

Data-driven and validated multiscale computational models and neuromorphic implementations
(D2.6- SGA3)

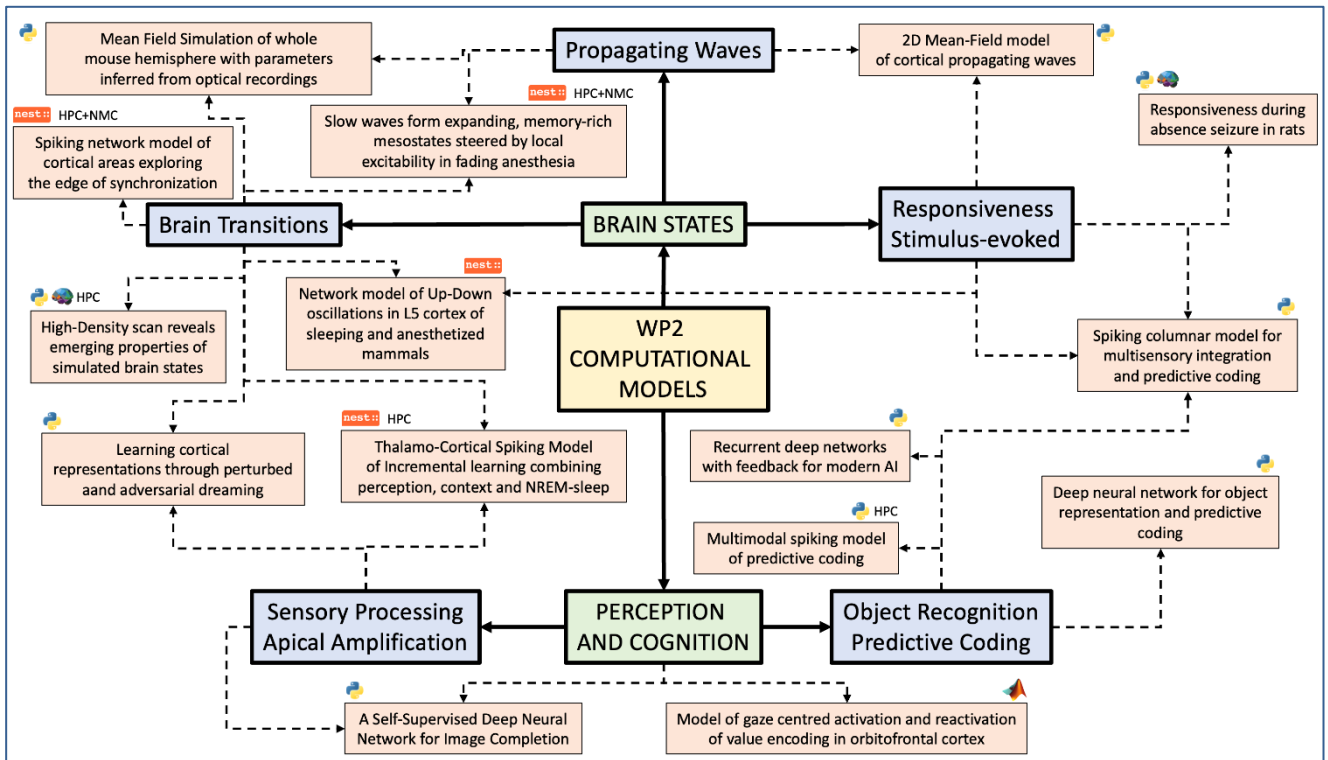


Figure 1: Diagram of the WP2 computational models

Diagram showing the computational models delivered by HBP SGA3 WP2 to the neuroscientific community. These models are mainly related to the investigation of brain states (brain transitions, propagating waves and responsiveness/stimulus-evoked) as well as to perception and cognition (Sensory Processing, Apical Amplification, Object Recognition and Predictive Coding).

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Description in GA:	Our models will be mainly mesoscopic and will be integrated into the full brain models generated in WP1. They will reproduce emergent activity in various brain states, responsiveness, sensory processing, and cognitive processes, departing from		



	<p>vision and reaching motor manipulation. Our NEST models will be used as a benchmark for analysis workflows, for execution on HPAC platforms. Network models will be adapted for real-time or faster-than-real-time execution on neuromorphic architectures (Spinnaker and BrainScaleS). Dendritic apical amplification will be integrated.</p>
<p>Abstract:</p>	<p>In this Deliverable we include computational models (n=15) generated in WP2 for the investigation of emergent activity generation in various brain states, brain responsiveness, sensory processing, multisensory integration, and object representation. We effectively integrated multiscale computational brain models, employing mean-field models to shed light on the relationship between different scales, from the mesoscale to the whole human brain macroscale activity. Through the TVB-AdEx model, we also explored pathological states in the rat brain. In the area of multisensory integration and predictive coding, three distinctive models were introduced. The knowledge gained from the three models will improve our understanding of perception and sensory predictions, offer valuable insights in neural mechanisms of brain disorders such as autism or schizophrenia, and inspire neuromorphic, artificial intelligence and robotic applications. Another approach is based on apical amplification, where deep neural networks use a feed-forward tuning model in which top-down connections regulate the bottom-up flow of information via contextual inputs to dendrites of pyramidal neurons in the neocortex for visual processing and image completion. These models have been inspired and tuned by experimental data obtained for this purpose, and often published along with the data. Some of them are executed in HPC platforms, and some in NMC. Most importantly, all of them have been made available to the community through EBRAINS, enhancing the impact of this work on a broad community not only of computational neuroscientists, but of students, clinicians, and general neuroscientists.</p>
<p>Keywords:</p>	<p>Computational models; NEST; mean field models; TVB; brain states; spiking models; slow waves; predictive coding; object representation; apical amplification; thalamo-cortical model; cortical model</p>
<p>Target Users/Readers:</p>	<p>Clinicians, computational neuroscience community, neuroinformaticians, neuroscientific community, neuroscientists, platform users, researchers, scientific community, and students.</p>

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1. Introduction

Investigating brain dynamics at multiple scales, and in particular how different scales interact, is a very difficult task that necessarily requires the use of computational models tightly linked to experiments. The goal of the research described in this deliverable D2.6 is to investigate various aspects of brain function and behaviour by creating computational models (n=15) that then are shared through EBRAINS.

The models cover a wide range of topics, including brain states, brain responsiveness, sensory processing, and cognitive processes (see Fig. 1 and Table 1). In the present Deliverable, we illustrate this approach at multiple levels.

First, we introduce computational models of **Brain responsiveness at multiple scales**. We show that mean-field models can be very powerful to investigate the link between scales, as also shown in Deliverable 2.3 (Showcase 3). This will be investigated using the recently introduced mean-field models either at mesoscale, modelling V1, or at macroscales, modelling the activity states in the whole human brain model. We will also show that the TVB-AdEx model of the rat brain can be used to investigate pathological activity states.

Then, we present models of **Multisensory integration and predictive coding**. Three computational models about multisensory integration and predictive coding which incorporate different levels of biological realism are presented: A neurobiological model, which simulates a realistic spiking cortical column using available connectivity data from the literature and the Knowledge Graph; A neurobiological-cognitive hybrid model, which depending on the version is constructed with a biologically realistic neuron model (i.e. spiking neuron) or a differentiated cellular circuitry (i.e. PV-SST-VIP circuits) and a local learning rule (i.e. Hebbian learning) to perform object reconstruction; and finally a cognitive model, which is built with rate-based neurons to focus on extending the cognitive ability of the hybrid model by introducing movement and visuomotor corrections. The knowledge gained from the three models will improve our understanding of perception and sensory predictions, offer valuable insights in neural mechanisms of brain disorders such as autism or schizophrenia, and inspire neuromorphic, artificial intelligence and robotic applications (see Deliverable D2.4 - Showcase 4).

We also present models of **Apical Amplification**: We are bridging multiscale empirical frameworks and machine learning to elucidate mechanisms of cognition and perception based on top-down context-dependent processing. We reframe sensory processing from a feed-forward, feature tuning model to a cooperative process in which top-down connections regulate the bottom-up flow of information via contextual inputs to dendrites of pyramidal neurons in the neocortex. Laminar resolution human brain imaging can probe microcircuit function during cognitive states and top-down information flow, that can be assimilated with neural models, specifically the characterisation of dendritic mechanisms that, in turn, inspire advancements in machine learning. Apical amplification, where feedback inputs to apical dendrites of pyramidal neurons would selectively amplify the cell's output, predicts a potential mechanism for recurrent processing which requires empirical testing.

Finally, we also present models of **brain states**. These models play a vital role in the exploration and understanding of brain states. They provide insights into various aspects of the spatio-temporal brain activity patterns, such as slow oscillations occurring in sleep and anaesthesia. Together, they contribute to unravelling the intricate nature of brain states and their underlying mechanisms, enhancing our comprehension of brain function.

In the table below, all the computational models are listed along with their main characteristics: 1) code implementation (MATLAB or Python), whether they use The Virtual Brain (TVB), whether they use NEST, or if Apical Amplification is accounted in the model if they apply Predictive Coding and whether they make use of High-Performance Computing (HPC) or Neuromorphic Computing (NMC).

