Use-cases integrating analysis workflows and algorithms in EBRAINS and at least 3 largely collaborative "Live Scientific Papers"
(D2.7 - SGA3)

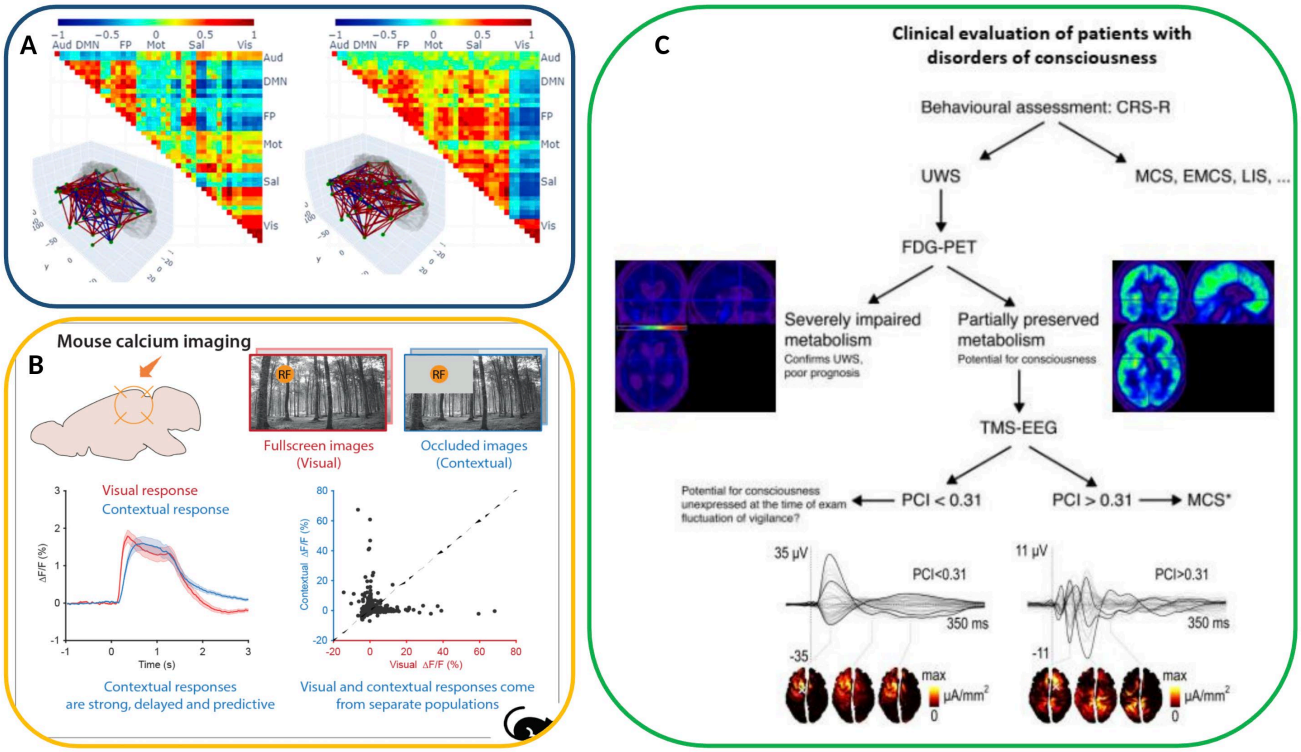

Figure 1: Examples of Live Figures from three WP2 Live Papers

The figures presented here are part of the WP2 Live Papers. These figures are live in the sense they can be reproduced in the EBRAINS Research Infrastructure by means of interactive Python notebooks. A) Figure from the paper: *Identification and neuromodulation of brain states to promote recovery of consciousness* (P4198) in which different patterns of functional connectivity are shown to the user, where they can vary different parameters and interact with the data. B) Figure from the paper: *The cortical microcircuitry of predictions and context - a multi-scale perspective* (P4201). The user can directly interact with the data and visualize the visual and contextual responses to a given image in mouse calcium imaging data. C) Figure from the paper: *Advancing the science of consciousness: from ethics to clinical care (P4183)*. In this case, the reader can access a live figure that will present five clinical cases and depending on the Positron Emission Tomography (PET) image and Perturbational Complexity Index (PCI) chosen, a clinical diagnosis will be produced.

Project Number:	945539	Project Title:	HBP SGA3

Document Title:	Use-cases integrating analysis workflows and algorithms in EBRAINS and at least 3 largely collaborative "Live Scientific Papers" (D2.7 – SGA3)
Document Filename:	D2.7 (D18) SGA3 M42 RESUBMITTED 231208.docx
Deliverable Number:	SGA3 D2.7 (D18)
Deliverable Type:	Report
Dissemination Level:	PU = Public
Planned Delivery Date:	SGA3 M42 / 30 SEP 2023
Actual Delivery Date:	SGA3 M42 / 29 SEP 2023 (resubmitted 08 Dec 2023)
Author(s):	Arnau MANASANCH, IDIBAPS (P93), Mavi SANCHEZ-VIVES, IDIBAPS (P93)
Compiled by:	Arnau MANASANCH, IDIBAPS (P93)
Contributor(s):	Jorge MEJÍAS, UvA (P98), contributed to section 2.1 Jitka ANNEN, ULG (P97), contributed to section 2.2, 3.1 Diana CASAS-TORREMOCHA, IDIBAPS (P93), contributed to section 2.2, 3.1 Maurizio MATTIA, ISS (P96), contributed to section 2.3 Andrea GALLUZZI, ISS (P96), contributed to section 2.3 Pier Stanislao PAOLUCCI, INFN (P92), contributed to section 2.3 Andrea PIGORINI, UMIL (P94), contributed to section 2.4 Ezequiel MIKULAN, UMIL (P94), contributed to section 2.4 Alain DESTEXHE, CNRS (P10), contributed to section 2.4 Michele FARISCO, UU (P83), contributed to section 3.1 Michele SVANERA, UGLA (P87), contributed to section 3.1 Lucy PETRO, UGLA (P87), contributed to section 3.1 Lars MUCKLI, UGLA (P87), contributed to section 3.1 Glenn VAN DER LANDE, ULG (P97), contributed to section 2.2, 3.1 Ben von Huenerbein, UBERN (P71), contributed to section 3.2 Francesco MANNELLA, CNR (P12), contributed to section 3.2 Alessandra CAMASSA, IDIBAPS (P93), contributed to section 3.2 Leonardo DALLA PORTA, IDIBAPS (P93), contributed to section 3.2
WP QC Review:	Angelica DA SILVA LANTYER, UVA (P98) / Eurídice ÁLVARO, IDIBAPS (P93)
WP Leader / Deputy Leader Sign Off:	Mavi SANCHEZ-VIVES, IDIBAPS (P93)
T7.4 QC Review:	N/A
Description in GA:	Novel measures of perceptual integration and joint multisensory object features, network perturbation and responsiveness, neuromodulatory network impact, wave propagation, network complexity and network synchronization will be made available to the community. They will be associated with relevant data collections

	and validated models. The "live papers" will be associated with data, analysis tools and models in EBRAINS to act as platform demonstrators of WP2 activities.
Abstract:	The goals of the research described in this deliverable D2.7 are divided in two topics. On one hand we provide a set of use cases that are related to the topics of perceptual integration and joint multi-sensory object features, network perturbation and responsiveness, neuromodulatory network impact and wave propagation. These use cases have been released in scientific publications and some have been made publicly available to the neuroscientific community through EBRAINS. The related data and models are also shared in the EBRAINS Knowledge Graph. On the other hand, we also share here a collection of 3 Live Papers, which were collaboratively developed within WP2. These Live Papers showcase two important aspects. First, they are a demonstration of how data, models, and figures from scientific papers can be reproduced online, enabling researchers to validate and build upon existing findings. Second, they highlight the use of the EBRAINS Research Infrastructure, showcasing its capabilities and providing a practical example of how it can be effectively used for accessing and reproducing findings obtained from data, models, and figures. This helps to increase collaboration and knowledge-sharing and provide advances in neuroscience research within the broader scientific community.
Keywords:	Use-cases, live Papers, EBRAINS, data, models, ethics, Consciousness, wave propagation, multisensory perception, network complexity
Target Users/Readers:	Clinicians, computational neuroscience community, neuroinformaticians, neuroscientific community, neuroscientists, platform users, researchers, scientific community, and students.

Table of Contents

Table of Tables

Table of Figures

History of Changes made to this Deliverable (post Submission)

Date	Change Requested / Change Made / Other Action
Sep 23rd 2023	Deliverable submitted to EC
Dec 8th 2023	Resubmission with specified changes requested in Review Report Main changes requested: • Change 1 (Please make clear whether the closed loop experiment with coma patients is part of D2.7, and if so, then provide more specifications): Please, see Section 2.2, **Page 10**. • Change 2 (*The TMS-EEG work is described in Live Paper, whose link in Sec 2.2 is broken. It is not clear whether the Live Paper is in preparation or has been finished*): Please, see Section 2.2, **Page 10**. The link has been fixed. It is available now. See Live Paper https://live-papers.brainsimulation.eu/#2023-vanderlande-et-al • Change 3 (*In Figure 3 a one-subject average is shown. It would be interesting to plot a grand average over the entire cohort of its associated PCI indices*): (Please, see Section 2.2 **Page 10**.
	•

1. Introduction

The current Deliverable D2.7 is divided into two main blocks. First, we provide a set of use cases that are related to the topics of perceptual integration and joint multi-sensory object features, network perturbation and responsiveness, neuromodulatory network impact and wave propagation. These use cases have been released in scientific publications and some have been made publicly available to the neuroscientific community through EBRAINS, as described in the following sections. The related data and models are also shared in the EBRAINS Knowledge Graph.

Second, we present here a collection of 3 Live Papers, all of which were collaboratively developed within WP2. These Live Papers showcase two important aspects. In the first place, they are a demonstration of how data, models, and figures from scientific papers can be non-only shared but reproduced online, enabling researchers to validate and build upon existing findings. Further, they highlight the use of the EBRAINS Research Infrastructure, showcasing its capabilities and providing a practical example of how it can be effectively used for accessing and reproducing findings obtained from data, models, and figures. This helps to increase collaboration and knowledge-sharing, facilitating advances in neuroscience research for the broader scientific community.

In WP2 we were committed to deliver at least three Live Papers by the end of SGA3. The WP2 Live Papers have been a challenge and an intensive collaborative effort from tasks T2.1 to T2.7. As acceptance for publication in peer-reviewed journals often takes considerable time, it will not be possible to have them published in peer reviewed journals by September 2023, but we have made them available as pre-prints in open repositories such as bioRxiv or Zenodo and they are under review in journals. All of them have their Figures and associated materials (data, models, or analysis tools) ready in EBRAINS. In addition to the three Live Papers presented in this document as submitted, there are four other Live Papers that are in different phases of development, some already made available in total or part, and they will be available after the end of SGA3. These are also included in this Deliverable.

The Live Papers feature dynamic Live Figures, which offer an interactive representation of the data/models presented in each paper. Readers can actively engage with the data and models, exploring and reproducing the main research findings.

The work of the use-cases and Live Papers described in this Deliverable will be of interest to multiple communities within the field of neuroscience, computational modelling, and the broader scientific research community including students, as our research addresses a wide variety of topics that provide insights into how 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 even beyond the end of the Human Brain Project.

Some of the EBRAINS services we use in the work presented here are the EBRAINS Knowledge Graph for data and model sharing, the EBRAINS Collaboratory for use-cases, and the EBRAINS Live Papers Service, including the EBRAINS Jupyter Lab, where users can actively interact with the data, models, and figures presented. During SGA3, these services have evolved and improved significantly. We tried to provide all types of feedback to these services when integrating our work in order to enhance their functionality and utility, fostering a more collaborative and easy-to-access environment for neuroscience research.

