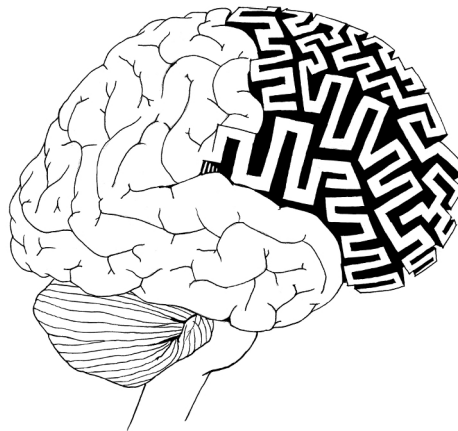


# AREADNE 2026

Research in Encoding and Decoding of Neural Ensembles  
Eliopoulos Conference Center, Milos, Greece  
23-27 June 2026



Conference Information  
Schedule and Program  
Invited Speaker Abstracts  
Poster Abstracts  
Attendee and Author Index

**AREADNE 2026**

*Research in Encoding and Decoding of Neural Ensembles*

*Eliopoulos Conference Center, Milos, Greece, 23–27 June 2026*

Nicholas G. Hatsopoulos, John S. Pezaris, editors

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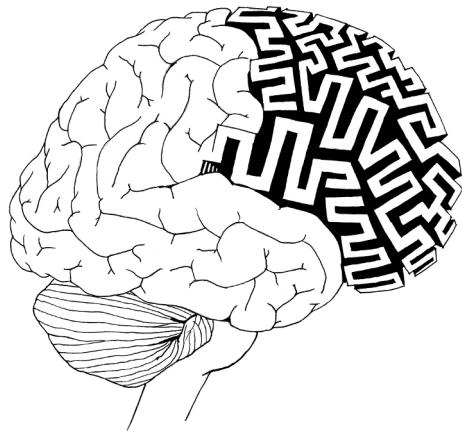
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# FOREWORD



## Foreword

It is a pleasure to mark the twentieth anniversary of AREADNE Conferences. Since 2006, we have brought together scientists working across systems neuroscience from a wide variety of backgrounds, working in nearly every area of the brain, with tools as varied as intracellular electrophysiology, bi-directional two-photon microscopy, and large language models. Despite twenty years of progress the central question remains the same: how do ensembles of neurons encode and manipulate information to establish perception, action, memory, and thought?

In his poem *Helen*, Seferis asks a disarming question: “What is a god? What is not a god? And what is there in between them?” [1]. The force of the line is epistemic rather than theological. It reminds us that the most dangerous errors arise from certainty that has gone unexamined.

As scientists, we are often pressured toward answers that are clean, authoritative, and final. But our calling is the opposite. It is to resist diktats, to be wary of inherited categories, and to remain attentive to what lies between them: the ambiguous, the unresolved, the inconvenient, the ignored. Science advances through interrogation of what appears to be self-evident, and through the difficult work of distinguishing understanding from persuasion. In that sense, the place in between that Seferis names is precisely where our work belongs: where truth is sought rather than asserted, and where explanation is earned rather than proclaimed.

AREADNE is a meeting devoted to those ideas, that place where data are considered neither to be self-explanatory nor as ornaments for preexisting claims; where models are judged by the understanding they produce, not by their elegance alone; where measurements are used to probe our assumptions, not merely confirm them. It is where competing descriptions are held in cooperative tension, and where disagreement, pursued amicably, drives progress rather than friction.

Here are our hopes for this meeting. We hope that our discussions will be vigorous and direct, because scientific progress requires clarity about what has, and has not been shown. We hope they will be gracious, because difficult work is almost always incomplete when it first becomes interesting. And we hope they will be exacting, because our understanding of the brain should not yield to rhetoric or fashion. Our knowledge will grow with vitality only through a healthy combination of rigorous observation and open discourse.

As we return to AREADNE twenty years after its first gathering, we are thankful to the organizing committee members who have contributed their efforts to curate a meeting that has become widely recognized with a reputation for excellence. We are thankful for the community that has propelled the conference with unwavering interest. And we are thankful for the sponsors who have supported our efforts with their sustained generosity. This anniversary is a reminder of why the meeting began: to bring together our love of Greece and of neuroscience to benefit the worldwide community of researchers devoted to understanding the brain, and ultimately to contribute to our understanding of the nervous system.



Nicholas G. Hatsopoulos, Ph.D.



John S. Pezaris, Ph.D.

1. Seferis, “Helen” from *Log Book III*, 1955, Ithaka.



**WELCOME**



## **Welcome**

Welcome to AREADNE 2026, the eleventh AREADNE Conference on Research in Encoding and Decoding of Neural Ensembles, and our 20th anniversary session.

A central challenge in neuroscience is to understand how the activity within networks of neurons gives rise to the higher-order functions of the brain including learning, memory, cognition, perception, action, and ultimately conscious awareness. Over fifty years of electrophysiological recordings in behaving animals have produced significant insights into what the firing patterns of single neurons encode in isolation, but many of the mysteries of how collections of neurons interact to perform these functions remain.

Technological advances have allowed us to glimpse into the global functioning of the brain. Tools such as multielectrode electrophysiology, multiphoton microscopy and connectomics have expanded our understanding beyond single neurons and into ensembles. We routinely observe the activity of dozens and even thousands of individual neurons simultaneously, and deduce the connectivity between them.

At the same time, our understanding of how neuronal ensembles carry information has allowed the development of brain-machine interfaces (BMIs) to enhance the capabilities of patients with sensory and motor deficits. Knowledge of how neuronal ensembles encode sensory stimuli has made it possible to develop perceptual BMIs for the hearing and visually impaired. Likewise, research in how neuronal ensembles decode motor intentions has resulted in motor BMIs by which people with severe motor disabilities can control external devices.

## **Conference Mission Statement**

There are three major goals of this conference. First and foremost, this conference is intended to bring scientific leaders from around the world to present their most recent findings on the functioning of neuronal ensembles. Second, the meeting provides an informal and beautiful setting on Milos in which attendees can discuss and share ideas outside of the presentations at the conference center to develop professional relationships and collaborations. Third, this conference continues our long-term goals to promote systems neuroscience within Greece by creating a forum for scientists from around the world to interact with Greek researchers and students.

## **Organizing Committee**

The Organizing Committee for AREADNE 2026 has been co-chaired by Nicholas Hatsopoulos and John Pezaris, with highly-valued contributions from members Dora Angelaki, Kenny Blum, Yiota Poirazi, Thanos Siapas, Jiannis Taxidis, and Andreas Tolia.

Local organization effort has been provided by Nike Makres with assistance from Olympia Tziampiri and Graydon Genieser.

## **Sponsors and Support**

Our conference is being sponsored with generous gifts from Mrs. Daphne Hatsopoulos through the NIMA Foundation, The Gatsby Charitable Foundation, and Blackrock Neurotech to the University of Chicago, along with a gift from the Simons Foundation to the Massachusetts General

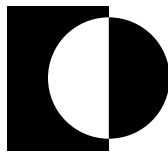
Hospital. We have received generous in-kind support from Foley & Lardner, LLP, and both the University of Chicago and Massachusetts General Hospital, where the conference is co-administered.



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Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors, for invited or contributed material, and The AREADNE Foundation, Inc., for organizational material, and do not necessarily reflect the views of any of our sponsoring individuals or institutions.

### **The Myth of Ariadne**

The conference name AREADNE is a combination of the conference title, Research in Encoding and Decoding of Neural Ensembles, and the name of the mythological figure Ariadne. Our brain-to-maze logo was inspired by the central role Ariadne played in the myth of Theseus and the Labyrinth.

In Greek Mythology, Ariadne was the daughter of Minos, king of Crete. King Minos built a large, intricate maze called the Labyrinth to house the Minotaur, a fearsome creature that was half bull, half human. Any who attempted to face the Minotaur perished, either by becoming lost

in the maze or from the Minotaur's vicious attack. When the hero Theseus came from Athens to slay the Minotaur, Ariadne gave him a sword and a ball of silk thread. Theseus tied one end of the thread at the Labyrinth entrance and unwound it as he went along, so that after he had found and slain the Minotaur, he could escape from the maze by following the thread back out.



## **LOCAL INFORMATION**



## Local Information

We have assembled a small selection of local information on Adámas and the island of Milos. For more information, select among the many guidebooks and web sites written for travel in Milos.

### Restaurants

Greeks normally eat their evening meal quite late, with restaurants being busiest from 10 PM to midnight. The largest meal of the day is often lunch, leading naturally to the habitual afternoon siesta. Tipping at restaurants is not expected, as the cost of service is normally included in the price of the meal. Each euro symbol in the list below is about € 10.

#### *Restaurants in Adámas*

O! Hamos!	+30-22870-21672	€ €	traditional Greek
Yankos Restaurant	+30-22870-23615	€ € €	souvlaki stand
Nostos	+30-697-196-4981	€ € €	seafood, on the water
Alevromilos	+30-22870-23117	€ € €	modern Greek
O Zygos	+30-22870-23120	€	grilled meats
Mikros Apoplous	+30-22870-24207	€ € €	seafood, on the water
Flisvos	+30-22870-22275	€ € €	seafood, traditional Greek; by the port
Volta Restaurant	+30-22870-22858	€ € €	seafood, traditional Greek; by the port

#### *Restaurants and Bars in Plaka*

Archontoula	+30-22870-21384	€ €	traditional Greek food
Glaronisia	+30-22870-23480	€ €	Milos specialty
Kyra	+30-22870-27350	€ €	modern Greek food
Methysemi Politia	+30-22870-23100	€ € €	Greek grilled meats
Utopia Cafe-Bar	+30-22870-23678	€ €	great sunset view

### Recommended Activities

Milos offers many diversions, including excellent beaches, interesting ancient as well as modern history, high-quality museums, enticing restaurants, and, above all, natural beauty. Some ideas are given below.

#### *Mining Museum*

Open 10:00–14:00 and 18:00–21:00 (closed Mondays), +30-22870-22481, located on the main road in Adámas.

#### *Archeological Museum*

Open 08:30–15:30 Monday, Wednesday–Saturday; 09:00–22:00 Sunday; closed Tuesday, +30-22870-28026, located in Plaka.

#### *Catacombs of Milos*

Open 09:00–18:45 Monday–Sunday; closed Tuesday, +30-22870-21625, located near Trypiti. Among the most important early Christian monuments in Greece.

#### *Klima Village*

A charming fishing village with traditional colorful houses built right on the water's edge.

### *Trypiti Village*

A quaint village known for its windmills and the ancient theater of Milos.

### *Sulfur Mines*

Abandoned sulfur mines give a glimpse into the island's industrial past.

### *Sunset at Plaka*

Watch a breathtaking sunset from Utopia Cafe in Plaka, offering one of the best views on the island. If the bar is full, you can get the same view from the nearby churches.

## **Main Beaches**

The beaches on Milos are beautiful and varied. They appear both on the inner bay and around the outside of the island. Arrays of lounges and umbrellas that appear on many beaches are available for rent. A short while after sitting down, someone will approach you and ask for payment, often in cash. Typical rates are EUR 5 to 10 for the day, although some beaches can be significantly higher.

*Tsigrado Beach*, not suitable for children

*Firiplaka Beach*, narrow, pebbly, volcanic cliffs

*Provatas Beach*, family friendly, can get crowded

*Sarakiniko Beach*, small, the most photographed on Milos

*Papafragas Caves*, stunning, tiny, not suitable for small children

*Achivadolimni Beach*, longest sandy beach on Milos, shallow, family friendly

*Firopotamos Beach*, small-pebbled beach, family-friendly, no restaurants

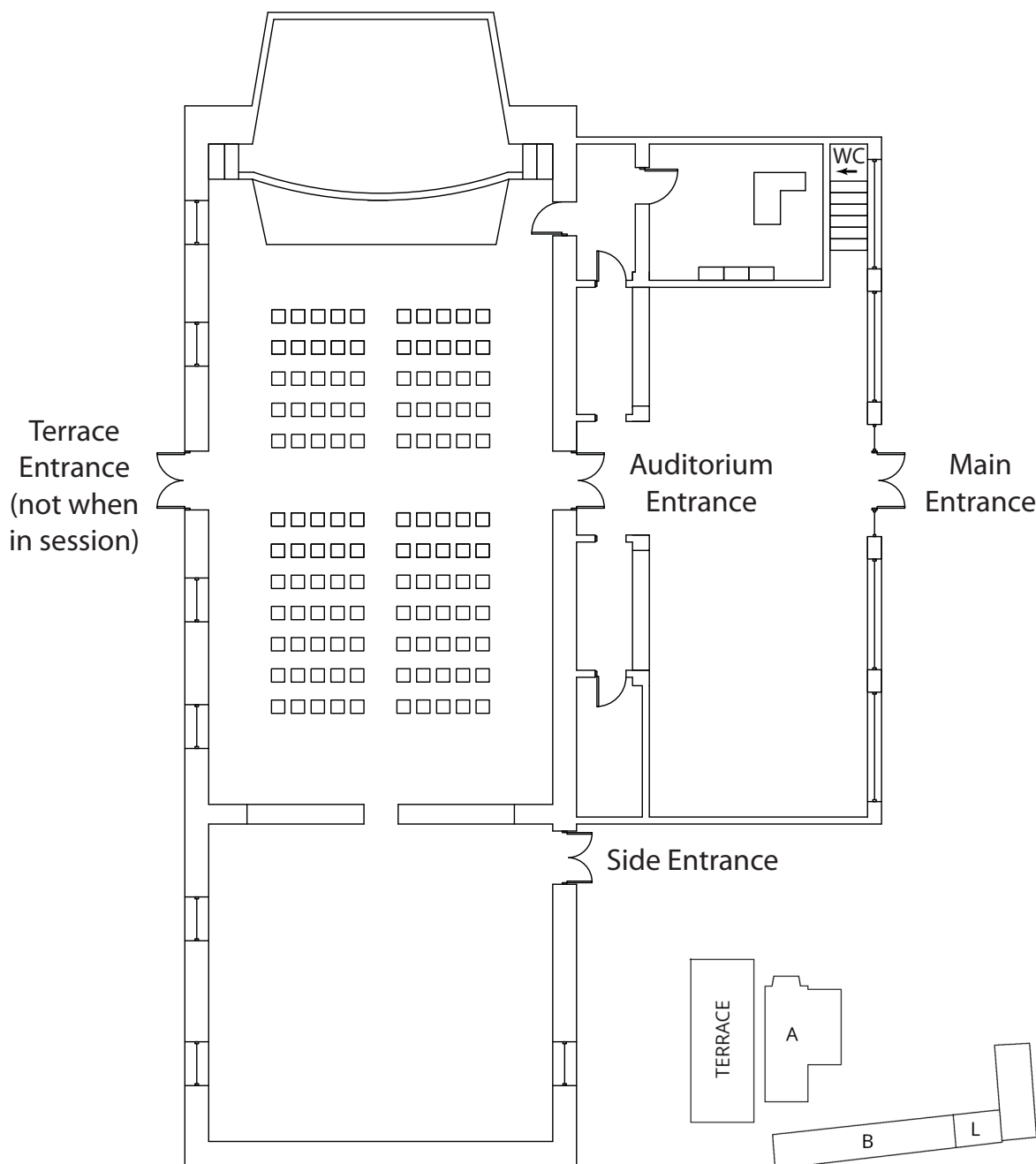
*Paleochori Beach*, most popular, water sports available

*Agia Kyriaki Beach*, sand and fine pebbles, no sun beds

### Conference Center Map

Oral presentations will be held in the main auditorium of Building A (map below) at the Eliopoulos Conference Center. Posters will be hung on stands placed on the terrace, or near the adjacent Building B (see inset), depending on the wind. Coffee breaks and lunches will be on the terrace or near Building B (L on the inset), again based on current conditions. Restrooms are in Building B and the lower level of Building A, while a first aid station is available in Building B, along with a room for extended internet use.

Please do not use the Terrace Entrance when we are in session to avoid disturbing the talks. Instead, please come in through either the Main or Side Entrances.





# **DAILY SCHEDULE AND PROGRAM**



## **Overall Schedule**

The schedule for the four-day conference follows the Greek lifestyle of having a long lunch, with the afternoon free for siestas or swimming, and a late dinner.

### *Tuesday*

19:30-22:00 Welcome Reception and Registration

### *Wednesday*

08:00-08:45 Registration

08:45-09:00 Opening Remarks

09:00-12:30 Lectures and Coffee Break

12:30-14:00 Lunch

17:00-21:30 Lectures and Coffee Break, Posters

### *Thursday*

09:00-12:30 Lectures and Coffee Break

12:30-14:00 Lunch

17:00-21:30 Lectures and Coffee Break, Posters

### *Friday*

09:00-12:00 Optional Excursion (no lunch provided)

17:00-21:30 Lectures and Coffee Break, Posters

### *Saturday*

09:00-12:30 Lectures and Coffee Break

12:30-14:00 Lunch

17:00-19:00 Lectures and Coffee Break

19:00-19:15 Closing Remarks

20:30-24:00 Banquet Dinner at Kipos Cafe in Kipos Beach

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**TUESDAY, 23 JUNE 2026**

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19:30-22:00 welcome reception at Eliopoulos Conference Center

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**WEDNESDAY, 24 JUNE 2026**

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08:00-08:45 registration

08:45-09:00 opening remarks

**MORNING SESSION** Andreas Tolia, moderator

09:00-09:45 **Naoshige Uchida** (Harvard University)  
*Neural circuits for learning to predict, 54*

09:45-10:30 **Julijana Gjorgjieva** (Technical University of Munich)  
*Shaping neural circuit structure and function through biologically plausible learning, 39*

10:30-11:00 coffee break

11:00-11:45 **Brent Doiron** (University of Chicago)  
*The geometry of globally optimal neural representations, 37*

11:45-12:30 **Nina Miolane** (University of California, Santa Barbara)  
*Fourier intelligence in brains and machines, 48*

12:30-14:00 lunch

**AFTERNOON SESSION** Nicholas Hatsopoulos, moderator

17:00-17:45 **Stephanie Palmer** (University of Chicago)  
*What to throw away? How brains make efficient codes, 49*

17:45-18:15 coffee and light snacks

18:15-19:00 **Emmanouil Froudarakis** (University of Crete)  
*From neural activity to behavior: Shaping object representations in the mouse brain, 38*

19:00-19:20 **Desmond Patterson** (University of Texas at Austin)  
*A talk in two parts: The geology of Milos, and the 2025 Aegean seismic swarm, 50*

19:20-19:40 **Andronike Makres** (University of the Peloponnese)  
*Who is Venus de Milo?, 46*

20:00-21:30 Poster Session (i), listed by presenting author

**Amirmasoud Ahmadi** (MPI Biological Intelligence)

*Spectral-temporal neuronal selectivity in the awake zebra finch auditory fore-brain, 57*

**Stamatios Aliprantis** (FORTH, IMBB and University of Crete Medical School)

*Are dynamics necessary in a temporally coherent world? Probing temporal continuity in mice during visual object recognition, 59*

**Nikolaos Armeniakos** (Friedrich Miescher Institute)

*Amygdala dynamics during value-based decision-making, 62*

**Katharina Bracher** (University of Freiburg)

*Unbiased detection of neural sequences, 67*

**Diana Burk** (National Institute of Mental Health)

*Coordinated neural activity across the limbic system predicts motivational state, 68*

**R. James Cotton** (Shirley Ryan AbilityLab / Northwestern University)

*Seeing the neural control of movement through neuromuscular imitation learning to analyze neurologic gait impairments, 74*

**Maria Diamantaki** (IMBB-FORTH)

*Ethopy: Reproducible behavioral neuroscience, 76*

**Dimokratis Karamanlis** (University of Geneva)

*Prefrontal correlates of a social learning strategy during joint decision-making in mice, 82*

**Julia Leeman** (Duke University)

*Neural multiplexing versus place coding: Multiplexing steps in when most needed, 86*

**Adamantia-Ilianna Mantouka** (University of Crete Medical School / FORTH)

*Local and global visual processing in the mouse brain: From receptive fields to population codes, 89*

**Savannah Maw** (University of California, Davis)

*Dopamine and stimulus discrimination in the dentate gyrus, 90*

**James McAllister** (Ulster University)

*Exact dynamics of linear recurrent neural networks in cognitive tasks, 91*

**Anahita Nazari** (German Primate Center)

*Neural correlates of continuous perceptual decisions in rhesus macaques in solo and social context, 92*

**Christos Paschalidis** (IMBB-FORTH / University of Crete School of Medicine)  
*Dimensionality and geometry of object coding across the mouse visual hierarchy, 97*

**Alessio Quaresima** (Hearing Institute – Pasteur Institute)  
*Data optimized biophysical model identifies parallel subnetworks underlying functional and statistical properties of auditory cortex, 99*

**Daniel Ramirez Gordillo** (University of Colorado Anschutz Medical Campus)  
*Restoring CaMKII function in hippocampus and olfactory bulb enables odor association learning in CaMKIIalpha knockout mice, 96*

**Dina Theodosiadou** (University of Bath)  
*Loss-based directed graph constraints for recurrent flow network dynamics, 109*

**Aleksejs Timčenko** (Hertie Institute for AI in Brain Health)  
*Low-dimensional population codes for natural videos in mouse superior colliculus, 110*

**Christopher Trombley** (University of Chicago)  
*Progressive changes in motor cortical replay across extended motor learning, 111*

**Sofia Zangila** (INSERM PACA)  
*Non-monotonic emergence of behavioral modulation in a neonatal cortical circuit, 119*

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**THURSDAY, 25 JUNE 2026**

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**MORNING SESSION** Maneesh Sahani, moderator

- 09:00-09:45 **Dmitriy Aronov** (Columbia University / HHMI)  
*A neural code for episodic memories in food-caching chickadees, 32*
- 09:45-10:30 **Mark Cembrowski** (University of British Columbia)  
*Cholinergic drive toggles cell-type-specific output modes of the hippocampus, 36*
- 10:30-11:00 coffee break
- 11:00-11:45 **Attila Losonczy** (University of Texas Southwestern Medical School)  
*The meaning of dendrites: Dynamic subcellular representation of the past and the future in the hippocampus, 45*
- 11:45-12:30 **Jaideep Bains** (Krembil Brain Institute, University Health Network)  
*Hypothalamic CRH neurons sustain defensive escape to modulate outcome-driven strategy update, 33*
- 12:30-14:00 lunch

**AFTERNOON SESSION** Alexander Ecker, moderator

- 17:00-17:45 **Christian Hansel** (University of Chicago)  
*The little brain supervises learning in the big brain, 40*
- 17:45-18:15 coffee and light snacks
- 18:15-19:00 **Jennifer Raymond** (Stanford University)  
*Cerebellar metaplasticity, 51*
- 19:00-19:45 **Andreas Tolias** (Stanford University)  
*Decrypting the brain with AI, 53*
- 20:00-21:30 Poster Session (ii), listed by presenting author
- Athina Apostolelli** (University College London)  
*Structural learning of reward patterns in the mouse prefrontal cortex, 60*
- Aditi Aravind** (University of Crete / FORTH)  
*Altered functional connectivity in V1 of MECP2 duplication syndrome mice during spontaneous conditions, 61*
- Haicang Chen** (Radboud University)  
*Decoding V1 surround modulation: Decoding performance negatively correlates with contextual receptive-field center predictability, 72*

**Alexander Ecker** (University of Göttingen)

*Omnimouse: Scaling properties of multi-modal, multi-task brain models on 150B neural tokens, 115*

**Clemens Engelhardt** (University of Cologne)

*Mechanisms of cerebellar feed-forward inhibition in a spiking attractor model of primate motor cortex, 77*

**Arno Feinstein** (Aix Marseille Université)

*Segregation of sensory, cognitive control and decision representation across V4, LIP and PFC under distractor competition, 78*

**Emmanouil Giannakakis** (Imperial College London)

*Network structure as an inductive bias for meta-learned plasticity rules in a connectome constrained network, 79*

**Sven Goedeke** (University of Freiburg)

*Differential geometry of neural manifolds: Connecting network mechanisms to information encoding, 80*

**Sze Chai Kwok** (Duke Kunshan University)

*Behavioral and neural representations of intertwined episodes in the macaque, 83*

**Laura López-Galdo** (University of Strasbourg)

*Coordinated multilaminar dynamics underlie multiplexed computation in motor cortex, 88*

**Konstantinos Ladakis** (University of Crete / FORTH)

*From ensembles in visual cortex to deep spiking networks: Conserved functional connectivity properties, 84*

**Nina Nellen** (Goettingen University)

*Learning to cluster neuronal function, 93*

**Virginie Oberto** (KU Leuven)

*Investigating task-dependent modulation of visual cortical activity using large-scale recordings and optogenetics, 94*

**Riina Pöllänen** (Aalto University)

*Cortical dynamics of pose invariance during visual object recognition, 98*

**Mario Alexios Savaglio** (University of Crete / FORTH)

*Temporal robustness and brain-state stability of functional connectivity in the mouse visual hierarchy, 102*

