BARRELS XXXIX 2026

Barcelona, Spain

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Barrels Program
July 4th, 2026

SATURDAY MORNING: 8:00 AM - 12:45 PM

8:00 AM – 9:00 AM **Breakfast and Coffee**

9:00 AM – 9:05 AM **Welcome:** *Randy Bruno,* Oxford University

9:05 AM – 9:35 AM **Invited Talk: "Origins and Relevance of Sensory-Evoked Cortical Output"** *Marcel Oberlaender, Vrije Universiteit Amsterdam*

9:35 AM – 10:05 AM **Invited Talk: "Not too early, not too late: Adaptive tuning of sensory feedback delay for motor control"** *Valerie Ego-Stengel, CNRS / Paris Saclay University*

10:05 AM – 10:30 AM **Stretch Break**

10:30 AM – 11:00 AM **Invited Talk:** **"Thalamocortical pathways to somatosensory areas S1 and S2: single-cell and synaptic-level diversity"** *Francisco Clascá, Universidad Autónoma de Madrid, Spain*

10:30 AM – 11:00 AM **Invited Talk:** **"Functional Connectomics of Secondary Somatosensory Cortex"** *Jerry Chen, Boston University*

11:00 AM – 11:30 AM **Coffee Break**

11:30 AM – 11:45 AM **Short Talk: "Cell-type-specific sustained value representations in the claustrum"** *Ahmad B. Taha, Seong Yeol An, Su-Jeong Kim, Rowhan Daly, Jeremiah Y. Cohen, **Solange P. Brown**. Johns Hopkins University School of Medicine and Allen Institute for Neural Dynamics USA.*

11:45 AM – 12:00 PM **Short Talk: "Human layer 6b contains a neuronal subtype linked to brain state-control in mice"** ***Timothy A. Zolnik***, *Aasha Meenakshisundaram, Marissa Mueller, Julia Onken, Thomas Sauvigny, Ulrich-Wilhelm Thomale, Ulf Schneider, Pawel Fidzinski, Martin Holtkamp, Angela Kaindl, Jörg Geiger, Bettina Brokowski, Thorsten Trimbuch, Christian Rosenmund, Robert NS Sachdev, Zoltán Molnár, Dietmar Schmitz, Britta J. Eickhlt, Matthew E. Larkum. Charité – Universitätsmedizin Berlin, Oxford*

University, United Kingdom, University Med. Ctr. Hamburg-Eppendorf, Germany and Humboldt Univ. of Berlin Germany.

12:00 PM – 12:30 PM	**Invited Talk: "Rapid reorganization of barrel cortex activity during goal-directed reward-based sensorimotor learning"** ***Carl Petersen****, EPFL.*
12:30 PM – 12:45 PM	**Short Talk: "Brain-wide neural dynamics underlying goal-directed single-session learning"** ***Axel Bisi,*** *Myriam Hamon, Robin Dard, Anthony Renard, Sylvain Crochet, Carl Petersen. EPFL, Switzerland.*
12:45 PM – 3:00 PM	**Lunch Break**

SATURDAY AFTERNOON 3:00 PM - 5:00 PM

3:00 PM – 3:30 PM	**Invited Talk: "Shared Algorithms of Tactile Memory and Decision Making Across Rats and Humans"** *Mathew Diamond, SISSA.*
3:30 PM – 4:00 PM	**Invited Talk: ″Cortical circuits for cross-modal generalisation of a goal-directed behaviour″** *Sami El-Boustani, University of Geneva.*
4:00 PM – 4:15 PM	**Stretch Break**
4:15 PM – 4:30 PM	**Short Talk: "A transient, sex-dependent window for recovery of tactile behavior after cortical lesions"** *Rawan Fakhreddine, Margaret Monhan, Jonah Henderson, and* ***Y. Kate Hong****. Carnegie Mellon University, USA.*
4:30 PM – 5:00 PM	**Invited Talk: "Dynamics of learning in many option foraging"** *Laura Grima, HHMI Janelia.*
5:00 PM – 8:00 PM	**DINNER AND POSTER SESSION**

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July 5th, 2026

<u>SUNDAY MORNING: 8:00 AM - 12:30 PM</u>

8:00 AM – 9:00 AM **Breakfast and Coffee**

9:00 AM – 9:30 AM **Invited Talk: "Overlapping functional tuning to non-sensory and sensory signals across different interneuron classes in mouse barrel cortex"** *Miguel Maravall, University of Sussex.*

9:30 AM – 10:00 AM **Invited Talk "Peri-Head Distance Coding in the Mouse Brainstem"** *Fan Wang, Massachusetts Institute of Technology.*

10:00 AM – 10:15 AM **Stretch Break**

10:15 AM – 10:30 AM **Short Talk: "Identifying Neuro-Immune Signatures of Stress Resilience: A Multi-Omics Approach"** ***Ahmed Ibrahim****. The American University in Cairo, Egypt.*

10:30 AM – 10:45 AM **Short Talk: "Differences in Subcellular Geometry of Thalamocortical Contacts on Excitatory vs Inhibitory Cortical Neurons"** *Y Zaman, G Mirzaee, N Egawa, Y Kubota and* ***A Agmon****, West Virginia University School of Medicine, USA and National Institute for Physiological Sciences, Japan.*

10:45 AM – 11:00 AM **Short Talk: "Unique Spatial Organization of Perisynaptic Astrocytic Processes in Layer 1 of the Primary Motor Cortex After Motor Skill Learning"** ***Yoshiyuki Kubota****, Yuri Yanagawa, National Institute for Physiological Sciences, Okazaki and Jichi Medical University, Shimotsuke, Japan.*

11:00 AM – 11:30 AM **Coffee Break**

11:30 PM – 11:45 PM **Short Talk: "Voltage-imaging of mouse dorsal cortex during a water reaching task reveals fast subnetwork and oscillatory dynamics"** *Yunmiao Wang, Soon Ho Kim, Hannah Choi,* ***Dieter Jaeger****. Emory University & Georgia Inst. Technology, USA.*

11:45 PM – 12:00 PM **Short Talk: "Tuft dendrites in frontal motor cortex enable flexible learning"** ***E. Maristany de las Casas,*** *K. Killmann, L. Münster, M. Drüke, C. Ebner, R. Sachdev, D. Jaeger, M. Larkum.*

Humboldt University Berlin, Germany, Emory University, Atlanta, USA.

12:00 PM – 12:15 PM **Short Talk: "Uncertainty and learning leave a lasting trace in sensory cortex"** ***Alison Barth***, Ajit Ray, Matt Mosso, and Xiaoyang Ma. Carnegie Mellon University, USA.

12:15 PM – 12:30 PM **Short Talk: "Excitatory and Inhibitory Signal Flow in a Cortical Column Connectome"** ***Apoorva Vikram Singh***, *Meike Sievers, Alessandro Motta, Martin Schmidt, Yagmur Yener, Sahil Loomba, Kun Song, Johannes Bruett, Moritz Helmstaedter. MPI, Frankfurt am Main, Germany.*

12:30 PM – 12:45 PM **Short Talk: "Neural and behavioral substrates of maternal nursing"** ***Eduard Maier***, *Viktoriya Tsay, Antonella Daresta, Sebastian Einsiedler, Valery Grinevich*; Central Institute for Mental Health, Medical Faculty Mannheim, University of Heidelberg, Germany.

