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


Alicia Garrido Peña

Advisor: Pablo Varona Martínez

**Escuela Politécnica Superior.**
**Universidad Autónoma de Madrid**


Alicia Garrido Peña. PhD thesis Seminar

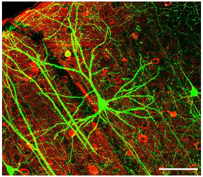
Tuesday 23rd July, 2024


Universidad Autónoma de Madrid | Escuela Politécnica Superior

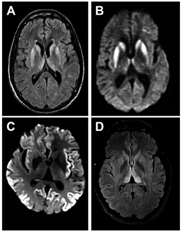
# Contents

# Introduction

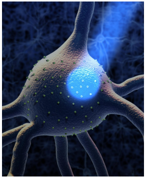
# Neuroscience



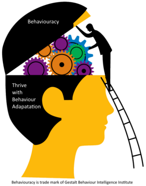
**Neurobiology**



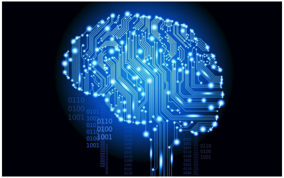

**Clinical Neuroscience**



**Neurotechnology**




**Cognitive Neurosience**



**Computational Neurosience**

# Approach

- Neurocomputational Perspective

# Approach

- Neurocomputational Perspective
- Bottom-up approach

# Approach

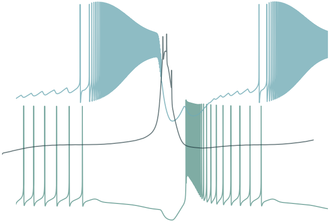
- Neurocomputational Perspective
- Bottom-up approach

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, computational work

# Approach

- Neurocomputational Perspective
- Bottom-up approach
- Combining electrophysiology, computational work and novel neurotechnology.

# Neuronal and Networks Dynamics

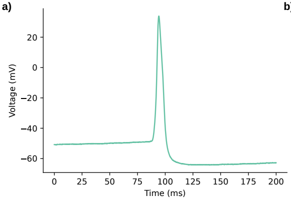
Neuronal electrical activity is often described in terms of the evolution of membrane voltage caused by the flow of ionic channels between the inside and outside of the cell.

# Neuronal and Networks Dynamics

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

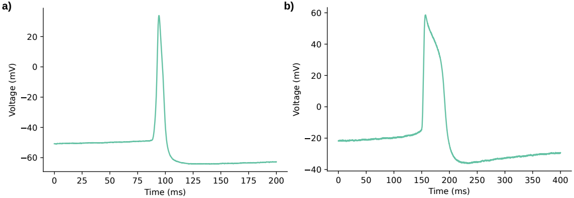
# Neuronal and Networks Dynamics

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

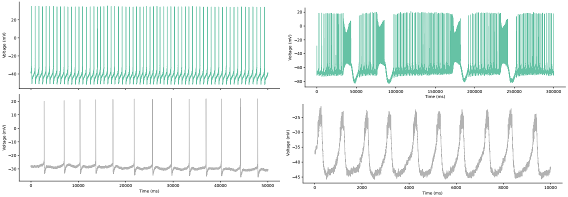


# Neuronal and Networks Dynamics

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.

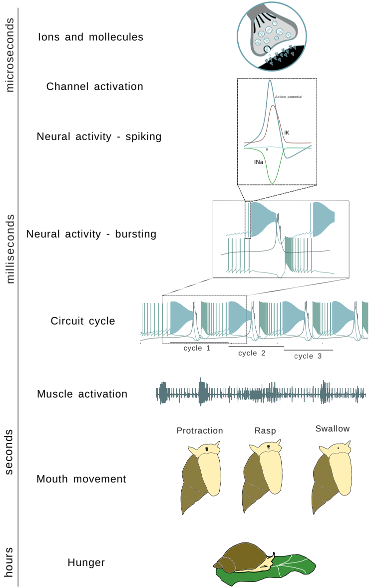


# The sequential nature of neural dynamics

- There are sequential processes at different time-scales.

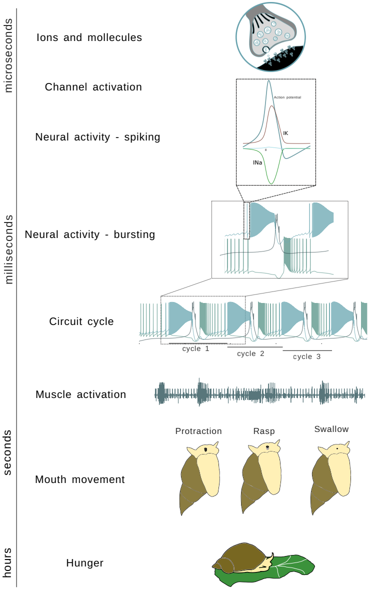
# The sequential nature of neural dynamics

- There are sequential processes at different time-scales.



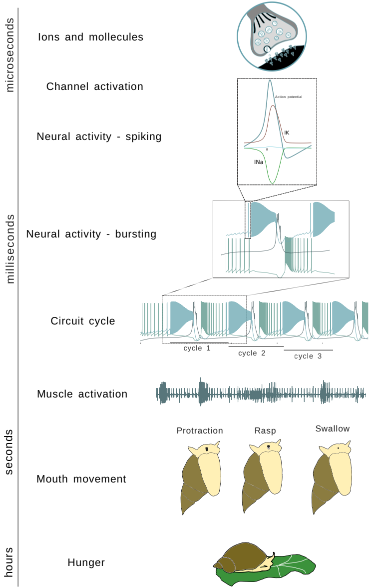
# The sequential nature of neural dynamics

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



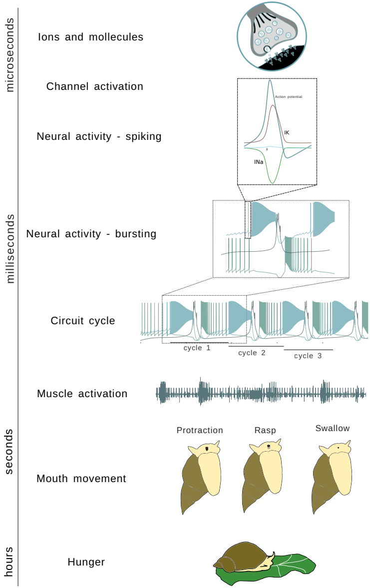
# The sequential nature of neural dynamics

- There are sequential processes at different time-scales.
- Many behaviors and actions are governed by sequential processes
- In humans: 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
- In humans: Motor control, speech, decision making, etc.
- Study of sequential activity might have a crucial role in neural coordination to autonomously establish a balance between the robustness and flexibility required for effective motor 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 system

# Studying neural dynamics in computational models

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

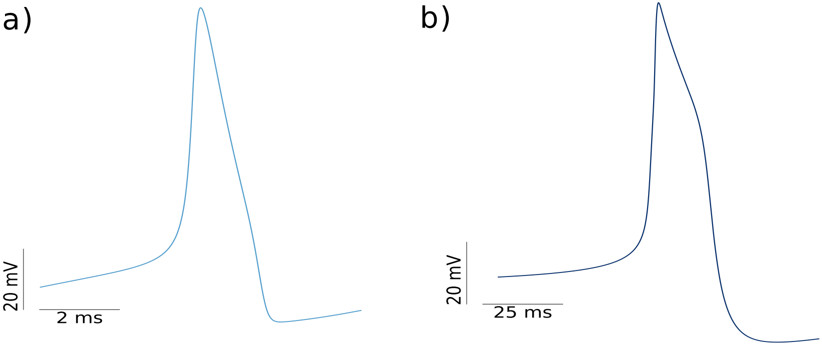
**Conductance-based models**

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

# 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

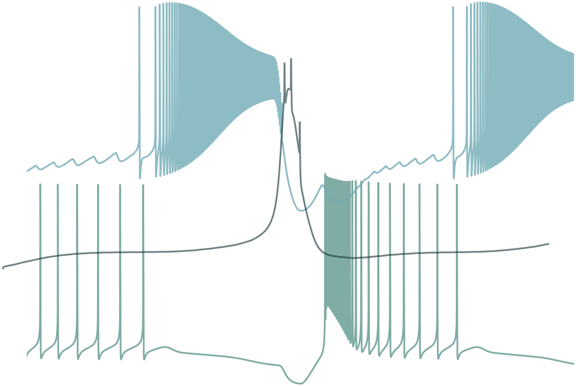
**Conductace-based models**

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

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

# 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

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

# Motivation and Objectives

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

# Motivation and Objectives

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

# Motivation and Objectives

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

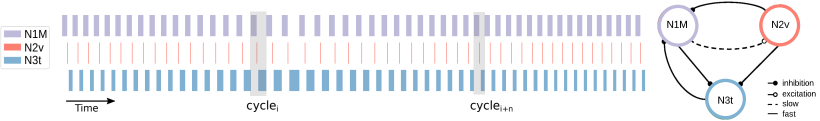
# Motivation and Objectives

5. To test the capability of **CW-NIR laser stimulation to modulate** neuronal dynamics by:
   - 5.1 Characterizing the CW-NIR effect in the spike waveform dynamics.
   - 5.2 Analyzing the ability of this neurotechnology to change the spiking rate and the circuit dynamics.
6. To study the possible **biophysical candidates** underlying the CW-NIR effect in model simulations.
7. To design and implement a **new technique** for CW-NIR stimulation in **closed-loop**.

