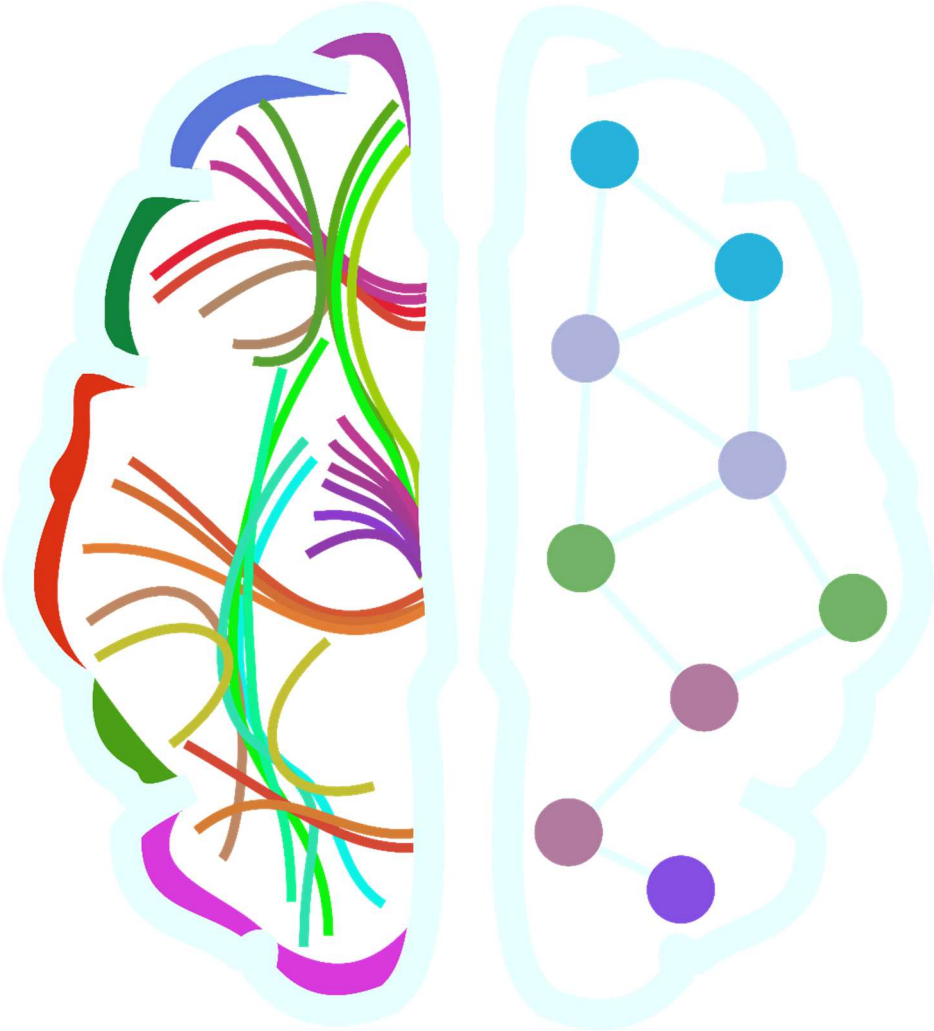
B R A D Y



Kick-off meeting

Prague, Národní 1009/3

29. 4. 2024

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

Kick-off meeting

EVENT PROGRAM

PRE KICK-OFF WORKSHOP: MODELLING BRAIN DYNAMICS (CONFERENCE HALL N. 206)

10:00 Opening	**Ing. Mgr. Jaroslav Hlinka, Ph.D.** (ICS)
10:10 Lecture 1	**Helmut Schmidt, Ph.D.** (ICS)
10:40 Lecture 2	**Mgr. Pavel Šanda, Ph.D.** (ICS)
11:10 Coffee break	*(Lobby of the hall n. 206)*
11:40 Lecture 3	**Mgr. Ján Antolík, Ph.D.** (CU)
12:10 Lecture 4	**Mgr. Nikola Jajcay, Ph.D.** (ICS)
12:40 Lunch	*(Lobby of the hall n. 206)*

KICK-OFF (CONFERENCE HALL N. 206)

13:40 Welcoming remarks	**doc. Ing. Petr Cintula, Ph.D., DSc.** (ICS)
13:45 Intro to the project	**Ing. Mgr. Jaroslav Hlinka, Ph.D.** (ICS)
14:10 Admin	**Mgr. Michaela Lutišanová** (ICS)
	Who is who, administrative team, basic info
14:20 WP 1	**Jajcay, Schmidt, Šanda, Bakštein, Novák** (ICS, NIMH, CTU)
	Introducing expertise and objectives
15:00 WP 2	**Jiruška, Španiel, Hammer, Antolík, Kremláček** (CU/NIMH)
	Introducing expertise and objectives
15:40 WP 3	**Horáček, Klírová, Sieger, Páleníček, Brunovský** (NIMH/CTU)
	Introducing expertise and objectives
16:25 Coffee break	*(Lobby of the hall n. 206)*

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

16:50 Training 1	**Mgr. Pavel Šanda, Ph.D., Mgr. Nikola Jajcay, Ph.D.** (ICS) Open science publishing guidelines, open source software and licencing
17:20 Training 2	**Ing. Eduard Bakštein, Ph.D.** (CTU) Scientific programming
17:50 Training 3	**MUDr. Filip Španiel, Ph.D., Ing. Pavel Dvořák** (NIMH) Working with medical data
18:20 Questions/Discussion	
18:50 Dinner	*(Lobby of the hall n. 206)*
Poster session	**Poster wine reception**

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

ABSTRACTS

Intro to the project

Presenter: Ing. Mgr. Jaroslav Hlinka, Ph.D., research project manager

Jaroslav Hlinka *is a senior scientist and the Head of the Department of Complex Systems at the Institute of Computer Science of the Czech Academy of Sciences. He develops and applies methods for analysis of complex systems. He is expert in the area of uncovering the mechanism of brain activity dynamics, both in healthy subjects and in disease, by developing and applying methods to model and analyze data obtained by combination of neuroimaging and psychological methods. As the BRADY research project manager, he will coordinate the research activities, participating across Objectives, in particular leading the research activity RA1.2. Data driven model inversion.*

Jaroslav Hlinka, after welcoming to the Kick-off proper part of the program, will re-introduce the BRADY project. Particular attention will be paid to its main goals and activities, and then to the structure of its research program and the complementary expertise of the team we have put together. A brief overview of the research work packages and their objectives will set the stage for the more detailed presentations that will follow during the afternoon.

