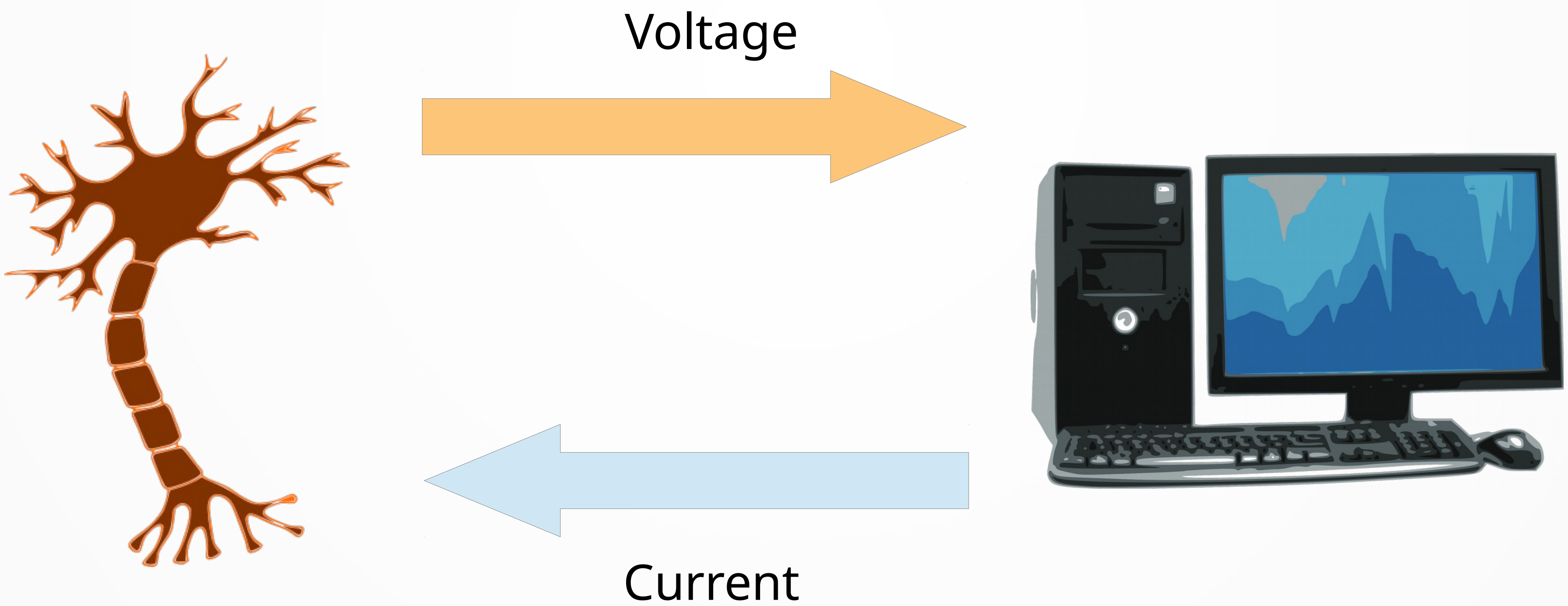
Hybrid circuits: interacting living neurons, model neurons and robots

