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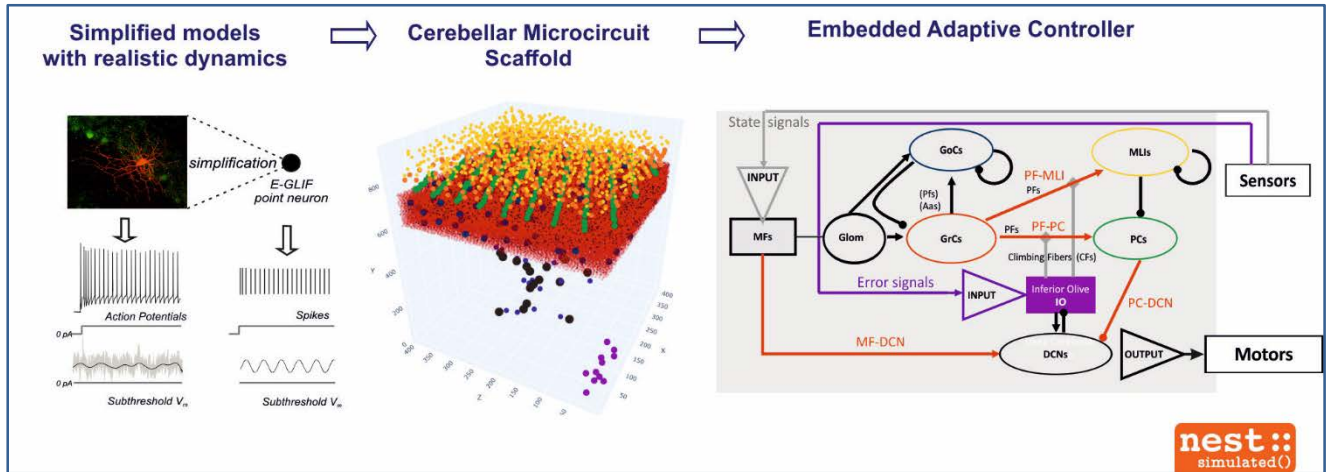

Figure 1: Cerebellar modular circuit into an adaptive control system

Model transformation from multi-compartmental single neurons to point neurons allows to embed realistic dynamics into scaffold networks models, which are then integrated into sensori-motor system controllers to predict accurate control of actions.

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Description in GA:	For consistent presentation of HBP results, SGA2 M24 Deliverables describing the accomplishments of an entire SP, WP or CDP have been prepared according to a standard template, which focuses on Key Results and the outputs that contribute to them. Project management elements such as Milestones and Risks will be covered, as per normal practice, in the SGA2 Project Periodic Report.
Abstract:	CDP2: "Mouse-Based Cellular Cortical and Subcortical Microcircuit Models" aims to integrate molecular/cellular properties into large-scale simulations and to develop whole-brain scaffold models using detailed rodent cortical and sub-cortical microcircuits. The models will exploit the infrastructure resources and will be implemented in the Joint Platform.
Keywords:	Scaffold models, cerebellum, neocortex, hippocampus, basal ganglia
Target Users/Readers:	Computational neuroscience community, Consortium members, Experts in neurophysiology, Funders, General public, Neuroscientific community, Neuroscientists, Platform users, Researchers, Scientific community.

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1. Overview

Mouse-Based Cellular Cortical and Subcortical Microcircuit Models (CDP2) aims to develop whole-brain scaffold models using rodent cortical and subcortical microcircuit models capable of multiscale integration of molecular/cellular properties into large-scale simulators. CDP2 is unique for its capacity to develop and showcase the whole process going from neuronal simplification to implementation of large-scale scaffold models that are then integrated into closed-loop controllers and used in specific sensori-motor control simulations. For example, in this way relevant datasets on cerebellar synaptic plasticity and network dynamics have been transformed and integrated into closed loop simulators. CDP2 has thereby strengthened the collaboration between data production and model generation and simulations involving SP1 (data for model construction and validation), SP6 (neuron and microcircuit modelling), SP7 (HPC), SP9 (neuromorphic computing), SP10 (neurorobotics), SP5 (neuroinformatic processing of data and models on the Data Catalog, Model Catalog and Knowledge Graph).

