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

Alicia Garrido Peña

Universidad Autónoma de Madrid

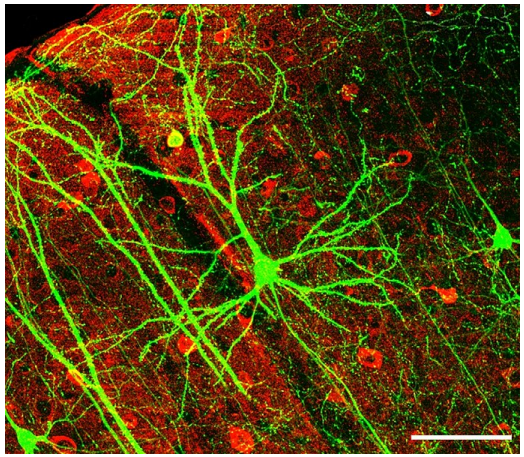
Alicia Garrido Peña. PhD thesis Seminar
Sunday 21st July, 2024

UAM Universidad Autónoma de Madrid | Escuela Politécnica Superior

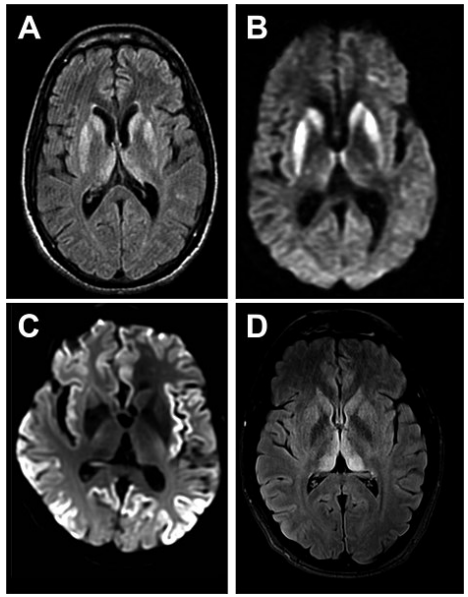
Contents

Introduction

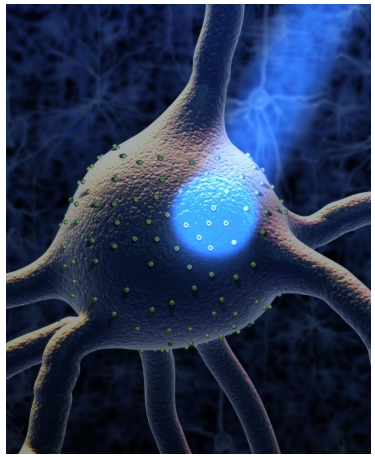
Neuroscience



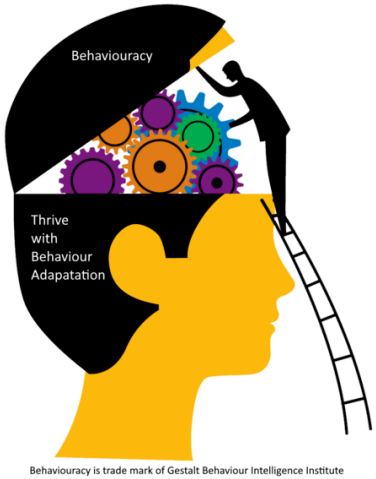
Neurobiology



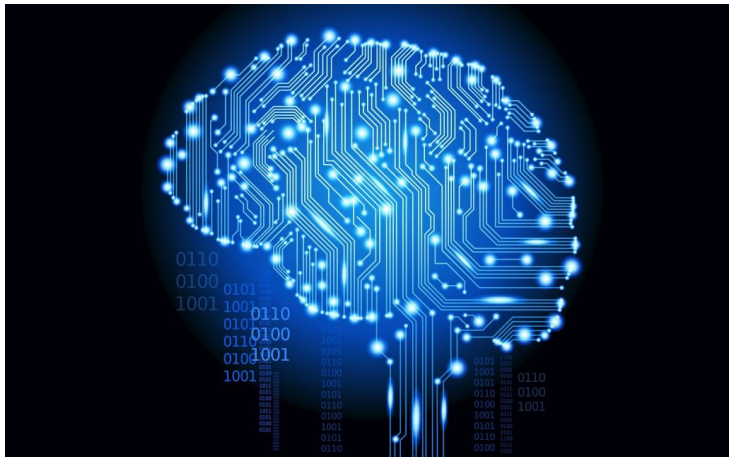
Clinical Neuroscience



Neurotechnology

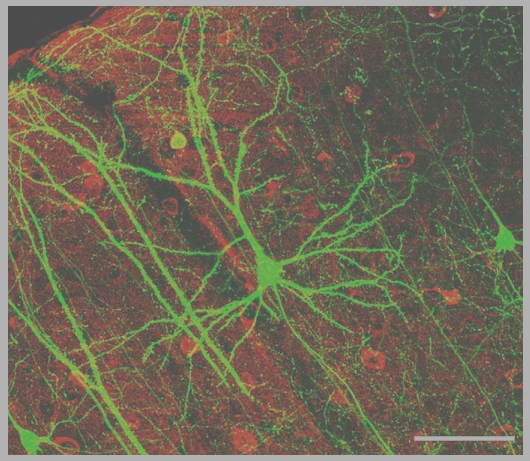


Cognitive Neurosience

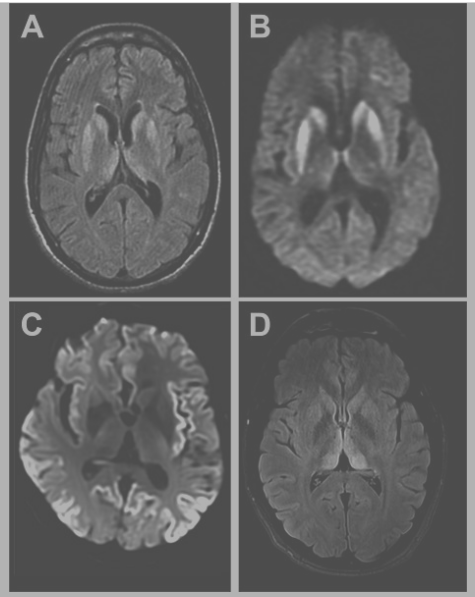


Computational Neurosience

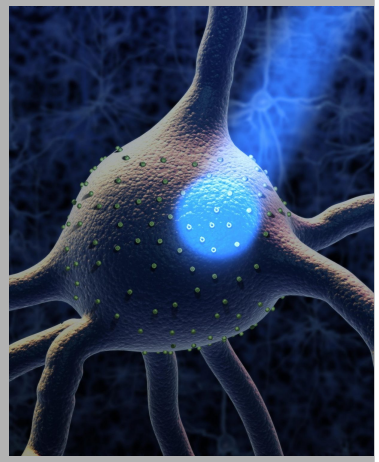
Neuroscience



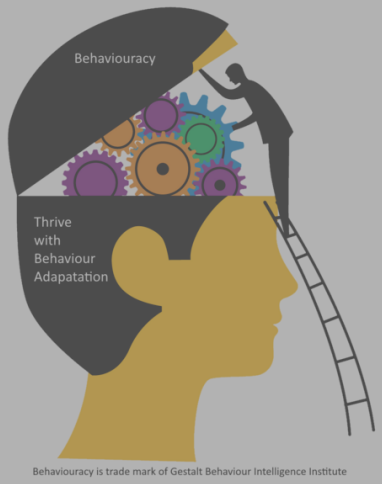
Neurobiology



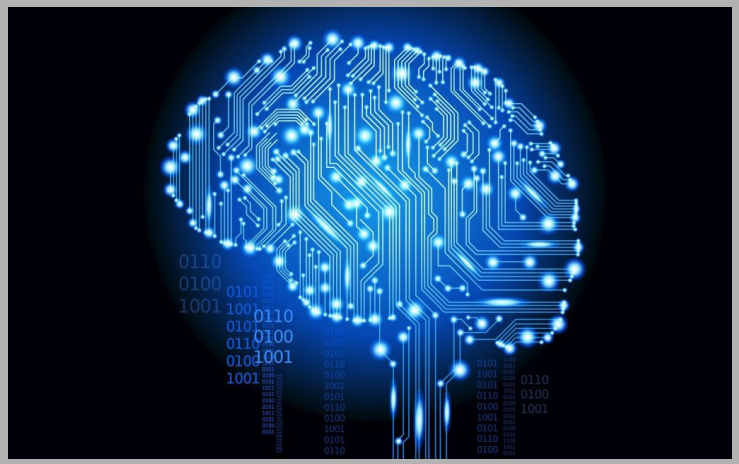
Clinical Neuroscience



Neurotechnology



Cognitive Neurosience



Computational Neurosience

Approach

- Neurocomputational Perspective

Approach

- Neurocomputational Perspective
- Bottom-up approach

Approach

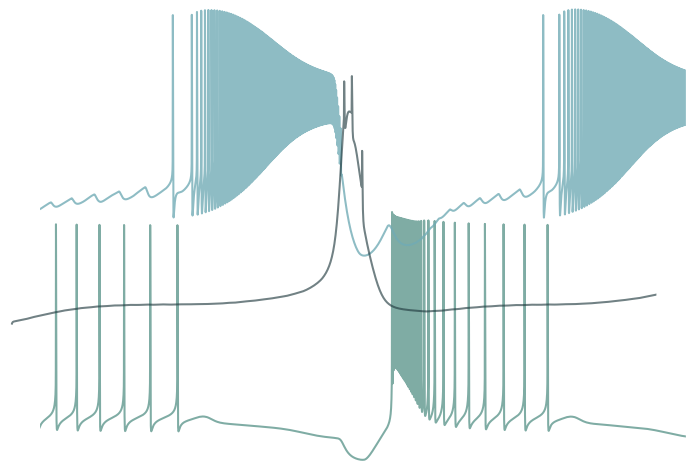
- Neurocomputational Perspective
- Bottom-up approach

From ionic channels

Approach

- Neurocomputational Perspective
- Bottom-up approach

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

Neuronal and Networks Dynamics

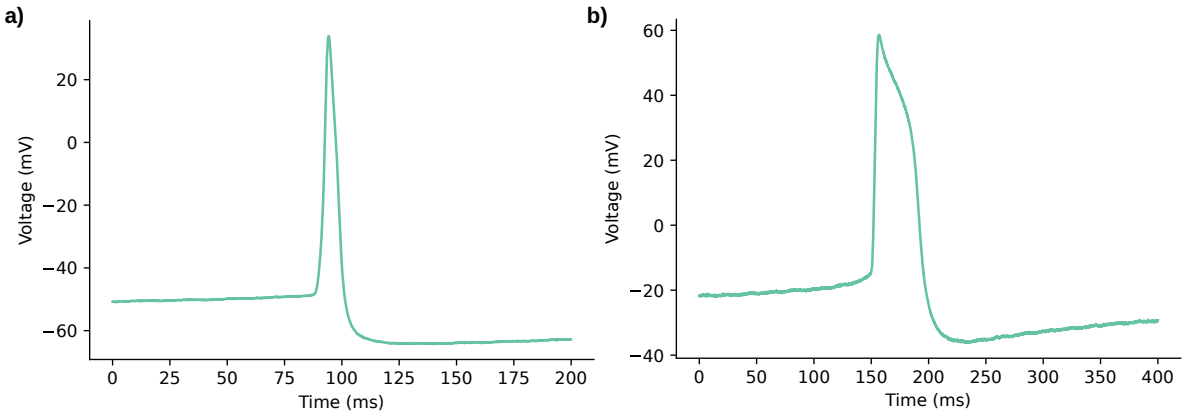
Neuronal electrical activity is often described in terms of the evolution of membrane voltage caused by the flow of ionic channels between the inside and outside of the cell.

Neuronal and Networks Dynamics

Depending on the channels that constitute the neuron and the circuit it is immersed in, the activity varies.

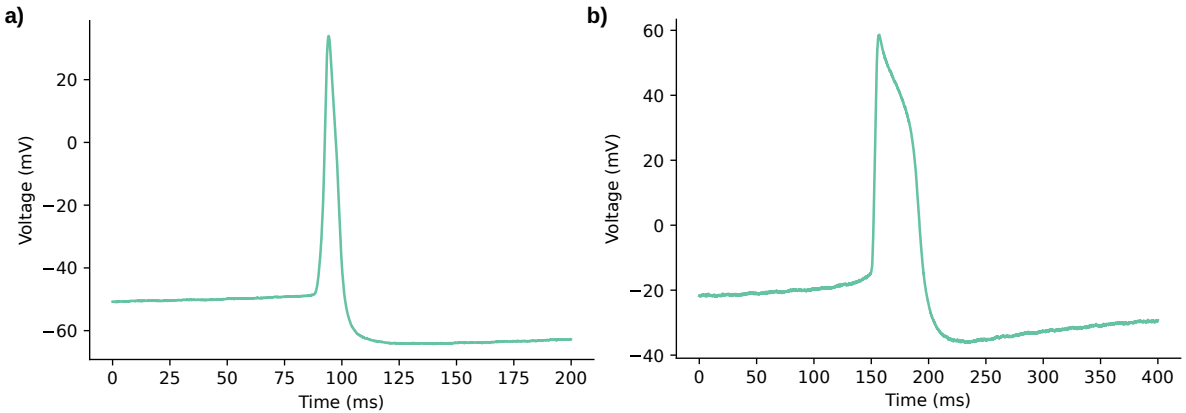
Neuronal and Networks Dynamics

Depending on the channels that constitute the neuron and the circuit it is immersed in, the activity varies.
In terms of the spike waveform:

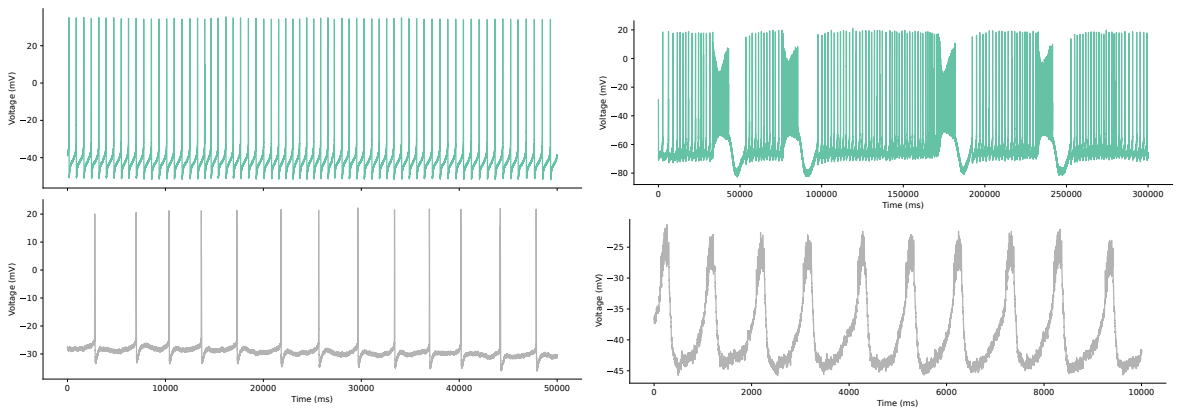


Neuronal and Networks Dynamics

Depending on the channels that constitute the neuron and the circuit it is immersed in, the activity varies.
In terms of the spike waveform:



