ICSC
Centro Nazionale di Ricerca in HPC, Big Data and Quantum Computing

Plenary meeting
Casalecchio di Reno
25 June 2024

UNIVERSITÀ DI PAVIA

Brain Digital Twins in Ataxia

Atax-BDT

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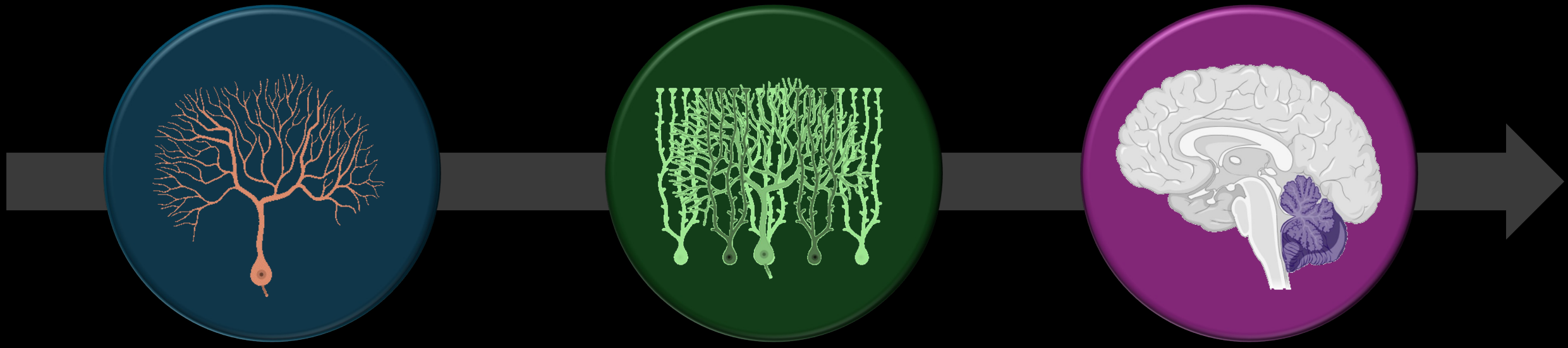
AIM

Creating a **Digital Brain Twin for Ataxia**: simulating brain activity in specific pathological conditions using a multiscale approach.



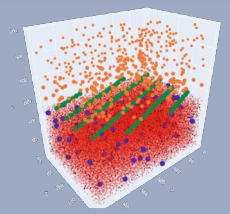
Microscale

Mesoscale

Macroscale

Brain digital twins in ataxia - *Multiscale workflow*

Microscale

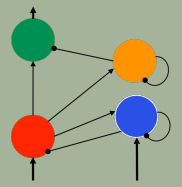


Microcircuit

Cerebellar spiking neural network (SNN)
Neuron & Nest

Structural and functional changes of the SNN adapting to ataxia

Mesoscale

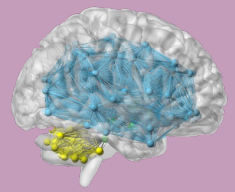


Nodes

Cerebellar mean field (MF) model

Obtain a MF specific for ataxia (change parameters or re-fitting the transfer function)

Macroscale



Brain

The Virtual Brain

Considering the atrophy of the cerebellum (nodes rescaling)

Add MEG data

JOUBERT SYNDROME (JS)

JS is a rare **autosome** recessive syndrome (1:80 000-1:100 000)

over 40 distinct mutations

All the identified genes encode for proteins of the **primary cilium**: ciliopathy

Mutated genes have been linked to altered **Sonic Hedgehog** (shh) signalling.