Rodrigo Amaducci

Grupo de Neurocomputación Biológica (GNB)
Universidad Autónoma de Madrid

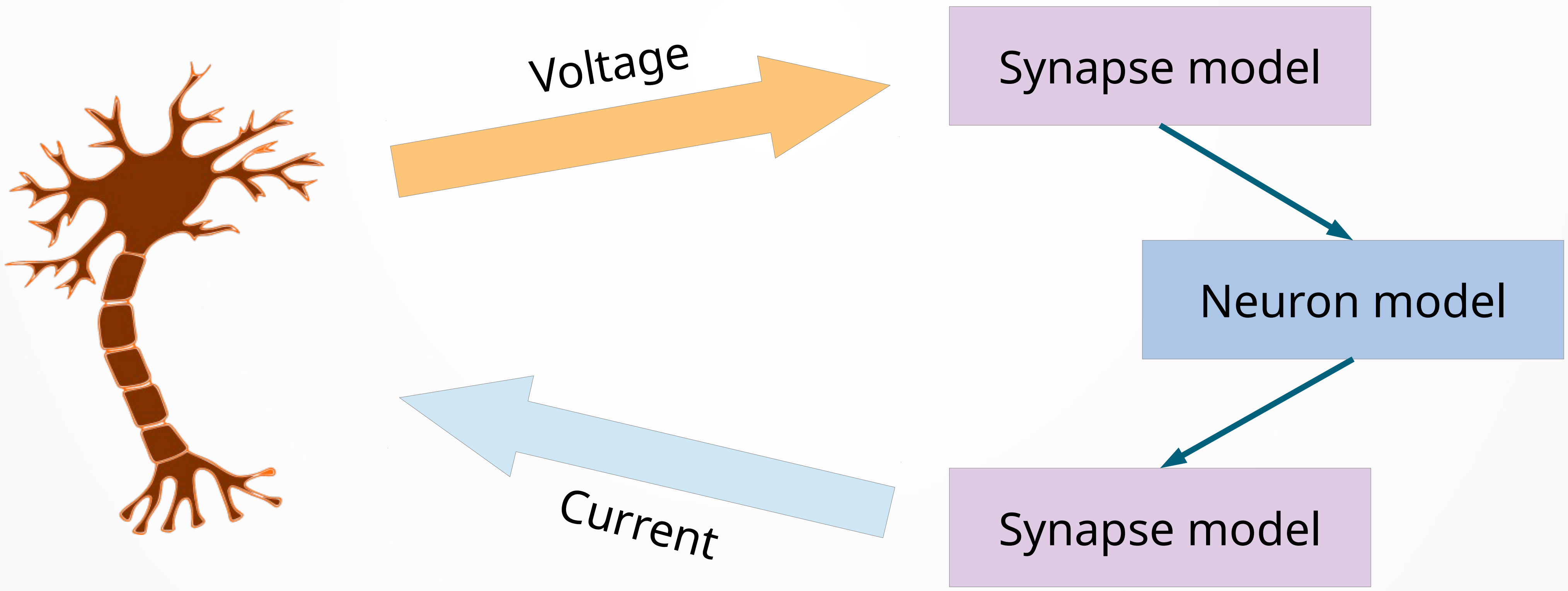
Hybrid circuits

- Networks built by connecting computational models with living cells.



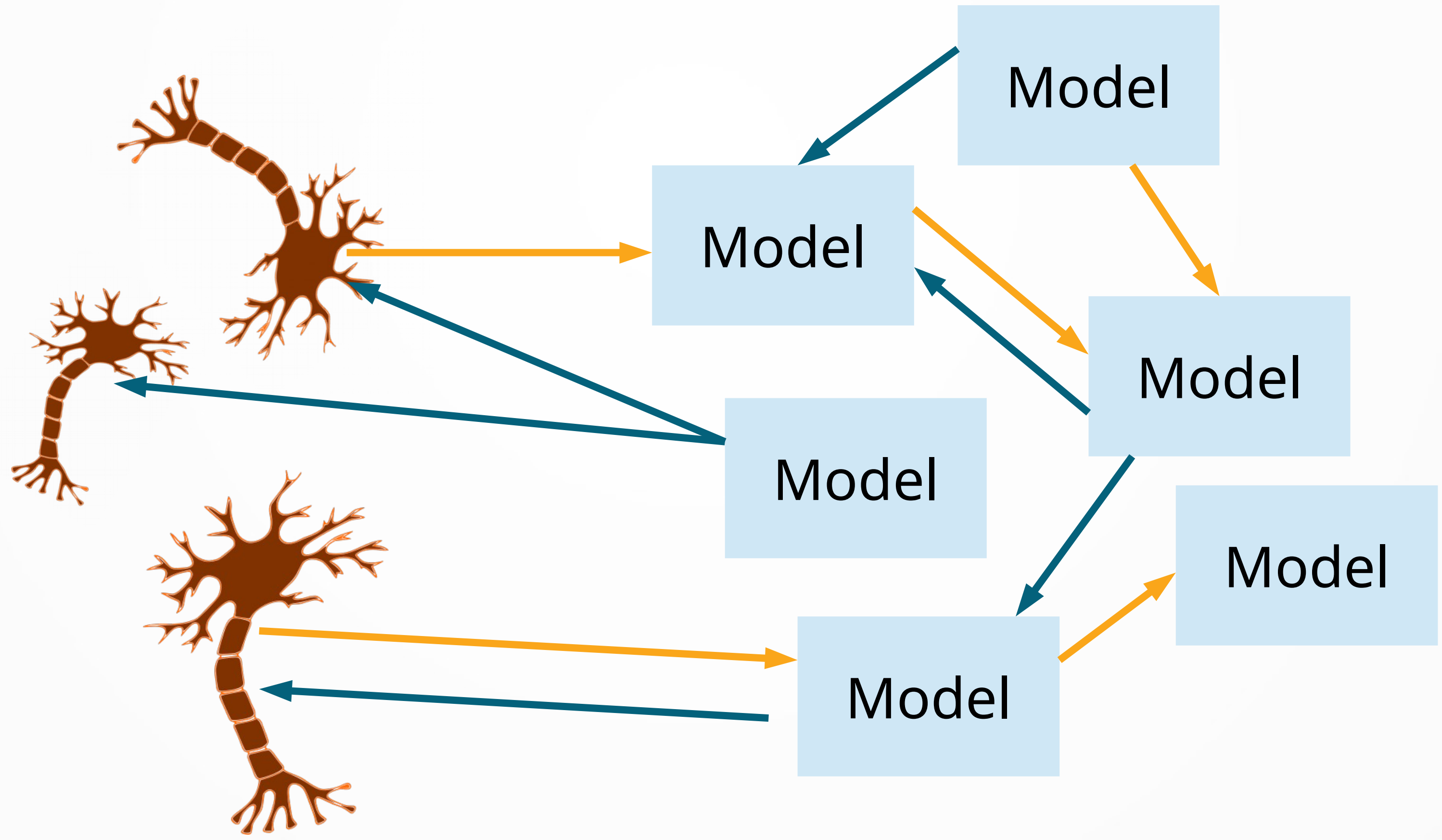
Hybrid circuits

- Networks built by connecting computational models with living cells.