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

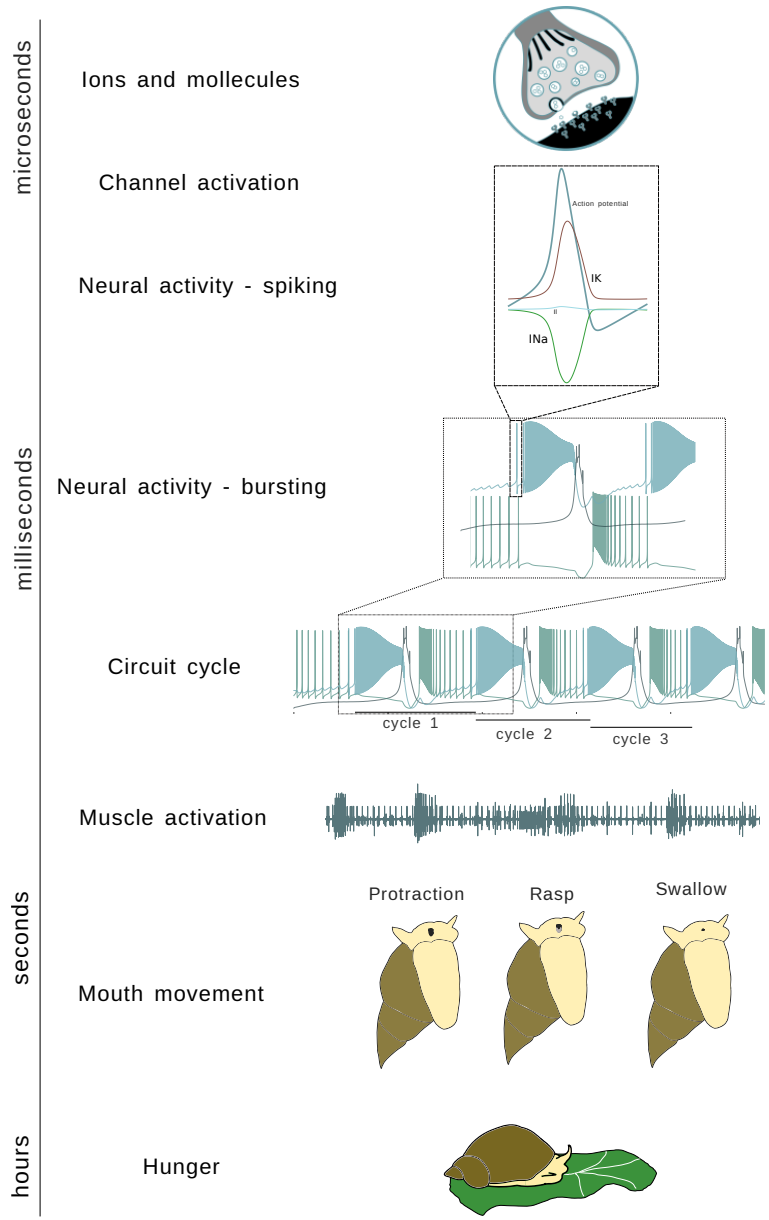


The sequential nature of neural dynamics

- There are sequential processes at different time-scales.

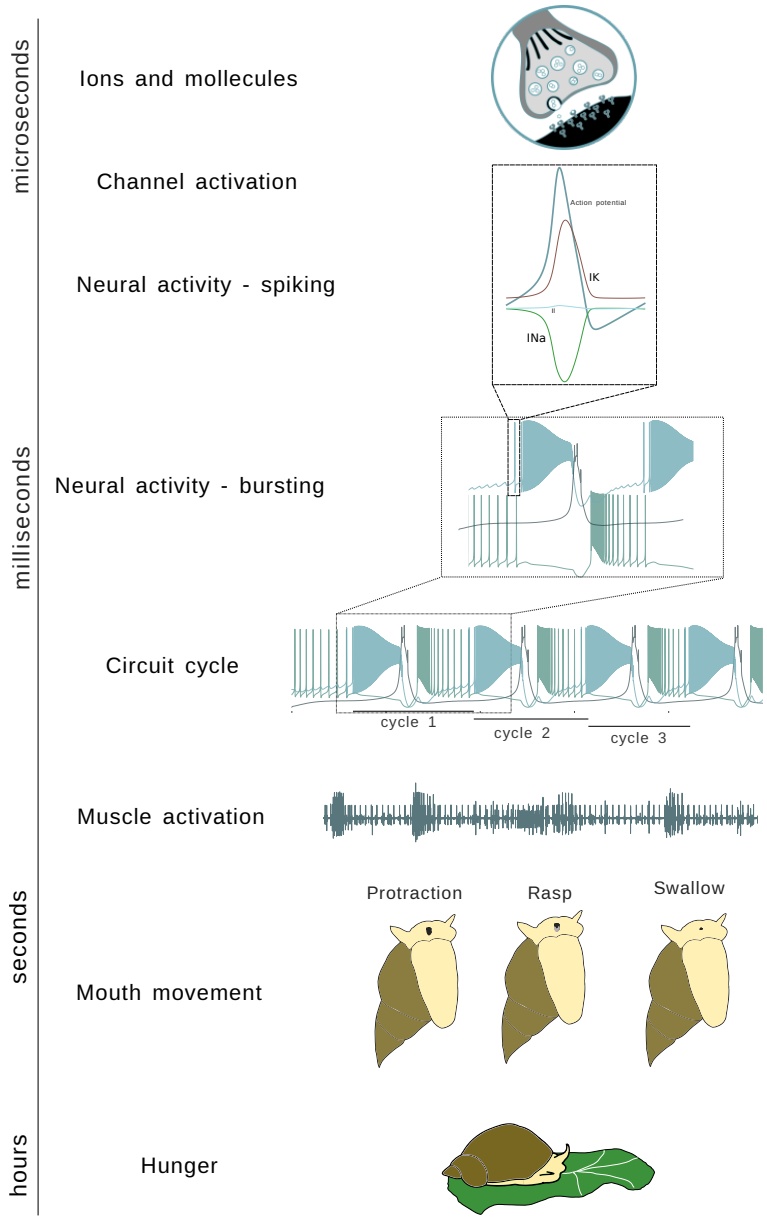
The sequential nature of neural dynamics

- There are sequential processes at different time-scales.



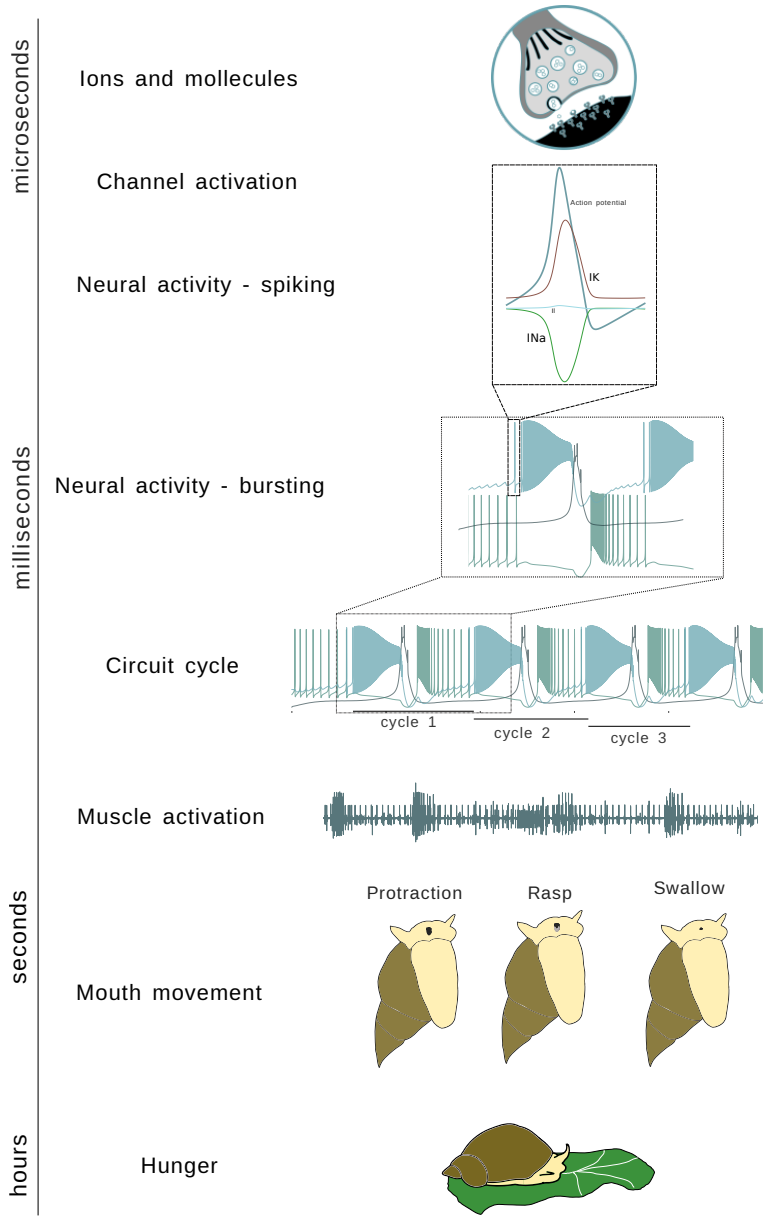
The sequential nature of neural dynamics

- There are sequential processes at different time-scales.
- Many behaviors and actions are governed by sequential processes



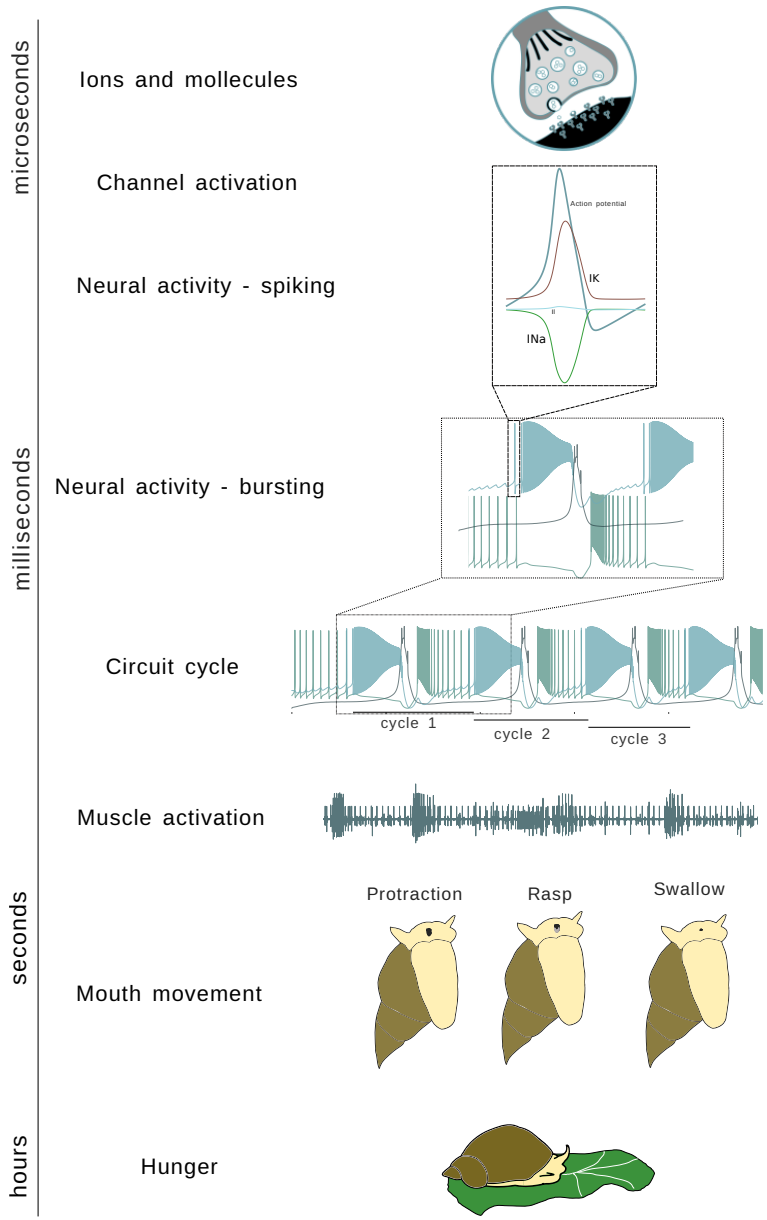
The sequential nature of neural dynamics

- There are sequential processes at different time-scales.
- Many behaviors and actions are governed by sequential processes
- Motor control, speech, decision making, etc.



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

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the
  - Detailed reproduction of the living activity

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the
  - Detailed reproduction of the living activity
- Limitations

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the
  - Detailed reproduction of the living activity
- Limitations
  - Restricted variability

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the
  - Detailed reproduction of the living activity
- Limitations
  - Restricted variability
  - The description may depend on the information about the living system

Studying neural dynamics in computational models

- Computational models are powerful tools to study neural dynamics
- Advantages
  - Full accessibility to the
  - Detailed reproduction of the living activity
- Limitations
  - Restricted variability
  - The description may depend on the information about the living system