Lecture 1: From Adaptive Spiking Neural Networks to Neural Mass Models

Presenter: Helmut Schmidt, Ph.D.

Helmut Schmidt *is a computational neuroscientist and researcher who focuses on computational techniques to understand and reproduce the dynamics of biological neural networks, ranging from small-scale networks to the entire (human) brain. Applications encompass neuronal information processing (working memory, language acquisition) as well as disorders of large-scale neuronal networks, especially epilepsy. His expertise in mean-field modeling makes him a key scientist working on Objectives O1.1.2 and O1.1.3.*

Neuronal networks are endowed with a multitude of mechanisms that modulate their spiking activity and connectivity structure, such as spike frequency adaptation (SFA) and short-term

synaptic plasticity. Typically, these mechanisms add long time scales on top of membrane time scales and synaptic transmission times, and are commonly studied using large-scale simulations at the spiking neuron level. We present methods for deriving the macroscopic equations for networks composed of non-identical quadratic integrate-and-fire neurons (based on [1]) that incorporate such mechanisms.

First, we focus on SFA and analyse the resulting equations by means of bifurcation analysis. SFA leads to the emergence of bursting behaviour, which can coexist with steady state behaviour providing a bistable regime that enables transient switches between synchronised and non-synchronised states of population dynamics. The macroscopic equations provide an accurate and efficient description of phase transitions between bursting and steady state population dynamics, which are organised by Hopf and homoclinic bifurcations. We also show that the macroscopic equations generalise well to networks of biologically plausible size and coupling probability [2].

Next, we incorporate short-term synaptic depression and facilitation into the model equations. The straightforward derivation of the macroscopic equations is no longer possible in this case, and we propose two approaches to obtain an approximate macroscopic description: (a) an adiabatic approximation of the network dynamics, which yields a low-dimensional, but somewhat inaccurate description of the macroscopic dynamics; and (b) a more accurate multi-population approximation of the network dynamics. The latter is based on dividing the network into sub-networks of neurons with nearly identical properties, for which the macroscopic dynamics can be easily obtained. Both approaches outperform standard mean field methods in terms of their accuracy [3].

Our work provides a comprehensive account of the effects of SFA and short-term synaptic plasticity on the macroscopic dynamics of spiking neural populations, and the mathematical tools to predict population-level effects of SFA and short-term plasticity from single neuron properties.

References

[1] Montbrió, E., Pazó, D., Roxin, A.: Macroscopic description for networks of spiking neurons. Phys. Rev. X 5 (2015) 021028.

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

[2] Gast, R., Schmidt, H., Knösche, T. R.: A mean-field description of bursting dynamics in spiking neural networks with short-term adaptation. Neur. Comp. 32 (2020) 1615-1634.
[3] Gast, R., Knösche, T. R., Schmidt, H.: Mean-field approximations of networks of spiking neurons with short-term synaptic plasticity. Phys. Rev. E 104 (2021) 044310.

Lecture 2: Spiking perspective on different vigilance states

Presenter: Mgr. Pavel Šanda, Ph.D.

Pavel Šanda *is a computational neuroscientist and researcher at the Institute of Computer Science. He is focused on detailed biophysical models of neuronal networks. He has expertise in modelling sleep, whole-brain resting state networks and their neuromodulation which makes him a key scientist for working on Objectives O1.1.1 and O1.1.3.*

We will introduce some modeling approaches for description of different brain vigilance states. We will use small (spiking) networks to build the systems-level depiction of sleep processes related to memory consolidation and characterization of large-scale network dynamics affected by cholinergic neuromodulation during the resting state.

Lecture 3: From modeling of visual system to cortical implant for vision restoration

Presenter: Mgr. Ján Antolík, Ph.D.

Ján Antolík *is an Assistant Professor at the Faculty of Mathematics and Physics. The objective 2.1.1 lead by Dr. Antolík is a natural extension of his previous research activities and will involve techniques in which he has extensive experience: modeling of multi scale neural data, analysis of neurophysiological recordings and neuroinformatics.*

The goal of the presentation will be to briefly introduce the large-scale spiking neural network model of the early visual system that is being developed in our group, We will then show how we extended the model with a model of optogenetic stimulation from the cortical

surface. Finally, we will demonstrate how we use this modeling framework to evaluate effectiveness of optogenetic stimulation protocols for vision restoration.

Lecture 4: Model inversion of biophysically realistic models and their role in computational psychiatry

Presenter: Mgr. Nikola Jajcay, Ph.D.