# Sequential constrains in CPG circuits: Dynamical invariants

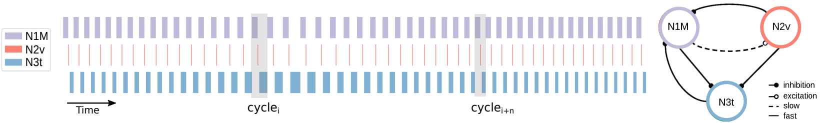
# Central Pattern Generators

- Neural circuits generating robust sequences of neural activity



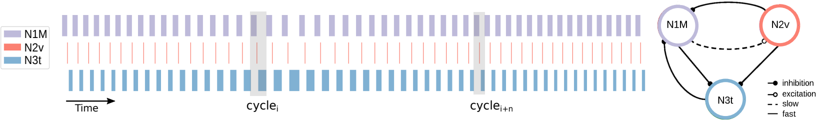
# Central Pattern Generators

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



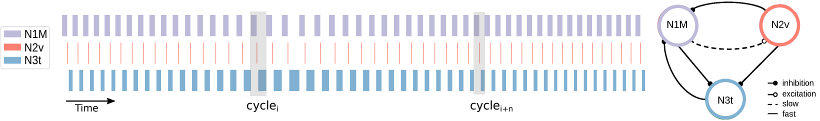
# Central Pattern Generators

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



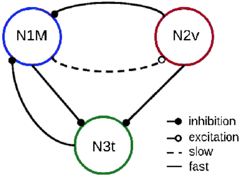
# Central Pattern Generators

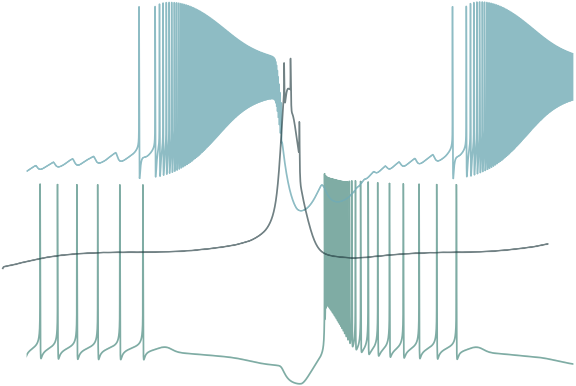
- Neural circuits generating robust sequences of neural activity
- Control motor rhythms in an autonomous manner
- Present in vertebrates and invertebrates
- Flexible enough to adapt the rhythm to the variability keeping a robust sequential activity



# Central Pattern Generators

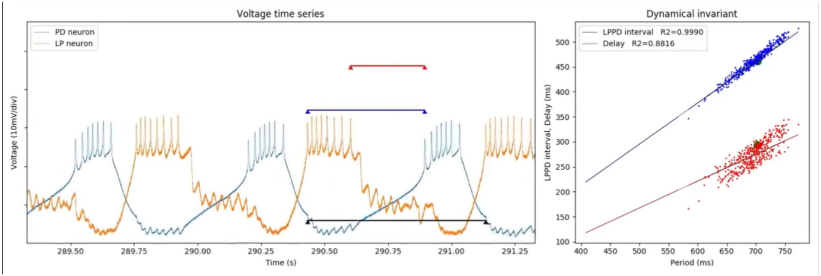
- Non-open topologies
- Based on mutual inhibition
- Temporal sequences maintained cycle-by-cycle



# Temporal constrains: Sequential Dynamical invariants

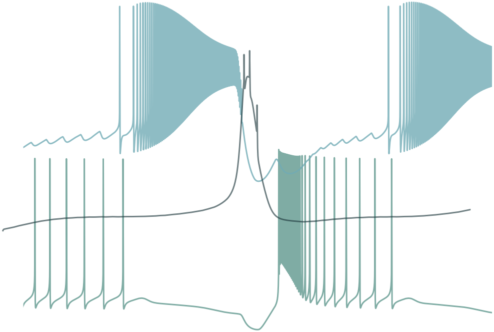
- Recently found in pyloric CPG (experimental study). (Elices et al.)
- Specific intervals that build the sequence are highly correlated cycle-by-cycle.
- Consistent under high variability induced situations (Ethanol).



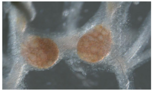
# Feeding CPG of Lymnaea stagnalis

Triphasic rhythm:

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



# Computational and Experimental approach



Buccal Ganglia of Lymnaea stagnalis Microscope Image

Lymnaea stagnalis

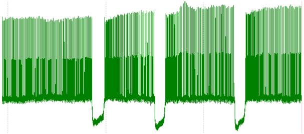
$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l)$$

$$dn/dt = \alpha_n (1 - n) - \beta_n n$$

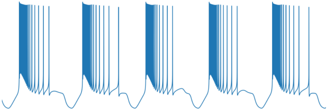
$$dm/dt = \alpha_m (1 - m) - \beta_m m$$

$$dh/dt = \alpha_h (1 - h) - \beta_h h$$

Intracellular recording



Model simulation

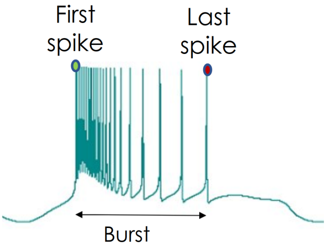


)

# Characterization of the time-intervals cycle-by-cycle

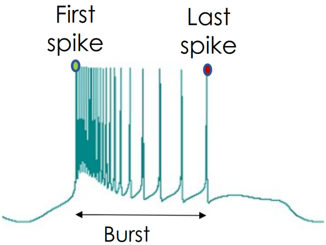
# Characterization of the time-intervals cycle-by-cycle

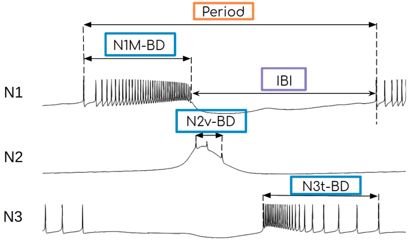
To analyze the dynamics of the sequential activity cycle-by-cycle we need to define time references to characterize the time-intervals in the sequence.



# Characterization of the time-intervals cycle-by-cycle

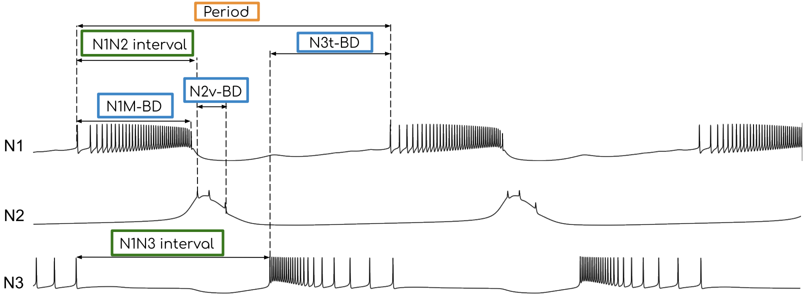
To analyze the dynamics of the sequential activity cycle-by-cycle we need to define time references to characterize the time-intervals in the sequence.



