



COSYNE

2022

MAIN MEETING

Lisbon, Portugal

17–20 March

WORKSHOPS

Cascais, Portugal

21–22 March

cosyne.org

Program Summary

All times are GMT (Greenwich Mean Time)

Thursday, 17 March 2022

12:00	Cosyne Tutorial: Spiking neural network models in neuroscience
16:00	Registration opens
16:45	Welcome reception
18:15	Opening remarks
18:30	Session 1: Behavior and the brain Invited speaker: Sandeep Robert Datta; 3 accepted talks
20:30	Poster Session I

Friday, 18 March 2022

09:00	Session 2: Action selection, learning, and dopamine Invited speaker: Valerio Mante; 2 accepted talks
10:45	Session 3: Communication within and between brains Invited speaker: Michael Long; 4 accepted talks
12:30	Lunch break
15:00	Session 4: Spatial memory and beyond Invited speaker: Andre Fenton; 3 accepted talks
17:00	Session 5: Oscillations, network states, and arousal Invited speaker: Susanne Schreiber; 3 accepted talks
18:30	Dinner break
19:00	Professional Development Panel and Social: Pathways to research beyond Academia
20:30	Poster Session II

Saturday, 19 March 2022

09:00	Session 6: Population codes and connectivity Invited speaker: Christian Machens; 3 accepted talks
11:00	Session 7: Multiscale brain networks Invited speaker: Pamela Douglas; 3 accepted talks
12:30	Lunch break
15:00	Session 8: Immune responses and the brain Invited speaker: Asya Rolls
16:00	Panel discussion on inequities and the pandemic's effects
17:00	Session 9: Navigating space and time Invited speaker: Ann Hermundstad; 3 accepted talks
18:30	Dinner break
20:30	Poster Session III

Sunday, 20 March 2022

- | | |
|-------|---|
| 09:00 | Session 10: Working memory, decision making, and value
Invited speaker: Albert Compte; 3 accepted talks |
| 11:00 | Session 11: Sensory, motor, and in-between
Invited speaker: Eugenia Chiappe; 3 accepted talks |
| 12:30 | Lunch break |
| 15:00 | Session 12: Codes for (spatial) behaviors
Invited speaker: Kate Jeffery; 3 accepted talks |

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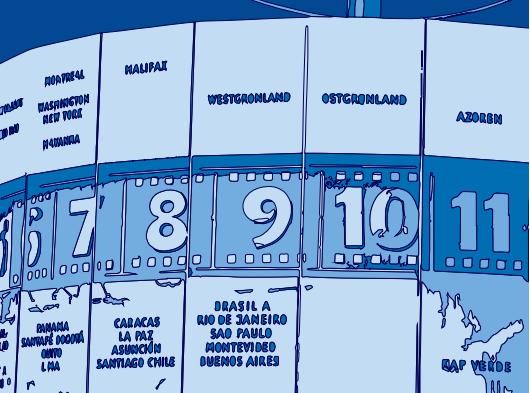
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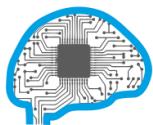


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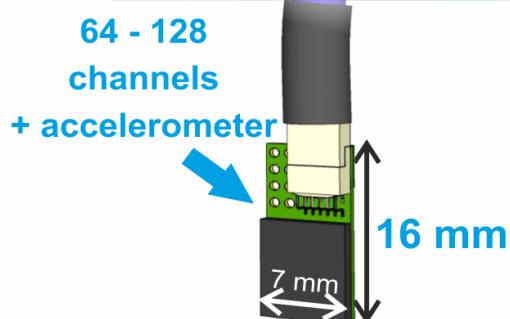
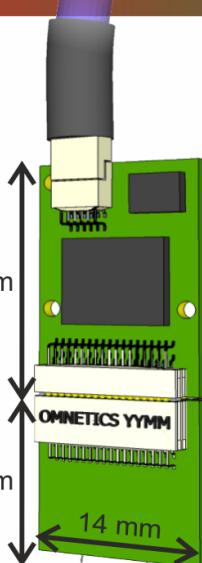
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About Cosyne

The annual Cosyne meeting provides an inclusive forum for the exchange of experimental and theoretical/computational approaches to problems in systems neuroscience.

To encourage interdisciplinary interactions, the main meeting is arranged in a single track. A set of invited talks are selected by the Executive Committee and Organizing Committee, and additional talks and posters are selected by the Program Committee, based on submitted abstracts.

Cosyne topics include (but are not limited to): neural basis of behavior, sensory and motor systems, circuitry, learning, neural coding, natural scene statistics, dendritic computation, neural basis of persistent activity, nonlinear receptive field mapping, representations of time and sequence, reward systems, decision-making, synaptic plasticity, map formation and plasticity, population coding, attention, machine learning for neuroscience, and computation with spiking networks. Participants include pure experimentalists, pure theorists, and everything in between.

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Special thanks to Titipat Achakulvisut, Daniel Acuna, and Konrad Kording for writing and managing the automated software for reviewer abstract assignment.

About Cosyne

Conference Support

Administrative Support, Registration, Hotels

Leslie Weekes, Cosyne

Travel Grants

The Cosyne community is committed to bringing talented scientists together at our annual meeting, regardless of their ability to afford travel. Thus, a number of travel grants are awarded to students, postdocs, and PIs for travel to the Cosyne meeting. Five award granting programs were available for Cosyne 2020. Each award covers at least \$1,000 towards travel and meeting attendance costs (less for Childcare grants).

The generosity of our sponsors helps make these travel grant programs possible. Cosyne Travel Grant Programs are supported entirely by the following corporations and foundations:

- The Gatsby Charitable Foundation
- Burroughs Wellcome Fund
- Simons Foundation
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Cosyne Presenters Travel Grant Program

These grants support early career scientists with highly scored abstracts to enable them to present their work at the meeting.

The 2022 recipients are

Kadjita Asumbisa, Ryszard Auksztulewicz, Federico Bolanos, Zoe Boundy-Singer, Karolina Farrell, Priyanka Gupta, Daniel Herrera, Nora Alicia Herweg, Nizar Islah, Habon Issa, Kathleen Jacquerie, Zilong Ji, Justin Jude, Thomas Morvan, Ugurcan Mugan, Nathaniel Powell, Luisa Ramirez, Camille Rullan, Sofia Skromne Carrasco, and Patricia Stan.

Cosyne New Attendees Travel Grant Program

These grants help bring scientists that have not previously attended Cosyne to the meeting for exchange of ideas with the community.

The 2022 recipients are

Alisha Ahmed, Rana Alkhoury Maroun, Simone Azeglio, Shiva Azizpourlindi, Robert Bruce, Ferenc Csikor, Kira Düsterwald, Richard Sebastian Eydam, Michael Gachomba, Divyansh Gupta, Madhura Ketkar, Kyveli Kompatsiari, Chiara Mastrogiovanni, Haleigh Mulholland, Amarachi Oleru, Tiffany Oña Jodar, Hyein Park, Srikanth Ramaswamy, Laura Silva, Sarah Solomon, Ayesha Vermani, and Gabriel Yancy.

Cosyne Mentorship Travel Grant Program

These grants provide support for early-career scientists of underrepresented minority groups to attend the meeting. A Cosyne PI must act as a mentor for these trainees and the program also is meant to recognize these PIs ("Cosyne Mentors").

The 2022 Cosyne Mentors and mentees are:

Rui Ponte Costa and Samia Mohinta, Becket Ebitz and Akram Shourkeshti, Kevin Lloyd and Sahiti Chebolu, and Lucas Sjulson and Eliezyer de Oliveira.

Cosyne Undergraduate Travel Grant Program

These grants help bring promising undergraduate students with strong interest in neuroscience to the meeting.

The 2022 recipients are

Noemie Eustachon, Samira Glaeser-Khan, Chaten Jessel, Mohit Kulkarni, Nancy MacKenzie, Darwing Santiago Padilla Rolon, Yeritmary Rodriguez Delgado, Arianna Rodriguez-Rivera, Tat Hei Tsin, Raymond Wang, Forrest Wargo, and Liu Zhang.

Cosyne Childcare Travel Grant Program

Cosyne Childcare Grants help cover childcare expenses incurred by participation in Cosyne 2022.

The 2022 recipients are

Brian DePasquale, Zahara Girones, Ulkar Isayeva, Barbara Peysakhovich, Frederic Roemischied, and Noa Sadeh.

Social media policy

Cosyne encourages the use of social media before, during, and after the conference, so long as it falls within the following rules:

- Do not capture or share details of any unpublished data presented at the meeting.
- If you are unsure whether data is unpublished, check with the presenter before sharing the information.
- Respect presenters' wishes if they indicate the information presented is not to be shared.

Stay up to date with Cosyne 2022 #cosyne22

Cosyne Code of Conduct

Purpose

At Cosyne, we strive for open and honest intellectual debate as part of a welcoming and inclusive atmosphere. This requires a community and an environment that recognizes and respects the inherent worth of every person.

Sources

This code of conduct is based on standards and language set at other meetings, whose organizing boards convened special working groups of scientific and legal experts to set their policies. We follow, in particular, those guidelines established for the Gordon Research Conferences, the Society for Neuroscience Annual Meeting, and NeurIPS.

The following code of conduct has been adapted from:

<https://www.grc.org/about/grc-policies-and-legal-disclaimers>

<https://www.sfn.org/about/professional-conduct/code-of-conduct-at-sfn-events>

<https://nips.cc/public/CodeOfConduct>

Other online resources:

<http://changingourcampus.org>

<https://www.sfn.org/about/professional-conduct/sfn-ethics-policy>

Responsibilities

All participants, volunteers, organizers, reviewers, speakers, sponsors, and volunteers (referred to as “Participants” collectively throughout this document) at our Conference, workshops, and Conference-sponsored social events—are required to agree with this Code of Conduct both during an event and on official communication channels, including social media.

Sponsors are equally subject to this Code of Conduct. In particular, sponsors should not use images, activities, or other materials that are of a sexual, racial, or otherwise offensive nature. This code applies both to official sponsors as well as any organization that uses the Conference name as branding as part of its activities at or around the Conference.

Organizers will enforce this Code, and it is expected that all Participants will cooperate to help ensure a safe and inclusive environment for everyone.

Policy

The conference commits itself to providing an experience for all Participants that is free from the following:

Harassment, bullying, discrimination which includes but is not limited to:

- Offensive comments related to age, race, religion, creed, color, gender (including transgender/gender identity), sexual orientation, medical condition, physical or intellectual disability, pregnancy, or medical conditions, national origin or ancestry.
- Intimidation, personal attacks, harassment, unnecessary disruption of talks or other conference events.

Inappropriate or unprofessional behavior that interferes with another's full participation including:

- Sexual harassment, stalking, following, harassing photography or recording, inappropriate physical contact, unwelcome attention, public vulgar exchanges, derogatory name-calling, and diminutive characterizations.
- Use of images, activities, or other materials that are of a sexual, racial, or otherwise offensive nature that may create an inappropriate or toxic environment.
- Disorderly, boisterous, or disruptive conduct including fighting, coercion, theft, damage to property, or any mistreatment or non-businesslike behavior towards participants.
- “Zoom bombing” or any virtual activity that is not related to the topic of discussion which detracts from the topic or the purpose of the program. This includes inappropriate remarks in chat areas as deemed inappropriate by presenters/monitors/event leaders.

Scientific misconduct: including fabrication, falsification, or plagiarism of paper submissions or research presentations, including demos, exhibits or posters. Cosyne asks each session chair and organizing and reviewing committee member to promote rigorous analysis of all science presented for or at the meeting in a manner respectful to all attendees.

This Code of Conduct applies to the actual meeting sites and Conference venues where Cosyne business is being conducted, including physical venues, online venues, and official virtual engagement platforms, including video, virtual streaming, and chat-based interactions. Cosyne is not responsible for non-sponsored activity or behavior that may occur at non-sponsored locations such as hotels, restaurants, or physical or virtual locations not otherwise a sanctioned space for sponsored events. *Nonetheless, any issues brought to the Hotline Relations Counselors will be explored.* Moreover, Cosyne will not actively monitor social media platforms but will follow up on issues of harassment and violations of the code of conduct that occur on those platforms that are specifically related to the Cosyne program, during the course of Cosyne, if and when they are brought to our attention.

Complaint reporting

The Conference encourages all Participants to immediately report any incidents of discrimination, harassment, unprofessional conduct, and/or retaliation so that complaints can be quickly and fairly resolved. There will be no retaliation against any Participant who brings a complaint or submits an incident report in good faith or who honestly assists in investigating such a complaint. If you have concerns related to your participation/interaction at the Conference or Conference sanctioned events, or observe someone else's difficulties, or have any other concerns you wish to share, please write to *CosyneHotline@gmail.com* or by calling the *Cosyne Hotline phone number at +1-858-208-3810* where you can speak with an HR Consultant.

Action

If a Participant engages in any inappropriate behavior as defined herein, the Conference organizers may take action as deemed appropriate, including: a formal or informal warning to the offender, expulsion from the conference with no refund, barring from participation in future conferences or their organization, reporting the incident to the offender's local institution or funding agencies, or reporting the incident to local authorities or law enforcement. A response of “just joking” is not acceptable. If action is taken, an appeals process will be made available. There will be no retaliation against any Participant who brings a complaint or submits an incident report in good faith or who honestly assists in investigating such a complaint. All issues brought forth to the onsite HR Consultant during the course of a Conference will be immediately investigated.

Program

Note: Institutions listed in the program are the primary affiliation of the first author. For the complete list, please consult the abstracts.

All times are UTC (Greenwich Mean Time, GMT)

Thursday, 17 March 2022

12:00	Spiking neural network models in neuroscience <i>Cosyne 2022 Tutorial session sponsored by the Simons Foundation</i>
	Dan Goodman
16:00	Registration opens
16:45	Welcome reception
18:15	Opening remarks

Session 1: Behavior and the brain

(Chair: Bing Brunton)	
18:30	Dopamine specifies the structure of spontaneous behavior Sandeep Robert Datta, Harvard University (invited) 29
19:45	Interpretable behavioral features have conserved neural representations across mice A. Syeda, W. Long, R. Tung, M. Pachitariu, C. Stringer, HHMI Janelia Research Campus 32
20:00	Operative Dimensions in High-Dimensional Connectivity of Recurrent Neural Networks R. Krause, M. Cook, V. Mante, G. Indiveri, UZH / ETH Zurich 33
20:15	Joint coding of visual input and eye/head position in V1 of freely moving mice E. Abe, P. Parker, D. Martins, E. Leonard, C. Niell, University of Oregon 33
20:30	Poster Session I

Friday, 18 March 2022

Session 2: Action selection, learning, and dopamine

(Chair: Cristina Savin)	
09:00	From plans to outcomes: Continuous representations of actions in primate prefrontal cortex Valerio Mante, ETH Zurich (invited) 29
09:45	Distinct dynamics in projection-specific midbrain dopamine populations for learning and motivation J. Elum, L. Zweifel, University of Washington 34
10:00	Computational strategies and neural correlates of probabilistic reversal learning in mice K. Mishchanchuk, A. MacAskill, University College London 34
10:15	Coffee break

Session 3: Communication within and between brains

(Chair: Il Memming Park)	
10:45	What can birds and rodents tell us about human speech? Michael Long, New York University (invited) 29
11:30	A new tool for automated annotation of complex birdsong reveals dynamics of canary syntax rules Y. Cohen, D. A. Nicholson, Weizmann Institute of Science 35

Program

11:45	Linking tonic dopamine and biased value predictions in a biologically inspired reinforcement learning model S. Romero Pinto, N. Uchida, Harvard University	35
12:00	Integrating deep reinforcement learning agents with the <i>C. elegans</i> nervous system C. Li, G. Kreiman, S. Ramanathan, Harvard University	36
12:15	Dynamical systems analysis reveals a novel hypothalamic encoding of state in nodes controlling social behavior A. Nair, T. Karigo, B. Yang, A. Kennedy, D. Anderson, California Institute of Technology (Caltech)	36
12:30	Lunch break	

Session 4: Spatial memory and beyond

(Chair: Brad Wyble)

15:00	To remap or reregister, that is the question: how hippocampus represents different spaces Andre Fenton, New York University (invited)	30
15:45	Isolating the role of synaptic plasticity in hippocampal place codes M. Plitt, K. Kaganovsky, J. Ding, T. Sudhof, L. Giocomo, Stanford University	37
16:00	A hierarchical representation of sequences in human entorhinal cortex A. Shpektor, J. Bakermans, A. Baram, T. Fedele, D. Ledergerber, L. Imbach, H. Barron, J. Sarnthein, T. Behrens, University of Oxford	37
16:15	Neocortical feature codes drive memory recall N. Yadav, C. Noble, J. Niemeyer, A. Terceros, J. Victor, C. Liston, P. Rajasethupathy, Rockefeller University	38
16:30	Coffee break	

Session 5: Oscillations, network states, and arousal

(Chair: Jennifer Groh)

17:00	(De-)Synchronizing neural networks with homoclinic action potentials Susanne Schreiber, Humboldt University of Berlin (invited)	30
17:45	Basal Ganglia feedback loops as possible candidates for generation of beta oscillation S. Azizpourlindi, A. Leblois, Institute of Neurodegenerative Diseases (IMN), University of Bordeaux	38
18:00	Neocortical long-range inhibitory neurons coordinate state-dependent network synchronization J. Ratliff, R. Batista-Brito, Albert Einstein College of Medicine	39
18:15	Metastable circuit dynamics explains optimal coding of auditory stimuli at moderate arousals L. Papadopoulos, M. Wehr, L. Mazzucato, University of Oregon	39
18:30	Dinner break	

19:00 Professional Development Panel and Social: Pathways to research beyond Academia

Sponsored by Meta Reality Labs

David Sussillo (Meta Reality Labs), Claire Warriner (Meta Reality Labs), Maria Eckstein (Deep Mind), Dawer Jamshed (Vanguard)

The paths to research jobs outside of academia are not always obvious. What jobs exist? How do you find them? What industry research opportunities are available? In this session, each panelist will share their career paths to industry research positions, why they transitioned to a career outside of academia, and the nature of the research programs they work on. There will be time for questions from the audience. Following the panel, there will be a free reception.

20:30 Poster Session II

Saturday, 19 March 2022

Session 6: Population codes and connectivity

(Chair: Omri Barak)		
09:00	Coordinated spike coding Christian Machens, Champalimaud (invited)	30
09:45	Large retinal populations are collectively organized to efficiently process natural scenes W. Mlynarski, D. Gupta, O. Symonova, M. Josch, Institute of Science and Technology Austria	40
10:00	A two-way luminance gain control in the fly brain ensures luminance invariance in dynamic vision M. Ketkar, S. Shao, J. Gjorgjieva, M. Silies, University of Mainz	40
10:15	Direct measurement of whole-brain functional connectivity in <i>C. elegans</i> F. Randi, A. Sharma, S. Dvali, A. M. Leifer, Princeton University	41
10:30	Coffee break	

Session 7: Multiscale brain networks

(Chair: Anne-Marie Oswald)		
11:00	Exploring ephaptic coupling in white matter Pamela Douglas, University of Central Florida (invited)	31
11:45	Optogenetic mapping of circuit connectivity in the motor cortex during goal-directed behavior A. Finkelstein, K. Daie, R. Darshan, K. Svoboda, Janelia Research Campus	41
12:00	Invariant neural subspaces maintained by feedback modulation L. B. Naumann, J. Keijser, H. Sprikeler, Berlin Institute of Technology	42
12:15	Dynamic causal communication channels between neocortical areas M. Javadzadeh, J. Rapela, M. Sahani, S. B. Hofer, University College London	42
12:30	Lunch break	

Session 8: Immune responses and the brain

(Chair: Carlos Ribeiro)		
15:00	A physiological take on the mind-body question. Asya Rolls, Technion (invited)	31
16:00	Panel discussion on inequities and the pandemic's effects Gabrielle Gutierrez, Megan Carey, Andre Fenton	
16:30	Coffee break	

Session 9: Navigating space and time

(Chair: Adrien Peyrache)		
17:00	A navigational network hardwired for rapid flexibility Ann Hermundstad, HHMI Janelia Research Campus (invited)	31
17:45	The secret Bayesian lives of ring attractor networks A. Kutschireiter, M. Basnak, R. Wilson, J. Drugowitsch, Harvard Medical School	42
18:00	A hindbrain ring attractor network that integrates heading direction in the larval zebrafish L. Petrucco, H. Lavian, V. Stih, Y. K. Wu, F. Svara, R. Portugues, Technical University of Munich	43
18:15	A reservoir of timescales in random neural networks M. Stern, N. Istrate, L. Mazzucato, University of Oregon	43
18:30	Dinner break	
20:30	Poster Session III	

Program

Sunday, 20 March 2022

Session 10: Working memory, decision making, and value

(Chair: Elizabeth Buffalo)

09:00	Neural circuits of visuospatial working memory Albert Compte, Barcelona (invited)	31
09:45	Orbitofrontal cortex is required to infer hidden task states during value-based decision making S. Schiereck, A. Mah, C. Constantinople, New York University	44
10:00	Reorganizing cortical learning: a cholinergic adaptive credit assignment model M. Filipovica, H. W. Zhu, W. Greedy, R. P. Costa, University of Bristol	44
10:15	Integrating information and reward into subjective value: humans, monkeys, and the lateral habenula E. Bromberg-Martin, Y. Feng, T. Ogasawara, J. K. White, K. Zhang, I. Monosov, Washington University School of Medicine	45
10:30	Coffee break	

Session 11: Sensory, motor, and in-between

(Chair: Daniela Vallentin)

11:00	Brain-body interactions for rapid and flexible control of walking Eugenia Chiappe, Champalimaud (invited)	32
11:45	The emergence of fixed points in interlimb coordination underlies the learning of novel gaits in mice H. Stein, A. Andrianarivelo, J. Gabillet, C. Batifol, M. Graupner, N. A. Cayco Gajic, Ecole Normale Supérieure	45
12:00	Differential encoding of innate and learned behaviors in the sensorimotor striatum K. Hardcastle, J. Marshall, B. Olveczky, Harvard University	46
12:15	Deep neural network modeling of a visually-guided social behavior B. Cowley, A. Calhoun, N. Rangarajan, J. Pillow, M. Murthy, Princeton Neuroscience Institute	46
12:30	Lunch break	

Session 12: Codes for (spatial) behaviors

(Chair: Kevin Franks)

15:00	The synaptic origins and functional role of diverse cortical responses during behavior J. Toth, B. Albanna, B. DePasquale, S. Fadaei, T. Gupta, K. Rajan, R. Froemke, M. Insanally, University of Pittsburgh	47
15:15	Correlation-based motion detectors in olfaction enable turbulent plume navigation N. Kadakia, D. Clark, T. Emonet, Yale University	47
15:30	A temporal context model of spatial memory N. A. Herweg, M. Kahana, Ruhr University Bochum	48
15:45	Symmetries and asymmetries in the neural coding of space Kate Jeffery, University College London (invited)	32
16:30	Closing remarks	

Poster Session 1

Thursday 17 March, 2022

1-001. Signatures of rapid synaptic learning in the hippocampus during novel experiences	48
James Priestley, John Bowler, Sebi Rolotti, Stefano Fusi, Attila Losonczy, Columbia University	
1-002. Differential effects of time and experience on hippocampal representational drift	49
Nitzan Geva, Alon Rubin, Yaniv Ziv, Weizmann Institute of Science, Israel	
1-003. Time cell encoding in deep reinforcement learning agents depends on mnemonic demands	49
Dongyan Lin, Blake Richards, McGill University	
1-004. Hippocampal networks support continual learning and generalisation	
Samia Mohinta, Dabal Pedamonti, Martin Dimitrov, Hugo Malagon-Vina, Stephane Ciochetti, Rui Ponte Costa, University of Bristol	50
1-005. The dynamical regime of mouse visual cortex shifts from cooperation to competition with increasing visual input	
William Podlaski, Lloyd Russell, Arnd Roth, Brendan Bicknell, Michael Hausser, Christian Machens, Champalimaud Centre for the Unknown	50
1-006. Thalamic role in human cognitive flexibility and routing of abstract information.	
Ali Hummos, Bin Wang, Sabrina Drammis, Burkhard Pleger, Michael Halassa, Massachusetts Institute of Technology	51
1-007. The geometry of map-like representations under dynamic cognitive control	
Seongmin Park, Jacob Russin, Maryam Zolfaghari, Randall O'Reilly, Erie Boorman, University of California, Davis	51
1-008. Multi-task representations across human cortex transform along a sensory-to-motor hierarchy	
Takuya Ito, John D Murray, Yale University	52
1-009. Neural network size balances representational drift and flexibility during Bayesian sampling	
Jacob Zavatone-Veth, Abdulkadir Canatar, Cengiz Pehlevan, Harvard University	52
1-010. Latent Equilibrium: A unified learning theory for arbitrarily fast computation with arbitrarily slow neurons	
Paul Haider, Benjamin Ellenberger, Laura Kriener, Jakob Jordan, Walter Senn, Mihai A Petrovici, University of Bern	53
1-011. Single-phase deep learning in cortico-cortical networks	
Will Greedy, Heng Wei Zhu, Jack Mellor, Rui Ponte Costa, University of Bristol	53
1-013. Biological multi-task learning with top-down signals	
Matthias Tsai, Willem Wybo, Bernd Illing, Jakob Jordan, Abigail Morrison, Walter Senn, University of Bern	54
1-014. Fine-tuning hierarchical circuits through learned stochastic co-modulation	
Caroline Haimerl, Eero Simoncelli, Cristina Savin, New York University	54
1-015. Insight moments in neural networks and humans	
Anika T Lowe, Andrew Saxe, Nicolas W Schuck, Leo Touzo, Paul S Muhle-Karbe, Christopher Summerfield, Max Planck Institute for Human Development	55
1-016. What do meta-reinforcement learning networks learn in two-stage decision-making?	
Li Ji-An, Marcelo G Mattar, University of California, San Diego	55
1-017. Neural optimal feedback control with local learning rules	
Johannes Friedrich, Siavash Golkar, Shiva Farashahi, Alexander Genkin, Anirvan Sengupta, Dmitri Chklovskii, Flatiron Institute	56
1-018. Principled credit assignment with strong feedback through Deep Feedback Control	
Alexander Meulemans, Matilde Tristany Farinha, Maria R Cervera, Joao Sacramento, Benjamin F Grewe, Institute of Neuroinformatics, University of Zurich and ETH Zurich	56
1-019. A closed-loop emulator that accurately predicts brain-machine interface decoder performance	
Ken-Fu Liang, Jonathan C Kao, University of California, Los Angeles	57
1-020. Learning input-driven dynamics from neural recordings	
Marine Schimel, Ta-Chu Kao, Kristopher Jensen, Guillaume Hennequin, University of Cambridge	57
1-021. Bayesian Inference in High-Dimensional Time-Series with the Orthogonal Stochastic Linear Mixing Model	
Rui Meng, Kristofer Bouchard, Lawrence Berkeley National Laboratory	58
1-022. Bayesian active learning for latent variable models of decision-making	
Aditi Jha, Zoe C Ashwood, Jonathan Pillow, Princeton University	58
1-023. Identifying latent states in decision-making from cortical inactivation data	
Zeinab Mohammadi, Zoe C Ashwood, Lucas Pinto, David W Tank, Carlos D Brody, Jonathan Pillow, Princeton University	59

Posters 1

1-024. Modeling multi-region neural communication during decision making with recurrent switching dynamical systems	
Orren Karniol-Tambour, David Zoltowski, Lucas Pinto, Eftymia Diamanti, David W Tank, Carlos D Brody, Jonathan Pillow, Princeton Neuroscience Institute	59
1-025. Rapid fluctuations in functional connectivity of cortical networks encode spontaneous behavior	
Hadas Benisty, Andrew Moberly, Sweyta Lohani, Daniel Barson, Ronald Coifman, Gal Mishne, Jessica Cardin, Michael Higley, Yale university	60
1-026. Fitting recurrent spiking network models to study the interaction between cortical areas	
Christos Sourmpis, Anastasiia Oryshchuk, Sylvain Crochet, Wulfram Gerstner, Carl Petersen, Guillaume Bellec, EPFL	60
1-027. Inter-areal patterned microstimulation selectively drives PFC activity and behavior in a memory task	
Joana Soldado Magraner, Yuki Minai, William Bishop, Matthew Smith, Byron Yu, Carnegie Mellon University / Neuroscience Institute & Center for the Neural Basis of Cognition	61
1-029. Predicting connectivity of motion-processing neurons with recurrent neural networks	
Whit Jacobs, Matthew Loring, Joseph Choo-Choy, Maxim Nikitchenko, Timothy Dunn, Eva Naumann, Duke University	61
1-030. Heterogeneous prediction-error circuits formed and shaped by homeostatic inhibitory plasticity	
Loreen Hertag, Claudia Clopath, Imperial College London	62
1-031. Novelty modulates neural coding and reveals functional diversity within excitatory and inhibitory populations in the visual cortex	
Farzaneh Najafi, Iryna Yavorska, Marina Garrett, Alex Piet, Peter Groblewski, Anton Arkhipov, Stefan Mihalas, Shawn Olsen, Allen Institute	62
1-032. A transcriptomic axis predicts state modulation of cortical interneurons	
Stephane Bugeon, Joshua Duffield, Mario Dipoppa, Anne Ritoux, Isabelle Pranker, Dimitris Nicoloutsopoulos, David Orme, Maxwell Shinn, Han Peng, Hamish Forrest, Aiste Viduolyte, Charu Bai Reddy, Yoh Isogai, Matteo Carandini, Kenneth D Harris, University College London	63
1-033. Impact of single gene mutation on circuit structure and spontaneous activity in the developing cortex	
Zhuoshi Liu, Jan Hendrik Kirchner, Juliette Cheyne, Christian Lohmann, Julijana Gjorgjieva, Max Planck Institute for Brain Research	64
1-034. The operating regime of primate sensory cortex	
Jagruti J Pattadkal, Boris Zemelman, Ila R Fiete, Nicholas Priebe, The University of Texas at Austin	64
1-035. Gain-mediated statistical adaptation in recurrent neural networks	
Lyndon Duong, Colin Bredenberg, David Heeger, Eero Simoncelli, New York University	65
1-036. Unifying model of contextual modulation with feedback from higher visual areas	
Serena Di Santo, Mario Dipoppa, Andreas Keller, Morgane Roth, Massimo Scanziani, Kenneth D Miller, Columbia University	65
1-037. An interpretable spline-LNP model to characterize feedforward and feedback processing in mouse dLGN	
Lisa Schmors, Yannik Bauer, Ziwei Huang, Lukas Meyerolbersleben, Simon Renner, Ann H Kotkat, Davide Crombie, Sacha Sokoloski, Laura Busse, Philipp Berens, University of Tübingen	66
1-038. A discrete model of visual input shows how ocular drift removes ambiguity	
Richard Lonsdale, Tim Vogels, Independent researcher	66
1-039. Efficient Coding of Natural Movies Predicts the Optimal Number of Receptive Field Mosaics	
Na Young Jun, Greg Field, John Pearson, Duke University	67
1-040. Identifying the nonlinear structure of receptive fields in the mammalian retina	
Dimokratis Karamanlis, Tim Gollisch, University Medical Center Goettingen	67
1-041. Biological learning of local motion detectors	
Tiberiu Tesileanu, Alexander Genkin, Dmitri Chklovskii, Flatiron Institute	68
1-042. Predictive processing of natural images by V1 firing rates revealed by self-supervised deep neural networks	
Cem Uran, Alina Peter, Andreea Lazar, William Barnes, Johanna Klon-Lipok, Katharine A Shapcott, Rasmus Roese, Pascal Fries, Wolf Singer, Martin Vinck, Ernst Strungmann Institute for Neuroscience in Cooperation with Max Planck Society (ESI)	68
1-043. Hypothesis-neutral models of higher-order visual cortex reveal strong semantic selectivity	
Meenakshi Khosla, Leila Wehbe, McGovern Institute for Brain Research, Massachusetts Institute of Technology	69

1-044. Evolution of neural activity in circuits bridging sensory and abstract knowledge	70
Francesca Mastrogiosse, Naoki Hiratani, Peter Latham, University College London	70
1-045. A distributional Bayesian learning theory for visual perceptual learning	70
Li Wenliang, University College London	70
1-046. Representation of sensory uncertainty by neuronal populations in macaque primary visual cortex	71
Zoe Boundy-Singer, Corey Ziemba, Robbe Goris, UT Austin	71
1-047. The emergence of gamma oscillations as a signature of gain control during context integration.	71
Joseph Emerson, Audrey Sederberg, Cheryl Olman, University of Minnesota	71
1-048. Selective V1-to-V4 communication of attended stimuli mediated by attentional effects in V1	72
Christini Katsanevakis, Andre Moraes Bastos, Hayriye Cagnan, Conrado Arturo Bosman, Karl John Friston, Pascal Fries, Ernst Strungmann Institute	72
1-049. A neural circuit model of hidden state inference for navigation and contextual memory	72
Isabel Low, Scott Linderman, Lisa Giocomo, Alex Williams, Stanford University	72
1-050. Rapid approximation of successor representations with STDP and theta phase precession	73
Tom George, William de Cothi, Kimberly Stachenfeld, Caswell Barry, UCL	73
1-052. Oscillatory and fractal biomarkers of human memory	73
Joseph Rudoler, Michael Kahana, Nora A Herweg, University of Pennsylvania	73
1-053. Neural signatures of memory retrieval in the hippocampus of freely caching chickadees	73
Selmaan Chettih, Dmitriy Aronov, Columbia University	73
1-054. Computational principles of systems memory consolidation	74
Jack Lindsey, Ashok Litwin-Kumar, Columbia University	74
1-055. Hierarchical interaction between memory units with distinct dynamics enables higher-order learning	74
Yoshinori Aso, Ashok Litwin-Kumar, Daichi Yamada, Toshihide Hige, Janelia Research Campus, HHMI	74
1-056. Purely STDP-based learning of stable, overlapping assemblies	75
Paul Manz, Raoul Martin Memmesheimer, University of Bonn	75
1-057. Spatio-Temporal Pattern Selectivity from Homeostatic Hebbian Plasticity	75
Klaus Pawelzik, Mohammad Dehghani Habibabadi, University of Bremen	75
1-058. Heavy-tailed connectivity emerges from Hebbian self-organization	76
Christopher Lynn, Caroline Holmes, Stephanie Palmer, Princeton University	76
1-059. Input correlations impede suppression of chaos and learning in balanced rate networks	76
Rainer Engelken, Alessandro Ingrosso, Ramin Khajeh, Sven Goedeke, Larry Abbott, Columbia University	76
1-060. Identifying key structural connections from functional response data: theory & applications	77
Tirthabir Biswas, Tianzhi Lambus, James Fitzgerald, HHMI Janelia Research Campus	77
1-061. Emergence of time persistence in an interpretable data-driven neural network model	77
Sebastien Wolf, Guillaume Le Goc, Georges Debregas, Simona Cocco, Remi Monasson, Ecole Normale Supérieure	77
1-062. Auxiliary neurons in optimized recurrent neural circuit speed up sampling-based probabilistic inference	77
Wah Ming Wayne Soo, Mate Lengyel, University of Cambridge	77
1-063. The neural code controls the geometry of probabilistic inference in early olfactory processing	78
Paul Masset, Jacob Zavatone-Veth, Venkatesh N Murthy, Cengiz Pehlevan, Harvard University	78
1-064. Optimal information routing to cerebellum-like structures	78
Samuel Muscinelli, Marjorie Xie, Mark Wagner, Ashok Litwin-Kumar, Columbia University	78
1-065. Microcircuits and the compressibility of neural connectomes	79
Alexis Benichou, Jean-Baptiste Masson, Christian L Vestergaard, Institut Pasteur	79
1-066. Weighted clustering motifs and small-worldness in connectomes	79
Anna Levina, Tanguy Fardet, University of Tübingen	79
1-067. A circuit library for exploring the functional logic of massive feedback loops in Drosophila brain	80
Mehmet Turkcan, Yiyin Zhou, Aurel A Lazar, Columbia University	80
1-068. Sex-specific network topology of the nociceptive circuit shapes dimorphic behavior in <i>C. elegans</i>	80
Gal Goldman, Vladyslava Pechuk, Meital Oren-Suissa, Elad Schneidman, Weizmann Institute of Science	80
1-070. Unsupervised inference of brain-wide functional motifs underlying behavioral state transitions	81
Matthew Perich, Tyler Benster, Aaron Andelman, Daphne Cornelisse, Eugene Carter, Karl Deisseroth, Kanaka Rajan, Icahn School of Medicine at Mount Sinai	81

Posters 1

1-071. Spatiotemporal dynamics and targeted functions of locus coeruleus norepinephrine in a learned behavior	
Gabi Drummond, Vincent Breton-Provencher, Mriganka Sur, Massachusetts Institute of Technology	81
1-072. Revealing latent knowledge in cortical networks during goal-directed learning	
Celine Drieu, Ziyi Zhu, Aaron Wang, Kylie Fuller, Sarah Elnozahy, Kishore Kuchibhotla, Johns Hopkins University	82
1-073. Neural sequence representation of stimulus value, response and surprise in hippocampus and prefrontal cortex	
Bryan Souza, Jan Klee, Luca Mazzucato, Francesco Battaglia, Donders Institute for Brain, Cognition and Behaviour, Radboud University	82
1-074. Simultaneous mnemonic and predictive representations in the auditory cortex	
Ryszard Auksztulewicz, Drew Cappotto, Hijee Kang, Kongyan Li, Lucia Melloni, Jan Schnupp, European Neuroscience Institute Gottingen	83
1-075. Transformation of population representations of sounds throughout the auditory system	
Sophie Bagur, Jacques Bourg, Alexandre Kempf, Thibault Tarpin, Khalil Bergaoui, Yin Guo, Etienne Gosselin, Alain Muller, Jean Luc Puel, Jerome Bourien, Brice Bathellier, Institut Pasteur, Institut de l'audition	83
1-076. Differential encoding of temporal context and expectation across the visual hierarchy	
David Wylick, Hannah Choi, Marina Garrett, Luca Mazzucato, Nicholas Cain, Ryan Larsen, Matthew Valley, Jerome Lecoq, University of Oregon	84
1-077. Perceptual and neural representations of naturalistic texture information in developing monkeys	
Gerick M Lee, Carla L Rodriguez-Deliz, Najib J Majaj, J Anthony Movshon, Lynne Kiorpes, New York University	85
1-078. Coarse-to-fine processing drives the efficient coding of natural scenes in mouse visual cortex	
Rolf Skyberg, Seiji Tanabe, Hui Chen, Jianhua "JC" Cang, University of Virginia	85
1-079. Coordinated multiplexing of information about distinct objects in visual cortex	
Jennifer Groh, Na Young Jun, Douglas Ruff, Lily Kramer, Brittany Bowes, Surya Tokdar, Marlene Cohen, Duke University	86
1-080. Moving bar of light evokes vectorial spatial selectivity in hippocampal place cells	
Shonali Dhingra, Chinmay Purandare, Mayank Mehta, CRTD, TUD	86
1-081. Neural mechanisms for collision avoidance exploiting positional geometry	
Ryosuke Tanaka, Damon Clark, Yale University	87
1-082. Investigation of a multilevel multisensory circuit underlying female decision making in Drosophila	
Edna Normand, Talmo Pereira, Nivedita Rangarajan, David Deutsch, Megan Wang, Mala Murthy, Princeton University	87
1-083. Multiscale Hierarchical Modeling Framework For Fully Mapping a Social Interaction	
Shruthi Ravindranath, Talmo Pereira, Junyu Li, Jonathan Pillow, Mala Murthy, Princeton Neuroscience Institute	88
1-084. Parvalbumin-positive interneuron regulation of maternal pup retrieval behavior	
Alexa Pagliaro, Julia Wang, Deborah Rupert, Stephen D Shea, Cold Spring Harbor Laboratory	88
1-085. Anterior cingulate cortex enables rapid set-shifting behaviour via prediction mismatch signalling	
Nicholas Cole, Matthew Harvey, Dylan Myers-Joseph, Aditya Gilra, Adil Khan, King's College London	89
1-087. Improved striatal learning with vector-valued errors mediated by diffusely transmitted dopamine	
Emil Warnberg, Konstantinos Meletis, Arvind Kumar, Karolinska Institutet	89
1-088. Reward Bases: instant reward revaluation with temporal difference learning	
Beren Millidge, Mark Walton, Rafal Bogacz, University of Oxford	90
1-089. A striatal probabilistic population code for reward underlies distributional reinforcement learning	
Adam Lowet, Qiao Zheng, Sara Matias, Naoshige Uchida, Jan Drugowitsch, Harvard University	90
1-090. Deliberation gated by opportunity cost adapts to context with urgency in non-human primates	
Maximilian Puelma Touzel, Paul Cisek, Guillaume Lajoie, University of Montreal	91
1-091. Mesolimbic dopamine encodes subjective value and predicts time investment decisions	
Sue Lynn Ren, Torben Ott, Apoorva Arora, Victoria Vega, Thiago Gouveia, Adam Kepecs, Washington University School of Medicine in St. Louis	91
1-092. Monkeys exhibit combinatorial reasoning during economic deliberation.	
Tao Hong, William Stauffer, Carnegie Mellon University / Neuroscience Institute & Center for the Neural Basis of Cognition	92
1-093. Optimal reward-rate in multi-task environments, and its consequences for behavior	
Lucas Silva Simoes, Alexandre Pouget, Peter Latham, UCL	92

