Systems and Cognitive Neuroscience - Results for SGA2 Year 1 (D3.6.1 – SGA2)

Figure 1: Generating new hypotheses for cognition based on the power of real neurons

An artist's impression of "apical amplification in human and rodent pyramidal neurons", one of the key outputs of SGA2 (T1.3.1). This relates to a unifying hypothesis for the operation of the cortex based on the active properties of the dominant neuronal cell type in the cortex, the pyramidal neuron. Artwork by Thomas SPLETTSTOESSER (SciStyle).

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Description in GA:	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:	The Subproject 3 (SP3) of the Human Brain Project is devoted to provide data, models and tools to understand important cognitive processes such as memory, sleep and consciousness, from the microscopic level in rodents to the human behaviour. This Deliverable brings the currently available outputs.
Keywords:	Multisensory processing, perception, memory, context-dependent visual recognition, cognitive architecture, sleep, consciousness.
Target Users/Readers:	Neuroscientific community, neuroscientists, platform users, researchers, students, computational neuroscience community, consortium members, clinicians and the general public.

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1. Overview

The Systems and Cognitive Neuroscience Subproject of the Human Brain Project is devoted to provide data, models and tools to understand important cognitive processes, such as memory, sleep and consciousness, from the microscopic level in rodents to human behaviour.

In relation to sleep, it is known that human brains need healthy sleep, as chronic sleep deprivation reduces cognitive performances. Our aim is to unveil the underlying mechanisms of deep sleep, anaesthesia and coma and the emergence toward wakefulness. Taking advantage of cortical slow wave activity (SWA), we contribute with experimental data, analysis tools, modulation techniques, theoretical models and simulations of such states and of the transition to wakefulness.

Regarding memory, we have advanced on modelling the integration between bottom-up and top-down processes into recurrent convolutional neural networks in order to explain and predict high-resolution human fMRI data, and electrophysiological, optogenetic and 2-photon calcium imaging rodent data.

We also continued to acquire human and rodent brain imaging and rodent electrophysiological recordings in order to model episodic and spatial memory at the systems level. We are developing models of multisensory integration, spatial memory and navigation, and brain-inspired robots (i.e. a visual-tactile rodent-like robot and a humanoid robot).

Furthermore, we have been testing and developing measures of (un)conscious states *in vivo*, *in vitro*, and *in silico*, resulting in the reported advancements (both practical and theoretical). The next year will see consciousness measures defined more explicitly, standard practices developed, and measures comparisons in broad and specific terms.

Additionally, our aim is to build an overarching cognitive architecture for biomimetic agents which can perform a wide range of tasks (see the outputs of Key Result KR3.5). This architecture will be built by integrating the models of specific brain phenomenon like sleep and large-scale models with multiple cortical and subcortical regions.

2. Introduction

This Compound Deliverable addresses the main developments in the Key Results proposed in the current phase (SGA2) of the Human Brain Project. Our five work packages (WPs) - WP3.1, WP3.2, WP3.3, WP3.4 and WP3.5) have written this document to unite the available tools, data and models each of them released in this first year of SGA2.

WP3.1 studies cortical contextual processing at multiple levels of systems neuroscience (neuronal signalling, interactions between cortical layers, within cortical columns, between neighbouring areas, and between remote cortical areas). This WP has expanded the study of contextual processing beyond visuospatial and multi-sensory context to include temporal context. WP3.1 is a collaborative effort of three institutions (UGLA, KNAW, and UBER), developing a sophisticated understanding of large-scale neural interactions and network models that integrate recurrent information processing in context-sensitive object recognition. Experimental work within WP3.1 produces high-resolution human fMRI data and electrophysiological, optogenetic and 2-photon calcium imaging mouse data to inform neural network models.

WP3.2 focuses on the cortical activity during sleep and during different states of consciousness (i.e. coma or anaesthesia) that share with deep sleep the phenomenon of cortical slow wave activity (SWA). This WP also studies the transition to wakefulness and contributes to the investigation of the cognitive functions of sleep. In a joint effort of five institutions (UMIL, IDIBAPS, IBEC, ISS and INFN), WP3.2 provides HBP platforms with experimental data and tools (like simultaneous scalp high-density electroencephalography (HD-EEG) and intracranial electroencephalography (EEG) in humans, micro-electrocorticography (micro-ECOG) in mice), modulation methodologies and models at multi-scales and at different levels of sleep, anaesthesia and excitability. WP3.2 has also started the integration of data and analysis pipelines into the HBP platforms.

WP3.3 works on understanding episodic memories and their dependency on the integration of multisensory information into long-term memory. This WP is acquiring human and rodent brain imaging and rodent electrophysiological recordings, developing models of multisensory integration, spatial memory and navigation, and brain-inspired robots (i.e. visual-tactile rodent-like robot and a humanoid robot). These multi-species and multi-level data are being integrated into a theory for multisensory integration and neural compression, storage and reconstruction of memories, with the contribution of five institutions (DZNE, UCL, UVA, USFD and UWE). On this basis, we have constructed a multimodal memory system for the iCub humanoid robot that we have deployed for human-robot interaction.

WP3.4 studies the brain capability of conscious representations of the world and itself. It represents a collaboration between four institutions (UIO, UMIL, ULG and UVA) aiming at improving our understanding of neuronal mechanisms of consciousness, and developing new, theoretically driven methods for evaluation of consciousness, for both clinical and basic scientific purposes. This WP uses structural and functional brain imaging, as well as electroencephalography (EEG) and stereoelectroencephalography (SEEG, with intracranial electrodes) in humans and 2-photon imaging in animals, to record both spontaneous brain activity, responses to cortical perturbations, and sensory evoked potentials, combined with simulation of *in silico* brain network models.

WP3.5 builds neurobiologically plausible models of interconnected cognitive phenomena and develops methods to integrate these models into a single cognitive architecture for biomimetic robots that can perform a multitude of tasks. In a combined effort of five institutions (INFN, UIO, UGLA, USFD, and UVA), this WP advanced the understanding of the role of sleep in memory. WP3.5 built deep neuronal models for learning and inferring the causes of sensory inputs, developed multi-compartment network models for Artificial Intelligence (AI)-style tasks and created a generic framework for integrating different models into a comprehensive cognitive architecture. WP3.5 also contributed to an assimilation of the integrative cognitive architecture into the neurorobotics platform and developed models of specific aspects like sleep to large scale models of multiple cortical and/or subcortical regions that address higher order function like cross-modal recall in multisensory integration.

3. Key Result KR3.1 Context-sensitive vision and recognition models (DNN)

Our goal is to develop deep neural network models for visual recognition with novel context-modulation units. These units have separate integration sites for bottom-up driving input and for contextual input. They will be based on high-resolution human brain imaging and neuronal recordings (2-photon calcium and electrophysiology data from mouse somatosensory and visual cortices) relating to temporal expansion of context in neuronal computations.

3.1 Outputs

The Key Result (KR3.1) expected from WP3.1 at the end of the SGA2 period is a combination of modelling and experimental efforts, which culminates in biologically plausible, contextual processing in deep recurrent neural networks at a scale capable of tackling modern image classification tasks. This Key Result also delivers novel cross-species data, investigating key aspects of contextual processing and temporal expansion in humans (high-resolution fMRI data) and mice (electrophysiological, optogenetic and 2-photon calcium imaging data). Data differentiate processes in different cortical layers, providing fundamental insights to contextual integrative processes, and informative validation for models. These data enable testing of computational theories with human and mouse brain activity data, leading to biologically inspired contributions to computer vision and artificial intelligence.

3.1.1 Overview of Outputs

The following is a list of key outputs produced during the period M1-M12 of SGA2 (April 2018 – March 2019):

1) Output 1: Recurrent Convolutional Neural Networks (C2381, C2385)

2) Output 2: Functional MRI data aligned to Big Brain (C2381)

3.1.2 Recurrent Convolutional Neural Networks

We have expanded network models developed in the SGA1 phase to process real-world images. These networks incorporate bottom-up, lateral and top-down convolutional connections (T3.1.4: Layer-specific fMRI data of temporal predictions; C2381, C2385). Networks exhibit robust performance dominance over parameter-matched state-of-the-art feedforward control models and provide interesting theoretical and engineering implications. We are currently finalising a manuscript for submission and preprint posting. Networks will be publicly available on Github upon publication. This manuscript explores how lateral connections improve performance on scaled-up networks trained on imagenet and ecoset[1]. We show superior classification performance compared to feedforward control models, explore how RCNNs with lateral connections can trade off speed and accuracy (contributing to CDP4 through Task T3.5.1), discuss how network behaviour compares to human behaviour and how learned lateral connectivity in early layers compares to lateral connectivity in early visual areas. Models will be released publicly through Github upon publication of the descriptive manuscript. Model URLs will be announced via Twitter (@KriegeskorteLab) and featured on the HBP website (prior to October 2019). Validation will therefore be through the community.