Table 1: List of models with the different tools used

Model	Python/ MATLAB	TVB	NEST	Apical Amplification	Predictive Coding	HPC	NMC
Mean Field Simulation of whole mouse hemisphere with parameters inferred from optical recordings	X						
Spiking network model of cortical areas exploring the edge of synchronization	X		X			X	X
Slow waves form expanding, memory-rich mesostates steered by local excitability in fading anaesthesia	X		X			X	X
High-Density scan reveals emerging properties of simulated brain states	X	X				X	
Network model of Up-down oscillations in L5 cortex of sleeping and anaesthetised mammals	X		X				
Learning cortical representations through perturbed and adversarial dreaming	X			X			
Thalamo-cortical spiking model of incremental learning combining perception, context, and NREM-sleep	X		X	X		X	
A self-supervised deep neural network for image completion	X			X			
2D Mean-Field model of cortical propagating waves	X						
Responsiveness during absence seizure in rats	X	X					
Spiking columnar model for multisensory integration and predictive coding	X				X		
Recurrent deep networks with feedback for modern AI	X						
Multimodal spiking model of predictive coding	X				X	X	
Deep neural network for object representation and predictive coding	X				X		
Model of gaze centred activation and reactivation of value encoding in orbitofrontal cortex	X						

The computational models presented here would be of interest to multiple communities within the field of neuroscience, computational modelling, and the broader scientific research community, as our research addresses a wide variety of topics that provide insights on how the brain networks function and interact. Moreover, our work directly involves the EBRAINS platform, making it of interest to the community of researchers who intend to use this infrastructure for accessing, reproducing, and collaborating on neuroscience research. The models are publicly shared.

2. Computational Models

2.1 Models of brain responsiveness at multiple scales

2.1.1 2-D mean-field model of cortical propagating waves

Link to the KG: <https://search.kg.ebrains.eu/instances/a94b0808-9693-4f74-afc8-d9a29bb9d952>

Responsiveness to external stimuli can occur as propagating waves, as shown for example in primary visual cortex (V1) of awake monkey, where visual stimuli systematically induce a propagating wave across V1 (Muller et al., 2014). Such travelling waves were modelled by 1D networks of AdEx mean-field units (Zerlaut et al., 2018), which were recently extended in 2D networks to better reflect the V1 topology (Roques and Destexhe, 2023, in preparation). This 2D array of AdEx mean-field models is illustrated in Figure 2.

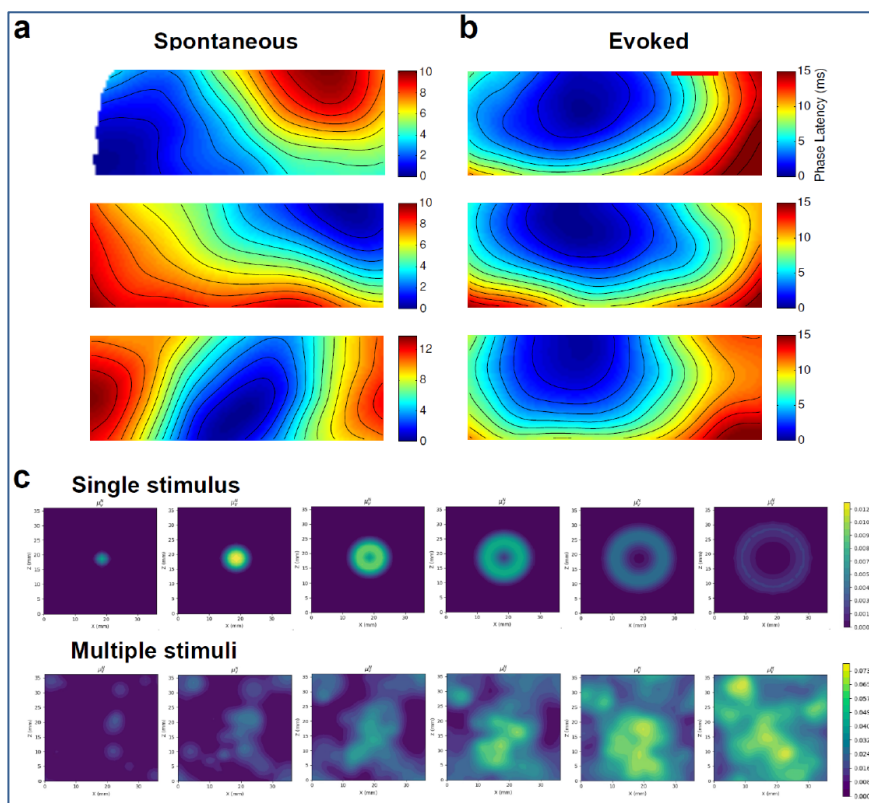


Figure 2: Cortical responses occurring as travelling waves.

a. Spontaneous travelling waves occurring in awake monkey primary visual cortex, imaged by VSD. Each panel shows a phase latency map for 3 examples of spontaneous travelling wave. b. Travelling waves evoked by visual inputs. Three examples of the same visual input and the travelling wave evoked. c. Model of travelling waves using a 2D array of AdEx mean-field units. The top row shows snapshots of the simulated VSD signal for a single visual input evoking a travelling wave. The bottom row shows the response evoked by more complex inputs in the same conditions.

2.1.2 High-density scan reveals emerging properties of simulated brain states

Link to the model: https://github.com/davidaquilue/TVBAdEx_ParSweep

The TVB-AdEx model presented in Showcase 3: <https://wiki.ebrains.eu/bin/view/Collabs/showcase-3-tvb-brain-states-modelling> and published recently (Goldman et al., 2022, P3023) could successfully reproduce asynchronous and slow-wave synchronized brain states, as well as their responsiveness to external inputs.

To extend this model further, we performed a high-density parameter scan, and explore the parameter space of the TVB-AdEx model (Aquilue et al., 2023; P4143). We explored a few features related to the emergence of collective properties of brain states: (1) the parameter space was extensively scanned to verify that the asynchronous and slow-wave states are a defining feature of this model and were present in a considerable domain of parameters. (2) We verified that the synchrony of slow-waves - an emerging property - was present widely in the model. (3) We also analysed another emerging property, the relation between functional connectivity (FC) with the structural connectivity (SC). We found that the model generally exhibits a higher FC-SC relation in the slow-wave oscillatory state, as we also observed in data (see Deliverable 2.4 - Showcase 3). These properties were not « built-in » and were therefore emerging properties of the model.

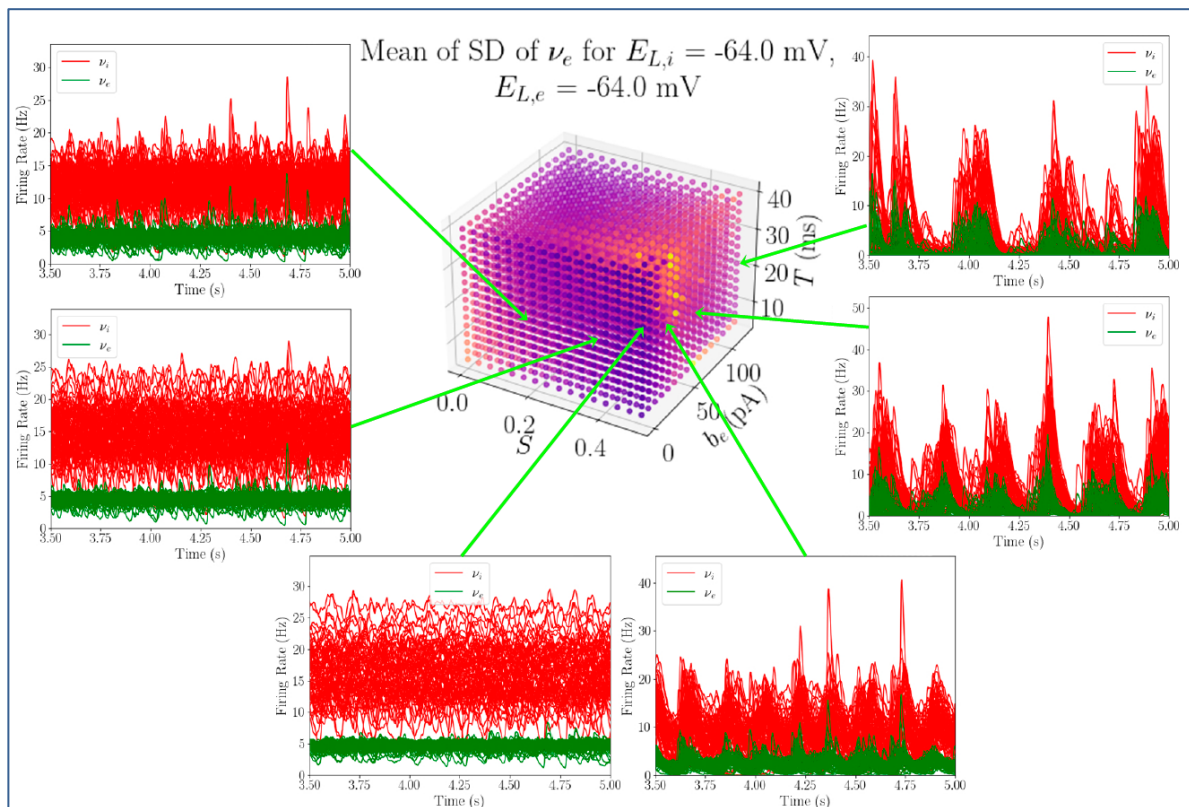


Figure 3: Mapping of the excitatory firing rate as a function of three parameters.