12:45 PM – 3:00 PM **Lunch and Business meeting**

SUNDAY AFTERNOON: 3:00PM - 5:00PM

3:00 PM – 3:30 PM **Invited Talk: "Thalamocortical bursts encode reward contingencies and drive associative learning"** *Alexander Groh, Heidelberg University.*

3:30 PM – 4:00 PM **Invited Talk "A hierarchical cortical circuit for multisensory evidence accumulation and adaptive learning"** *Simon Musall, Forschungszentrum Jülich.*

4:00 PM – 4:15 PM **Stretch Break**

4:15 PM – 4:30 PM **Short Talk: "Behavioural Context Shapes Sensory Responses in Vibrissal Motor Cortex"** ***Florian Freitag***, *Jelte de Vries, Liv Grete-Harder, Matthew E. Larkum and Robert N. S. Sachdev. Humboldt Universität zu Berlin, Germany.*

4:30 PM – 5:00 PM **Invited Talk: "GABAergic control of developmental dynamics and the emergence of behavioral encoding"** *Laura Modol, Hospital del Mar Research Institute.*

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Concluding Remarks

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Invited Talks

Functional Connectomics of Secondary Somatosensory Cortex
Jerry Chen
Boston University

Sensory cortices do not passively relay information but actively transform inputs according to behavioral context. How local circuit organization supports this context-dependent processing remains poorly understood. Here, we investigated the relationship between functional response properties and synaptic connectivity in whisker secondary somatosensory cortex (wS2) during a tactile working memory task. Using two-photon calcium imaging, we characterized the task-evoked activity of large neuronal populations across multiple behavioral epochs. We then performed serial-section electron microscopy (ssEM) of the same imaged cortical volume, enabling direct structure-function mapping of individual neurons. Automated synapse detection and classification revealed distinct subnetworks defined by their local connectivity motifs. These subnetworks exhibited markedly different task-related response profiles. Critically, subnetworks also differed in their excitatory and inhibitory synaptic density and synapse size, suggesting that differences in synaptic drive and gain control may underlie their divergent functional roles. Together, these findings suggest that wS2 is organized into structurally distinct subnetworks whose synaptic properties are tuned to support specific computations during context-dependent sensory processing.

Shared Algorithms of Tactile Memory and Decision Making Across Rats and Humans
Mathew Diamond
Cognitive Neuroscience PhD, International School for Advanced Studies

In tactile psychophysics, there are obvious differences between rats and humans. Perhaps the most striking distinction lies in learning: rats typically require months of shaping and training, whereas humans achieve task competence after little more than half an hour of instruction. Yet once individuals of both species reach stable performance, a set of surprising similarities emerges. I will focus on two tactile psychophysical tasks: (1) judging the intensity of a vibration and (2) judging its duration. I will show that, across these tasks, many of the principles governing the encoding, storage, and retrieval of information are remarkably shared between rats and humans. In particular, I will demonstrate that – with the adjustment of only a small number of parameters – the same computational framework can account for reference memory and working memory in both species. These results suggest that, despite differences in sensory apparatus and learning trajectories, some fundamental components of cognitive architecture underlying perceptual memory and decision making are conserved across species. Funded by HFSP, ERC, and Italian Ministry for Research.

Not too early, not too late: Adaptive tuning of sensory feedback delay for motor control
Valerie Ego-Stengel
NeuroPSI, CNRS & University Paris-Saclay, France

To explore their environment, find food, and perform most actions, animals need ongoing sensory feedback. The brain indeed learns to generate complex motor commands while integrating seamlessly sensory cues, enabling the body to reach an exquisite level of movement precision. Many studies suggest that learning and executing dexterous voluntary motor skills involve the sensorimotor cortex, particularly through plasticity of somatosensory-motor cortical circuits. We ask how somatosensory feedback is integrated into motor commands during novel skill learning using a bidirectional prosthesis. This strategy allows to manipulate the spatial and temporal characteristics with which somatosensory information is provided to the brain. Thus, we developed an ultra-fast sensory and motor brain-machine interface using chronic recordings from whisker-related primary motor cortex (wM1) and 2D patterned optogenetic stimulation of whisker primary somatosensory cortex (wS1) in mice. Mice had to control a virtual cursor by modulating the spiking activity of wM1 neurons, in order to reach a reward location. A photostimulation pattern on wS1 provided feedback about the cursor position, thus allowing the mouse to adapt its motor command online. Our results show that the somatosensory information provided directly to the cortex has to respect both spatial and temporal constraints in order to be integrated efficiently for motor task completion. Funded by CNRS, ANR, and ED Biosigne.

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Cortical circuits for cross-modal generalisation of a goal-directed behaviour
Sami El-Boustani
University of Geneva

Decision-making, a fundamental cognitive process, provides valuable insights into how internal states and representations shape behavior. Mice use internal representations of peri-personal space to rapidly generalize sensorimotor associations across vision and touch. Using multiscale calcium imaging and anatomical tracing, we identified key visuo-tactile associative regions in the dorsal cortex, characterized by aligned spatial maps and supramodal coding at the single-neuron level. Targeted neuronal silencing and optogenetic sensory substitution allowed us to pinpoint a specific cortical area crucial for cross-modal generalization. These insights not only deepen our understanding of the neural basis of decision-making but also reveal fundamental principles of how the brain integrates and generalizes information across different sensory modalities.

Dynamics of learning in many option foraging
Laura Grima
HHMI Janelia

How animals efficiently learn to make foraging decisions and plan sequential actions when faced with multiple simultaneously available sources of sustenance is largely unknown. Progress on this question requires paradigms in which we can record and monitor the evolution of behavior in naive animals introduced to a complex environment with many concurrent options. In this talk, I will discuss a novel paradigm in which naïve mice rapidly learn to forage amongst six options (water sources) of varying quality distributed across a large (~2 m) arena.

Mice (N=24) intelligently adapted their behavior to the environment by matching their choices to the integrated option quality within as little as ten minutes. This efficient learning was consistent with a computational model in which a representation of the 6 option structure of the environment was rapidly acquired and used to select sequential option visits in a near optimal manner. A dynamic global learning rate that balanced rapid updating of option quality with long run estimate stability was critical.

We find that reward-evoked dopamine signals in the nucleus accumbens core (NAcC) uniquely reflect the requisite global learning rate shared across options. In a separate cohort of mice, we provide evidence that hippocampal activity in CA1 is consistent with an abstract representation of option structure and including option-specific transitions. Together, these findings suggest that dopamine-dependent learning and hippocampal representations of environment structure work in concert to support rapid and effective foraging decisions in novel environments.

Thalamocortical bursts encode reward contingencies and drive associative learning
Filippo Heimburg, Nadin Mari Saluti, Lars-Lennart Oettl, Josephine Timm, Katharina Ziegler, Maria Helena Bortolozzo-Gleich, Thomas Kuner & **Alexander Groh**
Heidelberg University

Learning requires adaptive changes in neuronal circuits, but how neurons encode learning content in their activity patterns to construct memories remains poorly understood. Using longitudinal multi-site recordings in freely moving mice performing a sensory discrimination task, we discover the emergence of burst-coding neurons (BCNs) across cortical, thalamic, and extrathalamic regions. BCNs encoded task rules through the presence or absence of bursts, with their proportion increasing as learning progressed. Decoding analyses reveal that BCNs act as the principal carriers of rule information within the thalamocortical system. BCN burst rates scaled with stimulus valence, collapsed when contingencies were degraded, and inverted after repeated rule reversals, demonstrating that bursts dynamically track associative context to instruct memory formation. Indeed, pharmacological and focal genetic suppression of thalamocortical bursting disrupted learning and task performance, establishing neuronal bursts as context-sensitive drivers of associative learning. These findings identify a previously unknown burst-based neural code for stimulus–outcome associations in the thalamocortical system and provide causal evidence linking cellular firing dynamics to reward contingency learning.