2. WP2 Use-cases

2.1 Perceptual integration and joint multisensory object features

The use-case on measures of perceptual integration and multisensory feature coding contains several components1. The main component is defined by the Live Paper "An active inference model of rodent whisking behaviour during multimodal object recognition" by Mannella et al. (a collaboration of the groups of Pezzulo, CNR Rome, and Pennartz, UvA Amsterdam, as well as with the EBRAINS RI; under preparation). Based on integrative modelling and experimental work, in this first component we have developed novel measures of perceptual-cognitive integration as captured by predictive processing. This is best illustrated by a multisensory object recognition task that we have tested in experiments as well as in a computational model (see Table 1).

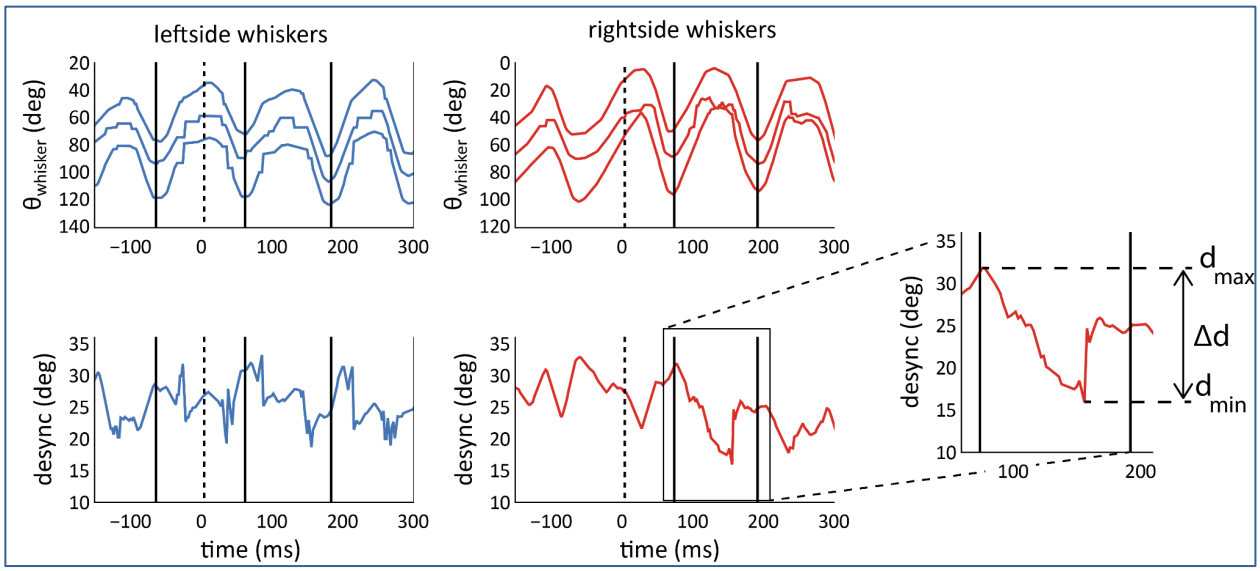

Figure 2: Experimental data on whisker dynamics and measure of model predictability

Upper panels plot the angle of whisker deflection (Theta-whisker) for individual whisker on the left and right side of the rat's head. Each plot shows traces from 3 example whiskers. Dynamics is plotted as a function of time, where time zero marks the onset of first object touch in an object recognition task. Lower panels plot the whisker De-synchronization measure, where high De-synchronization corresponds to poor object predictability (large error; novel, unpredicted input) and low De-synchronization means high predictability (i.e., the model makes proper object predictions). These empirical data were used to test the computational model (Mannella et al., 2023, in prep.).

Rodents use whisker movements to probe and recognize objects, sometimes in combination with other senses such as vision. However, we still lack a comprehensive understanding of how they combine multiple sensory modalities during object recognition. Here, we combine experimental data with a novel computational model of rodent whisking behaviour during multimodal object recognition, using the framework of active inference (see Figure 2). In the model, object recognition originates from a competitive process, based on prediction error minimization and bottom-up information from sensory systems for vision and whisking. Whisking is conceptualized as an active process: the rodent controls the amplitude of its whiskers until they touch the object at the end of their protractions. Since each object corresponds to a set of object-specific (predicted) whisker amplitudes, the amplitude of whiskers can be used as evidence about the object the animal is interacting with. Crucially, active whisking can also be guided from the top down or via another, non-tactile sense: when vision provides prior information about object identity, the model can already set whisker amplitudes to their object-specific values. The model therefore predicts that

[1] See also deliverable D2.2, submitted in June 2022 and resubmitted in Dec 2023 after EC reviewers comments: Early version of use-case for cognitive performance integrating data and models.

whisker movements will be more accurate, and the model convergence process will be faster, in the presence of multimodal information. We validate this model prediction with the help of in vivo recorded rodent whisking data acquired during a multisensory object discrimination task, in two conditions. In one condition (tactile-only), rodents gather tactile information by actively whisking, with the light turned off. In another condition (multimodal), the light is turned on and hence the rodents receive both visual and tactile information.

To compare model and rodent data, we developed a novel behavioural measure of multisensory processing-based predictability, based on the synchrony between individual whisker movements during object recognition. Our results indicate that, in multimodal trials, the synchrony between whiskers after object contact initially declines, but then recovers faster than in tactile-only trials, providing support for the multisensory integration account provided by the active inference model.

In addition to this main component, the responsible HBP team has worked on other measures and methods for quantifying perceptual integration and multisensory feature coding in the brain. For instance, Meijer et al. (2020) quantified multisensory interactions in both low- and high-level visual areas of the mouse cortex, using two-photon Ca_{2+} imaging data (ensemble recording with single-cell resolution). In work that is closely related to the Live Paper described above, Fiorilli et al.(P4074) and Ruikes et al. (eNeuro, in revision; 2023) quantified multisensory (tactile-visual) interactions in simultaneous four-area ensemble recordings from sensory cortical, perirhinal, and hippocampal areas, yielding measures at the single-cell, population, and LFP (mass field potential) levels. Work by Oude Lohuis et al. (P3308)) presented novel generalized linear model (GLM) applications to quantify multisensory integration (and visual-motor integration) components in visual cortex (V1) of the mouse. Related data from Oude Lohuis et al. (P3301) were used by the Senn group (U. Bern) to test a model wherein multisensory integration is quantified in terms of spike train and membrane potential irregularities, reflecting (un)certainty about sensory evidence at the level of cortical pyramidal cell dendrites. The latter work has been accepted for a conference presentation ("Certainty-weighted integration of information in individual cortical neurons", by Von Hünerbein, Oude Lohuis, et al., CCN conference 2023) and is prepared for a Live Paper publication (Von Hünerbein et al., in preparation, 2023). Finally, these experimental and modelling results are taken on board in the work on multilevel, multiarea predicting coding models (see Showcase 4[2], D2.4) which are also being used by the team to study multisensory integration in robots in the Neuro Robotics Platform NRP (e.g., to improve place recognition; Pearson et al. 2021)

Table 1: Data and models related to perceptual integration

Title	KG link	Embargo status
Neural correlates of multisensory detection behaviour in primary and higher-order visual cortex	https://search.kg.ebrains.eu/instances/Dataset/97d45335-6757-4a42-9824-2d652d9a9721	Public
Multi-area recordings from visual and somatosensory cortices, perirhinal cortex and hippocampal CA1	https://search.kg.ebrains.eu/instances/2077efac-09f6-47c1-aabe-632e08ed148b	Public
Audio-visual change detection task in mice	https://search.kg.ebrains.eu/instances/ba41de6c-1b30-4f48-89c4-a6eb47b2c549	Public
Sensory, perirhinal and hippocampal tetrode recordings during visual, tactile and visuotactile discrimination task in the freely moving rat	https://search.kg.ebrains.eu/instances/d406a98c-ae5c-4fb3-9f0c-4cf4de9b1094	Under embargo
Multimodal predictive coding network with WhiskEye and the NRP	https://search.kg.ebrains.eu/instances/Model/2164c2b9bbb66b42ce358d108b5081ce	Public
A generative network model of visual perception that learns invariant object	https://search.kg.ebrains.eu/instances/0b219bf1-dead-4a06-811a-fdce66f2ec7d	Public

[2] https://www.youtube.com/watch?v=yr1bho_iTv4

representations through local minimization of prediction errors		

Related Publications:

- P2685: Meijer GT, Mejias JF, Marchesi P, Montijn JS, Lansink CS, Pennartz CMA (2020) Neural correlates of multisensory detection behavior: comparison of primary and higher-order visual cortex of the mouse. Cell Reports 31: 107636. doi: https://doi.org/10.1016/j.celrep.2020.107636.
- P4074: Fiorilli J, Marchesi P, Ruikes T, Huis van 't Veld GJ, Buckton R, Duque Quintero M, Reiten I, Bjaalie J, Pennartz CMA (2023) Neural correlates of object identity, spatial choice and reward outcome in perirhinal cortex, hippocampus and sensory cortices. Biorxiv. https://doi.org/10.1101/2023.05.24.542117
- P3308: Oude Lohuis, MN Pietro Marchesi P, Olcese U, Pennartz CMA (2022) Triple dissociation of visual, auditory and motor processing in primary visual cortex. BioRxiv 2022.06.29.498156; doi: https://doi.org/10.1101/2022.06.29.498156.
- P3301: Oude Lohuis, MN, Marchesi, P, Pennartz CMA, Olcese U (2022) Functional (ir)relevance of posterior parietal cortex during audiovisual change detection. J. Neurosci. 42 (26): 5229-5245. https://doi.org/10.1523/JNEUROSCI.2150-21.2022
- P3027: Pearson MJ, Dora D, Struckmeier O, Knowles TC, Mitchinson B, Tiwari K, Kyrki V, Bohte S, Pennartz CMA (2021) Multimodal representation learning for place recognition using Deep Hebbian predictive coding. Frontiers in Robotics and AI. 8: 732023. doi: https://doi.org/10.3389/frobt.2021.732023

2.2 Neuromodulatory network impact

Neuromodulation provides promising avenues for the treatment of patients with disorders of consciousness (DoC). Although several neuromodulation techniques exist such as deep brain, vagus nerve stimulation or ultrasound, transcranial direct current stimulation (tDCS) seems to be one of the most promising avenues. About half of the patients in the minimally conscious state (MCS; a condition with periods of arousal and fluctuating yet consistent signs of awareness) seem to respond positively to stimulation, evidenced by the appearance of new behaviours (P1351). Also more recently, the effectiveness of tDCS in other configurations (other stimulation sites and fewer application) has been confirmed and their neurophysiological correlates have been investigated (e.g., P2740, P3064).

Building on work performed in the Human Brain Project SGA2, transcranial magnetic stimulation combined with electroencephalography (TMS-EEG) offers unique insight into network activity after exogenous perturbation. A strength of this technique is that it is independent from collaboration of the investigated subject. It has been shown that the differentiation and integration within the network can be synthesized in a metric sensitive to classify DoC patients in MCS or with unresponsive wakefulness syndrome (UWS; a condition in which patients are awake but totally unaware of themselves or the environment) (P1215). This metric, coined the perturbational complexity index (PCI), co-varies with cortical structural integrity (P907) and metabolism (P1002). TMS-EEG has been used to study brain state changes induced by therapy in healthy subjects (P2211). It provides a robust marker of cerebral function and could be used to study treatment induced network alterations even in the absence of behavioural changes.

tDCS is hypothesized to increase cortical reactivity, a hypothesis that can directly be tested by assessing tDCS-induced effects with TMS-EEG. By combining recent effects in the fields of tDCS and TMS-EEG, in SGA3 we have investigated the effect of TMS stimulation on EEG before and after tDCS treatment (20 min at 2 mA on the dorsolateral pre-frontal cortex, with cathode over the right supra-orbital area; P2594). The TMS target was the medial pre-motor cortex (just outside the primary effect location of the tDCS), for 400 trials separated by random intervals between 2 and 3 s using a figure-of-eight coil (Focal Bipulse, Nexstim Plc, Finland). The end product is an EEG dataset of event-related spectral perturbation and event related evoked-potentials from preprocessed data of a 60-

channel EEG system recording at 1450 Hz sampling rate (eXimia, Nexstim Plc, Finland). This dataset has been shared through the EBRAINS Knowledge Graph: https://search.kg.ebrains.eu/instances/Dataset/ab2d4db0-4c97-442c-82f9-a3dade301e9f (publicly available for EBRAINS users).

