LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

HARVARD UNIVERSITY

LMU–Harvard Young Scientists' Forum

From Molecules to Organisms XVII
Munich, June 30 – July 02, 2025

The **LMU-Harvard Young Scientists' Forum (YSF)** seeks to unite PhD students and Postdoctoral fellows from the Harvard University and the Ludwig-Maximilians-Universität (LMU Munich) with core faculty from the two universities to create a framework for an interdisciplinary exchange of ideas.
The YSF was initiated as a yearly event in 2009 and is held alternately in Munich and Cambridge (Massachusetts).

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- **LMU-Harvard Young Scientists' Forum at the LMU Biocenter:** From Molecules to Organisms, June 30 – July 02, 2025
- **Under the auspices of** Prof. Dr. Francesca Biagini, Vice President for International Affairs, LMU
- **Program Management:** Angelika Doebbelin (LMU International Office), Sylvia Zehner (LMU Munich Center for Neurosciences)
- **Participating academic units:** Munich Center for Neurosciences (MCN^{LMU}), Graduate School for Systemic Neurosciences (GSN^{LMU})
- **Academic Management:** Prof. Dr. Oliver Behrend, Prof. Dr. Benedikt Grothe (MCN^{LMU}/GSN^{LMU})
- **Institutional Responsibility:** LMU International Office, LMU Biocenter

Conference Agenda

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Sunday, June 29

Arrival (LMU International Office, or individually arranged)
IZB Residence CAMPUS@HOME (address below)

Monday, June 30

LMU Biocenter, Grosshadernerstr. 2, 82152 Martinsried, D00.003

09:00 – 09:15	*Walk* from IZB Residence to Biocenter
09:15 – 09:30	**Welcome address** (F.Biagini, Vice President LMU International and O.Behrend, Munich Center for Neurosciences)
09:30 – 10:30	**Lecture 1** – Kanaka Rajan: **"Brain-Wide Compositionality and Learning Dynamics in Biological Agents"** (Intro: W.Młynarski)
	Coffee break (catered; foyer D00.003)
11:00 – 13:00	**Session 1** – **"Neural Computation and Learning"** Burrell/Graetsch/Kumar/Ruben/Stemmler (Chair: W.Młynarski)
	Lunch break (catered; foyer)
14:30 – 16:30	**Session 2** – **"Neuropathologies and Clinical Perspectives"** De Weerd/Landgraf/Marvian/Muehlhofer/Mittas (Chair: D.Keays)
	Coffee break (catered; foyer)
17:00 – 18:00	**Lecture 2** – Thomas Misgeld: **"Dynamics of Cortical Myelination"** (Intro: D.Keays)
18:45 – open	Bavarian Conference Evening (Fürstenrieder Schwaige, Forst-Kasten-Allee 114, 81475 München; transfer pre-arranged at IZB Residence)

Tuesday, July 01

LMU Biocenter Martinsried, D00.003

08:45 – 09:00	*Walk* from IZB Residence to Biocenter
09:00 – 10:00	**Lecture 3** – Venkatesh Murthy: **"Tracking Scent Trails: Algorithms and Mechanisms"** (Intro: A.Herz)
	Coffee break (catered; foyer)
10:30 – 12:30	**Session 3** – **"Active Sensing and Behaviour"** Karamihalev/Mizes/Watkins-Kröger/Sepela/Sumser (Chair: A.Herz)
	Lunch break (catered; foyer)
14:30 – 16:30	**Session 4** – **"Neuronal Circuits and Sensory Processing"** Berger/Lewin/McCalmon/Meyerolbersleben/Winhart (Chair: L.Busse)
	Coffee break (catered; foyer)
17:00 – 18:00	**Lecture 4** – Lisa Fenk: **"Neural mechanisms for active eye movements in *Drosophila*"** (Intro: L.Busse)
18:00 – open	*At free disposal (student representative activities)*

Wednesday, July 02

	LMU Biocenter Martinsried, D00.003
08:45 – 09:00	*Walk* from IZB Residence to Biocenter
09:00 – 10:00	**Lecture 5** – Michael Pecka: **"Neuronal Representations of Active Audition During Unrestricted Behaviour"** (Intro: A.Schroeder)
	Coffee break (catered; foyer)
10:30 – 12:30	**Session 5** – **"Orientation, Navigation and Memory"** Chen/Cohen/David/Hohendorf/Mei (Chair: A.Schroeder)
	Lunch break (catered) & **YSF poster session** (foyer) & **YSF faculty meeting** (B03.015)
	Poster – Dogru/Hoffelner/Müller-Karoza/Nicholls/ Righetti/Rovere/ Rullan Buxo/Schiffl/Wang
14:30 – 15:30	**Lecture 6** – Albert Lee: **"Hippocampal Representations and Their Uses"** (Intro: A.Sirota)
15:30	**Closing remarks** (O.Behrend MCN[LMU]; K.Blum CBS-HRVD)
15:45	*Walk* from Biocenter to IZB Residence / *individually: beergarden*

Thursday, July 03

IZB Residence CAMPUS@HOME,
Am Klopferspitz 21, 82152 Martinsried
Departure (LMU International Office, or individually arranged)

Participants*

*Participating PhD students and Postdoctoral fellows have been nominated by selected faculty members of LMU and Harvard University (please note the heads of the nominees' "home laboratories" at the end of each entry).

Harvard University Delegation

- **Kenneth Blum**, Executive Director, Harvard Center for Brain Science
- **Daniel Berger**, Postdoctoral Fellow, Department of Molecular and Cellular Biology, Laboratory of Jeff W. Lichtman
- **Mark Burrell**, Postdoctoral Fellow, Center for Brain Science, Laboratory of Naoshige Uchida
- **Albert Chen**, PhD student, Harvard Medical School, Laboratory of Jan Drugowitsch
- **Zach Cohen**, PhD student, Harvard Medical School, Laboratory of Jan Drugowitsch
- **Ganesh Kumar**, Postdoctoral Fellow, Harvard John A. Paulson School of Engineering and Applied Sciences, Laboratory of Cengiz Pehlevan
- **Albert Lee**, Professor, Harvard Medical School, Department of Medicine & Beth Israel Deaconess Medical Center
- **Hannah McCalmon**, Harvard Department of Molecular and Cellular Biology, Laboratory of Venkatesh Murthy
- **Kevin Mizes**, Postdoctoral Fellow, Harvard Medical School, Laboratory of Christopher Harvey
- **Venkatesh Murthy**, Professor, Academic Director, Harvard Center for Brain Science
- **Kanaka Rajan**, Professor, Harvard Medical School
- **Benjamin Ruben**, PhD student, Harvard John A. Paulson School of Engineering and Applied Sciences, Laboratory of Cengiz Pehlevan
- **Camille Rullán Buxó,** Postdoctoral Fellow, Harvard Medical School, Laboratory of Jan Drugowitsch
- **Rebecka Sepela**, Postdoctoral Fellow, Harvard Department of Molecular and Cellular Biology, Laboratory of Nicholas Bellono

Harvard University Nominating Faculty

- **Nicholas Bellono**, Professor, Harvard Department of Molecular and Cellular Biology
- **Jan Drugowitsch**, Professor, Harvard Medical School
- **Christopher Harvey**, Professor, Harvard Medical School
- **Jeff Lichtman**, Professor, Harvard Center for Brain Science
- **Venkatesh Murthy**, Professor, Academic Director, Harvard Center for Brain Science
- **Cengiz Pehlevan**, Professor, Harvard John A. Paulson School of Engineering and Applied Sciences
- **Naoshige Uchida**, Professor, Harvard Department of Molecular and Cellular Biology

Ludwig-Maximilians-Universität München (LMU)
Max Planck Institute of Biological Intelligence (MPI-BI)
Max Planck Institute of Psychiatry (MPI Psych)
Technische Universität München (TUM)
Representatives

- **Oliver Behrend**, Managing Director, LMU, Munich Center for Neurosciences (MCN^{LMU}), Graduate School of Systemic Neurosciences (GSN^{LMU})
- **Francesca Biagini**, LMU, Vice President International
- **Martin Biel**, Professor, LMU Department of Chemistry and Pharmacy
- **Laura Busse**, Professor, LMU Department Biology, Division of Neurobiology
- **Erwan David**, Assoc. Prof., Le Mans University, and LMU Psychology Department, Laboratory of Melissa Võ
- **Lis De Weerd**, PhD student, German Center for Neurodegenerative Diseases (DZNE), Laboratory of Christian Haass
- **Angelika Doebbelin**, Project Manager, LMU International Office
- **Merve Dogru**, PhD student, LMU BioMedical Center, Department of Physiological Genomics, Laboratory of Antje Grosche
- **Lisa Fenk**, Principal Investigator, MPI-BI, Active Sensing Group
- **Nadine Gogolla**, Director, MPI of Psychiatry, Department Emotion Research
- **Swantje Graetsch**, Postdoc, MPI-BI, Laboratory of Herwig Baier
- **Antje Grosche**, LMU BioMedical Center, Department of Physiological Genomics
- **Christian Haass**, Professor, LMU Biomedical Center, Metabolic Biochemistry, German Center for Neurodegenerative Diseases (DZNE), SyNergy Excellence Cluster of Systems Neurology
- **Jochen Herms**, Professor, LMU, German Center for Neurodegenerative Diseases (DZNE)
- **Andreas Herz**, Professor, LMU Department Biology, Division of Neurobiology, Computational Neuroscience
- **Patricia Hoffelner**, PhD student, LMU BioMedical Center, Department of Physiological Genomics, Laboratory of Antje Grosche
- **Günther Höglinger**, Professor, LMU University Hospital, Neurology Department
- **Victoria Hohendorf**, PhD student, TUM, Translational Neurotechnology, Laboratory of Simon Jacob
- **Mark Hübener**, Professor, MPI-BI, Department Synapses, Circuits, Plasticity
- **Simon Jacob**, Professor, TUM, Translational Neurotechnology