The core CDP2 activity is summarised by the Key Result (KRc2.3) "Demonstrating microcircuit activity in closed-loop neurorobotic simulations with learning", which entails the full development of the cerebellum scaffold model along with its applications:

1) point-neuron version for pyNEST

2) multi-compartment-neuron version for pyNEURON

3) pilot version in the new modelling platform ARBOR

4) PYNN version that implemented in neuromorphic hardware, SpiNNaker

5) reduced version applied to neurorobotic simulations

6) full-scale cerebellum model adapted to Allen Brain Atlas morphology

7) neural mass version in preparation for the Virtual Brain (TVB)

This activity has involved community engagement through the Partnering Project (PP) "CerebNEST" and the infrastructure Vouchers SpinnCER (now turned into a PP) and VM-CerebNEST. For SGA3, CDP2 has been involved in proposing new Vouchers, 7 of which have been approved. Moreover, CDP2 promoted the organisation of the Erice Golgi School on "Modelling the brain and its pathologies" and the "Hackathon on Cerebellum" supported by the Education Programme; these events were open to all members of the research community allowing to extend the use of microcircuit scaffold models and to promote their application to neuromorphic hardware, neurorobotics and virtual brains.

2. Introduction

The aim of CDP2 is to run large-scale detailed model simulations of brain dynamics and plasticity, to embed simplified network models into robots for closed-loop testing, to promote model transformation into neuromorphic hardware.

"Demonstrating microcircuit activity in closed loop neurorobotic simulations with learning" (KRc2.3) aims to refine and apply molecular/cellular level models of the main brain microcircuits to

1) simulate dynamic control of plasticity in trial-and-error learning

2) integrate the microcircuits for large-scale network simulations

3) simplify such models and integrate them into whole-brain robotic simulators

4) extend modelling through the Collaboratory

All these activities are coordinated to develop and refine neuro-informatic tools. Moreover, CDP2 has coordinated the neuroinformatic processing of data and models in the Model Catalog and Knowledge Graph, together with SP5. Finally, CDP2 has integrated the activity of two Vouchers (SpinnCer and VM-CerebNEST) and of the Partnering Project (CerebNEST).

During the second year of SGA2, CDP2 has integrated cellular properties into large-scale simulations and developed large-scale scaffold models using detailed rodent cortical and sub-cortical microcircuits. We aligned data gathering from SP1 with model implementation in SP6 and in the Brain Simulation Platform (BSP), with model transformation in SpiNNaker in SP9, with model simplification and application to closed-loop controllers in SP10 and in the Neurorobotics Platform. In doing so, CDP2 has continued its action towards platform development.

The actions taken by CDP2 are listed below:

- simplification strategies have been applied to closed loop controllers (Geminiani *et al.* 2019, P2023) that are now running sensori-motor simulations in cortico-cerebellar loops using original datasets on synaptic plasticity and network dynamics.

- the technologies for the simplification of detailed neurons have been pursued further. A manuscript is under final review at Nature Comms and the live paper is already available on the BSP (Masoli *et al.* 2019, P1878; https://humanbrainproject.github.io/hbp-bsp-live-papers/2019/masoli_et_al_2019/masoli_et_al_2019.html).