Nikola Jajcay *is a junior scientist at the Center for Advanced Studies of Brain and Consciousness, National Institute of Mental Health, and the Department of Complex Systems at the Institute of Computer Science of the Czech Academy of Sciences. He currently holds an individual fellowship in the Horizon Europe scheme from the European Research Executive Agency in the field of computational psychiatry. His focus spans modelling and analysis of complex systems with a particular interest in brain dynamics in health and disease, and he has apt experience with modelling, data analysis, and machine learning from academia and industry. He will benefit from his experience and expertise in overseeing the whole research work package RWP1 and (co-)leading objectives O1.2.2, O3.2.1, and O3.2.2.*

This short talk will introduce the field of computational psychiatry, which involves applying computational modelling and theoretical approaches to psychiatric questions. Its goal is to characterise psychopathology in mathematical terms with the hope that it might serve to identify specific neural circuits or processes responsible for psychiatric disorders. We will briefly summarise various tools it typically uses and how they might relate to the BRADY project. Finally, we will dive deeper into model inversion, mainly using Dynamic Causal Modelling and Simulation-Based Inference methods, and what their caveats and potential gains are.

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

Training 1: Open science, open source software and licencing

Presenter: Mgr. Pavel Šanda, Ph.D., Mgr. Nikola Jajcay, Ph.D.

Pavel Šanda *is a computational neuroscientist and researcher at the Institute of Computer Science. He is focused on detailed biophysical models of neuronal networks. He has expertise in modelling sleep, whole-brain resting state networks and their neuromodulation which makes him a key scientist for working on Objectives O1.1.1 and O1.1.3.*

Nikola Jajcay *is a junior scientist at the Center for Advanced Studies of Brain and Consciousness, National Institute of Mental Health, and the Department of Complex Systems at the Institute of Computer Science of the Czech Academy of Sciences. He currently holds an individual fellowship in the Horizon Europe scheme from the European Research Executive Agency in the field of computational psychiatry. His focus spans modelling and analysis of complex systems with a particular interest in brain dynamics in health and disease, and he has apt experience with modelling, data analysis, and machine learning from academia and industry. He will benefit from his experience and expertise in overseeing the whole research work package RWP1 and (co-)leading objectives O1.2.2, O3.2.1, and O3.2.2.*

The tutorial will summarize open science publishing guidelines for BRADY project, types of software contributions and philosophy of open source licensing. Focus will be on streamlining activities and sharing good practice in order to 1) fulfil formal requirements, 2) maximize research impact through open results and methods dissemination, 3) minimise administrative burden of scientists and support staff.

Training 2: Scientific programming

Presenter: Ing. Eduard Bakštein, Ph.D.

Eduard Bakštein *is a researcher, working on application of AI and advanced data science and signal processing methods to diagnosis, clinical state monitoring and outcome prediction in neurology and psychiatry. He is co-author of 16 journal publications and coauthor of 10 conference publications. He co-supervised 3 PhD students and 15+ Bc and MSc theses and*

taught courses on Artificial intelligence, Biometric identification and Computational neuroscience. He will lead O1.2.1 and T1.2.3b.

The typical scientific programming tasks deal with analysis of experimental data. The contribution will pinpoint some good/bad practices in organizing data analytic programming projects, with special focus on effective data handling and maintenance of reproducible results. Links to additional resources and tools specific for BRADY will be also provided.

Training 3: Working with medical data

Presenter: MUDr. Filip Španiel, Ph.D., Ing. Pavel Dvořák

Filip Španiel *is the Head of the Center for Applied Research in Early Stage of Serious Mental Illnesses at National Institute of Mental Health, Czech Republic. He has actively participated as PI and co-PI in more than 15 national (AZV, GAČR, TAČR) and international projects (HORIZON). Dr. Spaniel's research and clinical work focus on the identification, characterization and treatment of patients with mood disorders and schizophrenia spanning all disease stages from the prodrome to first and multi-episode illness and up to refractory illness. He focuses primarily on MRI neuroimaging in schizophrenia. He is an author of telemedicine relapse prevention programs in schizophrenia and bipolar disorder.*

This tutorial addresses the management of neuroimaging medical data in academic research, covering study design, ethical considerations including informed consent and ethics committee approval, data security, and anonymization. It delves into computational requirements for data analysis, strategies for data storage, and emphasizes reproducibility through rigorous documentation and public sharing of research components. Principles of open science and their application in research transparency are discussed, with a practical example from the NUDZ HYDRA system, demonstrating effective implementation of these practices.

WORK PACKAGE 1 – WHOLE BRAIN SPONTANEOUS DYNAMICS

Objective 1.1.1: Detailed biophysical modelling of neurotransmitter actions

Presenter: Mgr. Pavel Šanda, Ph.D. (Research objective O.1.1.1 leader)

Pavel Šanda *is a computational neuroscientist and researcher at the Institute of Computer Science. He is focused on detailed biophysical models of neuronal networks. He has expertise in modelling sleep, whole-brain resting state networks and their neuromodulation which makes him a key scientist for working on Objectives O1.1.1 and O1.1.3.*

Neuromodulatory systems provide the basis for cognitive actions in the brain and strongly influence human behaviour. Each system is linked with a specific brain centre(s) and any disbalance in neurotransmitter release, delivery or interaction leads to various disease states. Capturing neurotransmitter influence on the microcircuit level leads to the proper description of the circuit dynamics and allows prediction of pharmaceutical interventions typically targeting particular neuromodulatory systems. We will study the transitions between different functional modes in awake/sleep states and link their aberrations to potential neurochemical disease mechanisms at the cellular level.

Tasks:

Task T1.1.1.a: Detailed biophysical models of neurotransmission

Task T1.1.1.b: Astrocytic influence on the dynamics of the microcircuitry

Task T1.1.1.c: Pharmacological modulation of vigilance states

Objective 1.1.2: Computationally efficient mean-field models

Presenter: Helmut Schmidt, Ph.D. (Research objective O1.1.2 leader)

Helmut Schmidt *is a computational neuroscientist and researcher who focuses on computational techniques to understand and reproduce the dynamics of biological neural networks, ranging from small-scale networks to the entire (human) brain. Applications encompass neuronal information processing (working memory, language acquisition) as well*

as disorders of large-scale neuronal networks, especially epilepsy. His expertise in mean-field modeling makes him a key scientist working on Objectives O1.1.2 and O1.1.3.