Overlapping functional tuning to non-sensory and sensory signals across different interneuron classes in mouse barrel cortex
Chrysovalantis Fekos, Abdoreza Asadpour, **Miguel Maravall**

University of Sussex

As shown by several labs, neurons in the barrel cortex respond to multiple non-sensory behavioural signals, including the animal's decisions to act in a task and the outcomes of such actions, e.g., whether they go rewarded or unrewarded. We wished to understand how such task-dependent tuning is distributed across molecularly defined interneuron classes. We recorded from PV, SST and VIP interneurons in mice performing a whisker sequence discrimination task in which excitatory neurons have already been shown to acquire diverse sensory and non-sensory tuning (Bale et al, Current Biology, 2021), and used a data-driven approach to identifying functional categories. Neurons of different molecular classes overlapped in their tuning rather than acting as separate functional clusters; in particular, PV and SST cells displayed very similar distributions of responses. Funded by the BBSRC (BB/V00817X/1) and University of Sussex (studentship to C. Fekos).

GABAergic control of developmental dynamics and the emergence of behavioral encoding
Laura Modol
Hospital del Mar Research Institute

Early postnatal development is marked by profound changes in cortical activity that drive circuit maturation. We examine how specific inhibitory interneuron subtypes control these transitions in network dynamics and guide the functional development of cortical circuits. Using longitudinal in vivo calcium imaging in mice, we track how neural activity evolves over time. We find that the emergence of behavioral encoding critically depends on these developmental changes. Together, these results identify inhibitory circuits as key drivers linking network maturation to the emergence of behaviorally relevant computations.

A hierarchical cortical circuit for multisensory evidence accumulation and adaptive learning
Simon Musall
Forschungszentrum Juelich, RWTH Aachen, University of Bonn

How do cortical circuits integrate multisensory information to support flexible decision-making? Answering this requires understanding both cortical hierarchy and cell-type-specific computations. We therefore performed functional imaging and optogenetic perturbations in mice performing a visuotactile evidence-accumulation task. Despite superadditive multisensory responses in parietal and frontal cortex, behavioral performance matched an additive combination of unisensory evidence. Visual and tactile evidence was preferentially accumulated in distinct cortical regions and converged into modality-independent choice signals late in the trial in frontal cortex. To further dissect the underlying circuit mechanisms, we separately measured cortex-wide activity of pyramidal-tract (PT) and intratelencephalic (IT) neurons. PT and IT neurons showed pronounced differences in sensory coding, spatial specificity, and choice-related dynamics. Across learning, the two cell types showed opposite changes: PT activity in frontal cortex became less prominent as animals improved, while IT activity became more tightly coupled to behavioral performance. Axonal recordings in subcortical targets confirmed that these divergent dynamics propagate along distinct output pathways. Together, these findings reveal a hierarchical cortical circuit in which modality-specific evidence accumulation and cell-type-specific output channels jointly enable flexible multisensory choices and adaptive learning.

Origins and Relevance of Sensory-Evoked Cortical Output
Marcel Oberlaender
Vrije Universiteit Amsterdam

The cerebral cortex continuously transmits information to subcortical regions. These descending cortical output streams drive interactions between cortex and subcortical regions that are crucial for cognitive processes and for generating behavior. The pyramidal tract neurons (PTs) in layer 5 are the major source of these descending output streams. Along elaborate dendrites, PTs combine multiple input streams that arrive at all cortical layers. Approaches that could dissect how multiple input streams interact across all dendritic domains are presently unavailable. Even if this technical limit was resolved, the enormous computational complexity of the dendrites poses another challenge for inferring causality between inputs that PTs receive *in vivo* and their somatic outputs. Thus, mechanistic origins of cortical output patterns, and hence, their relevance for downstream processing, may only be revealed if the dendritic locations, strengths and activation times of all local and long-range inputs are known, and integration of these input patterns could be studied with respect to the complex active properties of the PTs' dendrites. We tackled these challenges by combining *in vivo* recordings and neuroanatomical reconstructions at synaptic resolution with multi-scale simulations. Our multidisciplinary approaches reveal how PTs in the barrel cortex transform sparse input streams into a dense population code that both robustly and efficiently broadcasts multiple stimulus and non-stimulus related features to different subcortical targets.

Rapid reorganization of barrel cortex activity during goal-directed reward-based sensorimotor learning
Anthony Renard*, Georgios Foustoukos*, Maya Iuga, Pol Bech, Axel Bisi, Robin F. Dard, Sylvain Crochet and **Carl C.H. Petersen**
EPFL

Sensorimotor associations are typically thought to require days of training to consolidate in sensory cortex, yet adaptive behavior can emerge within minutes. Here, we developed a barrel cortex-dependent whisker-based detection task in which mice learned to associate a novel tactile stimulus with reward within a single behavioral session. Longitudinal two-photon calcium imaging of layer 2/3 excitatory neurons revealed that reward-driven learning rapidly reorganised the neuronal representation of the whisker-deflection within a single session. Population decoding tracked this transition trial-by-trial during learning with neuronal trajectories mirroring behaviour. Critically, neurons that gained stimulus responsiveness across training preferentially took part in spontaneous reactivation events during learning, suggesting that online reactivations could act as a potential upstream selection mechanism. These results suggest that reward-based learning evokes rapid sensory cortical reorganisation on a minute timescale which could be mediated by a concurrent reactivation-based mechanism driving plasticity. Funding : Swiss National Science Foundation.

Peri-Head Distance Coding in the Mouse Brainstem
Fan Wang
Massachusetts Institute of Technology

Perceiving the location of nearby objects relative to the body is essential for guiding movement and avoiding danger. Many organisms use touch to estimate object distance, yet how somatosensory circuits extract this information from tactile inputs remains unclear. Here, we investigate how neurons in the mouse whisker brainstem compute peri-head distance. Using in vivo extracellular recordings in the brainstem principal trigeminal nucleus (PrV) in awake mice during naturalistic wall-passing stimulations, we discover two coding schemes that collectively tile peri-head space: "proximity", showing monotonically increasing activity as objects approach the face, and "map", showing peaked tuning at specific distances. The map code enables more precise readout of peri-head distance. Perturbation experiments suggest that long-range inter-subnucleus inhibition is important for the generation of the PrV map code, through subtracting heterogeneous peripheral signals either from different whiskers or within the same whisker. Together, these findings reveal an underappreciated computational role for brainstem circuits, where inhibition acts as a neural comparator to transform multiplexed peripheral inputs into a stable representation of peri-head distance.

