Abstracts (organized alphabetically by presenting author for each category of presentation)

1. Invited Talk

Network influence determines the impact of cortical ensembles on stimulus detection

Hayley Bounds, Hillel Adesnik
UC Berkeley Department of Neuroscience

Observation of neural firing patterns can constrain theories for the types of activity patterns that the brain uses to guide behavior. However, directly perturbing these patterns, ideally with great specificity, is required to causally test any particular theory. We combined two-photon imaging and cellular resolution optogenetic photo-stimulation to causally test how neural activity in the mouse visual cortex is read out to detect visual stimuli. Contrary to expectations, targeted activation of highly sensitive neural ensembles did not preferentially modify behavior compared to random ensembles, contradicting a longstanding hypothesis for how neural activity drives stimulus detection. Instead, the main predictor of a targeted neural ensemble's impact on perception was its effect on network activity. This argues that downstream regions summate visual cortex activity without preferentially weighting more informative neurons to make sensory detection decisions. Comparing mouse behavioral performance to decoding models of neural activity implies that mice employ this simple, albeit suboptimal strategy to solve the task. This work challenges conventional notions for how sensory representations mediate perception and demonstrates that specific neural perturbations are critical for determining which features of neural activity drive behavior.

2. Invited Talk

Long-lasting, subtype-specific regulation of SST neurons during sensory learning

Alison L. Barth, Mo Zhu, Matt B. Mosso, Xiaoyang Ma
Carnegie Mellon University

Somatostatin-expressing (SST) inhibitory neurons are a major class of neocortical inhibitory neurons, with at least 14 distinct subtypes exhibiting significant morphological, electrophysiological, and transcriptomic diversity. However, whether this diversity is related to specific roles in cortical computations and plasticity remains unclear. In this study, we identify learning-dependent, subtype-specific plasticity in layer 2/3 SST neurons of the mouse somatosensory cortex. Martinotti-type, SST-Calb2 neurons show a selective decrease in excitatory synaptic input and stimulus-evoked Ca^{++}responses as mice learn a stimulus-reward association. This insight enabled the development of a classifier using basal activity from *in vivo* imaging that accurately predicts learning-associated response plasticity. Our data indicate that SST neuron subtypes play specific and highly-regulated roles in sensory information processing and learning.

3. Invited Talk

Coordinated development of inhibitory and excitatory networks

Natalia De Marco García
Center for Neurogenetics, Brain and Mind Research Institute, Weill Cornell Medicine, New York, NY 10021, USA.

During neonatal development, sensory cortices generate spontaneous activity patterns shaped by both sensory experience and intrinsic influences. How these patterns contribute to the assembly of neuronal circuits is not clearly understood. Using in vivo calcium imaging in young mouse pups, we show that spatially segregated assemblies of interneuron and pyramidal cells are already active at neonatal stages in the somatosensory cortex. In this talk, I will cover recent work from my lab indicating that GABAergic inputs and L-type calcium channels shape network patterns that balance the number of interneurons and pyramidal cells during a critical window of development. In addition, I will discuss how imaging approaches including longitudinal 2-photon and widefield calcium imaging can be used to study the link between genetic predispositions for neurodevelopmental disorders and their impact on early network dynamics, and functional connectivity. Current Funding:2R01MH110553; 1R01MH1250061R01NS116137; Irma Hirschl/Monique Weill-Caulier Career Scientist Award; DREAM (Dup15q Research Endeavors, Activities, and Mechanisms) Fund Award.

4. Invited talk
Heterarchical cortical and subcortical control of limb movements
Joshua Dudman Jason Keller; Junchol Park
Janelia & Princeton
In this talk I will elaborate on two of our recent studies that attempt to identify some important principles for understanding how the distributed premotor areas in cortex and subcortical structures including basal ganglia and brainstem act together to shape voluntary movements of the limbs.

5. Invited talk
From circuits to subspaces: The control of movements by the mouse motor cortex
Michael N. Economo
Boston University
Decades of research in neuroscience, control theory, and robotics has provided a rich theoretical framework for the control of movements. Much less is known about movements are controlled mechanistically at the level of cells and circuits in the mammalian brain. Confronting this knowledge gap requires the development of new approaches for dissecting neural circuits across molecular, structural, and functional domains. My talk will focus on our efforts to develop new technologies for understanding neural circuit function and how we've applied them to reveal new insights into motor system function. Funding: NIH R01NS121409; NIH RF1MH126882; NSF CAREER 2239412.

6. Invited talk
Barrel cortex interactions with posterior parietal cortex
Adrian Roggenbach, Shuting Han, Fritjof Helmchen
Brain Research Institute; University of Zurich
Sandwiched between primary visual cortex and the barrel field of primary somatosensory cortex (S1) lies the posterior parietal cortex (PPC) as a higher-order, multi-sensory cortical area. I will report on our recent two-photon imaging studies in mice investigating sensory representations in PPC subregions (areas RL and A) and their interactions with the barrel cortex. First, in spontaneously behaving mice, we characterized the integration of tactile and visual information about a pole object in front of the snout. We find multi-sensory responses in a subset of PPC neurons, organized along a shared gradient of rostro-caudal location coding. Second, we trained mice in an auditory-cued tactile discrimination task. We find that PPC communicates with the neighboring S1 and that behavioral responses based on auditory-tactile sequences are governed by predictions conveyed from subarea A in PPC to the barrel cortex. Third, we analyzed how S1/PPC responses and interactions adapt during task learning using a multi-area microscope. We identify changes in single-neuron responses as well as in population subspace organization that are associated with learning-related refinement of sensory processing and decision-making. Our results provide insights into the dynamic processing across hierarchical levels of cortical regions and highlight the relevance of the appropriate configuration and coordination of bottom-up and top-down information flows. Funding: Swiss National Science Foundation.

7. Invited Talk
Population codes across cortex: Generalization and specialization in inhibitory microcircuits
Caroline A. Runyan
University of Pittsburgh
The cerebral cortex performs incredibly diverse functions, from sensory processing to decision-making. Local cortical computations across the cortex are performed by a generalized circuit comprised of specific neuron types and local connectivity. It has become increasingly clear though that variations in the structure of this local circuit exist across the cortical processing hierarchy, such as in the pattern of local connectivity and in cell type composition. These variations possibly contribute to the flexibility of cortical circuits to perform such diverse functions across cortical regions. In my lab, we focus on three major aspects of cortical circuits: 1) inhibitory microcircuits and their function, 2) the state-dependence of local processing, and 3) information routing through cortical networks. I will discuss recent findings from my lab that uncover key differences in the function of excitatory and inhibitory microcircuits in auditory and parietal cortex.

8. Invited Talk

Neural circuits of thermal perception

James Poulet
Max Delbrück Center (MDC), Berlin

Whether warm and cool are represented in the nervous system as anatomically and functionally separate 'labelled lines' or rather as a mixed encoding scheme has polarized the debate about thermal encoding since Magnus Blix first identified cool and warm spots on the skin in 1882. Prior work has examined primary sensory afferent neurons and their thermal ion channels, in contrast the encoding of innocuous temperature in the central nervous system has remained unclear. Here I will discuss the remarkable ability of mice to detect innocuous temperatures, as well as the neural circuits of the thermal system.Funding: European Research Council (ERC), German Science Foundation (DFG), National Institutes of Health (NIH), Helmholtz Foundation.

9. Invited Talk

Local and long-range control of gamma-band synchrony in cortical circuits

Julia Veit
University of Freiburg

Gamma band synchronization is thought to facilitate local and long-range neural communication. In the primary visual cortex, visual stimulus properties within a specific location determine local synchronization strength, while matching stimulus properties between distant locations control long-range synchronization. The neural basis for the differential control of local and global gamma band synchronization is unknown. Combining electrophysiology, optogenetics, and computational modeling, we found that VIP interneurons in mouse cortex reduce the gain of gamma power locally without changing its stimulus tuning. Conversely, they suppress long-range synchronization when two regions process non-matched stimuli, tuning gamma coherence globally. Modeling shows that like-to-like connectivity across space and specific VIP/SST inhibition capture these opposing effects. VIP neurons thus differentially impact local and global properties of gamma rhythms depending on visual stimulus statistics.Funding: DFG (VE 938/2-1, VE 938/2-2).

1. Short Talk

Single-branch preference in thalamocortical axodendritic synaptic targeting

A. Agmon and Y. Kubota

Dept. of Neuroscience, West Virginia University, Morgantown, WV and Section of Electron Microscopy, National Institute of Physiological Sciences, Okazaki, Japan

Thalamocortical innervation properties have been studied exhaustively over the last 5 decades, however relatively little is known about the detailed geometry of thalamocortical connectivity at the local, single-axon-to-single-dendrite level. We are applying correlated light-electron microscopy (CLEM) to follow and reconstruct in 3D genetically labeled thalamocortical axons and their postsynaptic target elements in layer 4 of mouse barrel cortex. Unexpectedly, thalamocortical axons entering layer 4 from below are thick (>1 micrometer diameter) and myelinated. They retain their myelin sheath for up to 100 micrometer of their initial trajectory within layer 4, then continue their upward trajectory while emitting several thin lateral branchlets. The unmyelinated main branch and branchlets form large varicosities, each making synaptic contact with 2-4 postsynaptic targets. Most surprisingly, postsynaptic dendritic branches, both spiny and smooth, often make multiple (2-4) contacts with a single axonal branch or branchlets, usually on neighboring varicosities but in some cases up to 20 micrometer apart and even on different branchlets of the same axon. This selectivity at the level of single axonal and dendritic branches implies highly non-random connectivity, likely guided by molecular cues during early development and adult plasticity. Supported by NSF OIA grant 2242771 to AA, JSPS KAKENHI grants 23H04689, 24H02314 to YK.