Hybrid circuits

- Networks built by connecting computational models with living cells.



Hybrid circuits

- Powerful tool to explore and characterize neural system dynamics.
- Useful to assess the role of specific circuit components.
- Set a baseline for machine and biological elements interaction.

How to build hybrid circuits

Living circuit preparation

- Typically dynamic-clamp.
- DAQ and amplifier specifications.
- Temporal precision:
  - Milliseconds scale or higher?
    - Soft real-time
  - Under milliseconds scale?
    - Hard real-time

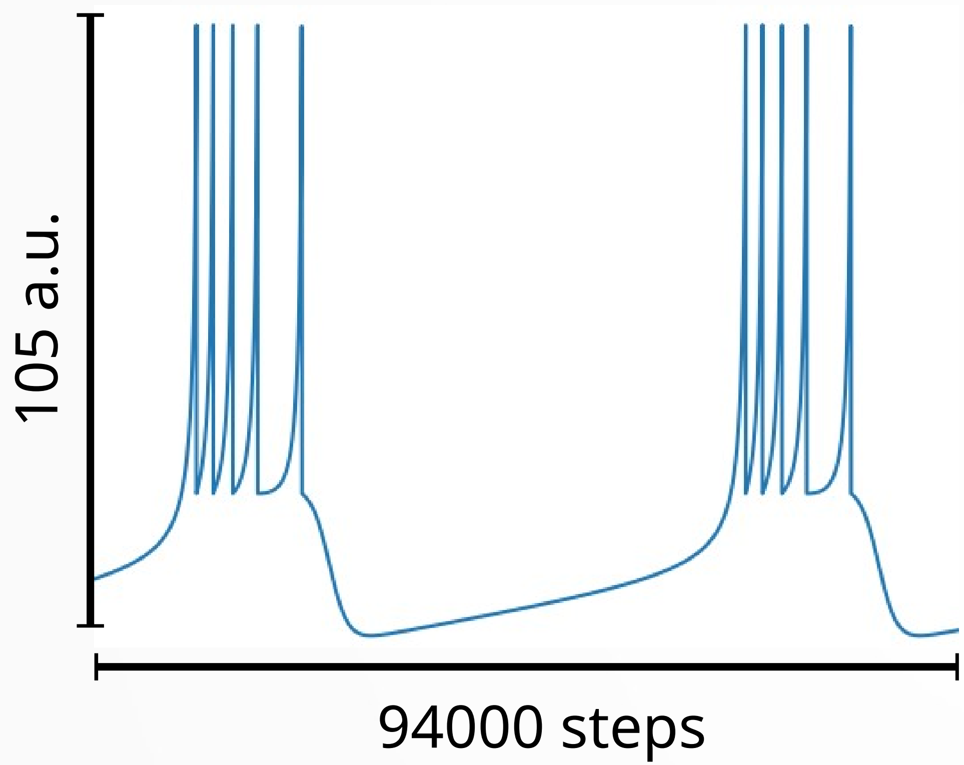
How to build hybrid circuits

Computational setup

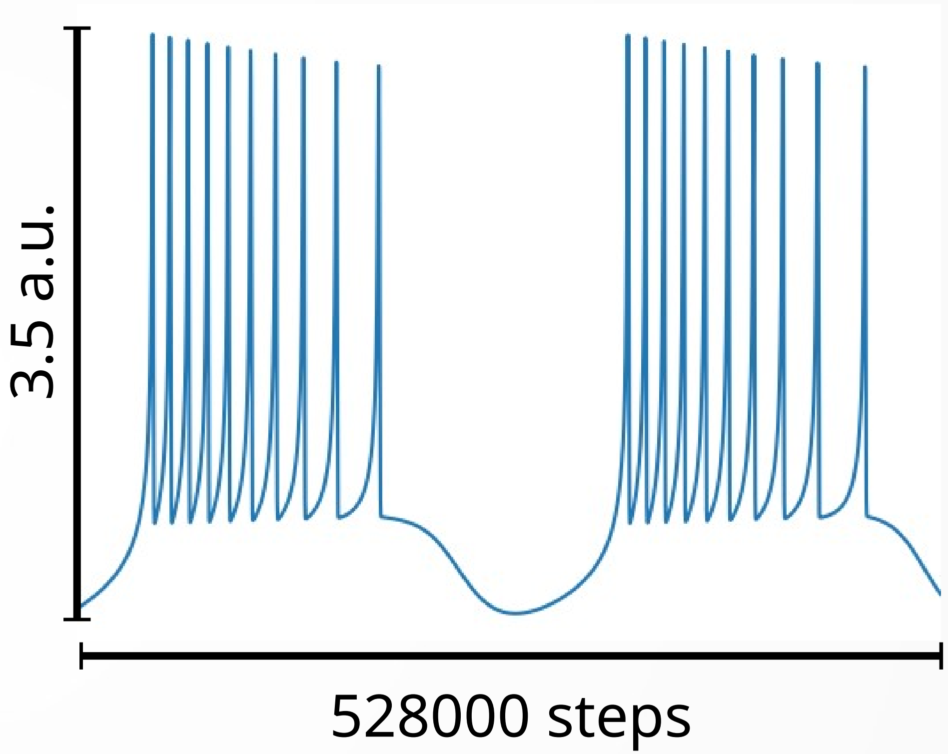
- Hardware-based:
  - Electronic circuits
  - Microcontrollers (Arduino, Teensy, etc)
- Software-based:
  - Soft real-time:
    - Normal OS (Windows, Linux, MacOS, etc)
  - Hard real-time:
    - Real-time OS (Preempt-RT, Xenomai, etc)