- the SONATA format has been finalised in collaboration with EPFL/BBP and the Allen Institute leading to a publication on PLOS Computation Biology (Dai *et al.* 2020, P2184)

- the cerebellar network has been fully implemented and adapted for incorporation into large-scale loops. Plasticity rules of the cerebellum microcircuit have been developed, embedded into the scaffold (Casali *et al.* 2019, P1877) and applied to virtual neurorobots (Antonietti *et al.* 2019, P1647)

- a hippocampus CA1 microcircuit has been successfully deployed to various HPAC sites and tested the connection of the web-based online use cases for *in-silico* experimentation of the BSP (https://collab.humanbrainproject.eu/#/collab/1655/nav/66856)

- the results have been presented at the International School of Brain Cells & Circuits "Camillo Golgi"-Ettore Majorana Foundation and Centre for Scientific Culture, Erice (Italy) (ID 167) entitled "Modelling the brain and its pathologies" (27 August 2019 - 1 September 2019, https://www.erice-golgi.org/). The Course was promoted by CDP2 in order to engage the scientific community

- the Hackathon on cerebellum modelling (ID 1223) has been promoted by CDP2 and organised at the University of Pavia, Italy (13-15 January 2020, talks and tutorials available here https://collab.humanbrainproject.eu/#/collab/77410/nav/524402).

3. Key Result KRc2.3 Demonstrating microcircuit activity in closed loop neurorobotic simulations with learning

This Key Result (KR) demonstrates how molecular/cellular level models of the main brain microcircuits can be used to investigate complex microcircuit dynamics. The full system implementation has been demonstrated by embedding the simplified cerebellum model into large-scale robotic controllers. The cerebellum model incorporated multiple plasticity rules enabling the development of plasticity during trial-and-error learning. The other models (neocortex, basal ganglia and hippocampus) are achieving maturity and their exploitation in large-scale controllers is foreseen in the next phase of HBP (2020-2023). Our integrated modelling/experimental/robotic approach is providing a strong scientific driver for platform implementation, refinement of informatics tools and co-design of science and infrastructure activities. In summary, we have demonstrated that, with the available HBP data and modelling services, it is possible to generate multiple outcomes at the level of brain modelling, theoretical understanding of brain function and disease and infrastructure implementation.

3.1 Outputs

3.1.1 Overview of Outputs

3.1.1.1 List of Outputs contributing to this KR

- Output 1: Cerebellum (C3128)
- Output 2: Neocortex (C1670, C3132, C3137)
- Output 3: Hippocampus (C3133)
- Output 4: Basal Ganglia (C3131, C3134)

3.1.1.2 How Outputs relate to each other and the Key Result

These Outputs are all contributing to whole brain modelling. The 4 different Outputs are examples of us building models using the cross-group approach outlined above. We tested this with the cerebellum model, which has advanced already to the exploitation phase (see Life Cycle Model for Data-Driven Models[1] for different phases) and applied this to the other 3 regions after it was shown that this approach worked.

3.1.2 Output 1: Cerebellum

Table 1: Output 1 links

Component	Link to	URL
C3128	Model Repository	https://github.com/dbbs-lab/extra-cereb-nest https://github.com/dbbs-lab/cereb-nest https://github.com/dbbs-lab/scaffold
	Technical Documentation	https://collab.humanbrainproject.eu/#/collab/75138/nav/534938

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[1] https://collab.humanbrainproject.eu/#/collab/1655/nav/368782

	User Documentation	https://collab.humanbrainproject.eu/#/collab/75138/nav/534938

The cerebellum model has reached maturity and has been used in large-scale closed-loop controllers. For the first time, a tandem model of the cerebellum (forward + inverse cerebellar modules) has been implemented by means of a realistic point-neuron Spiking Neural Network, embedded with distributed plasticity. The model is being already tested in closed-loop protocols, with the perspective to integrate the cerebellum modules with simplified cortical modules (for motor planning and motor actuation).

Sensorimotor signals are integrated and processed by the cerebellar circuit to predict accurate control of actions. To investigate how single neuron dynamics and geometrical modular connectivity affect cerebellar processing, we have exploited an olivocerebellar Spiking Neural Network with advanced point neuron models capturing essential non-linear neuronal dynamics.

Distributed long-term plasticity has been introduced at multiple synaptic sites (a cerebellar circuit property called "distributed plasticity"); in the scaffold configuration, at multiple connection sites, the synaptic strengths are modulated through bidirectional (long-term potentiation and depression) learning rules.