The dataset also forms the basis of a Live Figure in preparation in a collaboration of the members of T2.3 (See Live Paper https://live-papers.brainsimulation.eu/#2023-vanderlande-et-al). A static version of this image is provided in Figure 3 (see also Table 2), which shows that tDCS induced decreased evoked slow activity in patients with DoC (P1489). However, high-frequency activity was not affected, which is often related to higher levels of consciousness. This might be why no behavioural improvements were found in the current study. The wave shape of TMS-evoked potentials is highly variable across individuals, what makes grand averaging non-informative. A single case is thus used for illustration.

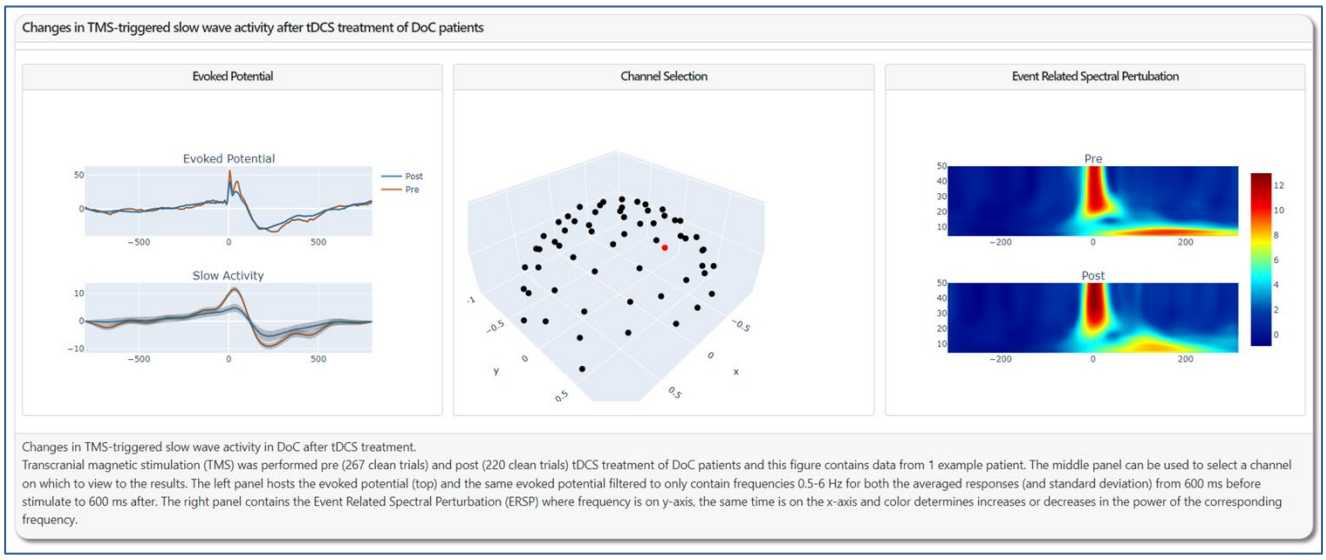

Figure 3: Changes in TMS-triggered slow wave activity in DoC after tDCS treatment

States of high and low vigilance, like the circadian sleep-wake cycle in the healthy population, alternate quickly in the DoC population. These Up and Down states can be another reason for the varying effect of tDCS. Up- and Down-states refer to the set of cellular and network properties that causes neurons to respond to synaptic input in a two-state manner, easily reaching the threshold for action potentials or not. They can be tracked by calculating the spectral entropy, a measure of complexity of the system, from EEG measurements. Hypothetically, a more complex brain state, and a more vigilant patient, is more receptive to tDCS treatment, giving importance to the time of stimulation. In anticipation of this, to increase the effectiveness of tDCS, we have developed a new protocol that tracks in real time the spectral entropy of the EEG and applies the tDCS to the bilateral prefrontal cortex in the targeted state (P2856). The site of stimulation is currently the most promising target for tDCS in patients with disorders of consciousness. The added value for treatment in a closed-loop approach is currently being tested, with an inclusion of 13 MCS patients so far. The study is a double-blind randomised trial across 3 days of measurement (i.e., randomized double-blinded high vigilance stimulation, low vigilance stimulation and random stimulation), 5 days apart with pre-, during- and post-measurements of EEG and pre- and post-tDCS behavioural assessments. Since tDCS seems to affect the bistability of Up- and Down states when stimulated in random moments (P1489), the current protocol allows us to investigate if stimulation in specific states amplifies the effects on network function, and potentially reach supra-threshold behavioural effects. This might provide patients with tailored treatment options, currently lacking in the field of DoC.

Table 2: Data and models related to neuromodulatory network impact

Title	KG link	Embargo status

TMS-EEG perturbation in patients with disorders of consciousness	https://search.kg.ebrains.eu/instances/Dataset/ab2d4db0-4c97-442c-82f9-a3dade301e9f	Public with an EBRAINS account
Spontaneous Direct Current (DC) modulated activity in in vitro ferret slice	https://search.kg.ebrains.eu/instances/d4460b07-73fd-4bd1-bfd7-01d23f32f8b3	Under embargo
Optimisation of photostimulation targeting muscarinic receptors	https://search.kg.ebrains.eu/instances/Dataset/b5998ae0-7237-4626-8ca6-e9fe2e8389c9	Embargo lift requested

Related Publications:

- P1351: Martens G, Lejeune N, O'Brien AT, Fregni F, Martial C, Wannez S, Laureys S, Thibaut A. Randomized controlled trial of home-based 4-week tDCS in chronic minimally conscious state. Brain Stimul. 2018 Sep-Oct;11(5):982-990. doi: https://doi.org/10.1016/j.brs.2018.04.021 . Epub 2018 May 2. PMID: 29759943.
- P2740: Martens G, Kroupi E, Bodien Y, Frasso G, Annen J, Cassol H, Barra A, Martial C, Gosseries O, Lejeune N, Soria-Frisch A, Ruffini G, Laureys S, Thibaut A. Behavioral and electrophysiological effects of network-based frontoparietal tDCS in patients with severe brain injury: A randomized controlled trial. Neuroimage Clin. 2020;28:102426. doi: https://doi.org/10.1016/j.nicl.2020.102426 . Epub 2020 Sep 15. PMID: 32977212; PMCID: PMC7511767.
- P3064: Carrière M, Mortaheb S, Raimondo F, Annen J, Barra A, Binda Fossati MC, Chatelle C, Hermann B, Martens G, Di Perri C, Laureys S, Thibaut A. Neurophysiological Correlates of a Single Session of Prefrontal tDCS in Patients with Prolonged Disorders of Consciousness: A Pilot Double-Blind Randomized Controlled Study. Brain Sci. 2020 Jul 21;10(7):469. doi: https://doi.org/10.3390/brainsci10070469 . PMID: 32708119; PMCID: PMC7408434.
- P1215: Casarotto S, Comanducci A, Rosanova M, Sarasso S, Fecchio M, Napolitani M, Pigorini A, G Casali A, Trimarchi PD, Boly M, Gosseries O, Bodart O, Curto F, Landi C, Mariotti M, Devalle G, Laureys S, Tononi G, Massimini M. Stratification of unresponsive patients by an independently validated index of brain complexity. Ann Neurol. 2016 Nov;80(5):718-729. doi: https://doi.org/10.1002/ana.24779 . Epub 2016 Nov 2. PMID: 27717082; PMCID: PMC5132045.
- P907: Cortese S, Castellanos FX, Eickhoff CR, D'Acunto G, Masi G, Fox PT, Laird AR, Eickhoff SB. Functional Decoding and Meta-analytic Connectivity Modeling in Adult Attention-Deficit/Hyperactivity Disorder. Biol Psychiatry. 2016 Dec 15;80(12):896-904. doi: https://doi.org/10.1016/j.biopsych.2016.06.014 . Epub 2016 Jun 24. PMID: 27569542; PMCID: PMC5108674.
- P1002: Bodart O, Gosseries O, Wannez S, Thibaut A, Annen J, Boly M, Rosanova M, Casali AG, Casarotto S, Tononi G, Massimini M, Laureys S. Measures of metabolism and complexity in the brain of patients with disorders of consciousness. Neuroimage Clin. 2017 Feb 6;14:354-362. doi: https://doi.org/10.1016/j.nicl.2017.02.002 . PMID: 28239544; PMCID: PMC5318348.
- P2211: Gosseries O, Fecchio M, Wolff A, Sanz LRD, Sombrun C, Vanhaudenhuyse A, Laureys S. Behavioural and brain responses in cognitive trance: A TMS-EEG case study. Clin Neurophysiol. 2020 Feb;131(2):586-588. doi: https://doi.org/10.1016/j.clinph.2019.11.011 . Epub 2019 Nov 27. PMID: 31843502.
- P2594: Mensen A, Bodart O, Thibaut A, Wannez S, Annen J, Laureys S, Gosseries O. Decreased Evoked Slow-Activity After tDCS in Disorders of Consciousness. Front Syst Neurosci. 2020 Sep 25;14:62. doi: https://doi.org/10.3389/fnsys.2020.00062 . PMID: 33100977; PMCID: PMC7546425.
- P1489: Engemann DA, Raimondo F, King JR, Rohaut B, Louppe G, Faugeras F, Annen J, Cassol H, Gosseries O, Fernandez-Slezak D, Laureys S, Naccache L, Dehaene S, Sitt JD. Robust EEG-based cross-site and cross-protocol classification of states of consciousness. Brain. 2018 Nov 1;141(11):3179-3192. doi: https://doi.org/10.1093/brain/awy251 . PMID: 30285102.

- P2856: Martens G, Ibáñez-Soria D, Barra A, Soria-Frisch A, Piarulli A, Gosseries O, Salvador R, Rojas A, Nitsche MA, Kroupi E, Laureys S, Ruffini G, Thibaut A. A novel closed-loop EEG-tDCS approach to promote responsiveness of patients in minimally conscious state: A study protocol. Behav Brain Res. 2021 Jul 9;409:113311. doi: https://doi.org/10.1016/j.bbr.2021.113311 . Epub 2021 Apr 18. PMID: 33878429.

2.3 Wave propagation

2.3.1 Slow wave propagation in fading anaesthesia

In the arousal process from sleep and anaesthesia, the brain restores its integrative and complex activity from the synchronized state of slow-wave activity (SWA) characteristic of NREM sleep. The mechanisms and dynamics of the cortical network underpinning this state transition remain to be elucidated. We investigated the progressive shaping of SWA propagating through the cortex on the way to wakefulness. Using micro-electro-cortico-graphical recordings in the mouse, we pharmacologically increased levels of slow-wave frequency and complexity from deep unconsciousness toward wakefulness and probed several single neuronal assemblies throughout the whole cortex. We found a form of memory in the SWA at deep anaesthesia, with an alternation of posterior-anterior-posterior modes of slow-wave propagation. When approaching wakefulness, metastable patterns of spiking cortical activity propagated in many more directions, reflecting an increased complexity in network dynamics. We unveil a temporal component of the dynamics of the waves' mesostates, predicted by simulations of a model network of spiking neurons and confirmed in our experimental data. Local excitability suffices to explain the transition from sleep to wakefulness without requiring modifications in network connectivity (see Figure 4 and Table 3). These results shed new light on the functional reorganization of the cortical network in the awakening brain.

This approach, exemplified by Pazienti et al 2022 (P3230), highlights the significance of wave propagation in understanding brain states like sleep and anaesthesia. The study demonstrates that altering local excitability while maintaining network connectivity can reproduce experimental findings, revealing the pivotal role of intrinsic neuronal properties in shaping slow wave propagation patterns. This insight deepens our understanding of local-global dynamics and unveils the complex interactions between cortical and sub-cortical structures during different anaesthesia stages.

The integrated-and-fire network model is simulated using NEST where neurons are connected with a spatial-dependent distribution. The modules are distributed on a 13×13 grid and connected with cortico-cortical horizontal connections. By changing the excitability and spike frequency adaptation of excitatory neurons, the model replicates different brain states observed in mice during slow-wave activity under various levels of anaesthesia. The model can be easily adapted for neuromorphic systems like Spinnaker with minimal modifications to study large-scale brain dynamics in real-time on specialized hardware components. It currently runs on HPAC platforms via EBRAINS.