How to build hybrid circuits

Izhikevich model (2003)



Hindmarsh and Rose model (1984)



- Each model have different temporal and amplitude scales.
- Every electrophysiological experiment is different (and can change over time).

How to build hybrid circuits

- All amplitude and time scale adjustments have to be addressed specifically for each preparation.
- This can be done by hand, but takes a lot of precious time.
- Automatic adaptation and mappings of hybrid circuits help to solve this issue.
- More about this techniques in the following talk.

Some existing tools

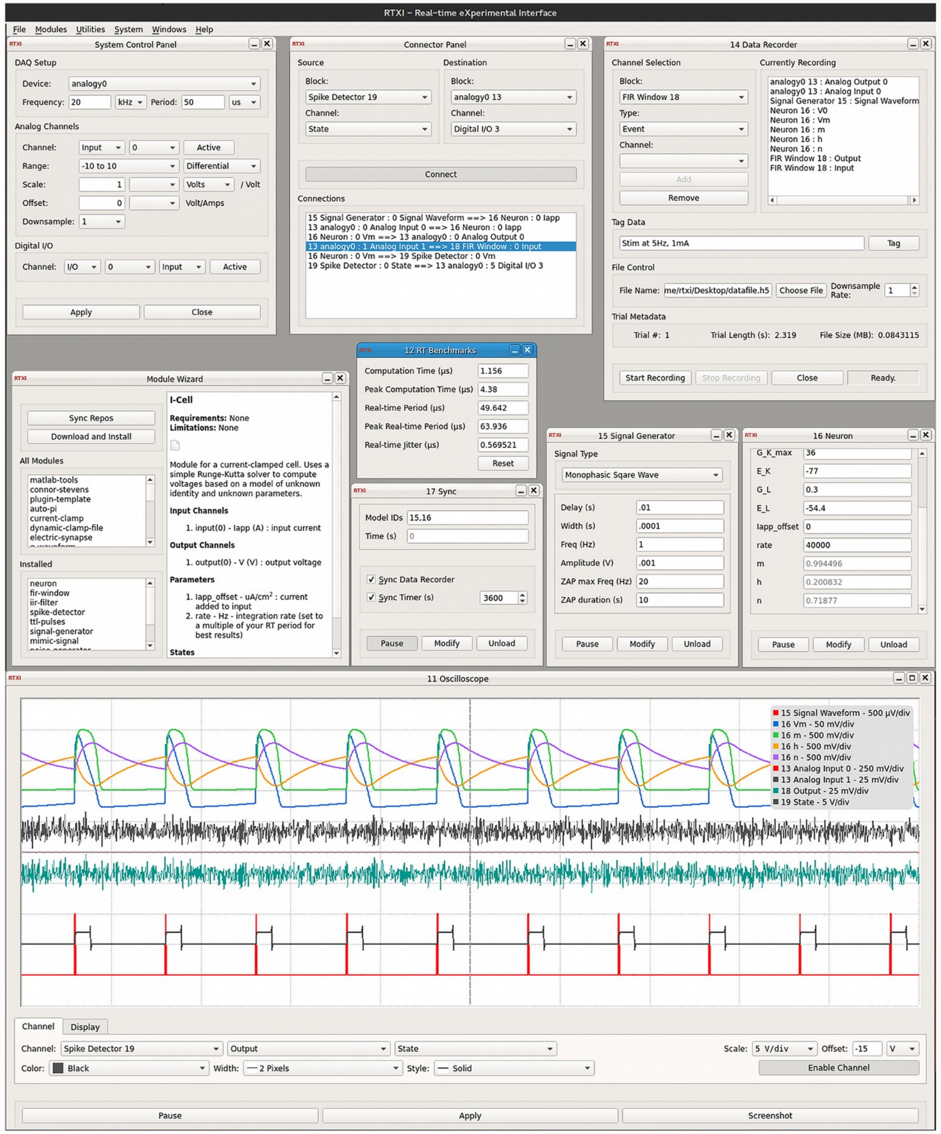
Name	Platform	Real-time support	Reference
LCG	Linux	Soft real-time	Linaro et al., 2014
StdpC	Windows	Soft real-time	Nowotny et al., 2006
PC NEURON Simulink	Windows	Hard real-time (xPC and Simulink)	Biró and Giugliano, 2015
CLEM	Windows	Soft real-time	Hazan and Ziv, 2017
Falcon	Windows	Soft real-time	Ciliberti and Kloosterman, 2017
Open Ephys GUI	Windows/Linux/ MacOS	Soft real-time	Siegle et al., 2017
RTXI	Linux	Hard real-time (Xenomai)	Patel et al., 2017
RTHybrid	Linux	Soft and hard real-time (Xenomai or Preempt-RT)	Amaducci et at, 2019