1-094. Using Markov Decision Processes to benchmark the performance of artificial and biological agents	93
Alexander Kazakov, Ana Polterovich, Maciej M Jankowski, Johannes Niediek, Israel Nelken, The Hebrew University of Jerusalem	93
1-095. Rethinking Tolman's latent learning with metacognitive exploration	93
Su Jin An, Benedetto De Martino, Sang Wan Lee, Korea Advanced Institute of Science and Technology	93
1-096. Long-term consequences of actions affect human exploration in structured environments	94
Lior Fox, Ohad Dan, Gal Yarden, Yonatan Loewenstein, The Hebrew University of Jerusalem	94
1-097. Constructing behaviour in structured environments	94
Jacob Bakermans, Joseph Warren, James Whittington, Timothy Behrens, University of Oxford	94
1-098. Consolidation of Sequential Experience Supports Flexible Model-Based Planning	95
Oliver Vikbladh, Evan Russek, Neil Burgess, University College London	95
1-099. Neural basis of transferable representations for efficient learning	95
Ai Phuong Tong, Vishnu Sreekumar, Mark Woolrich, Huijing Tan, Sara Inati, Kareem Zaghloul, National Institutes of Health/University of Oxford	95
1-100. Model architectures for choice-selective sequences in a navigation-based, evidence-accumulation task	96
Lindsey Brown, Jounhong Ryan Cho, Scott S Bolkan, Edward H Nieh, Manuel Schottdorf, Sue Ann Koay, David W Tank, Carlos D Brody, Ilana B Witten, Mark S Goldman, Princeton University	96
1-101. Temporal Dynamics in an Attractor Model of the Songbird's Premotor Nucleus.	96
Fjola Hyseni, Arthur Leblois, Nicolas P Rougier, Institute of Neurodegenerative Diseases	96
1-102. Motor cortex isolates skill-specific dynamics in a context switching task	97
Eric Trautmann, Elom Amematsro, Sean Escola, Daniel Wolpert, Najja Marshall, Hannah Chen, Elijah Aliyari, Francisco Sacadura, Michael Shadlen, Mark Churchland, Columbia University	97
1-103. What is the snow in a neural avalanche?	97
Chaitanya Chintaluri, Tim Vogels, Institute of Science and Technology Austria	97
1-104. Action recognition best explains neural activity in cuneate nucleus	98
Alessandro Marin Vargas, Axel Bisi, Alberto Chiappa, Chris Versteeg, Lee E Miller, Alexander Mathis, EPFL	98
1-105. Facial movements and their neural correlates reveal latent decision variables in mice	98
Fanny Cazettes, Alfonso Renart, Zachary Mainen, Champalimaud Foundation	98
1-106. Distinct neural substrates for flexible and automatic motor sequence execution	99
Kevin Mizes, Jack Lindsey, Sean Escola, Bence Olveczky, Harvard University	99
1-107. Modeling the formation of the visual hierarchy	99
Mikail Khona, Sarthak Chandra, Talia Konkle, Ila R Fiete, Massachusetts Institute of Technology	99
1-108. Normative models of spatio-spectral decorrelation in natural scenes predict experimentally observed ratio of PR types	100
Ishani Ganguly, Matthias Christenson, Rudy Behnia, Columbia University	100
1-109. Chromatic contrast and angle of polarization signals are integrated in the Drosophila central complex	100
Sharon Su, Larry Abbott, Rudy Behnia, Columbia University	100
1-110. Accurate Engagement of the Drosophila Central-Complex Compass During Head-Fixed Path-Constrained Navigation	101
Hessameddin Akhlaghpour, Jazz Weisman, Gaby Maimon, Rockefeller University	101
1-111. Nonlocal Spatiotemporal Representation in the Hippocampus of Freely Flying Bats	101
Nicholas Dotson, Michael Yartsev, The Salk Institute for Biological Studies	101
1-112. A cortico-collicular circuit for accurate orientation to shelter during escape	102
Dario Campagner, Ruben Vale, Panagiota Iordanidou, Oriol Pavon Arcas, Yu Lin Tan, Federico Claudi, Anna Vanessa Stempel, Sepideh Keshavarzi, Rasmus Strange Petersen, Troy Margrie, Tiago Branco, Sainsbury Wellcome Centre and Gatsby Unit- University College London	102
1-113. Dendritic integration of thalamic HD signals and retrosplenial input in presubiculum neurons	102
Desdemona Fricker, Merie Nassar, Nathalie Sol-Foulon, Louis Richevaux, CNRS / U Paris	102
1-114. Large-scale paired recordings reveal strong and specific connections between retina and midbrain.	103
Jeremie Sibille, Carolin Gehr, Jonathan Benichov, Hymavathy Balasubramanian, Kai Lun Teh, Tatiana Lupashina, Daniela Vallentin, Jens Kremkow, Charite	103
1-116. Neuromodulatory changes in the efficiency of information transmission at visual synapses	103
Leon Lagnado, Jose Moya-Diaz, Ben James, University of Sussex	103
1-117. Cellular mechanisms of dorsal horn neurons shape the functional states of nociceptive circuits	104
Anaelle De Worm, Pierre Sacre, University of Liege	104

Posters 1

1-118. The timescale and magnitude of 1/f aperiodic activity decrease with cortical depth in humans, macaques, and mice	
Mila Halgren, Raphi Kang, Bradley Voytek, Istvan Ulbert, Daniel Fabo, Lorand Eross, Lucia Wittner, Joseph Madsen, Werner Doyle, Orrin Devinsky, Eric Halgren, Mark T Harnett, Sydney Cash, MIT	105
1-119. Mechanisms of surround facilitation and suppression to holographic perturbations	
Ho Yin Chau, Ian Oldenburg, William Hendricks, Hillel Adesnik, Kenneth D Miller, Agostina Palmigiano, Center for Theoretical Neuroscience, Columbia University	105
1-120. An inhibitory network model explains the transient dynamics of hippocampal ripple oscillations	
Natalie Schieberstein, Tilo Schwalger, Richard Kempter, Benjamin Lindner, Humboldt University of Berlin .	106
1-122. Efficient learning of low dimensional latent dynamics in multiscale spiking and LFP population activity	
Parima Ahmadipour, Omid Sani, Yuxiao Yang, Maryam Shanechi, University of Southern California	106
1-123. Explainable Machine Learning Approach to Investigating Neural Bases of Brain State Classification	
Evie Malaia, Sean Borneman, Katie Ford, Brendan Ames, University of Alabama	107
1-124. Inter-individual alignment and single-trial classification of MEG data using M-CCA	
Leo Michalke, Jochem Rieger, Carl von Ossietzky University Oldenburg	107
1-125. Fast inter-subject alignment method for large datasets shows fine-grained cortical reorganisations	
Alexis Thual, Huy Tran, Bertrand Thirion, Stanislas Dehaene, CEA, Neurospin	108
1-126. Approximate gradient descent and the brain: the role of bias and variance	
Arna Ghosh, Konrad Kording, Blake Richards, McGill University	108
1-127. A new approach to inferring the eigenspectra of high-dimensional neural representations	
Dean Pospisil, Jonathan Pillow, Princeton University	109
1-128. Optimal dynamic allocation of finite resources for many-alternatives decision-making	
Francesco Damiani, Ruben Moreno Bote, Center for Brain and Cognition, Universitat Pompeu Fabra, 08002 Barcelona, ES;	109
1-129. A biophysical counting mechanism for keeping time	
Klavdia Zemlianova, Amitabha Bose, John Rinzel, New York University	110
1-130. Encoding of natural movies based on multi-neuron temporal spiking patterns	
Boris Sotomayor, Francesco Battaglia, Martin Vinck, Ernst Strungmann Institute for Neuroscience in Co-operation with Max Planck Society (ESI)	110
1-131. Awake perception is associated with dedicated neuronal assemblies in cerebral cortex	
Anton Filipchuk, Alain Destexhe, Brice Bathellier, NeuroPSI	111
1-132. Isolated correlates of somatosensory perception in the posterior mouse cortex	
Michael Sokoletsky, David Ungarish, Ilan Lampl, The Weizmann Institute of Science	111
1-133. Grid cells rapidly integrate novel landmarks	
John Wen, Ben Sorscher, Surya Ganguli, Lisa Giocomo, Stanford University	111
1-135. Soft-actor-critic for model-free reinforcement learning of eye saccade control	
Henrique Granado, Akhil John, Reza Javanmard, John Van Opstal, Alexandre Bernardino, Institute for Systems and Robotics, Instituto Superior Tecnico, Universidade de Lisboa	112
1-136. Neural Representations of Opponent Strategy Support the Adaptive Behavior of Recurrent Actor-Critics in a Competitive Game	
Mitchell Ostrow, Guangyu Robert Yang, Hyojung Seo, Yale University	112
1-138. Cerebellum learns to drive cortical dynamics: a computational lesson	
Joseph Pemberton, Rui Ponte Costa, University of Bristol	113
1-139. Modelling Systems Memory Consolidation with neural fields	
Lisa Blum Moyse, Hugues Berry, INSA de Lyon	113
1-140. A stable memory scaffold with heteroassociative learning produces a content-addressable memory continuum	
Sugandha Sharma, Sarthak Chandra, Ila R Fiete, Massachusetts Institute of Technology	114
1-141. A cable-driven robotic eye for the study of oculomotor behaviors	
Akhil John, Bernardo Dias, Reza Javanmard, John Van Opstal, Alexandre Bernardino, Institute for Systems and Robotics, Instituto Superior Tecnico, Universidade de Lisboa	114
1-142. Frontal cortex neural correlations are reduced in the transformation to movement	
Noga Larry, Mati Joshua, The Hebrew University of Jerusalem	115
1-144. Engagement of the respiratory CPG for songbird vocalizations	
Eszter Kish, Kevin Yackle, Michael Brainard, UCSF	115
1-145. Cortical adaptation to sound reverberation	
Aleksandar Ivanov, Andrew King, Benjamin Willmore, Kerry Walker, Nicol Harper, University of Oxford . .	115

1-146. "This Is My Spot!": Social Determinants Regulate Space Utilization in Macaques.	
Sylvia Wirth, Tadeusz Kononowicz, Felipe Rolando, Lucas Maigre, Sebastien Ballesta, Angela Sirigu, Jean-Rene Duhamel, Centre National de la Recherche Scientifique	116
1-147. Investigating effort and time sensitivities in rodents performing a treadmill-based foraging task	
Thomas Morvan, Stefania Sarno, Christophe Eloy, David Robbe, Aix-Marseille University	116
1-148. Paradoxical effect of exercise on the long-term stability of hippocampal place code	
Yoav Rechavi, Alon Rubin, Yaniv Ziv, Weizmann Institute of Science, Israel	117
1-149. Data-driven dynamical systems model of epilepsy development simulates intervention strategies	
Danylo Batulin, Fereshteh Lagzi, Annamaria Vezzani, Peter Jedlicka, Jochen Triesch, Frankfurt Institute for Advanced Studies	117

Poster Session 2**Friday 18 March, 2022**

2-001. Exceptionally large rewards lead to a collapse in neural information about upcoming movements	118
Adam Smoulder, Patrick Marino, Nicholas Pavlovsky, Emily Oby, Sam Snyder, William Bishop, Byron Yu, Steven Chase, Aaron Batista, Carnegie Mellon University	
2-002. State-dependent Reward Encoding in Cortical Activity During Dynamic Foraging	119
Nhat Minh Le, Mriganka Sur, Murat Yildirim, Hiroki Sugihara, Yizhi Wang, MIT	
2-003. Hippocampal representations emerge when training recurrent neural networks on a memory dependent maze navigation task	119
Justin Jude, Matthias Hennig, University of Edinburgh	
2-004. Epiphenomenal representations of abstract rules in a connectionist model of the Delayed Match to Sample task	120
Badr AlKhamissi, Muhammad ElNokrashy, Zeb Kurth-Nelson, Sam Ritter, Sony AI	
2-005. Learning-to-learn emerges from learning to efficiently reuse neural representations	120
Vishwa Goudar, Barbara Peysakhovich, Elizabeth A Buffalo, David Freedman, Xiao-Jing Wang, New York University	
2-006. Capturing the evolution of low-dimensional dynamics in large scale neural recordings with sliceTCA	121
Arthur Pellegrino, Heike Stein, N Alex Cayco Gajic, The University of Edinburgh	
2-007. Disentangling neural dynamics with fluctuating hidden Markov models	121
Sacha Sokoloski, Ruben Coen-Cagli, University of Tübingen	
2-008. Online neural modeling and Bayesian optimization for closed-loop adaptive experiments	122
Anne Draelos, Pranjal Gupta, Na Young Jun, Chaichontat Sriworarat, Matthew Loring, Maxim Nikitchenko, Eva Naumann, John Pearson, Duke University	
2-009. Hida-Matern Gaussian Processes	122
Matthew Dowling, Piotr Sokol, Memming Park, Stony Brook University	
2-010. How coding constraints affect the shape of neural manifolds	123
Allan Mancoo, Christian Machens, Champalimaud Centre for the Unknown	
2-011. Neuromodulation as a path along the model manifold for spiking networks	123
Jacob Crosser, Braden Brinkman, SUNY Stony Brook	
2-012. Thalamic head-direction cells are organized irrespective of their inputs	124
Guillaume Viejo, Adrien Peyrache, McGill University	
2-013. Environment-dependent firing in rigidly organized head-direction cells is stable across weeks	124
Sofia Skromne Carrasco, Guillaume Viejo, Adrien Peyrache, McGill University	
2-014. Goal-directed remapping of entorhinal cortex neural coding	124
Alexander Gonzalez, Lisa Giocomo, Stanford University	
2-016. Developmental experience of scarcity affects adult responses to negative outcomes and uncertainty	125
Wan Chen Lin, Christine Liu, Polina Kosillo, Lung-Hao Tai, Ezequiel Galarce, Helen Bateup, Stephan Lammel, Linda Wilbrecht, University of California, Berkeley	
2-017. Indirect-projecting striatal neurons constrain timed action via ‘ramping’ activity.	125
Robert Bruce, Rachael Volkman, Nandakumar Narayanan, University of Iowa	
2-018. Exploration of learning by dopamine D1 and D2 receptors by a spiking network model of the basal ganglia	126
Carlos Enrique Gutierrez, Jean Lienard, Benoit Girard, Hidetoshi Urakubo, Yuko Ishiwaka, Kenji Doya, Softbank Corp., Advance Technology Promotion Office	
2-019. Learning and expression of dopaminergic reward prediction error via plastic representations of time	126
Ian Cone, Claudia Clopath, Harel Shouval, Imperial College London	
2-020. Learning rules underlying operant matching in <i>D. melanogaster</i>	127
Adithya Rajagopalan, Ran Darshan, James Fitzgerald, Glenn Turner, HHMI Janelia Research Campus	
2-021. The neurocognitive role of working memory load when motivation affects instrumental learning	128
Heesun Park, Hoyoung Doh, Harhim Park, Woo-Young Ahn, Seoul National University	
2-022. Counterfactual outcomes affect reward expectation and prediction errors in macaque frontal cortex	128
Jan Grohn, Caroline Jahn, Mark Walton, Sébastien Bouret, Jerome Sallet, Nils Kolling, University of Oxford	
2-023. Optimists and realists: heterogeneous priors in rats performing hidden state inference	129
Andrew Mah, Christine Constantinople, New York University	

2-025. A virtual rodent predicts the structure of neural activity across natural behavior	
Diego Aldarondo, Josh Merel, Jesse Marshall, Leonard Hansclever, Ugne Klibaite, Amanda Gellis, Yuval Tassa, Greg Wayne, Matthew Botvinick, Bence olveczky, Harvard University	129
2-026. A feedback model for predicting targeted perturbations of proprioceptors during fly walking	
Pierre Karashchuk, Sarah Walling-Bell, Chris Dallmann, John Tuthill, Bing Brunton, University of washington-seattle	130
2-027. Sensory feedback can drive adaptation in motor cortex and facilitate generalization	
Barbara Feulner, Matthew G Perich, Lee E Miller, Claudia Clopath, Juan A Gallego, Imperial College London	130
2-028. Widespread representations of sensory evidence with distinct temporal dynamics across the sensorimotor axis	
Andrei Khilkevich, Michael Lohse, Ivana Orsolic, Tadej Bozic, Thomas Mrsic-Flogel, Sainsbury Wellcome Centre	131
2-029. Auditory cortex represents an abstract sensorimotor rule	
Samuel Picard, Andrew King, Yves Weissberger, Samuel Lippl, Johannes Dahmen, University College London	131
2-030. Experience early in auditory conditioning impacts across-animal variability in neural tuning	
Kathleen Martin, Colin Bredenberg, Cristina Savin, Jordan Lei, Eero Simoncelli, Robert Froemke, New York University	132
2-031. Holographic activation of neural ensembles reveals both space and feature based cortical micro-circuitry	
Ian Oldenburg, Gregory Handy, Brent Doiron, Hillel Adesnik, William Hendricks, UC Berkeley	132
2-032. Development of orientation selective receptive fields via Hebbian plasticity	
Bettina Hein, Francesco Fumarola, Kenneth D Miller, Columbia University	133
2-033. Clustered recurrent connectivity promotes the development of E/I co-tuning via synaptic plasticity	
Emmanouil Giannakakis, Oleg Vinogradov, Anna Levina, University of Tubingen	133
2-034. Recurrent suppression in visual cortex explained by a balanced network with sparse synaptic connections	
Jonathan O'Rawe, Zhishang Zhou, Anna Li, Paul LaFosse, Mark Histed, Hannah Goldbach, National Institutes of Health	134
2-035. Statistics of sub-threshold voltage dynamics in cortical networks	
Oren Amsalem, Hidehiko Inagaki, Jianing Yu, Karel Svoboda, Ran Darshan, Harvard Medical School	134
2-036. Cortex-wide decision circuits are shaped by distinct classes of excitatory pyramidal neurons	
Simon Musall, Xiaonan R Sun, Hemanth Mohan, Xu An, Steven Gluf, Anne Churchland, Research Center Juelich	135
2-037. Goal-directed processing flexibly controls the flow of interhemispheric tactile cues	
Hyein Park, Hayagreev Keri, Chengyu Bi, Daniel Butts, Scott Pluta, Purdue University	136
2-038. Dynamics of interhemispheric prefrontal coordination underlying serial dependence in working memory	
Melanie Tschiersch, Joao Barbosa, Akash Umakantha, Matthew Smith, Albert Compte, IDIBAPS	136
2-039. Phase dependent maintenance of temporal order in biological and artificial recurrent neural networks	
Stefanie Liebe, Matthijs Pals, Johannes Niediek, Jakob Macke, Florian Mormann, University Clinic Tubingen	137
2-040. Can time dependent and invariant decoders co-exist?	
Ayesha Vermani, Ke Chen, Joshua Kogan, Alfredo Fontanini, Memming Park, Stony Brook University	137
2-041. Top-down optimization recovers biological coding principles of single-neuron adaptation in RNNs	
Victor Geadah, Giancarlo Kerg, Stefan Horoi, Guy Wolf, Guillaume Lajoie, Princeton University	138
2-043. Emergence of convolutional structure in neural circuits	
Alessandro Ingrosso, Sebastian Goldt, The Abdus Salam International Centre for Theoretical Physics	138
2-044. Feedforward and feedback computations in V1 and V2 in a hierarchical Variational Autoencoder	
Ferenc Csikor, Balazs Meszena, Gergő Orban, Wigner Research Centre for Physics	139
2-045. Similar reformatting of object manifolds across rat visual cortex and deep neural networks	
Paolo Muratore, Sina Tafazoli, Alessadro Laio, Davide Zoccolan, SISSA	139
2-046. Causal inference can explain hierarchical motion perception and is reflected in neural responses in MT	
Sabyasachi Shivkumar, Zhixin Xu, Gabor Lengyel, Gregory DeAngelis, Ralf Haefner, University of Rochester	140
2-047. Structure in motion: visual motion perception as online hierarchical inference	
Johannes Bill, Samuel J Gershman, Jan Drugowitsch, Harvard University	140

Posters 2

2-048. Learning static and motion cues to material by predicting moving surfaces	141
Kate Storrs, Roland Fleming, Justus Liebig University Giessen	
2-049. Task-dependent contribution of higher-order statistics to natural texture processing	141
Daniel Herrera, Ruben Coen-Cagli, Universidad de la Republica	
2-050. Local low dimensionality is all you need	142
Thomas Yerxa, Eero Simoncelli, New York University	
2-051. Initialization choice leads to different solutions in trained RNNs	142
Friedrich Schuessler, Francesca Mastrogiosse, Srdjan Ostojic, Omri Barak, Technion - Israel Institute of Technology	
2-052. Beyond accuracy: robustness and generalization properties of biologically plausible learning rules	143
Yuhan Helena Liu, Guillaume Lajoie, University of Washington	
2-053. Supervised learning and interpretation of plasticity rules in spiking neural networks	143
Basile Confavreux, Friedemann Zenke, Everton J Agnes, Timothy Lillicrap, Tim Vogels, IST Austria	
2-054. Adversarial learning of plasticity rules	144
Poornima Ramesh, Basile Confavreux, Tim Vogels, Jakob Macke, University of Tübingen	
2-055. Revisiting the flexibility-stability dilemma in recurrent networks using a multiplicative plasticity rule	144
Bin Wang, Johnatan Aljadeff, University of California, San Diego	
2-056. Efficient inference of synaptic learning rule with Conditional Gaussian Method	145
Shirui Chen, Sukbin Lim, Qixin Yang, University of Washington-seattle	
2-057. Bayesian synaptic plasticity is energy efficient	145
James Malkin, Cian O'Donnell, Conor Houghton, Laurence Aitchison, University of Bristol	
2-058. Turning spikes to space through plastic synaptic dynamics	146
Robert Gutig, Qiang Yu, Misha Tsodyks, Haim Sompolinsky, Charite Medical School	
2-059. Rapid compressed sensing of synaptic circuitry enabled by holographic neural ensemble stimulation	146
Marcus Triplett, Marta Gajowa, Hillel Adesnik, Liam Paninski, Columbia University	
2-060. Real-time neural network denoising of 3D optogenetic connectivity maps	147
Benjamin Antin, Marta Gajowa, Masato Sadahiro, Marcus Triplett, Amol Pasarkar, Hillel Adesnik, Liam Paninski, Columbia University	
2-062. Unsupervised representation learning of neuron morphologies	147
Marissa A Weis, Timo Luddecke, Laura Pede, Alexander Ecker, University of Gottingen	
2-063. Wiring diagram of a central sensory projection revealed by dense Brainbow labeling	148
Katie Matho, Minh Son Phan, Lamiae Abdelladim, Nelly Vuillemin, Dragos Niculescu, David Mou, Morgane Roche, Marie Guirguis, May Zhang, Laura Dumas, Francesco Boato, Pierre Mahou, Ignacio Arganda-Carreras, Jonathan Bradley, Willy Supatto, Alexis-Pierre Bemelmans, Jeff Lichtman, Anatole Chessel, Emmanuel Beaurepaire, Jean Livet, Cold Spring Harbor Laboratory	
2-064. Parallel functional architectures within a single dendritic tree	149
Young Joon Kim, Balazs Ujfalussy, Mate Lengyel, University of Cambridge	
2-065. Synaptic diversity naturally arises from neural decoding of heterogeneous populations	149
Ben Scholl, Jacob Yates, The Pennsylvania State University	
2-066. Random compressed coding with neurons	150
Simone Blanco Malerba, Mirko Pieropan, Rava Azeredo da Silveira, Yoram Burak, Ecole Normale Supérieure	
2-067. Diverse covariates modulate neural variability: a widespread (sub)cortical phenomenon	150
David Liu, Theoklitos Amvrosiadis, Nathalie Rochefort, Mate Lengyel, University of Cambridge	
2-068. Relating Divisive Normalization to Modulation of Correlated Variability in Primary Visual Cortex	151
Oren Weiss, Hayley Bounds, Hillel Adesnik, Ruben Coen-Cagli, Albert Einstein College of Medicine	
2-069. Electrical but not optogenetic stimulation drives nonlinear contraction of neural states	151
Daniel O'Shea, Lea Duncker, Saurabh Vyas, Xulu Sun, Maneesh Sahani, Krisha Shenoy, Stanford University	
2-070. Disrupting periodic neuronal synchrony with closed-loop stimulation in vitro	152
Domingos Leite de Castro, Miguel Aroso, A Pedro Aguiar, David B Grayden, Paulo Aguiar, Instituto de Investigacao e Inovacao em Saude	
2-071. Hierarchy of brain oscillations emerges from recurrent error correction	152
Trevor McPherson, Alexander Kuczala, Tatyana Sharpee, University of California, San Diego	
2-072. How spiking neural networks can flexibly trade off performance and energy use	153
Sander Keemink, William Podlaski, Nuno Calaim, Christian Machens, Donders Institute for Brain, Cognition and Behaviour	

2-073. Optimal Multimodal Integration Supports Course Control Under Uncertainty in Walking Drosophila	Tomas Cruz, Andre Marques, Terufumi Fujiwara, Nelia Varela, Eugenia Chiappe, Fundacao Champalimaud	153
2-074. Sensory tuning in neuronal movement commands	Matthias Baumann, Amarender R Bogadhi, Anna Denninger, Ziad M Hafed, Centre for Integrative Neuroscience	154
2-075. Movement and stimuli are differentially encoded in on- or off-manifold dimensions revealed by sleep	Eliezyer Fermino de Oliveira, Soyoung Kim, Tian Qiu, Adrien Peyrache, Renata Batista-Brito, Lucas Sjulson, Albert Einstein College of Medicine	154
2-076. A control space for muscle state-dependent cortical influence during naturalistic motor behavior	Zhengyu Ma, Natalie Koh, Amy Kristl, Abhishek Sarup, Andrew Miri, Northwestern University	155
2-077. Stabilizing brain-computer interfaces through nonlinear manifold alignment with dynamics	Brianna Karpowicz, Yahia H Ali, Lahiru N Wimalasena, Mohammad Reza Keshtkarani, Andrew R Sedler, Kevin Bodkin, Xuan Ma, Lee E Miller, Chethan Pandarinath, Emory University	155
2-078. Multitask computation in recurrent networks utilizes shared dynamical motifs	Laura Driscoll, Krisha Shenoy, David Sussillo, Stanford University	156
2-079. Reduced dynamics - a tool for describing RNNs activity as a directed graph	Elia Turner, Omri Barak, Technion	156
2-080. Gaussian Partial Information Decomposition: Quantifying Inter-areal Interactions in High-Dimensional Neural Data	Praveen Venkatesh, Gabriel Schamberg, Adrienne Fairhall, Shawn Olsen, Stefan Mihalas, Christof Koch, Allen Institute	157
2-081. Towards hierarchical predictive coding with spiking neurons and dendritic errors	Fabian Mikulasch, Lucas Rudelt, Michael Wibral, Viola Priesemann, Max Planck Institute for Dynamics and Self-Organization	157
2-082. Self-supervised learning in neocortical layers: how the present teaches the past	Kevin Kermani Nejad, Dabal Pedamonti, Paul Anastasiades, Rui Ponte Costa, University of Bristol	158
2-083. Multiscale encodings of memories in hippocampal and artificial networks	Louis Kang, Taro Toyoizumi, RIKEN Center for Brain Science	158
2-084. A GABAergic plasticity mechanism for world structure inference by CA3	Zhenrui Liao, Darian Hadjibabai, Satoshi Terada, Ivan Soltesz, Attila Losonczy, Columbia University	159
2-085. Experience-Driven Rate Modulation is Reinstanted During Hippocampal Replay	Daniel Bendor, Marta Huelin Gorri, Masahiro Takigawa, Lilia Kukovska, Margot Tirole, University College London	159
2-086. The anterior thalamus drives hippocampal replay following spatial learning	Sandybel Angeles Duran, Adrien Peyrache, McGill University	160
2-087. Hippocampal Neocortical Coupling Varies as a Function of Depth of NREM Sleep	Rachel Swanson, Jayeeta Basu, Gyorgy Buzsaki, New York University	160
2-088. Conjunctive theta- and ripple-frequency oscillations across hippocampal strata of foraging rats	Pavithra Seenivasan, Reshma Basak, Rishikesh Narayanan, Indian Institute of Science	161
2-089. Comparable theta phase coding dynamics along the CA1 transverse axis	Aditi Bishnoi, Sachin Deshmukh, Indian Institute of Science	161
2-090. Acetylcholine in amygdala does not encode outcome uncertainty	Jacob Dahan, Quentin Chevy, Fitz Sturgill, Melissa Cortez, Adam Kepecs, Washington University School of Medicine in St. Louis	162
2-091. Universality of modular correlated networks across the developing neocortex	Nathaniel Powell, Bettina Hein, Deyue Kong, Jonas Elpelt, Haleigh Mulholland, Matthias Kaschube, Gordon Smith, University of Minnesota	162
2-092. Environmental Statistics of Temporally Ordered Stimuli Modify Activity in the Primary Visual Cortex	Scott Knudstrup, Jeff Gavornik, Boston University	163
2-093. State Prediction in Primary Olfactory Cortex	Hanne Stensola, Tor Stensola, Megha Patwa, Eric DeWitt, Zachary Mainen, Champalimaud Centre for the Unknown	163
2-094. Shared representational features in Drosophila olfactory centers	Camille Rullan, Hamza Giaffar, Mikio Aoi, New York University	164
2-095. High-level prediction signals cascade through the macaque face-processing hierarchy	Tarana Nigam, Caspar M Schwiedrzik, European Neuroscience Institute Gottingen	164

Posters 2

2-096. Neural network mechanisms underlying post-decision biases	
Klaus Wimmer, Bharath Chandra Talluri, Tobias Donner, Alex Roxin, Jose M Esnaola-Acebes, Centre de Recerca Matematica	165
2-097. The interplay between prediction and integration processes in human perception	
Alexandre Hyafil, Pau Blanco-Arnau, Centre de Recerca Matematica	165
2-098. Tracking human skill learning with a hierarchical Bayesian sequence model	
Noemi Elteto, Dezso Nemeth, Karolina Janacsek, Peter Dayan, Max Planck Institute for Biological Cybernetics	166
2-099. Dynamic and structured action bias masks learned task contingencies early in learning	
Ziyi Zhu, Celine Drieu, Kishore Kuchibhotla, Johns Hopkins University	166
2-100. Selection from working memory can lead to catastrophic misbinding errors	
Matteo Alleman, Matthew F Panichello, Timothy J Buschman, W Jeffrey Johnston, Center for Theoretical Neuroscience, Columbia University	167
2-101. One-shot learning of paired associations by a reservoir computing model with Hebbian plasticity	
M Ganesh Kumar, Cheston Tan, Camilo Libedinsky, Shih-Cheng Yen, Andrew Tan, National University of Singapore	167
2-102. The role of hippocampal CA1 in relational learning in mice	
Svenja Nierwetberg, David Orme, Karel Kieslich, Andrew MacAskill, University College London	168
2-103. Internally Organized Abstract Task Maps in the Mouse Medial Frontal Cortex	
Mohamady El-Gaby, Adam Harris, James Whittington, Mark Walton, Thomas Akam, Timothy Behrens, University of Oxford	168
2-104. Mice identify subgoal locations through an action-driven mapping process	
Philip Shamash, Tiago Branco, University College London	169
2-105. Automatic Task Decomposition using Compositional Reinforcement Learning	
Pablo Tano, Peter Dayan, Alexandre Pouget, University of Geneva	169
2-106. Environmental complexity modulates the arbitration between deliberative and habitual decision-making	
Ugurcan Mugan, Samantha Hoffman, Paul J Cunningham, Paul S Regier, Seiichiro Amemiya, A David Redish, University of Minnesota	170
2-107. The rodent medial prefrontal cortex is composed of functionally distinct subregions	
Geoffrey Diehl, A David Redish, University of Minnesota	170
2-108. Defining the role of a locus coeruleus-orbitofrontal cortex circuit in behavioral flexibility	
Cameron Ogg, Hunter Franks, Hunter Nolen, Benjamin Lansdell, Abbas Shirinifard, Lindsay Schwarz, St. Jude Children's Research Hospital	171
2-109. Input-specific regulation of locus coeruleus activity for mouse maternal behavior	
Chloe Bair-Marshall, Robert Froemke, New York University	171
2-110. Mechanisms of plasticity for pup call sounds in the maternal auditory cortex	
Christoph Miehl, Soomin Song, Robert Froemke, Julijana Gjorgjieva, MPI Brain Research Frankfurt	172
2-111. Emergence of functional circuits in the absence of neural activity	
Daniel Barabasi, Gregor Schuhknecht, Andrew Bolton, Florian Engert, Harvard University	172
2-112. Social cues modulate circuit dynamics to control the choice between communication signals in flies	
Afshin Khalili, Elsa Steinfath, Kimia Alizadeh, Adrian Palacios Munoz, Jan Clemens, European Neuroscience Institute Gottingen	173
2-113. Flexible circuit mechanisms for context-dependent song sequencing	
Frederic Roemschied, Diego Pacheco, Elise Ireland, Xinping Li, Max Aragon, Rich Pang, Mala Murthy, Princeton University	173
2-114. Modeling tutor-directed dynamics in zebra finch song learning	
Miles Martinez, Samuel Brudner, Richard Mooney, John Pearson, Duke University	174
2-115. Many, but not all, deep neural network audio models predict auditory cortex responses and exhibit hierarchical layer-region correspondence	
Greta Tuckute, Jenelle Feather, Dana Boebinger, Josh McDermott, Massachusetts Institute of Technology	174
2-116. Identifying and adaptively perturbing compact deep neural network models of visual cortex	
Benjamin Cowley, Patricia Stan, Matthew Smith, Jonathan Pillow, Princeton Neuroscience Institute	175
2-117. Mind the gradient: context-dependent selectivity to natural images in the retina revealed with a novel perturbative approach	
Matias Goldin, Alexander Ecker, Baptiste Lefebvre, Samuele Virgili, Thierry Mora, Ulisse Ferrari, Olivier Marre, Institut de la Vision - Sorbonne Universite	175

2-118. Divergence of chromatic information in GABAergic amacrine cells in the retina	176
Sarah Strauss, Maria M Korympidou*, Timm Schubert, Katrin Franke, Philipp Berens, Thomas Euler, Anna L Vlasits, University of Tübingen	
2-120. Organization of local directionally selective neurons informs global motion vision encoding	176
Arthur Zhao, Aljoscha Nern, Edward Rogers, Nirmala Iyer, Miriam Flynn, Connor Laughland, Henrique Ludwig, Alex Thomson, Michael Reiser, Janelia Research Campus	
2-121. Evaluating Noise Tolerance in Drosophila Vision	177
Hyosun Kim, Anmo Kim, Hanyang University	
2-122. Affine models explain tuning-dependent correlated variability within and between V1 and V2	177
Ji Xia, Ken Miller, Columbia University	
2-123. Disentangling Fast Representational Drift in Mouse Visual Cortex	177
Jinke Liu, Martin Vinck, Ernst Strungmann Institute for Neuroscience in Cooperation with Max Planck Society (ESI)	
2-124. A brain-computer interface in prefrontal cortex that suppresses neural variability	178
Ryan Williamson, Akash Umakantha, Chris Ki, Byron Yu, Matthew Smith, Carnegie Mellon University / Neuroscience Institute	
2-125. Behavior measures are predicted by how information is encoded in an individual's brain	179
Jennifer Williams, Leila Wehbe, Carnegie Mellon University	
2-126. Fast ACh signals and the optimal control of attention in a detection task	179
Sahiti Chebolu, Peter Dayan, Kevin Lloyd, Indian Institute of Science Education and Research Pune	
2-127. Perceptography: Reconstruction of visual percepts induced by brain stimulation	179
Elia Shahbazi, Timothy Ma, Walter Scheirer, Arash Afraz, National Institutes of Health	
2-128. Using 1D-convolutional neural networks to detect and interpret sharp-wave ripples	180
Andrea Navas Olive, Rodrigo Amaducci, Teresa Jurado-Parras, Enrique R Sebastian, Liset Menendez de la Prida, Instituto Cajal - CSIC	
2-129. Cross-Frequency Coupling Increases Memory Capacity in Oscillatory Neural Networks	180
Connor Bybee, Alex Belsten, Friedrich Sommer, University of California Berkeley	
2-130. Intrinsic neural excitability induces time-dependent overlap of memory engrams	181
Geoffroy Delamare, Douglas Feitosa Tome, Claudia Clopath, Imperial College London	
2-131. Dynamic and selective engrams emerge with memory consolidation	181
Douglas Feitosa Tome, Ying Zhang, Sadra Sadeh, Dheeraj Roy, Claudia Clopath, Imperial College London	
2-132. Mice can do complex visual tasks	182
Lin Zhong, Carsen Stringer, Marius Pachitariu, Janelia Research Campus, HHMI	
2-133. 'Silent' olfactory bulb mitral cells emerge from common feature subtraction.	182
Sina Tootonian, Mihaly Kollo, Andreas Schaefer, The Francis Crick Institute	
2-134. A neural mechanism for the termination of perceptual decisions in the primate superior colliculus	183
Gabriel M Stine, Eric Trautmann, Danique Jeurissen, Michael Shadlen, Columbia University	
2-135. Serotonergic Control of Model-based Decision Making	183
Masakazu Taira, Thomas Akam, Mark Walton, Kenji Doya, Okinawa Institute of Science and Technology .	
2-136. Dopamine and norepinephrine signaling differentially mediate the exploration-exploitation tradeoff	184
Cathy Chen, Evan Knep, Becket Ebitz, Nicola Grissom, University of Minnesota Twin Cities	
2-137. Multimodal cues displayed by submissive rats facilitate prosocial choices by dominants	184
Michael Gachomba, Joan Adrian Esteve Agraz, Kevin Caref, Aroa Sanz Maroto, Maria Helena Bortolozzo Gleich, Diego Andres Laplagne, Cristina Marquez, Institute of Neuroscience of Alicante	
2-138. Confidence-guided waiting as an evidence accumulation process	185
Tyler Boyd-Meredith, Carlos D Brody, Alex Piet, Princeton Neuroscience Institute	
2-139. Rats employ a task general strategy to report calibrated confidence during learning	185
Amelia Christensen, Torben Ott, Steven Ryu, Adam Kepecs, Washington University School of Medicine in St. Louis	
2-140. An Analytical Theory of Curriculum Learning	186
Luca Saglietti, Stefano Sarao Mannelli, Andrew Saxe, EPFL	
2-141. SemiMultiPose: A Semi-supervised Multi-animal Pose Estimation Framework	186
Ari Blau, Anqi Wu, Christoph Gebhardt, Andres Bendesky, Liam Paninski, Columbia University	
2-142. Attractor neural networks with metastable synapses	187
Yu Feng, Nicolas Brunel, Duke University	
2-143. Activity-dependent dendrite growth through formation and removal of synapses	187
Lucas Euler, Julijana Gjorgjieva, Jan Hendrik Kirchner, Max Planck Institute for Brain Research	

Posters 2

2-144. Faithful encoding of interlimb coordination by individual Purkinje cells during locomotion	
Hugo Marques, Jorge Ramirez*, Pedro Castelhanito, Ana Goncalves, Megan Carey, Champalimaud Centre for the Unknown	188
2-145. Neural Representation of Hand Gestures in Human Premotor Cortex	
Nishal Shah, Donald Avansino, Foram Kamdar, Frank Willett, Leigh Hochberg, Jaimie Henderson*, Krishna Shenoy, Stanford University	188
2-146. Time-warped state space models for distinguishing movement type and vigor	
Julia Costacurta, Alex Williams, Blue Sheffer, Caleb Weinreb, Winthrop Gillis, Jeffrey Markowitz, Sandeep Robert Datta, Scott Linderman, Stanford University	189