Studying neural dynamics in computational models

Studying neural dynamics in computational models

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

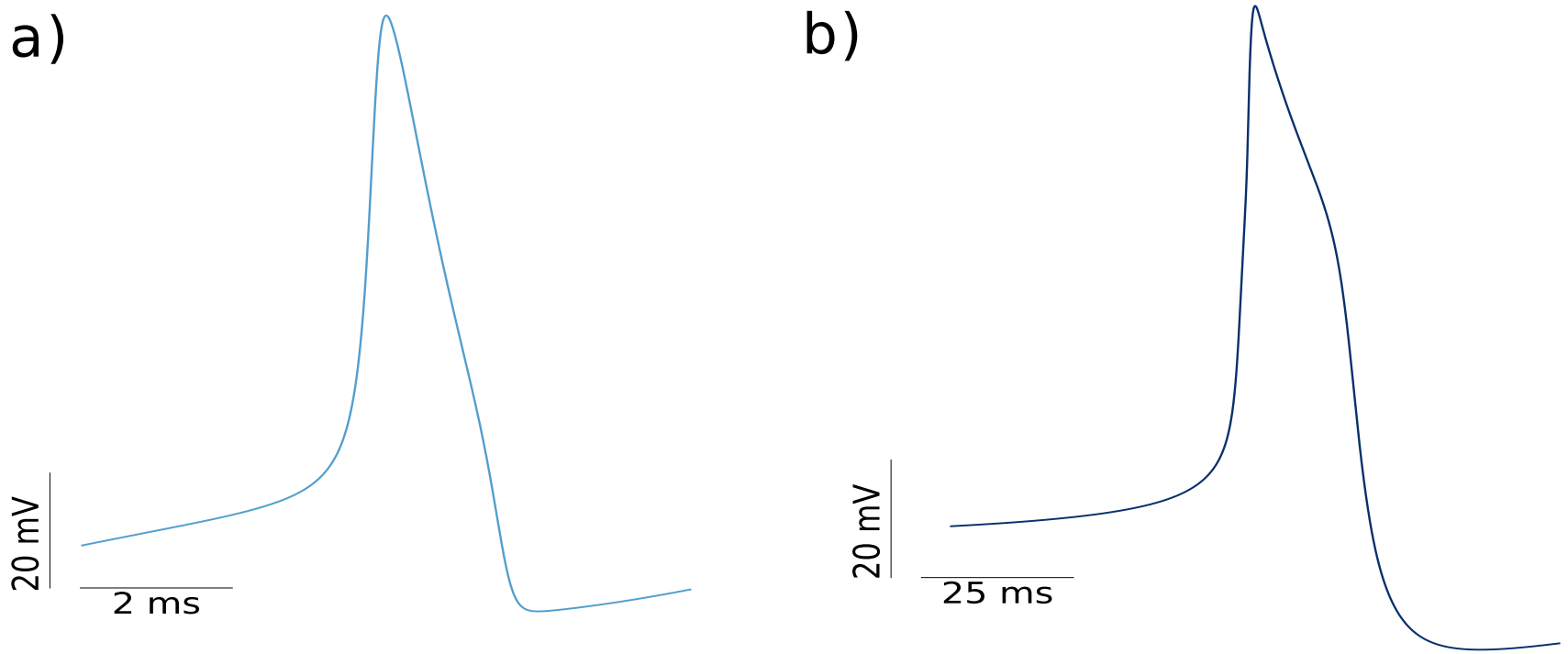
Conductance-based models

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

Studying neural dynamics in computational models

Conductance-based models

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



Studying neural dynamics in computational models

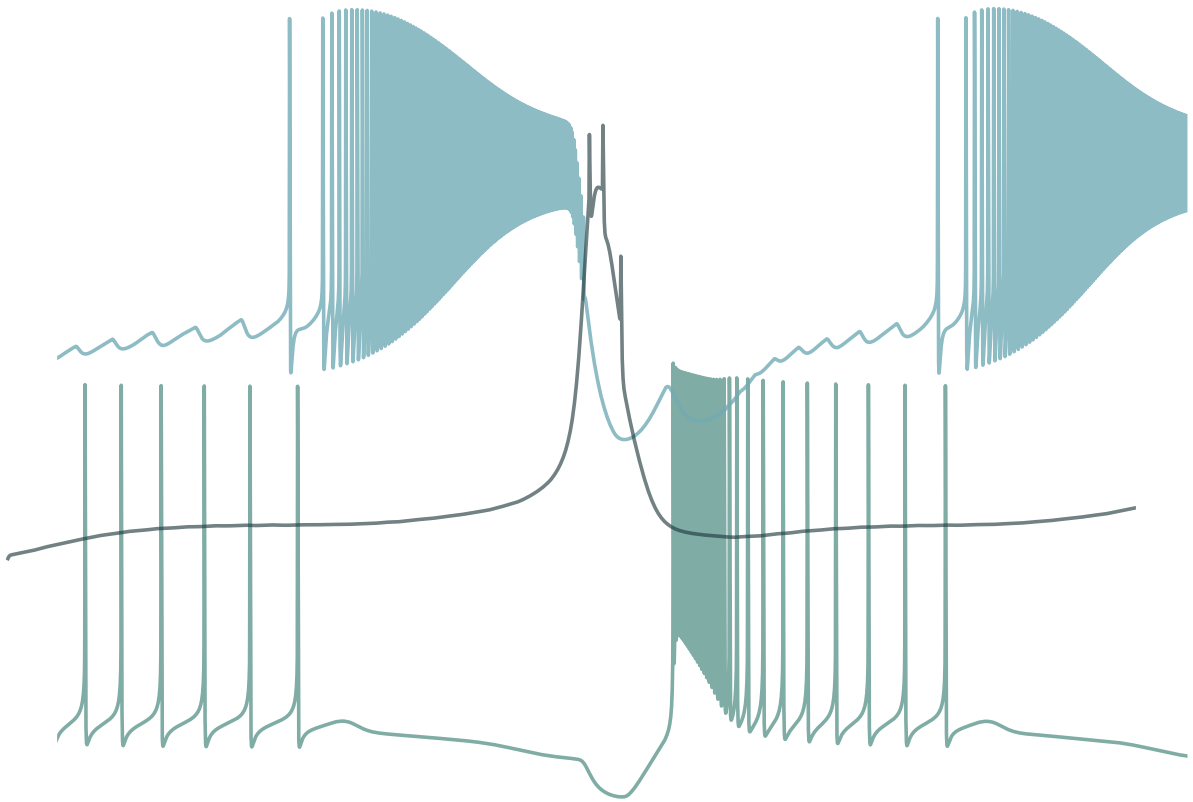
Conductace-based models

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

Studying neural dynamics in computational models

Conductace-based models

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



Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.
- Using invertebrates as animal models have different advantages:

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.
- Using invertebrates as animal models have different advantages:
  - Ease of accessibility to the nervous system.

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.
- Using invertebrates as animal models have different advantages:
  - Ease of accessibility to the nervous system.
  - Longer survival times of the preparations.

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.
- Using invertebrates as animal models have different advantages:
  - Ease of accessibility to the nervous system.
  - Longer survival times of the preparations.
  - Ease of breeding and reproduction.

Vertebrate and invertebrate animal studies

- In addition to the well known vertebrate models, there have been invaluable findings using invertebrates.
- There are many universal characteristics of nervous systems and behaviors that can be extrapolated to humans.
- Using invertebrates as animal models have different advantages:
  - Ease of accessibility to the nervous system.
  - Longer survival times of the preparations.
  - 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.

- To study different conditions.

Neural stimulation

When studying neural systems, we need neuromodulatory technics.

- To study different conditions.
- Test their robustness.

Neural stimulation

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
- The source of the stimulation:
  - Chemical
  - Electrical

Neural stimulation

We can classify them based on:

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

Neural stimulation

We can classify them based on:

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

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive
- The source of the stimulation:
  - Chemical
  - Electrical
  - Magnetic
  - Mechanical
  - Optical

Neural stimulation

We can classify them based on:

- The change in the system: Invasive / non-invasive
- The source of the stimulation:
  - Chemical
  - Electrical
  - Magnetic
  - Mechanical
  - Optical

Motivation and Objectives

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.
2. To study sequence interval variability constraints and relationships in neural models and living circuits.

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.
2. To study sequence interval variability constraints and relationships in neural models and living circuits.
3. To analyze the feeding CPG of *Lymnaea stagnalis* to provide evidence of the universality of sequential dynamical invariants found in the pyloric CPG by:

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.
2. To study sequence interval variability constraints and relationships in neural models and living circuits.
3. To analyze the feeding CPG of *Lymnaea stagnalis* to provide evidence of the universality of sequential dynamical invariants found in the pyloric CPG by:
   - 3.1 Characterizing the sequential invariants cycle-by-cycle in a bursting CPG model.

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.
2. To study sequence interval variability constraints and relationships in neural models and living circuits.
3. To analyze the feeding CPG of *Lymnaea stagnalis* to provide evidence of the universality of sequential dynamical invariants found in the pyloric CPG by:
   - 3.1 Characterizing the sequential invariants cycle-by-cycle in a bursting CPG model.
   - 3.2 Analyzing intracellular recordings with spontaneous activity and with different rhythm initiation stimulation protocols.

Motivation and Objectives

1. To explore the sequential nature of neuronal dynamics at distinct description levels.
2. To study sequence interval variability constraints and relationships in neural models and living circuits.
3. To analyze the feeding CPG of *Lymnaea stagnalis* to provide evidence of the universality of sequential dynamical invariants found in the pyloric CPG by:
   - 3.1 Characterizing the sequential invariants cycle-by-cycle in a bursting CPG model.
   - 3.2 Analyzing intracellular recordings with spontaneous activity and with different rhythm initiation stimulation protocols.
4. To illustrate the possible functionality of sequential dynamical invariants in biohybrid robotics.

Motivation and Objectives

1. To test the capability of CW-NIR laser stimulation to modulate neuronal dynamics by:

Motivation and Objectives

1. To test the capability of CW-NIR laser stimulation to modulate neuronal dynamics by:
   1.1 Characterizing the CW-NIR effect in the spike waveform dynamics.

Motivation and Objectives

1. To test the capability of CW-NIR laser stimulation to modulate neuronal dynamics by:
   - 1.1 Characterizing the CW-NIR effect in the spike waveform dynamics.
   - 1.2 Analyzing the ability of this neurotechnology to change the spiking rate and the circuit dynamics.

Motivation and Objectives

1. To test the capability of CW-NIR laser stimulation to modulate neuronal dynamics by:
   - 1.1 Characterizing the CW-NIR effect in the spike waveform dynamics.
   - 1.2 Analyzing the ability of this neurotechnology to change the spiking rate and the circuit dynamics.
2. To study the possible biophysical candidates underlying the CW-NIR effect in model simulations.

Motivation and Objectives

1. To test the capability of CW-NIR laser stimulation to modulate neuronal dynamics by:
   - 1.1 Characterizing the CW-NIR effect in the spike waveform dynamics.
   - 1.2 Analyzing the ability of this neurotechnology to change the spiking rate and the circuit dynamics.
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 constrains in CPG circuits: Dynamical invariants

Central Pattern Generators

- Neural circuits generating robust sequences of neural activity

Central Pattern Generators

- Neural circuits generating robust sequences of neural activity
- Control motor rhythms in an autonomous manner

Central Pattern Generators

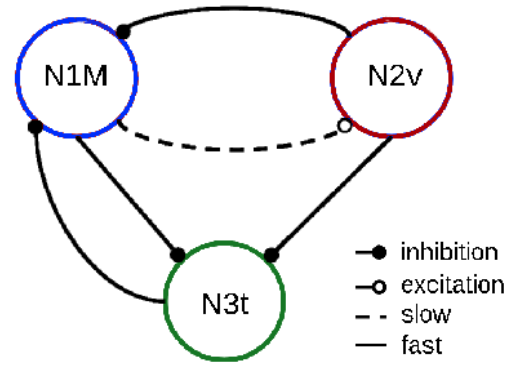
- Neural circuits generating robust sequences of neural activity
- Control motor rhythms in an autonomous manner
- Present in vertebrates and invertebrates

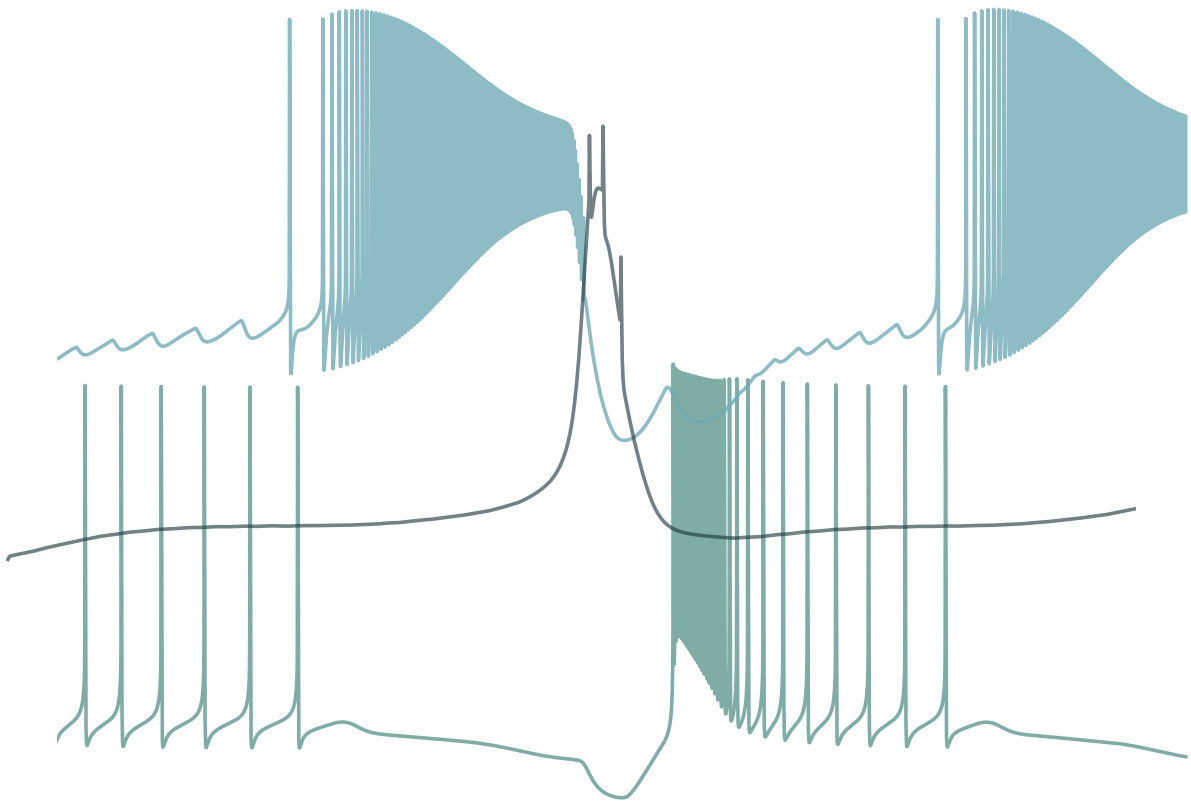
Central Pattern Generators

- 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

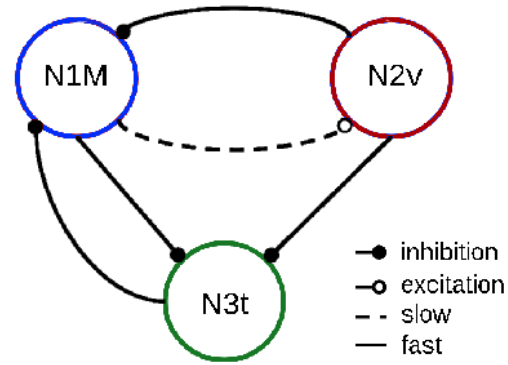
- Non-open topologies

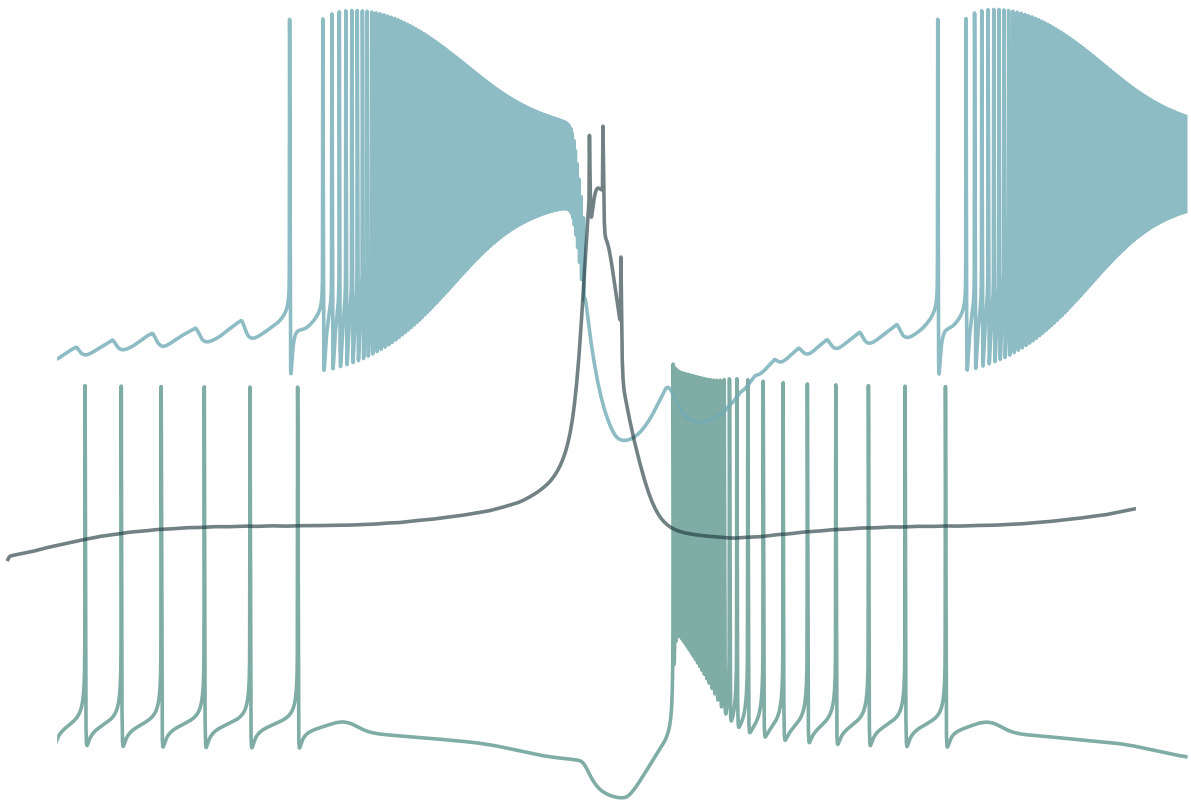




Central Pattern Generators

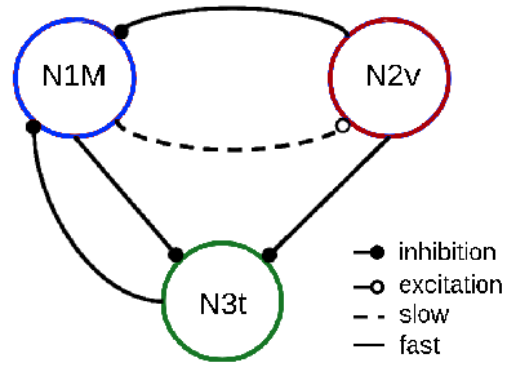
- Non-open topologies
- Based on mutual inhibition