Dr. Schmidt will summarize his research area, and goals under Objective 1.1.1. In particular, mean-field models will include key neuron types and astrocytes, using advanced mean-field approaches for modeling. These models will explore the interaction of neurons and astrocytes in detail. The model extends to incorporate EEG and fMRI data links, explaining how these relate to neuronal and astrocytic activities, assisting in understanding their correlation and impact on brain conditions. Additionally, a mean-field model for the visual cortex will analyze cortical connectivity and patterns, using realistic brain structure data. Lastly, these models will be evaluated against detailed spiking neuron networks to verify their biological accuracy and compare findings from various studies.

Tasks:

Task T1.1.2.a: Mean-field models of cortical microcircuits

Task T1.1.2.b: EEG-fMRI forward model

Task T1.1.2.c: Neural field models of V1

Task T1.1.2.d: Establishing correspondence with spiking network models

Objective O1.1.3: Whole-brain dynamics

Prof. Dr. phil. Dr. rer. nat. habil. Gustavo Deco (Research objective O1.1.3 leader)

Gustavo Deco *is Research Professor at the Institució Catalana de Recerca i Estudis Avançats (ICREA) and Professor (Catedrático) at the Pompeu Fabra University (UPF) where he leads the Computational Neuroscience group. The main aim of his research is to elucidate precisely the computational principles underlying higher brain functions and their breakdown in brain diseases. He is perfectly positioned to lead the research activity RA1.1.*

This research activity aims to move beyond standard brain network models and develop mathematical descriptions of cortical and whole-brain activity that bridge different brain states, neurotransmitter action, and disease dynamics. This involves the development of

computational models of (biological) neural networks at various spatial scales and levels of complexity, which will be integrated into whole-brain networks models. The strength of this approach lies in developing equivalent model descriptions at different scales (e.g. spiking neural networks vs. neural masses), with which we will validate the computationally most efficient approaches. The goal of this activity is to develop an in-silico framework that is flexible and adaptable to various research paradigms, and that generates testable hypotheses.

Tasks:

Task T1.1.3.a: Link biophysical and mean-field models to whole-brain models

Task T1.1.3.b: Efficient implementation of subcortical influences

Task T1.1.3.c: Spatial heterogeneity of cortex

Task T1.1.3.d: Modelling complex spatiotemporal dynamics

Objective O1.2.1: Extracting features from large databases

Presenter: Ing. Eduard Bakštein, Ph.D. (Research objective O1.2.1 leader)

Eduard Bakštein *is a researcher, working on application of AI and advanced data science and signal processing methods to diagnosis, clinical state monitoring and outcome prediction in neurology and psychiatry. He is co-author of 16 journal publications and coauthor of 10 conference publications. He co-supervised 3 PhD students and 15+ Bc and MSc theses and taught courses on Artificial intelligence, Biometric identification and Computational neuroscience. He will lead O1.2.1 and T1.2.3b.*

Research activity RA 1.2 focuses on preprocessing and analysis of neuroimaging and electrophysiology data from consortium partners, as well as from large public datasets. The application scenarios include modeling of brain activity for tasks ranging from understanding brain dynamics to predicting clinical status and disease course. I will describe our previous work in development of preprocessing methods for electrophysiological data, fusion of invasive microelectrode electrophysiology and structural imaging data in Parkinson's disease patients, and clinical outcome prediction in Schizophrenia.

Tasks:

Task T1.2.1.a: Database construction and curation

Task T1.2.1.b: Feature extraction

Task T1.2.1.c: Efficient dimension reduction and data representation

Objective O1.2.2: Personalised parameter identification

Presenter: Mgr. Nikola Jajcay, Ph.D. (Junior Research work package 1 leader, objective 1.2.2 leader)

Nikola Jajcay *is a junior scientist at the Center for Advanced Studies of Brain and Consciousness, National Institute of Mental Health, and the Department of Complex Systems at the Institute of Computer Science of the Czech Academy of Sciences. He currently holds an individual fellowship in the Horizon Europe scheme from the European Research Executive Agency in the field of computational psychiatry. His focus spans modelling and analysis of complex systems with a particular interest in brain dynamics in health and disease, and he has apt experience with modelling, data analysis, and machine learning from academia and industry. He will benefit from his experience and expertise in overseeing the whole research work package RWP1 and (co-)leading objectives O1.2.2, O3.2.1, and O3.2.2.*

Dr. Jajcay will summarize his research area, and goals under Objective 1.2.2. In particular, to simplify complex forward models from RA1.1 for better parameter estimation, we will fix certain parameters based on biological likelihood and use Bayesian techniques to derive model probabilities. We'll also consider parameter inference in the Fourier domain, especially for resting-state data. Additionally, we'll assess using Dynamic Causal Models (DCMs) for model inversion through Variational Bayes and other methods, to clarify neuroimaging mechanisms. For more complex scenarios, Simulation-based Inference (SBI) will employ deep learning to analyze simulation data. Finally, parameter estimation will be tackled as an optimization issue, utilizing evolutionary algorithms and Gaussian Processes, optimizing for multi-modal neuroimaging data fitting.