Some existing tools

Name	Platform	Real-time support	Reference
LCG	Linux	Soft real-time	Linaro et al., 2014
StdpC	Windows	Soft real-time	Nowotny et al., 2006
PC NEURON Simulink	Windows	Hard real-time (xPC and Simulink)	Biró and Giugliano, 2015
CLEM	Windows	Soft real-time	Hazan and Ziv, 2017
Falcon	Windows	Soft real-time	Ciliberti and Kloosterman, 2017
Open Ephys GUI	Windows/Linux/ MacOS	Soft real-time	Siegle et al., 2017
RTXI	Linux	Hard real-time (Xenomai)	Patel et al., 2017
RTHybrid	Linux	Soft and hard real-time (Xenomai or Preempt-RT)	Amaducci et at, 2019

RTXI

- Open-source.
- Hard real-time:
  - Linux with Xenomai
- Designed for general data acquisition and control in biological research.
- Users can add custom modules.
- Great flexibility.



[Patel et al, 2017]

RTHybrid

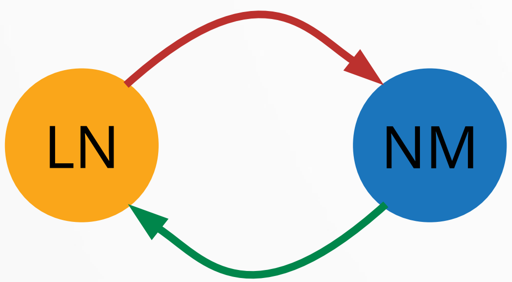
- Open-source.
- Soft real-time:
  - Standard linux
- Hard real-time:
  - Linux with Xenomai
  - Linux with Preempt-RT
- Designed specifically to build hybrid circuits.
- Includes neuron and synapse model library and adaptation algorithms.

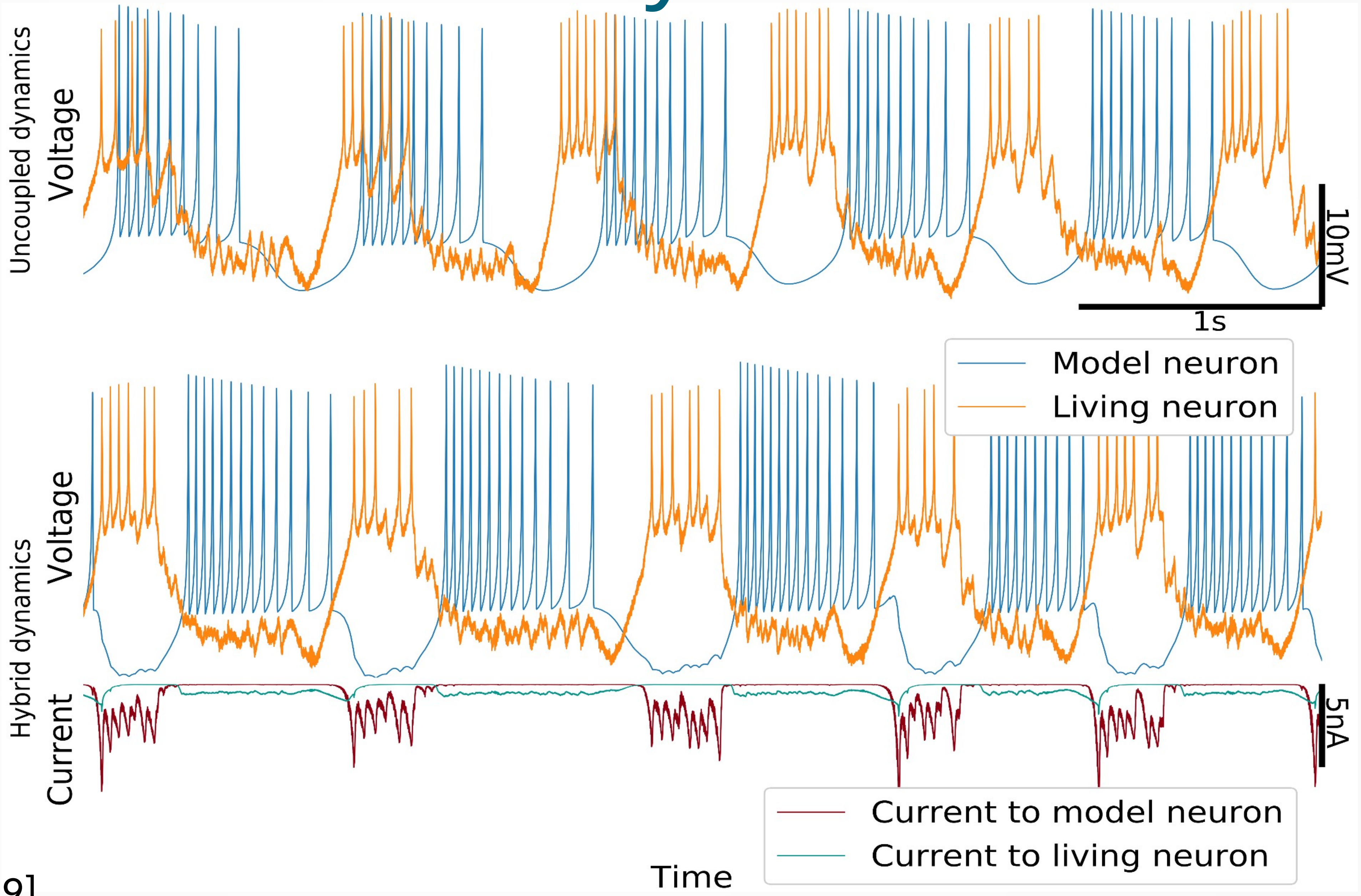
[Amaducci et al, 2019]