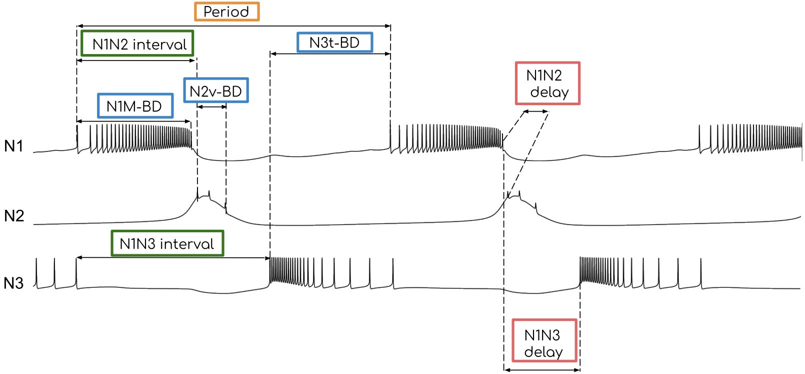
# Characterization of the time-intervals cycle-by-cycle

We can also define intervals combining the time references of two bursts



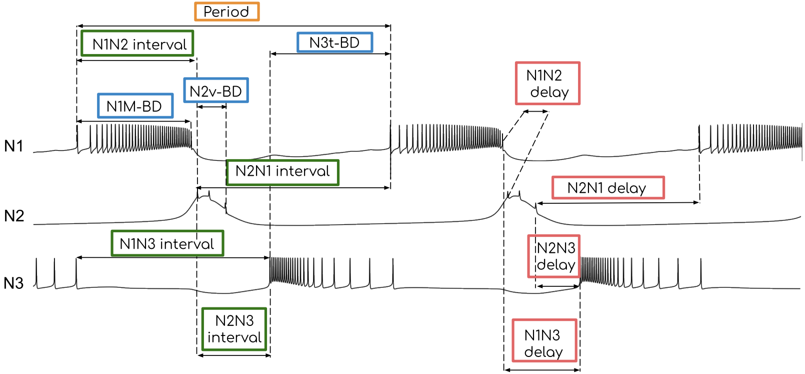
# Characterization of the time-intervals cycle-by-cycle

We can also define intervals combining the time references of two bursts



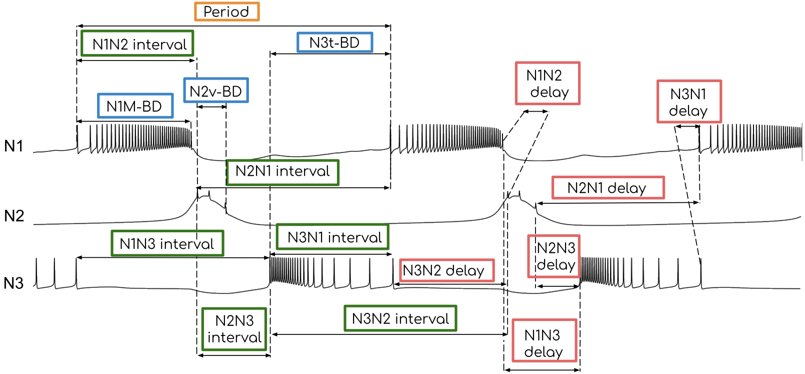
# Characterization of the time-intervals cycle-by-cycle

We can also define intervals combining the time references of two bursts



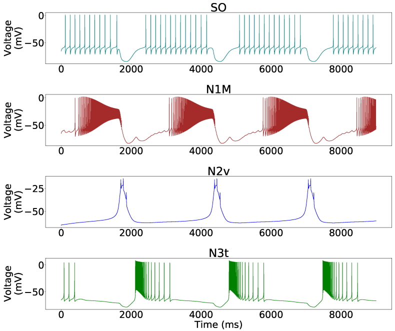
# Characterization of the time-intervals cycle-by-cycle

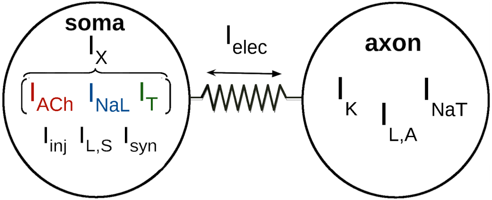
We can also define intervals combining the time references of two bursts



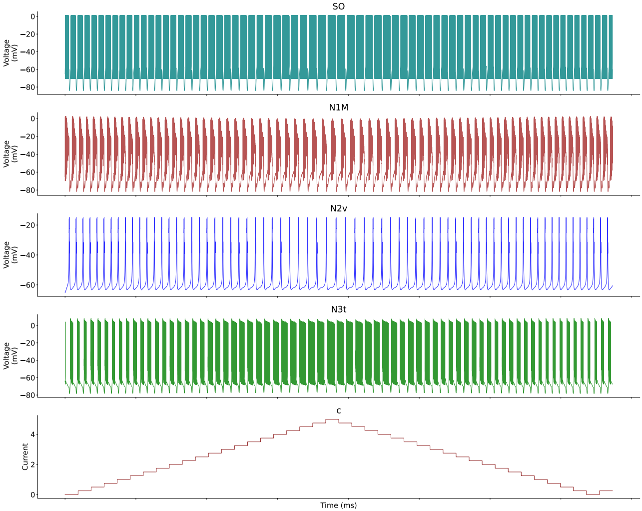
# Computational Approach: Model description

- (Vavoulis et al.)
- Conductance-based model.
- Specific waveforms and gradual synapse.
- Two compartments.
- Feeding CPG Model.

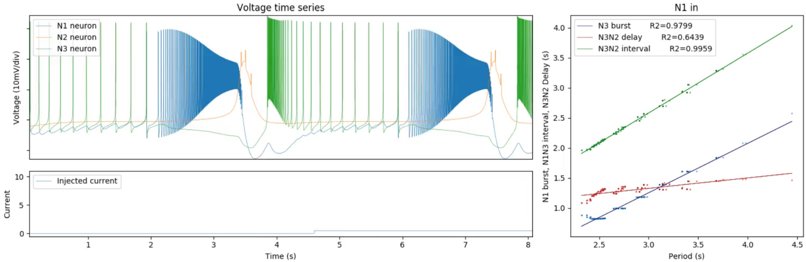


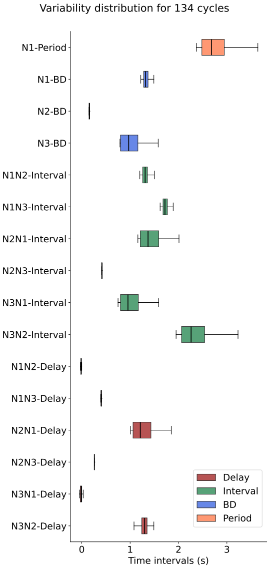
# Computational Approach: Ramp stimulation protocol

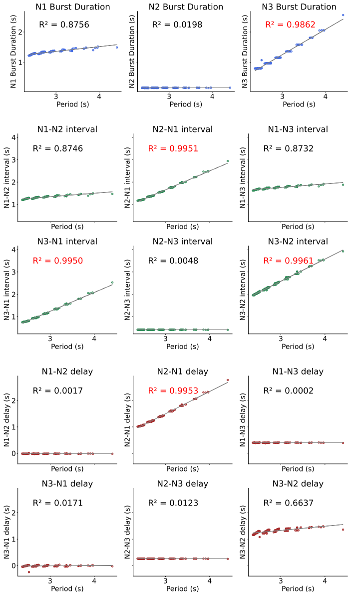


# Cycle-by-cycle restrictions

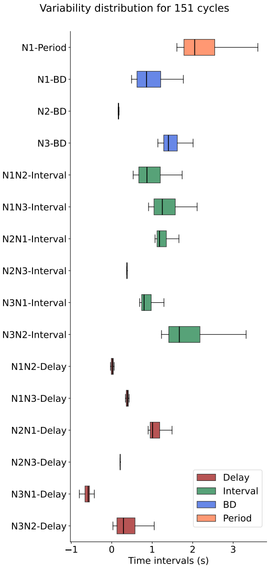


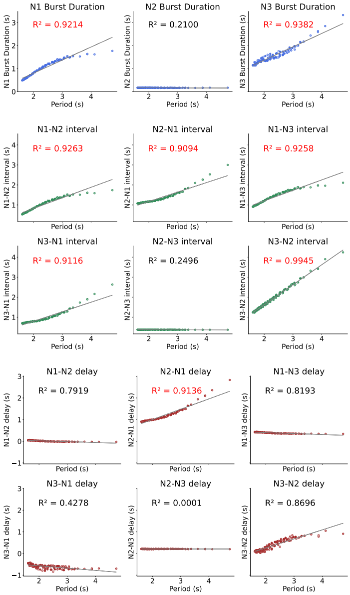
# N1M stimulation



# SO stimulation



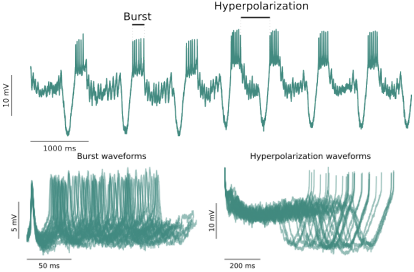
# Models with chaotic activity

Variability in models is usually limited. The variability can be induced by a current ramp as in this case, but with a chaotic activity the variability could be more realistic.

