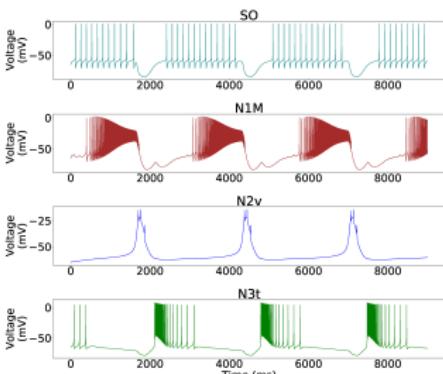
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Characterization of the time-intervals cycle-by-cycle



Computational Approach: Model description

○ Feeding CPG Model



Computational Approach: Ramp stimulation protocol

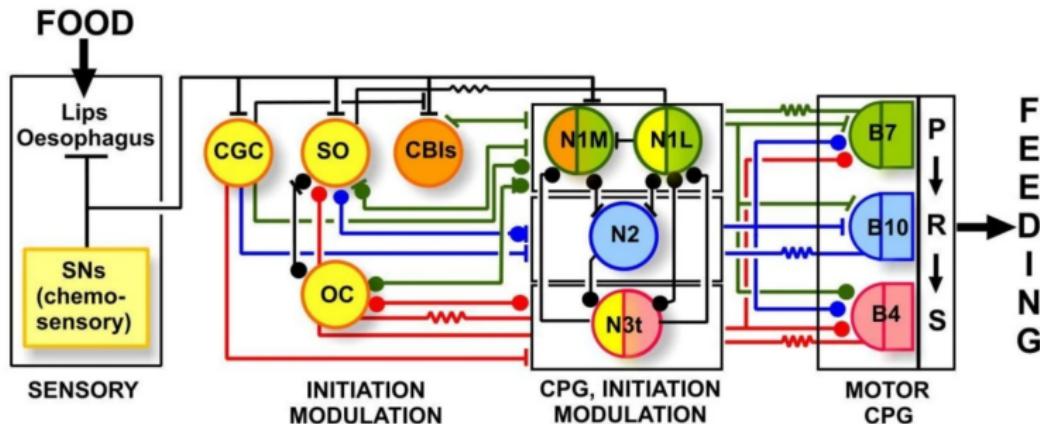
