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Abstract:	This deliverable describes the different theoretical models that will be investigated in the Human Brain Project (HBP) Subproject 4: Mathematical and Theoretical Foundations of Brain Research. These models are structured according to the four different scientific Work Packages of SP4: Bridging Scales (WP4.1), Models of Plasticity, Learning and Memory (WP4.2), Large-Scale Models of Cognitive Processes (WP4.3), and Principles of Brain Computation (WP4.4). We describe the different models and provide a timeline taking each one from conception, programming, simulation, validation, and finalisation to integration in the HBP Brain Simulation Platform. We also include a set of Key Performance Indicators (KPIs) to track progress.
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Table of Contents

List of Figures and Tables

Executive Summary

This deliverable describes the different theoretical models that will be investigated in the Human Brain Project (HBP) Subproject 4: Mathematical and Theoretical Foundations of Brain Research. These models are structured according to the four different scientific Work Packages of SP4: Bridging Scales (WP4.1), Models of Plasticity, Learning and Memory (WP4.2), Large-Scale Models of Cognitive Processes (WP4.3), and Principles of Brain Computation (WP4.4). We describe the different models and provide a timeline taking each one from conception, programming, simulation, validation, and finalisation to integration in the HBP Brain Simulation Platform. We also include a set of Key Performance Indicators (KPIs) to track progress.

1. Introduction

The Human Brain Project (HBP) is a ten-year research project, backed by the European Commission (EC) that is laying the foundation for a new approach brain research. The HBP is integrating data and knowledge from different disciplines, and catalysing a community effort to develop a new understanding of the brain, new treatments for brain disease, and new brain-like computing technologies. To support this effort, the HBP is creating an integrated system of ICT platforms, offering services to neuroscientists, clinical researchers and technology developers. Other Subprojects (SPs) are responsible for generating strategic brain data, theoretical aspects and ethical issues.

The HBP's SP4 works on the Mathematical and Theoretical Foundations of Brain Research and its goals are to:

- Investigate mathematical techniques to link models used or developed in other modelling and simulation-oriented Subprojects
- Investigate different scales that are observed in experimental data and that need to be present in the simulation platforms
- Develop plasticity rules for brain circuits that continually change during development and learning
- Theoretically characterise different cognitive functions that are compiled in other Subprojects.

This document describes the theoretical models that will be developed during the ramp-up phase in the four scientific Work Packages of the Subproject. This description includes the algorithms and computing principles that will be studied, and indicators of progress for the planned work.

Models are used to explore the computation of neural circuits. This work is performed in close collaboration with the partners responsible for experimental and cognitive neuroscience and for neuromorphic computing. We also plan to establish a European Institute for Theoretical Neuroscience (EITN) to interact closely with the theoretical community and involve new ideas in the project.

This deliverable is structured to match the four scientific Work Packages, each of which comprises several different Tasks. We describe the models investigated in each Task, estimate a timeline for the work and present the Key Performance Indicators (KPIs) that will be used to measure progress.

2. Process of Work

2.1 WP4.1 Bridging Scales

2.1.1 Derive Simplified Neuron and Neural Circuit Models from Biophysically and Morphologically Detailed Models (T4.1.1)

The purpose of the first Task, T4.1.1, is to construct simplified models of neurons and their dendritic processing. Idan Segev's group (HUJI) is already developing new strategies for obtaining simplified conductance-based models of neurons with passive dendrites. This work is based on the large database of morphologically and physiologically characterised neocortical cells measured *in vitro* in Henry Markram's laboratory (EPFL). In parallel, Alain Destexhe's group (CNRS-UNIC) is studying the principles of synaptic integration in dendrites

in vivo, taking into account dendritic excitability/nonlinearity. Wulfram Gerstner's group (EPFL) is reducing the Hay-Segev model for L5 cortical pyramidal cell to a noisy, generalised, integrate-and-fire model and GLM model.

The results from all three groups will be merged to produce the following outputs:

1) A set of simplified models for various neocortical cell types.
2) A set of systematic methods for reducing any neuron model complexity while keeping the essential I/O properties of the full model.
3) A set of criteria for assessing the quality of the reduction against the benchmark of the full model.
4) Publications in peer-reviewed journals.
5) Released models in public databases.