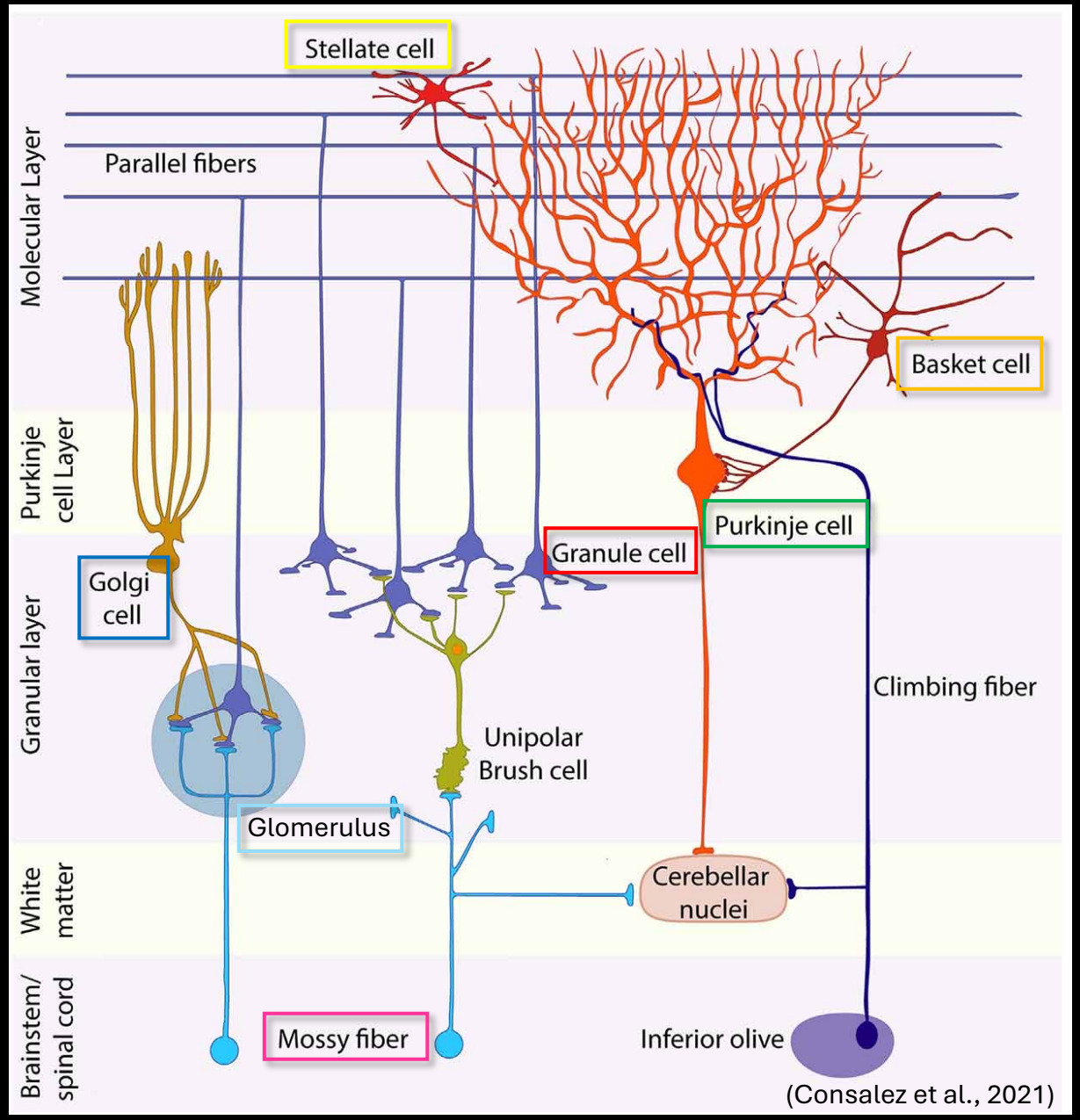
(Brancati et al, 2010) (Andreu-Cervera et al., 2021) (Sattar and Gleeson, 2011)

ALTERATIONS

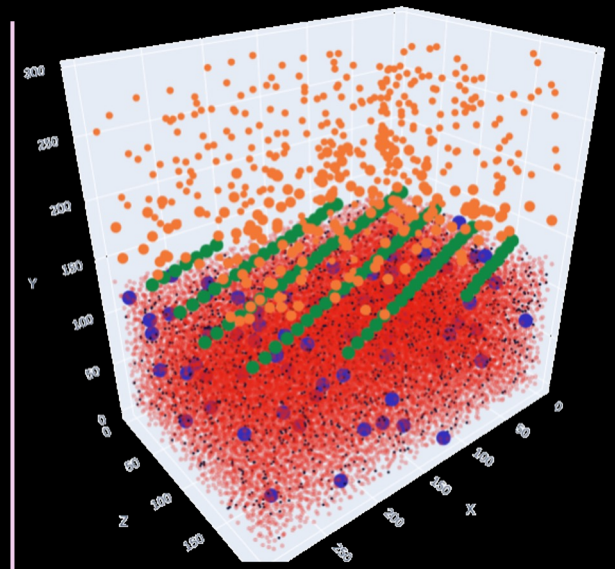
WHO	WHAT
Vermis	Aplasia/hypolasia
Granule cell (GrC)	Density reduced (50%)
Purkinje Cell (PC)	Density reduced (50%), heterotopic
Dentate nuclei	Fragmented
Cerebellar cortex	Hypoplastic

