





<u>All Models for Bridging Scales developed during SGA2:</u> (D4.1.1 - SGA2)



Figure 1: Modelling of brain signals generated by neural networks Unitary field potentials illustrated here for the hippocampus.





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Abstract:	This report describes the pro Bridging Scales in SGA2 toget	ogress made on the vario her with related outputs a	us models developed in WP4.1 and publications.
Keywords:	Mean-fields models, Brain activity models, single cell and population levels.		
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### 1. Overview

The theoretical and computational models developed in SP4 occupy a central position in the HBP. On the one hand, they are derived from experimental data produced in the HBP. On the other hand, models are implemented in the HBP Platforms, where they serve as "first users". These models also constitute the building blocks of work that will be continued in SGA3, such as bridging scales, network models, models of plasticity, models of cognitive processes and whole-brain models.

This Deliverable describes the models developed for "bridging scales", so it spans from the cellular level (models of single neurons, and their dendrites), up to the level of neuron populations, using mean-field techniques inspired from physics. Mean-field models are ideal to link scales because they find their source in the single-cell models and try to formulate equations to describe the dynamics of populations of neurons, which can then be used at larger scales, up to the whole brain. Such combination of scales must be accompanied by appropriate modelling of the different brain signals involved, from single cell signals up to population signals such as the local field potential (LFP), voltage-sensitive dye (VSD) imaging, calcium imaging, neuronal magnetic fields and up to the electro-encephalogram (EEG).

The highlights of the work in SGA2 are that multiple models were successively developed, published and are now available on the Platforms. Some of these models are running on neuromorphic hardware. It must be noted that these models were published in a total of 40 publications in SGA2 from 7 laboratories, which is an exceptionally high level of publication for this Work Package. Most of these models are open access and available not only in the HBP but also to the entire community.

PU = Public







### 2. Introduction

In WP4.1, the goal is to bridge scales from neurons up to the whole-brain. The lowest scale is actually sub-cellular, it concerns the dendrites of neurons, and in particular how they integrate synaptic inputs. This is a long-standing problem which must be mastered to generate efficient single-cell models. The approach followed here is to apply a systematic complexity reduction procedure from detailed morphological models to obtain simplified models. A similar approach is also needed for collapsing the complexity of non-linear dendrites. Integrating biophysical mechanisms, such as the genesis of fast dendritic spikes in neurons, can potentially lead to fundamentally different types of computational capabilities. Here again, models of different complexity are needed to capture such computations. The simplified models conceived are done in a way compatible with the second-generation neuromorphic hardware, which places HBP in a unique position to integrate the results of biophysical simulations into neuromorphic computers.

Another important theme of WP4.1 is to link cellular models to population models using mean-field techniques. Mean-field models are well used in the literature, but none of such models are "realistic" in the sense that they apply in general to very simple systems. By following a procedure to derive mean-field models for complex neurons, this allows us to go one step further and envision integrating realistic models into whole-brain simulations, a work that will be done in SGA3. We consider properties such as neuronal stochasticity, spikes, spike-frequency adaptation, the different gain of excitatory and inhibitory neurons, conductance-based interactions, etc. Such properties are essential to shape large-scale interactions in the brain, and the availability of such realistic mean-field models will be an important step as they will constitute the basis of several models in SGA3. The derivation of mean-field models in SGA2, and their implementation in SGA3 to model large-scale up to whole-brain activity, is a combination of expertise unique to HBP.

Finally, another aspect investigated in WP4.1 is the genesis of brain signals. This theme of modelling is very important to the HBP, because to properly constrain models from experimental data, it is necessary to have good models of brain signals. This is true for single-cell models which are traditionally based on methods such as intracellular or extracellular recordings. It is also true for population models which are based on measurements such as LFP, VSD, calcium or EEG, and to properly constrain such models, it is necessary to have a good understanding of what population signals tell us about the underlying neural networks. This type of modelling is therefore inherently multiscale, as it combines different levels from cells to large populations.

Note that most of the models will be available in the Knowledge Graph and are in the process of being transferred.