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Short Talks

Differences in Subcellular Geometry of Thalamocortical Contacts on Excitatory vs Inhibitory Cortical Neurons
Y. Zaman[1], G. Mirzaee [1], N. Egawa [2], Y. Kubota [2] and **A. Agmon** [1]
1. Dept. of Neuroscience, West Virginia University School of Medicine, Morgantown, WV, USA. 2.Section of Electron Microscopy, National Institute for Physiological Sciences, Okazaki, Japan

Thalamocortical axons relay sensory information to postsynaptic excitatory (spiny) and inhibitory (aspiny) cortical neurons, but the responses in inhibitory interneurons (basket cells) are consistently earlier, faster and stronger. Proposed explanations include differences in receptor properties, convergence ratios and even presynaptic conduction velocities; however differences in subcellular geometry of thalamocortical contacts on these two targets were not explored. Using a correlated LM-EM volume, we generated 3D reconstructions of thalamocortical axons with their postsynaptic layer 4 targets. We found that thalamocortical axons contact basket cells shortly after losing their myelin sheath but contact excitatory neurons further along the unmyelinated branch, delaying the arrival of the sensory signal in the latter. Thalamocortical axons often make multiple contacts with a given basket cell, allowing each incoming action potential to generate a large postsynaptic conductance. Lastly, contacts are almost always found on cell bodies or thick proximal dendrites of basket cells but on thin distal branches of excitatory cells, further attenuating the integrated postsynaptic signal in the latter. Together, these differences explain the earlier, faster and stronger thalamocortical activation of inhibitory cells, consistent with previous electrophysiological findings by us and others.
Supported by NSF OIA grant 2242771 to AA and JSPS grants 23H04689 and 24H02314 to YK.

Uncued rewards prevent learning-associated thalamocortical plasticity via serotonin signaling
Ajit Ray and **Alison Barth**
Department of Biological Sciences, Carnegie Mellon University Pittsburgh PA USA

Causal inference is an important function of intelligent systems. Here we investigated how stimulus-reward contingencies modulate input- and target-specific synaptic plasticity in mice learning a whisker-dependent sensory association task (Sensory Association Training; SAT). When the sensory stimulus was perfectly predictive of a water reward during SAT, mice developed strong anticipatory licking to the predictive sensory input and thalamocortical inputs onto L2/3 pyramidal neurons in primary somatosensory cortex (S1) strengthened. To degrade causal inference, we introduced uncued rewards (all-reward SAT; AR-SAT), a training paradigm that prevented learning and also thalamocortical plasticity. Unpredicted rewards have been shown to increase serotonergic activity, and serotonin depresses excitatory synapses in sensory cortex. We found that S1 depletion of serotonin during AR-SAT was sufficient to restore thalamocortical plasticity. Thus, unpredicted rewards during AR-SAT suppress thalamocortical synaptic strengthening via serotonin signaling. These data suggest that serotonin signaling is a critical pathway by which uncued rewards reduce causal attribution to unreliable sensory cues.

Brain-wide neural dynamics underlying goal-directed single-session learning
Axel Bisi, Myriam Hamon, Robin Dard, Anthony Renard, Sylvain Crochet, Carl Petersen
EPFL, Switzerland

Animals flexibly learn new associations by leveraging prior knowledge and using rewards as teaching signal, a process affected by changes in behavioural strategies and internal states. Understanding how distributed neural circuits reorganize during learning requires measuring population dynamics continuously at the single-trial level, yet most studies compare static snapshots in naive versus expert animals or sample intermittently across days, missing how specific neuronal populations reorganize as learning unfolds. Here, we leveraged brain-wide Neuropixels recordings from ∼100,000 neurons ∼40,000 well-isolated) spanning 60+ brain regions (288 insertions across 80 mice) to investigate how neural activity reorganizes as mice rapidly acquire a novel whisker- reward mapping in a single session. Mice were first pretrained to lick for a reward following an auditory cue. After reaching expert performance, mice were then confronted with a novel whisker-reward contingency, with separate cohorts experiencing either Go or No-Go whisker stimuli, while maintaining auditory performance in interleaved trials. Both cohorts rapidly acquired the new sensorimotor mapping within tens of trials. Learning trajectories were highly individualized, with fast transitions between low- and high-performance, and correlated with ongoing movements and pupil area. Single-unit

analyses revealed a brain-wide encoding of performance states and licking, and sparse encoding of sensory and choice variables. The activity of a distributed but sparse subset of neurons reflected rapid changes in performance and behavioural history. This brain-wide simultaneous recording dataset provides a foundation for dissecting the coordinated activity of distributed circuits during rapid learning.

Cell-type-specific sustained value representations in the claustrum
Ahmad B. Taha[*#], Seong Yeol An[*], Su-Jeong Kim[*], Rowhan Daly[*], Jeremiah Y. Cohen[$], **Solange P. Brown**[*#]
*Johns Hopkins University School of Medicine, #Kavli Neuroscience Discovery Institute, $Allen Institute for Neural Dynamics

Flexible decision-making relies on interactions between frontal cortex and subcortical structures. The claustrum, a subcortical nucleus highly interconnected with frontal cortex, influences cortical activity and has been implicated in cognitive functions. Recording from claustrum neurons as mice performed a reinforcement learning task, we found that the activity of almost half of recorded neurons scaled with reward rate and predicted trial- by-trial adjustments in reaction time and choice switching. Individual neurons sustained this activity over seconds between trials. Our recordings identified two electrophysiologically distinct populations. One was excited during task execution and bidirectionally scaled its activity with reward rate. The other was suppressed during task execution, scaled activity inversely with reward rate and projected to frontal cortex, indicating that claustrocortical outputs produce graded increases in activity with decreasing reward rate. Our results identify the claustrum as a subcortical locus for stable value representations and integrate it into neuronal circuits for value-based decision-making. Funding: Kavli Neuroscience Discovery Institute Distinguished Graduate Student Fellowship Natural Sciences and Engineering Research Council, PGS-D NIMH R56MH138416 NINDS R01NS085121.

Thalamocortical pathways to somatosensory areas S1 and S2: single-cell and synaptic-level diversity
Francisco Clascá
Universidad Autónoma de Madrid, Spain

Thalamocortical projections from the ventral posteromedial (VPM) and posterior (Po) nuclei to the barrel subfield of the primary somatosensory cortex (S1) in rodents have become a leading model for studying thalamus–cortex interactions and for computational modeling. These pathways have been thoroughly characterized. However, VPM and Po neurons also provide substantial input to other subfields of S1 and to the secondary somatosensory area (S2), whose axonal organization and synaptic architecture remain less well understood. In our laboratory, we combined micropopulation and single-cell axonal tracing, in vivo recordings, and volumetric electron microscopy of selectively labeled VP or Po axons and synapses to selectively visualize, quantify, and compare the thalamocortical connections from VPM and Po to S1 and S2. Our data reveal multiple distinct axonal and synaptic phenotypes targeting different S1 subfields and S2. The organization of these pathways supports the view that S1 and S2 process, in parallel, distinct streams of ascending somatosensory information.

Behavioural Context Shapes Sensory Responses in Vibrissal Motor Cortex
Florian Freitag, Jelte de Vries, Liv Grete-Harder, Matthew E. Larkum and Robert N. S. Sachdev
Institute of Biology, Humboldt Universität zu Berlin, Charitéplatz 1 / Virchowweg 6, Berlin

Understanding how motor cortical circuits flexibly transform sensory and contextual information into behavior remains a central challenge. Whether neurons in primary vibrissal motor cortex (M1) multiplex across behaviors or are selectively engaged in context-specific actions is still unclear. To address this question, we trained mice on multiple vibrissal sensorimotor tasks, including a cue-triggered whisking-to-touch task and an air-puff–triggered licking task. Fast-spiking and regular-spiking neurons in layers 2/3 and 5 in vM1 responded robustly within ~15 ms to air-puff stimulation. In contrast, these same neurons were only weakly modulated during goal-directed whisking-to-touch behavior. Unexpected air-puffs evoked responses in fewer neurons than expected stimuli. Trials in which stimulation elicited whisker movements produced smaller neural responses than trials without whisking. Stimulus-evoked activity in M1 was organized along a spectrum of response profiles with neurons exhibiting varying responses dynamics that cut across laminar and physiological distinctions. This organization of responses is consistent with context-dependent recruitment of M1 neurons. Together, these findings indicate that M1 activity is strongly context dependent and more closely associated with the selection of specific behavioral responses than with generalized sensory-motor encoding.