# Models with chaotic activity

Variability in models is usually limited. The variability can be induced by a current ramp as in this case, but with a chaotic activity the variability could be more realistic.

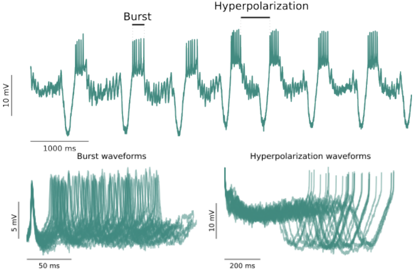
Neuronal recording variability



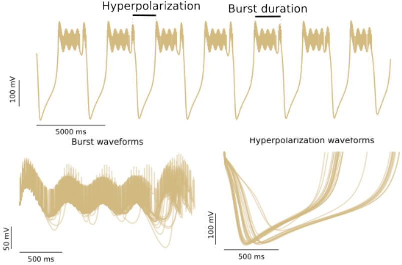
# Models with chaotic activity

Variability in models is usually limited. The variability can be induced by a current ramp as in this case, but with a chaotic activity the variability could be more realistic.

Neuronal recording variability




Model simulation with chaotic activity



# Experimental approach

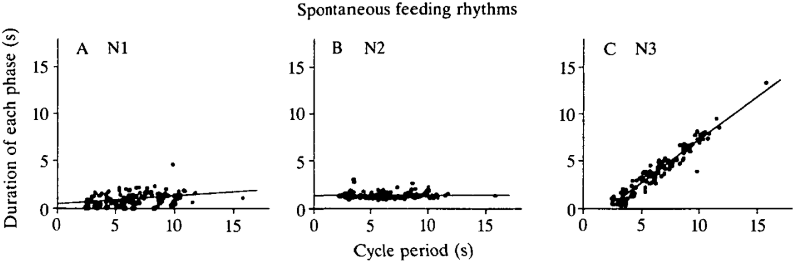
- Are sequential invariants present also in the experimental recordings?

# Experimental approach

- Are sequential invariants present also in the experimental recordings?
- Do the invariants change under different stimulation conditions?

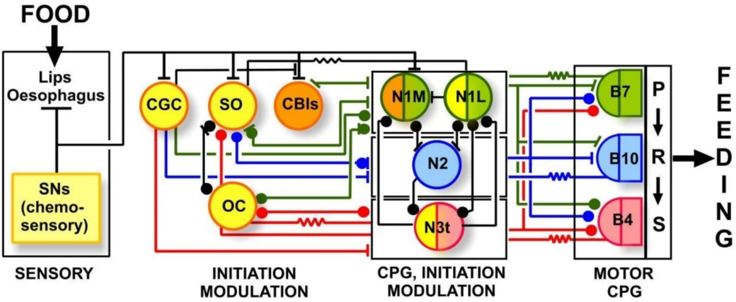
# Experimental approach

Previous studies point to the linear relation between some phases and the period



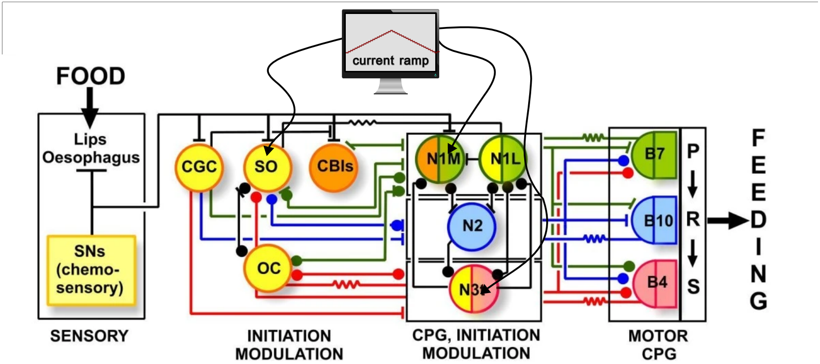

Elliott, C. J. H., & Andrew, T. (1991). Temporal Analysis of Snail Feeding Rhythms: A Three-Phase Relaxation Oscillator. Journal of Experimental Biology, 157(1), 391–408. Figure 5.

# Distributed neural system of L. stagnalis



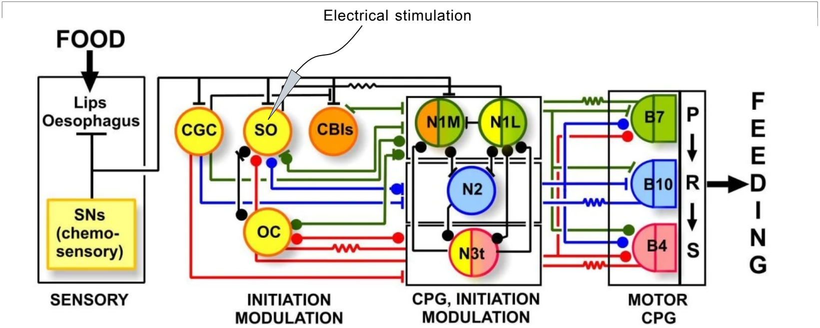

Benjamin, P. R. (2012). Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Systems & Circuits, 2(1), 1–16. https://doi.org/10.1186/2042-1001-2-4

# Distributed neural system of L. stagnalis



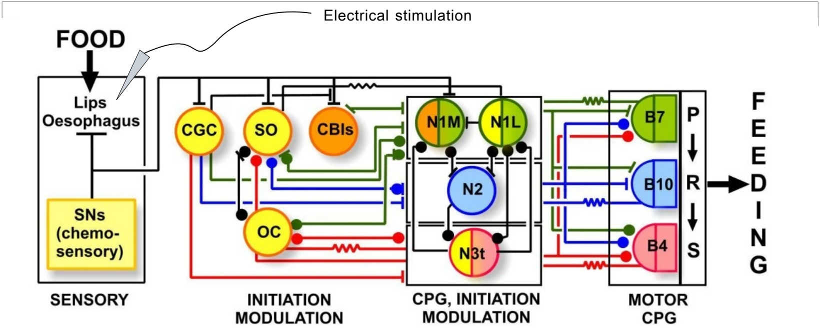

Benjamin, P. R. (2012). Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Systems & Circuits, 2(1), 1–16. https://doi.org/10.1186/2042-1001-2-4

# Distributed neural system of L. stagnalis



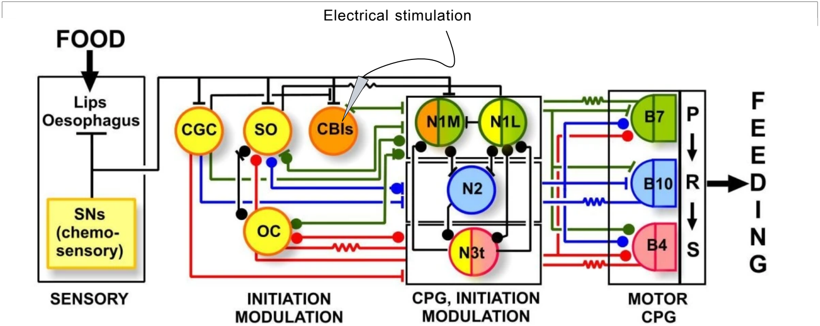

Benjamin, P. R. (2012). Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Systems & Circuits, 2(1), 1–16. https://doi.org/10.1186/2042-1001-2-4