**Paolo Scaccia** (Institut de la Vision - Sorbonne Université)

*Large correlated noise improves decoding for similarly tuned neurons, 103*

**Shushruth Shushruth** (University of Pittsburgh)

*Neural correlates of the interaction of working memory and decision-making in prefrontal cortex, 104*

**Polina Turishcheva** (University of Goettingen)

*Early results linking neuronal function and morphology in mouse visual cortex, 112*

**Klaus Wimmer** (Centre de Recerca Matemàtica)

*Non-uniform spatial integration of motion signals in area MT shapes motion perception, 116*

**Xiaoran Yuan** (LMU Munich)

*Nonstationary dynamics of sensory population codes during active behavior, 117*

**Pietro Zamberlan** (Institut de la Vision – Sorbonne Université)

*Predicting neural responses using scalable Gaussian processes in closed-loop, 118*

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**FRIDAY, 26 JUNE 2026**

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09:00–12:00 optional excursion (no lunch provided)  
*Sign-ups taken on Wednesday and Thursday.*

**AFTERNOON SESSION** John Pezaris, moderator

17:00–17:45 **Michael Hausser** (University College London / HKU)  
*Swaying decisions with light, 41*

17:45–18:15 coffee and light snacks

18:15–19:00 **Hillel Adesnik** (University of California, Berkeley)  
*Optogenetic network clamp reveals the features of neural dynamics that drive perception, 31*

19:00–19:45 **Farran Briggs** (NIH)  
*How cortical feedback influences visual thalamic neuronal activity, 34*

20:00–21:30 Poster Session (iii), listed by presenting author

**Ali Alamri** (University of Chicago)  
*Imagination strategies for generalizable brain computer interfaces, 58*

**Costas Anastassiou** (Cedars-Sinai / Caltech)  
*Cell type-specific neuronal dynamics revealed in the living human brain, 71*

**Abhishek Banerjee** (University of Oxford)  
*Reprogramming sensory cortex for adaptive task learning, 108*

**Joao Barbosa** (Neuromodulation Institute)  
*Distributed computations of flexible decisions, 63*

**Georgios Bardanikas** (Institut de Neurosciences de la Timone)  
*Movement anticipation modulates motor-parietal interactions during goal-directed movements, 64*

**Chiara Boscarino** (Institut de la Vision – Sorbonne Université)  
*Decoding retinal ensembles to improve vision restoration therapies, 65*

**Celia Bougou** (Caltech)  
*Neural representations of intuitive physics in human posterior parietal cortex, 66*

**Juan Salvador Calanni** (Institut de la Vision)  
*A barcode stimulus to classify retinal ganglion cell types, 69*

**Lamine Camara** (University of Chicago)

*Orofacial motor cortex preferentially encodes tongue posture, 70*

**Simone Ciceri** (TU Berlin)

*Innate development of cognitive functions and motor programs by chemoaffinity, 73*

**Ioannis Delis** (National Technical University of Athens)

*EEG signatures of multisensory processing in autism and schizophrenia, 75*

**Ralf Haefner** (University of Rochester)

*Task learning increases redundancy of V4 responses reflecting a flexible redistribution of information, 87*

**Anna-Maria Jürgensen** (University of Cambridge / Imperial College London)

*Diverse plasticity rules for temporal credit assignment in fly-connectome-based parallel learning circuits, 81*

**Alexandre Lainé** (Aix-Marseille Université – AMIDEX – INT)

*Population decoding of visual motion direction, 85*

**Timothée Proix** (ETH Zurich)

*Wave-spike interactions encode overt and imagined speech, 95*

**Maneesh Sahani** (Gatsby Computational Neuroscience Unit)

*Inference, manifolds, and learning, 100*

**Ophelie Saussus** (KU Leuven)

*Neural innovation reveals task-dependent (mis)alignment between neural intent and shared-control policies in iBCI navigation, 101*

**Shi-Hai (Scott) Sun** (Mass General Hospital)

*Single-nucleus transcriptomics reveals hidden heterogeneity in macaque LGN relay pathways, 106*

**Bahareh Taghizadeh** (Marburg University)

*Neural activity in the macaque lateral intraparietal area during a visual metronome saccade task, 107*

**Nikolaos Tzanakis** (University of Crete)

*Decoupling stimulus encoding from internal state dynamics in mouse visual cortex, 113*

**Ben von Hünenbein** (University of Bern)

*Brain-inspired computing for brain-computer interfacing, 105*

**Yuval Wasserman** (Weizmann Institute)

*Spatial coding going wild: High-dimensional neural manifolds in bats flying freely outdoors on a remote oceanic island, 114*

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**SATURDAY, 27 JUNE 2026**

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**MORNING SESSION** Tatiana Pasternak, moderator

09:00–09:45 **Mehrdad Jazayeri** (MIT)

*Adaptive problem solving in the primate frontal cortex, 43*

09:45–10:30 **Marie Carlén** (Karolinska Institutet)

*A prefrontal cortex map based on single neuron activity, 35*

10:30–11:00 coffee break

11:00–11:45 **Jennifer Linden** (University College London)

*The mechanisms of minding the gap: Neural coding at the limits of temporal acuity, 44*

11:45–12:30 **Michèle Insanally** (University of Pittsburgh School of Medicine)

*Contributions of heterogeneous cortical neuron responses to auditory perceptual learning, 42*

12:30–14:00 lunch

**AFTERNOON SESSION** Tatiana Pasternak, moderator

17:00–17:45 **Mackenzie Mathis** (EPFL)

*Neuro-musculoskeletal modeling reveals muscle-level neural dynamics of adaptive learning in sensorimotor cortex, 47*

17:45–18:15 coffee and light snacks

18:15–19:00 **Bill Rinaldi** (University of Chicago)

**Scott Imbrie** (University of Chicago)

**Marcus Gerhardt** (Blackrock Neurotech)

**Nicholas Hatsopoulos** (University of Chicago)

*Living with a brain-computer interface, 52*

19:00–19:15 closing remarks

20:30–24:00 banquet dinner at Kipos Cafe in Kipos Beach

**INVITED SPEAKER ABSTRACTS**  
**(in alphabetical order by speaker)**



## **OPTOGENETIC NETWORK CLAMP REVEALS THE FEATURES OF NEURAL DYNAMICS THAT DRIVE PERCEPTION**

*Daniel Quintana<sup>1,†</sup>, Hayley Bounds<sup>1</sup>, Julia Veit<sup>2</sup>, Hillel Adesnik<sup>1,3,\*</sup>,†*

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Whether the millisecond-timescale temporal dynamics of cortical activity drive perception has remained unresolved for decades. The obstacle is largely methodological: every available circuit perturbation that alters spike timing also changes mean activity, so rate codes and timing codes cannot be cleanly separated in causal experiments. To overcome this, we developed optogenetic network clamp that uses balanced, fast bidirectional optogenetics to inject arbitrary time-varying patterns of excitation and inhibition into a brain area while mitigating changes in spike rates. Neuropixels recordings in awake mouse visual cortex (V1) confirm that optogenetic network clamp can drive strong frequency-locked activity or whiten the spike and LFP power spectrum, all with minimal change in mean firing rate. Applying it during a visual contrast detection task in mice revealed a striking specificity in the features of cortical dynamics that visual perception depends on. Clamping the network into a balanced oscillatory state had no behavioral effect at any frequency tested, despite producing massive frequency-locked cortical activity. Balanced illumination with no temporal structure (square pulses), was also benign, even when red (silencing) and blue (stimulating) intensities were independently reshuffled across trials. By contrast, noisy balanced optogenetic input substantially impaired detection whether or not the red and blue waveforms were temporally correlated. Finally, injecting oscillatory structure, but with random phase perturbations, also disrupted behavior. Thus, the cortex tolerates large, structured perturbations of its temporal dynamics, but cannot tolerate randomization of fine-scale temporal structure — implicating endogenous fast dynamics, not merely mean activity, as a causal substrate of perception. More broadly, network clamp offers a general route to causally dissect which features of neural dynamics underlie behavior and cognition across the brain.

## **A NEURAL CODE FOR EPISODIC MEMORIES IN FOOD-CACHING CHICKADEES**

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Throughout each day the brain captures snapshots of distinct experiences, forming episodic memories that often last a lifetime. This function depends on the hippocampus — a brain region that is evolutionarily conserved across vertebrates. My lab studies the relationship between neural activity and episodic memory using a unique model organism — the black-capped chickadee. Chickadees are specialist food-caching birds that store thousands of food items at concealed locations in their environment and use memory later in time to retrieve their caches. I will describe our effort in designing behavioral arenas and neural recording techniques to study these behaviors in laboratory conditions. I will share our discoveries of spatial representations in the chickadee hippocampus, on how neural activity in this region represents distinct memories, and how vision plays a role on this process.

## **HYPOTHALAMIC CRH NEURONS SUSTAIN DEFENSIVE ESCAPE TO MODULATE OUTCOME-DRIVEN STRATEGY UPDATE**

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The ability to escape from a predator is essential for survival, yet it remains unclear whether escape is a momentary commitment or requires sustained drive throughout the maneuver. Defensive escape to a looming stimulus that simulates an aerial predator involves threat detection followed by escape initiation. Corticotropin-releasing hormone-synthesizing neurons in the paraventricular nucleus of the hypothalamus (CRH-PVN) are active across all stages of escape, showing anticipatory activity required for initiation and sustained activity throughout execution. Using behaviour, optogenetics, and *in vivo* recordings, we show that animals complete escape regardless of continued stimulus presence, with stimulus-independent CRH-PVN activity persisting during execution. Single-cell imaging in freely moving animals revealed bimodal recruitment of CRH-PVN neurons, with distinct pools engaged before and after escape initiation. Disrupting CRH-PVN activity after escape onset aborts the maneuver, preventing shelter entry and reducing escape probability in subsequent trials. We propose that sustained CRH-PVN activity represents the perceived threat, enabling completion of escape and informing outcome-driven strategy updating.

## **HOW CORTICAL FEEDBACK INFLUENCES VISUAL THALAMIC NEURONAL ACTIVITY**

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The early visual pathways of highly visual mammals like primates and carnivores are efficiently organized into separate processing streams optimized to convey information about different visual features to the cortex in parallel. The first feedback step in the visual processing hierarchy, corticogeniculate feedback from primary visual cortex (V1) to the dorsal lateral geniculate nucleus of the thalamus (LGN), is also organized into parallel streams aligned with the feedforward streams. We have demonstrated that corticogeniculate feedback regulates the temporal precision of LGN responses to incoming retinal input and that this effect is global, *i.e.*, shared across the streams. In contrast, we find that corticogeniculate feedback also regulates spatial resolution in a stream-specific manner, selectively for the magnocellular/Y stream. Several open questions remain, however, regarding the impact of corticogeniculate feedback on LGN neuronal responses. In order for corticogeniculate influence to be functionally stream-specific, its connections with LGN neurons must be functionally like-to-like. New electrophysiological results from our lab show that corticogeniculate-to-LGN connectivity is indeed functionally like-to-like. Prior studies have suggested that corticogeniculate feedback modulates the activity of LGN neuronal ensembles in a coordinated fashion. We therefore applied optogenetics to examine whether and how corticogeniculate feedback alters LGN ensemble activity. Finally, as our previous findings overall suggest a role for corticogeniculate feedback in shaping LGN response variability in both the temporal and spatial domains, we report preliminary findings demonstrating how optogenetic perturbation of corticogeniculate feedback in behaving animals performing visual discrimination tasks disrupts performance. Together, these results paint a more complete picture of how feedback from the cortex controls the flow of visual information through the thalamus, providing important insight into conditions in which sensory filtering is disrupted.

## **A PREFRONTAL CORTEX MAP BASED ON SINGLE NEURON ACTIVITY**

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The intrinsic organization underlying the central cognitive role of the prefrontal cortex (PFC) remains poorly understood. It is unclear to what extent subregions of the PFC exhibit functional specialization, and existing structural descriptions of the PFC have yet to be integrated with the neuronal activity underlying information processing in this region. Furthermore, it remains an open question whether neuronal activity in the PFC is distinct from that of other cortical regions, and which activity patterns may support PFC-specific functional demands.

I will present our current work, in which we investigate the organization of the PFC at the level of single-neuron activity and evaluate neuronal firing patterns across multiple spatial scales. Our mouse studies incorporate spontaneous activity patterns, sensory responses, and tuning to aspects of goal-directed behavior, and address the relationship between single-unit activity and brain anatomy, as well as the distinctive activity characteristics and internal organization of the PFC.

Overall, our results demonstrate how distinct aspects of neuronal activity provide unique and complementary insights into the functional organization of the PFC. The findings also challenge the traditional emphasis on cytoarchitecture. I will discuss how our data-driven framework provides a scalable roadmap for studying functional organization across brain regions and species.

## **CHOLINERGIC DRIVE TOGGLES CELL-TYPE-SPECIFIC OUTPUT MODES OF THE HIPPOCAMPUS**

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The hippocampus, a brain region critical for learning and memory, is often conceptualized as a serial processor. Here, we examine the output region of the hippocampus, and reveal that excitatory neurons within this brain region can be coherently separated across molecular profiles, morphological structure, and circuit wiring. Functionally, these subtypes have different representational properties and causal contributions to behaviour, with cholinergic drive being sufficient to toggle between subtype-specific activity. Our results here illustrate highly specialized dissociable pathways for learning and memory in the brain.

## **THE GEOMETRY OF GLOBALLY OPTIMAL NEURAL REPRESENTATIONS**

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It is widely believed that neurons across a population coordinate their responses to best represent salient sensory, cognitive, and motor features. Large population sizes and noisy neuronal responses are significant obstacles for understanding how responses should be organized for optimal representation. Past theories have made simplifying concessions, such as considering discrimination only between similar inputs, or assuming restrictive parametric forms of neuronal response tuning. We present a novel theory that overcomes these past limitations and definitively identifies the globally optimal geometry of population codes for a circular variable. We validate core predictions with population activity data from the head direction system in mice, showing that it is close to optimal. Our framework is broadly applicable and makes substantial progress toward a theoretical understanding of the global structure of optimal neural representations, which has remained elusive largely due to a lack of appropriate mathematical tools.

## **FROM NEURAL ACTIVITY TO BEHAVIOR: SHAPING OBJECT REPRESENTATIONS IN THE MOUSE BRAIN**

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How does the brain construct object representations that support robust and flexible behavior? In this work, we combine large-scale neural recordings and behavior to investigate object processing in the mouse visual system. Using automated, high-throughput behavioral training approaches, we train mice on object recognition tasks and examine how population activity encodes object identity and how these representations evolve across the visual hierarchy and with experience. We further explore the structure of these representations in neural state space, asking how they generalize across transformations and learning, as well as across animals. By linking neural activity to behavior and model predictions, we aim to identify the principles that govern the formation of invariant and actionable object representations. Together, this approach provides a unified framework for studying how neural circuits shape object representations to support perception and behavior.

## **SHAPING NEURAL CIRCUIT STRUCTURE AND FUNCTION THROUGH BIOLOGICALLY PLAUSIBLE LEARNING**

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Neural circuits learn, stabilize, and flexibly combine representations through multiple plasticity mechanisms operating across synapses, dendrites, and inhibitory cell types. Yet how these mechanisms jointly shape circuit structure and computation remains poorly understood. I will discuss our recent results showing that inhibitory synaptic plasticity can go beyond homeostatic rate control to self-organize structured excitatory and inhibitory (E/I) connectivity, including E/I co-tuning and lateral inhibition, to generate surround suppression, and modular spontaneous activity. I will then show how dendritic nonlinearities and context-dependent inhibitory gating can regulate excitatory plasticity to form stable, overlapping neuronal assemblies without catastrophic interference. Together, these mechanisms provide a biologically plausible framework in which plasticity both stabilizes recurrent dynamics and creates the structured connectivity needed for flexible assembly-based computations across brain areas.

## **THE LITTLE BRAIN SUPERVISES LEARNING IN THE BIG BRAIN**

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In the cerebellum, climbing fibers (CFs) provide instructive signals for supervised learning at parallel fiber to Purkinje cell synapses. It has not been tested so far whether CF signaling may also influence plasticity in other brain areas. Here, we show that optogenetic CF activation suppresses potentiation of whisker responses in layer 2/3 pyramidal cells in the primary somatosensory (S1) cortex of awake mice that is observed after repeated whisker stimulation. Using two-photon imaging and chemogenetics, we find that CFs control plasticity by modulating SST- and VIP-positive interneurons in S1 cortex. Transsynaptic labeling identifies zona incerta (ZI) to thalamic posterior medial nucleus projections as a pathway for cerebellar output reaching S1 cortex. Chemogenetic inhibition of PV-positive neurons in the ZI prevents CF co-activation effects, identifying the ZI as a critical relay. Our findings demonstrate that CFs impact sensory signal processing and plasticity in S1 cortex and thus may convey instructive signals.

## **SWAYING DECISIONS WITH LIGHT**

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Understanding how neural circuits perform computations during decision making is crucial for understanding the brain. This requires that we can read and write activity patterns in genetically defined neurons at cellular resolution and with millisecond precision during behaviour. I will describe experiments using an all-optical strategy for interrogating neural circuits which combines simultaneous two-photon imaging and two-photon optogenetics. This strategy allows the physiological patterns of network activity to be read out, reproduced and manipulated on the fly, enabling closed-loop feedback control of activity. I will discuss how we are using this approach to manipulate decision-making in real time to identify the neural circuit determinants of behaviour.

## **CONTRIBUTIONS OF HETEROGENEOUS CORTICAL NEURON RESPONSES TO AUDITORY PERCEPTUAL LEARNING**

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The ability to flexibly respond to sensory cues in dynamic environments is essential to adaptive auditory-guided behaviors such as navigation and communication. How do neural circuits flexibly gate sensory information to select appropriate behavioral strategies based on sensory input and context? Auditory neural responses during behavior are heterogeneous, ranging from highly reliable classical responses (*i.e.*, robust, frequency-tuned cells) to irregular or seemingly random non-classically responsive firing patterns (*i.e.*, from nominally non-responsive cells) that fail to demonstrate any significant trial-averaged responses to sensory inputs or other behavioral factors. While classically responsive cells have been extensively studied for decades, the contribution of non-classically responsive cells to behavior has remained underexplored despite their prevalence. Recent work has shown that non-classically responsive cells in auditory cortex (AC) and secondary motor cortex (M2) contain significant stimulus and choice information and encode flexible task rules. While it has been shown that both classically and non-classically responsive units are essential for asymptotic task performance, their role during learning is unknown.

In this talk, I will discuss how heterogeneous cortical responses emerge and evolve during flexible behavior. We recorded single-unit responses from AC while mice performed a reversal learning task. Cortical response profiles during learning were highly heterogeneous spanning the continuum from classically to non-classically responsive. Strikingly, we found that the proportion of task-encoding non-classically responsive neurons significantly increased during late learning when the largest behavioral improvements occur demonstrating that non-classically responsive neurons are preferentially recruited during learning. To identify the role of top-down feedback on AC circuits during key learning phases we optogenetically silenced M2→AC projection neurons while recording AC spiking responses. Remarkably, silencing M2 inputs selectively modulated non-classically responsive cells and impaired behavioral performance during post-reversal learning. Our findings demonstrate that task-encoding non-classically responsive cells are preferentially recruited during learning by top-down inputs enabling neural and behavioral flexibility.

## **ADAPTIVE PROBLEM SOLVING IN THE PRIMATE FRONTAL CORTEX**

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Humans solve problems adaptively by selecting strategies suited to the situation. For example, when missing the bus to an appointment, we may wait for the next bus, call a taxi, cancel, or reschedule depending on the circumstances. Yet the neural and computational principles that support such flexible problem solving remain poorly understood. To address this question, we designed a moderately complex decision task for monkeys that admits multiple plausible solution strategies. Animals learned the task rapidly, generalized to novel maze geometries, and their choices were inconsistent with any single fixed strategy. We then recorded large-scale neural activity from the frontal cortex and found that population dynamics varied systematically with maze geometry. Neural responses clustered into two distinct dynamical regimes with separable initial states, consistent with hierarchical and sequential strategies. A decoder trained on population activity revealed time-resolved decision dynamics that aligned with these regimes, and an unsupervised latent-space analysis provided convergent evidence that strategy use varied across trials. A behavioral model grounded in neurally inferred strategies accounted for choices better than fixed-strategy alternatives and captured trial-by-trial variability. Together, these results provide a neural and computational account of how the brain selects and implements distinct strategies during adaptive problem solving.

## **THE MECHANISMS OF MINDING THE GAP: NEURAL CODING AT THE LIMITS OF TEMPORAL ACUITY**

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Humans and other animals can detect brief silent gaps (interruptions) in otherwise continuous sounds with extraordinary temporal acuity. Duration thresholds for gap detection typically approach 1–2 milliseconds — nearly two orders of magnitude shorter than the timescale of neural responses to the transient cues that mark the gap. How are these millisecond-timescale sound interruptions encoded by neural ensembles in the auditory system? In this talk, I will illustrate how neural population activity in the auditory cortex evolves during gap-in-noise events. I will also demonstrate that the sensitivity of auditory cortical dynamics to millisecond-timescale interruptions in sound reflects convergence of neural responses to both sound disappearances (offsets) and reappearances (onsets).

## **THE MEANING OF DENDRITES: DYNAMIC SUBCELLULAR REPRESENTATION OF THE PAST AND THE FUTURE IN THE HIPPOCAMPUS**

*Attila Losonczy*

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Why do neurons possess amazingly complex dendritic arbors? Long-standing and influential theories posit that dendrites are not merely passive conduits that merely integrate synaptic inputs but also perform independent, active, and nonlinear computations that greatly expand neuronal computational capacity. Empirical support for this “dendritic autonomy” has, however, largely come from *ex vivo* preparations, while direct evidence for dendritic computational units in behaving animals has been lacking, due primarily to pervasive technical limitations in measuring membrane potential along the somato-dendritic membrane surface. To address this limitation, we implemented ultrafast, motion-stabilized three-dimensional voltage imaging along the dendrites and somata of CA3 pyramidal neurons in the mouse hippocampus during virtual reality-guided navigation. Our results reveal that the dendritic arbor of CA3 pyramidal neurons comprises multiple independent computational units that can be either dynamically coupled to or distinct from somatic activity, depending on task conditions. Furthermore, spatially co-tuned dendrites retain their coordination during subsequent sharp-wave ripple events. These findings demonstrate that active dendritic properties in CA3 pyramidal neurons enable parallel processing of synaptic inputs, shaping somatic output and behaviorally relevant coding. This result expands the computational capacity of CA3 pyramidal neurons within the hippocampal network.

## **WHO IS VENUS DE MILO?**

*Andronike Makres*

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The *Venus de Milo* or *Aphrodite of Melos* is an ancient Greek marble sculpture of the Goddess of Love that was discovered in modern times on Milos. She is displayed at the Louvre in Paris and along with the Mona Lisa and the Nike of Samothrace, she is one of the three famous works of art in that museum.

*When* and *how* did Aphrodite make her way from Milos to Paris? What were the circumstances of her discovery on Milos? Why did the French take her? Was the statue complete or broken? What was she holding in her hand before she lost her arms? And, most importantly: when was the statue created? Is Aphrodite of Milos a true masterpiece or not?

Why did Venus de Milo become so famous? Should she return to Greece and to Milos in particular? With many copies of the statue displayed in museums across the world, and one official copy in Milos, who should have the original, the Louvre in Paris, the National Archeological Museum in Athens, or the Archeological Museum of Milos? How important is the material aspect of Aphrodite, i.e. the statue itself as opposed to her immaterial existence (the history of the statue, the symbolisms, etc)?

All the above questions will be addressed in my talk with some thought-provoking discussion to follow.

## **NEURO-MUSCULOSKELETAL MODELING REVEALS MUSCLE-LEVEL NEURAL DYNAMICS OF ADAPTIVE LEARNING IN SENSORIMOTOR CORTEX**

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The neural activity of the brain is intimately coupled to the dynamics of the body. In order to predict and adapt to the sensorimotor consequences of our actions, compelling behavioral studies in humans, non-human primates, and in rodents have shown the existence of internal models — predictive models of our body in the environment. These internal models are theoretically used to compute an updated state estimate with prediction errors. Here, we directly test whether such errors are encoded in primary somatosensory (S1) or motor (M1) cortex during a motor adaptation task in mice. Using control theory-derived features that include prediction errors, we find that functionally distinct neurons are mapped onto specific computational motifs. We find that layer 2/3 population dynamics encode command-like signals and sensorimotor prediction errors (SPEs). S1 neurons encode SPEs more prominently than M1, and the neural latent dynamics change in S1 more than in M1 during this within-session learning. Then we asked, in which coordinate frameworks are such errors computed? To answer this question, we developed a novel 50-muscle model of the adult mouse forelimb that is capable of studying motor control and learning in a physics simulator. We identify both high-level 3D position and muscle spaces as coordinate frameworks for SPEs. Together, our results provide a new model of how neural dynamics in S1 enables adaptive learning.