Funding: DFG (257 Neurocure); ERC 670118; 72070/HBP SGA1, 785907/HBP SGA2, 785907/HBP SGA3, 670118/ERC

A transient, sex-dependent window for recovery of tactile behavior after cortical lesions
Rawan Fakhreddine, Margaret Monhan, Jonah Henderson, and **Y. Kate Hong**
Carnegie Mellon University, USA

Chronic lesions are widely used to probe circuit function, but the variables that define the extent and constraints on functional recovery are not clearly defined. We examined how tactile function recovers after ischemic lesions in barrel cortex (wS1) in a whisker-based detection task in mice. Following wS1 lesions, behavioral recovery was strongly dependent on the timing of retraining: mice retrained within a day of lesioning rapidly recovered behavioral performance, while longer periods of rest showed decreased recovery outcomes, consistent with a limited time window of enhanced plasticity following ischemia. Strikingly, the length of this window was sex-dependent: while both males and females recovered when trained within 1 day of lesions, only females recovered after 7-days of rest, and neither group recovered after 14-days of rest. Blocking estrogen signaling abolished the extended recovery observed in the 7-day female group, suggesting that the window of plasticity is regulated by estrogen-sensitive mechanisms. Together, these results suggest that the window of plasticity after ischemic lesions is not fixed, but hormone-regulated and potentially modifiable. Moreover, these findings have important implications for interpreting lesion-based studies and inform future rehabilitation strategies, reflecting differences in circuit plasticity across biological sex.

Identifying Neuro-Immune Signatures of Stress Resilience: A Multi-Omics Approach
Ahmed Ibrahim,
The American University in Cairo

The rising prevalence of stress-related mental health disorders highlights the need to understand individual differences in stress resilience. While most research emphasizes vulnerability, this research examines the neurobiological and immunological foundations of adaptive coping. The goal is to identify neuro-biomarkers that facilitate resilience and support personalized mental health interventions. A cohort of 200 adults was exposed to a controlled psychosocial stressor. A multi-omics approach was used, integrating functional magnetic resonance imaging (fMRI) with comprehensive peripheral blood analysis. fMRI assessed neural connectivity and activity in stress-related regions: the prefrontal cortex, amygdala, and hippocampus. Blood analysis used RNA sequencing to profile gene expression, quantify key protein levels, and identify metabolic signatures. Participants were followed for 6 months for evaluation. Findings showed distinct neuro-immune signatures distinguishing resilient individuals from those who developed transient stress-related symptoms. Resilient participants demonstrated enhanced resting-state functional connectivity between the ventromedial prefrontal cortex and hippocampus, accompanied by a transient, adaptive upregulation of IL-10 anti-inflammatory gene expression and reduced TNF-alpha levels immediately after stress exposure. These integrated neuro-immune patterns significantly predicted faster recovery and sustained positive mental health.

Voltage-imaging of mouse dorsal cortex during a water reaching task reveals fast subnetwork and oscillatory dynamics
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Wide-field voltage imaging in mice allows capturing fast dynamics of cortical cell populations across the entire surface of dorsal cortex during behavior. We expressed a JEDI-1P voltage sensor in excitatory neurons that restricted expression to excitatory cell bodies. We co-injected an AAV9-hsyn-mCherry vector in order to have a data preprocessing pipeline available where hemodynamic and movement artifacts could be regressed out using the mCherry signal. Pan-cortical voltage-imaging focused on layer 2/3 cell bodies was obtained in the adult mice after undergoing training in a cued forelimb water reaching task. Multiple sessions of imaging with 50-150 trials per session were obtained in 7 mice. Using temporal independent component analysis we could reveal specific fast temporal dynamics in several overlapping cortical networks that were aligned to sensory cues, reward delivery, or reaching movements. Networks could also be defined through shared oscillatory dynamics. Prominent oscillations were found at around 8 Hz that were related to a task-disengaged quiescent state, and gamma oscillations at 40-60 Hz there spanned a bilateral cortical network related to reward processing. We also found that imaged activity in selected regions of interest could be used to decode the presented cues, or predict reaching behavior. Overall, a picture emerged of highly integrated cortex-wide sensorimotor task processing with specific temporal dynamics in overlapping subnetworks.

Unique Spatial Organization of Perisynaptic Astrocytic Processes in Layer 1 of the Primary Motor Cortex After Motor Skill Learning

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Astrocytes play a key role in regulating synaptic transmission as part of the tripartite synapse. Each astrocyte typically occupies a distinct, non-overlapping domain. However, the plasticity of these domains—especially during learning-related synaptic remodeling—remains largely unknown. Using two-photon imaging in Thy1-GFP mice trained for 8 days on a forelimb seed-reaching task, we first identified dendritic segments of the apical tuft of a layer 5 pyramidal neuron that exhibited high spine turnover (Sohn et al., Science Advances, 2022). Correlative light and electron microscopy using large-scale volume EM data collected from these mice with automated tape-collecting ultramicrotome and scanning electron microscopy revealed that these active dendritic segments were contacted by perisynaptic astrocytic processes (PAPs) originating from 3–6 distinct astrocytes, which was analyzed quantitatively using our in house developed measurement methods. Notably, these astrocytic processes extended directly and specifically toward each active dendritic segment. Despite the convergence of processes from multiple astrocytes at the level of dendritic segment, individual dendritic spines were typically contacted by PAPs from only a single astrocyte, indicating highly organized astrocyte-synapse interactions. In addition, astrocyte cell bodies in layer 1 were arranged in a tiled pattern beneath the pia mater, forming a sheet-like organization.

Neural and behavioral substrates of maternal nursing

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Infant nursing is a conserved feature across mammals and requires precise coordination between mother and infant to ensure effective attachment and suckling. In humans, successful breastfeeding—often supported by interventions targeting maternal posture and positioning—is associated with substantial health benefits, yet the neural mechanisms underlying such maternal bodily adjustments remain poorly understood. While hardwired subcortical circuits mediate core parental behaviors, fine-tuned postural and sensorimotor coordination during nursing is likely supported by experience-dependent plasticity in cortical circuits. Oxytocin has been implicated in maternal plasticity across multiple brain regions, including the cortex, but its role in shaping cortical mechanisms for precise mother–infant coordination during nursing is unknown. Here, we investigate oxytocinergic modulation of the somatosensory cortex (S1) ventrum/limb representation and its contribution to cortical plasticity and maternal coordinative behaviors during nursing. Using a local oxytocin receptor (OTR) knock-out (KO) in lactating rats, we find that receptive field plasticity in S1 is impaired. OTR-KO in S1 also impaired maternal bodily adjustments, reduced oxytocin neuron bursting, and affected litter weight. Together, our results identify oxytocin-dependent plasticity in somatosensory cortical circuits as a potential mechanism supporting mother–infant coordination for successful nursing. Funding: DFG