2.Short Talk

Perceptual decision-making correlates in the primary somatosensory cortex

Alex G. Armstrong & Yurii A. Vlasov

University of Illinois, Urbana-Champaign

The primary somatosensory cortex (S1) is thought to process sensory input and feed it forward to higher order cortices for perceptual decision making. In contrast, we found surprisingly strong modulation of spiking across all S1 populations correlated with accumulation of evidence during decision making. We harnessed the natural whisker-guided navigation of mice using tactile virtual reality combined with Neuropixels recording. Head-fixed mice navigate at elevated speeds through a virtual corridor defined by a pair of motorized walls using only a pair of C2 whiskers. An alternative forced choice (AFC) is introduced by the sudden approach of one wall closer to the snout, that forces the mouse to turn to avoid this virtual obstacle. As opposed to traditional trained AFC tasks (i.e. left and right licks), our task is unrewarded and almost untrained, as it takes only 2-3 habituation sessions to perform at 90% success rate. Fitting of reaction time distribution is accurately predicted using a drift diffusion model (DDM). The spiking variance across S1 population, while initially high dimensional, collapses within just 100ms to a single latent variable during the decision-making process. Simultaneous strong modulation of spiking is correlated with the decision variable (DV) extracted from DDM fitting and can be interpreted as gradual accumulation of sensory evidence driving the decision to turn. We hypothesize that representation of DV in S1 is a top-down regulation feedback signal

3. Short Talk

Cortical circuits for context-dependent sensory processing

P Bech-Vilaseca, R Dard, S Crochet, CCH Petersen, EPFL

In nature, humans and animals are constantly bombarded with sensory information, which needs to be promptly contextualized to elicit the appropriate motor sequences through a process known as sensorimotor transformation. In this project, we investigate how context affects sensorimotor transformations by training water-restricted mice in a context-dependent multisensory detection task. Mice are required to detect two sensory stimuli of different modalities. The first stimulus (whisker deflection) is rewarded upon licking in a context-dependent manner, while the second stimulus (auditory tone) is always rewarded upon licking, irrespective of context. Context is provided by two different auditory background textures that change every block of 20 trials. Upon learning, mice were able to switch their behavior according to the contextual cues and perform on average 10 switches per session. To investigate the cortical regions required for the execution of this task, we are carrying out a random-access optogenetic inactivation screening of the dorsal cortex in VGAT-ChR2 mice, as well as pharmacological inactivation using muscimol. We are also investigating how different subpopulations of excitatory neurons in the cortex are involved in context-dependent sensory processing using widefield calcium imaging in mice expressing GCaMP6f selectively in L2/3 excitatory neurons and in mice expressing jRGECO1a across all cortical layers.

4. Short Talk

Learning enhances behaviorally relevant representations in apical dendrites

Sam E. Benezra, Kripa B. Patel, Citlali Pérez Campos, Elizabeth M.C. Hillman, and Randy M. Bruno
University of Oxford

Learning alters cortical representations and improves perception. Apical tuft dendrites in Layer 1, which are unique in their connectivity and biophysical properties, may be a key site of learning-induced plasticity. We used both two-photon and SCAPE microscopy to longitudinally track tuft-wide calcium spikes in apical dendrites of Layer 5 pyramidal neurons as mice learned a tactile behavior. Mice were trained to discriminate two orthogonal directions of whisker stimulation. Reinforcement learning, but not repeated stimulus exposure, enhanced tuft selectivity for both directions equally, even though only one was associated with reward. Selective tufts emerged from initially unresponsive or low-selectivity populations. Animal movement and choice did not account for changes in stimulus selectivity. Enhanced selectivity persisted even after rewards were removed and animals ceased performing the task. We conclude that learning produces long-lasting realignment of apical dendrite tuft responses to behaviorally relevant dimensions of a task.Funding: The Wellcome Trust, the Academy of Medical Science Professorship program, NIH/NINDS R01 NS069679, and NIH/NINDS R01 NS094659 (RMB); a Kavli Institute for Brain Science Postdoctoral Fellowship (SEB); NIH/NINDS/NIMH/BRAIN U01 NS094296, UF1 NS108213, U19 NS104649, and RF1 MH114276 (EMCH)

5. Short Talk

Representation of Body State in the Barrel Cortex of Freely Moving Mice

Luka Gantar¶, Matthew A. Burgess¶, Neveen Mansour¶, Joaquín Rusco-Portabella, Alžbeta Námešná, David Gill, Isabella Harris, Patrycja Orlowska-Feuer, Aghileh S. Ebrahimi, Riccardo Storchi, Rasmus S. Petersen**
The University of Manchester

Decades of research on anesthetized preparations have provided extensive insights into how neurons in the brain's ascending sensory pathways respond to sensory stimulation. However, the function of sensory cortices in a natural setting, where animals are awake and unrestrained, remains less understood due to technical challenges. To address this, we implanted Neuropixels probes into the barrel cortex of mice and recorded neural activity as the mice explored objects in a dark arena illuminated by infrared light. We reconstructed the object, arena, and tracked mouse body landmarks in 3D, allowing us to extract snout-to-surface distance (SSD) and several body state parameters describing the pose and movements of the mouse. We then trained a supervised learning algorithm (XGBoost) to predict the firing rate of neurons based on SSD. SSD was a statistically significant predictor for 92% of the neurons. However, when the algorithm was trained using both SSD and body state parameters, the mean explained variance increased from 11 to 18% (84% neurons significant). To ensure this result wasn't due to a correlation between body state and whisker touch, we repeated the experiment in mice with an infraorbital nerve transection. In these mice 93% of neurons significantly encoded body state. Overall, our data suggest that barrel cortex is an embodied representation, which not only processes signals from its associated whisker sense organ, but integrates these signals within a body schema.

6. Short Talk

Three-dimensional architecture and linearized mapping of vibrissa follicle afferents

Ben Gerhardt, Michael Brecht, BCCN Humboldt Universitaet, Berlin

Understanding the vibrissa follicle has been challenging, given the intricate afferent innervation, which maps onto an encapsulated and complex internal structure. While serial sections and identified afferent recordings have clarified overall anatomy and response properties, the precise mapping of the afferent population onto the vibrissa follicle remains elusive. Here, we reveal rat C2 vibrissa follicle innervation along with its mechanosensory machinery through synchrotron X-ray phase contrast tomograms. Morphological analysis identified 5% superficial, ~32% unmyelinated and 63% myelinated deep vibrissal nerve axons. Myelinated afferents consisted of each one third Merkel- and club-like-, and one sixth Ruffini-like- and lanceolate-endings. Unmyelinated and thin myelinated axons innervate proximal, whereas thick myelinated axons innervate distal follicle regions, indicating a proximal-to-distal axon conduction velocity gradient along the follicle. Afferents innervate preferentially posterior to the vibrissa, presumably to sample contacts from vibrissa protraction. Further, afferents organize in axon-arms innervating discrete angular territories. The radial axon-arm-arrangement around the vibrissa maps into a linear representation of axon-arm-bands in the nerve. Such follicle linearization presumably instructs downstream linear (tube-like) brainstem barrelettes. Synchrotron imaging provides a synopsis of afferents and mechanotransductory machinery.

7. Short Talk

Cortical and collicular role in multimodal self-initiated sequential behaviors

Myriam Hamon, Tatiana Lupashina, Jeremie Sibille, Matthew E Larkum, Robert NS Sachdev, Jens Kremkow
BCCN Berlin, Humboldt Univ., Neurosci. Res. Ctr. Charité-Universitätsmedizin, Berlin, Germany

Navigation to achieve a goal --to forage and explore the world -- is one of the most basic, and routine acts in the daily lives of people and animals. This action has many complex dimensions: it requires orienting to the environment, while predicting the effect of the movement. The colliculus is thought to control orienting behaviors. Here we trained head-fixed mice in self-initiated behavior that engages multiple sensory motor modalities, as mice plan, decide and execute whisker, eye, and body movements during navigation in a "real-world" maze. Here we examined whether the plan to move can be revealed in the activity of cortical and collicular neurons, whether individual neuron activity is related to a single dimension in behavior or is related to a sequence of related behaviors. Our recordings in the superior colliculus and motor cortex (M2) reveal that in both areas neurons are best related to a single dimension of behavior eye movement, or turning or onset of backward movement. For both colliculus and M2, activity could be related to eye movement in multiple directions. Activating inhibitory neurons in colliculus unilaterally generated contraversive eye, body and whisker movement and triggered activity and suppression in contralateral colliculus. Our work suggests that even though both M2 and colliculus contain a sensory motor map that encompasses the entire spectrum of planning, and movement of the entire body, individual neurons are tuned to single class of movements.

