CDP2 Annual Compound Deliverable Year 1 (M12) (D6.2.1 – SGA2)

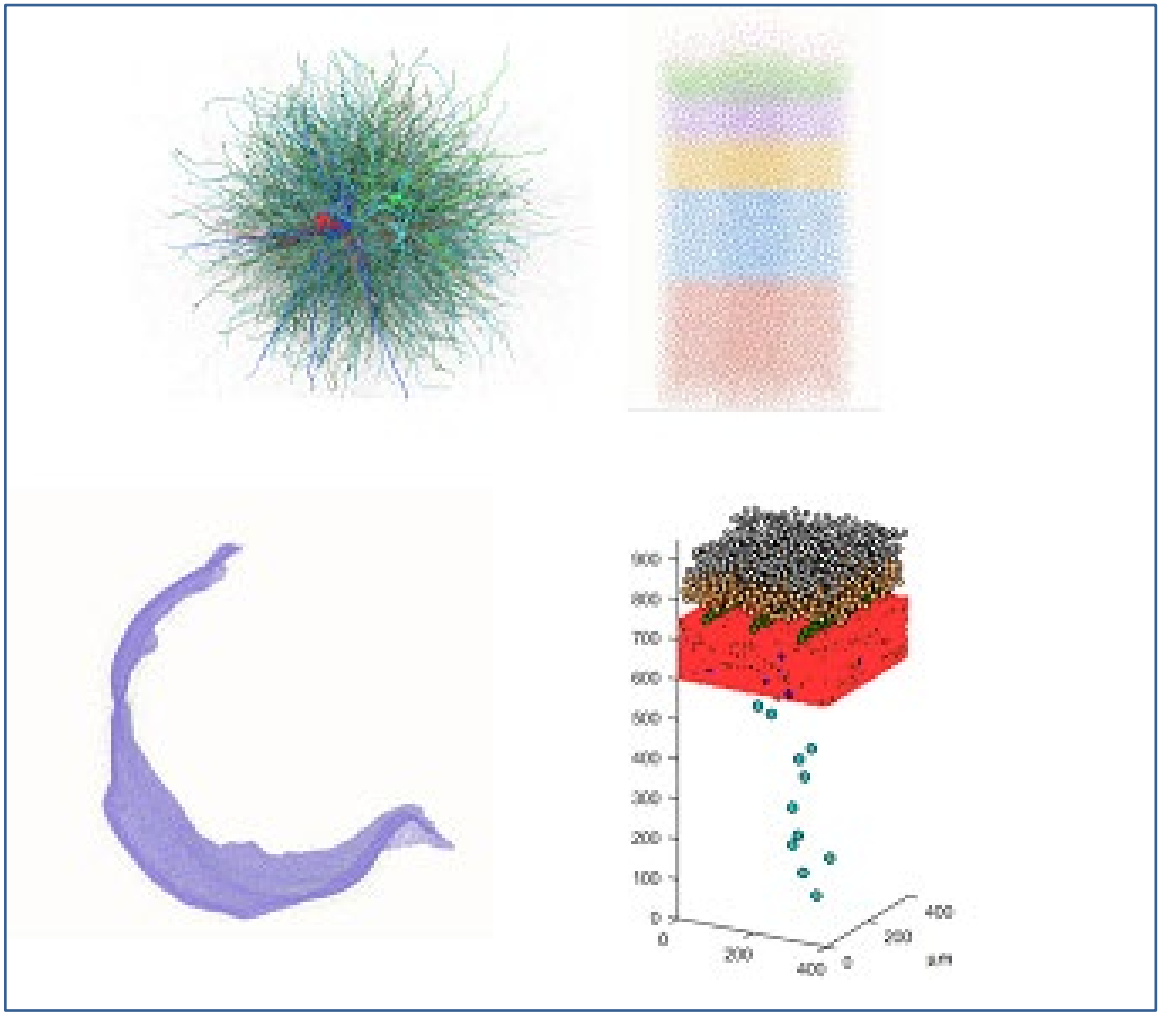

Figure 1: Scaffold models of the four brain regions (cerebellum, striatum, neocortex and hippocampus)