The cerebellar circuits have been inserted into loops and receive input signals coding both the system status information and sensory or motor attentional/error signals driving the plasticity. The architecture is modular, including the cerebellum working both as forward and inverse model. To interface the cerebellar spiking networks with other control blocks, encoding and decoding strategies have been designed. In particular, in closed-loop testing protocols, sensory feedback and intentional planning signals are converted into spike patterns and fed to the neural structures; while, the spiking network outputs are sent as actuation commands to a peripheral system (eventually a neurorobot). The scaffold model has been split to geometrically define adjacent micro-complexes, to topographically segregate information on matching sensory and motor signals (e.g. target overshooting and agonist corrective commands, or target undershooting and antagonist corrective commands). The inputs to the network come through the mossy fibres, which branch into the granular layer. The connectivity principles let spontaneously emerge areas of consistent incoming signals.

One protocol-dependent control system has been designed: the learning is driven by the cerebellar activity evolving along task repetitions. The behaviour emerges from network dynamics. We emulate a pointing task perturbed by prismatic glasses, including into the control system abstract cerebral cortex modules and multiple instances of the cerebellar model. The latter allows to achieve complementary processing able to predict a sensory discrepancy and compensatory motor commands. Therefore, the cerebellum works as a general-purpose massive predictive machine in whole-brain modular systems.

The results are on the BSP at https://collab.humanbrainproject.eu/#/collab/1655/nav/66856 and on the Neurorobotic Platform (NRP) at https://collab.humanbrainproject.eu/#/collab/79149/nav/535740; the results have been showcased at the Athen's Open Day and Summit (Cerebellar modular circuit into an adaptive control system, Antonietti *et al.* 2020, P1557) and presented at the CodeJam#10 (Integrating virtual brains with virtual bodies. Simulated robots for closed-loop *in-silico* experiments", event contribution 2182).

3.1.1   Output 2: Neocortex

Table 2: Output 2 links

Component	Link to	URL
C1670	Software Repository	https://github.com/AllenInstitute/sonata
	Technical Documentation	https://github.com/AllenInstitute/sonata/blob/master/docs/SONATA_DEVELOPER_GUIDE.md
	User Documentation	https://doi.org/10.1371/journal.pcbi.1007696 (P2184)

Component	Link to	URL
C3132	Software Repository	https://bbp.epfl.ch/public/simulationapp/index.html#/circuits/mouse_ncx_hbp_microcircuit https://github.com/bluebrain/snap https://github.com/BlueBrain/SimulationRunner/ https://github.com/blueBrain/DMT
	Technical Documentation	https://bbp.epfl.ch/public/simulationapp/index.html#/circuits/mouse_ncx_hbp_microcircuit https://github.com/bluebrain/snap https://github.com/BlueBrain/SimulationRunner/ https://github.com/blueBrain/DMT
	User Documentation	https://bbp.epfl.ch/public/simulationapp/index.html#/circuits/mouse_ncx_hbp_microcircuit https://github.com/bluebrain/snap https://github.com/BlueBrain/SimulationRunner/ https://github.com/blueBrain/DMT
C3137	Software Repository	https://github.com/orena1/neuron_reduce
	Technical Documentation	https://github.com/orena1/neuron_reduce
	User Documentation	https://www.nature.com/articles/s41467-019-13932-6 (P2295) https://humanbrainproject.github.io/hbp-bsp-live-papers/2020/amsalem_et_al_2020/amsalem_et_al_2020.html

This Output focuses on the improvement of the use of models. The specific contributions entail:

1) advancement of the open file format for networks of simplified and detailed neurons, SONATA (C1670), which has now been published (P2184)

2) creation of an online use case allowing *in silico* experimentation on the mouse neocortical microcircuit as a service (C3132) and open sourcing of a Network and Simulation Analysis Productivity framework (Blue Brain SNAP) that supports SONATA and allows powerful analysis of network models and a validation suite for Data-Model-Test (DMT)

3) peer-reviewed publishing (P2295) and open sourcing of the Neuron reduce method (C3137) and platform integration as a live paper with online use case.