8. Short Talk

Morphological simplification of the motor control of whisking

Chris S. Bresee, Yifu Luo, Jasmine L. Alade'Fa, Megan E. Black, Kevin J. Kleczka, Nicholas E. Bush, Kevin Zhang, Mitra J.Z. Hartmann, Northwestern University Evanston, Illinois, 60208

Animal nervous systems must generate commands for the sequence and timing of numerous muscles – a difficult control problem. The problem is particularly acute for highly mobile sensing structures with many degrees of freedom, such as the eyes, pinnae, hands, forepaws, and whiskers; these low-mass, distal sensors require complex coordination of multiple muscles. The present work demonstrates that the morphology of the rat whisker array simplifies the motor control of "whisking" behavior. During whisking, intrinsic ("sling") muscles control the rapid, rhythmic protractions of whiskers that vary more than 6-fold in length and more than 3-fold in base diameter. In addition, although whisking is a rhythmic, centrally-patterned behavior, the rat can change the position, shape, and size of the whisker array about its head, implying considerable voluntary control. To begin to understand how rats exert precision control over such disparately-sized sensors, we aimed to identify a "baseline protraction," i.e., the protraction that would result if all motor neurons controlling the sling muscles fired at the same rate. Three-dimensional anatomical reconstructions were first used to quantify follicle and sling muscle geometry across the whisker array. Simulations using these reconstructions then demonstrated that a baseline protraction will cause all follicles to rotate through approximately equal angles, regardless of size, and that sensing resolution will increase monotonically during protraction. These results sugest that the rat may use muscle synergies to simplify motor control.

9. Short Talk

The role of primary somatosensory cortex and the superior colliculus in tactile detection

Alice Y. Nam, Jiwook Shin, Morgan Tenney, Baihe Zhang, and Y. Kate Hong, Carnegie Mellon University

For even the simplest form of sensation such as tactile detection, the function of primary somatosensory cortex is still debated. Animals without neocortex, such as fish and birds, can detect stimuli using the tectum, the non-mammalian homolog of the superior colliculus (SC). What does S1 contribute to evolutionarily ancient subcortical structures during tactile detection? Our previous work indicated that acute inactivation barrel cortex (S1) partially impairs tactile detection; yet permanent ablation of S1 only transiently disrupts detection behavior, with recovery to pre-lesion levels within days. In the absence of S1, the SC is thought to mediate tactile detection, but SC's functional contribution in the intact animal remains unclear. One possibility is that SC, which receives direct input from the brainstem and S1, can quickly learn to compensate for the prolonged loss of S1. Alternatively, acute S1 inactivation might cause an imbalance in downstream areas that are important for tactile detection. We examine the roles of S1 and SC in mice performing a whisker-mediated tactile detection task. Using a combination of perceptual decision-making behavior, lesions, optogenetics, and simultaneous recordings from S1 and SC, we provide evidence that behavioral impairments caused by S1 inactivation are primarily due to downstream effects that alter SC's sensory-evoked activity and bias decision-making processes, rather than due to loss of sensory information in S1.

10. Short Talk

JEDI-1P wide-field cortex voltage imaging during a forelimb reaching task reveals task-related network processing

Dieter Jaeger and Yunmiao Wang, Emory University

To understand fast signal processing at the cortical network level, we employed the JEDI-1P voltage sensor with soma-targeted expression in excitatory neurons to perform wide-field imaging during a left/right water reaching task cued by whisker stimuli. Independent component analysis (ICA) revealed a distinct low-dimensional manifold of temporal dynamics related to the task that were exhibited in specific subnetworks. Generally, an ICA with 6 components sufficed to account for 90% of cortical activity variance. Notably functional networks revealed by ICA were remarkably similar between mice. Activity was in most cases bilaterally symmetric, though specific contralateral activity in S1 barrel cortex was seen for unilateral air-puff train stimuli, and a contralateral sensorimotor network was activated aligned with the reaching movement. Narrow band-pass filtered activity showed distinct frequency components in the delta, beta and gamma ranges at specific times in the task. We trained feedforward neural networks to classify either the stimulus or behavioral outcome based on neural activity at different task periods. Stimulus side was decoded most accurately from neural activity immediately after stimulus presentation (92.6±0.9% test accuracy). The neural classifiers were also able to predict the behavioral outcome of the task (reach or no-reach) based on neural activity preceding the response period (84.0±1.1%). Funded by NIH BRAIN Initiative grant NINDS 1 R01 NS111470.

11. Short Talk

Behavioral relevance shapes motor cortical representation of bilateral tactile space

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Many behaviors involve coordination between the left and right sides of the body. The neural computations and brain areas supporting bilateral coordination are unclear. Our recent findings revealed that the primary somatosensory cortex (S1) serves as the first stage for bilateral integration during goal-directed, active touch. We now extend this study to the motor cortex (MC), to understand how the neural representation of bilateral space changes with behavioral context. In one behavioral context, mice discriminated between different categories of bilateral tactile stimuli, requiring them to share tactile information between the hemispheres. In the other context, mice performed a task that required tactile discrimination between two whiskers on one side of the face. Electrophysiology recordings revealed that MC neurons formed enhanced stimulus- and task-specific representations of bilateral space, but only when performing bilateral discrimination. In contrast, MC neurons in mice trained on a unilateral task did not integrate sensory features across hemispheres. Our results suggest that bilateral integration in the MC depends on the behavioral context.

12. Short Talk

Traveling waves support dynamic rerouting of communication subspaces across the motor cortical hierarchy

Hammad F. Khan1,2, Om T. Kolhe1,2, Meisem Habibimatin1,2, Eduard Tanase3, Krishna Jayant1,2

1. Weldon School of Biomedical Engineering; 2. Purdue Institute for Integrative Neuroscience; 3. Elmore School of Electrical and Computer Engineering

Most brain functions involve interactions among multiple, distinct areas or nuclei. For instance, generating reliable volitional movement requires multiple neural populations to work together to produce a desired action. Yet, how populations of neurons separated by millimeters reliably communicate is still unclear. Here, we investigate how moment-to-moment fluctuations of population dynamics in the secondary (M2) motor cortex relate to stable population codes in the primary motor cortex (M1) during a context-dependent volitional motor task. Using state-space analysis, we find that M2-M1 spiking trajectories occur through a communication subspace, which changes as a function of task variables, suggesting that a small fraction of selective neural dimensions interact across motor areas. This was accompanied by the timing in phase directionality of propagating traveling waves recorded across the brain's surface. Changes in wave phase directionality were correlated to the quenching of neural variability, which is tightly coupled with ongoing wave dynamics within a lower dimensional state-space. Using focal cooling and optogenetic inhibition, we show that M2 modulates the structured generation of traveling waves and neural trajectories in M1 for correct motor execution via distinct pathways: cortical and trans thalamic. Thus, traveling waves may support the dynamic rerouting of neural dynamics within communication subspaces to guide optimal motor output. Fund: AFOSRFA9550-22-1-00

13. Short Talk

An cortical network for tongue control in probabilistic motor sequences

Jeong Jun Kim, Daniel H. O'Connor
Johns Hopkins University

The mammal nervous system can generate complex sequences of movements that are planned and executed on the fly based on sensory feedback. Here we developed a probabilistic sequence licking task in head-fixed mice that mimics such motor sequences, requiring lick-by-lick adjustment of tongue targeting based on somatosensory feedback. Optogenetic inhibition of orofacial cortical areas, including the tongue-jaw premotor cortex (anterolateral motor cortex, ALM), tongue-jaw primary motor cortex (M1TJ) and tongue-jaw primary somatosensory cortex (S1TJ), revealed that these areas are crucial for controlling lick kinematics during the task. Silencing orofacial cortical areas affected lick-by-lick adjustments in tongue angle. Perturbations in cortical activity during the current lick cycle disrupted the tongue angle for the subsequent lick and the tongue length for the current lick. Photoinhibition during a single lick cycle showed the interaction between cortical activity and lick cycle timing. Our work demonstrates how a high level cortical network simultaneously plans and executes flexible motor sequences. Funding: NIH Award 1U19NS137920

14. Short Talk

Disruption of Efficient Maternal Behavior Through Cortical PNN Manipulation

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Cortical perineuronal nets (PNNs) are extracellular matrix structures thought to play a role in long-term memory. Previously, we found adult female wild-type mice (WT) learn from the mother to retrieve scattered pups, an ethologically relevant social behavior. The learning is associated with increased PNN expression in the right hemisphere of the primary somatosensory (S1) barrel field cortex (rS1BF). These results suggest increased PNN expression is important for consolidating maternal learning via tactile sensation. To test this hypothesis, we removed PNNs from the WT rS1BF via chondroitinase ABC (ChABC) injection, and assessed their pup retrieval performance for 6 consecutive days. Compared to control-injected WT, ChABC-injected WT exhibited more variable performance on the first 2 days of testing, but improved to control level in later days. As S1 is a large brain region, the early-day variable performance may be explained by the extent of PNN degradation. To address this possibility, we used QUINT to map the entire S1 and determine PNN degradation efficacy along the rostral-caudal axis. We found variable PNN degradation in multiple S1 subregions due to variability of injection sites. We are currently performing multivariate analysis to determine the impact of PNN reduction in individual subregions have on efficient retrieval. Together, these results suggest that PNNs in rS1 are important for acquisition, rather than maintenance, of pup retrieval learning.