## **FOURIER INTELLIGENCE IN BRAINS AND MACHINES**

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Many behavioral tasks—arithmetic, perception, navigation, and planning—share a common structure: learning to compose transformations, such as translations, rotations, and more complex operations. Motivated by this observation, we introduce the group composition task, a unifying abstraction of computations in biological and artificial neural networks, whose objective is to map a sequence of group elements to their cumulative product.

We prove that two-layer networks solve this task one irreducible representation at a time, in an order dictated by the Fourier statistics of the input encoding. We show that this learning dynamic persists in deeper architectures, and that it predicts empirical signatures observed in biological neural systems—offering a principled account for the emergence of grid cells and other Fourier-like patterns in neuronal firing maps.

Taken together, these results suggest that intelligence, across brains and machines, may admit unifying mathematical laws.

## **WHAT TO THROW AWAY? HOW BRAINS MAKE EFFICIENT CODES**

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Biological systems must selectively encode partial information about the environment, as dictated by the capacity constraints at work in all living organisms. For example, we cannot see every feature of the light field that reaches our eyes; temporal resolution is limited by transmission noise and delays, and spatial resolution is limited by the finite number of photoreceptors and output cells in the retina. Classical efficient coding theory describes how sensory systems can maximize information transmission given such capacity constraints, but it treats all input features equally. Not all inputs are, however, of equal value to the organism. Our work quantifies whether and how the brain selectively encodes stimulus features, specifically predictive features, that are most useful for fast and effective movements. We have shown that efficient predictive computation starts at the earliest stages of the visual system, in animals from flies to salamanders to rats and mice. Recent work extends this principle of efficiency, and thus encoding what is most relevant to the organism, for mission-critical behaviors like mate selection. For that question, we focus on the rapid evolution of color vision in butterflies and have discovered new circuit motifs that may underpin how new wing coloration patterns are introduced in these charismatic species.

## **A TALK IN TWO PARTS: THE GEOLOGY OF MILOS, AND THE 2025 AEGEAN SEISMIC SWARM**

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### *The geology of Milos*

Milos covers an area of 151 km<sup>2</sup> and is predominantly, but not exclusively, of volcanic origin. The region is tectonically active with numerous extensional faults forming areas of high and low relief with vertical offsets that can exceed several 100 meters. The most obvious of these is the large embayment of the Gulf of Milos which, in contrast to Santorini, is not a volcanic crater or caldera.

Volcanic activity began approximately 3.5 Ma ago and has continued until historical times. Individual eruptions appear to have been comparatively small, with a maximum total thickness of 700 meters, with no evidence for any large-scale cataclysmic events. Eruptions have occurred from over 20 individual centers scattered across the island. Volcanic deposits are highly variable depending on interaction with seawater and proximity to the vent, and deposits from different vent locations are commonly interleaved. When combined with extensive post-eruption hydrothermal alteration and significant erosion, the field geology of Milos is challenging. As a generalization, the oldest volcanics are in the western areas and along the eastern coast (3 to 2 Ma), with younger deposits in the north (Trachilas 500 to 300 ka), and south-central regions (Fyriplaka 70 to 60 ka). The youngest events, near Agia Kiriaki in the southeast, are <sup>14</sup>C dated 200 BCE to 200 CE. This area also hosts a large geothermal reservoir which feeds active surface fumaroles and warm springs.

### *The 2025 Aegean seismic swarm*

Between 26 January and 24 February 2025 there was a significant seismic swarm (over 30,000 events) near Milos, between the islands of Santorini and Amorgos in the vicinity of the active Amorgos Fault. The majority were relatively small (below M3.5), but there were 50 quakes between M4.5 and M5.3. Uncertainty over the origin of the swarm (volcanic versus tectonic) and the memory of the catastrophic 1956 Amorgos Earthquake (M7.7) prompted a State of Emergency between 6 February and 3 March 2025 for Santorini and surrounding islands (but not including Milos).

A multi-national investigation combining seismic data, satellite geodesy, and seabed deployed sensors [1] subsequently determined that the earthquake swarm was associated with movement of magma at mid-to-shallow crustal levels. High resolution mapping of the earthquake focal locations, and modelling of ground deformation (up to 18 cm vertically and 4.5 cm laterally) indicate the flow of approximately 0.31 km<sup>3</sup> of magma into a NE-SW oriented 13-km-long dike (vertical sheet-like structure). The magma source was a large partially-molten magma storage reservoir in the mid to lower crust (deeper than 10 km) which also feeds the magma chambers of Santorini and Kolumbo (a submarine volcano 7 km NE of Santorini). Ultimately the dike stopped 3 to 5 km below the seafloor rather than continuing upward to eruption.

### **Reference**

1. Isken *et al.*, 2025, *Nature*, 645:939-948, 10.1038/s41586-025-09525-7

## **CEREBELLAR METAPLASTICITY**

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Metaplasticity, *i.e.*, the plasticity of plasticity, could serve a number of important computational functions in neural circuits. However, experimental studies of metaplasticity have been limited. I will describe two forms of metaplasticity in the cerebellum and evidence for their role in cerebellum-dependent learning in health and disease. Cerebellar parallel fiber-Purkinje cell synapses exhibit experience-dependent changes in *(i)* the threshold and *(ii)* the timing rules for associative long-term depression (LTD). Our results suggest that the induction of LTD triggers a transient elevation in the threshold for LTD that dramatically reduces its availability to support new learning. In wild type mice, this threshold metaplasticity may support the stability of recently acquired memories. However, in a mouse model of autism, it seems to contribute to learning impairments. A second form of metaplasticity alters the timing contingencies for LTD in response to experience. This temporal metaplasticity can solve the temporal credit assignment problem, ensuring that synapses that could have contributed to the error signal are selectively weakened.

## **LIVING WITH A BRAIN-COMPUTER INTERFACE**

*William Rinaldi*<sup>1</sup>, *Scott Imbrie*<sup>1</sup>, *Marcus Gerhardt*<sup>2</sup>, *Nicholas G. Hatsopoulos*<sup>1,\*</sup>

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Bill Rinaldi and Scott Imbrie became the first two subjects in the Chicago area to be implanted with electrodes in the motor and somatosensory cortices as part of our Cortical Bionics Research Group (CBRG), a consortium which includes teams from the University of Chicago, the University of Pittsburgh, and Northwestern University. The goal of our research program is to develop a bi-directional brain computer interface (BCI) for dexterous object manipulation; this BCI uses control signals from motor cortex to produce movement in combination with electrical stimulation of somatosensory cortex to provide artificial tactile feedback. In this presentation, Bill and Scott will discuss what led them to this study, how it feels to control devices through thought, and what their prosthetic percepts feel like. Bill and Scott will discuss these topics first with Marcus and Nicho, prior to taking questions from the audience.

## **DECRYPTING THE BRAIN WITH AI**

*Andreas Tolias*

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“You, your memories and ambitions, your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells,” — Crick’s words capture the profound challenge of decrypting the neural code. This challenge has long been hindered by two limitations: our ability to record activity from large neuronal populations under the complex, variable conditions in which brains evolved, and our capacity to model the intricate relationships between stimuli, behaviors, and neural activity. Recent breakthroughs are beginning to overcome these barriers. Cutting-edge technologies now enable large-scale recordings, while artificial intelligence (AI) can construct predictive brain models that link stimuli, neural activity, and behavior. These digital twins open the door to virtually limitless *in silico* experiments, testing theories that would otherwise be impossible to probe at sufficient scale in living brains. I will discuss our work building brain foundation models and digital twins to uncover the mechanisms of neural representation, with predictions validated through closed-loop experiments.

## **NEURAL CIRCUITS FOR LEARNING TO PREDICT**

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The ability to predict future outcomes is a fundamental basis of flexible behavior. In the brain, the neuromodulator dopamine is thought to play a central role in learning to predict future rewards. A large body of evidence suggests that dopamine supports this predictive learning by signaling a moment-by-moment prediction error, called a temporal difference (TD) error, analogous to those used in reinforcement learning algorithms. However, whether reinforcement learning algorithms are truly implemented in the brain, and if so how, remains unclear. In this talk, I will present our recent work addressing two key issues: *(i)* how dopamine signals are computed, and *(ii)* how core parameters of reinforcement learning models may be instantiated within neural circuits.

**POSTER ABSTRACTS**  
**(in alphabetical order by first author)**



## **SPECTRAL-TEMPORAL NEURONAL SELECTIVITY IN THE AWAKE ZEBRA FINCH AUDITORY FOREBRAIN**

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The perception of complex acoustic signals, such as birdsong or human speech, depends critically on the brain's ability to process both spectral (frequency content) and temporal (timing) information. While hierarchical processing within the avian auditory system is established, how these distinct features are encoded and integrated, particularly in awake, behaving animals, remains largely unresolved, as previous studies mainly used anesthetized preparations, which may not have the same neural dynamics as awake preparations.

In this study, we investigated single units that encode spectral and temporal features in the auditory forebrain of awake, freely moving zebra finches (*Taeniopygia guttata*). We recorded units from primary (Field-L) and secondary (caudomedial nidopallium or NCM; caudomedial mesopallium or CMM) auditory regions while presenting natural conspecific songs alongside song versions selectively filtered to degrade either spectral or temporal information. Using demixed Principal Component Analysis (dPCA), we disentangled neural population responses according to spectral features versus temporal structure of ten different unfamiliar zebra finch songs.

We found distinct subpopulations of neurons preferentially tuned to either spectral or temporal features, supporting a modular organization of auditory processing. Notably, neurons in the NCM exhibited strong selectivity for spectral information, responding preferentially to natural songs, while neurons in Field-L showed noticeable temporal selectivity and included a subset of neurons that responded more robustly to spectrally filtered playbacks. Further analysis identified temporally selective neurons, especially in Field-L and NCM, often located in deeper cortical layers. The dPCA encoding weights clustered into distinct neural groups, suggesting a potential temporal manifold, indicating that Field-L consists of low-dimensional subspaces that represent temporal song features. These findings were corroborated by spectrotemporal receptive field (STRF) analysis of neurons, which revealed different tuning properties that were consistent with different spectral and temporal encoding strategies.

This study highlights neuron populations that are functionally specialized for processing different spectral and temporal acoustic features within the avian auditory hierarchy, with NCM neurons showing preferential tuning to spectral features while Field-L contains subpopulations with enhanced temporal selectivity, organized in low-dimensional manifolds that collectively enable the robust encoding of complex acoustic signals such as conspecific vocalizations.

## IMAGINATION STRATEGIES FOR GENERALIZABLE BRAIN COMPUTER INTERFACES

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Intracortical brain-computer interfaces (BCIs) predominantly rely on biomimetic control strategies, in which neural activity associated with attempted or imagined movements is mapped onto congruent movements of a cursor or prosthetic device. While this approach is intuitive, it assumes the availability of strong and stable movement-related neural signals, an assumption that does not always hold across individuals, recording sites, or task contexts [1]. These limitations motivate the exploration of alternative control strategies that relax strict biomimetic constraints while remaining learnable and reliable.

We developed a modular task framework designed to evaluate two key factors in BCI generalization. First, a neural decoder is trained once and then held fixed across all tasks within a session, allowing generalization to be assessed without confounds introduced by decoder retraining. Second, the framework contrasts biomimetic mappings with non-biomimetic mappings derived from the strongest, most stable, and separable neural signals rather than their natural motor correlates. Using a fixed two-dimensional continuous velocity decoder, participants performed a sequence of cursor-based tasks spanning these conditions, including a center-out reaching task, a visually distinct but kinematically matched UFO abduction task, a bounding-box task requiring concurrent control of position and scale, and an abstract color-size matching task in which decoded signals controlled non-spatial task variables.

Using this framework, participants successfully generalized control across multiple task contexts using a single fixed decoder. Effective performance was observed for both biomimetic and non-biomimetic mappings derived from strong, stable, and separable neural signals. Performance improved with practice, and transitions between tasks revealed distinct behavioral signatures associated with task demands and mapping type.

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## **ARE DYNAMICS NECESSARY IN A TEMPORALLY COHERENT WORLD? PROBING TEMPORAL CONTINUITY IN MICE DURING VISUAL OBJECT RECOGNITION**

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In natural vision, objects typically remain coherent over time, even as their appearance changes. This temporal continuity suggests that the brain might take advantage of not only which patterns of activity occur but also how they evolve to build stable object representations. Here we ask: in a world where objects are temporally coherent, are neural dynamics themselves important for recognition?

We approach this complex question in three stages. First, using a high-throughput visual behavior paradigm in mice, we examine different aspects of temporal continuity of object identity across a plethora of changing latent parameters and quantify how performance changes when identity is preserved versus switched. This provides a purely behavioral readout of the cost or benefit of temporal coherence in an object discrimination setting. Second, we analyze large-scale extracellular recordings from mice passively viewing objects. Using a linear decoder, we project high-dimensional activity into a decoder state space and compare trials in which object identity repeats (cis) versus switches (trans) from the previous trial. Across sessions, cis trials show higher decoding performance than trans trials, and their population trajectories exhibit less abrupt state changes between trials, as well as faster stabilization within a trial. Trans trials instead involve larger and faster state changes but slower convergence towards a stable representation, revealing a dynamic signature of violated temporal continuity that is not apparent from static decoding accuracy alone. Finally, we combine our behavioral paradigm with dense neural recordings to ultimately link these neural trajectories to trial-by-trial performance.

Together, these behavioral and neural results point to temporal continuity as an organizing constraint for object representation: when identity is preserved over time, the visual system appears to reuse and refine existing population states rather than recomputing them from scratch, whereas identity changes are accompanied by larger reconfigurations of activity. By extending the same analysis to simultaneous behavior and recordings, we directly link moment-by-moment trajectories in neural state space to successful recognition decisions in a temporally structured world.

### **Acknowledgments**

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## STRUCTURAL LEARNING OF REWARD PATTERNS IN THE MOUSE PREFRONTAL CORTEX

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Learning and memory studies often focus on associations between pairs of stimuli, or stimuli and rewards. However, it is also possible to learn more abstract structures governing the reward environment. Here we test how mice rely on both strategies, using a task that can tease them apart at the level of behaviour and neural representation.

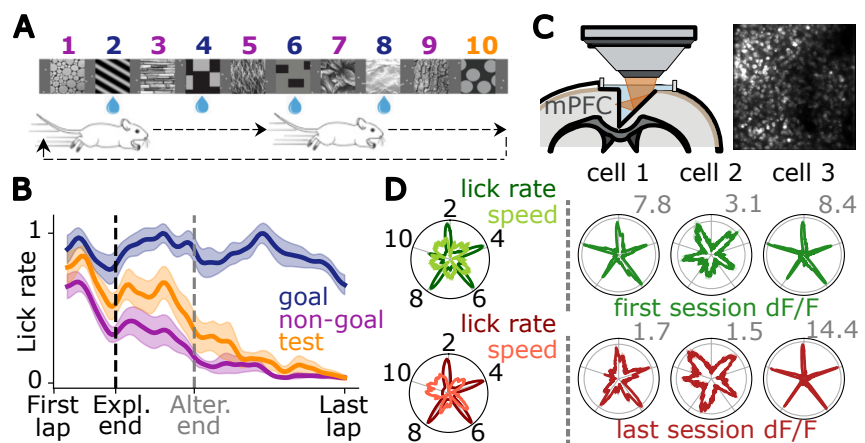
Mice ran on a virtual corridor with ten landmarks, and were rewarded at four goal locations 2, 4, 6, 8 (Fig. 1A). To learn the reward structure, the mice could develop ten independent landmark-reward associations. Alternatively, they could learn a structural pattern that predicts reward every other stimulus. Behavior at the test, unrewarded 10th landmark distinguishes these strategies, as only the latter predicts a response there.

We found that mice continued responding to the 10th landmark even after responses to all other non-rewarded landmarks stopped, in line with structure learning, before ultimately learning the correct reward pattern (Fig. 1B). We recorded individual mPFC cells in task and examined neural activity as a function of progress towards different behavioural steps (Fig. 1C). Neurons initially tracked progress to the four goals, but also the test landmark. Surprisingly, a subset of neurons maintained this alternating landmark representation even after mice learned the true reward structure (Fig. 1D).

These findings suggest that even in a simple stimulus-reward association paradigm, mice may favour a structural explanation for rewards, if one is available. Characterising representations of similar structural regularities is critical to understand how they could be used as building blocks for more complex structures.

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**Figure 1.** (A) Schematic of the landmark sequence on the virtual corridor. (B) Average lick rate by landmark type; dashed lines mark the end of exploration and alternation periods (mean  $\pm$  s.e.m.,  $n = 10$  mice) (C) Two-photon imaging setup using a prism implant in mPFC (left; adapted from [1]) and example field of view during behaviour (right). (D) Projections onto the circular task structure of average lick rate and speed (left), and neuronal activity from the same cells (right) in the 2nd (top) and last (bottom) sessions; grey lines mark goal times; the maximum activity is in the top right of the neuronal activity plots.

## **ALTERED FUNCTIONAL CONNECTIVITY IN V1 OF MECP2 DUPLICATION SYNDROME MICE DURING SPONTANEOUS CONDITIONS**

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MECP2 duplication syndrome (MDS) is a neurodevelopmental disorder characterized by intellectual disability, autism, and seizures [1]. Cortical hyperexcitability and altered GABAergic signaling have been reported in MDS models [2], yet circuit-level mechanisms of sensory processing dysfunction remain unclear. Understanding how MDS affects functional connectivity in visual cortex may reveal how MECP2 dosage disrupts cortical network organization.

We performed two-photon calcium imaging to record activity from 3000+ neurons in the primary visual cortex (V1) from 4 MDS and 4 control mice during spontaneous activity (absence of visual stimulus). Functional connectivity matrices were constructed using the spike time tiling coefficient (STTC) [3], which provides pairwise correlation estimates resistant to firing rate variations. Statistical significance was determined by circular permutation testing (100 shuffles per neuron pair). MDS mice exhibited significantly reduced functional connectivity compared to controls: fewer neuron pairs showed significant functional connections, and individual neurons had significantly lower connection counts (degree). This suggests MDS disrupts the typical synchronization patterns within V1 networks, resulting in sparser functional structure.

We also examined the relationship between neuronal activity and arousal state by computing spike-triggered averages of z-scored pupil radius, established proxies for cortical arousal [4]. V1 neurons were stratified into quartiles based on their functional connectivity degree. In control mice, neurons showed positive coupling to pupil dynamics regardless of connectivity level, indicating uniform arousal coupling across the network. MDS mice exhibited quartile-dependent heterogeneity: weakly connected neurons (lower quartiles) displayed inverse coupling to pupil activity, while highly connected neurons (upper quartile) showed enhanced positive coupling.

These findings reveal that MDS fundamentally alters V1 functional organization, fragmenting the network into modular subpopulations with opposing arousal dependencies. This architecture may reveal sensory processing deficits and cortical dysfunction in MDS.

### **Acknowledgments**

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## **AMYGDALA DYNAMICS DURING VALUE-BASED DECISION-MAKING**

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Adaptive behavior requires learning the value of environmental options and flexibly updating actions when contingencies change. The basolateral amygdala (BLA) has been implicated in affective learning and goal-directed behavior [1], yet how local neuronal populations coordinate activity during ongoing decision-making remains unclear.

To address this gap, we developed a freely moving two-alternative unforced choice task in which mice continuously adapt their choices following unsignaled changes in outcome value. Using head-mounted miniscope calcium imaging, we recorded large populations of genetically identified BLA neurons across learning- and expert-stage performance, including both glutamatergic neurons and multiple inhibitory interneuron subtypes.

Population activity evolved with learning and exhibited structured dynamics that tiled different behavioral epochs. Distinct neuronal subgroups were preferentially active during reward expectation, exploitation, and action adaptation after contingency switches, across all excitatory and inhibitory populations, pointing to a role for BLA micro-circuits in organizing task engagement and action selection rather than solely encoding reward outcomes [2].

Together, these findings suggest that BLA activity is organized into coordinated neuronal ensembles comprised of parallel canonical circuit-motifs whose dynamics track task variables and behavioral transitions, consistent with a population-level encoding of motivational state and action selection. This work provides a framework for linking amygdala ensemble dynamics to adaptive decision-making.

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**DISTRIBUTED COMPUTATIONS OF FLEXIBLE DECISIONS**

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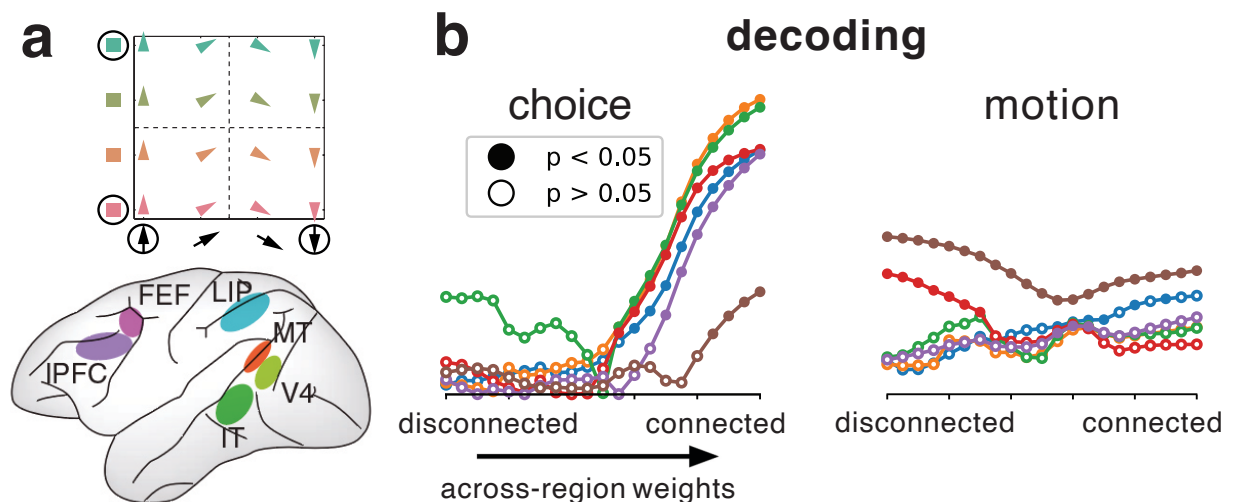
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Previous work investigating the neural dynamics underlying context-dependent decision making typically analyses a single brain region or recurrent neural network. However, evidence suggests that the information required to solve these tasks is distributed across multiple regions. Here, we investigate the neural dynamics across six cortical regions (Figure 1A) of the non-human primate brain where such distributed information has been observed [1]. By examining within-region geometry and dynamics, we identified significant differences not captured by classical decoding analyses (see [2] for details). Using multi-regional, rank-regularized RNNs constrained on condition-averaged data, we explored how cross-area interactions shaped neural representations. Specifically, we set out to test two different hypotheses: one in which prefrontal cortex acts as a central hub for context-dependent decision making versus a distributed model in which multiple brain regions flexibly modulate behavior without central control. Our analyses support the latter hypothesis: data-constrained networks in which across-region interactions were blocked could represent stimuli (Figure 1B, right), but gradually disconnecting regions led to an abrupt breakdown of task-solving capabilities (Figure 1B, left). Finally, perturbation experiments (not shown) highlighted the differential contributions of various regions, offering predictive insights for future experimental validation. These results underscore the critical role of inter-regional communication in task performance and provide a framework for understanding distributed neural processing.

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## **MOVEMENT ANTICIPATION MODULATES MOTOR-PARIETAL INTERACTIONS DURING GOAL-DIRECTED MOVEMENTS**

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It is widely hypothesized that coordinated activity between parietal and motor areas is essential for transforming sensory information into goal-directed actions. However, a comprehensive understanding of how their interactions adapt when upcoming movements can be anticipated remains limited. This study investigates the modulation of motor-parietal interactions by movement anticipation during predictive visuomotor coordination.

To this end, two rhesus macaques performed a visually-guided sequential reaching task, in which the predictability of the next target location increased within the sequence. Behavioral analyses of eye and hand movements revealed signs of movement anticipation as the predictability of the next target location increased. We recorded simultaneous neural activity from the dorsal premotor and primary motor cortex (PMd/M1) and the parietal area 7A.

To examine whether anticipation modulated the directional encoding in both areas, we trained a Linear Discriminant Analysis classifier on the envelope of Multi-Unit Activity (MUA) after unpredictable target onsets. The goal direction could be decoded from the MUA responses in both areas before the presentation of predictable targets, suggesting that neural representations of direction were temporally advanced by movement anticipation. Finally, using a novel information theoretic measure, we found that information about the forthcoming target direction was processed and broadcast across 7A and PMd/M1 at similar latencies, through bi-directional, yet asymmetric, interactions that occurred earlier during movement anticipation.