Tuft Dendrites in Frontal Motor Cortex Enable Flexible Learning

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Flexible learning relies on integrating sensory and contextual information to adjust behavioral output in different environments. The anterolateral motor cortex (ALM) is a frontal area critical for action selection in rodents, yet the cellular mechanisms enabling behavioral adaptation remain poorly understood. Using anatomical tracing, we found that inputs critical to decision-making converge on the apical tuft dendrites of layer 5b pyramidal neurons in ALM. We therefore investigated the role of these dendrites in a rule-switching paradigm using two-photon calcium imaging combined with optogenetic manipulation. Activation of dendrite-inhibiting NDNF-positive layer 1 interneurons selectively impaired the acquisition of new rules, without affecting previously learned behavior. This inhibition

profoundly suppressed global calcium activity in dendritic shafts but left local calcium transients in spines largely intact, while additionally reducing somatic burst firing. Furthermore, we observed that excitatory synaptic inputs to tuft dendrites exhibited rule-dependent spatial clustering, indicating that the organization of synaptic inputs dynamically restructures according to task demands. Together, our results demonstrate that active dendritic integration in layer 5b pyramidal neurons is a key computational component of flexible learning, providing a cellular substrate for context-dependent behavioral adaptation.

Human layer 6b contains a neuronal subtype linked to brain state-control in mice

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At the bottom of the cortex in mice, a subpopulation layer 6b neurons responsive to the arousal peptide orexin-B was recently found to drive and sustain higher-order thalamocortical loops essential for attention. Here, we examined human orexin sensitive cortical neurons using electrophysiology, molecular labeling, and anatomical reconstructions in cortical slices from surgical resections. Across species, we found a striking overlap in neuronal properties suggesting that the human cortex contains an orexin-gated circuit positioned to influence human cognition. The following funding sources have supported this project: Einstein Stiftung Berlin (EVF-2020-571), the European Union's Horizon 2020 research and innovation programme (under grant agreement no. 101055340/ERC Cortical Coupling), and the German Research Foundation (EXC 257 NeuroCure, project no. 327654276 – SFB 1315).

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Posters

VIP neuron subtypes differentially provide inhibitory input onto excitatory neurons across layers in mouse barrel cortex

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Cortical computations depend on layer- and cell-type–specific microcircuits in which inhibitory interneurons shape excitatory activity with high temporal and spatial precision. VIP interneurons are often described as primarily disinhibitory because they preferentially inhibit other interneurons, yet multiple lines of evidence indicate that VIP cells can also provide direct inhibition to excitatory neurons. Because VIP neurons are heterogeneous, it remains unclear which marker-defined VIP subtypes deliver inhibitory input to excitatory neurons across cortical layers. Here, we used an intersectional Flp/Cre genetic strategy (Ai80; membrane-targeted opsin) and whole-cell voltage-clamp recordings from excitatory neurons across layers in mouse barrel cortex, in order to quantify light-evoked IPSCs following subtype-specific stimulation of three VIP subtypes (VIP-CCK, VIP-CR, and VIP-ChAT). In our current dataset, VIP-CCK stimulation evoked IPSCs broadly in L2 (22/27), L4 (15/16), and L5 (18/18) excitatory neurons. In contrast, VIP-ChAT stimulation evoked IPSCs predominantly in L5 excitatory neurons (5/6), with no detectable responses in L2 (0/23) or L4 (0/4). VIP-CR stimulation evoked IPSCs in L4 (6/6) and L5 (3/3) excitatory neurons but not L2 (0/9). Together, these findings reveal pronounced subtype- and layer-specific inhibitory output from VIP interneurons onto excitatory neurons, supporting distinct circuit roles for VIP-CCK, VIP-CR, and VIP-ChAT subtypes. Supported by DFG

Distinct behavioural states during tactile discrimination in mice revealed by a modular automated open-source maze for sensory-guided foraging

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Rodents exhibit sophisticated context-dependent decision-making and navigation capacities. We developed an experimental, modular maze to study these behaviors, featuring automated, real-time stimulus presentation and reward delivery triggered by mouse tracking. This approach facilitates the study of naturalistic foraging without restricting movement or nutrition, providing robust experimental control and flexible task design. Flexible reconfiguration was achieved by replacing standard walls with reward/stimulus devices, motion-triggered by animal entry into regions of interest (ROIs). Mice quickly habituated and were intrinsically motivated, learning to navigate to arbitrary reward locations. They exhibited shifting behavioral states—engaged, exploratory, and settled/nest-building—often triggered by collecting a reward. Our results demonstrate the complexity of state modulation during naturalistic exploration and highlight the need for fuller characterization of state-dependent sensory processing. We also provide testing approaches to detect neural activity in exploring animals.

The computational basis of aesthetic reward: Auditory Sequence perception in mice and implications for model-based Reinforcement Learning

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Computational theories of aesthetics posit that aesthetic value is a function of both immediate sensory fluency and long-term gains in predictive efficiency. This could account for phenomena like the preference for intermediate predictive complexity, repeated exposure, and the appeal of symmetry. We aimed to investigate the biological generality of this model by exploring how structural and semantic complexity drive intrinsic reward in the mouse. We developed an automated 8-arm maze acting as a state machine. Spatial navigation into an arm triggered one of several

sounds in real time. Each sound was linked to a specific arm in a block-by-block design, implementing a dynamical conditioned place paradigm. We generated synthetic auditory stimuli with varying sensory complexity, quantifying interval consonance/ dissonance and amplitude modulation to vary acoustic roughness, and including semantically meaningful stimuli such as ultrasonic vocalisations (USVs). Consistent with the literature, mice exhibited a general preference for silence over synthetic stimuli, but not over USVs, which drove a significant preference over the silent arm. Across individuals, exploratory drive correlated with the overall motivation to engage with unrewarded sounds. These findings underscore the role of semantics as a driver of intrinsic reward. We are currently further investigating this role by associating abstract grammars with specific environmental contexts.

Distributed context-dependent transformations in thalamocortical sensorimotor circuits
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How sensory motor circuits flexibly transform sensory input into context-appropriate behavior remains incompletely understood. In particular, it is unclear how activation of the primary vibrissal somatosensory cortex (S1bf) is interpreted to drive distinct actions. Mice were trained in two whisker-based tasks: active whisker touch of a sensor within a 2s cue window, and directional licking in response to a passive air puff to the whisker. Orofacial behavior and posture were tracked while neural activity was recorded from S1bf, primary motor cortex (vM1), and posteromedial thalamus (VPM/PoM) using Neuropixels probes. On recording days, in a subset of trials, S1bf was electrically stimulated with a tungsten microprobe. Unexpected intracortical stimulation drove orofacial behavior and was encoded both locally in S1bf and in downstream projection targets including vM1. The same sensory modality recruits distinct activity patterns across thalamocortical circuits depending on context. Thalamic neurons were active across multiple task contexts, consistent with multiplexed representations, whereas cortical neurons displayed structured responses that differentiated active touch, air-puff stimulation, and microstimulation. These results indicate that context-dependent transformations emerge across distributed sensorimotor circuits rather than within a single locus. Ongoing analyses examine whether local activity predicts long-range context-dependent recruitment and behavior.