15. Short Talk

Nonuniform NMDA Expression in L2/3 dendrites Allows Differential Processing of Bottom-up and Top down Inputs

Viktor J Olah & Matthew JM Rowan
Emory University

Although the dendrites of L2/3 PCs are impressive, they lack the distinct compartments of L5 PCs. Whether local nonlinearities emerge preferentially in specific sub-compartments of L2/3 dendrites remains unclear. Like L5 PCs, L2/3 PCs receive both ‘bottom-up’ and ‘top-down’ inputs, biased to their proximal and distal dendrites, respectively. In principle, nonuniform receptor distributions could serve to differentially modulate the L2/3 responses to these distinct information streams. Our recent work suggests that L2/3 PC dendrites are indeed computationally unique. Here, using region-specific optogenetics, we found that NMDA receptors are readily recruited by activation of ‘bottom-up’ primary thalamic axons. However, this was not true for ‘top-down’ inputs, for example, those originating from higher-order cortical regions. In complementary CRISPR knock-in experiments to label endogenous NMDA receptors, we observed a significant enrichment of NMDA in basal and proximal apical L2/3 spines with respect to distal apical spines. This novel dendritic organization likely

underlied the preferential NMDA recruitment by thalamic input. Interestingly, we observed that NMDA recruitment via thalamic input generated prolonged recurrent network responses. Conversely, activation of top-down inputs did not result in sustained network activity. Together, our findings indicate a unique NMDA distribution in L2/3 dendrites, allowing for distinct responses to bottom-up and top-down information.

16. Short Talk
Understanding the Role of Neural Synchrony in Motor Control Using Holographic Optogenetics
Ian Anton Oldenburg
Rutgers University
Perception, action, and cognition require the coordinated activity of many neurons across brain regions. These neurons fire in complex, time-varying patterns – presumably leading to the rich repertoire of behaviors that animals engage in. However, while we can observe the activity of these neurons, our ability to reproduce these complex patterns is much more limited. This restricts our ability to understand the causal relationship between neural activity and behaviors. Until recently, we lacked the tools necessary to drive activity with the specificity required to test theories of neural population activity. Multiphoton Holographic Optogenetics, specifically expanded spot approaches like 3D-SHOT, offer the ability to control populations of neurons with millisecond timing independently across dozens or hundreds of user-chosen neurons.We address a classic question in motor systems neuroscience: how are movements evoked? Are evoked movements driven by individual specific cells, the total number of active cells, or the pattern of firing of the population? Taking advantage of the incredible temporal precision of 3D-SHOT, we show that neural synchrony plays an outsized role in driving behaviors – far greater than the number or identity of driven cells.

17. Short Talk
Context representation in mouse frontal cortex during a short-term memory task
Parviz Ghaderi, Sylvain Crochet and Carl C.H. Petersen
EPFL, Switzerland
Flexible integration of sensory information in a context-dependent manner is a key cognitive process required to generate appropriate behavior. An intriguing question, then, is how the same sensory stimulus can be interpreted differently according to context in order to generate different behavioral responses. We designed a task in which mice were trained to lick for reward in response to a brief single whisker stimulus if it was preceded by a brief Go-Tone presented one second before the whisker stimulus, but not if it was preceded by a NoGo-Tone. We recorded neuronal activity using multiple Neuropixels probes simultaneously. Prominent persistent activity following the Go-tone presentation was found selectively in wM2 and ALM, even in trials devoid of delay period movements. Consistently, inactivation of wM2 and ALM during the delay between the Go-tone and the whisker stimulus also reduced licking in the reward window. These findings suggest a crucial role of the frontal areas wM2 and ALM in the encoding and maintenance of contextual information in a short-term memory task.Funding: Swiss National Science Foundation.

18. Short Talk
Consequences of individual PV and VIP interneuron firing on the output of postsynaptic SST neurons in mouse barrel cortex
F. Preuß, M. Möck, M. Witte, J. F. Staiger
University Medical Center Goettingen, Department of Neuroanatomy, Goettingen, Germany
In recent years, parvalbumin- (PV) and vasoactive intestinal polypeptide- (VIP) expressing neurons have been described as potential disinhibitors via inhibition of pyramidal cell-targeting somatostatin- (SST) expressing neurons. However, little is known about to what extend individual PV and VIP ells are able to modulate the output of postsynaptic SST cells. Therefore, we performed paired patch clamp recordings in acute slices mouse barrel cortex. Despite their elementary differences in inhibitory postsynaptic potential (IPSP) parameters and short-term synaptic plasticity, PV and VIP cells were able to significantly reduce firing in postsynaptic SST cells. Surprisingly, there was no significant difference in spike loss between the PV to SST and VIP to SST connection. Within both connections there was a large variability within effect strength. Short presynaptic stimulation of PV and VIP cells applied before SST cell firing was able to significantly delay firing in SST cells. Again, effects were not significantly different between both groups. In line, morphological analysis of putative contact sites (PCS) did not reveal differences in PCS location. We propose that individual GABAergic

neurons are indeed able to modulate the firing output of SST neurons without principle cell type specificity. Thereby, these findings challenge the concept of a strict separation of input versus output control by different types of inhibitory cells.Funded by the German research foundation.

19. Short Talk
Real world neuroscience
Saikat Ray,
Weizmann Institute of Science
Animal brains and behaviors have evolved to allow species to meet their daily life challenges. However, our understanding of how the brain deals with such diverse natural conditions stems from constrained laboratory experiments, leaving the fundamental question unexplored: How does the brain actually represent the real world – in natural and multi-animal settings?To answer this, we caught wild fruit-bats, and observed their group behaviour in a naturalistic laboratory-based cave, while conducting wireless neural recordings from their brain. We found that hippocampal neurons invariantly encoded the identities of conspecifics – and represented pertinent social factors, like the sex, dominance hierarchy, and social affiliation of other individuals. These representations were conjoined with spatial representations, indicating that the hippocampal cognitive map evolved to also include social information – forming a socio-spatial cognitive map.We then pioneered neural recordings in the real world – in bats navigating on a remote oceanic island. We found that the head-direction system, that encodes the orientation of an animal in small rooms, can function as a global compass in the real world and maintain a stable heading over large spatial scales and in the face of dynamic celestial cues – providing the first view on spatial-coding during real-world navigation. Together, these studies provide the first insights into the neural encoding of real-world places and societies.

20. Short Talk
Simultaneous Targeting of Layer 2/3 and Layer 5 Cortical Neurons using an Enhancer-AAV Only Approach
Matthew JM Rowan, Viktor J Olah, Jenni Issac, Annie Goettemoeller, Emory University
In the canonical view of cortical signal processing, sensory information arrives via thalamus and is sent through a series of hierarchically organized layers (i.e., thalamus_ L4_ L2/3 _ L5_) before being relayed to subcortical regions. However, a multitude of in vivo and ex vivo experiments challenge the model, including recent work showing that superficial (L2/3) and deep (L5) PCs both receive shared bottom-up information from thalamus, as well as from shared top-down cortical inputs. Despite this apparent redundancy of inputs to L2/3 and L5 PCs, these cells encode information in distinctive patterns during sensory behavior. Thus, development of approaches to simultaneously monitor/modulate the activity or gene expression of L2/3 and L5 PCs would be hugely beneficial in deciphering the roles of these unique PC populations. Here we demonstrate an all-AAV approach to tackle this problem that is suitable for implementation across different mouse lines and potentially across species. This was achieved using a combination of recently discovered and unpublished enhancer-AAVs. This method allows for simultaneous 2-color imaging and optogenetic control of L2/3 and L5 PC activity, allowing unparalleled access to these two cell populations and their (intermingled) dendritic trees simultaneously, without the need for Cre lines, for the first time.

21. Short Talk
Pre-neuronal biomechanical filtering supports tactile encoding
Neeli Tummala[1,2], Gregory Reardon[1,2], Bharat Dandu[2], Yitian Shao[2], Hannes P. Saal[3], Yon Visell[2].
[1]Northwestern University, [2]University of California Santa Barbara, [3]University of Sheffield
As rodents use their whiskers to gather tactile information from the environment, humans often use their hands. Manual touch interactions evoke skin oscillations across the entire upper limb, exciting spatially distributed populations of tactile afferents. These skin oscillations are filtered by the biomechanics of the hand in a frequency- and location-dependent manner before mechanotransduction. Previous work has demonstrated that this pre-neuronal biomechanical filtering influences tactile perception. For example, low-frequency stimulation (<100 Hz) at the fingertip evokes widespread skin oscillations, producing sensation across the whole hand, while high-frequency stimulation (>200 Hz) evokes oscillations and sensation localized to the fingertip. Despite its perceptual relevance, the influence of biomechanical filtering on subsequent neural responses remains poorly understood. By combining optical vibrometry measurements and neural simulation, my work demonstrates that biomechanical filtering diversifies the responses of whole-hand afferent populations, thereby increasing their information encoding capacity. These findings challenge conventional

characterizations of tactile afferents and emphasize the need for a population-level understanding of tactile encoding that integrates both neural and biomechanical factors. I will conclude by discussing the implications of my work for research in the rodent vibrissal system.