- **David Keays, Professor**, LMU Department Biology and University of Cambridge Department of Physiology
- **Stephan Kröger**, Professor, LMU BioMedical Center
- **Nicolas Landgraf**, PhD student, LMU, German Center for Neurodegenerative Diseases (DZNE), Laboratory of Jochen Herms
- **Uwe Lewin**, PhD student, GSN[LMU], MPI-BI, Laboratory of Mark Hübener
- **Meryl Malzieux**, Postdoc, MPI Psych, Laboratory of Nadine Gogolla
- **Amir Marvian**, Postdoc, LMU, German Center for Neurodegenerative Diseases (DZNE), Laboratory of Günther Höglinger
- **Siyuan Mei**, PhD student, LMU Department Biology, Division of Neurobiology, Computational Neuroscience, Laboratory of Andreas Herz
- **Lucas Meyerolbersleben**, PhD student, LMU, Department Biology, Division of Neurobiology, Laboratory of Laura Busse
- **Wiktor Młynarski**, Professor, LMU Department Biology, Division of Neurobiology, Computational Neuroscience
- **Thomas Misgeld**, Professor, TUM, Institute of Neuronal Cell Biology, German Center for Neurodegenerative Diseases (DZNE)
- **David Mittas**, PhD student, LMU Department of Chemistry and Pharmacy, Laboratory of Martin Biel
- **Maria Muehlhofer**, PhD student, LMU BioMedical Center, Metabolic Biochemistry, Laboratory of Christian Haass
- **Lea Mueller-Karoza**, PhD student, LMU Psychology Department, Laboratory of Melissa Võ
- **Jonas Neher**, Professor, LMU BioMedical Center, Division of Biochemistry
- **Vicky Nicholls**, Postdoc, LMU Psychology Department, Laboratory of Melissa Võ
- **Michael Pecka**, Principal Investigator, LMU, Department Biology, Division of Neurobiology
- **Beatrice Righetti**, PhD student, TUM, Translational Neurotechnology, Laboratory of Simon Jacob
- **Matteo Rovere**, PhD student, LMU BioMedical Center, Metabolic Biochemistry, Laboratory of Christian Haass
- **Laura Schiffl**, Postdoc, TUM, Translational Neurotechnology, Laboratory of Simon Jacob
- **Anna Schroeder**, Professor, LMU Department Biology, Division of Neurobiology
- **Anton Sirota**, Professor, LMU Department Biology, Division of Neurobiology, Computational Neuroscience
- **Martin Stemmler**, PI, LMU Department Biology, Division of Neurobiology, Computational Neuroscience

- **Anton Sumser**, Postdoc, LMU Department Biology, Division of Neurobiology, Laboratory of Laura Busse
- **Melissa Võ**, Professor, LMU Psychology Department, Neuro-Cognitive Psychology
- **Miao Wang**, PhD student, LMU Department Biology, Division of Neurobiology, Computational Neuroscience, Laboratory of Anton Sirota
- **Bridgette Watkins**, PI, LMU BioMedical Center, Laboratory of Stephan Kröger
- **Valentin Winhart,** PhD student, LMU Department Biology, Division of Neurobiology, Laboratory of Michael Pecka

Munich Nominating Faculty

- **Herwig Baier**, Professor, Director, MPI-BI, Department Genes, Circuits, Behavior
- **Martin Biel**, Professor, LMU Department of Pharmacy
- **Laura Busse**, Professor, LMU Department Biology, Division of Neurobiology
- **Nadine Gogolla**, Director, MPI of Psychiatry, Department Emotion Research
- **Benedikt Grothe**, Professor, LMU Department Biology, Division of Neurobiology, Munich Center for Neurosciences (MCN[LMU]), Graduate School of Systemic Neurosciences (GSN[LMU])
- **Antje Grosche**, LMU, Department of Physiological Genomics, BioMedical Center (BMC)
- **Christian Haass**, Professor, LMU Biomedical Center, Metabolic Biochemistry, German Center for Neurodegenerative Diseases (DZNE), SyNergy Excellence Cluster of Systems Neurology
- **Jochen Herms**, Professor, LMU, German Center for Neurodegenerative Diseases (DZNE)
- **Andreas Herz**, Professor, LMU Department Biology, Division of Neurobiology, Computational Neuroscience
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- **Mark Hübener**, Professor, MPI-BI, Department Synapses, Circuits, Plasticity
- **Simon Jacob**, Professor, TUM, Translational Neurotechnology
- **Stephan Kröger**, Professor, LMU BioMedical Center
- **Thomas Misgeld**, Professor, TUM, Institute of Neuronal Cell Biology, German Center for Neurodegenerative Diseases (DZNE)
- **Michael Pecka**, Professor, LMU, Department Biology, Division of Neurobiology
- **Anton Sirota**, Professor, LMU, Department Biology, Division of Neurobiology, Computational Neuroscience
- **Melissa Võ**, Professor, LMU Psychology Department, Neuro-Cognitive Psychology

Abstracts of lecturers and posters

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Circuitry of double bouquet cells in human cortex

Daniel R. **Berger**, Jeff W. Lichtman
[1] **Department of Molecular and Cellular Biology, Laboratory of Jeff W. Lichtman**
[2] **Harvard Center for Brain Science**

The Lichtman lab recently published a large electron microscopic data set of human cortex (Shapson-Coe et al., Science, 2024). One of the main findings was the existence of very strong synaptic connections between pairs of neurons in the data, comprised of dozens of synapses. Further investigation suggests that many of these strong connections are inputs and outputs of morphological Double Bouquet Cells (DBCs). We found that DBCs receive multi-synaptic inputs from individual local layer 2 pyramidal neurons (up to 63 synapses) and send strong inhibitory outputs to individual layer 3 pyramidal neurons with cell bodies directly below (up to 125 synapses), within the narrow vertical axon bundle of the DBC. This circuit suggests that activity of layer 2 pyramidal neurons may cause selective inhibition of layer 3 pyramidal neurons in the same minicolumn, via DBCs.

Prospective contingency explains behavior and dopamine signals during associative learning

Mark **Burrell**, Lechen Qian, Jay A. Hennig, Sara Matias, Venkatesh N. Murthy, Samuel J. Gershman & Naoshige Uchida
Harvard University, Department of Molecular and Cellular Biology

Associative learning depends on contingency, the degree to which a stimulus predicts an outcome. Despite its importance, the neural mechanisms linking contingency to behavior remain elusive. In the present study, we examined the dopamine activity in the ventral striatum—a signal implicated in associative learning—in a Pavlovian contingency degradation task in mice. We show that both anticipatory licking and dopamine responses to a conditioned stimulus decreased when additional rewards were delivered uncued but remained unchanged if additional rewards were cued. These results conflict with contingency-based accounts using a traditional definition of contingency or a new causal learning model (ANCCR) but can be explained by temporal difference (TD) learning models equipped with an appropriate intertrial interval state representation. Recurrent neural networks trained within a TD framework develop state representations akin to our best 'handcrafted' model. Our findings suggest that the TD error can be a measure that describes both contingency and dopaminergic activity.

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The role of feedback in dynamic inference for spatial navigation

Albert **Chen**, Jan Drugowitsch
Harvard Medical School

Efficient behavior in our noisy and ambiguous world calls for the strategic use of the arising uncertainty by probabilistic inference. Probabilistic inference in complex dynamic environments is challenging as it requires tracking not only individual latent variables but also the interactions among them. As a result, a neural circuit that optimally encodes these variables would need to be recurrently wired to relay information between them via feedback connections. Given the additional cost of evolving and maintaining these feedback connections, we sought the circumstances under which the brain could get away with simpler circuits lacking some of the feedback connections necessary for optimal inference. We focused on spatial navigation, in which self-motion and landmark cues inform estimates of our velocity and position, respectively, across time. As velocity and position are coupled by kinematics, optimal inference predicts that velocity information is used to improve the inference of position and vice versa. Whereas animals are known to use path integration to integrate self-motion cues to estimate their position, it remains unclear whether they use successive landmark observations, which provide position information, to infer their velocity. To assess the impact of lacking position-to-velocity feedback on inference performance, we developed a general mathematical framework to compare two inference models: (1) optimal inference and (2) constrained inference, which lacks particular feedback pathways. We found that lacking position-to-velocity feedback only causes significant performance loss if landmark observations are reliable, but self-motion observations are unreliable. We further found that this performance deficit is, in fact, negligible at most biologically realistic noise levels. Thus, a heuristic algorithm without all the necessary components for optimal inference could nevertheless support efficient navigation. Ongoing work seeks to identify signatures of position-to-velocity feedback, or the lack thereof, in neurophysiological data to discriminate between optimal and constrained inference models.