Layer-specific ECoG biomarkers of columnar input–output shift with cognitive engagement
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How is sensory information transferred and broadcast across cortical areas? We investigated the mechanisms of perceptual readout from primary sensory cortex by combining patterned whisker stimulation, mesoscale µECoG recordings (~columnar resolution), and optogenetic perturbations in mice. In the first series of experiments, we optogenetically suppressed superficial (L2/3) or deep (L5) populations of pyramidal neurons during whisker-evoked responses. L5 inhibition strongly reduced the high-gamma (65–170 Hz) component of early sensory responses, whereas L2/3 inhibition primarily attenuated theta-beta (4–30 Hz) activity. This indicates a frequency-specific segregation of columnar input (low-frequency) and output (high-frequency) processes in ECoG signals. In ongoing work, we relate mesoscale ECoG dynamics to behavioral readout. Mice integrate sequential whisker inputs over a temporal window of ~150 ms, beyond which delayed inputs fail to summate perceptually. In awake mice, ECoG signals show state-dependent shifts from low- to high-frequency activity with increasing cognitive engagement, coupled with enhanced sensory-evoked high gamma. We are investigating whether these state changes reflect transitions from input to output processing modes.

Neuronal dynamics during inital learning vs expert performance of a sensorimotor transformation
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Learning operates across multiple timescales, from rapid initial association to long-term consolidation. To dissect these processes, we developed a rapid learning paradigm where mice pre-trained in an auditory-detection task learned a novel whisker-reward association within their first exposure session, with performance improving over subsequent days. One cohort learned whisker-reward associations while for the other cohort the whisker stimulus was not associated to reward. We recorded neuronal activity using up to five simultaneous Neuropixels probes targeting motor cortex, somatosensory areas, prefrontal cortex, striatum, thalamus, and superior colliculus in over 80 mice during initial learning and in over 30 expert mice. To map sensory representations, passive whisker and auditory stimuli were presented at the beginning and end of each recording session. Comparing expert to initial sessions revealed consolidation of the learning of the new association. Expert rewarded mice demonstrated elevated whisker-evoked neuronal responses in the passive trials at the start of the expert session across primary whisker somatosensory cortex, caudate putamen, and superior colliculus, suggesting consolidation of initial representations. In contrast, expert non-rewarded mice overall showed lower neuronal responses to the whisker stimulus. Ongoing analyses investigate how population dynamics and inter-area functional connectivity evolve from rapid learning to consolidated expertise.

Pathway-specific ultrastructure comparison of thalamocortical synapses in mouse somatosensory and motor cortical areas

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The synaptic circuits established by thalamocortical axons from the ventral posteromedial (VPM) and posterior (Po) nuclei in the primary somatosensory cortex (S1) have become a paradigm for modelling interactions between the thalamus and cerebral cortex. Beyond S1, VPM and Po neurons also innervate the second somatosensory cortex (S2), while Po and the ventral lateral nucleus (VL) jointly innervate the motor cortex. Despite their relevance, the synaptic organization of these projections remains incompletely characterized. To address this gap, we combined anterograde axon labeling with serial section transmission electron microscopy (ssTEM) and focused ion beam-s (FIB-SEM) in adult male mice. This approach allowed us to measure and compare functionally relevant ultrastructural parameters of synaptic boutons (SBs), including bouton and mitochondrial volume, vesicle pool size, and the distribution and area of the postsynaptic density (PSD). Our results show that SBs in caudal VPM and rostral Po axons in S2 exhibit similar ultrastructural features. Similarly, Po and VL synaptic boutons in the motor cortex are comparable in volume size. Furthermore, comparison of S2 SBs with previously published data on S1 SBs reveals a striking resemblance in thalamocortical synaptic organization across both areas findings, supporting the view that S1 and S2 operate in parallel. Funding: This work was supported by Spain's MICINN-AEI grants (PCI2019-111900-2 and PID2020-115780GB-IO

Effect of social isolation and sensory stimulation on locomotor behavior and exploratory patterns in mice

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The primary somatosensory cortex exhibits experience-dependent plasticity. Healthy behaviors require coordinated large-scale network activity across sensory, prefrontal, motor, and hippocampal regions; dysregulation triggers pathologies like schizophrenia and dementia. This study assessed how opposing contexts—social isolation (SI) versus sensory stimulation (SS)—modulate the barrel cortex-hippocampal-prefrontal axis and locomotor activity. Male C57Bl/6 mice (8 weeks old) underwent 14–16 days of SI (1/cage) or SS (3/cage with bead strands). Locomotor profiles were quantified in open field (OF) assays at midpoint and endpoint. SI mice exhibited elevated locomotion trends, traveling longer distances across peripheral zones, alongside increased scanning behaviors. Conversely, SS mice

manifested peripheral locomotion increase exclusively at endpoint. SI induced more pronounced behavioral alterations than SS, likely due to its stressful nature. Tissue was harvested for future analysis. Funding: University of Costa Rica, grant number FEES-Max Planck 2023 CVI-462-2022

Cortical Representation of Touch: Transfer of Perception from Artificial to Natural Stimulation

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In rodents, artificial stimulation of the primary somatosensory cortex (S1) can replace whisker touch during tactile discrimination tasks. Optogenetics allow to apply precisely defined patterns on the known topography of sensory cortices, mimicking natural spatiotemporal patterns evoked by peripheral stimuli. In this project, we want to characterize how similar optogenetic and peripheral stimulation are, regarding perception, integration into behavior, and underlying neural activity. We trained mice to discriminate the position of an optogenetic bar rotating on the barrel cortex. Similarly, mice could learn to discriminate the position of a physical bar rotating across the whiskers. We further interrogated the ability of mice to transfer such perceptual learning when tactile inputs guide motor learning. We implemented a closed-loop brain-machine interface in which mice learned to control the position of a virtual cursor by modulating the activity of primary motor cortex neurons. Mice were guided by an optogenetic feedback, which was a light bar projected on the barrel cortex. When switching to a peripheral bar feedback, mice managed to control the virtual cursor from the first session. To understand this transfer, we recorded activity in the barrel cortex of anesthetized mice using voltage-sensitive dye imaging. The rotation of a bar across the whiskers evoked a sequence of blobs, whose location moved on the barrels topography in synchrony with the bar.

Probing Cortical Plasticity and Prefrontal Coupling with an Mtl-Dependent Microstimulation Paradigm

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Memory consolidation relies on activity-dependent plasticity, with long-range inputs from medial temporal lobe (MTL) structures playing a key role in associative learning. In the neocortex, these inputs predominantly target layer 1 (L1), yet how they alter local microcircuits to support information storage remains unclear. We employ an MTL-dependent cortical microstimulation paradigm in which mice learn to associate intracortical direct current stimulation of primary somatosensory cortex (S1) with a water reward. Simultaneous Neuropixels recordings provide high-resolution electrophysiological data across cortical layers, allowing us to track dynamic changes before, during, and after learning. Using advanced quantitative analyses, we identify how each layer adapts its response within the behavioral timescale and how these changes reflect associative memory formation. In S1, most neurons showed increased firing and bursting after learning, while only a subset decreased activity. The overall distribution of firing patterns remained consistent, indicating no emergence of distinct populations between naïve and expert animals. Layer-specific adaptations in S1 were linked to coordinated activity within medial and lateral prefrontal cortex (mPFC and lPFC), revealing large-scale interactions between sensory and frontal regions. Together, these findings show how associative learning reshapes cortical dynamics to form and consolidate memory traces. Funded by DFG - SfB1315