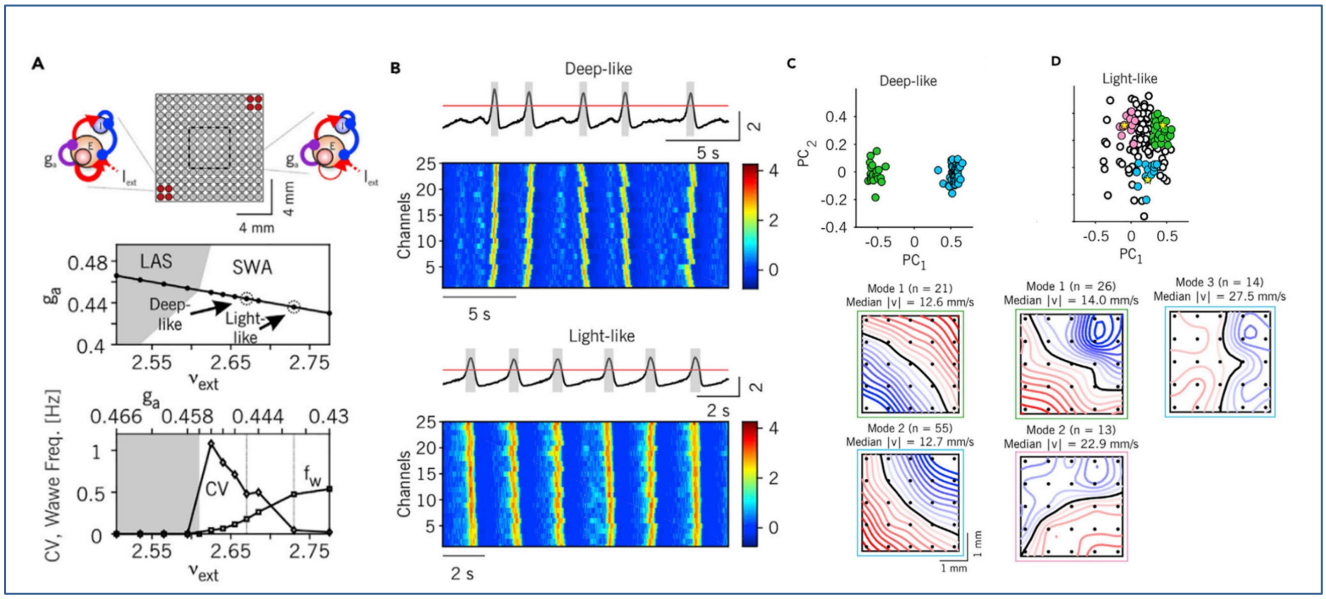

Figure 4: Multiscale model of a multiarea cortical network during anaesthesia fade-out

(A) Top: Sketch of the multiarea network of excitatory and inhibitory integrate-and-fire neurons. Middle: bifurcation diagram displaying various network activity states as the spike frequency adaptation (g_a) and the rate of external spikes (ν_{ext}) are altered. To model anaesthesia fade-out, these parameters are adjusted along the black line connecting the low-firing asynchronous (LAS) and slow-wave states (SWA). Bottom: coefficient of variation of Up-Down cycles (circles) and frequency of wave occurrence (f_w, squares) measured in simulations along the aforementioned 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") (deep and light anaesthesia levels, respectively). (C and D) Distributions of time lag arrays of spontaneously occurring activation waves in the network in the plane of the first two principal components (PC1, PC2). Coloured dots highlight the wavefronts belonging to the modes of propagation identified in the bottom panels using k-means clustering.

Table 3: Data and models related to wave propagation

Title	KG link	Embargo status
Slow waves form expanding, memory-rich mesostates steered by local excitability in fading anaesthesia	https://search.kg.ebrains.eu/instances/39526a60-0c72-4b20-b850-a2bffbf02049	Public (Model)
Propagation modes of slow waves in mouse cortex	https://search.kg.ebrains.eu/instances/7866daf2-7064-4fa0-b6a2-0b1c899ba35f	Public (Data from SGA2)

2.3.2 Cobrawap and SWA propagation inferred from data

Cobrawap (Collaborative Brain Wave Analysis Pipeline) is a computational workflow used to evaluate statistical properties of spatially organized cortical activity, developed in a collaboration of INFN, JUELICH, IDIBAPS, LENS, and ISS. It enables robust comparisons across a spectrum of multimodal activity data types (see Table 4) from experiments and simulations.

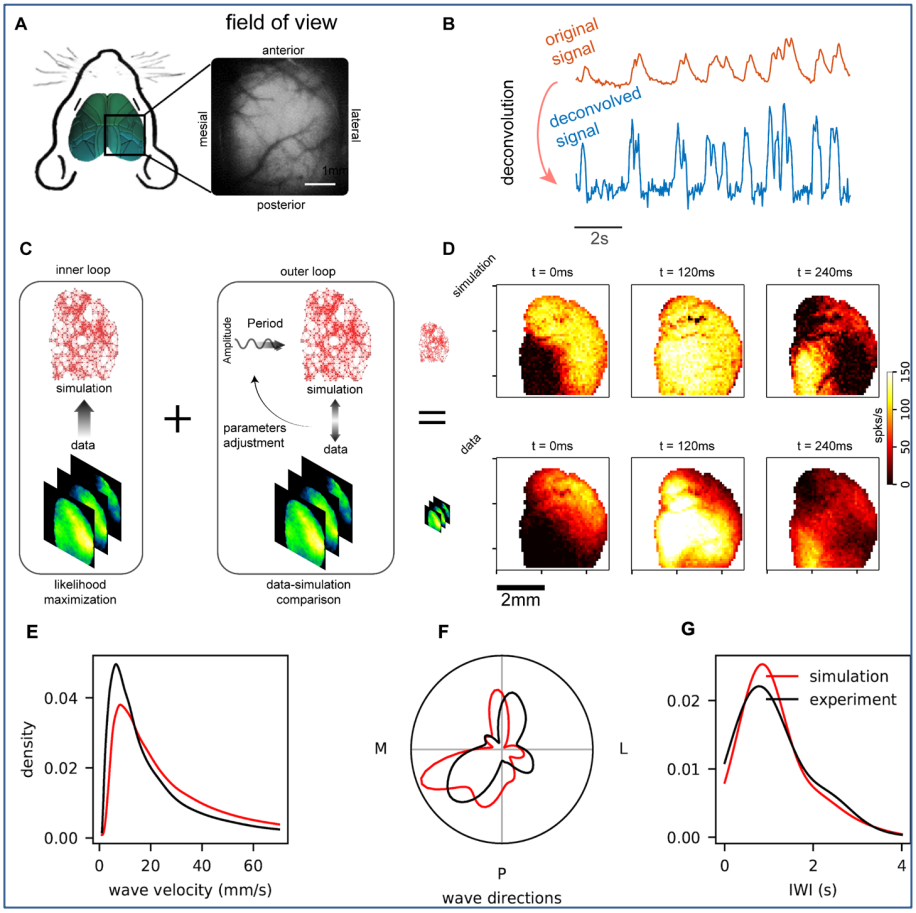

Figure 5: Slow-wave propagation in experimental data and simulations. Adapted from P3907

This figure illustrates the application of the Cobrawap pipeline to compare experimental data. (A and B: Wide-field calcium imaging recording of the dorsal view of the mouse cortex under ketamine/xylazine anaesthesia) with simulations of propagating slow waves inferred from data (C and D). Experimental data and simulations are compared using a set of observables about the spatiotemporal features of slow waves extracted by Cobrawap. In particular, the pipeline measures the distributions of local velocities (E), local direction of propagation (F) and inter-wave intervals on experimental data (black curves) and inferred simulations (red curves, panel G), but also the distribution of individual waves in main modes of propagation (not shown).

To accommodate data heterogeneity (ECoG, Widefield Ca Imaging, Utah arrays, simulation outputs), the Cobrawap workflow is fully configurable in a user-friendly manner. Its components leverage EBRAINS standards such as Neo and Elephant for data handling. The multistage pipeline supports a dual approach, based on Snakemake and CWL. It is being made available on multiple platforms, including JupyterHub, FENIX resources, and the EBRAINS task launching system. The modular

structure and reconfiguration support promotes a flexible development of science-driven analysis and processing steps and the standardization of metrics and terminology for brain wave investigation.

It is available as an open-source software (https://github.com/INM-6/cobrawap), within a reproducible/cooperative framework and responding to FAIR principles. It is written in Python and structured as a collection of modular building blocks arranged along sequential stages (see Figure 6), implementing data processing steps and analysis methods (e.g., spatial down sampling, wave clustering), directed by a workflow manager. Each block can be flexibly added, removed or replaced.

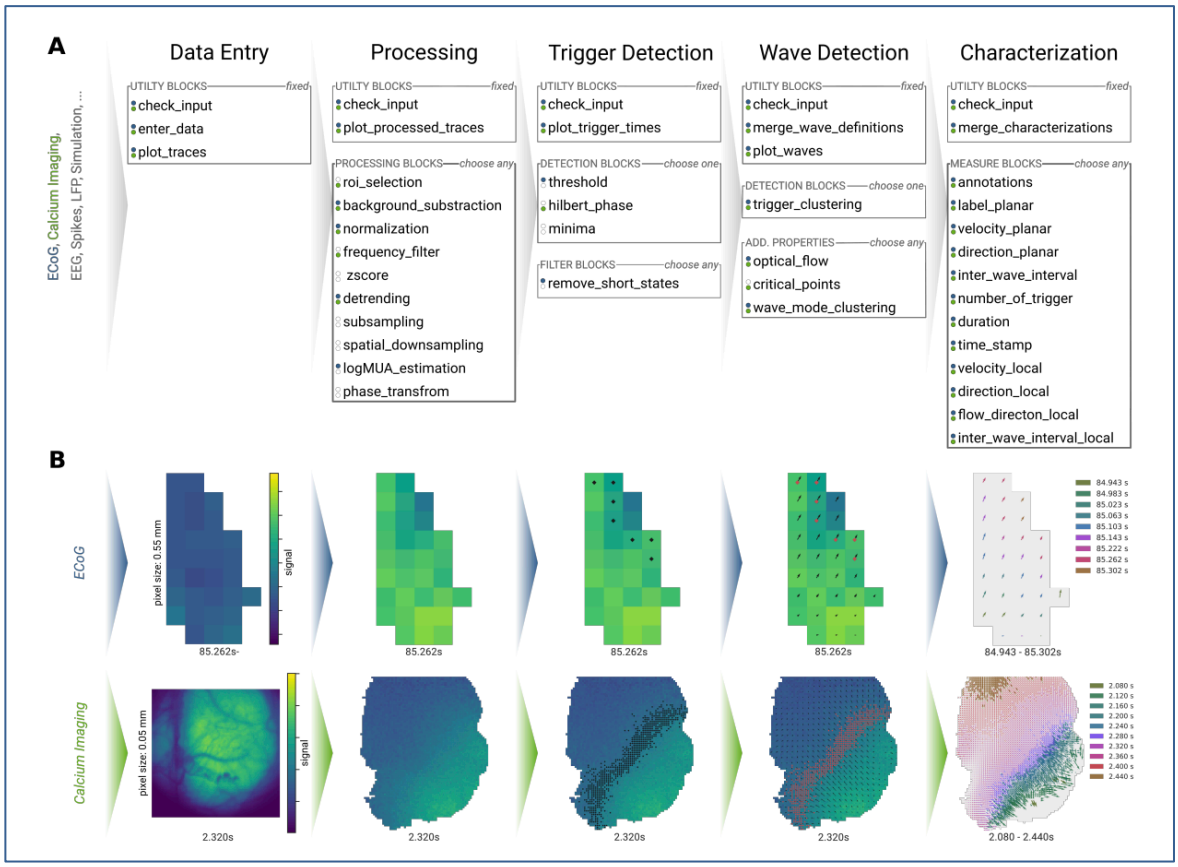

Figure 6: Cobrawap pipeline

The pipeline structure in sequential stages and modular blocks (A) and its application to benchmark datasets (B). From: P3927, under review.