We will also port these models to the AdEx framework so that they can be integrated on VLSI hardware. We are in contact with Karlheinz Meier's group (UHEI) to make these dendritic neurons fully compatible with new VLSI chips developed for this purpose.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.1.2 Modelling Brain Signals at Different Scales, from Intracellular, Local Field Potentials, VSD up to EEG and MEG signals (T4.1.2)

Task 4.1.2, starting in Year 2, will design models of the different signals. These models will be conceived so that they are compatible with the SP6 Brain Simulation Platform's detailed models, with the Meier group (UHEI)'s simplified models, and with the cognitive model simulations of WP4.3 and SP3. The theoretical results of this Task will influence the way the large-scale simulation researchers in the HBP think about collective and cognitive phenomena in the detailed simulation models.

This Task will produce the following outputs:

1) Research results describing the correspondence between unit activity and local field potentials (LFP).
2) Models of extracellular spikes and LFP, as well as more global electrical activity, such as surface EEG or EcoG.
3) Publications in peer-reviewed journals.
4) Released models in public databases.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 20)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.2 WP4.2 Synaptic Plasticity, Learning and Memory

Neurons are connected to each other with axons: cable-like extensions that touch the soma or dendrites of other neurons. At the touch point, synapses can be formed. Synapses are not fixed in size or strength, but can change over time. Synaptic changes are the foundation of learning and memory formation. Hence, synaptic plasticity is a key concept for linking microscopic phenomena at the cellular level to cognitive phenomena observable in behavioural experiments.

2.2.1 Derive Learning Rules from Biophysical Synapse Models (T4.2.1)

Task 4.2.1 will formulate synaptic plasticity rules that are biologically plausible and functionally useful for learning. The groups of Wulfram Gerstner (EPFL), Walter Senn (Universität Berne) and Misha Tsodyks (Weizmann Institute) are exploring biologically plausible learning rules and their potential functional relevance for learning, memory formation, and memory recall. Particular attention is devoted to the potential role of global modulators, which contain information on reward, alertness, stress, attention, etc.

The success of plasticity models can be measured by comparing model complexity (a simple model is better) with the number of experimental data points that the model can qualitatively account for (a model that can explain a lot of data is better). A further measure of success is whether the model is mathematically structured such that it can, in principle, be implemented in neuromorphic hardware or in the large-scale simulation platforms developed by other HBP Subprojects. Experimental data are typically extracted from the published literature on slice electrophysiology or cognitive experiments. In later years, models will also connect to data collected within other HBP Subprojects. A second success criterion is that the synaptic plasticity model should be functionally relevant, which implies that we have to measure whether synaptic plasticity as summarised in the model can indeed explain memory formation and memory recall.

The outputs of this Task will result in several publications in peer-reviewed journals, as well as the release of the models in public databases. The outputs will influence the development of neuromorphic hardware in other HBP Subprojects and guide the development of plasticity implementations in the large-scale simulations of HBP.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.2.2 Unsupervised Learning Rules and Emergent Connectivity (T4.2.2)

In T4.2.2, Wulfram Gerstner's group (EPFL), in collaboration with the Blue Brain Project (EPFL), studies the mathematical relation between synaptic plasticity models and the development of cortical microcircuits. The aim is to compare microcircuits that are subject to on-going synaptic plasticity with those in the HBP's connectivity database.

The success of an unsupervised learning rule in the context of developmental plasticity and microcircuit wiring can be measured by evaluating whether the synaptic dynamics display at least one stable fixed point . Success can also be measured by determining how many circuit connectivity motifs resulting from the learning rule correspond to circuit motifs in the reconstructed microcircuits produced by other HBP Subprojects.

The output of T4.2.2 will include a publically available model of unsupervised developmental plasticity, which will be published in a peer-reviewed journal. The model will be

implementable in large-scale simulations and will influence the thinking of researchers in other Subprojects of the HBP.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.3 WP4.3 Large-Scale Models of Cognitive Processes

The HBP will develop simplified large-scale models of specific cognitive functions. These models will provide a bridge between "high-level" behavioural and imaging data and detailed multi-level models of brain physiology. Topics for modelling will include perception-action, attention, and the sleep/wakefulness cycle. These models will make a direct contribution to the design of architectures for neuromorphic computing systems.

Computational models aiming to explain the mechanisms underlying specific brain functions (perception, cognition) developed in WP4.3 cover two scales: detailed biophysical neuronal models of single brain areas, and detailed neurophysiological models of the whole brain. The first category (microscopic models) will be fitted against neuronal recordings (microscopic measurements), whereas the second category (macroscopic brain models) will be fitted against fMRI/MEG data (macroscopic measurements).