Poster Session 3

Saturday 19 March, 2022

3-001. Biological learning in key-value memory networks	Danil Tyulmankov, Ching Fang, Ling Liang Dong, Annapurna Vadaparty, Guangyu Robert Yang, Columbia University	189
3-002. Local dendritic balance enables the learning of efficient representations in networks of spiking neurons	Lucas Rudelt, Fabian Mikulasch, Viola Priesemann, Max Planck Institute for Dynamics and Self-Organization	190
3-003. A Theory of Coupled Neuronal-Synaptic Dynamics	David Clark, Larry Abbott, Columbia University	190
3-004. Top-down modulation in canonical cortical circuits with inhibitory short-term plasticity	Yue Kris Wu, Felix Waitzmann, Julijana Gjorgjieva, Max Planck Institute for Brain Research	191
3-005. Linking neural dynamics across macaque V4, IT, and PFC to trial-by-trial object recognition behavior	Kohitij Kar, Reese Green, James DiCarlo, Massachusetts Institute of Technology	191
3-006. Selective signal processing by spontaneous synchronization	Maik Schunemann, Udo Ernst, University of Bremen	192
3-007. Learning accurate path integration in ring attractor models of the head direction system	Pantelis Vafidis, David Owald, Tiziano D'Albis, Richard Kempter, California Institute of Technology (Caltech)	192
3-008. Neural Circuit Architectural Priors for Motor Control	Nikhil Bhattachari, Anthony Zador, Tatiana Engel, Cold Spring Harbor Laboratory	193
3-009. Hebbian plasticity with a predictive component enables local learning in deep networks	Manu Srinath Halvagal, Friedemann Zenke, Friedrich Miescher Institute	193
3-010. Meta-learning biologically plausible feedback learning rules	Klara Kaleb, Claudia Clopath, Imperial College London	194
3-011. Cerebro-cerebellar networks facilitate learning through feedback decoupling	Ellen Boven, Joseph Pemberton, Paul Chadderton, Richard Apps, Rui Ponte Costa, University of Bristol .	194
3-012. Subcortical modulation of cortical dynamics for motor planning: a computational framework	Jorge Jaramillo, Ulises Pereira, Karel Svoboda, Xiao-Jing Wang, European Neuroscience Institute	194
3-013. Contextual modulation of mesoscale functional connectivity	Matthew Harvey, Adil Khan, King's College London	195
3-014. Multi-region Poisson GPFA isolates shared and independent latent structure in sensorimotor tasks	Gabriel Yancy, Eric Hart, Adrian Bondy, Carlos D Brody, Alex Huk, Jonathan Pillow, Stephen Keeley, Fordham University	195
3-015. Flexible inter-areal computations through low-rank communication subspaces	Joao Barbosa, Srdjan Ostojic, Ecole Normale Supérieure	196
3-016. Neuronal implementation of the representational geometry in prefrontal working memory	Xiaoxiong Lin, Simon Jacob, Technical University of Munich	196
3-017. Learning generalised representations of behaviour within the hippocampal-entorhinal-prefrontal system	Joseph Warren, Jacob Bakermans, David McCaffary, Timothy Behrens, James Whittington, University College London	197
3-018. Efficient task representations for habitual and model-based behaviour	Severin Berger, Christian Machens, Champalimaud Centre for the Unknown	197
3-019. Arithmetic value representation for hierarchical behavior composition	Hiroshi Makino, Nanyang Technological University	198
3-020. Understanding rat behavior in a complex task via non-deterministic policies	Johannes Niediek, Maciej M Jankowski, Ana Polterovich, Alexander Kazakov, Israel Nelken, The Hebrew University of Jerusalem	198
3-021. Inferring implicit sensorimotor costs by inverse optimal control with signal dependent noise	Dominik Straub, Matthias Schultheis, Constantin Rothkopf, TU Darmstadt	199
3-022. In silico manipulation of cortical computation underlying goal-directed learning	Jae Hoon Shin, Sang Wan Lee, Jee Hang Lee, KAIST	199
3-023. Identifying the control strategies of monkeys and humans in a virtual balancing task	Mohsen Sadeghi, Reza Sharif Razavian, Salah Bazzi, Raeed Chowdhury, Patrick Loughlin, Aaron Batista, Dagmar Sternad, Northeastern University	200

Posters 3

3-024. Identifying changes in behavioral strategy from neural responses during evidence accumulation	200
Brian DePasquale, Carlos D Brody, Jonathan Pillow, Princeton University	
3-025. Divisive normalization shapes evidence accumulation during dynamic decision-making	201
Victoria Shavina, Valerio Mante, University of Zurich	
3-026. How cerebellar architecture facilitates rapid online learning	201
Adriana Perez Rotondo, Dhruva Raman, Timothy O'Leary, University of Cambridge	
3-027. Synaptic and mesoscale plasticity in auditory cortex of rats with cochlear implants	202
Ariel Edward Hight, Erin Glennon, Silvana Valtcheva, Mario A Svirsky, Robert Froemke, NYU Grossman School of Medicine	
3-028. Reward modulates visual responses in mouse superior colliculus independently of arousal	202
Liad J Baruchin, Sylvia Schroeder, University of Sussex	
3-029. VIP interneuron-mediated disinhibition does not interact with endogenous attention modulation in V1	203
Dylan Myers-Joseph, Adil Khan, King's College London	
3-030. A parallel channel of state-dependent sensory signaling by the cholinergic basal forebrain	203
Fangchen Zhu, Sarah Elnozahy, Jennifer Lawlor, Kishore Kuchibhotla, Johns Hopkins University	
3-031. A biophysical account of multiplication by a single neuron	204
Lukas Groschner, Jonatan Malis, Birte Zuidinga, Alexander Borst, Max Planck Institute of Neurobiology	
3-032. Characterization of neuronal resonance and inter-areal transfer using optogenetics	204
Ana Clara Silveira Broggini, Athanasia Tzanou, Irene Onorato, Cem Uran, Martin Vinck, Ernst Strungmann Institute	
3-033. Cortical inhibitory tuning reflects the Fourier components of locally encoded features	205
Adrian Duszkiewicz, Sofia Skromne Carrasco, Pierre Orhan, Elliott Owczarek, Eleonor Brown, Emma Wood, Adrien Peyrache, McGill University	
3-034. Inception loops reveal novel spatially-localized phase invariance in mouse primary visual cortex	205
Zhiwei Ding, Dat Tran, Erick Cobos, Taliah Muhammad, Kayla Ponder, Santiago Cadena, Alexander Ecker, Xaq Pitkow, Andreas Tolias, Baylor College of Medicine	
3-035. Learning to combine sensory evidence and contextual priors under ambiguity	206
Nizar Islah, Guillaume Etter, Tugce Gurbuz, Eilif Muller, University of Montreal	
3-036. Predictability in the spiking activity of mouse visual cortex decreases along the processing hierarchy	206
Daniel Gonzalez Marx, Lucas Rudelt, Viola Priesemann, Max Planck Institute for Dynamics and Self-Organization	
3-037. Mechanistic modeling of Drosophila neural population codes in natural social communication	207
Rich Pang, Christa Baker, Diego Pacheco, Jonathan Pillow, Mala Murthy, Princeton Neuroscience Institute	
3-038. Unsupervised sparse deconvolutional learning of features driving neural activity	207
Bahareh Tolooshams, Hao Wu, Naoshige Uchida, Venkatesh N Murthy, Paul Masset, Demba Ba, Harvard University	
3-039. An interpretable dynamic population-rate equation for adapting non-linear spiking neural populations	208
Laureline Logiaco, Sean Escola, Wulfram Gerstner, Columbia University	
3-040. Reduced stochastic models reveal the mechanisms underlying drifting cell assemblies	208
Sven Goedeke, Christian Klos, Felipe Yaroslav Kalle Kossio, Raoul Martin Memmesheimer, University of Bonn	
3-041. Frustrated synchronization and excitability in hierarchical-modular brain networks	209
Victor Buendia, Pablo Villegas, Raffaella Burioni, Miguel A Munoz, University of Tübingen	
3-042. Towards using small topologically constrained networks in-vitro in combination with in-silico models	209
Stephan Ihle, Sean Weaver, Katarina Vulić, Janos Voros, Sophie Girardin, Thomas Felder, Julian Hengsteler, Jens Duru, Csaba Forró, Tobias Ruff, Benedikt Maurer, ETH Zurich	
3-043. Emergence of modular patterned activity in developing cortex through intracortical network interactions	210
Haleigh Mulholland, Matthias Kaschube, Gordon Smith, University of Minnesota	
3-044. Reduction of entropy specific to cortical outputs during anesthetic-induced loss of consciousness	210
Arjun Bharioke, Martin Munz, Emilie Mace, Botond Roska, Alexandra Brignall, Georg Kosche, Max Ferdinand Eizinger, Nicole Ledergerber, Daniel Hillier, Brigitte Gross-Scherf, Karl-Klaus Conzelmann, Institute of Molecular and Clinical Ophthalmology Basel	

3-045. A manifold of heterogeneous vigilance states across cortical areas	211
Julia Wang, Sylvain Chauvette, Robert Kwapich, Igor Timofeev, Tatiana Engel, Cold Spring Harbor Laboratory	
3-046. Walking elicits global brain activity in adult Drosophila	212
Karen Cheng, Sophie Aimon, Julijana Gjorgjieva, Ilona Grunwald Kadow, TUM	
3-047. How neuronal axons get from here to there using gene-expression maps derived from their family trees	212
Stan Kerstjens, Gabriela Michel, Rodney Douglas, ETH Zurich	
3-048. Self-assembly of the mammalian neocortex, from mouse to macaque	213
Gabriela Michel, Andreas Hauri, Sabina Pfister, Marion Betizeau, Frederic Zubler, Colette Dehay, Henry Kennedy, Rodney Douglas, Janelia Research Campus	
3-049. Emergence of an orientation map in the mouse superior colliculus from stage III retinal waves	213
Kai Lun Teh, Jeremie Sibille, Jens Kremkow, Charite Berlin University of Medicine	
3-050. Natural scene expectation shapes the structure of trial to trial variability in mid-level visual cortex	214
Patricia Stan, Matthew Smith, University of Pittsburgh	
3-051. Sensory specific modulation of neural variability facilitates perceptual inference	214
Hyeyoung Shin, Hillel Adesnik, University of California Berkeley	
3-052. Processing of visual textures in the mouse visual cortex	215
Federico Bolanos, Javier G Orlandi, Akshay V Jagadeesh, Justin L Gardner, Andrea Benucci, RIKEN Center for Brain Science and The University of Tokyo	
3-053. The geometry of cortical representations of touch in rodents	215
Ramon Noguera, Stefano Fusi, Chris C Rodgers, Randy M Bruno, Columbia University	
3-054. Nonlinear manifolds underlie neural population activity during behaviour	216
Catia Fortunato, Jorge Bennasar-Vazquez, Junchol Park, Lee E Miller, Joshua Dudman, Matthew Perich, Juan Gallego, Imperial College London	
3-055. Dissecting emergent network noise compensation mechanisms in working memory tasks	216
Colin Bredenberg, Maximilian Puelma Touzel, Rainer Engelken, Guillaume Lajoie, New York University	
3-056. A genetic algorithm to uncover internal representations in biological and artificial brains	217
Guido Maiello, Kate Storrs, Alexandra Quintus, Roland Fleming, Justus Liebig University Giessen	
3-057. How many objects can be recognized under all possible views?	217
Blake Bordelon, Matthew Farrell, Shubhendu Trivedi, Cengiz Pehlevan, Harvard University	
3-058. Map Induction: Compositional spatial submap learning for efficient exploration in novel environments	218
Sugandha Sharma, Aidan Curtis, Marta Kryven, Josh Tenenbaum, Ila R Fiete, Massachusetts Institute of Technology	
3-059. Occam's razor guides intuitive human inference	218
Eugenio Piasini, Shuze Liu, Vijay Balasubramanian, Joshua Gold, International School of Advanced Studies (SISSA)	
3-060. A high-throughput pipeline for evaluating recurrent neural networks on multiple datasets	219
Moufan Li, Nathan Cloos, Xun Yuan, Guangyu Robert Yang, Christopher J Cueva, Tsinghua University	
3-061. An adaptive analysis pipeline for automated denoising and evaluation of high-density electrophysiological recordings	219
Anoushka Jain, Alexander Kleinjohann, Severin Graff, Kerstin Doerenkamp, Bjorn Kampa, Sonja Grun, Simon Musall, Forschungszentrum Julich	
3-062. Automated processing of calcium imaging videos for densely labeled dendritic and somatic ROIs	220
Jason Moore, Shannon K Rashid, Naomi Codrington, Dmitri Chklovskii, Jayeeta Basu, NYU Grossman School of Medicine; Simons Foundation	
3-063. Bias-free estimation of information content in temporally sparse neuronal activity	220
Liron Sheintuch, Alon Rubin, Yaniv Ziv, Weizmann Institute of Science	
3-064. Single cell measures of tuning to imagined position during replay show preserved spatial tuning but quenched neural variability in place cells.	221
John Widloski, Matt Kleinman, David Foster, University of California, Berkeley	
3-065. Neural adaptation in attractor networks implements replay trajectories in the hippocampus	221
Zilong Ji, Xingsi Dong, Tianhao Chu, Si Wu, Peking University	
3-066. Multiple bumps can enhance robustness to noise in continuous attractor networks	222
Raymond Wang, Louis Kang, University of California, Berkeley	
3-067. Long-term motor learning creates structure within neural space that shapes motor adaptation	222
Joanna Chang, Matthew Perich, Lee E Miller, Juan Gallego, Claudia Clopath, Imperial College London	

Posters 3

3-068. Coordinated cortico-cerebellar neural dynamics underlying neuroprosthetic learning Aamir Abbasi, Andrew Fealy, Nathan Danielsen, Tanuj Gulati, Cedars-Sinai Medical Center	223
3-069. Regionally distinct striatal circuits support broadly opponent aspects of action suppression and production Bruno Cruz, Goncalo Guiomar, Sofia Soares, Asma Motiwala, Christian Machens, Joseph J Paton, Cham-palimaud Foundation	223
3-070. Distinct aversive states in the mouse medial prefrontal cortex. Pierre Le Merre, Daniela Calvignoni, Janos Fuzik, Marina Slashcheva, Felix Jung, Marie Carlen, Kon-stantinos Meletis, Karolinska Institutet	224
3-071. Dentate gyrus inhibitory microcircuit promotes network mechanisms underlying memory consoli-dation Hannah Twarkowski, Victor Steininger, Min Jae Kim, Amar Sahay, Massachusetts General Hospital, Har-vard Medical School	224
3-072. Neuromodulation of synaptic plasticity rules avoids homeostatic reset of synaptic weights during switches in brain states Kathleen Jacquerie, Caroline Minne, Guillaume Drion, University of Liege	225
3-073. A synaptic plasticity rule based on presynaptic variance to infer input reliability Julia Gallinaro, Claudia Clopath, Imperial College London	225
3-074. An anatomically accurate circuit for short- and long-term motivational learning in fruit flies Evripidis Gkantas, Barbara Webb, University of Edinburgh	226
3-075. One engram, two ways to recall it Mehrab Modi, Adithya Rajagopalan, Herve Rouault, Yoshinori Aso, Glenn Turner, Janelia Research Cam-pus, HHMI	226
3-076. Stimulus-specific olfactory processing via nonlinear transient dynamics Palka Puri, Shiuan-Tze Wu, Chih-Ying Su, Johnatan Aljadeff, University of California, San Diego	227
3-077. Inferring olfactory space from glomerular response data Yakov Berchenko-Kogan, Min-Chun Wu, Matt Wachowiak, Vladimir Itskov, Pennsylvania State University .	227
3-078. Exploiting color space geometry for visual stimulus design across animals Matthias Christenson, S Navid Mousavi, Rudy Behnia, Columbia University	228
3-079. Photoreceptor dynamics in the context of optimal chromatic codification Luisa Ramirez, Ronald Dickman, Universidade Federal de Minas Gerais	228
3-080. The smart image compression algorithm in the retina: recoding inputs in neural circuits Gabrielle Gutierrez, Fred Rieke, Eric Shea-Brown, Columbia University	229
3-081. Localized balance of excitation and inhibition leads to normalization Yashar Ahmadian, University of Cambridge	229
3-082. Normative Network Regularization for Neural System Identification Yongrong Qiu, David Klindt, Klaudia Szatk, Laura Busse, Matthias Bethge, Thomas Euler, University of Tuebingen	229
3-083. Bayesian active learning for closed-loop synaptic characterization Camille Gontier, Simone Carlo Surace, Jean-Pascal Pfister, University of Bern	230
3-084. AutSim: Principled, data driven model development and abstraction for signaling in synaptic protein synthesis in Fragile X Syndrome (FXS) and healthy control. Nisha Viswan, Upinder Bhalla, National Centre for Biological Sciences	230
3-085. Semi-supervised sequence modeling for improved behavior segmentation Matt Whiteway, Anqi Wu, Mia Bramel, Kelly Buchanan, Catherine Chen, Neeli Mishra, Evan Schaffer, Andres Villegas, The International Brain Laboratory, Liam Paninski, Columbia University	231
3-086. Visual association cortex immediately reactivates sensory experiences Nghia Nguyen, Andrew Lutas, Jesseba Fernando, Mark Andermann, Harvard University	231
3-087. Abstract cognitive encoding in the primate superior colliculus Barbara Peysakhovich, Stephanie Tetrick, Ou Zhu, Guilhem Ibos, W Jeffrey Johnston, David Freedman, The University of Chicago	232
3-088. Hippocampal spatio-temporal cognitive maps adaptively guide reward generalization Tankred Saanum, Mona Garvert, Eric Schulz, Nicolas W Schuck, Christian Doeller, Max Planck Institute for Biological Cybernetics	232
3-089. Modeling Hippocampal Spatial Learning Through a Valence-based Interplay of Dopamine and Serotonin Carlos Wert Carvajal, Claudia Clopath, Melissa Reneaux, Tatjana Tchumatchenko, University of Bonn .	233

3-090. The role of inhibition in shaping memory-encoding hippocampal sequences	233
Jiannis Taxidis, Blake Madruga, Michael Lin, Peyman Golshani, University of California - Los Angeles	233
3-091. Probing neural value computations in the nucleus accumbens dopamine signal	234
Tim Krausz, Alison Comrie, Loren Frank, Nathaniel Daw, Joshua Berke, UCSF	234
3-092. VTA dopamine neurons signal phasic and ramping reward prediction error in goal-directed navigation	234
Karolina Farrell, Aman Saleem, Armin Lak, University College London	234
3-093. Neurons in dlPFC signal unsigned reward prediction error independently from value	235
Michael Shteyn, Carl Olson, University of Pittsburgh, Carnegie Mellon University	235
3-094. Irrational choice via curvilinear value geometry in ventromedial prefrontal cortex	235
Becket Ebitz, Benjamin Hayden, Katarzyna Jurewicz, Brianna Sleezer, Priyanka Mehta, Universite de Montreal	235
3-095. Imagining what was there: looking at an absent offer location modulates neural responses in OFC	236
Demetrio Ferro, Anna Rife Mata, Tyler Cash-Padgett, Maya Zhe Wang, Benjamin Hayden, Ruben Moreno Bote, Universitat Pompeu Fabra	236
3-096. How does the dorsal striatum contribute to active choice rejection?	237
Jaclyn Essig, Albert Jiaxu Qu, Zichen Zhou, Lung-Hao Tai, Linda Wilbrecht, University of California, Berkeley	237
3-097. Balancing safety and efficiency in human decision-making.	237
Pranav Mahajan, Sang Wan Lee, Ben Seymour, University of Oxford	237
3-098. Dual pathway architecture in songbirds boosts sensorimotor learning	237
Remya Sankar, Nicolas P Rougier, Arthur Leblois, Inria Bordeaux	237
3-099. Contextual motor learning in birdsong reflects two distinct neural processes	238
Lena Veit, Lucas Tian, Michael Brainard, University of Tübingen	238
3-100. Saccade preparation does not benefit visual change detection	238
Priyanka Gupta, Devarajan Sridharan, Indian Institute of Science, Bangalore	238
3-101. Associative memory of structured knowledge	239
Julia Steinberg, Haim Sompolinsky, Princeton University	239
3-102. Learning sequences with fast and slow parts	239
Matthew Farrell, Cengiz Pehlevan, Harvard University	239
3-103. Phase precession and theta sequences in the hippocampus are spatially and temporally segregated	240
Federico Stella, Matteo Guardamagna, Francesco Battaglia, Donders Centre for Neuroscience, Department of Neuroinformatics, Radboud University Nijmegen	240
3-104. Long-term dynamics of the entorhinal grid code	240
Noa Sadeh, Alon Rubin, Meytar Zemer, Yaniv Ziv, The Weizmann Institute of Science	240
3-105. Object × position coding in the entorhinal cortex of flying bats	241
Gily Ginosar, Nachum Ulanovsky, Liora Las, The Weizmann Institute of Science	241
3-106. Hippocampal representations during natural social behaviors in a bat colony	241
Saikat Ray, Itay Yona, Liora Las, Nachum Ulanovsky, Weizmann Institute of Science	241
3-107. The representational geometry of social memory in the hippocampus	242
Lorenzo Posani, Lara Boyle, Sarah Irfan, Steven A Siegelbaum, Stefano Fusi, Columbia University	242
3-108. Using navigational information to learn visual representations	242
Lizhen Zhu, Brad Wyble, James Wang, Pennsylvania State University	242
3-109. Talking Nets: Neural Networks Trained to Understand and Communicate Task Instructions	242
Reidar Riveland, Alexandre Pouget, University of Geneva	242
3-110. Covert reinstatement predicts recall initiation	243
David Halpern, Michael Kahana, University of Pennsylvania	243
3-111. You don't always forget: Mechanisms underlying working memory lapses.	243
Tiffany Ona Jodar, Genis Prat-Ortega, Eva Carrillo, Chengyu Li, Josep Dalmau, Albert Compte, Jaime de la Rocha, IDIBAPS	243
3-112. Predictive coding of global sequence violation in the mouse auditory cortex	244
Sara Jamali, Stanislas Dehaene, Timo van Kerkoerle, Brice Bathellier, Institut Pasteur, Institut de l'audition	244
3-113. Clear evidence in favor of adaptation and against temporally specific predictive suppression in monkey primary auditory cortex	244
Tobias Teichert, University of Pittsburgh	244

Posters 3

3-114. The role of temporal coding in everyday hearing: evidence from deep neural networks Mark Saddler, Josh McDermott, MIT	245
3-115. An insect vision-based flight control model with a plastic efference copy Angel Canelo, Sungyong Kim, Anmo Kim, Hanyang University	245
3-116. Multiple stimulus features are encoded by single mechanosensory neurons in insect wings Alison Weber, Abigail von Hagel, Thomas Daniel, Bing Brunton, University of Washington	246
3-117. A visuomotor pathway underlies small object avoidance in flying Drosophila Anmo Kim, Hayun Park, Joowon Lee, Hyosun Kim, Hanyang University	246
3-118. Feedforward thalamocortical inputs to primary visual cortex are OFF dominant Jun Zhuang, Naveen Ouellette, R Clay Reid, Allen Institute for Brain Science	247
3-119. Sparse coding predicts a spectral bias in the development of V1 receptive fields Andrew Ligeralde, Michael DeWeese, University of California, Berkeley	247
3-120. Do better object recognition models improve the generalization gap in neural predictivity? Yifei Ren, Pouya Bashivan, McGill University	247
3-121. Energy efficient reinforcement learning as a matter of life and death Jiamu Jiang, Mark van Rossum, University of Nottingham	248
3-122. A Model for Representational Drift: Implications for the Olfactory System Farhad Pashakhanloo, Alexei Koulakov, Cold Spring Harbor Laboratory	248
3-123. Stable memories without reactivation Michael Fauth, Jonas Neuhof, Christian Tetzlaff, Bernstein Center for Computational Neuroscience, University of Gottingen	249
3-124. Sharing weights with noise-canceling anti-Hebbian plasticity Roman Pogodin, Peter Latham, Gatsby Computational Neuroscience Unit, University College London . .	249
3-125. Relating local connectivity and global dynamics in excitatory-inhibitory networks Yuxiu Shao, Srdjan Ostojic, Ecole Normale Superieure	250
3-126. A White Matter Ephaptic Coupling Model for 1/f Spectral Densities Pamela Douglas, Garrett Blair, Jack Vice, UCLA; UCF	250
3-127. Deep Reinforcement Learning mimics Neural Strategies for Limb Movements Muhammad Noman Almani, Shreya Saxena, University of Florida	250
3-128. A novel experimental framework for simultaneous measurement of excitatory and inhibitory conductances Daniel Muller-Komorowska, Ben Title, Gal Elyasaf, Yonatan Katz, Alexander Binshtok, Heinz Beck, Ilan Lampl, Institute of Experimental Epileptology and Cognition Research, University of Bonn	251
3-129. A latent model of calcium activity outperforms alternatives at removing behavioral artifacts in two-channel calcium imaging Matthew Creamer, Kevin Chen, Andrew M Leifer, Jonathan Pillow, Princeton University	251
3-130. Emergent behavior and neural dynamics in artificial agents tracking turbulent plumes Satpreet Harcharan Singh, Floris van Breugel, Rajesh PN Rao, Bing Brunton, University of Washington .	252
3-131. Optimization of error distributions as a design principle for neural representations Ann Hermundstad, Wiktor Mlynarski, Janelia Research Campus	252
3-132. Uncertainty-weighted prediction errors (UPEs) in cortical microcircuits Katharina Wilmes, Constanze Raltchev, Sergej Kasavica, Shankar Babu Sachidanandam, Walter Senn, University of Bern	253
3-133. Inference of the time-varying relationship between spike trains and a latent decision variable Thomas Luo, Brian DePasquale, Carlos D Brody, Timothy Kim, Princeton University	253
3-134. Mutual gaze with a robot influences social decision-making Kyveli Kompatsiari, Marwen Belkaid, Davide de Tommasao, Ingrid Zablith, Agnieszka Wykowska, Italian Institute of Technology	254
3-135. Near-optimal time investments under uncertainty in humans, rats, and mice Torben Ott, Paul Masset, Joshua I Sanders, Marion Bosc, Thiago Gouvea, Adam Kepecs, Washington University School of Medicine	254
3-136. Optimal search strategies under energetic constraints Yipei Guo, Ann Hermundstad, Janelia Research Campus	255
3-137. Pupil size anticipates exploration and predicts disorganization in prefrontal cortex Akram Shourkeshti, Gabriel Marrocco, Katarzyna Jurewicz, Tirin Moore, Becket Ebitz, University of Montreal	255
3-138. Exploring too much? The role of exploration in impulsivity Magda Dubois, Tobias Hauser, University College London	256

3-139. Theories of surprise: definitions and predictions Alireza Modirshanechi, Johanni Brea, Wulfram Gerstner, EPFL	256
3-140. Spontaneous emergence of magnitude comparison units in untrained deep neural networks Woochul Choi, Hyeonsu Lee, Se-Bum Paik, Korea Advanced Institute of Science and Technology	257
3-141. Dissecting the Factors of Metaplasticity with Meta-Continual Learning Hin Wai Lui, Emre Neftci, University of California, Irvine	257
3-142. Modeling and optimization for neuromodulation in spinal cord stimulation Hongda Li, Yanan Sui, Tsinghua University	257
3-143. Flexible cue anchoring strategies enable stable head direction coding in blind animals Kadjita Asumbisa, Adrien Peyrache, Stuart Trenholm, McGill University	258
3-144. Task demands drive choice of navigation strategy and distinct types of spatial representations Sandhiya Vijayabaskaran, Sen Cheng, Ruhr-University Bochum	258
3-145. The role of prior experience in the replay of both novel and familiar contexts Marta Huelin Gorri, Daniel Bendor, University College London	259
3-146. Orienting eye movements during REM sleep Yuta Senzai, Massimo Scanziani, University of California, San Francisco	259
3-147. Integration of infant sensory cues and internal states for maternal motivated behaviors Habon Issa, Silvana Valtcheva, Kathleen Martin, Kanghoon Jung, Hyung-Bae Kwon, Robert Froemke, New York University School of Medicine	260

Abstracts

Abstracts for talks appear first, in order of presentation; those for posters next, in order of poster session and board number. An index of all authors appears at the back.

T-1. Dopamine specifies the structure of spontaneous behavior

Sandeep Robert Datta

Harvard University

Spontaneous behavior exhibits structure. Ethologists describing animals in the wild have long appreciated that naturalistic, self-motivated behavior is built from modules that are linked together over time into predictable sequences. And yet, it remains unclear how the brain regulates the selection of individual behavioral modules for expression at any given moment, or how it dynamically composes these modules into the fluid behaviors observed when animals act of their own volition, and in the absence of experimental restraint, task structure or explicit reward. Here we use novel methods for characterizing and manipulating behavior in freely-moving mice in real time to reveal that learning and variability interact to create the architecture of self-guided behavior. Our findings suggest a broad model in which the composition of spontaneous behavior from elemental components is supported by the same circuits and mechanisms that enable action selection in structured tasks.

T-2. From plans to outcomes: Continuous representations of actions in primate prefrontal cortex

Valerio Mante

ETH Zurich

Dorsal-lateral prefrontal cortex in primates (dlPFC) is thought to contribute to flexible decisions primarily by selecting, maintaining, and combining contextually relevant information to select an action. This view was strongly shaped by the discovery in dlPFC of tuned, persistent activity that bridges the time interval between the planning and execution of an action. I will present evidence that these classic findings may have provided a somewhat misleading view of the function of dlPFC, in that they disregarded the activity which follows an action. We analyzed large-scale recordings from monkeys engaged in saccade-based decisions for which rewards were delayed with respect to the choice saccades. In this setting, we found that dlPFC is persistently active before and after an action, and maintains a continuous representation of actions lasting from planning and execution to the resulting outcome and beyond. Several properties of these action representations suggest a key role for dlPFC in remembering actions that may be eligible for rewards and in updating future plans based on past actions.

T-3. What can birds and rodents tell us about human speech?

Michael Long

New York University

Vocal communication is central to our everyday lives, facilitating social exchange. Despite significant recent discoveries, the neural mechanisms underlying coordinated vocal exchanges remain poorly understood. We examine the brain processes involved in interactive vocal behaviors, focusing on forebrain circuitry in the songbird and the rodent, and we relate these to emerging human studies that employ a range of methods to manipulate and monitor cortical areas relevant for speech.

T-4. To remap or reregister, that is the question: how hippocampus represents different spaces

Andre Fenton

New York University

The hippocampus is crucial for solving complex navigation and memory problems and has been the focus of intense investigations at virtually all levels of biological organization. I will report on our studies of hippocampal physiology, in particular the activity of spatially-tuned cells called place cells and related head-direction cells and grid cells in the medial entorhinal cortical inputs to hippocampus. Within this context, the lecture will focus on the phenomenon called remapping, in which place fields rearrange according to cell-specific rules when the environment changes; cells with nearby place fields in one environment are likely to have distant place fields in another environment or turn off or turn on in different environments. The field interprets place field remapping to mean that the neural cofiring relationships reorganize, and this would maximize the information coding capacity needed for a memory system. However, I will discuss a number of observations that challenge the very idea of remapping, going so far as to suggest it may be a misnomer. Hippocampal neural activity appears to be internally-organized in a manner such that momentary cofiring relationships amongst the cells are largely invariant across distinct environments, despite the cell-specific rearrangement of place fields. This is because activity is organized on a low-dimensional (non-linear surface) manifold that maintains across environments like a solid object would. Instead of remapping the cofiring relationships, only the registration between the manifold and the environment changes across environments. The subset of environment-specific anti-cofiring cells seems to set the orientation of the manifold, and perhaps its registration with external information. Beyond such reregistering, these observations promote a view that rather than represent external information, a subjective, internally-organized hippocampal representation is actively fit to the environment for processing information that enables navigation and promotes memory.

T-5. (De-)Synchronizing neural networks with homoclinic action potentials

Susanne Schreiber

Humboldt University of Berlin

Supported by the success of artificial neural networks, neural computation is viewed as a phenomenon predominantly shaped by the connectivity among neurons whose individual dynamics can be largely neglected. Yet in this talk, I will demonstrate how the properties of cells – and in particular their dynamics of action-potential generation – can have a decisive impact on network behavior and the way information is processed. Our recent theoretical work shows that, among regularly firing neurons, the homoclinic type (characterized by a spike onset via a saddle homoclinic orbit bifurcation) stands out: (i) spikes of this type foster synchronization in inhibitory as well as splayed-out or frustrated states in excitatory networks and (ii) can easily be induced by changes in a variety of physiological parameters (like temperature, extracellular potassium, or dendritic morphology). Providing first experimental evidence and discussing functional consequences of homoclinic spikes for the design of efficient pattern-generating motor circuits in insects as well as for mammalian pathologies like febrile seizures, we predict a role for homoclinic action potentials as an integral part of brain dynamics in both health and disease.

T-6. Coordinated spike coding

Christian Machens

Champalimaud

Models of neural networks can be largely divided into two camps. On the one side are rate networks that can perform a multitude of functions and have led to many recent breakthroughs in ML/AI, but ignore well-established biological facts. On the other side are spiking network models that incorporate and replicate a lot of our knowledge, but then fail to perform interesting functions. I will review work that has tried to bridge this gap. I will specifically focus on spiking networks that produce functionality in low-dimensional subspaces, and I will argue that they force us to reconsider the very basics of how we think about neural networks.

T-7. Exploring ephaptic coupling in white matter

Pamela Douglas
University of Central Florida

T-8. A physiological take on the mind-body question.

Asya Rolls
Technion

Thoughts and emotions can impact physiology. This connection is evident by the emergence of disease following stress or recovery in response to placebo treatment. Nevertheless, this fundamental aspect of physiology remains largely unexplored. By targeted manipulations of the brain, we aim to uncover how specific brain activity affects the immune system, the organism's main protection mechanism. In this talk, I will focus on the brain's involvement in regulating the peripheral immune response and explore the question of how the brain evaluates and represents the state of immune system it regulates.

T-9. A navigational network hardwired for rapid flexibility

Ann Hermundstad
HHMI Janelia Research Campus

Many flexible behaviors are thought to rely on internal representations of an animal's spatial relationship to its environment and of the consequences of its actions in that environment. While such representations—e.g. of head direction and value—have been extensively studied, how they are combined to guide and modify behavior is not well understood. We use a combination of theory and modeling, together with behavioral, neural, and connectomic data, to study these questions in a visual learning paradigm that requires fruit flies to simultaneously map a new environment and infer goals within that environment. To perform this task, animals must modify their behavior within a matter of minutes, an ability that we think relies on genetically-specified circuits that incorporate structured relationships between an animal and its surroundings, and on continually-evolving internal representations maintained within these circuits. I will discuss how these anatomical constraints, and the internal and behavioral dynamics that emerge from them, can shed light on rapid learning and behavioral flexibility in biological and artificial agents more broadly.

T-10. Neural circuits of visuospatial working memory

Albert Compte
Barcelona

One elementary brain function that underlies many of our cognitive behaviors is the ability to maintain parametric information briefly in mind, in the time scale of seconds, to span delays between sensory information and actions. This component of working memory is fragile and quickly degrades with delay length. Under the assumption that behavioral delay-dependencies mark core functions of the working memory system, our goal is to find a neural circuit model that represents their neural mechanisms and apply it to research on working memory deficits in neuropsychiatric disorders. We have constrained computational models of spatial working memory with delay-dependent behavioral effects and with neural recordings in the prefrontal cortex during visuospatial working memory. I will show that a simple bump attractor model with weaker angular resolution in the visual periphery can link neural data with fine-grained behavioral output in a trial-by-trial basis and account for the main delay-dependent limitations of working memory: precision, interference between simultaneous memories, foveal biases and serial dependence. I will finally present data from participants with neuropsychiatric disorders that suggest that serial dependence in working memory is specifically altered, and I will use the model to infer the possible neural mechanisms affected.

T-11. Brain-body interactions for rapid and flexible control of walking

Eugenio Chiappe

Champaulimaud

Without a continuous correction system, intended movements are executed as expected only rarely. This is because of the unpredictable nature of natural environments, and the presence of noise within sensorimotor circuits. To correct movements, sensorimotor circuits must estimate self-motion with high precision to adjust maneuvers at a timescale specific to the task, and at a proper context that is specified by the behavioral goals of the animal. Here, I will discuss our attempts to understand the functional organization of circuits controlling such movement adjustments in the context of an exploratory walking fly. We found that recurrent interactions between premotor circuits in the brain and the ventral nerve cord of the fly —the insect analogue of the spinal cord, support rapid and context-dependent steering adjustments that are critical to maintain straight walking and a stable gaze when the fly intends to do so. Ascending signals from the ventral nerve or vertebrate spinal cords have been observed in premotor circuits in different animal species, but their nature and functional role remains unclear. Our findings in flies highlight a critical role for these multimodal ascending signals on context-dependent computations supporting the coordination of goal-directed movement across the body.

T-12. Symmetries and asymmetries in the neural coding of space

Kate Jeffery

University College London

The neural coding of space centres on three foundational cell types: place cells, head direction cells and grid cells. One interesting characteristic of these neurons is the symmetry properties of their spatial firing patterns. Place cells are distinguished by firing in focal regions of space, and they do so asymmetrically even if the environment is symmetrical. Head direction cells also fire asymmetrically, when the head is facing in a single direction (a different direction for each cell). Grid cells, by contrast, are remarkable for the six-fold symmetry of their firing, each cell producing a close-packed hexagonal pattern of circular firing fields that spreads across the environment, and has six-fold symmetry, both rotationally and translationally. Six-fold rotationally symmetric activity has also been reported in human brain scanning experiments. This talk will review a number of experiments in which these firing symmetries have been altered by environmental manipulations. Place cell firing can be made translationally symmetric but never (at least so far) rotationally symmetric. Some types of (normally asymmetric) head direction cell firing can be made rotationally symmetric. Grid cell firing can have its symmetries reduced, or in some cases abolished. These symmetries are modulated by three types of inertial cue: gravity, translational motion and rotational motion, and also by some types of static environmental information. This talk will discuss how these factors interact, and speculate on the consequences of the resultant firing symmetries and asymmetries for spatial coding.

T-13. Interpretable behavioral features have conserved neural representations across miceAtika Syeda¹Will Long¹Renee Tung¹Marius Pachitariu²Carsen Stringer²

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Quantitative behavioral analyses have become an essential tool for understanding neural circuits. For example, recent studies have shown that ongoing “spontaneous” behaviors drive large fractions of neural activity in the mouse brain. However, the specific behavioral features encoded and their consistency across mice remain unknown. To study the neural representation of interpretable behavioral features, we recorded the activity of ~50,000 neurons in the mouse visual cortex during spontaneous behaviors. We used simultaneous five-camera video recordings to show that orofacial behaviors contain all of the neurally-related behavioral information. Focusing on the face, we tracked several key points from which we computed pose relationships. These behavioral features predicted a higher proportion of neural activity compared to previous models. To compare against mice, we developed a fast, generalist deep-learning model for tracking 13 distinct points on the mouse face recorded from arbitrary camera angles. The model obtained a median error of less than 3 pixels on test frames from a new mouse with

novel camera views. The model was several times faster than state-of-the-art pose estimation tools, making it a powerful tool for closed-loop behavioral experiments. Next, we aligned facial key points across mice in order to train a universal model to predict neural activity from behavior. The universal mouse model could predict neural activity as well as a model fit to a single mouse, showing that neural representations of behaviors are conserved across mice. The latent states extracted from the universal model contained interpretable mouse behaviors, such as grooming and wincing. In summary, we developed a robust end-to-end framework for modeling neural activity based on orofacial behaviors, and found that neural representations of behavior are similar across mice.

T-14. Operative Dimensions in High-Dimensional Connectivity of Recurrent Neural Networks

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Recurrent Neural Networks (RNN) are useful models to study neural computation. Several approaches are available to train RNNs on neuroscience-related tasks and reproduce neural population dynamics. However, a comprehensive understanding of how the generated dynamics emerge from the underlying connectivity is largely lacking. Previous work derived such an understanding for specific types of constrained RNNs (Mastrogiuseppe and Ostojic, 2020; Curto et al., 2019; Biswas and Fitzgerald, 2020), but if and how the resulting insights apply more generally is unclear. In this work, we study how network dynamics are related to network connectivity in RNNs trained without specific constraints to solve two previously proposed tasks, contextual evidence integration and sine wave generation. We find that the weight matrix of these trained RNNs is consistently high-dimensional, even though the dynamics they produce is low-dimensional. Unlike in RNNs constrained to have low-rank connectivity, the functional importance of a particular dimension of the weight matrix is not predicted by the amount of variance it explains across the matrix. Despite this apparent high-dimensional structure, we show that a low-dimensional, functionally relevant subspace of the weight matrix can be found through the identification of local “operative” dimensions, which we define as dimensions in the row or column space of the weight matrix whose removal has a large influence on local RNN dynamics. Notably, a weight matrix built from only a few operative dimensions is sufficient for the RNN to operate with the original performance, implying that much of the high-dimensional structure of the trained connectivity is functionally irrelevant. The existence of a low-dimensional, operative subspace in the weight matrix simplifies the challenge of linking connectivity to network dynamics, and suggests that independent network functions may be placed in separate subspaces of the weight matrix to avoid catastrophic forgetting in continual and multitask learning.