These findings suggest that motor-parietal interactions are not strictly hierarchical, but instead reveal more reciprocal architecture. Within this framework, PMd/M1 and 7A form a fronto-parietal network that facilitates eye-hand coordination through distributed information processing to support the anticipation of predictable movements.

### **Acknowledgments**

Supported by the Marie Skłodowska Curie Actions Innovative Training Network In2PrimateBrains (Grant agreement n°956669 – H2020). We would also like to thank Neuroschool for partly funding this work.

## **DECODING RETINAL ENSEMBLES TO IMPROVE VISION RESTORATION THERAPIES**

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Optogenetic gene therapy is a promising strategy to restore vision in patients blinded by retinal degeneration: previous studies have shown that the artificial expression of light-sensitive proteins, called opsins, in surviving retinal cells can reactivate light-driven responses and partially restore functional vision. However, current approaches do not restore sufficient visual acuity for everyday tasks, leaving patients below the threshold of legal blindness [1].

There is evidence that the expression of faster and more sensitive opsins as well as targeting upstream neurons could lead to substantial improvements [2, 3]. However, the impact of these strategies on recovered visual acuity remains difficult to predict. Most studies focus on single-cell sensitivity and dynamics, offering limited insight into population-level information transfer to the brain, thereby limiting predictions of achievable visual resolution and clinical efficacy.

To address this gap, we developed a computational framework that links single-neuron recordings to population-level predictions of visual acuity [4]. Using multi-electrode array recordings from optogenetically treated retinas in a blind mouse model, we model light-driven responses at the single-unit level and assemble a synthetic human-like retinal population. This allows us to simulate population responses to moving visual stimuli of varying size and speed. Through maximum-likelihood decoding, we estimate the smallest discriminable size and highest discriminable velocity, which we translate into predicted performance on standard visual acuity tests. This framework thus enables quantitative predictions and direct comparisons of the clinical efficacy of different optogenetic strategies in the context of natural visual dynamics.

Applying this framework to ganglion- and bipolar-cell targeting allowed us to identify the key factors that make an optogenetic strategy effective at restoring high resolution vision and estimate the benefit of leveraging biological processing through upstream cell targeting. Ongoing work is addressing potential gains from faster and more efficient opsins.

### **Acknowledgments**

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## NEURAL REPRESENTATIONS OF INTUITIVE PHYSICS IN HUMAN POSTERIOR PARIETAL CORTEX

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Studies using fMRI have identified parietal regions that respond preferentially during intuitive physics judgments [1] and shown that multivariate activity patterns encode physical properties of visual scenes [2]. However, the underlying neural computations remain poorly understood.

Here, we recorded single unit activity and local field potentials (LFPs) from posterior parietal cortex in two individuals (RD, JJ) with chronic spinal cord injury implanted with Utah arrays. In RD, one array was implanted in superior parietal lobule (SPL) and one in supramarginal gyrus (SMG), yielding over 500 units per array across sessions. Participant JJ was implanted with one array in SPL that contributed only LFPs due to the long duration of implantation. Participants performed established intuitive physics tasks, including a tower falling task contrasting physical stability judgments with a color-based control judgment, passive viewing of short videos depicting physical versus social events, and a spatial working memory task. In RD, population decoding reliably distinguished physics from color judgments in both regions, with maximum accuracies of approximately 80% in SPL and SMG. Using the same arrays, physical events were strongly discriminated from social events, particularly in SPL (accuracy: 95.7%). In contrast, neither region showed increased responses or above chance decoding for difficult versus easy spatial working memory trials. In JJ, SPL high gamma activity showed the same pattern, with larger responses and above chance decoding for physics versus color judgments and for physical versus social events, but no effects of working memory difficulty.

These findings provide electrophysiological evidence that posterior parietal cortex is engaged in intuitive physical reasoning, consistent with prior work showing that these areas encode internal models of the body and environment and contribute to action planning [3], making intuitive physics a natural component of their function.

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## UNBIASED DETECTION OF NEURAL SEQUENCES

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Cell assemblies are commonly defined by co-firing, but when temporal order is taken into account, a neural population can express a large number of distinct sequence motifs, substantially increasing the capacity to encode information [1]. In this work, we treat the temporal ordering of spikes across many neurons as the primary structure of population activity in the hippocampus. Most existing approaches to hippocampal sequence analysis rely on decoding with respect to predefined behavioral variables and firing-rate tuning curves, such as spatial position. However, limiting analyses to predefined variables risks missing additional, potentially functionally relevant motifs, especially those that do not map onto known behavioral events [2]. Recent work further suggests that additional sequence motifs may exist beyond those tied to specific behavioral interpretations [3]. Identifying repeating sequences within population bursts may reveal how brain activity reorganizes with learning and allows us to track memory-related processing without reference to external variables.

We developed an unbiased method for detecting recurring sequence motifs directly from spiking activity, independent of behavioral variables or tuning properties. Our approach assigns each neuron a mean activation time within population bursts, producing ordered index sequences. Applying rank correlation-based similarity measures and clustering across bursts reveals distinct temporal motifs. Unlike assembly-based or dimensional-reduction methods, our approach explicitly captures temporal ordering within population activity. We validate the method using simulated sequences generated from a parametric statistical model, allowing systematic control over firing variability, participation, and temporal precision. This analysis identifies regimes where the method reliably recovers ground-truth motifs and revealed how firing statistics constrain detectability. The simulation framework thus provides a link between theoretical assumptions about sequence generation and observable population structure.

We applied the method to CA1 tetrode recordings from two rats performing either a memory-guided task or a non-memory control, tracking sequence motifs across pre-, mid-, and post-task sleep. Comparing motif rates across sleep phases revealed distinct recruitment patterns: in both animals, new motifs emerged during task-intermittent resting periods, indicating experience-dependent reorganization. However, only in the memory condition did these motifs reappear at similar rates during post-task sleep, consistent with consolidation, whereas the control animal showed little correspondence in motif rates, indicating memory-specific consolidation.

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## COORDINATED NEURAL ACTIVITY ACROSS THE LIMBIC SYSTEM PREDICTS MOTIVATIONAL STATE

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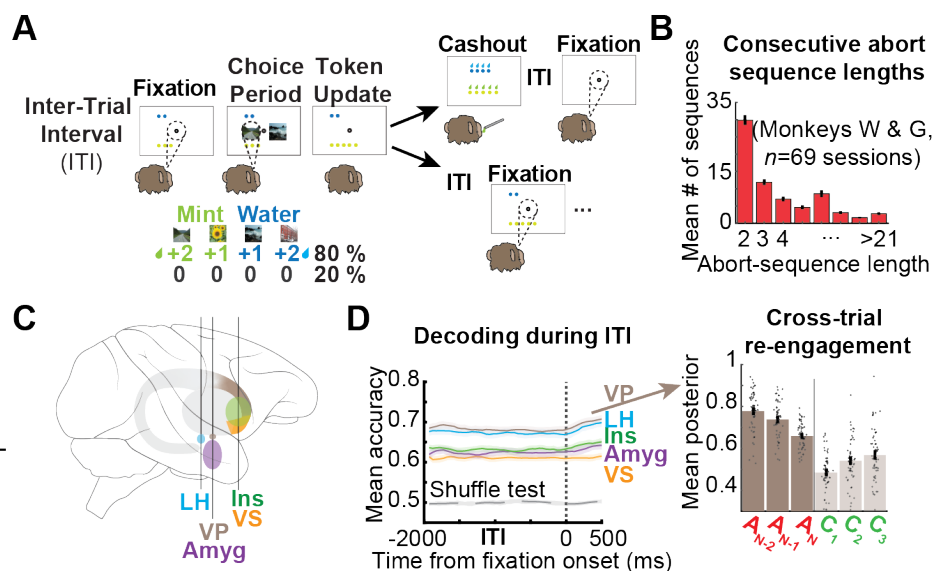
Motivation fluctuates dynamically even when task demands and rewards are stable. Yet how such fluctuations are represented across limbic circuits that regulate reward remains unclear. We trained two rhesus monkeys on a token-based reinforcement learning task that dissociated immediate reward from motivation (Fig. 1A). Through the requirement to repeat an aborted trial until completed, the monkeys entered sequences of aborted trials that revealed slow fluctuations in engagement over multiple trials (Fig. 1B). We conducted simultaneous neural recordings in the Ventral Striatum (VS), Ventral Pallidum (VP), Lateral Hypothalamus (LH), Insula (Ins), and Amygdala (Amyg) (Fig. 1C).

Model-estimated state values, reflecting immediate and future expected rewards, were higher before continued engagement and lower before abort sequences. This pattern indicated that higher state value was associated with sustained engagement. We observed a distributed representation of this fast correlate of motivation across 8,000 neurons recorded from the limbic structures.

Intertrial-interval (ITI) activity reflected slower motivational dynamics. Neural activity across

areas predicted whether the next trial would be completed or aborted before fixation onset (Fig. 1D), with the strongest decoding performance in VP and LH. Engagement-related activity recovered as monkeys resumed task performance, revealing a slow-timescale motivational signal (Fig. 1D). Further analysis of the ITI dynamics revealed that the attractor basin for abort trials deepens when state value, a task-driven correlate of motivation, is low.

Together, these results show that coordination in the limbic system forecasts transitions in engagement before overt behavioral change. This systems-level framework connects value, motivation, and limbic circuit dynamics and provides insight into how disruptions in these processes may contribute to apathy and anergia in psychiatric disease.



**Figure 1.** (A) Tokens task. (B) Average length of abort trial sequences. (C) Five areas for semi-simultaneous neural recordings. (D) Average decoding performance of abort versus completed during intertrial interval before fixation. Right inset: Mean posterior probabilities from decoding across re-engagement in the task at the end of a sequence of aborts (example shown is from VP).

## **A BARCODE STIMULUS TO CLASSIFY RETINAL GANGLION CELL TYPES**

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Retinal ganglion cells (RGCs) are the sole output neurons of the retina, providing a unique system for understanding how sensory perception is transformed into neural representations. RGCs are divided into several functional types that encode complementary features of the visual scene, each organized in mosaic-like patterns that tile the entire visual field. Yet despite decades of study [1, 2], the number of RGC functional types remains unresolved, in part because robust, precise functional classification at scale is still lacking.

Standard functional typing for large-scale recordings relies mainly on responses to the chirp stimulus—a full-field modulation of light intensity over time—. However, full-field stimulation disregards spatial computations that are known to occur in the retina (e.g., center-surround interactions) and often fails to distinguish similarly responding RGC types.

To address this issue, we developed a barcode stimulus: a moving pattern of black-and-white stripes spanning multiple spatial frequencies and applied it to *ex vivo* mouse retinas recorded with a multi-electrode array (MEA). Compared with the chirp, the barcode evoked stronger and more reliable responses across trials (higher SNR and lower CV). Crucially, its spatial richness exposes consistent differences between cells that appear indistinguishable under chirp stimulation. We analyzed barcode responses using a combination of t-SNE (t-distributed stochastic neighbor embedding) and a targeted feature-extraction approach that quantifies each neuron’s response to every stripe in the barcode. Preliminary results indicate that this clustering pipeline organizes cells into broad neighborhoods consistent with canonical response classes (ON/OFF; transient- versus sustained-like). Within each neighborhood, it further resolves finer clusters whose receptive-field locations form mosaic-like patterns. These results were consistent across independent experiments.

Together, our results highlight two key points. First, achieving fine resolution of neuronal functional types requires a stimulus that elicits sufficiently rich responses—here, the barcode separated groups that chirp-based procedures could not reliably distinguish. Second, beyond improving cluster resolution, the barcode also drove stronger and more trial-to-trial reliable responses than the chirp, supporting more consistent functional type assignment. We expect that the barcode will provide a fast and reliable approach for assessing functional types in large-scale RGC recordings, a key step toward understanding how visual information is transformed into neural representations.

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## **OROFACIAL MOTOR CORTEX PREFERENTIALLY ENCODES TONGUE POSTURE**

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Precise control of tongue and hyoid musculature is critical for fundamental behaviors such as feeding and speech production, yet the neural mechanisms underlying control of soft-bodied effectors remain poorly understood. Previous research suggests cortical motor neurons encode movement velocity during reaching arm movements but preferentially encode joint posture over hand movement dynamics during grasping tasks. Given the tongue's role in object interaction and manipulation during feeding, analogous to the hand during grasping, we hypothesized that orofacial motor cortex would preferentially encode tongue postural features over movement dynamics.

Here we investigated cortical motor encoding of the tongue by simultaneously recording multicellular neural activity in orofacial primary motor cortex and three-dimensional tongue kinematics using X-ray Reconstruction of Moving Morphology (XROMM) during naturalistic feeding in rhesus macaques. Using regularized Poisson generalized linear models, we found results consistent with our hypothesis that orofacial motor neurons preferentially encoded tongue posture over velocity (paired *t*-tests,  $p < 0.0001$ ), replicating across both subjects. Nested model comparisons revealed that detailed kinematic features explained substantially more neural variance than parameters related to gape cycle and magnitude alone, suggesting that neural encoding reflects active control of tongue morphology beyond the rhythmic structure of feeding.

These findings indicate that postural encoding is a shared computational principle across cortical motor regions controlling manipulatory movements, whether of the hand or tongue, despite fundamentally different effector biomechanics. Understanding these principles provides insights for developing brain-computer interfaces for speech restoration and clinical interventions for hyolingual motor dysfunction.

## CELL TYPE-SPECIFIC NEURONAL DYNAMICS REVEALED IN THE LIVING HUMAN BRAIN

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A fundamental goal of neuroscience is to understand how neurons organize to produce cognition [1–4]. The human brain’s unique cognitive capabilities emerge from the activity of diverse neuronal cell types, yet we lack fundamental knowledge of how these types organize in human neural circuits — a gap that has constrained our understanding of human cognition and brain disorders. While animal studies routinely identify and monitor specific cell types *in vivo*, to date this is impossible in humans.

We bridge this critical divide by developing a computational framework that identifies distinct neuronal types in the living human cortex. We generated thousands of biophysically faithful single-cell models of eight human cell types, simulated their extracellular signatures, and trained classifiers to identify cell types from extracellular recordings. Applying these classifiers to *in vivo* recordings from three neurosurgical patients, we successfully detected six cortical cell types — three excitatory and three inhibitory — with compositions matching recent single-nucleus RNA sequencing and electron microscopy data.

The newly found cell type resolution in living humans revealed organizational principles of ongoing cortical activity: while standard activity metrics showed no differences between types, their participation in circuit dynamics diverged. We show that emergent theta-gamma phase-amplitude coupling across patients does not synchronize all cortical neurons equally. Instead, we discovered cell type-specific coupling, with less populous excitatory ITL35 and ITL46 units showing significantly stronger neocortical theta band (2–14 Hz) synchronization than the more numerous excitatory ITL23 neurons while inhibitory units exhibit strong but non-specific theta coupling between PVALB, VIP and LAMP5. We also observed neocortical gamma band (30–70 Hz) synchronization where, again, ITL35 and ITL46 exhibit stronger coupling but, unlike for theta, inhibitory VIP show strong and specific coupling compared to PVALB and LAMP5.

Our approach opens a new window into human brain function and dysfunction, enabling cell type-resolution in studies in living patients.

### Acknowledgments

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## DECODING V1 SURROUND MODULATION: DECODING PERFORMANCE NEGATIVELY CORRELATES WITH CONTEXTUAL RECEPTIVE-FIELD CENTER PREDICTABILITY

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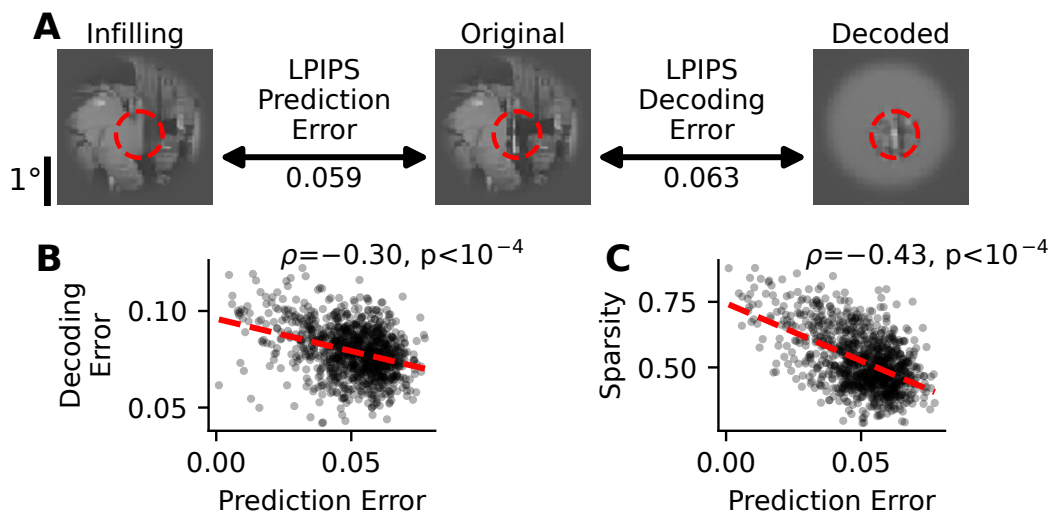
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Surround modulation is essential for information processing in primary visual cortex (V1), yet how it adapts to natural scene statistics and what functional role it plays in population neural coding is not fully understood. Here, we adopt a decoding-based framework to study surround modulation under naturalistic stimulation. Using a large dataset of V1 neuronal responses to natural images, we examine the relationship between predictability of the receptive field (RF) center given its surrounding context [1], population sparsity [2], and decoding performance.

We used two-photon imaging signals from 299 V1 neurons with overlapping RFs in an awake macaque viewing 49,000 ImageNet-derived natural images. We fitted a deep learning encoding model, which allowed us to decode image stimuli from population activity using gradient-based optimization. Predictability was quantified by a deep learning based perceptual distance (LPIPS) between generative infilling samples and the original images at the RF center, while decoding performance was also assessed using RF LPIPS. We found that decoding performance is negatively correlated with predictability, and sparsity positively correlates with predictability.

These preliminary results suggest a possible link to predictive coding: surround modulation may reduce decodability of the RF center when it is less surprising, potentially through sparsification of the neural code [2]. Future work will employ guided flow-matching to extend this framework to a Bayesian formulation, examining the balance between prior and likelihood.



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## INNATE DEVELOPMENT OF COGNITIVE FUNCTIONS AND MOTOR PROGRAMS BY CHEMOAFFINITY

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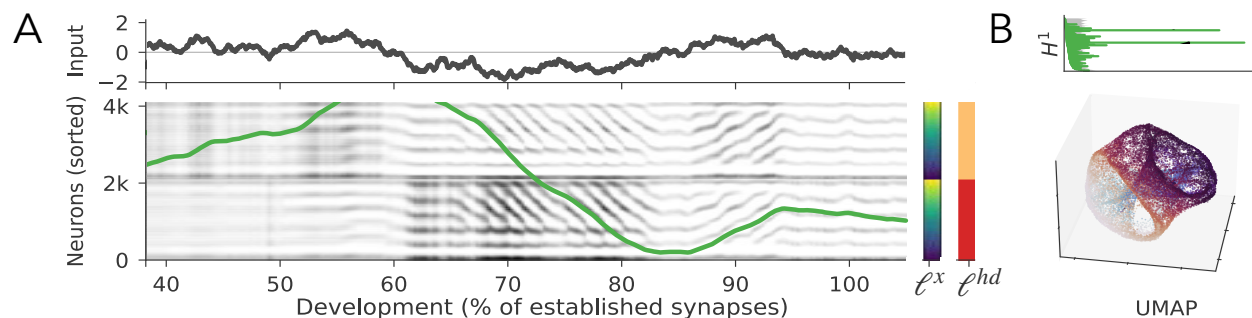
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Humans and animals are equipped with a rich innate repertoire of cognitive and behavioral skills. Yet, the developmental programs that establish the underlying neural structures are unknown. During early development, neural connectivity is shaped by molecular axon guidance and cell adhesion programs that connect neurons based on the affinity between presynaptic receptors and postsynaptic ligands [1]. Here, we show how such chemoaffinity-based connectivity rules can establish innate cognitive functions and motor programs by structuring recurrent architectures prior to experience. To this end, we simulate networks of unconnected neurons with stochastic, uncorrelated expression levels of guidance molecules. We show that different functional networks develop depending on the expression statistics. We present chemoaffinity systems that establish (i) continuous attractor networks for path integration [2] (Fig. 1A) with a toroidal grid cell topology [3] (Fig. 1B), (ii) networks with an exponentially large number of neuronal assemblies and sequences [4] as categorical, hierarchical, or temporal priors, and (iii) networks for arbitrary innate motor trajectories. The model predicts that the expression levels of guidance molecules are directly linked to the semantics of neural representations: neurons belonging to the same ensemble and exhibiting similar sensory or spatial tuning should share a similar expression pattern. Hence, chemoaffinity may shape not only the anatomical organization of the brain but also its innate cognitive and motor functions.



**Figure 1.** Innate development of a path-integration network. **(A)** 1-dimensional path integration. Top: head-direction ( $hd$ ) input encoding velocity. Bottom: Network activity over development; neurons ordered by ligand expression  $\ell^x$ ,  $\ell^{hd}$ . At later stages of development, the activity is periodic and tracks the integrated input (green). **(B)** 2-dimensional path integration network. Toroidal topology in neural activity is revealed by persistent cohomology (top) and nonlinear dimensionality reduction (UMAP, bottom).

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## SEEING THE NEURAL CONTROL OF MOVEMENT THROUGH NEUROMUSCULAR IMITATION LEARNING TO ANALYZE NEUROLOGIC GAIT IMPAIRMENTS

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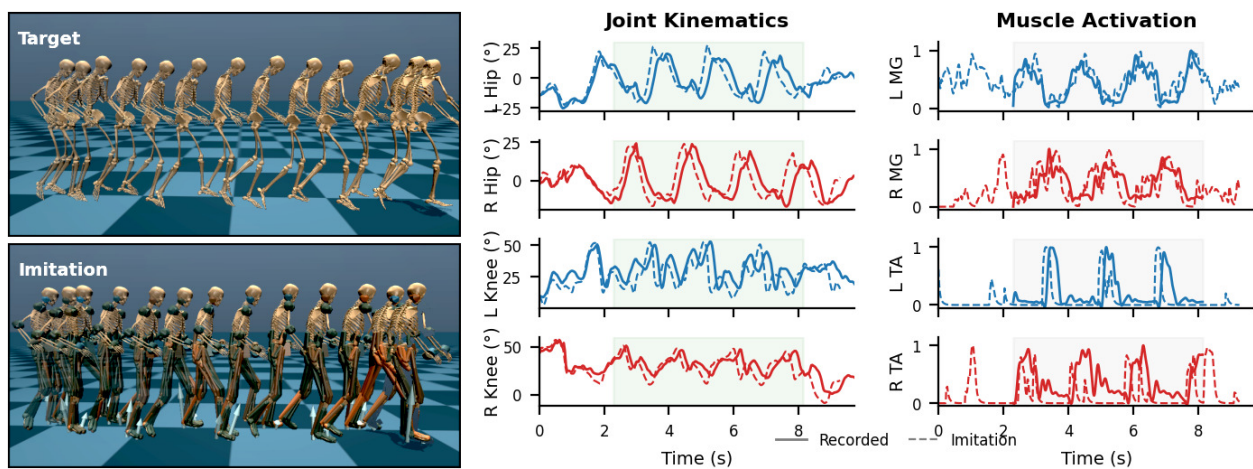
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Advances in human pose estimation now enable measurements of 3D kinematics from multiview and even monocular video. The methods for this have steadily progressively to give deeper insights into the movement, from 2D keypoints in the image plane to 3D keypoints and to the kinematic joint angles for the movements. However, is it possible to obtain an even deeper embodied understanding and infer the muscle activations underlying these observed movements?

We address this question through neuromuscular imitation learning, training a control policy to drive a 92-muscle musculoskeletal model to reproduce observed kinematics within a physics simulator. The control policy has been trained on 34 hours of data from 467 participants, including individuals with neurological injuries being assessed during inpatient rehabilitation. It solves the inverse dynamics problem and learns to infer muscle activations and ground reaction forces that are consistent with the observed motion. We then validated the inferred neuromuscular parameters with paired recordings in a clinical motion analysis laboratory, which also includes surface electromyography. The figure below shows an example trial in which the system reproduces the measured kinematics and predicts muscle activations similar to those measured experimentally.

By applying this model to gait kinematics measured longitudinally during inpatient rehabilitation, we can go beyond purely observing changes in kinematics after a neurologic injury to understanding changes in the neural control of movement.