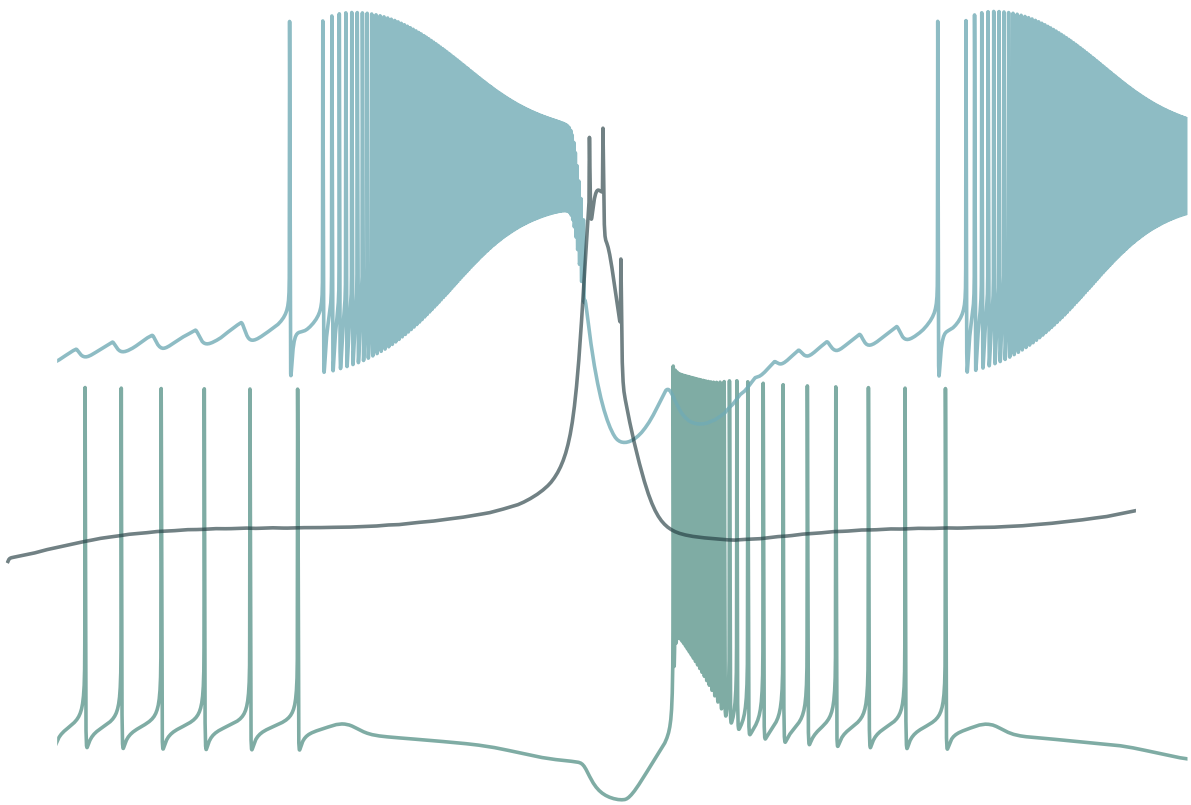




Central Pattern Generators

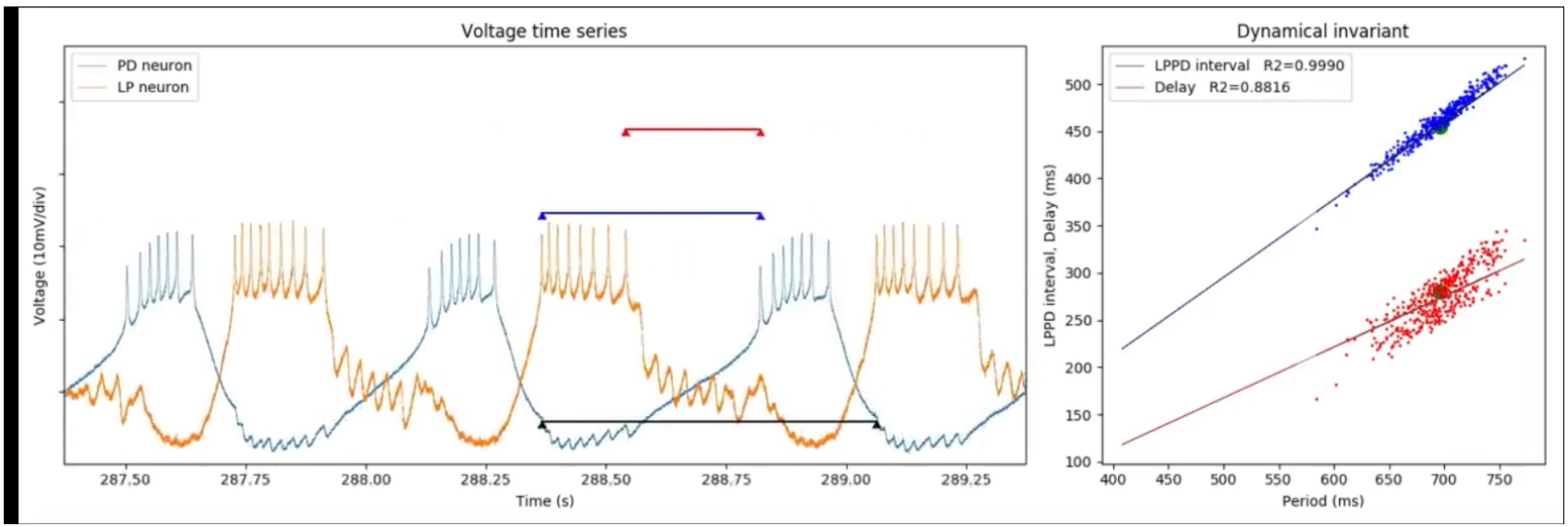
- Non-open topologies
- Based on mutual inhibition
- Temporal sequences maintained cycle-by-cycle





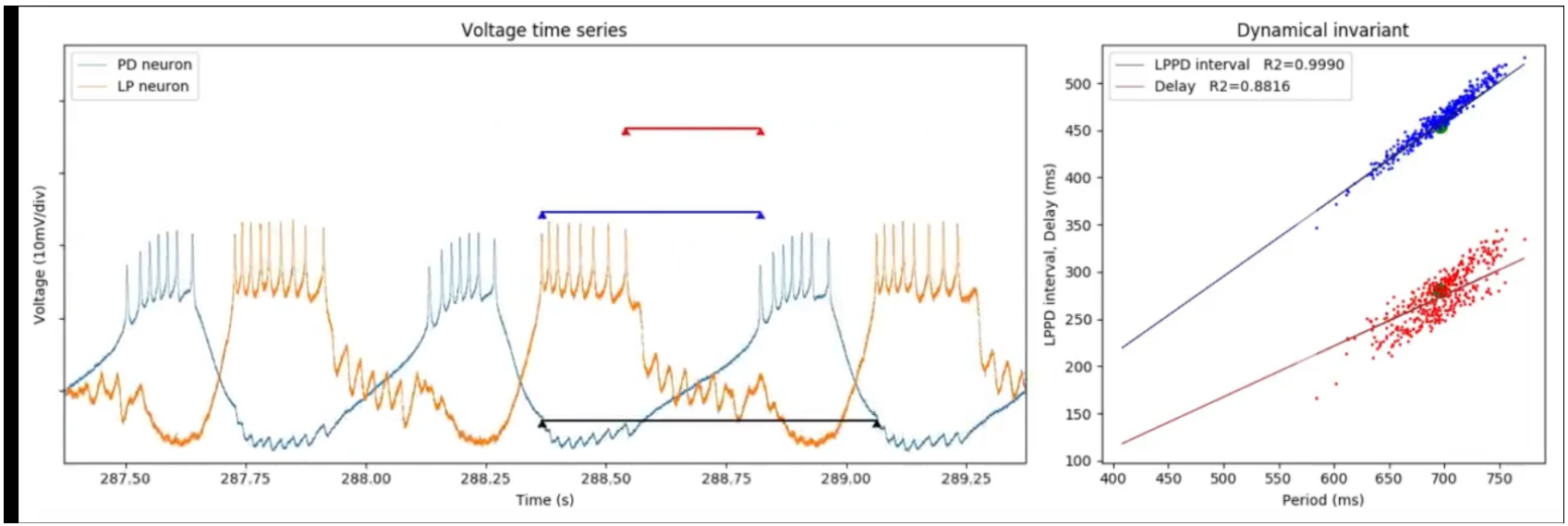
Temporal constrains: Sequential Dynamical invariants

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



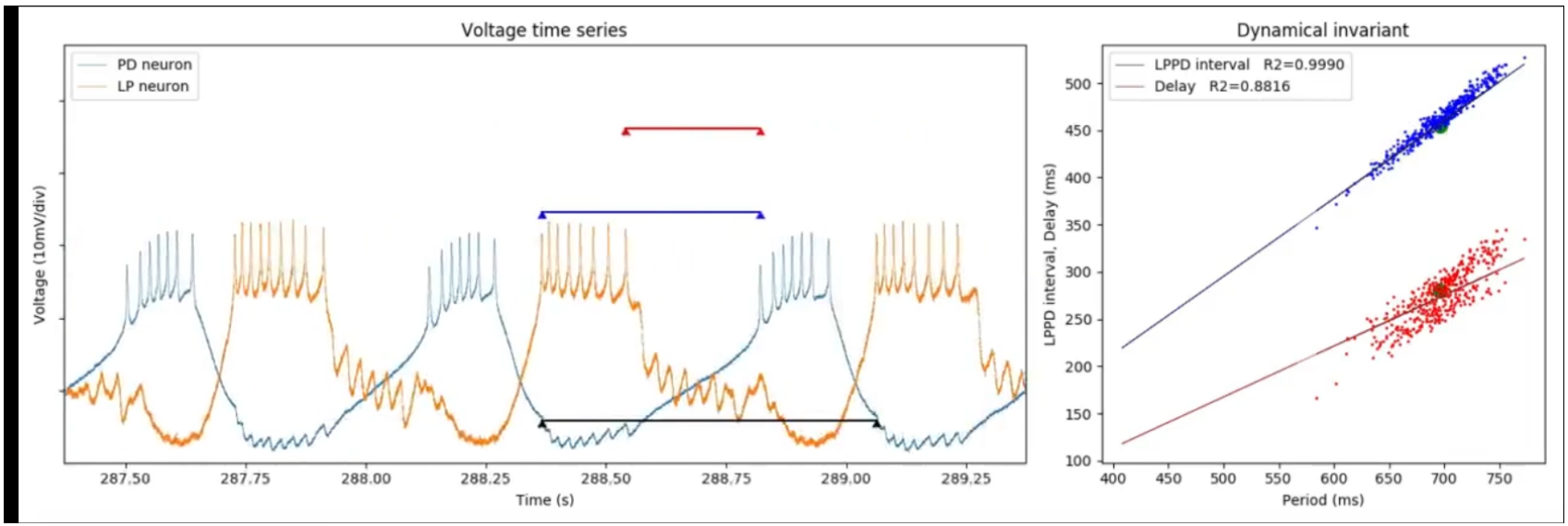
Temporal constrains: Sequential Dynamical invariants

- Recently found in pyloric CPG (experimental study). (Elices et al.)
- Specific intervals that build the sequence are highly correlated cycle-by-cycle.



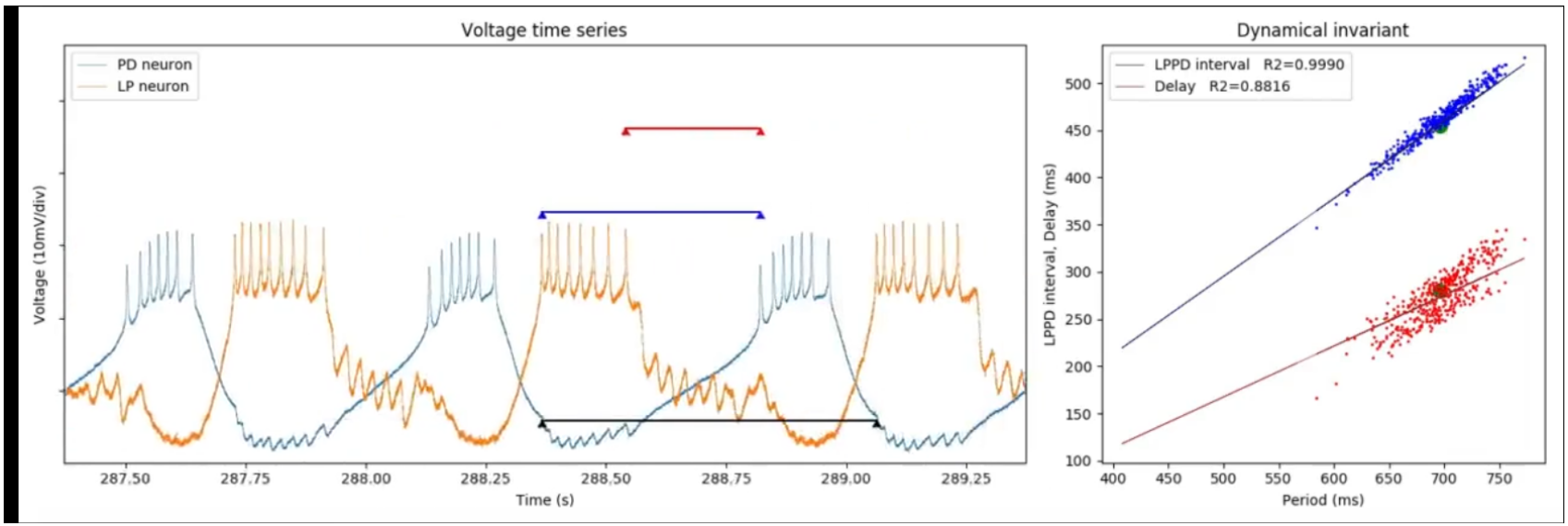
Temporal constrains: Sequential Dynamical invariants

- Recently found in pyloric CPG (experimental study). (Elices et al.)
- Specific intervals that build the sequence are highly correlated cycle-by-cycle.
- Consistent under high variability induced situations (Ethanol).