22. Short Talk

Dopaminergic Signaling Drives Rapid Increases in BBB Permeability

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Forebrain circuits could benefit in many ways from rapid, local access to the blood-brain barrier (BBB). Vessels contain a unique, high-dimensional aggregation of body state signals, and tuned moments of elevated sampling could provide an ideal snapshot. Metabolic delivery and clearance of waste, timed to the locally active circuits, could also be ideal for brain health. We recently found that behavioral events predict brief, spatially-localized moments of BBB permeability, ‘Plume Events,’ occurring just after Valid Cues and prior to choice, and during and after Reward. Dopaminergic (DA) inputs from the VTA are ideal to drive such BBB dynamics: They index behavioral relevance and learning in real time, and are in close contact with vessels. Endogenous spiking and optogenetic activation of DA VTA Axons next to vessels also drive Plume Events without accompanying vasodilation. These findings in Primary Somatosensory Neocortex (SI) are consistent with our anatomical data, showing DA VTA Axons make repeated, direct vessel appositions. To test the possible role of DA specifically, we infused the D1/D5 partial agonist SKF38,393 across SI through an implanted cannula during simultaneous 2-Photon Imaging of awake mice. Application of 100 uM SKF38,393 activated dLight on DA VTA varicosities contacting vessels. This agonist also drove rapid, large-scale opening of the BBB, extravasation of 70kD RhoB into the parenchyma, effects not found with control infusions (N = 7 mice).

23. Short Talk

Depth-dependent variations in morphoelectric properties reveal the molecular identity of cortical interneurons

Felipe Yáñez, Fernando Messore, Guanxiao Qi, Dirk Feldmeyer, Bert Sakmann, Marcel Oberlaender
Max Planck Institute for Neurobiology of Behavior

Cortical interneurons are characterized by a variety of cellular attributes that enable their specialized roles in regulating information processing in the brain. Molecular identity provides the major subtype specification, with striking differences in morphology and electrophysiology across layers. However, it is unknown whether such diverse morphoelectric properties systematically relate to molecular identity to organize the structure underlying cortical circuits. Here we assess variations in morphoelectric properties across the entire depth of rat barrel and mouse visual cortices. These variations define relationships that reveal the molecular identity of interneurons based on their respective morphoelectric properties. In both species, the overall axonal and dendritic arborizations increase as a function of cortical depth. The spike-frequency also increases with cortical depth, whereas the spike-frequency adaptation remains unaffected by it. Interneurons with high spike-frequency and low spike-frequency adaptation z-scores delineate the parvalbumin class, including small to large basket, chandelier, and translaminar cells. This relationship is conserved across layers. Strong correspondences between morphoelectric properties and molecular identity are also observed in the remaining major interneuron subtypes. Thus, simple organizing principles may largely account for the diversity of interneurons through the adjustment of their morphoelectric properties in cortex. [DFG]

24. Short Talk

Parvalbumin interneurons regulate circuit plasticity in the healthy and injured somatosensory cortex

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It has been hypothesized that plasticity and remapping of cortical circuits underlies recovery after brain injury. Using a mouse model of focal cortical injury, we previously found that sensory-evoked activity was reduced for a prolonged period after injury and that whisker trimming-induced circuit remapping was impaired. These results suggest that plasticity in the peri-lesional cortex may be maladaptive and limit recovery. We

hypothesized that Parvalbumin (PV) inhibitory interneurons might contribute to this maladaptive plasticity and used longitudinal two-photon calcium imaging to record the activity of individual PV cells in the healthy and injured S1. We find that the spatial distribution of sensory-evoked responses in PV cells mirrors that of pyramidal cells. In the healthy cortex, whisker trimming leads to recruitment of PV cells responsive to the spared whisker in deprived cortical barrels and long-lasting shifts in responsivity to the spared whisker in the spared barrel. Chemogenetic inhibition of PV cells during experience-dependent plasticity blocks whisker trimming-induced remapping. In the injured cortex, sensory-evoked responses of PV cells to the principal whisker of the lesioned barrel are selectively impaired after stroke. Together, these results suggest that proper functioning of PV cells is essential for adaptive plasticity in the healthy and injured cortex. Funding: NINDS 1K08NS114165-01A1 and American Academy of Neurology NRTS 2199 to W.Z.

1. Poster

Hand-jaw coordination as mice handle food is organized around intrinsic structure-function relationships

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Rodent jaws evolved structurally to support dual functionality, and rodent hands also function dually during food handling. How are these functions coordinated? We combined electromyography recording and kilohertz kinematic tracking to analyze masseter and hand actions as mice handled food. Masseter activity was organized into two modes synchronized to hand movement modes. In holding/chewing mode, mastication occurred as rhythmic (~5 Hz) masseter activity while the hands held food below the mouth. In oromanual/ingestion mode, bites occurred as lower-amplitude aperiodic masseter events that were precisely timed to follow regrips (by ~200 ms). Thus, jaw and hand movements are flexibly coordinated during food handling: uncoupled in holding/chewing mode, and tightly coordinated in oromanual/ingestion mode as regrip-bite sequences. Key features of this coordination were captured in a simple model of hierarchically orchestrated mode-switching and intra-mode action sequencing. We serendipitously detected an additional masseter-related action, tooth-sharpening, identified as bouts of higher-frequency (~13 Hz) rhythmic masseter activity, which was accompanied by eye displacement, including rhythmic proptosis, attributable to masseter contractions. These results reveal intricate, high-speed coordination of the hands and jaw, and show how natural forms of dexterity can serve as a model for understanding the behavioral neurobiology of multi-body-part coordination in general.

2. Poster

Large-scale neuronal dynamics underlying rapid goal-directed sensorimotor learning

Axel Bisi, Sylvain Crochet, Carl C. H. Petersen
EPFL

Animals adapt their behaviour to novel situations, quickly learning to respond appropriately to external stimuli. It remains unclear where and how new associations are formed in the brain through reward-based learning. Here, we developed a behavioral paradigm that allows us to probe rapid reward-based sensorimotor learning in mice, overcoming the limitations of longitudinal recordings. Thirsty mice are first pre-trained on an auditory detection task where they must lick for a reward after an auditory stimulus. Once experts in this task, these mice are transferred to a whisker-based tactile detection task, where they must also learn to lick for a reward after a novel whisker stimulus. First, we observed that mice can learn the new whisker-reward association in minute timescales and go from novice to high-performance levels in a single session. Second, this learning required only a few trials to emerge and is reward-dependent, since this association was not observed in a group of mice that did not receive a reward when licking after whisker stimulation. During this single-session learning, we performed large-scale simultaneous multi-probe Neuropixels recordings across several brain areas aligned to a reference atlas. We observed widespread task-related activity across areas of the brain beyond those typically considered in whisker detection tasks, including the auditory, somatosensory, motor and prefrontal cortices, dorsal striatum, and thalamus.

3. Poster

Presynaptic inhibition of higher-order thalamocortical and corticocortical inputs to mouse somatosensory cortex

Kelly E Bonekamp, M. Lea Ratz-Mitchem, Grant R Gillie, Mya K Sebek, Lingxi Xiong, Shane R Crandall
Michigan State University

The strength of a given synapse is dictated by its own previous activity. Repetitive activation of synapses as well as various chemical messengers can change the strength of synaptic transmission across time. Presynaptic inhibition is mediated by neurotransmitters with receptors located on presynaptic terminals, one in particular being GABAB receptors. Previous studies show that GABAB-mediated presynaptic modulation occurs at local corticocortical but not core thalamocortical synapses, suggesting potential pathway specificity to this presynaptic modulation. This work aims to investigate the modulation of synaptic strength in higher order thalamocortical and corticocortical pathways through presynaptic inhibition. Here we assess how presynaptic glutamate release in barrel cortex from either primary motor cortex or the posterior medial nucleus of the

thalamus is influenced by a GABAB agonist. Preliminary work shows that applying GABAB agonists suppresses excitatory vM1 responses onto L2/3 pyramidal neurons in vS1. Our research is poised to enhance our understanding of the role of presynaptic inhibition across various types of synapses and its dynamic regulation of synaptic communication. Funding: NIH Grant R01-NS117636, Michigan State Startup

4. Poster

In vivo high-speed voltage imaging of action potentials of cerebellar molecular layer interneurons reveals synchronous spiking to sensory input in awake mice

Spencer Brown, Michelle Land, Shuyuan Yang, Alex McDonald, Francois St-Pierre, Indira Raman
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Multiple lines of evidence suggest that cerebellar neurons encode distinct information in the rate and timing of their action potentials, depending on the behavioral task and cerebellar region studied. With single unit recordings, we previously found that crus I Purkinje cells respond to whisker deflections with 2-4 ms synchronous suppressions of spiking that drive well-timed spiking in cerebellar nuclear cells via disinhibition. Since molecular layer interneurons (MLIs) are the primary source of synaptic inhibition to Purkinje cells, they may underlie the observed suppression of simple spikes. Here, we developed a low magnification, 1-photon microscope for 2-kHz voltage imaging of action potentials in awake mice. Groups of 10-30 MLIs expressing a novel genetically encoded voltage indicator were imaged using targeted illumination. In resting mice, crus I MLIs fired narrow (1-2 ms) action potentials at 30-50 spikes/sec. With the application of air puffs to the whisker pad, MLIs fired synchronous, short-latency spikes across the imaged population. On a large fraction of trials, 4-ms synchrony among MLIs exceeded 50%. The puff also evoked whisking, during which spike rates increased in MLIs, without ms-scale temporal coherence. These results offer direct measurements of single-trial, ms-scale spike synchrony in the cerebellum and provide further evidence that synchronous inhibition encodes the onset of a sensory event while motor input is encoded by a rate code. NIHR35-NS116854.