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

Tasks:

Task T1.2.2.a: Exploring model reduction schemes

Task T1.2.2.b: Bayesian model inversion (Dynamic Causal Models)

Task T1.2.2.c: Simulation-based inference (SBI) approach

Task T1.2.2.d: Parameter fitting as a general optimization problém

Objective O1.2.3: Neuro multimodal data visualisation and exploration

Presenter: doc. Ing. Daniel Novák, Ph.D. (Research objective O1.2.3 leader)

Daniel Novák *is head of Analysis and Interpretation of Biomedical Data Group working in the area of application of AI in the neurological and psychiatric area. He is co-author of 26 journals (16 publications in Q1) and co-author of 90 conference publications. He directed 5 PhD thesis and more than 100 master and bachelor thesis. He will be responsible for leading research activities in Objective O1.2.3. Concerning application area, Daniel is cofounder of start-ups Blindshell Ltd (2014) focusing on design alternative interface for visually impaired people, MindPax Ltd (2015) developing tele-care system in psychiatry and Adiquit Ltd (2018), therapeutic program for smoking cessation.*

Standard methods of data analysis assume that data are clean, non-missing, following apriori well-known distributions, sampled randomly and that they reside in relatively low-dimensional space. In contrast, experimental neuro-multimodal data often contain missing and outlying values, follow diverse and exotic distributions, are serially correlated due to suboptimality of the sampling, and reside in high-dimensional space, as many features get measured on the studied units of interest. To bridge this gap, there has been a need to develop advanced methods capable of processing and analyzing real-world data. Missing data need to be carefully detected and accounted for (Molenberghs & Kenward, 2007), data need to be transformed (Shachar et al., 2018) and may need to be projected into more convenient lower-dimensional space (McInnes et al., 2018; Kratochvíl et al., 2020). Furthermore, data need to be explored prior entering analytical pipelines to identify potential invalid values and to learn the intrinsic structure of the data, which can be eased with the use of hierarchical clustering

(Fišer et al., 2012) and interactive means of inspection of the so called dendrogram resulting from the hierarchical clustering (Sieger et al., 2017). At the same time, research and development of data preprocessing methods is still outgoing in order to satisfy the specific needs of new experiments. In addition, models describing brain functional connectivity and assessing short/long-term effects of neuro stimulations will be developed. The outcomes of the objective will be applied in further objectives in RWP 2 and 3.

Tasks:

Task T.1.2.3.a Development and application of neuro multimodal data visualisation methods

Task T1.2.3.b Electrophysiology low level processing and visualisation

Task T1.2.3.c Clinical course assessment, visualisation and prediction on different temporal scales

WORK PACKAGE 2 – OBSERVING (DYS)FUNCTIONAL DYNAMICS

Objective O2.1.1: Biophysically detailed models of neural dynamic in early visual processing

Presenter: Mgr. Ján Antolík, Ph.D. (Research objective O2.1.1 leader)

Ján Antolík *is an Assistant Professor at the Faculty of Mathematics and Physics. The objective 2.1.1 lead by Dr. Antolík is a natural extension of his previous research activities and will involve techniques in which he has extensive experience: modeling of multi scale neural data, analysis of neurophysiological recordings and neuroinformatics.*

Objective 2.1.1 focuses on developing detailed biophysical models of neural dynamics in the early visual processing areas V1 and V2. Leveraging previous work by the MFF team, we aim to enhance whole-brain models by integrating a high-density model that can accurately simulate visual stimuli processing. This integration will enable the study of mesoscopic brain dynamics and their effects on global brain networks. The research will include expanding the existing V1 model to encompass deeper cortical layers and extend into V2, thereby allowing for a comprehensive understanding of both spontaneous and visually evoked brain states. Additionally, this project will refine models for cortical implants used in vision restoration,

with the end goal of improving stimulation protocols based on human electrophysiological and perceptual data.

Tasks:

Task T2.1.1.a: Multi-layer model of early visual pathway: from retina to V2

Task T2.1.1.b: Dynamics of cortical visual networks: spontaneous vs. visually evoked state

Task T2.1.1.c: Modelling of cortical neural visual prosthetic implants

Objective O2.1.2: Intracortical view of brain dynamics from simple to complex stimuli

Presenter: Mgr. Jiří Hammer, Ph.D. (Research objective O2.1.2 leader)

Jiří Hammer *is a computational neuroscientist and researcher at the Second Faculty of Medicine, Charles University. In his research, he is focusing on analysis of intracranial EEG (iEEG) data acquired from epilepsy patients, both during rest or different cognitive tasks. His expertise and experience is well fitting to the research objective O2.1.2.*

Our research objectives focus on neural dynamics obtained from intracranial EEG (iEEG) signals. The iEEG offers a unique opportunity to measure the electrophysiological activity directly in the human brain of the epilepsy patients, while they perform different cognitive tasks. In my talk, I will introduce the research objectives, as well as the methodological concepts of our work, which will, hopefully, facilitate the inter-disciplinary cooperation with other research teams within the BRADY project.

Tasks:

Task T2.1.2.a: From simple to natural and ecologically valid stimuli

Task T2.1.2.b: Higher cognitive functions (self-agency)

Task T2.1.2.c: Public library of the battery of cognitive tests and their implementations for epilepsy patients with intracerebral electrodes

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

Objective O2.1.3: Brain dynamics of normal and pathological visual perception

Presenter: prof. Ing. Jan Kremláček, Ph.D. (Research objective O2.1.3 leader)

Jan Kremláček *is the Head of the Institute of Medical Biophysics, Faculty of Medicine, Charles University in Hradec Králové. He has long experience in the field of neurophysiology of vision and has been involved in grant projects dealing with the dynamics of visual information processing. His team will mainly address the topic Brain dynamics of normal and pathological visual perception.*

Neurophysiological methods monitoring or interfering with human visual information processing to address Tasks 2.1.3a-b will be presented: visual evoked potentials, transcranial magnetic stimulation evoked potentials and accompanying morphological (optical coherence tomography), and psychophysical examinations (perimetry, contrast sensitivity, visual acuity, eye movement monitoring). We descriptively model the relationships between stimulus space parameters and physiological and perceptual levels of visual perception. Present ed will be examples of former studies in the domains of perceptual learning, neural adaptation, and variability.