(Aguilar et al., 2012) (Dan Doherty et al., 2009) (Juric-Sekhar et al., 2012) (Bashford AL et al, 2019)

CEREBELLUM CIRCUIT & SIMULATION



(Consalez et al., 2021)



BSB

(https://www.ebrains.eu/tools/bsb)

MOSSY FIBER

GLOMERULUS

GRANULE CELLS

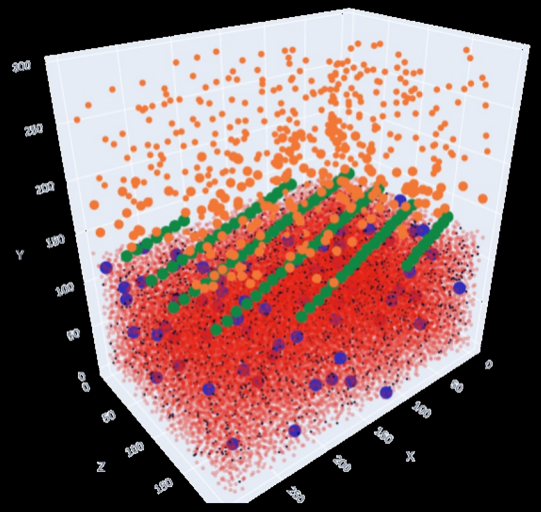
GOLGI CELLS

PURKINJE CELLS

BASKET CELLS

STELLATE CELLS

THE FIRST SIMULATIONS



SIMULATION DETAILS

Network size:
[300 μm, 295 μm, 200 μm]

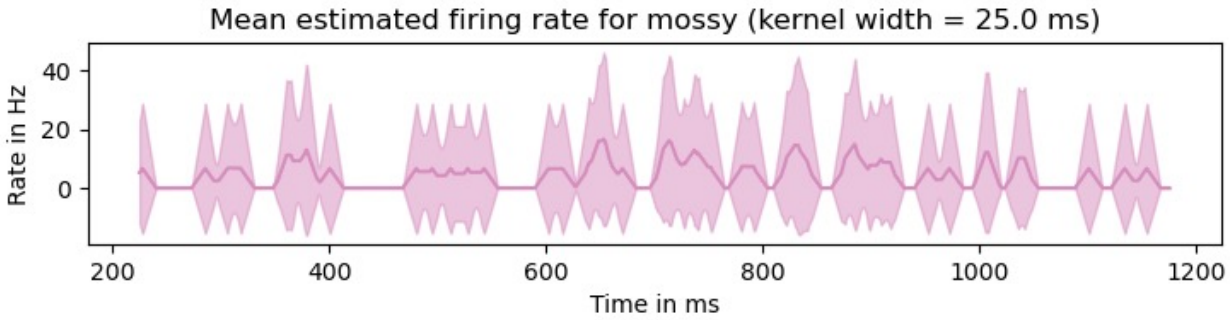
Basal activity:
Background noise at 4 Hz