T-15. Joint coding of visual input and eye/head position in V1 of freely moving mice

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Visual input to the brain is highly dynamic during natural behavior due to movements of the eyes, head, and body through complex environments. Previous studies have shown that neurons in mouse primary visual cortex (V1) respond to eye and head movements, but how these signals are integrated with visual processing during free movement is unknown since visual physiology is generally performed under conditions of head-fixation. To address this, we performed the first measurements of visual receptive fields (RFs) from freely moving animals by using single-unit electrophysiology in V1 while simultaneously measuring the mouse's visual scene and eye/head position using head-mounted cameras and an inertial measurement unit (IMU). These RFs, estimated using a generalized linear model (GLM), explained a significant amount of neural activity and closely matched RFs measured in the same cells under head-fixed conditions. Many V1 neurons also showed significant tuning for eye position and head orientation during free movement. By incorporating these variables into the GLM, we found that this tuning was best explained by different combinations of multiplicative and additive integration of visual scene

and eye/head position across the population, consistent with theoretical models of gain fields and linear/nonlinear mixed selectivity. Our results provide new insight into coding in mouse V1, with implications for visual processing beyond traditional head-fixed preparations. More generally, this work provides a paradigm and requisite tools for performing visual physiology under natural conditions, including active sensing and ethological behavior.

T-16. Distinct dynamics in projection-specific midbrain dopamine populations for learning and motivation

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The mesolimbic dopamine system is believed to regulate both reinforcement learning and motivation to obtain rewards. A central question is how the mesolimbic dopamine system influences these distinct functions. A classical neural circuit model proposes a two-component system in which dopamine release in the nucleus accumbens core encodes prediction error signals to regulate reinforcement learning while dopamine release in the nucleus accumbens shell signals incentive salience and promotes motivated responses. Here we record bulk calcium dynamics in projection-specific ventral tegmental area (VTA) dopamine populations during instrumental conditioning, as mice undergo acquisition, extinction, and reinstatement of a food-reinforced operant task. We show that both accumbens core- and shell-projecting dopamine populations are activated by actions, cues, and rewards. However, we find differential activity dynamics in action, cue, and reward encoding between projection-specific dopamine populations. Accumbens shell-projecting VTA dopamine neurons preferentially encode animals' action initiation (lever press) and display a sustained increase in activity during the cue and reward outcome periods. In contrast, these signals in the accumbens core-projecting population return to baseline between discrete events. Further, during unexpected reward omission, the accumbens core-projecting population displays temporally discrete decreases in calcium signals consistent with a prediction error-encoding model that are not observed in the shell-projecting dopamine cells. By contrast, during unexpected reward delivery, the accumbens shell-projecting population preferentially encodes high saliency reward outcomes. By optogenetically manipulating both the accumbens shell-projecting and core-projecting VTA dopamine populations we tested and confirmed the prediction that these populations differentially regulate motivation during cued reinstatement. These findings suggest that accumbens core-projecting dopamine neurons provide prediction error signals to facilitate reinforcement learning while accumbens shell-projecting dopamine neurons provide incentive salience signals to promote motivated behavioral responses. These results also provide evidence for a two-component neural circuit model of mesolimbic dopamine's dual functions in reinforcement learning and motivation.

T-17. Computational strategies and neural correlates of probabilistic reversal learning in mice

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When faced with a constantly changing, uncertain environment it is necessary to infer its underlying structure to guide behaviour. This has often been formalised as a value updating problem – where actions are chosen based on an incrementally updated weighted average of past reward. Activity of midbrain dopamine neurons has been commonly associated with the error in such value prediction, and it has been proposed to be crucial for learning and updating of values that inform decision making. However, it has become increasingly apparent that both humans and animals often use an alternative strategy – based on the use of inferred hidden states to make predictions and to guide their choices. In this study we hypothesised that, as is commonly seen in humans, mice might use hidden state strategies even in simple tasks such as reversal learning, and that midbrain dopamine activity would reflect the use of such strategies.

To investigate this, we used a probabilistic reversal learning task in mice. In this paradigm, for optimal performance it is necessary to continuously integrate past trial outcomes to predict reward contingencies associated with different actions across reversals. Probing animals' behaviour with computational modelling, we found that mouse behaviour was consistently best fit by models that utilised hidden states, as opposed to value updating or alternate strategies. Furthermore, by recording dopamine release in the nucleus accumbens during the task using the dopamine sensor dLight, we found phasic dopamine was most strongly predicted by error associated with hidden state inference, rather than error in reward prediction.

Overall, we find that mouse behaviour and midbrain dopamine activity during probabilistic reversal learning task is best described by a belief state rather than value updating strategy. Ongoing work is investigating the sources of the belief state prediction that influence dopamine signalling during decision making.

T-18. A new tool for automated annotation of complex birdsong reveals dynamics of canary syntax rules

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Songbirds provide a powerful model system for studying sensory-motor learning. Many analyses require time-consuming manual annotation of the units of song, often called syllables. However, songbirds produce many more songs than can be annotated by hand, creating a bottleneck that limits the questions researchers can answer. Methods exist for automated annotation[1], but, as we show, these methods exhibit limitations when applied to songs with many syllable types and variable transitions. To address these issues, we developed an artificial neural network, TweetyNet[2], that segments and labels spectrograms. We first show how our approach mitigates issues faced by methods that rely on segmented audio. Then we demonstrate TweetyNet achieves low error across individuals and across two species, Benaglese finches and canaries. We also show that using TweetyNet, we can accurately annotate very large datasets, containing song recorded in multiple days, and that these predicted annotations replicate key findings from behavioral studies in both species[3,4]. TweetyNet is the first algorithm to automate annotation of canary song at the syllable level, processing minutes-long bouts with as many as 50 syllable types. We demonstrate that access to thousands of songs yields an order of magnitude precision improvement in statistical syntax models and allows measurements of previously-unknown diurnal changes. Specifically, probabilities of different first-order Markov sequences exhibit uncorrelated changes. This observation suggests that beyond global parameters, like temperature and neuromodulator tone, there may be additional mechanisms that affect canary syntax. We then estimate the diurnal change in transition entropy and find decrease in second-order but not in first-order Markov processes. These differences indicate dynamics in the long-range structure of song, similar in trend to the known diurnal decrease in syllable acoustic variability, but on tenfold longer time scales. Our results suggest TweetyNet will make it possible to address a wide range of new questions about birdsong.

T-19. Linking tonic dopamine and biased value predictions in a biologically inspired reinforcement learning model

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Some psychiatric disorders are characterized by excessively optimistic or pessimistic predictions of future events, as well as changes in dopamine levels. However, how changes in dopamine could lead to biased value predictions is unknown. Here, we draw this link by examining the role of baseline dopamine levels in value learning. Value learning is thought to depend, in part, on synaptic plasticity driven by dopamine reward prediction errors (RPEs) acting upon D1 and D2 receptors in medium spiny neurons (MSNs) of the striatum. At reported striatal dopamine levels, D1 and D2 receptors are mostly unoccupied and occupied by dopamine, making them sensitive to increases and decreases of dopamine, respectively. Accordingly, studies have reported that potentiation in MSNs expressing D1 or D2 receptors is triggered by phasic increases or decreases of dopamine [1,2]. Moreover, given the sigmoidal dose-occupancy relationship of these receptors, shifts in dopamine baseline should change their sensitivity to dopamine transients (i.e., take the baseline to a “steep” or “shallow” region of the dose-occupancy curve). Here, we show that a reinforcement learning (RL) model incorporating these plasticity rules develops positive or negative biases in predictions of probabilistic rewards when baseline dopamine is increased or decreased, respectively. We validate this model using data from a previous study [3]. This study showed that lesions of the habenula resulted in positive biases both in reward-seeking behavior (anticipatory licking) and dopamine neurons responses to cues predictive of probabilistic rewards. In our model, an increase in baseline firing of dopamine neurons, which was observed in the data, is sufficient to lead to optimistic biases. Taken together, our biologically inspired RL model highlights a causal impact of baseline dopamine on biasing value predictions, which may underlie abnormalities in psychiatric patients, including altered risk preferences.

T-20. Integrating deep reinforcement learning agents with the *C. elegans* nervous system

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Deep reinforcement learning (RL) has successfully trained machines to excel in video games, board games, and robotics. It has been argued that together, deep RL and robotics can be used to study biological learning by virtue of being embodied intelligence in the real world (Tan et al., 2021). In fact, RL itself was originally formulated to model animal behavior (Sutton & Barto, 1998). Here we go one step further and directly interface deep RL agents with a living neural network: that of the nematode *C. elegans*. We present a hybrid deep RL - *C. elegans* closed-loop computational system wherein an agent reads animal states through a camera and uses optogenetics to control neuronal activity. We trained the system to move animals to target locations. Agents successfully learned to control the movement of three genetic lines, each with different neurons that responded to optogenetic control. Building and training our system led to insights about which algorithmic choices mattered in learning the task; notably, appropriate agent regularization and data augmentation were important for success. In parallel, analyzing the policies of trained agents shed light on how neurons involved in each line could guide target-finding. Finally, we found that neither agent nor animal was always in complete control. Instead, existing sensory and motor systems in *C. elegans* integrated with RL agents to avoid obstacles during target-finding, or to override optogenetic input when animals reached a desirable state (like a patch of food). Remarkably, these behaviors emerged without any retraining of the system. Thus, we demonstrate that biologically-integrated deep RL can be used to control *C. elegans* behavior, to learn about neuron capabilities, to find key algorithmic principles for coordinating animal behaviors, and to study the interaction of biological and artificial neural networks.

T-21. Dynamical systems analysis reveals a novel hypothalamic encoding of state in nodes controlling social behavior

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All animals possess a repertoire of survival behaviors, such as aggression and reproduction, that are under strong evolutionary constraints. In vertebrates, the hypothalamus plays a key role in regulating these behaviors. The prevailing view of this neural system posits that hypothalamic nuclei are organized as ‘labeled lines’ – populations of behavior-specific neurons with characteristic transcriptional and connectomic profiles. This model seems to fit regions such as the medial preoptic area (MPOA, whose activation causes reproductive behaviors), which contains multiple behavior-specific neuronal populations with distinct transcriptional profiles. However other structures, such as the ventromedial hypothalamus (VMHvl, whose activation causes scalable aggression), have rich dynamics but only weak tuning for experimenter-identified behaviors like attack and mating. We adopt an unsupervised dynamical systems framework to characterize neural activity of ESR1 neurons in the MPOA and VMHvl of interacting mice in a user-unbiased manner. Strikingly, we find activity in the VMHvl is organized by state rather than behavior: the low-dimensional dynamics of our fit model reveal one dimension with slow-ramping dynamics and persistent activity that correlates with escalating aggressive or reproductive behavior. Intriguingly, the time constant of this dimension is a strong predictor of time animals spend fighting. These ramping representations suggest a generic function for the VMHvl to encode intensity of motivational states and are compatible with results of functional perturbation experiments. Importantly, ramping dynamics are not an arbitrary result of our fitting process, as models fit to MPOA activity revealed states that precisely correlate with the animals’ behavior. The low-dimensional dynamics of the MPOA contained behaviorally tuned factors that display rotational dynamics during mating episodes, suggesting an encoding of actions rather than state. Thus, our analysis of dynamics reveals two distinct organizations of computation in the hypothalamus, one based on action encoding populations in MPOA and another population encoding motivational state in VMHvl.

T-22. Isolating the role of synaptic plasticity in hippocampal place codes

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Long-term potentiation (LTP) is thought to be a key plasticity mechanism underlying the formation and maintenance of hippocampal place codes. It is unclear, however, which properties of these neural codes are inherited from upstream processing and which are learned through plasticity. To disentangle these influences on place codes, we utilized a method for abolishing LTP specifically in hippocampal region CA1 of the adult mouse without affecting basal synaptic processing: conditional genetic deletion of a necessary component of the postsynaptic membrane fusion machinery, Syntaxin3 (Stx3). Surprisingly, most hippocampal dependent behaviors were spared by Stx3 deletion. However, mice lacking CA1 LTP did not express typical novel environment preferences. By imaging calcium activity of CA1 neurons during a novel environment virtual reality behavior, we find that LTP is not required to form stable neural representations of context and space. This result is accounted for by a simple computational model that predicts stable CA1 codes can be passively inherited from upstream CA3 inputs. This model also correctly predicts differences in place field properties between mice with and without LTP such as place field width and the number of place fields per cell. Expanding on this hypothesis, LTP is necessary for endowing population codes with the properties that are unique to CA1 but not present in CA3. First, LTP is required for the overrepresentation of reward locations. Second, LTP is necessary for the experience dependent backward shift of place fields in novel environments. Third, LTP is essential for the increased population activity in novel environments. Collectively, these results suggest that LTP in CA1 serves a unique role in processing reward and novelty, but its role in spatial coding may most often be to augment existing biases in presynaptic connectivity.

T-23. A hierarchical representation of sequences in human entorhinal cortex

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Cells in the rodent hippocampal (HP) formation contain representations of space and time. In entorhinal cortex (EC), spatial (grid) cells are organised along a hierarchical gradient with smaller spatial scales dorsal and larger scales ventral (homologous to a posterior-anterior axis in humans). Recent models suggest these patterns of cellular activity might be the consequence of a more general mechanism that optimally represents the structure of possible sequences in the world. If so, it should be possible to find similar signatures for arbitrary (non-spatial) sequences. Using extracellular recordings in epilepsy patients, we show “position in sequence” is also represented in HP/EC cells when subjects are asked to memorise an arbitrary sequence of stimuli. Using fMRI in healthy volunteers (where we can train subjects on long (113 element) sequences with rich hierarchical structure), we show that these sequence positions are represented in a factorised hierarchical form along a posterior-anterior EC gradient, exactly as grid cells are in space. In both cells and fMRI, the EC representation of sequence position was abstracted - it generalised over multiple sequences with different stimuli (analogous to grid cells generalising over multiple environments). Overall, using single-unit recordings and fMRI we show that the human HP formation contains abstracted representations of sequential structures. Moreover, these representations are organized hierarchically along posterior-anterior axis in EC. The hierarchical levels factorised (as with grid cells). Notably, the temporal structure of our daily life is also hierarchical: breakfast-lunch-dinner sequences form days, days form months etc. Thus, similar representational principles of sequence hierarchy and abstraction would permit efficient inferences and generalisations in the experiences that make up every-day life.

T-24. Neocortical feature codes drive memory recall

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The neural basis underlying the relationship between a contextual memory and its constituent features is not well understood; in particular, where features are represented in the brain and how they drive memory recall. To gain insight into this question, we developed a behavioral task where mice use features to recall an associated contextual memory. We performed longitudinal imaging in hippocampus as mice performed this task and identified robust representations of global context. To identify putative brain regions that provide feature inputs to the hippocampus, we inhibited cortical afferents while imaging hippocampus during behavior. We found that while inhibition of entorhinal inputs led to broad silencing of hippocampus, inhibition of prefrontal anterior cingulate inputs led to a highly specific silencing of context neurons and deficits in feature-based recall. Single neurons in AC displayed feature-selectivity as well as mixed-selectivity to combinations of features, in contrast to the strong conjunctive tuning that was observed with CA1 neurons. These multiplexed single neuron activities gave rise to robust population level representations of features. Interestingly, we observed that AC feature representations 1) lag hippocampus context representations during training, but 2) dynamically reorganize to lead and target recruitment of context ensembles in hippocampus during recall. This AC-CA1 interaction is further enhanced by the saliency of the memory, as suggested by tight coupling of feature-context ensembles in reinforced compared to non-reinforced contexts. Together, we provide neurophysiological insights into how feature representations emerge, stabilize, and access long-range episodic representations to drive memory recall.

T-25. Basal Ganglia feedback loops as possible candidates for generation of beta oscillation

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An increase in beta-band frequency (13-30 Hz) activity has been observed in different nuclei of the basal ganglia (BG) of patients with Parkinson's disease (PD). However, recent studies have shown that beta oscillations are not only specific to pathological conditions. They have been shown to occur during sensorimotor tasks in healthy subjects. In this study, we used both a rate model and a spiking neural network to investigate the mechanisms responsible for the generations of beta oscillations. Results show that using a rate model with realistic time constants, the classical candidate - a recurrent network between the Subthalamic nucleus (STN) and external globus pallidus (GPe)- produces frequencies beyond the beta range and is consequently unlikely to be the main source of beta oscillations as previously suggested. We then propose two alternative circuits made of pallidostratial feedback loops that can generate network oscillations in this range. Moreover, we show that with the pathophysiological changes due to dopamine depletion in PD, the network can transition from a steady-state where firing is asynchronous to a pathological state with synchronous oscillatory firing in beta-band frequencies. We explore how each of these loops behaves around the point of transition between the normal steady-state and the oscillatory regime depending on synaptic connection strengths. Finally, one by one, we add the aforementioned loops together and show that in a complete BG network we can reproduce the oscillatory behavior and phase-locking observed in Parkinsonian rats. Our results suggest that pathological oscillations are the product of the interactions between two or more feedback loops.

T-26. Neocortical long-range inhibitory neurons coordinate state-dependent network synchronization

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Cortical activity changes dramatically upon changes in behavioral state, such as between sleep versus wake (McGinley et al 2015). Though the mechanisms enabling these distinct modes of cortical operation remain largely unknown, inhibitory neurons (INs) have been suggested repeatedly as a regulator of behavioral-state dependent neocortical activity (Batista-Brito et al 2018, Cardin et al 2019, Bugeon et al 2021). Here we investigate how a unique subpopulation of long-range INs impact cortical states. These cells are defined by the co-expression of somatostatin (SST) and neuronal nitric oxide synthase (nNOS), namely SST/nNOS cells. Although they constitute a very small minority of neocortical INs, SST/nNOS cells are evolutionarily old and conserved from reptiles to humans. Further, they have unique morphology for neocortical INs, with long-range projections that span millimeters and cross cortical areas (Tomioka et al 2005). Their remarkably distinctive features and deep evolutionary conservation suggest that SST/nNOS cells play an important role in neocortical function. Until recently, the genetic targeting of SST/nNOS cells has been difficult. We have used intersectional genetic tools to manipulate neocortical SST/nNOS cells in mice to interrogate their *in vivo* functional roles. Using 2-photon calcium imaging with high precision state monitoring, we find that SST/nNOS cells are specifically active during low-arousal states characterized by low movement and synchronized local field potentials. Using optogenetic manipulation of SST/nNOS cells in combination with *in vivo* extracellular recordings we show that the activity of SST/nNOS cells is sufficient to induce a synchronized network state, with both increases in low-frequency LFP power and increases in spiking entrainment to these low-frequencies. These observations are specific to SST/nNOS cells as optogenetic activation of SST+/nNOS- cells leads to reduced neocortical network synchrony.

T-27. Metastable circuit dynamics explains optimal coding of auditory stimuli at moderate arousals

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Behavioral states in humans and animals vary over time, and these shifts alter cortical processing and cognitive function. For example, one striking result is an observed inverted-U relationship between arousal and performance on signal detection tasks. However, there is currently a need for mechanistic models that can explain these state-dependent effects. Here we address this challenge in the context of arousal-dependent auditory processing in rodents. In experiments where mice were presented tones of different frequencies, we found that frequency information could be best decoded from population activity during states of moderate arousal, compared to either low or high arousal. We explain the computational mechanism of this optimal stimulus processing with a spiking network model composed of excitatory and inhibitory cells arranged in clusters. Neural activity in this circuit unfolds through metastable attractors representing transiently activated neural assemblies. By modeling varying arousal levels as perturbations to excitatory cells' baseline external inputs, we show that increasing input heterogeneity modulates stimulus decoding in a manner consistent with the data. That is, intermediate levels of heterogeneity – modeling intermediate arousals – yield optimal discriminability. Moreover, comparison to a model with homogeneous architecture reveals that clustered organization is necessary to explain the observed inverted-U relationship between decoding performance and arousal. Using mean-field theory, we then show that variations in stimulus decoding arise due to a perturbation- (i.e. arousal-) induced shift in the dynamical regime of the circuit. Increasing arousal in the model from low to moderate levels accelerates the network's metastable dynamics, leading to an optimal coding regime. But at high arousals, metastable dynamics disappear and decoding performance degrades, explaining the empirical results. Beyond the current application, the framework we present can be extended to understand context-dependent neural computation more broadly. For example, it could be utilized to study pharmacologically- or optogenetically-induced shifts in cortical state.

T-28. Large retinal populations are collectively organized to efficiently process natural scenes

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Sensory systems are adapted to efficiently process natural stimuli. Such adaptation has been particularly well documented in the retina. Theoretical and experimental studies have demonstrated that multiple properties of retinal coding and architecture – from receptive field (RF) shapes to RF mosaic alignment – are optimized for efficient sensory coding. These adaptations have been primarily studied in small regions of the retina, however stimulus statistics vary systematically across the entire visual field (VF). It therefore remains unknown whether the collective structure of large neural populations, such as those covering the entire VF, could be shaped by global statistics of natural scenes.

A particularly salient global property of the natural VF is the contrast inhomogeneity. Local contrast increases with elevation and rapidly drops-off at the horizon, inducing changes in signal-to-noise ratio (SNR) of the photoreceptor output. To understand how SNR variation could globally shape RFs of retinal ganglion cells (RGCs), we developed an encoding model related to the predictive coding (PC) theory. The theory postulates that RGCs recode photoreceptor output to minimize the metabolic cost of information transmission. Our model predicts two kinds of change in RF shapes induced by the contrast variation: increase of the surround strength along the VF elevation, and concentration of asymmetric RFs at the horizon. To test these predictions, we established a novel epi-fluorescent imaging approach that enables simultaneous recording of approximately 1000 neurons per field-of-view. Using this novel technique, we mapped RFs of 26558 RGCs, distributed across the entire VF.

We found that large-scale retinal organization closely recapitulates theoretical predictions. The relative strength of the surround increases along the dorso-ventral axis, while the RGCs with vertically asymmetric RFs form a streak along the horizon line. Our results demonstrate that the statistics of natural scenes can shape the organization of neural populations at a previously unappreciated scale.

T-29. A two-way luminance gain control in the fly brain ensures luminance invariance in dynamic vision

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For visual perception to be unaffected by viewing conditions, animals must adapt their sensitivity to changing visual statistics, such as mean illumination. Consistently, photoreceptors in many species control their luminance gain and encode relative changes in luminance [1,2], termed contrast. However, this early gain control is insufficient for luminance invariant contrast estimation in dynamic conditions. Sudden transitions to dim or bright environment would lead to an erroneous, reduced or enhanced perception of contrasts, thus imposing a two-way challenge on contrast estimation. Yet, visual behaviors are luminance invariant [3,4], and it is not understood how the brains achieve such invariance. In fruit flies, a distinct visual pathway preserves luminance information past photoreceptors and enhances contrast estimation in sudden dim light [4]. Here, we show that the pathway implements a generalized gain correction to tackle the two-way contrast coding deficits in dynamic conditions. When blocking the output of the luminance-sensitive interneurons L3, the flies underestimate large contrasts in sudden dim light and overestimate smaller contrasts in sudden bright light. Furthermore, the gain correction improves visibility of very dim stimuli at all contrasts. To explain how the gain correction is implemented in these widely differing scenarios, we formulated an algorithmic model. Here, the luminance channel plays a dichotomous role: when correcting contrast deficits in dynamic conditions, it interacts with contrast signals in a multiplicative way; in absolute dim light, it acts as an independent contrast channel to improve signal detection. Together, our work combines experimental and computational modelling approaches to demonstrate how post-receptor gain correction is key to perceptually relevant vision. Given that visual systems of all behaving animals face similar challenges, and that luminance information is preserved in the vertebrate retina too [5], the corrective gain control

might be a universal strategy of visual systems.

T-30. Direct measurement of whole-brain functional connectivity in *C. elegans*

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Understanding how neural perturbations propagate in the nervous system is important for understanding neural dynamics, to elucidate specific circuits, and to reveal how neuroanatomy relates to neural function. Here, we systematically perturb individual neurons in *C. elegans* while measuring the responses of all neurons in its brain in order to directly measure functional connectivity at brain scale and cellular resolution. Specifically, we measure the sign, strength, direction, and temporal properties of the connections between neurons. We present a preliminary functional connectome, currently with 68 neuron classes from 24 animals (including mutants), comprising more than half of all neuron classes. Our preliminary atlas comprises more than 900 stimulation-whole-brain-response events. We investigate the stereotypy and timescale of evoked responses in the network, and compare connections to the known connectome and gene expression data. We explore in detail the role of one specific well-characterized neuron, RID, which outputs neural signals almost exclusively via extrasynaptic communication. We use this neuron to both validate our system and compare against predictions from gene expression data. We identify 20 neurons that respond to RID activation at timescales consistent with extrasynaptic communication. 18 of them were predicted from recent gene expression data (CeNGEN) to express receptors for transmitters released by RID, and two more were predicted to receive indirect signals from RID. This demonstrates that our direct measures of functional connectivity resolve wireless signaling between neurons that would not otherwise be visible in the wired connectome.

T-31. Optogenetic mapping of circuit connectivity in the motor cortex during goal-directed behavior

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Behavior-related neural dynamics in the frontal cortex is an emergent property of network connectivity. The network structure at the level of individual neurons, and its relationship to neural coding are largely unknown. We developed an optical method for rapid (500k pairwise connections / 30 minutes) mapping of effective connectivity in the neocortex *in vivo*. To this end, we combined 2-photon optogenetic stimulation of individual excitatory neurons and measurement of responses in non-stimulated neurons ('effective connection') using 2-photon volumetric calcium imaging. We applied this method in anterior lateral motor cortex (ALM) in a novel behavioral task in which untrained mice performed multidirectional tongue-reaching for water rewards presented at multiple (up to 25) locations on a grid in front of the mouse face. A majority of ALM neurons were modulated by task variables with a subset of neurons (~25%) exhibited strong tuning to the reward location. Specifically, some neurons showed tuning to direction of the reward location with respect to the mouse face, whereas other neurons were selective for particular reward locations. We then mapped effective connectivity between 10,000,000 pairs of layer 2/3 neurons imaged in this task. Nearby neurons were more strongly connected and shared directional selectivity, revealing a fine-scale columnar architecture. We next analyzed effective connectivity between these neurons using methods borrowed from network science. The distribution of the number of out-degree connections could not be explained by random connectivity, but instead displayed a long tail – with a subset of neurons having unexpectedly large numbers of connections. These hub neurons had weak tuning to reward location, showed highly reliable responses on a trial-by-trial basis, and exhibited a strong influence on neighboring neurons. Hub neurons may act as local conductors of the neural orchestra.

T-32. Invariant neural subspaces maintained by feedback modulationLaura Bella Naumann^{1,2}

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Sensory systems reliably process incoming stimuli in spite of changes in context. Most recent models accredit this context invariance to an extraction of increasingly complex sensory features in hierarchical feedforward networks. Here, we study how context-invariant representations can be established by feedback rather than feedforward processing. We show that feedforward neural networks modulated by feedback can dynamically generate invariant sensory representations. The required feedback can be implemented as a slow and spatially diffuse gain modulation. The invariance is not present on the level of individual neurons, but emerges only on the population level. Mechanistically, the feedback modulation dynamically reorients the manifold of neural activity and thereby maintains an invariant neural subspace in spite of contextual variations. Our results highlight the importance of population-level analyses for understanding the role of feedback in flexible sensory processing.

T-33. Dynamic causal communication channels between neocortical areasMitra Javadzadeh¹

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Dynamic pathways of information flow between distributed brain regions underlie the diversity of behavior. However, it remains unclear how neuronal activity in one area causally influences ongoing population activity in another, and how such interactions change over time. Here we introduce a causal approach to quantify cortical interactions by pairing simultaneous electrophysiological recordings with neural perturbations. We found that the influence primary visual cortex (V1) and higher visual area LM had on each other was surprisingly variable over time. Both feedforward and feedback pathways reliably affected different subpopulations of target neurons at different moments during processing of a visual stimulus, resulting in dynamically rotating communication dimensions between the two areas. The influence of feedback on V1 became even more dynamic when visual stimuli were behaviorally relevant and associated with a reward, impacting different subsets of V1 neurons within tens of milliseconds. Importantly, these fast changes in inter-areal influences were in stark contrast to, and could not be explained by, the much slower dynamics of activity in either area. To understand the function of dynamically rotating communication dimensions, we used a linear dynamical system to model the recurrent dynamics and external inputs that shape V1 activity. We found that the fast rotation of feedback communication dimensions momentarily aligned feedback influences with dynamical modes in V1 and with the visual input, creating a selective, transient time window for signal integration. Interestingly, only during this brief (<100 ms) time window, the feedback input to V1 was relevant for behavioral performance in a visual discrimination task. In summary, using a causal method for measuring long-range cortical interactions, we found that communication subspaces between visual areas are dynamically rotating. This rotation leads to momentary alignment of external inputs with V1 dynamics, consistent with the formation of transient windows for signal integration and sensory processing.

T-34. The secret Bayesian lives of ring attractor networksAnna Kutschireiter^{1,2}

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Efficient navigation requires animals to track their position, velocity and heading direction (HD). Some animals'

behavior suggests that they also track uncertainties about these navigational variables, and make strategic use of these uncertainties, in line with a Bayesian computation. Ring-attractor networks have been proposed to estimate and track these navigational variables, for instance in the HD system of the fruit fly *Drosophila*. However, such networks are not designed to incorporate a notion of uncertainty, and therefore seem unsuited to implement dynamic Bayesian inference. Here, we close this gap by showing that specifically tuned ring-attractor networks can track both a HD estimate and its associated uncertainty, thereby approximating a circular Kalman filter. We identified the network motifs required to integrate angular velocity observations, e.g., through self-initiated turns, and absolute HD observations, e.g., visual landmark inputs, according to their respective reliabilities, and show that these network motifs are present in the connectome of the *Drosophila* HD system. Specifically, our network encodes uncertainty in the amplitude of a localized bump of neural activity, thereby generalizing standard ring attractor models. In contrast to such standard attractors, however, proper Bayesian inference requires the network dynamics to operate in a regime away from the attractor state. More generally, we show that near-Bayesian integration is inherent in generic ring attractor networks, and that their amplitude dynamics can account for close-to-optimal reliability weighting of external evidence for a wide range of network parameters. This only holds, however, if their connection strengths allow the network to sufficiently deviate from the attractor state. Overall, our work offers a novel interpretation of ring attractor networks as implementing dynamic Bayesian integrators. We further provide a principled theoretical foundation for the suggestion that the *Drosophila* HD system may implement Bayesian HD tracking via ring attractor dynamics.

T-35. A hindbrain ring attractor network that integrates heading direction in the larval zebrafish

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To successfully navigate their environment, animals may generate an internal, abstract and stable representation of the environment that can be updated based on sensory cues, such as visual landmarks or vestibular feedback, or internally generated motor commands. In mammals, neurons that fire when the animal faces a particular direction in the world reference frame have been recorded in mammillary bodies and entorhinal cortex. The heading direction can be read out using a weighted sum of the activation of those cells. This dynamics is well described by a “ring attractor” model: the network has an attractor with a ring topology in its phase space, positions along the ring represent the heading direction, and input signals translate the network activation along this circular attractor. Although this model has found remarkable validation in the *Drosophila* ellipsoid body, the precise anatomical dissection of a ring attractor circuit has been elusive in the vertebrate brain. Here we describe a group of ~100 GABAergic neurons in the anterior hindbrain (aHB) of the larval zebrafish with highly constrained dynamics lying on a ring manifold in phase space. Clockwise and counterclockwise shifts along this manifold happen when the fish performs left and right movements, so that the network phase keeps track of current heading direction. This heading representation is stable over tens of minutes even without external visual or vestibular feedback. We show that neurons are anatomically organized according to their proximity in activity space and connect with each other in the interpeduncular nucleus (IPN), a structure implicated in navigation in fish and mammals. Moreover, their morphologies suggest a mechanistic model for the organization of the ring network dynamics. Together, our data represent the first observation of a full ring attractor network with an anatomical organization that integrates heading direction in the vertebrate brain.

T-36. A reservoir of timescales in random neural networks

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The temporal activity of neural circuits exhibits fluctuations simultaneously varying over a large range of timescales (Murray et al. 2014). Recent experimental evidence presents a heterogeneity of timescales across neurons within the same local cortical circuit, ranging from milliseconds to minutes (Bernacchia et al. 2011). While this phenomenon is well documented, the underlying neural mechanism is still unknown. We present a novel random neural network whose units represent functional neural clusters of different sizes, given by a heterogeneous distribution of self-couplings. We find that the network activity varies over multiple timescales spanning several orders of magnitude. When the self-couplings are strong and heterogeneous, a reservoir of numerous timescales emerges in the chaotic phase, where a neural cluster's timescale is proportional to its self-coupling. In the limit of large size, the dynamics of a network cluster can be studied analytically, revealing a new metastable regime described by colored noise-driven transitions between potential wells. In this regime, we provide a novel analytical treatment for recurrent neural networks, capturing their time-dependent metastable dynamics. When driving such a network with a time-dependent broadband input, given by a superposition of multiple frequencies, slow and fast neural clusters preferentially entrain slow and fast input frequencies, respectively, thus providing a potential mechanism for spectral demixing in cortical circuits. Our work establishes the basis of a novel framework for studying heterogeneity of timescales in neural circuits as well as artificial neural networks, highlighting the advantages of generating multiple timescales for encoding complex time-varying signals.

T-37. Orbitofrontal cortex is required to infer hidden task states during value-based decision making

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The orbitofrontal cortex (OFC) has long been considered critical for value-based decision making, but its precise role is a point of contention. One hypothesis is that OFC computes subjective value and drives economic choice [1]. A second hypothesis is that OFC represents a cognitive map or state space (i.e., a representation of the different states in a task and the transitions between them) [2]. We trained rats on a novel temporal wagering task with partially hidden states (blocks of trials with low or high rewards). Rats must determine how long to wait for a reward, providing an explicit behavioral readout of subjective value. Rats' wait times are modulated by both the offered reward volume and the hidden block. Bilateral muscimol inactivation of lateral OFC (IOFC) reduces modulation of wait time by block but does not impair modulation of wait time by reward volume. This suggests that IOFC is necessary to infer the current block based on knowledge of the task structure but is not required to compute subjective value, per se. We extend these findings using behavioral modeling to address how IOFC contributes to inference. We fit a behavioral model that uses Bayes' Rule to predict the identity of the current block. The model includes parameters representing the opportunity cost in each block (which dictates the wait time in different blocks), and a parameter capturing the extent to which rats use an optimal prior, which contains knowledge about block length and transition probabilities. Results suggest that rats use a less informative prior when IOFC is inactivated, but other parameters are not affected. Electrophysiological recordings from IOFC reveal encoding of hidden states (blocks). These data suggest that IOFC promotes the use of a prior that incorporates knowledge of the task structure for inferring partially observable states of the environment.

T-38. Reorganizing cortical learning: a cholinergic adaptive credit assignment model

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The cholinergic system has been associated with learning, but also with cognitive decline in dementia and aging. Yet, to date no computational models have been put forward to explain how the cholinergic system contributes to both learning and cognitive decline. Here we introduce a model that combines a recently proposed biologically plausible model of credit assignment with a cholinergic adaptive module based on adaptive deep learning rules. Using a multi-class perceptual discrimination task we show that cholinergic adaptive learning leads to rapid

learning when compared with non-adaptive models. Our results suggest that this is a consequence of the reorganizing effect that these forms of adaptive learning have, which encourages the network to develop distributed neuronal representations with mixed-selectivity. As a consequence, we show that the network becomes more robust to perturbations such as simulated cell death. Moreover, we demonstrate that in order to obtain such rapid and robust learning, it is not sufficient for cholinergic modulation to operate at a purely global level, suggesting an important function for local sources of acetylcholine in the cortex, such as ChAT-VIP interneurons. Overall, our work provides a novel theoretical framework for cellular-systems neuroscience with which to link cholinergic modulation of cortical learning to its function in health and disease.

T-39. Integrating information and reward into subjective value: humans, monkeys, and the lateral habenula

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Humans and several animal species, including monkeys, rats, and pigeons, are often strongly motivated to seek information about uncertain future rewards. Remarkably, they prefer information even when it has no objective value for controlling the outcome, suggesting that information has subjective value of its own. In recent years there has been an explosion of research on information seeking in humans and animal models. However, a critical unanswered question is whether the computations that assign subjective value to information are conserved between humans and other species. If so, we could leverage animal models to uncover the neuronal populations that are responsible for conserved information value computations and their causal influence on decisions.

To address this, we designed analogous multi-attribute information choice tasks for humans and monkeys. Individuals choose between options with multiple attributes, including cues that are either informative or non-informative about future outcomes, and different probability distributions of rewards (money for humans, juice for monkeys). This let us measure and model the subjective value individuals assign to information; how they compute information value using reward uncertainty, expected reward, and other attributes; and integrate information and reward into the total value of an option. We find human and monkey value computations are remarkably similar on all these fronts.

We then investigated the neuronal networks responsible for these value computations by recording in monkeys in two interconnected areas with information-related activity, the anterior/ventral pallidum (Pal) and lateral habenula (LHb). Both areas respond to all attributes needed for decisions, but only LHb predominantly integrates information and reward in a manner resembling subjective value. Furthermore, trial-to-trial fluctuations in LHb value signals predict ongoing decisions, while electrical stimulation coincident with LHb value signals modifies ongoing decisions. Our results thus implicate LHb in conserved information value computations that guide online decisions.

T-40. The emergence of fixed points in interlimb coordination underlies the learning of novel gaits in mice

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Complex motor behaviors involve the precise coordination of different body parts. While motor coordination has

been extensively studied in expert animals, the behavioral and neural processes involved in its emergence through learning are still not well understood. To answer this question, we combined longitudinal behavioral analyses with population recordings from the cerebellum, which is a key region for movement coordination and motor learning. We trained mice to walk on a motorized runged treadmill over multiple days while Ca²⁺-activity was recorded from cerebellar molecular layer interneurons (MLIs). Motorization and rungs obliged mice to walk slower and with different stride lengths than in their natural gait. High-speed behavioral video recordings allowed us to extract paw trajectories and to assess how mice learned to control stepping patterns in this novel task that required coordination both between limbs, and the coordination of single limbs with the runged treadmill. Over learning, mice acquired a novel gait pattern (lateral sequence walk) not typically used for locomotion. We found that across animals, fixed pairwise swing-stance phase differences between limbs emerge over days. Using a neural population decoder, we show that cerebellar MLIs encode pairwise phase differences of limbs. We finally asked whether fixed pairwise phase relationships emerge through stronger interlimb coupling or rather by an increase in regularity of single-paw stepping patterns. To address these possibilities, we fit paw position dynamics to a coupled oscillator model in which intrinsic frequencies change stochastically according to a Hidden Markov Model (HMM). With this model we find that over learning, mice adjust single-limb stepping frequencies so that fixed-point dynamics in interlimb coordination become possible.

T-41. Differential encoding of innate and learned behaviors in the sensorimotor striatum

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We can perform a diverse range of innate and learned behaviors – from running and jumping to a swift tennis serve – with remarkable coordination and grace. While skillful execution of innate and learned behaviors is supported by sensorimotor striatum, how this region encodes behavior remains poorly understood. Studies based on learned skills suggest striatal neurons represent skills as neural sequences, with each neuron locked to a feature of the stereotyped motor output. However, whether this coding scheme generalizes to innate behaviors or emerges through learning is not known. One possibility is that striatum functions as a general controller and codes for movement kinematics similarly across innate and learned behaviors. Such a scheme, however, may cause neural interference if kinematically similar movements appear in distinct action types. A degenerate kinematic code, in which similar behaviors are represented differently depending on context, may solve this problem.

To arbitrate between these coding schemes, we combined in-vivo electrophysiology with whole-body 3D kinematic recordings in behaving rats expressing both a learned skill and spontaneous natural behaviors. Examining the striatal code for natural behaviors, we identified a subpopulation of neurons that were tuned to specific behaviors, such as rearing and grooming. Activity of these neurons was well-described by whole-body movement kinematics, with ‘trial-by-trial’ activity during a given behavior comparably precise to what has been described for learned skills. Comparing this subpopulation to that encoding movement kinematics in the learned skill revealed an overlap. Intriguingly, we found that similar movements exhibited during innate and learned behaviors were associated with different patterns of activity. This suggests that striatum has a precise but degenerate kinematic code that is a function of context. This many-to-one mapping between activity and behavior may thus afford the motor system the flexibility to refine behaviors in context-specific ways without undue interference across behavioral domains.

T-42. Deep neural network modeling of a visually-guided social behavior

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An important problem in systems neuroscience is to understand how animals transform complex, high-dimensional sensory inputs into neural signals that drive behavior. Here we propose a novel modeling approach for this sensorimotor transformation to identify a one-to-one mapping between real and model neurons. Our approach involves

training a deep neural network to produce behavioral data from a range of different inactivation experiments. Crucially, we train the model while perturbing its hidden units with the same perturbations applied to neural activity—a process we call ‘knockout’ training. We applied this approach to understand the sensorimotor transformation of *Drosophila melanogaster* males during a complex, visually-guided social behavior. We explicitly modeled a population of visual projection neurons known as Lobula Columnar or LC cells (Wu et al., eLife 2016), which receive inputs from the optic lobes and send their axons to the central brain. Our model identified a one-to-one mapping from model neurons to LC cells, providing an overview into how LCs coordinate their activity to transform visual input to drive behavior. We verified that the model correctly predicted responses recorded from LC neurons—even though the model had no access to neural recordings during training. We then systematically analyzed our model and found that most of the model LCs had mixed selectivity and contributed to multiple behavioral actions (e.g., movement and song production). This suggests that, contrary to the current prevailing view, LC neurons form a distributed population code to sculpt social behavior. Overall, we propose a novel modeling framework for relating deep neural network models to real neurons and to shed light on the neural computations performed during sensorimotor transformations.