Tasks:

Task T2.1.3.a Predictive coding in visual processing

Task T2.1.3.b Simulation of visual disturbance and its effect on visual processing

Task T2.1.3.c Brain dynamics of normal and pathological visual perception

Objective O2.2.1: Understanding the multiscale nature of epilepsy dynamics

Presenter: prof. MUDr. Přemysl Jiruška, Ph.D. (Research work package 2 leader, research objective O2.2.1 leader)

Přemysl Jiruška *is Head of the Department of Physiology at the Second Faculty of Medicine. He is internationally recognized for his research on the pathophysiology of epilepsy, the organization of epileptic networks, and pathological oscillations. He started his career as a pediatric neurologist interested in epilepsy and epilepsy surgery. After completing his Ph.D. studies, he worked as a postdoctoral research fellow in Prof John Jeffery's group in the United*

Kingdom. In 2008 he was awarded a personal research fellowship from Epilepsy Research UK, a competitive and prestigious award for the most promising epilepsy researchers. Currently, his research group focuses on the mechanisms regulating seizure genesis within abnormally connected epileptic networks and on the network principles governing seizure dynamics in experimental models and humans. He has expertise in both in vitro and in vivo electrophysiological techniques, digital signal processing, and several experimental models of epilepsy. Prof. Jiruska is a Project Manager of the Epilepsy Research Centre Prague, which brings together scientists and clinicians who share an interest in epilepsy research.

Epilepsy is the most common neurological disorder that affects 0,5-1% of the population in developed countries. Approximately every third person with epilepsy doesn't respond to currently available drugs. Our main goal is to provide new insights into the cellular and network mechanisms of drug-refractory epilepsies and identify new and innovative approaches to cure epilepsy. To reach our research objective, we use a multidisciplinary approach and a wide range of experimental techniques to dissect the pathophysiological mechanisms of epilepsy, seizures, and epileptic tissue organization. In the project, we aim to combine computational and experimental approaches to understand the dynamic principles of long-term seizure risk fluctuations and changes in tissue resilience governing these fluctuations and transition to seizure. The study results should identify new therapeutic targets to control seizure emergence and promote brain resilience by neurostimulation or genetic modification.

Tasks:

Task T2.2.1.a Long-term changes in brain stability/resilience in epilepsy

Task T2.2.1.b Multi-scale modelling of complex brain dynamics in epilepsy

Task T2.2.1.c Computationally derived stimulation parameters to stabilize the brain dynamics

Objective O2.2.2: Brain dynamics at different temporal scales in schizophrenia

Presenter: MUDr. Filip Španiel, Ph.D. (Research objective O2.2.2 leader)

Filip Španiel *is the Head of the Center for Applied Research in Early Stage of Serious Mental Illnesses at National Institute of Mental Health, Czech Republic. He has actively participated as PI and co-PI in more than 15 national (AZV, GAČR, TAČR) and international projects (HORIZON). Dr. Spaniel's research and clinical work focus on the identification, characterization and treatment of patients with mood disorders and schizophrenia spanning all disease stages from the prodrome to first and multi-episode illness and up to refractory illness. He focuses primarily on MRI neuroimaging in schizophrenia. He is an author of telemedicine relapse prevention programs in schizophrenia and bipolar disorder.*

Modern technological advances increasingly permit deep phenotyping in large samples of patients, making simultaneous neuroimaging assessments, -omic measurements, and neurocognitive testing available at substantial scales. This research objective is aimed at leveraging one of such initiatives. The goal will be based on NIMH's research flagship – a national-wide multimodal ESO database that contains data from an ongoing large-scale longitudinal study focused on first-episode psychosis patients (FES). At each study visit, participants undergo a complex examination repeated at intervals over subsequent years (Siemens Magnetom 3T Prisma MRI scanner). The longitudinal study comprises three consecutive visits: Baseline visit V1 (on average, three months after the disease onset). The initial sample group is re-examined one year after the baseline (visit 2, V2), and the same is repeated four years after V1 (Visit 3, V3). To date, we dispose of longitudinal data from 500 FES patients and 350 healthy controls (HS), totaling 1500 complex MRI examinations altogether. This represents the world's most extensive samples ever applied to the multimodal, longitudinal survey in the early schizophrenia stage. Thus we have the necessary statistical power and data multidimensionality to enable the development and testing of the data-driven sophisticated re-phenotypization of the historically set schizophrenia concept.

Tasks:

Task T2.2.2.a Dynamic phenotypes and longitudinal trajectories in multimodal MRI during early-stage schizophrenia spectrum

Task T2.2.2.b Astrocytes as generators of ultra-slow brain dynamic oscillations

Task T2.2.2.c A structural equation model of dynamic multimodal variables: confirming the causal theory of astrocytopathy in schizophrenia

WORK PACKAGE 3 – INTERVENING INTO BRAIN DYNAMICS

Objective O3.1.1: Modelling therapeutical (noninvasive) stimulation in Depression and Schizophrenia

Presenter: MUDr. Monika Klírová, Ph.D. (Research objective O 3.1.1 leader)

***Monika Klírová**, internationally recognized neuroscientist in the field of non-invasive brain stimulation as a diagnostic and therapeutic method in neuropsychiatric disorders. Since 2015, head of the Laboratory of Non-invasive Brain Stimulation at the National Institute of Neuroscience, winner of national and international awards for research on non-invasive brain stimulation. She is/was the principal investigator of several grant projects.*