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Description in GA:	Overview of key results and impact achieved in M1-M12, tailored for presentation to the relevant audiences (research/industry/public). References to HBP/SP/CDP objectives and use cases for navigation between multiple Subprojects. Linkage of results to components/a set of component factsheets (lower-level information: component ownership, technology readiness level, performed quality control checks, etc.). *For consistent presentation of HBP results, SGA2 M12 Deliverables describing the accomplishments of an entire SP 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 Year 1 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

CDP2 Mouse-Based Cellular Cortical and Subcortical Microcircuit Models fully addresses platform implementation and testing for multiscale simulations of spatio-temporal dynamics and plasticity as a scientific driver for the main brain microcircuits (neocortex, cerebellum, basal ganglia, and hippocampus). So far, the main results of this Co-Designed Project are the definitions of schemas for simplified circuits in the HBP Knowledge Graph. The data-driven circuit descriptions have been made compatible with the last release of PyNN with the help of the SONATA file format, thus supporting the simulation pipeline.

The cerebellar network has been adapted for incorporation into large-scale loops. Plasticity rules of the cerebellum microcircuit have been developed, embedded into the scaffold and applied to virtual neurorobots, resulting in a publication from Antonietti *et al*. This pipeline will be applied to basal ganglia and the hippocampus.

The models are based on molecular/cellular mechanisms and allow bottom-up detailed biophysical reconstructions of neurons and microcircuits of the mouse brain. The microcircuit models are assembled into interconnected networks allowing large-scale simulations up to whole-brain. The neuron models are simplified in order to be embedded into robotic controllers. CDP2 supports a multiple fall-out at the level of brain modelling, theoretical understanding of brain function and infrastructure implementation. CDP2 is intended to generate a reference frame for data-driven modelling applied to a broad field of HBP users including simulation of brain states and pathological mechanisms, robotic applications and neuromorphic hardware. CDP2 is also intended to extend the use of the Brain Simulation Platform capabilities to the external community through the Collaboratories.

2. Introduction

Mouse-Based Cellular Cortical and Subcortical Microcircuit Models are progressing through co-design of experimental activity with modelling and platform implementation. This work covers the multiscale data-driven reconstruction and testing of the four main brain microcircuits: cerebral cortex, cerebellum, basal ganglia and hippocampus. During the first year of the project, the core activity has been to integrate subcellular mechanisms into neuronal models and to bring them up to the level of entire microcircuits and whole brain. The main goals have been to explore the impact of neuronal dynamics and plasticity in the main microcircuits and the whole brain using models and their robotic implementations.

The main focus of CDP2 is summarised in three Key Results.

- The first two of them (KR6.1 “Multi-scale models of plasticity” and KR6.2 “Scaffold models of brain regions/whole brain ready for community use”) are implemented directly through the Brain Simulation Platform (SP6) and are described in the SP6 Deliverable D6.1.1.
- The third one (KRc2.3 “Demonstrating microcircuit activity in closed-loop neurorobotic simulation with learning”) is described here.

This Deliverable is based on the last version of the workplan for CDP2, which is currently under revision as part of Amendment 2.

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 and the development of plasticity during trial-and-error learning. This concept has been exemplified in Figure 2, where starting from a realistic model, a simplified microcircuit has been developed and embedded into a large scale network in a closed loop simulation.

An exemplar case is provided by a series of works on cerebellum models. The cerebellum scaffold model is complete (https://www.biorxiv.org/content/10.1101/532515v1) and validated (Tognolina M, Casali S, D'Angelo E, *in preparation*). New simplified single-point versions of the multi-compartmental neuron models have been produced in order to maintain non-linear second-order dynamics (Geminiani A *et al.*, 2018). The scaffold with these simplified neurons has been embedded into robotic controllers for closed-loop simulations of motor control and of its pathologies (Antonietti A *et al.*, 2018; Geminiani A *et al.*, 2018). The extension of these closed-loop controllers toward integration of cortex, basal ganglia and hippocampus and the implementation of cognitive architectures (D'Angelo E, 2019) is under development.

The integrated modelling/ experimental/ robotic approach of KRc2.3 is providing a strong scientific driver for platform implementation, refinement of informatics tools and co-design of science and infrastructure activities. Moreover, the work involves large-scale network simulations based on converging PRACE and ISCRA-B supercomputing projects and provides the basis to extend modelling through the collaboratory and the Brain Simulation Platform.