Temporal constrains: Sequential Dynamical invariants

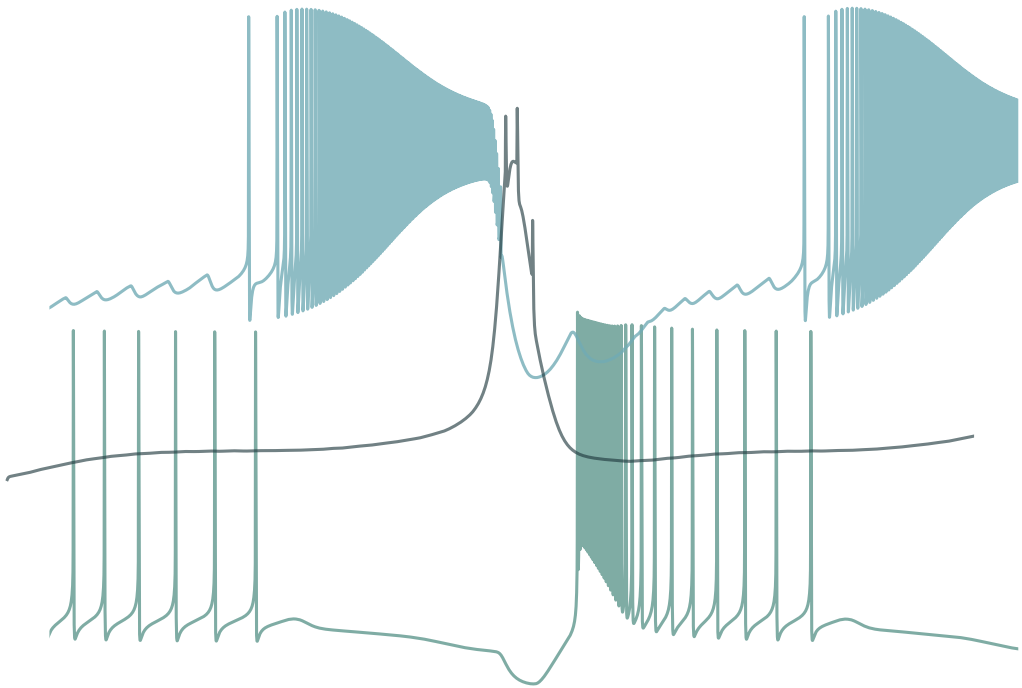
- Recently found in pyloric CPG (experimental study). (Elices et al.)
- Specific intervals that build the sequence are highly correlated cycle-by-cycle.
- Consistent under high variability induced situations (Ethanol).



Feeding CPG of Lymnaea stagnalis

Triphasic rhythm:

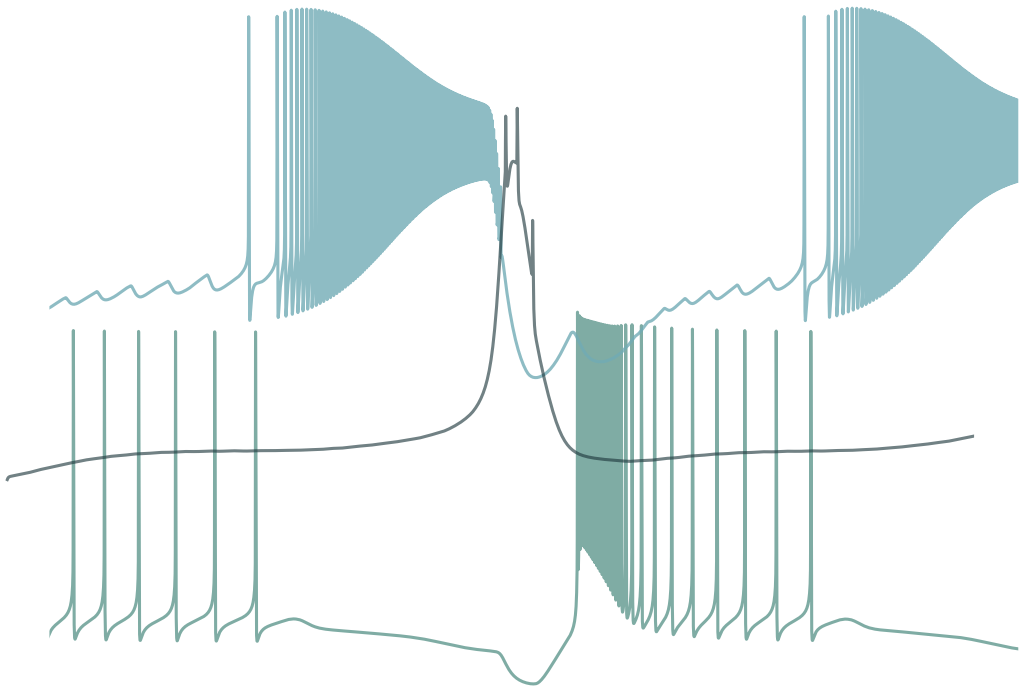
- N1 phase → Protraction



Feeding CPG of Lymnaea stagnalis

Triphasic rhythm:

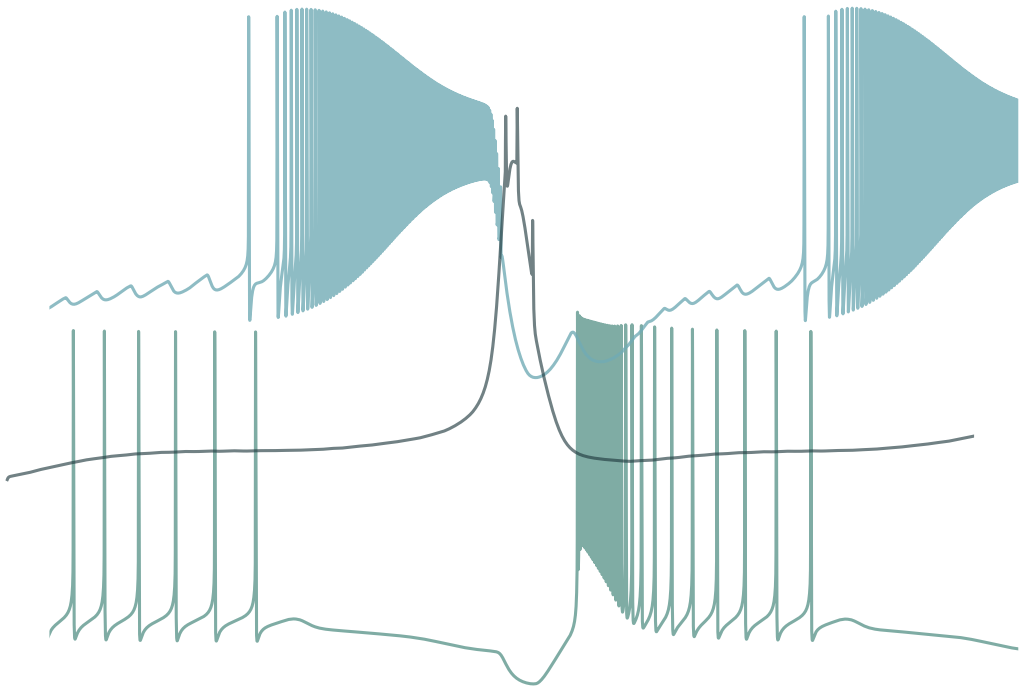
- N1 phase → Protraction
- N2 phase → Rasp



Feeding CPG of Lymnaea stagnalis

Triphasic rhythm:

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



Computational and Experimental approach

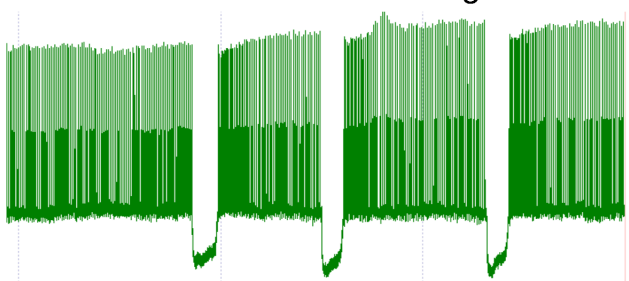
Buccal Ganglia of Lymnaea stagnalis Microscope Image

Lymnaea stagnalis

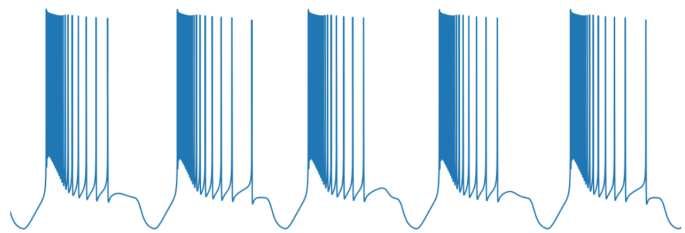
$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l)$$

$$dn/dt = \alpha_n(1-n) - \beta_n n$$
$$dm/dt = \alpha_m(1-m) - \beta_m m$$
$$dh/dt = \alpha_h(1-h) - \beta_h h$$

Intracellular recording

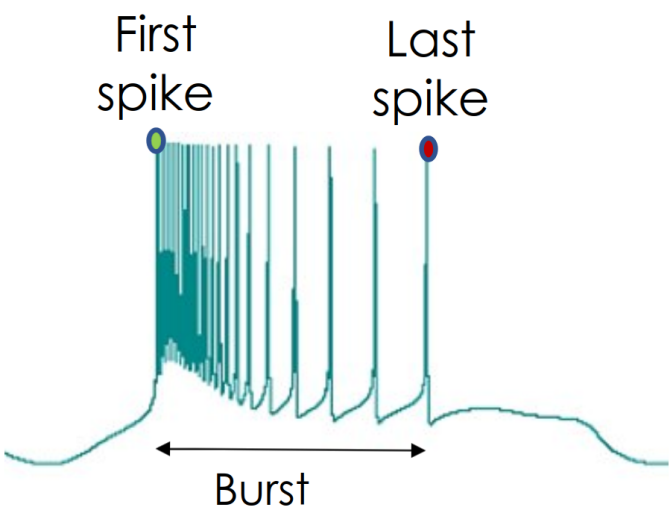


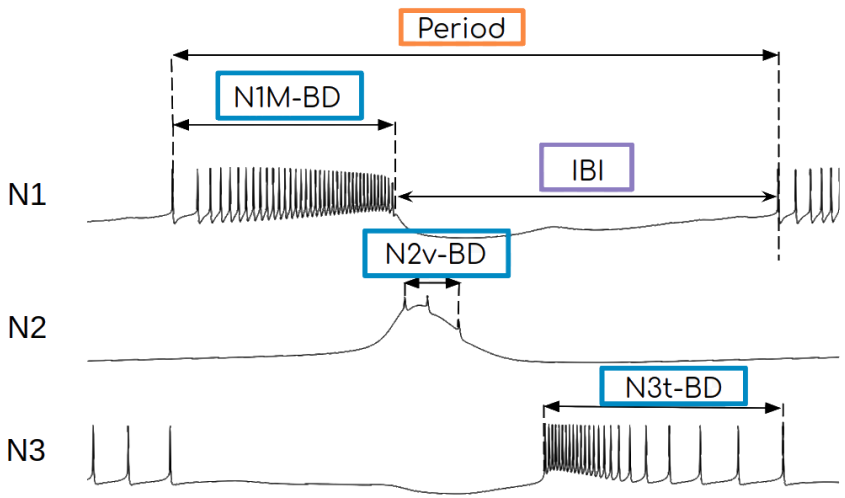
Model simulation



)

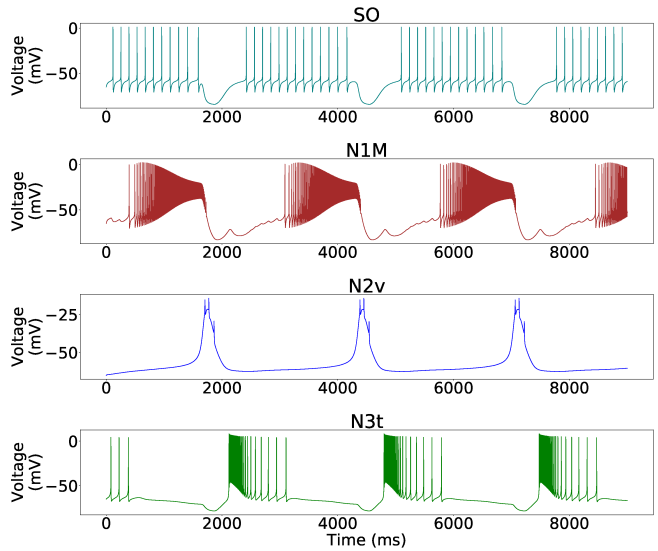
Charaterization of the time-intervals cycle-by-cycle