Neuro-computational techniques are capable of interpretable description of brain activity both in health and disease. When appropriate neuroimaging data (EEG, fMRI, TMS-EEG) are available the computational models can be designed and used for prediction of the effects of a stimulation therapy (Gornerova et al., 2023, Klirova et al. 2013, 2021). This objective is to increase the impact and reproducibility of therapeutic and diagnostic interventions in Major Depressive Disorder (MDD) and Schizophrenia (SCH), with particular focus on non-invasive brain stimulation methods, specifically repetitive transcranial magnetic stimulation (rTMS) and deep rTMS in MDD, and transcranial alternating current stimulation (tACS) in SCH. This will be achieved by a combination of advancement of EEG signal artifact correction methods, novel algorithms for characterization of a brain network excitability using concurrent EEG-fMRI measurement and data-driven as well as modelling-based prediction and optimization of brain stimulation paradigms to probe and modulate network excitability aberrations.

Tasks:

Task T3.1.1.a: Develop advanced methods for cleaning MRI-corrupted EEG signals

Task T3.1.1.b: Develop methods to characterize brain excitability at network level

Task T3.1.1.c: Predict and optimize the stimulation effects by integration of EEG-fMRI analysis and neuro-computational techniques

Objective O3.1.2: Modelling therapeutical DBS stimulation in Parkinson's disease

Presenter: Mgr. Tomáš Sieger, Ph.D. (Research objective 3.1.2 leader)

Tomáš Sieger *is a researcher, focused on development of advanced signal processing and data analytic methods, which he applies to different areas of medicine with special focus on neurology. Apart from Charles University in Prague (MSc) and Czech Technical University Prague (Ph.D.), he studied biostatistics at University of Hasselt, Belgium (MSc). He completed research stay at Max Planck institute in Leipzig, Germany and was an invited lecturer at the Summer school in mining and modelling neuroscience data, UC Berkeley, USA. He is coauthor of more than 60 publications and conference proceedings. His applied results include the idendro package for interactive dendrograms. He is leading T1.2.3a.c.*

Psychiatric and/or motor side effects may be aggravated or even directly caused by DBS. However, they are difficult to appreciate during the clinical programming due to their insidious gradual development, again stemming from network-scale alterations of brain function (Appleby et al., 2007). Unfortunately, little is known about their drivers and exact properties and network states related to their development. The presented project proposes a fundamentally different approach to previous largely descriptive studies – the development of a model of the positive therapeutical effect of DBS in Parkinson's disease, capturing the characteristics necessary to deliver the expected motor benefits to the patients. The ultimate goal would be the fitting of this general model to individual preoperative data of DBS candidates with Parkinson's disease to be able to estimate the possible future effects and/or optimize the DBS treatment after the implantation utilising more complex settings than feasible under the currently standard clinical workflows.

Tasks:

Task T3.1.2.a: Evaluating the immediate effect of stimulation

Task T3.1.2.b: Evaluating the long-term effect of DBS treatment using multimodal assessment

Task T3.1.2.c: Optimization of DBS treatment using computational models

Objective O3.2.1: Pharmacological models of schizophrenia

Presenter: MUDr. Tomáš Páleníček, Ph.D. (Research objective 3.2.1 leader)

Tomáš Páleníček *has been employed at National Institute of Mental Health, Czech Republic (NIHM CR, formerly Prague Psychiatric Centre) since 2001. He started his career as a PhD student in preclinical research, studying the neurobiology of schizophrenia in animal models. Shortly after, he received his first grant funding and extended his research interests towards the neurobiology of psychedelic drugs (e.g., LSD, psilocin, mescaline, 2C-B), entactogens (ecstasy / MDMA) and new synthetic drugs. Simultaneous to working on his PhD he passed his training as a clinical psychiatrist with a specialism in clinical electroencephalography (EEG). He defended his thesis in early 2009 and in 2012 he became a licensed psychiatrist. Over the last few years he has contributed significantly to human clinical research. He is involved as a co-investigator of ketamine projects in NIHM CR, where ketamine is used to model psychosis and to treat depression in humans. For the last four years he has been a principal investigator of the first project in the Czech Republic that is intended to study the acute effects of cannabis* in *healthy volunteers. Finally, he is also a principal investigator of the first human clinical trial in the Czech Republic studying the effects of psilocybin in human volunteers. Currently his research interests are oriented to the area of EEG functional connectivity.*

Schizophrenia is a severe mental illness with an unclear etiopathogenesis. The glutamatergic system is primarily involved in the development of schizophrenia, but the role of monoaminergic neuromodulators is also undisputed. Elucidation of the role of these systems is then not only crucial for understanding the origins of schizophrenia but is also an essential prerequisite for the development of novel therapeutic interventions. This translational objective will systematically map the induced brain dynamics changes in a model of schizophrenia induced by glutamate NMDA receptor blockade (ketamine) and 5-HT2A receptor agonism (psilocybin). The brain dynamics effect (EEG) following both

pharmacological manipulations will be studied in both rat and human samples. In addition, the complementary value of the EEG and fMRI approach will be utilized in the human sample. The validity of all observed changes in brain dynamics in these models will then be determined by comparison with schizophrenic patients examined with multimodal EEG and fMRI protocol.