[1] Mehrer J, Kietzmann Tim, Kriegeskorte N. Deep Neural Networks Trained on Ecologically Relevant Categories Better explain human IT. *Cognitive Computational Neuroscience 2017.* Archived at https://ccneuro.org/2017/abstracts/abstract_3000198.pdf

3.1.3 Functional MRI data aligned to Big Brain database

The MUCKLI lab at UGLA has shown that predictive information arrives at superficial layers of early visual cortex (T3.1.4: Layer-specific fMRI data of temporal predictions; C2381). Feedforward input was blocked to subsections of retinotopic visual cortex by occluding one quarter of the visual field while participants viewed 384 real-world scenes and recorded V1 responses using high-resolution 7T fMRI (0.8mm). V1 responses exhibited predictive and contextual response properties, in addition to feedforward orientation and spatial frequency properties typically associated with V1 responses. These predictive and contextual responses were primarily associated with superficial layers of the cortex. Findings suggest that feedback connections terminating in superficial layers provide V1 neurons with contextual information, not available via localised feedforward input. These experimental data contribute to CDP3 and will be integrated into a retinotopic alignment with the Big Brain atlas, allowing for comparisons between functional responses to natural stimuli and high-resolution anatomical markers in Big Brain data. Data will initially be released internally (within HBP) to validate alignment with the Big Brain. After embargo, during which experimental data will be published, data will be made available publicly through a recognised MRI repository.

3.2 Validation and Impact

3.2.1 Actual Use of Output(s) / Exploitation

The Neuroinformatics Platform (SP5/CDP3) has demonstrated retinotopic alignment of functional MRI data from the UGLA lab (Lars MUCKLI, Task T3.1.4) to the Big Brain atlas, allowing users to relate functional responses in cortical and visual space to anatomical markers already available through the atlas.

3.2.2 Potential Use of Output(s)

The addition of retinotopically-aligned responses to natural stimuli to the Big Brain will allow users to compare more specific functional properties to anatomical markers already available in the atlas. Examples include the possibility to calculate tuning properties (stimulus orientation and spatial frequency tuning) of retinotopic areas to receptor densities.

Modern AI neural networks depend primarily on feedforward connections to transform data into meaningful task representations. Since network models in first output (Recurrent Convolutional Neural Networks) are robustly dominant due to added lateral and top-down connections, networks here could have substantial impact on the AI community.

3.2.3 Publications

Data from the second Output mentioned in Section 3.1.1 (Functional MRI data aligned to Big Brain) are high-resolution, layer-specific fMRI in Primary Visual Cortex. Data will therefore allow users to examine laminar responses relating to predictive processing. The following publications relate to the function of cortical layers, predictive processing, and computational modelling of fMRI responses:

- P1357: Larkum M.E., Petro, L.S., Sachdev, R.N.S. and Muckli, L. (2018) A Perspective on Cortical Layering and Layer-Spanning Neuronal Elements. *Frontiers in Neuroanatomy*. doi: 10.3389/fnana.2018.00056
- P1356: Sterzer, P., Adams, R.A., Fletcher, P., Frith, C., Lawrie, S.M., Muckli, L., Petrovic, P., Uhlhaas, P., Voss, M., Corlett, P.R. (2018). The predictive coding account of psychosis. *Biological Psychiatry*. 84:9. p634-43. doi:10.1016/j.biopsych.2018.05.015

- P1709: Svanera M, Savardi M, Benini S, Signoroni A, Raz G, Hendler T, Muckli L, Goebel R, Valente G. (2018). Transfer learning of deep neural network representations for fMRI decoding. *BioRxiv*. doi:10.1101/535377

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

Results relating to the two outputs above were presented internationally at the 2018 Conference on Cognitive Computational Neuroscience in Philadelphia, USA (September 2018) by the MUCKLI (Output 2) and KRIEGESKORTE (Output 1) labs. Niko KRIEGESKORTE also contributed to establishment and planning of this conference. Data from the second output was presented by Lars MUCKLI at the 1st international Workshop on Predictive Processing in San Sebastian, Spain on 22 June 2018 and at the workshop, PRECISE Brains: Predictive Coding, Inference and Unsupervised Learning, at EITN, Paris on 17 January, 2019. Lars MUCKLI discussed the transformative nature of interdisciplinary multiscale neuroscience approach that works so successful in the Human Brain Project in an interview with Horizon, The EU Research & Innovation Magazine (https://www.humanbrainproject.eu/en/follow-hbp/news/theory-of-predictive-brain-as-important-as-evolution-prof-lars-muckli/).

4. Key Result KR3.2 Multiscale user-accessible data, models and analysis tools for slow wave activity and sleep/awake transitions

Our goal is to develop a user-accessible collab including experimental data, simulation models and analysis tools to characterise high-resolution spontaneous and perturbed multi-areal slow wave activity expressed under different levels of activation at different scales.

4.1 Outputs

4.1.1 Overview of Outputs

The following is a list of key outputs produced during the period M1-M12 of SGA2 (April 2018 – March 2019):

1) Output 1: Slow Waves Analysis Pipeline, area-dependence of slow oscillations and integration in HBP infrastructure (C2051, C2052, C2053, C1786)
2) Output 2: Cortical dynamics at different excitability/anesthesia levels (C1854, C1852, C1788, C2051)
3) Output 3: PAI (Phthal Azobenzene Iperoxo), a photo-switchable drug to produce brain state transitions with light in vivo (C2047, C2048, C2049)
4) Output 4: Data curation and containers for electrophysiological data simultaneously recorded from scalp HD-EEG and intracranial EEG (C1790, C1791, C1793)

4.1.2 Slow Waves Analysis Pipeline (SWAP), area-dependence of slow oscillations and integration in HBP infrastructure

We (INFN, ISS, IDIBAPS) delivered a prototype of the Slow Waves Analysis Pipeline (characterisation of the cortex activity during deep sleep and anaesthesia) to the Elephant teams (JUELICH - C348). The cooperation with JUELICH produced a preliminary version that can be downloaded from this github. SWAP is currently a python pipeline based on Elephant, but the plan is to integrate SWAP pipeline as a module into Elephant and offer it through the HBP platform by May 2020. SWAP can be applied to experimental data and simulation outputs. It has been validated on an extensive *in vivo* data set, collected from the cerebral cortex of mice by Multi-Electrode Array. SWAP differentiates by area key-parameters related to the onset of slow oscillations. For example, it demonstrates gradients of key observables along the fronto-lateral to occipito-medial direction in recordings of anaesthetised mice. The pipeline discriminates between brain states, specifically different levels of anaesthesia. It also allows comparing simulation outputs obtained with different simulation engines (for example NEST or DPSNN simulations). The process of data curation and integration in the Knowledge Graph is ongoing.

4.1.3 Cortical dynamics at different excitability/anaesthesia levels

A new dataset of cerebral cortex electrophysiological data at different excitability levels induced by: (1) anaesthesia (isoflurane) levels with micro-ECOG (32 channels); and (2) electric fields *in vitro* (16 channels) has been produced in a collaboration between the institutions IDIBAPS, ISS, INFN and

UPF. Sample data are available in this Google Folder, and a complete data set will be available in May 2020, registered in the Knowledge Graph. Our objective is to identify the dynamics of the emergent activity of the cerebral cortex at different levels of excitability/anaesthesia. This provides building blocks for identifying brain states, underlying mechanisms and transitions between them. While varying activation levels of the cortical network, different features (including complexity of the network, functional connectivity, travelling wave properties etc.) vary, reflecting the state of the underlying network. This offers valuable information regarding transitions across states, critical for modelling of the cerebral cortex and the functional connectome.

4.1.4 PAI (Phthal Azobenzene Iperoxo), a photoswitchable drug to produce brain state transitions with light in vivo

Our goal is to control slow wave activity in the brain using light-regulated drugs to alter muscarinic receptors (mAChRs) activity. We synthesised several compounds and carried out the photochemical characterisation, *in vitro* and *in vivo* testing. Among those, PAI displayed outstanding properties (picomolar activity, photo-reversibility to control the frequency of cortical slow wave activity in mice). PAI's properties are reported in a submitted manuscript, and a sample of electrophysiological data on brain state transitions will be available on a dedicated section in this Google Folder, while a complete data set will be available in May 2020, registered in the Knowledge Graph. This work is a collaboration between the institutes IBEC and IDIBAPS.

4.1.5 Data curation and containers for electrophysiological data simultaneously recorded from scalp HD-EEG and intracranial EEG

During the SGA1 phase of HBP, we collected a dataset (updated during SGA2) of HD-EEG and intracranial EEG, both spontaneous and evoked by single pulse electrical stimulation (SPES), simultaneously acquired during wakefulness and sleep. A sample dataset can be found at this link.

UNIMI performed pre-processing and conversion to BIDS format and created, in collaboration with JULICH, a container for the delivery of a preliminary dataset of 10 subjects at the end of March 2019 (M12). After that, the Knowledge Graph will be updated accordingly.

4.2 Validation and Impact

4.2.1 Actual Use of Output(s)

The first output (SWAP) is a prototype available in its current form on a collaboration github and it has been validated on a first set of experimental data. See next section for the integration plan in the HBP infrastructure.