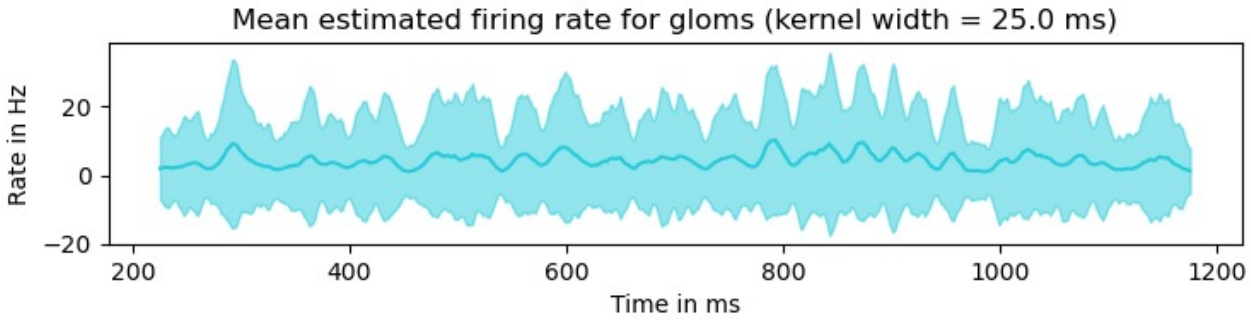
01

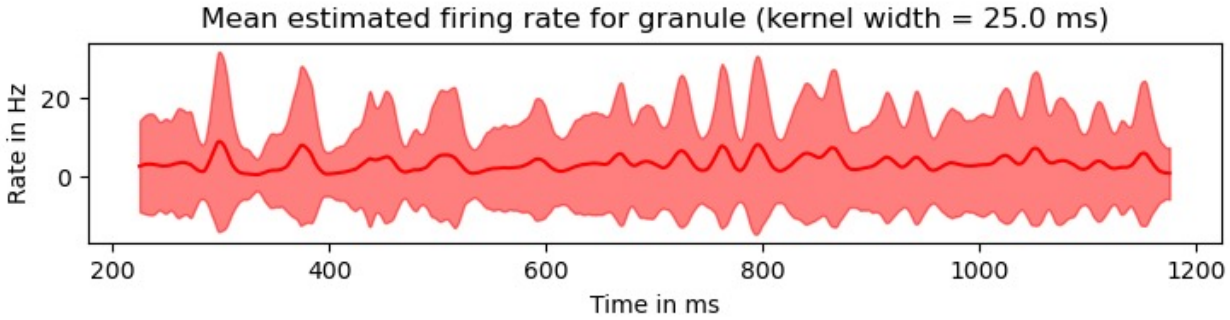
Healthy control case

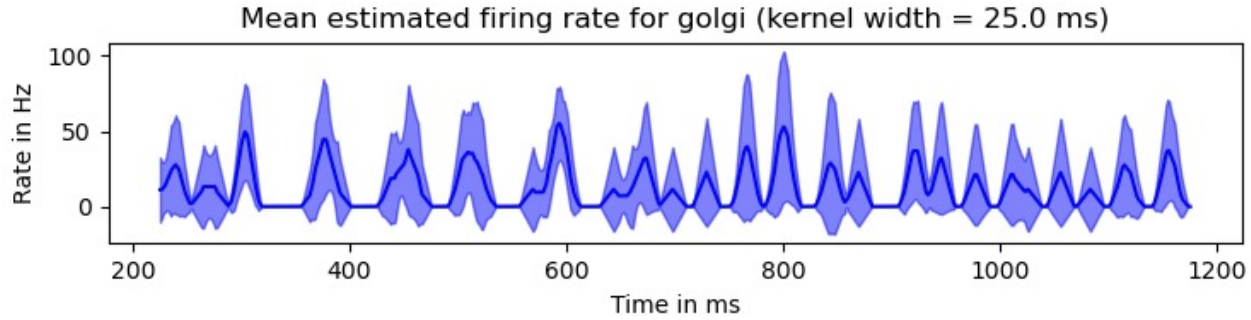
02

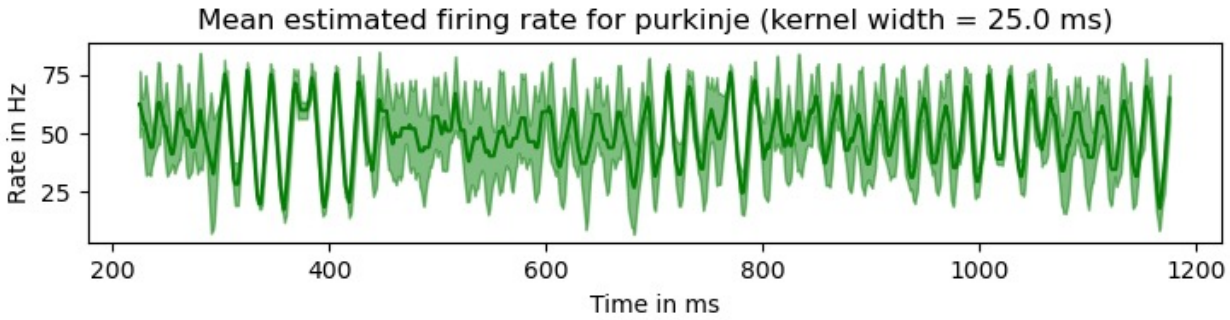
50% reduction in granular cell (GrC) density