PU = Public





# 3. Key Results KR4.1 Develop models single cell and population levels

### 3.1 Outputs

### 3.1.1 Overview of Outputs

### 3.1.1.1 List of Outputs

- Output 1: Develop models single-cell and population levels
- Output 2: Detailed spiking models from 3D anatomical reconstructions of L2/3 cortical human neuronal morphologies
- Output 3: Models with active dendrites
- Output 4: Biologically-realistic mean-field models
- Output 5: Development of theory and simulation techniques for population density methods
- Output 6: Mean-field models of formal networks
- Output 7: Mean-field models, from dendrites to visual processing

### 3.1.1.2 How Outputs relate to each other and the Key Result

The different models developed span multiple scales, ranging from single-cell models, network models, mean-field models and large-scale models. They are all integrated in EBRAINS and will be among the building blocks of the models developed in SGA3. These models will also be combined with models of brain signals at multiple scales (see KR4.3).

### 3.1.2 Output 1: Develop models single-cell and population levels

During the SGA2 period, Idan SEGEV's team from the Hebrew University of Jerusalem, has successfully achieved two key challenges.

- 1) To develop first-ever analytical method for reducing complex nonlinear neuron models (*Neuron\_Reduce*) (see Figure 2) while preserving the Neuron's I/O properties. This holds for any neuron type and enables for a 100-folds speedup in simulating large realistic neuronal networks (Amsalem *et al.*, *Nature Commun.* 2020) [1].
- 2) To develop detailed compartmental and cable models for human neurons (both layer 2/3 cortical pyramidal cells as well as CA1 hippocampal neurons); (Eyal *et al.*, *Front. Cell Neurosci*, 2018; Benavides-Piccione *et al.*, *Cereb. Cortex* 2019[2]). In yet another study we have demonstrated a surprising effect regarding how the neuron asymmetrical geometry underlies a universal (innate) local architecture in neuronal networks (Gal *et al.*, 2019, BioXiv)









Figure 2: Illustration of the method to simplify the morphology of detailed pyramidal neuron models.

# 3.1.3 Output 2: Detailed spiking models from 3D anatomical reconstructions of L2/3 cortical human neuronal morphologies

In SGA2, we (UA) built detailed spiking models from 3D anatomical reconstructions of L2/3 cortical human neuronal morphologies (from SP2, H. MANSVELDER). We then explored the functional consequences of dendritic trees' size by these models, as we quantified the bandwidth of information processing in these cells. We found that larger dendrites correlate 1) with more rapid action potentials at the onset and 2) with a broader transmission bandwidth, well above 100 cycles/s. This work appeared in eLife (Goriounova *et al.*, 2018, P1630, [1]).

We further investigated the model reduction of rodent L5 cortical pyramidal cells and interneurons, simplified into single-compartmental exponential integrate-and-fire units. We then successfully validated *in silico* our own *in vitro* experimental findings, concerning the transfer of correlated input synaptic activity into output spike trains. This work appeared in the Journal of Neuroscience (Linaro *et al.*, 2019, P2054, [2]).

We finally investigated the spike-initiation mechanisms in rodent cortical model neurons (as released from the Blue Brain Project), in terms of the impact of the Axon Initial Segment location plasticity. We found that across all 13 different excitatory electrical phenotypes, the information processing properties display a significant heterogeneity, with L4 cortical neurons outperforming all the other (Figure 3). This work is currently under review (Verbist *et al.*, 2020, *submitted for publication*).









Figure 3: Cut-off frequency of excitatory neocortical models from rodents

Information processing bandwidth of distinct excitatory cortical neuron models (from the Blue Brain Project) is examined systematically against the location of the Axon Initial Segment (AIS).

This work also contributes to Key Result KR4.5 Validation of spiking network model against experimental data.

### 3.1.4 Output 3: Models with active dendrites

Linktomodel'sinformationhttps://kg.ebrains.eu/search/instances/Model/74671c8d4f6e590452f6ceaebb780e03

During SGA2, we (CNRS) have investigated several models with dendrites. First, we have investigated dendritic integration mechanisms in the presence of fast dendritic spikes (Gorski *et al.* 2018; Figure 4) [1]. This model showed that the presence of dendritic spikes can provide an inverse response to correlations to neurons, which is a type of computation that is not possible using point neurons. The model also generates intense spiking activity, as observed experimentally. We are presently investigating networks of such neurons. Second, we have used morphologically reconstructed models of cortical and hippocampal pyramidal cells to understand how they generate extracellular fields (Telenczuk *et al.*, 2018, 2020) [2][3]. This work is also part of Task T4.1.4 on modelling brain signals.