The second output (Cortical dynamics at different excitability/anaesthesia levels) is a data set and related analysis methods developed by several groups (IDIBAPS, ISS, INFN, JUELICH) that can be used to identify markers of different levels of excitability/anaesthesia, markers of transitions, dynamics of the process, underlying mechanisms. A prototype is shared in a dedicated section of the collaboration github. See next section for the integration plan in the HBP infrastructure.

The third output of KR3.2 (PAI) is shown in the photocontrol of brain waves with PAI, validated by IDIBAPS and IBEC in cell lines expressing mAChRs using calcium imaging, in ferret brain slices using MEA and field/focalized illumination, and in the exposed cortex of live anesthetized mice (extracellular recordings, field illumination). This is the first report of photocontrol of brain state transitions. It can be applied to wild-type animals without optogenetic manipulation, and a first set of electrophysiological data about photomanipulation is made available through a dedicated section of the collaboration github. See next section for the integration plan in the HBP infrastructure.

The last output (HD-EEG + iEEG) includes an internal release as a collab (restricted to selected HBP collaborating institution) sharing data with SP4 (EINEVOLL, UIO) for analysis of co-registered iEEG/EEG data and another collab (also restricted to selected HBP collaborating institution) sharing data with SP4 (JIRSA, TVB Platform) aiming at the parameter inference for TVB models, using the stimulation as a data feature (i.e. iEEG/EEG empirical data use case). Meanwhile, a container on CSCS was created to share, within HBP, embargoed, curated (Tier 1, in BIDS format) data from 10 subjects (200 stimulation sessions). Data delivery in the container is planned for 31 March 2019 (M12 Deliverable). The end of SGA2 (M24) will remove the embargo.

4.2.2 Potential Use of Output(s)

The final release of the SWAP analysis pipeline, integrated in the HBP infrastructure, and the related set of curated examples of experimental data will be offered after the embargo period (May 2020) to the external community. Researchers will then either apply SWAP to their own experimental data or to the analysis of HBP curated data accessible through the HBP Knowledge Graph.

The dataset of cortical dynamics at different excitability/anaesthesia levels can be used to test different analysis methods to be integrated in a future release of the SWAP pipeline, in particular to compare across different anaesthetics

Reversibly photocontrolling brain states with PAI is a novel tool for research purposes, with therapeutic applications in brain state transitions involved in diverse pathologies. Photoswitching with tissue-penetrating light will allow reducing the invasiveness of brain modulation techniques, because it does not require optogenetic manipulation.

Finally, the collabs and container with HD-EEG and iEEG data will be publicly opened, and the embargo will be removed at the end of SGA2 to make these data open source. These data can be used for connectivity analysis, they can be integrated in models and on platforms (e.g TVB) and can be used in the human brain atlas, to add a perturbational perspective.

4.2.3 Publications

The following three manuscripts are directly related to the KR3.2 outputs produced during the last year. The first is about the “HD-EEG + iEEG” output, the second about the “SWAP” output, the last about the “Cortical dynamics at different excitability/anaesthesia levels” output.

- P1669: "BIDS-iEEG: an extension to the brain imaging data structure (BIDS) specification for human intracranial electrophysiology". Christopher Holdgraf et al. Psyarxive (2018), (submitted).
- P1720: "Slow Waves Analysis Pipeline for extracting features of slow oscillations from the cerebral cortex of anesthetized mice." G. De Bonis et al. (2019) (submitted: preprint https://arxiv.org/abs/1902.08599)
- P1659: “Attractor competition enriches cortical dynamics during awakening from anesthesia”. Tort-Colet et al. (2019). BioRxiv, 1–24. https://doi.org/10.1101/517102

4.2.4 Measures to Increase Impact of Output(s): disseminations

WP3.2 co-organised with WP3.3 and WP3.4 the conference: “Understanding Consciousness, A Scientific Question for the 21st century.”, held in Barcelona 21-22, June, 2018. WP3.2 is participating in the organisation of a special issue on Frontiers of System Neuroscience directly related to KR3.2 topics. Also, WP3.2 organised and chaired the “High-Performance Computing for Neuroscience” session at PDP2019, the 27th Euromicro International Conference on Parallel, Distributed and

Network-Based Processing, Pavia, 15-18 February 2019. PDP 2019 IEEE proceedings will include peer-reviewed contributions from several HBP partners. Lastly, WP3.2 co-organised with EBRI on 11 March 2019 a scientific divulgation event dedicated to Brain Simulation in Roma, on occasion of the World Brain Awareness Week.

5. Key Result KR3.3 Models of multisensory integration, spatial memory and navigation

Our goal is to acquire human and rodent brain imaging and rodent electrophysiological recordings, and to develop models of multisensory integration, spatial memory and navigation, and brain-inspired robots (i.e. visual-tactile rodent-like robot and a humanoid robot). In humans, we have so far developed tasks to investigate multimodal integration and memory retrieval with which we are probing the functional organisation of the perirhinal and entorhinal cortex and hippocampus in young and older adults and older individuals with amyloid deposits in their brain. Research in rodents complements human research, in a sense that we could obtain direct recordings from the perirhinal cortex. We have developed a method to visualise the recording tracks and export this information to a common reference atlas for the Neuroinformatic Platform. These multi-species and multi-level data are being integrated into a theory for neural compression, storage and reconstruction of memories. On this basis, we have constructed a multimodal memory system for the iCub humanoid robot that we have deployed for human-robot interaction.

5.1 Outputs

5.1.1 Overview of Outputs

The following is a list of key outputs produced during the period M1-M12 of SGA2 (April 2018 – March 2019):

1) Output 1: Systems-level modelling of episodic and spatial memory (C2451) Work in progress (Behavioural Task 1.1: 70% finished; Behavioural Task 1.2: 50% finished; Behavioural Task 2: 20% finished).
2) Output 2: Episodic memory dynamics for mental time travel (C2450 and C2451)
3) Output 3: Sensory integration, episodic memory and object recognition in rodents (C2060)
4) Output 4: Visual-tactile mobile robot "WhiskEye" ported into the NRP (C2301).

5.1.2 Systems-level modelling of episodic and spatial memory

We developed two tasks to investigate multimodal integration and retrieval in humans.

The first task (Behavioural Task 1.1) focuses on pattern completion across domains (scene – object) in retrosplenial, hippocampal, entorhinal and perirhinal cortices. Task development is successfully completed and we are acquiring functional MRI data (3 Tesla) in a cohort of younger adults, and – to investigate the effect of Alzheimer's related pathology (amyloid and tau accumulation) – in a cohort of preclinical Alzheimer's dementia patients with determined pathology status (Behavioural Task 1.2). Data analysis will start subsequently to examine multimodal retrieval processes on representational level on collaboration with the UVA.

The second task (Behavioural Task 2) focuses on a multisensory integration and pattern completion across domains (scene – object) and sensory inputs (auditory – visual) and will be used to investigate these processes on a layer-specific level in the entorhinal-hippocampal circuitry as well as to identify the functional topography of convergence zones for these different modalities in humans. Initial behavioural data has been acquired to inform task adjustments and enable implementation of the task as a functional MRI paradigm (7 Tesla).

5.1.3 *Episodic memory dynamics for mental time travel*

Using findings from neuroscience (Cyriel PENNARTZ, UVA), brain imaging (Emrah DUEZEL, DZNE), and the psychology of human memory, Tony PRESCOTT (USFD) has assembled an integrated theory of the brain sub-systems and pathways that allows the compression, storage and reconstruction of memories for past events and their use in contextualising the present and reasoning about the future. Through machine learning techniques, specifically, Gaussian process latent variable models, or *simple synthetic memories* (SSMs), we have constructed a multimodal memory system for the iCub humanoid robot that we have deployed for human-robot interaction. A major integrative review describing this research is currently *in press* (see publications section). We have also published a book chapter describing progress towards the robot model of the temporally-extended self (C2450, C2451).

5.1.4 *Sensory integration, episodic memory and object recognition in rodents*

Assessing the neural code of multisensory integration (MI) requires a consistent metric of MI. Mice have been subjected to a behavioural paradigm for high quality audio-visual detection, where the mice report detection and absence of the stimulus, a 2-alternative forced choice paradigm. Mice readily learn this task, providing us with psychometric data on multisensory integration. Enhanced detection of stimuli in multisensory conditions versus unisensory conditions indicated true multisensory integration. In next steps mice will be recorded during this task. Neurophysiological recording paradigms for behaving animals have been piloted successfully for primary visual area, with pilots for primary auditory area happening at this moment (C2060). Dual-recordings (visual and auditory areas) of animals performing the multisensory detection task are planned for March 2019, providing us with behavioural data and electrophysiological data (single units and local field potential - LFP) during multisensory integration in primary visual and auditory cortex.

To investigate how memories are stored and retrieved as rich and multisensory episodic experiences, we acquired simultaneous single-unit and LFP data in secondary visual cortex, barrel cortex, Perirhinal cortex and hippocampus in rats while they performed a multisensory object recognition task (C2061). Electrophysiological data have been preprocessed and more in-depth analysis of single unit activity recently started.