The 3D plot shows the standard-deviation of the firing rate as a function of three parameters (time constant τ , coupling strength S and adaptation b_e). The floating panels show examples of 68 AdEx mean-field nodes, plotted for six different parameter combinations. When $b_e = 0$ pA, for intermediate values of S , one can see how asynchronous states appear, consistent with the low value of SD shown in the 3D plot. For $S = 0.5$, one can see the transition between AI and UD states when increasing b_e . Modified from Aquilue et al. 2023.

2.1.3 Responsiveness during absence seizures in rats

Link to KG: <https://search.kg.ebrains.eu/instances/d19d8e53-b755-406e-b559-d22e2b6eb89e> (although this is a dataset entry, the model is stored in the same folder).

In a recent study (Stenroos et al., 2023, preprint available¹), it was shown using fMRI measurements in rats, that the responsiveness and associated brain-wide spread of activity are strongly diminished during absence seizures (data in E BRAINS). In this case, the input was sensory (whisker stimulation), and the EEG of the animal was recorded simultaneously with fMRI, to identify acquisition windows with and without seizures. During non-seizure (inter-ictal) awake activity, sensory stimuli evoked a spread of information from sensory areas to multiple brain areas, whereas during absence seizures (ictal), the sensory stimulation effect tended to remain confined to somatosensory cortex.

¹ <https://www.biorxiv.org/content/10.1101/2023.07.26.550701v1.abstract>

We have designed computational models, using a custom-made rat version of TVB (using a published connectome, BAMS; Bota and Swanson, 2007). The AdEx mean-field model used previously (di Volo et al., 2019) was used to simulate either normal or seizure dynamics (Fig.4 A-D). Implementing this mean-field in TVB using a similar implementation as the TVB-AdEx introduced previously (Goldman et al., 2022), but here using the BAMS rat connectome could reproduce these findings (Fig. 4 E).

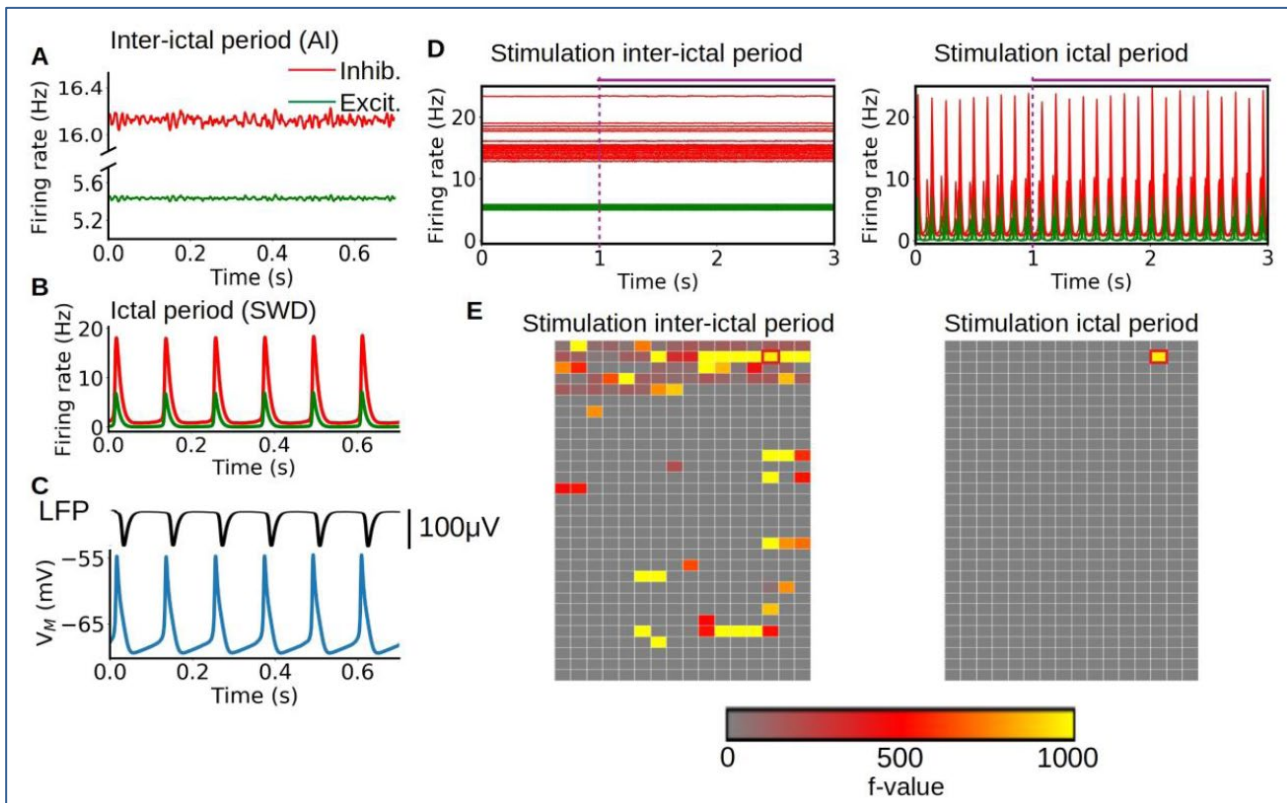


Figure 4: Simulation of sensory stimulation during ictal and interictal periods

A-B: asynchronous irregular (AI) and spike-and-wave discharge type of dynamics obtained from the mean-field model, representing interictal and ictal periods respectively. The change between the two dynamics is given by the strength of the adaptation current in the AdEx mean-field model. C: LFP and membrane potential obtained from the mean-field model. The model can capture the SWD pattern observed experimentally in LFP measurements which is correlated with periods of hyper-polarization in the membrane potential. D-E: time-series and statistical maps of the simulated sensory stimulus in the whole brain simulations of the rat, showing the results of a stimulation of the primary visual cortex during ictal and inter-ictal periods. The onset and duration of the stimulus is indicated by the dashed vertical line and horizontal line at the top of the time-series. The statistical maps are built from a 2D representation of the 496 brain regions of the BAMS rat connectome (Bota and Swanson, 2007).

2.2 Models of multisensory integration and predictive coding

2.2.1 Deep neural network for object representation and predictive coding

Link to the KG: <https://search.kg.ebrains.eu/instances/0b219bf1-dead-4a06-811a-fdce66f2ec7d>.

This model describes the computations underlying object invariant recognition, typical of ventral stream processing of visual images, under a predictive coding framework. It is based on biologically plausible principles such as modular architectures composed of firing rate units and plasticity elicited by Hebbian learning rules and displays a low representational dissimilarity among items of the same class and temporal correlations in agreement with experimental data.

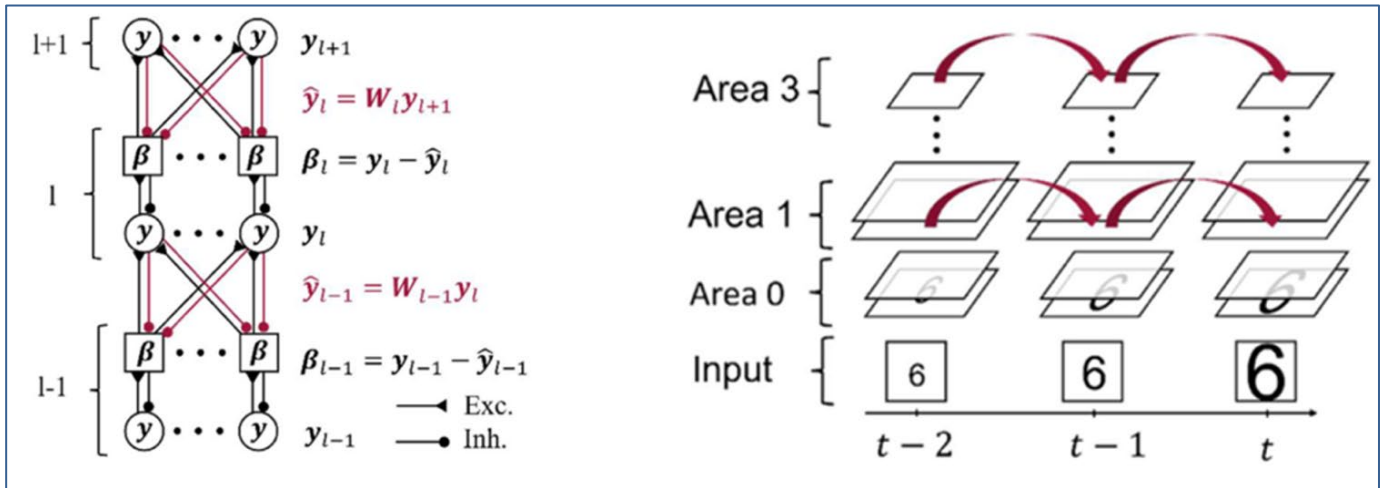


Figure 5: Schematic of the cognitive model

Cognitive model for invariant object recognition (left), and illustration of temporal iterations (right)

Related publications:

P3919: Brucklacher M, Bohte SM, Mejias JF, Pennartz CMA, Local minimization of prediction errors drives learning of invariant object representations in a generative network model of visual perception, bioRxiv, p. 2022.07.18.500392, 2022.

