Release of scaffold model including basal ganglia, cerebellum, and cerebral cortex (D3.4 – SGA3)

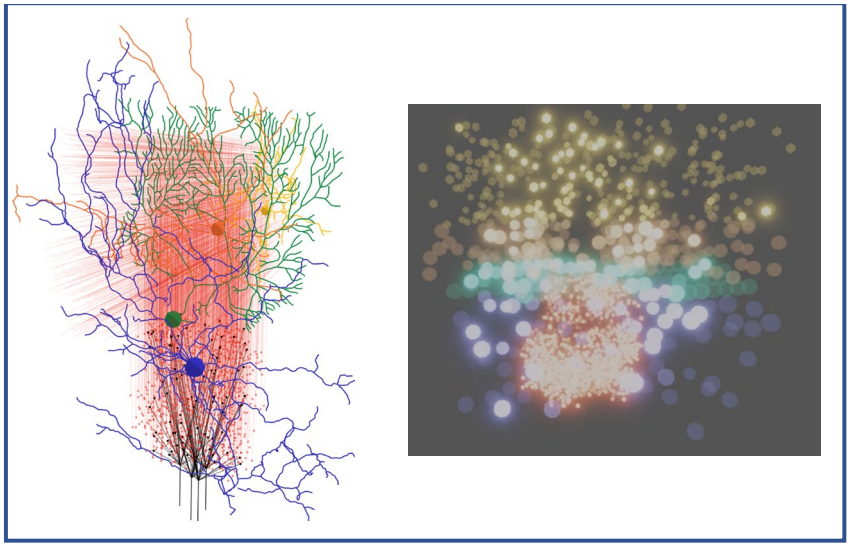

Figure 1: The brain regions are modularly ("scaffold") reconstructed and simulated in an advanced neuroinformatic framework, the Brain Scaffold Builder (BSB).

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Description in GA:	Detailed basal ganglia and cerebellar network models incorporating multiple plasticity mechanisms will be simplified to obtain point neuron network models retaining the main biological learning characteristics, and integrated into a functional model together with a cortical component
Abstract:	This deliverable describes anatomically and physiologically based modelling of mouse cerebellar-basal ganglia-cortical networks, with a focus on the former two structures, along with a tool for the flexible reconstruction and simulation of multiple brain regions, the Brain Scaffold Builder. Existing multicompartment models were translated to point neuron models to enable full-scale simulations in

	future. The circuits perform sensorimotor learning using spike-timing-dependent plasticity.
Keywords:	cerebellum, basal ganglia, scaffold modelling, point neuron networks, functional cortical module, closed-loop sensorimotor learning, long-term plasticity
Target Users/Readers:	Computational neuroscience community, computer scientists, Consortium members, experts in modelling, funders, general public, HPC community, neuroinformaticians, neuroscientific community, neuroscientists, platform users, policymakers, researchers, scientific community, students

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1. Introduction

The goal of this work is to develop a model system of multiple brain regions, in a closed-loop configuration to generate sensorimotor behaviours. The individual region models need to be scalable, in size, and the considered structural and dynamical features need to have different levels of detail. Finally, their specific internal dynamics and plasticity mechanisms will drive adaptation and learning of an actuated physical plant, performing sequences of motor tasks (in simulation). Such a modular system will be fundamental to fill a gap across multiple scales, from microcircuit dynamics to changes in motor actions. This addresses one of the key avenues of investigation in neuroscience: relating detailed, biologically plausible neural models to emerging macro-level functions and behaviours.

As long-standing vision, this can be used to generate a digital twin of the specific subject's motor system, to investigate brain dynamics of healthy subjects or patients, and the bidirectional causal relationships between changes in movements and in brain network activities. This is in synergy with the Work Package (WP) 1 approach, by including the peripheral systems connected to the brain models. In summary, the modular system can host multiple networks reconstructed with different levels of detail, e.g. local connectivity among single neurons generated through intersection of morphologies in 3D space, or functional equations reproducing the algorithmic operations of the network dynamics. A dedicated neuroinformatic framework, the Brain Scaffold Builder (BSB), has been designed to address specific properties of network architecture, allowing easy reconfigurations of brain networks, and offering flexible interfacing for simulations (De Schepper et al. 2021) (this is in synergy with WP5/ Service Category (SC)3 tool development tasks).

This document provides an update on the implementation status, as of December 2021, of scaffold modelling of some brain microcircuits fundamental in sensorimotor functions, with as goal to connect them in a functional adaptive system (D'Angelo et al. 2016). We focus on cerebellar and basal ganglia networks. The work builds on our previously developed detailed single-neuron models of cerebellar cortex and basal ganglia. Atlas-derived quantitative data on cell compositions and local connectivity were exploited (voxel-based density, cell compositions, etc.). The developed BSB framework is able to host and tune these data, and we have validated the network reconstruction. Extensive work has been performed at a detailed modelling level (De Schepper et al. 2021; Hjorth et al. 2020), where multi-compartmental neurons were embedded in a realistic, structurally validated connectome. For simulations, we have considered two network variants plugging in i) biophysically detailed compartmental neuronal models or ii) point neuron models. Both are constrained by experimental measurements and are able to reproduce multiple observations from electrical recordings *in vivo* and *in vitro*. This allows elucidating relationships between network structure and function.

The point neuron networks maintain the salient properties of the specific single neurons and microcircuits. Spike-time-based plasticity rules, previously designed and tested (Antonietti et al., 2016), have been introduced in the cerebellar network to support learning of sensorimotor task sequences (Figure 2). Using the developed BSB framework, initially used to address the cerebellum as a use case, we will finalise the basal ganglia network and augment it with specific plasticity mechanisms.

A prototype model, composed of multiple brain networks, connected in feedback and feedforward loops, has been designed. The resulting model will feature cerebellar and basal ganglia modules at high granularity, connected through the thalamus and cerebral cortical modules (mainly M1, S1). Some of the building blocks (e.g., primary motor cortex, state estimator) are represented by simplified functional counterparts of the brain regions considered. They are able, by ad hoc interfaces, to work with spike signals. This developed model will allow simulation of learning in sensorimotor tasks, investigating, among others, mechanisms related to the prediction of sensory consequences based on efference copies of motor plans, sensory feedback, delays, error compensation, selection of the motor plan, and suppression of competing plans. The range of functions considered typically emerge from the concerted activity of several brain regions. Implementing a detailed digital model of such a neural system would prove excessively computationally intensive, to the point of being impractical (if at all possible currently). The developed framework directly addresses such issues, allowing construction of streamlined

counterparts to detailed models, retaining their key functional features, and composing different models, at different levels of detail, to investigate emerging behaviour.

The work presented directly contributes to the **co-design of EBRAINS** and thereby to its unique value proposition. Results discussed in this document rely on neural simulation tools (NEST, NEURON) from EBRAINS' Brain simulation and simulation workflow Service Category (SC3), the aforementioned BSB (developed in coordination with SC3), and dedicated High Performance Computing (HPC) resources provided by EBRAINS' interactive workflows on HPC or NMC Service Category (SC6). The technology offers the perspective of ground-breaking developments, only possible using EBRAINS. In the middle term, we will work on aspects related to embodiment, facilitating faithful expression of the sensorimotor functions under consideration, with contributions from EBRAINS' Closed-loop, AI and robotics workflows Service Category (SC4). The development of the BSB and of workflows tying this framework to EBRAINS simulation tools directly expands the range of services provided to EBRAINS users, making it possible for neuroscientists to approach the same type of multiscale modelling work discussed below. Second, the functional model, whose properties are discussed hereafter, will be made accessible, serving as a blueprint illustrating use of the developed digital modelling technology. The resulting set of tools, supported by a combination of services not found anywhere else, will empower EBRAINS users to break new ground in computational neuroscience.