Cycle-by-cycle restrictions

Video

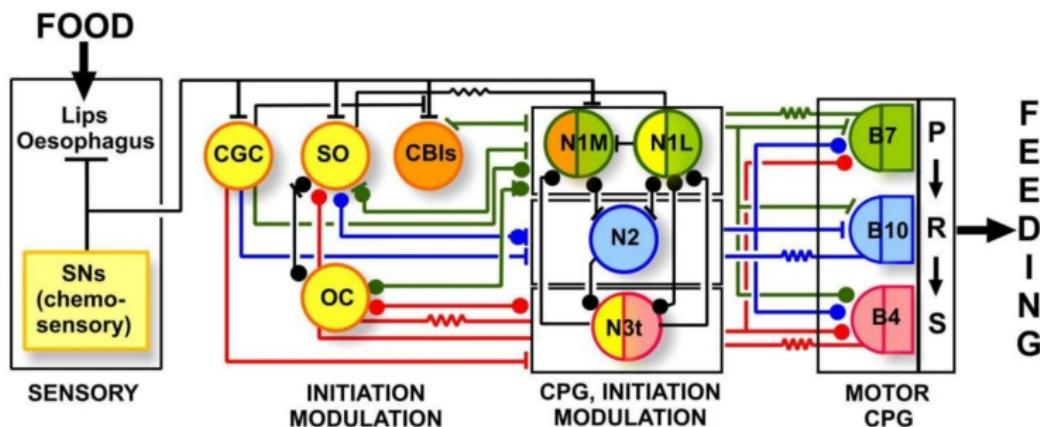
N1M stimulation

SO stimulation

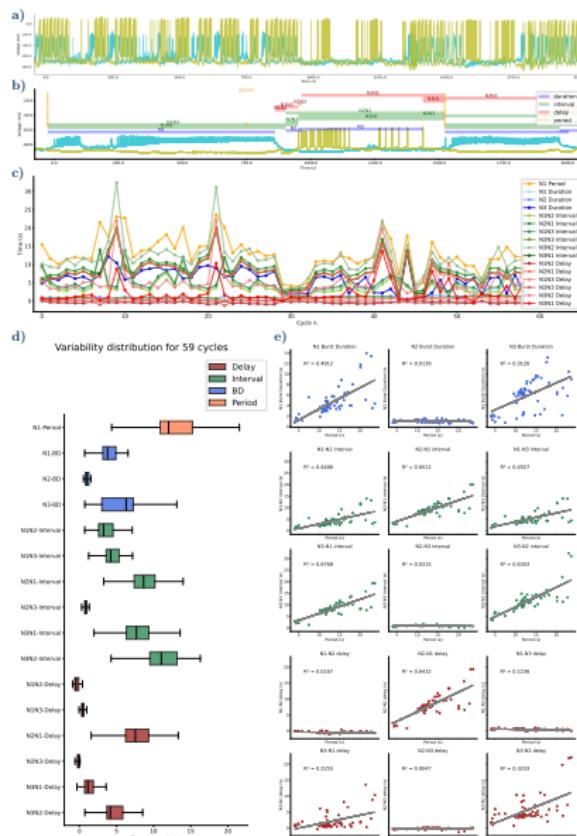
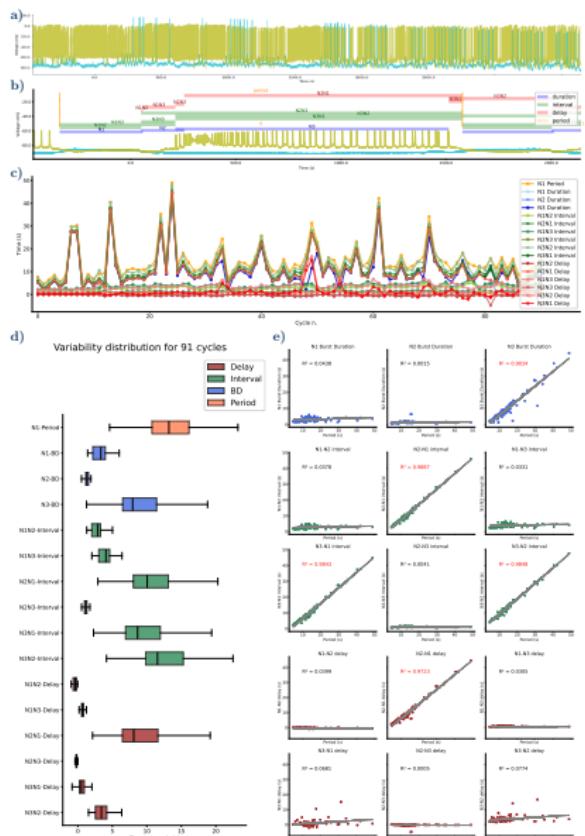
Models with chaotic activity



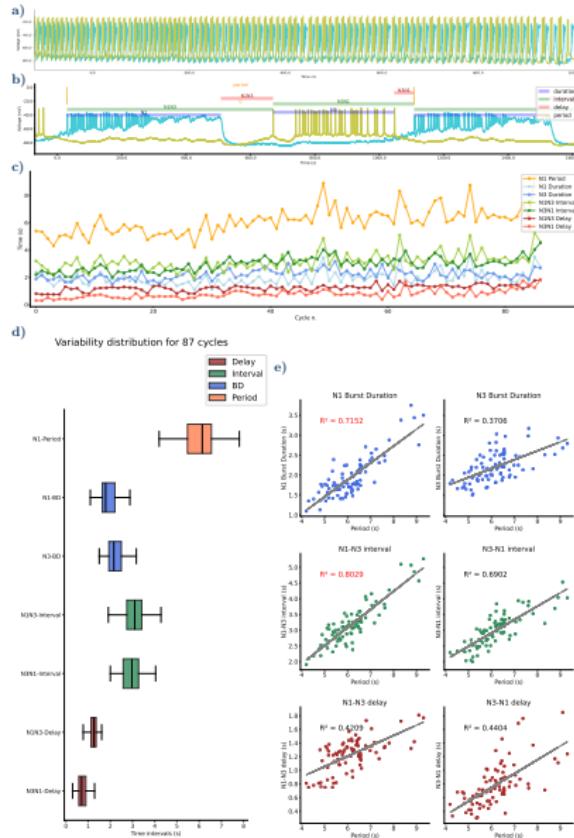
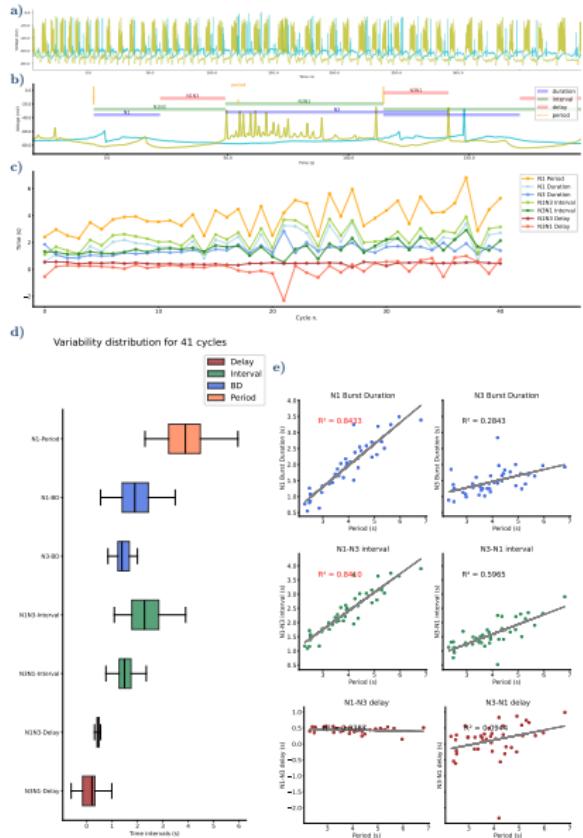
Experimental approach