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Hippocampal spatial maps exhibit information maximizing field anisotropy

Zach **Cohen** and Jan Drugowitsch
Harvard Medical School

Neural populations across cortex exhibit heterogeneity in the sizes and shapes of their receptive fields (RFs). However, little is known about the computational role of RF heterogeneity. Here we investigate how tuning heterogeneity impacts the stimulus information encoded in neural populations. We do so by deriving closed-form expressions for population information as a function of population tuning properties. We found that populations with heterogeneously tuned RF widths broadly exhibit a computational advantage over homogeneously tuned populations, and that the magnitude of this advantage is dependent upon the dimensionality of the encoded stimulus. Intriguingly, we found that for populations encoding 2- and 3-dimensional stimuli, heterogeneous tuning only confers a computational advantage if RFs exhibit tuning anisotropy (tuning curves are more likely elliptical than perfectly spherical). For populations encoding stimuli of higher dimensionality, width heterogeneity across the population remains advantageous, but tuning anisotropy becomes computational detrimental. Our framework thus predicts that hippocampal place cells, which putatively encode 2D allocentric spatial position through spatially localized receptive (or place) fields (PFs), can maximize spatial information through width heterogeneity and tuning anisotropy. In first attempting to test this prediction, we found that existing methods for measuring PF widths are sensitive to heuristic assumptions and fail to properly measure tuning heterogeneity and anisotropy. To circumvent this issue, we developed a fully Bayesian PF tuning inference method to determine the empirical distribution of PF sizes and degree of field anisotropy. We show that this novel method is far less impacted by bias in stimulus presentation inherent in measuring neural activity – particularly for freely moving animals – than traditional methods. We also show that our method more robustly recovers key tuning characteristics than traditional methods on synthetic data. Applying our method to CA1 recordings of freely moving rats, we found that place fields indeed exhibit highly heterogeneous and anisotropic RFs, thereby increasing spatial information, as predicted by our model. While we primarily study place cells here, our framework makes testable predictions about the interplay between field anisotropy, population heterogeneity, and encoded stimulus dimensionality that can be studied in populations across the brain.

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Virtual reality and visual search: Unlocking new perspectives in the quasi-natural world

Erwan **David**[1, 2], Melissa Le-Hoa Võ[2]
[1] **Computer Science Lab of Le Mans University, France**
[2] **LMU Department of Psychology, Scene Grammar Lab**

Virtual reality (VR) offers significant advantages for testing visual search behaviors in conditions that closely resemble real-world environments. By immersing participants in 3D spaces, VR allows for complete control of the virtual environment, tracking of the participant, unrestricted movement and interaction with complex scenes, which traditional on-screen methods cannot replicate. This talk will showcase various protocols I have developed using eye tracking in VR: such as gaze-contingent protocols, studies examining gaze dynamics while searching for hidden objects in interactable virtual scenes, and tracking more than just head movements to learn how the whole body accompanies eye movements. These studies highlight eye tracking in VR as a powerful experimental tool, providing valuable insights into how individuals navigate and search for targets in their surroundings.

We will introduce the principles of eye tracking and how it can be integrated with VR to gather real-time data on gaze patterns and visual attention. The session will highlight key findings from our studies that investigate how factors such as central and peripheral visual fields, object visibility, and spatial relationships influence search strategies in 3D environments. By examining these elements, we can gain a deeper understanding of the cognitive processes involved in visual search.

The talk will also address practical aspects of using VR and eye tracking in research, providing attendees with insights on how to implement these technologies in their own studies. This includes discussing the challenges and considerations involved in designing experiments that leverage eye tracking in VR for visual tasks. We will introduce toolboxes that make gathering data in VR experiments and processing 3D eye tracking data easier.

Overall, this session aims to encourage young scientists to consider the potential of eye tracking in VR as a research tool. By exploring the intersection of computer science and cognitive science, we can deepen our understanding of how individuals look, navigate and interact with their environments, ultimately advancing our understanding of visual behavior in complex natural scenes.

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Aducanumab-mediated clearance of amyloid plaques decreases microglial activation and induces a peri-plaque microglial phenotype associated with antigen presentation

Lis **de Weerd**
LMU Haass Lab, Munich Cluster for Systems Neurology (SyNergy)

Anti-amyloid β-peptide (Aβ) immunotherapy was developed as treatment for Alzheimer's disease to reduce and prevent amyloid plaque pathology and its downstream consequences. Efficient amyloid plaque clearance has been proven in clinical trials with Aducanumab, Lecanemab and Donanemab. At least two of these antibodies slow memory decline to some extend and have beneficial effects on daily living activities. The therapeutic effects correlate with the efficacy of plaque removal. However, treatment is associated with adverse side-effects, such as oedema and haemorrhages, which are potentially linked to the induced immune response. To improve therapeutic safety, it is therefore imperative to understand the consequences of anti-Aβ antibody treatment on immune cell function. We investigated the effects of long-term chronic Aducanumab treatment on amyloid plaque pathology and microglial response in the APP-SAA knock-in mouse model. Mice were treated weekly with Aducanumab from 4-8 months of age. Long-term treatment with Aducanumab results in a robust and dose-dependent removal of amyloid plaque pathology, with a higher efficiency for removing diffuse over dense-core plaques. Analysis of the CSF proteome indicates a reduction of markers for neurodegeneration including Tau and α-Synuclein, as well as immune cell related proteins. Bulk RNAseq confirms a dose-dependent decrease in brain-wide disease-associated microglial (DAM) and glycolytic gene expression, which is supported by a parallel decrease of glucose uptake and protein levels of the Triggering receptor of myeloid cells 2 (Trem2) protein, a major immune receptor involved in DAM activation of microglia. Microglial DAM activation is however still induced around remaining plaques regardless of treatment dose. In addition, we observe a dose-dependent increase in genes associated with antigen-presentation and immune signaling in microglia. In addition to increased microglial clustering, mAducanumab treatment is associated with a selective increase these proteins around remaining plaques. These findings demonstrate that long-term chronic Aducanumab-mediated removal of Aβ leads to a dose dependent decrease in brain-wide microglial DAM activation and neurodegeneration, but does not affect DAM activation around remaining plaques and induces an antibody treatment-related microglial phenotype associated with antigen presentation and immune signaling.

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Single-cell analysis reveals TSPO's therapeutic potential, highlighting its role in ischemia and early AMD

Rüya Merve **Dogru**, Oliver Bludau, Patricia Hoffelner, Antje Grosche
LMU Department of Physiological Genomics, Biomedical Center

Introduction: Müller glia cells are the very specialized and predominant glial cells of the retina. They provide homeostatic, metabolic and functional support to neurons and own critical roles in the regulation of the extracellular space, ion and water homeostasis and the maintenance of blood-retinal barrier. Furthermore, these cells exhibit remarkable resilience to damage and respond to retinal injury and disease through reactive gliosis, altering their morphology, biochemistry, and physiology. The Translocator protein 18 kDa (TSPO) is an integral outer mitochondrial membrane protein. One of its potential functions is the transport of cholesterol into the mitochondrial matrix, a prerequisite for steroid biosynthesis. In the retina, TSPO is expressed at highest levels in Müller glia, microglia and vascular cells. Although it is known from studies in mouse models that microglia and Müller cells upregulate TSPO in response to tissue damage, it remains unclear whether a similar glial response occurs in the stressed human retina. Using a published single-cell RNA sequencing (scRNA-seq) dataset, we examine whether this regulatory pattern occurs in early age-related macular degeneration (AMD) to assess TSPO as a potential pharmacological target. We then compare these findings with our recent scRNA-seq study on Müller cell-specific TSPO knockout (KO) mouse models subjected to ischemic stress.

Method: A single cell suspension retrieved from both wild-type (WT) and Müller cell-specific TSPO KO mouse retinae from control and ischemic, 7 days post-injury, eyes were subjected to magnetic activated cell sorting (MACS) by which Müller cells were enriched using CD29 antibody. Afterward, single-cell sequencing was performed, and the data were analyzed in RStudio (version 4.3.2) with the Seurat package. Single-cell RNA sequencing data of early AMD patients vs. healthy donors (GSE188280; Zahuar et al., 2022) was reanalyzed in RStudio (version 4.3.2) with the Seurat package. TSPO expression in microglia and Müller glia from both mouse and human donor retinae was analyzed using immunohistochemistry.

Results: In our analysis, we first identified the TSPO expression and its interaction partners in Müller cell-specific TSPO KO and WT mice under control and ischemic conditions at the single-cell level. Our findings revealed that many TSPO interaction partners (e.g., Atad3a, Cyp11a1, Acbd3, Vdac1, Vdac3, Dbi, Hk2, Mgst1, Tomm20, Tomm40) were upregulated in the TSPO KO ischemic mouse retina. Next, repeated this analysis comparing respective expression profiles for retinal cell types of healthy donors and patients suffering from early AMD. We found that TSPO and many of its interaction partners were dysregulated in microglia and Müller cells of early AMD patients, mirroring our findings in the ischemic mouse retina.

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Conclusion: Our findings reveal that TSPO-related pathways, which may influence glial function, are dysregulated already in early AMD well in line with findings from our mouse model. Therefore, TSPO ligands might have potential as a novel therapeutic strategy for AMD and should be investigated in relevant disease models.

Neural mechanisms for active eye movements in *Drosophila*

Lisa **Fenk**
Max Planck Institute for Biological Intelligence

Almost all animals move, and when they do, they alter the stream of information reaching their auditory, mechanosensory, visual, and other sensory systems. Our work focuses on two fundamental aspects of such active sensation. First, how do brains ignore those components of the changing sensory stream that are irrelevant or even detrimental to the task at hand? Second – and perhaps more remarkably – how do brains actively move their sensors to create sensory patterns of activity to enhance perception?

We use the fruit fly visual system to study both of these challenges in a powerful genetic model organism. Fruit flies move their retinas beneath the stationary lenses of their compound eyes using tiny muscles. These movements share surprising similarities with vertebrate eye movements – we observe retinal movements in response to visual motion that resemble the optokinetic reflex, as well as spontaneous, self-timed movements reminiscent of microsaccades in primates.