3.1.3   Output 3: Hippocampus

Table 3: Output 3 links

Component	Link to	URL
C3133	Model Repository	1- https://kg.ebrains.eu/search/instances/Model/2d5ecf4a-2962-4a04-a42d-4a680664bea0 2- https://kg.ebrains.eu/search/instances/Model/92cec93d952a201a53b84eb31fa3b842
	Technical Documentation	3- https://collab.humanbrainproject.eu/#/collab/1655/nav/66854 (online use case - single cells) 4- https://collab.humanbrainproject.eu/#/collab/1655/nav/66855 (online use case - paired recordings) 5- https://collab.humanbrainproject.eu/#/collab/1655/nav/66856 (online use case - *in silico* exp on circuit) 6- https://collab.humanbrainproject.eu/#/collab/1655/nav/66858 (online use case - validation)
	User Documentation	7- https://www.humanbrainproject.eu/en/brain-simulation/hippocampus/

		8- https://humanbrainproject.github.io/hbp-bsp-live-papers/2018/migliore_et_al_2018/migliore_et_al_2018.html (live paper)
		9- https://appukuttan-shailesh.github.io/hbp-bsp-live-papers-dev/2020/romani_et_al_2020/romani_et_al_2020.html (live paper - in preparation)
		10- https://appukuttan-shailesh.github.io/hbp-bsp-live-papers-dev/2020/saray_et_al_2020/saray_et_al_2020.html

Models of hippocampal neurons and networks were developed [7 – numbers in this Section refer to numbers in Table 3] and validated in a data-driven manner using systematic, general workflows. Morphologically and biophysically detailed models of a variety of different hippocampal cell types were built by fitting the physiological behaviour of the neurons to experimental data using advanced parameter-optimisation methods [1, 3, 8]. The models were further validated by the tests of HippoUnit, a test suite for the validation of hippocampal single cell models [6,10], which was also developed in this component. A detailed cellular-level model of the hippocampal CA1 region was then constructed based on the cellular and synaptic models using a customised version of the general workflow for brain region models in the HBP; drafting of the paper is in progress and the model is made available to the reviewers in a preview [2, 10]. A microcircuit of this CA1 model is already released for *in silico* experimentation [5] and forms a central component of the *In Silico* Experimentation MOOC that is ongoing. This output led the co-design process with SP7 to implement/improve back-end and HPC tools and services (e.g. UNICORE for launching simulations and fetching results, ICEI for resources allocation, FENIX storage to build a centralised file system accessible from the Collaboratory).

3.1.4 Output 4: Basal Ganglia

Table 4: Output 4 links

Component	Link to	URL
C3131	Model Repository	Enhanced MSN (dSPN, iSPN) models and mechanisms (Data and metadata in curation before release in KG) https://github.com/Hjorthmedh/Snudda/snudda/data/cellspecs/dspn https://github.com/Hjorthmedh/Snudda/snudda/data/cellspecs/ispn https://github.com/Hjorthmedh/Snudda/snudda/data/cellspecs/mechanisms
	Technical Documentation	https://senselab.med.yale.edu/modeldb/ShowModel.cshtml?model=237653#tabs-1 (ModelDB)
	User Documentation	https://collab.humanbrainproject.eu/#/collab/376/nav/3413 https://humanbrainproject.github.io/hbp-bsp-live-papers/2018/lindroos_et_al_2018/lindroos_et_al_2018.html (live paper)
C3134	Model Repository	Striatal microcircuit simulation (Data and metadata in curation before release in KG) https://github.com/Hjorthmedh/Snudda/
	Technical Documentation	https://collab.humanbrainproject.eu/#/collab/9102/nav/312979 https://collab.humanbrainproject.eu/#/collab/376/nav/3413 https://collab.humanbrainproject.eu/#/collab/7598/nav/57859
	User Documentation	https://collab.humanbrainproject.eu/#/collab/376/nav/3413

This Output focuses on simulation at the striatal cellular/microcircuit level, in which the molecular/subcellular and systems levels meet. Enhanced models of the striatal projection neurons, SPN (same as medium spiny neurons, MSN), are developed together with low threshold-spiking, LTS, and cholinergic, ChIN, interneuron models which are new for this study. We present for the first

time a nearly full-scale model of the mouse striatum using available data on synaptic connectivity, cellular morphology and electrophysiological properties to create a microcircuit mimicking the real network. A striatal volume is populated with reconstructed neuronal morphologies with appropriate cell densities, and then we connect neurons together based on appositions between neurites as possible synapses and constrain them further with available connectivity data. Moreover, we simulate a subset of the striatum involving 10,000 neurons, with input from cortex, thalamus and the dopamine system, as a proof of principle. Simulation at this biological scale should serve as an invaluable tool to understand the mode of operation of this complex structure. This platform will be updated with new data and expanded to simulate the entire striatum.

3.2   Validation and Impact

The Hackathon on cerebellum modelling (Pavia, Italy, 13-15 January 2020) counted 63 participants from all over the HBP and outside as indicated in Table 5, (see Figure 1).

Table 5: number of participants at the Hackathon on Modelling the Cerebellum

Country	Institutions	Number of participants
Italy	UNIPV, CNR, SSSA, POLIMI, CINECA	39
Spain	UPM, UGR	5
Sweden	KI, KTH	4
Switzerland	EPFL, CSCS	4
Japan	University of electro-communication Tokyo	3
Germany,	Juelich	2
Israel	HUJI, Tel-Aviv University	2
UK	Manchester University	2
France	AMU	1
The Netherlands	ERASMUS-MC	1

The event alternated presentations and tutorials with hands-on experience guided by expert scientists in the field (links to program[2] and to talks and tutorials[3]) illustrating multiscale modelling techniques and applications. These included the use of pyNEST, pyNEURON and TVB with illustration of examples running on the BSP and (NRP). The event was quite successful in creating and consolidating working groups (single neuron modelling, microcircuit scaffold modelling, cerebellum modelling, hippocampus modelling, NEURON development, NEST development, ARBOR development, HPC implementation, large-scale circuit modelling, TVB modelling and applications, neurorobotics, neuromorphic computing) forming the core of a scientific community working around the HBP aims. The message passed nicely demonstrating the maturity of the HBP modelling system and infrastructure.

The focus on cerebellum allowed to illustrate specific use cases but also to extend them to a general modelling scheme applicable to other brain structures including the hippocampus, basal ganglia and cerebral cortex and to large scale networks and the whole brain. This last step is illustrated by the introduction of cerebellar microcircuit models into large-scale closed-loop controllers (collaborations with the Partnering project CEREBNEST), in robots (collaboration with UGR and ISSA) and in TVB (collaboration with CNRS Aix-Marseille) and neuromorphic computers (collaboration with University of Manchester).

Very useful also was the consolidation of the working groups (see above) that have made the point on the ongoing works, from cellular level up to whole brain models, with identification of problems and elaboration of possible solutions to run them on BSP, NRP and TVB. The Hackathon was streamed

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[2] https://flagship.kip.uni-heidelberg.de/jss/HBPm?m=showAgenda&meetingID=198
[3] https://collab.humanbrainproject.eu/#/collab/77410/nav/524057

and has been recorded in full in digital format at the Hackathon on Cerebellum Modelling collab (https://collab.humanbrainproject.eu/#/collab/77410/nav/524402).