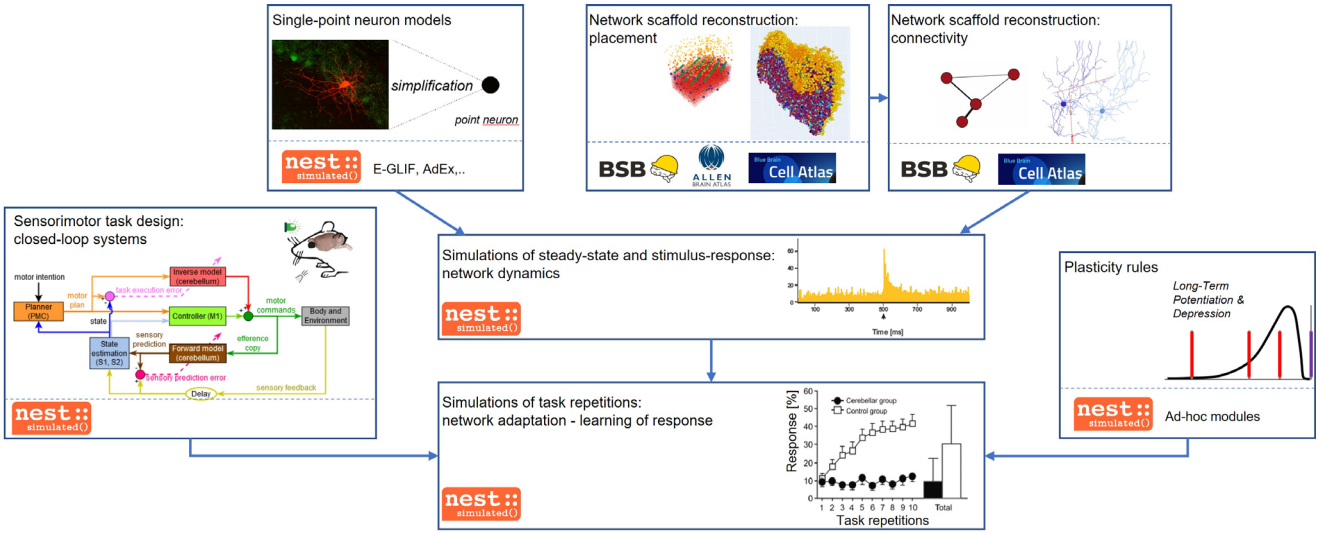

Figure 2: Workflow: from neurons to behaviour

2. Main achievements

2.1 Scaffold modelling for brain circuit reconstruction and simulation

Data-driven modelling of the brain requires a neuroinformatic framework implementing a general strategy to accommodate experimental data at different scales. To this end, we have developed the Brain Scaffold Builder (BSB), an advanced framework for neuronal circuit modelling, with specific modules for network reconstruction and simulation. The "scaffold" design allows an easy model reconfiguration reflecting variants across brain regions, animal species, and physio-pathological conditions without changing the basic network structure. The BSB provides an organised staged workflow allowing reconstruction of networks with arbitrary volume and geometry. It provides multiple strategies for cell placement and connectivity, a configuration system managing detailed neuronal and synaptic models, and the support for multiple simulators with transparent parallel processing. The interfaces with several simulators (NEURON, NEST, Arbor) allow investigation of the same brain region at different levels of resolution, depending on the scientific question about

structure-function relationships. The BSB[1] is provided as an open-source package[2], applicable for multi-scale modelling of different brain areas. In principle, the BSB workflow may be applied to any neuronal circuit, promoting an ecosystem of modelling packages compatible with one another, for long-term value and extended use of brain modelling in the scientific community.

2.2 Cerebellar circuit reconstruction and simulation

With the BSB, for the first time, the mouse cerebellar cortex was reconstructed and simulated at cellular/subcellular resolution using morphologically realistic multi-compartmental neuron models. Embedded connection rules allowed the BSB to generate the cerebellar connectome, unifying a collection of scattered experimental data into a coherent construct. Naturalistic background and sensory burst stimulation were used for functional validation against *in-vivo* recordings, monitoring the impact of subcellular mechanisms on signal propagation and spatiotemporal processing. Molecular and cellular properties reverberate across scales controlling spike timing and distribution. In particular, different properties emerged matching experimental values and observations: background frequency of all cerebellar populations, synchronous theta-band oscillatory behaviour of granular layer in resting state, vertical organisation of the impulsive responses of the cerebellar populations, burst-pause response of Purkinje cells, and feedforward and lateral inhibition from molecular layer interneurons (stellate and basket cells) to Purkinje cells. The integration of structural and functional properties through the model provides a new "ground truth" about cerebellar circuit organisation capable of predicting neural dynamics *in vivo*. The model appears to confirm the possible existence of a vertical column structure, activated in the cerebellar cortex by peripheral inputs. Our simulations provide the first prediction of neural dynamics in the cerebellar network revealing the formation of vertical columns of activity that might represent the emergence of cerebellar computational modules (De Schepper et al. 2021).

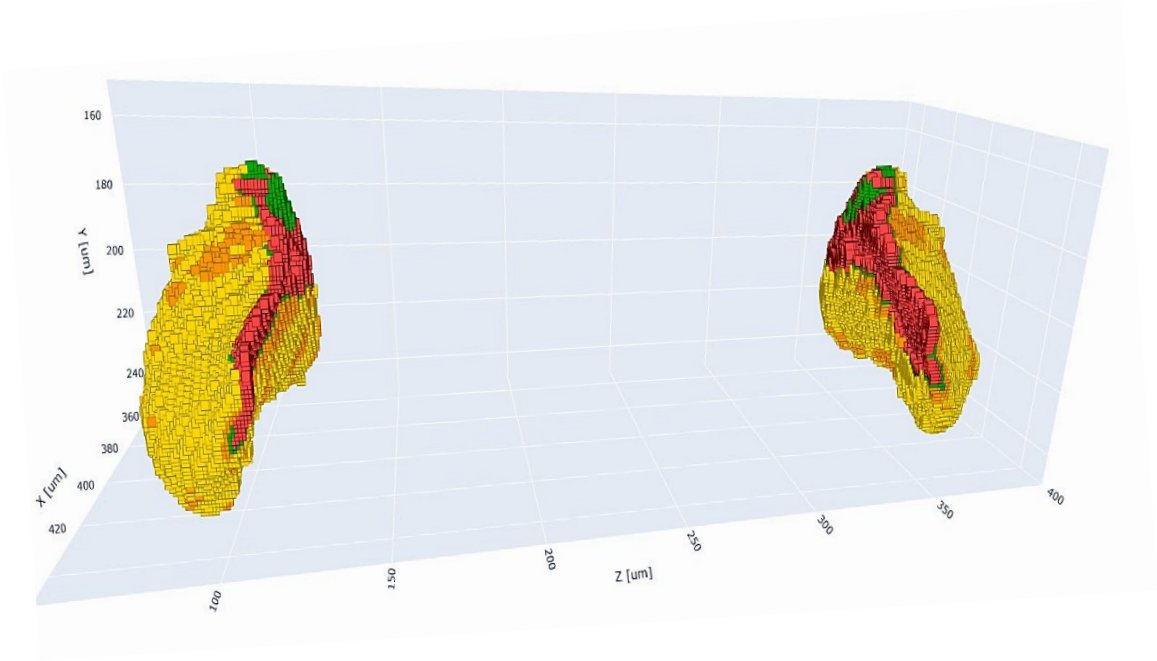

Figure 3: Voxelized cerebellar flocculus reconstruction

One of the final goals is to reconstruct full-scale atlas-mapped cerebellar regions and simulate them with ad hoc task-specific protocols, which means with ad hoc encoding-decoding strategies. In this context, we have scaled up the original scaffold architecture to large-scale networks mapped on the Allen Brain Atlas (ABA), developing full cerebellar region networks (e.g. the vermis, the flocculus,

[1] https://bsb.readthedocs.io/
[2] https://github.com/dbbs-lab/bsb

and the hemispheres). To do so, the placement and connectivity strategies of the original scaffold have been generalised (considering real folding and orientation) to account for region-specific anatomical data derived from the ABA. They are used to generate full-scale models of mouse cerebellar regions. Eventually, this will yield the first full-scale spiking neural network model of the mouse cerebellum, to be integrated with large-scale models of further brain areas (e.g. co-simulations in The Virtual Mouse Brain). The BSB reconstruction stage can directly use the voxel-based density and cell composition data coming from atlases. Technically, full-scale reconstruction is feasible thanks to the parallel reconstruction feature (on HPC) supported by the latest version of the BSB. The intra-cerebellum structural specificities will allow investigation of specific functionalities ascribed to cerebellar lobules. In a system of multiple brain regions, emergence of such structure-function relationships is also affected by specific connection pathways. Figure 3 shows an example of reconstruction of the cerebellar flocculus, using voxel-based density from the Allen Brain Atlas and specific annotations/corrections in collaboration with Blue Brain Project at EPFL. The total number of voxels is 88,216; the floccular volume 1.4 mm^3; and 1,325,206 neurons are positioned. Functional simulations of this region are ongoing using point neuron models (in NEST).