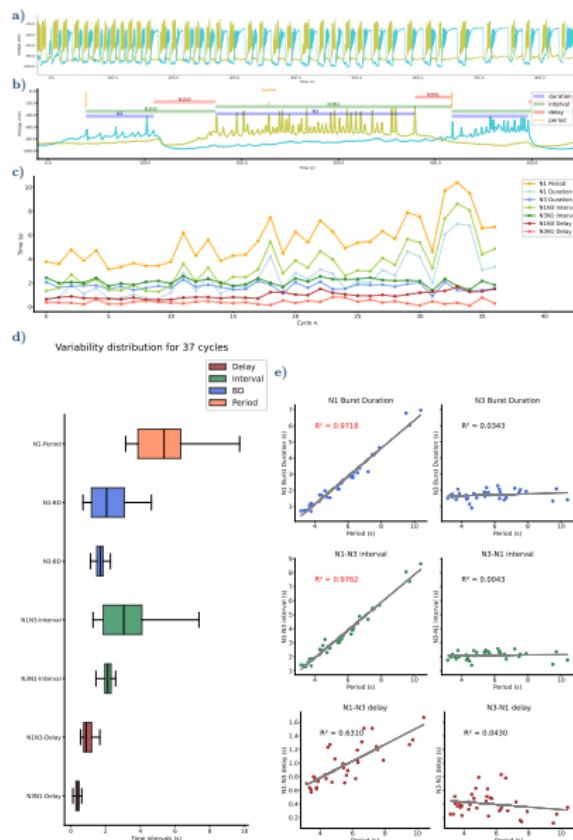
Spontaneous activity



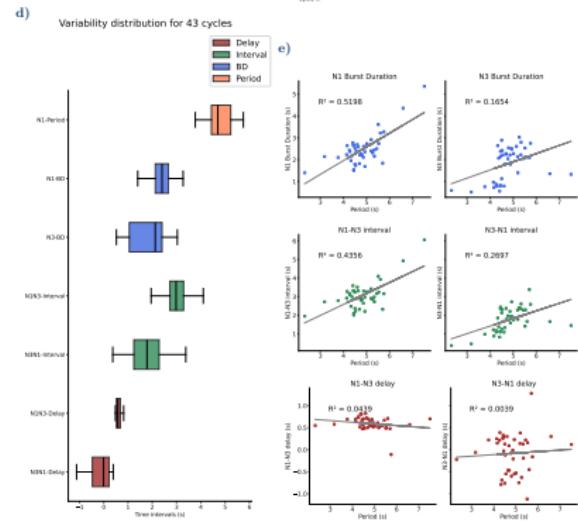
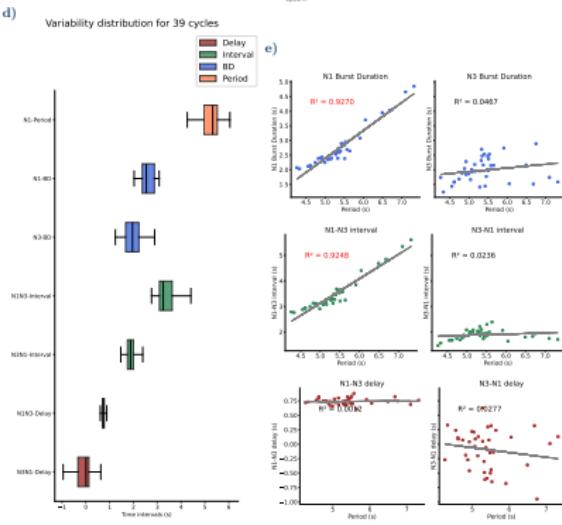
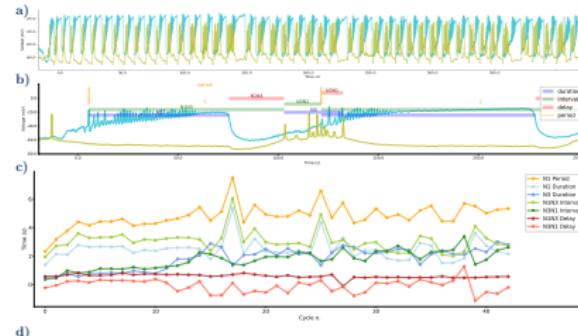
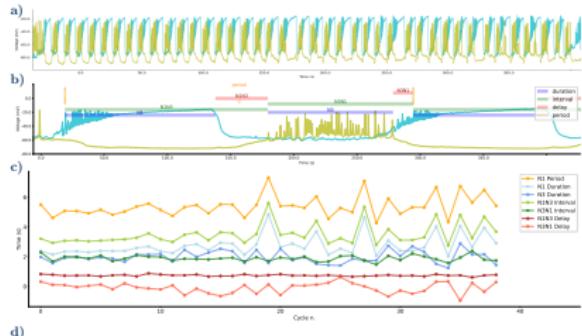
SO driven activity