5. Poster

Sensory responses evoked in motor cortex of mice engaged in a whisking to touch task

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The function of motor cortex in decision making, preparing for movement and in executing movements is an active area of research. Whether individual neurons in cortex are active in one or more behavioral contexts, whether preparation to move affects responses to sensory input are still open questions. In this study, we trained mice to perform a whisking to touchtask, or to simply lick in response to an air puff. The trials were intermixed randomly between whisking to touch, air-puff alone, and with some unexpected air-puffs delivered while mice were actively engaged in whisking to touch. We used behavioral tracking of whiskers, and face, with high-speedcameras and multichannel probe recordings of M1 in head-fixed mice. Analysis of the data revealed strong and widespread encoding of the air-puff stimulus in the motor cortex across all layers whereas active whisking to touch, and the expected touch against the contact sensor, elicited only minimal changes in the firing rate of recorded neurons. Even though the task on each trial was chosen randomly, mice prepared to whisk to touch, by subtly shifting their posture, and preparing their whiskers and jaw. This study highlights the multimodal nature of motor cortical function and shows the potential for online readout of motor planning and sensory responses in motor cortex in situations of high uncertainty.Funding: DFG, NIH, ERC

6. Poster

Dexterous food-sniffing: a unique form of multi-motor coordination for active sensing as mice feed

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Natural, ethologically critical behaviors often involve rapid orchestration of multiple body parts for coordinated complex actions. Food-handling is such a behavior, involving coordination of the hands and oral apparatus. In a recent study (Barrett et al., 2020), we found that mice, while handling food, briefly bring to the nares, appearing to take a single sniff. This “sniff maneuver” raises basic questions, including: during these single sniffs of hand-held food, are hand and head actions coordinated with breathing activity? How precisely, if at all, are “manual” sniff movements timed to coincide with an inspiratory breath? How does this type of “manually dexterous sniffing" compare to exploratory and other forms of sniffing? To address these questions, we developed an approach based on multi-camera high-speed videography with computer vision controlled robotic camera, DeepLabCut-based kinematic tracking, intranasal measurement of breathing, and electromyography of muscles involved in food-handling. Analysis of the multi-modal data sets indicates a rich diversity of intricately coordinated activity across multiple phases of food-handling behavior, showing that mice dexterously sniff the food in their hands using a unique form of high-speed multi-motor-system coordination for active sensing. Key features of this complex behavior exhibit millisecond-scale temporal precision.

7. Poster

Cortical and collicular role in multimodal self-initiated sequential behaviors

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Navigation to achieve a goal --to forage and explore the world -- is one of the most basic, and routine acts in the daily lives of people and animals. This action has many complex dimensions: it requires orienting to the environment, while predicting the effect of the movement. The colliculus is thought to control orienting behaviors. Here we trained head-fixed mice in self-initiated behavior that engages multiple sensory motor modalities, as mice plan, decide and execute whisker, eye, and body movements during navigation in a "real-world" maze. Here we examined whether the plan to move can be revealed in the activity of cortical and collicular neurons, whether individual neuron activity is related to a single dimension in behavior or is related to a sequence of related behaviors. Our recordings in the superior colliculus and motor cortex (M2) reveal that in both areas neurons are best related to a single dimension of behavior eye movement, or turning or onset of backward movement. For both colliculus and M2, activity could be related to eye movement in multiple directions. Activating inhibitory neurons in colliculus unilaterally generated contraversive eye, body and whisker movement and triggered activity and suppression in contralateral colliculus. Our work suggests that even though both M2 and colliculus contain a sensory motor map that encompasses the entire spectrum of planning, and movement of the entire body, individual neurons are tuned to single class of movements.

8. Poster

Traveling waves enables reliable volitional motor movement

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Weldon School of Biomedical Engineering; 2. Purdue Institute for Integrative Neuroscience; 3. Elmore School of Electrical and Computer Engineering

Traveling waves (TWs) are an emergent phenomenon observed in complex dynamical systems throughout nature. These TWs mediate various aspect of animal cognition such as stimuli perception and volitional movement. Yet their potential functional and behavioral relevance remains unknown. In this work, by using custom flexible neuro-electronics in mice performing a motor task, we demonstrate that TWs distinctly reflect task relevant information. Specifically, propagating TW phase-directionality reflected impending movement after an external stimulus while the propensity of precise wave generation relied on the presence of external context. This was reflected by changes in the reliability of local spiking populations of cortical neurons across task conditions, which tightly coupled with onging wave dynamics within a lower dimensional state-space. Using focal cooling and optogenetic inhibition, we show that M2 modulates the structured generation of TWs and correct motor execution via distinct pathways: cortical and subcortical through motor thalamus. Thus, our results suggest that TWs reflect task-specific computations required to generate reliable volitional movement and can dynamically coordinate activity between distinct brain regions. Moreover, a 3D temporal convolutional neural network trained on the phase gradients of surface LFP can accurately predict behavioral outcomes, suggesting that the TWs carry behaviorally relevant information. (Funding - AFOSR FA9550-22-1-0078)

9. Poster

Body state encoding in primary and secondary somatosensory cortex of freely moving mice

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The University of Manchester

How do neurons function during natural behaviour, when animals are unconstrained and free to move? The aim of this study was to address this issue by comparing primary (wS1) vs associational (wS2) whisker somatosensory cortices. We recorded neural activity simultaneously from wS1 and wS2 (Neuropixels) while mice explored an object-containing open-field arena in the dark. Using four cameras, we tracked 11 head and body landmarks using DeepLabCut and reconstructed their 3D coordinates. By tracking points on the

walls/floor/object, we reconstructed the internal arena surfaces and calculated snout-to-surface distance (SSD) as a proxy for whisker-surface touch. We characterised the body state as 3D body velocity, head angles, their temporal derivatives, and principal components of body shape. We trained a supervised learning algorithm (XGBoost) to predict the firing rates of wS1 and wS2 neurons based on SSD and body state. We also sectioned the infra-orbital nerve to eliminate whisker afferent input and better understand the extent of body state encoding. As expected from whisker somatosensory areas, we found that SSD predicted firing rates for most wS1 and wS2 neurons but, surprisingly, adding body state substantially improved prediction accuracy in both areas. Our findings suggest that body state modulation is widespread, affecting both primary and associative sensory cortices and that both areas integrate signals from the whiskers within an overall body schema.

10. Poster

Cell-type specific representation of temporal signals in behaving mice

Yicong Huang, Laurence Copeland, Tim Stamm, Sana Naji, Ali Shamsnia, Hosala Patil, Farzaneh Najafi
Georgia Institute of Technology

Temporal expectation is the ability to anticipate the timing of future events based on prior experience, and is essential for learning, perception, and action in a dynamic environment. However, the neuronal mechanisms underlying temporal expectation signaling in the brain remain poorly understood. While previous studies have identified distributed temporal signals across brain regions, particularly in the cerebellum and visual-parietal cortical areas, the underlying cell-type specific circuits and interactions among these brain regions during temporal processing are yet to be determined.We addressed this question in behaving mice by presenting a temporally regular sequence of auditory and visual stimuli, which included infrequent temporal violations. To investigate the cell-type specific mechanisms underlying temporal processing, we performed two-photon calcium imaging from Purkinje cells in the cerebellar cortex, as well as from excitatory and inhibitory neuronal subtypes in the visual and posterior parietal cortex of awake, behaving mice. To identify the potential interactions among these brain regions during temporal processing, we manipulated one brain region while performing calcium imaging from the other regions. Our results suggest functionally diverse clusters of neurons in cerebellar and visual-parietal cortical regions, with distinct temporal coding properties. While some neurons are stimulus driven, some other neurons demonstrate temporal signaling.

11. Poster

Inactivating S1 impairs detection behavior by acting through downstream superior colliculus

Alice Y Nam, Jiwook Shin, Morgan Tenney, Baihe Zhang, Y. Kate Hong
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The primary somatosensory cortex (S1) has long been thought to mediate sensory perception and play a crucial role in sensory processing. However, recent work showed that mice rapidly recover in a detection task after S1 lesion, and that optogenetic inactivation of S1 only leads to a partial behavioral impairment. Together, these suggest that alternative regions may mediate detection even without S1. Out of several candidates, we chose to explore the superior colliculus (SC) based on its known function. We hypothesized that inactivating S1 leads to downstream changes in SC, and the changes within SC explain the observed behavior impairment. Here we show that silencing S1 leads to decreased detection performance, the majority of which is explained by a shift in decision criterion. Directly inactivating SC also shifted animals' criterion, which was determined by the balance between SCs in the two hemispheres. While both areas robustly encoded the stimulus, S1 inactivation-induced changes in sensory activity in SC correlated significantly better with behavior than in S1. Finally, in contrast to inactivating S1 with an intact SC, inactivating S1 after SC ablation did not lead to additional behavior impairment. Our work provides further compelling evidence against S1's long-standing importance and illuminates the role of SC in tactile detection, a vastly understudied brain region in somatosensation.

12. Poster

The topography of ipsilateral response in the mouse barrel cortex

Yael Oran, Ilan Lampl
Hebrew University of Jerusalem

We studied sensory integration across brain hemispheres by analyzing bilateral and ipsilateral responses to whisker stimulation in anesthetized and awake mice using widefield imaging. Previous studies indicated dense callosal fiber innervation near the S1-S2 border, suggesting enhanced ipsilateral responses in nearby barrels.