2.2.2 Spiking columnar model for multisensory integration and predictive coding

Link to the KG: <https://search.kg.ebrains.eu/instances/dcb14321-9294-43bc-9bcd-26d3bda1ef54>

This model constitutes a neurobiologically precise spiking neural network model of a cortical column in primary visual cortex V1 of the mouse. It is constrained by state-of-the-art connectivity data from experiments, and includes laminar modules, four different cell types (pyramidal, PV, SST and VIP), post-synaptic receptors for AMPA, GABA and NMDA, and spike-timing-dependent plasticity rules for learning. The model can reproduce spontaneous and stimulus-evoked activity across all layers and cell types, as well as provide insight into the conditions for the emergence of complex dynamical patterns such as stimulus-specific oscillations.

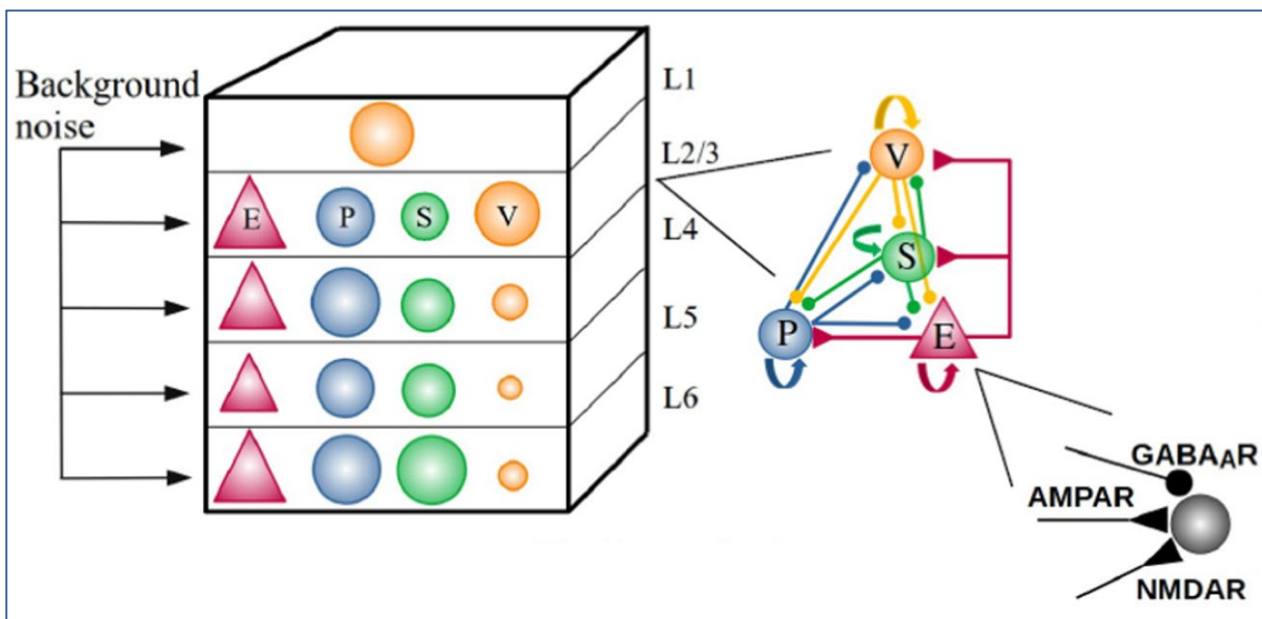


Figure 6: Schematic of the spiking neural network (SNN)

SNN for the V1 cortical column, displaying the laminar modules, cell types and receptor types included in the model.

Related publications:

P4133: G Moreni, CMA Pennartz, JF Mejias, Synaptic plasticity is required for oscillations in a V1 cortical column model with multiple interneuron types, BioRxiv, 2023.08. 27.555009, 2023 <https://www.biorxiv.org/content/10.1101/2023.08.27.555009v1>

2.2.3 Multimodal spiking model of predictive coding

Link to the KG: <https://search.kg.ebrains.eu/instances/7d29bdc5-ac3d-4b59-aed7-fdcf1b667d03>

This model constitutes a hybrid approach which combines neurobiologically plausible features (such as the use of spiking neural networks) with the computational power of cognitive models (reflected in a good model performance, low within-class dissimilarity of neural representations, and realistic neural spiking dynamics) in the context of predictive coding. The model also highlights the importance of a fast feedforward ‘gist-like’ pathway to trigger sensory priors in higher cortical areas.

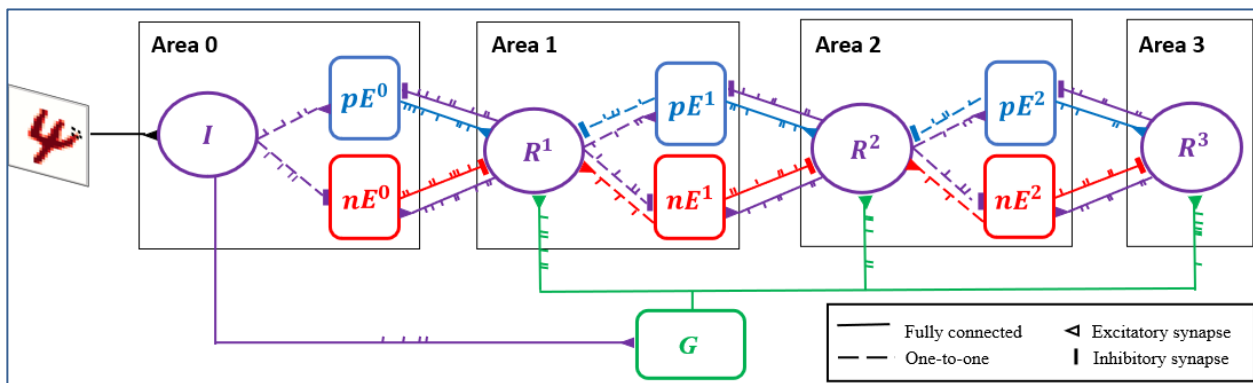


Figure 7: Schematic of the spiking neural network for predictive coding

Each module (beyond the first one) contains representational neurons and two types of error-prediction circuits, plus a feedforward gist.

Related publications:

P3898: K Lee, S Dora, J Mejias, S Bohte, C Pennartz, Predictive coding with spiking neurons and feedforward gist signalling, bioRxiv, 2023.04. 03.535317, 2023

2.3 Models of apical amplification

We are bridging multiscale empirical frameworks and machine learning to elucidate mechanisms of cognition and perception based on top-down context-dependent processing. We re-frame sensory processing from a feed-forward, feature tuning model to a cooperative process in which top-down connections regulate the bottom-up flow of information via contextual inputs to dendrites of pyramidal neurons in the neocortex. Laminar resolution human brain imaging can probe microcircuit function during cognitive states and top-down information flow, that can be assimilated with neural models, specifically the characterisation of dendritic mechanisms that, in turn, inspire advancements in machine learning. Apical amplification, where feedback inputs to apical dendrites of pyramidal neurons selectively amplify the cell’s output, offers a possible mechanism for recurrent processing but such two-point neuronal processes require model-based and empirical demonstration.

In this direction, our model, ‘Recurrent deep networks with feedback for modern AI’, demonstrates that recurrent connectivity, a hallmark of biological visual systems that we are also testing with human laminar fMRI, is critical for understanding the accuracy and dynamics of human visual recognition performance (P1137). In line with this model, we have also trained a self-supervised deep convolutional neural network (CNN) with an encoder/decoder architecture to fill in a partially occluded image. Our network outperformed a classical object-recognition supervised network (VGG16) in terms of similarity to brain data recorded from humans viewing the same occluded images, providing further support that there is information in sensory areas (V1) not related to bottom-up features but to generative internal models, in line with the theory that dendritic

computations process feedback inputs related to top-down context (P2886). Lastly, we present a functional model of dreaming (Depperois et al., 2022) that can be reconciled with cellular models of dreaming (Aru et al., 2022) by postulating that forward encoding pathways and feedback generative pathways are represented by separate streams of L2/3 pyramidal neurons. These L2/3 streams likely do not reach awareness, while their integration in L5 pyramidal neurons that encode the match between the encoding and generative pathway through dendritic calcium spikes (Aru et al., 2019, Takahashi et al., 2020). These L5 pyramidal neurons may also be active when a subject dreams, opposed to cortical activity during sleep that is not perceived as dream. Together these models align with data-driven theories suggesting that top-down projections contextually modulate sensory processing, via dendritic-specific computations.