MLN driven activity



CV1 driven activity

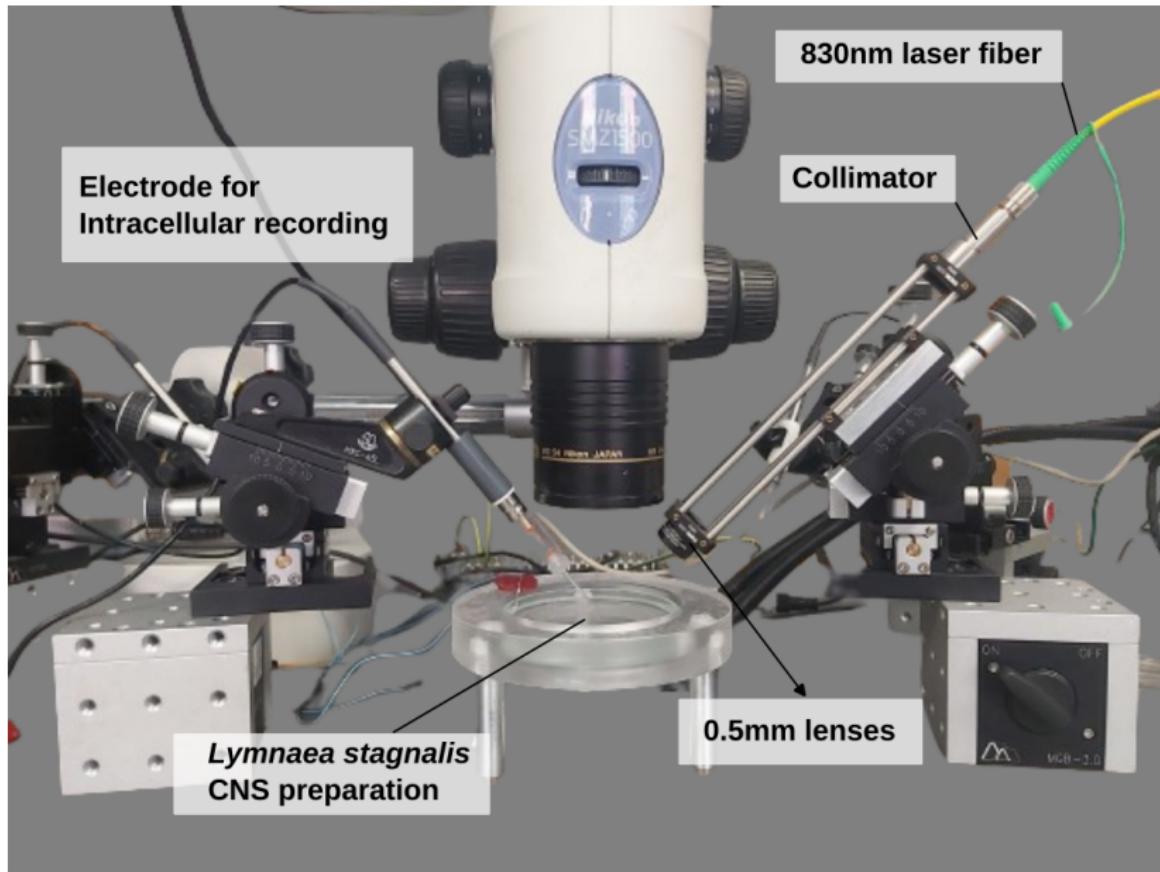


Robot

CW-NIR laser as an effective neuromodulation technique

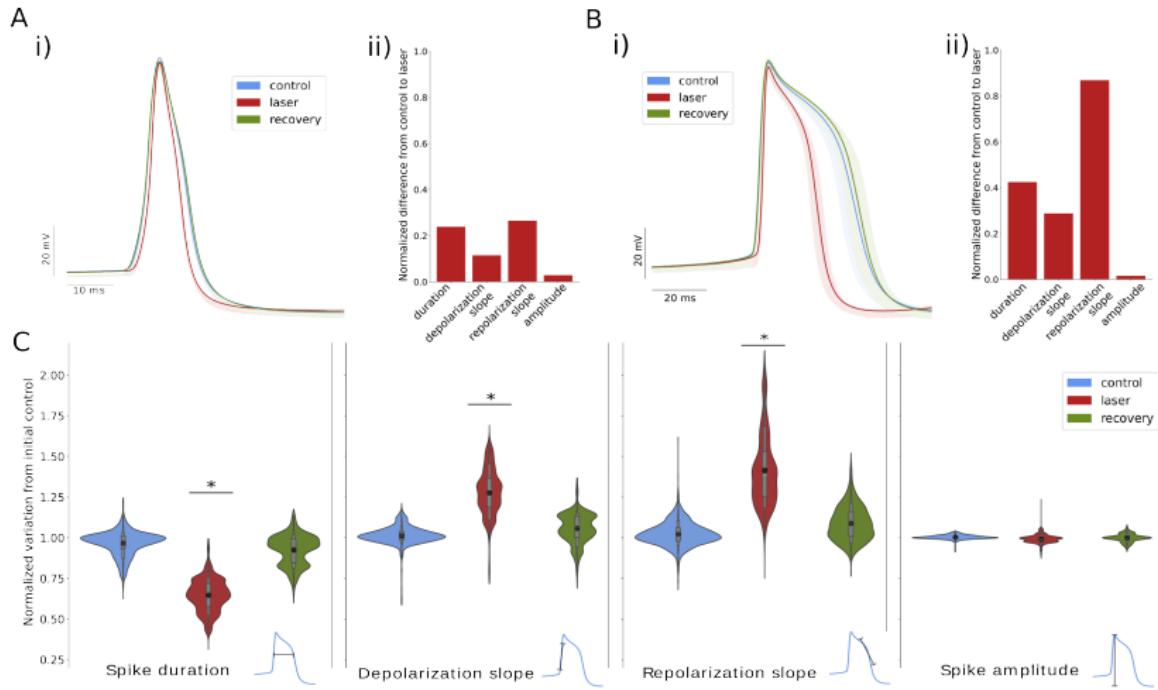
Current findings

Experimental setup

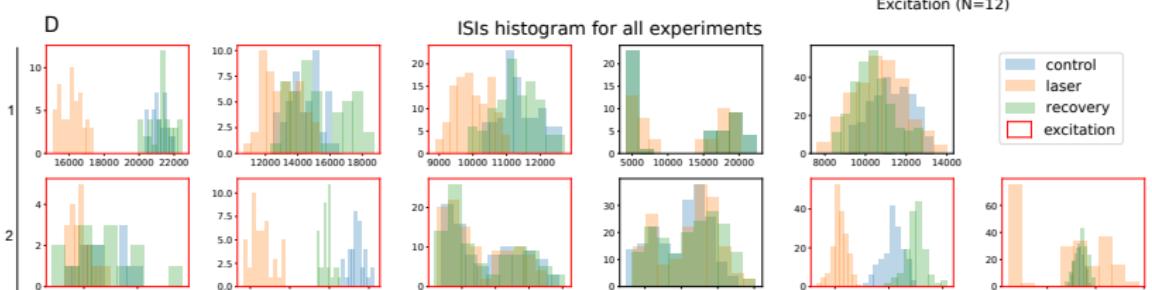
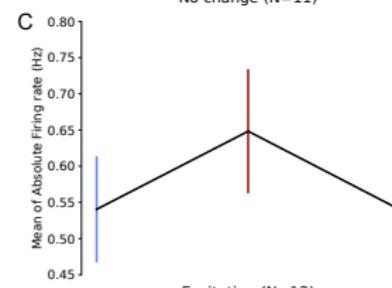