# Distributed neural system of L. stagnalis




Benjamin, P. R. (2012). Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Systems & Circuits, 2(1), 1–16. https://doi.org/10.1186/2042-1001-2-4

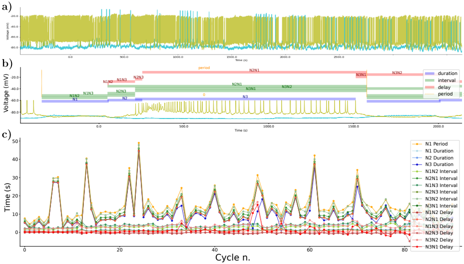
# Distributed neural system of L. stagnalis



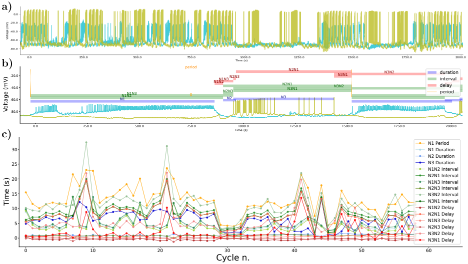

Benjamin, P. R. (2012). Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Systems & Circuits, 2(1), 1–16. https://doi.org/10.1186/2042-1001-2-4

# Spontaneous activity

## Case 1

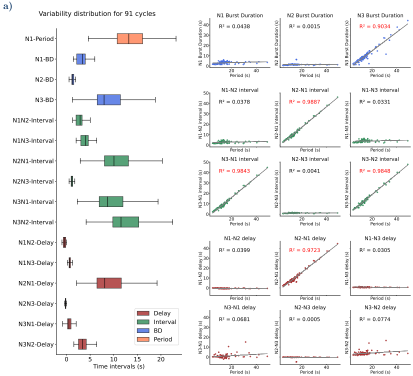



## Case 2

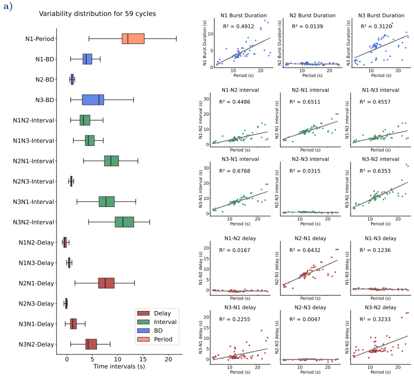


# Spontaneous activity

## Case 1

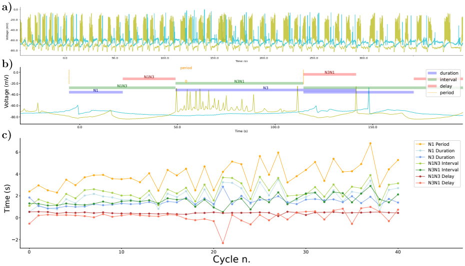



## Case 2

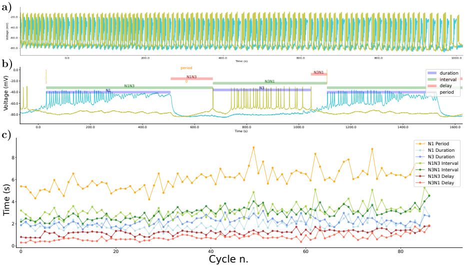


# SO driven activity

## SO driven by stimulation

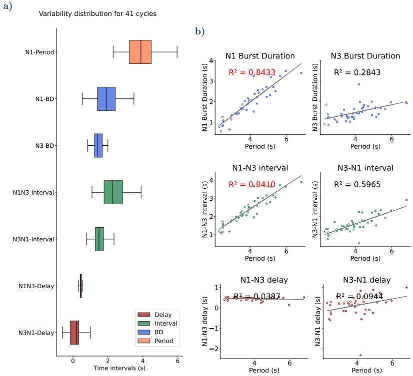



## SO spontaneous driven

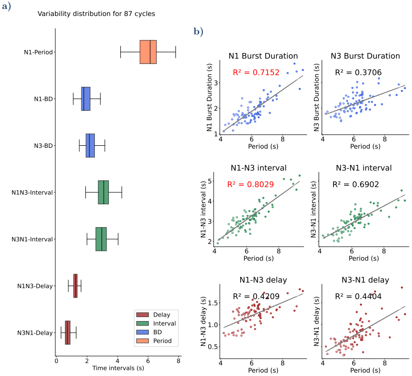


# SO driven activity

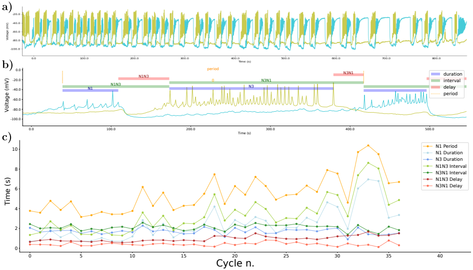
## SO driven by stimulation



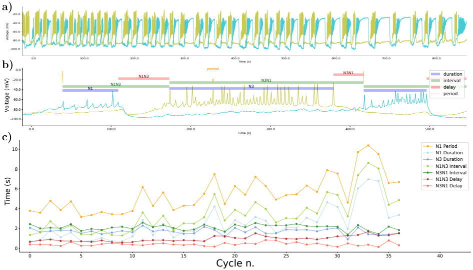

## SO spontaneous driven

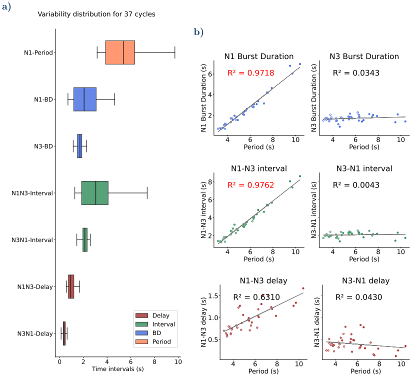


# MLN driven activity



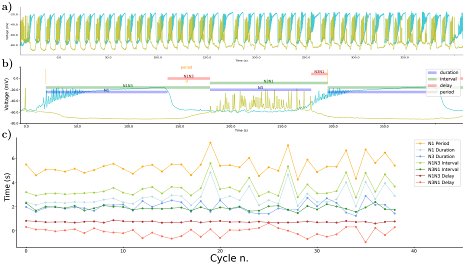
# MLN driven activity



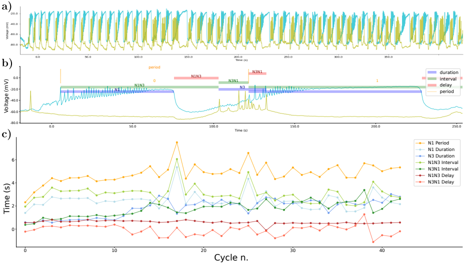



# CV1 driven activity

CV1a driven by electrical stimulation. Case 1

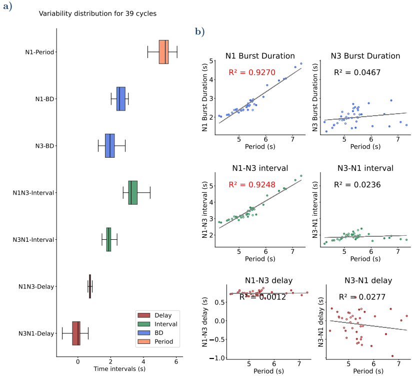



CV1a driven by electrical stimulation. Case 2

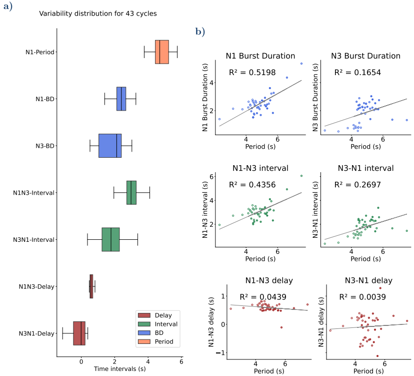


# CV1 driven activity

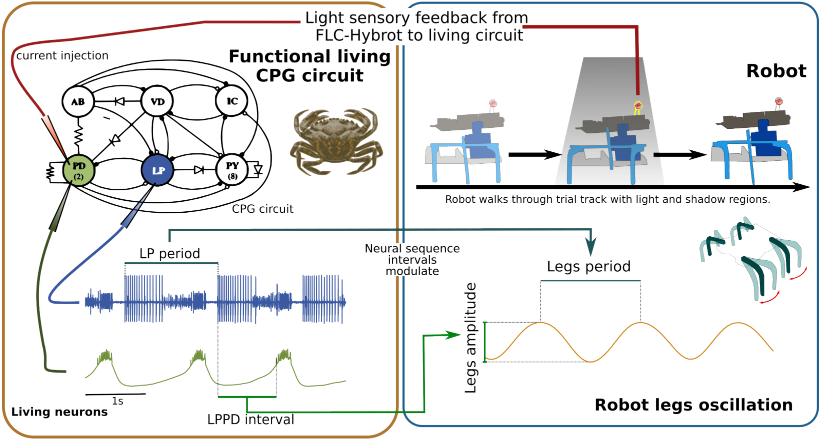
## CV1a driven by electrical stimulation. Case 1