The interfaces with several simulators allow simulation of the same brain region at different levels of resolution, depending on the scientific question about structure-function relationships under investigation. For our point neuron network models (Cerebellar Spiking Neural Network – SNN), we developed and used an Extended Generalised Leaky Integrate-and-Fire (E-GLIF) neuron model (Geminiani et al., 2018) and alpha-shaped conductance-based synapses. We had previously (SGA2) optimised the E-GLIF for each cerebellar cell type (granule, Golgi, Purkinje, stellate, basket cells) (Geminiani et al., 2019a) (Figure 4).

A reconstructed cerebellar cortical module of 17.7 10-3 mm^3 including 29,230 neurons was simulated using naturalistic background and sensory burst stimulation, imitating whisker/facial sensory stimulation *in vivo* (Rancz et al., 2007). The outputs of the simulations in NEURON and NEST are reported in Figure 5.

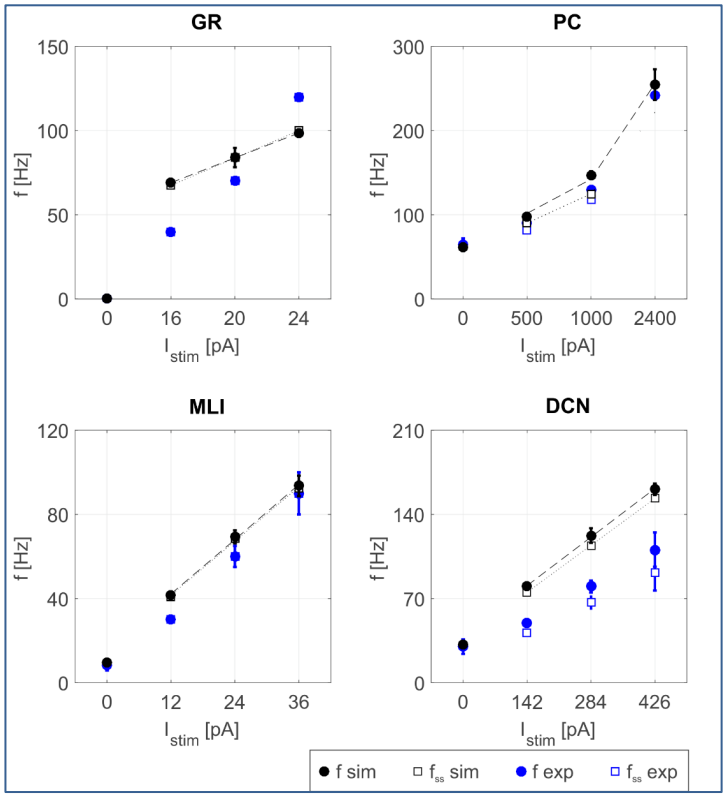

Figure 4: Simulations of optimised E-GLIF point neuron models vs experimental electroresponsiveness.

GR: granule cell; PC: Purkinje cell; MLI: molecular layer interneurons (stellate and basket cells); DCN (deep cerebellar nucleus cell). The panels depict the relationship between the output frequency and current injection, showing f-I_{stim} slope, adaptation (initial and steady-state output frequency as solid disks and open squares, and basal discharge (at I_{stim} = 0 pA). Adapted from (Geminiani et al., 2019a).

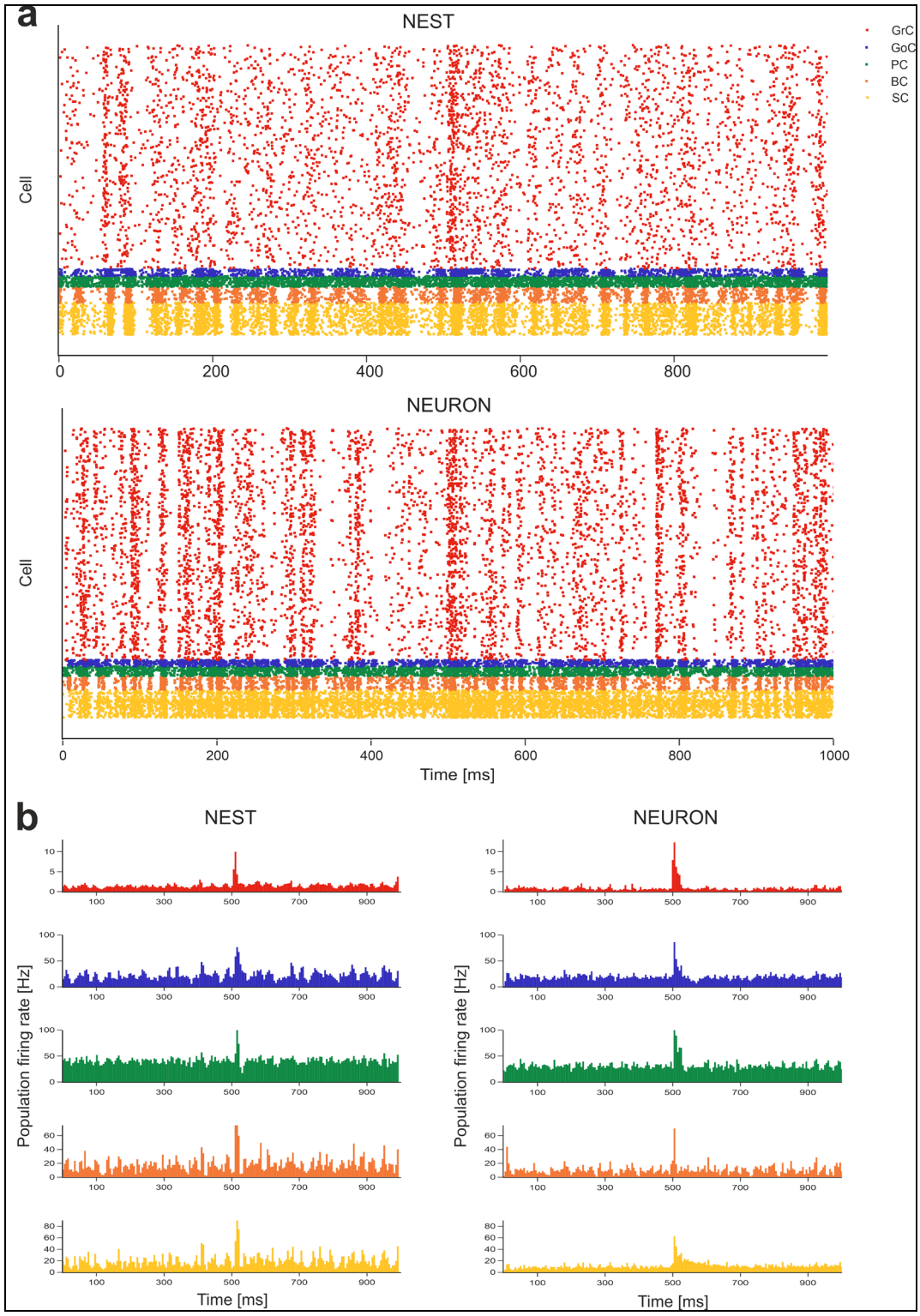

Figure 5: The reconstructed cerebellar network was simulated using the BSB NEST and NEURON Adapters.