2.3.1 *Recurrent deep networks with feedback for modern AI*

Link to the KG: <https://search.kg.ebrains.eu/instances/ae6a13b-4006-49df-bdcc-ec27c2409e72>

Here we compared recurrent convolutional neural networks (rCNNs) to feed-forward (fCNN) control models in terms of their object-recognition performance and their ability to account for human visual recognition behaviour. We report that recurrent processing can improve recognition performance compared to similarly complex feed-forward networks. Deep feed-forward neural network models of vision dominate in both computational neuroscience and engineering. The primate visual system, by contrast, contains abundant recurrent connections. Recurrent signal flow enables recycling of limited computational resources over time, and so might boost the performance of a physically finite brain or model. Here we show: (1) Recurrent convolutional neural network models outperform feed-forward convolutional models matched in their number of parameters in large-scale visual recognition tasks on natural images. (2) Setting a confidence threshold, at which recurrent computations terminate and a decision is made, enables flexible trading of speed for accuracy. At a given confidence threshold, the model expends more time and energy on images that are harder to recognise, without requiring additional parameters for deeper computations. (3) The recurrent model's reaction time for an image predicts the human reaction time for the same image better than several parameter-matched and state-of-the-art feed-forward models. (4) Across confidence thresholds, the recurrent model emulates the behaviour of feed-forward control models in that it achieves the same accuracy at approximately the same computational cost (mean number of floating-point operations) (P2284). However, the recurrent model can be run longer (higher confidence threshold) and then outperforms parameter-matched feed-forward comparison models. These results suggest that recurrent connectivity, a hallmark of biological visual systems, may be essential for understanding the accuracy, flexibility, and dynamics of human visual recognition.

2.3.2 *Learning cortical representations through perturbed and adversarial dreaming*

Link to the KG: <https://search.kg.ebrains.eu/instances/26bcf978-cddf-420d-8e7c-fff7ab2a892f>

We are exposed to different visual stimuli during our waking experience. The brain builds semantic context from this visual experience without explicit supervision. How does the brain build high level representations about visual inputs, and how does sleep help? Humans and other animals learn to extract general concepts from sensory experience without extensive teaching. This ability is thought to be facilitated by offline states like sleep where previous experiences are systemically replayed. However, the characteristic creative nature of dreams suggests that learning semantic representations may go beyond merely replaying previous experiences. We support this hypothesis by implementing a cortical architecture inspired by generative adversarial networks (GANs), (P2911). Learning in our model is organized across three different global brain states mimicking wakefulness, non-rapid eye movement (NREM), and REM sleep, optimizing different, but complementary, objective functions (figure above). We train the model on standard datasets of natural images and evaluate the quality of the learned representations. Our results suggest that generating new, virtual sensory inputs via adversarial dreaming during REM sleep is essential for extracting semantic concepts, while replaying episodic memories via perturbed dreaming during NREM sleep improves

the robustness of latent representations. The model provides a new computational perspective on sleep states, memory replay, and dreams, and suggests a cortical implementation of GANs.

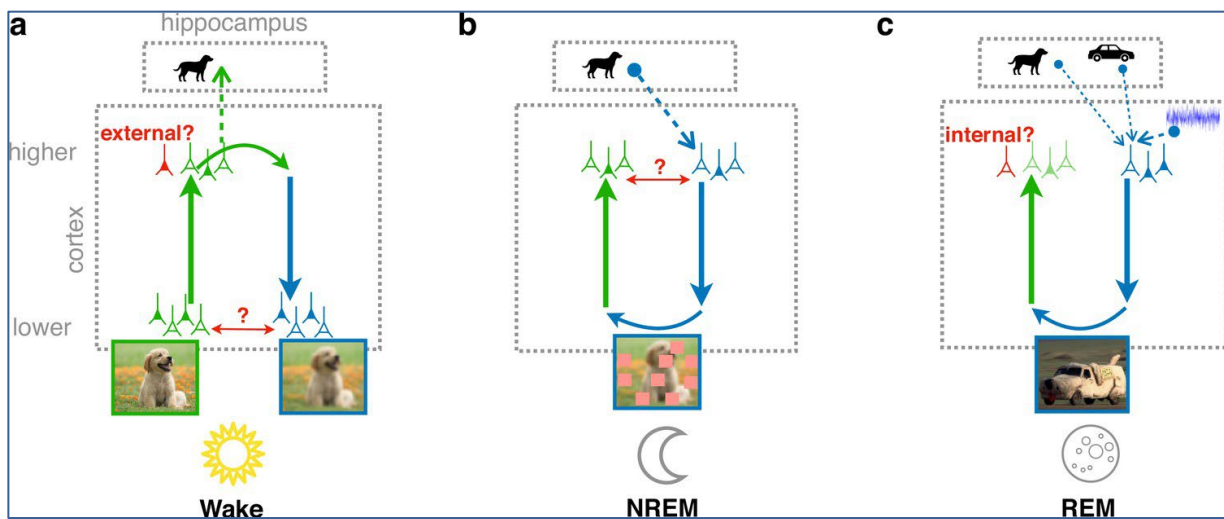


Figure 8: Cortical representation learning through perturbed and adversarial dreaming (PAD)

(a) During wakefulness (Wake), cortical feed-forward pathways learn to recognize that low-level activity is externally driven, and feedback pathways learn to reconstruct it from high-level neuronal representations. These high-level representations are stored in the hippocampus. (b) During non-rapid eye movement sleep (NREM), feed-forward pathways learn to reconstruct high-level activity patterns replayed from the hippocampus affected by low-level perturbations, referred to as perturbed dreaming. (c) During rapid eye movement sleep (REM), feed-forward and feedback pathways operate in an adversarial fashion, referred to as adversarial dreaming. Feedback pathways generate virtual low-level activity from combinations of multiple hippocampal memories and spontaneous cortical activity. While feed-forward pathways learn to recognize low-level activity patterns as internally generated, feedback pathways learn to fool feed-forward pathways (figure 1, P2911).

2.3.3 A Self-Supervised Deep Neural Network for Image Completion

Link to the KG: <https://search.kg.ebrains.eu/instances/01f9cfbc-d45f-4ae3-866a-c13c006ec390>

Here we investigated the similarity in representations between an artificial neural network trained to fill occlusions and early visual cortical fMRI activity acquired from humans viewing occluded images. Specifically, we wanted to investigate whether an artificial neural network with encoder/decoder architecture would better approximate brain data acquired during a task involving cortical feedback signals, than a purely feedforward network. We have two main findings. First, training an artificial network to solve the same task as humans revealed increased similarity to brain data compared to a generic supervised network for classification. Furthermore, the CNN decoder pathway was more similar to brain processing than the encoder pathway. In fact, there was an increase in similarity going further along the network, in line with the integration of multiple feature levels in early visual cortex. This work provides additional evidence that optimal models of the visual system might come from less feedforward architectures trained with less supervision. We also find that CNN decoder pathway activations are more similar to brain processing compared to encoder activations, suggesting an integration of mid- and low/middle-level features in early visual cortex. Challenging an artificial intelligence model to learn natural image representations via self-supervised learning and comparing them with brain data can help us to constrain our understanding of information processing, such as neuronal predictive coding.

2.4 Models of brain states

2.4.1 Network model of Up-Down slow oscillations in L5 of the visual cortex of sleeping and anaesthetized rats

Link to the KG: <https://search.kg.ebrains.eu/instances/4b13fe21-28f9-4373-9a05-04f450cb6e1d>