Hybrid circuit with RTHybrid

Neuron model:
[Hindmarsh and Rose, 1984]

Synapse models:
[Golowasch et al., 1999]



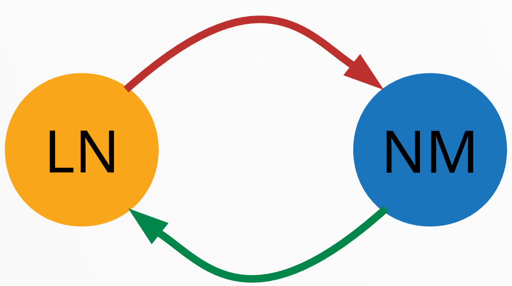


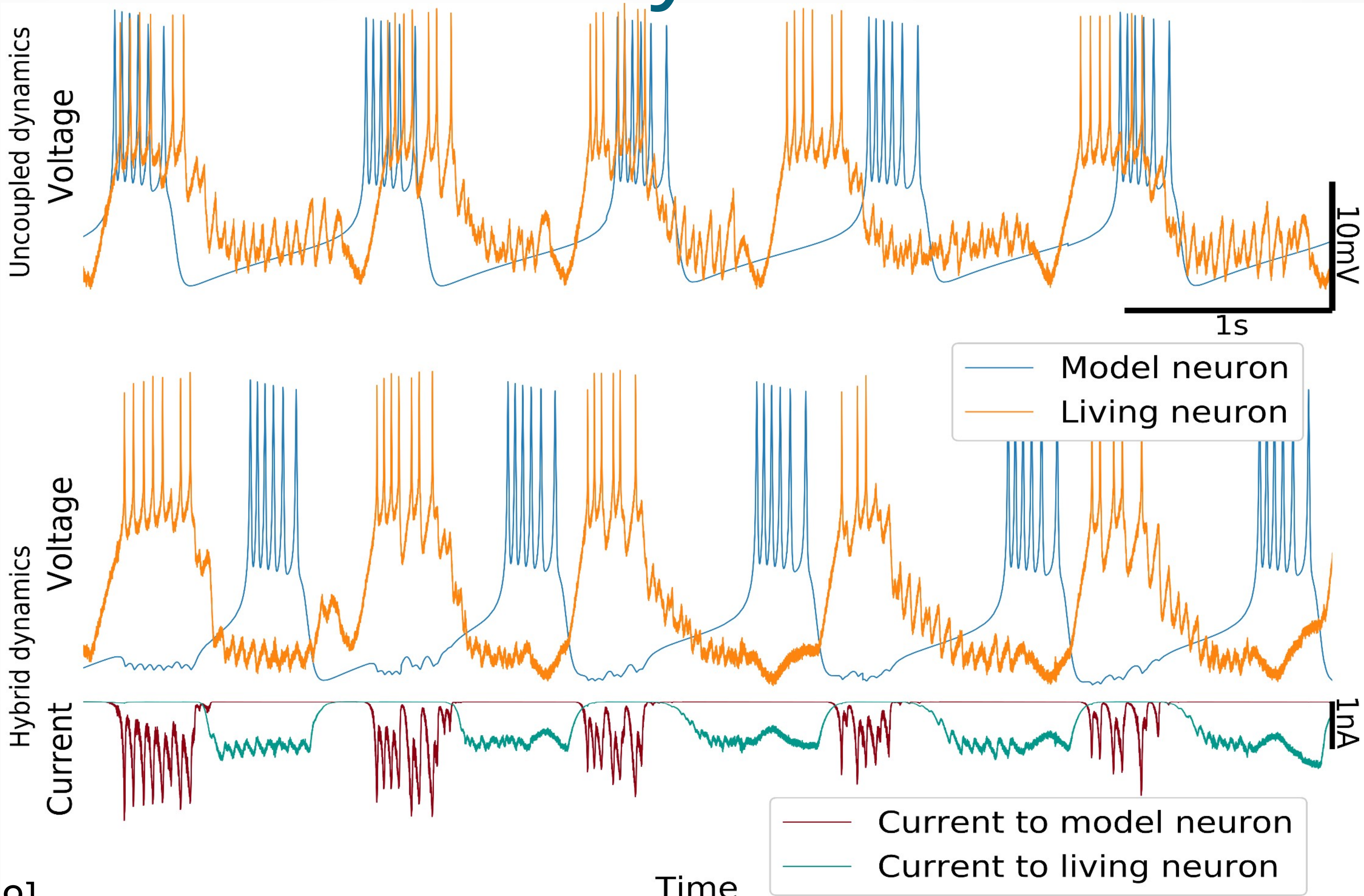
[Amaducci et al, 2019]