The models use the AdEx mechanism and their implementation in the 2nd-generation BrainScaleS hardware is in progress.











The dendrites are subject to an intense spiking activity (top), while the soma displays lower levels of firing (bottom). From Gorski *et al.* 2018.

### 3.1.5 Output 4: Biologically-realistic mean-field models

During SGA2, we (CNRS) have worked on a framework for building mean-field models using a semianalytic procedure which allows one to design mean-field models even for complex neurons. This formalism was applied to gradually more complex models such as the leaky integrate and fire (IF) model (work in SGA1), the AdEx model (di Volo *et al.*, 2019, Figure 5) [4] and more recently the Hodgkin-Huxley model (Carlu *et al.*, 2020) [2]. This formalism will be used in SGA3 to design mean-field models to even more complex neuronal types, with dendrites. The mean-field approach was also extended to model Up-Down state dynamics, using either a mean-field model with adaptation (di Volo *et al.*, 2019) [4] or a state-dependent formalism (Capone *et al.*, 2020) [1]. The mean-field model approach was combined with voltage-sensitive dye recordings in awake monkey, to account for propagating waves of activity in V1, and how such propagating waves participate to visual information processing (Chemla *et al.*, 2019) [3]. This study was very important for modelling because it allowed us to calibrate mean-field models and create "networks of mean-fields", applied here to V1 recordings. The same approach will be continued in SGA3, towards larger scales, as reviewed in a recent paper (Goldman *et al.*, 2019) [5].

This model is now implemented in The Virtual Brain (TVB). This implementation (joint work with Viktor JIRSA in Marseille) is in progress and is described in the SGA2 Deliverable D4.6.1 (D26.1 D39).









Figure 5: State-dependent network response, that can be captured by a mean-field model.

The simulations in A, B illustrate the response of the same network (AdEx neurons) in two different states, to the same input. (From di Volo *et al.*, 2019). C. Comparison between mean-field models showing that an adapting mean-field optimally captures this state dependence.

### 3.1.6 Output 5: Development of theory and simulation techniques for population density methods

During SGA2, we (University of Leeds) completed a method for modelling two-dimensional population density methods [1]. We have demonstrated that this algorithm can simulate networks of hundreds of populations, using a GPGPU [1]. The algorithm has been made publicly available as simulator MIIND<sup>1</sup> and installation and usage has been facilitated by providing Docker containers and virtual machines. We gave a tutorial on its usage during CNS2019 in Barcelona<sup>2</sup>. MIIND has been installed on JURON and is directly available for anyone with an account on this machine, including but not restricted to all HBP members. After extensive validation, against Monte Carlo simulation and comparisons with DIPDE, the only other population density simulator, we are satisfied that our algorithms are very robust. Unlike DIPDE we are not restricted to leaky-integrate-and-fire neurons but can handle any 1D or 2D neuron model. We are now in a position that we can construct large-scale networks. We have recently reimplemented the Potjans-Diesmann model and have applied MIIND to a model of afferent feedback in spinal cord circuits [2]. We have managed to implement and evaluate the Hindmarsh-Rose model as well as a reduced version of Hodgkin-Huxley, which is remarkable because they are 3D models (Figure 6). 3D visualisations provide novel insight into how these complex dynamical systems evolve when subjected to noise. In summary, we can make models more complex by extending the network architecture, or by including more realistic models for individual populations. A model catalogue has been submitted as a preprint to arXiv [3]

<sup>&</sup>lt;sup>1</sup> <u>http://miind/sf.net</u>

<sup>&</sup>lt;sup>2</sup> Osborne H, de Kamps M, Deutz L, <u>Simulating Multiple Interacting Neural Populations using Population Density</u> <u>Techniques (using MIIND)</u>, whole day tutorial at CNS2019, Barcelona. (<u>https://www.cnsorg.org/cns-2019-tutorials#T4</u>)









Figure 6: Implementation of models in MIIND.

A-C: Validation MIIND vs DIPDE. D: Potjans-Diesmann model dynamics, an 8 population recurrent network. E: Hindmarsh-Rose model subject to shot noise, F: reduced Hodgkin-Huxley.