Related publications:

- P3230: Pazienti, A., Galluzzi, A., Dasilva, M., Sanchez-Vives, M. V., & Mattia, M. (2022). Slow waves form expanding, memory-rich mesostates steered by local excitability in fading anaesthesia. Iscience, 25(3).
- P3907: Capone, C., De Luca, C., De Bonis, G. et al. Simulations approaching data: cortical slow waves in inferred models of the whole hemisphere of mouse. Commun Biol 6, 266 (2023). https://doi.org/10.1038/s42003-023-04580-0
- P3927: Gutzen, R., De Bonis, G., De Luca, C., Pastorelli, E., Capone, C., Mascaro, A. L. A., ... & Denker, M. (2022). Comparing apples to apples--Using a modular and adaptable analysis pipeline to compare slow cerebral rhythms across heterogeneous datasets. arXiv preprint arXiv:2211.08527.

Table 4: Data and models related to wave propagation II

Title	KG link	Embargo status
Interactive Exploration of Brain states and spatiotemporal activity patterns in data-constrained simulations	https://search.kg.ebrains.eu/instances/3ebdd555-f965-477c-8a0e-4c220014d138	Public (Model)
Study of Slow Waves propagation through wide-field calcium imaging of the right cortical hemisphere of GCaMP6f mice	https://search.kg.ebrains.eu/instances/Dataset/71285966-8381-48f7-bd4d-f7a66afa9d79	Public (Data)

2.4 Perturbation Complexity Index as a measure of network complexity and responsiveness

PCI State Transition: under curation for the EBRAINS Knowledge Graph, by now available at https://github.com/renzocom/PCIst. (to be available in the EBRAINS KG at: https://search.kg.ebrains.eu/instances/f84a966d-5916-4716-a738-5c828e346044).

2.4.1 PCI method

To explore the neuronal underpinnings of PCI across experimental models and scales, the original measure, PCI Lempel-Ziv (PCI_{LZ}), available at https://search.kg.ebrains.eu/instances/04abd640-6335-4ccb-92b4-638648f0bece), has been adapted to other types of recordings.

PCI_{LZ} is an empirical measure of brain complexity, introduced by Casali et al. 2013, that gauges the amount of information contained in the deterministic brain response to a direct cortical perturbation. In essence, the PCI is defined as the normalized Lempel-Ziv complexity of the deterministic spatiotemporal pattern of cortical activation triggered by direct cortical perturbation; for this reason the original formulation of PCI has been later named PCI_{LZ} (to distinguish from other alternative versions; see below) PCI_{LZ} has been validated in a benchmark population encompassing 150 healthy subjects and communicative brain-injured patients in various states including aware wakefulness, deep sleep (Massimini, Science 2005), dreaming and (Massimini, Eur J Neurosc, 2007) different types of anaesthesia (Sarasso, Curr Biol 2015). Based on this data, an optimal cut off to separate conscious and unconscious subjects has been identified via a receiver operating characteristic curve analysis (PCI_{LZ}=0.31), yielding an accuracy of ~100%. Finally, PCI has been applied to cohorts of non-communicative patients affected by DoC, offering a reliable stratification independent of behavioural responsiveness (Casarotto, Ann of Neuro 2016). Crucially, the reliability of PCI_{LZ} for the diagnosis and stratification of patients depends on TMS-EEG data quality, thus standards, procedures and tools have been made available to optimize the signal-to-noise ratio of TMS-evoked potentials (P3736 and P3738).

The adaptation of PCI_{LZ} to other types of experimental models and scales are not calibrated against the ground truth of conscious and unconscious humans and therefore do not allow direct inference on the presence of awareness but can be used to gain insight into the neuronal and network mechanisms of complexity. Comolatti and colleagues (Brain Stim, 2019) proposed and validated an alternative, fast, and generalizable method for empirically estimating the complexity of sparse intracerebral local field potentials in response to perturbations. This method does not require source modelling nor a homogeneous distribution of recording electrodes and is based on PCA in combination with state transitions quantification (namely PCI state transitions—PCI_{ST}), a method that can be applied to sparse continuous signals.

PCI_{ST} has been applied to invasive intra-cranial stimulation and recordings both in humans (P1719) and in rodents (P2916, Cavelli et al. 2023), effectively distinguishing between synchronous and asynchronous states (i.e. awake vs sleep/anaesthesia).

2.4.2 PCI in humans

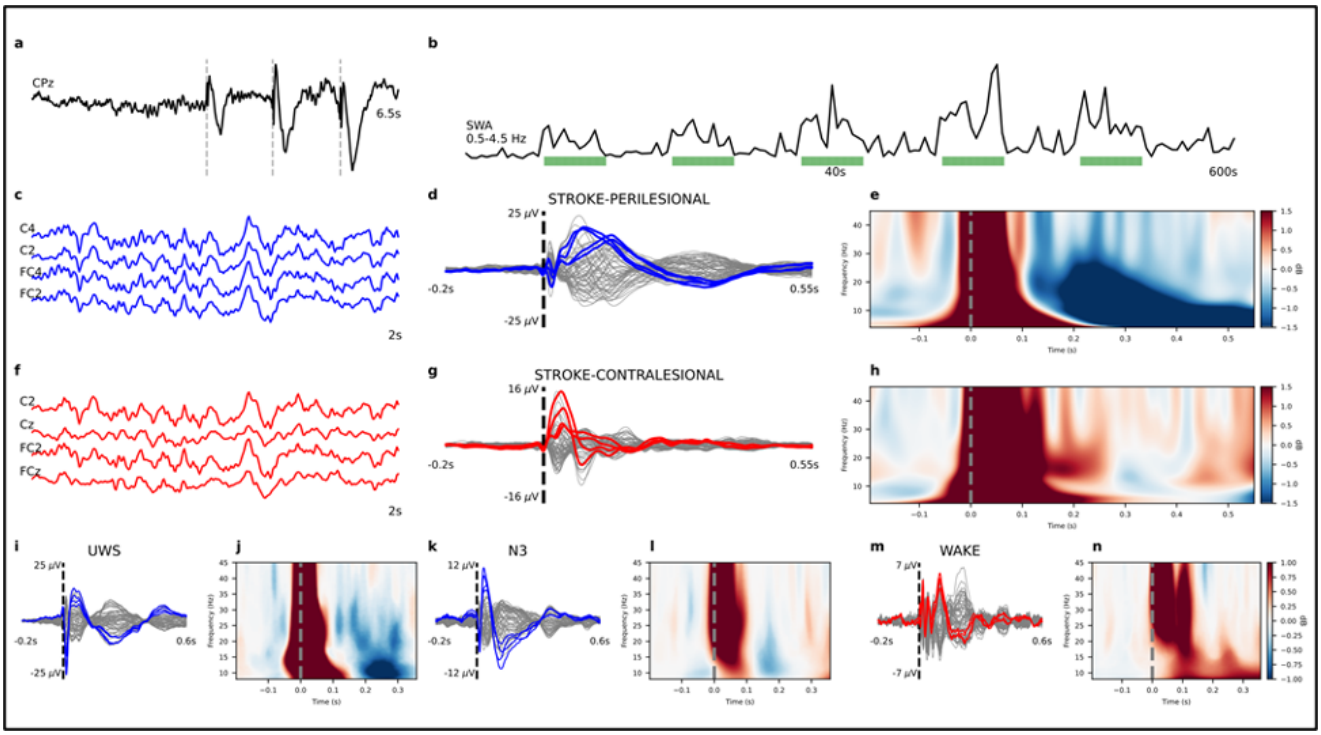

Figure 7: TMS-EEG evoked responses in stroke-perilesional and stroke-contralesional areas

(a) Time course of one channel of scalp EEG during N3 sleep showing spontaneous activity and single trial responses to TMS (vertical dashed lines). (b) Time course of average delta activity across all EEG channels during periods of spontaneous activity and TMS (green horizontal bars). (c) Spontaneous activity from four EEG channels in the perilesional area of a stroke patient. (d) Responses to TMS when stimulating the perilesional area of the same patient shown in (c). Highlighted channels correspond to the four channels showing the largest responses and correspond to those shown in (c) and l Time-frequency representation of the responses to TMS of the four channels highlighted in (d). (f-h) Same as (c-e), respectively, but from a contralesional area. (i-n) Responses to TMS and time-frequency representations of the four highlighted channels for a UWS patient, and a neurotypical subject during N3 sleep and wakefulness

The datasets related to this topic include data collected with TMS-EEG in healthy subjects as well as in brain-lesioned patients; it also includes intracranial recordings in human and subdural recordings in rodents. They are all used to compare brain responsiveness across states, as shown for example in Figure 7 and Table 5. All datasets are available in the KG as listed below.

Table 5: Data and models related to PCI in humans

Title	KG link	Embargo status
Coregistration of simultaneous HD-EEG and intracranial EEG during single pulse intracerebral stimulation in wakefulness and sleep	https://search.kg.ebrains.eu/instances/Dataset/a3e9cd95-d601-40ed-b5fa-e5a9fd01005a	Under embargo
Results for complexity measures and a read-out of the state of cortical circuits after injury	https://search.kg.ebrains.eu/instances/9a05f491-3ef7-47be-93b2-0a6d8cd43ae0	Public with an EBRAINS account
From focal stroke to cortical islands: the impact of lesions on brain complexity and consciousness	https://search.kg.ebrains.eu/instances/a857b9b9-da46-48e7-953d-200e75dbc8e3	Public with an EBRAINS account

2.4.3 PCI in animals

The multiscale investigation of cortical complexity and the mechanisms underlying and modulating it were investigated in different preparations, giving access to the involved circuits and regulatory

factors. In the early period of SGA3, a WP2 article P2595 adapted to the mouse *in vivo* the PCI measure carried out in humans, revealing a lower complexity in deep anaesthesia versus lighter levels of anaesthesia. This measure of complexity (PCI) was applied in P2595 in parallel with other measures that also inform about the emerging complexity and that are based on spontaneous activity, such as wave propagation (further developed in P3230) and functional complexity (first developed in 2016 P905). Further expansions of this work *in vivo* have investigated the perturbational complexity in different cortical areas, as well as comparing thalamic and cortical perturbation (P4124), which is currently being prepared as a full scientific paper.

To investigate in more detail the local mechanisms contributing to cortical complexity, we used cortical slices, where we can mimic various brain states such as slow oscillations and awake-like states. In an earlier study in HBP, we demonstrated how these different states are reflected in the perturbational complexity, which significant increases in desynchronized states (awake-like) with respect to synchronized ones (P758).

We investigated other mechanisms that may influence PCI, such as network excitability. As demonstrated earlier, changes in excitability mediated by depolarizing the membrane potential, either chemically (P758), or by means of electric fields (P1660) did not change the perturbational complexity; however, this may be a limitation of PCI in that it is not sensitive to small changes in network excitability. A certain dependence of PCI on excitability levels is expected based on the original formulation of this index (Casali et al., 2013): PCI measures the information content of brain responses that are integrated in space and time. Low levels of cortical excitability prevent the network from producing sustained responses and thus integration. Hence, a certain level of excitability may be necessary but not sufficient to attain high PCI. This principle is relevant for developing measures in humans, as there are different conditions, such as seizures, sleep, and some types of anaesthesia, in which the cortex produces large, hyper-excitable responses that lack information content or complexity.

We also tested in cortical slices whether PCI was modulated in the presence of different channel blockers such as potassium channel blockers (tetraethylammonium, 4-aminopyridine) or M-current (XE991), without obtaining significant PCI changes.

More recently we investigated the role of $GABA_A$ and $GABA_B$ inhibition on complexity for different states, regulated using neurotransmitters (adrenergic and cholinergic) (P2975). Gradual $GABA_A$ receptor blockade resulted in a significantly higher synchronization, being able to drive the network from a desynchronized to a synchronous state, with a progressive decrease in complexity (PCI). Blocking $GABA_B$ receptors also resulted in a reduced PCI, in particular when in a synchronous, slow-wave state. Our findings demonstrate that physiological levels of inhibition contribute to the generation of dynamical richness and spatiotemporal complexity. However, if inhibition is diminished or enhanced, cortical complexity decreases. Using a computational model, we explored a larger parameter space in this relationship and demonstrate a link between excitatory/inhibitory balance and the complexity expressed by the cortical network.