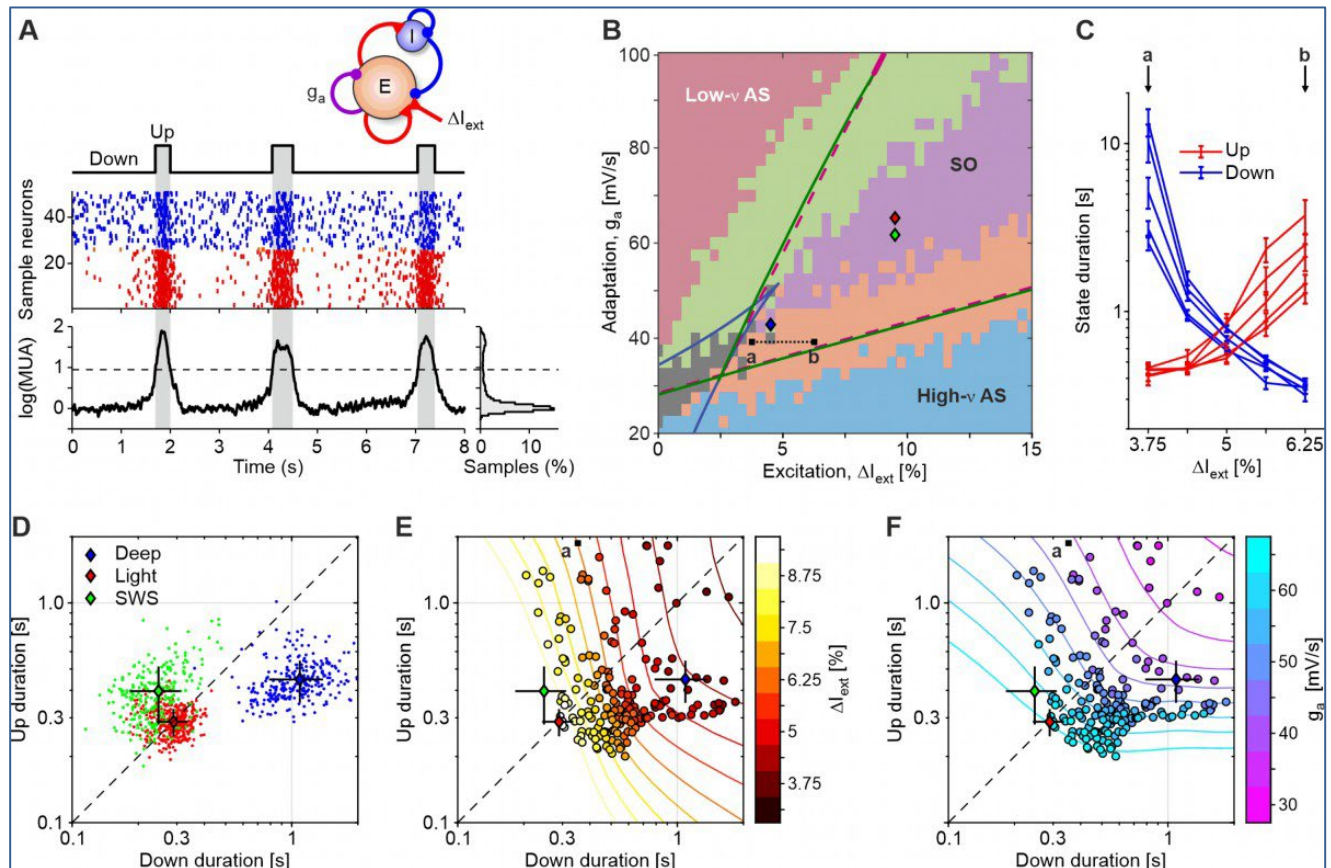


Figure 9: Spontaneous activity of L5 module in a mammalian cortical column

(A) Spontaneous slow oscillations in a network of excitatory and inhibitory leaky integrate-and-fire (LIF) model neurons with spike-frequency adaptation modelling a mammalian cortical column as a L5 network model showing Up-Down slow oscillations (SO). From the firing rate of the excitatory neurons is extracted the multi-unit activity (bottom). (B) Bifurcation diagram of the dynamical regimes expressed by the network model (Mattia & Sanchez-Vives, 2012; Cattani et al., 2023). For each value of excitation (change in input current, ΔI_{ext}) and adaptation strength (g_a , 100 s of simulations in five independent networks (randomly selected synaptic matrix)). Low- and high-firing rate AS (asynchronous state), neuronal spiking is irregular and firing rate fluctuates around a fixed value. Bistable (bottom-left corner), both low- and high-firing rate AS coexist. SO, the quasi-periodic slow alternation between Up and Down metastable states. Coloured diamonds, networks with Up and Down state statistics as in deep and light anaesthesia, and sleep experiments (D). (C) Average Up and Down state durations (red and blue, respectively) computed in five independent networks with parameter changes depicted by the a-b dotted line in panel (B). (D) Distributions of average Up and Down durations from experiments under deep (blue) and light (red) anaesthesia, and during natural NREM sleep (SWS, green). Coloured diamonds, grand averages (centroids) of the state durations for these three distributions. Black lines, standard deviations of the state durations. (E, F) Distribution of average Up and Down state durations from simulated networks (circles) used to work out the diagram in panel (B). Contour lines, iso-level curves of excitation and adaptation obtained by fitting with a smoothed surface the mean state durations from simulations. Diamonds as in panel (D). Fitted surfaces were used to infer the effective ΔI_{ext} needed to reproduce experimental state duration statistics in simulations (diamonds in panel B).

Here, we provide a simulation of a cortical-like module endowed with activity-dependent adaptation. Fundamental aspects of spontaneous activity (Torao-Angosto et al., 2021) and local responsiveness elicited in mammals in different brain states by direct cortical stimulation (Cattani et al., 2023) can be replicated by systematically varying the relationships between adaptation strength and excitation level in the network. Excitatory neurons incorporate the activity-dependent fatigue mechanism modelling spike-frequency adaptation (SFA), which is a key ingredient to

generate Up-Down slow oscillations typical of deep sleep and anaesthesia. The network was built using anatomical data collected in the literature on L5 of the visual cortex (V1) of sleeping and anaesthetized rats and aims at bridging the microscopic scale of single neuron activity and the mesoscopic level of neuronal network modules composing a cortical column.

Related publications:

P2697: Torao-Angosto et al., Front Syst Neurosci 2021; DOI: [10.3389/fnsys.2021.609645](https://doi.org/10.3389/fnsys.2021.609645)²

P4081: Cattani et al., eNeuro 2023; DOI: [10.1523/ENEURO.0435-22.2023](https://doi.org/10.1523/ENEURO.0435-22.2023)³

2.4.2 Slow waves form expanding, memory-rich mesostates steered by local excitability in fading anaesthesia

Link to the KG: <https://search.kg.ebrains.eu/instances/39526a60-0c72-4b20-b850-a2bffb02049>

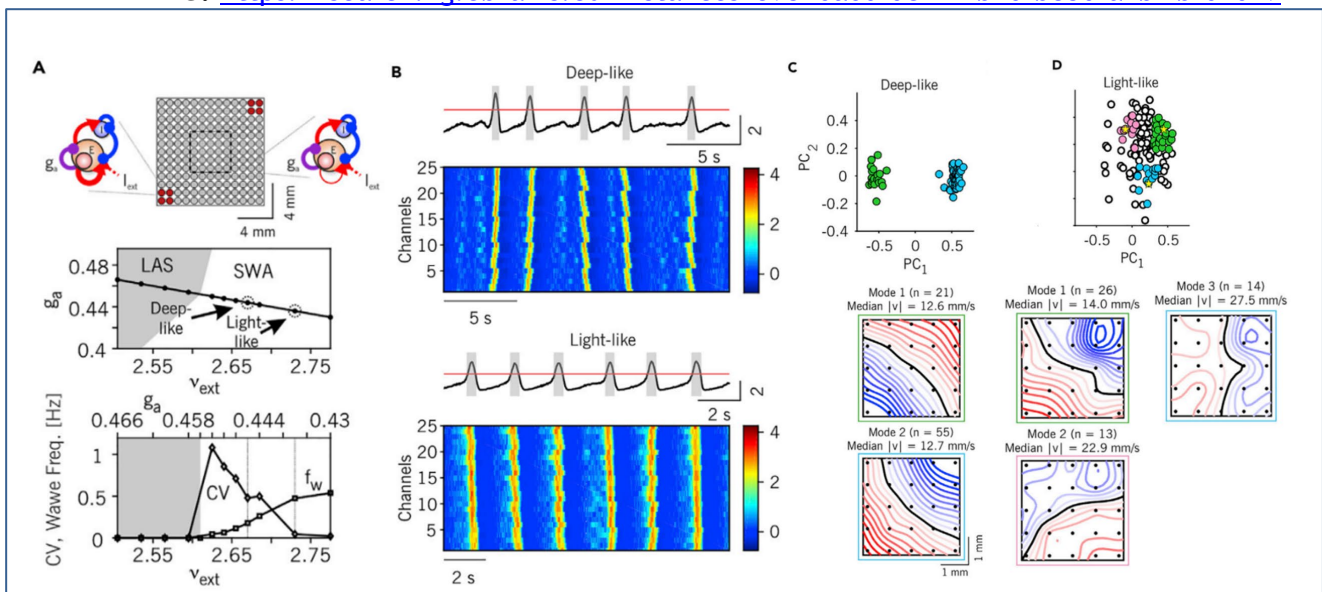


Figure 10: Increased excitability in model explains observed changes as anaesthesia lightens.

(A) Schematic representation of the simulated network, consisting of 13x13 local cell assemblies. Cell assemblies are composed of excitatory and inhibitory integrate-and-fire neurons and are sketched on the left those with increased excitability (stronger synaptic self-excitation, red circles) and on the right the ones with reference excitability in the rest of the grid. Middle: bifurcation diagram showing the different activity regimes displayed by spiking neuron network simulations as the level g_a of the firing rate adaptation and the rate of spikes from other (external) areas are changed. To model anaesthesia fading, these parameters are changed according to the depicted black line connecting the low-firing asynchronous (LAS) and the slow wave state. Bottom: coefficient of variation of Up-Down cycles (circles) and frequency of waves (f_w , squares) measured in simulations along the above black trajectory. (B) Representative average and single-channel log (MUA) in the simulated network for low wave frequency/high CV (top, “deep-like”), and high frequency/low CV (bottom, “light-like”) modelling deep and light levels of anaesthesia, respectively. (C and D) Distributions of time lag arrays of spontaneously occurring activation waves in the model network in the plane of the first two principal components (PC1, PC2). Model networks in both the deep-like and the light-like conditions are shown (panel C and D, respectively). Coloured dots highlight the wavefronts belonging to the modes of propagations singled out in bottom panels, relying on k-means clustering. For the “light-like” case (D) three representative groups of wavefronts were selected; these included the points centred at the yellow stars.