T-43. The synaptic origins and functional role of diverse cortical responses during behavior

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Spike trains recorded from the cortex of behaving animals can be complex, highly variable from trial to trial, and therefore challenging to interpret. A fraction of cells exhibit obvious trial-averaged, task-related responses such as pure tone frequency tuning in auditory cortex. However, a substantial number of cells do not appear to fire in a task-related manner and are often neglected from analysis. Previous work used a novel single-trial, spike-timing-based analysis to show that both classically and non-classically responsive cortical neurons contain significant information about sensory stimuli and behavioral decisions suggesting that non-classically responsive cells may play an underappreciated role in perception and behavior. A recent study presented at Cosyne 2021 introduced a novel, task-performing spiking recurrent neural network (RNN) model incorporating excitatory and inhibitory spike-timing-dependent plasticity (STDP) that successfully recapitulates the distribution of classically and non-classically responsive neurons measured from the cortex of behaving animals. Here, we leverage this model to explore the synaptic origin and functional contribution of heterogeneous response profiles. Detailed inactivation experiments revealed that both response types contribute to task performance albeit via distinct mechanisms providing evidence for a double-dissociative function of these subpopulations. Excitatory and inhibitory plasticity rules independently increased the fraction of non-classically responsive units however both were required in tandem to improve performance and maintain engagement of all network units. We discovered unique local synaptic signatures that explain the heterogeneity of single-unit response profiles and made predictions that we compared to *in vivo* whole-cell recordings taken from the auditory cortex of behaving animals. Remarkably, parameters derived *in silico* accurately predicted the spiking response profiles of individual *in vivo* neurons. Our approach successfully accounts for the synaptic origins of heterogeneous neural responses and provides a powerful lens for exploring large-scale neuronal dynamics and the plasticity rules that shape them.

T-44. Correlation-based motion detectors in olfaction enable turbulent plume navigation

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Insects navigate to odor sources by combining information from the intensity, timing, and spatial distribution of odor encounters. One key information stream is the difference in odor signals between the antennae. This bilaterally-resolved information enables gradient sensing, helping navigation in simple environments like static odor ribbons.

In turbulent plumes, however, gradients are of limited use since they are hard to resolve and carry little information about the source location. Here, we have discovered a distinct role for bilateral odor sensing—detecting the direction of motion of odors. This discovery was enabled by decoupling wind from odor using spatially and temporally precise optogenetic stimulation of freely-moving *Drosophila*. We used stimuli previously designed for visual motion detection studies, which decompose natural stimuli landscapes into their “building blocks” of spatiotemporal correlations. Using this paradigm, we demonstrate that flies compute the direction of odor motion using a correlation-based algorithm equivalent to the Hassenstein-Reichardt correlator (HRC) proposed to describe motion detection in vision. Moreover, we replicated “olfactory illusions” analogous to the well-known “reverse phi” visual illusion, providing direct evidence of correlation-based motion detection outside of vision.

What is the value of odor direction sensing for navigation in the natural world? Is odor motion simply redundant with the wind? We use computational modeling to show that odor motion is a critical information stream in turbulent plumes, complementary to the wind direction. We then use a novel paradigm to present fictive plumes with artificially reversed odor motion, finding that navigation is significantly degraded. Finally, simulations of olfactory navigators in silico revealed that odor motion significantly improves previously-proposed navigation algorithms. Our work (1) reveals a critical role for bilaterality in olfaction; (2) shows that olfactory navigation exploits odor motion direction independent of wind direction; and (3) provides direct, causal evidence for analogous motion computations in olfaction and vision.

T-45. A temporal context model of spatial memory

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Decades of research have shown that temporal encoding context is a powerful organizing principle in memory. When remembering lists of words, subjects tend to recall items together that were presented in nearby list positions (“temporal clustering”). The retrieved context framework explains these results by assuming that new memories are stored along with a slowly changing context representation, which cues similar memories at retrieval. Outside of the laboratory, our experiences unfold over both time and space, raising the question of how spatial context affects memory organization. Studies using virtual environments to simulate a varying spatial encoding context, show that spatial distances likewise organize subjects’ memories, such that subjects recall items together that were encoded in nearby spatial locations. Unlike temporal recall organization, this “spatial clustering” effect depends on a learned cognitive map of an environment’s spatial layout. The hippocampus has been implicated in both spatial navigation and episodic memory, and the discovery of hippocampal place cells, time cells and concept cells has motivated an ongoing effort to establish an overarching theory of MTL function. Here, we present a formal computational model that (1) learns spatial maps from a slowly changing temporal context vector and (2) stores and retrieves individual items along with their spatio-temporal context. By running simulations, we show that our model acquires spatial knowledge over time, resulting in both spatial and temporal clustering effects during episodic recall. As such, our model provides a parsimonious, unified account of cognitive mapping and episodic memory in medial temporal lobe circuits.

1-001. Signatures of rapid synaptic learning in the hippocampus during novel experiences

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Neurons in the hippocampus exhibit striking selectivity for specific combinations of sensory features, forming representations which are thought to subserve episodic memory. Even during a completely novel experience,

ensembles of hippocampal “place cells” are rapidly configured such that the population sparsely encodes visited locations, stabilizing within minutes of the first exposure to a new environment. What cellular mechanisms enable this fast encoding of experience? Recent work has implicated a novel “behavioral-timescale” synaptic plasticity (BTSP) rule in hippocampal area CA1 which can rapidly modify neuronal tuning, but it remains unclear how ubiquitous this mechanism is during novel learning.

We leveraged virtual reality and large scale neural recordings to dissect how novelty and experience affect the dynamics of place field formation. We show that the place fields of many CA1 neurons transiently shift locations and modulate the amplitude of their activity immediately after place field formation, rapid changes in tuning that are predicted by BTSP. Place fields exhibited firing motifs consistent with underlying plateau potentials and somatic burst spiking, and these signatures were particularly enriched during initial exploration of a novel context and decayed with experience. Our data indicate that novelty modulates the effective learning rate in CA1, favoring burst-driven field formation to support fast synaptic updating during new experience.

To probe the mechanisms underlying these transient representational changes, we also recorded calcium dynamics from axonal projections of the locus coeruleus (LC) as they terminate in CA1, using the same context switching paradigm. Exposure to the novel environment briefly altered the pattern of LC activation, congruent with the hypothesis that broader novelty detection circuits may open a temporary window of heightened plasticity via adjusting neuromodulatory tone. In CA1, we suggest one consequence of this may be to transiently increase the probability of plateau potentials, which could upregulate BTSP during novel experiences.

1-002. Differential effects of time and experience on hippocampal representational drift

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Hippocampal place-cell activity is thought to support the formation of a cognitive map that allows the association of an event to its spatial context. It has long been thought that within familiar spatial contexts, such neuronal representations should be stable over time, and that individual place cells should retain their coding properties. However, recent findings have demonstrated that hippocampal codes gradually change over timescales of minutes to weeks. Several studies have suggested that this gradual drift in the ensemble activity patterns of hippocampal neurons could serve as a mechanism for the encoding of the temporal aspect of episodic memory, by linking or separating in memory experienced events based on their temporal proximity. These findings raised several fundamental questions: What are the contributions of the passage of time and the amount of experience to drift in hippocampal representations? To what extent are different aspects of place-code stability affected by time and experience? To address these questions, we used Ca2+ imaging to record CA1 activity in mice that repeatedly explored two familiar environments. The different environments were visited at different intervals (every 2 or 4 days), which allowed distinguishing between the contribution of time and experience to representational drift. We found that time and experience differentially affected distinct aspects of hippocampal place codes: changes in activity rates were mostly affected by time, whereas changes in spatial tuning were mostly affected by experience. Overall, our results demonstrate that the time-driven changes in activity rates are shared across contexts while experience-driven changes in tuning are context-specific. These findings suggest that different biological mechanisms underlie different aspects of representational drift in the hippocampus.

1-003. Time cell encoding in deep reinforcement learning agents depends on mnemonic demands

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The representation of “what happened when” is central to encoding episodic and working memories. Recently discovered hippocampal “time cells” are theorized to provide the neural substrate for such representations by forming distinct sequences that encode both time elapsed and sensory content. However, while multiple neurophysiological studies have presented contradictory results on the role of “time cells” in memory, little work has directly addressed this discrepancy. Here, we hypothesize that this discrepancy is a result of different studies

using tasks that involve different cognitive demands, which affect what the brain optimizes for, and thus, the emergence and informativeness of “time cells”. To test this, we trained deep reinforcement learning (DRL) agents on a simulated trial-unique nonmatch-to-location (TUNL) task, and analyzed the activities of artificial recurrent units using neuroscience-based methods. We show that, after training, representations resembling “time cells” naturally emerged in the artificial recurrent units. Furthermore, using a modified version of the TUNL task that did not require the agent to remember the sample during the delay period, we show that a task with memory demands is necessary for the “time cells” to encode information about the sensory stimuli for long periods of time. Our findings help to reconcile current discrepancies regarding the involvement of “time cells” in memory-encoding by providing a computational, normative explanation. Our modelling results also provide concrete experimental predictions for future studies.

1-004. Hippocampal networks support continual learning and generalisation

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The ability to continually adapt to the environment is key for survival. How the brain learns continuously while retaining previous knowledge is not known. Using a combination of neural and behavioural data analysis together with deep learning modelling, we studied the role of the hippocampus in continual spatial reinforcement learning. First, we introduce a deep recurrent Q-learning agent consistent with the hippocampal architecture (hcDRQN) along with three control models: a non-recurrent model (hcDQN) and two standard machine continual learning algorithms. We trained all these reinforcement learning agents in a virtual environment with partial observability mimicking the experimental neuroscience setup. Our results show that not only does the hcDRQN model achieve the best performance across tasks, but that is the model that best captures animal behaviour during continually interleaved ego- and allocentric tasks. Next, we used demixed Principal Component Analysis (dPCA) to analyse neural recordings from 612 neurons of hippocampal CA1 as animals were trained over multiple days on the same ego-allocentric tasks. We found that CA1 neurons encode reward, task rule and time specific components. Next, we performed the same dPCA analyses in our reinforcement learning models, which show that hcDRQN is the model that best captures the neural data. Finally, to test how well the different models learnt ego-allocentric tasks we conducted a range of generalisation tests in which hcDRQN clearly outperformed all the other models. Overall, our results suggest that hippocampal networks support continual learning in the brain.

1-005. The dynamical regime of mouse visual cortex shifts from cooperation to competition with increasing visual input

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Recent experiments have revealed that visual cortex operates as an inhibition-stabilized network (ISN), in which unstable excitatory coupling is balanced by strong inhibition. Computational models like the stabilized supralinear network (SSN) describe the mechanisms behind this regime, and also postulate that a transition occurs from non-ISN to ISN dynamics with increasing visual input. However, while some studies find input-dependent effects that support a shift in dynamical regime, others have shown ISN-like dynamics in the spontaneous state, leaving open questions about the existence and nature of such a transition, and how it might be measured experimentally. To resolve these unknowns, we combined photostimulation experiments in mouse primary visual cortex and

computational network modelling to study cortical dynamics over different visual input levels. We performed simultaneous all-optical recordings and stimulation of groups of L2/3 excitatory neurons to infer the influence of each stimulated neuron on the local excitatory network. Focusing on this influence as a function of signal correlation, we observed a shift from an excitatory influence at spontaneous and low-input regimes to an inhibitory influence with high visual input. To elucidate the circuit mechanisms behind these results, we modelled the perturbation experiments using a rate network. We observed that this shift in influence can be explained by an increase in synaptic connectivity efficacy as a function of visual input. Finally, we found that an SSN-like power-law non-linearity could act as a plausible mechanism behind this efficacy change. Together, these results show that the dynamical regime of mouse visual cortex becomes more inhibition dominated as visual input increases, transitioning from excitatory cooperation towards more inhibitory competition. Moreover, this dynamical regime change is feature-specific, which could explain why it is not observed in population-level perturbation experiments, thereby reconciling previously conflicting results and supporting the SSN as a plausible model of cortical dynamics.

1-006. Thalamic role in human cognitive flexibility and routing of abstract information.

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Interactions across the frontal cortex are critical for cognition. Animal studies suggest a role for mediodorsal thalamus (MD) in these interactions, but the computations performed and direct relevance to human reasoning are unclear. Here, inspired by animal work, we build a neural model to derive computational insights and find consistent evidence in fMRI data of humans performing the same probabilistic reversal learning task. We used a reservoir recurrent neural network as a model of the dorso-lateral prefrontal cortex (dlPFC) and found that adding an MD layer with multiplicative inputs to dlPFC supports flexible learning and behavioral switching. In addition, we found a novel computational mechanism where the dlPFC-MD interactions enable the circuit to integrate inputs from other frontal regions, such as the orbitofrontal cortex (OFC), to coordinate the selection of behavioral strategy. Model simulations revealed that integrating votes on behavioral strategy was dependent on an intact MD, and routing votes to MD, rather than dlPFC, required far fewer parameters. Human fMRI data supported these predictions and demonstrated activity from OFC routed to the MD thalamus, when human participants switched behavioral strategies. Collectively, our findings reveal a thalamic role in flexible representations and routing of abstract task information across frontal cortical areas in the human brain.

1-007. The geometry of map-like representations under dynamic cognitive control

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Recent work has shown that abstract, non-spatial relationships between task-relevant states or entities are organized into map-like neural representations^{1–5}. Here, we investigate how these map-like representations interact with changing task goals in the context of cognitive control, where the features most relevant to the current goal benefit from top-down biasing. Classic computational neuroscience studies of cognitive control have focused on explicitly presented categorical features rather than map-like representations retrieved from memory, and have typically found facilitation of task-relevant features and suppression/compression of task-irrelevant features^{6–8}. Here, we explore the relationship between cognitive control and the geometry of map-like representations by combining neural network models and fMRI of the same task³. Consistent with previous findings, we found that although only one of two task attributes was behaviorally relevant for current decisions, hippocampus (HC), entorhinal cortex (EC), and orbitofrontal cortex (OFC) spontaneously organized pairwise relationships into 2D

map-like representations. Consistent with the predictions of the neural-network models, new analyses of the fMRI data show that task-irrelevant dimensions were compressed relative to task-relevant dimensions dynamically as a function of which dimension is currently relevant, in dorsomedial frontal (DMFC) and posterior and medial parietal cortex (PMC). Furthermore, the model's underlying 2D representations were also affected by task demands in a different way: representations were skewed along the 2D axis that remains unchanged across conditions requiring focus on each dimension separately. This finding was confirmed by fMRI analyses showing that this same skewing phenomenon occurs in the HC, and that the degree of skewing was correlated with individual differences in cognitive control. Further simulations showed that this skewed geometry reflects the natural tendency of neural networks to learn context-invariant maps, consistent with behavioral and fMRI results.

1-008. Multi-task representations across human cortex transform along a sensory-to-motor hierarchy

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Hierarchical cortical organization unifies the brain's structural and functional organization, yet its relationship to task-evoked cognitive processes remains unclear. How might intrinsic hierarchical properties shape and constrain the cognitive processes required to perform the wide variety of tasks encountered in daily life? By analyzing a human functional magnetic resonance imaging (fMRI) data set with 26 unique cognitive tasks collected per participant, we characterized the geometry and topography of multi-task representations across the cortical hierarchy using representational similarity analysis. Empirically, we found that task representations in unimodal (sensorimotor) areas were high dimensional and segregated from other functional networks, while task representations in transmodal (association) areas were low dimensional but integrated across networks. Further analysis of whole-cortex representational organization revealed a sensory-association-motor axis that first compressed, then expanded multi-task representations from sensory to motor cortices. To identify the computational mechanisms underlying the compression-then-expansion of task representations, we trained a multi-layer artificial neural network modeling (ANN) to model the transformation of empirical task activations. We found that the compression-then-expansion of task representations exclusively emerged in a "rich" training regime, when ANNs were initialized with low-norm weights. In this rich training regime, the ANNs' internal representations had greater similarity to empirical fMRI representations across the cortical hierarchy. Further analysis of the ANN's organization revealed that richly trained ANNs learned low-dimensional connectivity weights with heavy-tailed distributions, resulting in hierarchically structured internal representations. In contrast, ANNs trained in the so-called "lazy" regime, where ANNs were initialized with large-norm weights, ANNs failed to learn hierarchically structured representations. Together, these results provide a characterization of multi-task representations across the cortical hierarchy, while establishing computational mechanisms for building brain-like, hierarchical representations in ANN models.

1-009. Neural network size balances representational drift and flexibility during Bayesian sampling

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A hallmark of natural intelligence is the ability to sustain stable memories while flexibly learning new associations, allowing animals to adapt to dynamic environments while executing precise behaviors years after they were first learned. Yet, recent experiments have revealed that neural representations of fixed stimuli change continuously over time, contravening the classical assumption that learned features should remain static to maintain task proficiency. The phenomenon of representational drift can be reconciled with normative principles for neural computation within the framework of probabilistic inference: drift in neural responses arises naturally during Bayesian sampling, which is a minimal model for noisy synaptic updates in the brain. However, our theoretical understanding of representation learning in deep Bayesian neural networks (BNNs) is generally poor. Here, we take the first step towards developing a rigorous theory of representation learning and drift by characterizing the statistics of the representational similarity kernels of each layer of large but finite BNNs. We show that network size controls the tradeoff between representational stability and flexibility: infinite BNNs are stable but have inflexible internal representations, while finite networks are flexible, but their kernels inevitably drift. In linear networks, we obtain

a precise analytical description of how network architecture and the similarity between input stimuli affect the statistics of learned representations. During equilibrium sampling, representations of dissimilar stimuli drift more over time than representations of similar stimuli. Taken together, our results begin to elucidate how stimulus-dependent representational drift can arise in normative Bayesian models for neural computation. Moreover, they provide experimentally testable predictions for the structure of drift.

1-010. Latent Equilibrium: A unified learning theory for arbitrarily fast computation with arbitrarily slow neurons

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Fast cortical processing is required in many scenarios where both sensory input and the corresponding cognitive responses change rapidly. Therefore, efficient learning in such networks needs to tackle the issue of credit assignment continuously, in real time. Recent years have witnessed a surge of cortical learning models which address this question by approximating the error backpropagation algorithm. However, all of these either require long relaxation phases following a change in sensory stimuli, which renders them unable to cope with the fast time scales imposed by, e.g., saccades, or impose some form of rapidly phased learning, which is difficult to reconcile with experimental observations. We introduce Latent Equilibrium, a framework for inference and learning in networks of slow components which avoids these issues by harnessing the ability of biological neurons to phase-advance their output with respect to their membrane potential. This mechanism enables quasi-instantaneous inference independent of network depth and avoids the need for computationally expensive relaxation phases, allowing networks to learn from stimulus-target pairs with dynamics on near-arbitrarily short time scales. We derive neuron morphology, network structure, and in particular disentangled neuronal and synaptic weight dynamics from a single prospective energy function. The resulting model can be interpreted as a real-time, biologically plausible approximation of error backpropagation in deep cortical networks with continuous-time, leaky neuronal dynamics and continuously active, local synaptic plasticity. We demonstrate successful learning from continuous input streams, achieving competitive performance with both fully-connected and convolutional architectures on standard benchmark datasets. We further show how our mathematical framework can be embedded within cortical microcircuits. Finally, we study the robustness of our model to spatio-temporal substrate imperfections to demonstrate its feasibility for physical realization, both *in vivo* and *in silico*.

1-011. Single-phase deep learning in cortico-cortical networks

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The error-backpropagation (backprop) algorithm has stood at the forefront as a solution to the credit assignment problem in artificial neural networks. Whether the brain adopts a similar strategy to ensure that the correct synapses are modified remains unclear. Recent work has attempted to bridge this gap with backprop-like learning mechanisms that are consistent with several cortical experimental observations. However, these models are either unable to effectively backpropagate error signals across several brain areas or require a multi-phase learning process, neither of which are reminiscent of learning in the brain. Here, we introduce a new model, bursting cortico-cortical networks (BurstCCN), which solves these issues by integrating biologically-plausible bursting, dendritic feedback and cell-type specific functional connectivity. Our model uses a burst-dependent synaptic plasticity rule and connection-type-specific short-term synaptic plasticity to enable burst multiplexing. In addition, our model relies on apical dendrite-targeting (SST) interneurons to maintain E/I balance and facilitate the encoding of error signals. We show that our model can efficiently backpropagate errors across several brain areas, a core

property of backprop, using a learning process with just a single phase. We also demonstrate successful credit assignment with Dalián constraints, proposing a role for both inhibitory (SST, PV, NDNF) and disinhibitory (VIP) cell-types. Overall, our work suggests that specific excitatory-inhibitory cortico-cortical connectivity with both short- and long-term synaptic plasticity, jointly underlie single-phase efficient deep learning in the brain.

1-013. Biological multi-task learning with top-down signals

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Animals naturally display a wide range of behaviours in varying contexts. Not only do their actions depend on their internal states, but also how their early sensory cortex processes information. Here, we propose that contextual top-down afferents adapt the receptive fields of sensory neurons to accommodate varying task demands. Although this view is widely supported by connectomic and electrophysiological evidence, a mechanistic and, in particular, a normative understanding is still lacking. We investigate how task-dependent top-down signals can reshape the functional mapping of sensory processing networks with fixed feedforward synaptic weights in order to solve multiple different tasks. In computational terms, the contribution of these modulations can be framed as a shift in gains and/or biases of artificial neurons. In biological neurons, we show that N-methyl-D-aspartate (NMDA) spikes in dendritic subunits are well suited to implement such modulations. Our work demonstrates that a single set of feedforward synaptic weights together with task-specific biases and/or gains can indeed solve multiple tasks, when fine-tuned by supervised learning. This approach is also suitable for transfer learning, as the top-down modulation can be adapted for new tasks without further changes in the feedforward network connections. This type transfer learning framework provides a novel criterion to evaluate the quality of a set of feedforward weights. With this in mind, we infer an unsupervised learning algorithm derived from a geometrical argument based on the structure of decision boundaries to derive synaptic weights that perform well in concert with contextual modulation. We demonstrate that the resulting method outperforms networks using common neuronal unsupervised learning algorithms. Overall, our work represents a new framework for understanding sensory processing, and sheds light on the computational mechanisms by which top-down afferents can flexibly adapt feedforward pathways for a variety of tasks.

1-014. Fine-tuning hierarchical circuits through learned stochastic co-modulation

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Humans and animals can quickly adapt to new task demands while retaining previously-developed capabilities, but the neural mechanisms of such flexibility remain unclear. While neural computations are governed by synaptic interactions, adjusting the strength of all synapses to allow this behavioral adaptation would likely be slow and not easily reversible. Here we use intrinsic, structured gain fluctuations to rapidly and transiently fine-tune hierarchical neural networks for a particular task. This mechanism takes inspiration from well documented low-dimensional covariability in visual areas of the brain, which has been attributed to shared gain modulation in task-informative neurons (Rabinowitz et al., 2015; Bondy et al., 2018; Haimerl et al., 2021). We construct a multi-layer neural network whose primary encoding stage is modulated by a stochastic gain signal, with learned task-specific targeting. These fluctuations act as a label of informative neurons, and accompany the stimulus signal as it traverses the hierarchy. Upon reaching the decision layer, this label facilitates task-specific decoding, without relying on changes in network weights. Trained stochastic gain modulation allows the circuit to adapt to novel tasks, achieving good performance with minimal task experience. It is not only faster than relearning all network weights but also instantly reversible (disabling modulation restores initial network computation). This mechanism also achieves better performance than deterministic gain increases traditionally used to model attentional mechanisms. Overall,

these results provide a novel explanation of how the brain can flexibly, robustly and reversibly adapt to changes in task structure.

1-015. Insight moments in neural networks and humans

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The success of neural networks derives from the fact that they can learn useful representations of observed inputs. However, the dynamics of when and how fast a network will discover good representations are not well understood, even when network training is governed by gradient descent. The potential complexity of learning dynamics is particularly apparent in so called insight moments, when useful task representations are discovered suddenly following a delay during which no learning is noticeable. Such insights are commonly observed in animals and humans, where they are often taken to reflect explicit strategy discovery or shifts of attention, but whether they arise in neural networks trained with incremental gradient descent is unknown. Here, we study how and when insight moments arise in neural networks and humans. We employ a two-alternative forced choice task in which input feature relevance changes after initial training, such that previously learned input representations can be relearned to improve behavioural efficiency. We reasoned that this non-stationary feature relevance poses unique computational challenges that could trigger insight-like learning dynamics. In line with previous research, we show that about half of human volunteers performing this task showed insight-like learning about newly relevant features. A simple linear neural network with three nodes trained on the same task with baseline performance matched to humans and regularised gate modulation on the two input nodes, exhibited abrupt learning dynamics resembling insight-like behaviour – despite its gradual learning rule and simple architecture. Finally, we show analytically that L1 regularisation of gain factors is a core mechanism behind insight-like learning in neural networks, whereby frequency and delay depended on the regularisation parameter lambda. Our results suggest that insight phenomena can arise from regularised gradual learning mechanisms and shed light on learning dynamics and representation formation in intelligent agents more generally.

1-016. What do meta-reinforcement learning networks learn in two-stage decision-making?

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The striatum and prefrontal cortex (PFC) play critical roles in reinforcement learning (RL). The striatum implements a model-free RL algorithm by driving synaptic plasticity modulated by dopaminergic prediction errors. The PFC, in turn, is thought to implement a model-based algorithm through its neuronal dynamics. The role and interplay of both regions can be successfully modeled in the meta-RL framework, whereby a striatal model-free learning algorithm is used to adjust synaptic weights of the PFC network, enabling a free-standing learning algorithm through neuronal dynamics. However, it is unclear which free-standing learning algorithm emerges in PFC from the training procedure. To answer this question, we trained recurrent neural networks on the widely-studied two-stage task, in which two first-stage actions probabilistically lead to two rewarding second-stage states. We then analyzed networks' representational geometry. We found that the networks acquired a representation with neural activity grouped by second-stage state and reward. In this space, points (i.e., neural activity on one trial) in each group formed curves. The relative location of points along these curves roughly corresponded to action probabilities. To elucidate mechanisms giving rise to these curves, we fit behavioral models to networks' action probabilities, including model-free, reward-as-cue, model-based (MB), and latent-state (LS) algorithm families. The MB and LS families provided the best fits. Surprisingly, trial-by-trial choice probabilities predicted by the LS, but not the MB model, were consistent with networks' action probabilities. Additionally, the more training the networks received, the more the networks sharpened their dynamics towards the LS representation. Our results

demonstrate that the networks learned an augmented latent-state representation in the two-stage task. More generally, we offer a systematic approach for "opening the black box" of meta-RL agents, identifying emergent algorithms, and adjudicating model families (e.g., MB vs. LS) previously thought to be difficult to distinguish in animal experiments.

1-017. Neural optimal feedback control with local learning rules

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A major problem in systems neuroscience, specifically in sensory-motor control, is understanding how the brain plans and executes proper movements in the face of delayed and noisy stimuli. A prominent framework for addressing such control problems is Optimal Feedback Control (OFC). OFC generates control actions that optimize behaviorally relevant criteria by integrating noisy sensory stimuli and the predictions of an internal model using the Kalman filter or its extensions. However, a satisfactory neural model of Kalman filtering and control is lacking because existing proposals have the following limitations: not considering the delay of sensory feedback, training in alternating phases, and requiring knowledge of the noise covariance matrices, as well as that of systems dynamics. Moreover, the majority of these studies considered Kalman filtering in isolation, and not jointly with control. To address these shortcomings, we introduce a novel online algorithm which combines adaptive Kalman filtering with a model free control approach (i.e., policy gradient algorithm). We implement this algorithm in a biologically plausible neural network with local synaptic plasticity rules. This network performs system identification and Kalman filtering, without the need for multiple phases with distinct update rules or the knowledge of the noise covariances. It can perform state estimation with delayed sensory feedback, with the help of an internal model. It learns the control policy without requiring any knowledge of the dynamics, thus avoiding the need for weight transport. In this way, our implementation of OFC solves the credit assignment problem needed to produce the appropriate sensory-motor control in the presence of stimulus delay. To test the performance of our network, we considered, among others, the task of making reaching movements in the presence of externally imposed forces. Our network successfully captures the characteristics of human trajectories in the null field, the force field, as well as during adaptation.

1-018. Principled credit assignment with strong feedback through Deep Feedback Control

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The success of deep learning sparked interest in whether the brain similarly learns its hierarchical representations. However, current biologically-plausible models for hierarchical credit assignment (HCA) –i.e., determining how to adjust synapses across hierarchies– assume that the effect of feedback on forward processing is negligible. This weak feedback assumption is problematic in biologically realistic noisy environments and is at odds with experimental evidence showing that the effect of feedback on neural activities can be strong. To overcome this limitation, we revisit the recent Deep Feedback Control (DFC) method. In DFC, a feedback controller nudges a deep neural network to match a desired output target and uses the resulting control signal for HCA through a learning rule local in space and time. Unlike DFC, we now let feedback strongly influence the neural activity, by taking the supervised label as target instead of a nudged output, thereby invalidating the original theoretical foundation of DFC. Using the implicit function theorem, we show that DFC with strong feedback gradually reduces

the amount of feedback required from the controller, resulting in a novel view of learning that can be intuitively understood as help minimization. Further, we show that overcoming the need for help is equivalent to achieving zero output loss with a traditional training objective. We complement our theory with standard computer-vision experiments, showing competitive performance to less biologically-plausible methods like backpropagation and standard DFC. To summarize, by drawing inspiration of how feedback affects neural activity in the brain and by combining dynamical systems and optimization theory, we offer a new theoretical framework to investigate how the brain can learn hierarchical representations through principled optimization. This initiates a novel line of research that can lead to testable experimental predictions, such as the presence of feedback that substantially changes neural activity and whose magnitude decreases with learning.

1-019. A closed-loop emulator that accurately predicts brain-machine interface decoder performance

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Intracortical brain-machine interfaces (iBMIs) aim to provide naturalistic communication and movement for those with paralysis by decoding neural spikes into actions 1–10. iBMIs traditionally require closed-loop *in vivo* experiments to develop, design, optimize, and benchmark decoder algorithms. Although offline evaluation provides insight into what algorithms are promising, the discrepancy between offline and online performance may lead to incorrect conclusions that mislead algorithm design 11–15. We therefore aim to build an emulator that accurately characterizes online decoder performance without neurosurgery. We build on a prior emulator that correctly optimized decoder bin width by generating synthetic neural spike counts from hand kinematics using a tuning model 11. A limitation of this study is that a tuning model is insufficient to reproduce complexities in neural firing rates and population activity, including multiphasic PSTHs, neural trajectories, and neural dynamics 16. To address this, we used neural network based encoder to transform hand kinematics to synthetic neural activity in our emulator.

We evaluated our emulator by performing three published iBMI experiments and quantitatively compared the emulator's predictions to the empirical results. We chose these three studies to test: linear decoders (FIT-KF and VKF) 17, a two-stage trained decoder (ReFIT-KF) 18, and a nonlinear decoder (FORCE) 19. Our emulator correctly reproduced the conclusions of these studies, in addition to reproducing precise details of control, including: (1) distance-to-target profiles, closely matching the first touch time (FTT) and the dial-in time (DIT), (2) the distribution of trial times, and (3) cursor trajectories observed in prior monkey online experiments. These results suggest it is feasible to accurately predict iBMI performance without neurosurgery, enabling quantitative comparisons between different types of decoding algorithms. We anticipate this system can facilitate and accelerate the development of iBMI decoders.

1-020. Learning input-driven dynamics from neural recordings

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Large scale neural recordings are typically found to embed lower-dimensional structure that reflects behaviour. Empirically, the best models of such low-dimensional structure – by several statistical measures – tend to be those that describe neural recordings via a latent dynamical system. Importantly, as recordings are typically made in one or a subset of areas within the brain, the dynamics that best capture the data cannot in general be expected to be fully autonomous, but may instead be driven by unobserved inputs. Learning the parameters of a probabilistic dynamical system whilst simultaneously inferring any unobserved inputs is a difficult and somewhat ill-posed problem. Here, we propose a new method to tackle this that harnesses recent developments in differentiable control and faithfully recovers ground-truth dynamics in a range of synthetic input-driven systems. Similarly to Pandarinath et al. (2018) we formulate our model as a variational auto-encoder where the generator is an input-driven recurrent neural network (RNN). However, instead of using yet other RNNs to parametrize the decoder, we perform amortized inference using iLQR, a powerful nonlinear controller that finds the set of inputs most likely to

have given rise to the data. This greatly reduces the number of (hyper)-parameters in our model, thus facilitating learning. Moreover, iLQR enables flexible inference on trials of varying duration and population size with no further modifications, which was difficult with previous RNN-based decoders. We demonstrate the utility of our method on several synthetic and real datasets. We first show that it can successfully learn the dynamics of a variety of low-dimensional systems. Next, we validate it on two sets of neural recordings from monkey M1 during reaching tasks, and dissect the dynamics and inputs inferred in both cases.

1-021. Bayesian Inference in High-Dimensional Time-Series with the Orthogonal Stochastic Linear Mixing Model

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The activity of 100s-1000's of neurophysiological signals can be recorded during behaviors and in response to sensory stimuli, creating high-dimensional time-series data. Understanding such data is often aided by methods that extract low-dimensional latent structure present in the high-dimensional recordings. Multi-output Gaussian process models leverage the nonparametric nature of Gaussian processes to capture structure across multiple outputs. However, this class of models typically assumes that the correlations between the output response variables are invariant in the input space (e.g., sensory stimuli). We present the stochastic linear mixing model (SLMM), which utilizes a conditional linear mapping function between latent variables and observations without loss of the geometric interpretation of the subspace. In our formulation, the mixture coefficients depend on inputs, making SLMM flexible and effective to capture complex output dependencies. However, the inference for SLMMs is intractable for large datasets, making them inapplicable to modern neuroscience data. Thus, we propose a new regression framework, the orthogonal stochastic linear mixing model (OSLMM), that introduces an orthogonality constraint amongst the stochastic mixing coefficients. This constraint dramatically reduces the computational burden of inference while retaining the capability to handle complex output dependencies, and also contributes to extraction of more interpretable latent trajectories. Moreover, we put a uniform prior on the orthogonal subspace (Stiefel manifold) to manage the variability of subspaces. We provide Markov chain Monte Carlo (MCMC) inference procedures for both SLMM and OSLMM, and demonstrate superior model scalability and reduced prediction error of OSLMM compared with state-of-the-art methods in several real-world data-sets. In neurophysiology recordings from auditory cortex, we use the inferred latent functions for compact visualization of population responses to stimuli, and demonstrate superior results compared to a competing method (GPFA). Together, these results demonstrate that OSLMM will be useful for analysis of large-scale time-series data increasingly common in neuroscience.

1-022. Bayesian active learning for latent variable models of decision-making

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Characterizing perceptual decision-making is an important goal of systems neuroscience. Recent work has shown that animal decision-making behavior is not stationary, but exhibits switches between discrete latent states within a single experimental session. However, fitting these complex models requires large amounts of data, a crucial impediment to progress. Here we propose to overcome this obstacle by introducing active learning methods for discrete latent variable models of decision-making. Active learning seeks to improve the efficiency of experiments by selecting highly informative stimuli on each trial. However, past work has largely overlooked active learning for latent variable models (LVMs). To address this gap, we propose a novel framework for "infomax" stimulus selection in discrete latent variable regression models. Our approach relies on sampling of the joint distribution over latents and model parameters to evaluate information gain, which we use to select the maximally informative stimulus on each trial. We begin with an application to a simple "mixture of linear regressions" (MLR) model; although it is well known that active learning confers no advantage in standard linear regression settings, we show that for mixtures of linear regressions, our method can provide dramatic gains. We then proceed with an application to Input-Output Hidden Markov Models (IO-HMMs), a family of highly expressive regression models for time series data, which have proven useful in diverse applications including perceptual decision-making. We show that our method substantially reduces the number of trials needed to learn the parameters of these models. We expect this method to have broad applicability for improving experimental efficiency in neuroscience and beyond.

1-023. Identifying latent states in decision-making from cortical inactivation data

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Recent work has shown that rodent decision-making relies on distinct latent or hidden states that switch on a timescale of tens to hundreds of trials [Ashwood 2021; Bolkan, Stone 2021; Weinhammer 2021]. However, the neural basis for these states, and the contributions of different brain regions to state-dependent decision-making strategies, remains an important open problem. Here we address this challenge by performing a model-based analysis of decision-making data acquired during multi-region laser-scanning inactivation of dorsal cortex. We analyzed optogenetic inactivation data from mice performing a visual-evidence-accumulation task while navigating in a virtual environment (a publicly available dataset from Pinto et al. 2019). In this dataset, 29 different individual cortical regions were bilaterally inactivated during a randomly interleaved subset of trials. We fit choice data from these experiments using a Hidden Markov Model (HMM) with Bernoulli Generalized Linear Model (GLM) observations. The resulting GLM-HMM framework describes choice behavior with state-specific GLMs that quantify how the animal combines different features (e.g., sensory evidence, bias, choice history) to make decisions in each state, and a matrix of transition probabilities governing the switches between states. To incorporate the effects of neural perturbations on behavior, we grouped the 29 inactivation sites into three clusters. We then extended the model by adding GLM weights for each cluster, allowing inactivation of each cluster to have distinct, state-specific effects on choice. Our preliminary analyses revealed that a multi-state GLM-HMM substantially outperformed a basic GLM at predicting behavior, and suggested that the effects of bilateral inactivations in dorsal cortex were highly state-dependent, with the sign and strength of the effect on choice varying substantially across states.

1-024. Modeling multi-region neural communication during decision making with recurrent switching dynamical systems

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Understanding how multiple brain regions interact to produce behavior is a major challenge in systems neuroscience. Sensory-driven decision making, in particular, has been shown to involve context-dependent processing in multiple brain regions, but a precise description of the interactions between regions remains an open problem. Addressing this problem requires new methods for inferring multi-region activity that account for sensory inputs and communication between brain regions. Here we develop multi-region switching state space models with higher-order autoregressive dynamics, allowing for time-varying estimation of directed, multi-region interactions. The approach models high dimensional multi-region observations as emissions from coupled, low dimensional dynamical systems with explicit local dynamics and communication across time-lags. To fit the model, we derive variational Laplace EM (vLEM) for autoregressive dynamical systems, extending vLEM to the case of higher order AR dynamics. We additionally introduce a measure of the volume of communications between brain regions across time in the model, allowing us to quantify the directional ‘messages’ communicated between regions at each timepoint. We use the model to analyze two calcium imaging datasets in mice performing a sensory decision making task: mesoscale wide-field recordings, and cellular-resolution two-photon mesoscope recordings, simultaneously from 16 and 3 brain regions, respectively. In both cases, our method reveals multiple distinct, task-driven dynamical states, and produces rich estimates of communication flows across regions, revealing in-

teractions that match known connectivity and hypothesized functional roles of different areas. Preliminary analysis suggests large-scale cortico-cortical interactions are a more important determinant of cortical dynamics than the sensory input, despite the sensory nature of the task. Thus, we introduce an important approach to analyzing and understanding multiregion neural activity and communication in decision making tasks.

1-025. Rapid fluctuations in functional connectivity of cortical networks encode spontaneous behavior

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Experimental work across a variety of species has demonstrated that spontaneously generated behaviors are robustly correlated to variation in neural activity within the cerebral cortex. Indeed, functional magnetic resonance imaging (fMRI) data suggest that functional connectivity in cortical networks varies across distinct behavioral states, providing for the dynamic reorganization of patterned activity. However, these studies generally lack the temporal resolution to establish links between cortical signals and the continuously varying fluctuations in spontaneous behavior typically observed in awake animals. Here, we take advantage of recent developments in wide-field mesoscopic calcium imaging to monitor neural activity across the neocortex of awake mice. Diverging from traditional analysis of functional connectivity as a static entity, we explored the temporal dynamics of connectivity as expressed by instantaneous correlations between functional brain parcels. We develop a novel analysis, termed “graph-of-graphs”, that views the temporal fluctuations of correlations as high dimensional observations of a dynamical system and aims to extract their latent dynamics. We use Riemannian geometry and diffusion geometry to extract a low dimensional representation capturing the intrinsic dynamics of the functional connectivity. Using this novel approach, we demonstrate that spontaneous behaviors are more accurately represented by fast changes in the connectivity structure versus the activity of large-scale network. Moreover, the dynamics of the extracted functional connectivity representation reveals subnetworks that are not evident in traditional anatomical atlas-based parcellation of the cortex. For a small-scale network such as cells in the primary visual cortex, we show that there is no significant difference in the representation of behavioral variables using either embedded activity or embedded correlations, which means that the internal mechanisms of behavior encoding vary with scale. These results provide insight into how behavioral information is represented across the mammalian neocortex and demonstrate a new analytical framework for investigating time-varying functional connectivity in neural networks.