In summary, KRc2.3 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. These results are presented in the papers mentioned above and have been presented during many outreach events that are illustrated in the next pages.

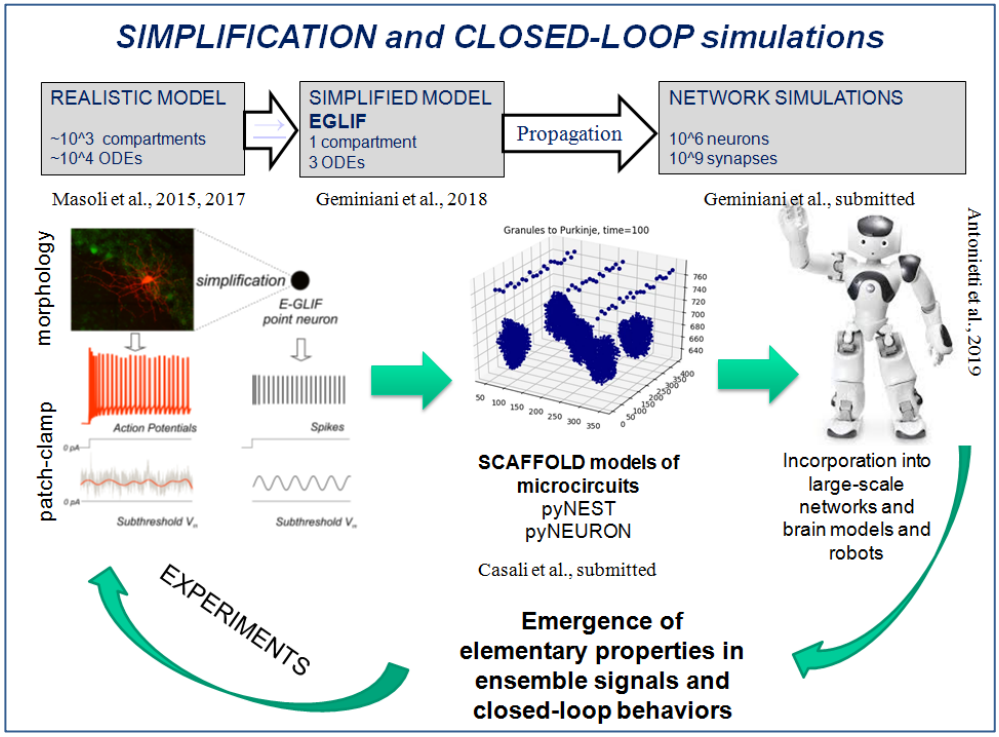

Figure 2: Simplification and closed loop simulations

3.1 Outputs

3.1.1 Overview of Outputs

3.1.2 Neocortex

The work on the cerebral cortex model has been intended mostly to provide specific tools and pipelines for microcircuit modelling. Following a previous paper that published a simplification method (Roessert *et al.*, 2017), the current focus is on automation of this process. A tangible outcome so far has been the definition of schemas (SHACL) for simplified circuits in the HBP Knowledge Graph (the schemas definitions are publicly available under https://github.com/INCF/neuroshapes and the 1.0.3RC release, Feb 5, 2019; INCF International Neuroinformatics Coordinating Facility). The SP6 data-driven circuit descriptions have been made compatible with PyNN (PyNN v0.9.3 (http://neuralensemble.org/docs/PyNN/releases/0.9.3.html) with the help of the SONATA file format (https://github.com/AllenInstitute/sonata). This allows point-neuron network models in SONATA format to be loaded by PyNN, simulated with NEST, NEURON, SpiNNaker, etc., and then the results saved in the SONATA data report format. It also allows models and simulation plans defined as a PyNN script to be exported in SONATA format and hence simulated using any SONATA-supporting simulation pipeline.

3.1.3 Cerebellum

A new tool for model simplification has been developed (E-GLIF) in collaboration with cerebNEST (Geminiani *et al.*, 2018).