We now leverage fly retinal movements as a relatively simple model to examine the cellular underpinnings of active visual processing. We take advantage of the rich experimental toolbox in *Drosophila* and combine these efforts with comparative experiments in other insect species. Ultimately, we aim to understand how fly eye movements are controlled neuronally, how the brain processes input from moving eyes, and how visual perception benefits from these movements.

From innate motor programs to learned precision: Nest building in a shell-dwelling cichlid, *Lamprologus ocellatus*

Swantje **Grätsch**[1], Alessandro Dorigo[1], Vaishnavi Agarwal[1], Ash Parker[1], Manuel Stemmer[1], Abdelrahman Adel[1], Isabela Hernández Murcia[1], Alex Jordan[2], and Herwig Baier[1]
[1] **MPI-BI Department Genes – Circuits – Behavior**
[2] **MPI for Animal Behavior, Konstanz**

Nest-building behavior has evolved across many animal taxa – from termites to spiders and from birds to the great apes. And while this behavior has been studied in detail in a great variety of species, the neurogenetic underpinnings of it have remained obscure. We are investigating nest-building behavior in *Lamprologus ocellatus*, a shell-dwelling cichlid fish from Lake Tanganyika. *L. ocellatus* builds nests by manipulating empty snail shells, inserting them apex-down into the sandy substrate, and covering them with sand. Using computer vision and object detection algorithms, we show that they are doing this by executing a sequence of stereotyped behavioral motifs. Furthermore, by using immediate-early gene mapping, we have begun to localize the brain regions activated during nest building.

To determine whether this complex behavior is genetically programmed or learned, we examined nest building of shell-naïve fish that were reared in a shell-deprived environment. When presented with empty snail shells, these fish constructed nests executing the same behavioral motifs as experienced animals and their nests resembled the characteristic phenotype of *L. ocellatus* nests. However, shell-naïve individuals initially took longer to engage with the shells and needed more time to complete their nests. Following this first clumsy attempt, these individuals learned fast, and their following nest-building activity resembled experienced animals in duration and dexterity. Fascinatingly, in a different experimental approach, we found that a single building opportunity in an otherwise shell-deprived animal was sufficient to perform skilled nest construction even months later, suggesting the formation of a long-term memory by a single trial. In summary, we propose that nest-building behavior in *L. ocellatus* constitutes an innate program that is unfolded through one-trial motor learning.

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Human retinal organoids mimic the cholesterol storage disease Niemann-Pick type C in vitro

Patricia **Hoffelner**, Oliver Bludau[1], Valerio Zenatti[2], Lina Dinkel[2], Laura Sebastian Monasor[2], Dominik Paquet[3, 4], Matthias Prestel[2], Sabina Tahirovic[2], Antje Grosche[1]
[1] **LMU Department of Physiological Genomics, Biomedical Center**
[2] **German Center for Neurodegenerative Diseases (DZNE) Munich**
[3] **LMU Institute for Stroke and Dementia Research, University Hospital Munich**
[4] **Munich Cluster for Systems Neurology (SyNergy), Munich**

Introduction: Niemann-Pick type C (NPC) disease is caused by a malfunction of either of the two cholesterol transporters NPC1 (95 % of patients) or NPC2 (5 % of patients). NPC1 dysfunction in patients leads to intracellular accumulation of cholesterol in lipid vesicles and mitochondria with brain and liver being the most affected tissues resulting in neurodegeneration, visual impairment and ultimately premature death. We aim to mimic a retinal phenotype in NPC1-deficient human retinal organoids (hRO) co-cultured with iPSC-derived microglia.

Methods: hRO were generated from a healthy human iPSC line as well as a NPC1 mutant line (NPC1mut) derived from the latter. As neuroepithel-derived hRO do not contain hematopoietic lineage-derived microglia, we co-cultured hRO with iPSC-derived microglia from the same cell line. By morphometric analysis of different cell populations using immunolabeling, the cellular composition of hRO and the activation state of iMicroglia was investigated.

Results: First results indicate a shift in the cellular composition or differentiation pattern/timing upon NPC1 mutation. While there were more photoreceptors in NPC1mut hRO (indicated by an increased recoverin intensity and a thicker ONL), there is a tendency to less neurons of the INL (indicated by less calretinin and calbindin positive cells). In contrast, no differences between both lines were found for Müller cells (Vimentin) and VGlut1 (Synapses). 18 kDa translocator protein (TSPO), which is hypothesized to be a mitochondrial cholesterol transporter in Müller cells, is upregulated in NPC1mut hRO at later time points, indicating a possibly altered cholesterol shuttling upon NPC1 mutation.
In co-culture experiments, microglia readily integrate into hROs regardless of the genotype and could be maintained for up to 60 days. Cholesterol accumulation in microglia soma, a hallmark of NPC, was confirmed by filipin staining.

Conclusion and Outlook: Although initial retinogenesis and microglia integration appears to be unaffected by NPC1mut hROs, there may be an effect on the maturation and/or survival of distinct cell populations at later developmental time points. Since cell number does not necessarily indicate cell functionality, we will characterize hRO glial cells in terms of their functionality upon NPC1 loss in live cell assays already established in the lab.

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Single-neuronal signatures of short-term memory in the mouse and human prefrontal cortex

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Maintenance of sensory information in short-term memory is an important function of the prefrontal cortex (PFC) and the foundation of intelligent behaviour. Here, we investigated how differing task demands shape the underlying neuronal representations and directly compared mouse and human recordings at single-neuron resolution. We administered a spatial short-term memory task in two variants that differed with respect to behavioural requirements. In the delayed response (DR) task, spatial information (sample locations) could be directly translated to a choice (motor action after a delay), but did not need to be maintained in memory. In the working memory (WM) task, spatial information had to be actively maintained in memory, and the correct motor output could only be determined after a subsequently presented test location. Mice showed faster learning and higher performance in DR compared to WM tasks. In expert sessions of both tasks, we microendoscopically imaged medial PFC (mPFC) pyramidal neurons expressing GCaMP6f (1319 neurons from 6 mice). Individual neurons encoded spatial locations and the animals' behavioural choices, exhibiting monotonic and labelled line tuning patterns. Importantly, during presentation of the sample, the fraction of selective units increased earlier and more strongly in the WM task than in the DR task (peaking at 25% and 14%, respectively). More units also remained selective during the memory delay (17% and 8%, respectively). The same task was performed by a human subject chronically implanted with intracortical microelectrode arrays, with one placed in the middle frontal gyrus, the human analog of the rodent mPFC. DR trials were completed faster and more accurately than WM trials. Single neurons were tuned to task variables just as in mice. Importantly, the fraction of sample-selective units was again higher in the WM task than the DR task, both during sample presentation (peaking at 23% and 10%, respectively) and during the memory delay (17% and 32%, repectively). In summary, our results demonstrate that delayed response and working memory tasks, often indiscriminately grouped as short-term memory tasks, differ significantly with respect to their cognitive requirements and neuronal underpinnings. Strikingly, these differences are phlyogenetically conserved, underscoring the translational value of rodent models for our understanding of higher cognitive functions in humans.

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A model of place field reorganization during reward maximization

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When rodents learn to navigate in a novel environment, a high density of place fields emerges at reward locations, fields elongate against the trajectory, and individual fields change spatial selectivity while demonstrating stable behavior. Why place fields demonstrate these characteristic phenomena during learning remains elusive. We develop a normative framework using a reward maximization objective, whereby the temporal difference (TD) error drives place field reorganization to improve policy learning. Place fields are modeled using Gaussian radial basis functions to represent states in an environment, and directly synapse to an actorcritic for policy learning. Each field's amplitude, center, and width, as well as downstream weights, are updated online at each time step to maximize cumulative reward. We demonstrate that this framework unifies three disparate phenomena observed in navigation experiments. Furthermore, we show that these place field phenomena improve policy convergence when learning to navigate to a single target and relearning multiple new targets. To conclude, we develop a normative model that recapitulates several aspects of hippocampal place field learning dynamics and unifies mechanisms to offer testable predictions for future experiments.

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Paradoxical excess dopamine upon Locus Coeruleus axon loss in the hippocampus drives cognitive impairment in prodromal PD

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder, characterized by motor symptoms such as resting tremor, bradykinesia, and rigidity. Pathologically, misfolded α-synuclein (α-syn) aggregates into Lewy bodies, leading to neurodegeneration. Early diagnosis remains challenging, often occurring after substantial dopaminergic neuron loss in the substantia nigra pars compacta (SNc), highlighting the need for earlier diagnostic methods to slow disease progression.

Prodromal symptoms, including hyposmia, sleep disturbances, and psychiatric manifestations, are critical for identifying patients in the premotor stage. Notably, the locus coeruleus (LC), a small noradrenergic brainstem nucleus, controls physiological function impaired at early PD stages, suggesting a potential link between LC dysfunction and prodromal PD.

Here, we established a mouse model of prodromal PD by virally inducing A53T-α-syn expression in the LC. We utilized behavioral tests, immunohistochemistry and *in vivo* imaging techniques including fiber photometry, two-photon microscopy and microendoscopy to investigate LC involvement in non-motor symptoms PD stages.

Our findings reveal behavioral impairments in the A53T-α-syn animals, particularly in working memory and spatial learning during the Y-maze test. In the dorsal hippocampus, dopamine is predominantly released from LC axons. We hypothesize that altered dopamine release from the LC to the hippocampus underlies these deficits, supported by significant reductions in LC cell count, LC axonal degeneration in hippocampal CA1/CA3 regions and changes in local dopamine concentration in CA1 observed *in vivo*. Paradoxically, we prove increased DA release despite LC axon loss.