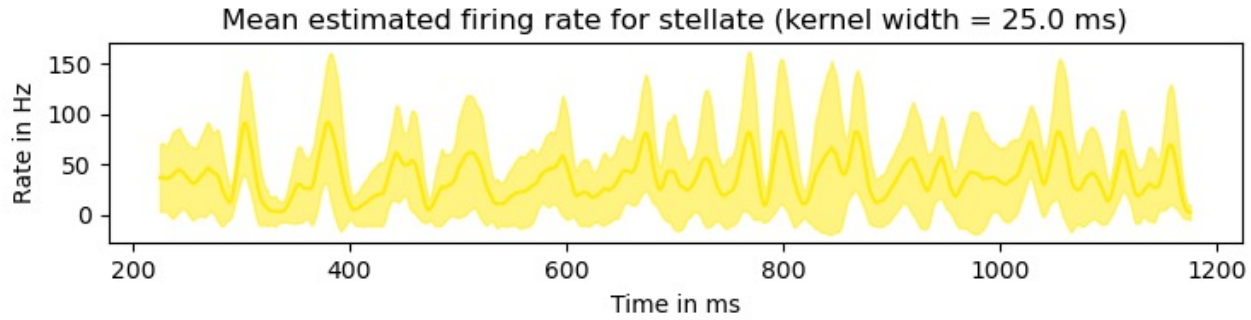


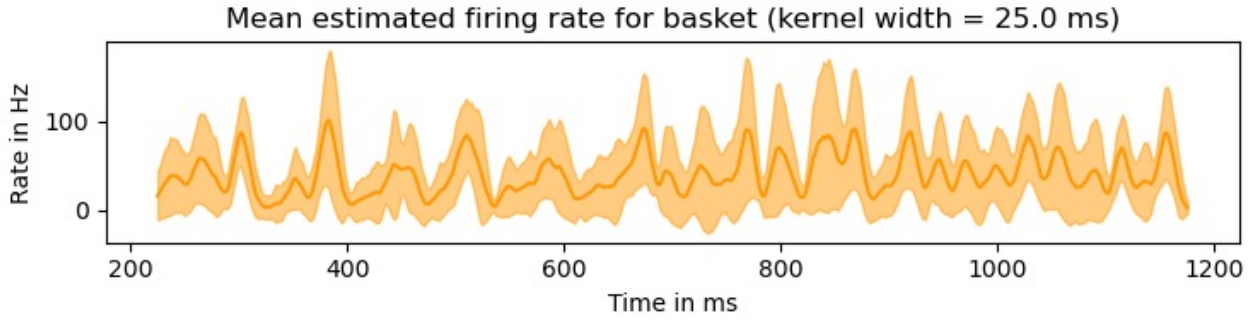






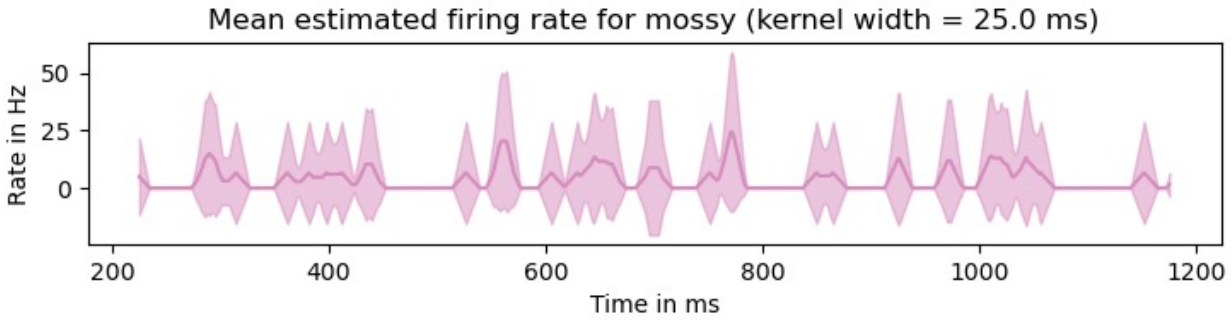


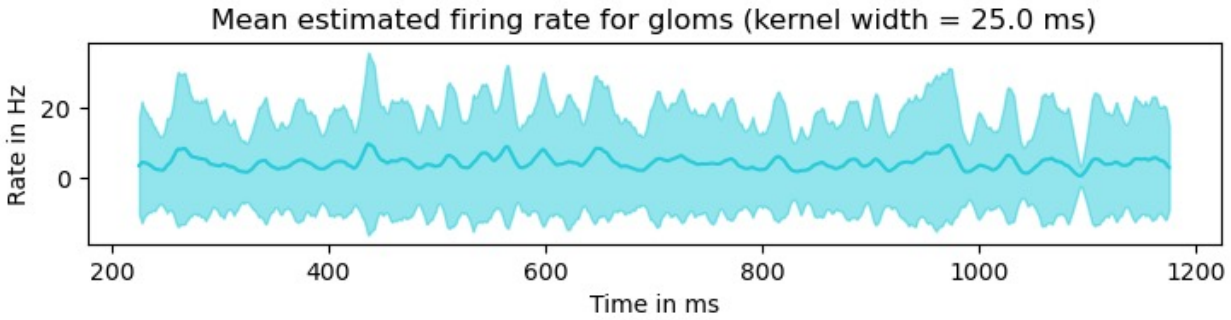


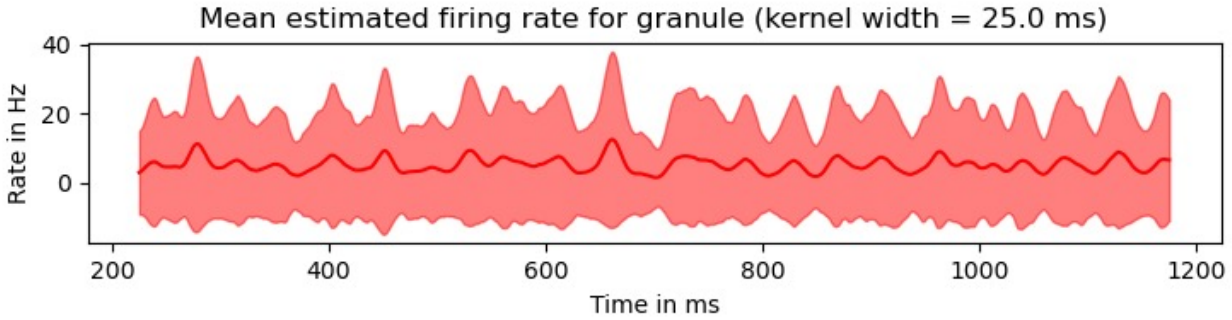


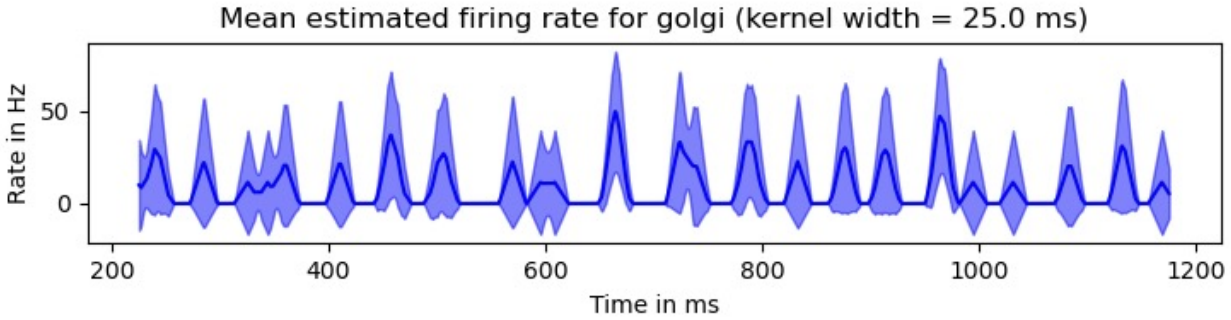
mossy 117
granule 30077
purkinje 27
basket 150