### 3.1.7 Output 6: Mean-field models of formal networks

Schuecker *et al.* 2018<sup>3</sup> show that optimal information-processing capabilities do not coincidence with the transition to chaos in networks that receive time-varying inputs. Dynamic mean-field theory shows how fluctuating inputs suppress chaos and lead to a dynamical regime that is optimal to memorize past inputs. In SGA2, using beyond mean-field methods, Dahmen *et al.* 2019 [1] show that motor cortex of the awake macaque monkey operates in a second type of critical regime, that is hidden from macroscopic brain signals but essential for high performance in such concepts as reservoir computing.



Figure 7: Phase Diagram of a recurrent, driven network. Optimal sequential memory arises in regime beyond linear stability

<sup>&</sup>lt;sup>3</sup> Jannis Schuecker, Sven Goedeke, Moritz Helias (2018), Optimal Sequence Memory in Driven Random Networks, Phys. Rev. X 8, 041029 (P1577)







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### 3.1.8 Output 7: Mean-field models, from dendrites to visual processing

Link to model's information https://kg.ebrains.eu/search/instances/Model/66f3f5ce6aa337c9dec89cf7843fe5d9

During SGA2, we (INRIA) have worked on building several new and challenging mean field models of interacting neurons. In a first work [1], we developed a framework to describe a network of spiking neurons with a dendritic compartment (Ball and Stick neurons) which takes into account dendritic spikes (see Figure 8). A second research axe was directed to mean field of generalised Integrate and Fire neurons for which a fast simulation procedure was described [2] and the long term behaviour of the network was characterised [3]. A third research axe was directed to Mean-field dynamics of networks with random synaptic weights.

We proved that the size of the synaptic weights can be of the order  $1/\sqrt{N}$  instead of 1/N in the deterministic setting [4,5]. Moreover, for correlated synaptic weights, the limit equation does not satisfy the propagation of chaos property. In other words, even in the mean-field limit, the activity of two typical neurons is still correlated. In a last research axe, we also developed a model of visual cortex with colour perception (A. Song, O. Faugeras, and R. Veltz., 2019) which reproduces in a unified way two opposing perceptual phenomena, known as simultaneous contrast and chromatic assimilation. We fitted our model to experimental data. We also developed a model of memory lifetime based on a stochastic synaptic rule and a statistical test. We were able to generalise a previous result concerning the memory lifetime which scales as  $1/f^2$  where is f is the (small) coding level of the signal.



Figure 8 : Network of spiking neurons with dendrites

Top: Comparison of the Firing rate for the finite size network and the mean field limit. Middle: plot of the density of the membrane potentials g(t,v) for the mean field. BoPom: empirical density for the finite size network (From [2]).

### 3.2 Validation and Impact

### 3.2.1 Actual and Potential Use of Output(s)

The actual and potential Use of the Outputs are already described within the Outputs.



### 3.2.2 Publications

### 3.2.2.1 Output 1: Develop models single-cell and population levels

[1] Amsalem O, Eyal G, Rogozinski N, Gevaert M, Kumbhar P, Schürmann F, Segev I. An efficient analytical reduction of detailed nonlinear neuron models. Nat Commun. 2020 Jan 15;11(1):288. doi: 10.1038/s41467-019-13932-6. PubMed PMID: 31941884; PubMed Central PMCID: PMC6962154. (P2295)

[2] Benavides-Piccione R, Regalado-Reyes M, Fernaud-Espinosa I, Kastanauskaite A, Tapia-González S, León-Espinosa G, Rojo C, Insausti R, Segev I, DeFelipe J. Differential Structure of Hippocampal CA1 Pyramidal Neurons in the Human and Mouse. Cereb Cortex. 2019 Jul 3. pii: bhz122. doi: 10.1093/cercor/bhz122. [Epub ahead of print] PubMed PMID: 31268532. (P1963)

[3] Doron M, Segev I and Shahaf D. Discovering Unexpected Local Nonlinear Interactions in Scientific Black-box Models, Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining - KDD '19, 2019. (P2050) <u>http://dx.doi.org/10.1145/3292500.3330886</u>

### 3.2.2.2 Output 2: Detailed spiking models from 3-D anatomical reconstructions of L2/3 cortical human neuronal morphologies