With respect to the mechanisms regulating PCI, it has been found in humans the relevance of sleep-like cortical OFF-periods as mechanisms that disrupt causality and complexity, such that highly synchronized and oscillatory states such as slow wave sleep or deep anaesthesia, are associated to large OFF-periods and low PCI (P1516). Since OFF-periods, also known as Down states, are so critical for breaking up the causal interactions across areas and thus lowering complexity, we investigated them in animal models (*in vivo* and in cortical slices) and in a cortical computational model in P3780, where we demonstrated how to identify two phases: a highly synchronized “deterministic” period, followed by a low-synchronization “stochastic” period. The balance between these two phases determines the dynamic properties of the resulting rhythm and responsiveness to incoming inputs, which vary with inhibition, anaesthesia levels, or network excitability (as explored previously in P1660).

Table 6: Data and models related to PCI in animals

Title	KG link	Embargo status
Large scale multi-channel EEG in rats	https://search.kg.ebrains.eu/instances/154e9d64-27aa-458d-a289-3e42e4269235	Public
PCI-like measure in rodents	https://search.kg.ebrains.eu/instances/9400031b-dc13-4444-b161-c574d184fdca	Public
Perturbational Complexity Index (PCI) protocol in the mouse (in vivo) and ferret (in vitro)	https://search.kg.ebrains.eu/instances/ae138e06-e565-4bc4-910c-b4eded3bb3c1	Under embargo

Related publications for PCI:

- P1516: Rosanova M, Fecchio M, Casarotto S, Sarasso S, Casali AG, Pigorini A, Comanducci A, Seregni F, Devalle G, Citerio G, Bodart O, Boly M, Gosseries O, Laureys S, Massimini M. Sleep-like cortical OFF-periods disrupt causality and complexity in the brain of unresponsive wakefulness syndrome patients. Nat Commun. 2018 Oct 24;9(1):4427. doi: https://doi.org/10.1038/s41467-018-06871-1 . PMID: 30356042; PMCID: PMC6200777.
- P1719: Comolatti R, Pigorini A, Casarotto S, Fecchio M, Faria G, Sarasso S, Rosanova M, Gosseries O, Boly M, Bodart O, Ledoux D, Brichant JF, Nobili L, Laureys S, Tononi G, Massimini M, Casali AG. A fast and general method to empirically estimate the complexity of brain responses to transcranial and intracranial stimulations. Brain Stimul. 2019 Sep-Oct;12(5):1280-1289. doi: https://doi.org/10.1016/j.brs.2019.05.013 . Epub 2019 May 15. PMID: 31133480.
- P2595: Dasilva M, Camassa A, Navarro-Guzman A, Pazienti A, Perez-Mendez L, Zamora-López G, Mattia M, Sanchez-Vives MV. Modulation of cortical slow oscillations and complexity across anesthesia levels. Neuroimage. 2021 Jan 1;224:117415. doi: https://doi.org/10.1016/j.neuroimage.2020.117415 . Epub 2020 Oct 1. PMID: 33011419.
- P2916: Arena A, Comolatti R, Thon S, Casali AG, Storm JF. General Anesthesia Disrupts Complex Cortical Dynamics in Response to Intracranial Electrical Stimulation in Rats. eNeuro. 2021 Aug 5;8(4):ENEURO.0343-20.2021. doi: https://doi.org/10.1523/ENEURO.0343-20.2021 . PMID: 34301724; PMCID: PMC8354715.
- P3736: Casarotto S, Fecchio M, Rosanova M, Varone G, D'Ambrosio S, Sarasso S, Pigorini A, Russo S, Comanducci A, Ilmoniemi RJ, Massimini M. The rt-TEP tool: real-time visualization of TMS-Evoked Potentials to maximize cortical activation and minimize artifacts. J Neurosci Methods. 2022 Mar 15;370:109486. doi: https://doi.org/10.1016/j.jneumeth.2022.109486. Epub 2022 Jan 21. PMID: 35074394.
- P3738: Russo S, Sarasso S, Puglisi GE, Dal Palù D, Pigorini A, Casarotto S, D'Ambrosio S, Astolfi A, Massimini M, Rosanova M, Fecchio M. TAAC - TMS Adaptable Auditory Control: A universal tool to mask TMS clicks. J Neurosci Methods. 2022 Mar 15;370:109491. doi: https://doi.org/10.1016/j.jneumeth.2022.109491. Epub 2022 Jan 31. PMID: 35101524.
- P3780: Camassa, A., Galluzzi, A., Mattia, M., & Sanchez-Vives, M. V. (2022). Deterministic and stochastic components of cortical Down states: dynamics and modulation. Journal of Neuroscience, 42(50), 9387-9400. https://doi.org/10.1523/JNEUROSCI.0914-22.2022
- P4124: Casas-Torremocha, D., Cortada, M., Camassa, A., Tort-Colet, N., Destexhe, A., & Sánchez-Vives, M. V. (2023). Perturbational cortical complexity evoked by thalamic versus motor cortex stimulation. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 16(1), 396.
- Casali AG, Gosseries O, Rosanova M, Boly M, Sarasso S, Casali KR, Casarotto S, Bruno MA, Laureys S, Tononi G, Massimini M. A theoretically based index of consciousness independent of sensory processing and behavior. Sci Transl Med. 2013 Aug 14;5(198):198ra105. doi: https://doi.org/10.1126/scitranslmed.3006294. PMID: 23946194.

- Casarotto S, Comanducci A, Rosanova M, Sarasso S, Fecchio M, Napolitani M, Pigorini A, G Casali A, Trimarchi PD, Boly M, Gosseries O, Bodart O, Curto F, Landi C, Mariotti M, Devalle G, Laureys S, Tononi G, Massimini M. Stratification of unresponsive patients by an independently validated index of brain complexity. Ann Neurol. 2016 Nov;80(5):718-729. doi: https://doi.org/10.1002/ana.24779 . Epub 2016 Nov 2. PMID: 27717082; PMCID: PMC5132045.
- Cavelli ML, Mao R, Findlay G, Driessen K, Bugnon T, Tononi G, Cirelli C. Sleep/wake changes in perturbational complexity in rats and mice. iScience. 2023 Feb 13;26(3):106186. doi: https://doi.org/10.1016/j.isci.2023.106186 . PMID: 36895652; PMCID: PMC9988678.
- Massimini M, Ferrarelli F, Huber R, Esser SK, Singh H, Tononi G. Breakdown of cortical effective connectivity during sleep. Science. 2005 Sep 30;309(5744):2228-32. doi: https://doi.org/10.1126/science.1117256 . PMID: 16195466.
- Sarasso S, Boly M, Napolitani M, Gosseries O, Charland-Verville V, Casarotto S, Rosanova M, Casali AG, Brichant JF, Boveroux P, Rex S, Tononi G, Laureys S, Massimini M. Consciousness and Complexity during Unresponsiveness Induced by Propofol, Xenon, and Ketamine. Curr Biol. 2015 Dec 7;25(23):3099-105. doi: https://doi.org/10.1016/j.cub.2015.10.014 . Epub 2015 Nov 19. PMID: 26752078.

2.4.4 PCI in models

In computational neuroscience, using human and animal empirical data is crucial for a proper refinement of the models, not only ensuring reliability but also providing a better comprehension of the neural processes behind.

In the context of Showcase 3 (see Deliverable D2.4 submitted) a mouse, macaque and human TVB-AdEx models were developed (Goldman et al. 2022 Frontiers P3023) to not only reproduce spontaneous dynamics (synchronous-sleep-like and asynchronous-awake-like) but also evoked ones. The notebooks (executable in EBRAINS) can be found at this EBRAINS Collaboratory: https://wiki.ebrains.eu/bin/view/Collabs/showcase-3-tvb-brain-states-modelling.

The same model was used to simulate the effect of anaesthesia. This was modelled by the effect of two parameters in the AdEx model, the excitatory and inhibitory synaptic decays, modelling the effect of NMDA-blockers and $GABA_A$ agonists (see Figure 8). The model that reproduces these effects can also be found in the previous Collab: https://wiki.ebrains.eu/bin/view/Collabs/showcase-3-tvb-brain-states-modelling/Drive#Anesthesia

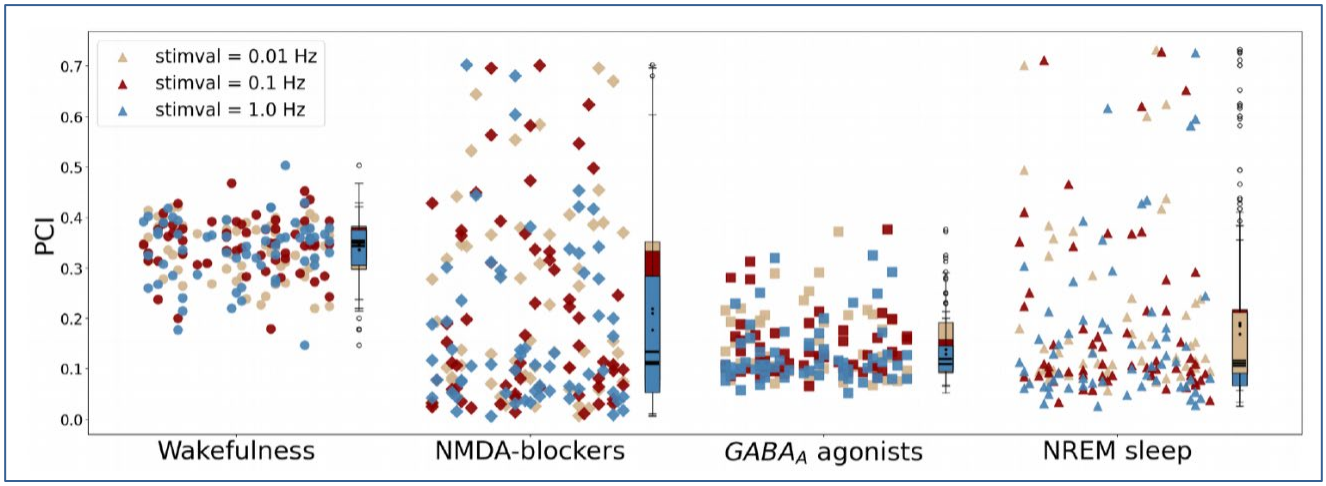

Figure 8: PCI values for the cases of wakefulness, anaesthesia and NREM sleep

3. Live Papers

3.1 Live Papers submitted

3.1.1 Advancing the science of consciousness: from ethics to clinical care

Link to the paper: P4183: Farisco, M., Evers, K., Annen, J., Blandin, V., Camassa, A., Cecconi, B., … Zamora-Lopez, G. (2023, September 22). Advancing the science of consciousness: from ethics to clinical care. https://doi.org/10.31234/osf.io/sutrc

Link to the Live Paper in EBRAINS: https://live-papers.brainsimulation.eu/#2023-farisco-et-al

Authors: Michele Farisco, Kathinka Evers, Jitka Annen, Veronique Baldin, Alessandra Camassa, Benedetta Cecconi, Gustavo Deco, Steven Laureys, Rajanikant Panda, Arnau Manasanch, Mavi Sanchez-Vives & Gorka Zamora-Lopez

3.1.1.1 Abstract

Significant advances in the scientific investigation of the neurobiology of consciousness have been slow to be translated into clinical settings, limited by factors of a conceptual (e.g., what is consciousness?), methodological (e.g., how do we identify reliable indicators of consciousness?), and technical (e.g., how do we improve sensitivity and specificity of the technological identification of consciousness?) nature. In the present paper we aim to reduce the gap between research, clinical practice, patient, and caregiver needs, regarding disorders of consciousness. By implementing a multidisciplinary and multidimensional approach, the paper focuses on disorders of consciousness: it starts from the review of some of the most promising measures of consciousness from brain activity (i.e., spectral measures, measures of functional connectivity, complexity-based measures). Next the paper introduces brain responses to illusions as a new indicator of consciousness (i.e., a feature that facilitates the attribution of consciousness), and illustrates the clinical operationalization of the indicators of consciousness through the case of virtual reality. Finally, in the paper we analyse a set of urgent ethical issues and describe a model for assessing and dealing with these issues, concluding by elaborating key recommendations for improving the clinical treatment of patients with disorders of consciousness through a better translation of research into clinics (see Table 7 for the resources used in the paper).