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## EEG SIGNATURES OF MULTISENSORY PROCESSING IN AUTISM AND SCHIZOPHRENIA

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Multisensory integration (MSI) — the process by which information from different senses is combined to enhance behavioural performance — can be altered in individuals with neurodevelopmental and psychiatric conditions. Here, we use machine learning to examine the neural signatures of MSI and characterise differences in multisensory processing among individuals with Autism Spectrum Disorder (ASD), Schizophrenia (SCZ), and neurotypical controls (CN). EEG data were collected from 23 participants with ASD, 35 with SCZ, and 32 CN while they responded to auditory (A), visual (V), and audiovisual (AV) stimuli.

Behaviourally, significant effects of both group and sensory condition were observed. CN exhibited the fastest reaction times, followed by ASD and SCZ. All groups showed multisensory facilitation with faster responses in the AV condition, though these gains were reduced in ASD and SCZ compared to CN. Drift diffusion modelling indicated that reduced MSI gains in ASD were driven by slower evidence accumulation, whereas those in SCZ stemmed from prolonged stimulus encoding.

To reveal neural markers of multisensory gains, we applied unsupervised machine learning in a transdiagnostic framework to capture task-relevant covariability across individuals. This approach uncovered an early (about 150 ms) occipital EEG component reflecting audiovisual amplification of visual signals, with reduced enhancement in ASD and SCZ. We further employed convolutional neural networks (CNNs) to differentiate EEG responses to multisensory versus unisensory stimuli within each group. Feature visualisation confirmed the involvement of the same spatiotemporal component, reinforcing its role in diminished multisensory gains in the two clinical populations.

Overall, this study provides a combined behavioural and electrophysiological assessment of MSI in ASD and SCZ. By identifying a shared neural signature associated with reduced multisensory facilitation, we highlight a common neurocognitive mechanism underlying atypical sensory processing in these conditions.

## **ETHOPY: REPRODUCIBLE BEHAVIORAL NEUROSCIENCE**

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Progress in neuroscience increasingly depends on sophisticated behavioral paradigms that capture complex and adaptive animal behavior. However, implementing such experiments at scale remains challenging, as behavioral training is often labor-intensive, costly, and difficult to standardize across laboratories and hardware platforms. To address these challenges, we present *EthoPy*, an open-source, Python-based framework for designing, running, and monitoring behavioral experiments, with a particular emphasis on automated, high-throughput home-cage training.

*EthoPy* employs a modular software architecture that separates task logic, stimulus control, hardware interfaces, and data management into independent components. This design enables reuse and extension of experimental code across behavioral paradigms, sensory modalities, and experimental systems, ranging from freely-moving to head-fixed configurations, while operating on affordable hardware such as Raspberry Pi. Database integration and comprehensive metadata tracking support scalable automation with minimal experimenter involvement, while ensuring reproducibility and standardized data handling. *EthoPy* is actively developed, released under an MIT license, distributed via PyPI, and integrates with widely used behavioral and experimental tools.

We demonstrate *EthoPy* across complex behavioral tasks, including visual object recognition and rule switching, across diverse experimental systems ranging from automated home-cage training to open-field and head-fixed setups, such as the Air-Track, and spanning visual, auditory, and olfactory stimulus modalities, highlighting its capacity for adaptive, high-level behavioral training. *EthoPy* provides an accessible and extensible platform for scalable, reproducible behavioral neuroscience, enabling laboratories to share, standardize, and build upon complex behavioral paradigms.

### **Acknowledgments**

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## MECHANISMS OF CEREBELLAR FEED-FORWARD INHIBITION IN A SPIKING ATTRACTOR MODEL OF PRIMATE MOTOR CORTEX

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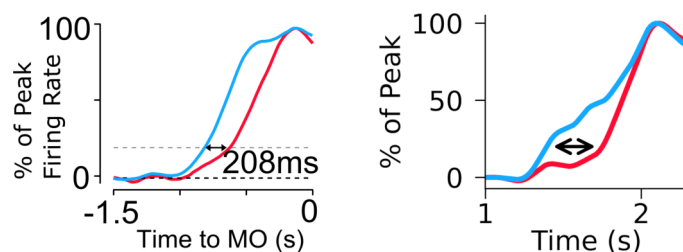
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The motor cortex plays a vital role in movement preparation and execution. During preparation, motor cortical (MC) population activity steadily increases until the movement is initiated. The cerebello-thalamo-cortical (CTC) pathway provides a major input to the MC with thalamo-cortical (TC) cells projecting to both excitatory and inhibitory neurons in the cortex. A recent study [1] found that shortly before movement onset and in response to thalamic input, inhibitory cortical activity *precedes* that of the excitatory pyramidal neurons (Fig. 1A). This phenomenon was termed TC feed-forward inhibition (FFI). Yet the mechanism and computational role of this effect remain unclear.

Here we propose short-term depression (STD) in TC projections [2] differentially tuned for inhibitory and excitatory postsynaptic neurons as the underlying mechanism of FFI. We study the role of CTC input in a large-scale spiking attractor model of the motor cortex that can reproduce experimentally observed spiking statistics, action selection and reaction time modulation in a delayed center-out arm reaching task

[3]. Introducing STD in the TC projections [3] can qualitatively and quantitatively reproduce the experimentally observed FFI effect in single neurons and in the excitatory and inhibitory population averages (Fig. 1B). We explore to which extent our model and experimental FFI data can explain the movement related potential in the local field potential recorded from the monkey motor cortex. Our results allow for an important step towards a comprehensive and mechanistic CTC network model for action selection and movement initiation based on the accumulation of task-relevant sensory input.



**Figure 1.** Experimentally observed (left) and simulated (right) FFI. In both plots, inhibitory (blue) precedes excitatory (red) cortical population activity by 200–300 ms.

### Acknowledgments

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## **SEGREGATION OF SENSORY, COGNITIVE CONTROL AND DECISION REPRESENTATION ACROSS V4, LIP AND PFC UNDER DISTRACTOR COMPETITION**

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Adaptive behavior requires maintaining task-relevant information while selectively processing competing sensory inputs [1]. We analyze population activity from three cortical areas (PFC 3200 units, LIP 1200 units, V4 2000 units across two macaques) during a covert, head-fixed delayed-match to sample task. The task probes sequential comparison of test stimuli against a remembered sample under persistent distractor competition.

Each trial starts with one of four learned sample stimuli (2 orientations x 2 colors, drawn from an 8 orientations x 8 colors feature set), followed by a variable delay and a sequence of 1 to 5 test epochs. At each epoch, a test stimulus from the 8 x 8 set appears at the sample location while a distractor from the same set appears simultaneously in the opposite hemifield. Monkeys report whether test stimuli match the remembered sample conjunction (location, orientation, and color) by releasing a manual lever. Across trials, test and distractor stimuli can fall inside or outside recorded receptive fields (RF), providing a manipulation of attentional selection.

Our analyses follow two decoding approaches. First, SVM decoding on pseudo-populations pooled across sessions assesses how sensory and decision-related information are distributed across LIP, PFC and V4. Coupled to detailed analyses of behavioral strategies, these results suggest a dissociation between areas: LIP match encoding reflect binary decisions, whereas PFC match selectivity reflect continuous cognitive control. Second, to preserve genuine within-session population covariances and day-specific network states, we perform session-by-session time-resolved decoding on real simultaneously recorded populations. Elastic Net classifiers are trained on sliding spike-count windows (100 ms width, 25 ms step) aligned to each test onset. We decode test features (orientation; color ongoing) per test epochs and quantify attentional-dependent readout via in-RF/out-RF and cross-decoding across attentional configurations.

Pilot results reveal time-locked orientation information: decoding is strongest in V4 (macro-AUC 0.7-0.8 in non-match conditions) weaker in PFC (0.58-0.65 depending on test epoch), and near chance in LIP. Ongoing work extends these analyses across sessions and animals, adds decoding match/non-match status, and relates neural readouts to behavioral variability (e.g., reaction times, pupil size, micro-saccade rates, d-prime or decision criterion). It will help us disambiguate parieto-frontal functions for sensory processing, cognitive control and decision making.

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## **NETWORK STRUCTURE AS AN INDUCTIVE BIAS FOR META-LEARNED PLASTICITY RULES IN A CONNECTOME CONSTRAINED NETWORK**

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Unlike artificial neural networks, which typically learn tasks *de novo*, with minimal initial architecture, animal brains are characterized by complex connectivity and diverse modulatory systems refined by evolution. These structures, formed primarily during early development, interact strongly with synaptic learning mechanisms [1], enabling organisms to efficiently learn complex tasks over their lifetime. However, understanding the interplay between innate connectivity, dynamic neuromodulation, and synaptic plasticity remains a challenging problem that has only recently become tractable.

The recent explosion of high-resolution connectomic data, including the full wiring diagram of the *Drosophila* brain [2], has created unprecedented opportunities to study large-scale functional neural networks. One particularly promising approach focuses on the development, training, and analysis of artificial neural networks that emulate biological connectomes. Studying such networks can provide critical insights into the underlying logic of the original biological circuits [3].

Here, we aim to utilize this approach to investigate dependencies between the form of synaptic learning rules, cell type-specific connectivity motifs, and modulatory signaling patterns in the *Drosophila* mushroom body, a well-studied center of associative learning. We develop a large artificial network of adaptive rate neurons that emulates the plastic connectivity between the Kenyon cell layer and the mushroom body output neurons (MBONs), as well as the fixed connections of these populations to dopaminergic neurons (DANs) that modulate the learning process. The network is trained on a range of temporal conditioning tasks involving combinations of reward delays, which fully exploit the intricate recurrent connectivity between different neuronal populations.

We employ a meta-learning approach [4] that identifies general forms of plasticity rules capable of achieving different learning objectives, providing an unbiased framework for studying effective learning mechanisms. Through targeted perturbations of network connectivity, as well as the specificity and timescales of modulatory signaling, we systematically investigate the relationships between these structural features and the resulting forms of synaptic plasticity.

Our work offers insights into how the structure of biological neural networks can act as a strong inductive bias for local learning algorithms, and provides a basis for developing experimentally testable predictions about the interactions between network architecture and learning in insect brains.

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## **DIFFERENTIAL GEOMETRY OF NEURAL MANIFOLDS: CONNECTING NETWORK MECHANISMS TO INFORMATION ENCODING**

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Understanding how network connectivity shapes neural ensemble representations is central to systems neuroscience [1]. While dimensionality reduction methods uncover low-dimensional manifold structure in population recordings, a rigorous framework connecting manifold geometry to network mechanisms and information encoding remains lacking. We develop a differential geometric approach for analyzing neural manifolds in rate-based recurrent networks receiving tuned feedforward inputs. We derive expressions for the pullback metric of neural manifolds, showing how input tuning curves, feedforward synaptic connectivity, and recurrent weights shape manifold geometry. Critically, we establish that the Fisher information matrix, which bounds decoding performance via the Cramér-Rao bound, also has the structure of a pullback metric. This directly links intrinsic manifold geometry to stimulus discriminability and information encoding [2].

Our framework reveals important principles of how connectivity determines neural representations. For noise with slow temporal correlations propagated through the network, we show that recurrent effects on information geometry cancel: Fisher information depends only on the feedforward connectivity. Thus, feedforward connectivity critically determines representational geometry. As an example, we demonstrate that a linear feedforward transformation can map random, spatially broad input tuning curves into a population of regular grid cells with hexagonal periodicity. The resulting neural manifold exhibits toroidal topology [3] and is intrinsically flat, despite the complex embedding in high-dimensional neural state space. This illustrates how feedforward connectivity alone can generate structured spatial representations without requiring carefully tuned recurrent connectivity or continuous attractor dynamics.

Our framework provides quantitative tools for interpreting dimensionality reduction in neural population recordings. By decomposing how connectivity determines manifold structure and linking geometry to information encoding via Fisher information, we offer mechanistic understanding of how ensembles encode information. This unifies geometric and information-theoretic perspectives.

### **Acknowledgments**

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## DIVERSE PLASTICITY RULES FOR TEMPORAL CREDIT ASSIGNMENT IN FLY-CONNECTOME-BASED PARALLEL LEARNING CIRCUITS

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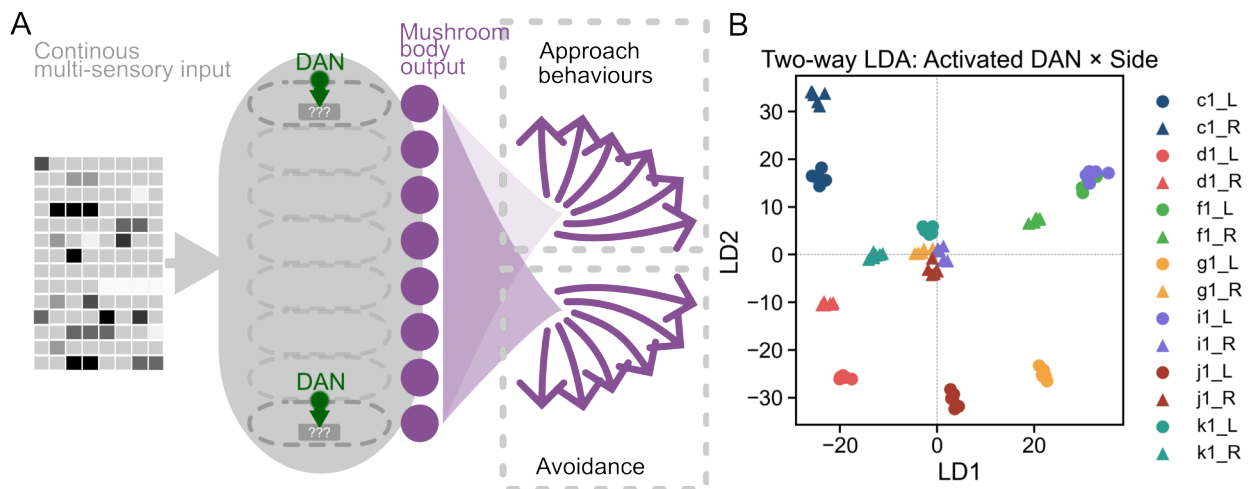
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In high-dimensional, dynamic environments, where sensory cues and reinforcements vary in intensity, modality, source, timing, valence and contextual significance, effective and flexible anticipatory behaviour depends on accurately predicting specific reinforcements from the appropriate sensory cues. Parallel learning and memory circuits are needed for the maintenance, updating, and retrieval of these complex and potentially conflicting predictions.

In the insect brain, the mushroom body serves as the central hub for sensory integration, learning, and reinforcement prediction. Its compartmental organization, defined by anatomically segregated domains of individual dopaminergic reinforcement input, is hypothesized to act as such parallel learning circuits that encode differences in stimulus-reinforcement timing via diverse plasticity rules (Figure 1A).

Using a comprehensive whole-brain synaptic-resolution rate model of the *Drosophila* larva connectome, we investigate the dynamic neural representation of sensory input and reinforcement. We show that the mushroom body output encodes learned valence, specific reinforcement profiles, and location (Figure 1B).

We evaluate the computational advantages of parallel, interconnected learning circuits with diverse plasticity rules for: (i) Maximising the information content of the mushroom body output to instruct specific, high-dimensional behaviour; (ii) encoding, maintaining and selectively retrieving parallel memories with less interference; and (iii) performing temporal credit assignment to predict specific reinforcement profile, source location and timing to support specific and flexible anticipatory behavior.



**Figure 1.** (A) The compartmental organization with distinct dopaminergic innervation (DAN) creates parallel learning circuits. (B) Their output encodes valence, reinforcement profile, and location.

## **PREFRONTAL CORRELATES OF A SOCIAL LEARNING STRATEGY DURING JOINT DECISION-MAKING IN MICE**

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Social animals observe others to guide their behavior and strategically choose when and from whom to learn [1]. Although prefrontal cortical areas are believed to encode the actions and attributes of others [2], how these representations adapt to varying task demands and decisional uncertainty remains unclear. To probe these computations, we designed a behavioral paradigm where pairs of mice, separated by a transparent divider, jointly perform a visually guided, two-alternative forced-choice task. Trial-by-trial, we independently varied visual cue contrast for each mouse to create different levels of perceptual uncertainty between the pair. We observed that mice facing low-contrast stimuli reliably copied the decisions of partners with high-contrast cues, a stereotyped behavior consistent with a strategy that follows the examples of others when uncertain. This reliance on social information was abolished when the partner was replaced by a mechanical slider, confirming the social nature of the computation.

Whole-brain c-Fos mapping revealed increased medial prefrontal cortex (mPFC) activation in mice performing the task jointly compared to those performing it solo. Enhanced activity in regions anatomically and functionally connected to the mPFC suggests that this area acts as a hub for integrating private sensory evidence with social information. We performed large-scale electrophysiological recordings from the mPFC during task execution and revealed functional diversity of single-neuron responses that consistently varied with the mouse's choice, reward, motor activity, and combinations thereof. We also identified neurons with ramping activity that preceded stimulus presentation. This activity was boosted by stimulus onset in a contrast-dependent manner and was higher in trials where mice copied their partner compared to behaviorally-matched solo trials.

We demonstrate that mice actively monitor conspecifics to guide their own decisions under perceptual uncertainty and suggest that social evidence is integrated with visual evidence into a decision variable in mPFC.

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## **BEHAVIORAL AND NEURAL REPRESENTATIONS OF INTERTWINED EPISODES IN THE MACAQUE**

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Real-world episodic recall often requires comparing earlier-later relations across days [1], yet the neural mechanisms supporting such cross-context temporal judgments remain poorly understood.

Two rhesus macaques were trained on a temporal order judgment (TOJ) task using naturalistic video episodes [2] learned across two encoding days. During a mixed-retrieval test on a third day, images sampled from all previously learned episodes were presented in interleaved pairwise comparisons. Behavioral performance was quantified using a Bradley-Terry paired-comparison model to recover latent temporal-order structure. Population spiking activity was recorded from the medial posterior parietal cortex (precuneus/mPPC), yielding 3,000 single units in the main experiment, and analyzed using cross-temporal decoding, demixed principal component analysis (dPCA), and nonlinear manifold geometry methods. To verify specificity, we conducted a control experiment using the same TOJ procedure with images unrelated to those encoded video episodes, recording 800 single units.

Behaviorally, the inferred latent temporal rankings closely matched the ground-truth episode order. Neurally, cross-day temporal order information became decodable 200 ms after stimulus onset, with correct trials exhibiting stable cross-temporal decoding and coherent low-dimensional population trajectories that rapidly separated source-day context. These dynamics formed a structured temporal memory subspace with a concentric organization, in which earlier temporal positions occupied peripheral regions and later positions clustered centrally. In contrast, the control experiment showed no reliable temporal distance effects, no systematic latent ordering, and no stable temporal decoding or structured neural manifold.

These findings show that temporal order memory during mixed episodic retrieval depends on stable population-level dynamics in the macaque precuneus and is specific to meaningful episodic representations. A dynamically maintained temporal manifold supports a population-based neural architecture of episodic time [3].

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## FROM ENSEMBLES IN VISUAL CORTEX TO DEEP SPIKING NETWORKS: CONSERVED FUNCTIONAL CONNECTIVITY PROPERTIES

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Although the properties of individual neurons in the visual cortex are well-studied, far less is known about how ensembles that co-activate more often than expected by chance operate as units of cortical computation. Spontaneous and stimulus-driven population activity exhibits non-random, structured patterns indicative of ensemble organization [1, 2]. Synchronously-firing ensembles are thought to efficiently relay shared information to downstream targets [3] and participate in networks subserving similar functions.

Using large field-of-view, high-resolution two-photon imaging, we analyzed activity in granular (L4) and supragranular (L2/3) layers of mouse V1 and higher visual areas. Functional connectivity was identified using the spike time tiling coefficient (STTC) [4] that measures pairwise neuronal correlation strength. We characterized a neuron's first-order functional connections (1FC) as its connections with statistically significant correlations (z-scored above 4). We argue that neurons, together with their 1FC groups, define ensembles that serve as information processing primitives.

The firing probability of L2/3-pyramidal neurons is conditioned on the co-firing of their L4-1FC partners, following a ReLU-like pattern, increasing sharply when  $\geq 13\%$  of their L4-1FC partners co-fire. This behavior defines a weak/no-response regime and a strong-response regime (rare event), which supports sparse yet reliable firing, adapting to the dynamic range of L4-1FC co-firing. The number, rather than the identity, of co-firing L4-1FC partners affects L2/3 responses. These properties persist across different conditions (e.g., quiet wakefulness, stimulus presentation, alertness).

We observed the same properties in trained spiking neural networks when we applied our methodology during testing with unseen images from the CIFAR-100 dataset. Similar results were obtained with other models.

These findings suggest that structured, task-relevant connectivity patterns naturally arise in both biological and artificial systems, providing a foundation for embedding cortical-like principles to enhance learning efficiency, robustness, and interpretability in neuroAI models.

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## POPULATION DECODING OF VISUAL MOTION DIRECTION

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Understanding how information is internally represented in the primary visual cortex (V1) is essential for explaining the way the external world is perceived. Studies of planar motion direction selectivity in non-human primates, particularly using naturalistic stimuli such as MotionClouds [1], reveal a high degree of diversity and the coexistence of multiple encoding mechanisms within neuronal populations [2]. Here, we investigate how a large population of V1 neurons jointly encodes stimulus direction and orientation by systematically manipulating the precision of both orientation and spatial frequency.

Using an explainable decoding approach, test-set accuracy shows, first, that a broad distribution of spatial frequencies improves decoding performance, and second, that orientation precision is a critical factor in the representation of motion direction. Specifically, high orientation precision gives rise to the aperture problem, leading to ambiguity in motion direction encoding.

Weights extracted from the optimized decoder were projected into a new subspace using principal component analysis (PCA). Direction-related weights, originally organized along a circular structure, progressively lost cluster discriminability as orientation precision decreased. These weights could then be used to reconstruct tuning curves in a fully data-driven manner.

Finally, our results suggest that orientation precision may play a major role in shaping the interaction between orientation and motion direction representations.

### Acknowledgments

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## NEURAL MULTIPLEXING VERSUS PLACE CODING: MULTIPLEXING STEPS IN WHEN MOST NEEDED

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Sensory scenes contain many different stimuli. How does the brain maintain information about each item separately? Two complementary theories are that the brain segregates such signals via (i) place codes, such that different populations of neurons encode each item; and/or (ii) time division multiplexing, such that neurons switch back between encoding each item over time [1–3]. Such time division multiplexing would appear to be required when the population of neurons responsive to each stimulus overlaps, as place coding lacks the granularity to resolve the two stimuli. If multiplexing functions to segregate information about concurrent stimuli with largely overlapping neural responses, we would expect that as neural responses to component stimuli become more similar, there would be a greater incidence of multiplexing.

We tested this hypothesis using responses in the macaque inferior colliculus to combinations of two sounds of varying frequencies (sound frequency being the chief sensory dimension that is place coded in this structure). Bayesian posterior probabilities of multiplexing were calculated for each dual-stimulus condition [2, 4]. We investigated whether the difference in neural spike count in response to each individual stimulus affected the probability of a neuron being classified as multiplexing for the dual-stimulus condition.

We found that as the neural response to each individual stimulus condition became more similar, the proportion of neurons classified as multiplexing increased. This suggests that when the neural responses to component stimuli are similar, multiplexing is needed to differentiate the response to each individual stimulus. However, when the responses are sufficiently different, place coding likely suffices and multiplexing may not be required.

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## TASK LEARNING INCREASES REDUNDANCY OF V4 RESPONSES REFLECTING A FLEXIBLE REDISTRIBUTION OF INFORMATION

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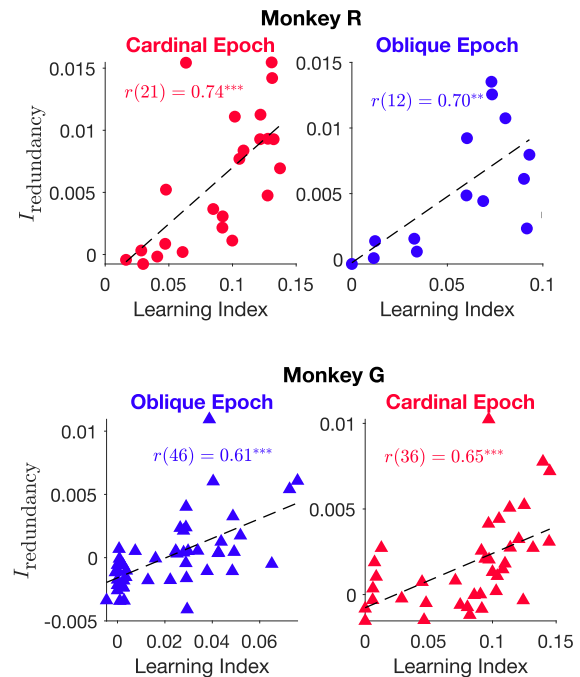
† equal contribution

How the activity of sensory neurons supports perceptual decisions remains one of the central questions of systems neuroscience, with two primary frameworks guiding thought. One framework, following ideas of redundancy reduction and information maximization, focuses on the decision-related information represented by neural responses and how it is extracted from sensory populations. In the other framework, based on the Bayesian brain hypothesis, neural activity encodes posterior beliefs about the outside world, which then guide decision making. Interestingly, these two perspectives make opposing predictions for whether redundancy (*information-limiting* correlations) should decrease or increase over the course of task learning [1].