1-026. Fitting recurrent spiking network models to study the interaction between cortical areas

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We performed extra-cellular recordings simultaneously from the whisker primary sensory cortex (wS1) and the medial prefrontal cortex (mPFC) of mice performing a tactile detection task and then fit a recurrent spiking neural network (RSNN) to the recorded activity. We assume that neural dynamics are defined by standard conductance-based spiking neurons with adaptation. We optimize the entire connectivity matrix (within and across areas) using back-propagation through time (BPTT) for spiking neural networks [1, 2] and synaptic rewiring [3] while respecting Dale’s law. After optimization, the resulting matrix provides a possible connectivity pattern that explains the

recorded activity statistics in wS1 and mPFC. To validate this modelling approach, we perform a virtual ablation on the fitted model and compare the resulting activity with experimental manipulations affecting the late response component in wS1. Our model reproduces the finding that a secondary-late response of the whisker stimulation is due to feedback from higher-order cortical areas [4, 5]. Since many other areas are involved in this task in a real mouse brain, we cannot claim that we built a full model of wS1 and mPFC. However, we believe that this modelling approach can help us to understand better the activity in cortical circuits and test hypotheses concerning possible neural computations such as the importance of feedback from high-order areas to wS1.

1-027. Inter-areal patterned microstimulation selectively drives PFC activity and behavior in a memory task

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A central problem in neuroscience is to understand how areas in the brain communicate. Inputs to brain areas largely influence the intrinsic dynamics of each region, which shapes ongoing computations. Hence, characterizing how inputs drive different population responses is key to understanding how brain circuits are controlled to generate different behaviors. To this end, we developed an inter-areal patterned microstimulation (uStim) protocol that allowed us to finely manipulate the activity of a neural population in one brain area while simultaneously recording the activity of a second population in a different area. In macaques implanted with dual 96-channel Utah arrays, we manipulated the activity of different brain regions by electrically stimulating combinations of electrodes in one of the arrays while recording the effect on the other. We were able to generate a rich repertoire of activity patterns and to identify the dimensions along which different inputs drove the neural population. We used our protocol to study how the prefrontal cortex (PFC), a high-order cognitive area that displays robust memory encoding, is influenced by inter-hemispheric inputs. For this, we assessed the impact that different uStim patterns applied to the right-hemisphere PFC (RH-PFC) had on the contralateral PFC (LH-PFC) during a memory task. We found that the stimulation patterns selectively affected PFC activity in different dimensions and biased performance and reaction times. Our approach provides a causal tool to link brain activity and behavior at greater granularities, and paves the way towards data-driven models that explain how brain areas dynamically interact to produce computations.

1-029. Predicting connectivity of motion-processing neurons with recurrent neural networks

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The conversion of visual input into behavior requires whole-brain circuits of diverse neurons. Due to the inaccessibility of mammalian model systems, there exists a gap in understanding how these neurons are connected and influence neural response dynamics that underlie behavior. Recent studies into the visually guided optomotor response (OMR) in larval zebrafish have attempted to bridge this gap by proposing circuit models that predict connectivity among functionally identified response classes of motion-processing neurons driving the OMR [1,2]. However, these models only consider responses of overrepresented classes averaged across many fish and therefore ignore large swaths of the motion-responsive population, fail to capture inherent circuit dynamics, and cannot describe idiosyncrasies in neural responses and behavior. Here, we train recurrent neural networks (RNNs) with calcium imaging data to model all neurons in the pretectum (Pt), the central sensory processing

region underlying the OMR, responding to eye- and direction-specific visual motion. These models generate predictions of local and inter-hemispheric connectivity, including the signs, strengths, and numbers of synapses. Our model estimates connections between individual neurons, providing insight into the potential role of underrepresented response classes, previously from models [2]. To drive the RNNs with visual stimuli, we implemented a novel, biologically plausible set of directional-selective retinal ganglion cells providing external input to the population. We show the RNNs to be exceptional at reproducing activity from neurons with diverse responses to motion. We find the RNNs predict excitatory connections among neurons with shared motion preference and of inhibitory connections among neurons responsive to conflicting stimuli, supporting the hypothesis of shared functional roles of previously identified neural response classes. Our RNNs provide a realistic, dynamic circuit model of a complete sensory population and generates hypotheses about the nature of vertebrate information processing that will inform future photostimulation experiments to illuminate neural circuitry underlying the OMR.

1-030. Heterogeneous prediction-error circuits formed and shaped by homeostatic inhibitory plasticity

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The remarkable ability of neural networks to make predictions about the immediate future and recognize unexpected events is a ubiquitous hallmark of intelligent life. In recent years, researchers have begun to unravel the neural substrates underlying this predictive information processing [1]. An integral part of predictive processing is a subset of excitatory neurons that encode prediction errors: while negative prediction-error (nPE) neurons are only activated when sensory signals are weaker than predicted, positive prediction-error (pPE) neurons respond only when sensory signals exceed the internal predictions [1-3]. How these different types of prediction-error neurons can co-exist and simultaneously form in the same recurrent neural circuit they are embedded in, and how they are shaped by the rich diversity of cell types [4] is still largely unresolved.

To unravel the circuit-level mechanisms that underlie the parallel formation and refinement of nPE and pPE neurons, we make use of a computational model of a cortical circuit with excitatory pyramidal cells and three types of inhibitory interneurons: parvalbumin-expressing, somatostatin-expressing, and vasoactive intestinal peptide-expressing interneurons [4]. By means of a mathematically tractable model and network simulations, we show that the presence of nPE and pPE neurons requires balanced pathways that can be learned simultaneously with homeostatic inhibitory plasticity with low baseline firing rates. The resulting robust PE circuits generalize to sensory stimuli not seen during learning. Furthermore, we show that the responses to unexpected events are mainly determined by the network's initial connectivity and the distribution of actual and predicted sensory inputs onto the interneurons. Finally, we demonstrate that PE neurons can support biased perception and may underly faster learning as well as generalization across stimuli statistics. In summary, our results shed light on the formation, refinement, robustness, and computational role of PE circuits.

1-031. Novelty modulates neural coding and reveals functional diversity within excitatory and inhibitory populations in the visual cortex

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Stimulus novelty modifies perception and promotes exploration and learning. What are the neural circuit mechanisms that underlie the effects of novelty? To address this question, we trained mice on a visual change detection task, while we performed two-photon calcium imaging of neural activity from excitatory and inhibitory (VIP and SST) neuron classes across multiple layers of the visual cortex (areas V1 and LM; 82 mice, 551 sessions, 34,619 neurons). The behavioral task required detecting image changes that occurred amid repeated image presen-

tations. Additionally, flashed images were periodically (5%) omitted, thereby allowing the study of expectation violation signals. To study how novelty modulates the neural encoding of sensory and behavioral events, mice experienced two image sets across sessions: one familiar set that was used during training, and another novel set that mice had never seen before. Using population decoding, regression and clustering techniques we reveal cell-type specific changes in neural activity as a result of stimulus novelty that unfold on multiple timescales: novelty exerts rapid and transient changes in the visual responses of SST and particularly VIP neurons, in contrast to excitatory neurons. Additionally, we studied functional diversity within each cell class as a result of exposure to novelty. Individual VIP neurons encode a variety of features; while excitatory or SST neurons tend to be less multiplexed in their coding properties. Together, our results reveal functional roles for different neuron cell classes, providing a new model of microcircuitry between excitatory and inhibitory neurons. Overall, VIP activity in response to novelty is consistent with a role in gating plasticity in excitatory neurons, allowing the brain to update its predictions about the external world. Moreover, the distinct functional clusters indicate that novelty defines new microcircuits of excitatory and inhibitory neurons, which contrast the classical disinhibitory microcircuitry.

1-032. A transcriptomic axis predicts state modulation of cortical interneurons

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Transcriptomics has revealed the exquisite diversity of cortical inhibitory neurons, but it is not known whether these fine molecular subtypes have correspondingly diverse activity patterns in the living brain. Here, we show that inhibitory subtypes in primary visual cortex (V1) have diverse correlates with brain state, but that this diversity is organized by a single factor: position along their main axis of transcriptomic variation. We combined *in vivo* 2-photon calcium imaging of mouse V1 with a novel transcriptomic method to identify mRNAs for 72 selected genes in *ex vivo* slices. We used transcriptomic clusters (*t*-types) to classify inhibitory neurons imaged in layers 1-3 using a three-level hierarchy of 5 Families, 11 Subfamilies, and 35 *t*-types. Visual responses differed significantly only across the Families, but modulation by brain state differed at all three hierarchical levels. Nevertheless, this diversity could be predicted from the first transcriptomic principal component, which predicted a cell type's brain state modulation and correlations with simultaneously recorded cells. Inhibitory *t*-types with narrower spikes, lower input resistance, weaker adaptation, and less axon in layer 1, as determined *in vitro*, fired more in resting, oscillatory brain states. Transcriptomic types with the opposite properties fired more during arousal. The former cells had more inhibitory cholinergic receptors, and the latter more excitatory receptors. Thus, despite the diversity of V1 inhibitory neurons, a simple principle determines how their joint activity shapes state-dependent cortical processing.

1-033. Impact of single gene mutation on circuit structure and spontaneous activity in the developing cortex

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Understanding how neural circuits in the brain wire up during development is important for the implementation of numerous functions in adulthood, but also for the prevention and treatment of many neurological disorders that result from bad wiring. Before the onset of sensory experience, spontaneous activity in the developing brain organizes and refines circuits. Hence, alterations in spontaneous activity can lead to severe deficits in wiring. One such alteration occurs in the Fragile X mouse model, where a single genetic mutation reduces cortical inhibition and increases the number of neurons recruited in spontaneous activity. The mechanisms behind the generation of spontaneous activity remain unclear, especially regarding how genetic mutations affect spontaneous activity. To address this, we investigated how biologically realistic spontaneous activity can emerge in recurrent networks with excitatory and inhibitory neurons and background input representing the sensory periphery. We find that our model successfully captures two distinct types of spontaneous activity, local (L-) and global (H-) events, that match experimentally characterized activity originating in the sensory periphery or the cortex. During local events strong inputs from the sensory periphery result in dominant inhibition which limits lateral spread of activity. Conversely, during global events intrinsically triggered inputs produce dominant excitation which spreads laterally without restriction. We next analyzed calcium imaging data from the developing cortex of Fragile X mice revealing spontaneous activity with an increase of global and decrease in local events. Finally, we explored two plausible mechanisms that lead to this altered activity: weakened feedforward connectivity vs. reduced inhibitory recurrent connectivity. These alternatives make different experimentally-testable predictions for the relative ratio between local and global events. Our model allows us to investigate the role of connectivity profiles, intrinsic excitability, and correlations in shaping normal and genetically-altered spontaneous activity, and the implications for receptive field refinements in development.

1-034. The operating regime of primate sensory cortex

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Neuronal sensitivity and selectivity to our environment arise from the transformation of external inputs by the cortical circuitry. We dissect the circuitry for this emergence using a combination of large-scale simultaneous measurements from single cells in awake animals and computational models. In area MT, an area of the neocortex that processes visual motion, even weak motion signals evoke selective responses in the presence of noise. We also observe tuned patterns of activity in the absence of visual motion that suggest feature-selective amplification within the circuit. In addition, responses in MT have fast dynamics, posing critical constraints on the nature of the underlying amplification mechanisms. We identified different regimes in computational models capable of generating high amplification. These computational regimes exhibit distinct activity signatures, including the speed of amplification dynamics, the response to sudden shifts in input, as well as the structure and statistics of spontaneous activity. We examined the activity of large populations of primate MT neurons across the same conditions and compared the results with the computational models. We find that our recorded responses from MT network match a regime where amplification arises from separate excitatory and inhibitory populations operating in a balanced regime with tuned recurrent interactions. This allows the internal circuitry of the sensory cortex to strongly amplify incoming inputs, while maintaining sensitivity to and rapid tracking of input changes because of strong inhibitory contributions that quench amplification (Murphy and Miller, Neuron, 2009). This balanced amplification regime only emerges in models composed of segregated excitatory and inhibitory populations. Our

discovery provides a potential explanation for the specialization of neurons into distinct excitatory and inhibitory populations: the fundamental asymmetry that arises from coupling these populations is essential to the generation of large but rapid amplification without response persistence.

1-035. Gain-mediated statistical adaptation in recurrent neural networks

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Sensory neurons in different species, brain areas, and modalities adjust their sensitivity (gain) in response to recent stimulus history. This gain control offers a mechanism for single neurons to rapidly and reversibly adapt to different stimulus contexts while preserving synaptic weights that serve to represent features that remain consistent across contexts. From a normative perspective, this allows an individual neuron to adjust the dynamic range of its responses to accommodate changes in input statistics – a core tenet of Barlow's efficient coding theory. However, experimental measurements reveal that adaptation induces more complex changes in neural responses: tuning-dependent reductions in both response maxima and minima; tuning curve repulsion; and stimulus-driven decorrelation. Although coding efficiency and gain-mediated adaptation is well-studied in single neurons, this combination of normative principle and simple mechanism appears insufficient in accounting for these nuanced effects. Indeed, to explain these phenomena, previous studies have relied on adaptive changes in feedforward or recurrent synaptic efficacy, mechanisms which, while more flexible, are unlikely to operate as transiently as simple gain modulation.

We propose a normative framework for adaptive gain control in which recurrently-connected neurons dynamically adjust their gains in response to novel stimulus statistics. Specifically, gains are modulated to optimize an objective enforcing an accurate representation of their inputs while minimizing total population activity. We compare model predictions to experimental measurements of V1 neurons responding to a sequence of gratings drawn from an ensemble with either uniform or biased orientation probability. The model captures the full set of adaptation phenomena in the data simply by propagating the effects of single-neuron gain changes through the network. Thus, single-neuron gain control within a recurrent circuit, coupled with a coding efficiency objective, is sufficient to capture the observed diversity of neural adaptation responses.

1-036. Unifying model of contextual modulation with feedback from higher visual areas

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Neurons in primary Visual Cortex (V1) have a receptive field (RF) or "center", the region in visual space in which appropriate stimuli drive the neuron to fire. Stimuli surrounding the RF modulate these responses, a phenomenon known as contextual modulation. Here we consider 3 types of contextual modulation: i) classical surround suppression: the response of cells in V1 decreases when the stimulus size is increased beyond the RF size; ii) inverse surround suppression: neurons in layer L2/3 –but not layer L4– of mouse V1 respond to a lack of contrast in their RF when the surround is filled with a drifting grating ('hole' stimulus), and this response shows tuning for the size of the hole similar to i) and iii) surround facilitation: the response of cells in V1 increases when a grating stimulus in the RF is presented together with an orthogonal surround. We devise a large-scale stabilized supralinear model of rate units representing L2/3 cells, receiving recurrent, bottom-up (L4) and top-down (higher

visual areas HVA) inputs. The model is endowed with anatomically realistic length scales and physiologically constrained input patterns and is able to account for all three contextual modulation phenomena. Given the recorded inputs to L2/3 in [Keller-Nature2020], we develop a conceptual model to analytically compute the firing rate profile across layer L2/3. We shed light on the mechanisms and different factors that contribute to classical and inverse surround suppression. We predict the specific role of Somatostatin interneurons in inverse response and propose a link between inverse response and surround facilitation. We then present a ‘full’ model with three interneuron subclasses showing the robustness of the identified mechanisms. The full model is built to match recordings during the classical stimulus condition and generalizes to reproduce inverse size-tuning curves.

1-037. An interpretable spline-LNP model to characterize feedforward and feedback processing in mouse dLGN

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The dorsolateral geniculate nucleus (dLGN) of the thalamus is an essential processing stage for retinal signals to reach the primary visual cortex (V1). How these feedforward signals are modulated by corticothalamic (CT) feedback and behavior remains an open question. To quantify how feedforward, feedback and behavior combine in shaping dLGN responses, direct and selective control of CT feedback in behaving animals is needed, as well as a computational model that takes the various contributing factors into account. We here recorded extracellular responses in dLGN of awake mice to a rich, dynamic movie stimulus, while we selectively and reversibly photo-suppressed V1 layer 6 CT pyramidal cells and simultaneously tracked locomotion behavior and pupil size. We predicted dLGN responses using a Linear-Nonlinear-Poisson (LNP) model with a spline basis (RFEst toolbox [1]) to estimate spatiotemporal receptive fields (RFs) and kernels for CT feedback and behavioral modulations. We found that the spline-LNP model successfully captured diverse spatial and temporal RF shapes, such as different RF polarities and uni- vs. bimodal temporal responses. The shapes of the modulatory kernels allowed to independently quantify their contributions: we found, on average, positive kernels for running and pupil size, consistent with the overall enhancement of dLGN responses with behavioral state; we also found, on average, negative kernels for optogenetic feedback suppression, capturing the removal of top-down excitation. Interestingly, effects of CT feedback varied between spontaneous and stimulus-driven periods, and between different contrasts within RFs. Finally, training models on either movies or artificial noise stimuli revealed RFs with similar characteristics, although the noise stimulus elicited overall lower firing rates. By integrating feedforward drive, feedback modulation, and behavior into an interpretable spline-LNP model for dLGN activity, this work presents an important step towards a quantitative understanding of how responses to complex, naturalistic stimuli are modulated by CT feedback and behavior.

1-038. A discrete model of visual input shows how ocular drift removes ambiguity

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Understanding the neural code for vision remains a major challenge for neuroscience, with recent efforts influenced by the success of convolutional neural networks. However, spiking neurons make biological vision fundamentally different from the firing rate model implicit in these artificial neural networks. In region V1 of the primate

visual cortex, a flashed image is processed in tens of milliseconds, allowing time for only a few action potentials, typically across a small subset of neurons. Moreover, persistent eye motion (ocular drift) changes the location of retinal responses, and thus cortical input, as an image is encoded. Here, we develop a discrete computational model, to explore how these characteristics of the visual system can generate cortical representations that match experimental observations and encode images unambiguously. Our model explicitly represents retinal cone cells, lateral geniculate nucleus (LGN) neurons, and V1 layer 4 (V1L4) neurons, in a feedforward circuit with binary (0 or 1) neural activity and binary connection weights. We incorporate random eye motion, to present each image as a sequence of retinal activity patterns. Hebbian learning, from natural images, determines LGN-V1L4 connectivity. Despite its relative simplicity, our model successfully reproduces phenomena observed in V1L4 simple cells, including: separate on/off receptive fields, orientation tuning, end-inhibition and contrast invariance. Quantitative comparisons with experimental data, for receptive field shapes and tuning curve bandwidths, show good agreement. To investigate ambiguity in the cortical encoding of sensory input, we probe the system with an adversarial attack that finds an alternative image creating exactly the same V1L4 activity pattern as the original image. We discover that microscopic eye movements substantially reduce ambiguity, compared to a static retina. This demonstrates a beneficial role for ocular drift, removing ambiguity from cortical representations.

1-039. Efficient Coding of Natural Movies Predicts the Optimal Number of Receptive Field Mosaics

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Efficient coding theory, which stipulates that the nervous system attempts to minimize redundancy in stimulus coding, has proven widely successful in predicting observed features in early sensory systems, including center-surround receptive fields (RFs), ON and OFF parallel pathways, and the relative arrangement of ON and OFF RF mosaics. However, relatively limited work has addressed the encoding of spatiotemporal stimuli. Ocko et al. (2018) examined spatiotemporal encoding in the retina using an approach based on a convolutional autoencoder, replicating known features of retinal ganglion cell (RGC) receptive fields like midget and parasol cells. However, this work assumed a configuration consisting of exactly two cell types with a global stride factor to represent the size and density of the RFs, and the input data were synthetic Gaussian noise. This leaves a number of questions unanswered, including the optimal number of RF types, their size/mosaic arrangements, and the impact of natural movies' higher-order statistics. Extending a previously proposed efficient coding model for images, we trained a model to maximize mutual information between natural movies and neural firing rates. We found that the model produced four distinct types of RGC mosaics: One ON/OFF subgroup exhibited large, temporally precise filters, while the other exhibited spatially precise, temporally slow filters. These resemble the known distinctions between parasol and midget RGCs (in the monkey retina). Moreover, when given a larger population of neurons, the model produced additional sets of ON and OFF RF types/mosaics by subdividing the group of temporally precise filters. These results suggest a principle by which the visual system might specialize neural response types based on available channel capacity and further validate efficient coding as a theoretically grounded computational framework for reasoning about the roles of specialized RF types and their diversity.

1-040. Identifying the nonlinear structure of receptive fields in the mammalian retina

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Sensory neurons can integrate their inputs nonlinearly, and this nonlinear pooling allows the extraction of complex features from the natural environment. Such nonlinear computations are ubiquitous in the visual system, and can be captured with encoding models that partition receptive fields into subunits whose outputs are nonlinearly combined. In the retina, the nonlinearities that transform subunit signals before integration by retinal ganglion cells affect the cells' sensitivity to the spatial structure of natural scenes. Fitting subunit models to neural responses remains a challenge, as available solutions largely ignore integration nonlinearities. Here, we introduce the sub-unit grid method, which offers a generic parametrization of nonlinear subunit models and a stimulus that efficiently

probes the subunit layout and that evokes reliable responses for effective parameter fitting. Using multielectrode-array recordings from the isolated mouse retina, we fit subunit grid models to spiking responses of ganglion cells under flashed gratings with varying spatial frequency and orientation. Fitted models capture nonlinear grating responses with small subunits that can display rectification or saturation to different degrees, even in the presence of a subunit surround. Additionally, subunit layouts and nonlinearities consistently differ between ganglion cell types. Compared to spatially linear models, subunit grids improve response predictions to both spatially structured artificial stimuli and natural images. Using data from rapidly flickering gratings, we extend our models to the time domain, and show improved response predictions to natural movies with imprinted mouse eye movements. Finally, we show that subunit grids can fit receptive fields with multiple inputs, such as the ON and OFF subunits of ON-OFF direction-selective retinal ganglion cells. Together, we introduce a novel method for mapping nonlinear receptive fields, showcase how subunit grids extend functional descriptions of neuronal types beyond linear receptive fields, and thereby reduce the gap in predicting the retinal output to natural visual inputs.

1-041. Biological learning of local motion detectors

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Motion detection is a fundamental task for the visual system, with cells as early as the retina showing selectivity to specific directions of motion. These cells typically have localized connectivity and receptive fields. Why not pool information from locations that are far apart to improve motion sensing?

Here we provide a normative model that relates the lack of distant connections in motion-sensitive cells to the statistics of natural videos, which exhibit localized patterns undergoing localized motion. These local motions largely conserve contrast in a visual scene, allowing us to treat the transformations between consecutive frames as rotations in the high-dimensional pixel space. Motion can occur at different speeds, so we focus on the infinitesimal generators for these transformations. We show that, when trained on patches from whitened natural videos, a sparse-coding approach learns receptive fields involving small sets of nearby pixels. For biological plausibility, we implement the sparse-coding step in our model using non-negative similarity matching, a method rooted in multidimensional scaling that starts from an optimization problem and produces circuits with local learning rules that perform their functions in an online setting. This makes our approach both normative and biologically plausible.

Our model shows that unsupervised training on natural videos prunes long-range connections between visual receptors, resulting in localized connectivity. This connectivity is dependent on the statistics of visual scenes during learning, allowing future experimental tests of our theory. Specifically, we predict that the organization of motion-detecting circuits in different species should depend on their visual environments.

1-042. Predictive processing of natural images by V1 firing rates revealed by self-supervised deep neural networks

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The responses of neurons in primary visual cortex depend strongly on the spatial context in which stimuli are

embedded. This context-dependence has been theorized to reflect efficient and/or predictive coding of natural scenes. Critical tests of these theories in a generic form for natural images are currently lacking, because it is unclear how predictions, and measures of predictability, should be operationalized for natural scenes. Further, it is unclear whether there is just one type or level of predictability given the hierarchical processing in the primate visual system. Here, we trained neural networks that learn both linear and non-linear natural scene statistics (i.e. priors) across a very large number of images in a self-supervised manner. We hypothesize that this training will ensure that the networks develop a similar internal model as the primate visual system uses to generate predictions. The natural scene statistics contain low-level (pixel structure) to high-level (object information) features. Biological neurons, with encoding properties shaped by natural scene priors, could encode sensory predictions or prediction errors for this broad spectrum of features. Here, we derived measures to assess predictability in natural images in order to investigate the contextual modulation of firing rates, and distinguished between lower- and higher-order image features using convolutional neural networks for object recognition. We performed parallel recordings from awake macaque V1 viewing natural scenes of different sizes. Surprisingly, we found that firing rates are only weakly modulated by structural (pixel-wise) predictability and image compressibility. We find that the main factor determining a decrease in V1 firing rates is the contextual predictability of higher-level features of stimuli falling into the RF. These higher-order features correlated strongly with human perceptual similarity judgements, and with image salience. Our model provides improved prediction of surround modulation compared to state-of-the-art models based on Gabor filters. Our findings suggest that V1 neurons encode higher-order mismatch signals about features that are relevant for object recognition.

1-043. Hypothesis-neutral models of higher-order visual cortex reveal strong semantic selectivity

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Modeling neural responses to naturalistic stimuli has been instrumental in advancing our understanding of the visual system. Dominant computational modeling efforts in this direction have been deeply rooted in preconceived hypotheses. Here, we develop a hypothesis-neutral computational methodology which brings neuroscience data directly to bear on the model development process. We demonstrate the effectiveness of this technique in modeling as well as systematically characterizing voxel tuning properties.

We leverage the unprecedented scale of the Natural Scenes Dataset to constrain parametrized neural models of higher-order visual systems with brain response measurements and achieve novel predictive precision, outperforming the predictive success of state-of-the-art models. Next, we ask what kinds of functional properties emerge spontaneously in these response-optimized models? We examine trained networks through structural and functional analysis by running ‘virtual’ fMRI experiments on large-scale datasets.

Strikingly, despite no category-level supervision, since the models are optimized for brain response prediction from scratch, the units in the networks after optimization act strongly as detectors for semantic concepts like ‘faces’ or ‘words’, thereby providing one of the strongest evidences for categorical selectivity in these areas. The observed selectivity raises another question: are these units simply functioning as detectors for their preferred category or are they a by-product of a non-category-specific processing mechanism? To investigate this, we create selective deprivations in the visual diet of these models and study semantic selectivity in the ‘deprived’ networks, thereby also elucidating the role of specific visual experiences in shaping neuronal tuning.

Beyond characterizing tuning properties, we study the transferability of representations in response-optimized networks on different perceptual tasks. We find that the sole objective of reproducing neural targets, without any task-specific supervision, grants these networks intriguing functionalities. Together, this new class of response-optimized models combined with novel interpretability techniques reveal themselves as a powerful framework for probing the brain.

1-044. Evolution of neural activity in circuits bridging sensory and abstract knowledge

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The ability to associate sensory stimuli (e.g., apples and cookies) with abstract knowledge (e.g., “healthy” versus “unhealthy”) is critical for survival. How are these associations implemented in the brain? And what governs how neural activity changes during abstract knowledge acquisition? To investigate these questions, we consider a circuit model that learns to map sensory stimuli into abstract categories via gradient-descent plasticity. We focus on typical neuroscience tasks (simple, and context-dependent categorization), and use simulations and mathematical analysis to uncover how neural activity evolves during learning. We find that activity of single neurons becomes, over learning, selective to abstract variables: these include variables that are explicitly reinforced, such as category, and variables that represent task rules and are indirectly cued, such as context. Such behaviour is universal, and independent of model details; this is in agreement with experiments, where the emergence of selectivity has been consistently reported across studies. On the other hand, how the population as a whole responds to categories and contexts does depend on details - and thus carries valuable information on the circuitry that implements the task. For instance, over learning, category and context correlations (i.e., correlations among population activity in response to different categories and contexts) can become either positive or negative. Also, the population can exhibit either symmetric or asymmetric responses: the number of neurons that most strongly respond to a given category can be similar or very different across categories. Negative and positive correlations, as well as symmetric and asymmetric responses, have been observed in experiments; our model provides a single explanation for these seemingly contradictory studies. We determined how, in the model, correlations and symmetry depend on circuit (gain and sparsity of activity, relative learning rates) and task (number of stimuli, context-dependence) parameters; these dependencies make experimentally testable predictions about the underlying circuitry.

1-045. A distributional Bayesian learning theory for visual perceptual learning

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Training subjects to discriminate fine details of stimuli can improve perceptual capabilities, a phenomenon known as perceptual learning (PL). Experiments have discovered intriguing psychophysical findings despite the simple stimuli (e.g., Gabor patches) and training procedures (e.g., 2AFC task) involved. Finding explanations for these learning effects could shed light on sensory plasticity in adulthood and constraints in sensory processing. A profound feature of (visual) PL is its slow learning speed, which can take days of training and hundreds or thousands of trials for the performance to saturate. This is sometimes attributed to the low signal-to-noise ratio in the sensory activities, which poses a challenging classification problem for decision neurons that readout these activities. How could the decision neurons learn when the signal is so weak? We hypothesize that, rather than relying on the short-lived activities at each trial, the brain may learn according to the distribution of sensory activities summarized by sensory neurons over multiple stimulus presentations. In such a noisy condition, we also assume that the decision neurons combine sensory signals using uncertain readout weights modeled as probabilistic (Bayesian) synapses (e.g. with a mean and sd). During PL, the weights are updated by averaging over the stimulus distribution of the presented category; during perception, the decision neuron acts according to the probability of the perceived category computed by a sample of the posterior weights. This model can explain several behavioral results obtained by Dosher and Lu (1998, 2005). We show that the model replicates the uniform downward shift of threshold-versus-noise contrast (TVC) curves, the power-law decrease of the signal threshold with training, and the asymmetric transfer between noisy and clean displays. This theory thus offers an alternative to the Hebbian reweighting model (Dosher and Lu, 2010) and connects the theoretical literature of probabilistic synapses to visual perceptual learning.

1-046. Representation of sensory uncertainty by neuronal populations in macaque primary visual cortex

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Perception is uncertain. Repeated presentations of the same stimulus elicit variable perceptual impressions. To robustly guide behavior, the neural circuits that mediate perception must therefore extract both feature estimates and feature uncertainty from sensory inputs. How they do so is not well understood. We addressed this question using an approach that combines three components. First, a rich stimulus set which varies in feature value and uncertainty. Second, observation of neural population activity in a sensory circuit that represents these features. And third, a maximum likelihood decoder of neural activity, tasked to estimate feature value and uncertainty on each trial. We took this approach to macaque primary visual cortex (V1), where neural activity encodes local image orientation. We made extracellular recordings of V1 population activity and described each neuron's responses with a stimulus-response model built from operations of linear filtering, nonlinear transduction, gain control, and a doubly stochastic noise process. We then used this model to derive the maximum likelihood estimator of stimulus orientation. Orientation estimates were on average unbiased, even in the presence of nuisance variation (contrast and spread). On individual trials, orientation estimation error tended to be small for high contrast, small spread stimuli, but could be substantial when contrast was low, or spread was high. This was reflected in the uncertainty estimates of the decoder, which we obtained by computing the width of the orientation likelihood function. We then asked which aspect of neural activity distinguishes uncertain from certain trials. We identified two candidate representations. First, the overall level of activity (the higher the population firing rate, the more precise the orientation estimate). And second, a model-based estimate of variability in response gain (the higher this variability, the less precise the orientation estimate). Our findings clarify how sensory circuits jointly encode stimulus features and their uncertainty.

1-047. The emergence of gamma oscillations as a signature of gain control during context integration.

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Context integration is a fundamental feature of the human visual system contributing to basic visual processing routines such as contour integration, visual pop-out, and texture segmentation. Two perceptual hallmarks of context integration are orientation-dependent surround suppression (ODSS) and the orientation tilt illusion. In these contextual effects, either the magnitude (ODSS) or the orientation (tilt illusion) of a neural population vector code is shifted depending on the relative orientation of the spatial surround. Supported by past modeling studies, these perceptual effects have been attributed to a divisive gain control mechanism, in which the spatial surround exerts an orientation-tuned modulatory influence on the center. Electrophysiological measures have shown that oscillations in the gamma band (30-100Hz) of the local field potential (LFP) in visual cortex may serve as a biomarker for gain control. However, previous models of context integration have not explained this aspect of neural dynamics in connection to gain control. To address this issue, we use oscillatory recurrent gated neural integrator circuits (ORGaNICs), a model based on a biological implementation of long short-term memory (LSTM) networks, that has been shown to generate oscillatory dynamics in V1. By constraining the model using a recurrent circuit motif consistent with primate neurophysiology, we explain both perceptual effects and oscillatory dynamics observed in ODSS. We show that the model is capable of matching both psychophysical measures of the tilt illusion and narrowband gamma power observed in LFPs recorded from human visual cortex. Furthermore, the model predicts that similarly oriented surround stimuli increase the strength of gain pools for the center causing an increase in gamma power, an experimentally testable prediction.

1-048. Selective V1-to-V4 communication of attended stimuli mediated by attentional effects in V1

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Selective attention implements the preferential routing of attended stimuli, likely through increasing the gain of the respective synaptic inputs to higher-area neurons. As the synaptic inputs conveying competing stimuli converge and intermingle on postsynaptic neurons, impeding selective attentional addressing, presynaptic circuits might be the best target of top-down signals from higher areas of attentional control. If those signals enabled presynaptic circuits to selectively entrain postsynaptic neurons, this would be a mechanism for selective routing in accordance with the Communication-through-Coherence hypothesis (CTC) [1]. Indeed, when two visual stimuli induce two gamma rhythms in separate local populations in macaque V1, only the gamma rhythm induced by the attended stimulus entrains gamma in V4 and establishes coherence [2]. Here, we modeled those electrocorticographic data [2] with a Dynamic Causal Model (DCM) for Cross-Spectral Densities (CSD) [3] and found that the selective entrainment can be caused by modulations of intrinsic V1 connections alone. Specifically, local inhibition was decreased in the granular input layer and increased in the supragranular output layer of the V1 circuit processing the attended stimulus. Our model reproduces attentional effects even in the absence of V4-to-V1 feedback connections, suggesting that a purely feed-forward mechanism can achieve the selective entrainment of V4. Thus, we propose that a mechanism of attentional addressing can act on V1 inhibitory circuitry and induce the experimentally observed effects, thereby increasing communication through coherence and implementing the selective routing of information during attention.

1-049. A neural circuit model of hidden state inference for navigation and contextual memory

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Neural circuit computations are modulated by combinations of internal and external factors. For example, neurons in the medial entorhinal cortex (MEC) change their firing patterns or “remap” during a reward-seeking task, responding to changing task conditions and environmental cues. Why does this remapping occur? What unifying principles (if any) underlie remapping? Recent work proposes that remapping reflects hidden state inference—changes to an animal’s internal beliefs about the world. Recent experimental evidence suggests that remapping can indeed arise from latent behavioral or cognitive state changes without changes to the environmental or task cues. There remains, however, a critical gap between our theoretical and biological perspectives on neural remapping. Sanders et al. frame remapping as hidden state inference, but do not propose a circuit mechanism to implement this inference. Low et al. used Neuropixels recordings of MEC neural ensembles to characterize remapping as transitions between geometrically aligned neural activity manifolds, but they do not attribute remapping to any functional purpose, such as hidden state inference. Here we leverage recurrent neural network (RNN) models to bridge this gap. We find that, when RNNs are trained to simultaneously track a hidden state (“context cue”) and perform a path integration task, the RNN dynamics converge to a similar solution as MEC neurons. Namely, the number of hidden states reflects the number of neural manifolds (spatial maps of the environment) in the RNN and, critically, these manifolds are geometrically aligned in the precise manner described by Low et al. This geometric alignment allows for remapping along an orthogonal dimension to ongoing circuit computations, supporting flexible hidden state inference alongside reliable spatial coding in a single circuit. We thus propose a normative model for neural remapping with a biologically plausible implementation, reconciling prior theoretical and experimental work and generating hypotheses for future studies in both fields.

1-050. Rapid approximation of successor representations with STDP and theta phase precession

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The successor representation (SR) is a promising candidate principle for hippocampal function. Theory proposes that each place cell encodes the expected state occupancy of its target location in the near future. This framework has desirable consequences on the generalisability and efficiency of reinforcement learning algorithms operating over these representations and is supported by behavioural and electrophysiological evidence. However, it is unclear how the SR might be learnt in the brain. Temporal difference learning, commonly used to learn SRs in artificial agents, is not known to be implemented in hippocampal networks. Instead, we demonstrate that spike-timing dependent plasticity (STDP), a modified form of Hebbian learning, acting on temporally compressed trajectories known as “theta sweeps”, is sufficient to rapidly learn a useful approximation to the SR. Our model is biologically plausible: it maps onto validated aspects of hippocampal circuitry, it uses spiking neurons modulated by theta-band oscillations, diffuse and overlapping place cell-like states and experimentally matched parameters. It explains substantial variance in the true successor matrix and gives rise to place cells demonstrating key experimentally observed phenomena associated with the SR including policy-dependent backwards expansion on a 1D track and elongation near walls in 2D. In our model, larger place cells encode longer timescale SRs. We shed insight on the observed topographical ordering of place cell size down the dorsal-ventral axis by showing this is necessary to prevent the detrimental mixing of these timescales.

1-052. Oscillatory and fractal biomarkers of human memory

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Human direct brain recordings have implicated 4-8 Hz theta-band activity in a wide range of cognitive processes including spatial navigation, working memory, and associative recall (Kahana et al. (2001); Nyhus & Curran (2010)). Yet, many highly-powered memory studies indicate that good memory appears during periods of reduced theta and alpha (8-12 Hz) activity and enhanced high-frequency (>40 Hz activity), a pattern known as the spectral tilt (Burkeet et al., 2015). In a meta-analysis of prior work, Herweg et al. (2020) suggest several possible resolutions to these discrepant results: They hypothesize that theta increases appear under specific conditions: (1) measures that isolate narrow-band oscillatory effects by filtering out broad-band power fluctuations like spectral tilt, (2) contrasts that isolate retrieval processes, and specifically associative effects during retrieval, (3) measures that aggregate neural activity over larger brain areas, thus picking up synchronous oscillations. We evaluate each of these three hypotheses in a large dataset of human hippocampal depth recordings (674 electrode pairs across 144 patients). Using the IRASA method to separate broad and narrow-band components of the field potential we show that (1) isolating the narrow-band components of the signal does recover an increase in theta power at both encoding and retrieval. (2) theta does not reliably increase as a function of associative strength during retrieval, and (3) employing an average reference scheme - which aggregates neural activity over the entire brain - rather than the more localized bipolar reference scheme does not produce significantly different results.

1-053. Neural signatures of memory retrieval in the hippocampus of freely caching chickadees

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How does the brain record individual experiences, and recall them to adaptively guide future behavior? This ‘episodic-like’ memory regime involves the hippocampus, but it has been difficult to identify specific neural signatures with recollection of specific memories, hindering a mechanistic understanding of recall. Studying food caching behaviors may provide a clearer picture. Scatter hoarding species, such as chickadees, cache individual food items, and use hippocampal-dependent memory to later retrieve them. However tools for behavioral and neural measurement in chickadees are underdeveloped, and so neural correlates of cache memories have not been identified.

We designed a behavioral arena where chickadees spontaneously cache and retrieve seeds, without explicit training or reinforcement. In order to parse this unconstrained behavior, we collect multi-view, high-speed, video data. We combined recent advances in 3D postural tracking with conventional 2D tracking networks into a 2-stream algorithm, which achieved high accuracy with only moderate computational demands. Postural tracking enabled automated detection of multiple discrete behaviors, including interaction with cache sites and gaze location. Finally we developed a light-weight implant for chronic silicon probe recordings compatible with freely moving behavior in small birds, enabling simultaneous recording of ~100 hippocampal neurons. Hippocampal activity during caching exhibited strong modulation preceding cache site interaction. This activity was distinct for each cache site, encoded the hidden contents of the site, and was dissociable from a representation of spatial or other behavioral variables. This activity is consistent with the reactivation of hippocampal codes underlying the recollection of individual caching events.