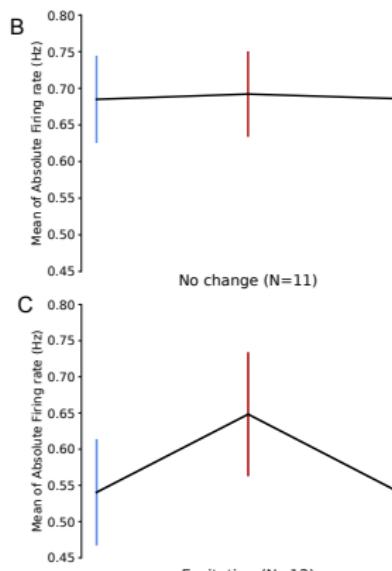
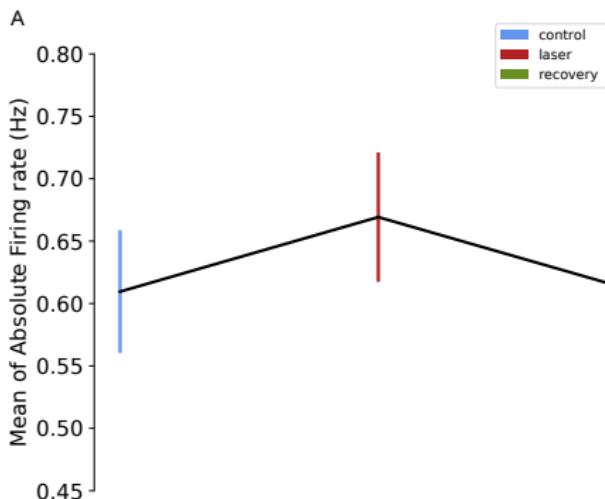


Effect on single neurons dynamics

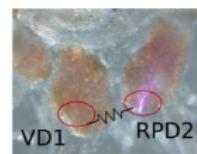
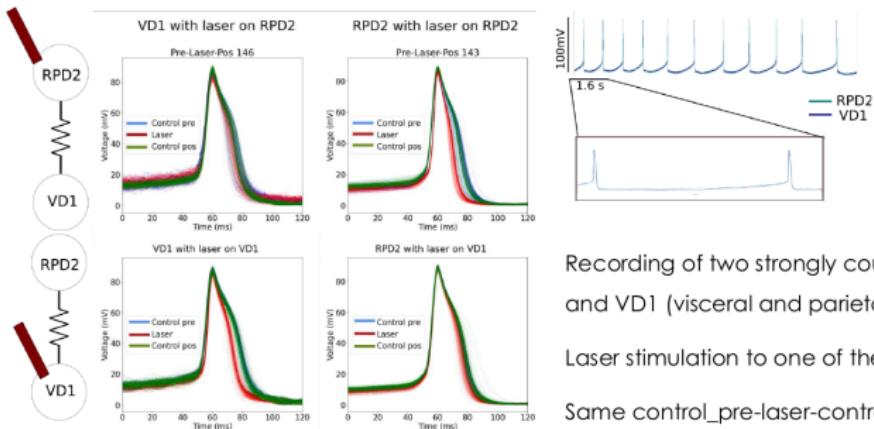
Modulation of the spike waveform



Effect on the firing rate



Effect on a minimal circuit



Recording of two strongly coupled neurons RPD2 and VD1 (visceral and parietal ganglia).

Laser stimulation to one of the neurons at a time.

Same control_pre-laser-control_pos protocol.

Model analysis to explore candidates

Model with temperature description

Activity-dependent stimulation

Conclusion

Conclusion



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