2.3.1 Models for Perception-Action (T4.3.1)

In Task 4.3.1, Gustavo Deco, Neil Burgess, Olivier Faugeras will develop models for perception-action. Functions emerge from distributed processing across brain areas[1],. A key goal is to understand how bottom-up and top-down processes interact in this scheme. T4.3.1 addresses the fundamental question of how the cortical dynamical state observed at rest – presumably reflecting noise or spontaneous cognitive activity – is shaped during task performance, in which sensory-driven and cognitive-driven processes are both at work. T4.3.1 aims to develop a model of cortical activity closely tied to experimental protocols, which allows for predictions and verifications of fMRI and M/EEG data during rest and task conditions. In doing so, we examine relevant methods to measure cortical activity (mean level, fluctuations, periodicity, phase distribution, etc.), as well as develop algorithms to fit empirical data and methods to characterise the dynamical state of the cortex.

Unlike many previous cortical models using neural fields[2], our model relies on regions and connectivity between them, defined according to experimental data. So far, we have exploited data obtained from diffusion tensor imaging (DTI), a technique that allows to evaluate the quantity of nervous fibres connecting two loci in the cortex[3].

Our model will influence the thinking of researchers in other HBP Subprojects – particularly in SP3 (Cognitive Architectures), which aims to characterise successive stages in visual recognition using fMRI. Modelling output from T4.3.1 is expected to benefit the design of focused experimental protocols, and influence the large-scale simulation work of other Subprojects. Outputs for this Task include:

1) Establishment, via modelling, of a relationship between structural connectivity and functional connectivity (expressed activity). Our approach is based on the study of the dynamic principles in model-based networks that allow functional processes taking place in distant places to cooperate via forms of synchronisation.
2) Reproduced correlation patterns exhibited by the whole cortex, both at the resting state and when performing tasks.

3) Algorithms to adjust the interregional cortical projections individually in order to reproduce the empirical correlated patterns of activity. This will indicate which connections are necessary to reproduce experiments, and complement available data obtained using DTI.
4) Publications in peer-reviewed journals.
5) Publicly available models of large-scale activity.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.3.2 Models of Working Memory and the Effects of Attention (T4.3.2)

T4.3.2, led by Misha Tsodyks, will focus on models of working memory. Human subjects can retain lists of items (e.g., words), but not all items have the same likelihood of being retained. Moreover, memory recall is often sequential, jumping from one item to the next. The aim of this Task is to develop models that can qualitatively describe these phenomena. Success of working memory models can be measured by comparing the model complexity (a simple model is better) with the number of experimental data points that the model can qualitatively account for (a model which explains a lot of data is better).

The outputs of T4.3.2 will include a publically available model of working memory, and publications in peer-reviewed journals. Our model will be implementable in the large-scale simulations and will influence the thinking of researchers in other HBP Subprojects.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.3.3 Models of Biologically Realistic Network States; Wakefulness and Sleep (T4.3.3)

T4.3.3 will start in Year 2. We will design network models of spontaneous activity states, as well as wake and sleep type activity (such as Up/Down states). The models will be constrained by extracellular recordings of a large number of units (ensemble recordings) in humans or monkeys.

The success of the model can be measured by the extent to which:

1) The firing frequencies in the model match those measured in the extracellular data.
2) The irregularity of firing patterns in the model matches that measured in extracellular data.
3) The correlation patterns in the model match those found in the ensemble recordings.
4) The conductance measurements in the model match those in cortical neurons *in vivo*
5) It can be translated into Adaptive Exponential (AdEx) type models, so that succeeding models will be implementable directly in the hardware.

The outputs of this Task will include the model code, which will be made available in PyNN format so that the models can be simulated in various platforms (e.g. NEST or hardware). A

further output of this Task will be the publication of different models, which will be made available to the HBP Consortium, as well as publications in peer-reviewed journals.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 20)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.4 WP4.4 Principles of Brain Computation

The overall aim of WP 4.4 is to derive principles of brain computation that could be used in other HBP Subprojects, in neuromorphic hardware, or outside the HBP.

