Human Brain Project

EBRAINS

POLITECNICO MILANO 1863

UNIVERSITÀ DI PAVIA

CerebNEST

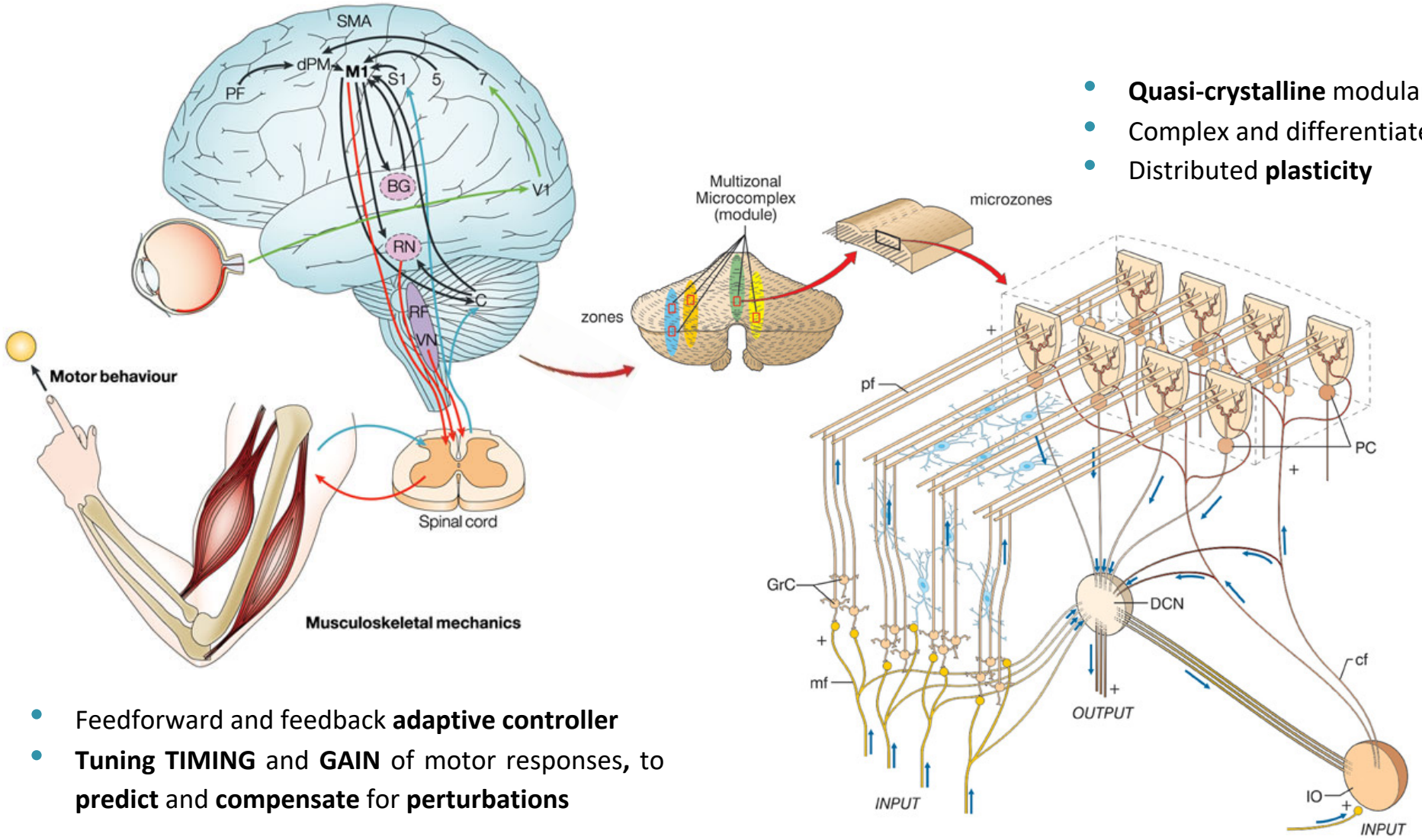
A Bioinspired Multiscale Modelling of The Cerebellar Network

HBP Partnering Projects Meeting: Status quo & outlook

5-7 September 2022 | Nijmegen, The Netherlands

Co-funded by the European Union

Why simulate the cerebellum?



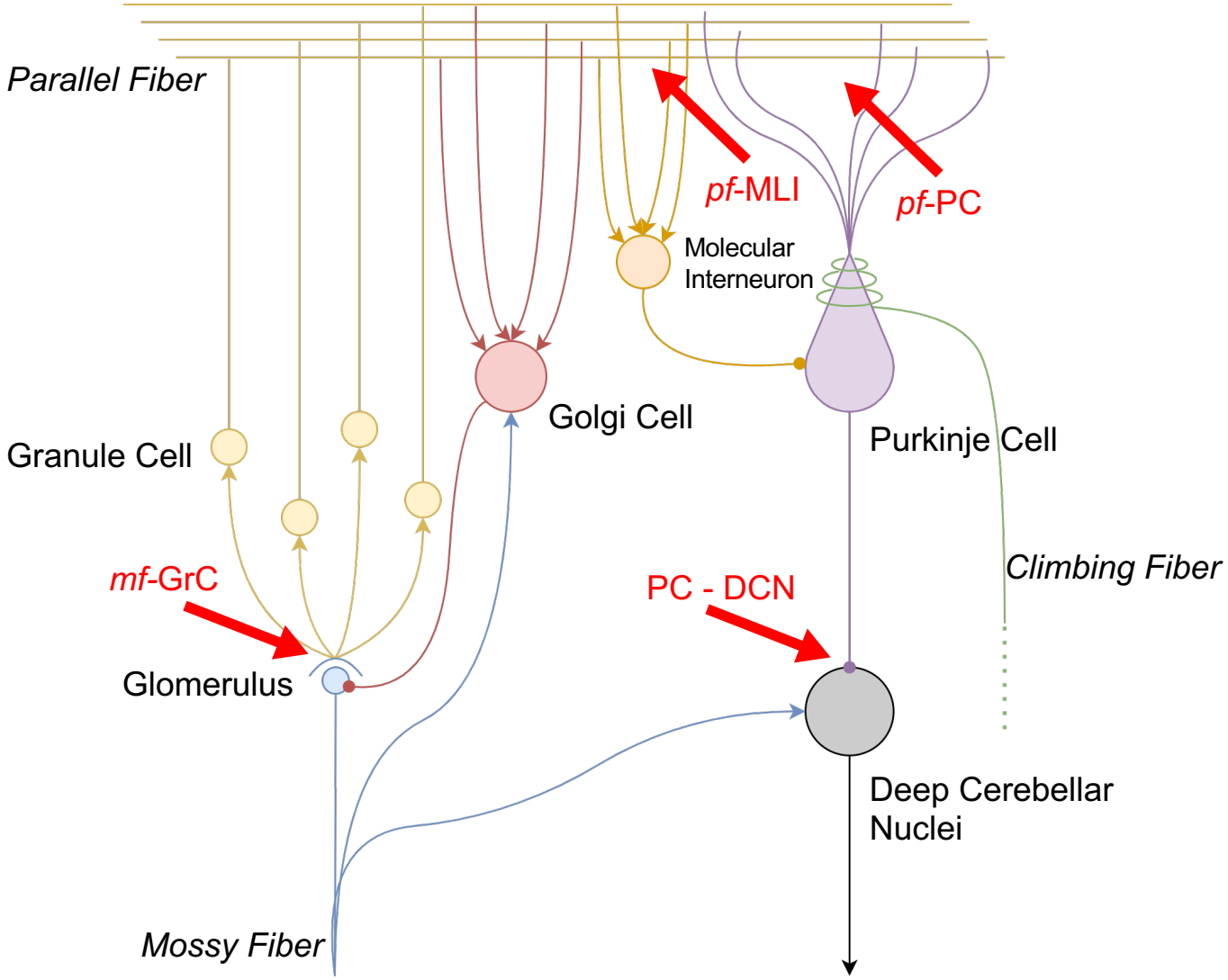
- **Quasi-crystalline** modular microcircuit structure
- Complex and differentiated single **neuron and synapse dynamics**
- Distributed **plasticity**

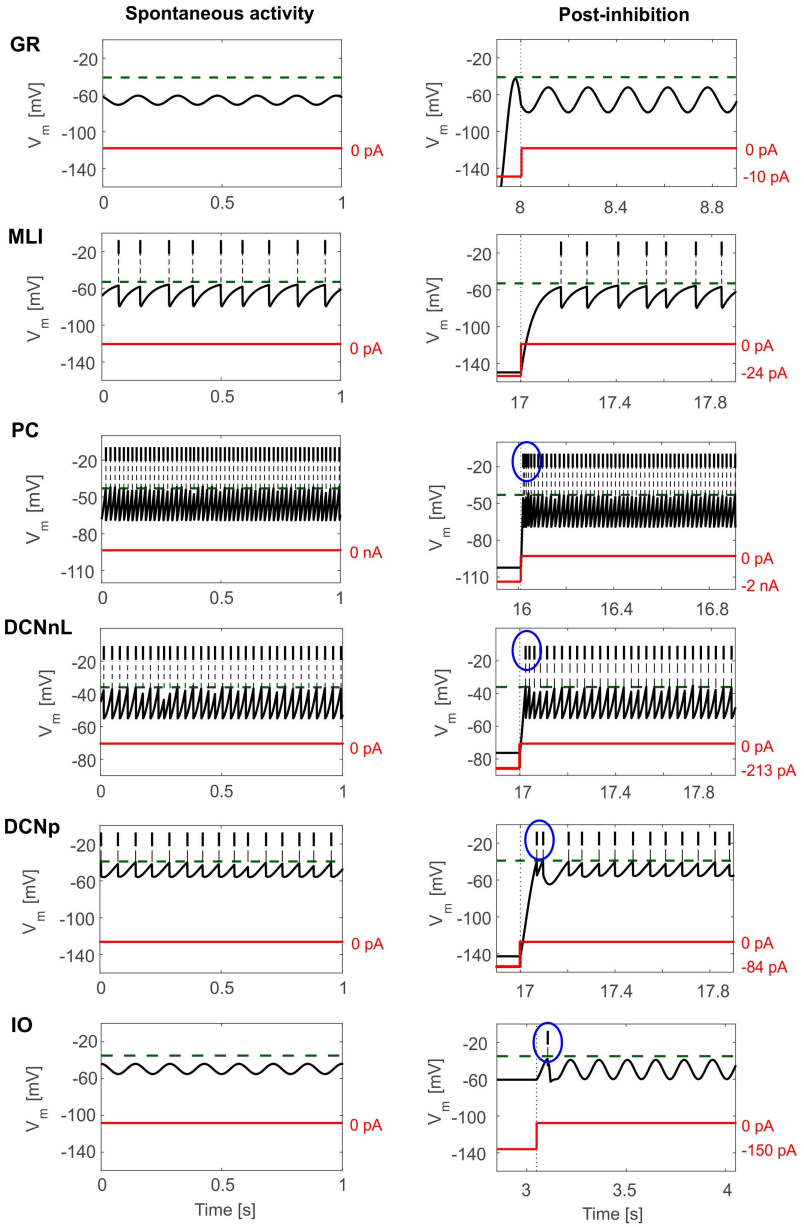
- Feedforward and feedback **adaptive controller**
- **Tuning TIMING** and **GAIN** of motor responses**,** to **predict** and **compensate** for **perturbations**

mf: mossy fiber
cf: climbing fiber
pf: parallel fiber
GoCs: Golgi cells
GrCs: granule cells
SCs: stellate cells
BCs: basket cells
PCs: Purkinje Cells
DCN: deep cerebellar nuclei

Taken from: D'Angelo E. and Casali S., 2013

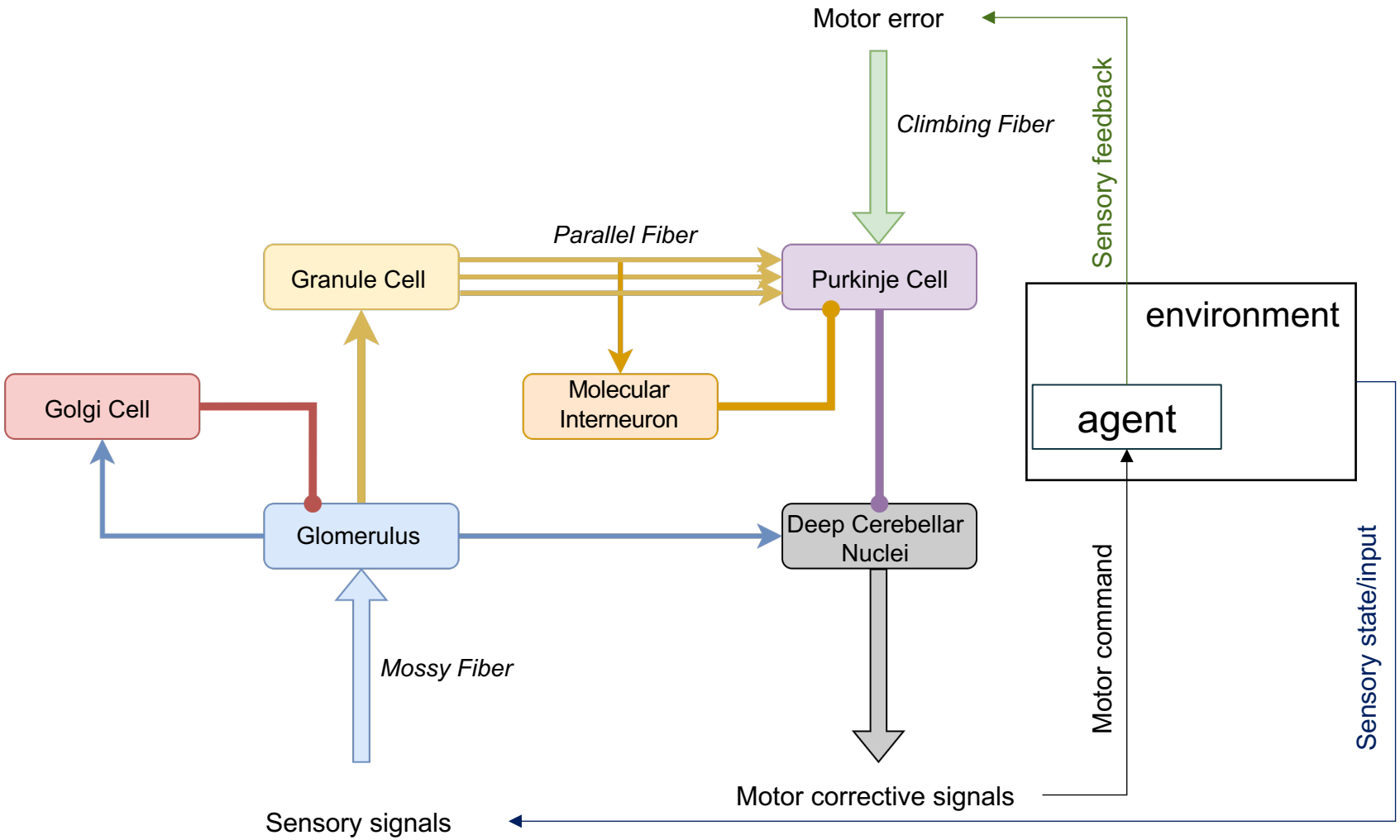
Why simulate the cerebellum?



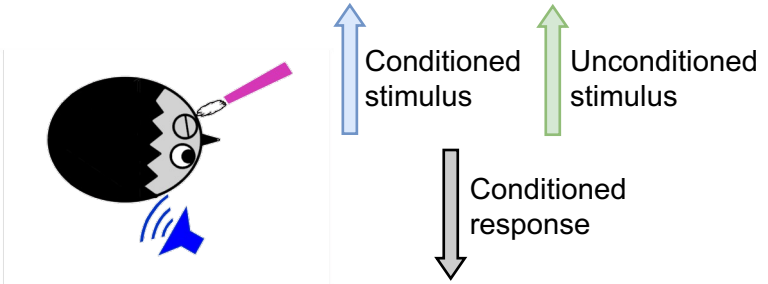


Taken from: Geminiani A et al.., 2019

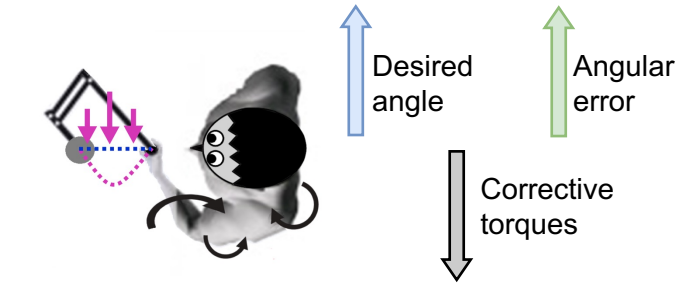
Why simulate the cerebellum?



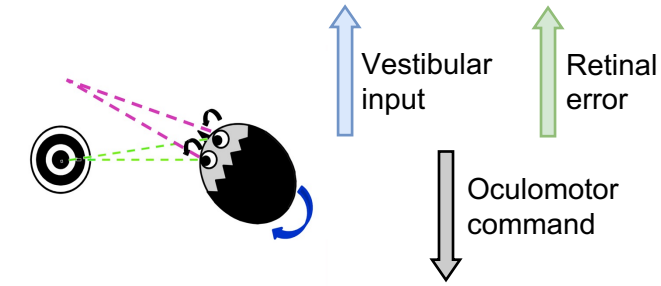
Eye Blink Classical Conditioning (EBCC)



Movements perturbed by Force Fields (FF)



Vestibulo-Ocular Reflex (VOR)



Adapted from: Casellato et al., 2014

Story of cerebNEST project

CerebNEST

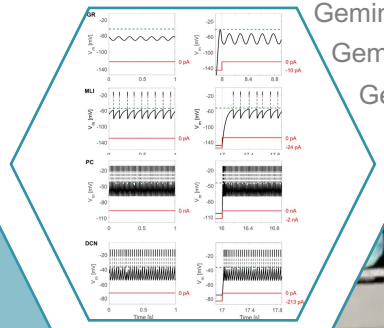
Design experimental protocols

Advanced models of single point neuron EGLIF

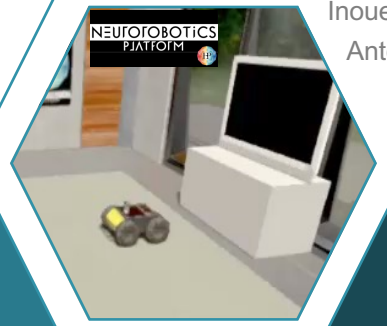
Develop microcircuits models

Robotic embodiment

...

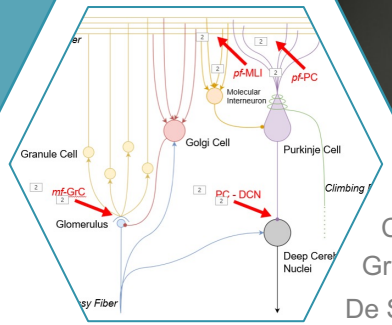


Geminiani et al., 2018
Geminiani et al., 2019 a
Geminiani et al., 2019 b

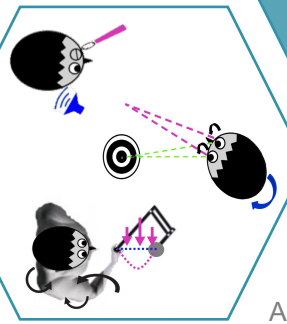


Inoue et al., 2021
Antonietti et al., 2022

Antonietti et al., 2018
Antonietti et al., 2019



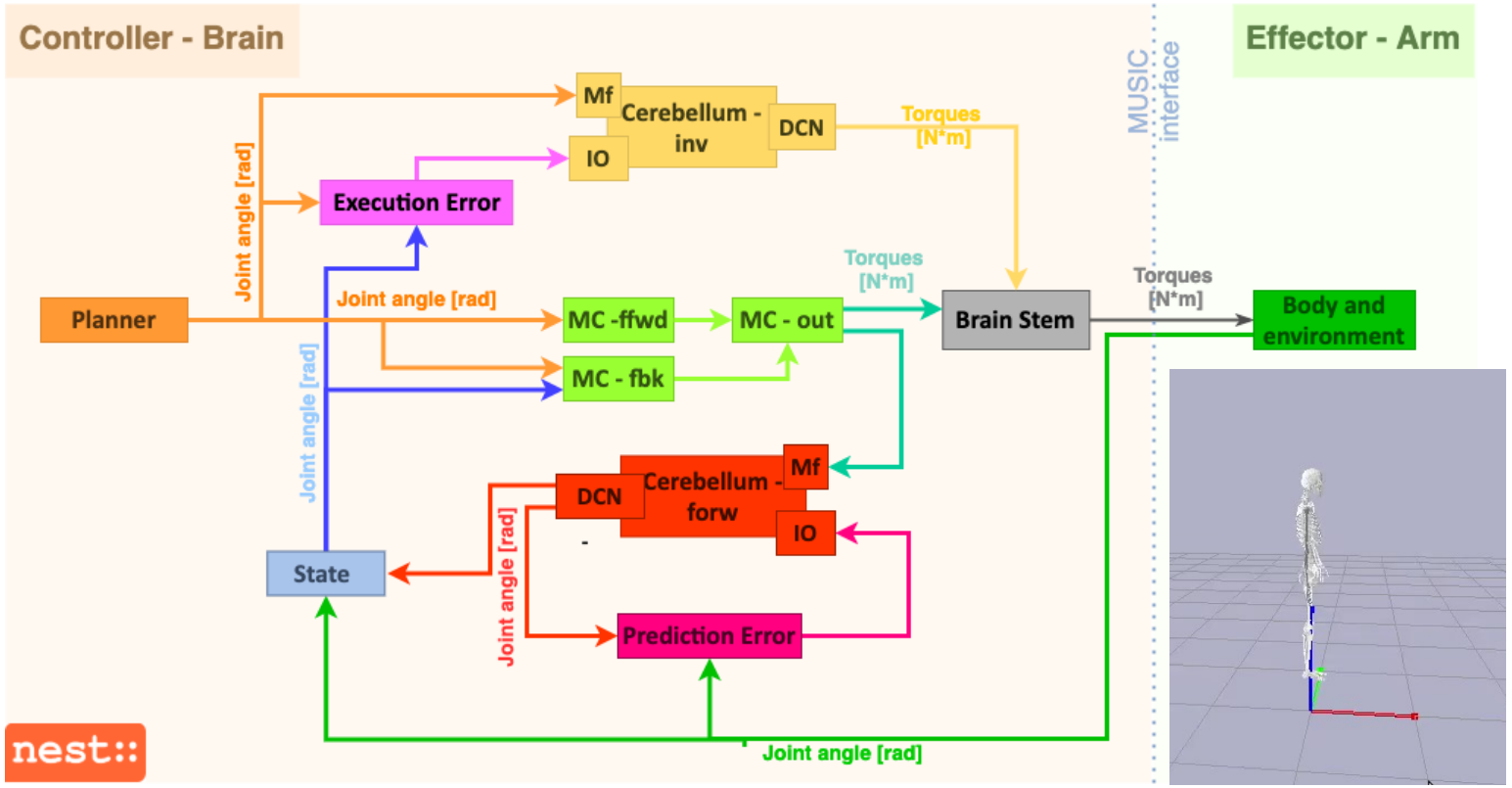
Casali et al., 2019
Grillo et al., 2021
De Schepper et al., 2021

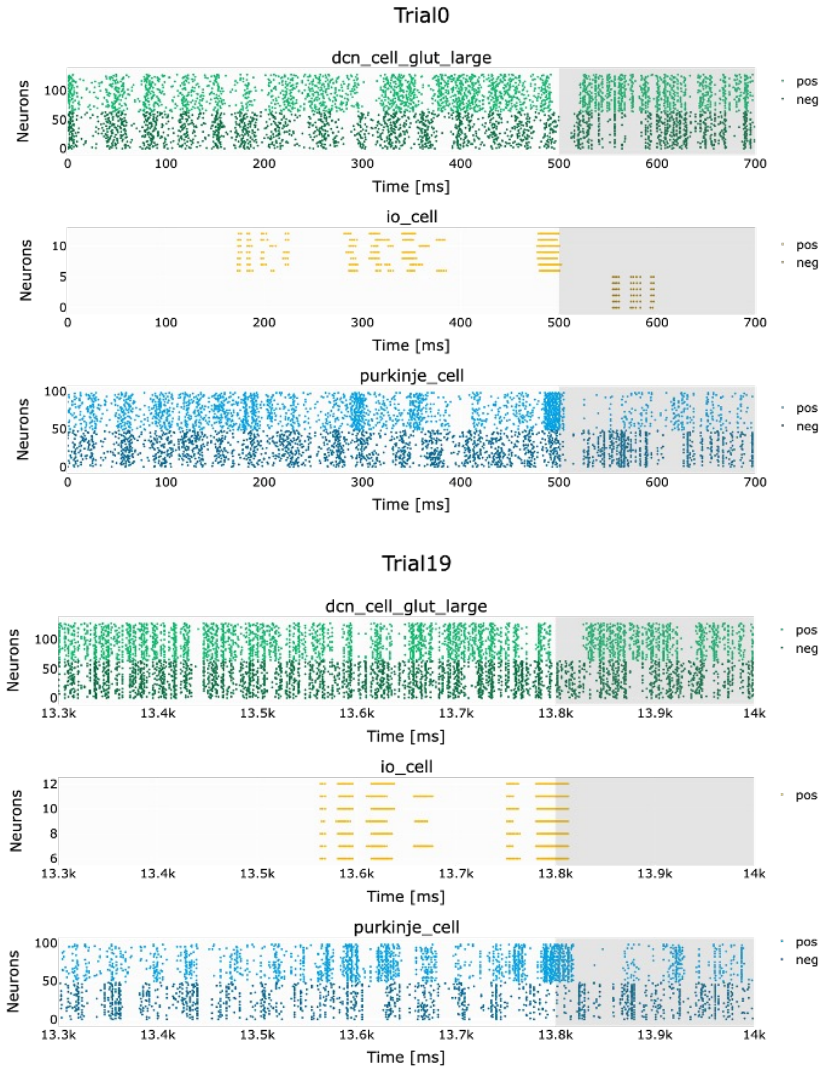


Casellato et al., 2014
Antonietti et al., 2015

cerebNEST today – Robotic embodiment

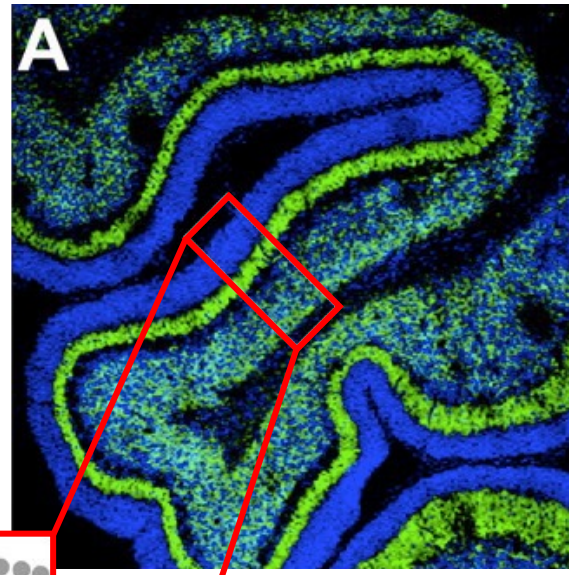
Benedetta Gambosi
benedetta.gambosi@polimi.it

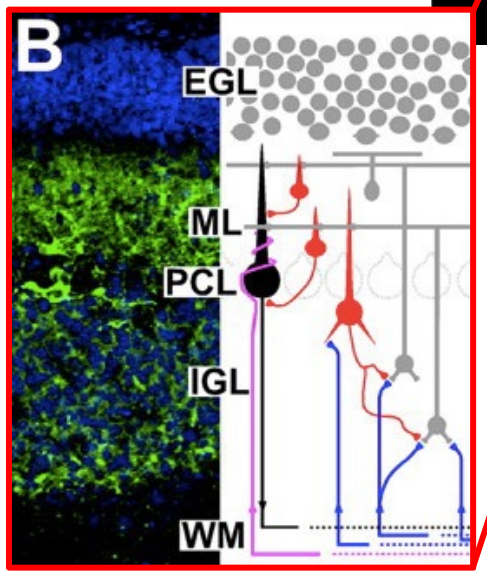




cerebNEST today – Diffusive plasticity mechanism

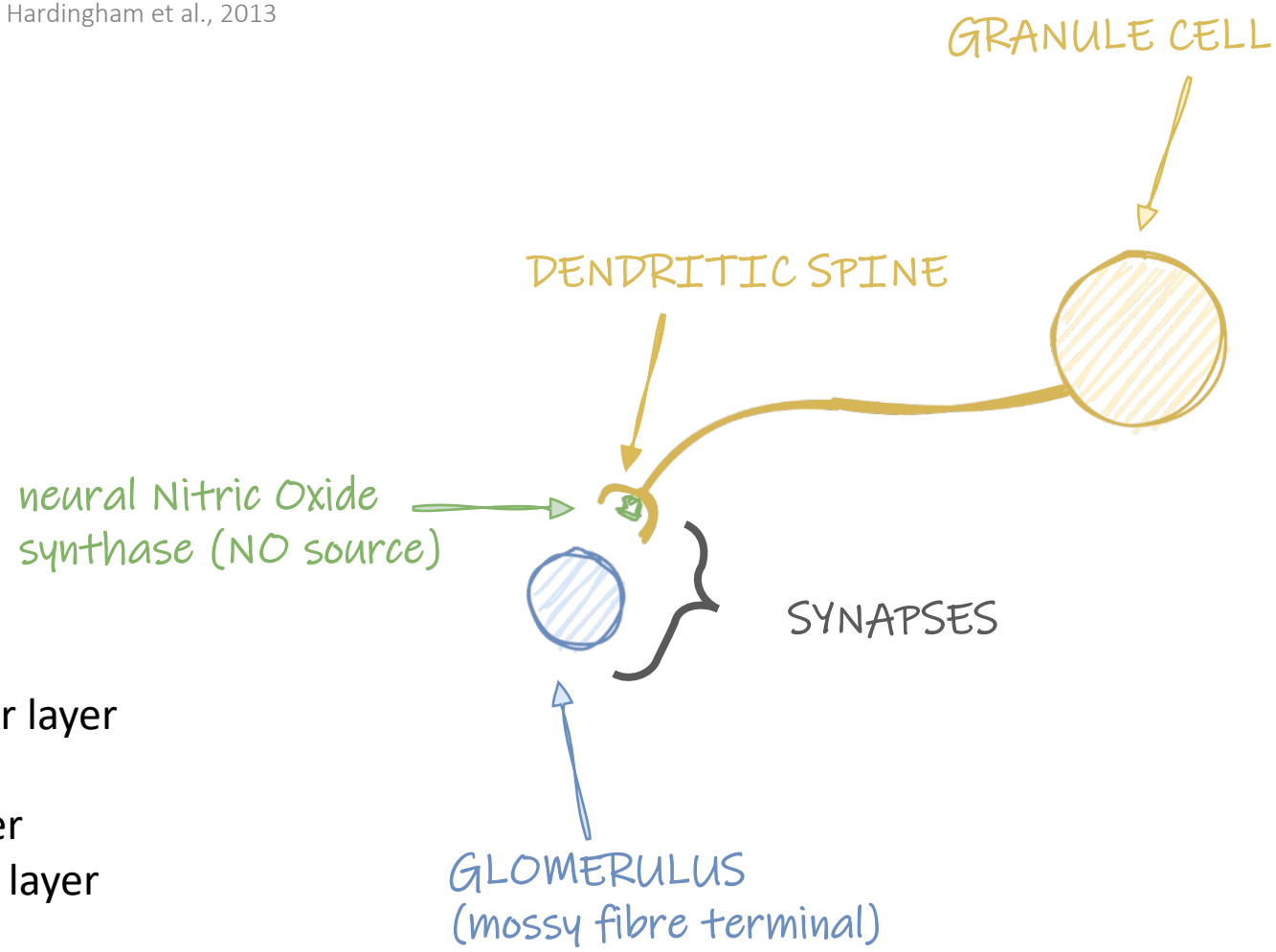
Cerebellar cortex





Garthwaite, et al. 1988
Wood, et al. 2001
Hardingham et al., 2013

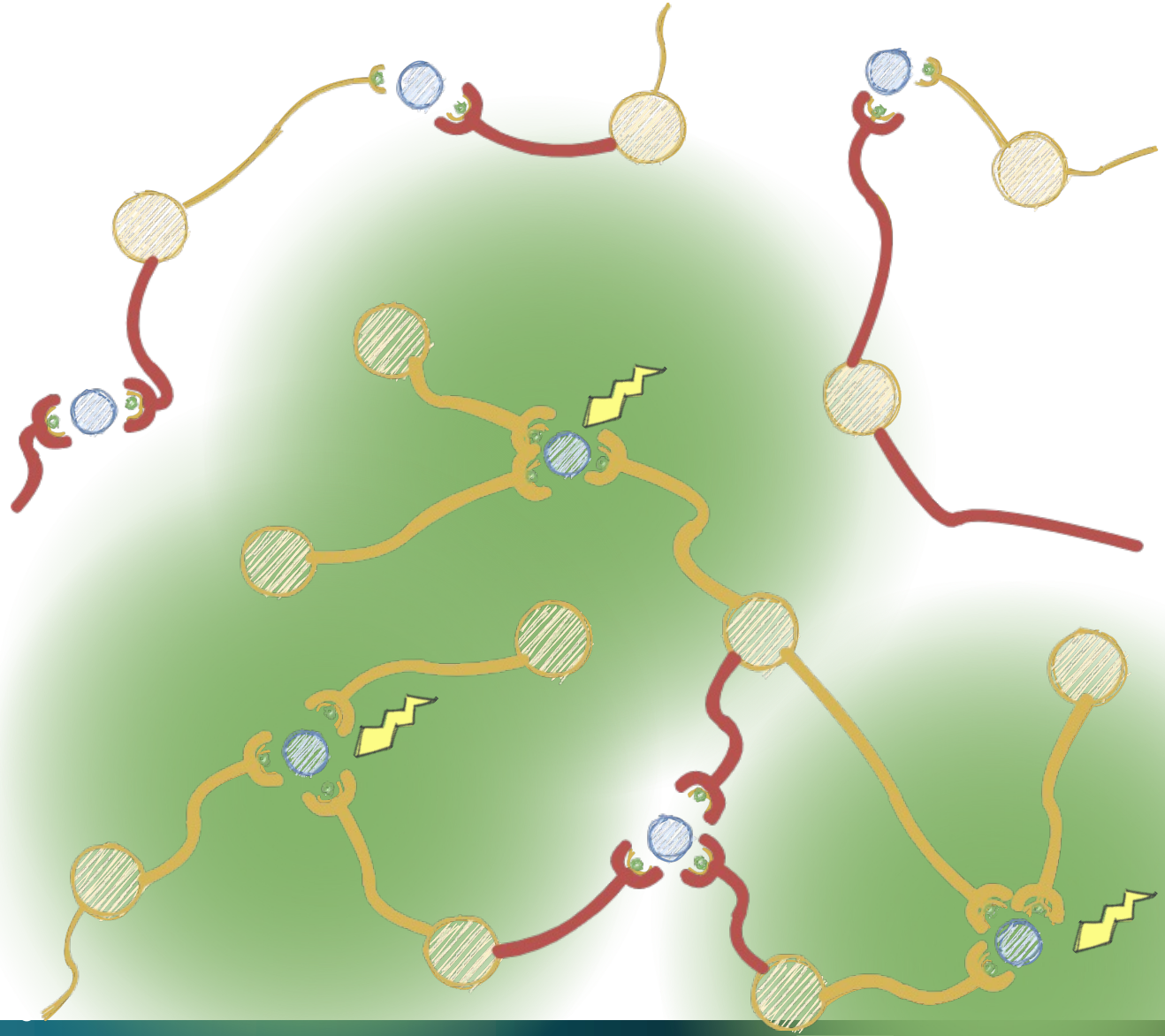
nNOS
Nuclei
EGL: external granular layer
ML: molecular layer
PCL: Purkinje cell layer
IGL: internal granular layer
WM: white matter



Nitric Oxide production and diffusion model in SNN

NO signal

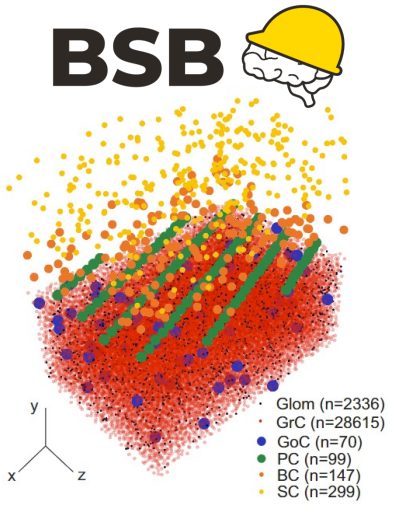
Volume transmitter

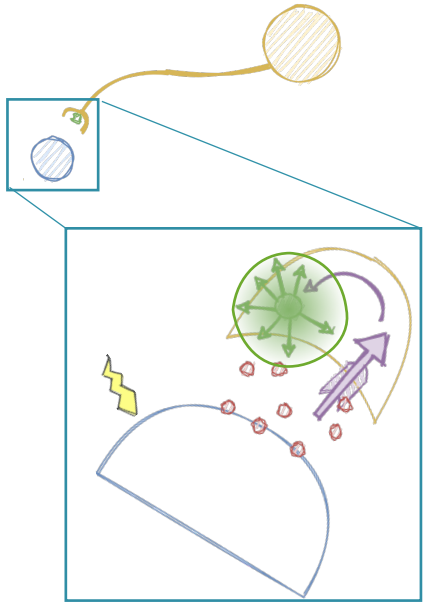


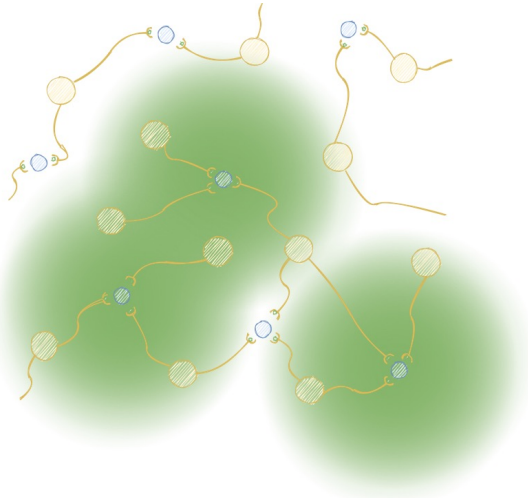
Hardingham et al., 2013
Garthwaite, et al. 2016

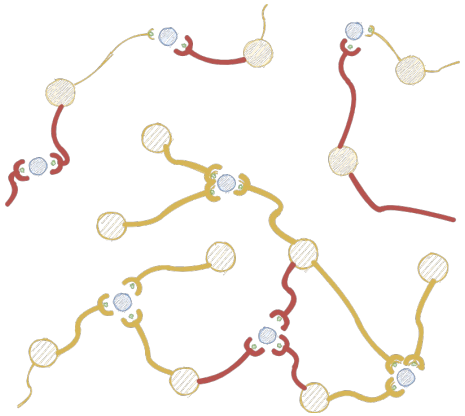
Nitric Oxide production and diffusion model in SNN

Geometry of the network → Single source model → Network diffusion → Plasticity model





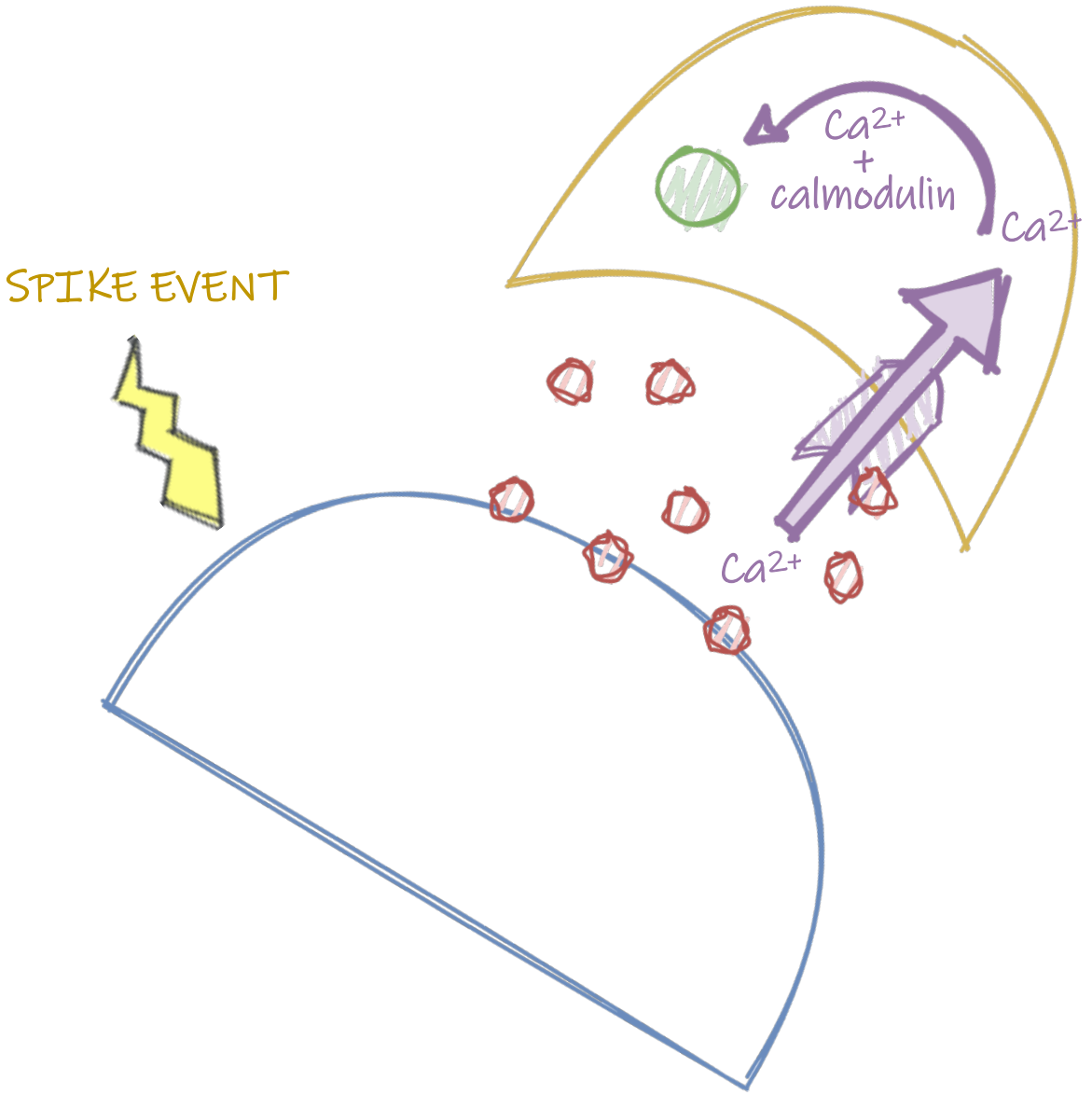




De Schepper, Robin, et al. *bioRxiv* (2021).

NO single source model

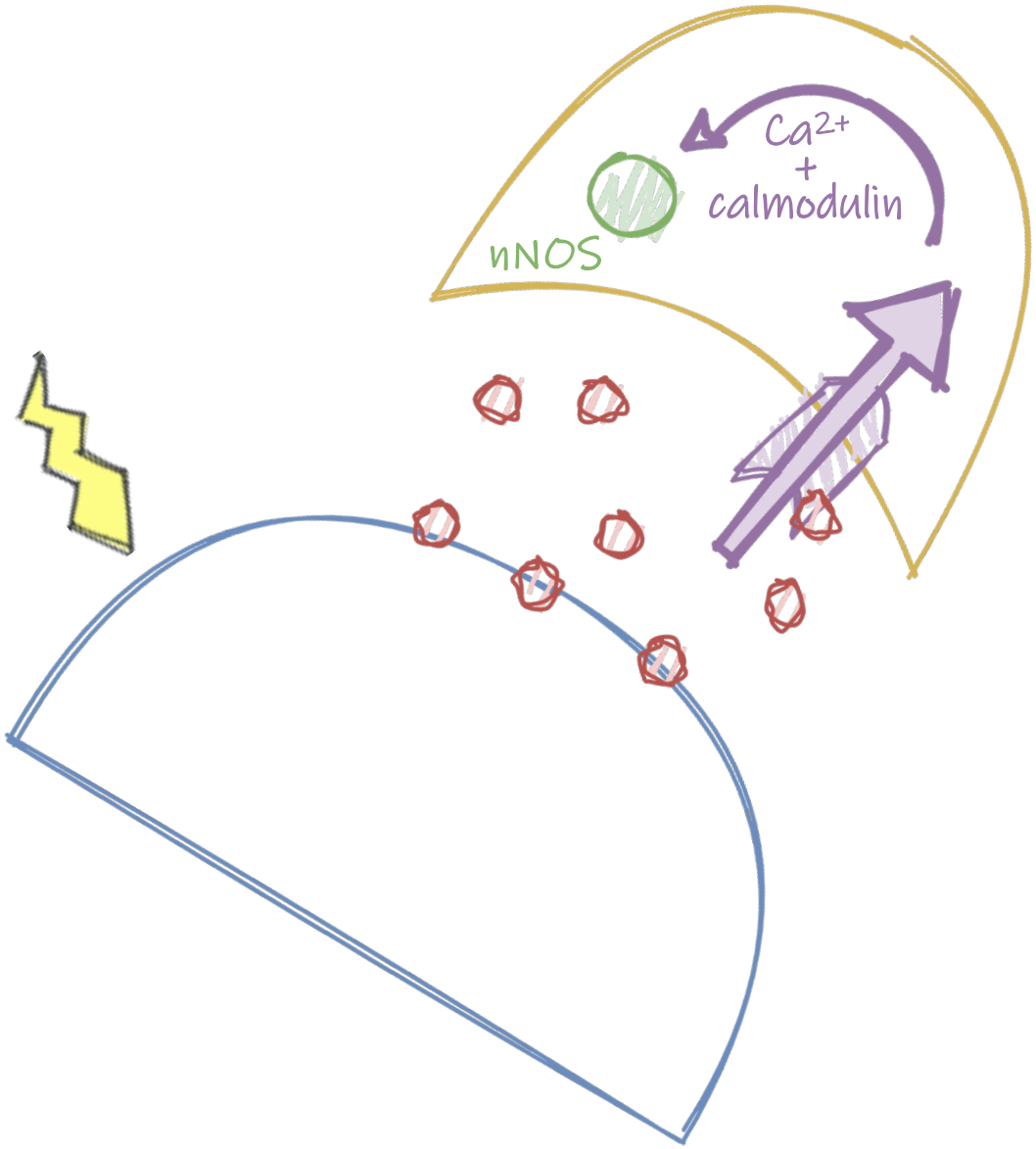
$$\frac{dCalm2C(t)}{dt} = -\frac{Calm2C(t)}{\tau_c} + \delta_{spike}$$



NO single source model

$$\frac{dCalm2C(t)}{dt} = -\frac{Calm2C(t)}{\tau_c} + \delta_{spike}$$

$$\frac{dnNOS(t)}{dt} = -\frac{nNOS(t)}{\tau_{n1}} + \frac{1}{\tau_{n2}}\left(\frac{Calm2C(t)}{Calm2C(t)+1}\right)$$

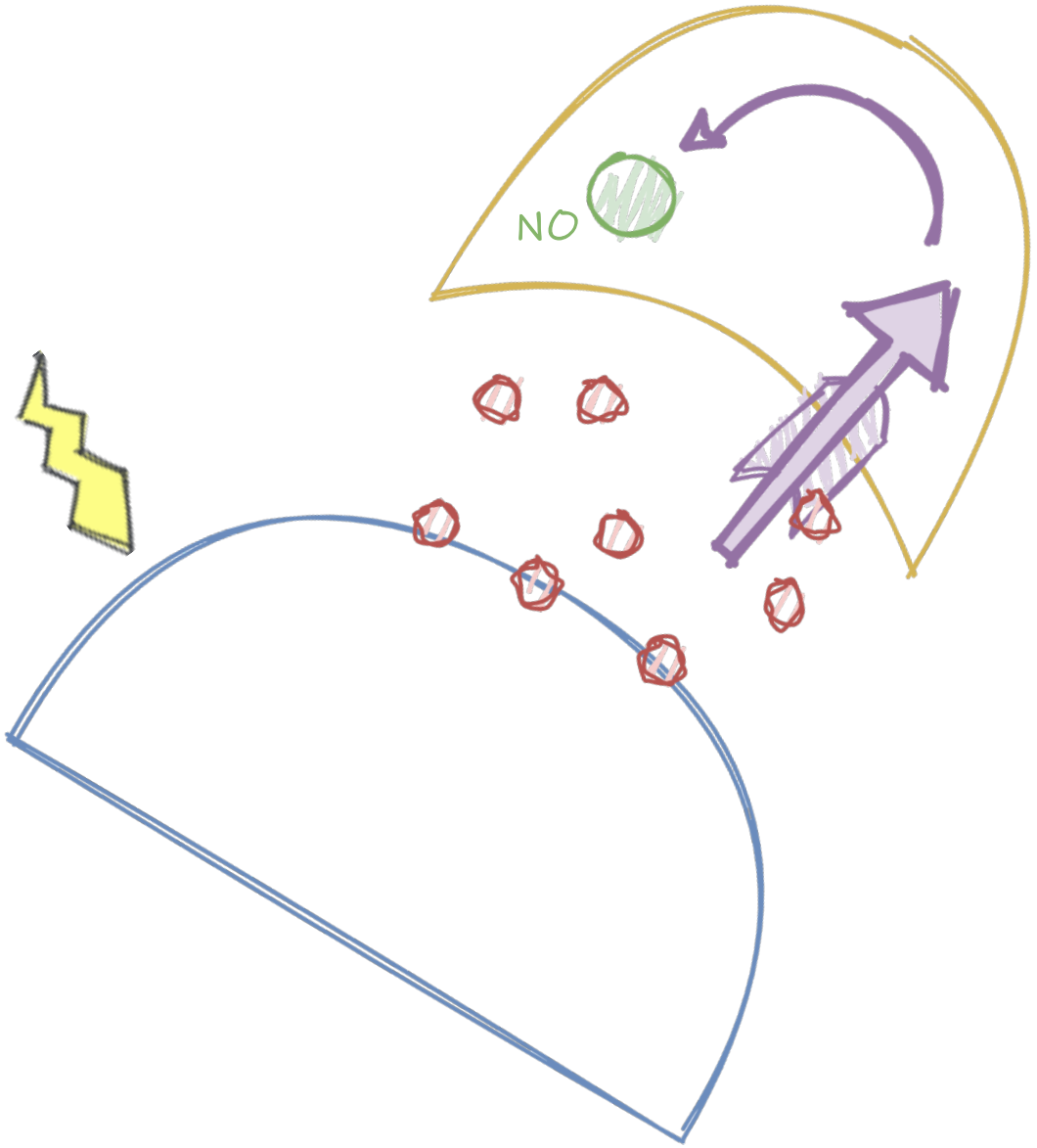


NO single source model

$$\frac{dCalm2C(t)}{dt} = -\frac{Calm2C(t)}{\tau_c} + \delta_{spike}$$

$$\frac{dnNOS(t)}{dt} = -\frac{nNOS(t)}{\tau_{n1}} + \frac{1}{\tau_{n2}}\left(\frac{Calm2C(t)}{Calm2C(t)+1}\right)$$

$$\frac{dNO(t)}{dt} = A * \frac{dnNOS(t)}{dt}$$



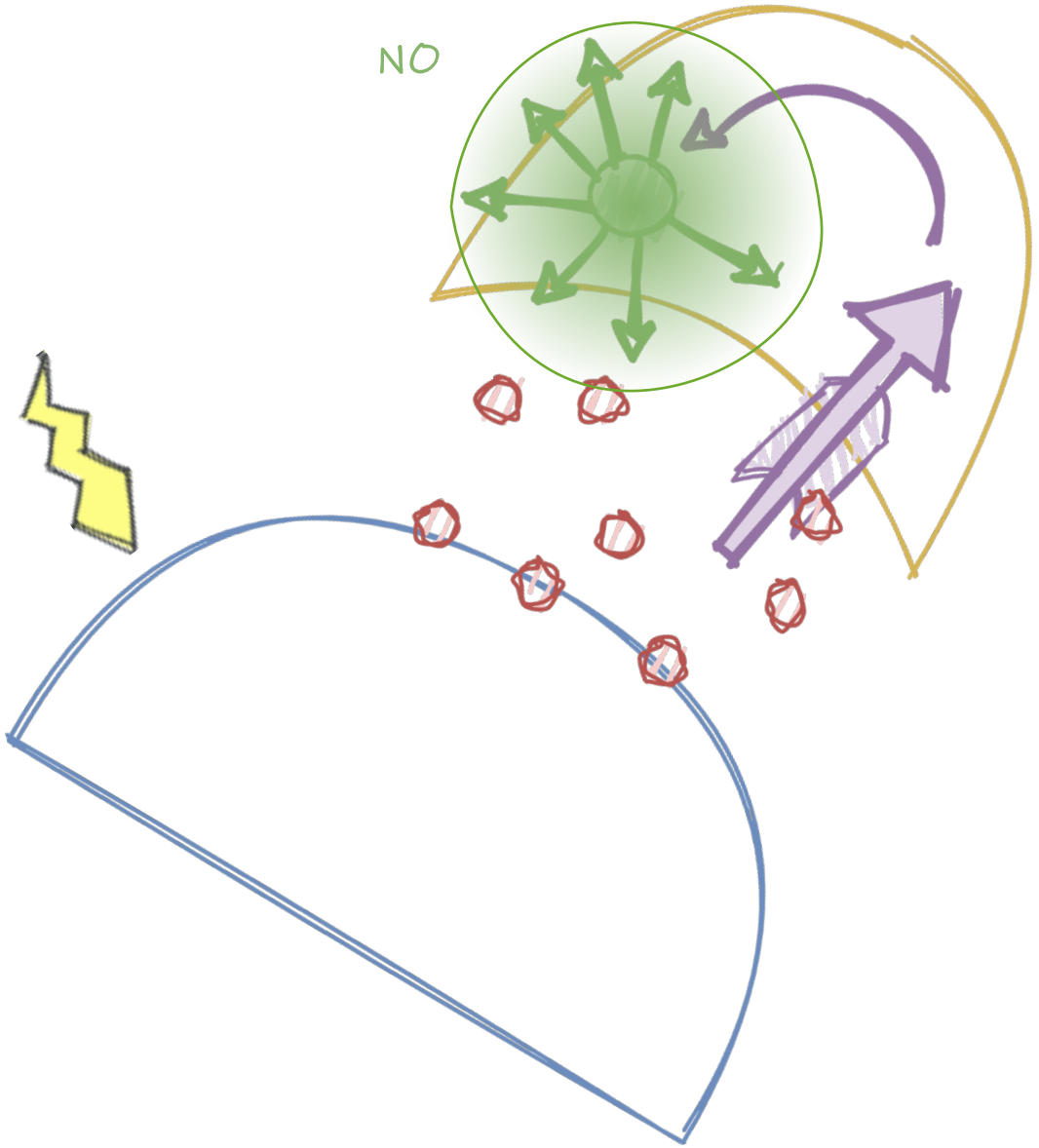
NO single source model

$$\frac{dCalm2C(t)}{dt} = -\frac{Calm2C(t)}{\tau_c} + \delta_{spike}$$

$$\frac{dnNOS(t)}{dt} = -\frac{nNOS(t)}{\tau_{n1}} + \frac{1}{\tau_{n2}}\left(\frac{Calm2C(t)}{Calm2C(t)+1}\right)$$

$$\frac{dNO(t)}{dt} = A * \frac{dnNOS(t)}{dt}$$

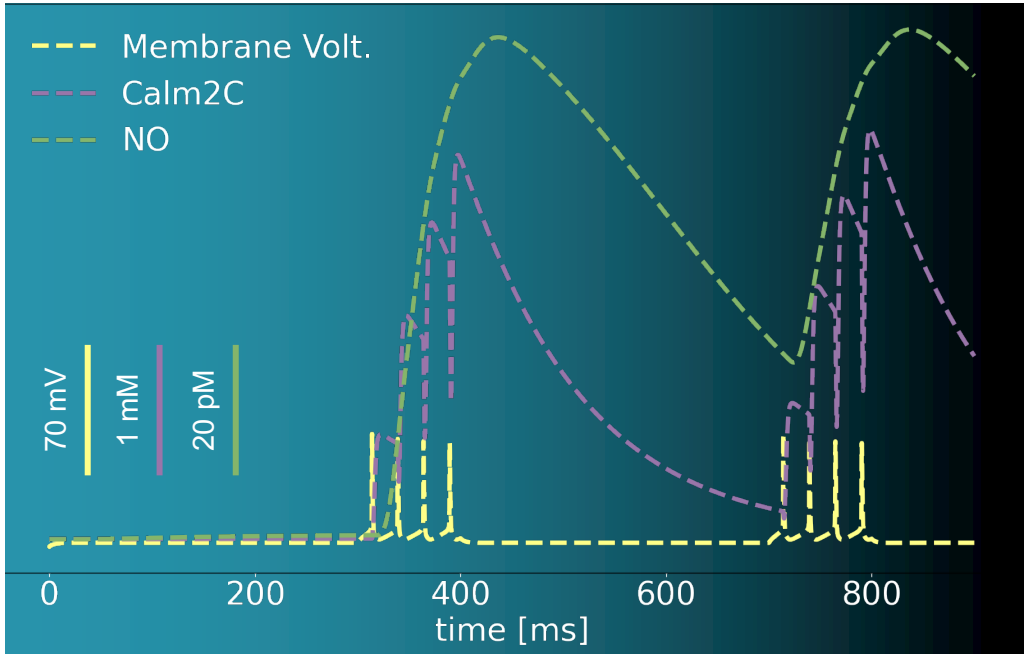
$$\frac{\partial C_{no}(r,t)}{\partial t} - D\nabla^2 C_{no}(r,t) + \lambda C_{no}(r,t) = NO(t)$$



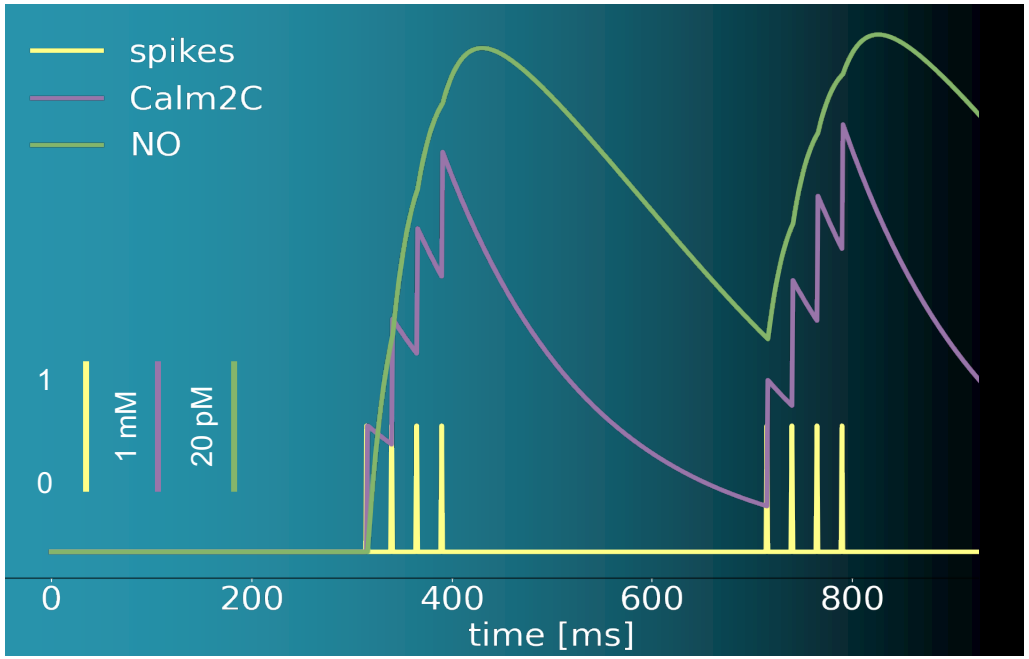
H. Carslaw and J. Jaeger. *Conduction of heat in solids.* Oxford University Press, 1959

NO single source model

Simulation in NEURON (Reaction&Diffusion)

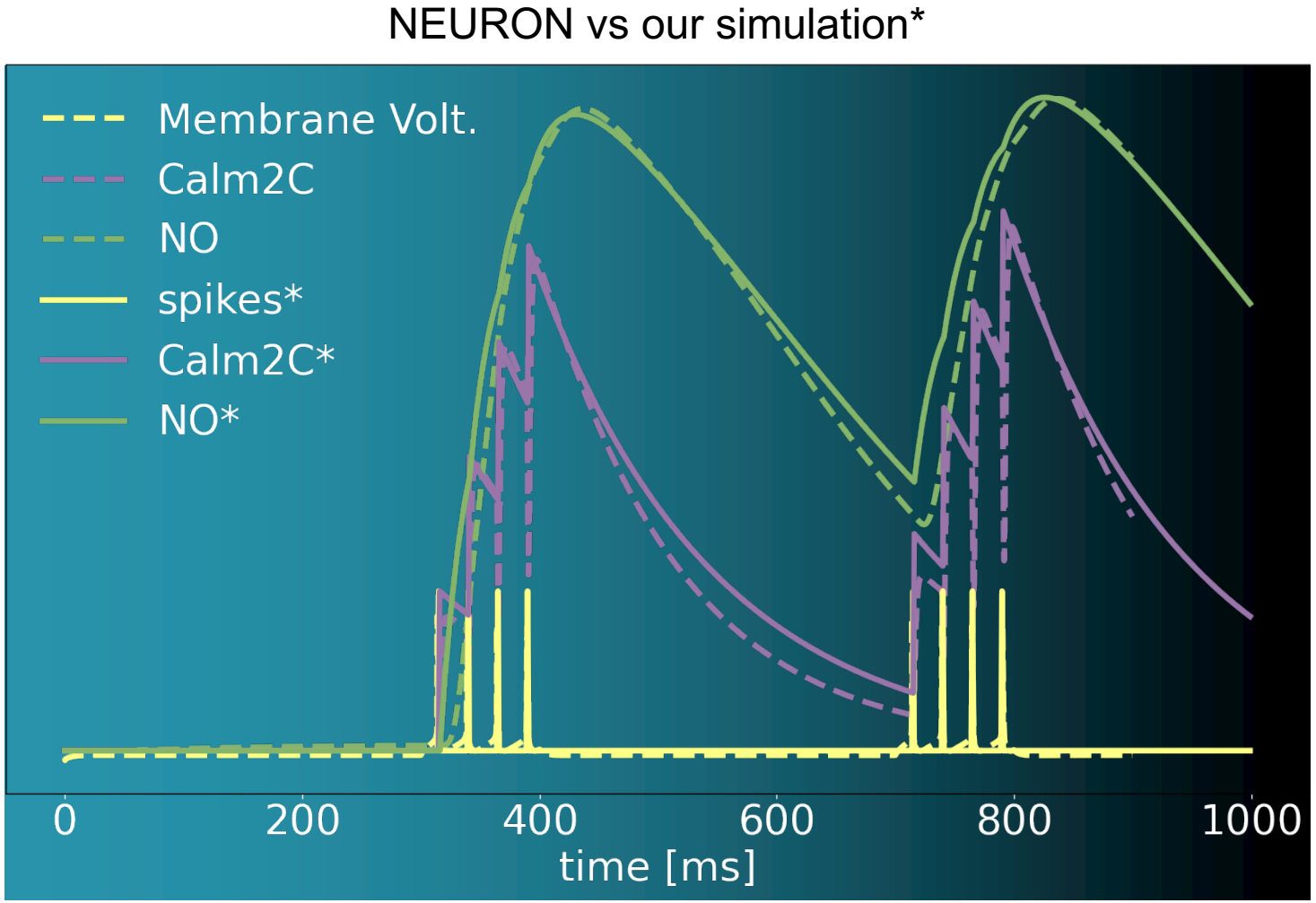


Simulation in python (our implementation)



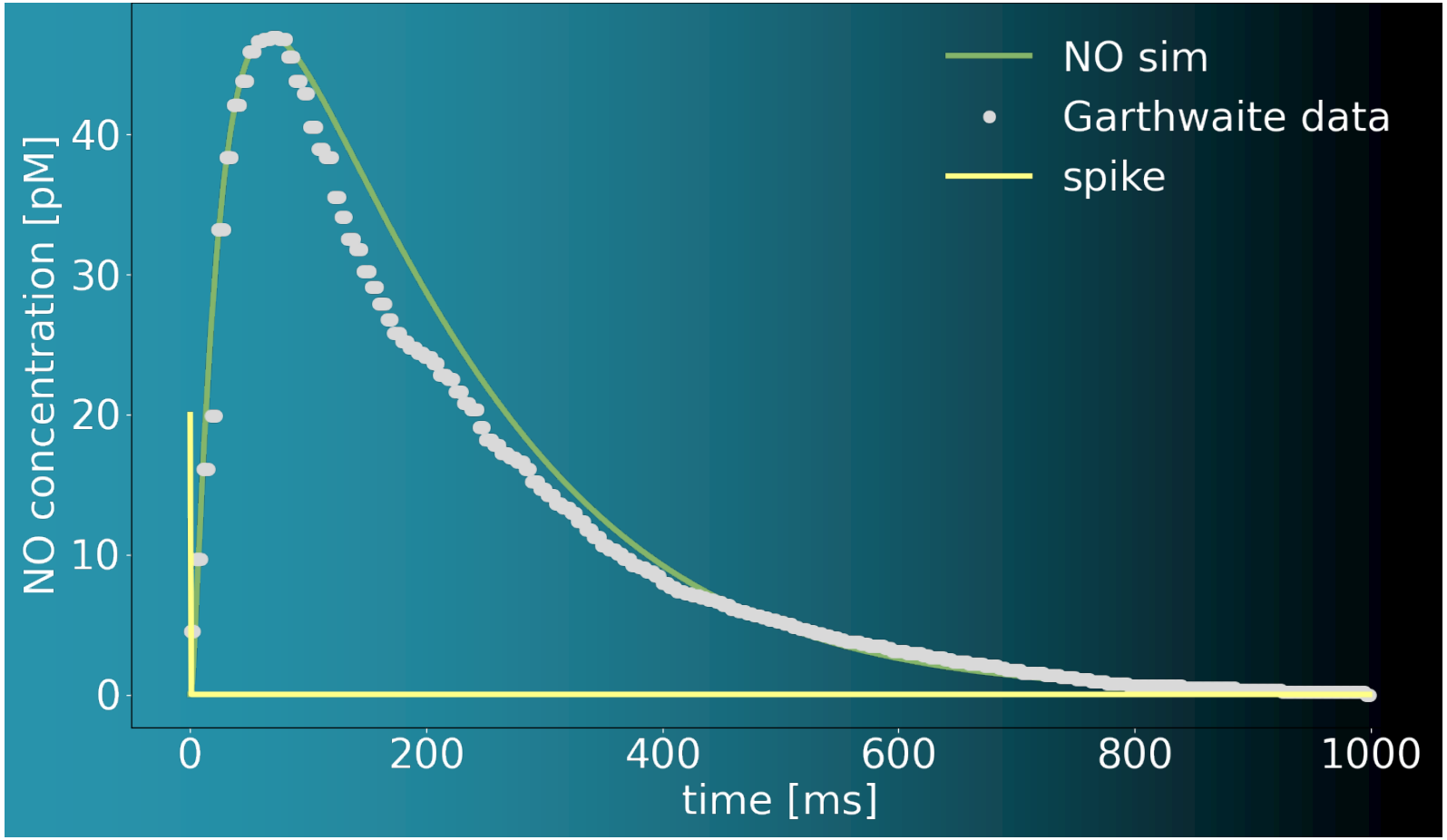
ACKNOWLEGMENT: Simulations run by Stefano Masoli, Ph.D. University of Pavia

NO single source model - production



NO single source model - diffusion

Literature data vs our simulation*



J. Garthwaite, 2016

NO network diffusion

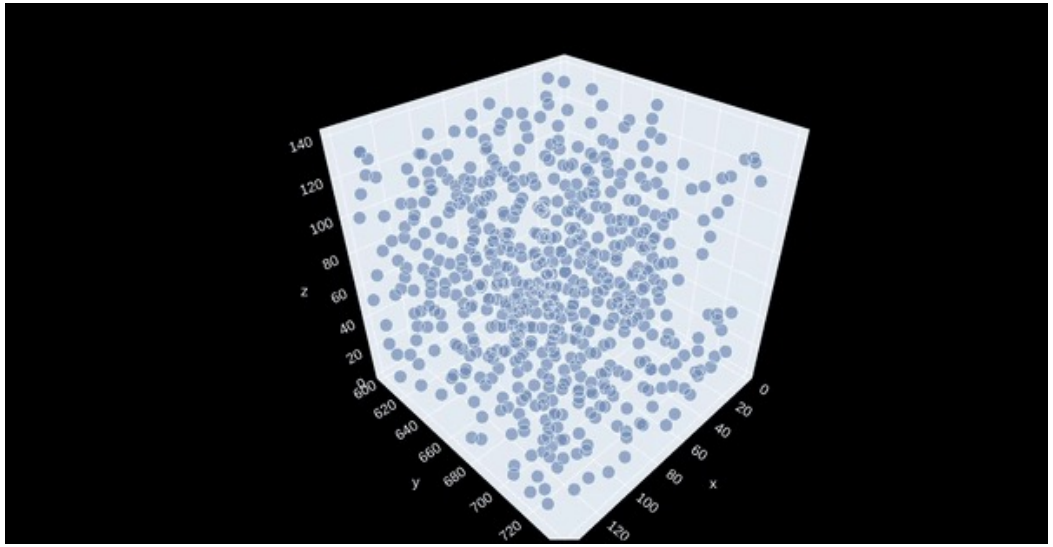
Source positioning

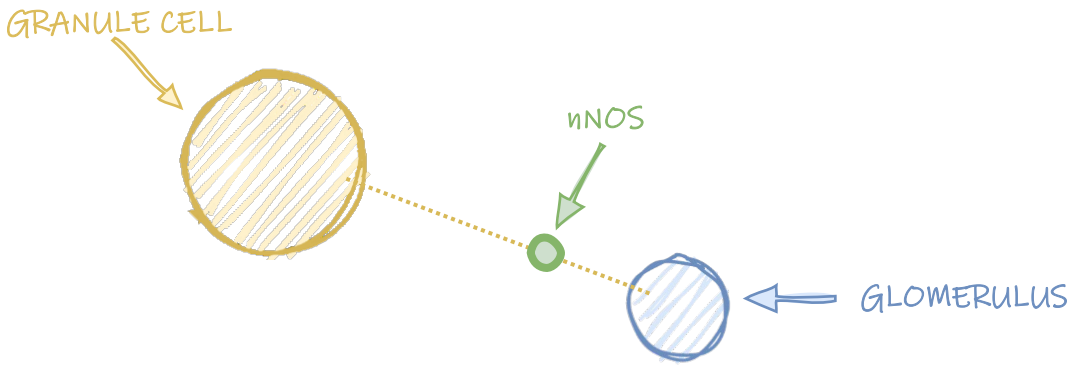
⇩

Single source computation

⇩

Overall [NO] on “Probes”





NO network diffusion

Source positioning

⇩

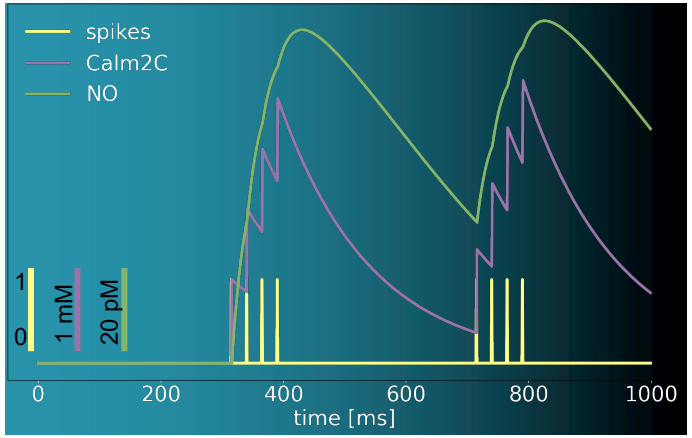
Single source computation

⇩

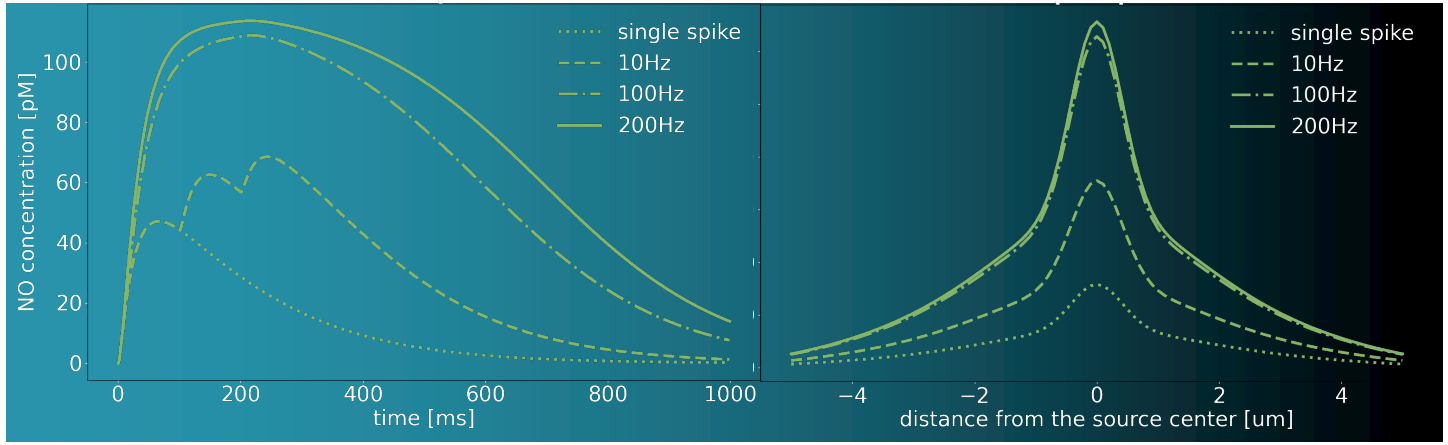
Overall [NO] on “Probes”

⟹

Production



Diffusion



Trapani et al., 2021

NO network diffusion

Source positioning

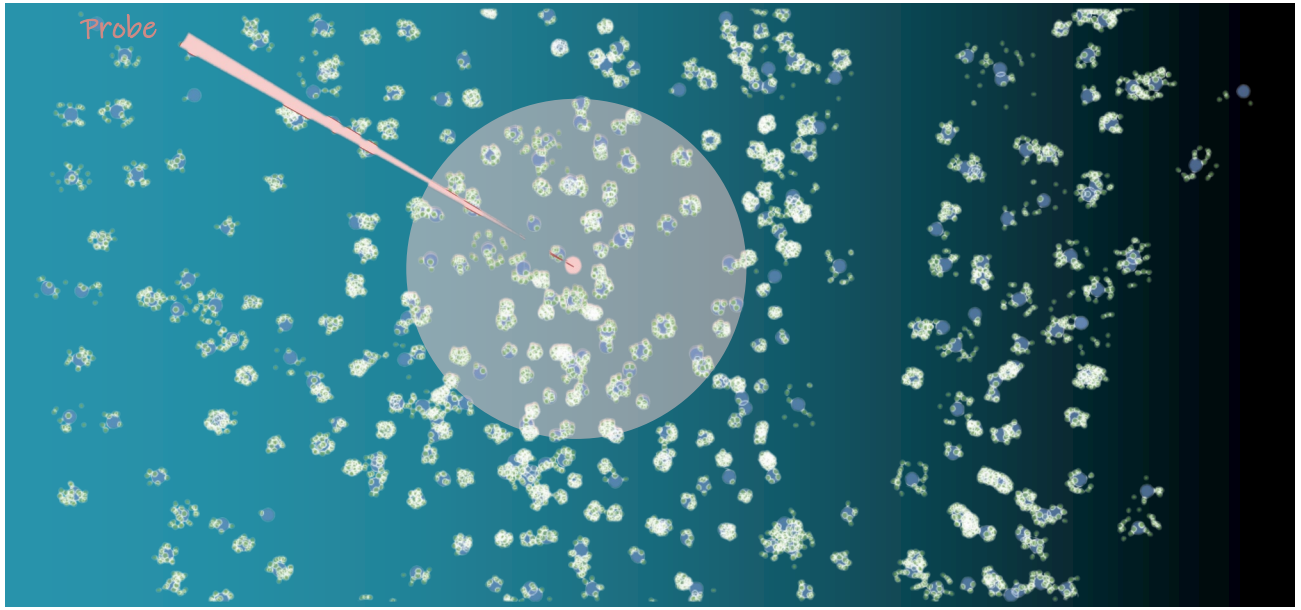
⇩

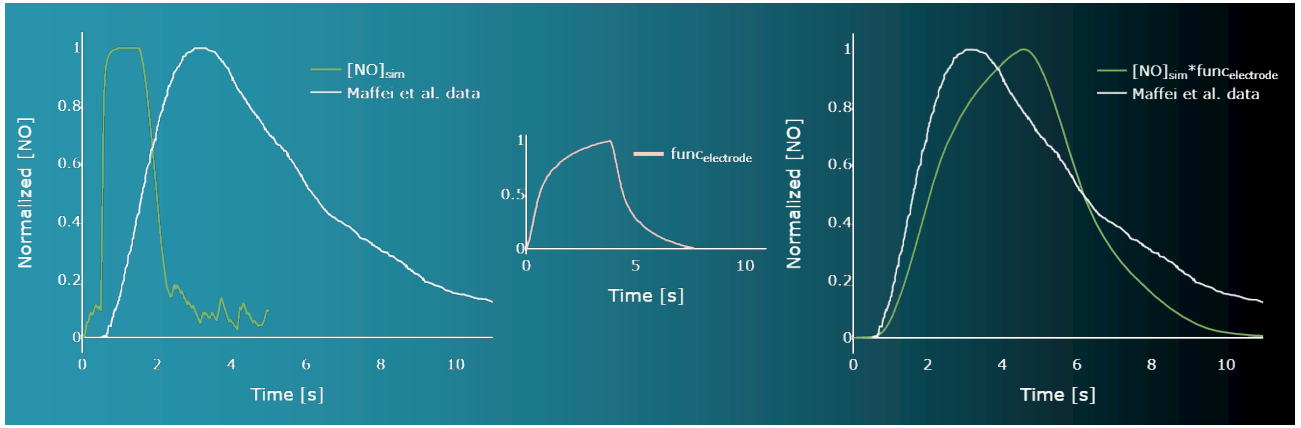
Single source computation

⇩

Overall [NO] on “Probes”

⟹





Shibuki et al., 1990

Co-funded by the European Union

NO role in plasticity mechanism

Nitric Oxide Is a Volume Transmitter Regulating Postsynaptic Excitability at a Glutamatergic Synapse

Joern R. Steinert,[1] Cornelia Kopp-Scheinpflug,[2] Claire Baker,[1] R.A. John Challiss,[3] Raj Mistry,[3] Martin D. Haustein,[1] Sarah J. Griffin,[1] Huaxia Tong,[1] Bruce P. Graham,[4] and Ian D. Forsythe[1,*]

Asymmetric spike-timing dependent plasticity of striatal nitric oxide-synthase interneurons

E. Fino, V. Paille, J.-M. Deniau, L. Venance

Nitric Oxide Is an Activity-Dependent Regulator of Target Neuron Intrinsic Excitability

Joern R. Steinert,[1] Susan W. Robinson,[1] Huaxia Tong,[1] Martin D. Haustein,[1] Cornelia Kopp-Scheinpflug,[1] and Ian D. Forsythe[1,*]

J Neurophysiol. 2003 Oct;90(4):2478-83. doi: 10.1152/jn.00399.2003.

NO enhances presynaptic currents during cerebellar mossy fiber–granule cell LTP

Arianna Maffei [1], Francesca Prestori, Katsuei Shibuki, Paola Rossi, Vanni Taglietti, Egidio D'Angelo

The role of nitric oxide in pre-synaptic plasticity and homeostasis

Neil Hardingham*[‡], *James Dachtler*[†‡] *and Kevin Fox*

School of Biosciences, Cardiff University, Cardiff, UK

Nitric Oxide Is Required for L-Type Ca^{2+} Channel-Dependent Long-Term Potentiation in the Hippocampus

Beatrice M. Pigott and John Garthwaite*

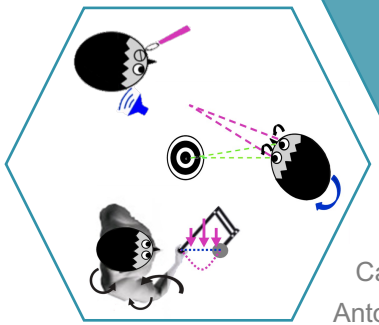
The Wolfson Institute for Biomedical Research, University College London, London, UK

Co-funded by the European Union

Future development

CerebNEST

Design experimental protocols

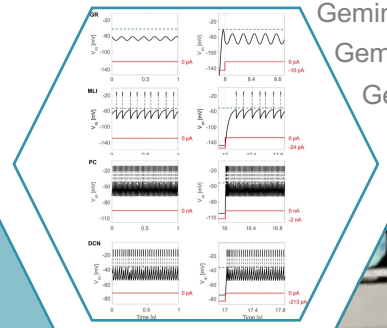


Casellato et al., 2014
Antonietti et al., 2015

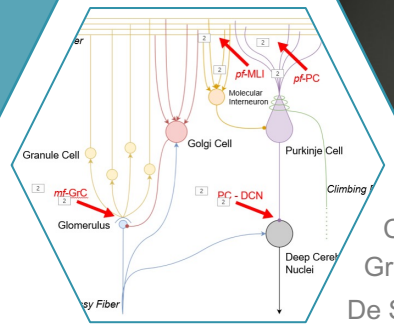
Advanced models of single point neuron EGLIF

Develop microcircuits models

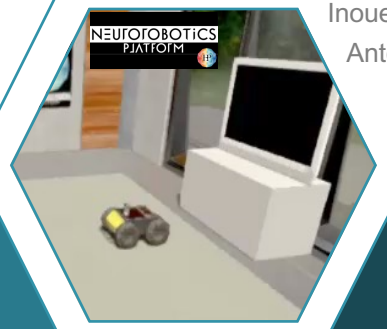
Robotic embodiment



Geminiani et al., 2018
Geminiani et al., 2019 a
Geminiani et al., 2019 b



Casali et al., 2019
Grillo et al., 2021
De Schepper et al., 2021

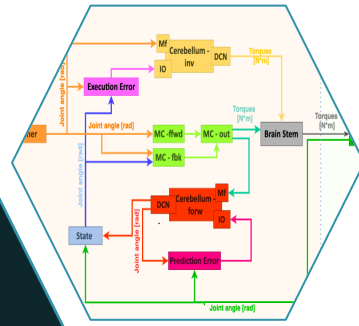


Inoue et al., 2021
Antonietti et al., 2022

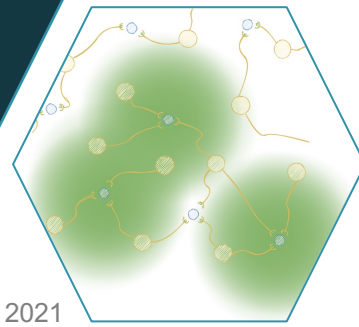
Antonietti et al., 2018
Antonietti et al., 2019

Work in progress

Bio-inspired robotic controller and effector



Diffusive plasticity model



Trapani et al., 2021

Human Brain Project

EBRAINS

POLITECNICO MILANO 1863

UNIVERSITÀ DI PAVIA

Thank you


Alessandra Pedrocchi, PhD


Alberto Antonietti, PhD


Alice Geminiani, PhD


Alessandra Trapani


Benedetta Gambosi

Egidio D'Angelo, PhD

Claudia Casellato, PhD

www.humanbrainproject.eu

www.ebrains.eu

Co-funded by
the European Union