Figure 2: Participants in Hackathon on cerebellum modelling

3.2.1   Actual and Potential Use of Output(s)

Output 1 cerebellum: the modular cortico-cerebellar circuit has spread over the HBP providing an interesting use case for different Platforms: the BSP (where the cortico-cerebellar model can be directly launched by the users, eventually exploiting UNICORE HPC resources) and the NRP (where the same cortico-cerebellar model can be used to test adaptation in different closed-loop protocols). The developed models can be used by both users external to the HBP Consortium, through an easy access provided by the BSP and NRP, and by other HBP partners.

Output 2 Neocortical Microcircuit: the functionality used for the sharing large scale network models of simplified and detailed neurons, SONATA, is already used by other groups. In particular, the Allen Institute for Brain Science has released network models of visual cortex in this format. Furthermore, the mouse neocortical microcircuit is featured in different use cases of the Brain Simulation Platform.

Output 3 Hippocampus: the hippocampal single cell models, microcircuit and CA1 region circuit are featured in multiple online use cases in the Brain Simulation Platform. Furthermore, the hippocampal microcircuit is a centre point on the newly generated massive open online course (MOOC) on *In silico* experimentation using the HBP Brain Simulation Platform (hosted by EPFL) that is in final stages of preparation.

Output 4 Basal Ganglia: the model of the striatum is presented in a live paper and awaiting further exploitation. Models of the striatal projection neuron with dopaminergic modulation are available in a live paper. Single cell model optimisation workflow is illustrated in BSP on the example of the fast-spiking interneuron. All underlying experimental data is shared via KG infrastructure. Data and models are used in neuroscience and biomodelling courses for engineers (DD2401 and DD2435, KTH Royal Institute of Technology).

3.2.2   Publications

P2184 The SONATA data format for efficient description of large-scale network models. Dai K, Hernando J, Billeh YN, Gratiy SL, Planas J, Davison AP, Dura-Bernal S, Gleeson P, Devresse A, Dichter BK, Gevaert M, King JG, Van Geit WAH, Povolotsky AV, Muller E, Courcol JD, Arkhipov A. PLoS Comput Biol. 2020 Feb 24;16(2): e1007696. doi: 10.1371/journal.pcbi.1007696.

P2023 Response Dynamics in an Olivocerebellar Spiking Neural Network With Non-linear Neuron Properties Geminiani A, Pedrocchi A, D'Angelo E, Casellato C 2019-10-01 Frontiers in Computational Neuroscience, Vol. 13 2417 http://dx.doi.org/10.3389/fncom.2019.00068

P2112 The Amyloid Precursor Protein C-Terminal Domain Alters CA1 Neuron Firing, Modifying Hippocampus Oscillations and Impairing Spatial Memory Encoding Pousinha PA, Mouska X, Bianchi D, Temido-Ferreira M, Rajão-Saraiva J, Gomes R, Fernandez SP, Salgueiro-Pereira AR, Gandin C, Raymond EF, Barik J, Goutagny R, Bethus I, Lopes LV, Migliore M, Marie H 2019-10-08 Cell Reports, Vol. 29, No. 2 http://dx.doi.org/10.1016/j.celrep.2019.08.103

P2110 The subthreshold-active KV7 current regulates neurotransmission by limiting spike-induced Ca^{2+} influx in hippocampal mossy fiber synaptic terminals Martinello K, Giacalone E, Migliore M, David A. Brown, Mala M. Shah 2019-04-26 Communications Biology, Vol. 2, No. 1 http://dx.doi.org/10.1038/s42003-019-0408-4

P1866 A kinetic model for Brain-Derived Neurotrophic Factor mediated spike timing-dependent LTP Solinas S, Edelmann E, Leßmann V, Migliore M., Article in Journal 2019-04-24PLOS Computational Biology, Vol. 15, No. 4 http://dx.doi.org/10.1371/journal.pcbi.1006975

P2489 (*in press – will be published in SGA3*) Hjorth, J., Kozlov, A., Carannante, I., Frost Nylén, J., Lindroos, R., Johansson, Y., Tokarska, A., Dorst, M. C., Suryanarayana, S. M., Silberberg, G., Hellgren Kotaleski, J., & Grillner, S. (2020). The microcircuits of striatum in silico. Proceedings of the National Academy of Sciences of the United States of America, 202000671. Advance online publication. https://doi.org/10.1073/pnas.2000671117

4.   Conclusion and Outlook

By exploiting the case of building a cerebellar model, we have provided a full pipeline of multiscale model construction, simplification and application that extends from data acquisition to realistic and simplified neuron models and to the generation of a scaffold strategy for microcircuit reconstruction. This has allowed to propagate molecular and cellular properties through the network, to embed plasticity and to generate closed-loop controllers that have been applied to simulated and physical neurorobots. Finally, appropriate model transformations are now used to generate SpiNNaker neuromorphic hardware of the cerebellum and cerebellar neural masses for large-scale brain simulators (TVB). All these activities have been integrated into the BSP and NRP as an anticipation of the future EBRAINS. The generalisation of this pipeline to include the hippocampus, basal ganglia and neocortex is in progress and will be fully developed in WP1 and WP3 of SGA3.

As a whole, we believe that CDP2 has substantially contributed to expand HBP activities, to coordinate experimental research with modelling, to implement modelling and data-processing workflows, and to gather the interest of the scientific community around the HBP targets. By bridging science and technology, CDP2 has provided substantial feedback from models toward experimental data sampling. CDP2 has given substantial support and feedback for platform implementation and refinement, especially for the Brain Simulation Platform and the Neurorobotic Platform. CDP2 has promoted and participated in:

- The Partnering Projects (cerebNEST), which implements the neurorobotic controllers generated in CDP2

- The Voucher Project VM-cerebNEST, that expands the cerebellum scaffold networks to a whole cerebellar network mapped onto the Allen Brain Atlas

- The Voucher SpinnCer, which generates a SpiNNaker version of the cerebellum scaffold.

- The FLAG-ERA project "NeuronsReunited", which analyses in detail cerebello-thalamo-cortical connectivity for extended brain simulators.

- The ETN project "Cerebellum and Emotional Networks" (CEN), which analyses the experimental and modelling underpinning of cerebellar control of emotional responses.

- The 7 new Vouchers that have been approved for SGA3: BOLD signal reconstruction and simulation from cellular data-driven models (BOLDsim); Enhanced mouse atlas for cerebellar connectivity (ATLAS-cer); SODIUM signal reconstruction and simulation from cellular data-driven models (SODIUMsim); Integration of NetPyNE into EBRAINS Platform (EBRnetpyne); Multiscale Mathematical Modeling: from Neurons to Networks (M3N2); Integrating a Multimodal Olfactory Bulb Model into EBRAINS (INDOME); Modeling Synaptic Plasticity in the Hippocampal Trisynaptic Circuit: Integration to the Brain Simulation Platform (HippoTrisynPlasticity).

CDP2 has effectively promoted dissemination of the multiscale modelling strategies of the HBP through a series of initiatives including:

- The international courses on Brain Modelling by the Center Ettore Majorana in Erice (Italy)

- The Hackathon on Cerebellum modelling in Pavia (Italy).

As such, it has been gathering the scientific community around core themes like multiscale brain modelling. Through these actions, CDP2 has substantially contributed to put the seeds for future developments of HBP activities, in SGA3 and beyond.

CDP2 has extended the validity of the HBP Modelling/Simulation approach for integrating neuroscience research and technological development. This has required a continued coordination of data production in SP1 and modelling in SP6 to fuel single neuron and *in silico* microcircuit experimentation integrated on the Brain Simulation Platform and the Neurorobotic Platform. Moreover, CDP2 has remarkably extended its interaction with the external community through dissemination, outreach initiatives and collaboratories. CDP2 has therefore continued to implement and extend the concept of multiscale brain organisation and modelling through a bottom-up approach that is now integrating with system theory and top-down inferences coming from integrated brain signals analysis, further applying the models to large-scale brain simulations, neurorobotics and neuromorphic computing.