These results suggest that A53T-α-syn overexpression in the LC induces neuronal loss and axonal degeneration in the hippocampus, potentially contributing to early cognitive impairment in PD via disrupted dopamine signaling. Further investigations are ongoing to elucidate the mechanisms linking LC degeneration to cognitive decline in PD.

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Hippocampal representations and their uses

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The hippocampus is critical for recollecting and imagining experiences. This is believed to involve voluntarily drawing from hippocampal memory representations of people, events, and places, including map-like representations of familiar environments. We developed a brain-machine interface to test whether rats can volitionally activate representations from such cognitive maps in a flexible, goal-directed manner. We found that rats can efficiently navigate or direct objects to arbitrary goal locations within a virtual reality arena solely by activating and sustaining appropriate hippocampal representations of remote places. We have also performed memory and decision-making experiments in freely moving rats in which the animals activate planning-related, remote activations of the hippocampus. These results should lead to insight into the mechanisms underlying memory recall, mental simulation and planning, and imagination.

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Representational stability despite sustained circuit disinhibition in mouse visual cortex

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Neuronal representations in cortex are not fixed but gradually change over time – a phenomenon known as representational drift. While several studies have characterized the phenomenology of drift, its underlying mechanisms remain unclear. The preferred orientation of neurons in adult mouse primary visual cortex offers a well-suited model system for investigating the principles that govern stable feature representations. It offers both a detailed understanding of the underlying circuitry and shows moderate but reliable representational drift.

Inhibitory interneurons, particularly parvalbumin-positive (PV) cells, are strong candidates for regulating drift of orientation preference, given their central role in controlling pyramidal neuron excitability and modulating plasticity across development. PV interneuron activity sharpens excitatory tuning, and since broader tuning curves have been linked to greater drift in a computational model, we hypothesized that PV interneuron activity stabilizes orientation representations by limiting the tuning width of excitatory neurons.

To test this, we chemogenetically reduced PV interneuron activity in the primary visual cortex of adult mice for one week, while performing repeated two-photon calcium imaging to track the orientation preference of excitatory neurons over several weeks. As expected, PV interneuron inhibition increased pyramidal neuron activity, broadened tuning curves, and elevated pairwise correlations. Surprisingly, however, these circuit-level changes had no effect on the magnitude of representational drift.

Thus, while PV interneurons in primary visual cortex shape the activity and tuning of excitatory neurons, they do not govern the long-term stability of preferred orientation. Given that the local circuit architecture of excitatory and inhibitory neurons is largely conserved across cortical areas, our results suggest that increasing feature selectivity via inhibition does not limit representational drift.

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Interoceptive cardiac signals guide emotion state coding in the posterior insular cortex

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Emotions are evolutionary conserved functional states eliciting prominent changes in behavior and bodily physiology. Classical and modern theories of emotion suggest that emotions drive peripheral physiological responses, but also that changes in bodily signals themselves can influence the emergence and persistence of emotions. A key brain region implicated in emotions as well as interoception across species is the insular cortex. Specifically, the posterior Insular Cortex (pInsCtx) is a highly multimodal brain region processing and influencing interoception. Recent research has demonstrated that artificially elevating heart-rate increases pInsCtx activity and is sufficient to induce anxiety (Hsueh*, Chen*, et al., 2023). Furthermore, disrupting heart-to-brain communication impedes fear extinction, a process dependent on pInsCtx activity (Klein, et al., 2021). However, we currently lack a mechanistic understanding of how the pInsCtx processes cardiac signals at the cellular level, and how this processing influences emotions.

To investigate the relationship between heart-rate and pInsCtx activity, we conducted whole-cell and silicone probe recordings in awake, head-fixed mice. By monitoring heart-rate, pupil diameter, and locomotion, we characterized the behavioral and physiological responses associated with positive and aversive emotion states. Finally, we used the adrenergic beta-blocker metoprolol to manipulate heart-rate.

Our findings reveal that cardiac signals are the strongest modulator of insula activity. pInsCtx neurons can become tuned to single heartbeats, with both their membrane potential and firing rate modulated by the cardiac cycle. Cardio-insular coupling is increased during positive and aversive states, showing that cardiac signal processing by the insula is enhanced during emotion states. Finally, long-lasting decrease in heart-rate prevents the representation of cardiac signals by the pInsCtx and disrupts emotion state encoding at the neuronal and behavioral levels. Taken together, our study provides mechanistic evidence that processing of cardiac signals by the pInsCtx is necessary for the encoding of emotion states.

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Physiology versus pathology-related Tau transport into neurons

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Tau pathology is the most common co-pathology observed across neurodegenerative diseases and is strongly associated with neurodegeneration and cognitive decline. Although its underlying cause remains unresolved, accumulating evidence supports the hypothesis that Tau pathology propagates through a cell-to-cell transport mechanism, contributing to the progression of clinical symptoms. Therefore, elucidating the mechanisms driving this pathological spread and identifying effective strategies to block it are of critical importance. Despite substantial efforts, efficient inhibition of Tau propagation remains elusive. In this study, we investigated the neuronal internalization of extracellular Tau as a key step in the prion-like spreading model. We identified distinct uptake mechanisms for physiological monomeric Tau and pathology-relevant Tau aggregates. Using two independent human neuronal cell models, our data indicate that physiological Tau uptake is mediated by LDL receptor-related protein 1 (LRP1), whereas internalization of pathological Tau aggregates occurs via heparan sulfate proteoglycans. Interestingly, both forms utilize shared general endocytic pathways. These findings underscore the importance of specifically targeting disease-associated mechanisms to achieve robust inhibition of Tau spreading while minimizing off-target effects and preserving physiological processes.

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Stimulus sensitivity, not feature learning, explains olfactory scene analysis in mice

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Navigating natural environments requires animals to identify behaviorally relevant cues amidst complex and variable sensory inputs. In olfaction, this challenge is compounded by fluctuations in both environmental and source odors. Although mice can detect target odors embedded in mixtures of distracting background odors, it remains unclear whether this ability reflects flexible feature learning or sensitivity to stable, stimulus-driven cues. Here, we trained mice to perform an odor-guided two-alternative forced choice task in which target odors at varying concentrations were presented concurrently with randomly selected combinations of background odors. Behavioral performance declined systematically with decreasing target concentration but remained stable across background complexities, suggesting that perceptual limitations are primarily driven by target detectability rather than mixture complexity. To investigate the underlying mechanisms, we applied a biophysically grounded model of olfactory bulb glomerular responses, enabling precise control over stimulus composition, receptor sensitivity, and neural noise. Simulations revealed that target odor decodability was constrained chiefly by the ratio of receptor sensitivity to neural response noise, rather than background complexity – closely mirroring the behavioral data. These findings suggest that olfactory scene analysis is limited more by signal strength than by interference from background odors and highlight the robustness of the olfactory system in preserving target identity within complex sensory environments.

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Rotation-direction preference distinguishes path integration mechanisms in ring-attractors: A case study with zebrafish head-direction dells

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A head direction (HD) cell fires when an animal faces a particular azimuthal direction (Taube and Bassett 2003). Recurrent connections among HD cells create a ring-attractor network that continuously encodes HD (Ajabi et al. 2023).

Indeed, in the Drosophila HD system, three rings interact to linearly integrate angular head velocity (AHV), with two of the rings receiving countervailing velocity-dependent inputs (Turner-Evans et al. 2017). In contrast, for the desert locust, an alternative mechanism has been proposed (Zittrell et al. 2023; Pabst et al. 2024). There, velocity modulates synaptic strengths to integrate AHV.

Here, we put forward a theoretical framework that distinguishes the two models of AHV integration. The ring-attractor network that operates via countervailing inputs should consist of conjunctive HD×AHV cells, with one group of cells preferring clockwise rotations while the other group preferring counterclockwise rotations. In contrast, the activity of the network that operates via synaptic modulation is only affected by HD. This distinction allows us to infer the path integration mechanisms of the ring attractor network from single-cell activity without reference to the cells' structural connectivity.

Applied to Drosophila, our framework deduces the presence of three interacting rings, in agreement with the findings of Turner-Evans et al. (2017). In zebrafish, an activity bump rotates across anatomical structures as the HD changes (Petrucco et al. 2023), but the exact structure of the ring-attractor is still unknown. When we apply our approach to the zebrafish data, we find that the zebrafish HD system is composed of three functional rings, even though these rings are only partially segregated anatomically. Our findings suggest that HD systems exhibit a high similarity across distant species and show that our theoretical approach holds promise for inferring the ring-attractor structures in other species, too.

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Anatomically resolved oscillatory bursts reveal dynamic circuit motifs of thalamocortical activity during naturalistic stimulus viewing

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Natural vision requires circuit mechanisms which process complex spatiotemporal stimulus features in parallel. In the mammalian forebrain, one signature of circuit activation is fast oscillatory dynamics, reflected in the local field potential (LFP). Using data from the Allen Neuropixels Visual Coding project, we show that local visual features in naturalistic stimuli induce in mouse primary visual cortex (V1) retinotopically specific oscillations in various frequency bands and V1 layers. Specifically, layer 4 (L4) narrowband gamma was linked to luminance, low-gamma to optic flow, and L4/L5 epsilon oscillations to contrast. These feature-specific oscillations were associated with distinct translaminar spike-phase coupling patterns, which were conserved across a range of stimuli containing the relevant visual features, suggesting that they might constitute feature-specific circuit motifs. Our findings highlight visually induced fast oscillations as markers of dynamic circuit motifs, which may support differential and multiplexed coding of complex visual input and thalamocortical information propagation.