The simulation lasted 1 second, with background rate 4 Hz on all mossy fibres (mf), and a burst on 4 adjacent mfs starting at 500 ms and lasting 20 ms. For the NEST version, optimised E-GLIF neuron models and alpha-shaped conductance-based synapses (Geminiani et al., 2019a) were inserted. a) Raster plot of all cells; GrCs are undersampled (random 10%) for clarity. b) Peri-Stimulus Time Histogram (PSTH) of each population (number of spikes in 5 ms time bins, normalised on the total number of cells). GrC: granule Cell, GoC: Golgi Cell, PC: Purkinje Cell, BC: basket Cell, SC: stellate Cell.

2.3 Learning capability of the cerebellar circuit (point neuron network with plasticity)

When dealing with cerebellar-driven sensorimotor behavioural loops and learning, the cerebellar cortical microcircuit needs to be connected with the deep cerebellar nuclei and the inferior olive, at a mesoscale level. We have developed a microcomplex network model (Figure 6) embedding long-term plasticity rules at multiple connection sites. To challenge the plastic cerebellar microcomplex in different sensorimotor tasks, task-specific systems have been designed, wiring the plastic cerebellar microcomplex with the appropriate structures to reconstruct the main loops involved in those tasks.

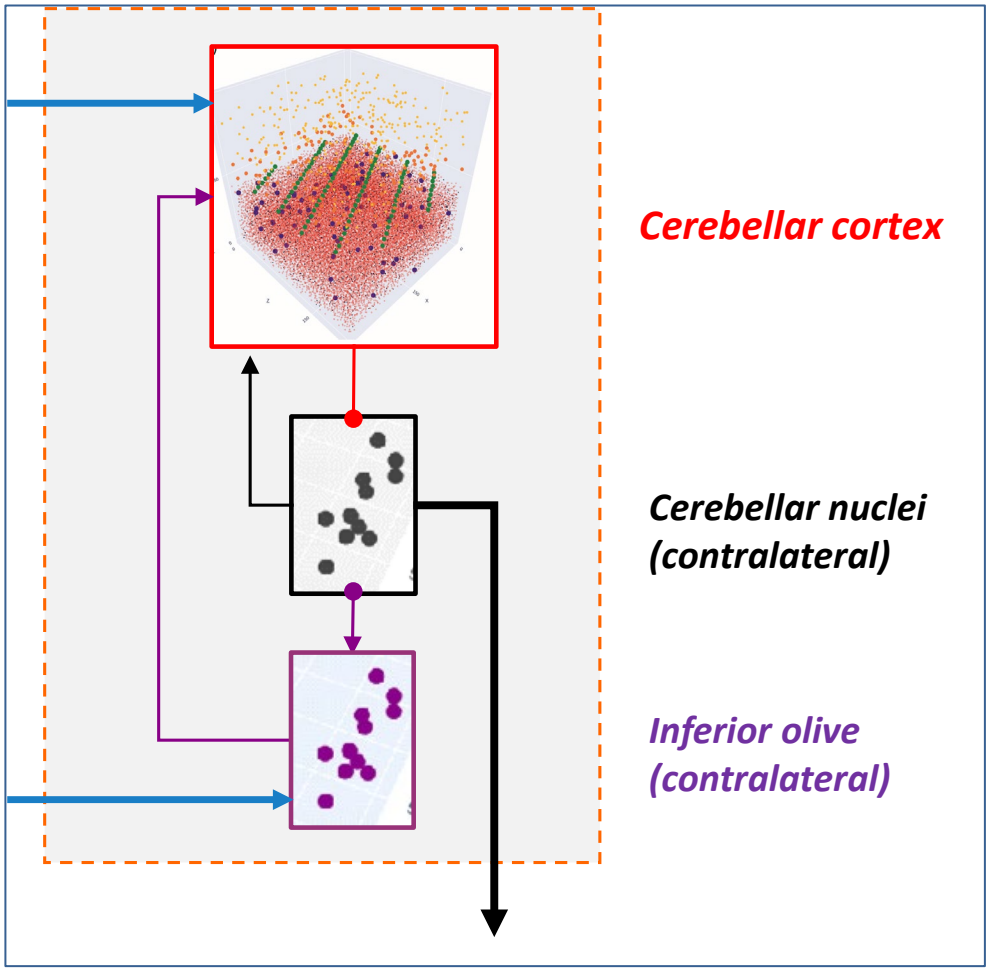

Figure 6: Cerebellar microcomplex.

The first example concerns the spiking cerebellar circuit embedded in a system able to generate and adapt saccadic eye movements (cf. Figure 7). This study investigates how synaptic mechanisms in the Purkinje cell populations of the cerebellum lead to predictive control and encoding of saccadic eye movements. Bioinspired plasticity rules in the spiking neural network model of cerebellum lead to improvement in both movement accuracy and speed, despite receiving just the end foveation error to evaluate the movement quality for trial-by-trial movement improvement. This work "*Dual STDP processes at Purkinje cells contribute to distinct improvements in accuracy and vigour of ballistic eye movements*" was presented at the HBP Summit 2021 and now is submitted for publication (in collaboration with the BioRobotics Institute, Scuola Superiore Sant'Anna, Italy).

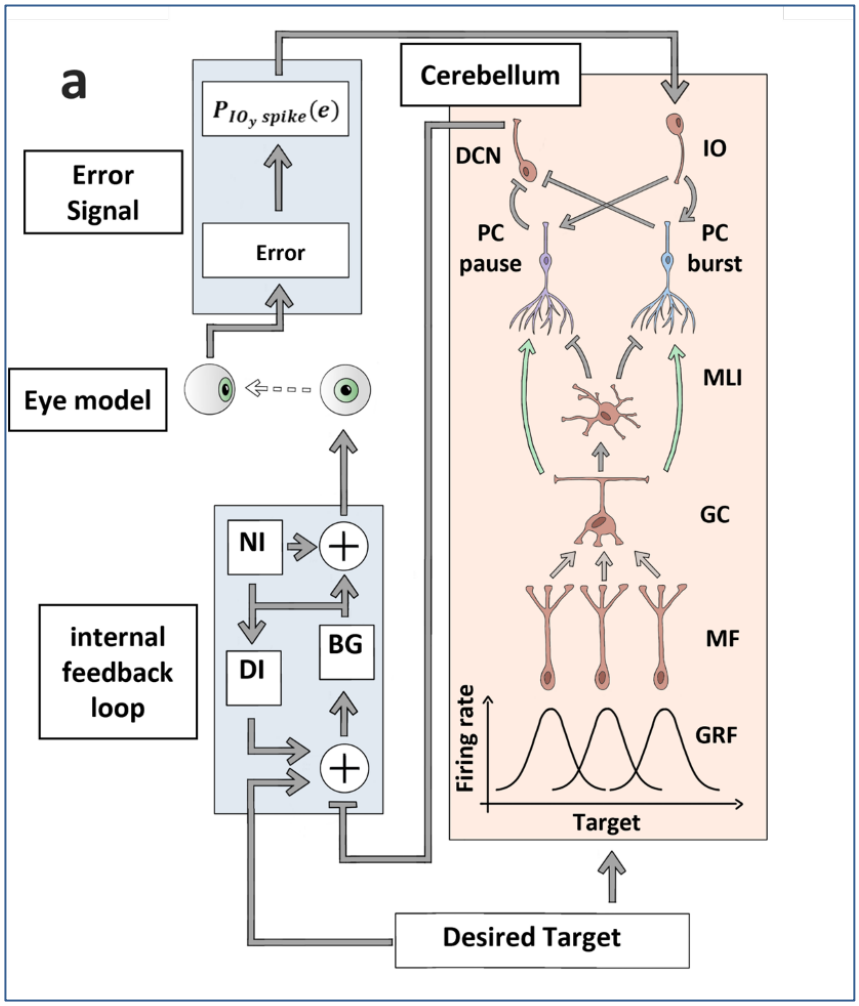

Figure 7: Schematic of the saccadic control loop.