5.1.5 *Visual-tactile mobile robot "WhiskEye" ported into the NRP*

The integrated visual-tactile mobile robot platform called WhiskEye, that was developed in previous phase of the HBP, has been ported into the robot simulator adopted by the Neurorobotics Platform in HBP (C2301). This includes the visual and collision meshes, kinematic chain and coding of the Gazebo-ROS plugin to control the virtual robot as if it were the physical WhiskEye platform. The preliminary cognitive architecture that controls for WhiskEye is being instantiated into the NRP brain engine using the transfer functions and CLE architecture available to enable further development of the mammalbot cognitive architecture (C2452). The virtual WhiskEye platform has been used to gather visual-tactile data sets to support studies into cross modal recall (C2226) and toward spike-based model of spatial navigation (C2300).

5.2 Validation and Impact

5.2.1 Actual Use of Output(s)

Histology of tetrode tracks in rat brains has been used to validate data integration methods through brain atlasing (C2166). The Neuroinformatics Platform (SP5) demonstrated that this can be used to reconstruct tetrode tracks to a common 3D reference atlas. This allows accurate comparison of electrophysiological data across different recording locations and different experiments[2].

We are continuing to develop the synthetic episodic memory system modelled at USFD. For example, we are in discussion with the USFD's Advanced Manufacturing Research Centre, and with Imperial College London, about extending the system towards applications in human-robot co-working. We are also advancing this work towards application by evaluating the usefulness of brain-inspired memory systems for social robots including the animal-like robot MiRo, which is being developed towards applications in robot-assisted therapy for people with Alzheimer's Disease. A presentation was given to a symposium on assistive technology at the annual meeting of the Alzheimer's Society concerning this potential.

We provide a manually segmented ultra-high resolution 7Tesla human MRI data set to Task T4.2.1 to validate new, automated deep-learning-based atlas segmentation algorithms. Our atlas has the most detailed segmentation of medial temporal regions currently possible in humans and will provide an important basis for validating automated approaches.

The Virtual WhiskEye platform in the NRP has been used to gather visual-tactile data sets to inform cross modal recall models of predictive coding and in the development of a behavioural model of haptic object exploration (C2525).

5.2.2 Potential Use of Output(s)

Functional neuroimaging data from humans that perform a multimodal integration and retrieval paradigm can inform and constrain computational models that solve pattern completion problems across domains (object – context) and across multiple sensory inputs. In addition, to provide the human brain atlas with human data on a meso-level (hippocampal subfields) and macrolevel (cortex), we share our data with the DICKSCHEID lab at JUELICH (Human Brain Atlas, SP2) and the Human Brain Project partner "Virtual Brain project" under supervision of Petra RITTER.

Single unit recordings and LFP data will be used to assess if and how phase-locking is relevant for multisensory integration in behaving animals, providing us with an additional framework to be used in the coding scheme of multisensory integration.

Synthetic systems that model the temporal dynamics of episodic memory outputs have potential application in the areas of assistive robotics, human-robot interaction and human-robot co-working. For example, a capacity for human-like episodic memory could assist a robot to fill out its current understanding of a social setting both by recognising actors and their actions and by recalling aspects of past interactions with those actors, including their emotional associations. Pattern completion triggered by social cues could help the robot to retrieve information that is relevant and assist the robot to select behaviour that is more appropriate to the current setting and better matched to user needs. The capacity to reconstruct past episodes, and to imagine future ones, enabled by synthetic episodic memory could serve as the basis for planning, using memory for past outcomes to decide if sequences of action are applicable and worth repeating.

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[2] Bjerke IE, Øvsthus M, Andersson KA, Blixhavn CH, Kleven H, Yates SC, Puchades MA, Bjaalie JG, Leergaard TB, 2018. Navigating the Murine Brain: Toward Best Practices for Determining and Documenting Neuroanatomical Locations in Experimental Studies. Front Neuroanat. 2018 Nov 2;12:82. doi: 10.3389/fnana.2018.00082.

5.2.3 Publications

The following papers provide the first empirical evidence in humans for a specific involvement of the locus coeruleus in memory and decision making and in the pathogenesis of Alzheimer's Disease. The locus coeruleus is important for hippocampal function because it supplies noradrenaline and dopamine.

- P1756: Hämmerer, D., Callaghan, M.F., Hopkins, A., Kosciessa, J., Betts, M., Cardenas-Blanco, A., Kanowski, M., Weiskopf, N., Dayan, P., Dolan, R.J., Düzel, E., 2018. Locus coeruleus integrity in old age is selectively related to memories linked with salient negative events. PNAS 115, 2228-2233. https://doi.org/10.1073/pnas.1712268115

For an integrative review of work on robot modelling of human episodic memory and mental time travel, see:

- P1710: Prescott: Prescott, T. J., Camilleri, D., Martinez-Hernandez, U., Damianou, A., & Lawrence, N. D. (In Press, to be published 11/3/2019). Memory and Mental Time Travel in Humans and Social Robots. Philosophical Transactions of the Royal Society. B: Biological Sciences.

For insight into the cognitive architecture of the self with emphasis on the "temporally extended" self, see:

- P1712: Prescott, T. J., & Camilleri, D. (2018). The Synthetic Psychology of the Self. In J. Sequeira, R. Ventural, & I. Ferraira (Eds.), Cognitive Architectures. Berlin: Springer Verlag.

5.2.4 Measures to Increase Impact of Output(s): disseminations

We would like to highlight specifically the dissemination activities related to the output of the episodic memory dynamics for mental time travel. Tony PRESCOTT has given three lectures to the Sage Center for the Study of Mind, Santa Barbara, CA, as Distinguished Fellow (April 2018). He was invited for a symposium talk "A Personalized Animal-like Robot Companion to Support People with Dementia" on the use of animal-like robots in therapy to the annual meeting of the Alzheimer's Association (AAIC 2018), Chicago, July 2018. Other outreach activities included using brain-based robots at BlueDot Festival 2018, London Tech Week 2018, Cheltenham Science Festival 2018, Manchester Science Festival 2018, Sheffield Festival of Mind 2018 and other events reaching a public audience of 5,000+.

6. Key Result KR3.4 Neural mechanisms of consciousness

Our goal for Key Result KR3.4 is to develop a collab that gathers different measures of consciousness and their generalisation from different pathophysiological (e.g. brain injuries), physiological functional states and anaesthesia conditions in humans, animal models, computer simulations and neuromorphic circuits.

For our goal, to deliver a public collaboratory space by March 2020 with access to a set of easily applicable measures of consciousness, research on multiple fronts has been conducted. Experiments with humans, animal models, and computer simulations have been performed to understand how the measures are affected in different pathophysiological (e.g. brain injuries), and physiological functional states, as well as under anaesthesia conditions with and without alterations in brain state and phenomenal consciousness.

6.1 Outputs

6.1.1 Overview of Outputs

The following is a list of key outputs produced during the period M1-M12 of SGA2 (April 2018 – March 2019):

1) Output 1: Perturbational Complexity Index measurements in rats (C2068)
2) Output 2: Implementation of a thalamocortical network model in the neural simulator NEST (C2086, C2090)
3) Output 3: Generalisation of the application of the PCI pipeline (C2101, C2102, C1647, C1859)
4) Output 4: Multimodal integration of brain connectivity measures (C2106)
5) Output 5: Consciousness measures in healthy humans (C2223, C2224)

6.1.2 Perturbational Complexity Index measurements in rats

We elaborated a procedure for replicating Perturbational Complexity Index (PCI) measurements in rats. PCI has been shown to be a reliable neurophysiological marker of consciousness in humans. Using our new method in rats, we have now found a loss of cortical complexity (PCI reduction) in response to local electrical stimulations, from wakefulness to anaesthetised state, as observed in humans. The reduction of complexity was associated with suppression of high frequencies and reduced phase synchrony in the evoked potentials, indicating neuronal bistability, another potential signature of unconsciousness. We are revising the Matlab code for evaluation of high frequency suppression and phase synchrony in evoked potentials. The final code will be shared publically in the HBP Knowledge Graph together with the data, to make them accessible to other researchers. We are comparing PCI to other measures of consciousness (e.g. Lempel Ziv Complexity, Coalition Entropy and Integrated Information) (Component ID:C2067). The histology data that we collected for detecting the position of stimulating electrodes in rat cortex will be shared with the HBP Neuroinformatics Platform and anchored to a public 3D reference atlas, validating our method and contributing to Component ID:C2068.