Tasks:

Task T3.2.1.a: Sensitivity analysis and exploration of NMDA and 5-HT2A related parameters

Task T3.2.1.b: Model validation on animal data

Task T3.2.1.c: Model cross-validation and translation to human resting-state EEG

Task T3.2.1.d: NMDA and 5-HT2A receptors profiling in schizophrenia

Objective O3.2.2: Assessing pharmacological manipulations via psilocybin and ketamine for the treatment of depression

Presenter: prof. MUDr. Jiří Horáček, Ph.D., FCMA (Research work package 3 leader, research objective 3.2.2 leader)

Jiří Horáček *is Head of Centre of Advanced studies of Brain and Consciousness and Chairman of Dept. of Psychiatry and Clinical Psychology, 3rd Medical Faculty, Charles University in Prague. He has been actively involved in 40 scientific research projects. His research activities involve the use of brain imaging (PET, fMRI and qEEG) in the fields of schizophrenia, depression and OCD, psychiatric genetics and the animal modelling of mental disorders. He is* both the *editor of several books and the author of more than 100 scientific articles. He has received several national and international psychiatric awards from the International Pharmaco-EEG Society (Werner Hermann Memorial Award), the Czech Neuropsychopharmacological Society and ECNS-ISNIP. In his productive career he has been awarded the Senior Research Fellow of the Bedfordshire CMHR in association with the University of Cambridge. He acted also as the President of the Czech Neuropsychopharmacological Society.*

O3.2.2 is oriented toward the assessment of changes in brain dynamics after pharmacological manipulations involving two key mechanisms of neuronal function integration, i.e., neurotransmission and neuromodulation. The effect of altering neurotransmission will be

evaluated on a dataset of human subjects who have undergone EEG and fMRI scans following the administration of the NMDA receptor antagonist ketamine. To assess the effect of neuromodulation, we will use a unique human dataset of EEG and fMRI subjects examined after administration of the serotonin (5-HT2A) agonist psilocybin. RA3.2 thus provides an opportunity for cross-validation of the project's research activities, which include modeling brain dynamics at the level of individual neurons (e.g., *O1.1.2*) and the whole brain (*O1.1.3*) and both fast (EEG) and slow (fMRI) time scales of brain dynamics. In addition, both datasets used (ketamine and psilocybin) are complemented by animal EEG data, allowing a translational approach to analyses in two species.

The application potential of the project is then because both pharmaceuticals (ketamine and psilocybin) are now considered rapid-onset antidepressants and, as such, are being intensively studied. Thus, elucidating the changes in brain dynamics following their administration will contribute to understanding this unique clinical effect and allow the findings to be applied to other treatment modalities. It can be assumed that inducing identical changes using, for example, neurostimulation methods (rTMS, tDCS, and others) could be clinically effective and should be tested in future RCTs.

Tasks:

Task T3.2.2.a: Model validation on animal data

Task T3.2.2.b: Model cross-validation and translation to human resting-state EEG

Task T3.2.2.c: Exploring connectivity changes before and after pharmacological intervention using Dynamic Causal Models for fMRI data

Objective O3.2.3: Interventions into arousal dynamics

Presenter: MUDr. Martin Brunovský, Ph.D. (Research objective 3.2.3 leader)

Martin Brunovský *is an expert in the field of neurophysiology and QEEG (>60 publications), indispensable for the successful implementation of the project. He is the head of the clinical research program in the NIMH, a board-certified neurologist and neurophysiologist with more than 20 years of experience in research involving the application of neuroimaging techniques, especially quantitative electroencephalography (QEEG). His particular expertise lies in finding,*

evaluating and comparing the ability of individual QEEG parameters to predict response to treatment with pharmacological and non-pharmacological interventions in severe mental disorders. As a principal investigator, he has been awarded several national grant projects (AZV, GAČR) as well as an international LA CR-Austria grant. He collaborates with top scientists in the field of QEEG in psychiatry /Dr. Sebastian Olbrich (University of Zurich), Dr. Martijn Arns (Brainclinics & Maastricht University)/ and is also vice-president of the International Pharmaco-EEG Society (IPEG).

Sleep-wake dysregulation is a common feature of many mental disorders, including depression and insomnia. Patients with both depression and insomnia often experience sleep difficulties as well as daytime fatigue. The common denominator of their sleep and wake disorders is altered arousal, i.e. hyperarousal. A conceptual framework has been proposed that connects behavioural core dysfunction in depression, such as sleep disturbances and withdrawal from arousing environments, to an increased cortical tonic arousal (Hegerl et al., 2012). As a result, the disorder's symptoms are seen as a counter-regulatory response to the increased CNS arousal. Hyperarousal is a 24-h feature and as such it can be evaluated at various vigilance states such as wake and different sleep stages. In line with the theory by Hegerl et al. (2012) resting-state EEG features in MDD patients indeed indicated higher levels of CNS arousal compared to healthy controls and it was found that resting state arousal at baseline can predict treatment response (Ip et al., 2021). However it is not clear whether and how different drugs and interventions contribute to arousal alteration and whether arousal decrease is a general marker of clinical improvement.

Tasks:

Task T3.2.3.a: Alteration of arousal dynamics by pharmacological and electromagnetic interventions and the role of arousal modulation for depression treatment

Task T3.2.3.b: Alteration of sleep arousal and sleep dynamics by pharmacological and non-pharmacological interventions

Task T3.2.3.c: Investigating the link between arousal, mood and emotion regulation

BRAIN DYNAMICS

Registration number: CZ.02.01.01/00/22_008/0004643

Implementation time: 1. 1. 2024 – 30. 6. 2028

This project is co-funded by the EU.

This event was partialy supported by the Czech Academy of Sciences program Strategy AV21 „Breakthrough Technologies for the Future – Sensing, Digitisation, Artificial Intelligence and Quantum Technologies“

CONTACTS:

Ing. Mgr. Jaroslav Hlinka, Ph.D.: hlinka@cs.cas.cz

Mgr. Michaela Lutišanová: lutisanova@cs.cas.cz

Ing. Michaela Červíčková: cervickova@cs.cas.cz

Mgr. Anna Klímová: klimovaa@cs.cas.cz

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS