Schedule of SPP-2041 Final Review Meeting, January 27-29, 2026

- **Location:** Frankfurt Institute for Advanced Studies, Ruth-Moufang-Str. 1, 60437 Frankfurt am Main (how to get there)
- **DFG Representative:** Christoph Limbach
- **Reviewer for the DFG:** Jakob Heinzle, ETH Zürich
- **Zoom (new!):** https://us02web.zoom.us/j/87634184302?pwd=nJoj6ufTdCATi5HCir7nMpQa6YkdFa.1
- Meeting-ID: 876 3418 4302
- Kenncode: 630586
- **Wifi:** eduroam (preferred), guestGU (otherwise)

Tuesday, January 27, afternoon session: (talks are: 40+5 min, speakers are underlined)

12:00 - 13:00 **Arrival, light lunch**

Session Chair: Jochen Triesch

13:00 - 13:45 Simon Eickhoff, Götz Thomalla and Amir Omidvarnia, Marvin Petersen, Kaustubh Patil (remote): Machine-learning on brain connectomics: Individual prediction of cognitive functioning in health and cerebral small vessel disease

13:45 - 14:30 Sacha van Albada, Timo Dickscheid, Claus C Hilgetag: Cellular, connectional and molecular heterogeneity in a large-scale computational model of the human cerebral cortex

14:30 - 15:00 **Coffee Break**

Session Chair: Simon Rumpel

15:00 - 15:45 Evgeniya Kirilina, Markus Morawski, Siawoosh Mohammadi, Nikolaus Weiskopf: The comprehensive microstructural human connectome (COMIC): from long-range to short-association fibres

15:45 - 16:30 Nicolas Schuck, Mingbo Cai and Ronald Dekker: Mapping dynamic brain activity to spontaneous thoughts during rest

16:30 - 17:15 Philipp Berens, Kevin Briggman, Anna Vlasits, Thomas Euler (remote): Towards a connectomics-based predictive model of the inner retina

17:15 - 19:00 **Poster Session 1 and Snacks**

Wednesday, January 28, morning session: (talks are: 40+5 min, speakers are underlined)

Session Chair: Petros Evgenios Vlachos

09:00 - 09:45 Nataliya Kraynyukova, Nancy Mulaiese, Laura Busse, Tatjana Tchumatchenko: Combining theory and experiments to infer how Recurrent and top-down connectivity in the corticothalamic circuit gives rise to V1 selectivity

09:45 - 10:30 Fred Hamker, Andrea Kühn, Petra Ritter, Jil Meier, Oliver Maith, Johannes Achtzehn: Clinical Connectomics: A network approach to deep brain stimulation

10:30 - 11:00 **Coffee Break**

11:00 - 11:45 Juan Eduardo Rodriguez-Gatica, Jens Schweihoff, Heinz Beck, Martin Schwarz, Ulrich Kubitscheck (remote): The power of expansion: resolving neuronal connections from the meso- to the nanoscale

11:45 - 13:00 **Lunch**

Session Chair: David Edler von der Planitz

13:00 - 13:45 Daniel Baum, Jakob Macke, Marcel Oberlaender and Jan Bölts, Philipp Harth: Predicting the Impact of Connectomes on Cortical Function using Statistical Inference

13:45 - 14:30 Matthias Kaschube, Simon Rumpel, Jochen Triesch and Altug Kamacioglu, Pamela Osuna Vargas, Petros Vlachos: The dynamic connectome: dynamics of learning

14:30 - 15:00 **Coffee Break**

15:00 - 18:00 **Poster Session 2**

19:00 - 22:00 **Dinner at Lahmer Esel** (10 min walk from FIAS, subway stop “Niederursel”

along the lines U3, U8, U9)

Thursday, January 29: (talks are: 40+5 min, speakers are underlined)

Session Chair: Sacha van Albada

09:00 - 09:45 Lucius Fekonja, Thomas Picht, Petra Ritter (remote): The Language Connectome in Brain Tumor Patients

09:45 - 10:30 Gabriele Lohmann, Klaus Scheffler, Markus Siegel, Julius Steiglechner, Vinod Kumar and Antonino Greco: Next Generation Connectomics: Laminar and Spectral Specificity

10:30 - 11:00 **Coffee Break**

11:00 - 11:45 **Discussion & Outlook**

11:45 - 12:30 **Lunch, Farewell**

Poster List

P1: Connectome, transcriptome and task constrained modeling of the entire fly optic lobe

Zinovia Stefanidi, Linda Ulmer, Janne K. Lappalainen, Nathan Klapoetke, Byoungsoo Kim, Isaac Omolayo, Aljoscha Nern, Srinivas C. Turaga, Jakob H. Macke

In the fruit fly, over half of the brain is dedicated to visual processing. Recent connectome datasets now cover the entire optic lobe at synaptic resolution, providing a structural basis for modeling neural computations across the visual system. Connectome-constrained deep mechanistic network (DMN) models, task-optimized for motion detection, have previously captured single-cell tuning properties in the fly visual system, but were limited to convolutional approximations of a subset of the motion pathway. Our goal here is to build connectome-constrained DMN models of the whole optic lobe *in silico*, to generate detailed, cell-by-cell hypotheses of circuit mechanisms throughout the visual system. First, we constructed a connectome graph of the entire optic lobe from the *Nern et al.* connectome. Since the photoreceptors and lamina in this dataset are truncated, we imputed neurons and synaptic connections based on intact components and light microscopy data. We then built a DMN model using this connectome graph, and incorporated conductance-based synapse dynamics to capture nonlinear neural computations. After training the DMN on a motion detection task, it robustly predicted known tuning properties. Notably, it improved predictions, e.g. for OFF-motion direction selectivity in T5 cells, while reducing variability across an ensemble of trained models, in comparison with previous work. Finally, scaling connectome-constrained models to the full optic lobe poses a major challenge due to the vast number of unconstrained parameters. To address this, we leveraged transcriptome data by sharing network parameters based on transcriptomic similarity, enabling the propagation of parameter values even to pathways not effectively constrained by the motion detection task. In addition, we further constrained parameters by integrating neural activity measurements from visual projection neurons (LCs). Our results demonstrate a scalable approach for building detailed large-scale connectome-constrained models with a one-to-one mapping between biological and artificial neurons.

P2: Neuronal degeneracy: an information-energy trade-off?

Philip Sommer, Alexander D. Bird, Zahid Padamsey, Fleur Zeldenrust, Peter Jedlicka, Jochen Triesch

Neuronal biophysical parameters exhibit striking variability across cells and cortical areas, yet neural circuits operate under severe metabolic constraints. Here we show that this apparent diversity reflects a principled trade-off between information transmission and energy consumption. Using computational modeling constrained by experimentally measured neuronal properties, we identify structured manifolds of parameter combinations that transmit information with similarly high energy efficiency, forming degenerate solutions organized by Pareto-optimal trade-offs. Experimental data from visual and somatosensory cortex align with these predicted

Pareto fronts, indicating that neurons do not explore parameter space randomly but operate near optimal energy-information trade-offs that are specific to cortical area and cell type. We further show that information transmission per energy is maximized at low-to-medium firing rates, consistent with sparse activity observed in the mammalian neocortex. Under metabolic stress, such as food restriction, neurons adapt by moving along predictable trajectories in parameter space toward lower-energy configurations while preserving near-optimal coding performance. Together, our results suggest that neuronal diversity emerges from adaptive optimization under competing energetic and informational demands, providing a unifying framework linking metabolism, coding efficiency, and biophysical variability.

P3: Reaching the Tail: Validating MRI Axon Radius Mapping with MRI-Scale Histology
Laurin Mordhorst, Luke J. Edwards, Maria Morozova, Mohammad Ashtarayeh, Tobias Streubel, Björn Fricke, Francisco J. Fritz, Henriette Rusch, Carsten Jäger, Ludger Starke, Thomas Gladytz, Ehsan Tasbihi, Joao S. Periquito, Andreas Pohlmann, Thoralf Niendorf, Nikolaus Weiskopf, Markus Morawski, Siawoosh Mohammadi

Axons act as the brain's long-range cables, and their radius is increasingly recognized as a potential MRI-based biomarker for neurological disorders. We present a quantitative evaluation of MRI-based axon radius measurements using MRI-scale light microscopy of two human corpus callosum samples, comprising 46 million segmented axons. In vivo MRI measurements reproduce the coarse spatial pattern seen in histology and show a significant spatial correlation. Ex vivo MRI, however, shows very limited dynamic range and no significant correlation, likely due to strong signal attenuation and contributions from immobile water. These findings demonstrate that the MRI-visible axon radius is detectable in vivo and highlight its potential as a biomarker, as well as the need for improved modeling in ex vivo conditions.

P4: Predictive Coding Light
Antony W. N'dri, Céline Teulière, Jochen Triesch

Current machine learning systems consume vastly more energy than biological brains. Neuromorphic systems aim to overcome this difference by mimicking the brain's information coding via discrete voltage spikes. However, it remains unclear how both artificial and natural networks of spiking neurons can learn energy-efficient information processing strategies. Here we propose Predictive Coding Light (PCL), a recurrent hierarchical spiking neural network for unsupervised representation learning. In contrast to previous predictive coding approaches, PCL does not transmit prediction errors to higher processing stages. Instead it suppresses the most predictable spikes and transmits a compressed representation of the input. Using only biologically plausible spike-timing based learning rules, PCL reproduces a wealth of findings on information processing in visual cortex and permits strong performance in downstream classification tasks. Overall, PCL offers a new approach to predictive coding and its implementation in natural and artificial spiking neural networks.

P5: Defining Operating Regimes for Calcium/Light-dependent Genetic Labeling

Sergio Roberto Molina Ramirez, Liliia Shainberg, Beryth Emungu, Joyce Imaculate Jayakumar, Lydia Fischer, and Martin K. Schwarz

Calcium- and light-gated transcriptional systems enable selective genetic labeling of neuronal populations active within user-defined time windows by responding only when intracellular Ca^{2+} is elevated during illumination. In Cal-Light–derived designs, blue light uncages a TEV protease cleavage site (TEVcs) within a LOV domain, while Ca^{2+} promotes TEV protease activity (via split-protease reconstitution), enabling proteolytic release of a membrane-tethered tetracycline transactivator (tTA) that drives TRE/tetO-controlled reporter expression. ST-Cal-Light refines this architecture by adding a KA2 soma-targeting peptide to confine signaling to the cell body, thereby reducing dendritic/synaptic contributions and increasing response speed.
scFLARE was developed to mitigate expression- and stoichiometry-dependent variability inherent to multicomponent systems by consolidating light sensing, Ca^{2+} sensing, proteolysis, and transcriptional activation into a single membrane-anchored polypeptide. Its core innovation is a calcium-activated TEV protease (CaTEV), engineered by inserting a CaM/CaM-binding module into TEVp to allosterically couple Ca^{2+} binding to protease activity, paired with a tightly caged (hybrid) LOV-TEVcs module.
Despite their increasing use, comparative performance metrics for both systems remain insufficiently defined. Here, we present a standardized characterization framework that integrates a programmable optogenetic illumination chamber with a high-throughput, population-level analysis pipeline quantifying reporter induction across thousands of cells. Using this platform, we systematically benchmark scFLARE and ST-Cal-Light across stimulation and illumination parameters to delineate their operating regimes and identify conditions that maximize sensitivity and specificity. Together, these results establish a robust pipeline for the quantitative evaluation of calcium- and light-gated optogenetic transcription systems, providing practical guidance for selecting and tuning these tools in neuroscience research.

P6: Axon Terminal-Specific Corticothalamic Feedback Suppression in dLGN Modulates V1 Visual Responses

Nancy Mulaiese1,2,3, Oskar Markkula1,3, Conny Kopp-Scheinpflug1, Nataliya Kraynyukova4, Tatjana Tchumatchenko4,5, Lukas Meyerolbersleben1,3, Anton Sumser1, Steffen Katzner1, Laura Busse1,6

1Division of Neuroscience, Faculty of Biology, LMU Munich, Germany; 2International Max Planck Research School for Biological Intelligence - IMPRS-BI;
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Medical Center, Germany; 5Institute for Physiological Chemistry, University of Mainz Medical Center, Germany; 6Bernstein Centre for Computational
Neuroscience Munich, Germany

P7: Quantifying Changes in the Complexity of Large-Scale Brain Network Activity

Rafael Hein1,2, Ahmed Alramly1, Jorge Alejandro Valdez Soto3,4, Tobias Bauer3,4,5, Theodor Rüber3,4,5,6, Jochen Triesch1,2
1: Frankfurt Institute for Advanced Studies; 2: Goethe University Frankfurt; 3: Dept. of Neuroradiology, Univ. Hospital Bonn; 4: Dept. of Epileptology, Univ. Hospital Bonn; 5: German Center for Neurodegenerative Diseases (DZNE) Bonn, 6: Center for Medical Data Usability and Translation, Bonn

Quantifying the non-linear dynamics of large-scale brain networks is essential for distinguishing between diverse cognitive, pathological and developmental states. We utilized Lempel-Ziv Complexity (LZC) algorithms to analyze rs-fMRI data from hemispherotomy patients and EEG recordings from developing infants. In the hemispherotomy data complexity was locally reduced compared to healthy controls, graph analysis revealed that the isolated Default Mode Network (DMN) uniquely maintained structural connectivity. In the developmental cohort, we observed a significant positive correlation between age and signal complexity, consistent with established changes in the power spectrum density which support complexity analysis as a meaningful method. Validated with further entropy-based metrics, our results confirm that complexity algorithms provide a robust and flexible framework for capturing systematic differences in large-scale brain network activity.