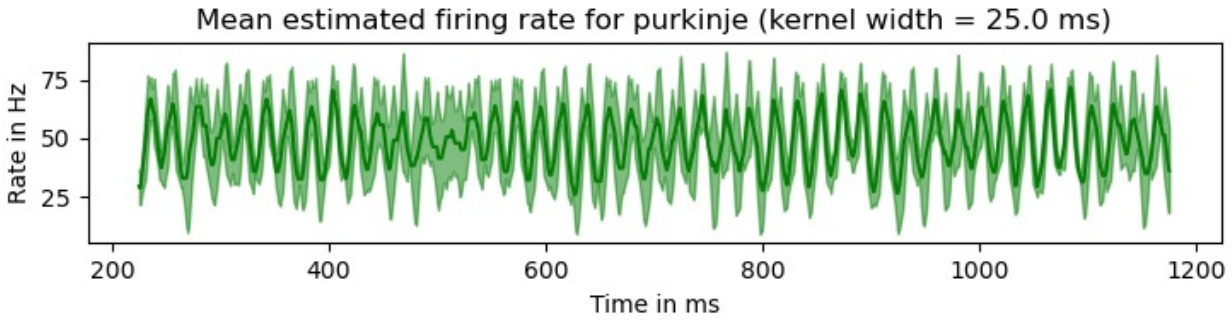
gloms 2322
golgi 70
stellate 297

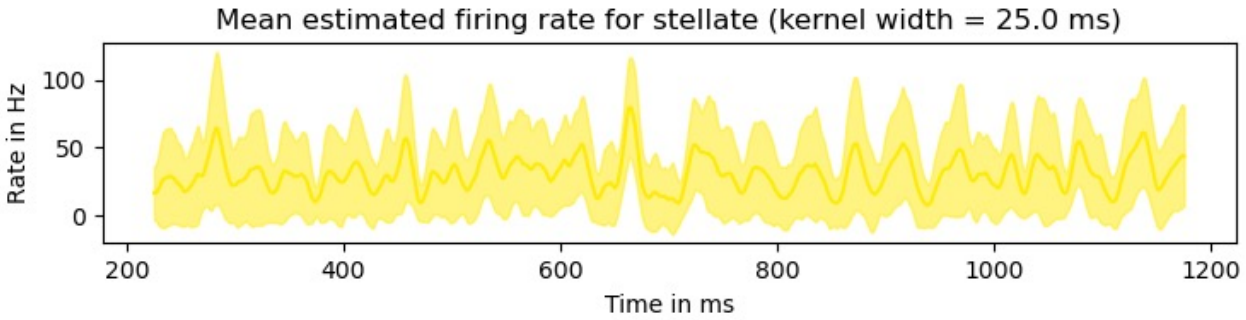


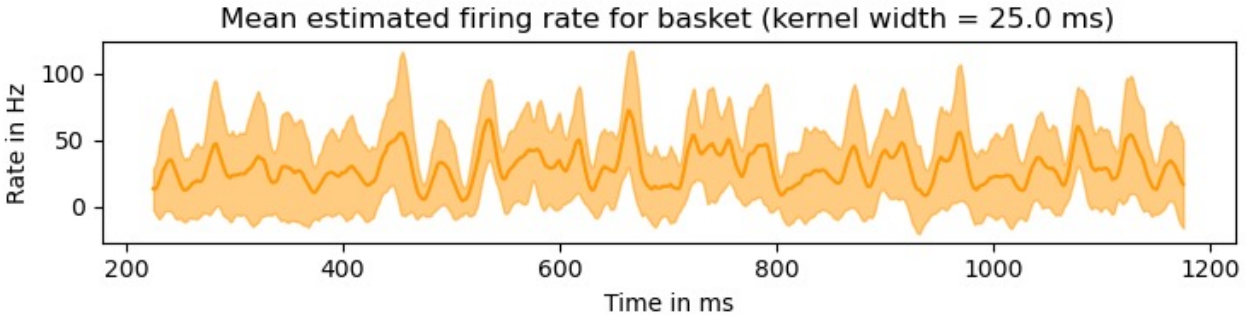












mossy 117
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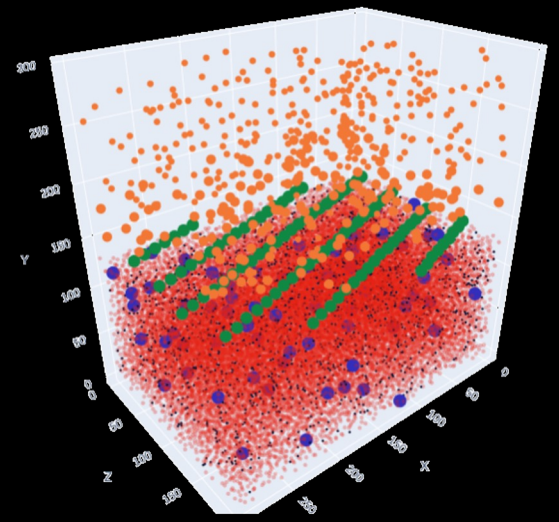
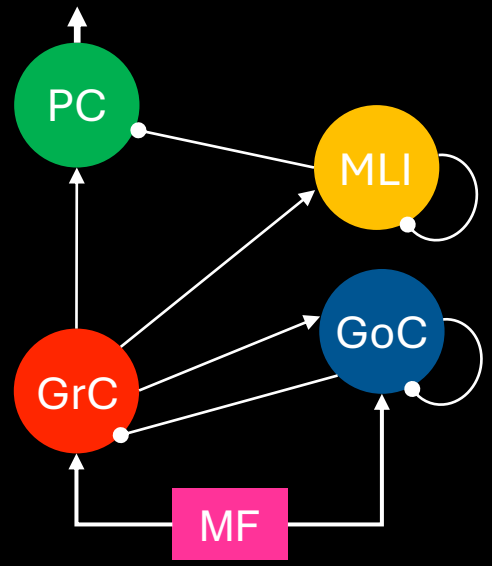
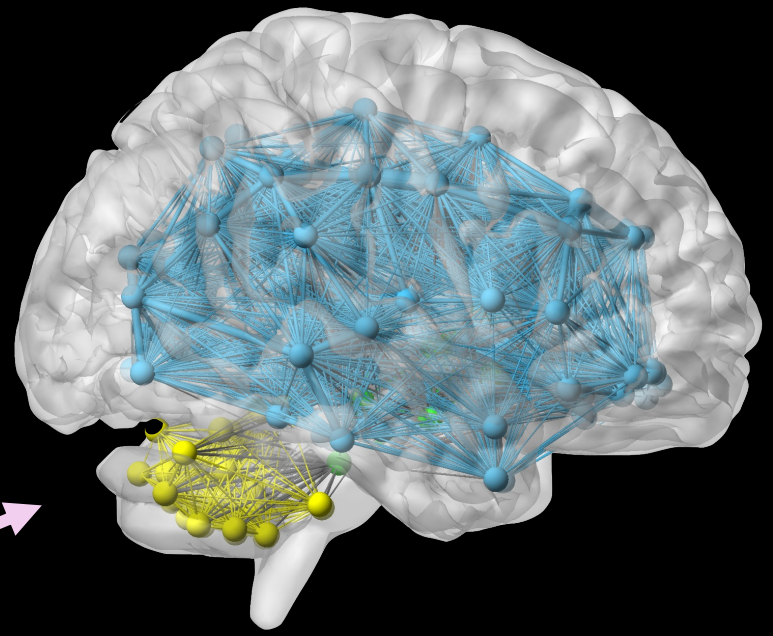
FUTURE STEPS



Pathological cerebellar spiking neural network (SNN)



Pathological mean field



The Virtual Brain (TVB) personalization

RAC request approved June 7

ACKNOWLEDGMENT

Gaviraghi M. et al., 2024 ” Finding the limits of deep learning clinical sensitivity with fractional anisotropy (FA) microstructure maps”, *Frontiers Neuroinformatics,* https://doi.org/10.3389/fninf.2024.1415085

Geminiani A. et al., 2024 “Mesoscale simulations predict the role of synergistic cerebellar plasticity during classical eyeblink conditioning”, *PLoS Computational Biology,* https://doi.org/10.1371/journal.pcbi.1011277