1-054. Computational principles of systems memory consolidation

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In many species and behaviors, learning and memory formation involve plasticity in at least two distinct neural pathways, responsible for short and long-term learning, and a process of consolidation requiring interaction between them. A well-known example is the consolidation of hippocampal memory traces into the neocortex in mammals. Consolidation mechanisms are also observed in motor learning (between cortical and subcortical structures) and associative learning in insects (between subregions of the mushroom body). Here, we propose a model that captures common computational principles underlying these phenomena. The key component of our model is recall-gated consolidation, in which the long-term pathway prioritizes the storage of memory traces that are familiar to the short-term pathway. This mechanism shields long-term memory from spurious synaptic changes, enabling it to focus on reliable signal in the environment. We show that this model has significant advantages, substantially amplifying the signal-to-noise ratio with which intermittently reinforced memories are stored. In fact, we demonstrate mathematically that these advantages surpass what is achievable by synapse-local mechanisms alone, providing a motivation for systems (as opposed to synaptic) consolidation. We describe neural circuit implementations of our general model for different types of learning problems, which make use of interpretable factors such as prediction accuracy, confidence, or familiarity to modulate the rate of consolidation. Our model makes a number of predictions, including (1) that the rate of memory consolidation should increase with the number and consistency of training repetitions (2) that short-term memory pathways benefit from sparser, higher-dimensional representations than long-term pathways, (3) that recall performance depends non-monotonically on the spacing of training trials, and the optimal training spacing depends on the time scale of evaluation. These predictions are largely consistent with existing evidence from the mammalian and insect memory consolidation literature, while also motivating new experiments to test them directly.

1-055. Hierarchical interaction between memory units with distinct dynamics enables higher-order learning

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Associative learning entails lasting changes in multiple, distributed neural circuits in different areas of the brain. Understanding the nature of information stored in individual memory circuits and how they interact cooperatively

and competitively to function as one network are key but highly challenging problems. In *Drosophila* mushroom body (MB), ~20 pairs of dopamine neurons (DANs) and mushroom body output neurons (MBONs) together form compartmental units of associative learning. Each DAN cell type is selectively tuned to rewards or punishments and write and update memories with cell-type-specific dynamics. Activity of MBONs is thought to be integrated by downstream neurons to guide memory-based actions and provide feedback to DANs to instruct future learning. However, its circuit mechanisms are still enigmatic. The latest EM connectome data revealed ~400 types of interneurons that have at least 100 synaptic connections with DANs and MBONs. The machine learning based prediction of their neurotransmitter and our new collection of genetic driver lines to manipulate them enable us to study how diverse local plasticity dynamics in each MB compartment and neural circuits for cross-compartmental interactions together define learning rules of the fly brain. Here we will present neural mechanisms of second-order conditioning. In the second-order conditioning, reward prediction by the first-order memory drives a formation of the second-order memory in the absence of reward. We found that the teacher compartment that has slow rate of learning and extinction instructs multiple student compartments with faster learning rate and higher flexibility. We identified two types of cholinergic interneurons that are 1) under control of competing inhibitory and excitatory drives from multiple MBONs whose activity represent memories about reward or punishment, 2) acquire enhanced response to reward-predicting cues after formation of appetitive memory and disinhibition from glutamatergic MBONs, 3) drive robust upwind steering when activated, 4) send highest number of excitatory outputs to multiple DANs, and thereby 5) induce secondary synaptic plasticity in their target compartments. This hierarchical interaction between MB compartments with distinct memory dynamics explains transient nature of second-order memory as originally described by Pavlov and Resorla and observed across animal phyla. Our results reveal the origin of action-correlated activity in DANs and how memory subsystems with distinct dynamics concertedly functions to enable higher-order learning.

1-056. Purely STDP-based learning of stable, overlapping assemblies

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Memories may be encoded in the brain via assemblies, groups of neurons that coactivate upon memory recall. The concept of Hebbian plasticity suggests that these assemblies are generated through synaptic plasticity, strengthening the recurrent connections within select groups of neurons that receive correlated stimulation. To remain stable in absence of such stimulation, these assemblies need to be self-reinforcing under the plasticity rule. Previous models of such assembly generation and maintenance required mechanisms of heterosynaptic competition or homeostatic plasticity often with biologically implausible timescales. Here we provide a model of neuronal assembly generation and maintenance without homeostatic plasticity. We assume that the neural networks are in a state of asynchronous irregular activity, allowing to model them as networks of linear Poisson neurons. Synaptic strengths change according to spike timing-dependent plasticity (STDP), with a simple pairwise, symmetric STDP function with negative integral and bounded weights. Our mathematical analysis and numerical simulations show that no further plasticity rules are required for stable network activity without pathological assembly evolution. Depending on the choice of parameters, the networks exhibit stationary assemblies, which consist of the same neurons over time, or drifting assemblies, which exchange neurons between each other. Further we show that neurons can be part of multiple assemblies at the same time for appropriate individual background firing rates.

1-057. Spatio-Temporal Pattern Selectivity from Homeostatic Hebbian Plasticity

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It is an open question to what extent neural coding and computation are based on precise patterns of spikes. Theoretically individual neurons can serve as detectors for given spatio-temporal spike patterns, however, this requires supervised adjustment of their input synapses. It is not known if existing activity dependent synaptic plasticity mechanisms can lead to unsupervised emergence of spatio-temporal pattern selectivity. Here, a combination of realistic mechanisms is demonstrated to self-organize the synaptic input efficacies such that neurons become detectors of patterns repeating in the input. The proposed combination of learning mechanisms yields a

balance of excitation and inhibition similar to observations in cortex, robustness of detection against perturbations and noise, and persistence of memory against ongoing plasticity. It enables groups of neurons to incrementally learn sets of noisy patterns thereby faithfully representing their ‘which’ and ‘when’ in sequences. These results suggest that computations based on spatio-temporal spike patterns might emerge without any supervision from the synaptic plasticity mechanisms existing in the brain.

1-058. Heavy-tailed connectivity emerges from Hebbian self-organization

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In networks of neurons, correlations and synaptic strengths are heavy-tailed, with a small number of neurons interacting much more strongly than the vast majority of pairs. Yet, it remains unclear whether, and how, such heavy-tailed connectivity emerges from simple underlying mechanisms. Building upon recent advances in neuroimaging, here we show that the correlations between thousands of neurons in the mouse visual cortex have heavy-tailed distributions spanning three decades in strength. Moreover, we find that these distributions are robust to variations in the visual stimuli, even persisting during spontaneous activity. To explain these heavy-tailed correlations, we propose a simple model of synaptic self-organization based on Hebbian plasticity: synapses are pruned at random, and the synaptic weight is redistributed throughout the network in either (i) a Hebbian fashion or (ii) randomly. Importantly, our model contains only a single parameter $0 \leq p \leq 1$, which represents the probability of Hebbian versus random growth. We predict analytically and confirm numerically that such dynamics generate scale-free distributions of connectivity strength, with a power-law exponent $\gamma = 1 + \frac{1}{p}$ that depends only on the probability of Hebbian growth. Finally, by generalizing our model to artificial neural networks, we demonstrate that Hebbian plasticity gives rise to heavy-tailed correlations similar to those observed in neuronal recordings. Generally, our results suggest that heavy-tailed distributions of correlations and synaptic weights may arise from general principles of self-organization, rather than the biophysical particulars of individual neural systems.

1-059. Input correlations impede suppression of chaos and learning in balanced rate networks

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Cortical circuits exhibit complex activity patterns, both spontaneously and evoked by external stimuli. Information encoding and learning in neural circuits depend on how well time-varying stimuli can control network activity. We show that in firing-rate networks in the balanced state, external control of recurrent dynamics, i.e., the suppression of the internally-generated chaotic variability, strongly depends on correlations in the input: One might expect that driving all neurons with a common input helps to control network dynamics. Surprisingly, we find that the network is far easier to control with independent inputs into each neuron. We discover that this discrepancy is explained by the dynamic cancellation of a common external input by recurrent feedback, an effect that is absent when inputs vary independently across neurons. We present a nonstationary dynamic mean-field theory that explains how autocorrelations and the largest Lyapunov exponent depends on input frequency, recurrent coupling strength, and network size, demonstrating that the discrepancy between common and independent input increases for larger networks and in the vicinity of the chaotic transition. Furthermore, we show that uncorrelated inputs facilitate learning in balanced networks.

1-060. Identifying key structural connections from functional response data: theory & applications

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Being able to identify key patterns of neural network connectivity that are specifically required to generate functional response patterns is a challenging and aspirational goal in neuroscience. The difficulty, in part, is because we are typically only able to probe a network with a limited number of stimulus conditions, and there exists huge degeneracies in the ways we can connect the neurons to reproduce the observed responses. Here we present a new geometric ensemble modeling approach to this problem. Inspired by whole-brain imaging approaches, we assume that we have access to a finite number of steady state response patterns of all the relevant neurons in a given network, and we then ask if we can identify key excitatory or inhibitory connections that must exist to generate the responses. We assume that the network can be modeled by a recurrent neural network of rectified linear units that receive feedforward inputs. We develop a geometric framework to analytically tackle the problem. We then apply our theory to predict biological connectivity required to generate binocular responses of zebrafish pretectal neurons to various optomotor stimuli, which were previously recorded using whole-brain imaging.

1-061. Emergence of time persistence in an interpretable data-driven neural network model

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Establishing accurate as well as interpretable models of neural networks activity is an open challenge in systems neuroscience. Here we infer an energy-based generative network model of the anterior rhombencephalic turning region (ARTR) of zebrafish larvae using calcium-imaging recordings of the spontaneous activity of hundreds of neurons. While our data-driven model is trained to solely reproduce the short-term statistics of the neural activity, its dynamics exhibits persistence on much longer time scales. The model's persistence time decreases with water temperature in agreement with neuronal and behavioral observations. Mathematical analysis of the model unveils a low-dimensional landscape-based representation of the population activity where the long-term dynamics reflects slow Arrhenius-like activated processes between metastable activity states. We show how this effective landscape is modified in the presence of light stimuli, which allows us to reinterpret previous experiments characterizing the visually-driven operation of the ARTR.

1-062. Auxiliary neurons in optimized recurrent neural circuit speed up sampling-based probabilistic inference

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It has been proposed that the visual cortex performs sampling-based probabilistic inference where neural responses represent stochastic samples from a posterior distribution. However, the highly-correlated nature of neural activity across time presents a computational ceiling on the effective sample size for any given time interval. Here, we show that auxiliary neurons, when implemented strategically, can speed up sampling rates in neural circuits to efficiently express an inferred posterior distribution. We train stabilized supralinear networks using a loss function that intrinsically rewards fast sampling. A base model comprising of 50 coding excitatory

and 50 inhibitory neurons is able to achieve an acceptable level of performance when trained to sample over 800ms but fails to produce enough effective samples under a more realistic time frame of 400ms. We construct the full network by installing an additional 100 auxiliary excitatory neurons. Our optimized network (trained for 400ms) attains competitive levels of performance compared to both the base network trained for 800ms and a naive duplication of the base model obtained by collecting samples from two concurrent base networks trained for 400ms despite having less sampling time or coding neurons. Two key temporal structures emerged from all models after optimization which are also experimentally observed: (1) positively-skewed membrane potential distributions at low contrast; and (2) gamma oscillations whose frequency increases with contrast. Additionally, oscillations expressed by the full network uniquely contain a well-hidden but computationally crucial temporal signature that evades typical spectral analyses in the form of reduced temporal co-kurtosis. We analytically show that the dynamics underlying these effects lead to improved sampling efficiency. Our results enhance the biological plausibility of sampling-based probabilistic inference and objectively attribute key experimental observations towards its computational efficiency, while our analysis on irregular oscillations brings to light the significance of analysing higher-order temporal moments in neural activity.

1-063. The neural code controls the geometry of probabilistic inference in early olfactory processing

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Neural circuits must perform probabilistic computations to efficiently process noisy sensory information. Sampling codes propose that single neuron variability is a signature of probabilistic computation, and corresponds to sampling the space of possible solutions in proportion to their posterior probability. Under this hypothesis, the neural code defines how variables inferred by the network are represented in single neurons. Compared to other proposed probabilistic codes, the capacity of sampling codes scales with the number of neurons, but their convergence speed scales poorly with dimensionality of the parameter space. To be useful to the organism, the proposed probabilistic computations should match perceptual speed. Work in statistics and machine learning shows that inference can be accelerated by sampling on a manifold with desirable geometry. However, these methods require structured noise, which in biological networks would imply strong electrical coupling across neurons. Here, we propose that the neural code can implement such favorable geometry in electrically uncoupled neurons, using the formalism of mirror descent. We first present a multivariate Gaussian model to highlight how distributed codes can implement a favorable geometry to achieve accelerated inference, independent of the dimensionality of the problem. Next, we apply these principles to neural circuits in the olfactory bulb, using a Poisson noise model for the activity of olfactory receptor neurons. Excitatory projection cells (mitral/tufted cells) implement a form of predictive coding, while inhibitory neurons (granule cells) implement sampling and control the geometry of representations. Since granule cells greatly outnumber mitral/tufted cells, they can implement such geometry through a sparse code. We show that this distributed code accelerates the inference and avoids interference by distractor odors. To conclude, choosing a neural code that implements a favorable geometry accelerates inference, and we map such an algorithm onto neural circuits in the early olfactory system.

1-064. Optimal information routing to cerebellum-like structures

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High-dimensional neural representations are observed in many brain areas and are believed to be a powerful substrate for flexible computation. Theories have suggested that the vertebrate cerebellum and other cerebellum-like structures produce such high-dimensional representations by expanding their input into a vast layer of granule-like cells. Signals are typically routed to such expanded representations by anatomical “bottlenecks”: in the mammalian cortico-cerebellar pathway, input from across the cortex converges in the pontine nuclei, from which

roughly half of the mossy fiber input to granule cells originates. Similarly, in the insect olfactory system, responses of odor receptor neurons in the antenna are compressed in the antennal lobe glomeruli, before being routed to Kenyon cells in the mushroom body (a cerebellum-like structure). This bottleneck motif has been largely ignored in models and is at first sight at odds with the goal of maximizing dimensionality. Here, we use a combination of simulations, analytical calculations, and analysis of neural data from flies and mice to develop a normative theory of cerebellum-like structures in conjunction with their afferent pathways. We propose that the bottleneck architecture of regions presynaptic to granule-like layers reformats the input representation to maximize the efficacy of the subsequent expansion. When applied to the insect olfactory system, our theory explains its glomerular organization and inter-glomerular interactions. The same objective, when applied to distributed input from motor cortex, implies that the pontine nuclei select the task-relevant subspace within cortical activity. Our theory predicts that cerebellar granule cells expand the task-relevant dimensionality, reconciling theories of dimensionality expansion with recent observations of high correlations among granule cells (Wagner et al., 2019). Our conclusions are not limited to cerebellum-like structures and relate the statistical properties of a neural representation to the architectures that optimally transform it to facilitate learning downstream.

1-065. Microcircuits and the compressibility of neural connectomes

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To understand how the brain is wired calls for investigating how the brain's wiring information (the connectome) is encoded in the genome. From small insects to humans, the apparent complexity of biological neural networks, in particular the information amount required to describe all connections in the connectome, far exceeds the genomic storage capacity. To explain the discrepancy in information volume between a direct description of the brain network and the coding genome's size, an emerging hypothesis, coined the genomic bottleneck principle, proposes that the wiring information must be compressed within the genome. Across diverse model animals, experiments both at the level of single neurons and of neural populations support this assumption, based on the observation of stereotyped "canonical" microcircuits. Such regular structural patterns throughout connectomes are hypothesized to have core roles in a wide range of biological functions. Information theory furthermore tells us that the presence of such statistically significant circuits, termed motifs, makes a compressed representation of the brain's wiring diagram possible. To test the genomic bottleneck and canonical microcircuits hypotheses, we relied on recent connectomic data acquired at single synapses resolution from whole-CNS EM volumes in *Drosophila melanogaster*. We developed lossless network compression techniques based on subgraph contractions and subgraph covers that allowed us to mine small network motifs and select the combination of motifs that maximally compresses a connectome with respect to a hierarchy of random graph null models such as Erdős-Renyi graphs or the configuration model. Our compression-based analysis circumvents problems related to multiple testing encountered when mining motifs individually using null hypothesis testing. Our results demonstrate the compressibility of neural connectomes and lend support to the canonical circuit hypothesis at the scale of single neurons, though with circuit motifs that may depend on brain region.

1-066. Weighted clustering motifs and small-worldness in connectomes

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Brain networks possess many non-random features that might present a key to the computational effectiveness and robustness of the nervous system. Information-transmission pathways in neuronal structure, especially in complex connectomes, seem to favor specific recurrent motifs. For intrinsically directional and weighted networks such as those in the brain, it is particularly important to use methods that are sensitive to the weight-encoded information. We use new weighted methods to assess statistics of motives in the connectomes of various animals: *C. elegans*, tadpole, drosophila, mouse. Except for drosophila, all connectomes showed an apparent overabundance of redundancy-enhancing clustering motifs. At the same time, a cyclic motive that can be considered the simplest structure for memory preservation was not more numerous than in the randomized network. We discuss potential relations between these structural patterns and the function of these neuronal circuits. Building on recent weighted and directed clustering methods, we properly define a measure of small-worldness in neuronal networks. In contrast with the consistent over-expression of clustering patterns associated with redundant information transfer, our analysis reveals that small-worldness is not a universal feature of connectomes. It can be

related to large distances between some nodes, a probable consequence of modular structures, or low clustering values for a significant fraction of the nodes. On the level of individual neurons, we show how specific motifs single out neurons with a particular function in a learning center of drosophila. We demonstrate that modulatory neurons sending converging information into two compartments within the mushroom body (MB) are at the center of a highly clustered group of neurons. This network feature might be essential for learning sparse encoding of conditioned stimuli. Altogether, our results highlight how the fully-weighted and directional methods can glean information about neuronal circuits.

1-067. A circuit library for exploring the functional logic of massive feedback loops in Drosophila brain

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The functional logic of brain circuits of Drosophila neuropils is largely determined by local/intrinsic neurons. The architecture of the antennal lobe (AL), for example, is numerically dominated by its local neurons (LNs) that interact with olfactory sensory neurons (OSNs) and projection neurons (PNs) within and across glomeruli. Detailed connectomic data, e.g., the Hemibrain dataset, reveal a massive number of nested feedback loops among these three classes of neurons. Dissecting the role of these feedback circuits is key to the understanding the computation taking place in AL and beyond. However, there has been little systematic study of the functional role of these feedback loops in the brain of the fruit fly.

In order to explore the functional logic of the feedback loops in the fruit fly brain, we developed a circuit library that brings together the available Drosophila connectomic, synaptomic and cell type data, with tools for 1) querying connectome datasets that automatically find and incorporate feedback pathways, 2) generation of interactive circuit diagrams of the feedback circuits, 3) automatic derivation of executable models based on feedback circuit abstractions anchored on actual connectomic data, 4) arbitrary manipulation (and/or ablation) of feedback circuits on the interactive circuit diagram for execution, and 5) systematic characterization and comparison of the effect of different feedback circuits on the I/O relationship.

We demonstrate the capabilities of the library using circuits of the DM4 and DL5 glomeruli of the Drosophila antennal lobe constructed either individually or together, from the Hemibrain dataset. We characterize the contribution of individual feedback motifs as well as their compositions on the circuit.

1-068. Sex-specific network topology of the nociceptive circuit shapes dimorphic behavior in C. elegans

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The effect of the detailed synaptic connectivity among neurons in a neural circuit on its function and the behavior of the organism, is a key question in many neural systems. *C. elegans* presents us with a particularly accessible system to explore these relations, thanks to its relative simplicity, the reconstruction of its connectome, and the range of molecular, imaging, and behavioral tools for studying it. We studied here the important circuit for nociception that is composed of the same set of neurons in the two sexes of *C. elegans*, which are connected in a sexually-dimorphic topology. As the two sexes demonstrate dimorphic behavioral response to aversive stimuli, we asked whether the distinct topologies are sufficient to explain these differences. We first showed, experimentally, that the sensory transduction is similar in the two sexes, and then explored the potential role of network connectivity as the source of behavioral dimorphism – by simulating the dynamics of the nociceptive circuits to external stimuli. As the biophysical parameters of these circuits are not known, we explored a wide range of realistic values for these parameters, and found the parameter sets that replicated the respective behavior of each sex. The number of overlapping parameter sets for the two sexes was relatively small, and, importantly – reproduced the behavioral differences observed experimentally. We then used our simulated model to identify critical potential rewiring of the networks that would switch behavior between sexes. Our model predictions were validated experimentally, where we showed that the male's network could be rewired to generate the responses of the opposite

sex, and in finding that the hermaphrodite's network is more robust to perturbations. We thus suggest that sexual identity sculpts neuronal circuits for the sex-specific needs of the organism and present an example of behavioral reprogramming by simple connectomic editing.

1-070. Unsupervised inference of brain-wide functional motifs underlying behavioral state transitions

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During prolonged periods of stress, animals switch from active to passive coping strategies to manage effort expenditure. These normally adaptive behavioral state transitions become maladaptive in disorders such as depression. Such behavioral state transitions occur as animals continually evaluate the fruitfulness or futility of their actions in response to stressors. This process is mediated by interactions across numerous brain regions over long timespans, integrating information about the stressor with the outcome of avoidance actions performed, and tracking the accrual of stress, ultimately driving transitions between different coping strategies. Here, we disentangled both the spatial and temporal dependencies of the neural mechanisms driving behavioral state transitions using computational models directly constrained by longitudinal, whole-brain, cellular-resolution neural recordings from larval zebrafish during active to passive coping in the face of persistent, inescapable stress [1]. We built and analyzed large-scale recurrent neural network (RNN) models that reproduced the long time-scale dynamics of over 10,000 simultaneously-recorded neurons. We combined this model's outputs—connectivity [1] and inter-region currents [2]—with tensor decomposition [3] to infer, in an unsupervised manner, separate “functional motifs” capturing multi-region dynamics that describe the time-varying flow of source and target currents. We found three distinct functional motifs corresponding to key behavioral signals: shocks, tail movements, and stress accumulation. All three motifs included the habenula and raphe nucleus—regions previously implicated in passive coping [4]—as key targets of brain-wide networks corresponding to each behavioral signal. We show that these two regions integrate distinct sets of input currents from a number of other regions, including dorsal thalamus and telencephalon to drive the transition from active to passive coping. We provide an unbiased mechanistic framework to disentangle the simultaneous encoding of behaviorally-relevant signals across interacting regions brain-wide and demonstrate that behavioral state transitions require simultaneous integration of inputs from distinct networks over slow timescales.

1-071. Spatiotemporal dynamics and targeted functions of locus coeruleus norepinephrine in a learned behavior

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The locus coeruleus (LC) serves as the primary source of the neuromodulator, norepinephrine (NE), in the brain. Through a widely divergent set of projections, LC neurons have been suggested to release NE ubiquitously to regulate arousal and attention. However, LC-NE is implicated in more precise roles such as mediating learning, promoting task execution, and signaling unexpected uncertainty. Whether and how LC-NE activity facilitates these distinct aspects of behavior is unknown. Here, we show that LC-NE activity displays distinct spatiotemporal dynamics to enable two functions during a learned behavior—facilitating task execution under conditions of uncertainty, and encoding reinforcement to improve performance accuracy. To examine these functions, we used a behavioral task with graded auditory stimulus detection and task performance. Optogenetic inactivation of the LC demonstrated that LC-NE activity was causal for both task execution and optimization. Targeted recordings of LC-NE neurons using photo-tagging, two-photon micro-endoscopy, and two-photon output monitoring showed that transient LC-NE activation preceded behavioral execution and followed reinforcement. These two compo-

nents of phasic activity were heterogeneously represented in LC-NE cortical outputs, such that the behavioral response signal was higher in motor cortex and facilitated task execution, whereas the negative reinforcement signal was widely distributed among cortical targets and improved performance on the subsequent trial. Modular targeting and spatiotemporal integration in target regions thus enable diverse functions, whereby some NE signal are segregated amongst targets while others are broadly distributed.

1-072. Revealing latent knowledge in cortical networks during goal-directed learning

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Behavioral performance during goal-directed learning is typically measured in the presence of reinforcement. In this context, learning has been described as a slow process with high inter-subject variability. Exploration of the neural mechanisms, therefore, has focused on identifying dynamics concomitant with these slow performance improvements. Recent work, however, has shown that task acquisition is much faster and more stereotyped than previously thought¹. Performance was evaluated daily in reinforced and non-reinforced ('probe') trials. These probe trials revealed a rapid and stereotyped acquisition of task contingencies early in learning which was only expressed much later in reinforced trials. Here we ask whether and how sensory cortical networks encode and control the acquisition of this latent knowledge. We used longitudinal, two-photon calcium imaging of the same large population of excitatory neurons in layer II/III of the auditory cortex (AC) while mice learned to lick to a tone to obtain a water reward (S+) and withhold from licking to another tone (S-) to avoid a timeout. We used unsupervised low-rank tensor decomposition to uncover low-dimensional network dynamics at different timescales. We identified a subset of neurons that were initially S+-driven but then shifted within the first 400 trials to firing at the time of reward, suggesting a role in reward learning. Another subset of S--responsive neurons exhibited a rapid enhancement of their stimulus-driven response, suggesting a role in behavioral inhibition. Latent knowledge of the task was thus manifest in cortical networks during reinforced trials despite poor task performance. To test the causal role of these dynamics, we optogenetically silenced the AC on reinforced trials and assayed performance on light-off probe trials. AC silencing led to a striking delay in the acquisition of stimulus-action associations. Overall, our work argues that latent task knowledge emerges rapidly in the AC and is crucial for goal-directed learning.

1-073. Neural sequence representation of stimulus value, response and surprise in hippocampus and prefrontal cortex

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The hippocampus and the medial prefrontal cortex (mPFC) participate in episodic and working memory, respectively. In trace conditioning, animals learn to associate a sensory stimulus (CS) and a reward (US) separated by a delay (trace period). Although the neural activity in both areas can be linked to memory representation formation, the neural mechanisms involved in learning the temporal association between CS and US are not known. In this work, we use auditory trace conditioning in head-fixed mice with simultaneous 128-channel silicon probe recordings from the hippocampal CA1 subfield and the medial PFC to investigate this. First, we found that both CA1 and mPFC encoded stimulus and reward onset through neuronal sequences. Interestingly, this temporal representation increased with learning for the rewarded stimulus (CS+), but not for the unrewarded one (CS-) in CA1. Moreover, stimuli and reward temporal representations, which were initially similar, disentangled from each

other after learning. The similarity between stimulus and reward temporal representations was partially recovered during incorrect trials, when the animal received an unexpected reward, suggesting that this representation included a component of surprise. Using hidden Markov models, we revealed the emergence of neural states encoding for either CS+ or CS- stimuli after learning. In PFC, CS+ coding states increased their activation specifically during stimulus and trace periods. Crucially, the occurrence of CS+ coding states during CS- trials predicted the onset of a wrong decision, namely a lick leading to an incorrect trial. Together these results help unveil the dynamics of stimulus encoding in the mPFC-hippocampal circuit, suggesting the hippocampus has a role in the initial processing of the stimulus, while mPFC is important to create the stimulus-reward association and to drive the animal's decision.

1-074. Simultaneous mnemonic and predictive representations in the auditory cortex

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Recent studies have shown that stimulus history can be decoded via the use of broadband sensory impulses to reactivate mnemonic representations. It has also been shown that predictive mechanisms in the auditory system demonstrate similar tonotopic organization of neural activity as that elicited by the perceived stimuli. However, it remains unclear if the mnemonic and predictive information can be decoded from cortical activity simultaneously and from overlapping neural populations. Here, we passively exposed anesthetized rats to complex auditory sequences consisting of artificial vowel triplets, while recording electrocorticography (ECoG) data from the auditory cortex. Occasionally, vowels were replaced by noise bursts, i.e., a completely uninformative stimulus. Although the noise bursts did not carry any information about the memory or prediction of stimuli, we could decode both mnemonic and predictive information from neural activity evoked by the bursts, showing that sensory cortical networks maintain both mnemonic and predictive representations independently of the currently processed sensations. Crucially, we also demonstrate that predictive representations are learned over the course of stimulation at two distinct time scales, reflected in two dissociable time windows of neural activity. These results are novel in that they show, for the first time, that during exposure to dynamically changing sequences, information about memory and prediction can be decoded from neural activity in the auditory cortex. More critically, they also show that the predictive representations are rapidly acquired and dynamically updated to match the stimulus statistics. Strikingly, these effects are observed under full anesthesia, indicating that learning of complex and rapidly changing contingencies can occur under passive stimulation and without awareness, providing novel evidence for the automaticity of memory and predictive computations. This largely empirical study will be of interest for computational neuroscientists working in the fields of predictive coding, population coding, memory encoding, and statistical learning.

1-075. Transformation of population representations of sounds throughout the auditory system

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The computational principles driving the transformation of sound information throughout the auditory system remains an intense subject of research. Here, we used large-scale samples of neuronal activity from the auditory cortex, thalamus and inferior colliculus in mice and from a detailed cochlea model to identify key transformations of population representations of simple, short (~500ms) time-varying sounds in the auditory pathway. Using noise-corrected metrics, we measured the similarity of evoked population patterns across sounds. In subcortical regions, this measure shows that the full temporal structure of population activity (sequence code) better separates sounds than time-averaged firing rates (cell identity code). However, in the cortex these two codes converge. This result is not due to a reduced temporal resolution but instead evidences a hybrid coding scheme in which the activity sequences and the identity of active neurons carry redundant information in the cortex. We also observed that deep networks trained to identify sounds or sound attributes show the same convergence of sequence and identity codes in the deeper layers. This suggests the emergence of a cell identity code is key to assign time-varying sounds to particular labels or decisions. In line with this, we found that the cell identity code and not the sequence code determines the speed of associative learning in a reinforcement-learning model with plausible synaptic learning rules. The emergence of the cell identity code in cortex is associated with a sparsening of single-neuron responses, which follows a dense and correlated code in thalamus. Because the introduction of a reduced-size layer in deep artificial networks leads to denser representations, the dense code in thalamus may result from its position as an anatomical bottleneck. Overall, our results reveal a cortical reformatting of information to generate a cell identity code, which seems crucial for associating sounds to behavior and meaning.

1-076. Differential encoding of temporal context and expectation across the visual hierarchy

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What information do cortical neurons along the visual hierarchy encode for? The classic view that neural populations in the visual cortex preferentially encode responses to visual stimuli has been strongly challenged by recent experimental studies. For example, a large fraction of variance in V1 responses in rodents can be attributed to behavioral state¹, trial-history², etc. Here, we present a comprehensive experimental and theoretical study demonstrating that the cortical visual hierarchy differentially encodes the temporal context and expectation of visual stimuli. We measured layer-specific neural responses to expected and unexpected sequences of natural scenes across three visual areas using *in vivo* 2p imaging in mice: the primary visual cortex (V1Sp), the posterior medial higher order visual area (V1SpM), and retrosplenial cortex (RSP). We found that all three areas predominantly encode for the temporal context in which the images were presented. Information about image identity was not present in neural populations when images were presented in randomized order. Only when presenting images within long repeated sequences, V1Sp and V1SpM, but not RSP, encoded image identity as well. We found that the conjunctive encoding of temporal context and image identity was modulated by the emergence of expectation about sequential events. We compared responses to expected vs unexpected image sequences, the latter one comprising an occasional oddball image replacing the last image in a familiar sequence. We found enhanced responses to oddball images when they disrupted the expected sequence order. The oddball response was strong in V1Sp and V1SpM but weak in RSP. In the latter, we found evidence for predictive coding where the oddball response recapitulated the identity of the missing image. Our results establish temporal context and expectation as new encoding dimensions in the visual hierarchy and suggest that differential responses along the visual hierarchy instantiate a predictive coding mechanism.

1-077. Perceptual and neural representations of naturalistic texture information in developing monkeys

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Neurons in intermediate visual cortical areas such as V2 and V4, unlike those in V1, respond preferentially to texture images containing naturalistic image statistics common to natural images. We wondered whether and how representations of these image statistics, which we term “naturalness”, changed during development. We made longitudinal behavioral and neural measurements from 2 infant macaque monkeys at the ages of 6 and 12 mo, using texture stimuli that were parametrically varied in naturalness. We used a novel visual search task to efficiently measure behavioral naturalness sensitivity. We also implanted multielectrode recording “Utah” arrays in areas V1/V2 and V4, and recorded neural responses to the same stimuli in interleaved testing sessions. We found a robust increase in behavioral naturalness sensitivity across the ages tested. Neural sensitivity was greater in V4 than in V1 or V2, at both the unit and population levels. In contrast to the behavioral data, neural naturalness sensitivity did not change consistently with age. We analyzed the time course of responses, measuring the dynamics of the response to textures and of the differential response to naturalness. In V2, the response to naturalness emerged later than the texture response, while in V4 the texture response and the naturalness response began together. The naturalness signal in V4 preceded the naturalness signal in V2. Both visual and naturalness latencies in V4 shortened with age. In summary, our longitudinal data suggest that developmental performance improves at least in part as a result of changes downstream to V2 and V4. Our analysis of response dynamics suggests that naturalness sensitivity in the ventral visual stream may emerge first in V4 and be fed back to earlier areas.

1-078. Coarse-to-fine processing drives the efficient coding of natural scenes in mouse visual cortex

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The sequential analysis of information in a coarse-to-fine (CtF) manner is a fundamental processing strategy of the visual system. Previous studies have shown that neurons in the primary visual cortex (V1) of anesthetized animals can process spatial information in a CtF fashion, shifting their spatial frequency (SF) preference from low (coarse) to high (fine) throughout their response to static grating stimuli. However, many central questions regarding CtF processing, such as whether it occurs in awake behaving mice and potential computational advantages it may provide, remain unexplored. Here, we performed large-scale single unit recordings to characterize CtF processing in both anesthetized and awake mice, determine its developmental profile, and study its role in encoding ethologically relevant natural scenes. Using high-density multielectrode silicon probes and subspace mapping of receptive fields, we found that the vast majority of V1 neurons from awake adult mice displayed two temporally discrete peaks in their spatiotemporal receptive field, each with distinct SF preferences. The SF shift between these 2 peaks was large and nearly always from low to high (i.e. CtF). Additionally, we discovered CtF processing is significantly attenuated in anesthetized mice and develops postnatally via experience-dependent mechanisms. Finally, we show that awake mice process the complex spatial statistics of natural scenes in a CtF manner. Excitingly, we demonstrate that this CtF processing reduces redundancy in the neural representation of natural scenes by shifting the population response away from the high-power, low-SF statistical regularities in these stimuli. This redundancy reduction drove an increase in the representational efficiency of natural images that did not occur in anesthetized or dark-reared mice with significantly attenuated CtF processing. Collectively, these findings establish a novel, state-dependent, computation of cortical circuitry that develops after vision onset to allow the animal to efficiently encode the complex spatial statistics of natural scenes.

1-079. Coordinated multiplexing of information about distinct objects in visual cortex

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How the brain separates information about multiple objects despite overlap in the neurons responsive to each item is not well understood. It has recently been proposed that when more than one stimulus is present, single neurons can fluctuate between coding one vs. the other(s) across some time period, i.e. a form of neural multiplexing in the time domain (Caruso et al., 2018). However, it is not known (a) whether such fluctuations occur specifically when two distinct objects are present and not in other cases, and (b) how fluctuations in individual neurons might be coordinated with one another to ensure the representation of both objects across the population. Here we investigated these questions in visual cortex (V1, V4) using two visual gratings that could be presented adjacent to one another (two objects), or superimposed to form a single "plaid" object. We found fluctuating activity in V1 only for the two-object case. The fluctuations were coordinated across the neural population to produce a pattern of V1 noise correlations that had not previously been detected with single stimuli: distinct distributions of positive and negative values, depending on whether the two neurons in the pair had similar or different preferences for the individual grating stimuli. A similar pattern was also seen in V4 for adjacent stimuli, but was not observed in either structure for single stimuli or when the two gratings were superimposed and formed a single object. Importantly, the bimodal correlation patterns were most pronounced among pairs of neurons showing the strongest evidence for multiplexing. These findings suggest multiple stimuli evoke different response dynamics than those evoked by single stimuli, lending support to the multiplexing hypothesis and suggesting a means by which information about multiple objects can be preserved despite the apparent coarseness of sensory coding.

1-080. Moving bar of light evokes vectorial spatial selectivity in hippocampal place cells

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Visual cortical neurons are known to encode the position and motion direction of specific stimuli retrospectively, without any locomotion or task demand. Hippocampus, though receives projections from these visual cortical areas, is hypothesized to require self-motion or cognitive task to generate allocentric spatial selectivity that is abstract and prospective. In an attempt to bridge these disparities, we measured hippocampal responses to a moving bar of light in a body-fixed rat, without imposing any task demand on the animal. For a revolving bar, about 70% of dorsal CA1 neurons showed stable activity modulation as a function of the bar's angular position, independent of behavior and rewards. A third of tuned cells also encoded the direction of revolution. For a linearly moving bar, neurons encoded for distance of the bar from the animal, with a preference for the approaching motion. Collectively, we term these results as visually evoked vectorial selectivity (VEVS) in CA1 cells. Unlike most place cells, VEVS was found to be largely retrospective. Changes in the visual stimulus or its trajectory did not lead to remapping, but only caused gradual changes in these responses. Most VEVS tuned neurons behaved like place cells during spatial exploration and the selectivity in these two domains were found to be correlated. We thus hypothesize that VEVS responses could form basic hippocampal building blocks, through which responses from the visual cortex get relayed after some filtering, for further processing and context-associations. When combined with self-motion, reward, or multisensory stimuli, these can generate the diversity of abstract and prospective representations including space, time, and episodes.

1-081. Neural mechanisms for collision avoidance exploiting positional geometry

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Visual motion provides us with rich cues about the three-dimensional structure of our environment. However, it is generally unknown how circuits of neurons decode spatial information carried by patterns of visual motion. Here, we study the neural mechanisms of a collision avoidance behavior in walking *Drosophila* fruit flies as a simple model of motion-based spatial vision. In psychophysical experiments, we observed that flies exhibit slowing upon encountering small objects moving back-to-front in the frontolateral visual field. With a simple simulation, we demonstrate that this slowing can be seen as a behavior to avoid collisions with conspecifics that exploits the geometry of objects in near-collision courses. Next, we identified a visual neuron called lobula plate-lobula columnar type 1 (LPLC1) cells to be necessary and sufficient for the collision avoidance slowing behavior through synaptic silencing and optogenetic activation experiments. The visual response property of LPLC1 neurons measured with two-photon calcium imaging closely resembled the visual tuning of the collision avoidance behavior, notably in its spatially biased direction selectivity. Taking advantage of connectomic analyses, optogenetics, as well as neurochemical imaging and manipulations, we demonstrate that the peculiar visual tuning of LPLC1 is implemented through the pooling of elementary motion- and object-detecting neurons, as well as spatially biased glutamatergic inhibition. Additionally, we identified a downstream pathway of LPLC1 that mediate the collision avoidance behavior. Overall, our results exemplify how a small neural circuit can combine different visual features to solve a specific spatial vision problem, exploiting a universal geometrical constraint of the visual world.

1-082. Investigation of a multilevel multisensory circuit underlying female decision making in *Drosophila*

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Multisensory integration plays an important role during decision-making in naturalistic settings. Here, we dissect circuit mechanisms underlying multisensory integration in *Drosophila melanogaster*, focusing on neurons that directly drive and modulate mated female rejection behavior (ovipositor extrusion or OE) during courtship. DNp13 is a descending neuron that is both necessary and sufficient for OE (Wang et al. Current Biology, 2020); pC2l neurons, which are activated by male courtship song (Deutsch et al. Current Biology, 2019), provide direct presynaptic input to DNp13 (Wang et al. Current Biology, 2020). Via connectomic analysis, we mapped putative sites of audiovisual integration onto both DNp13 and pC2l, identifying a previously uncharacterized group of visual projection neurons, called LC31, as important inputs to both cell types. Having uncovered that both pC2l and DNp13 receive auditory and visual inputs, we will investigate how these inputs are combined at both levels of the circuit to drive OE. To facilitate this work, we generated sparse driver lines to target the subset of LC31 neurons that serve as inputs to the OE circuit. We used SLEAP (Pereira et al. bioRxiv, 2020) to track the postures of virgin males and mated females during courtship, including tracking OE, in addition to recording and segmenting all song produced by the male, over a large dataset of behavioral recordings. We find that both song and changes in male position (in particular the subtended angle of the male on the female's retina) precede OE, and are examining differences in this behavior in females with cell types of the OE circuit silenced. Taken together, this study will ultimately provide insight into how neurons integrate multisensory cues directly from their unisensory inputs, and how they integrate multisensory signals over time, to inform dynamic decision making in ethologically relevant settings.

1-083. Multiscale Hierarchical Modeling Framework For Fully Mapping a Social Interaction

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Social behaviors result from processing social cues (sensory cues from a partner) and producing actions relative to both the other's behavior and one's own internal state. How these two (social sensory cues and internal states) come together to drive behavior on a moment-to-moment basis is not yet clear. Here we fill this gap focusing on social interactions in *Drosophila melanogaster*. During courtship, males chase females and sing; female responses to male cues serve as critical feedback signals that shape the male's ongoing behavior (Coen et al. 2014). In addition, we know that internal states shape these interactions (Calhoun et al. 2019 and Deutsch et al. 2020). Although courtship in *Drosophila* has been studied for decades (Yamamoto and Koganezawa 2013) we still lack a comprehensive map of the elaborate closed-loop social interactions, in both males and females, that comprise the courtship repertoire. This has been an impediment in interpreting manipulations of neural activity. To address this issue, we built a new behavioral phenotyping system that captures fine-scale postural descriptors of freely-moving, interacting fruit flies, and we leverage a deep learning framework (SLEAP) for multi-animal pose estimation to produce a rich, complex behavioral dataset of >90 pairs of freely moving, courting fruit flies. Finally, we introduce a novel computational framework that integrates both social sensory cues and internal states on multiple timescales to determine how they shape social dynamics.