6.1.3 Implementation of a thalamocortical network model in the neural simulator NEST

Our implementation of the Hill-Tononi thalamocortical network model in the neural simulator NEST is used to assist the development of *in situ* visualisation in NEST (WP7.3). In addition, in collaboration with Oliver Rhodes (SP9), the model is being implemented in the SpiNNaker neuromorphic computer, and in collaboration with the Tononi group it is further developed for the incorporation of Martinotti cells to assess their role in the wake/sleep cycle. In preparation for use at the FENIX infrastructure, the model has been extended to six thalamocortical areas on the Abel supercomputer at the University of Oslo, with simulated TMS and measures of LFP complexity and diversity, and measures of inter-area connectivity. LFP estimation has been improved by the use of summed synaptic current magnitudes. Simulation results are being related to ECoG data from rats (Task T3.4.1), contributing to components C2086 and C2090.

6.1.4 Generalisation of the application of the PCI pipeline

We have revisited the pipeline underlying the computation of the Perturbational Complexity Index (PCI) previously introduced as a neurophysiological TMS/EEG marker of the potentiality for consciousness in severely brain-injured patients (Component ID: 2102). The pipeline is coded in Python, it is based on the MNE module and can alternatively be computed at the sensor, as well as at the source levels. The overall work confirms that the classification of brain-injured patients, based on PCI, is robust to most of the parameters of the pipeline and in line with previous works. In addition, we assessed the impact of focal cortical lesions on brain complexity. In a group of patients, we found that complexity is reduced locally in the perilesional area as compared to the contra-lateral intact area (Component ID: 2101). We have also generalised the application of PCI pipeline to whole brain simulations (component ID: C1859) and to cerebellar brain slices (component ID: C1647). In the simulations we demonstrated that PCI is higher in the ‘wake’-like state with respect to ‘sleep’ and ‘anaesthesia’-like states. In the cerebellar slice experiments, we adapted the original definition of PCI to account for the different signal sources (i.e. LFPs for granule cells and spiking activities for the Purkinje cells).

6.1.5 Multimodal integration of brain connectivity measures

In the framework of a multimodal integration of brain connectivity measures (Component ID: 2104), we confronted brain metabolism (FDG-PET) and brain computer interface to assess covert command-following in patients with disorders of consciousness (DOC), we characterised the functional neuroanatomy of minimally conscious state (MCS) using rsfMRI, we measured heart-rate variability entropy to discriminate DOC patients, and we demonstrated that EEG markers of consciousness can be identified with machine learning in various clinical and acquisition contexts. We also acquired TMS/EEG data under anaesthesia and during meditation. These various datasets resulted in several publications (Annen *et al.*, 2018; Aubinet *et al.*, 2018; Riganello *et al.*, 2018; Engemann *et al.*, 2018; Bodart *et al.*, 2018). In addition, we showed that dynamic signal coordination provides specific and generalisable patterns pertaining to conscious and unconscious states after brain damage, suggesting that consciousness rests on the brain’s ability to sustain rich brain dynamics (Component ID: C2105, Demertzi *et al.*, 2019). A comparison between several markers of consciousness using EEG, TMS-EEG and FDG-PET is currently in progress. We also directed our efforts toward sharing our patient’s data and models through the Medical Informatics Platform (MIP). Regarding treatment, we are finalising the acquisition of neuroimaging data in DOC patients who were treated with the GABA-A receptor agonist Zolpidem (Component ID: C2106), and these data will be shared through the HBP Knowledge Graph.

6.1.6 Consciousness measures in healthy humans

In order to test, compare, and further develop measures of consciousness in healthy humans (Component ID: C2223), we have implemented algorithms for calculation of some of the most promising measures from EEG data (e.g. based on complexity and connectivity), and applied those in control and novel clinical conditions (e.g. low dose ketamine, cognitive load, Wada tests, muscle relaxants). To test predictions from leading theories of consciousness (Component ID: C2224), we started new collaborations to test specific theoretical predictions in split-brain and Wada test patients.

6.2 Validation and Impact

6.2.1 Actual Use of Output(s)

Work on the Hill-Tononi thalamocortical model has been shared with non-HBP collaborators at the University of Wisconsin (for modelling of Martinotti cell functions), and with HBP collaborators from SP7 (*in situ* visualisation in NEST) and SP9 (implementation of model in the neuromorphic computer SpiNNaker). The multi-area variant of the model is also informing work on PCI in rats (SP3).

A preliminary release of the code needed to compute PCI is available in an open Collab accessible to anyone requesting an HBP account. It has received interest also among non-HBP users and it has been downloaded and used by a senior researcher from Harvard University, for instance.

Multimodal neuroimaging datasets have been shared with HBP collaborators SP4 and SP5 and with non-HBP collaborators.

6.2.2 Potential Use of Output(s)

The measures and methods that are being tested can form the basis for tools that distinguish between patients with and without covert consciousness in behaviourally unresponsive states (e.g. general anaesthesia and disorders of consciousness). Such tools can impact therapy for patients with disorders of consciousness, improved administration of anaesthesia, and clinical decision making. The release of the revisited perturbational complexity index in the open source Python language will be valuable to any user inside and outside HBP.

Investigations of consciousness in rats can help to understand its neuronal mechanisms and to compare different measures within the same experimental conditions. Transferring anatomical information of our PCI method into public 3D reference atlas will allow accurate comparisons of electrophysiological data across different experiments.

The Hill-Tononi thalamocortical model can be further used to investigate and compare measures of consciousness that are currently developed and used in humans and rodents (SP3).

6.2.3 Publications

PCI depends on elaborate experimental setups and offline processing and has restricted applicability to other types of brain signals beyond transcranial magnetic stimulation and high-density EEG (TMS/hd-EEG) recordings. In the work below we aim to address these limitations by introducing a fast method for estimating perturbational complexity of any given brain response signal (Output 3, Generalisation of the application of the PCI pipeline):

- P1719: R Comolatti, A Pigorini, S Casarotto, M Fecchio, G Faria, S Sarasso, M Rosanova, O Gosseries, M Boly, O Bodart, D Ledoux, J F Brichant, L Nobili, S Laureys, G Tononi, M Massimini, A G Casali. A fast and general method to empirically estimate the complexity of brain responses to transcranial and intracranial stimulations. bioXxiv: https://doi.org/10.1101/445882.

The following article shows that consciousness rests on the brain's ability to sustain rich brain dynamics and allows to determine specific and generalisable fingerprints of conscious and unconscious states (Output 4, Multimodal integration of brain connectivity measures):

- P1704: Demertzi A, Tagliazucchi E, Dehaene S, Deco G, Barttfeld P, Raimondo F, Martial C, Fernández-Espejo D, Rohaut B, Voss HU, Schiff ND, Owen AM, Laureys S, Naccache L, Sitt JD. Human consciousness is supported by dynamic complex patterns of brain signal coordination. Sci Adv. 2019 Feb 6;5(2):eaat7603

Data gathered for the study "Investigating effects of sleep deprivation on cognitive control" is used to control measures proposed to specifically distinguish conscious from unconscious states (Output 5, Consciousness measures in healthy humans), see the selected paper:

- P1654: Kusztor A, Raud L, Juel BE, Nilsen AS, Storm JF, Huster RJ. Sleep deprivation differentially affects subcomponents of cognitive control. Sleep. (2019)

6.2.4 Measures to Increase Impact of Output(s): disseminations

Our main dissemination activities related to the outputs above include the following:

- Co-organisation of the first international HBP conference with Johan STORM, Marcello MASSIMINI, Cyriel PENNARTZ and Steven LAUREYS: "Understanding Consciousness, A Scientific Question for the 21st century.", held in Barcelona 21-22, June, 2018.
- Organisation of a symposium on Ethical issues with disorders of consciousness to be held in November 2019 in collaboration with SP12.
- Video: Biology winner and Audience Favorite of the contest "Dance my PhD" 2018 sponsored by AAAS and the journal Science. The video depicts 2 young woman who sustained a traumatic brain injury and who undergo behavioural and neuroimaging assessments of consciousness. https://youtu.be/eYMmVNei2Hc.

7. Key Result KR3.5 Computation modelling of multisensory deep predictive coding

Our goal for Key Result KR3.5 is: computational modelling of multisensory deep predictive coding with potential use in AI and robotics.

KR3.5 comprises several modelling components targeting different phenomena in the brain with the eventual goal of building a comprehensive neurobiologically plausible cognitive architecture for biomimetic agents. These models include studies of a specific process, like sleep, on the encoding and retrieval of memory (Component ID: 2086 and 2193), as well as large scale neural network models of cortical/corticohippocampal network (Component ID: C2226 and C2385) for higher-level processes, like multisensory integration. These models are being integrated into a single architecture for brain-inspired robots.