A new tool for constructing scaffold models has been developed and initially tested on the cerebellum microcircuit (https://www.biorxiv.org/content/10.1101/532515v1).

The cerebellar network has been adapted for incorporation into large-scale loops. Plasticity rules of the cerebellum microcircuit have been developed, embedded into the scaffold and applied to virtual neurorobots in collaboration with the partnering project cerebNEST (Antonietti *et al.*, 2018, 2019).

3.1.4 Hippocampus and basal ganglia

The main outputs for these two brain regions are the live papers on the Brain Simulation Platform (https://collab.humanbrainproject.eu/#/collab/1655/nav/306845).

3.2 Validation and Impact

3.2.1 Actual Use of Output(s) / Exploitation

The exploitation of outputs is documented by the interest that the CDP2 strategy is raising in the HBP community. The SP6 Partnering Project cerebNEST is transforming and transferring the cerebellum scaffold models into neurorobotic controllers and this, of course, fully engages the collaboration with CDP2 for the implementation of the cerebellar microcircuit. This operation has led to the essential demonstration that the main theory for motor control, the Motor Learning Theory by Marr-Albus-Ito, finds a precise correspondence in bottom-up reconstructions of the cortico-cerebellar loops in robotic settings and can be extended by adding numerous forms of plasticity not predicted by theory but discovered later on (reviewed by Mapelli *et al.*, 2015; D'Angelo *et al.*, 2015; Luque *et al.*, 2016). CDP2 results will be implemented also thanks to two new Voucher projects that will further extend its output during the second phase of SGA2. One Voucher project is "Virtual Mouse

cerebNEST" (VM-cerebNEST) that will allow extending the cerebellum scaffold model to full scale (35 M neurons) and to configure it according to the Allen Brain Atlas data-set. The other Voucher project is "Neuromorphic hardware simulations of cerebrocortical-cerebellar loop" (SpinnCer) that aims at implementing the currently available cerebellar models written in pyNEST into pyNN and then in SpiNNaker, in order to run the first neuromorphic hardware simulations of the cerebrocortical-cerebellar loop.

The expected outcome will be to simulate neuronal activity of the cerebro-cerebellar loops through the use of brain inspired hardware and to evaluate possible neurorobotic applications. Through the use of the parallel SpiNNaker platform, a consistent acceleration is expected and this will allow increasing the number of the involved cells making the simulations more significant and realistic. The target of the project, in fact, relates to the realism of the models simulated: the more they are realistic, the greater will be the inferences that can be taken.

This work will exploit the Joint Platform system (in particular the Neuromorphic Platform and the Brain Simulation Platform) providing the first example ever of a brain loop transferring realistic neuronal properties into hardware reproducing a major brain loop rather than a single brain region.

The direct applicability in HBP is related to SP10 and CDP2 experimentation for real-time acceleration of spiking robotic controllers. A more sophisticated use is expected for those interested in the simulation of continuous brain processing. Potential Use of Output(s)

With the continuation of SGA2, the work of CDP2 will advance toward full-scale implementation of the cerebellar scaffold, integration of the scaffold into robotic controllers and transformation into neuromorphic hardware. This will allow the models pursued by the HBP to be further used in several ways. We are aiming to involve external groups into the Voucher programs, FLAGERA projects (2 already submitted on cerebellum modelling and 2 on hippocampus modelling), ETN projects (1 submitted on cerebellum modelling). These groups will aim to exploit the HBP platform system for modelling aspects related to fundamental physiological research, biomedical applications, neuroengineering and robotics.

This work is intended to pave the road for broader applications toward more advanced software and hardware simulators involving the basal ganglia and the hippocampus in order to achieve integrated motor control systems and, in a future perspective, also cognitive control systems. The perspective is to generate workflows and hardware of broad applicability in the biomedical and technological fields.

3.2.2 Publications

The main publications of this Key Result are:

P1639 D'Angelo E. The Cerebellum Gets Social. Science 18 Jan 2019: Vol. 363, Issue 6424, pp. 229 DOI: 10.1126/science.aaw2571.

P1580 Geminiani A, Casellato C, Locatelli F, Prestori F, Pedrocchi A, D'Angelo E. Complex Dynamics in Simplified Neuronal Models: Reproducing Golgi Cell Electroresponsiveness. Front Neuroinform. 2018 Dec 3;12:88. doi: 10.3389/fninf.2018.00088. eCollection 2018.

P1647 Antonietti A., Martina D., Casellato C., D'Angelo E. and Pedrocchi A., "Control of a Humanoid NAO Robot by an Adaptive Bioinspired Cerebellar Module in 3D Motion Tasks," Computational Intelligence and Neuroscience, vol. 2019, Article ID 4862157, 15 pages, 2019. https://doi.org/10.1155/2019/4862157.

3.2.3 Measures to Increase Impact of Output(s): Dissemination

In September 2018, CDP2 has co-organised the Brain Simulation Platform - HBP School in Palermo (Italy). The aim of the School was to introduce participants to the Brain Simulation Platform (BSP)

of the Human Brain Project (HBP), with the main aim to train users on how to exploit the possibilities offered by the Platform to implement cellular level computational models, to use High Performance Analytics and Computing Platform systems to configure and run a simulation, and to visualise/analyse the results.

A maximum of 50 participants has been selected in a competitive application process based on an academic decision by the Scientific Chair and the HBP Education Programme.

Figure 3: pictures from the Brain Simulation Platform School in Palermo (Italy)

In December 2018, CDP2 has co-organised the fourth course of the School of Brain Cells & Circuits "Camillo Golgi" by the Ettore Majorana Foundation and Centre for Scientific Culture, Erice (Italy). The course focused on “The Neural Bases of Action – from cellular microcircuits to large-scale networks and modelling” and was preliminary to the CDP2 aim of integrating the main brain circuit to generate motor and cognitive control. The course directors for this year were Egidio D’ANGELO, Claudia GANDINI WHEELER-KINGSHOTT & Sten GRILLNER. The course had 80 attendees from all over Europe and outside of Europe. It was dedicated to multi-scale investigation and modelling of the motor system. Motor control is a fundamental function that characterises the animal kingdom and has driven brain evolution toward cognition. Therefore, understanding motor control is a fundamental step for understanding how the whole brain is organised and operates. The fundamental brain structures of vertebrates that are involved were covered in turn, including the cerebral cortex, basal ganglia, cerebellum, brainstem and spinal cord. Special attention was also given to pathologies emerging from dysfunctions of the motor system. Different aspects of the motor control were addressed at the level of cellular physiology, computational modelling and integrated brain signals using electrophysiological techniques and magnetic resonance imaging. Mathematical modelling was emphasized for its special effectiveness in tackling motor control problems and for explaining the function of the system across multiple complexity scales. By bringing together these communities and offering advanced teaching sessions and discussion panels on key topics, the course will foster future research in the field and will make a strong methodological case on how to combine experimental and modelling approaches in order to explain how the brain works (all outputs were showcased).

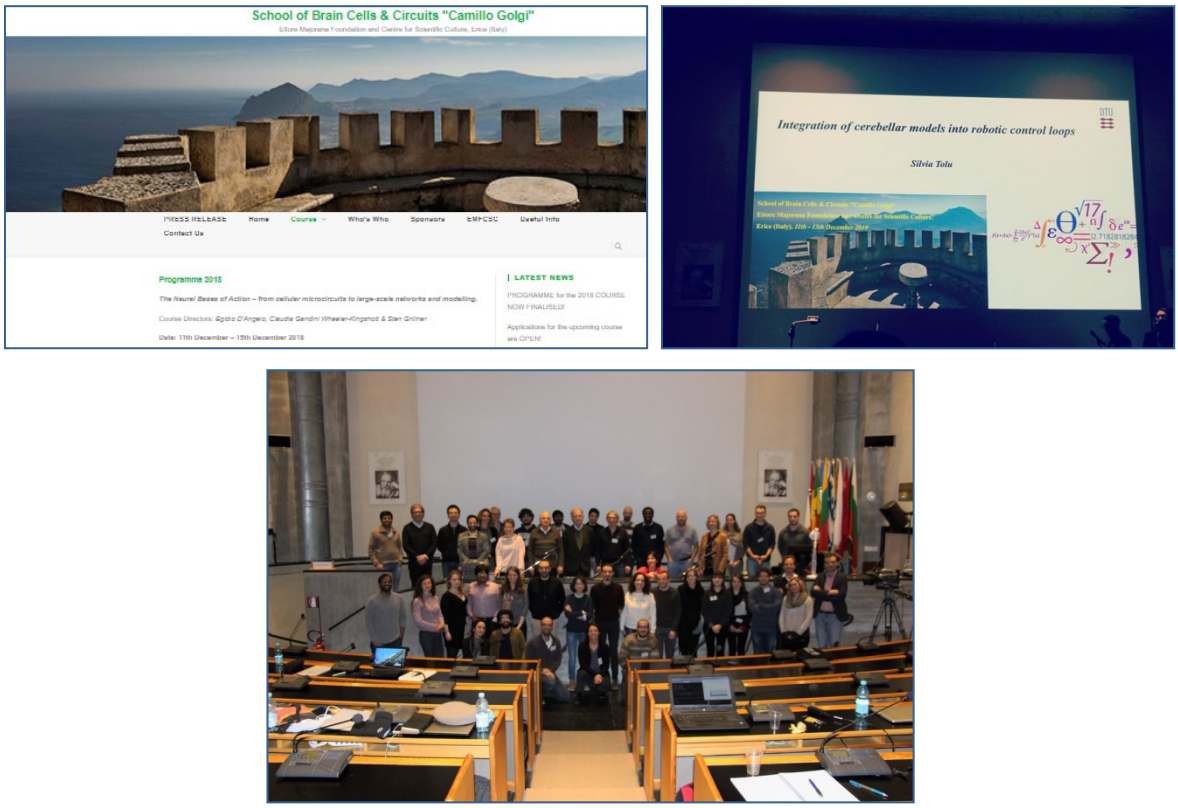

Figure 4: picture of the 2018 Erice Golgi School (The Neural Bases of Action - from cellular microcircuits to large-scale networks and modelling)

In January 2019, a Hackathon was organised in Geneva with participants of SP5, SP6 and SP10, to work out their respective schemas and to create a Joint Platform use case that includes a simplified model exchange with the Neurorobotics Platform.

Figure 5: a tweet from the Brain Simulation Platform on the Hackathon in Geneva

In July 2018, members of CDP2 participated in the 2nd HBP Curriculum Workshops Series, an ICT course for non-specialists: "Neuroscience for ICT: application to computation and robotics" (4-6 July 2018, Kalkscheune Berlin, Germany). Egidio D'ANGELO (UNIPV) and Carmen LUPASCU (CNR) were speakers of the session: “Bridging the gaps: computation and neuroscience - neuroscience and computation I and II”.

Three new CDP2 meetings are in preparation for the second year of SGA2, a Hackathon and a MOOC on Cerebellum modelling and the new ERICE course on BRAIN MODELLING.

Figure 6: CDP2 speakers at the 2nd HBP Curriculum workshops Series

4. Conclusion and Outlook

Conclusions

As a whole, 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 is providing substantial feedback from models toward experimental data sampling. CDP2 is giving substantial support and feedback for platform implementation and refinement, especially for the Brain Simulation Platform. CDP2 has promoted Partnering Projects (cerebNEST) and Voucher Projects (VM-cerebNEST and SpinnCer), as well as the submission of FLAG-ERA and ETN projects. CDP2 has promoted dissemination courses, including the ERICE and Palermo courses, CDP2 gathering the scientific community around core themes like multiscale modelling. Through these actions, CDP2 is substantially contributing to put the seeds for future developments of HBP activities, in SGA3 and beyond.

Outlook

In perspective, CDP2 will extend the validity of the HBP Modelling/Simulation approach for integrating neuroscience research and technological development (see SGA2 Grant Agreement). This will require a continued coordination of data production in SP1 and modelling in SP6 to fuel single neuron and *in silico* microcircuit experimentation integrated on the Joint Platform. Moreover, CDP2 will extend its interaction with the external community through dissemination, outreach initiatives and collaboratories. CDP2 will therefore continue to implement and extend the concept of multiscale brain organisation and modelling through a bottom-up approach, further extending its implications in large-scale brain simulations, neurorobotics and neuromorphic computing.