Here, we present new empirical and theoretical results to test these predictions. Training two macaques on two different orientation discrimination tasks each, while recording from area V4 with Utah arrays, we find that noise correlations systematically change with learning so as to *increase* information-limiting correlations, both over weeks with learning, and over hundreds of milliseconds within a trial. This finding confirms a critical prediction of the hierarchical generative inference framework and is compatible with prior studies that have found task-specific noise correlations at the end of learning. Importantly, it challenges the dominant interpretation of changes in noise correlations due to learning and attention: mediating the relationship between learning and attention with behavior by how much it reduces, or limits, information [2]. New analyses of a sampling-based hierarchical inference model [3] instead predict that the increase in information-limiting correlations does not reflect lower feedforward input information [4], but instead a redistribution of task-related information via top-down signals, leading to an increase in the redundancy of sensory responses, a prediction we confirm in our data. Finally, our data show that this redistribution is flexible and switches within a session between different tasks providing further evidence that it is controlled by feedback signals as predicted by hierarchical inference.

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**Figure 1.** Redundancy *increases* in *each* learning epoch, individually significantly. Training order counter-balanced across monkeys. Each data point represents one recording day.

## **COORDINATED MULTILAMINAR DYNAMICS UNDERLIE MULTIPLEXED COMPUTATION IN MOTOR CORTEX**

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Functional multiplexing is a signature of higher-order brain regions. Beyond single-unit mixed selectivity, the six-layered cortical microcircuit has been proposed as an optimal substrate for such parallel computations. Recurrent connections within and across layers allow cortical columns to retain incoming information for some time and integrate it into stable latent representations, thereby acting as functional units. The key question is whether the multiplexing capacity arises from specialized processing within individual layers or the collective coordination of multi-layer activity patterns.

Here, we analyzed laminar recordings from the motor cortex of macaque monkeys performing a complex delayed match-to-sample task. We identified laminarily distributed, behaviorally specific subspaces that captured the encoding of distinct task-related variables. These subspaces, spanning the entire column and expressed as coordinated activity patterns, were functionally reused to encode the same variable over time and flexibly recycled to encode new ones.

Subtle variations of laminar weights gave rise to multiple coexistent laminar coding subspaces, enabling multiplexing at the columnar level. Task-related information propagated across layers in temporally organized trajectories that transiently localized in superficial or deep layers at distinct trial epochs. These organized laminar trajectories were consistently observed across recording sites, but exhibited site-specific propagation patterns. The activity of the population on the other hand lacked structured dynamics. Thus, laminar trajectories of information emerged atop a background of spatially and temporally unspecific activity-fluctuations.

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EU Horizon 2020 Marie Skłodowska Curie Actions grant, In2PrimateBrains – 956669 FLAG-ERA grant PrimCorNet, ANR-19-HBPR-0005; ANR FunSy grant, ANR-25-CE45-2766; Neuroschool end-of-Ph.D. grant from the French government under the “France 2030” investment plan managed by the French National Research Agency and from Excellence Initiative of AixMarseille University.

## LOCAL AND GLOBAL VISUAL PROCESSING IN THE MOUSE BRAIN: FROM RECEPTIVE FIELDS TO POPULATION CODES

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Every day, we interact with thousands of objects, each composed of local features — such as edges and textures — and global features, including overall shape and structure. Object recognition relies on both the processing of fine details and their integration into coherent representations, commonly referred to as local and global processing respectively. Along the ventral visual stream, information flows from the primary visual cortex (V1) to higher-order visual areas (HVAs), where receptive field (RF) size typically increases [1]. However, a fundamental question remains: does combining information from neurons with spatially distributed RFs enhance or impair object discrimination?

We addressed this by analyzing two-photon calcium imaging data recorded simultaneously from V1 and HVAs (Lateromedial Area, LM; Anterolateral Area, AL; Rostrolateral Area, RL) while mice were head-fixed and passively viewing 3D moving objects. Objects underwent several transformations (translation, rotation, magnification, background changes) that modulated both local and global features. Using a linear classifier, we decoded object identity from neuronal sub-populations with varying spatial distributions of RF centers. In V1, LM, and RL, object discriminability decreased as the spatial spread of RFs increased, while AL did not show such effect-maintaining stable performance across all spatial scales.

To determine whether this scale-dependence could be due to the stimulus statistics, or a combination with either local connectivity and/or feedback connections, we generated a control model. Object stimuli were convolved with V1-like filters obtained through Independent Component Analysis to generate simulated neural responses [2]. The model reproduced the decreased discriminability with increasing spatial spread, particularly when background information was present, suggesting that stimulus statistics partially account for the observed effects.

Our findings reveal that different visual areas employ distinct strategies for integrating spatial information during object recognition. This work may shed light on how different object transformation parameters differentially modulate discrimination across the visual hierarchy, with implications for understanding the computational principles underlying hierarchical visual processing.

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## **DOPAMINE AND STIMULUS DISCRIMINATION IN THE DENTATE GYRUS**

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The ability to form distinct episodic memories about similar events in our lives allows us to distinguish between our many day-to-day experiences. The dentate gyrus (DG), a subregion of the hippocampus, is essential for this discrimination process, performing what is often called pattern separation. Research describes that dopamine (DA) is essential for DG plasticity and function, however, the precise timing of DA release into the DG during learning and the specific functions of D1 and D2 dopamine receptors in the DG is unknown.

First, we explored the source of DA to the DG. We lesioned dopaminergic hubs, the locus coeruleus (LC) or the ventral tegmental area (VTA) and measured DA release in the DG with fiber photometry while mice underwent a behavioral task. We found that mice with LC lesions had significantly less DA release in the DG compared to those with VTA or sham lesions, suggesting that the DG primarily receives DA from the LC.

Next, we probed the contribution of DA in the DG to pattern separation using a trace discrimination task (TD). In TD, mice learn to discriminate between two auditory cues, one that predicts shock (conditioned stimulus, CS+) and one that does not (CS-). A stimulus-free trace period separates the CS+ and shock. We measured DA release in the DG throughout TD. We found that during learning, DA is released to the CS+ and shock, but not to the CS- nor the trace interval. Then, we investigated how neurons expressing either D1 or D2 receptors behaved during TD. In a D1-Cre line of mice, we imaged D1+ neuron activity with fiber photometry during mouse learning. We found that D1+ neurons show a similar activation profile to general DA release. When we examined this in D2-Cre mice, we found that D2+ neurons are not active to either CS, fall below baseline activity during CS+ trace periods, and are active during shock. D1 receptors are primarily located in granule cells within the granule cell layer of the DG and D2 receptors have only been found in mossy cells within the hilus of the DG. Although located in different layers of the DG, D1+ and D2+ neurons likely receive similar dopaminergic input. D2 receptors exert an inhibitory effect on neurons, so we expected to see less activity in these cells when DA is released. This unexpected finding is likely due to stronger input from another neurotransmitter (*i.e.*, glutamate). We predict that mossy cells are encoding different task stimuli than D1+ granule cells. Finally, we antagonized either D1 or D2 receptors prior to mouse learning. We found that D1 antagonism results in significantly worse performance on the task while antagonizing D2 receptors results in a trend of better performance.

These results suggest that the DG primarily receives DA from the LC and that ensembles of D1 and D2 neurons differentially encode information about task-relevant stimuli. D1+ neurons may be encoding salient stimuli while D2+ neurons may be encoding the absence of stimuli in preparation for a shock.

### **Acknowledgments**

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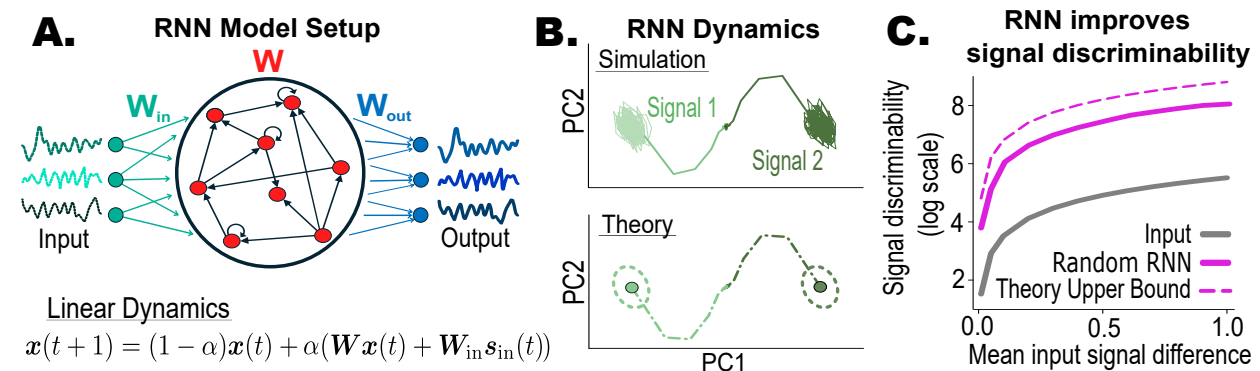
**EXACT DYNAMICS OF LINEAR RECURRENT NEURAL NETWORKS IN COGNITIVE TASKS***James McAllister\**, *Cian O’Donnell*

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Recurrent neural networks (RNNs) are widely used to model neural circuit dynamics and computation, but their internal mechanisms are difficult to interpret. This is a problem, as we don’t know how the geometry of the RNN’s signal representations contributes to task performance, nor how to interpret network readouts found via supervised learning or optimisation.

Here, we use theoretical analysis and simulation to study the dynamics of input-driven linear RNNs in settings relevant to working memory, decision-making, and fixation-response tasks. We first examine how these networks act as linear filters of past inputs, showing that temporal history is encoded geometrically in the network’s activity. We then derive closed-form expressions for the steady states and covariances of network activity as functions of input statistics, demonstrating that RNNs can significantly amplify signal discriminability between noisy stimuli, which enables robust classification or decision-making. Third, for fixation-response tasks, we characterise how appropriate input and recurrent structure can enforce a clean separation between the distinct input-driven or intrinsic dynamical regimes. We verified our theoretical analysis against numerical simulations of linear RNNs, finding an excellent match.



**Figure 1.** (A) Linear RNN model setup. (B) Agreement between simulation (upper) and theory (lower). (C) Signal discriminability improves in the RNN over the input.

Our results provide a geometric interpretation of network responses under different input regimes, and thus clarifies how these neural representations facilitate computation via interpretable linear input and output layers, while the RNN itself is left untrained. Based on this observation, we demonstrate how readouts can be constructed in unsupervised theory-driven or data-driven ways, avoiding the obscurity of supervised learning. We further show that biologically realistic learning, in the form of generalised Hebbian algorithms, can be used to train the relevant output layers.

**Acknowledgments**

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## **NEURAL CORRELATES OF CONTINUOUS PERCEPTUAL DECISIONS IN RHESUS MACAQUES IN SOLO AND SOCIAL CONTEXT**

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Social interaction shapes behavioral performance in cognitive tasks, yet the neuronal mechanisms underlying this influence remain unclear. Here, we aim to demonstrate where social information integrates during sensory processing and how it affects sensory and confidence representations, as well as choice encoding in the brain. We used a continuous perceptual report (CPR) task with a continuously changing stimulus and peri-decision wagering to investigate visual perception and confidence. During this task, rhesus monkeys reported their perceived direction of moving random dot patterns (RDP) using a joystick. A cursor around the fixation point indicated joystick direction, and its width decreased with stronger joystick tilt. A wider cursor increased the likelihood of catching a reward target, presented at random points in time along the current motion direction, but yielded smaller rewards. This peri-decision wagering greatly rewarded accurate and confident responses, while accurate low-confidence responses only produced small rewards. Inaccurate responses were not rewarded. Previously, we used this approach in humans for a real-time assessment of perceptual accuracy and corresponding confidence in solo and dyadic contexts [1].

Here, we report results from side-by-side monkey-human dyads (2 rhesus monkeys, 2 human partners). A shared display showed the stimulus and the continuous perceptual reports of monkey and partner. As in our previous study, human partners' confidence reports increased with RDP coherence, suggesting higher confidence with higher motion strength. The monkeys showed higher joystick tilt when the directional error was small, indicating real-time peri-decision wagering. In the social condition, the monkeys' joystick responses changed, with higher joystick tilt and lower accuracy compared to the solo CPR. However, the social modulation of behavior varied between the two monkeys and seemed to depend on stimulus coherence.

While the monkey performed the CPR task, we used two 32-channel Plexon V-probes to record extracellular spiking activity in area MT and along the intraparietal sulcus (primarily area LIP) in the right hemisphere of one rhesus monkey. Preliminary results indicate that around a fifth of stimulus-driven MT units showed a significant difference in response to the preferred direction of the neuron between the solo and dyadic condition. Some units displayed a suppression in average firing rates, while others increased their average spiking activity. Our results suggest behavioral and neural differences between dyadic and solo conditions, providing evidence that sensory neurons are involved in integrating social cues with sensory evidence during perceptual decision-making.

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## LEARNING TO CLUSTER NEURONAL FUNCTION

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Deep neural networks trained to predict neural activity from visual input and behaviour have shown great potential to serve as digital twins of the visual cortex. Per-neuron embeddings derived from these models could potentially be used to map the functional landscape or identify cell types. However, state-of-the-art predictive models of mouse V1 do not generate functional embeddings that exhibit clear clustering patterns which would correspond to cell types among excitatory neurons. This raises the question whether the lack of clustered structure is due to limitations of current models or a true feature of the functional organization of mouse V1.

In this work, we introduce DECEMber (Deep Embedding Clustering via Expectation Maximization based refinement), a method that incorporates an explicit clustering inductive bias into the training of neuronal embeddings to improve the identifiability of functional cell types. We see this as model-driven hypothesis testing: If clear functional cell types exist then such bias should improve the model performance, embeddings structure and/or cluster consistencies. Building on Deep Embedding Clustering (DEC) [1] we introduce an auxiliary clustering loss that jointly optimizes embeddings and clustering parameters via a learned multivariate t-mixture model, enabling non-isotropic clusters of varying sizes and yielding a flexible, biologically plausible embedding structure.

We demonstrate that these modifications improve cluster consistency while preserving high predictive performance and surpassing standard clustering methods in terms of stability. Moreover, DECEMber generalizes well across species (mice, primates) and visual areas (retina, V1, V4).

### Acknowledgments

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## **INVESTIGATING TASK-DEPENDENT MODULATION OF VISUAL CORTICAL ACTIVITY USING LARGE-SCALE RECORDINGS AND OPTOGENETICS**

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Understanding how sensory information is transformed into neural activity that supports flexible behavior requires identifying how cortical areas are engaged under different task demands. Sensory processing involves multiple interconnected cortical regions with distinct response properties, yet how their engagement changes with task context remains poorly understood.

We addressed this question using the mouse visual system, which comprises multiple higher visual areas (HVAs) with distinct functional and anatomical properties. Mice were trained on visual discrimination tasks based on stimulus location, size, or orientation. All tasks were learned and performed with comparable accuracy. To examine how visual circuits are engaged under different task demands, we combined patterned optogenetic perturbations, widefield population imaging, and multi-site cellular calcium imaging.

To assess causal contributions, we applied mesoscopic optogenetic suppression to visual cortical areas during behavior. During the size discrimination task, suppressing V1 and HVAs reduced performance, with the largest effects observed following inhibition of V1 and anterior visual areas (Anterolateral Area, AL; Rostrolateral Area, RL). In contrast, during the location detection task, suppressing most HVAs had little effect on accuracy, although reaction times tended to increase.

Consistent with these behavioral effects, area-averaged analyses of one-photon Ca<sup>2+</sup> imaging across the dorsal cortex during the size discrimination task showed the strongest activation in V1 and anterolateral HVAs (AL, RL, and Lateromedial Area, LM). These analyses were quantified using area-under-the-curve measures and Monte Carlo bootstrap statistics. Ongoing work applies linear encoding models to separate sensory and behavioral contributions to large-scale cortical activity

Together, these preliminary results indicate task-dependent differences in the engagement of visual cortical areas. To further examine the underlying cellular activity, we acquired a large dataset of simultaneous two-photon calcium recordings across HVAs. Our goal is to reveal how neuronal ensembles encode contextual and sensorial information. Current analyses use decoding approaches to dissociate sensory, contextual, and behavioral signals, and to evaluate how these signals relate to the causal involvement of specific cortical areas.

## **WAVE-SPIKE INTERACTIONS ENCODE OVERT AND IMAGINED SPEECH**

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The human ability to transform meaning into a coherent stream of imagined or overt speech involves a hierarchy of neural processing stages distributed across cortical regions. Recent evidence indicates that neuronal spiking activity in distinct brain regions encodes similar linguistic features [1–3]. Yet, at the neuronal level, the mechanisms by which information encoded in the spiking activity is coordinated across different brain regions and spatial scales remain unclear.

Here, we investigated interactions between neuronal ensemble spiking and local field potential (LFP) activity across multiple spatial scales in two human participants with epilepsy. We analyzed spiking and local LFP activity recorded from microelectrode Utah arrays (MEAs), simultaneously with large-scale LFP activity from surrounding electrocorticography (ECoG), while participants overtly or covertly produced single words. We characterized ensemble spiking activity and propagating LFP waves at both local (MEA) and large-scale (ECoG) levels.

We found a coordinated hierarchy of interactions across neural scales. Ensemble spiking activity was significantly modulated by the phase of local propagating waves, demonstrating robust wave-to-spike interactions. Phase-spike coupling was stronger during task performance than during baseline, peaking during the speaking period for overt speech and during the planning period for imagined speech. Overt and imagined speech were also associated with distinct preferential wave phases.

Large-scale propagating waves at the ECoG level reliably correlated with the emergence of local waves within the MEA, providing evidence for cross-scale wave-to-wave coupling. However, large-scale waves and their direct relationship to spiking did not predict trial type.

Together, our results suggest that large-scale waves primarily organize the timing of local neural dynamics, while local waves directly modulated spiking excitability, allowing the encoding of key aspects of overt and imagined speech.

### **Acknowledgments**

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## **RESTORING CaMKII FUNCTION IN HIPPOCAMPUS AND OLFACTORY BULB ENABLES ODOR ASSOCIATION LEARNING IN CaMKII $\alpha$ KNOCKOUT MICE**

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The alpha isoform of calcium/calmodulin-dependent protein kinase II (CaMKII $\alpha$ ) is a key molecular mediator of synaptic plasticity, long-term potentiation (LTP), and memory consolidation. CaMKII $\alpha$  is highly enriched in hippocampal pyramidal neurons and olfactory bulb granule cells, where its kinase activity supports experience-dependent circuit modification. Although CaMKII $\alpha$  knockout (KO) mice exhibit pronounced deficits in neuronal maturation and cognitive function, its specific mechanistic role within the olfactory-hippocampal network remains incompletely understood.

To address this gap, we combined behavioral training with simultaneous electrophysiological recordings to investigate how CaMKII $\alpha$  loss disrupts olfactory associative learning and interregional communication. Adult CaMKII $\alpha$  KO and wild-type littermates were trained on a go/no-go odor discrimination task while local field potentials were recorded concurrently from the hippocampal CA1 region and the olfactory bulb during awake behavior. KO mice displayed significant impairments in acquiring fine odor discriminations. Remarkably, targeted viral restoration of CaMKII $\alpha$  expression in both regions rescued learning performance, demonstrating that local CaMKII $\alpha$  activity is essential for sustaining effective cross-structure communication during odor-guided tasks.

Together, these findings identify CaMKII $\alpha$  as a critical integrative component that enables dynamic information flow between early sensory and mnemonic circuits required for associative learning. By linking disrupted kinase signaling to weakened hippocampal-olfactory coupling, this work reveals a molecular mechanism for multisystem coordination underlying sensory-based memory formation and establishes CaMKII $\alpha$  as a key modulator of cross-regional network plasticity.

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## **DIMENSIONALITY AND GEOMETRY OF OBJECT CODING ACROSS THE MOUSE VISUAL HIERARCHY**

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Object recognition requires the visual system to construct population-level representations that are robust to large variations in sensory input. A long-standing hypothesis is that such invariance emerges through transformations of neural population geometry along the visual cortical hierarchy. Despite extensive study, there is still no consensus on the dimensionality of visual cortical representations and whether geometric properties identified in primary visual cortex generalize across higher visual areas.

Here, we investigate the dimensionality and geometric organization of population activity across the mouse visual cortex using large-scale two-photon calcium imaging. We analyzed simultaneous recordings from head-fixed mice while viewing three-dimensional moving objects under varying stimulus conditions. We extracted the neural activity from the primary visual cortex (V1) and three higher visual areas of the mouse, lateromedial area (LM), anterolateral area (AL), and laterointermediate area (LI). Using linear analyses of population activity, we find that responses in all visual areas exhibit high apparent dimensionality, with the number of dimensions required to explain population variance scaling with the size of the recorded neural population. Importantly, this high dimensionality is stable across repeated subsampling of neurons, suggesting that it reflects genuine structure rather than noise or sampling artifacts. To test whether this high-dimensional variance reflects a lower-dimensional nonlinear structure, we estimated the intrinsic dimensionality, which is the minimum number of parameters to approximate the neural space. Intrinsic dimensionality was substantially lower than its linear counterparts, suggesting a low-dimensional manifold structure of the neural code.

Comparisons across visual areas reveal systematic differences in how variance is distributed across population activity dimensions, with areas such as LI and AL concentrating more variance into their primary dimensions, relative to V1. To interpret the functional relevance of this geometry, we leveraged the behavioral state as a natural modulation of cortical processing. In particular, during locomotion, object-identity decoding improves across all visual areas, indicating that active behavioral states enhance the alignment of population activity with task-relevant dimensions. Specifically, we compute a separation index that evaluates linear separability between object manifolds in the neural space, revealing that during locomotion decoding is improved by pushing object representations farther apart.

Together these results support a geometric view of object representations in which visual cortical population activity remains high-dimensional, yet exhibits area-specific and state-dependent organization. Thus it ultimately constrains how object information is embedded and accessed across the visual hierarchy.

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**CORTICAL DYNAMICS OF POSE INVARIANCE DURING VISUAL OBJECT RECOGNITION**

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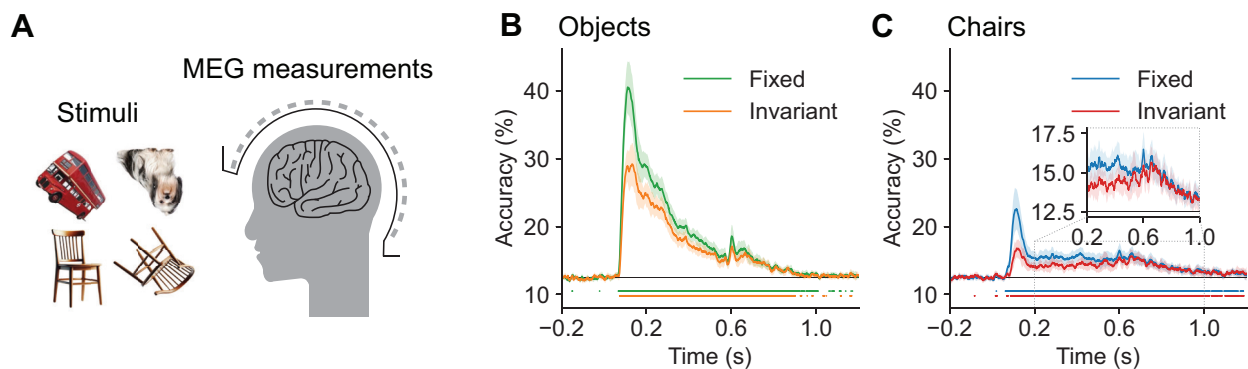
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Humans can recognize objects despite visual transformations such as changes in pose. During object recognition, cortical object representations become increasingly invariant to transformations [1]. While prior studies have investigated invariant object representation dynamics across distinct object categories [2, 3], focusing on visually similar objects within the same object category could better probe pose invariance due to increased discrimination difficulty.

To examine this question, we investigated temporal dynamics of invariance to changes in pose for both visually distinct objects and visually similar objects. Brain activity was recorded from 20 participants using magnetoencephalography (MEG) while they viewed images of eight distinct objects and eight chairs sharing similar low-level features (Fig. 1A). Each object was shown in five different in-plane orientations.

Time-resolved multivariate decoding analysis revealed for both visually distinct objects (Fig. 1B) and visually similar chairs (Fig. 1C) that pose-invariant and fixed-pose object information peaked around 120 ms. Importantly, for the chairs (Fig. 1C), we observed a significant progressive increase in pose invariance at 200–700 ms, which was absent for distinct objects and fixed-pose information. This indicates that later processing stages are required to build invariance for confusable objects. Overall, our findings suggest that pose invariance may depend on more extended recurrent processes than previously thought.