7.1 Outputs

7.1.1 Overview of Outputs

The following is a list of key outputs produced during the period M1-M12 of SGA2 (April 2018 – March 2019):

1) Output 1: Deep Predictive Coding Network, Generative model of sensory cortical hierarchy and corticohippocampal network (C2226)
2) Output 2: Multisensory Integration and crossmodal recall, Integration of corticohippocampal network in Cognitive Architecture (C2226)
3) Output 3: Sleep-memory interaction, Cortical spiking model of the interplay between sleep and plasticity (C2193)
4) Output 4: Effect of memory on Hill-Tononi model, Mechanisms of brain complexity and consciousness (C2086)
5) Output 5: Multi-compartment information theoretic neuron models, Information theoretic description of cognitive systems architectures (C6384), Recurrent deep networks with feedback for modern AI C2385)
6) Output 6: Multisensory mammalbot cortical architecture, Mammalnot layered control architecture (C2452)

7.1.2 Deep Predictive Coding Network

We developed a method to train deep neural networks as generative models using the neurobiologically plausible approach of predictive coding (Component ID: C2226). Inspired by the visual system, these networks employ an architecture in which the size of neuronal receptive fields increases from lower to higher regions in the model. The networks were trained using images (visual stimulus) from the CIFAR-10 dataset. We showed that the inferred representations in any layer of the model can be used to reconstruct a given stimulus. The trained model can also be used to infer representations for stimuli that have never been presented to the network during training. In this regard, the model generalises to stimuli beyond the training data set.

7.1.3 Multisensory Integration and Cross-modal Recall

We have developed a neurobiologically plausible approach to construct generative models on multisensory stimuli. This method is an extension to our previously developed approach which used predictive coding to train deep neural networks on unisensory stimuli. The model can be used to infer a single multisensory representation that can simultaneously reconstruct stimuli across multiple modalities. We also evaluated the trained model for the problem of cross modal recall in the brain (Component ID: C2226). For this purpose, we presented the trained model with a stimulus in one of the modalities while the corresponding stimulus in another modality is not presented to the trained model. The trained model is then used to infer representations using only the unisensory stimulus. We are able to reconstruct the stimulus that was not presented to the trained model using the representations inferred in this manner.

7.1.4 Sleep-Memory Interaction

Sleep is known to be beneficial to cognitive and mnemonic tasks, but a theoretical and computational approach demonstrating the underlying mechanisms was still lacking. We demonstrated interesting effects of deep-sleep-like slow oscillation activity on a simplified thalamo-cortical model which is trained to encode, retrieve and classify images of handwritten digits. During slow oscillations, spike-timing-dependent-plasticity (STDP) produces a differential homeostatic process. It is characterised by both a specific unsupervised enhancement of connections among groups of neurons associated to instances of the same class (digit) and a simultaneous down-regulation of stronger synapses created by the training. This is reflected in a hierarchical organisation of post-sleep internal representations. Such effects favour higher performances in retrieval and classification tasks and create hierarchies of categories in integrated representations. The model leverages on the interaction between of top-down cortico-thalamic predictions and bottom-up thalamo-cortical projections during deep-sleep-like slow oscillations. Such mechanism hints at possible applications to artificial learning systems (Component ID: C2193). The model is written in NEST, using standard neural model (AdEX) and STDP models available in the NEST library, and is therefore directly compatible with the HBP platform.

7.1.5 Effect of Memory on Hill-Tononi Model, Mechanisms of Brain Complexity and Consciousness

To test the effects of memory mechanisms on the stability of structural and dynamic properties of the Hill-Tononi model (Component ID: C2086), the previously non-plastic Nest-implemented version has been tested with STDP synapses. For now, no conclusions can be drawn from the work, but as the model adapts further, we hope it may elucidate the distinct effects sleep and wakefulness have on the plasticity of neural networks, and be used to test particular theories for the mechanistic effects of sleep on memory consolidation.

7.1.6 Multi-Compartment Information Theoretic Neuron Models

Large networks have been simulated with multi-compartment, L5-like context-sensitive neurons and L2/3-like additive neurons using information theoretic learning rules (T3.5.1: Information theoretic description of cognitive systems architectures; Component ID: C6384). Such networks are capable of completing AI-style tasks and are currently being compared to cortical architectures (T3.5.1: Recurrent deep networks with feedback for modern AI; Component ID: C2385). These neuron models have been officially delivered to NEST for integration into the package. Validation of these models is being completed by the NEST development team.

7.1.7 Multisensory Mammalbot Cortical Architecture

We have developed a specific model for a brain-based cognitive architecture for robots integrating cortical and sub-cortical systems including models of basal ganglia (action selection, learning), superior colliculus (orienting), hypothalamus (drives), and hippocampus (spatial and episodic memory) (Component ID: C2452). The technical specification of a new process control architecture “Brain Glue” for integrating heterogeneous brain models has been developed. Furthermore, a higher-level transparency layer called “PyGates” will allow the cognitive architecture to be used on different physical platforms as well as on the Neurorobotics Platform. We have also extended our existing model of action selection and orienting demonstrating this on the MiRo robot and preparing it for implementation on the WhiskEye robot.

7.2 Validation and Impact

7.2.1 Actual Use of Output(s)

In relation to the second output (Multisensory Integration and Crossmodal Recall), we want to study the feasibility of predictive coding as a mechanism that supports crossmodal recall in the brain (Component ID: C2228). For this purpose, we are using the model of crossmodal recall (Component ID: C2226) together with experimental data from (Component ID: C2061) and sensor data from Whiskeye robot (Component ID: C2301). Whiskeye robot will be presented with the same objects that have been used in multisensory experimental paradigms for gathering sensory input. The neuronal activities in the model will be partly constrained to the activities recorded in the experiment and remaining data from the model will be used to predict observations about experimental data.

The model used in the framework of the HBP Co-Designed Project 5 (CDP5) (plasticity) and part of KR3.5 is our third output (Sleep-memory interaction). This model is written in NEST using neural (AdEx) and STDP plasticity models available as standard NEST components, and therefore is ready for insertion among the models released by HBP. The results have been statistically validated and have been presented and discussed at the HBP summit (Oct 2018) and at the HBP CDP5 meeting in Heidelberg (Jan 2019).

Currently, USFD is working closely with UWE to extend the integrated cognitive architecture for demonstration on the WhiskEye robot platform (Component ID: C2301), regarding Output 6: Multisensory Mammalbot Cortical Architecture.

7.2.2 Potential Use of Output(s)

The model from Output 2 (Multisensory Integration and Crossmodal Recall) can be easily generalised to handle data in more than 2 modalities irrespective of the modalities used. In this regard, the model can be used to conduct further studies on data recorded from different sensory modalities, similar to the study described in section 7.2.1 and is a better way of robot interaction with the world by improved multisensory fusion.

For the third output in sleep-memory interaction, the plan is to extend the model to multisensory integration during 2019 for usage, starting from 2020, on neuromorphic and neurorobotic platforms. The explored mechanism hints at possible applications in artificial learning systems.

Neuron models will also be available from Output 5 (Multi-Compartment Information Theoretic Neuron Models) to test information theoretic hypotheses about biological neurons, as well as the capability of such neurons to complete common AI tasks.

The cognitive architecture we are developing in Output 6 (Multisensory Mammalbot Cortical Architecture) is intended to support real-time control for robots with brain-based capacities for perception, cognition, memory, and learning. There are wide-ranging possibilities for exploiting this architecture, particularly in areas of robotics that benefit from life-like control including social robotics, therapeutic robotics, prosthetics and human-robot interaction. The USFD spin-off companies Consequential Robotics and Cyberselves will identify commercial opportunities in telepresence robotics and education.

7.2.3 Publications

Three manuscripts are directly related to the KR3.5 outputs:

- P1528: C. Capone, E. Pastorelli, B. Golosio, P.S. Paolucci. “Sleep-like slow oscillations improve visual classification through synaptic homeostasis and memory association in a thalamo-cortical model”. https://arxiv.org/abs/1810.10498. 2018
- P1522: Shirin, D., Pennartz, C. and Bohte, S. "A deep predictive coding network for inferring hierarchical causes underlying sensory inputs." In International Conference on Artificial Neural Networks, pp. 457-467. Springer, Cham, 2018.
- P1755: T.J. Prescott, N. Lepora and P.F.M.J. Verschure, The Handbook of Living Machines: Research in Biomimetic and Biohybrid Systems. Oxford, UK: Oxford, 2018.

7.2.4 Measures to Increase Impact of Output(s): disseminations

Organised by Tony PRESCOTT, and hosted at the London Science Museum, the HBP Innovation Forum (https://www.humanbrainproject.eu/en/follow-hbp/events/first-annual-human-brain-project-innovation-forum-the-exhibition/) displayed HBP and HBP partners’ progress in science and innovation to the general public. The showcase included booths from multiple SP’s and SMEs with links to HBP, and talks of a fundamental, medical and innovative nature. We would also like to highlight the Predictive coding workshop given in the EITN in Paris, “PRECISE Brains”, which work was related to the first output, deep predictive coding network. For reaching a broader audience, Lars MUCKLI discussed the theory of the predictive brain in an interview with Horizon, The EU Research & Innovation Magazine (https://www.humanbrainproject.eu/en/follow-hbp/news/theory-of-predictive-brain-as-important-as-evolution-prof-lars-muckli/).