In search of a ‚common currency' circuit for social and non-social decision-making

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Social interactions shape many of our daily decisions, but studies of the neurobiology of decision-making typically lack social components. Since our real-world choices often require combining both social and non-social cues to make a single choice, these modalities theoretically must converge into a 'common currency', but how this occurs in our decision-making circuitry is not well understood.

To investigate how neural circuits and behavioral strategies combine social and non-social information to make single decisions, we developed a social foraging task for mice. Here, two mice simultaneously traverse a T-maze, making left or right choices for probabilistic water rewards. In contrast to when foraging alone, we found that mice in the social context were additionally influenced their partner's choices and outcomes when making decisions.

To directly measure the relative contributions of social and non-social information, we used a reinforcement learning framework and found that mice generally learned from their own experiences more than their partner's. These models also revealed that mice used different social strategies: while some mice learned from both the choice and outcome of their partner, others relied primarily on their partner's choice, regardless of outcome.

Then, to probe how social and non-social variables are encoded and combined in neural circuits, we recorded activity from the medial prefrontal cortex (mPFC), a region implicated in both decision-making and social behavior. Preliminary analyses suggest that mPFC neurons track multiple decision variables relevant to social and non-social choices.

Together, these preliminary findings promise to provide important insights into how social information is incorporated into our decision-making circuits.

Dynamics of cortical myelination

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Myelination is essential for cortical circuit function but can decay with age and in disease due to oligodendrocyte damage and death. This is exacerbated by reduced oligodendrocyte precursor cell (OPC)-mediated remyelination, which, in addition to cell senescence, has been ascribed to a non-permissive cortical neuropil lacking the pliability and signaling cues to support repair. Here, using single-cell ablations and intravital imaging in mice, we show that as cortical remyelination efficiency declines, OPCs lose motility, which can be modulated via CXCL12/CXCR4 signaling. Counter to prevailing notions, however, we find that even in old age, neuropil remains permissive and receptive to remyelination, which can be rekindled by a graded local demyelinating stimulus to induce a more juvenile dynamic state of OPCs. Our findings reveal the hitherto hidden remyelination potential of aged OPCs and a key role of OPC dynamics for cortical remyelination that could be targeted to improve myelin repair strategies.

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Gene supplementation or activation for treatment of Usher syndrome 1B

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Usher syndrome (USH) is the most common form of inherited deaf-blindness. According to the clinical phenotype and genetic background, different forms of USH can be distinguished. Mutations in the *MYO7A* gene are the predominant cause of USH1B, the most severe form of Usher syndrome. Currently, no therapy exists that can halt or mitigate retinal degeneration in USH1B patients. The *MYO7A* coding sequence (6.7 kb) exceeds the packaging capacity of adeno-associated viral (AAV) vectors for gene delivery, necessitating the employment of dual AAVs for gene supplementation. In this study, we employed our recently published dual AAV vector mRNA trans-splicing approach (REVeRT) to deliver *MYO7A* in mice, pigs, and human retinal organoids. Moreover, we used the same dual AAV approach to deliver CRISPRa designed to activate the endogenous murine *Myo7b* gene, a potential functional counterpart of MYO7A, in a conditional mouse model for USH1B.

Subretinal injection of dual REVeRT AAV vectors expressing human *MYO7A* resulted in high reconstitution efficiency of this gene in the retina of wild-type mice and pigs at the mRNA level. The transgenic MYO7A protein was found to be highly expressed and correctly localized to the retinal pigment epithelial (RPE) and photoreceptor cells of mice, pigs, and human retinal organoids. In a conditional *Myo7a*-KO-mouse model injected with the same dual REVeRT AAV vectors for *MYO7A* supplementation, we restored the MYO7A expression in the retina & RPE and the localization of melanosomes in RPE cells to wild-type levels.

Subretinal delivery of the dual REVeRT AAV vectors expressing CRISPRa to activate *Myo7b* resulted in high upregulation of this gene in the retina of wild-type mice at the mRNA and protein levels. In a conditional *Myo7a*-KO-mouse model subretinally injected with the same dual REVeRT AAV vectors for *Myo7b* activation, we partially restored the localization of melanosomes in RPE cells. The (sub)cellular localization of the activated MYO7B protein was similar to that of MYO7A.

Based on these results, we postulate that both strategies are, in principle, suitable for treating USH1B. Further experiments will show whether activating Myo7b can fully restore the molecular phenotype in the USH1B mouse model. Lastly, these results pave the way for future clinical trials aiming to supplement *MYO7A* or activate *MYO7B* in USH1B patients.

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Elevated brain legumain (LGMN) expression boosts TDP-43-like pathology in a progranulin (PGRN) deficient mouse model

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Mutations in the granulin (*GRN*) gene are causative for a subtype of frontotemporal dementia (FTD) with TDP-43-positive inclusions. *GRN* haploinsufficiency in patients results in cytoplasmic mis-localization, enhanced phosphorylation, proteolytic processing and aggregation of TDP-43. However, the link between PGRN deficiency and TDP-43 pathology remains elusive. Recent findings from our group indicate that in various model systems PGRN deficiency leads to enhanced maturation and activity of LGMN, a protease known to proteolytically process TDP-43 and other aggregating proteins in neurodegenerative diseases. To further study the role of LGMN in FTD *in vivo*, we overexpressed hLGMN in brain of *Grn* ko and wt mice using an adenoviral delivery system. Disease associated pathology was analysed with a focus on motor deficits, lysosomal activity and TDP-43 pathology. Grn ko mice overexpressing LGMN showed a severe decrease in motor function in a longitudinal Rotarod study. Overexpression of LGMN in *Grn* ko mice strongly affects the activity of lysosomal cathepsins. Additionally, DAM genes and cytokine mRNAs are elevated in LGMN overexpressing mice. Moreover, LGMN overexpression caused increased processing of TDP-43 and aggregation of phosphorylated TDP-43 as well as increased levels of plasma and CSF NfL. Thus, our results suggest that higher LGMN activity contributes to lysosomal abnormalities and microglial hyperactivation and is a driver of TDP-43 pathology in the context of PGRN deficiency and reducing LGMN activity might be a novel therapeutic approach to reduce increased processing and aggregation of TDP-43 in FTD.

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Actions in context: Contributions of scenes, phrases, and object affordances to action understanding

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Most actions occur in interaction with our environment, where scenes and objects provide cues for action possibilities. While scenes are best categorized by actions, completing actions usually requires objects. The scene grammar framework suggests that objects are grouped into „phrases," potentially reflecting functional organization. However, whether phrases are relevant for understanding actions remains largely unexplored. This study examines how objects and scene context influence action identification and scene-action fit assessment.

Across three experiments, participants viewed scenes, named actions, and identified necessary objects. Those used for the same actions were spatially closer than objects used for different actions, supporting the notion of functionally organized phrases. Sparse scenes lead to object-level actions (e.g., opening windows) while richer scenes evoked higher-level action-schemata involving multiple objects. Priming participants solely lexically elicited specific, higher-level actions predominantly (e.g., cooking with utensils and ingredients). Thus, the richness of our surroundings influences how we conceptualize actions; our scene concepts prioritize functions, whereas visual prompts shift the focus towards lower-level actions.

In an independent eye-tracking study, participants viewed scenes from the previous experiments, paired with the most frequently named and spatially distinct actions. Results showed a focus on objects in the action-related phrases when assessing a scene-action fit.

Our findings suggest that action identification and scene-action fit assessment rely on overlapping information. Participants predominantly selected objects within the same phrase when identifying items necessary for actions, and eye-tracking data confirmed a focus on these phrases during scene-action fit assessment. This highlights the functional organization of phrases in scenes.

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Tracking scent trails: algorithms and mechanisms

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Animals actively sense the environment to acquire features of interest to guide behaviors. We developed an experimental system to track mice as they follow dynamically varying odor trails drawn on an "infinite" paper treadmill. Mice spontaneously follow odor trails with no training but get better with experience. While mice with a single nostril blocked can track odor trails well, but with a lateral bias, animals with both nostrils intact but with interhemispheric communication disrupted within the brain were severely impaired. A respiratory sniff close to the trail triggered a rapid turn towards the trail in control mice, but not in those with impaired interhemispheric communication. Importantly, trail following was not simply reactive, but involved predictive strategies where mice form a short-term memory of the trail geometry and statistics. Our data indicate that mice combine immediate sensory information with an internal model of the environment to efficiently follow scent trails.

Neural representations of scene hierarchy

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We efficiently locate objects by narrowing our search using prior knowledge of our surroundings. For instance, to find a toothbrush in a bathroom, we focus on the sink. We suggest this previous knowledge is structured hierarchically, known as scene grammar. At the base of the hierarchy are local objects, smaller objects such as a toothbrush, followed by anchor objects that are predictive of the location of local objects, such as a sink. Combining local and anchor objects gives us phrases, and multiple phrases together form a scene. Using MEG, we investigated whether hierarchical scene representations, as described by scene grammar, are represented neurally. We recorded MEG data from 45 young adults (18-25 years, N female = 25). Participants were presented with an object as a world label or as a picture, followed by a blank period where participants imagined the object. Participants performed three tasks: In the first task participants rated how vividly they imagined the object, for the second task participants indicated whether they had seen a paperclip in the last 10 trials, and in the final task participants performed a search task. MEG data were analyzed using representational similarity analysis (RSA), comparing neural activity with models of object, phrase, and scene categories over time. The RSA results indicate that participants access object, phrase, and scene category information between 0.1 and 0.3s post-stimulus onset. These results indicate that participants do represent information contained at different points of the scene grammar hierarchy neurally.