3.1.1.2 Resources

Table 7: Resources for the Live Paper on Ethics

Title	URL	Embargo status
Results for complexity measures and read-out of the state of cortical circuits after injury	https://search.kg.ebrains.eu/instances/Dataset/9a05f491-3ef7-47be-93b2-0a6d8cd43ae0	Public with an EBRAINS account (Dataset)
The Virtual Brain: Brain states modelling	https://wiki.ebrains.eu/bin/view/Collabs/showcase-3-tvb-brain-states-modelling	Public collab (TVB Models)
Live Figure on clinical cases	https://wiki.ebrains.eu/bin/view/Collabs/live-paper-ethics-and-clinical-care/	Live Figure

3.1.2 The cortical microcircuitry of predictions and context - a multiscale perspective

Link to the paper: P4201: Lars Muckli, Lucy S. Petro, ... Michele Svanera , Wim Vanduffel, Walter Senn, Matthew E. Larkum (September 2023). The cortical microcircuitry of predictions and context - a multiscale perspective https://doi.org/10.5281/zenodo.8380094

Link to the Live Paper in EBRAINS: https://live-papers.brainsimulation.eu/#2023-muckli-et-al

Authors: Lars Muckli*, Lucy S. Petro*, Clement Abbatecola, Johanna Bergmann, Nicolas Deperrois, Alain Destexhe, Nikolaus Kriegeskorte, Christiaan N. Levelt, Wolfgang Maass, Andrew T. Morgan, Paolo Papale, Cyriel M. A. Pennartz, Benjamin Peters, Mihai A. Petrovici, William A. Phillips, Pieter R. Roelfsema, Robert N.S. Sachdev, Koen Seignette, Matthew W. Self, Fraser W. Smith, Johan F. Storm, Michele Svanera, Wim Vanduffel, Walter Senn* & Matthew E. Larkum

3.1.2.1 Abstract

Conscious cognition depends on the ability of the neocortex to generate internal models of the outside world. During wakefulness, the neocortex maintains and updates knowledge of the world and uses this knowledge through top-down projections to make predictions, test hypotheses, and/or contextualize input from the senses. How are these information streams combined in cortical microcircuitry? Is their computational function to test internal models on the basis of their predictions or to contextualize sensory signals, or both? In addition to their somatic integration zones, many pyramidal neurons have a site of top-down and other contextual information integration near the top of the apical dendrite's trunk. This enables the top-down contextualization of bottom-up information, amplifying or attenuating sensory responses depending on prior knowledge and current context. However, current deep neural network models of sensory processing lack such a mechanism, and cognitive theories often still lack intracellular two-compartment integration. We envision how a continued synthesis of multiscale, multispecies experimental data and theoretical and data-driven models will drive further insights into the biophysics, microcircuitry and dynamics of context-sensitive two-compartment neurons, and their role in predictive cognition (see Table 8 for the resources used in the paper).

3.1.2.2 Resources

Table 8: Resources for the Live Paper on The cortical microcircuitry of predictions

Title	URL	Embargo status
fMRI data of early visual cortex while viewing 24 occluded scenes	https://doi.org/10.25493/Z60A-BGY	Public with an EBRAINS account (Human Dataset)
Electrophysiological recordings in macaque V1 during passive viewing of full and occluded natural scenes	https://doi.org/10.25493/KABE-GS0	Public (Macaque Dataset)
Two-photon calcium imaging of layer 2/3 somas and layer 5 dendrites in mouse visual cortex during visual occlusion	https://doi.org/10.25493/NXRY-0W6	Public (Mouse dataset)
Learning cortical representations through perturbed and adversarial dreaming	https://doi.org/10.25493/A1WA-5RG	Public (Model)
Self-supervised Deep Neural Network for Image Completion	https://doi.org/10.25493/5Z86-K1Z	Public (Model)
Recurrent deep networks with feedback for modern AI	https://search.kg.ebrains.eu/instances/eae6a13b-4006-49df-bdcc-ec27c2409e72	Public (Model)

Live Figure Human data	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/The%20cortical%20microcircuitry%20of%20predictions%20and%20context%20-%20A%20multi-scale%20perspective/notebooks/Human%2BDNN.ipynb	Live Figure
Live Figure Mouse data	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/The%20cortical%20microcircuitry%20of%20predictions%20and%20context%20-%20A%20multi-scale%20perspective/notebooks/Mice.ipynb	Live Figure
Live Figure Macaque data	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/The%20cortical%20microcircuitry%20of%20predictions%20and%20context%20-%20A%20multi-scale%20perspective/notebooks/Monkey.ipynb	Live Figure

3.1.3 Identification and neuromodulation of brain states to promote recovery of consciousness

Link to the paper (preprint): P4198: Glenn J.M. van der Lande, Arnau Manasanch, Diana Casas-Torremocha, ..., Maria V. Sanchez-Vives, Gustavo Deco, Steven Laureys, Gorka Zamora-López, Jitka Annen (September 2023). Identification and neuromodulation of brain states to promote recovery of consciousness. https://doi.org/10.5281/zenodo.8377866

Link to the Live Paper in EBRAINS:

https://live-papers.brainsimulation.eu/#2023-vanderlande-et-al

Authors: Glenn J.M. van der Lande, Glenn J.M., Arnau Manasanch, Diana Casas-Torremocha, Leonardo Dalla Porta, Olivia Gosseries, Naji Alnagger, Alice Barra, Jorge F. Mejías, Rajanikant Panda, Fabio Riefolo, Aurore Thibaut, Vincent Bonhomme, Bertrand Thirion, Francisco Clasca, Pau Gorostiza, Maria V. Sanchez-Vives, Gustavo Deco, Steven Laureys, Gorka Zamora-López, Jitka Annen.

3.1.3.1 Abstract

Experimental and clinical studies of consciousness identify brain states (i.e., transient, relevant features of the brain associated with the state of consciousness) in a non-systematic manner and largely independent of the research into the induction of state changes. In this narrative review with a focus on patients with DoC, we synthesize advances on the identification of brain states associated with consciousness in animal models and physiological (sleep), pharmacological (anaesthesia) and pathological (DoC) states of altered consciousness in humans. We show that in reduced consciousness the frequencies in which the brain operates are slowed down and that the pattern of functional communication in the brain is sparser, less efficient, and less complex. The results also highlight damaged resting state networks, in particular the default mode network, decreased connectivity in long-range connections and in the thalamocortical loops. Next, we show that therapeutic approaches to treat DoC, through pharmacology (e.g., amantadine, zolpidem), and (non-)invasive brain stimulation (e.g., transcranial current stimulation, deep brain stimulation) have shown some effectiveness in promoting consciousness recovery. It seems that these deteriorated features of conscious brain states may improve in response to these neuromodulation approaches, yet targeting often remains non-specific and does not always lead to (behavioural) improvements. Furthermore, *in silico* model-based approaches allow the development of personalized assessment of the effect of treatment on brain-wide dynamics. Although still in their infancy, the fields of brain state identification and neuromodulation of brain states in relation to consciousness are showing fascinating developments that, when united, might propel the development of new and better targeted techniques for DoC. For example, brain states could be identified in a predictive

setting, and the theoretical and empirical testing (i.e., in animals, under anaesthesia and patients with a DoC) of neuromodulation techniques to promote consciousness could be investigated. This review further helps to identify where challenges and opportunities lie for the maturation of brain state research in the context of states of consciousness. Finally, it aids in recognizing possibilities and obstacles for the clinical translation of these diagnostic techniques and neuromodulation treatment options across both the multimodal and multispecies approaches outlined throughout the review. This paper presents interactive figures, supported by the Live Paper initiative of the Human Brain Project, enabling the interaction with data and figures illustrating the concepts in the paper through EBRAINS (see Table 9 for the resources used in the paper).

3.1.3.2 Resources

Table 9: Resources for the Live Paper on Identification and neuromodulation of brain states

Title	URL	Embargo status
FDG-PET/CT data of healthy volunteers and patients with disorders of consciousness	https://doi.org/10.25493/7TXP-WCF	Public with an EBRAINS account (Dataset)
Individual Brain Charting	https://doi.org/10.25493/SM37-TS4	Public with an EBRAINS account (Dataset)
Optimisation of photostimulation targeting muscarinic receptors	https://doi.org/10.25493/8X89-5VB	Under embargo (Dataset)
TMS-EEG perturbation in patients with disorders of consciousness	https://doi.org/10.25493/G8E3-DQE	Public with an EBRAINS account (Dataset)
Live Figure: Disorders of Consciousness and Brain State examples	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Live%20Paper%3A%20Identification%20and%20neuromodulation%20of%20brain%20states%20to%20promote%20recovery%20of%20consciousness/LiveFigure_ArousalAwareness/ArousalAwareness.ipynb	Live Figure
Live Figure: fMRI brain state dynamics in DoC	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Live%20Paper%3A%20Identification%20and%20neuromodulation%20of%20brain%20states%20to%20promote%20recovery%20of%20consciousness/LiveFigure_Dynamics/Dynamics.ipynb	Live Figure
Live Figure: TMS-triggered slow activity after tDCS treatment of DoC patients	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Live%20Paper%3A%20Identification%20and%20neuromodulation%20of%20brain%20states%20to%20promote%20recovery%20of%20consciousness/LiveFigure_tDCS/tDCS.ipynb	Live Figure
Live Figure: Brain state transitions with a photoswitchable muscarinic agonist	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Live%20Paper%3A%20Identification%20and%20neuromodulation%20of%20brain%20states%20to%20promote%20recovery%20of%20consciousness/LiveFigure_Photopharmacology/Photopharmacology.ipynb	Live Figure

3.2 Live papers under preparation

Apart from the three committed Live papers that are currently available as preprints and under review in journals, WP2 has generated additional ones that are in different stages of preparation and publication. All of them have all or part of the resources associated to their Figures and content already prepared in EBRAINS.

3.2.1 Active inference in tactile sensing during multisensory object recognition

Link to the paper: The paper is in preparation and will be available as a preprint after SGA3.

Link to the Live Paper in EBRAINS: The Paper is currently being built in the EBRAINS Live Papers Service. It will be published along with the paper.

Authors: Francesco Mannella, Giovanni Pezzulo, Jakob Jordan, Jorge Mejias, Julien Fiorilli, Lilian Emming, Martin Pearson, Mihai Petrovici, Pieter Roelfsema, Thijs Ruikes, Umberto Olcese, Cyriel Pennartz

3.2.1.1 Abstract

Rodents use whisker movements to probe and recognize objects, sometimes in combination with other senses, such as vision. However, we still lack a comprehensive understanding of how they combine multiple sensory modalities during object recognition. Here, we advance a novel computational model of rodent whisking behaviour during multimodal object recognition, using the framework of active inference. In the model, object recognition stems from a competitive process, based on prediction error minimization and bottom-up information from sensory systems for vision and whisking. Whisking is cast as an active process guided by prediction error minimization: the rodent controls the amplitude of its whiskers until they touch the object at the end of their protractions. Since each object corresponds to a set of object-specific (expected) whisker amplitudes, the amplitude of whiskers can be used as evidence about the object the animal is interacting with. Crucially, active whisking can also be guided from the top down: when vision provides prior information about object identity, the model sets whisker amplitudes to their object-specific values. The model therefore predicts that whisker movements are more accurate in the presence of multimodal information. We validate this model prediction with the help of in vivo recorded rodent whisking data acquired during a multisensory object discrimination task, in two conditions. In one condition (tactile-only), rodents gather tactile information by actively whisking, with the light turned off. In another condition (multimodal), the light is turned on and hence the rodents receive both visual and tactile information. To compare model and rodent data, we developed a novel behavioural measure of predictability, based on the synchrony between individual whisker movements during object recognition. Our results indicate that after object contact, the synchrony between whiskers decreases but it is recovered faster in multimodal trials, providing support for the multisensory integration based on active inference model (see Table 10 for the resources used in the paper).