The system is designed so that the target displacement information (desired target) is sent to the internal feedback loop (IFL) and to the cerebellum. In the cerebellum, the target displacement is encoded by the Gaussian receptive field (GRF) of the mossy fibres (MF), MF are connected to the granule cells (GrC), which, through their axonal endings (namely the parallel fibres, PFs) excite both the Purkinje cells (PC), and the molecular layer interneurons (MLI), composed of basket and stellate cells. The connection between PF and PC is the only plastic one in the model (represented by the green arrows). The MLI are connected to the PCs. The PCs are split into two subpopulations: PC pause (purple) and PC burst (light blue). PCs are connected to the deep cerebellar nuclei (DCN), which are the output of the cerebellum and project to the IFL. The IFL is composed of the neural integrator (NI), the burst generator (BG), and the displacement integrator (DI). The error information is then encoded by the firing rate of the inferior olive (IO), connected to the PC.

Another example in collaboration with Politecnico di Milano concerns the whisker system. The mouse whisker system has become a standard model to study active sensing and sensorimotor integration through feedback loops. In that work, we have developed a bioinspired spiking neural network model of the sensorimotor peripheral whisker system, modelling trigeminal ganglion, trigeminal nuclei, facial nuclei, and central pattern generator neuronal populations. This network was embedded in a virtual mouse robot, exploiting the HBP Neurorobotics Platform. The peripheral whisker system was connected to the adaptive cerebellar network. The whole system is able to drive active whisking with learning capability, matching neural correlates of behaviour experimentally recorded in mice (Figure 8). This work "Brain-inspired spiking neural network controller for a neurorobotic whisker system" was presented at the NeuroMatch 4.0 conference 2021 and now is submitted for publication.

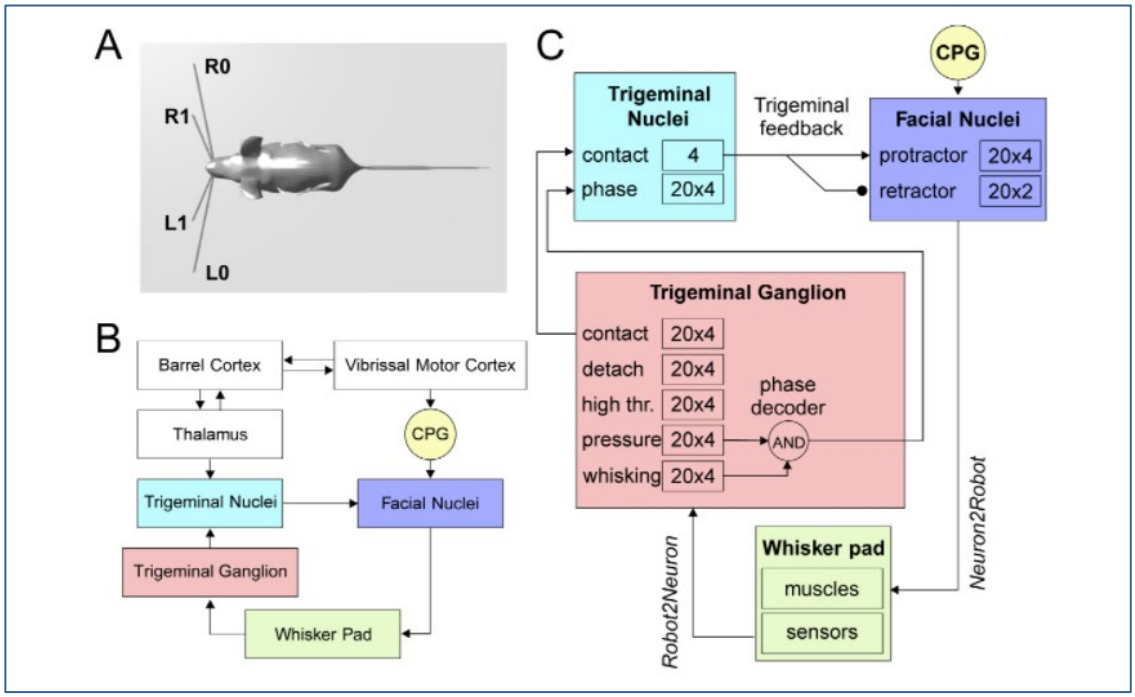

Figure 8: The rodent whisker system.

A) Virtual robotic mouse implemented in the NRP, with two whiskers per side. L0 and R0 are the lower left and right whiskers, L1 and R1 are the upper whiskers. B) Block diagram of the rodent whisker system, including sensory and motor pathways, and its integration with higher-order areas (thalamus and cortex). C) SNN implementation of the mouse peripheral whisker system; numbers in each block represent the size of the neural populations included in that brain region. Arrows represent excitatory connections, circles inhibitory connections.

Other systems have been designed to investigate the role of the cerebellar plasticity mechanisms in the eyeblink classical conditioning paradigm (EBCC). During this simple task, the cerebellum learns to associate two time-locked stimuli and drives a motor response (i.e. eyelid closure) that anticipates the second stimulus. Experimental evidence suggests that this association results from multiple mechanisms at neuronal and synaptic levels (Ten Brinke et al., 2017). The cerebellar network is able to simulate EBCC, driven by the complex balance of multiscale mechanisms found in experiments, reproducing realistic firing patterns and modulation of neural activity throughout learning. The new more realistic simulations started from SGA2 work, as the use case on this cerebellar-driven task provided on EBRAINS https://wiki.ebrains.eu/bin/view/Collabs/cerebellum (Geminiani et al. 2019b) (live paper https://doi.org/10.25493/3XVH-RS7)

In this context, ongoing work is related to pathological conditions by model reconfiguration. Specifically, when localised lesions in the cerebellar cortex are applied, the model should reproduce the alterations of behaviour found in experiments on knock-out mice, while suggesting hypotheses on the underlying modified neural mechanisms. Information on alterations in motor behaviour was derived from EBCC experiments in mutant mice. Specifically, EBCC was not impaired in GluR2Δ7 mutant mice with reduced PF-PC long-term depression (LTD), while L7-KCC2 and L7-Gamma2 mutant mice showed a decreased amplitude of CRs with altered timing, even though EBCC learning was not completely compromised (Boele et al., 2018).

2.4 Design of the system to host multiple brain region scaffold models

We have designed a more general-purpose control system, embedding realistic cerebellar circuits through the connectome. The main controller (Primary Motor Cortex M1) performs inverse dynamics operations and feedback control working with spiking signals (Figure 9). In the context of upper-limb coordinated movements, a reaching task disturbed by force fields has been designed. According to the target position, the planner model generates a certain trajectory, which, in turn, is translated into motor commands by the cortex-based controller. The sensory feedback and sensory prediction generated during the movement are optimally integrated by the state estimator, which updates the controller with the current status of the system. The cerebellar networks play a double role: forward and inverse model.

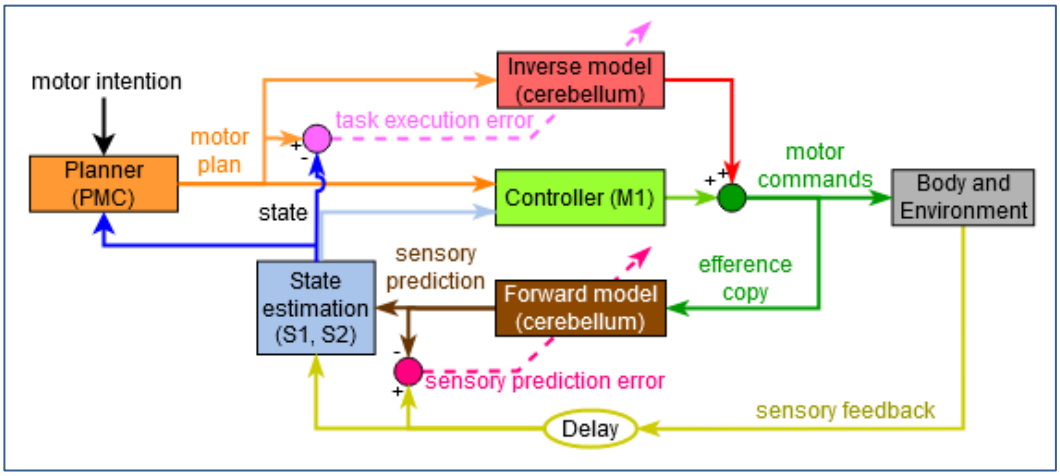

Figure 9: Sensorimotor control system.