Excitatory and Inhibitory Signal Flow in a Cortical Column Connectome

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The signal flow through a cortical column in mouse S1 has been studied for decades. We revisit this question using a dense, saturated volume electron microscopy reconstruction of the neuropil within a cortical column. First, we examined thalamic input to cortex. Consistent with prior work, we found strong input to layer 4 and layer 3 excitatory neurons, along with prominent feedforward inhibitory motifs associated with thalamic input onto layer 4 excitatory neurons. In contrast to canonical light microscopy studies, we found weaker innervation of layer 5 excitatory neurons because thalamocortical axons passing through these layers are often heavily myelinated. Next, we analyzed intralaminar excitatory connectivity and found extensive inhibitory mediation through both proximal- and distal-targeting interneuron channels. This inhibition is timed to precede excitation through early targeting of interneurons along excitatory axonal paths, larger axonal diameters, and selective myelination of inhibitory axons, supporting rapid conduction and timely inhibitory arrival. Finally, we found that feedforward inhibition is strong in the layer 4 to layer

3 pathway but much weaker in the layer 4 to layer 5 pathway, suggesting that layer 4 to layer 5 may provide a shortcut route for cortical processing. Together, these results define a cortical signal flow architecture in which excitation is tightly routed and gated by multiple inhibitory channels.

High-throughput mapping of defined populations across the whole mouse brain using iDISCO+ clearing and automated spot detection
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Understanding the spatial organization of specific neuronal populations requires whole-brain analysis at cellular resolution. We present an integrated experimental and computational pipeline for mapping fluorescently labeled cells across intact mouse brains. We labeled neurons by crossing Cre driver lines (inhibitory subtypes and layer-specific markers) or TRAP mice with a nuclear tdTomato reporter line. Following perfusion, brains were cleared using a modified iDISCO+ protocol optimized for direct immunofluorescence against tdTomato. Samples were imaged using a Zeiss Z1 lightsheet microscope with two channels, a background channel and a signal channel. We developed a computational pipeline for tile alignment and fusion, registration using Brainreg and automated cell detection using Spotiflow. Furthermore, implementation on High-Performance Computing platforms enabled high-throughput analysis of large datasets. Our pipeline successfully maps cellular distributions across the entire mouse brain with high specificity. We are currently testing registration accuracy and assessing layer-specific Cre line fidelity by quantifying labeled cell distributions relative to atlas annotations. We are also exploring whole brain distribution patterns of different inhibitory subtypes (PV, VIP and SST). Finally, application to a dataset of TRAP-labeled activity-dependent cells suggests the involvement of many brain areas in the single session learning of a new sensorimotor association.

High-throughput spatial transcriptomics on 50um-thick vibratome sections to enable integration with two-photon imaging
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In the mammalian brain, distinct neuronal types interact to generate diverse behaviors, yet the relationship between neural ensemble activity and molecular identity remains poorly understood. Spatial transcriptomics can identify fine cell types by localizing hundreds of genes at subcellular resolution, but thin cryostat sections represent a throughput bottleneck. CoppaFISH 3D (Prankerd et al., SfN 2023; Zhou et al., SfN 2024) adapts CoppaFISH for 50 µm-thick vibratome sections from PFA-fixed mouse brains, enabling easier tissue handling and more efficient registration to calcium recordings. Here, we optimize a more sensitive method, Direct Hybridization-based In Situ Sequencing (Lee et al., Scientific Reports 2022), for the same tissue preparation. We target a gene panel designed for cortical cell discrimination into supertypes as defined in the Allen Brain Cell Atlas (Yao et al., Nature 2023), using a six-round combinatorial barcoding scheme. We present a cell-typing workflow employing a quasi-3D heterogeneous graph transformer that transfers labels from a single-cell reference onto spatial data while incorporating local neighborhood information. This pipeline should facilitate registration between spatial transcriptomics data and in vivo two-photon recordings, providing a practical framework for investigating how transcriptomically defined cell types contribute to circuit function and behavior.

Providing artificial tactile feedback at different latencies in a Brain-Machine Interface
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Brain-Machine Interfaces aim to improve patient autonomy. Beyond restoring movement, fine control of prosthetic devices requires restoring tactile sensory feedback. While BMIs with artificial sensory inputs have recently been used in patients, few studies have explored the spatiotemporal constraints of feedback integration. This project examines how temporal latency between motor commands and sensory feedback affects control. We developed an ultrafast bidirectional BMI using chronic recordings from wM1 and 2D patterned optogenetic stimulation of wS1 in mice. We designed a task where single wM1 neuron spikes controlled the rotation of a virtual bar. A photostimulation pattern on wS1 provided feedback about the prosthesis angle during a reaching task. Our incremental algorithm enabled fine control, with well-guided trajectories achieved using a 50-ms feedback latency. Altering this latency to 5 or 500 ms disrupted the animals' ability to move and stabilize the prosthesis, suggesting a critical time window for S1-M1 interaction. We also explored the sensations evoked by optogenetic wS1 stimulation. After the mice mastered the BMI task with cortical stimulation, we replaced it with physical stimulation using a moving bar on the whisker array. This peripheral input targeted body regions corresponding to the previously stimulated cortical sites. The mice retained performance without relearning. Thus, S1 optostimulation appears to evoke perceptions similar to real tactile inputs,

Single-cell properties determine representational geometry of cortical layers
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Recent studies have moved us away from thinking about single cell sensory/motor representations and towards the activity of whole networks. What defines the geometry of network representations? The neocortex is organized into distinct layers, where the cells in each layer have unique physiological properties. We investigated whether these single-cell properties may change the geometry of representations at the population level. We measured how cells transform their current input into action potentials – the frequency-current (fI) curve. We recorded in awake head-fixed mice via whole-cell patch clamp (total N=80 neurons) and found differences among the cortical layers. In particular, we found that pyramidal neurons in Layer 2/3 have a higher threshold current and lower firing rates than those in Layer 5. Using abstractions of the fI curves as activation functions in artificial neural networks, we tested the resulting representational geometry. We trained the networks on classification tasks, modelling discrimination behaviours that are thought to require early sensory areas. Preliminary results suggest that networks with L5-like functions better represent the precise patterns of inputs, whereas networks with L2/3-like functions better encode global stimulus class. Overall, we conclude that the fI curve of single-cell types can impact network representations within cortical layers, which may allow the layers to specialise during sensory discrimination in vivo.

Sensory gating evoked by paw reaching in mice
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The brain is assumed to contain predictive systems that modify sensory flow during movement. Sensory gating (SG) is a candidate mechanism providing movement-related attenuation of sensory responses, yet its behavioral role and neuronal organization remain poorly understood. It is unclear how SG relates to other predictive mechanisms such as state estimation, as formalized in the reafference principle, which suppresses sensory signals precisely at expected sensory consequences. To address this question, we performed neuronal recordings across the depth of primary somatosensory cortex in head-fixed mice trained on a paw reach task. This behavioral paradigm allowed systematic manipulation of the temporal relationship between motor trajectories and tactile feedback by introducing multiple sensory delays. By comparing sensory responses across randomly interleaved delays, we tested whether SG reflects a temporally structured predictive process extending beyond reafference. We found robust sensory gating across a broad range of paw-related sensory delays. The strength of sensory gating varied systematically with delay, indicating structured temporal modulation rather than suppression confined to a single, precisely time-locked sensory consequence. Together, these findings suggest that sensory gating operates over an extended temporal window and reflects a predictive cortical process that is distinct from, and broader in temporal scope than, classical state estimation.

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