The network model shown in figure was simulated with NEST and composed of standard point-like integrated-and-fire (LIF) neurons. It was organized as a set of interacting modules, each consisting of two interconnected pools of excitatory and inhibitory spiking neurons. Each cortical module was composed of 250 inhibitory (I, 20%) and 1,000 excitatory (E, 80%) neurons with spike frequency adaptation (SFA). Such modules were spatially distributed on a two-dimensional grid of 13x13 sites. The inter-modular connectivity was greater than zero only between pairs of populations displaced at relative distance less than 3, thus modelling cortico-cortical horizontal connections. The model,

² <https://www.frontiersin.org/articles/10.3389/fnsys.2021.609645/full>

³ <https://www.eneuro.org/content/10/7/ENEURO.0435-22.2023>

changing the excitability and SFA (Spike Frequencies Adaptation) of excitatory neurons, can exhibit different brain states, reproducing the same complexity and variety of wave front propagation observed in mice during slow-wave activity under different levels of anaesthesia, thus simultaneously representing the micro- and macroscopic organization of cortical networks.

The model is structured and built in NEST. It is easily adaptable for implementation on neuromorphic systems. To adapt the model for neuromorphic architectures like Spinnaker, few specific modifications are required to map the spiking neuron dynamics and synaptic connections onto the specialized hardware components allowing the study of large-scale brain dynamics in real-time or faster, as it run on HPAC platforms via EBRAINS.

Related publications:

P3230: Paziienti et al., iScience 2022. DOI: 10.1016/j.isci.2022.103918⁴

2.4.3 *Spiking network model of cortical areas exploring the edge of synchronization.*

Link to the KG: <https://search.kg.ebrains.eu/instances/d55c5d70-1d6d-4a66-9dd6-00bc8d7346b6>

The network of spiking neurons aims at modelling a cortical area during slow-wave activity (anaesthesia), resting wakefulness and behavioural awake state expressed when a motor decision task is performed in separate trials. The network composed of 13x13 modules, each composed of 1,000 excitatory and 250 inhibitory neurons, connected with probability decaying with the distance (more than 200 103 neurons and 200 106 synapses per network). Using the external input current I_{ext} and the level of adaptation g_a as parameter handles, the network was set to operate in three relevant global brain states.

The model is simulated in NEST making use of the HPAC platforms made available via EBRAINS. In collaboration with E. Balaguer-Ballester (Bournemouth University, UK) and A. Rowley (University of Manchester, UK) the model has been ported onto the Neuromorphic platform Spinnaker within the framework of the project “Neuromorphic Hardware Operating at the Edge of Asynchrony (Async-Neuromorph)” funded by the EBRAINS Research Infrastructure Voucher Programme Call 2020. This neuromorphic implementation on Spinnaker will allow to explore the bifurcation diagram of the network at higher resolution. The Spinnaker implementation is in part available via GitHub and on the Spinnaker website. Its porting on the EBRAINS KG is ongoing.

Cortical-like field, Spiking 2D neuron network, Leaky integrate-and-fire neurons, Brain states, Sleep-Wake transition, Slow Wave Activity.

To adapt the model for neuromorphic architectures like Spinnaker, few specific modifications are required to map the spiking neuron dynamics and synaptic connections onto the specialized hardware components allowing the study of large-scale brain dynamics in real-time or faster.

Related publications:

P4082: Paziienti et al., Bernstein Conference 2023. DOI: 10.12751/nncn.bc2022.256 .

⁴ <https://www.sciencedirect.com/science/article/pii/S2589004222001882?via%3Dihub>

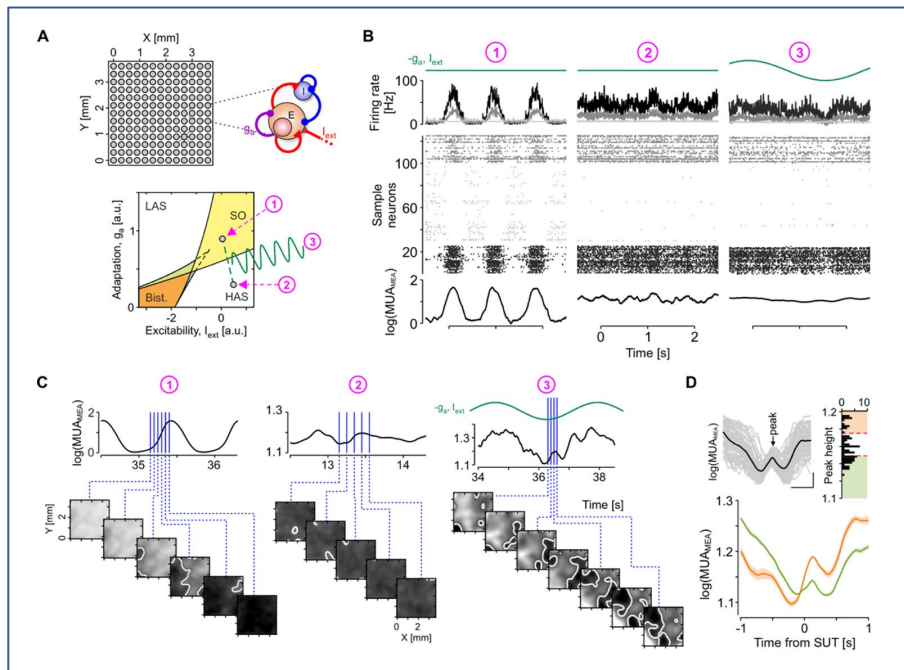


Figure 11: Network model dynamically exploring the edge of criticality.

(A) Sketch illustrating the in-silico network structure. The network is a two-dimensional grid composed of 13x13 modules, that communicate only through projecting excitation. Internally, each module consists of 1,000 excitatory and 250 inhibitory LIF neurons connected with probability equal to 0.8. Excitatory neurons receive an additional external current (I_{ext}) and are subject to spike-frequency adaptation (g_a). Bottom, qualitative phase diagram for a single module. By changing the value of the free parameters I_{ext} and g_a the dynamical regime of the network ranges from single to bistable point attractor (LAS, HAS and Bist. regions) including also stable limit cycles (SO region). (B) Activity of single in silico neurons for network at different states. From top to bottom, value of the I_{ext} ; average firing rate; dot displays of subsets of the network and $\log(MUAMEA)$. Dark grey: inhibitory neurons; light grey: excitatory background neurons; black: excitatory foreground neurons. A few seconds of activity are shown in the SO dynamical regime (left), in the asynchronous HAS dynamical regime (centre) and “moving” the network across the critical line between the former regimes. For the latter simulation, the network got back to same point of the phase space every three seconds. (C) $\log(MUAMEA)$ in a smaller time segment than in (B) (top) and snapshots of the $\log(MUA)$ on the grid taken at several time points. In the SO state (left), the snapshots are taken during the Down-to-Up transition. In the simulation across the critical line (right), the snapshots are taken around the point closest to the SO region, where the emergence of spatiotemporal patterns across the grid is observed. (D) Top left: $\log(MUAMEA)$ at the critical point for all crossing instances (grey) and their mean (black). Top right: distribution of the $\log(MUAMEA)$ value of the single times approaching the critical point at the peak (shown on the left panel). Two extreme regions are highlighted. Bottom, $\log(MUAMEA)$ activity at the critical point for the two groups of steepest and smoothest activations (orange and green, respectively). The waveforms cross each other shortly before the peak, switching from low activity preceding a steeper activation (orange) and from higher activity preceding a smoother activation (green).

2.4.4 Thalamo-Cortical Spiking Model of Incremental learning combining perception, context, and NREM-sleep

Link to the KG: <https://search.kg.ebrains.eu/instances/550e1364-8a3d-4c29-ba21-6ef7e0f47bf7>.

The model is published in Golosio et al. 2021 (P3089) in PLoS Computational Biology. This thalamo-cortical plastic spiking model (ThaCo) demonstrates beneficial cognitive and energetic effects of sleep during incremental awake learning and sleep cycles. Its endogenous dynamics enforces both the capability of association among memories and synaptic homeostasis. In the model, apical amplification is essential during incremental learning and classification. The endogenous dynamics expresses spectral densities and firing rates that match those of experimental data. The model is trained on handwritten digits (MNIST), it is coded in NEST and its execution requires the availability of adequate HPC resources due to the need of plastic simulation lasting several hours of simulated biological time to follow the plastic learning, sleep and the evaluation of pre-sleep and post-sleep classification ability during multiple learning and sleep cycles. A follow up paper (P3926) extends the model to the simulation of the specific effects of REM in a multi-area model.