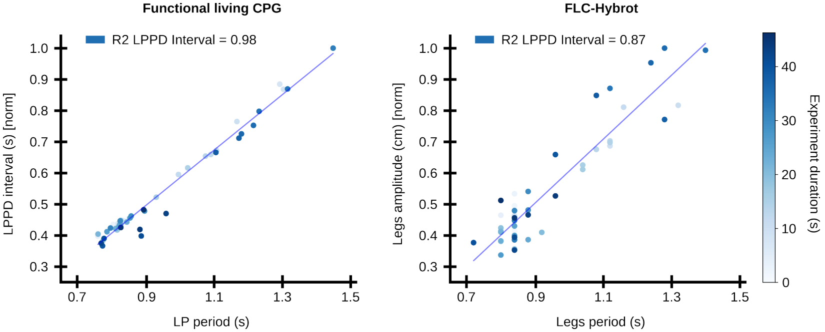

## CV1a driven by electrical stimulation. Case 2



# Study of functional the role of dynamical invariants in a Hybrot



# Study of functional the role of dynamical invariants in a Hybrot



# Summary of results

**Study of the Sequential nature in neuronal dynamics**

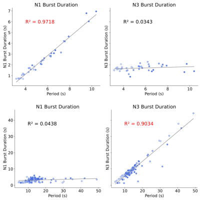
**Case of study**

**Feeding CPG**
***Lymnaea stagnalis***

**Experimental approach**

**Computational approach**

**1.**

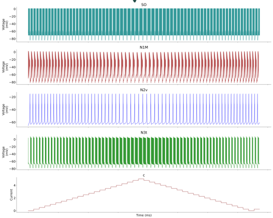



**Presence of dynamical invariants under different cases of stimulation**

**Universality of sequential dynamical invariants**

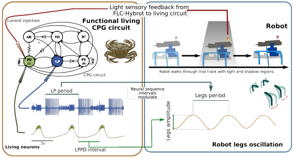
**The variability distribution is dependent on the CPG activity context**

**2.**



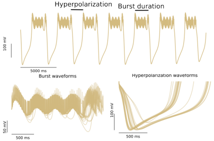

**3.**

**Transformation of sequential intervals into effective robot movement**




**4.**

**Importance of reproducing the functional variability in computational models**



# CW-NIR laser stimulation as an effective neuromodulation technique

# Current findings

- Laser stimulation accelerates neural activity.
- Most studies use pulsed laser and general dynamics
- Open questions:
  - Source of the effect: Photothermal, Photomechanical ...
  - Biophysical candidates: Capacitance, TRPV-4

Clinical applications

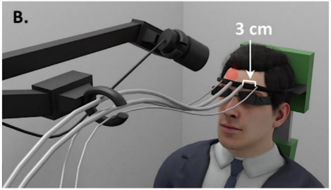



Figure 2 from Saucedo, C. L.et al (2021). Brain Stimulation, 14(2), 440–449. https://doi.org/10.1016/j.brs.2021.02.011

Stimulation technique

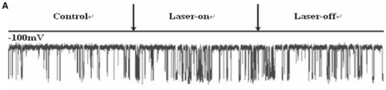
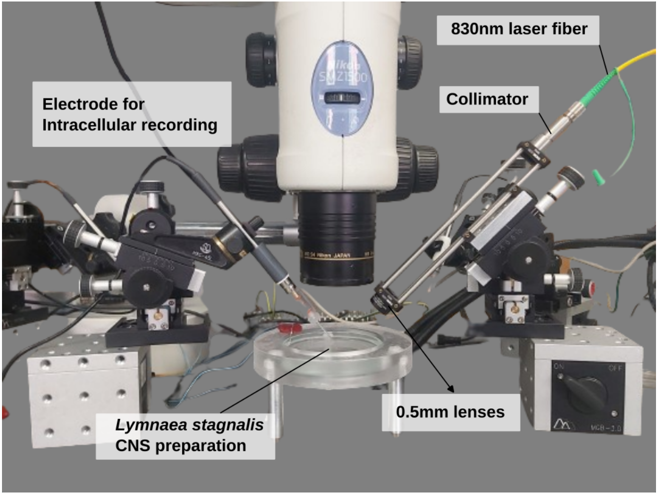


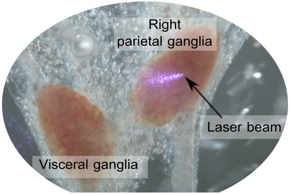

Figure 6A from Liang, S.et al. (2009). Cell Biochemistry and Biophysics, 53(1), 33–42. https://doi.org/10.1007/s12013-008-9035-2

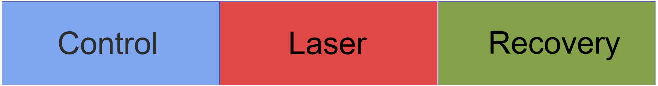
# Experimental setup



# Sustained stimulation protocol

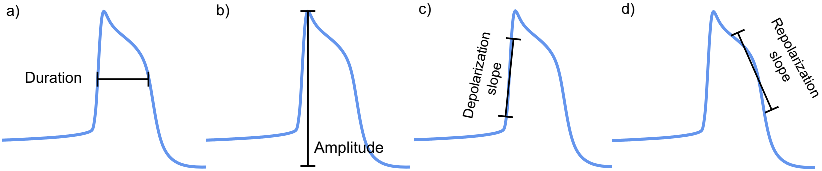
- The neuron was illuminated during the intracellular recording.
- The illumination lasted 1-3 min.
- We recorded a control before and after the illumination.



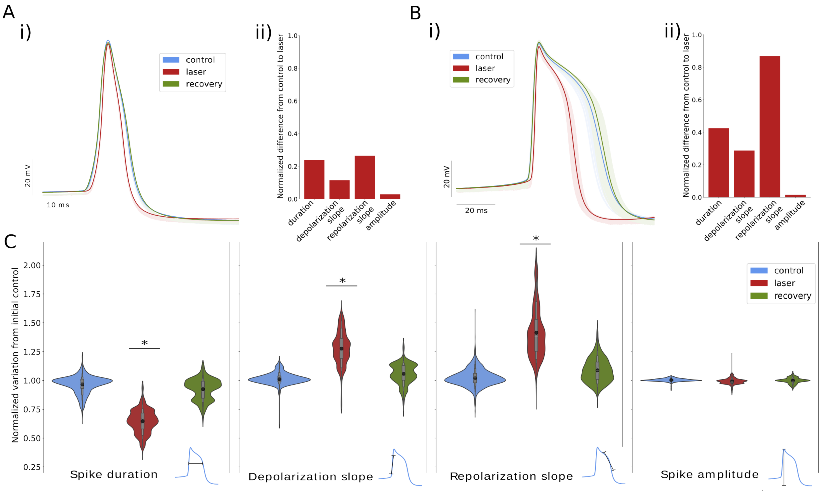



# Spike Waveform Characterization

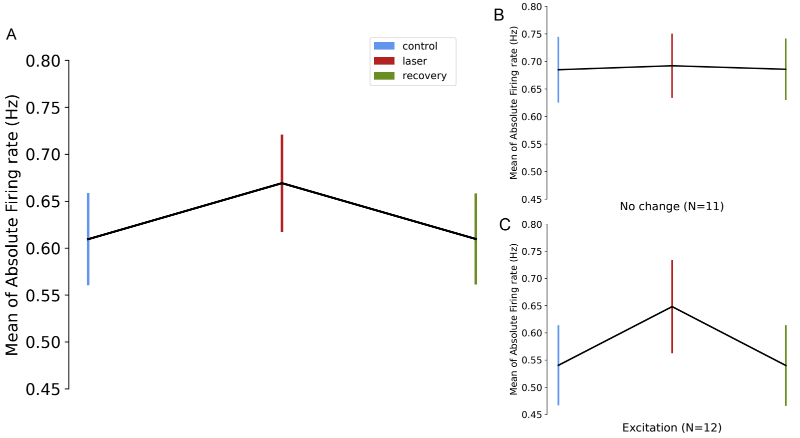
To characterize the change in the spike dynamics we defined waveform metrics.