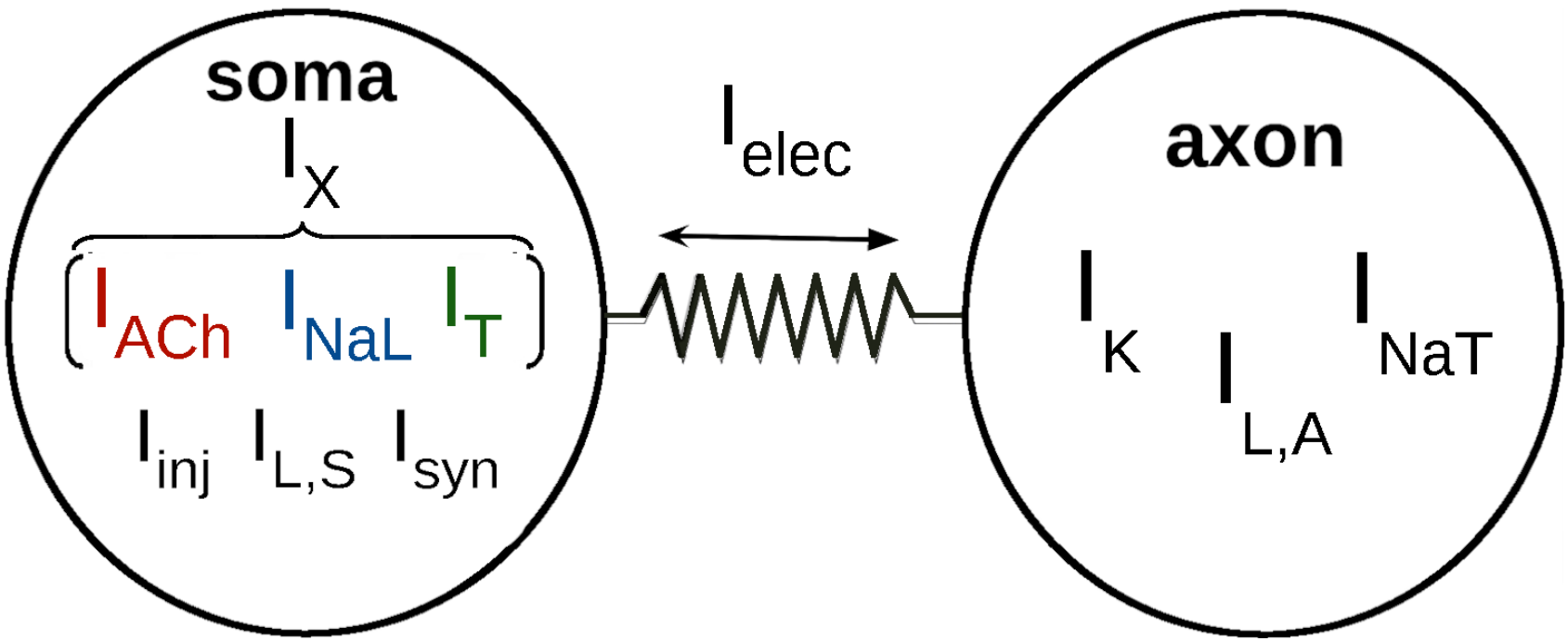




Computational Approach: Model description

- Feeding CPG Model





Computational Approach: Ramp stimulation protocol

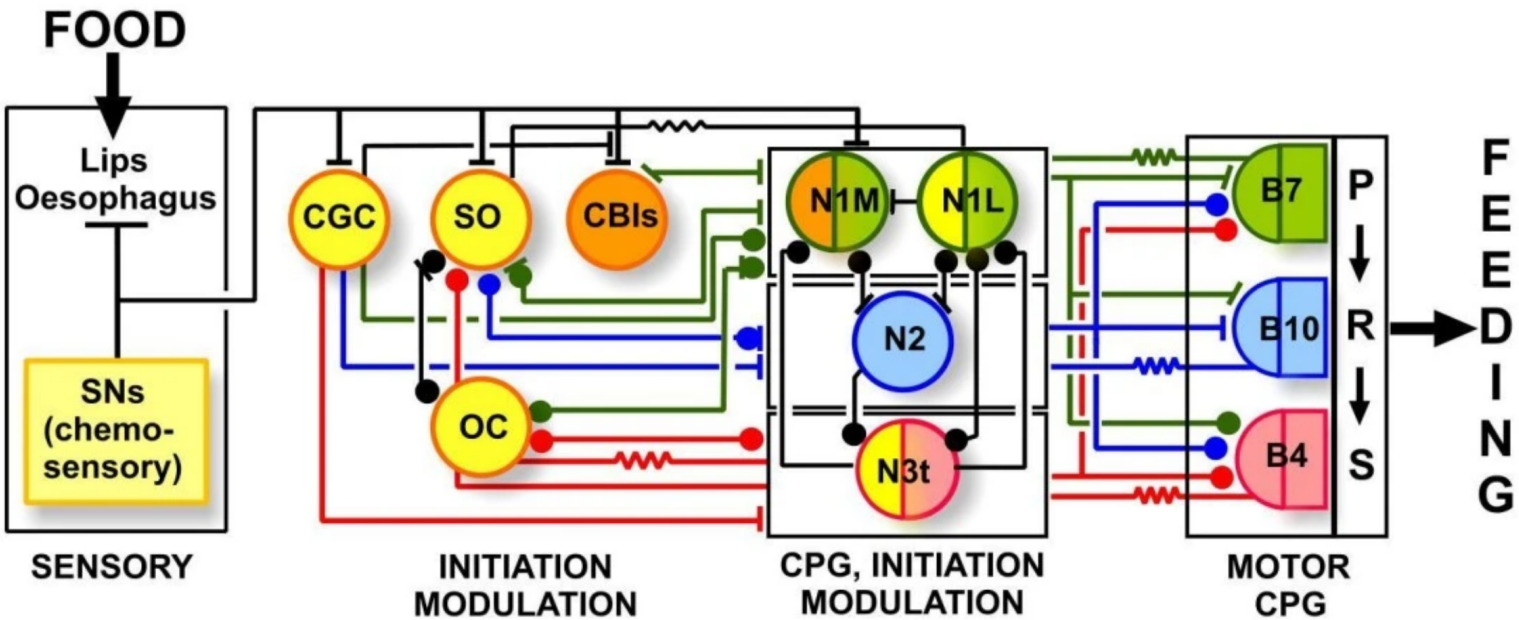
Cycle-by-cycle restrictions

Video

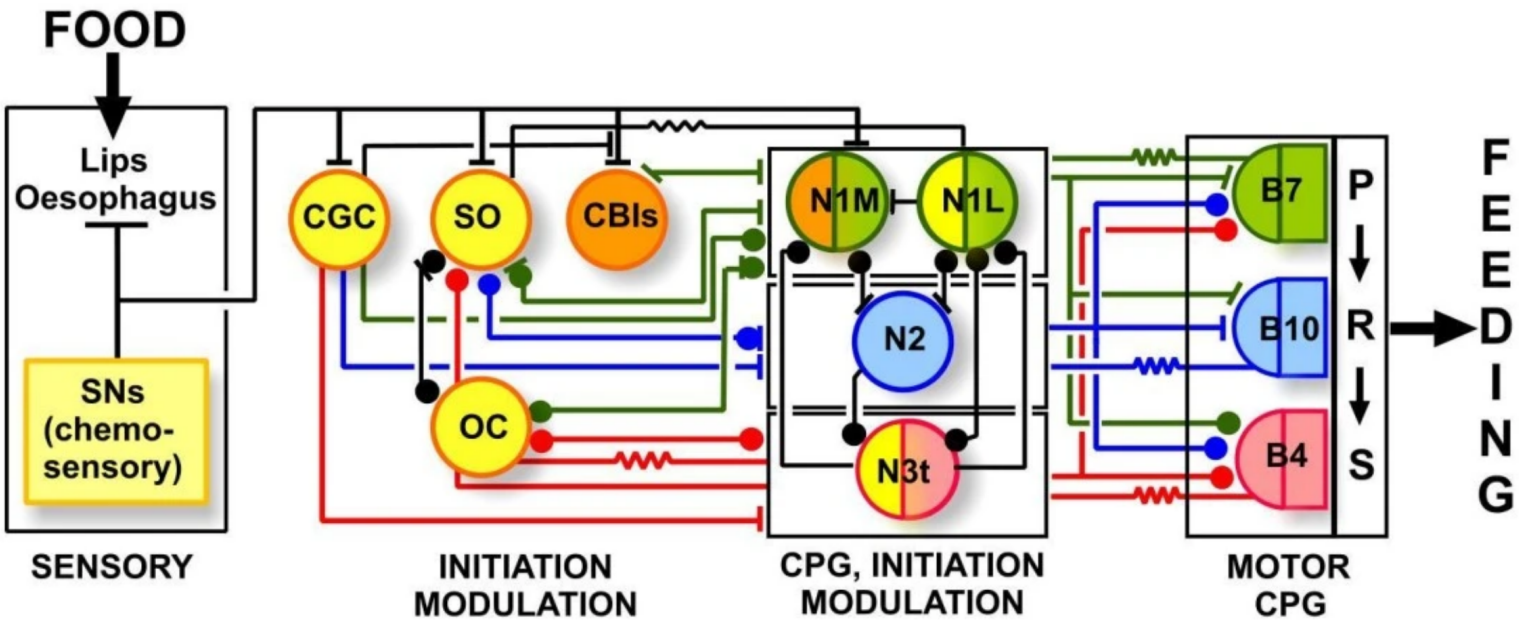
N1M stimulation

SO stimulation

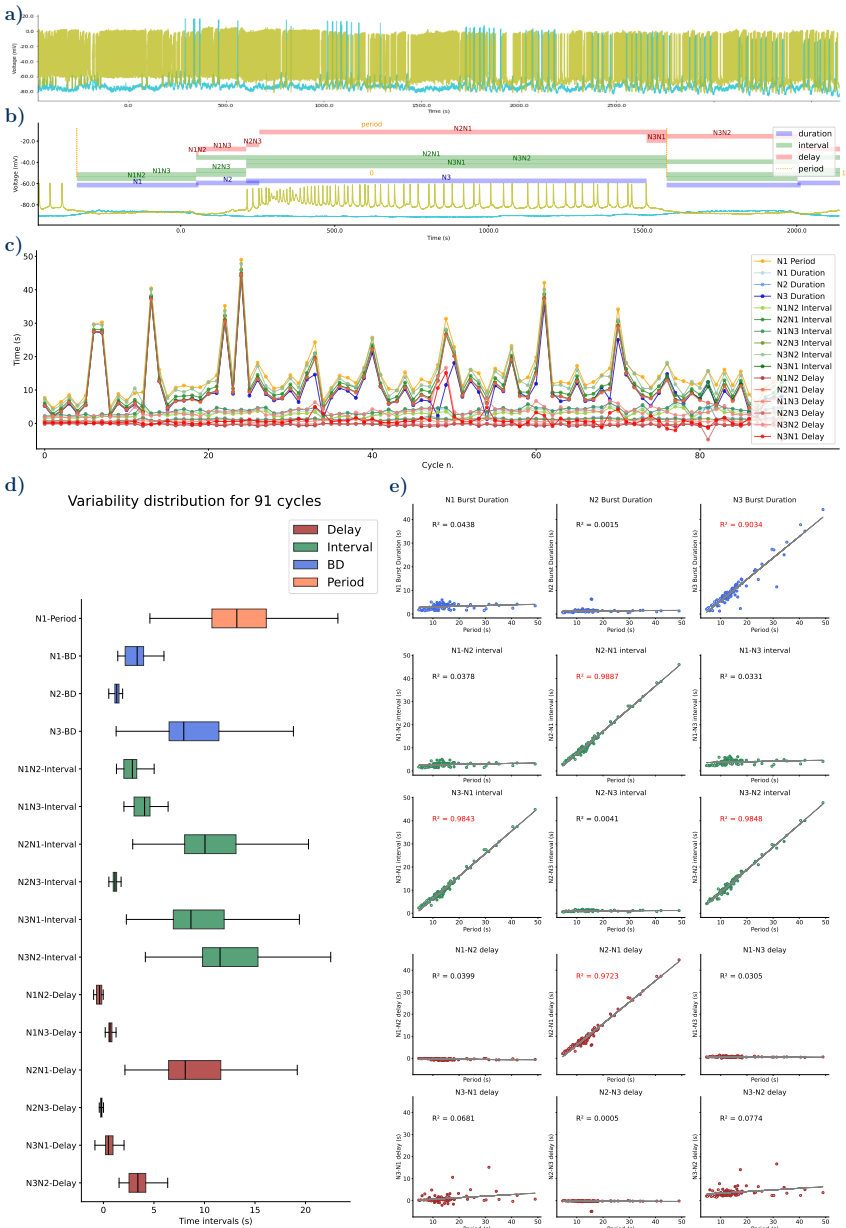
Models with chaotic activity

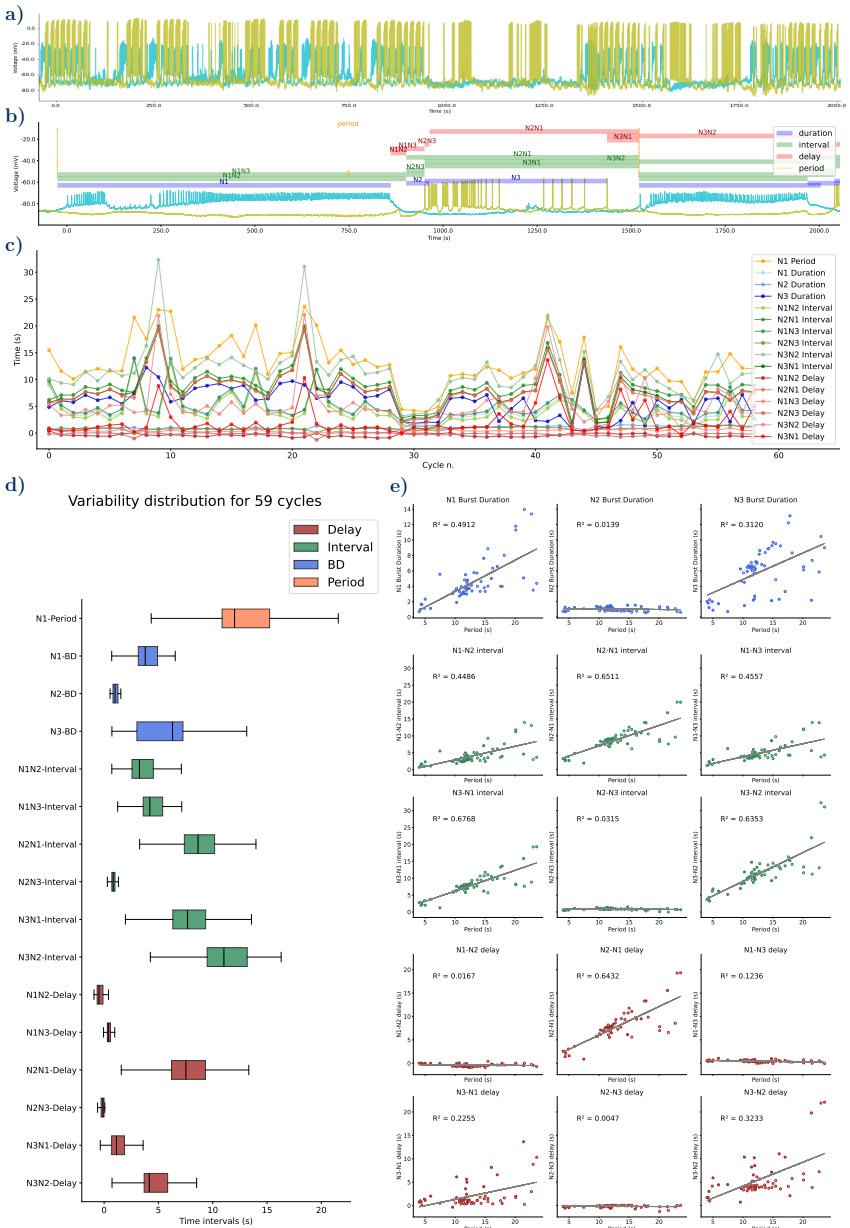


Experimental approach

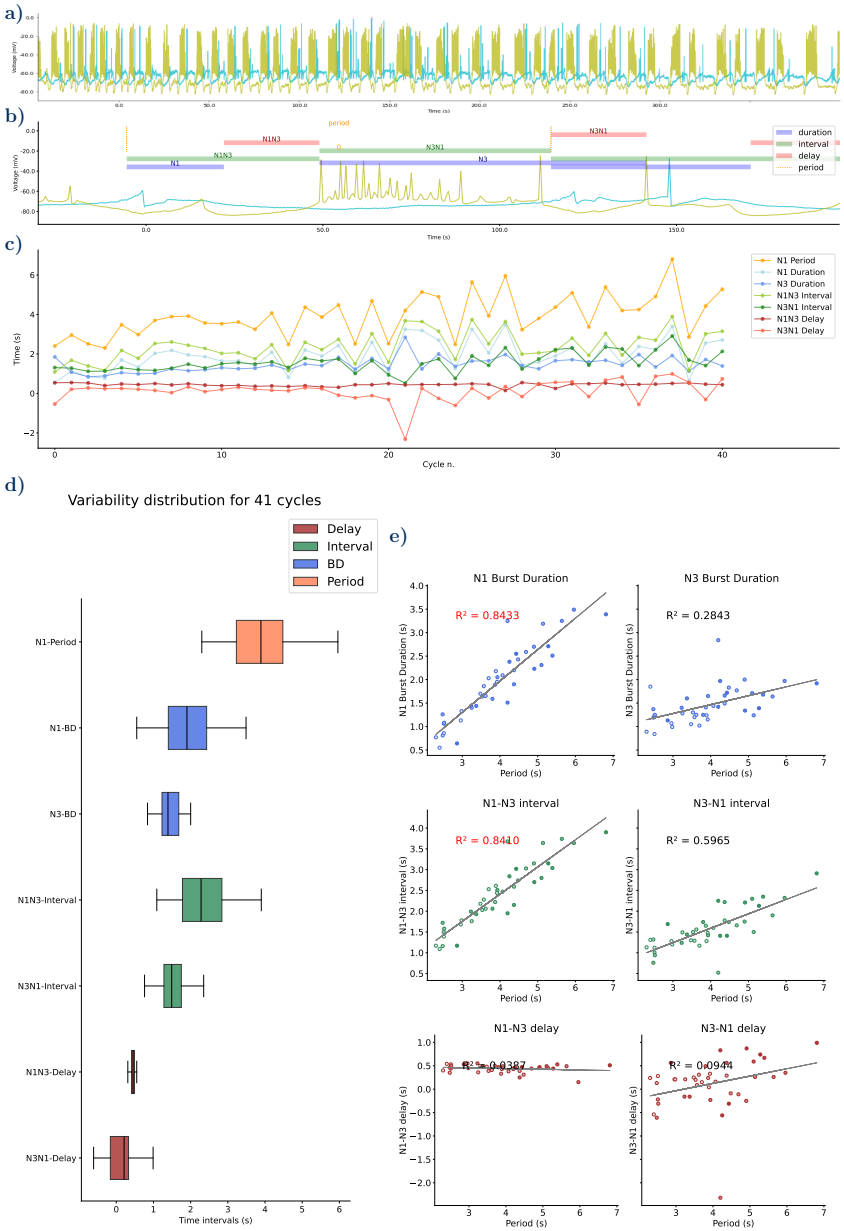