Hybrid circuit with RTHybrid

Neuron model:
[Ghigliazza and Holmes, 2004]

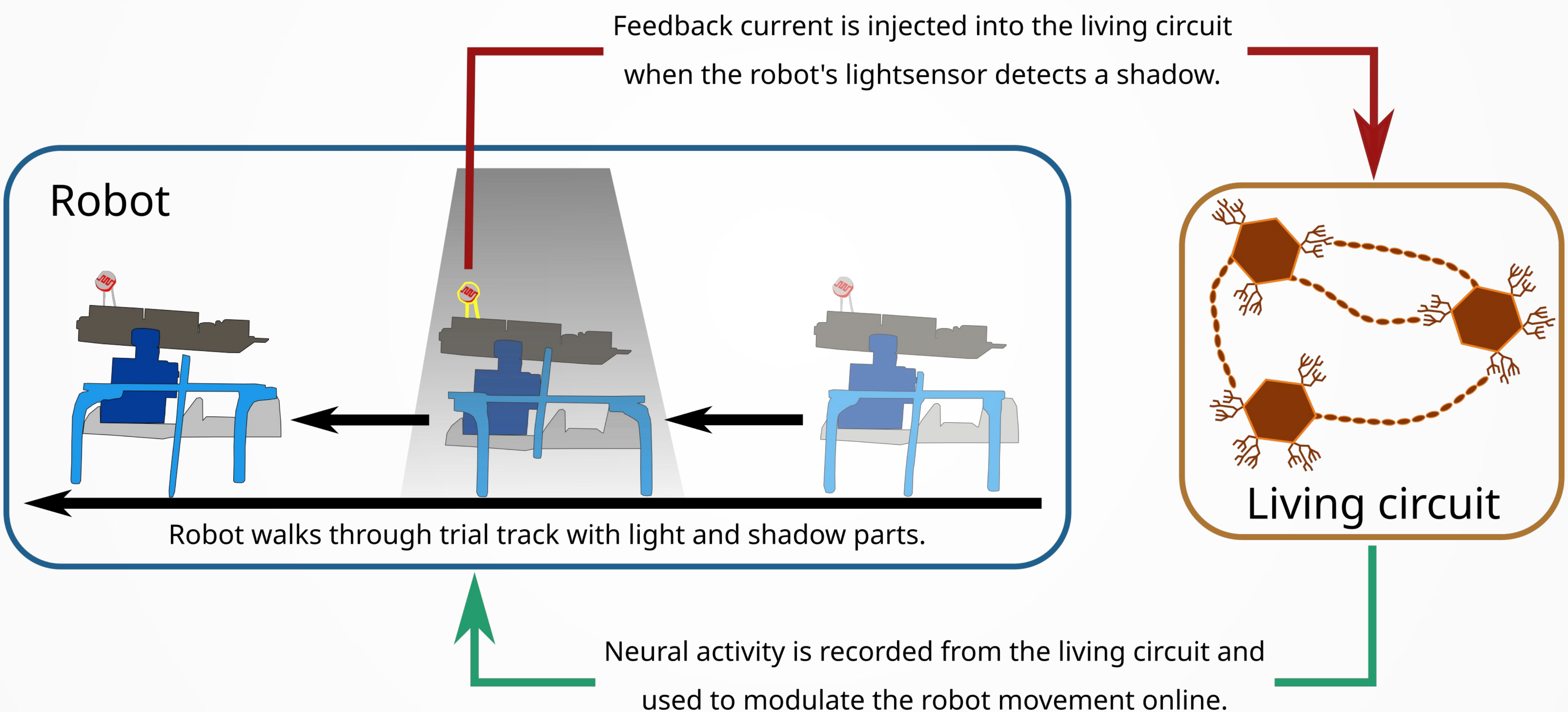
Synapse models:
[Golowasch et al., 1999]