P8: SynapFlow: A Modular Framework Towards Large-Scale Analysis of Dendritic Spines

Pamela Osuna-Vargas1,2, Altug Kamacioglu3, Dominik F. Aschauer3, Petros E. Vlachos1, Sercan Alipek4, Jochen Triesch1,2, Simon Rumpel3, Matthias Kaschube1,2
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Dendritic spines are key structural components of excitatory synapses in the brain. Given the size of dendritic spines provides a proxy for synaptic efficacy, their detection and tracking across time is important for studies of the neural basis of learning and memory. Despite their relevance, large-scale analyses of the structural dynamics of dendritic spines in 3D+time microscopy data remain challenging and labor-intense. Here, we present a modular machine learning-based pipeline designed to automate the detection, time-tracking, and feature extraction of dendritic spines in volumes chronically recorded with two-photon microscopy. Our approach tackles the challenges posed by biological data by combining a transformer-based detection module, a depth-tracking component that integrates spatial features, a time-tracking module to associate

3D spines across time by leveraging spatial consistency, and a feature extraction unit that quantifies biologically relevant spine properties. We validate our method on open-source labeled spine data, and on two complementary annotated datasets that we publish alongside this work: one for detection and depth-tracking, and one for time-tracking, which, to the best of our knowledge, is the first data of this kind. To encourage future research, we release our data, code, and pre-trained weights at https://github.com/pamelaosuna/SynapFlow, establishing a baseline for scalable, end-to-end analysis of dendritic spine dynamics.

P9: Disrupting E/I balance triggers rapid and reversible compensatory synaptic restructuring in vivo

Altug Kamacioglu1, Pamela Osuna-Vargas2,3, Petros E. Vlachos2, Dominik F. Aschauer1, Jochen Triesch2,3, Matthias Kaschube2,3, Simon Rumpel1

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Cortical networks operate in a regime of balanced excitation (E) and inhibition (I). Shifts from this balance have been linked to pathological disorders. To maintain this equilibrium, several homeostatic mechanisms are recruited. Understanding how these regulatory mechanisms respond to disruptions of E/I balance is key to developing targeted therapeutic interventions. Here, we explore the effects of E/I instabilities on the organisation and morphology of excitatory synaptic connectivity in the cortex and investigate their functional implications on single neuron models.

We pharmacologically disrupt E/I balance in the auditory cortex of GFP-M transgenic mice by increasing inhibitory synaptic transmission using diazepam. We acquire 2-photon live cell imaging data and develop a modular framework that allows us to automatically detect, track and analyse individual dendritic spines (N=15,500). We built a computational model of LIF neurons with excitatory and inhibitory synaptic inputs. Excitatory synapses are subject to spike-timing-dependent plasticity, stochastic restructuring, and synapse-mediated homeostatic regulation. Inhibitory synapses are static.

We observe rapid, multiplicative compensatory growth of dendritic spines in response to diazepam, in contrast to control, which is reversible as the effect of diazepam attenuates. We fit our computational model to the data and replicate the experimental observations. We use our model to study the timescales of different homeostatic mechanisms that allow and explain the observed dynamics and stability of spine size distributions. Our results suggest that cortical neurons utilise prompt regulatory mechanisms to allow swift control of E/I balance while preserving learned associations reflected in synaptic structures.

P10: Imaging collective synaptic dynamics in the mouse auditory cortex during learning

Altug Kamacioglu1, Pamela Osuna Vargas2, Dominik Aschauer1, Matthias Kaschube2, Simon Rumpel1

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There is strong evidence that alterations in the structural and functional properties of synaptic connections during learning underlie the formation of long-term memories. However, how learning-induced plasticity introduces specific changes in the architecture of the neuronal network is still poorly understood. A major limiting factor of current in vivo imaging studies of synaptic dynamics is that typically only a small number of synapses are assessed in a given animal, typically tens to hundreds. Here, we densely bulk-labeled endogenous PSD-95, a major postsynaptic scaffolding protein of excitatory synapses in layers 1-3 of the auditory cortex in mice using AAV-mediated expression of FINGR intrabodies. Applying longitudinal in vivo two-photon microscopy, we re-image the same volumes of neuropil in 12 imaging sessions over an 11-day period containing more than a million synapses in an individual mouse. Using the same imaging schedule, we image synaptic dynamics in mice in control groups during environmentally and behaviorally stable conditions as well as in mice undergoing classical conditioning using auditory cues, a paradigm we have previously shown to induce a transient imbalance in the ongoing formation and elimination of dendritic spines in the auditory cortex. In parallel, we are developing an automated detection and tracking methodology for PSD-95 puncta to quantitatively analyze synaptic changes. With this dataset, we hope to provide an entry point for the study of the collective dynamics of synapses during learning, but also basal conditions.