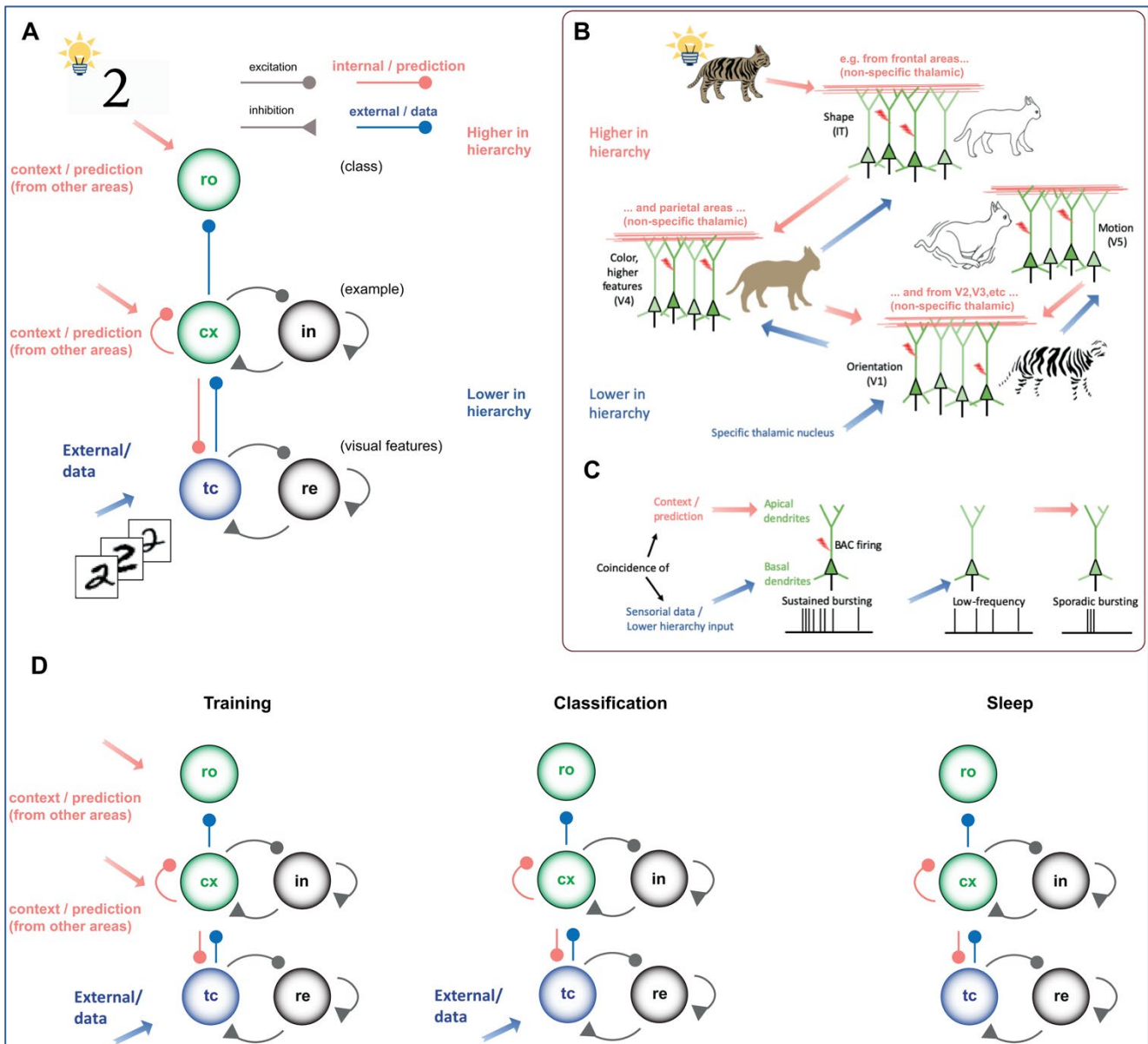


Figure 12: Plastic spiking model

Model leveraging apical amplification and demonstrating beneficial cognitive / energetic sleep effects during incremental learning and sleep cycles (figure from Golosio et al., PLOS 2021).

2.4.5 Interactive exploration of brain states and spatio-temporal activity patterns in Data-Constrained Simulations

Link to the KG: <https://search.kg.ebrains.eu/instances/3ebdd555-f965-477c-8a0e-4c220014d138>

The model is published in Capone et al., 2023 (P3907). How can the same network generate different brain states with their specific propagation patterns and rhythms? In this Jupyter lab environment, the user can interactively change the neuromodulation and adaptation parameters and observe in real-time the emergence of different categories of slow-wave wave-propagation patterns (spontaneous and stimulated) and the transition to an asynchronous regime on a columnar mean-field model equipped with lateral connections inferred from experimentally acquired cortical activity. The connectivity of the model was inferred from cortical activity acquired in the mouse using GECI imaging technique, on a dorsal view of a full hemisphere (25 mm² sampled at 100µm resolution). Even if the connectivity of the model was inferred from a single brain-state, the neuromodulated model supports the emergence of a rich dynamic repertoire of spatio-temporal

propagation patterns, from those corresponding to deepest levels of anaesthesia (spirals) to classical postero-anterior and rostro-caudal waves up to the transition to asynchronous activity, with the dissolution of the slow-wave features. The model has been validated by quantitative comparison among the spatio-temporal features of the activity expressed by the model and by the experimental data from which it has been derived has been executed using the Cobrawap analysis pipeline (P3927).

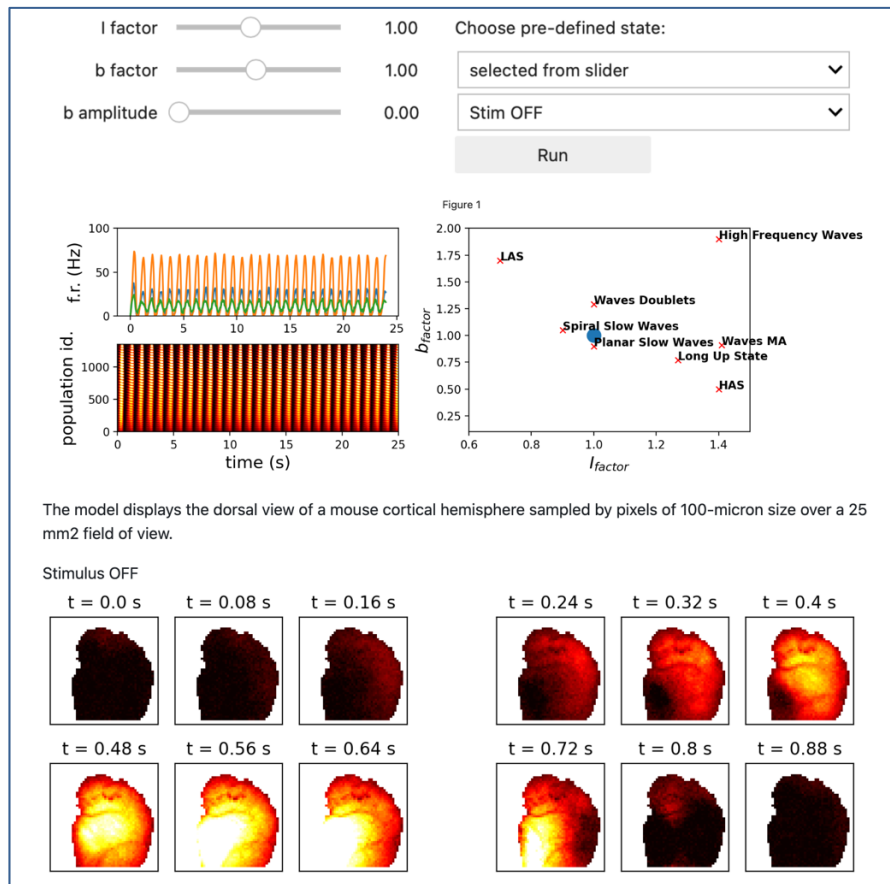


Figure 13: Simulated cortical waves.

Jupyter lab for interactive exploration of spontaneous and stimulated cortical waves generated by the same network at different levels of responsiveness.

2.5 Other models

2.5.1 Model of gaze centred activation of value encoding in orbitofrontal cortex

Link to the KG: <https://search.kg.ebrains.eu/instances/a2dce812-1d4b-4fc5-a69f-96005288c12e>

A broad set of studies in the field of value-based decision-making has long argued the role of orbitofrontal cortex in encoding the value of alternative reward offers to be chosen. Among other aspects, the community has wondered whether neural populations encoding alternative reward values do so via spatial segregation or by temporal alternation. In our model, we provide evidence for time-resolved alternation of the encoding of alternative offers, which are encoded by spatially overlapping groups of cells.

When combined with the analysis of simultaneous eye tracking data, our model provides insights about the way neural content relates to the value of the two alternative offers. We find that the encoding of alternative values matches the inspected offer presentation sites, both during offer presentation and at later delay times when the display screen is left blank, and subjects are left free to direct their gaze at their will.

Combined, our results allow making predictions about the activation and reactivation of the encoding of value during task execution time, both when subjects inspect presented stimuli and when they are freely exploring the visual display, following stimuli presentation.

3. Looking forward

In conclusion, the computational models presented in this document offer a multifaceted approach to understanding the intricacies of brain responsiveness, multisensory integration, apical amplification, and brain states. A further exploration of these models has the potential to reshape our understanding of neural processes and open new avenues for research in neuroscience and artificial intelligence.

Looking forward, the evolution of computational models in neuroscience promises exciting prospects. We anticipate the integration of more extensive datasets, advanced neuroimaging techniques, and the refinement of machine learning algorithms to enhance the accuracy and predictive power of these models. It is also important that these models continue to evolve in close alignment with empirical data, as the accuracy and fidelity of the models rely on the constant refinement and validation against real-world observations, ensuring that our scientific insights remain grounded. To achieve this, interdisciplinary collaborations between neuroscientists, computer scientists, and engineers are needed and will be pivotal in shaping the future of brain modelling. Initiatives like EBRAINS can play a vital role in facilitating these collaborations and accelerating progress in the field.

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