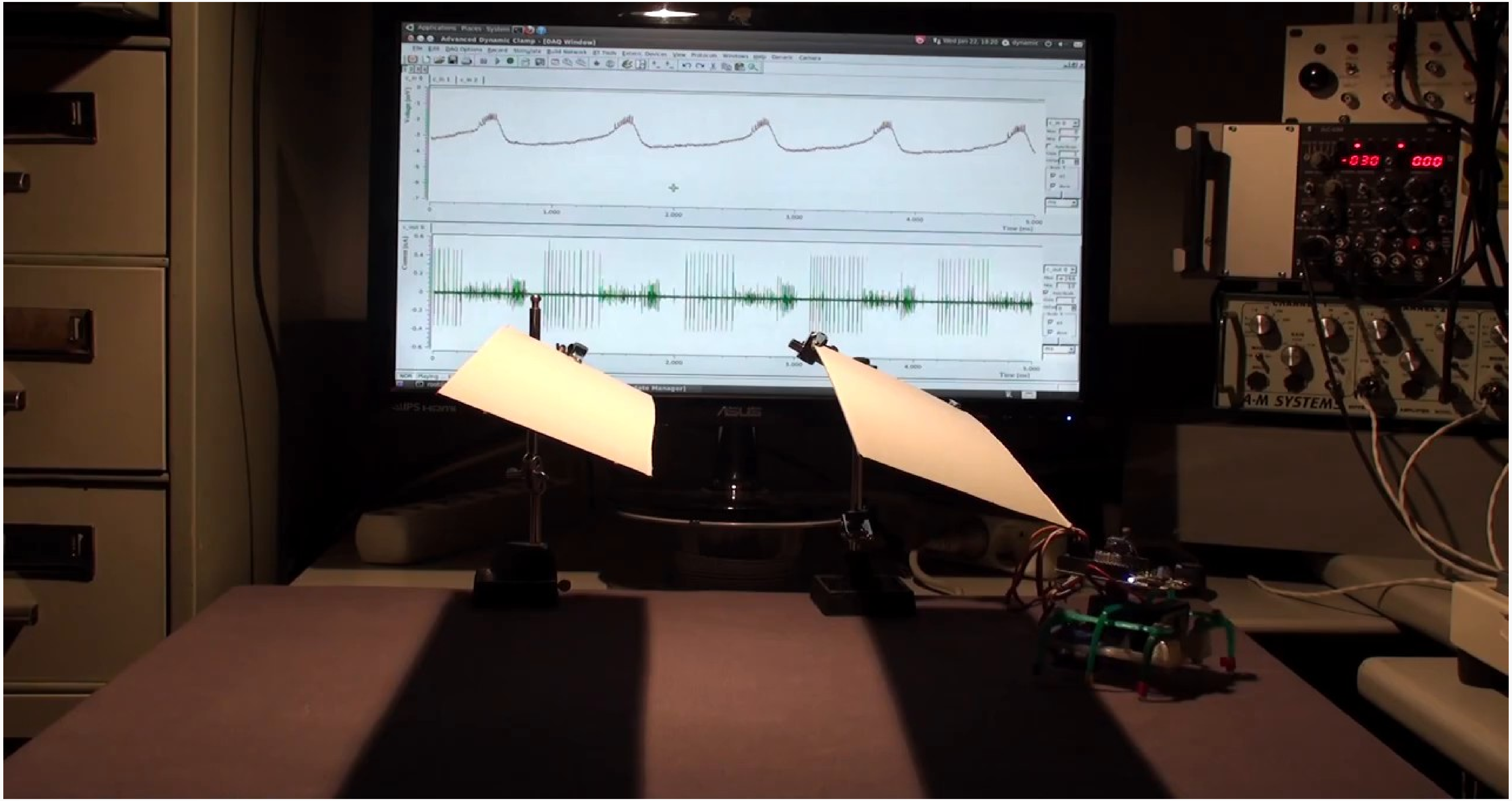




[Amaducci et al, 2019]

Hybrot (Hybrid robot)





https://www.youtube.com/watch?v=qFLPWpT1H7U

Conclusions

- Hybrid circuit closed-loop experiments are a great tool to study neural dynamics.
- However, technical requirements, such as temporal precision or adaptation to biological elements, make them difficult to implement.
- Standardization of real-time software beyond specific platforms will largely contribute to the use and dissemination of closed-loop protocols.

Thank you!

If you want to see more about closed-loops, check these posters and talks!

P206: Parameter exploration in neuron and synapse models driven by stimuli from living neuron recordings.

Sunday 19th - 9pm (Berlin Time)

P207: Hybrid robot driven by a closed-loop interaction with a living central pattern generator with online feedback.

Sunday 19th - 9pm (Berlin Time)

O11: Experimental and computational characterization of interval variability in the sequential activity of the Lymnaea feeding CPG.

Monday 20th - 9pm (Berlin Time)

- **R. Amaducci, M. Reyes-Sanchez, I. Elices, F.B. Rodriguez, P. Varona.** *2019*. RTHybrid: A Standardized and Open-Source Real-Time Software Model Library for Experimental Neuroscience. *Frontiers in Neuroinformatics 13:11*. https://doi.org/10.3389/fninf.2019.00011
- **M. Reyes-Sanchez, R. Amaducci, I. Elices, F.B. Rodriguez, P. Varona.** *2020*. Automatic adaptation of model neurons and connections to build hybrid circuits with living networks. *Neuroinformatics 18: 377–393*. https://doi.org/10.1007/s12021-019-09440-z
- **I. Elices, R. Levi, D. Arroyo, F.B. Rodriguez, P. Varona.** *2019*. Robust dynamical invariants in sequential neural activity. *Sci Rep 9, 9048*. https://doi.org/10.1038/s41598-019-44953-2