**Figure 1.** We measured MEG responses to object images (A). Time-resolved decoding of object identity for distinct objects (B) and similar chairs (C).

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## DATA OPTIMIZED BIOPHYSICAL MODEL IDENTIFIES PARALLEL SUBNETWORKS UNDERLYING FUNCTIONAL AND STATISTICAL PROPERTIES OF AUDITORY CORTEX

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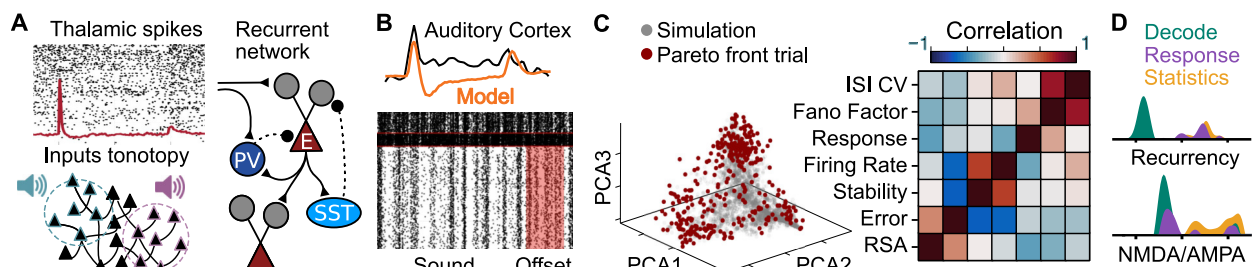
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The auditory cortex (AC) is crucial for processing complex sound patterns. Different AC neuronal populations activate in response to specific sound sequences, transforming auditory information into population codes [1, 2]. Theoretical research suggests that time-dependent computations require memory on the timescale of the input, supported by biophysical processes such as short-term synaptic plasticity (STP), recurrent connectivity, and cellular integration. However, how they contribute to integration of complex sounds remains unclear.

We address this question using a new approach to biophysical modelling with high-throughput genetic optimization to replicate AC's functional and statistical properties [3]. Networks are composed of 3200 excitatory and inhibitory cells, stimulated with spike trains recorded in mouse thalamus during passive listening of 88 distinct sounds (Fig. 1A). Neurons are sparsely connected to recurrent and input projections, and spatially organized to mirror tonotopy in AC. We compare model dynamics with voltage- and calcium-imaging recordings and optimize sound recognition, decorrelation of population activity, response dynamics, representation stability, and minimize the cross-entropy between model and AC spike statistics (Fig. 1B). The optimized parameters span recurrent and input connectivity, cell excitability, inhibitory homeostasis, and STP.

The genetic algorithm finds parameters that optimize each individual constraints, but no combination satisfies all constraints at once, creating a landscape of continuous local minima (Fig. 1C). By analyzing the local solutions, or Pareto front, we isolate subdomains that explain sound decodability, representation stability, and response statistics. Each subdomain has a different network dynamics, indicating that the AC may rely on distinct and loosely connected subnetworks to carry the computations associated with sound integration. These subnetworks have distinct underlying parameter distributions indicating that multiple physiological and connectivity factors are at play, and with different importance, to support AC computations (Fig. 1D).



**Figure 1.** (A) Biophysical model and thalamic inputs. (B) Model activity is fit to recordings. (C) Genetic optimization satisfies subset of constraints. (D) Distinct parameters underlie distinct functions.

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## **INFERENCE, MANIFOLDS, AND LEARNING**

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We present a theory of neural computation that brings together three fundamental observations regarding behaviour, neural dynamics of cortical circuits, and learning.

That inference is fundamental to cognition has been recognised since at least the time of Helmholtz. Effective inference depends on the integration of noisy and ambiguous sensory input with an accurate internal model of the sensory world, and of the consequences of one’s actions. Furthermore, this model—and the characteristics of the sensory input—must be learnt and updated from experience, usually without any separate access to the world-state that is to be inferred. Although the mathematical framework for inference itself is well worked out, less is known about how inferential processes may be implemented in neural dynamics, and how states may be learnt without explicit supervision or generation.

To resolve these issues, we link aspects of neural circuitry to inferential dynamics: specifically, we hypothesise that recurrent neural circuits have evolved to implement minimisation within the dual representation of exponential family distributions. The recurrent circuit then defines the family and the inferential process. Distributional families can be defined by a manifold of accessible states. We suggest that the bounding manifolds that describe experimental neural activations reflect these distributional forms. At a circuit level, broad inhibitory cell classes (such as parvalbumin-positive fast-spiking interneurons) combine with supralinear amplification along constrained dimensions to shape the manifold, and thus the probabilistic computation.

Exploiting a recently-developed theory of recognition-parametrised models, we also show how Hebbian-like learning rules are able to learn both the appropriate manifold (and thus the distributional family) and the evidence-dependent inputs that drive activity, without explicit supervision and without parametrised generation

We show that the hypothesised components are able to recapitulate both behavioural and neural observations. Specifically, we build models that: (i) learn to optimally combine complex high-dimensional sensory inputs; (ii) recover complex coding manifolds associated with orientation and spatial phase in visual inputs; and (iii) learn accurate forward models of complex controlled nonlinear motor dynamics, from babble-like motor activity.

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## **NEURAL INNOVATION REVEALS TASK-DEPENDENT (MIS)ALIGNMENT BETWEEN NEURAL INTENT AND SHARED-CONTROL POLICIES IN iBCI NAVIGATION**

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Adaptive behavior requires rapid updating of internal control policies when environmental contingencies change, particularly in closed-loop interactions mediated by shared-control systems. We investigated the neural dynamics underlying such updates in macaques performing closed-loop navigation in virtual reality using an invasive brain-computer interface (iBCI), during externally imposed perturbations including obstacle appearance and target displacement (respawn). Neural activity was decoded with a state-space model in which low-dimensional latent states captured the animal's intended control policy, and AI assistance was present in half of the trials. We quantified neural innovation as the mismatch between observed neural activity and that predicted by the current latent state, driving subsequent latent reconfiguration.

Across perturbation types, we observed transient increases in neural innovation time-locked to perturbation onset. These innovation responses preceded large latent deviations and corrective updates, indicating a violation of the ongoing internal model followed by rapid reconfiguration of the intended control policy. Innovation magnitude scaled with both latent displacement and the strength of subsequent state corrections, establishing it as a quantitative marker of internal replanning.

In the appearing-obstacle task, AI assistance substantially improved performance (+23 percentage points) and reduced early innovation responses on correct trials, consistent with a reduced need for internal corrective updates when environmental constraints were handled externally. In contrast, during target displacement (respawn task), AI assistance impaired performance (−13 percentage points) and was associated with sustained innovation, reflecting persistent conflicts between updated neural intent and AI temporal priors following rapid goal changes.

Together, these results identify neural innovation as a mechanistic link between environmental perturbations, latent policy reconfiguration, and closed-loop interaction with artificial controllers, highlighting how alignment—and misalignment—between neural intent, AI priors, and sensory feedback shapes adaptive behavior.

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## TEMPORAL ROBUSTNESS AND BRAIN-STATE STABILITY OF FUNCTIONAL CONNECTIVITY IN THE MOUSE VISUAL HIERARCHY

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Understanding how visual-cortex functional connectivity evolves over time and across brain states is crucial for revealing how neurons coordinate to process information and support behavior. In mice, higher-order visual areas exhibit distinct, segregated roles [1] and maintain stimulus representations across multiple time scales [2, 3]. However, the stability of their functional connectivity architecture across time and brain states remains less understood.

*In vivo* mesoscopic two-photon calcium-imaging was used to simultaneously record activity from thousands of neurons across V1 and three extra-striate areas in mice, during visual stimulation and at resting state (*i.e.*, absence of stimulus). We applied the spike time-tiling (STTC) coefficient [4] to estimate the pairwise correlations of neuronal firing and form the functional connectivity at the cell level. We assessed temporal stability by splitting each one-hour stimulus and resting-state recording into four consecutive 15-min intervals and computing statistically significant functional connections per interval. A connection was deemed stable if it remained significant across all four intervals.

Functional connectivity during stimulus presentation exhibits increasing temporal robustness as a function of hierarchical order. This trend is weaker during the resting state, suggesting it is driven by bottom-up visual input. Moreover, higher position in the hierarchy is associated with smaller changes in functional connectivity between stimulus and resting-state conditions, indicating that functional connectivity during quiet wakefulness more faithfully reflects the functional network elicited by visual stimulation in higher-order areas compared to lower-order areas.

Finally, we trained a spiking neural network (SNN) on image classification and applied the functional-connectivity analysis on the output of the SNN units during inference. We found that the temporal robustness of functional connections during inference increases relative to layer depth, mirroring the trend observed in the biological hierarchy.

Together, these results suggest that visual-cortex representations stabilize as signals approach cognitive areas, supporting consistent responses to similar stimuli.

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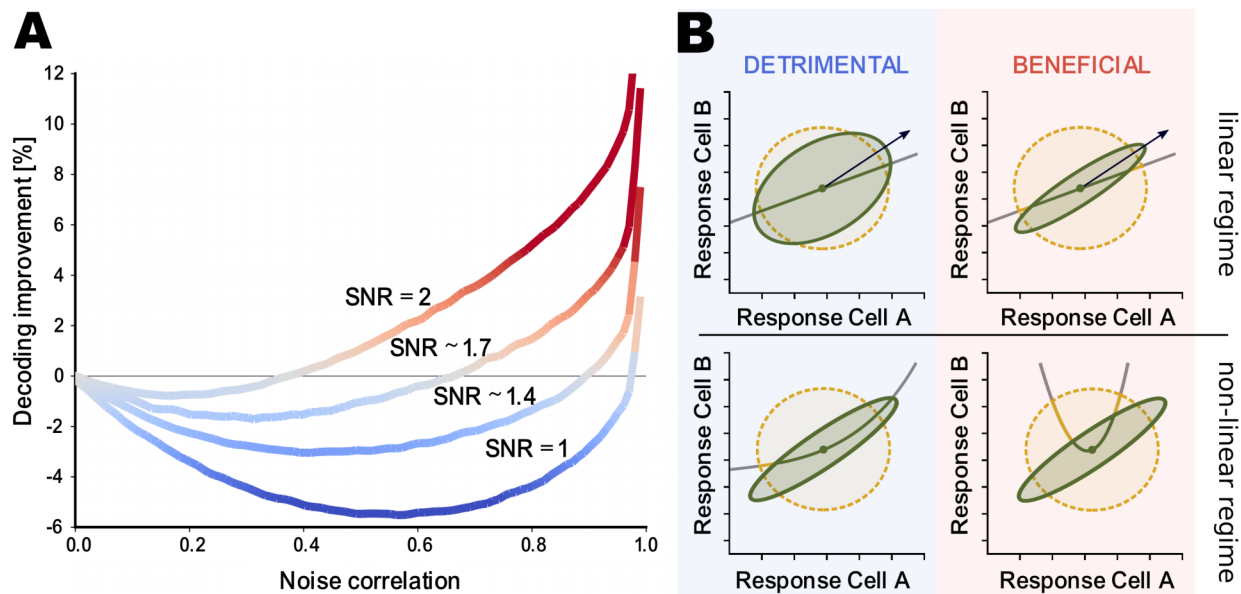
**LARGE CORRELATED NOISE IMPROVES DECODING FOR SIMILARLY TUNED NEURONS**Paolo Scaccia<sup>1,\*</sup>, Gabriel Mahuas<sup>1</sup>, Thierry Mora<sup>2</sup>, Ulisse Ferrari<sup>1,\*</sup><sup>1</sup> Institut de la Vision, INSERM, CNRS, Sorbonne University, Paris, France<sup>2</sup> Laboratoire de Physique de l'École Normale Supérieure, CNRS, Paris, France

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Biological neural networks can be remarkably reliable and precise despite their intrinsic noise. This noise is often correlated among neurons within the same layer. The role of this phenomenon, known as *noise correlations*, remains unclear and is still an active topic of research in neuroscience. This study seeks to determine whether noise correlations are merely a cost of neural connectivity or whether they can, in fact, enhance the information transmitted to downstream neural areas.

Experimental evidence indicates that similarly tuned neurons exhibit strong positive noise correlations. The widely accepted *Sign Rule* theory predicts that the observed regime is detrimental to the information encoded in the population activity. Despite its intuitive geometrical interpretation, this theory fails to account for an additional beneficial regime for positive correlations, identified in recent theoretical work.

We propose to resolve the inconsistencies between the two theories, providing an enhanced geometrical picture describing the impact of noise correlations on stimulus decoding. We simulated a bar experiment with a two-neuron model with Gaussian noise, in which external stimuli are reconstructed through an optimal Bayesian decoder. We compared the decoding performance of two models, with and without noise correlations (Figure 1A). By exploring a range of system parameters, we highlighted the impact of system geometry on decoding performance and identified the SNR-dependent regimes where the two theories are valid (Figure 1B).



**Figure 1.** (A) Comparison of decoding performance for correlated and uncorrelated models. Red regions mark regimes where noise correlations enhance decoding. (B) Main conditions under which noise correlations increase or decrease the overlap between neural responses and the manifold (gray) defined by the system's average activity. A larger overlap corresponds to a higher average decoding error.

## NEURAL CORRELATES OF THE INTERACTION OF WORKING MEMORY AND DECISION-MAKING IN PREFRONTAL CORTEX

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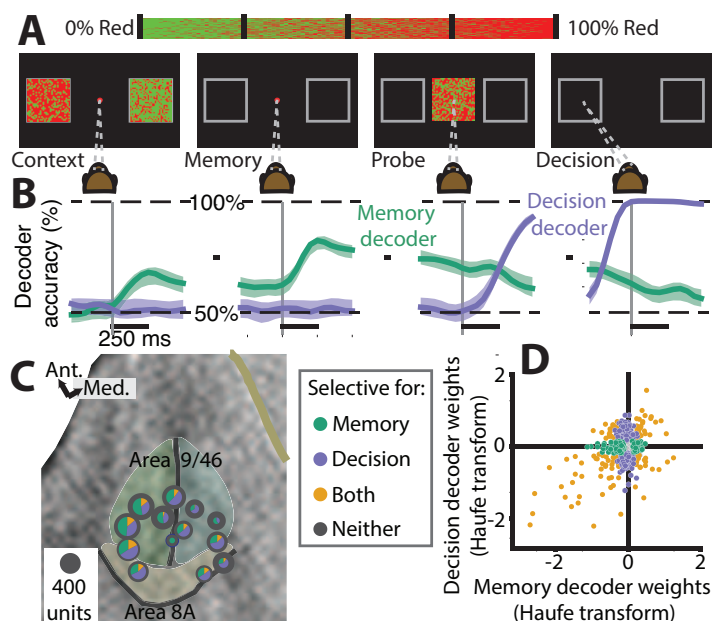
Perception and memory are closely intertwined. During perceptual decision-making (DM), sensory information is often evaluated in the context of other task-relevant information held in working memory (WM). Despite this interdependence, most neurophysiological studies have examined WM and perceptual DM in isolation.

To study how mnemonic and sensory information interact during DM, we developed a behavioral paradigm for macaque monkeys that parametrically varies both memory content and sensory evidence (Fig. 1A). On each trial, two *context* images, pseudorandomly sampled from a red-green spectrum, are presented for retention in WM. After a delay, a third *probe* image appears, and the monkey decides which context image is closer in color to the probe. By varying chromatic distances between context images and probe image, we can quantify how memory and sensory evidence are integrated for DM. We trained two monkeys on the task and their behavior varied systematically with the joint difficulty of the memory and perceptual components. In one animal, we recorded from multiple dorsolateral prefrontal cortex (dlPFC) subregions using NHP-Neuropixels probes (Fig. 1C). The high recording yields enabled population-level analyses at individual sites.

We first asked whether WM and DM signals are carried by distinct neural populations. At many sites, both WM content (context color red versus green) and decision (left versus right) were robustly decodable (Fig. 1B). WM content remained decodable through the decision epoch and the choice report. Analysis of decoder weights revealed partial segregation (Fig. 1D) with only a third of selective neurons contributing to both WM and DM decoding. This pattern suggests partial functional separation of WM and DM processing within dlPFC.

We next asked how WM representations are converted into decisions. Each trial requires a color decision (red or green) and a spatial decision (left or right). Population dynamics showed that the color decision variable emerged about 100 ms earlier than the spatial decision variable. Thus, an initial color decision is converted to a spatial decision.

Together, these results suggest that when perceptual decisions are made about information held in working memory, WM and DM signals are maintained in partly separable populations and integrated sequentially to drive behavior. Our results demonstrate a circuit-level mechanism for flexible memory-guided decisions.



## BRAIN-INSPIRED COMPUTING FOR BRAIN-COMPUTER INTERFACING

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Intracortical brain-computer interfaces (iBCIs) have the potential to restore lost motor functions in patients with neurological disorders. A critical component of iBCIs is the neural decoder translating recorded neural activity into control signals for external devices.

Current implementations often adopt simple models such as Optimal Linear Estimator (OLE) and Kalman Filter (KF) over higher performing deep learning models. This is because the latter require more extensive computational resources and larger datasets, hindering frequent retraining necessary to adjust to neural signal non-stationarities.

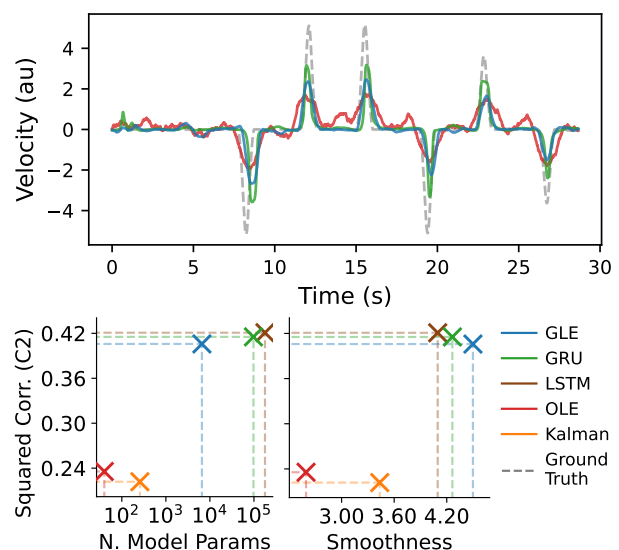
We use a novel cortex-inspired decoding approach designed for spatio-temporal computation and learning, called Generalized Latent Equilibrium (GLE) [1]. Combining different approximate past memories in a layered neural network structure, GLE is capable of efficiently processing sequential data, online real-time learning and has the potential for neuro-morphic on-chip implementation.

We evaluate GLE on neural data recorded during the observation calibration phase of an iBCI cursor control task performed by human tetraplegic participants [2], and compare it against other established decoder models such as OLE, KF, Gated Recurrent Unit (GRU) and Long Short-Term Memory (LSTM) among others. Our main evaluation metric is the squared Pearson’s Correlation Coefficient (C2) between the decoded and ground truth velocities, but we also consider other metrics including the smoothness related to the inverse jerk of decoded trajectories.

Our results show that GLE performs much better than OLE and KF in both C2 and smoothness. While performing at similar level as the conventional deep learning models (GRU and LSTM), it does so with much fewer model parameters (see Figure 1).

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**Figure 1.** Decoder model comparison on validation data showing (A) exemplary velocity predictions versus ground truth and C2 against (B) the number of model parameters and (C) smoothness.

## **SINGLE-NUCLEUS TRANSCRIPTOMICS REVEALS HIDDEN HETEROGENEITY IN MACAQUE LGN RELAY PATHWAYS**

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The primate lateral geniculate nucleus (LGN) is a critical hub in the thalamocortical ensemble, modulating and relaying retinal signals to cortex. While the LGN is classically divided into magnocellular (M), parvocellular (P), and koniocellular (K) pathways, electrophysiological evidence increasingly suggests functional heterogeneity within these canonical classes.

Here, we use single-nucleus transcriptomics to define molecular subtypes for understanding thalamic ensemble dynamics [1]. We analyzed 1,309 macaque LGN excitatory nuclei from a publicly available dataset sourced from the Allen Brain Map [2]. To resolve subtle and potentially pathway-specific structure, M, P, and K populations were analyzed separately using a standardized single-nucleus workflow with correction for technical variation and cross-sample alignment, followed by unsupervised clustering and silhouette-based assessment of cluster separation. We selected clustering parameters using a global optimization strategy to maximize cluster separation.

This approach reveals seven transcriptionally distinct excitatory subpopulations: two M, two P, and three K types. K cells show the strongest heterogeneity, refining prior K subdivisions by recovering one well-established K subgroup and resolving additional heterogeneity within the rest of the K population. Across pathways, differential markers suggest a clear distinction between subtypes enriched for fast signaling machinery (ion channels/glutamatergic components) versus subtypes enriched for cytoskeletal, transcriptional, and synaptic-adhesion programs, pointing to functional roles in high-throughput relay versus connectivity/plasticity and state-dependent modulation.

Together, these results propose a more nuanced LGN cellular taxonomy and provide molecular handles for future work that explicitly links transcriptomic identity to ensemble firing patterns, receptive-field computations, and circuit-level modulation underlying visual perception.

### **Acknowledgments**

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## **NEURAL ACTIVITY IN THE MACAQUE LATERAL INTRAPARIETAL AREA DURING A VISUAL METRONOME SACCADE TASK**

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When human participants are instructed to direct their gaze to a target that alternates between two known locations with constant frequency (the visual metronome task), within 2-3 target steps they adjust their response from reacting to the stimulus, to predicting the stimulus [1]. This adjustment is indicated by a change of saccade latency from the typical reaction times for reactive saccades (above 120 ms) to shorter (below 90 ms) and even negative reaction times for predictive saccades. The short and especially negative reaction times suggest that cognitive saccade control builds on an internal representation of space and time rather than exogenous stimuli. Although the visual metronome paradigm provides a useful tool to study brain areas within the oculomotor control circuit during predictive behavior, to the best of our knowledge, it was never tested in its original format to study the underlying neural mechanism of different predictive saccade behaviors. Here we show that monkeys can learn the visual metronome behavioral paradigm and show intrinsically driven reactive and predictive saccadic behavior to the rhythmic saccade target with different tempos, similar to human participants.

Using multi-channel U-Probes, we corded the neural activity from the Lateral Intraparietal (LIP) area when a monkey was performing the metronome saccade task. Area LIP is actively involved in the encoding of space, time and cognitive control of oculomotor behavior [2, 3]. Our preliminary analysis of the neural data suggests that not only neurons encode the tempo of the metronome [4], the temporal aspects of their activity is also correlated with the predictive saccadic behavior.

### **Acknowledgments**

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## REPROGRAMMING SENSORY CORTEX FOR ADAPTIVE TASK LEARNING

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Animals adapt their behaviour in response to variable changes in reward reinforcement. How animals employ specific behavioural strategies while learning tasks and how the prefrontal areas of the mammalian neocortex, especially the orbitofrontal cortex (OFC), contribute to such strategy-based learning remain understudied.

Using a tactile flexible learning task, longitudinal two-photon Ca<sup>++</sup> imaging, and tensor component analysis, combined with a novel temporal decoding method, we revealed the crucial contribution of the OFC and its hierarchically organised interactions with sensory areas. Our poster highlights such interactions between lateral OFC (lOFC) and a small ensemble of outcome/value-selective neurons in the primary somatosensory cortex (S1) during task reversal in mice [1] and briefly reviews similar circuits in operation in humans performing cognitive tasks combined with fMRI/EEG measurements [2, 3].

By implementing a Bayesian evidence accumulation model to analyse behavioural learning data in mice, we further revealed multiple exploratory strategies animals employ during key task-learning phases. Silencing lOFC impairs strategy deployment during behavioural flexibility, highlighting the role of the lOFC in leveraging prior knowledge to support reward and error-guided learning.

Furthermore, disinhibitory VIP interneurons in the OFC is found to encode a context-prediction error, signalling a loss of confidence that is mirrored in top-down signals modulating the apical activity of S1 pyramidal neurons [4]. A proposed theoretical model explains how contextual changes are detected in the brain and how a hierarchy of prediction errors in different cortical regions interacts to reshape and update the sensory representations [4].

Taken together, our experiments shed light on the circuit mechanisms underlying predictive teaching signals that drive adaptive changes in sensory cortices and in behaviour.

### Acknowledgments

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## **LOSS-BASED DIRECTED GRAPH CONSTRAINTS FOR RECURRENT FLOW NETWORK DYNAMICS**

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Accurate forecasting in directed flow networks requires capturing both temporal dynamics and structured interactions across interconnected nodes. Recurrent neural networks (RNNs) are effective at modeling nonlinear temporal dependencies, but they fail to explicitly account for network topology, limiting the physical consistency of the resulting dynamics. Graph-based approaches address this limitation by encoding connectivity but combining them with temporal models often leads to increased computational complexity. Bridging temporal modeling with structured network constraints in a scalable manner remains an open challenge.