However, the exact organization of ipsilateral inputs was unclear. Our findings show that ipsilateral response was localized to the homotopic region corresponding to the contralateral whisker response. In anesthetized animals, stimulating whiskers closest to the snout (rows A and B) showed the strongest ipsilateral responses. Bilateral stimulation of homotopic whiskers revealed sub-linear integration. In the secondary motor cortex, ventral whisker stimulation elicited a stronger response than caudal whisker stimulation. Similar effects were observed in awake animals, varying with behavioral state. Seed pixel correlation maps revealed strong motor area correlations. Moving from caudal to rostral whiskers shifted responses to more rostral secondary motor areas. Overall, the specific functional connectivity of whiskers influences interhemispheric integration and motor functions, aligning with their ecological.

13. Poster

Cortical dynamics in forelimb S1 and M1 evoked by brief photostimulation of the mouse's hand

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The synaptic circuits and spiking dynamics in primary somatosensory (S1) and motor (M1) areas are fundamental to sensorimotor integration in cortex. The ascending sensorimotor loop through these areas is important for conveying tactile and other somatosensory signals to influence output along corticospinal and other descending motor pathways. Recent studies have characterized synaptic connectivity along the ascending pathway through mouse hand/forelimb S1 and M1 (Yamawaki et al., 2021, eLife). Here, using linear arrays to record simultaneous spiking activity in S1 and M1, we investigated the peripherally evoked spiking dynamics in these two cortical areas. The brief (5 ms) optogenetic stimulation of sensory afferents in the hand of awake transgenic mice evoked short-latency barrages of activity appearing first in S1 and then in M1. The corticocortical latencies (from S1 to M1) were short. However, the estimated net propagation speed for S1-to-M1 was vastly slower than for hand-to-S1 signaling. Compared to S1, M1 responses were attenuated in amplitude and slightly shorter in duration. The main early sensory responses were followed by a prolonged period of suppressed activity, and an ensuing "rebound" response. These characterizations provide quantitative measures of spiking dynamics of cortical activity along the hand/forelimb-related transcortical loop.

14. Poster

Stimulus selection drives value-modulated somatosensory processing in superior colliculus

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A fundamental trait of intelligent behavior is the ability to respond selectively to stimuli with higher value. Where along the neural hierarchy does somatosensory processing transition from a map of stimulus location to a map of stimulus value? To address this question, we recorded single-unit activity from populations of neurons in somatosensory cortex (S1) and midbrain superior colliculus (SC) in mice conditioned to respond to a positive-valued stimulus and withhold responses to an adjacent, negative-valued stimulus. The stimulus preference of the S1 population was equally weighted towards either stimulus, in line with a somatotopic map. Surprisingly, we discovered a large population of SC neurons that were disproportionately biased towards the positive stimulus. This disproportionate bias was controlled by spike facilitation for the positive stimulus and spike suppression for the negative stimulus in single neurons. Removing the opportunity for mice to behaviorally select the positive stimulus reduced stimulus bias in SC but not S1, suggesting that sensory processing in SC neurons was partially controlled by movement preparation. Similarly, the spontaneous firing rates of SC but not S1 neurons predicted reaction times, suggesting that SC neurons played a persistent role in perceptual decision-making. Taken together, these data indicate that the somatotopic map in S1 is transformed into a value-based map in SC that encodes stimulus priority.

15. Poster

Short-term synaptic plasticity enables detection of novel somatosensory input by crus I/II Purkinje cells in awake mice

Meghana R Holla, Spencer T Brown & Indira M Raman, Department of Neurobiology, Northwestern University

Cerebellar Purkinje (Pkj) neurons receive synaptic inputs with different short-term plasticity (STP) profiles where EPSCs of parallel fiber show synaptic facilitation, and IPSCs from molecular layer interneurons, remain stable. Crus I/II Pkj cells in awake head-fixed mice during air puffs applied to the whisker pad show brief 2-4ms suppressions of Pkj simple spikes (SS), sufficient to drive cerebellar output. When 5-puff trains are applied with different intervals, SS suppression remains across stimuli with longer intervals (200, 100 ms) but decreases

with shorter intervals (50, 25 ms). The distinct STP of excitatory and inhibitory synaptic inputs permit Purkinje cells to respond to the onset of sensory events and filter repetitive stimuli. Here, we tested whether introducing a novel sensory event into a train of identical stimuli could engage feed-forward inhibition that might restore SS suppression. We show that SS suppression is reduced with trains of contralateral (contra) puffs given at 25 ms interval, but remained high when a novel ipsilateral (ipsi) puff was introduced. This suggests that Pkj cells receiving convergent ipsi and contral sensory inputs suppress their SSs to novel sensory inputs, even when that input arises on a background of repetitive stimuli to which they have adapted. Thus, STP of convergent feed-forward microcircuits allow Pkj cells to behave as novel event detectors, rather than processors of specific sensory features. Funding - NIH R35-NS116854

16. Poster

Whole-body motor control in freely moving mice

Lucas Williamson, Kai Park, Eliana Pollay, Joseph Chung, Valentina Esho, Rowan Gargiullo, Cedric Bowe, Jessica Mai, Abigail McElroy, Gordon Berman, Chris Rodgers, Emory University

In the laboratory, motor control is often studied by asking subjects to repeat the same movement of a single limb many times, such as in a reaching task. In contrast, everyday movements from tying shoes to leaping over an icy puddle require the flexible coordination of all parts of the body together. We seek to understand how neural circuits coordinate the whole body during naturalistic behaviors. In the course of unrelated behavioral experiments, we noted that freely moving mice in a sufficiently rich environment voluntarily engage in balancing, climbing, and leaping, without expectation of reward. After motor cortex lesion or in the MitoPark genetic model of Parkinson's Disease, mice are less likely to engage in these agile movements. To quantify whole-body motor control, we use multiple camera views to track the position of the entire body in 3D. In ongoing work, we are modeling these movements with unsupervised machine learning methods and correlating them with neural activity in the motor cortex using wireless recording. Our long term goal is to understand how motor areas coordinate movement with sensation to enable free and agile behavior.

17. Poster

Broad receptive fields in cortex facilitate efficient and robust population coding of sensory information

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In conventional views of cortical circuitry, sensory processing starts in layer 4 (L4), where inputs from primary thalamus evoke responses in neurons that are selective to specific stimulus features. However, it has become increasingly clear that in parallel to this canonical circuit, the same thalamic input also drives responses in L5. In contrast to the selective responses and hence narrow receptive fields (RFs) in L4, L5 pyramidal tract neurons (L5PTs) respond unselectively to any stimulus, having broad RFs. We recently reported the mechanism underling broad RFs of these major cortical output neurons, and now addressed the question: What information could L5PTs broadcast to downstream targets despite their broad RFs? We found that L5PTs constitute a population code that allows decoding any stimulus features. In fact, we show that sampling responses of any small L5PT subpopulation within and across any column of barrel cortex allows for such decoding. We demonstrate that broad RFs and cell-to-cell variability are necessary to constitute this population code. The broader the RFs, and the larger the variability, the fewer cells are required to encode specific features. Thus, broad RFs of L5PTs enable downstream targets to efficiently and robustly decode sensory information. Our findings indicate that sensory input from thalamus is transformed in parallel into two population codes, one that relies on selective responses in L4, and another one on unselective responses of L5PTs.

18. Poster

The timescales of layer 6 corticothalamic neuron activity in the recruitment of cortico-cortical and cortico-thalamo-cortical pathways

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Layer 6 corticothalamic (L6CT) neurons are an excitatory neuron type with projections to both cortical and thalamic neurons. L6CT neurons have been reported to have facilitatory and suppressive effects on cortical and thalamic neurons. We hypothesize that their functional effects depend on the timecourse of L6CT activation. We characterized the temporal patterns induced by L6CT neurons using optogenetic activation. Leveraging the Vibrissal pathway of awake, head-restrained mice, we presented different LED inputs while recording neuronal activity in the barrel cortex, the ventral posteromedial nucleus of thalamus (VPm), and the thalamic reticular nucleus (TRN) using silicon probes. We hypothesized that time-dependent dynamics of L6CT activity may influence their effect on cortical and thalamic neurons. To test this hypothesis, we measured the effect of prolonged L6CT activation and found activity-dependent increases and decreases in the firing rates of different layers and cell types over time, that we reduced to two components suggestive of different recruitment of the cortico-cortical vs cortico-thalamo-cortical pathways and reflected at the local field potential level. Our data suggests that different temporal dynamics of L6CT neurons modulate cortex through a complex interplay between cortico-cortical and cortico-thalamo-cortical pathways. This relates to L6CT activity in a variety of behavioral contexts and suggests a flexible role of L6CT neurons. GR00017821

19. Poster

Beyond the impact of morphology: Dissecting principles that constrain ion channel distributions in cortical dendrites

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How synaptic input, ion channel distribution and morphology relate to one another to implement function remains unclear. Capturing synaptic integration along complex dendrites via models is essential for dissecting such relationships. Here, we generate millions of biophysically detailed models for layer 5 pyramidal tract neurons (L5PTs) for a diverse set of in vivo labelled morphologies. We find highly degenerate ion channel distributions that account equally well for a wide range of dendritic and perisomatic responses observed in L5PTs, ex vivo and in vivo. By analyzing the relationships that characterize this degeneracy, we identify principles that describe how L5PTs can generate calcium action potential (Ca2+ AP) in their dendrites to facilitate somatic burst firing. These principles make predictions regarding the energy demand of Ca2+ AP generation, and the spatiotemporal organization of synaptic input patterns that are necessary to account for in vivo responses. Moreover, they are robust across variations in morphology and physiological responses used to generate the models. Thus, we reveal principles that underlie ion channel degeneracy in distributions beyond the impact of morpho-electric variations from cell-to-cell. Our database of L5PT models sets the stage to explore how synaptic input, ion channel distributions and morphology relate to one another to implement function, and how additional principles such as energy demand could impact these relationships.