The system is implemented as a Python-based flexible code using NEST for the brain spiking networks and MUSIC for the "body and environment" block, managing MPI simulations (https://github.com/cristianoalessandro/control_loops).

The State estimator block has been developed in collaboration with Politecnico di Milano. To allow the execution of complex movements, the brain continuously estimates the state of the body and the environment. To this end, specific brain regions are thought to act as a Bayesian estimator, optimally integrating the noisy and delayed sensory feedback with the sensory prediction generated by the cerebellum. This process is thought to be carried out by the parietal cortex, which receives, through the thalamus, projections from both the deep cerebellar nuclei (output of the cerebellum) and peripheral sensory structures. In the present work, we designed a spike-based computational model of this Bayesian estimator. The model receives spikes from neural populations encoding the sensory feedback and the cerebellar prediction signals and computes the spike-rate variability within each afferent population to estimate the reliability of these sources of information. Using these indices of reliability, the model implements a "spike-based Bayesian integration", so that its output encodes the current estimate of the state. We tested the system simulating a reaching task of a point mass, by imposing input trajectory signals that represent plausible snapshots of the movement learning process. The activity of the sensory feedback neurons encoded a noisy and delayed version of the executed trajectory, with a constant level of spiking variability throughout the learning process. The activity of the cerebellar output neurons emulated two different conditions, pre- and post-learning. In pre-learning, their firing rate did not encode any relevant signal, as the cerebellum should not be able to perform useful predictions yet, and their intra-population spiking variability was set to be higher than that of the sensory feedback, which conveyed useful, albeit noisy, information on the movement being executed. In post-learning, the firing patterns of the cerebellar output neurons encoded the trajectory before it was executed (accurate sensory prediction), and a spiking variability lower than that of the sensory feedback population was set. The designed model proved to be able to properly weight the two information sources based on their reliability, which depended on the learning stage and/or on any change during the ongoing movement (e.g. a sudden

loss of the sensory feedback information). The proposed tool will be a critical block for the development of general spiking brain-inspired control systems for sensorimotor tasks ("*Bayesian integration in a spiking neural system for sensorimotor control*": submitted for publication) (Figure 10).

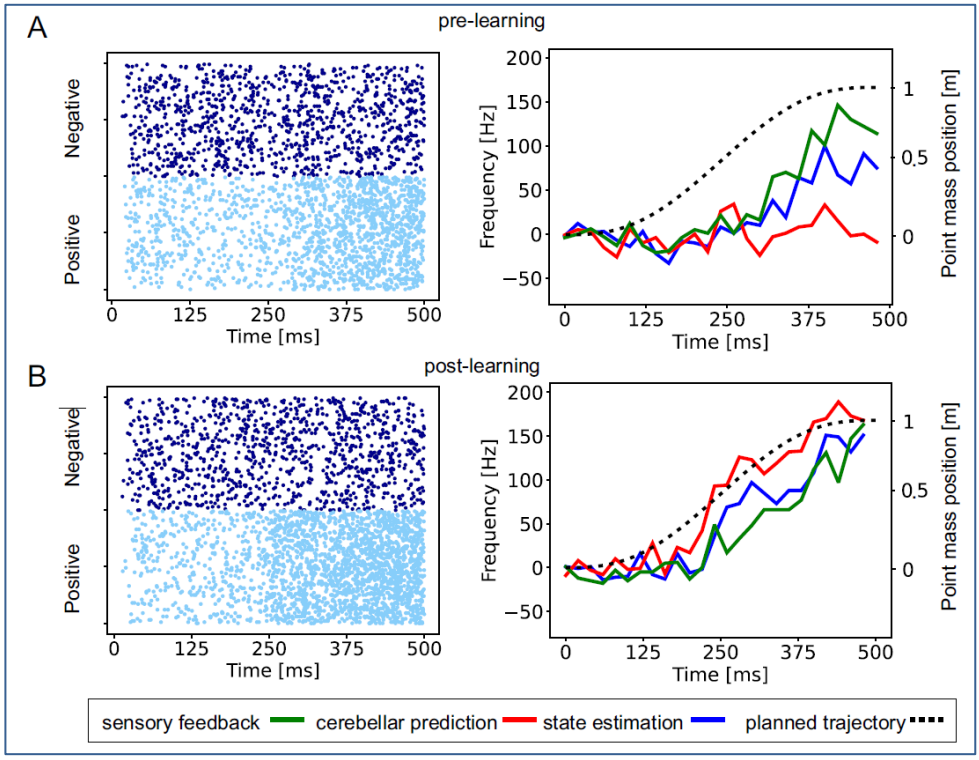

Figure 10: State estimator neurons.

The raster plot and the corresponding population rate signals (computed with time bins of 25 ms) of the state estimator neurons are reported in pre-learning (A) and in post-learning (B) conditions. While the negative group shows a constant background firing rate (~ 50 Hz), the positive group generates a number of spikes that depends on the progressive moving away of the point mass along x-axis. The corresponding net activity (blue rate profile) is reported on the right and compared with the net activity of the sensory feedback and cerebellar output populations in each condition.

More detailed models of the Deep Cerebellar Nuclei (DCN) and the Inferior Olive are under construction. Specifically, DCN neural populations are under reconstruction and functional characterisation, especially in the context of the signal integration process between sensorimotor inputs and cerebellar output internal feedback ("Implementation of the NucleoCortical pathways inside a Spiking Neural Network model of Cerebellar Nuclei" https://ieeexplore.ieee.org/document/9441361; https://www.youtube.com/watch?v=gW9Ca3109d0)

Also, the thalamic nuclei are under construction in collaboration with Politecnico di Milano. Indeed, they are intercalated nuclei fundamental for wiring together cerebellum, cerebral cortex, and basal ganglia. Atlas data and the BSB with the NEST interface are used.

Finally, also the system connectome is under refinement. In the context of cerebellar connectivity analysis, a comparison between Allen Mouse Brain Atlas data and the literature is being carried out to quantify the long-range connections.

2.5 Basal ganglia circuit reconstruction and simulation

Current work targets the *in-silico* reconstruction of the striatum. All major neuron types are characterised and placed in the network volume. Distance-dependent connection probability rules are applied. The point neuron models are tuned, axonal delays are introduced, and NEST simulations are run in the resting state and with an abstract cortical signal.

2.5.1 Neuron density maps for mouse striatum

Cell densities are estimated from *in-situ* hybridisation images of the Allen Mouse Brain Atlas. Molecular markers for all major cell types in the striatum are available: Drd1 for direct-pathway striatal projection neurons (dSPN), Adora2a for indirect-pathway striatal projection neurons (iSPN), Pvalb for the fast-spiking cells (FS), Sst for the low threshold-spiking interneurons (LTS) and Chat for cholinergic interneurons (ChIN). Striatal masks are obtained from the digital mesh definitions of the striatal volume (Allen Mouse Brain Atlas, structure ID 485). Cell counting is performed using spot registration algorithms from the scikit-image library. Combined cell counts per each slice provide a complete three-dimensional density map for all major neuron types with 200 µm spatial resolution (Figure 11). Density maps of dSPN cells (Figure 12), iSPN cells, FS cells, LTS cells, ChIN cells are extracted and used.