A framework is proposed that integrates RNNs with directed graph Laplacian loss regularization to enforce conservation principles in flow networks. We show that a continuity constraint can be mapped to a generalized directed graph Laplacian by introducing storage coefficients that relate changes in internal state to observed flow. This regularization encodes spatial proximity, connectivity, and directionality in the loss function, allowing physical structure to be imposed without modifying recurrent architectures or introducing trainable graph dynamics.

We evaluate the proposed framework on a large-scale directed flow network using diverse recurrent architectures. Across models, the regularization improves predictive accuracy and stability relative to unregularized baselines. On average, regularized models achieve a 1.9% improvement in overall error metrics and a 3.9% improvement in high peak-flow metrics, while reducing the variability of peak estimates by 26.9% and improving temporal alignment of extreme events by 8.6%.

Compared to a specialized mass-conserving recurrent model, the proposed loss-based regularization models achieves similar or better accuracy while using fewer parameters and requiring less training time. One limitation is that optimization can be sensitive to the choice of regularization strength. However, these results show that conservation constraints and directed interactions can effectively be incorporated through loss-based regularization, providing a scalable alternative to architecture-specific approaches.

## LOW-DIMENSIONAL POPULATION CODES FOR NATURAL VIDEOS IN MOUSE SUPERIOR COLLICULUS

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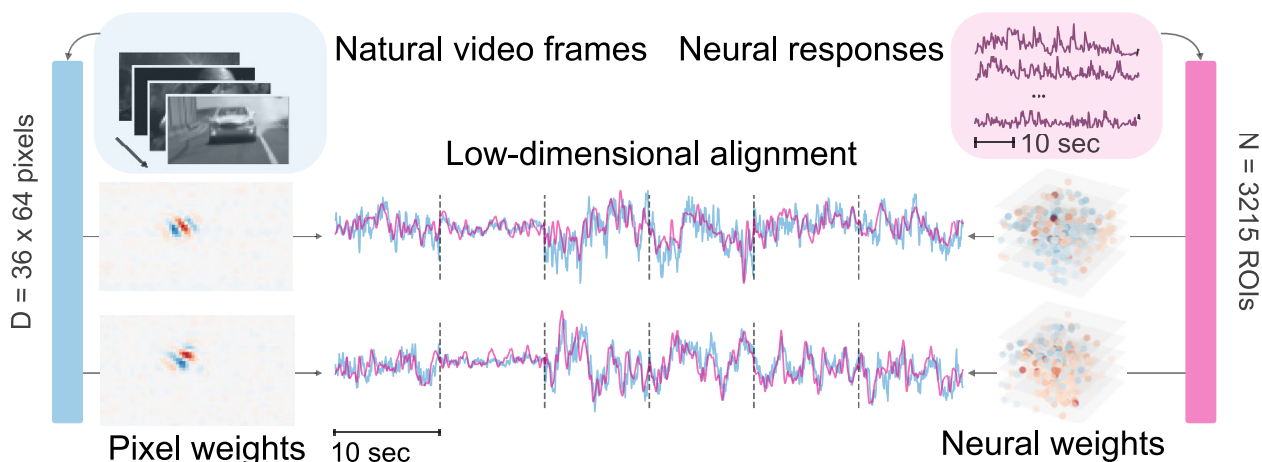
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The visual system represents and compresses high-dimensional inputs from natural environments. Despite their complexity, natural stimuli have strong statistical structure including pixel intensity correlations. At the same time, neural activity is organized at the population level through shared stimulus drive and correlated variability, limiting the representational power of single-neuron receptive-field descriptions. Here we ask how natural video streams are encoded by retinal inputs to mouse superior colliculus (SC), and whether stimulus and response structure can be used to uncover a robust low-dimensional population code.

We analyze functional calcium imaging (GCaMP8) of retinal axons in SC during presentation of 10 second natural video clips. We first characterize low-dimensional structure in population responses using principal component analysis (PCA), and then link stimulus features to response latents using low-rank stimulus-response models (CCA/RRR), interpreting the resulting weights and loadings as population-level basis functions.

Population responses to natural videos concentrate in a compact and interpretable latent space, which explains a significant fraction of stimulus-driven variance. The recovered basis patterns are highly structured, resembling Fourier-like spatial features rather than collections of independent center-surround receptive fields, suggesting a genuinely population-level representation. Thus, encoding models with a low-dimensional bottleneck show promise in characterizing processing of dynamic natural world in the early visual system.



**Figure 1.** Two high-dimensional information streams are related with a linear latent-space encoding model through weights for pixel and neural activations.

### Acknowledgments

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## **PROGRESSIVE CHANGES IN MOTOR CORTICAL REPLAY ACROSS EXTENDED MOTOR LEARNING**

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Sleep plays a critical role in motor skill consolidation, in part through the reactivation of neural activity patterns expressed during waking behavior. While prior studies of motor cortical reactivation have largely focused on population-level co-firing, motor skills such as reaching are inherently sequential, motivating investigation of sequential replay. Moreover, most studies have examined learning over short timescales, leaving unclear how replay evolves across extended motor learning.

Here, we trained marmoset monkeys on a precision reaching task over a two-week period while recording motor cortical activity during task performance and subsequent sleep. Learning was quantified by success rate, which increased over early learning and plateaued by the end of the two-week period. Sequential replay events during sleep were identified using a template-matching approach, in which population activity patterns from awake reaching trials served as templates. Replay was detected when sleep activity significantly matched these templates relative to temporally shuffled controls.

We found that motor cortical activity patterns expressed during awake reaching were replayed during subsequent sleep, whereas replay was minimal during a baseline pre-learning sleep period. Across learning, replay frequency increased during early learning and plateaued during mid to late learning, exhibiting a strong linear relationship with task performance ( $r = 0.8$ ). Replay diversity, defined as the number of distinct templates detected in an unsupervised analysis, scaled with between-day improvements in performance ( $r = 0.6$ ).

Together, these results demonstrate that motor cortical replay during sleep evolves across weeks of learning, with distinct replay features relating to overall performance. This finding suggests that sleep-related replay in motor cortex is dynamically modulated as motor skills are acquired.

## EARLY RESULTS LINKING NEURONAL FUNCTION AND MORPHOLOGY IN MOUSE VISUAL CORTEX

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Understanding the relationship between neuronal function and morphology is crucial for obtaining an objective taxonomy of cell types. Currently, many studies define functional activity via injected current, measuring biophysical properties rather than neuronal responses to naturalistic stimuli — the true *in vivo* functions. To focus on this function, we are relating 32-dimensional morphological embeddings [1] with 512-dimensional functional embeddings [2]. The embeddings are obtained from two independent deep learning models [1, 2]. Both models were trained on the MICrONS dataset, where the same neurons were registered across different modalities.

We used redundancy analysis [3] to extract the percentage of variance explained between the two modalities of morphology and function. First, linear regression was used to predict the embeddings dimension from joint x-y-z coordinates. Next, predictions were subtracted from original values to remove the coordinates as confounders. Then, canonical correlation analysis (CCA) was used to project modalities in the common subspace, maximizing correlation between projections while maintaining orthogonal axes. Finally, we computed a redundancy index as the product of the variance extracted (the normalized sum of squared correlation across samples for original and projected dimensions) and the squared canonical correlation.

This analysis shows that 18.6% of the functional variance is explained by morphology embeddings (or 26.6% if we subselect only V1 neurons). To gain insights into what features of a neuron’s morphology are predictive of its function, we asked which predefined morphological features [4] correlated most strongly with the functional projection to the latent space.

The top correlated features we found were the number of dendrite branches and, related to it, the dendritic area and skeletal length, as well as the total number of apical branches and the number of synaptic shafts. All features could be related to a feedback loop between neurons: more branches/shafts enable broader inputs, with extensive apical branching linked to top-down modulation of sensory processing.

The next step will be to integrate both modalities during model training to generate per-cell multimodal embeddings and assess whether this view can reveal distinct cell types in mouse visual cortex.

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## DECOUPLING STIMULUS ENCODING FROM INTERNAL STATE DYNAMICS IN MOUSE VISUAL CORTEX

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Disentangling sensory representations from single-trial variability remains a central challenge in systems neuroscience, as much response variability reflects shared excitability fluctuations rather than independent noise. Previous work showed that shared cortical variability can be modeled by a global gain scaling stimulus-driven responses and an additive offset shifting baseline activity [1], and that ongoing population dynamics form structured latent activity is separable from stimulus-evoked responses [2].

Motivated by these findings, we propose the Stimulus-State Factorized Variational Autoencoder (SSF-VAE), a generative encoder-decoder that decomposes neural activity into stimulus-driven and internal-state components with multiplicative coupling. SSF-VAE combines (i) deterministic stimulus latents optimized for stimulus decoding, (ii) probabilistic latents modeling shared internal-state variability supervised by state proxies, (iii) an encoder with a recurrent first hidden layer, and (iv) latent-level stimulus-state cross-covariance regularization. Unlike approaches that construct stimulus and spontaneous subspaces from separate recording epochs and analyze overlap via subspace projection, rely on linear additive mixing of stimulus-driven and spontaneous components, or use self-supervised latent decomposition without explicit internal-state supervision [2–4], SSF-VAE *jointly* learns stimulus-driven and internal-state components of neural population activity with multiplicative stimulus-state interaction and *explicit* stimulus-state decorrelation.

We applied SSF-VAE on large-scale mouse visual cortex two-photon calcium imaging data during visual stimulation of Gaussian noise with coherent orientation and motion (6 Hz sampling). Stimulus direction decoding accuracy is superior relative to linear decomposition methods. We have also applied SSF-VAE to neuropixels recordings and multimodal state measurements (e.g., pupil size, locomotion, and natural scenes). Part of our ongoing effort is to quantify neuronal contributions to stimulus and internal-state components and characterize their dynamics.

### Acknowledgments

HFRI neuronXnet 2285, neuron-AD 4058; EU MSCA neuronsXnets 101007926; MIS 5154714 under NextGenerationEU, R01 NS113890 and R21 NS127299. This work extends our paper Tzanakis *et al.*, IEEE BIBE, 2025.

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## **SPATIAL CODING GOING WILD: HIGH-DIMENSIONAL NEURAL MANIFOLDS IN BATS FLYING FREELY OUTDOORS ON A REMOTE OCEANIC ISLAND**

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The brain evolved to support complex behavior in natural environments, yet much of what we know about neural coding comes from highly constrained laboratory experiments that, until recently, largely focused on single-neuron activity. Here we combine, for the first time, large-scale neuronal population recordings with unconstrained behavior outdoors, to study hippocampal population activity during natural navigation. We tracked Egyptian fruit bats with high-precision GPS and used wireless electrophysiology to record simultaneously from over 100 hippocampal CA1 neurons, as the animals flew freely on an uninhabited island. Immediately before the outdoor session, we also recorded the same neuronal populations during simple back-and-forth flights in a small indoor environment, enabling a direct comparison of the neural activity across very different environments: a simple lab-like environment versus the complex real world outdoors. Beyond its larger scale, the outdoor environment offered a richer landscape — including beaches, rocks, and many landmarks [1] — as well as more diverse behavior. Consistent with prior work in large indoor arenas [1], many CA1 place cells exhibited multiple place fields outdoors.

Next, we estimated two common types of neural manifold dimensionality: intrinsic dimension, which roughly corresponds to the number of variables represented, and embedding dimension, which corresponds to the effective linear dimension spanning the population activity. Strikingly, the estimated dimensionality of the same neuronal ensembles was far higher outdoors than indoors: intrinsic dimension increased by more than two-fold, and embedding dimension increased four-fold. This increase in dimensionality could not be explained by changes in single-neuron firing characteristics. Interestingly, indoor dimensionality was similar to previously reported results from CA1 of mice performing a virtual reality task [2]. Moreover, estimating dimensionality using random subsets of neurons showed that indoor dimensionality quickly saturated as subset size increased, whereas outdoor dimensionality continued to increase and did not saturate. Thus, we find that the low dimensionality of neuronal population activity — which has been ubiquitously reported in constrained laboratory experiments in numerous brain areas — is not a fundamental neural property, but rather a consequence of behavioral and environmental simplicity.

We conclude that merely recording more neurons in simple experimental settings is insufficient to reveal the true, complex structure of neural activity manifested during natural behavior. Instead, brain research must combine recordings of large neuronal populations with complex naturalistic behaviors.

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## OMNIMOUSE: SCALING PROPERTIES OF MULTI-MODAL, MULTI-TASK BRAIN MODELS ON 150B NEURAL TOKENS

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The scaling of data to immense size coupled with advances in artificial neural networks have together transformed AI, driving breakthroughs in language and vision. Whether similar principles apply to modeling brain activity remains unclear. Here we leveraged a dataset of 3.3 million neurons from the visual cortex of 78 mice across 323 sessions, totaling more than 150 billion neural tokens recorded during natural movies, images and parametric stimuli, and behavior. We train multi-modal, multi-task transformer models (1M–300M parameters) that support three regimes flexibly at test time: *neural prediction*, predicting neuronal responses from sensory input and behavior; *behavioral decoding*, predicting behavior from neural activity; *neural forecasting*, predicting future activity from current neural dynamics; or any combination of the three.

We find that performance scales reliably with more data, but gains from increasing model size saturate, suggesting that current brain models are limited by data rather than computation. This observation inverts the standard AI scaling story: in language and computer vision, massive datasets make parameter scaling the primary driver of progress, whereas in brain modeling — even in the mouse visual cortex, a comparatively simple and low-resolution system — models remain data-limited despite vast recordings. These findings highlight the need for richer stimuli, tasks, and larger-scale recordings to build brain foundation models. The observation of systematic scaling raises the possibility of phase transitions in neural modeling, where larger and richer datasets might unlock qualitatively new capabilities, paralleling the emergent properties seen in large language models.

## NON-UNIFORM SPATIAL INTEGRATION OF MOTION SIGNALS IN AREA MT SHAPES MOTION PERCEPTION

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Interacting with the world often requires integrating noisy dynamic information across the visual field to discriminate stimuli and guide behavior. Studies using highly controlled visual stimuli have revealed how the instantaneous responses of sensory neurons are integrated *across time* to make decisions [1–3]. Nonlinear mechanisms underlying *spatial integration*, including surround suppression and facilitation, have been described at the single neuron level [4, 5], but these effects have not yet been linked to perception in a comprehensive computational model.

Here, we explore spatiotemporal motion representations in visual area MT and relate contextual effects in single neurons to perceptual responses. We find that monkeys integrate spatial evidence sublinearly in a highly spatiotemporally controlled motion discrimination task due to (i) surround suppression effects causing an attenuation of the responses to motion in the center of the stimulus, and (ii) weaker impact of peripheral motion. To test whether these effects originate in MT, we estimate spatiotemporal direction sensitivity kernels of MT neurons using nonlinear regression models. Our results reveal reliable non-uniform spatial modulation kernels in MT units that point towards visual spatial integration taking place in sensory areas. We propose a spatiotemporal decision making model in which choices rely on the pooled activity of sensory neural populations that weigh motion signals heterogeneously across space. Simulations reveal that the behavioral spatial suppression effects emerge from these instantaneous sensory representations of motion, demonstrating the impact of nonlinear spatial integration in MT on perception.

Taken together, our work challenges the assumption that spatially distributed stimuli are integrated uniformly and calls for a new class of decision making models that take into account spatial processing.

### Acknowledgments

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## NONSTATIONARY DYNAMICS OF SENSORY POPULATION CODES DURING ACTIVE BEHAVIOR

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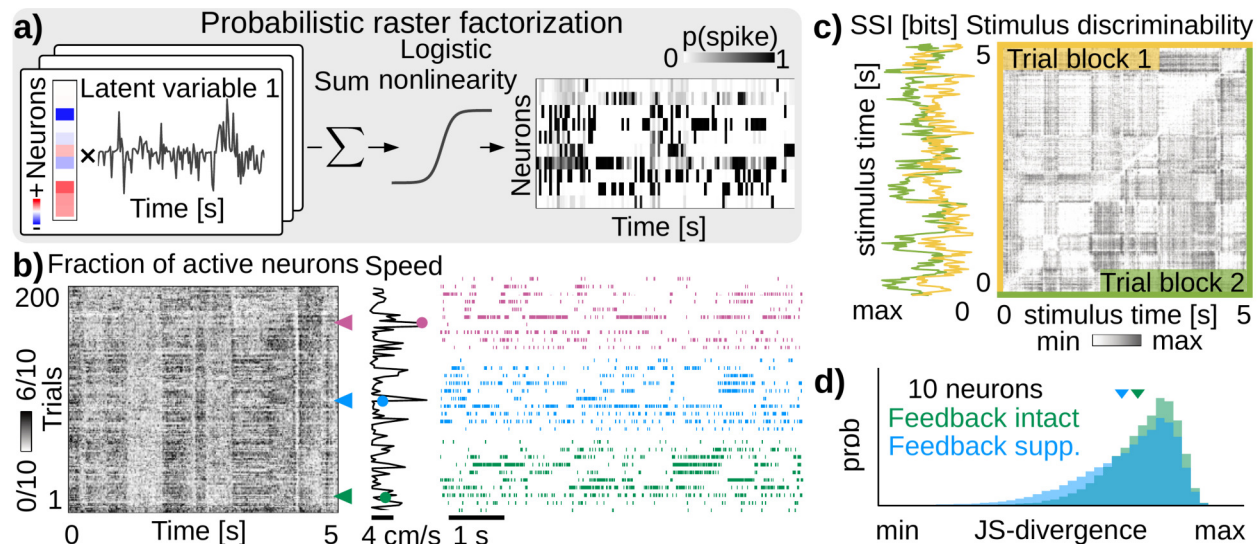
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Sensory neurons interact collectively to encode, process, and transmit stimulus information, and these interactions are not static. In behaving animals, sensory populations are constantly modulated by fluctuating internal and behavioral states. How these dynamic changes affect sensory encoding by population activity patterns, and to what extent signals from other brain areas shape collective sensory representations in behaving animals, remains unknown.

Here, we ask how thalamic neural populations encode natural stimuli in the presence of fluctuating internal states and how these fluctuations depend on corticothalamic input. We use extracellular recordings from dLGN of behaving mice with V1 feedback optogenetically suppressed. To study dynamically changing population codes with few trials, we develop a statistical model of neural activity, Probabilistic Raster Factorization (PRF; Figure 1a), which analyzes shared input patterns driving population activity at the level of individual spikes. Its probabilistic structure enables study of sensory coding in a non-stationary population.



**Figure 1.** (a) PRF model: The model infers latent variables and corresponding weights to characterize changing spiking probability. (b) Non-stationary population activity: (Left) active neuron counts across trials. (Middle) Average running speed on each trial. (Right) Rasters of all neurons in trials marked with colors in the left panel. (c) (Left) Stimulus specific information computed for individual trial blocks. (Right) Stimulus discriminability based on population states within different trial blocks. (d) Distributions of spike raster distances between trials. Feedback suppression (blue) visibly reduces the trial variability.

We find dLGN population codes vary through an experiment (Fig 1b). Within a trial block, information-theoretic measures of population activity distinguish different movie frames (Fig 1c). This discriminability varies, enabling a flexible coding scheme not arising in a stationary population. Suppressing V1 feedback reduces population variability (Fig 1d). These results suggest that sensory population codes change dynamically and are modulated by feedback signals.

## **PREDICTING NEURAL RESPONSES USING SCALABLE GAUSSIAN PROCESSES IN CLOSED-LOOP**

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Predicting the responses of sensory neurons to natural stimuli is a long-standing goal in neuroscience. In the early visual system, a primary approach has been to record the responses of neurons to flashed visual stimuli. These recordings are then used to train a model, which can be used to predict neural responses to novel stimuli.

However, the predictive performance of these models is limited by the data available for training. For example, if many stimuli do not elicit a response, then model performance may be reduced. This problem stems from limitations in experimental time that constraint the number of stimuli that can be presented. We proposed and experimentally tested a closed loop approach which chooses stimuli adaptively in real time, based on previous data collected during the experiment, to make efficient use of finite recording time.

The model used in our experiment faced two challenges. First, it required real-time speed, as it needed to be retrained in the time between two flashed images. Second, it needed to quantify the uncertainty at any moment in time, to identify where more data exploration would be most effective. The field of Bayesian active learning provides a principled framework for this problem. Bayesian models called Gaussian Processes (GPs) allow to estimate precisely how uncertain they are and have been shown to be competitive in predicting electrophysiological neural responses in mouse retinal ganglion cells, our model tissue [1, 2].

We conducted experiments implementing this approach and showed that the system could autonomously choose stimuli that span a more informative range of the natural input space. The closed loop protocol sought out stimuli that probed the entirety of neuronal tuning curves. Validation on held-out data revealed that models trained on these actively selected stimuli significantly outperformed those trained on the same number of images selected randomly. This performance gap extended to capturing the gradients of the tuning curve, enabling the model to learn non-linearities, such as context-dependent polarity inversions, that random sampling failed to detect.

This poses our closed-loop framework as a powerful tool for actively exploring the input space to investigate feature selectivity, expanding the range of analyses feasible with limited data in sensory systems.

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## NON-MONOTONIC EMERGENCE OF BEHAVIORAL MODULATION IN A NEONATAL CORTICAL CIRCUIT

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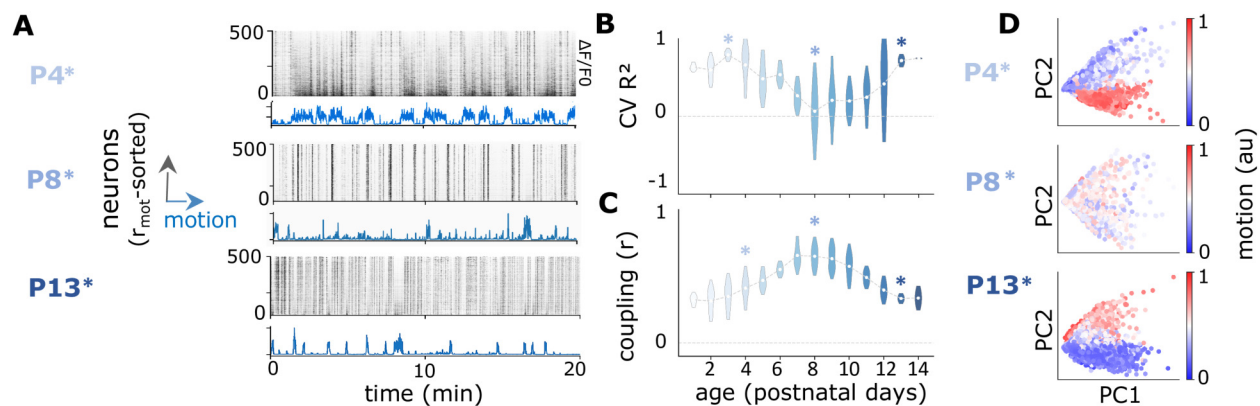
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Mature sensory circuits are strongly modulated by behavior, a feature thought to emerge monotonically by the end of the second postnatal week in mice [1, 2]. However, this view is largely extrapolated from recordings obtained after the first postnatal week, leaving the earlier but critical period for circuit formation underexplored. To address this gap, we performed *in vivo* 2-photon calcium imaging of spontaneous population dynamics in mouse barrel cortex, combined with videography to track global movements from postnatal day 1 (P1) to P14, spanning circuit maturation.

Linking population activity to movement, we uncovered a developmental window of strong behavioral modulation from P1–P5, with a spatially distributed neural ensemble consistently recruited at movement onset. This modulation declined to a minimum by P8, before re-emerging after P11 (Fig. 1A). Linear decoders trained to predict motion from activity revealed a parallel non-monotonic evolution of accuracy ( $R^2$ ) (Fig. 1B). Notably, the drop of modulation coincided with marked changes in network statistics: population coupling (synchrony) peaked by P8 (Fig. 1C), while firing rate transiently decreased (not shown). Moreover, leading neural principal components (PCs) encoded movement from P1–P5 and after P11, but not during P6–P10 (Fig. 1D), reflecting a temporary misalignment between neural dynamics and ongoing behavior.

Together, these results revise current views of cortical circuit development, from a behavior-isolated linear path, to a dynamic U-shaped trajectory with transient functional checkpoints. Further work aims to mechanistically investigate and perturb those checkpoints, to probe their role in shaping normative sensorimotor computation.



**Figure 1.** (A) Example rasterplots where rows are for neurons sorted by pairwise correlation ( $r$ ) to motion energy (blue trace). (B) Cross-validated decoding accuracy. (C) Population coupling (mean  $r$ ) across neurons. (D) Example neural trajectories projected on 2-dimensional PCA space (time color-coded by motion amplitude).

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