Brain-Wide Compositionality and Learning Dynamics in Biological Agents

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Biological agents continually reconcile the internal states of their brain circuits with incoming sensory and environmental evidence to evaluate when and how to act. The brains of biological agents, including animals and humans, exploit many evolutionary innovations, chiefly modularity – observable at the level of anatomically-defined brain regions, cortical layers, and cell types among others – that can be repurposed in a compositional manner to endow the animal with a highly flexible behavioral repertoire. Accordingly, their behaviors show their own modularity, yet such behavioral modules seldom correspond directly to traditional notions of modularity in brains. It remains unclear how to link neural and behavioral modularity in a compositional manner. We propose a comprehensive framework – compositional modes – to identify overarching compositionality spanning specialized submodules, such as brain regions. Our framework directly links the behavioral repertoire with distributed patterns of population activity, brain-wide, at multiple concurrent spatial and temporal scales.

Using whole-brain recordings of zebrafish brains, we introduce an unsupervised pipeline based on neural network models, constrained by biological data, to reveal highly conserved compositional modes across individuals despite the naturalistic (spontaneous or task-independent) nature of their behaviors. These modes provided a scaffolding for other modes that account for the idiosyncratic behavior of each fish. We then demonstrate experimentally that compositional modes can be manipulated in a consistent manner by behavioral and pharmacological perturbations. Our results demonstrate that even natural behavior in different individuals can be decomposed and understood using a relatively small number of neurobehavioral modules – the compositional modes – and elucidate a compositional neural basis of behavior. This approach aligns with recent progress in understanding how reasoning capabilities and internal representational structures develop over the course of learning or training, offering insights into the modularity and flexibility in artificial and biological agents.

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Sparse Hebbian learning for high-capacity pattern discrimination in cerebellar ensembles

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In the cerebellar cortex, mossy fiber inputs expand massively to the granule cells, which are subsequently read out by Purkinje Cells. Many recent works view this circuit as a random feature model, with a single PC playing the role of the output. Experimental observations, however, suggest an important role for coordination between PCs during cerebellar learning and operation. Here, we extend a simple model of cerebellar cortex to include ensembles of many Purkinje cells converging on a downstream output. Introducing multiple PCs adds an additional hidden layer to the network, but it is unclear whether a biologically plausible learning rule can leverage this increased expressivity. We propose a "sparse Hebbian learning" rule, where strong weight updates are applied to randomly gated subsets of the Purkinje cells in a microzone. We find that this plausible learning rule is indeed sufficient to improve the performance of an ensemble relative to a single-decoder network, and prove that these benefits require both nonlinear Purkinje cell activation functions and sparse learning. In agreement, numerical experiments demonstrate that ensembles of nonlinear PCs can significantly outperform linear ensembles when learning is sparse. We also analyze network capacity: while a single-decoder network can recall a number of patterns which scales linearly with input dimensionality, ensembles can achieve capacity which scales exponentially with input dimensionality. Finally, we find that SHL can outperform backpropagation on a noisy pattern recall task, suggesting that sparse Hebbian learning finds high-margin solutions that are robust to noise. Our results suggest sparse learning as a computational principle underlying Purkinje cell coordination in the cerebellar cortex. Furthermore, because of its simplicity and favorable performance to backpropagation, sparse Hebbian learning may be applied for on-device learning in neuromorphic hardware.

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Sound decisions: Deciphering the influence of dynamic brain state transitions on auditory cortical processing during natural, unrestricted behavior

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The dynamic integration of external sensory inputs with rapidly shifting brain states underpins perception. However, the specific impact of these transient state fluctuations on neural processing during natural, unrestricted behavior and decision-making remains largely uncharacterized. Here, we utilized chronic multi-electrode recordings alongside an innovative kinematic analysis framework, and inferred moment-to-moment latent brain states in freely behaving animals to investigate how intrinsic cognitive and motor fluctuations shape neural activity in the primary auditory cortex during an auditory change-detection task. Our results reveal that active task engagement and locomotion distinctly modulate auditory processing: while engagement reduces prolonged neuronal activity following stimulus presentation without compromising initial evoked activity, movement enhances these sustained responses. A generalized linear model confirmed that these behavioral variables are key predictors of cortical response variability. These findings advance our understanding of sensory coding by highlighting the dynamic and non-uniform influence of brain states on auditory processing, emphasizing the need for paradigms that capture the full complexity of natural behavior.

Mouse frontal cortical dopamine transients during cue-action-outcome association learning

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As a neurotransmitter with wide-ranging neuromodulatory effects, dopamine is essential for brain functions such as cognition, motivation, and reward. Studies show that midbrain dopamine neurons projecting to the medial prefrontal cortex (mPFC) and lateral orbitofrontal cortex (lOFC) influence high-level cognitive processes. These regions receive dopamine transients which are believed to be fundamental for reinforcement learning. Here, we examined the time course of dopaminergic transients in mouse mPFC and lOFC during abstract associative learning in order to investigate how frontal dopaminergic signatures evolve with increasing task competency. We trained mice (n = 23) on an auditory decision-making task with implicit rule switches, requiring the forming of associations between auditory cues (tones varying along the dimension of location and frequency) and motor responses to obtain rewards. Using the fluorescent dopamine sensor GRAB DA3h, we conducted subsecond measurements of dopaminergic signals with fiber photometry over the course of several months while the animals learned the different rules. Dopamine responses during cue presentation and reward consumption varied with the animals' task proficiency. In both regions, reward-triggered dopaminergic transients were largest in novice animals and decreased as the animals became experts. This effect was strongest for the first task rule. In contrast, omission of rewards in error trials triggered a reduction of dopamine levels, which also scaled with performance. This suggests that frontal dopamine contributes to modifying behavior based on feedback and reinforces learning. Dopamine activity was also triggered by auditory cues, particularly in the mPFC. After rule switches, cue triggered-dopamine transients were indicative of reward anticipation in the mPFC but, interestingly, not in the lOFC. In summary, our results suggest differential involvement of the mPFC and lOFC in cue-action association learning.

The late-onset Alzheimer's disease risk variant S209F ABI3 disrupts the recruitment of the scaffold protein 14-3-3γ to the WAVE regulatory complex

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Alzheimer's disease (AD) is the foremost cause of dementia and, despite recent breakthroughs, few therapeutic options are currently available. Genome-wide association studies have identified AD risk variants in several microglial genes, which could in turn emerge as druggable targets. One of these is ABI3, a cytoskeletal regulator whose S209F mutation was shown to increase late-onset AD risk. Our goal is a detailed molecular characterization of the interaction and post-translational modification landscape of wild-type and S209F ABI3, in order to understand its molecular underpinnings in health and disease.

Through the use of various biochemical methods, including detergent fractionation, size-exclusion chromatography, immunoprecipitation, and blue native gel electrophoresis, we establish ABI3 as an integral component of the WAVE regulatory complex (WRC), existing in an equilibrium with the "canonical" WRC containing its paralog ABI1. We show that the S209F mutation disrupts the physiological phosphorylation pattern of ABI3, reducing pSer216, and, to a lesser extent, pSer203 and pThr225. While phosphorylated ABI3 is enriched in the WRC-associated ABI3 pool, S209F ABI3 doesn't appear to have a reduced affinity towards the WRC, either in overexpression or endogenously. Rather, it shows a drastic reduction in the engagement of the pSer/pThr-binding scaffold protein 14-3-3γ.

We propose a model in which the S209F mutation, by disrupting the phosphorylation of Ser216, prevents the recruitment of the scaffold protein 14-3-3γ to the WRC, likely resulting in a loss-of-function phenotype. Further work will investigate the cytoskeletal changes associated with S209F ABI3 and characterize which other cellular components are recruited to the WRC by 14-3-3γ.

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Representational advantages of distributional reinforcement learning

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Efficient behavior often requires considering the statistical structure of the environment. For example, when navigating through environments with stochastic rewards, it might be preferable to remain in regions in which rewards are less variable, even if they are also smaller. Despite this, traditional reinforcement learning (RL) models of human and animal behavior only learn average reward, ignoring potentially useful stochastic information. Recent distributional RL (dRL) algorithms overcome these limitations by learning entire reward distributions, achieving state-of-the-art performance – even in environments where agents need only act on average rewards. Moreover, the predicted neural correlates of dRL algorithms were recently confirmed in mammalian reward learning areas. This suggests that dRL implements a more robust and efficient learning strategy, but the exact mechanisms underlying these advantages remain unknown. We investigate how artificial neural networks trained with dRL objectives learn structured representations of rewards and states and how these representations differ from those learned by traditional RL models. Using tasks inspired by navigation and foraging – where agents face multimodal rewards or ambiguous sensory cues – we analyze how distributional learning shapes exploration, state encoding, and generalization to new environments. Our findings suggest that learned state representations allow for faster transfer learning across environments with different reward statistics, and faster adaptation when these statistics change. Our work offers testable predictions for how biological circuits learn to represent distributional information and advances our understanding of dRL algorithms.

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Large-scale extracellular recordings reveal right-hemispheric language processing in aphasia

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The human language system is predominantly associated with the left hemisphere. Damage to left brain regions typically results in language impairment (aphasia). As patients regain language abilities, linguistic functions potentially redistribute to other brain regions, for example in the right hemisphere. To gain an in-depth understanding of the right hemisphere's role in residual language following brain injury, we chronically implanted a patient with stroke-induced aphasia with four intracortical micro-electrode arrays (totaling 256 channels) in right hemispheric regions homotopic to the language network, namely the inferior frontal gyrus (IFG), middle frontal gyrus (MFG), supramarginal gyrus (SMG) and angular gyrus (AG). Over several months, the patient performed word repetition, comprehension and naming tasks while we recorded large-scale extracellular neuronal activity from more than 10.000 single and multi-units. In line with symptoms of non-fluent aphasia, behavioral performance was high in comprehension and repetition, yet low in naming.

The majority of recorded units (60% in IFG, 77% in MFG, 57% in SMG, and 80% in AG) showed modulations of their activity with regard to the performed language task. These modulations were region- and event-specific, i.e. varied with electrode and task epoch and carried information about the individual word being processed. Furthermore, the neuronal responses were dissociable from purely sensorimotor-driven activity by triangulating response profiles across the three language tasks. For example, clusters of units in SMG encoded word information in naming, but not when repeating or viewing the same stimuli in the comprehension task.

Overall, our findings lend unique insights into the right hemisphere's role in post-stroke language functions. Understanding the neuronal mechanisms of language reorganisation will pave the way for novel treatments for language disorders. Our findings also highlight the potential of right-hemispheric neuronal resources to be leveraged for verbal communication in individuals with aphasia.

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Octopus "taste by touch" chemosensation is mediated by environmental microbiomes

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Three billion years after bacterial life originated, animals diverged from their protistan ancestors and began to evolve in this bacterial world. Captivating examples of interkingdom symbioses demonstrate the ramifications of animal and bacterial relationships across organ systems including those for digestion, immunity, and neural function. Despite the ubiquity of these interactions, how these pairings came to be and the chemical effectors that drive their physiological impacts are less well understood. In my postdoctoral studies, I have developed a conceptual and methodological framework that deploys animal chemoreceptors to discover bacterial chemicals that inform animal sensation of the bacterial world. In my current research, I explore how animals interrogate environmental microbiomes for sensory navigation using octopus as a model system. Octopuses use "taste by touch" chemotactile receptors (CRs) to explore the seafloor, but how they distinguish meaningful surfaces from the rocks and crevices they encounter is unknown. I find that secreted signals from microbiomes of ecologically relevant surfaces activate CRs to guide octopus behavior. Distinct molecules isolated from specific bacterial strains located on prey or eggs bind single CRs in subtly different structural conformations to elicit distinct mechanisms of receptor activation, ion permeation and signal transduction, and maternal care and predation behavior. From this work, I conclude that microbiomes on ecological surfaces act at the level of primary sensory receptors to inform navigation behavior. The study supports the future application of my framework across additional interdomain interactions to uncover chemical effectors that will broadly inform how animals evolved in a bacterial world.

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The entorhinal cortex's phase code for spatial navigation

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Grid cells in medial entorhinal cortex not only show spatially organized firing but also systematic phase advances and delays with respect to the population's multi-unit activity (MUA), which exhibits regular peaks every 120 milliseconds (theta-rhythm). Based on an analysis of 483 grid cells from Gardner et al. (2022), cells' phase- and firing-patterns fall into different classes. Conjunctive grid cells that are tuned both to head direction and spatial location tend to be phase-locked to the MUA. Other grid cells fire 180 degrees out of phase with the MUA. Most non-conjunctive grid cells, though, harbor a hidden head-direction signal in the temporal phase relative to the MUA. These cells often fire rapid bursts of spikes whose timing is a function of both head direction and spatial position, thereby multiplexing body-centered and world-centered information. The ensemble activity, measured in terms of the temporal phases, spans a 3-torus composed of two loops for the spatial coordinates and one loop for the head direction. By exploiting dihedral symmetries, we show how an ideal observer can decode these timing.

Thalamic coordination of vision in action

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For accurate perception and motor control, an animal must distinguish between sensory experiences elicited by external stimuli and those elicited by its own actions. The diversity of behaviors and their complex influences on the senses make this distinction challenging. Here, we uncover an action–cue hub that coordinates motor commands with visual processing in the brain's first visual relay – the superior colliculus (SC). We show that the ventral lateral geniculate nucleus (vLGN) acts as a corollary discharge center, integrating visual translational optic flow signals with motor copies from saccades, locomotion and pupil dynamics. The vLGN relays these signals to correct action-specific visual distortions and to refine perception, as shown for the SC and in a depth-estimation task. Simultaneously, brain-wide vLGN projections drive corrective actions necessary for accurate visuomotor control. Our results reveal an extended corollary discharge architecture that refines early visual transformations and coordinates actions via a distributed hub-and-spoke network to enable visual perception during action.

Behavioral and neuronal correlates of exploration and goal-directed avigation

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The balance between exploration and exploitation is crucial for an animal's survival, guiding the transition between gathering and using information. However, neither the behavioral features that characterize these states and their neural correlates have been elusive. Extending previous studies in our previous work, we identified a set of behavioral features that are associated with exploratory states: sniffing, associated rhythmic head movement, and low head pitch.

Conversely, the departure from this default "low" state of intense orofacial sampling to a "high" state is associated with slower breathing and high head pitch. Interestingly, these two states give rise to remapping of the hippocampal spatial representation.

In this study we extend this work in two directions. First, we analyzed rat behavioral features in a spatial memory task to identify the functional correlates of the two states. Multiple trajectory features distinguished between exploratory and goal-directed phases of the task, which in turn were predominantly associated with the "low" and "high" states. Second, we extended the analysis of the neural correlates of the behavioral states to a different allocentric spatial representation, a head direction system in the PostSubiculum of the mouse. We found similar remapping of head-direction cells between exploration and goal-directed states. We demonstrate it both at the single-neuron firing rate and preferred direction, and at population level via Baysian decoding and low-dimensional manifold analyses.

Our results demonstrate that distributed spatial allocentric representation is spontaneous fluctuating between exploration and goal-directed states in behaving rodents. Understanding this relationship provides new insights and the link between animal behavior, learning and spatial cognition.

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Muscles have feelings too – proprioception in healthy and diseased muscle

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Neuromuscular diseases encompass a broad and heterogeneous group of disorders that affect the peripheral nervous system and compromise skeletal muscle function. While research has focused on motor impairments associated with these conditions, growing evidence suggests that proprioceptive deficits, particularly those involving muscle spindle dysfunction, may play a significant role in disease progression and symptomatology. Proprioception is the body's sense of position and movement and is essential for maintaining balance, coordinated movement, and postural stability. Among the few specialized mechanosensory receptors that contribute to proprioception, muscle spindles are by far the most important. These encapsulated receptors are located within skeletal muscles and detect changes in muscle length, relaying that information to the central nervous system via sensory afferents, and are crucial in reflex arcs and fine motor control.

Despite their importance, muscle spindle function remains largely unexplored in the context of neuromuscular diseases, particularly at the molecular level. We hypothesised that muscle spindle dysfunction could contribute to the proprioceptive impairments and increased risk of falls observed in patients with these disorders. To investigate this, we examined mouse models of two distinct neuromuscular diseases – Pompe disease and Friedreich's Ataxia, using a combination of behavioural assays, functional proprioceptive tests, and detailed morphological analyses of muscle spindles.

Our findings reveal that both muscle spindle structure and sensory function are compromised in these models. We observed altered intrafusal fibre morphology and altered afferent signalling from muscle spindles. These deficits correlated with impairments in balance, gait, and coordination, suggesting a strong link between muscle spindle dysfunction and proprioceptive symptoms. Importantly, these results point to muscle spindle pathology not only as a secondary effect of muscle weakness or motor neuron loss, but as a contributing factor to the overall neuromuscular phenotype.

Our work illustrates the underappreciated role of proprioceptive dysfunction in neuromuscular disease and indicates the need for greater attention to sensory components in both research and clinical contexts. Understanding the mechanisms underlying impaired muscle spindle function could provide new therapeutic interventions aimed at preserving proprioceptive integrity, preventing falls, and prolonging motor independence in patients. Ultimately, our results support a broader and more integrated view of neuromuscular disease pathophysiology that includes both motor and sensory function of muscle tissue.

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Linking neural representations to precise perception: Insights from a naturalistic paradigm for studying sound duration discrimination

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Processing sound duration is a crucial aspect for comprehending speech and context, such as when listening to a podcast or music. However, the connection between perceptual judgments and the neural processing of sound duration remains ambiguous. Specifically, no distinct neural correlate has been identified for perceptual thresholds in duration discrimination. Previous studies on sound duration discrimination in rodents have consistently reported extraordinarily higher (approx. 2-3x) threshold levels compared to humans and other primates. This finding sharply contrasts with the notion of high temporal precision being a general hallmark of mammalian auditory processing, and raises the question to what extend other factors might be causing the reported high perceptual thresholds? Here, we investigate duration discrimination in gerbils using a paradigm that combines closed-loop auditory feedback during self-motion with natural free exploratory behavior, offering a more naturalistic way of probing perception and auditory processing. Remarkably, we observed that the animals could discriminate sounds that differed by only 5 to ~20ms in duration, matching human performance levels. To investigate neural processing motifs underlying this extraordinary perceptual discrimination ability, we conducted chronic extracellular recordings in the auditory cortex during task performance. Preliminary results show significant correlation between neural activity and the task-relevant saliency of the sound duration change. This suggests a neural correlate of the observed behavioral sensitivity on the early cortical level. Together, our findings provide valuable insights into the neural underpinnings of auditory perception during naturalistic behavior.

The **LMU-Harvard Young Scientists' Forum (YSF)** seeks to unite PhD students and Postdoctoral fellows from the Harvard University and the Ludwig-Maximilians-Universität (LMU Munich) with core faculty from the two universities to create a framework for an interdisciplinary exchange of ideas. The YSF was initiated as a yearly event in 2009 and is held alternately in Munich and Cambridge.

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