2.4.1 Principles of Computation in Single Neurons and Neural Microcircuits (T4.4.1)

For Task 4.4.1, simplified models for cortical microcircuits and columns based on data from EPFL and others (including simplified models from T4.1.1) will be analysed numerically and theoretically. The CNRS-UNIC group will evaluate measurements of computations in single neurons under *in vivo* conditions, while the group at TU Graz will consider a more theoretical perspective -- in particular, the question of which computational properties can emerge in microcircuits through learning. This work will utilise theoretical analysis and simulation of simplified versions of the EPFL column model (or of specific microcircuit motifs from this model).

Outputs for this Task include the following:

1) Experimentally observed functionalities that emerge in these models.
2) A theoretical understanding of the way these functionalities emerge.
3) At least one publication on the results of this research.

We currently estimate the following timeline for completion of planned actions:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

2.4.2 Novel Computing Systems Inspired by Biology (T4.4.2)

Wolfgang Maass's group (TU Graz) will investigate the applicability of biologically inspired models, concepts, and architectures of networks of spiking neurons with noise for solving difficult constraint satisfaction problems. The Task also will develop approximate solutions to NP-hard problems through spike-based networks. This research requires both theoretical work and computer simulations.

Outputs for this Task include the following:

1) Estimate of the number of constraints that can be satisfied simultaneously.
2) Evaluation of scalability, i.e., the performance of the computing system as a function of the size of the network.
3) At least one publication.

We currently estimate the following timeline:

- Stage 1: Model instantiated in software (Month 15)
- Stage 2: Model simulated, validated and delivered for use in the HBP Brain Simulation Platform (Month 30).

3. Measuring Progress Using Key Performance Indicators

Section 2 above describes the actions that will be undertaken by each Task, and the timeline for completing those actions. The Key Performance Indicator (KPI) for each Task consists of the proportion of actions completed by a specified date (percentage completion). For example: The target for T4.1.1 is to have two out of four actions – 50% - completed by the end of Month 12. If T4.1.1 reports that it is indeed 50% complete (i.e. two actions completed) by that date, then we know that this Task is on track.

WP4.1 Bridging Scales				
Task & Actions	Month		KPI - Target (%)	KPI - Actual (%)
T4.1.1 Derive simplified neuron and neural circuit models from biophysically morphologically detailed models	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use in Brain Simulation Platform		X	100% (2/2)	
T4.1.2 Modelling brain signals at different scales, from intracellular, local field potentials, VSD up to EEG and MEG signals	**20**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	

Table 1: Actions & KPIs – WP4.1 Bridging Scales

WP4.2 Synaptic plasticity, learning and memory				
Task & Actions	**Month**		**KPI - Target**	**KPI - Actual**
T4.2.1 Derive learning rules from biophysical synapse models	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	
T4.2.2 Unsupervised learning rules and emergent connectivity	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	

Table 2: Actions & KPIs – WP4.2 Synaptic plasticity, learning and memory

WP4.3 Large-scale models of human cognitive function				
Task & Actions	**Month**		**KPI - Target**	**KPI - Actual**
T4.3.1 Models for perception-action	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	
T4.3.2 Models of working memory and the effects of attention	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model delivered for use In Brain Simulation Platform		X	100% (4/4)	
T4.3.3 Models of biologically realistic network states; wakefulness & sleep	**20**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (4/4)	

Table 3: Actions & KPIs - WP4.3 Large-scale models of human cognitive function

WP4.4 Principles of brain computation				
Task & Actions	**Month**		**KPI - Target**	**KPI - Actual**
T4.4.1 Principles of computation in single neurons and neural microcircuits	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X		50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	
T4.4.2 Novel computing systems inspired by biology	**15**	**30**	**Actions completed**	**Actions completed**
Model instantiated in software	X	*X*	50% (1/2)	
Model simulated, validated and delivered for use In Brain Simulation Platform		X	100% (2/2)	

Table 3: Actions & KPIs – WP4.4 Principles of brain computation

4. Concluding notes

We have outlined the different models that will be investigated in SP4, as well as ways to measure their progress. All models investigated in SP4 will be validated against experimental data from SP3, or from existing data. Many of these models will be ported to a format (PyNN and AdEc) compatible with the neuromorphic hardware, allowing a strong interaction between this theoretical effort and neuromorphic approaches. Finally, all models will be posted to the Brain Simulation Platform so that HBP researchers can use them. Most will also be published and released in publically available databases.

References

[1] Cabeza and Nyberg, J Cogn Neurosci 2000

[2] Jirsa, Neuroinformatics 2004

[3] Hagmann et al, PLoS Biol 2008.