8. Conclusion and Outlook

With the goal of deciphering cortical contextual processing at multiple levels of systems neuroscience and to develop network models that integrate recurrent information processing in context-sensitive object recognition, WP3.1 (Context-Sensitive Multisensory Object Recognition) developed models showing that brain-inspired network architectures are able to outperform equivalent networks utilising simpler cortical architectures. Experimental work in WP3.1 has, and will continue to produce high-resolution human fMRI data. Electrophysiological, optogenetic and 2-photon calcium imaging mouse data will also be collected to inform neural network models in remainder of the phase, and will be made available for use to test computational and cortical architectural hypotheses.

WP3.2 (WaveScalES) aims to understand the multi-scale mechanisms sustaining cortical slow wave activity (SWA) expressed under deep sleep, anaesthesia and coma and the emergence toward wakefulness and consciousness. In this document, we reported about: data curation and containers for electrophysiological data simultaneously recorder from scalp HD-EEG and intracranial EEG in human subjects; a data set of electrophysiological data acquired on the cerebral cortex of mice at excitability levels induced by: (1) anaesthesia (isoflurane) levels, micro.ECOG (32 channels) and (2) electric fields in vitro (16 channels); the SWAP (Slow Wave Analysis Pipeline) for the measurement of areal dependence of slow oscillations; PAI (Phtal Azobenzene iperoxo), a photoswitchable drug to modulate brain state transitions with light in vivo. This is a first set of preliminary contributions to a collab, to be offered to the research community in 2020, including experimental data, acquired in humans and rodents, analysis tools, theoretical models and simulations.

WP3.3 develops a multi-scale understanding of multi-sensory integration in episodic memory and its implementation in humanoid robots. We have continued acquiring human and rodent brain imaging and rodent electrophysiological recordings, developing models of multisensory integration, spatial memory and navigation, and brain-inspired robots (i.e. visual-tactile rodent-like robot and a humanoid robot). By bridging multiple levels of representation ranging from single neurons, to meso-scale (7Tesla) and macro-scale (3T) mechanisms and computational models (humanoid robots), WP3.3. is making progress towards a comprehensive understanding of multi-sensory integration in episodic memory. A translational aspect of our work is to study multi-sensory integration in episodic memory also in older adults with preclinical Alzheimer's Disease who are known to have early impairment of perirhinal function, but where the exact mechanistic nature of memory problems is still poorly understood. We have constructed a multimodal memory system for the iCub humanoid robot that we have deployed for human-robot interaction. Electrophysiological datasets, human macro- and meso-scale MRI data and computational implementations are shared within HBP and contribute to HBP platforms. Our future plan is to integrate data, models and robotics and improve the data analysis methods.

The achievements in, and impact of, the work done by the ConsciousBrain (WP3.4) Work Package during this period have been centred on the testing, validation, and development of methods and measures intended for tracking consciousness. Data gathered using state-of-the-art neuroimaging techniques from patients and healthy controls in novel states and conditions have led to insights important for understanding structural and functional characteristics of the brain related to its capacity for consciousness. Applying the measures in rodents, slices, and computer models have also allowed for a more in-depth investigation of the mechanisms underlying changes in the measures in response to changes in brain states (e.g., anaesthesia and sleep). Altogether, this work is important for the development of measures and methods with the ability to robustly distinguish conscious from unconscious states. In the next twelve months, the work to test the measures in novel control conditions will continue and pipelines for application of the most promising measures will be made available for use.

Finally, WP3.5 is working to build detailed models of different brain phenomena and develop methods to integrate these models into a single framework that can be used by biomimetic agents, including robots, to perform a wide range of tasks. With this goal in mind, the work in the current phase has focused on modelling different processes like memory, perception, cognition and learning from two different perspectives. In the first perspective, that focus is on an observed phenomenon to understand its role in a simulation consisting of biologically plausible populations of neurons (e.g. effect of slow-wave activity observed during sleep in a thalamocortical circuit). In the second perspective, the focus is on developing neurobiological methods of learning and inference like deep generative models of visual cortical hierarchy. The future work will focus on connecting these models to data through collaborations with other Work Packages. Furthermore, with regards to the development of an integrative framework and cognitive architecture, the work in the current phase has created a skeleton of this framework and subsequent work will develop a usable implementation of this framework capable of real-time operation on physical robots.

Annex A: Component Details

Table 1: Overview of releases and major updates related to Key Result KR3.1

ID	Component Name	Type	Contact	Info on releases and major updates
C2381	T3.1.4 Layer-specific fMRI data of temporal predictions	Dataset	Lars MUCKLI (UGLA)	Recurrent Convolutional Neural Networks - models are publicly released through Github upon publication of the descriptive manuscript (https://github.com/nest/nest-simulator). Validation will therefore be through the community. Initial release of models will occur prior to October 2019. Functional MRI data aligned to Big Brain - data will initially be released internally (within HBP) to validate retinotopic alignment of V1 responses to natural stimuli with the Big Brain. After embargo, during which experimental data will be published, data will be made available publicly through a recognised MRI repository. Initial release of data is planned for prior to October 2019.
C2385	T3.5.1 Recurrent deep networks with feedback for modern AI	Model	Lars MUCKLI (UGLA)	Recurrent Convolutional Neural Networks (see above): https://github.com/nest/nest-simulator

Table 2: Overview of releases and major updates related to Key Result KR3.2

ID	Component Name	Type	Contact	Info on releases and major updates
C1786	T3.2.1(1) Inter-areal differences of multiscale organization of SWA	Report	Maurizio MATTIA (ISS)	https://github.com/INM-6/wavescalephant
C1788	T3.2.1(2)Multipurpose simplified neuronal network model of different cortical areas matching SWA/wake transitions	Model	Maurizio MATTIA (ISS)	Mean-field model of the awakening from anesthesia: publicly available in this pre-print: https://doi.org/10.1101/517102
C1790	T3.2.2 (4) The impact of neuronal bistability on global brain dynamics	Dataset	Marcello MASSIMINI (UMIL)	Release of data, from 6 patients undergoing presurgical evaluation, collected simultaneously from scalp HD-EEG and intracranial EEG during single pulse electrical stimulation, in wakefulness and sleep. https://github.com/iTCf/unimi_demo_dataset
C1791	T3.2.2 (3) The mesoscale correlates of the macroscale EEG	Dataset	Marcello MASSIMINI (UMIL)	Release of data, from 6 patients undergoing presurgical evaluation, collected simultaneously from scalp HD-EEG and intracranial EEG during single pulse electrical stimulation, in wakefulness and sleep.

				https://github.com/iTCf/unimi_demo_dataset
C1793	T3.2.2 (1) A multiscale (LFP and high-density EEG) human perturbational atlas	Dataset	Marcello MASSIMINI (UMIL)	Release of data, from 6 patients undergoing presurgical evaluation, collected simultaneously from scalp HD-EEG and intracranial EEG during single pulse electrical stimulation, in wakefulness and sleep. https://github.com/iTCf/unimi_demo_dataset
C1852	T3.2.3 (2) Propagation modes of slow waves	Dataset	Mavi SANCHEZ-VIVES (IDIBAPS)	The preliminary dataset can be found in this link: https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx
C1854	T3.2.3 (4) Mechanisms underlying cortical complexity	Dataset	Mavi SANCHEZ-VIVEZ (IDIBAPS)	The preliminary dataset can be found in this link: https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx
C2048	T3.2.4 (2) Development of photostimulation targeting GABA and glycine receptors	Report	Pau GOROSTIZA (IBEC)	InhibitoryPhotoswitches1: The first release can be found in this link (prior request required): https://drive.google.com/drive/folders/1NYOaH9Ogfbt02XtlHxGsYIexwVQ9Ha1b
C2049	T3.2.4 (3) In vivo characterisation of photostimulation and SWA manipulation	Dataset	Pau GOROSTIZA (IBEC)	PAIcharacterization1 - PAI (Phthal Azobenzene Iperoxo): a photoswitchable drug to produce brain state transitions with light in vivo- The goal is to control slow wave activity in the brain using light-regulated drugs to alter muscarinic receptors (mAChRs) activity. PAI's properties are reported in a submitted manuscript, and electrophysiological data on brain state transitions will be submitted soon in the HBP repositories. The reports can be found here: https://drive.google.com/drive/folders/1L86mvwNMyIGUKfSUWz3HCtItr-Hj2Wyi
C2051	T3.2.5 (1) High-efficiency analysis of (perturbed) SWA/transitions on single areas	Software	Pier Stanislao PAOLUCCI (INFN)	SlowOscillationTransitions1 and SlowOscillationTransitions2: Includes both a set of experimental data (acquisition of slow waves with 32 electrodes ECOG, from iDIBAPS, and the analysis pipeline applicable to this set of data jointly developed by ISS,and INFN. In collaboration with Juelich, at this date it is expected that a large part of the pipeline should have been ported from the original implementation (MATLAB) to the python Elephant environment. Find it in this link: https://github.com/INM-6/wavescalephant
C2052	T3.2.5 (2) High-efficiency, high-resolution distributed	Model	Pier Stanislao PAOLUCCI (INFN)	ApplicationOfSWAPtoSlowWaveSimulations - Application of the SWAP pipeline to Slow Wave simulations with the