[1] Goriounova N., Heyer D., Wilbers R., Verhoog M., Giugliano M., Verbist C., Obermayer J., Kerkhofs A., Smeding H., Verberne M., Idema S., Baayen J., Pieneman A., PJ de Kock C., Klein M., Mansvelder H. Large and fast human pyramidal neurons associate with intelligence. 2018 Dec 18. eLife, Vol7. DOI: <u>http://dx.doi.org/10.7554/elife.41714</u> (P1630)

[2] Linaro D., Ocker G., Doiron B., Giugliano M. Correlation Transfer by Layer 5 Cortical Neurons under Recreated Synaptic Inputs in Vitro. 2019 Sep 25. The Journal of Neuroscience, Vol. 39, No 39. DOI: <u>http://dx.doi.org/10.1523/jneurosci.3169-18.2019</u> (P2054)

### 3.2.2.3 Output 3: Models with active dendrites

[1] Gorski, T., Veltz, R., Galtier, M., Fragnaud, H., Goldman, J.S., Telenczuk, B. and Destexhe, A. Dendritic sodium spikes endow neurons with inverse firing rate response to correlated synaptic activity. J. Computational Neurosci. 45: 223-234, 2018. (P972)

[2] Telenczuk, M., Brette, R., Destexhe, A. and Telenczuk, B. Contribution of the axon initial segment to action potentials recorded extracellularly. eNeuro 5: 0068-18, 2018. (P1347)

[3] Telenczuk, M., Telenczuk, B. and Destexhe, A. Modeling unitary fields and the single neuron contribution to local field potentials in the hippocampus. Manuscript under review, 2019. (P2502) biorXiv preprint: <u>https://www.biorxiv.org/content/10.1101/602953v2</u>

### 3.2.2.4 Output 4: Biologically-realistic mean-field models

[1] Capone, C., di Volo, M., Romagnoni, A., Mattia, M. and Destexhe, A. A state-dependent mean-field formalism to model different activity states in conductance-based networks of spiking neurons. Physical Review E, in press, 2020. biorXiv preprint: <u>https://www.biorxiv.org/content/10.1101/565127v1</u>

[2] Carlu, M., Chehab, O., Dalla Porta, L., Depannemaecker, D., Herice, C., Jedynak, M., Koksal Ersoz, E., Muratore, P., Souihel, S., Capone, C., Zerlaut, Y., Destexhe, A., di Volo, M. A mean-field approach to the dynamics of networks of complex neurons, from nonlinear Integrate-and-Fire to Hodgkin-Huxley models. J. Neurophysiol., *in press*, 2020. (P2369- *SGA3 publication*)

[3] Chemla, S., Reynaud, A., diVolo, M., Zerlaut, Y., Perrinet, K., Destexhe, A. and Chavane, F. Suppressive traveling waves shape representations of illusory motion in primary visual cortex of awake primate. J. Neurosci. 39: 4282-4298, 2019. (P1510)







[4] di Volo, M., Romagnoni, A., Capone, C. and Destexhe, A. Biologically realistic mean-field models of conductance-based networks of spiking neurons with adaptation. Neural Computation 31: 653-680, 2019. (P1864)

[5] Goldman, J.S., Tort-Colet, N., di Volo, M., Susin, E., Boute, J., Carlu, M., Nghiem, T-A., Gorski, T. and Destexhe, A. Bridging single neuron dynamics to global brain states. Frontiers in Systems Neuroscience 13: 75, 2019 (P2222)

### 3.2.2.5 Output 5: Development of theory and simulation techniques for population density methods

[1] de Kamps M, Lepperød M, Lai YM (2019) Computational geometry for modeling neural populations: From visualization to simulation. PLoS Comput Biol 15(3): e1006729. https://doi.org/10.1371/journal.pcbi.1006729 (P1899)

[2]: Muscles Recruited During an Isometric Knee Extension is Defined by Proprioceptive Feedback York G, Osborne H, Sriya P, Astil SI, de Kamps M, Chakrabarty S, bioRxiv 802736; (P2189) doi: <u>https://doi.org/10.1101/802736</u>

[3] Osborne H, Lai Y M, de Kamps M (2020), Models Currently Implemented in MIND, (P2463) <u>https://arxiv.org/submit/3070798</u>

### 3.2.2.6 Output 6: Mean-field models of formal networks

[1] David Dahmen, Sonja Grün, Markus Diesmann, and Moritz Helias (2019), Second type of criticality in the brain uncovers rich multiple-neuron dynamics, PNAS 2019 116 (26) 13051-13060 (P1995)

#### 3.2.2.7 Output 7: Mean-field models, from dendrites to visual processing

[1] N. Fournier, E. Tanré, and R. Veltz "On a toy network of neurons interacting through their dendrites" Annales de l'Institut Henri Poincaré (B) Probabilités et Statistiques, 2019 (P2455)

[2] B. Aymard, F. Campillo, and R. Veltz. "Mean-Field Limit of Interacting 2D Nonlinear Stochastic Spiking Neurons." *ArXiv:1906.10232 [Cs, Math]*, June 24, 2019. <u>http://arxiv.org/abs/1906.10232</u>. (P2461)

[3] Q. Cormier, E. Tanré, and R. Veltz. "Long Time Behavior of a Mean-Field Model of Interacting Neurons." *Stochastic Processes and Their Applications*, July 22, 2019. <u>https://doi.org/10.1016/j.spa.2019.07.010</u>. (P1567)

[4] O. Faugeras, J. Maclaurin, and E. Tanré. "The meanfield limit of a network of Hopfield neurons with correlated synaptic weights." *arXiv preprint arXiv:1901.10248* (2019). (P2048)

[5] O. Faugeras, E. Soret, E. Tanré. "Asymptotic behavior of a network of neurons with random linear interactions". 2019. (hal-01986927) (P2131)

[6] P. Helson, "A Mathematical Analysis of Memory Lifetime in a simple Network Model of Memory" 2019, Arxiv 1910.04993, accepted for publication in Neural Computation (P2456)





## 4. Key Result KR4.3 Develop models of brain activity and function

### 4.1 Outputs

### 4.1.1 Overview of Outputs

### 4.1.1.1 List of Outputs contributing to this KR

- Output 1: Models of brain signals
- Output 2: Multi-modal calculation of vbrain signal

### 4.1.1.2 How Outputs relate to each other and the Key Result

The contribution of SP4 to KR4.3 is essentially to provide models of different brain signals. These models can be both microscopic (such as single-cell signals), mesoscopic (LFP, VSD, calcium imaging) or macroscopic (EEG, MEG, EcoG). They will be integrated in EBRAINS and will be available to calculate brain signals from neural simulations at multiple scales (see KR4.1).

### 4.1.2 Output 1: Models of brain signals

During SGA2, the CNRS partner has participated in the modelling of several brain signals, some of these will continue in SGA3. A first approach was to model voltage-sensitive dye (VSD) signals. These signals were modelled from mean-field models, and they were successfully used to account for propagating waves in V1 of awake monkey, as well as the suppressive effect mediated by these propagating waves (Chemla *et al.*, 2019) [1]. A second modelling effort was about the local field potential (LFP). Here a model was developed to study the role of the initial segment in the shape of the extracellular spike signal (Telenczuk *et al.*, 2018,) [4]. The unitary LFP was also modelled in the hippocampus, using detailed biophysical models (Figure 9; Telenczuk *et al.*, 2020a [5]). The latter yields a method to calculate LFPs from spiking neurons using kernel templates fit to the experimental data (Telenczuk *et al.* 2020b [6]). Third, the effect of extracellular electric stimulation was modeled using models of axon fibres (Dali *et al.*, 2020) [2]. Finally, CNRS also modeled calcium signals based on two-photon and wide-field measurements in mice (collaboration with Francesco PAVONE, SP1). This work is in progress and a paper is in preparation.

CNRS also participated to a review article in collaboration with several HBP partners, and the group of Gaute Einevoll (Einevoll *et al.*, Neuron 2019) [3].









Figure 9: Modelling of unitary field potentials (uLFPs) in hippocampus.

Detailed morphological models of hippocampal pyramidal cells were used, to model the stimulation of inhibitory (A) and excitatory (B) synapses. The resulting uLFPs are shown in C, D. It can be seen that inhibitory uLFP are more powerful than excitatory uLFPs, as in experiments. (From Telenczuk *et al.*, 2020).