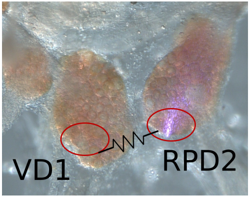
# Modulation of the spike waveform



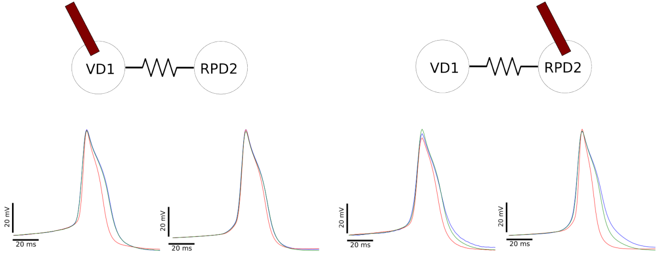
# Effect on the firing rate



# Effect on a minimal circuit

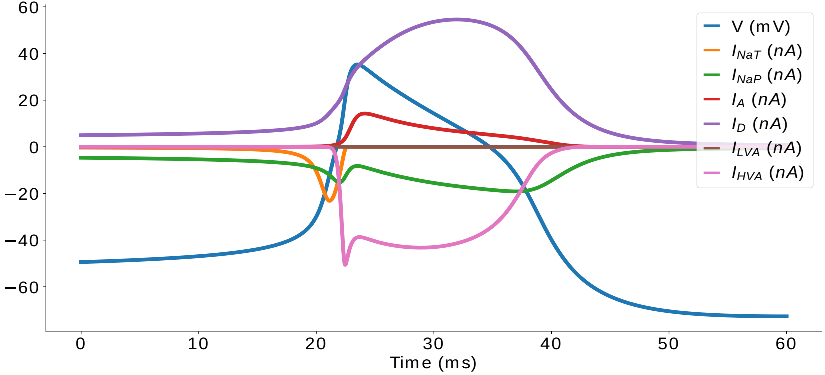



The stimulation of electrically coupled neurons, showed a first approximation to the capacity of the laser illumination to modulate neural dynamics.



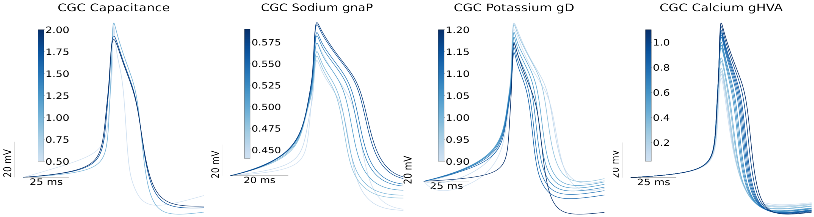
# Model analysis to explore biophysical candidates

$$C_m \frac{dV}{dt} = I_{inj} - I_{NaT} - I_{NaP} - I_A - I_D - I_{LVA} - I_{HVA} \qquad (1)$$



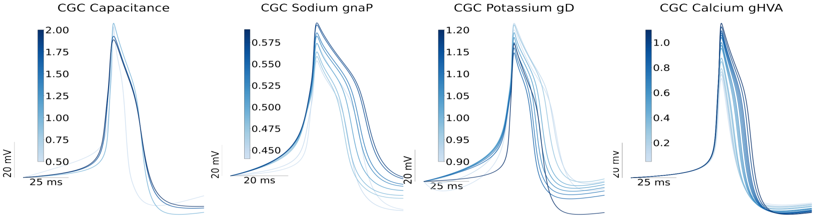
# Model analysis to explore biophysical candidates

Each candidate generated a change in the waveform, but each one fitted the experimental change only partly.



# Model analysis to explore biophysical candidates

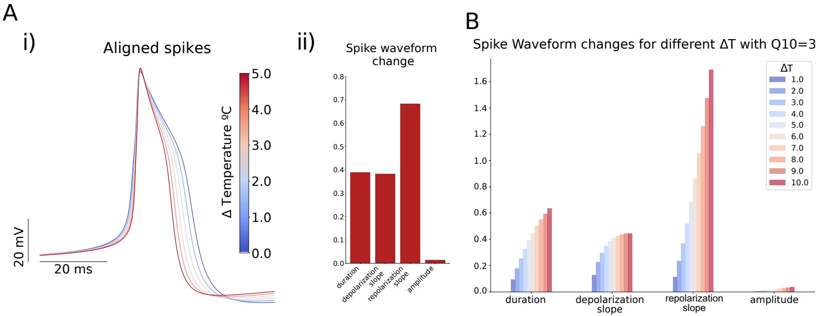
Each candidate generated a change in the waveform, but each one fitted the experimental change only partly.




The computational model study shows that no modulation of an individual candidate but a combination of them can explain the experimental quantification

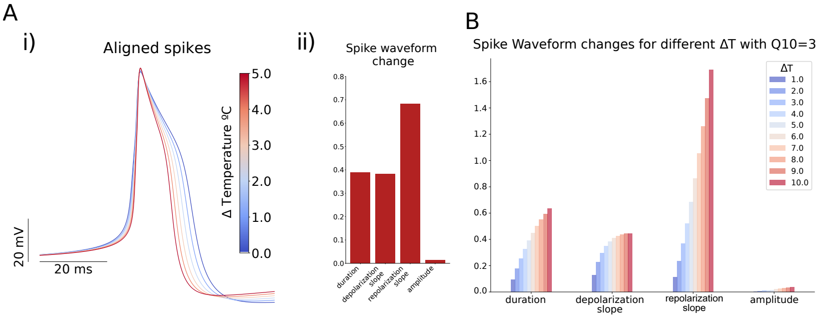
# Model with temperature description

Including temperature dependency in the model by a $Q_{10}$ factor showed the closest representation of the observed experimental modulation.



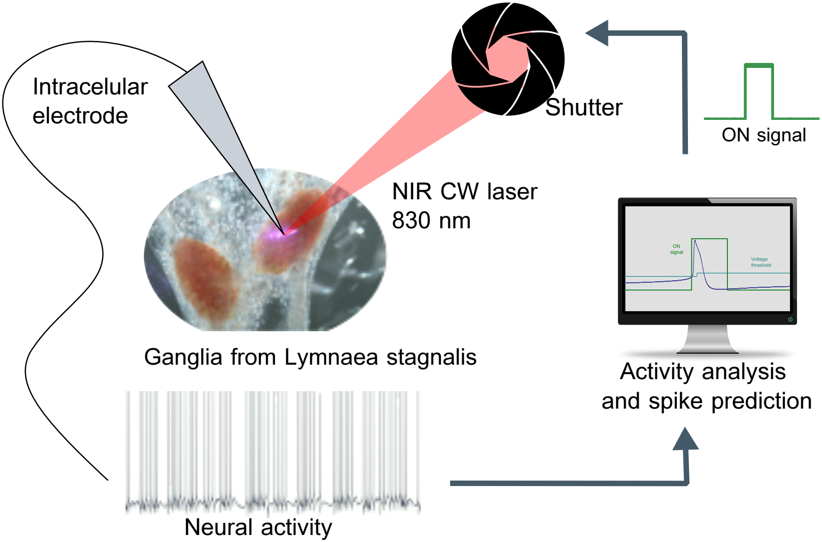
# Model with temperature description

Including temperature dependency in the model by a $Q_{10}$ factor showed the closest representation of the observed experimental modulation.