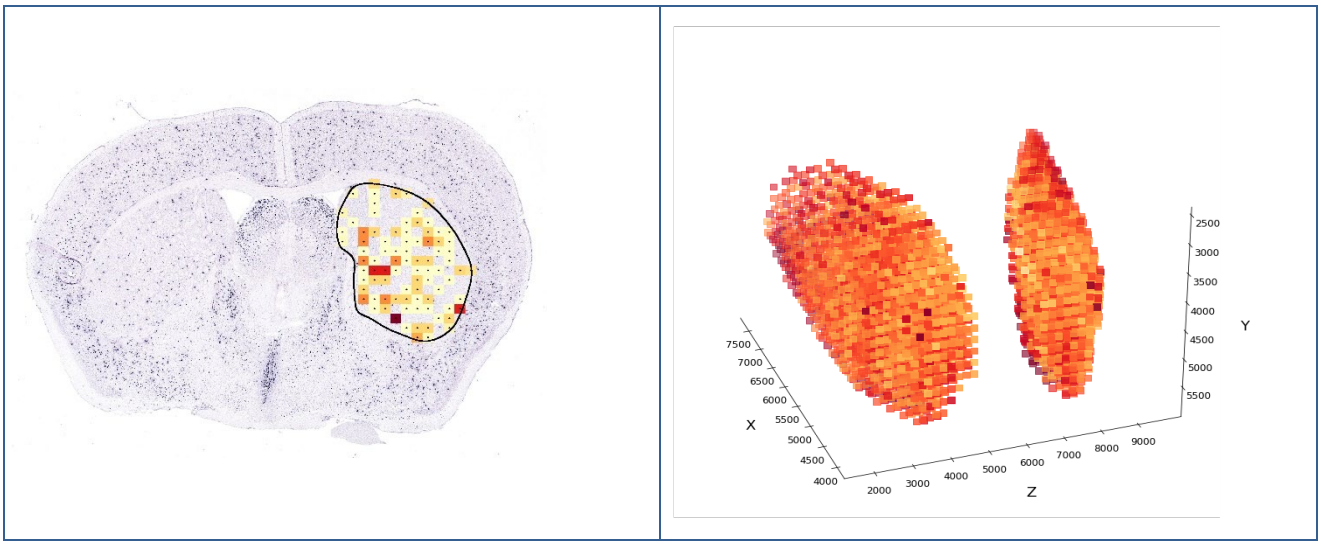

Figure 11: Three-dimensional density map for all major neuron types with 200 µm spatial resolution.

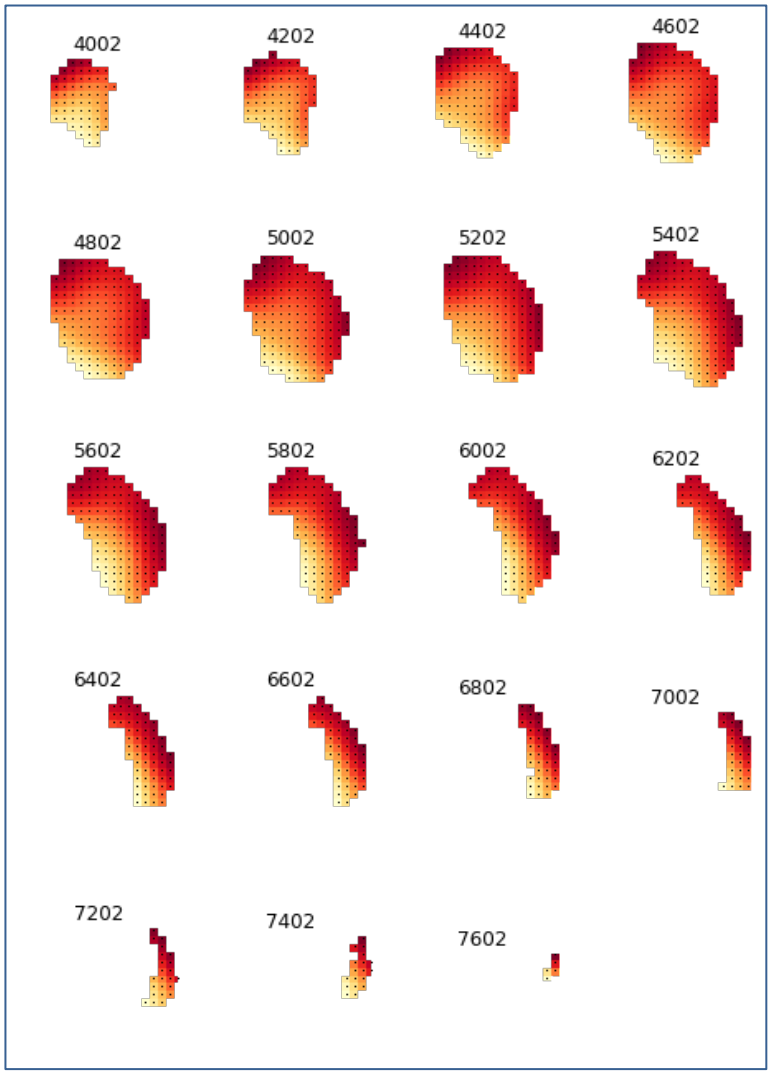

Figure 12: Density maps of dSPN cells.

Cell densities within the left part of the dorsal striatum obtained as in Figure 11 for multiple coronal slices in (z, y)-plane separated by 200 µm along the rostro-caudal axis (x-direction). Numbers above the maps correspond to the x-coordinate (in µm) of each slice.

2.5.2 Spike-based neuron models for the basal ganglia nuclei

Point neuron models, using adaptive exponential integrate-and-fire neuron AdEx (aeif_cond_exp in NEST), were tuned to represent direct-pathway striatal projection neurons (dSPN, experimental dataset 150917_c10_D1 from the previous work by Hjorth et al. (2020) publicly available on EBRAINS.eu, DOI: 10.25493/MZE0-BH5), indirect-pathway striatal projection neurons (iSPN, dataset 151123_c1_D2, DOI: 10.25493/MZE0-BH5), striatal fast-spiking cells (FS, dataset 161205_FS1, DOI: 10.25493/E883-NFA), as well as arkypallidal neurons from the globus pallidus externa (Arky), prototypical globus pallidus externa neurons (Proto), substantia nigra pars reticulate neurons (SNr), and subthalamic nucleus neurons (STN). The latter models were taken from our earlier studies (Lindahl et al., 2013; Lindahl and Hellgren Kotaleski, 2017). An example model of the principal cell of the dorsal striatum is shown below (dSPN, Figure 13, Figure 14, Figure 15).

Here, as example, dopamine receptor D1-expressing striatal projection neurons of the mouse striatum are modelled using the adaptive exponential integrate-and-fire neuron model, AdEx from the NEST simulation environment.