### 4.1.3 Output 2: Multi-modal calculation of brain signals

An essential part of computational neuroscience is comparing simulated and recorded neural activity [1-2], and our main work in SGA 2 has been centrred around the development and subsequent testing and use of a toolbox for calculating different brain signals from simulated neural activity, namely the software LFPy 2.0 [3-4] (https://lfpy.readthedocs.io/). This tool can now be used to calculate signals such as the local field potential (LFP), electrocorticogram (ECoG), electroencephalogram (EEG) and magnetoencephalogram (MEG) from arbitrary neural activity (Figure 10). We have applied LFPy 2.0 to (i) get a better understanding of extracellular potentials [5-7], to (ii) develop and test new methods [8 (also, one manuscript is under review<sup>4</sup>), and for (iii) gaining new insights into recorded LFP and EEG signals [9-10]. The work done in SGA2 lays the foundation for integrating LFPy 2.0 into the EBRAINS infrastructure in SGA3.

<sup>&</sup>lt;sup>4</sup> Martínez-Cañada P., Ness, T. V., Einevoll, G.T., Fellin, T, Panzeri, S (2020). Computing the electroencephalogram (EEG) from networks of point neurons. [Under review by PLoS Comp Biol]







Figure 10: Illustration of multi-modal calculation of brain signals.

Different waves of synaptic input (A) are projected to an unconnected population of 10,000 pyramidal cells (B). From this neural activity, we calculated the resulting LFP (C), and for either a radial or tangential population (D) corresponding to a neural population in a gyrus or a sulcus, the EEG (E) and MEG (F) at the head surface (for a snapshot in time marked by the vertical dashed line in panel A and C).

### 4.2 Validation and Impact

### 4.2.1 Actual and Potential Use of Output(s)

The actual and potential Use of the Outputs are already described within the Outputs.

### 4.2.2 Publications

### 4.2.2.1 Output 1: Models of brains signals

[1] Chemla, S., Reynaud, A., diVolo, M., Zerlaut, Y., Perrinet, K., Destexhe, A. and Chavane, F. Suppressive traveling waves shape representations of illusory motion in primary visual cortex of awake primate. J. Neurosci. 39: 4282-4298, 2019. (P1510)

[2] Dali, M., Goldman, J.S., Pantz, O., Destexhe, A. and Mandonnet, E. Modeling subcortical white matter stimulation. Manuscript under review, 2019 (P2539). biorXiv preprint: <u>https://www.biorxiv.org/content/10.1101/2019.12.12.872390v1</u>

[3] Einevoll, G.T., Destexhe, A., Diesmann, M., Gruen, S., Jirsa, V., de Kamps, M., Migliore, M., Ness, T.V., Plesser, H.E. and Schuermann, F. The scientific case for brain simulations. Neuron 102: 735-744, 2019. (P1913)

[4] Telenczuk, M., Brette, R., Destexhe, A. and Telenczuk, B. Contribution of the axon initial segment to action potentials recorded extracellularly. eNeuro 5: 0068-18, 2018. (P1347)

[5] Telenczuk, M., Telenczuk, B. and Destexhe, A. Modeling unitary fields and the single neuron contribution to local field potentials in the hippocampus. Manuscript under review, 2020a. (P2502) biorXiv preprint: <u>https://www.biorxiv.org/content/10.1101/602953v2</u>

[6] Telenczuk, B., Telenczuk, M. and Destexhe, A. A kernel-based method to calculate local field potentials from networks of spiking neurons, Manuscript under review, 2020b. (P2483) biorXiv preprint : <u>https://www.biorxiv.org/content/10.1101/2020.03.29.014654v1.full.pdf</u>







### 4.2.2.2 Output 2: Multi-modal calculation of brain signals

[1] Einevoll, G. T., Destexhe, A., Diesmann, M., Grün, S., Jirsa, V., de Kamps, M., ... Schürmann, F. (2019). The Scientific Case for Brain Simulations. Neuron, 102(4), 735-744. (P1913)

[2] Mäki-marttunen, T., Kaufmann, T., ... Andreassen, O. A. (2019). Biophysical Psychiatry–How Computational Neuroscience Can Help to Understand the Complex Mechanisms of Mental Disorders. Frontiers in Psychiatry, 10(534), 1-14. (P2005)

[3] Hagen, E., Næss, S., Ness, T. V., & Einevoll, G. T. (2018). Multimodal modeling of neural network activity: computing LFP, ECoG, EEG and MEG signals with LFPy 2.0. Front Neuroinform, 12(92). (P1847)