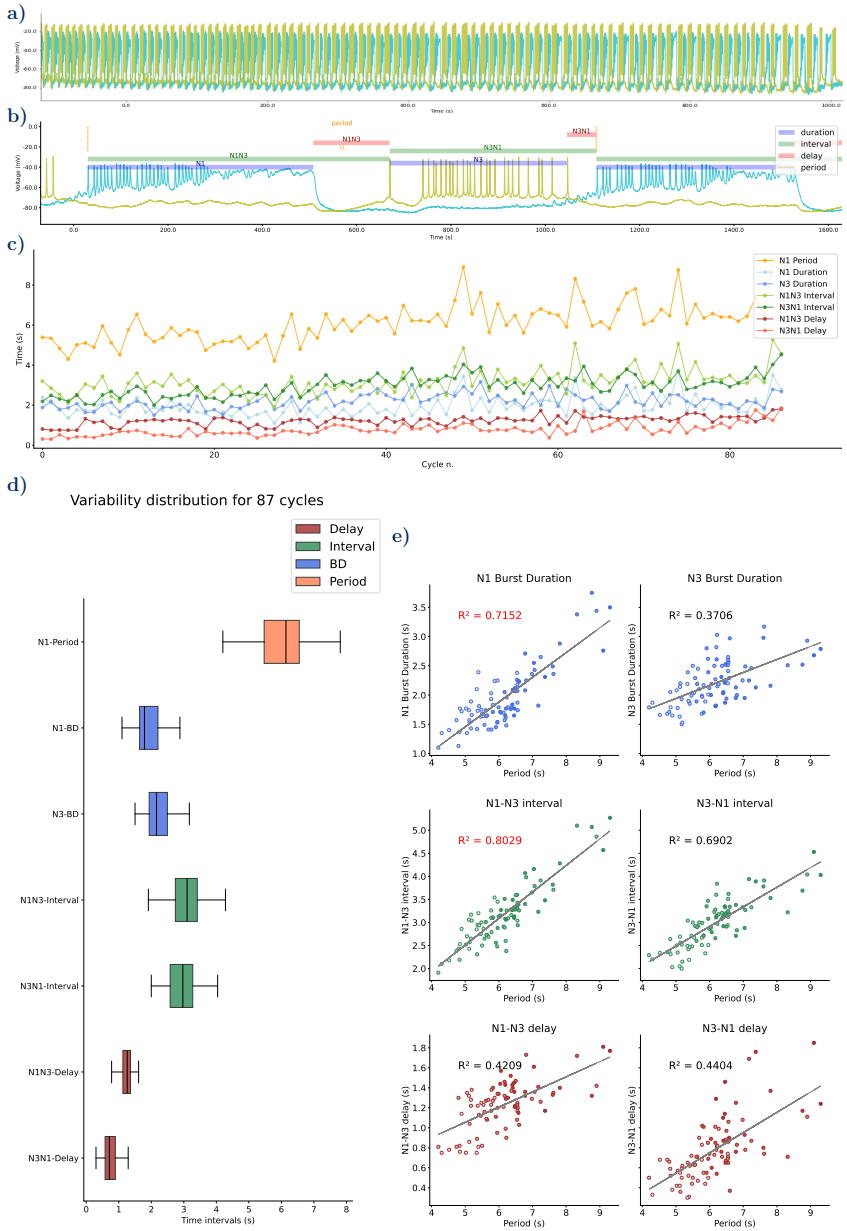
Spontaneous activity



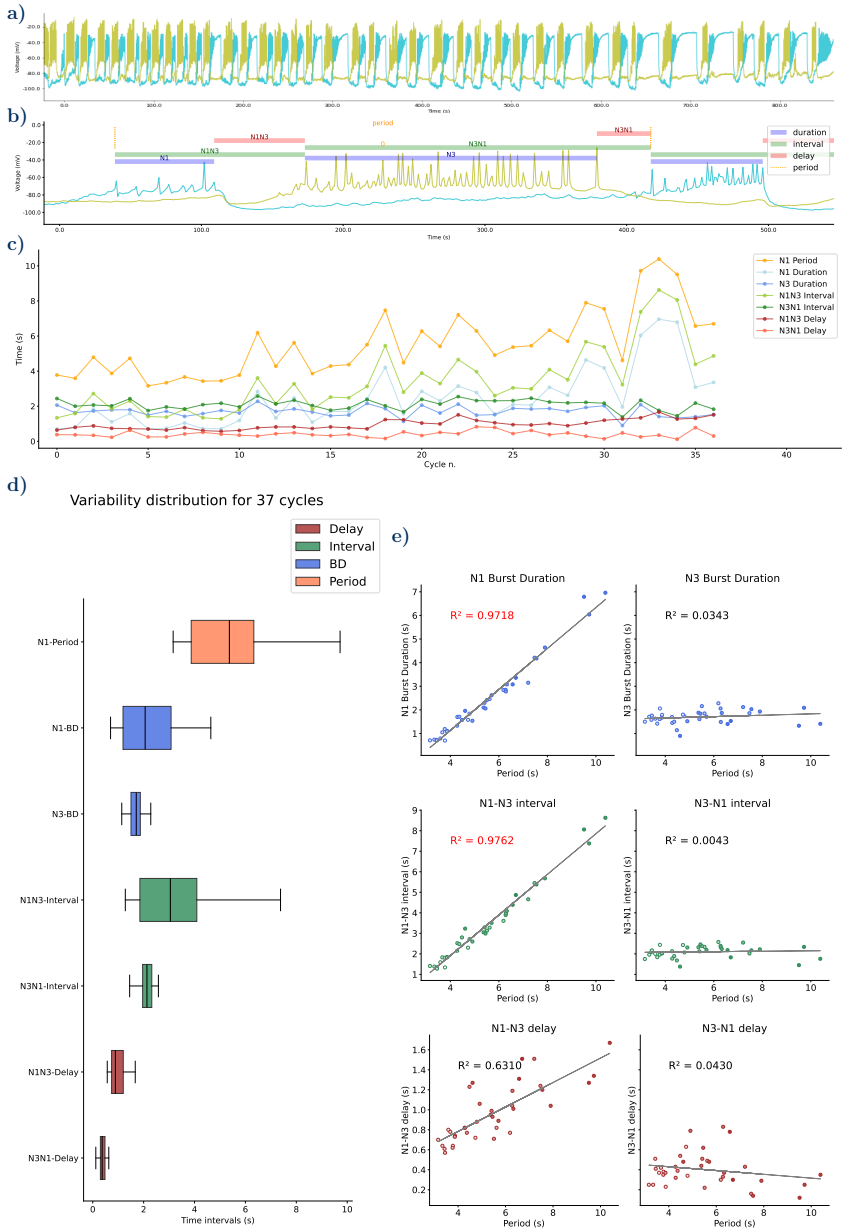


SO driven activity

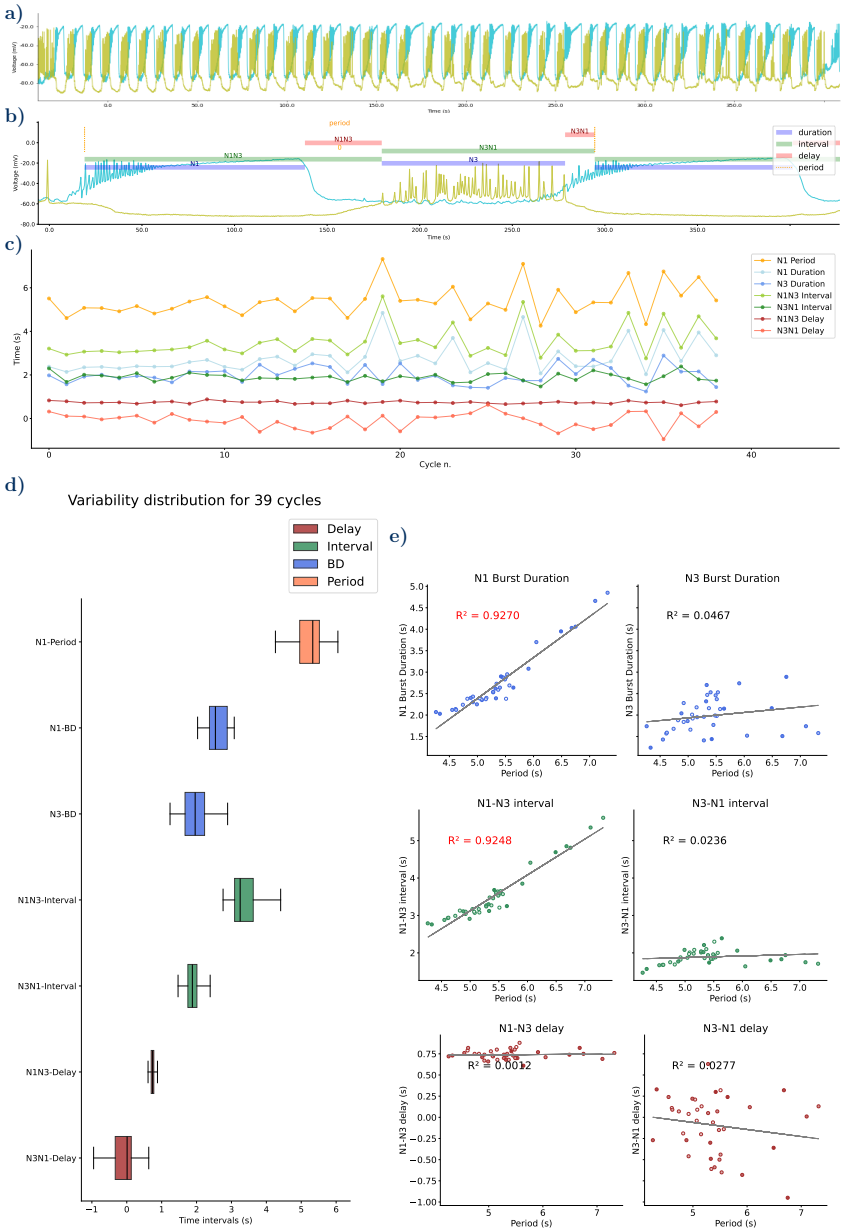


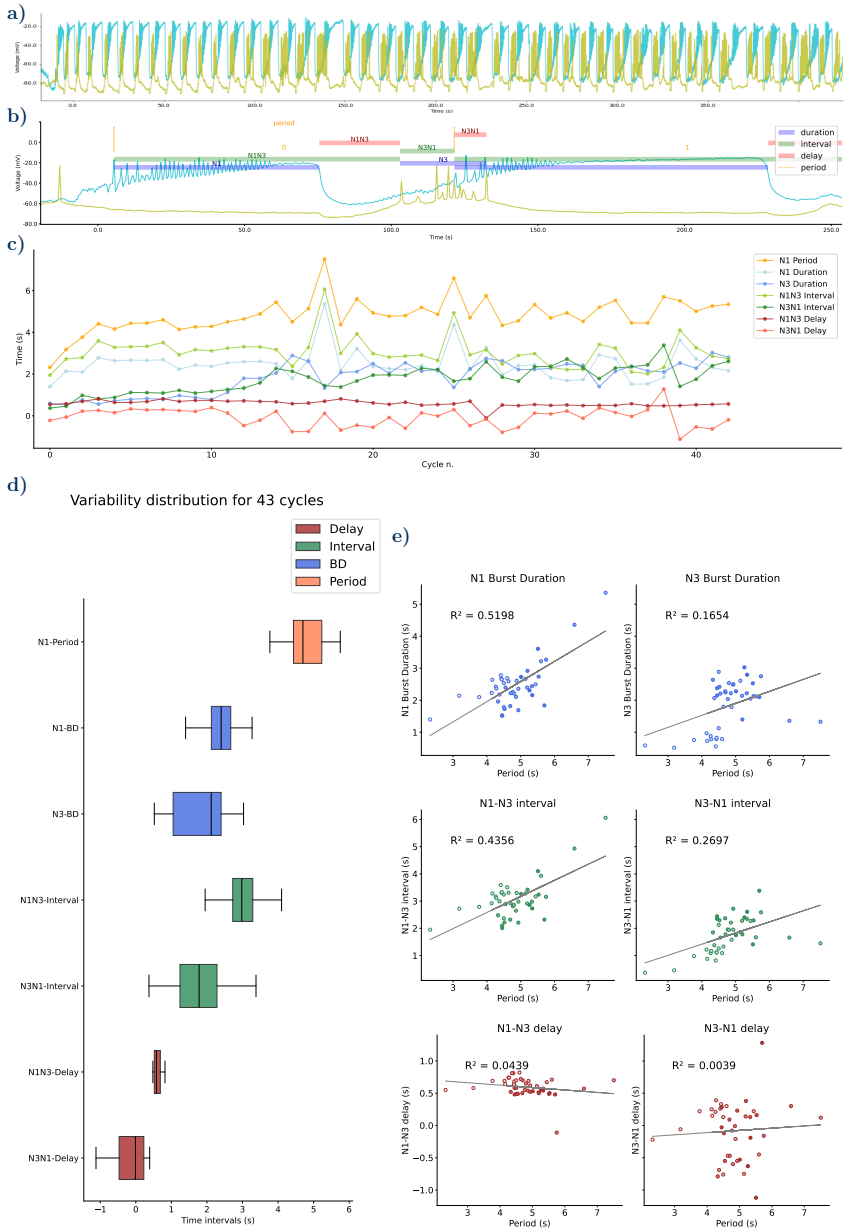


MLN driven activity



CV1 driven activity



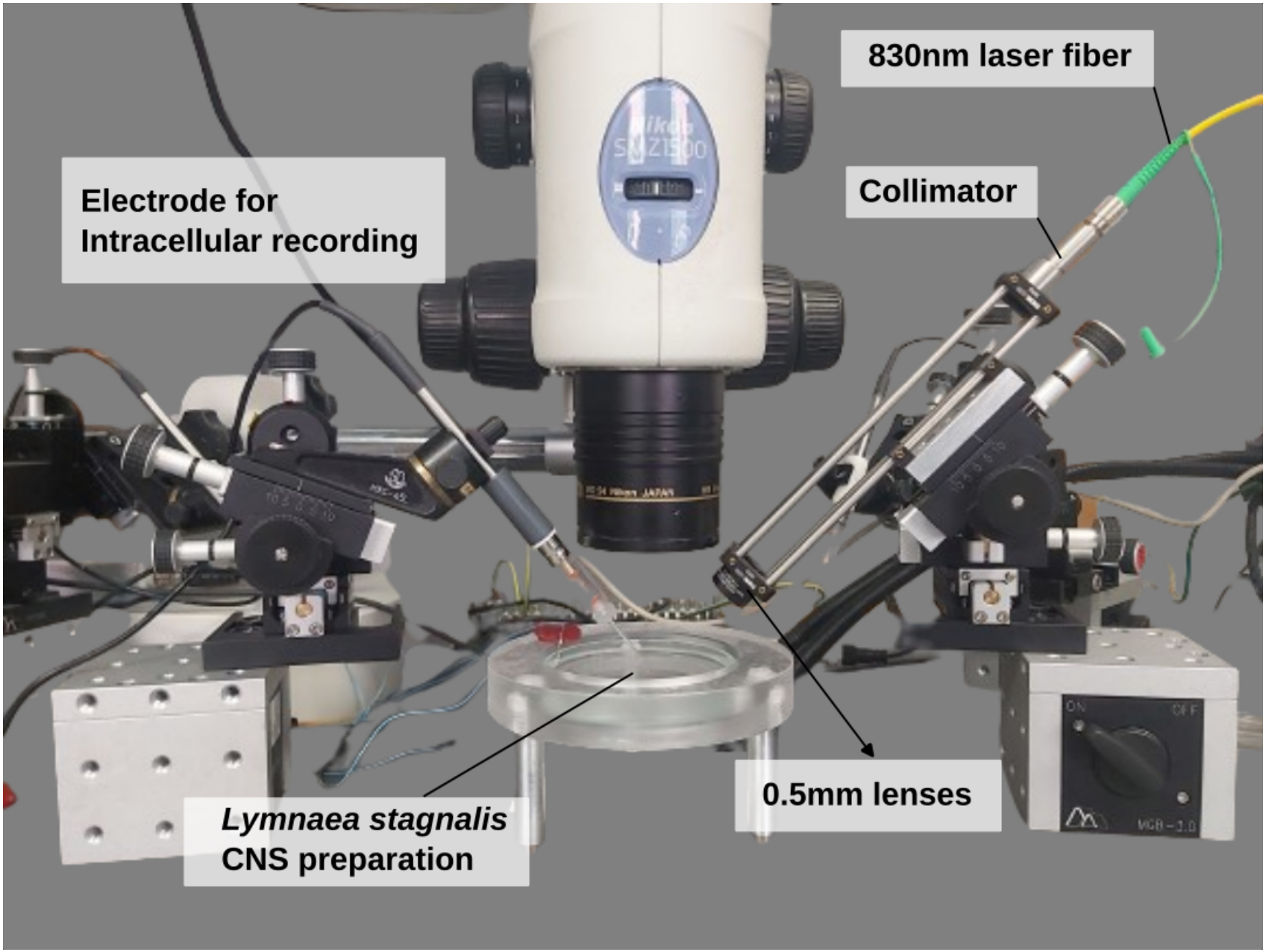


Robot

CW-NIR laser as an effective neuromodulation technique

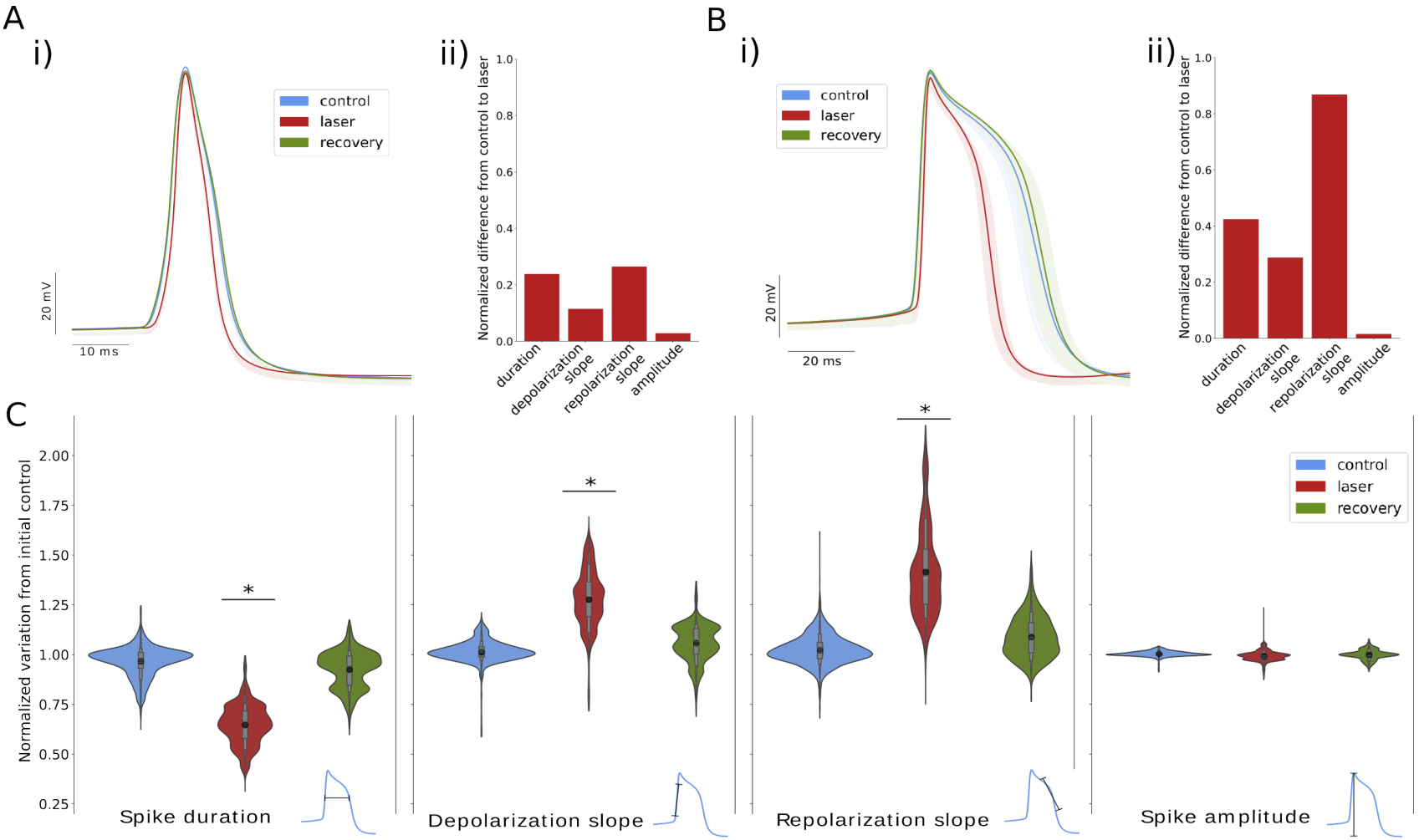
Current findings

Experimental setup

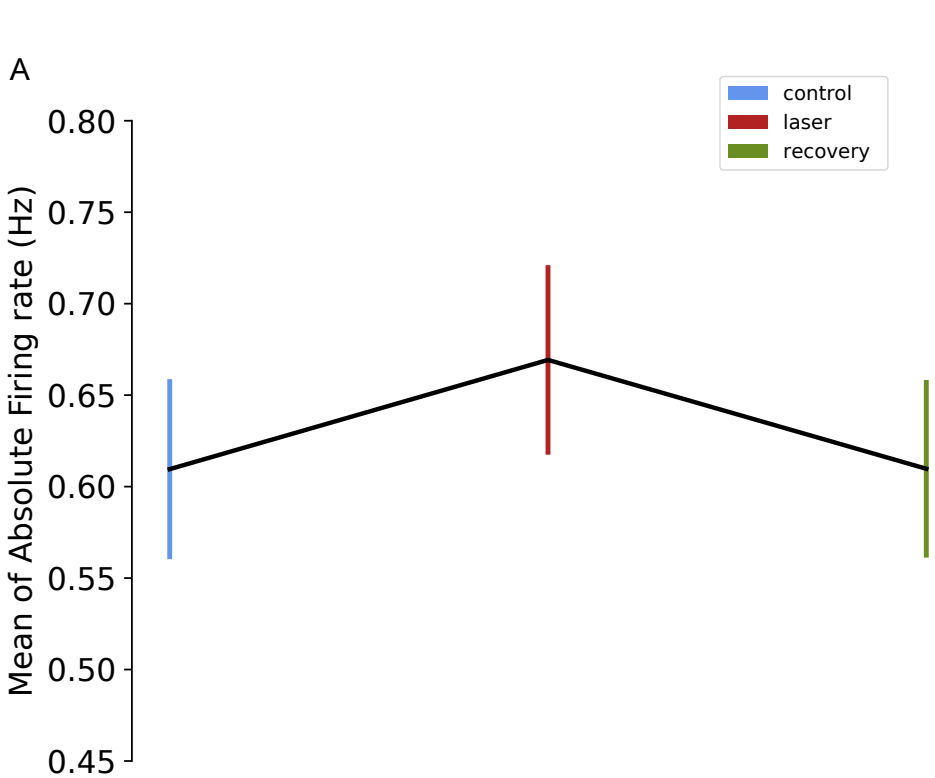