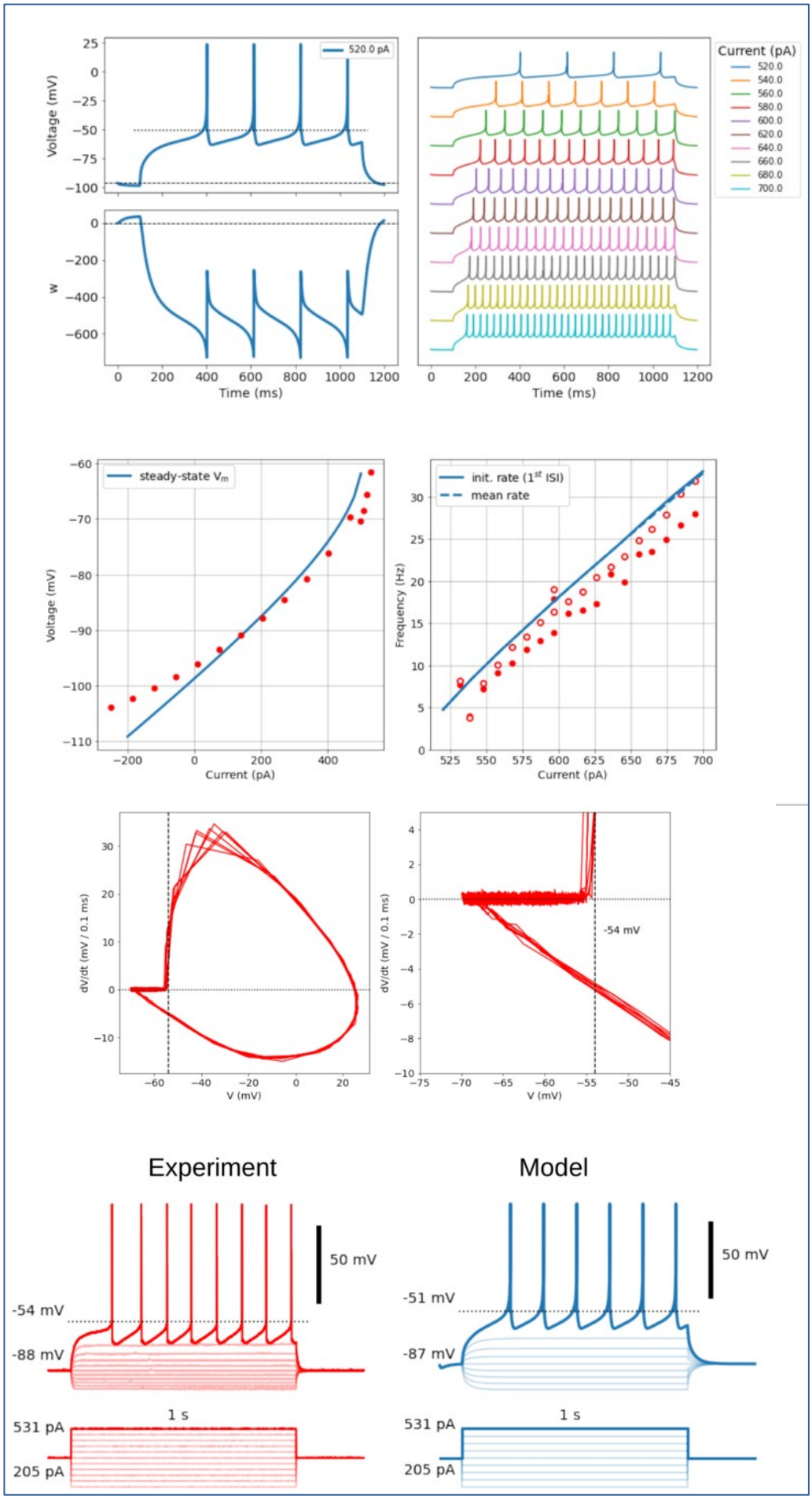

Figure 13: Fitting of the point neuron model (AdEx) of dSPN to the experimental data.

Parameters for 'aeif_cond_exp' model (NEST v.2.20) of dSPN cells are given in Table 1. Models of the other basal ganglia neuron types are similarly defined and will be available in an upcoming publication.

Table 1: Parameters of the point neuron model (AdEx) of dSPN.

C_m	123.5
g_L	35.002
E_L	-96.2
Ie	-80
a	-14.5
b	500
tau_w	15
V_th	-51
Delta_T	16
V_reset	-51
V_peak	23.5
t_ref	2.47

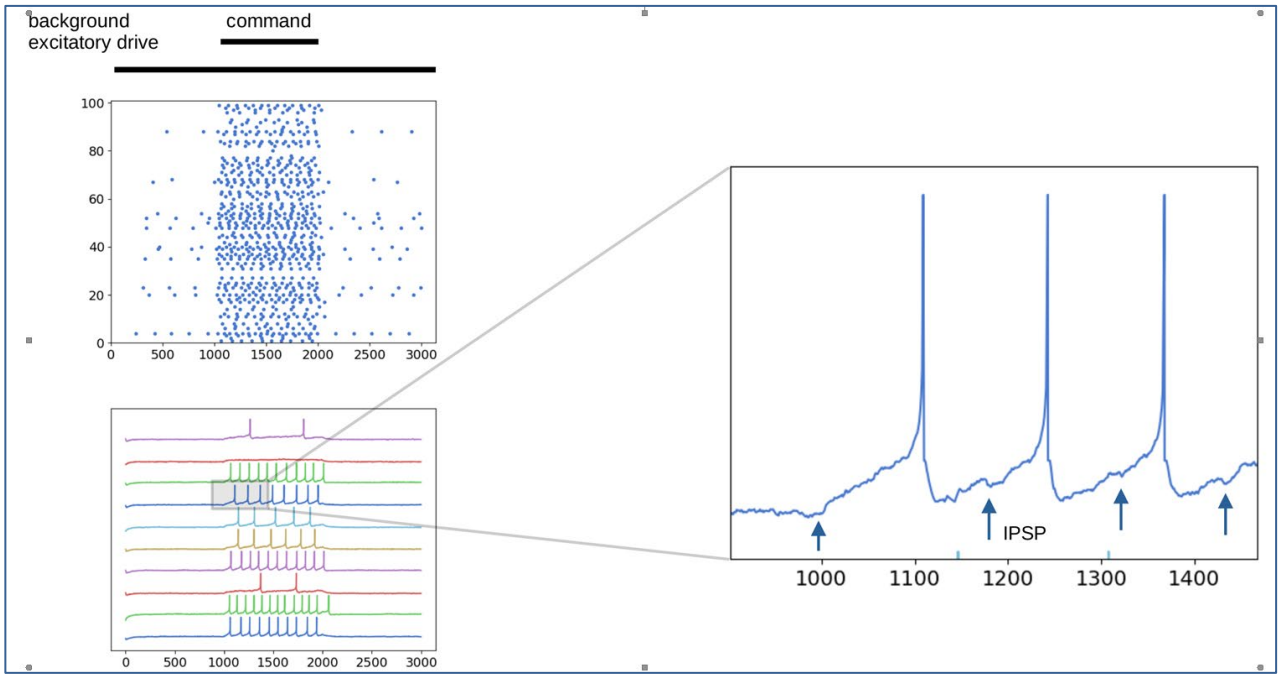

Figure 14: Baseline activity of dSPN population and response to the cortical command.

Arrows in the inset mark large IPSPs due to the lateral inhibition.

2.5.3 *Preliminary network simulations*

A neuron population is simulated as a homogeneous pool of cells with distributed excitability, distance-dependent connection probability and axonal delays. Cell density in the pool is estimated from three-dimensional density maps and the location of the simulated action channel. The synapse model is conductance-based with Tsodyks-Markram short-term plasticity. The baseline activity within the dSPN population due to the background excitatory drive as well as the response to the cortical command are shown in Figure 14.

The population response of a pool of the cells with distributed excitability involves increase of the firing rate of individual neurons and gradual recruitment of the cells, which are silent at baseline, as shown in Figure 15.

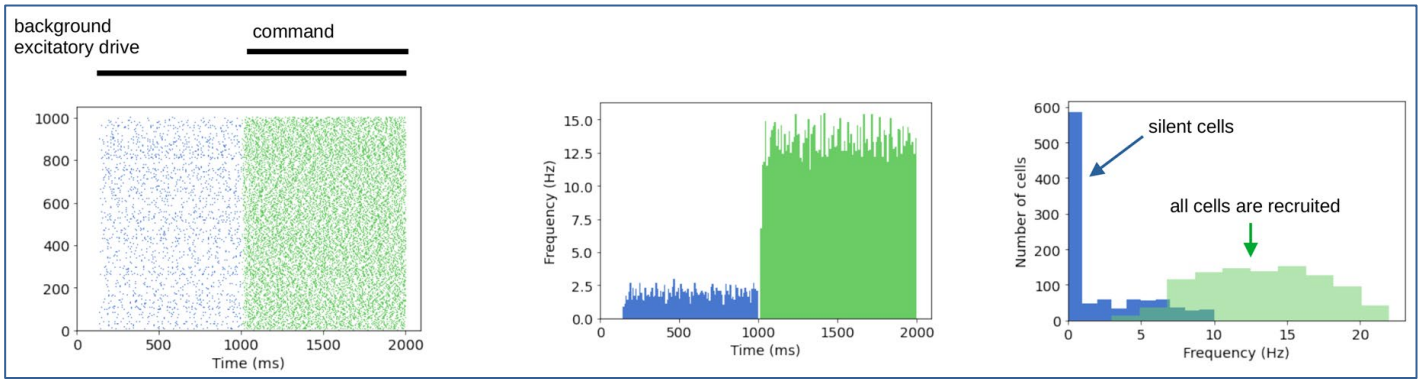

Figure 15: Population response of dSPN cells with distributed excitability.

Cells that are silent at baseline get gradually recruited by the excitatory cortical command.

3. Next steps

The cerebellar and basal ganglia spiking networks will be made compatible to be wired into the modular system. Ad hoc interfaces to connect them with functional non-spiking blocks will be inserted. The system blocks will be completely developed, and the entire connectome will be verified and tuned. Spike-based plasticity rules will be introduced also in the basal ganglia spiking network.

Specific tasks will be designed in order to challenge all the system blocks, especially the ones represented with high granularity (spiking circuits at single-cell resolution).

The functional multiscale model and testing sensorimotor protocols will be made accessible in EBRAINS.

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