[4] Hagen, E., Næss, S., Ness, T. V., & Einevoll, G. T. (2019). LFPy - multimodal modeling of extracellular neuronal recordings in Python. In Encyclopedia of Computational Neuroscience (p. 620286). Springer, New York, NY. (P2004)

[5] Skaar, J.-E. W., Stasik, A. J., Hagen, E., Ness, T. V., Einevoll, G. T. (2020). Estimation of neural network model parameters from local field potentials (LFPs). [Accepted for publication in PLoS Comp Biol.; Preprint: <u>https://www.biorxiv.org/content/10.1101/564765v1</u>] (P2439)

[6] Ness, T. V., Remme, M. W. H., & Einevoll, G. T. (2018). h-Type Membrane Current Shapes the Local Field Potential from Populations of Pyramidal Neurons. Journal of Neuroscience, 38(26), 6011-6024. (P1342)

[7] Buccino, A. P., Kuchta, M., Jæger, K. H., Ness, T. V., Berthet, P., Mardal, K.-A., ... Tveito, A. (2019). How does the presence of neural probes affect extracellular potentials? Journal of Neural Engineering, 16(2). (P1848)

[8] Buccino, A. P., Kordovan, M., Ness, T. V., Merkt, B., ..., Einevoll, G. T. (2018). Combining biophysical modeling and deep learning for multi-electrode array neuron localization and classification. Journal of Neurophysiology, 120, 1212-1232. (P1394)

[9] Luo, J., Macias, S., Ness, T. V., Einevoll, G. T., Zhang, K., & Moss, C. F. (2018). Neural timing of stimulus events with microsecond precision. PLoS Biology, 16(10), 1-22. (P1908)

[10] Mäki-Marttunen, T., Krull, F., Bettella, F., Hagen, E., Næss, S., Ness, T. V., ... Einevoll, G. T. (2019). Alterations in Schizophrenia-Associated Genes Can Lead to Increased Power in Delta Oscillations. Cerebral Cortex, 29(2), 875-891. (P1565)

[11] Heiberg, T., Kriener, B., Tetzlaff, T., Einevoll, G. T., & Plesser, H.-E. (2018). Firing-rate models for neurons with a broad repertoire of spiking behaviors. Journal of Computational Neuroscience, 45(2), 103-132. (P1402)







### 5. Conclusion and Outlook

In conclusion, we believe the work of WP4.1 has been successfully completed and according to the planned work for the SGA2 phase. Multiple models were developed, at the level of single cells and dendrites, the level of population of neurons, and for different brain signals spanning different scales from single neurons to brain scale. These models are now available in the Platforms. Some of these models are running on the 1<sup>st</sup> and 2<sup>nd</sup> generation of neuromorphic hardware. Nearly all models have been published and are available not only inside HBP, but also to the entire community.

It must be emphasised that WP4.1 reached an unusually high level of publications in SGA2, for dendritic models (10 publications from 3 laboratories), mean-field models (19 publications for 4 laboratories), and for the modeling of brain signals (17 papers in SGA2, from 2 laboratories). Most of these models are open access, and those who are not open-access will become open as soon as the corresponding paper is published.

Concerning the uniqueness of the work done here, we believe the combination of scales, from subcellular (dendrites) to large brain-size scales is unique to the HBP. It is also unique to the HBP that so many brain signals are modelled in a single project, from extracellular potential of single neurons, up to large scale signals such as imaging or EEG. Finally, all such models are (or will soon be) made available to the community, either in the form of open-code, or via tools such as LFPy.

The models developed in WP4.1 will all be continued in SGA3. The expertise in modelling dendrites will be used in the detailed models of human neurons in SGA3 WP1, for cerebral cortex, hippocampus, cerebellum and basal ganglia. The models for brain signals will be used there as well. The mean-field models are now implemented in The Virtual Brain (TVB), and will soon simulate brain dynamics at the level of the whole human brain, as well as the mouse brain (mouse TVB), respectively in WP1 and WP2 of SGA3. It must be noted that this modelling will be a true "bridging scales" since it will combine models estimated from cellular-level activity (in SGA1 and SGA2) and will be implemented to simulate the whole human brain (in SGA3).