3.2.1.2 Resources

Table 10: Resources for the Live Paper on Active inference

Title	URL	Type
Sensory, perirhinal and hippocampal tetrode recordings during visual, tactile and visuotactile discrimination task in the freely moving rat	https://search.kg.ebrains.eu/instances/d406a98c-ae5c-4fb3-9f0c-4cf4de9b1094	Dataset (under embargo upon publication)

Simulated rodent model	https://wiki.ebrains.eu/bin/view/Collabs/wp2-t2-1-livepaper-rootcollab/Drive	Collab where the code for Live Figures is stored
The computational model	https://drive.ebrains.eu/d/78ec7b7a34ca4e2496c4/files/?p=%2Fsrc%2Fpaper_notebooks%2Ffigure_1a.ipynb	Live Figure 1
Experimental data from the rodent study	https://drive.ebrains.eu/d/78ec7b7a34ca4e2496c4/files/?p=%2Fsrc%2Fpaper_notebooks%2Ffigure_2a.ipynb	Live Figure 2

All the code to reproduce the "Simulated rodent model" used in this Live Paper (and the two Live figures) has been uploaded in EBRAINS, see links in the table 8. The model is currently being inserted in the EBRAINS KG. The first live figure permits modifying the parameters of the computational model (e.g., parameters that regulate whisker amplitude of the simulated rodent) and observe the results. The second live figure permits selecting which rodent data to load (e.g., whisker data from a single tactile vs. multisensory trial) and compare it with equivalent data produced by the computational model.

3.2.2 Dendritic weighting during audiovisual cue detection: from experimental data to computational modelling

Link to the paper: The paper is in preparation and will be available as a preprint after SGA3.

Link to the Live Paper in EBRAINS: The Paper is currently being built in the EBRAINS Live Papers Service. It will be published along with the paper.

Authors: Ben von Hünerbein, Matthijs oude Lohuis, Pietro Marchesi, Umberto Olcese, Walter Senn, Cyriel Pennartz, Jakob Jordan & Mihai A. Petrovici

3.2.2.1 Abstract

Uncertainty is omnipresent. While humans and other animals take uncertainty into account during decision making, so far it remains unclear how it is represented in cortex. To investigate the effect of stimulus reliability on cortical neurons, we analysed single unit activity data recorded in mouse PPC, while animals performed a multisensory change detection task. Further we used simulation-based inference (SBI) to infer intracellular membrane potential statistics underlying the spiking activity. Spike data show that stimulus changes increase spiking activity while decreasing its variability. Inferred membrane potential statistics suggest that PPC neurons decrease their membrane potential variability in response to task relevant stimuli. Furthermore, more reliable stimuli lead to a larger decrease in membrane potential variability than weak stimuli. We discuss these results in the light of a recently proposed model of conductance-based Bayes-optimal cue integration in single neurons. Our findings suggest that individual cortical neurons track uncertainty, likely providing Bayesian benefits for downstream computations (see Table 11 for the resources used in the paper).

3.2.2.2 Resources

Table 11: Resources for the Live Paper on Dendritic weighting

Title	URL	Type
Audio-visual change detection task in mice	https://search.kg.ebrains.eu/instances/ba41de6c-1b30-4f48-89c4-a6eb47b2c549	Dataset (Public)
Certainty weighted integration of individual neurons	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/drive/Shared%20with%20groups/WP2_T2.1b_LivePaper_rootCollab/Live_Figure_T2.1b/live_fig.ipynb	Live Figure

3.2.3 *Multiscale dynamical characterization of spontaneous cortical brain states: from synchrony to asynchrony*

Link to the paper (preprint): https://doi.org/10.5281/zenodo.8384574

Link to the Live Paper in EBRAINS: The Paper is currently being built in the EBRAINS Live Papers Service. It will be published along with the paper.

Authors: Maria V. Sanchez-Vives, Arnau Manasanch, Andrea Pigorini, Alessandro Arena, Alessandra Camassa, Bjørn Erik Juel, Leonardo Dalla Porta, Cristiano Capone, Chiara De Luca, Jennifer Goldman, Maria Sacha, Andrea Galluzzi, Antonio Pazienti, Ezequiel Pablo Mikulan, Marcello Massimini, Johan F. Storm, Pier Stanislao Paolucci, Maurizio Mattia & Alain Destexhe

3.2.3.1 Abstract

The cerebral cortex spontaneously elicits different patterns of activity that evolve over time according to the brain state. Sleep, wakefulness, resting states, and attention are examples of a wide spectrum of physiological states that can be sustained by the same structural network. Furthermore, additional states are generated by drugs (e.g., different levels of anaesthesia), or by pathological conditions (e.g., brain lesions, disorders of consciousness). While the significance of understanding brain states in relation to brain dynamics and behaviour has become increasingly evident over the past two decades, a unified definition remains elusive. In this review we focus in two extremes of this spectrum, synchronous versus asynchronous states. These states predominantly underlie unconsciousness and consciousness, respectively, although exceptions exist. Our aim is to integrate a multiscale understanding ranging from local circuits to whole-brain dynamics, including properties such as cortical complexity, functional connectivity, synchronization, wave propagation and excitatory-inhibitory balance that vary across states and characterize them. Experimental and clinical data, as well as computational models (micro, meso and macrocortical levels) associated to the discussed brain states are made available to the readers (see Table 12 for the resources used in the paper).

3.2.3.2 Resources

Table 12: Resources for the Live Paper on Cortical brain states

Title	URL	Type
Human TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Human/human_notebook_GUI.ipynb	Model (interactive notebook)
Macaque TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Macaque/macaque_notebook_GUI.ipynb	Model (interactive notebook)
Mouse TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Mouse_working/Mouse_notebook_GUI.ipynb	Model (interactive notebook)
Interactive Exploration of Brain States and Spatiotemporal Activity Patterns in Data-Constrained Simulations	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Interactive%20Exploration%20of%20Brain%20States%20and%20Spatio-Temporal%20Activity%20Patterns%20in%20Data-	Model (interactive notebook)

	Constrained%20Simulations/spontaneous_simulation_v2/Interactive_MF_Inferred_v2.0.ipynb	
Spatiotemporal distribution of slow oscillations at different anaesthesia levels	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/live-figures-multiscale-brain-states/live_figure_idibaps/live_figure.ipynb	Live Figure
TMS-EEG evoked responses in different brain states, going from spontaneous to perturbed	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/live-figures-multiscale-brain-states/live_figure_unimi/live_figure.ipynb	Live Figure
Network model of Up-Down slow oscillations in L5 cortex of sleeping and anaesthetized mammals	https://search.kg.ebrains.eu/?category=Contributor&q=mattia#4b13fe21-28f9-4373-9a05-04f450cb6e1d	Model
Transitions between different naturally and artificially-induced brain states in in vivo rats	https://search.kg.ebrains.eu/instances/e07ab90a-6308-469c-8bc7-a41234103ad3	Dataset
Propagation modes of slow waves in mouse cortex	https://search.kg.ebrains.eu/instances/7866daf2-7064-4fa0-b6a2-0b1c899ba35f	Dataset
Coregistration of simultaneous HD-EEG and intracranial EEG during single pulse intracerebral stimulation in wakefulness and sleep	https://search.kg.ebrains.eu/?category=Contributor&q=massimini#a3e9cd95-d601-40ed-b5fa-e5a9fd01005a	Dataset
Dose-dependent effects of ketamine on spontaneous and evoked EEG activity in rats	https://search.kg.ebrains.eu/?category=Contributor&q=arena#68bce801-d06a-4b01-8d5a-b0e42f10b86d	Dataset

3.2.4 State-dependent brain responsiveness: from local circuits up to the whole brain

Link to the paper: The paper is in preparation and will be available as a preprint during the last quarter of 2023.

Link to the Live Paper in EBRAINS: The Paper is currently being built in the EBRAINS Live Papers Service. It will be published along with the paper.

Authors: Alain Destexhe, Andrea Pigorini, Anna Letizia Allegra Mascaro, Alessandro Arena, Alessandra Camassa, Cristiano Capone, Leonardo Dalla Porta, Olivier David, Giulia De Bonis, Chiara De Luca, Abhilash Dwarakanath, Jan Fousek, Andrea Galluzzi, Jennifer Goldman, Espen Hagen, Maciej Jedynak, Born Erik Juel, Arnau Manasanch, Ezequiel Mikulan, Elena Montagni, Antonio Pazienti, Spase Petkoski, Francesco Resta, Axel Roques, Johanna Senk, Núria Tort-Colet, Markuss Diesmann, Viktor Jirsa, Marcello Massimini, Maurizio Mattia, Theofanis Panagiotaropoulos, Pier Stanislao Paolucci, Francesco S Pavone, Johann F Storm & Mavi Sánchez-Vives

3.2.4.1 Abstract

The objective of this paper is to review physiological and computational aspects of the responsiveness of the cerebral cortex to stimulation, and how responsiveness depends on the state of the system. This correspondence between brain state and brain responsiveness (state-dependent responses) will be outlined at different scales from cellular/circuit level to the mesoscale and the macroscale level. At each scale, we will review how quantitative methods can be used to characterize brain responses, such as the Perturbational Complexity Index (PCI). This description will compare data and models, systematically and at multiple scale, with a focus on the mechanisms

that explain how brain responses depend on brain states (see Table 13 for the resources used in the paper).

3.2.4.2 Resources

Table 13: Resources for the Live Paper on Brain Responsiveness

Title	URL	Type
Human TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Human/human_notebook_GUI.ipynb	Model (interactive notebook)
Macaque TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Macaque/macaque_notebook_GUI.ipynb	Model (interactive notebook)
Mouse TVB Model Notebook	https://lab.ch.ebrains.eu/hub/user-redirect/lab/tree/shared/Showcase%203%20Brain%20Complexity%20and%20Consciousness/Mouse_working/Mouse_notebook_GUI.ipynb	Model (interactive notebook)
Coregistration of simultaneous HD-EEG and intracranial EEG during single pulse intracerebral stimulation in wakefulness and sleep	https://search.kg.ebrains.eu/instances/a3e9cd95-d601-40ed-b5fa-e5a9fd01005a	Dataset
Sensory and intracortical stimulations with simultaneous sEEG and hd-EEG recordings and subjective reports	https://search.kg.ebrains.eu/instances/a12a4d28-ca1c-4e03-9891-3ab696a1ac28	Dataset
Simultaneous human intracerebral stimulation and HD-EEG, ground-truth for source localization methods	https://search.kg.ebrains.eu/instances/f557d71e-fe11-43d7-8225-7c2d432f34b9	Dataset
Simultaneous stereo-EEG and high-density scalp EEG recordings to study the effects of intracerebral stimulation parameters	https://search.kg.ebrains.eu/instances/b1c3e79e-ca4a-4a05-9235-b93cf1cb678d	Dataset
2D Primary Visual Cortex Mean-Field Model	https://search.kg.ebrains.eu/instances/a94b0808-9693-4f74-afc8-d9a29bb9d952	Model
Wide-field imaging of cortical response to sensory stimulation in GCaMP6f mice at different brain states	https://search.kg.ebrains.eu/instances/5fbaeea7-fac2-472e-aefc-556c2cde1218	Dataset
Intracranial electrophysiological recordings from PFC and PPC during wakefulness and anaesthesia under electrical microstimulation	https://search.kg.ebrains.eu/instances/8c17072f-ff13-4467-882c-97a02ff37838	Dataset

4. Looking forward

As EBRAINS services continue to evolve and improve, we remain committed to providing feedback and remain as users, contributing to the development of a collaborative and accessible environment for neuroscience research. Our work has far-reaching implications, appealing to diverse communities within neuroscience, computational modelling, and the broader scientific research community, as we provide insights into critical aspects of brain network dynamics and their interaction with the EBRAINS platform. Sharing our Use-cases and Live Papers is an essential step toward advancing the frontiers of neuroscience and facilitating cross-disciplinary collaboration.