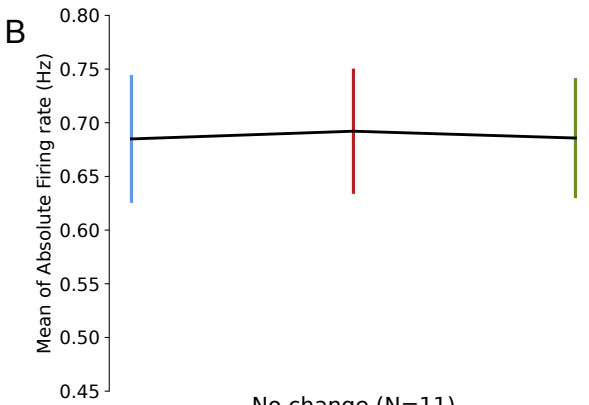
Effect on single neurons dyamics

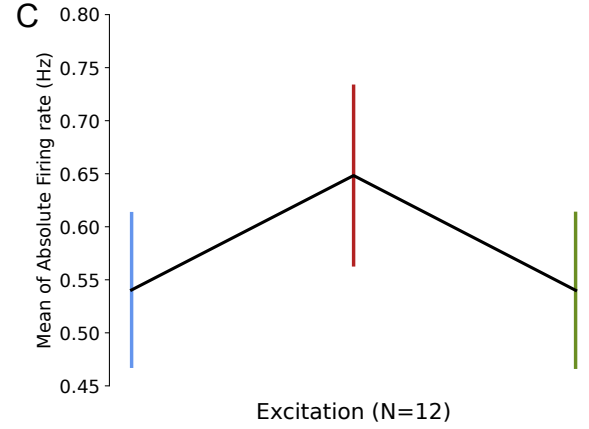
Modulation of the spike waveform

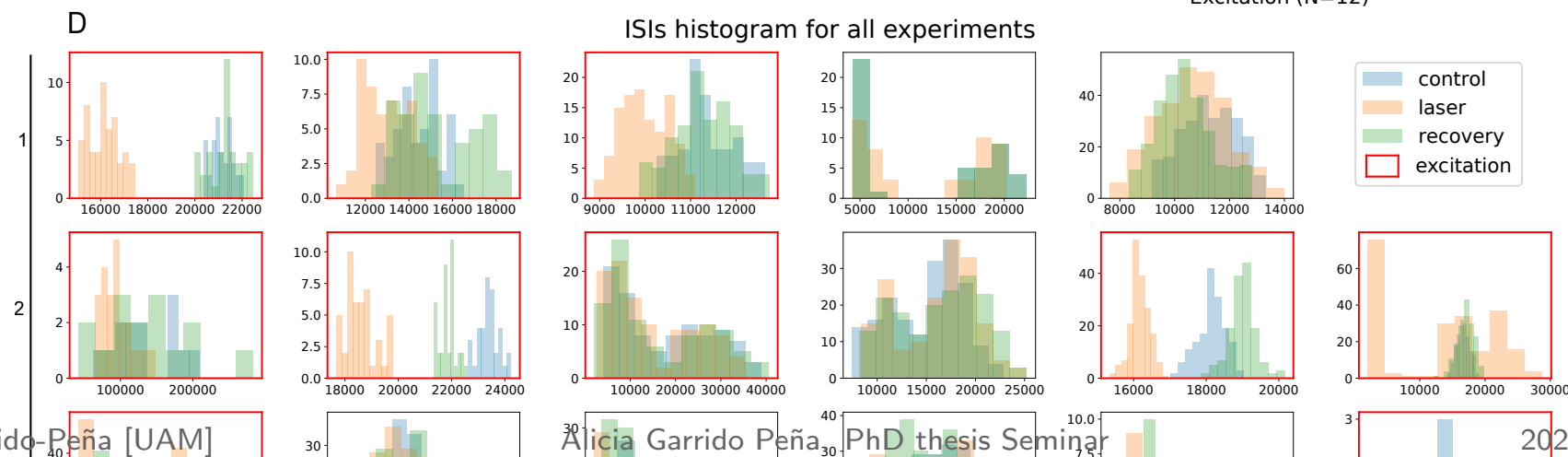


Effect on the firing rate

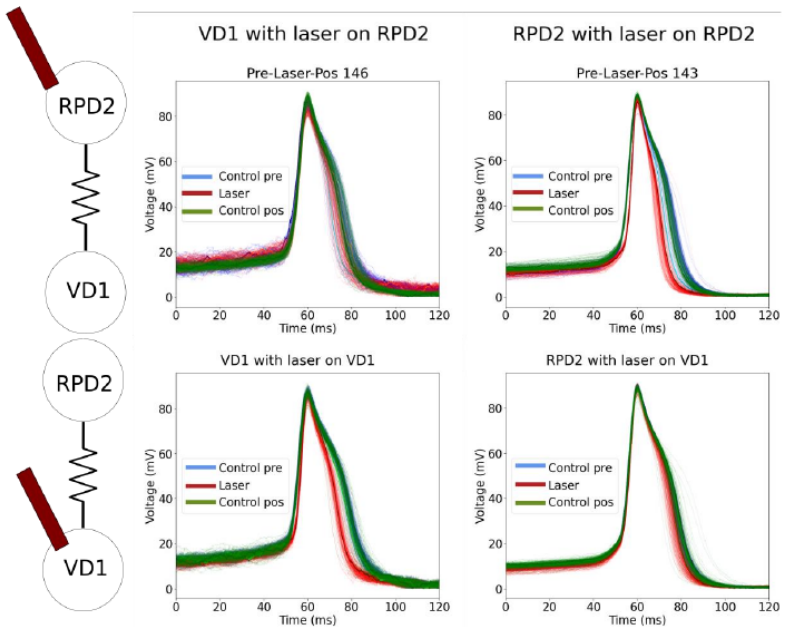


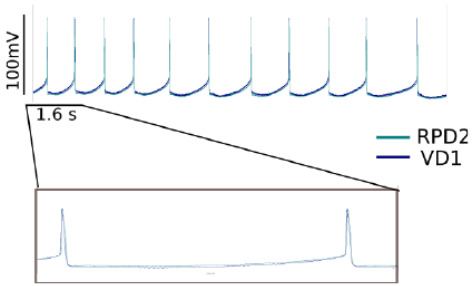


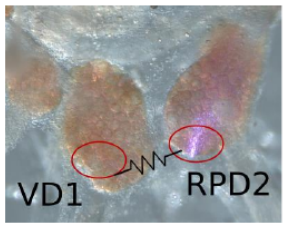




Effect on a minimal circuit







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

Escuela
Politécnica Superior