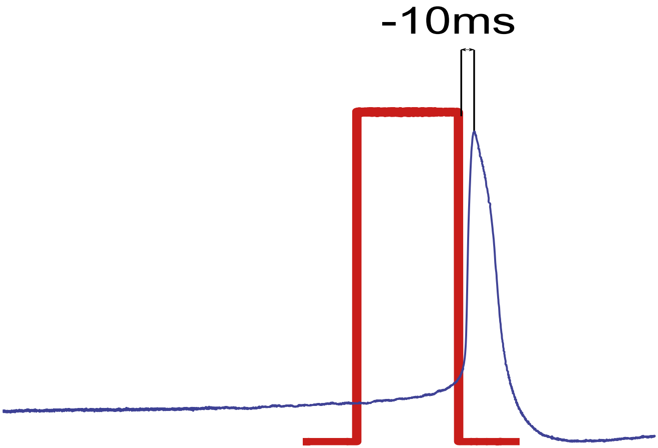



Temperature change plays a key role to explain the laser stimulation effect.

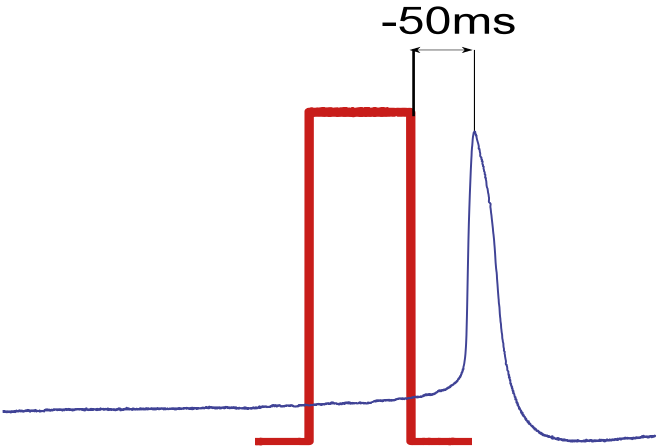
# Activity-dependent stimulation protocol



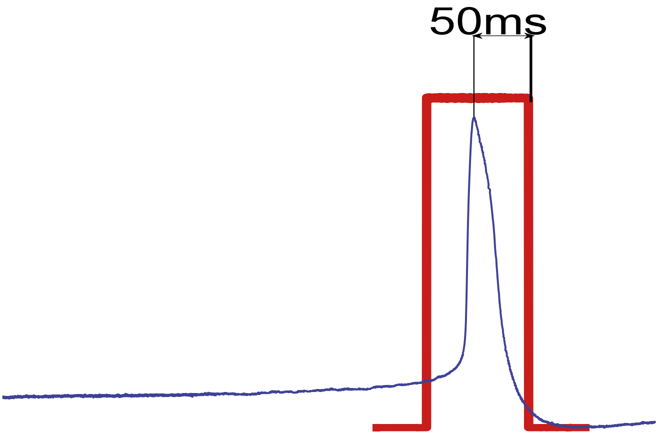
# Activity-dependent stimulation protocol



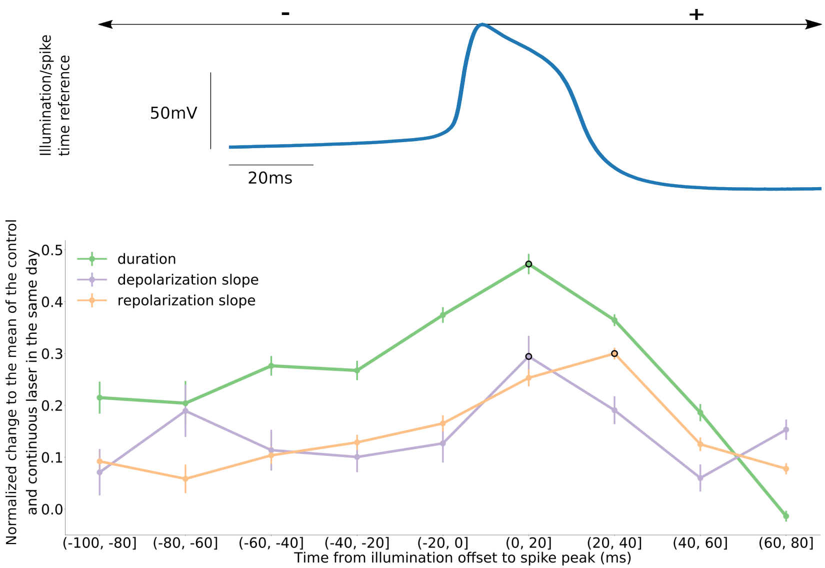
# Activity-dependent stimulation protocol



# Activity-dependent stimulation protocol



# Activity-dependent stimulation effect



# Summary of results

**Study of the Sequential nature in neuronal dynamics**

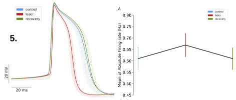
**Case of study** — **Feeding CPG *Lymnaea stagnalis***

**Stimulation Technique to study it** — **CW-NIR Infrared laser**

**Sustained illumination**

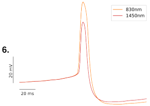
**Activity-dependent protocol**

5.



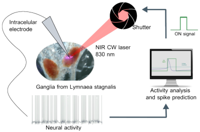

**Sutained laser stimulation accelerates the action potential**

6.



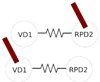

**Under the effect of different laser wavelengths, the metric changes are different**

9.



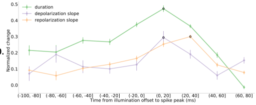

**The activity dependent protocol allows to assess the action potential sequential generation at different time instants**

7.



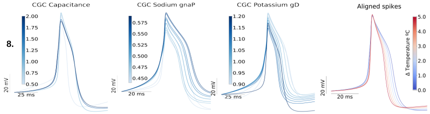

**CW-NIR laser stimulation of electrically coupled cells shows the potential of this technique to alter circuits dynamics**

10.




**The closed-loop protocol unveiled the CW-laser effect at different phases of the neuron dynamics**

8.




**No candidate alone in the model could reproduce the effect and a global change when simulating the temperature dependency reproduced better the observed effect**

# Conclusions

# Conclusions

- The study of neural sequences at multiple spatial and temporal scales can provide **novel insights to relate neural dynamics and behavior**.

# Conclusions

- The study of neural sequences at multiple spatial and temporal scales can provide **novel insights to relate neural dynamics and behavior**.
- We have **hinted the universality of sequential dynamical invariants** in experimental and modeling data in the feeding CPG.

# Conclusions

- The study of neural sequences at multiple spatial and temporal scales can provide **novel insights to relate neural dynamics and behavior**.
- We have **hinted the universality of sequential dynamical invariants** in experimental and modeling data in the feeding CPG.
- Dynamical invariants can be **indicators of the functional distribution** of variability in the CPG.

# Conclusions

- The study of neural sequences at multiple spatial and temporal scales can provide **novel insights to relate neural dynamics and behavior**.
- We have **hinted the universality of sequential dynamical invariants** in experimental and modeling data in the feeding CPG.
- Dynamical invariants can be **indicators of the functional distribution** of variability in the CPG.
- **Novel neurotechnologies** can contribute to identifying and exploiting the sequential nature of neural information processing.

# Conclusions

- Sustained CW-NIR laser illumination **asymmetrically accelerates action potential** dynamics and **the spiking rate** on single neurons.

# Conclusions

- Sustained CW-NIR laser illumination **asymmetrically accelerates action potential** dynamics and **the spiking rate** on single neurons.
- A model study of the effect of CW-NIR showed that **no biophysical candidate alone could fully reproduce the observed modulation** and the global modulation through **temperature change** in the simulation was **the closest approximation** to it.

# Conclusions

- Sustained CW-NIR laser illumination **asymmetrically accelerates action potential** dynamics and **the spiking rate** on single neurons.
- A model study of the effect of CW-NIR showed that **no biophysical candidate alone could fully reproduce the observed modulation** and the global modulation through **temperature change** in the simulation was **the closest approximation** to it.
- The **closed-loop protocol** unveiled the CW-laser **effect at different phases of the neuron dynamics**.

# Conclusions

- Sustained CW-NIR laser illumination **asymmetrically accelerates action potential** dynamics and **the spiking rate** on single neurons.
- A model study of the effect of CW-NIR showed that **no biophysical candidate alone could fully reproduce the observed modulation** and the global modulation through **temperature change** in the simulation was **the closest approximation** to it.
- The **closed-loop protocol** unveiled the CW-laser **effect at different phases of the neuron dynamics**.
- The results discussed in this thesis in the context of neural sequences can also have **strong implications** in the field of neurorrehabilitation, robotics, and artificial intelligence.

UAM Universidad Autónoma de Madrid

Escuela Politécnica Superior