20. Poster

Unveiling the role of protein synthesis in medial-temporal lobe-gated memory consolidation: insights from a neocortical stimulation paradigm

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The precise locus of memory formation remains elusive, with potential mechanisms involving cellular changes, circuit modifications, and protein synthesis. Building upon our previous findings (Doron et al., 2020) that demonstrated the necessity of the perirhinal cortex's pathway to L1 of the somatosensory cortex (S1) for memory formation, we employed a microstimulation paradigm to test the hypothesis that MTL-gated memory consolidation is contingent upon local protein synthesis. To investigate this we applied both non-specific (anisomycin) and specific (rapamycin) inhibitors of protein synthesis in L1 dendrites. While anisomycin had no significant impact on behavioral reporting of microstimulation, rapamycin—targeting the mTORC1 pathway—greatly impaired learning, evidenced by an ~80% decrease in stimulus sensitivity and increased response variability. Our results underscore that mTORC1 is crucial for learning. Additionally, we used Neuropixel recordings to extend previous findings of modulated L5 neuron firing after learning to all cortical layers and subcortical structures. Our preliminary results obtained show that that neuronal responses to microstimulation emerge within a session and modulate with repeated exposure, though this does not result in memory formation. We also found microstimulation-responsive neurons in the hippocampus and thalamus, revealing the need for further research into the timing and specific cortical locations critical for memory consolidation.

21. Poster

Larger Brains and Relatively Smaller Cerebella in Asian Compared to African Savanna Elephants

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Elephants are the largest terrestrial animals, but our knowledge of their brains is limited. We studied brain size, proportions, and development in Asian (Elephas maximus) and African savanna (Loxodonta africana) elephants. Specifically, we weighed, photographed, and analyzed postmortem MR-scans of elephant brains in addition to collecting elephant brain data from the literature. Despite their smaller body size, adult Asian female elephants have substantially and significantly heavier brains (mean 5345 ± 919 g SD) than adult African savanna female elephants (mean 4263 ± 377 g SD). In line with their larger body size, adult African savanna male elephants (mean 5764 ± 1274 g SD) have significantly heavier brains than African female elephants; the brain weight of the adult male Asian elephant remains unclear. Elephant brain weight increases approximately threefold postnatally. This postnatal increase is similar to that of the human brain, but is larger than that seen in non-human primates. Asian elephants likely have more cerebral cortical gray matter than African ones, the cerebellum is relatively smaller (19.3 % of brain weight) than in African elephants (22.7 %). Our data indicate a higher degree of encephalization in Asian than in African savanna elephants. The massive postnatal brain growth of elephants is likely related to prolonged adolescence and the important role of experience in elephant life history.Funding sources...- BrainPlay grant- Michael Brecht EXC-2049

22. Poster

Sensory-behavioral deficits in Parkinson's disease: Insights from a 6-OHDA mouse model

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Parkinson's disease (PD) is marked by the degeneration of dopaminergic neurons in the striatum, primarily causing motor symptoms. However, non-motor deficits, especially sensory symptoms, often appear before motor symptoms and provide an early diagnostic opportunity. The impact of these sensory deficits on behavior and their underlying mechanisms are not well understood. In our study, we used a mouse model of PD, induced by 6-hydroxydopamine (6-OHDA) to deplete striatal dopamine, to examine changes in tactile sensation using the conserved mouse whisker system. Through psychophysical experiments, we assessed sensory-driven behaviors in both healthy and Parkinson-like conditions. Our findings reveal that dopamine depletion significantly affects tactile sensation, beyond expected motor impairments, influencing detection performance, task engagement, and reward processes. Subjects with severe dopamine depletion consistently

exhibited pronounced sensory deficits, whereas others with substantial depletion showed minimal changes. Additionally, some showed moderate behavioral degradation likely due to sensory rather than motor impairment. Employing a sensory detection task helps quantify impairments from dopamine depletion, underscoring the need to include sensory evaluations in PD studies to fully capture the disease's diverse symptoms. Funding:NIH BRAIN Grant RF1NS128896NIH RO124764McCamish Blue Sky Grant 2023

23. Effect of surface material on whisker surface interaction

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In whisker-based texture sensing, whisker deformations induced by interaction with a surface create stresses that propagate to the follicle. These deformations may comprise combinations of bending, twisting, and buckling, as well as high-speed stick-slip events typical of frictional interactions. We produced 4000fps 3D reconstructions of the full lengths of mouse whiskers during whisking against surfaces, with simultaneous recordings from whisker-innervating mechanosensory neurons. The surfaces used were square wave gratings of varying frequency, material, and position. Whisker curvature and torsion reached larger magnitudes during whisking against the least slippery material (silicone) than the two more slippery materials (aluminum and photopolymer resin); whisking against silicone was also less likely to evoke a stick-slip event. These observations indicate two potential means of decoding the frictional properties of surfaces. Additionally, some neurons responded more strongly to whisking against silicone than aluminum or resin, suggesting sensitivity to the larger stresses that occurred during whisking against the silicone surface. This material is based upon work supported by the National Science Foundation Graduate Research Fellowship under Grant No. DGE-1746891.

24. Poster

Distinct somato-dendritic coupling dynamics in anatomically defined L5B pyramidal neuron subtypes

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Integrating bottom-up and top-down inputs in the sensorimotor cortices is crucial for accurate sensory perception. The thick tufted layer 5 pyramidal neurons (L5BPNs) play a central role in this framework, with their elaborate dendrites integrating long-range feedback in superficial layers and feedforward inputs across the basal regions. L5BPNs can be divided into subpopulations that project to various subcortical regions, yet little is known about the integration properties across these subtypes. We performed two-photon guided somato-dendritic patch-clamping and two-photon calcium imaging in retrograde-labeled barrel cortical L5BPNs in acute brain slices. We observed unique morphology and electrophysiology across L5BPNs with different downstream projections. Specifically, we found higher burstiness and earlier apical dendritic bifurcation in pons-projecting L5BPNs compared to Pom- and SC-projecting L5BPNs, accompanied with less apical dendritic compartmentalization including a lower threshold of global bursts, hallmarks of translaminar integration. Using biophysical simulations, we found that the distribution of dendritic Na+ channels and their rate of recovery from inactivation is a key factor in regulating the compartmentalized characteristics in these projection sub-types. Our findings suggest a critical role for unique dendritic integration properties in coordinating and broadcasting different top-down sensorimotor integration strategies across subcortical networks.

25. Poster

A rigid body model for simplifying mechanical signal analysis in whisker-based tactile sensing

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Accurately quantifying the mechanical signals acting at the whisker follicle during whisking behavior is an important component of understanding the entire process of tactile sensation. However, fully dynamic models of flexible whiskers such as WHISKiT Physics (Zweifel et al., 2021) are complex and can be difficult to use in the context of neurophysiology experiments. In some cases, a rigid body model may be an adequate representation of whisker-related mechanical signals. In the present work, we demonstrate that a rigid body model offers a good approximation for the mechanical signals generated during non-contact (“free-air”) whisking, predicting the reaction forces and moments at the base of the whisker largely in agreement with

flexible/dynamic models. This approach streamlines the modeling process, and also increases understanding of the significant mechanical effects underlying neural responses in the whisker system. We show that the approach can be effectively applied to analyze behavioral data from awake animals, further bridging the gap between theoretical modeling and practical applications. Supported by NIH award R01 NS-116277.

26. Poster

Parvalbumin interneurons regulate circuit plasticity in the healthy and injured somatosensory cortex

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It has been hypothesized that plasticity and remapping of cortical circuits underlies recovery after brain injury. Using a mouse model of focal cortical injury, we previously found that sensory-evoked activity was reduced for a prolonged period after injury and that whisker trimming-induced circuit remapping was impaired. These results suggest that plasticity in the peri-lesional cortex may be maladaptive and limit recovery. We hypothesized that Parvalbumin (PV) inhibitory interneurons might contribute to this maladaptive plasticity and used longitudinal two-photon calcium imaging to record the activity of individual PV cells in the healthy and injured S1. We find that the spatial distribution of sensory-evoked responses in PV cells mirrors that of pyramidal cells. In the healthy cortex, whisker trimming leads to recruitment of PV cells responsive to the spared whisker in deprived cortical barrels and long-lasting shifts in responsivity to the spared whisker in the spared barrel. Chemogenetic inhibition of PV cells during experience-dependent plasticity blocks whisker trimming-induced remapping. In the injured cortex, sensory-evoked responses of PV cells to the principal whisker of the lesioned barrel are selectively impaired after stroke. Together, these results suggest that proper functioning of PV cells is essential for adaptive plasticity in the healthy and injured cortex. Funding: NINDS 1K08NS114165-01A1 and American Academy of Neurology NRTS 2199 to W.Z.