	simulation of single areas in mice.			objective of constraining models to higher biological plausibility: https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx?usp=sharing ScalabilityMillionNeuronsBillionSynapses - Efficient simulation and scalability analysis on HBP distributed platforms of Slow Waves like activity and Awake-like asynchronous activity modeled by a grid of cortical columns. The status at M12 is described by arXiv:1902.08410. See https://github.com/APE-group/201903LargeScaleSimScaling for the code and https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx?usp=sharing for documentation. TestForComparisonBetweenSimulators - In the framework of the activity aiming at creating the Slow Wave Analysis Pipeline (SWAP) to be applied to experimental data and simulation results, that is the final joint result of C2051, C2052 and C2053, an intermediate step is the usage of Elephant tools to compare Slow Wave simulations produced by different simulators. A jupiter notebook performing an example of such comparison, using DPSNN and NEST models is included in the WaveScalephant GitHub: https://github.com/INM-6/wavescalephant
C2053	T3.2.5 (3) High-efficiency, multi-area wave propagation analysis	Software	Pier Stanislao PAOLUCCI (INFN)	MultiAreaSlowWavePropagationAnalysis2 - Release of a module integrated in the Elephant environment. See: https://github.com/INM-6/wavescalephant and https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx?usp=sharing MultiAreaSlowWavePropagationAnalysis1 - This component follows the local analysis features offered by the M12 release of the single area C2051 and it is a first step towards Multi-Areal Analysis. The plan is to offer Multi-Areal Slow-Wave analysis as an elephant module integrated in the offer of the HBP platform. This is the release of a MATLAB prototype to the Juelich Elephant team and constitutes a starting point for the joint activity of porting to the python

				environment. A description of the current status of the procedure and a set of sample experimental data are included in the Documentation folder accessible by the public at: https://drive.google.com/drive/folders/1A1UDfkWklRYqinyaX8ednXBa2DnK58Lx?usp=sharing

Table 3: Overview of releases and major updates related to Key Result KR3.3

ID	Component Name	Type	Contact	Info on releases and major updates
C2450	T3.3.4 (2) Episodic memory dynamics for mental time travel	Model	Tony PRESCOTT (USFD)	Integrative review of work on robot modelling of human episodic memory and mental time travel: http://eprints.whiterose.ac.uk/141650/
C2451	T3.3.4 (3) Systems-level modelling of episodic and spatial memory	Report	Tony PRESCOTT (USFD)	Integrative review of work on robot modelling of human episodic memory and mental time travel: http://eprints.whiterose.ac.uk/141650/
C2060	T3.3.3 (1) Multi-area ensemble mechanisms of multi-feature detection in rodents	Dataset	Cyriel PENNARTZ (UVA)	Neurophysiological recording paradigms for behaving animals in the primary auditory area is happening at this moment. Preliminary release is expected in September 2019.
C2061	T3.3.3 (2) Multi-area ensemble mechanisms of object recognition in rodents	Dataset	Cyriel PENNARTZ (UVA)	Dual-recordings (visual and auditory areas) during animals performing the multisensory detection task are planned for March 2019, providing us with behavioural data and electrophysiological data (single units and LFP) during multisensory integration in primary visual and auditory cortex. Preliminary release is expected in September 2019.

Table 4: Overview of releases and major updates related to Key Result KR3.4

ID	Component Name	Type	Contact	Info on releases and major updates
C2068	T3.4.1 Circuit and cellular mechanisms of consciousness explored by optical methods and/or pharmacology	Dataset	Johan STORM (UIO)	Single_neuron_rec - Single neuron and field recordings in vivo from rats during both wakefulness and general anesthesia in response to cortical stimulation. Initial release of preliminary data is planned for prior to SGA2 M18. Final release is planned for SGA2 M24.
C2086	T3.4.2 Mechanisms of brain complexity and consciousness	Dataset	Johan STORM (UIO)	Multiarea_thalamocortical_network_model_with_multicompartment_pyramidal_neurons-Results - Results of simulations using the multarea thalamocortical spiking network model with multicompartment pyramidal neurons.
C2090	T3.4.2 Novel measures of consciousness	Dataset	Johan STORM (UIO)	Hill-Tononi_multiarea_model-Novel_measures_of_consciousness-Results - Results of simulations on novel measures of consciousness using the

				multiarea thalamocortical network model based on the Hill-Tononi model. This is planned for March 2020.
C2101	T.3.4.3 (2) A reliable read-out of the state of cortical circuits after injury	Dataset	Marcello MASSIMINI (UMIL)	The data set will consist of focal cortical (~10 patients), sub-cortical (~10 patients) and multi-focal brain lesions (~10 patients) and is planned for March 2020.
C2102	T.3.4.3 (1) Generalising measures of complexity	Software	Marcello MASSIMINI (UMIL)	The released Python code allows to compute the perturbational complexity index from preprocessed TMS/EEG responses. The code comes as a notebook and will be extended to include the calculation of the inverse solution from raw data (https://github.com/iTCf/PCIcalc).
C2105	T3.4.4 (2) Characterisation of temporal dynamics underlying human arousal and awareness networks (internal/self and external/perceptual)	Dataset	Steven LAUREYS (ULG)	Publication of the data in a peer-reviewed journal can be found here: http://advances.sciencemag.org/content/5/2/eaat7603
C2223	T3.4.5 Test, compare, and develop measures of consciousness in healthy humans	Dataset	Johan STORM (UIO)	S cripts_for_calculating_consciousness - A package in Python 3.x for calculating proposed measures of consciousness, taking a 3D matrix of timeseries data and outputting values of a selection of measures of consciousness is planned to be released in March 2020.
C2224	T3.4.5 Test theoretical predictions	Dataset	Johan STORM (UIO)	Research_articles_on_studies_testing_measures_and_predictions_of_consciousness - Publications based on experiments aiming to test theoretical predictions of measures and theories of consciousness are planned for March 2020. Datasets_for_controls - Data aimed at testing theoretical predictions of measures of consciousness, focusing on possible confounding variables and edge cases where measures might report in conflict with expectations. Data will be released in January 2020.

Table 5: Overview of releases and major updates related to Key Result KR3.5

ID	Component Name	Type	Contact	Info on releases and major updates
C2086	T3.4.2 Mechanisms of brain complexity and consciousness	Dataset	Johan STORM (UIO)	Multiarea_thalamocortical_network_model_with_multicompartment_pyramidal_neurons-Results - Results of simulations using the multarea thalamocortical spiking network model with multicompartment pyramidal neurons are expected on March 2020.
C2193	T3.5.2 (1) Cortical spiking model of the	Model	Pier Stanislao PAOLUCCI (INFN)	InterplaySleepMemoriesClassificationTask1 - interesting effects of deep-sleep-like slow oscillation activity on a simplified

	interplay between sleep and plasticity			thalamo-cortical model which is trained to encode, retrieve and classify images of handwritten digits. See arXiv: 1810.10498 (submitted for pub) for a complete description of the model. During slow oscillations, spike-timing- dependent-plasticity (STDP) produces a differential homeostatic process. It is characterised by both a specific unsupervised enhancement of connections among groups of neurons associated to instances of the same class (digit) and a simultaneous down-regulation of stronger synapses created by the training. This is reflected in a hierarchical organisation of post-sleep internal representations. Such effects favour higher performances in retrieval and classification tasks and create hierarchies of categories in integrated representations. The model leverages on the interaction between of top-down cortico-thalamic predictions and bottom-up thalamo-cortical projections during deep-sleep-like slow oscillations. Such mechanism hints at possible applications to artificial learning systems. The model is written in NEST, one of the simulation engines at the hearth of the HBP Brain Simulation platforms, using standard neural model (AdEX) and STDP models available in the NEST library, and is therefore ready for integration among the set of models offered by the HBP Brain Simulation Platform and executable on the HBP HPC platforms. The model is currently available in a HBP collab (https://collab.humanbrainproject.eu/#/collab/44145/nav/303559) and will be made accessible on a GitHub on expiration of the embargo period.
C2226	T3.5.3 (1) Generative model of sensory cortical hierarchy and corticohippocampal network	Model	Cyriel PENNARTZ (UVA)	A manuscript is being prepared for submission based on the results from the model trained on unisensory stimuli. The code for the model will be open-sourced after publication of results. The results from the model trained using multisensory stimuli are being analysed. v1 - The details of the model have been published in ICANN' 2018: https://link.springer.com/chapter/10.1007/978-3-030-01424-7_45
C2385	T3.5.1 Recurrent deep networks with feedback for modern AI	Model	Lars MUCKLI (UGLA)	Recurrent Convolutional Neural Networks - models will be released publicly through Github upon publication of the descriptive manuscript. Validation will therefore be through the community. Initial release of models will occur prior to October 2019.

C2452	T3.5.5 (1) Mammalbot layered control architecture	Model	Tony PRESCOTT (USFD)	Information about the Mammalbot Cognitive Architecture, documentation, and links to the software and models, are available via the Mammalbot Collab in the Mammalbot Collab in the HBP Collaborator and at https://github.com/ABRG-Models/MammalBot