1-084. Parvalbumin-positive interneuron regulation of maternal pup retrieval behavior

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Learning requires the formation or modification of neural circuits – an extraordinary showcase of the brain's plasticity. Despite an established appreciation for the reorganizational capabilities of the brain, the exact mechanisms that enable experience-dependent plasticity remain unknown. The goal of this work is to uncover how circuitry of the auditory cortex (AC) facilitates learning of an auditory-driven maternal retrieval behavior in mice. Mouse pups emit ultrasonic vocalizations (USVs) when they are separated from the nest which cues maternal retrieval - a learned response to these distress cries. Interestingly, the transcription factor methyl-CPG binding protein 2 (MeCP2) is required for successful retrieval¹. Furthermore, a subpopulation of inhibitory cells, parvalbumin-positive (PV) interneurons, is particularly susceptible to MeCP2 perturbations. Females with an MeCP2 mutation (a Rett Syndrome model) exhibit deficits in pup retrieval, have elevated PV expression, and significantly more perineuronal nets encompassing AC PV cells - a hallmark signaling the closure of plasticity periods¹. This suggests that disruptions to the PV inhibitory circuitry of the AC underlie deficits in retrieval by limiting the cortical plasticity necessary to learn this behavior. However, PV activity has never before been probed during retrieval. Here, we aim to uncover the real-time PV network contributions to retrieval, and how disruptions to the network impair behavior. We used fiber photometry in the AC PV population during retrieval behavior in both wildtype and MeCP2 mutant females. AC PV activity was highly dynamic throughout the retrieval session in wildtypes, but not MeCP2 mutants. We found pronounced peaks in AC PV activity during both auditory events (USVs) and behavioral epochs such as the mouse contacting pups. This prompted us to implement a general linear model to uncover the signal's sensory and behavioral influences. In parallel, we are considering these peaks to reflect an attentional PV network state that may facilitate successful retrieval.

1-085. Anterior cingulate cortex enables rapid set-shifting behaviour via prediction mismatch signalling

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A key component of cognition is set-shifting, which requires animals to update their knowledge of current rules or context, allowing flexible behaviour in a changing environment. This updating of rules or context relies on constantly evaluating and detecting mismatches between expectation and observed outcomes of events. The anterior cingulate cortex (ACC) has been implicated in set-shifting behaviour, consistent with its well-established role in processing conflicts during cognitive tasks in primates and humans. However, the neural circuit mechanisms underlying set-shifting are largely unknown. Here we trained mice to perform an attentional set-shifting task in which they alternated between blocks of distinct task rules. Mice typically required a single experience of an expectation violation to accurately adapt their behaviour to respond to the same stimuli using different rules. The behaviour was well-fit to a reinforcement learning (RL) model incorporating context belief states, but not to a basic RL model. Optogenetic inhibition of the anterior cingulate cortex significantly impaired behavioural switching but had no effect on performance of the task once a behavioural switch was achieved. Inhibition of prelimbic cortex (PL) had no such effect. Chronic *in vivo* two-photon calcium imaging during the task identified prediction-mismatch tuned cells in the ACC but not in V1. These cells maximally fired when a stimulus was expected but not received, and these responses were inhibited when the expected stimulus was received. Crucially, the magnitude of the mismatch responses in the ACC could predict successful behavioural transitions in the subsequent trial. These results suggest an essential role for the ACC in driving rapid behavioural changes in response to changing context using prediction mismatch signals.

1-087. Improved striatal learning with vector-valued errors mediated by diffusely transmitted dopamine

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It is well established that midbrain dopaminergic neurons support reinforcement learning (RL) in the basal ganglia by transmitting a reward prediction error (RPE) to the striatum. In particular, different computational models and experiments have shown that a striatum-wide RPE signal can support RL over a small discrete set of actions (e.g. no/no-go, choose left/right). However, there is mounting evidence that the basal ganglia functions not as a selector between predefined actions, but rather as a dynamical system with graded, continuous outputs. To reconcile this view with RL, there is a need to explain how dopamine could support learning of dynamic outputs, rather than discrete action values.

Inspired by the recent observations that besides RPE, the firing rates of midbrain dopaminergic neurons correlate with motor and cognitive variables, we propose a model in which striatal dopamine carries a vector-valued error feedback signal (a loss gradient) instead of a homogeneous scalar error (a loss). Using a recurrent network model of the basal ganglia, we show that such a vector-valued feedback signal results in an increased capacity to learn a multidimensional series of real-valued outputs. The corticostriatal plasticity rule (based on the RFLO algorithm) we employed is a fully local, "three-factor" product of the presynaptic firing rate, a post-synaptic factor and the unique dopamine concentration perceived by each striatal neuron. Crucially, we demonstrate that under this plasticity rule, the improvement in learning does not require precise nigrostriatal synapses, but is compatible with random placement of varicosities and diffuse volume transmission of dopamine.

1-088. Reward Bases: instant reward revaluation with temporal difference learning

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The dominant theory of dopamine function in the basal ganglia system is model-free reinforcement learning (RL) where the dopaminergic neurons in the Ventral Tegmental Area (VTA) encode reward prediction errors which are used to modulate plasticity at cortico-striatal synapses so as to learn a value function of cortical states (Schultz et al 1998). However, a key assumption of this model (and model-free RL generally) is that the reward function being optimized is fixed, while for biological creatures the ‘reward function’ can fluctuate over time depending on physiological state – i.e. food is rewarding when hungry but not when sated. While experiments (Robinson et al 2013) have demonstrated that animals can instantly adapt their behaviour when their internal physiological state changes, the neurocomputational underpinnings of this capability are unknown and cannot be accounted for by standard model-free RL methods which must be retrained from scratch if the reward function changes. In this abstract, we propose a novel and simple extension to temporal difference learning that allows for zero-shot (instant) generalization to changing reward functions. Specifically, we demonstrate that if we interpret the reward function as a linear combination of reward basis vectors and then learn a separate value function for each reward basis using standard TD learning, then we can instantly compute the value function of any reward function in the span of the reward basis vectors. Moreover, this algorithm can be straightforwardly implemented in neural circuitry by simply parallelizing the circuits proposed in Schultz et al (1998). Here, we present the mathematical formalism underlying our algorithm, and demonstrate it can reproduce the behavioural effects of instant generalization (Robinson et al 2013) as well as dopamine responses in ventral striatum (VS) (Papageorgiou et al 2016)

1-089. A striatal probabilistic population code for reward underlies distributional reinforcement learning

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Research in machine learning has realized large performance gains on a variety of tasks by expanding the target of learning from the mean reward, as in traditional reinforcement learning (RL), to the entire distribution of rewards, an approach known as distributional RL. Dopamine (DA) neurons projecting from the midbrain to the striatum have long been thought to drive traditional RL in the mammalian brain. Moreover, a recent analysis of the response diversity of these neurons shows they have the appropriate properties to support distributional RL, and thus the learning of complete reward distributions. However, while representations of mean reward (frequently called “value”) abound across brain regions, particularly in the striatum, little is known about how neurons encode information about higher-order moments of reward distributions — much less the complete shapes of these distributions.

To fill this gap, we used Neuropixels probes to acutely record striatal activity from well-trained mice (n=9) in three classical conditioning tasks, in which unique odors were paired with particular reward distributions. We found that striatal neurons stably represent reward distributions, over and above mean reward, stimulus identity, and behavioral output. We then asked what mathematical form these codes take by modeling population responses as either probabilistic population codes (PPCs), distributed distributional codes (DDCs), quantile codes, or expectile codes, which differ in the particular statistics they use to characterize encoded probability distributions. We consistently found that PPCs outperformed the other code types, allowing us to decode from single-trial population responses not only the identity of reward distributions, but also their precise shapes. These results simultaneously bolster the core claim of distributional RL in neuroscience — that neurons encode full reward distributions — while challenging existing distributional RL models, which rely on other code types.

1-090. Deliberation gated by opportunity cost adapts to context with urgency in non-human primates

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Finding the right amount of deliberation, between insufficient and excessive, is a hard decision-making problem that depends on the value we place on our time. Average reward, putatively encoded by tonic dopamine, serves in existing reinforcement learning (RL) theory as the stationary opportunity cost of time. This cost often varies with context, however, which changes over time. Current RL approaches thus do not efficiently handle task non-stationarity. Yet, the brain's representation of and computation with time's value, including its impact on the neural dynamics of deliberation, must account for this variation. Using non-human primates as a model, here, we offer a two-part proposal for how the brain achieves time-sensitive deliberation. The opportunity cost of time is (1) estimated adaptively and on multiple timescales from reward history and (2) is represented directly as urgency, a previously characterized neural signal that lowers the threshold for decisions as within-trial deliberation goes on. We show that this simple, value-free strategy we call Performance-Gated Deliberation (PGD) is a heuristic approximation of the optimal, average-reward reinforcement learning (AR-RL) strategy. We highlight that the context variation of urgency from both PMd and LIP recordings in separate tasks favors a trial-aware versus trial-unaware cost of time. Using this version, we fit a PGD agent to decision times from recorded behaviour of two non-human primates in a prediction task with non-stationary reward context. This PGD agent outperforms AR-RL optimal solutions in explaining the state-dependence of the behaviour, with the model of the hastier subject having shorter inferred memory window and larger inferred reward bias. The opportunity cost profiles also match the urgency signals extracted from simultaneous PMd recordings. Our integrated research approach spanning cognitive and systems neuroscience grounds the value of time in its neural representation by revealing its impact on the dynamics of decision-making brain areas.

1-091. Mesolimbic dopamine encodes subjective value and predicts time investment decisions

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From picking dinner to college courses, the choices we make reflect our past experiences and momentary preferences. The value of a choice is inherently subjective, internal to a decision maker, yet we need to identify objective measures to study its neural basis. According to learning theory, value can be inferred from reinforcement history through an algorithmic computation ('model-inferred value'). In contrast, in behavioral economics, appropriately designed tasks can elicit choice patterns that reveal subjective preferences ('revealed choice value'). However, the relationship between these distinct measures of subjective value remains unclear, which limits studying its neural basis.

We designed a probabilistic reward learning task that brought together these two approaches. Rats chose between two options that were probabilistically 'baited' with rewards, varying across blocks. To earn a reward, rats committed to their choice by investing time for uncertain, delayed rewards. Choice value could be inferred from reward and choice history using generalized linear models or fitting reinforcement learning models. These model-inferred choice values robustly predicted rats' choice behavior, as well as the magnitude of time investment. In turn, shorter time investments predicted choosing the lower-valued ('model-inconsistent'), rather than the higher-valued ('model-consistent') option. Thus, time investment reflected the rats' subjective choice valuation, beyond model-inferred value alone, thereby behaviorally revealing choice value. To investigate the neural processes underlying choice valuation, we monitored dopamine release in the ventral striatum using fiber photometry with virally expressed, genetic dopamine sensors. We observed phasic dopamine release at the time of choice, which

strongly predicted trial-by-trial time investment seconds in advance, but was not correlated with model-inferred choice value based on reward history. Thus, mesolimbic dopamine encodes the subjective valuation of choice options that can be behaviorally read-out in single-trial time investment decisions.

1-092. Monkeys exhibit combinatorial reasoning during economic deliberation.

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Value optimization is a defining principle of economic behavior. To uncover the underlying psychological and neural processes, we developed a behavioral task based on the 'knapsack problem'. Given several items, each with a value and weight, the objective is to maximize value within the weight limit of the knapsack. Two rhesus monkeys solved a touchscreen-based version that equates weights with juice reward sizes. The animals performed well above chance and achieved at least 75% of the optimal reward value on 80% of all knapsack trials. We defined each unique set of items as an 'instance,' and estimated the difficulty of each instance. The animals adjusted their behavior based on the estimated difficulty. Specifically, they employed a 'satisficing' threshold that was lower when the difficulty was higher. Likewise, the animals took longer on individual selections and the entire solution when the difficulty was higher. These results indicate that the animals understood the complexity of the task and adjusted their behavior accordingly. To understand how the animals optimized, we categorized their solutions according to the solutions' proximity to established computer algorithms. The greedy algorithm described the animals' behavior on most trials. However, on approximately 15% of trials, combinatorial algorithms – and especially the Sahni-3 algorithm – provided the best match. During combinatorial trials, the animals spent more time deliberating, compared to noncombinatorial trials. Moreover, difficulty modulated deliberation time only during combinatorial trials. These results demonstrate that the animals adapted algorithmic strategies and employed combinatorial reasoning. Feedforward neural networks trained to mimic the greedy and Sahni-3 algorithms, the dominant algorithmic matches to the animals' behavior, showed stronger instance and solution representations, compared to networks trained to mimic other algorithms. These results establish a new behavioral paradigm for investigating the psychological and neural basis for combinatorial optimization and economic deliberation.

1-093. Optimal reward-rate in multi-task environments, and its consequences for behavior

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Consider a task where you're accumulating noisy evidence about two options, and the longer you collect evidence the more likely you are to choose the correct one. You get 1,000 for choosing the correct option and 900 for choosing the incorrect one. How long should you wait before making a decision? Tasks like this have been studied for decades, but typically in isolation. However, in the real world you always have the option of switching tasks. This can have a large effect on behavior: if, after making a choice, you are able to switch to an even more rewarding task, you won't take long at all, but if most tasks you encounter yield much lower rewards, you're likely to take a very long time. So the answer to how long you should take is: it depends on the reward statistics of other tasks.

Here we provide a formulation for the problem of maximizing reward rate in a multi-task setting, and present an efficient reinforcement learning algorithm for solving it; the algorithm extends results in foraging theory to stochastic environments. We argue that human behavior aligns with what is expected from our algorithm. We illustrate this for two-task environments, and show that the amount of time spent on one task depends strongly on the reward structure of the other, and the probability that it occurs. Our theory makes several experimentally testable predictions about human – and animal – behavior.

1-094. Using Markov Decision Processes to benchmark the performance of artificial and biological agents

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When an agent is trained on a complex episodic task, different task parts may be learned at different rates. How do we determine which part of the task challenged the agent the most? Since reward is provided usually only at the end of each trial, it cannot be used to infer within-trial learning trends. Behavioral features such as speed or trial duration capture trends in the agent's decision-making, but do not necessarily indicate that the agent is getting better at the task. We address this issue by modeling the task as a Markov Decision Process (MDP). The Q values of the optimal policy measure the quality of each and every action of the agent. We illustrate the use of two such measures, the well-established Optimality-Gap measure, and the Action-Rank – a new suggestion which is analytically shown to be less sensitive to the model's hyper-parameters. We first validated this approach on synthetic data from a deep reinforcement learning agent (Deep Q-network, DQN), and then used it to analyze the behavior of a rat, where both DQN and rat were trained on the same operant task (sound discrimination in a large arena). We observed that (1) Rat behavior approached the optimal policy gradually throughout training; (2) most of the policy refinement occurred at a specific, short ($\text{<}1\text{s}$) segment of the trial; (3) the first trials of each day showed sub-optimal performance. These results illustrate the ability of optimality-based measures to quantify fine features of the learning process. Importantly, optimality-based measures may contribute to cross-disciplinary research on learning in both artificial and biological agents.

1-095. Rethinking Tolman's latent learning with metacognitive exploration

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Previous studies have used the reinforcement learning theory to explain how animals explore a task space to maximize reward. While recent works argued that uncertainty in valuation is the key variable to guide exploration, little is known about the role of another variable - the uncertainty in state-space representation. One reason is that a simple task design consisting of only a few states and actions cannot accommodate the uncertainty of the environmental structure. Here, we hypothesize that metacognition, the human's unique ability to introspect and estimate one's level of uncertainty, guides the efficient exploration of a large state-space. For this, we designed a novel two-stage decision-making task with infinitely-many choices and sparse rewards and collected a total of 101 subjects' data (88 behavioural and 13 fMRI). We examined two key variables guiding exploration: uncertainty about the environmental structure (state-space uncertainty; SU) and the reward structure (value uncertainty; VU). We found that both variables are significantly correlated with the individual metacognitive ability measured using an independent perception task. Interestingly, we also found that high metacognitive subjects outperformed the low metacognitive subject group (test phase performance; $p < 10^{-10}$). In doing so, the former group relies on SU throughout learning, while the latter uses both SU and VU, suggesting that SU might be sufficient for metacognitive exploration. This finding is confirmed by the model comparison analysis with metacognitive exploration models that combine SU and VU in various ways. The preliminary fMRI analysis suggests that IPL, one of the regions previously known for metacognition, might be engaged in resolving SU. These results elucidate the role of metacognition in fostering a sample-efficient exploration strategy. Ultimately, our work may offer a new perspective on Tolman's latent learning: metacognition might be one of the key components to facilitate efficient learning of the latent environmental structure without value information.

1-096. Long-term consequences of actions affect human exploration in structured environments

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Exploration is an essential part of learning, and the question of how to achieve efficient exploration has been extensively studied in the field of Reinforcement Learning (RL). Recent works have demonstrated – both in theory and in practice – the importance and effectiveness of sophisticated methods of exploration which are sensitive to the long-term exploratory consequences of actions, and to the global structures of the environment. This is analogous to the standard concept of value in RL. How "good" an action is depends not only on the immediate reward gained by taking it, but also on the expected future rewards gained by taking it. Similarly, how "good" an action is for exploration also depends on whether it leads to future states from which new knowledge can be gained. Whether and how humans implement these computational principles in their exploratory behavior is largely unknown. The standard paradigm that is used to study exploration in humans, the Multi-Armed Bandit, cannot address these questions because it is characterized by a single state, and as such does not entail long-term consequences of actions. Ultimately, the exploration "utility" of an action in a Bandit problem can be expressed in a local quantity such as the number of times it has been previously visited. Based on recent RL algorithms for exploration in complex environments we developed a novel experimental task involving a multi-state structured environment. This task allowed us to test predictions of the models by parametrically changing some properties of the environment. We found that human participants take into the account long-term consequences of actions when making exploratory choices, and are sensitive not only to local, immediate exploration gains, but also to the global underlying structure of the environment.

1-097. Constructing behaviour in structured environments

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In reinforcement learning (RL), we try to learn a function f that maps a state representation s to actions a : $a=f(s)$. Learning f is hard, and is typically performed in each environment. What if, instead, we learn how to rapidly construct s out of general building blocks, for which the same f always works? We demonstrate (1) that this is possible in spatial worlds using object- and goal-vector representations that exist in the brain and (2) that this 'behavioural construction' dramatically outperforms traditional RL in simple spatial problems. In a companion paper, we demonstrate that the "building-block" representations can be learnt by predicting actions. For such a mechanism to work, each state representation (s) must contain information about the whole environment, so that actions (a) can be inferred directly from any s . To achieve this, whenever a new object or reward is encountered, we initialise a vector-representation centred on that object. Because vector representations path-integrate, the correct object-centred representations can immediately be inferred at all remote locations, either during exploration or, critically, in replay. These representations are bound to their locations in memory – effectively building memories of future behaviour. When the agent visits a new location, its s already contains information about all objects. We show it is possible to learn a function, f , that maps s to optimal a , including tortuous paths around multiple boundaries to the goal. Crucially, the same f works in all environments. Hence, instead of learning actions afresh in each environment, we construct a representation of the current situation from generalisable representations that predict good actions. By simply binding existing cortical representations in hippocampal memory, replay implicitly constructs state spaces (latent learning) and performs credit assignment. Although demonstrated in physical space, this approach will work in any structured space where actions have consistent meaning.

1-098. Consolidation of Sequential Experience Supports Flexible Model-Based Planning

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A variety of algorithms have been proposed to account for goal-directed planning, operationalized as sensitivity to reward revaluation i.e. flexibility in the face of reward changes. These algorithms use different representations which trade off computational cost with flexibility in the face of changes in the world. In particular, model-based (MB) reinforcement learning uses tree-search through 1-step relational representations that are often thought of as ‘semantic’. In contrast, models like the successor representation (SR) store representations of sequential experience. These algorithms can be distinguished based on MB sensitivity to transition revaluation, i.e. flexibility following changes in state-state transition relationships, which the SR lacks. It is believed that consolidation changes the way memories are represented and structured – transferring them from hippocampus to cortex and making them more abstract and semantic. This is important in light of recent findings, showing a transient hippocampal involvement in goal-directed planning, i.e. the hippocampus is required immediately after learning but not a week later (Bradfield et al, Nat Neuro, 2020). Further, the hippocampus has been proposed to specifically support SRs (Stachenfeld et al., Nat Neuro, 2017). We therefore sought to test how consolidation impacts the representations used for planning. To do this, we developed a new planning task which can detect either MB use of 1-step transition models, or use of sequential experience, like SRs. After training on fixed sequences, unique reward and transition revaluation problems are posed so as to map the relative use of either type of representation. We demonstrate that a week of memory consolidation pushes behaviour from SR-like insensitivity to transition revaluation towards flexible MB use of 1-step transitions that is sensitive to both reward and transition revaluations.

1-099. Neural basis of transferable representations for efficient learning

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We learn different rules that can switch depending on context. When the rule depends on context, the context is important to learn to differentiate the rewarded choice in different contexts. While it has previously been shown that the reinstatement of context guides decisions for reward, it is less clear how or whether context-based reactivation guides the efficient learning of reward and context associations. We hypothesize that representations of the context are used to guide learning of associations between context and reward. We test whether this context is retrieved from memory circuits prior to when a choice is made to optimize decisions. In this study, we assess how context representations in the high frequency 80-120 Hz ripple band transform and are retrieved using brain-wide oscillations recorded with intracranial EEG in 14 human participants who completed a rule learning task. We found that (1) context-related high frequency oscillatory patterns are reactivated for context dependent decisions when a reward is received, as indicated by good decoding prediction of context, (2) 4-8 Hz theta activity in medial temporal lobe and frontal cortex accompanies these reactivations, and (3) the dependence of decisions on context influences the speed of evidence accumulation necessary to reach a decision, modelled as a drift diffusion process. These findings suggest that coincident reactivation of context representations and theta activity in memory circuits during rewards for correct choices may influence subsequent decisions.

1-100. Model architectures for choice-selective sequences in a navigation-based, evidence-accumulation task

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Many classic decision-making paradigms require animals to select between alternative choices by accumulating evidence over time. Traditional models of decision-making posit that such accumulation is reflected in the activity of single neurons whose activity ramps up or down with evidence. However, recent experiments suggest that, in many settings, neurons do not exhibit persistent, ramping activity but rather are transiently and sequentially activated. Motivated by experiments in a navigation-based, accumulation of evidence task in which sequential activity is observed across multiple regions of neocortex, hippocampus, and striatum, we here propose two classes of networks that accumulate evidence in their sequential activity. First, we create a planar “bump attractor” model in which individual neurons are tuned to particular values of position and evidence, and the set of active neurons shifts along one axis with changes in evidence and along the other axis with changes in position. This model predicts unimodal tuning curves for individual neurons when plotted as a function of evidence and position, as has been observed in the response profiles for neurons in the hippocampus. Second, we develop a model consisting of two mutually inhibitory chains of neurons, in which each chain receives evidence cues for one of two alternative choices. Evidence for a given choice increases activity in one chain while decreasing activity in the other, while activity progresses forward in each chain with position. This model predicts tuning curves that are tuned to a specific position and that increase or decrease monotonically with evidence, as observed in our preliminary recordings in the anterior cingulate cortex. Overall, this work represents the first models of how circuits displaying sequential activity can solve accumulation-of-evidence decision-making tasks, and makes predictions about different underlying computational architectures in different brain regions.

1-101. Temporal Dynamics in an Attractor Model of the Songbird’s Premotor Nucleus.

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While temporal control is crucial for the generation of a wide range of sensorimotor tasks, its underlying mechanisms remain unclear. Like human speech, birdsong relies on a tight muscle coordination, and songbirds have proved to be an outstanding model to study the sequential pattern of neuronal activity encoding action timing. In male zebra finches, the premotor nucleus HVC is responsible for the precise control of song tempo. Current computational models of HVC rely on synfire chains, a purely feedforward network model that can account for HVC sequential activity. Synfire chains are however not robust to noise and function for a narrow range of feed-forward weights, thus requiring fine tuning during learning. On the contrary, attractor dynamics provide networks with robust functional properties that make them an attractive alternative to feedforward models. Here, we propose that HVC neuronal dynamics may be modelled using the ring model (Zhang, 1996; Hansel & Sompolinsky, 1998), where recurrent connections allow the formation of an activity bump that remains stable across a wide range of weights. In the case of asymmetrical connectivity, the bump of activity moves across the network. We show that the width of the activity bump, and thus the duration of transient neuronal activation, can be decreased to reproduce the brief activity bursts of HVC neurons. Relying on a reward covariance rule (Williams, 1992), we show that the duration of a syllable can be modified in response to a perturbed reward profile, as implemented

in a widely used lab conditioning paradigm. Consistent with behavioral data, the change in duration is specific to the target syllable. We derive a new prediction from the model and show that following local muscimol (GABAa agonist) injection in HVC, a perturbation in the initial phase of the pattern formation would delay song initiation, but singing would be sustained.

1-102. Motor cortex isolates skill-specific dynamics in a context switching task

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Performing two skills, such as swinging a tennis racquet or axe, requires both differences in typical motor output and different feedback-driven adjustments. The motor cortex (M1) is clearly involved in specifying motor output. Less-well understood is the extent and nature of its role in performing computations underlying skill-specific feedback control. In addressing this question, a technical hurdle is that it can be difficult to discern when skill-specific aspects of neural activity reflect different motor outputs versus skill-specific feedback control. To overcome this hurdle, we employed a simple 1D force production task with two contexts that required the same typical motor output, but opposite responses to sensory feedback. Using primate Neuropixels, we recorded thousands of neurons from M1 and dorsal premotor cortex. Despite the simplicity of motor output in this task, most neurons had complex time-dependent patterns of activity that did not directly reflect force or muscle activity, and were strongly context dependent. This demonstrates something unexpected: identical motor outputs can be driven by very different internal patterns of neural activity, even in an area closely tied to motor output. Context-dependent activity presumably enables transformation of the same sensory feedback into different motor corrections. Network simulations suggest this occurs via a simple mechanism: context-dependent neural trajectories allow each context to leverage different dynamics to transform the same sensory feedback into opposing outputs. The empirical data agreed with this hypothesis: small deviations from the typical neural trajectories reflected sensory inputs, motor corrections, and the flexible link between them. These results argue that skills are produced by skill-specific (not output-specific) neural trajectories that allow for flexible input-output relationships produced by dynamics close to that trajectory. A prediction of this hypothesis is that motor cortex activity may leverage the vast volume of a high-dimensional neural space to store the repertoire of distinct motor skills.

1-103. What is the snow in a neural avalanche?

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Neurons spike spontaneously in many experimental settings. Such firing patterns are often characterized by prolonged periods of silence followed by an unknown trigger of spontaneous activity that propagates throughout the slice. These were dubbed ‘neural avalanches’ as they resemble avalanches in which accumulated snow rapidly flows down a mountain slope. Expanding this analogy – if the network connectivity is equivalent to the mountain slope, what is the ‘snow’ that accumulates prior to a neural avalanche? Here, we propose that it is the accumulation of ATP in neuronal mitochondria, and that avalanches provide a respite from toxic conditions that arise during lower-than-baseline ATP consumption.

Neurons, presumably in anticipation of synaptic inputs, keep their ATP levels at a maximum. As metabolic recovery from synaptic inputs requires substantial energy resources, neurons are ATP-surplus/ADP-scarce during synaptic

quiescence. With ADP availability as the rate-limiting step, ATP production stalls in the mitochondria when energy consumption is low, leading to the formation of toxic Reactive Oxygen Species (ROS) which disrupt many cellular processes. We hypothesize that neurons actively sense their metabolic state and trigger ‘metabolic spikes’ to restore ATP production, to avoid ROS. To test this, we built a recurrent network in which neurons sense their metabolic state (based on recent inputs and outputs) and modulate an intrinsic metabolic current to control spiking when necessary. When the network goes silent, neurons initiate metabolic spikes to increase their own energy expenditure and avoid ROS poisoning. These first spikes trigger a domino effect of activity that ripples through the network and ceases when neurons have increased their ATP expenditure either through synaptic inputs or by spiking. This mitochondrially mediated homeostatic mechanism can account for many intrinsic firing patterns observed in neurons, as well as the avalanche-like activity, and it explains how networks maintain criticality without loss of stability.

1-104. Action recognition best explains neural activity in cuneate nucleus

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Adaptive motor control requires the integration of proprioceptive and other sensory signals. However, the principles, which govern the processing of proprioception, are poorly understood. Here, we employ a task-driven modeling approach to quantitatively test hypotheses about the functional role of proprioceptive neurons in cuneate nucleus, which is the projection target of ascending spindle neurons in the brain stem. We generated datasets of realistic proprioceptive, muscle spindle inputs for a large, diverse repertoire of movements (following Sandbrink et al., bioRxiv, 2020), and used them to train hundreds of temporal convolutional neural networks (TCNs) to perform three behavioral tasks: action recognition, hand localization and redundancy reduction. We contrasted these hypotheses about what the ascending proprioceptive pathway does by predicting single-neuron activity from the cuneate nucleus in macaques performing a center-out reaching task. We tracked limb movements with DeepLabCut and inferred the proprioceptive inputs via musculoskeletal modeling. We used these as input to the task-trained TCNs to linearly regress single-neuron activity. Firstly, we found that the models trained on action recognition provide significantly better neural predictions than the other tasks ($p < 0.05$ post-hoc Tukey’s test). Secondly, for three different architectural families of TCNs, we found that models that perform better on the action recognition task, explain the neural data in the cuneate nucleus better. This relationship was not true for the hand localization and redundancy reduction task. Overall, this suggests that action recognition is sufficient to develop brain-like postural representations in the cuneate nucleus. Furthermore, our work is the first to directly predict proprioceptive neurons from task-driven modeling and thus consolidates task-driven models as an optimization-based framework to understand sensory systems (beyond vision, audition and touch).

1-105. Facial movements and their neural correlates reveal latent decision variables in mice

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Signals related to self generated movements are broadcast to non-motor brain regions, and can be detected across wide regions of the forebrain in mice. Indeed, it has been observed that, even during the performance of a task, incidental movements, or ‘fidgets’, account for much more variance in neural activity than task-related movements and task-related variables. Some bodily movements or expressions, such as those of the face, reflect biologically significant expressions of internal state, that is, emotions, which have important relationships with ongoing cognitive processes such as decision-making. Therefore, it is possible that movements characterized as incidental actually express latent internal states that are in fact related to decision processes. Here, we trained mice to perform a probabilistic foraging task while video monitoring facial movements and simultaneously record-

ing large ensembles of neurons in frontal and premotor cortical regions using Neuropixels probes. In this task, mice had to combine a sequence of successful and failed foraging attempts to compute a latent decision variable (DV) in order to time the duration of their foraging bout. After training, this DV predicted the mice's behavior and accounted for a large degree of premotor activity, but consistent with a previous report, high dimensional facial movements dominated neural activity in premotor cortex and in all the other recorded brain regions. Remarkably, however, further analysis revealed that the explanatory power of facial movement was largely due to its correlation with the latent DV. The component of the movement uncorrelated with the latent DV had little predictive power. The premotor representation of the DV temporally preceded that of the movements, suggesting that premotor activity contributed to generating facial movements rather than reflecting proprioceptive feedback. These results show that seemingly 'incidental' bodily expressions can in fact reveal otherwise hidden task-relevant states.

1-106. Distinct neural substrates for flexible and automatic motor sequence execution

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The brain's ability to flexibly chain elementary movements into sequences enables rich behavior. For example, a concert pianist can play a never-before-seen sonata from the sheet music. However, to achieve the fluid and error-free performance required for a concert, she extensively practices a single piece until it is automatic. The neural circuits underlying automatic motor sequences are thought to differ from those for executing flexible ones, but the distinction is poorly understood. To address this, we trained rats to execute sequences of three lever presses in flexible sessions – where cues instructed the sequence order – or automatic ones – where a single uncued sequence was repeated. We found that neural activity in sensorimotor striatum primarily encodes low-level kinematics, regardless of the execution mode or sequence, whereas motor cortex activity reflects higher-level sequence information. Consistent with this, lesions to sensorimotor striatum disrupted movement kinematics in both modes, but only eliminated motor sequence execution in the automatic sessions. Lesions of motor cortex disrupted flexible sequence execution, indicating its vital role in sequencing motor elements. Intriguingly, automatic motor sequences were also affected by motor cortex lesions, unless we trained rats only on the automatic mode in which case performance was largely spared. This suggests that demands for flexibility interfere with subcortical consolidation of automatic motor sequences. We developed a neural network model with cortical and subcortical pathways, where the latter assumes control of behavior as it learns to recapitulate motor cortical commands. Our model reproduces the above findings, and suggests that flexible sequencing interferes with consolidation when the subcortical pathway lacks the sensory inputs needed to differentiate between sequences. This work provides important insights into the hierarchical and distributed control of flexible and automatic motor sequences and characterizes the circumstances under which the motor cortex is essential for sequence execution.

1-107. Modeling the formation of the visual hierarchy

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The human visual cortex is modular, parcellated into a hierarchy of visual areas (V1, V2, V3, etc.) that abut each other in the brain. The areas are each retinotopically organized with several characterizing higher-level organizational features — a notable example is that the polar angle of the retinotopic maps alternates (is mirrored) across area boundaries. Normative (task-trained) models of the dorsal visual stream capture important aspects of neural tuning, but typically only involve feedforward connections and already assume a hierarchical organization of a discrete set of areas. They also do not explain the spatial organization of these areas in the brain. On the

other hand, recent work with self-organizing maps has shown that it is possible to explain some of the spatial aspects of the organization of visual areas through multi-scale spatial relationships alone without requiring complex feature tuning relationships. Complementing this approach, here we take a developmental perspective in which the visual cortical connections are grown from simple bottom-up rules. These rules rely on an activity-dependent wiring process driven by spatial relationships implicit in the structure of retinal waves, and a synaptic pruning process dependent on wiring length, both grounded in biological data. Several features emerge as a result of the growth process: First, a discrete set of areas develops, with largely feedforward connections between them, defining a hierarchy. Second, each area exhibits retinotopy and characteristic mirror reversals in polar angle. The global eccentricity map is preserved. Third, connectivity is local: nearby neurons connect to nearby neurons in the preceding level of the hierarchy, together with a small fraction of recurrence. And lastly, receptive field sizes increase along the hierarchy. Altogether, this study demonstrates that many features of brain organization may arise not by direct optimization on particular tasks but as a consequence of low-level biophysical rules which unroll a cascade of developmental processes that determine structure and connectivity.

1-108. Normative models of spatio-spectral decorrelation in natural scenes predict experimentally observed ratio of PR types

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In line with the efficient coding hypothesis, the early visual system aims to minimize spectral and spatial redundancies arising from overlapping opsin sensitivities in retinal photoreceptors (PRs) and highly correlated structure in natural scenes. Encoding color information, or spectral information independent of intensity, requires comparing activities across different types of PRs. Mounting evidence shows that several species across the animal kingdom, such as the fruit fly *Drosophila Melanogaster*, have an uneven proportion of PR types in their retinas. However, it is unknown whether this uneven proportion is optimized for objectives relevant to the early color processing of natural scenes, as previous studies have modeled spectral and spatial processing in the early fly visual system independently. Here, we built a collection of models incorporating both spatial and spectral information to solve tasks relevant to the fly's early visual system, such as predictive coding at the level of PR inputs for spatial decorrelation in the retina as well as spatial and spectral decorrelation at the level of PR outputs via color opponency mechanisms. Using this framework, we asked how varying the ratio of the fly's two main PR types changed performance accuracy on these tasks. From this normative approach, we were able to conclude that the optimal ratio of PR types to best solve these tasks aligns with the experimentally observed distribution and showed this for multiple opsin sensitivity profiles determined within and across labs. Moreover, shuffling either spatial or spectral information in the input natural scene predicted an even PR type ratio, suggesting that biologically observed PR type ratios are optimized for spectral and spatial decorrelation. Altogether, these results suggest that natural scene statistics may have shaped the ratio of PR types in the fly retina through evolutionary mechanisms, providing important implications for understanding sensory systems in an ecologically relevant context.

1-109. Chromatic contrast and angle of polarization signals are integrated in the *Drosophila* central complex

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Many aspects of sensory information are linked in the natural environment, and evolution has shaped different navigational strategies across species to take advantage of this. A well-known example is celestial navigation in insects. Fruit flies use the position of the sun to navigate, but they can also orient successfully under the daytime sky even when the sun is not visible. This robustness is possible due to other global skylight cues—such as polarized light, spectral contrast, and intensity gradients—which all change in a stereotyped manner with respect to the position of the sun. Recent work in *Drosophila* shows that visual information about angles of polarized ultraviolet light (AOP) is conveyed to the central complex, the navigational center of the brain. However, the nature of how *Drosophila* use celestial cues to navigate is still not fully understood. Though the AOP pattern in the sky is used to infer a path that the observer and the sun lie on, it cannot provide information about which

direction the sun lies on that path due to its symmetry. Thus, flies must integrate another asymmetrical skylight cue, such as the chromatic contrast gradient, to resolve this directional ambiguity. Using *in vivo* calcium imaging, we show chromatic tuning in ER4m, a visual ring neuron that is polarization sensitive and part of the celestial compass pathway. Specifically, ER4m is color opponent, i.e., inhibited by long wavelengths of light and excited by short wavelengths—a hallmark of chromatically tuned neurons. Furthermore, ER4m also responds to chromaticity contrast changes, where overall intensity is constant, in a distinct stepwise way. The appearance of polarization and chromatic information in ER4m demonstrate that these cues are integrated together before compass (E-PG) neurons, suggesting that chromatic information is used to resolve the AOP pattern's directional ambiguity in the *Drosophila* celestial compass.

1-110. Accurate Engagement of the Drosophila Central-Complex Compass During Head-Fixed Path-Constrained Navigation

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Are there a set of basic operations that are used as building blocks of computation in the brain? If so, what are these operations? An ideal paradigm for studying this question is 2D path integration: the task of keeping track of one's spatial position over time through incremental addition of displacement vectors. Path integration is a compelling computation to study in that there are many constraints in how one can break it down into simpler operations. Moreover, small-brained organisms like bees, ants, and fruit flies with tractable nervous systems seem able to implement this computation (Heinze et al. 2018, Kim & Dickinson 2017). A major impediment to the study of insect path integration has been the absence of a head-fixed behavioral setup in a model organism like *Drosophila melanogaster* where the memory of a spatial location can be learned and reliably reported by the animal. As a step in this direction, we developed a new virtual reality preparation that constrains the head-fixed fruit flies to walk along circular or linear paths. We show that the flies' internal compass accurately reflects the fly's virtual orientation in this preparation. Furthermore, we have preliminary evidence of flies using spatial memory in this setup.

1-111. Nonlocal Spatiotemporal Representation in the Hippocampus of Freely Flying Bats

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Navigation occurs through a continuum of space and time. The hippocampus is known to encode the immediate position of moving animals. However, active navigation, especially at high speeds, may require representing navigational information beyond the present moment. Using wireless electrophysiological recordings in freely flying bats we demonstrate that neural activity in area CA1 predominantly encodes nonlocal spatial information up to meters away from the bat's present position. This spatiotemporal representation extends both forward and backwards in time with an emphasis on future locations and is found during both random exploration and goal directed navigation. The representation of position thus extends along a continuum, each moment containing information about past, present and future, and may provide a key mechanism for navigating along self-selected and remembered paths.

1-112. A cortico-collicular circuit for accurate orientation to shelter during escape

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Escaping towards shelter is an adaptive behaviour offering protection against predation. In mice, this is preceded by a fast, memory-guided head rotation towards the shelter[1]. It is not known how the escape circuit incorporates spatial information to execute rapid and accurate flights to safety. Here we show that retrosplenial cortex (RSP) and superior colliculus (SC) form a monosynaptic circuit that continuously encodes shelter direction and is necessary for spatially-accurate escape. Using Neuropixels probes, we found head-shelter angle cells (HSAC) in RSP and SC. Both multivariate tuning curve analysis and generalized linear models showed HSA to be a key predictor of their firing rate. HSACs tile angular space such that HSA can be decoded accurately at the population level. Rabies tracing and channelrhodopsin-assisted circuit mapping revealed that both excitatory and inhibitory SC neurons receive monosynaptic input from RSP. This synapse is critical for HSA encoding in SC and accurate escape: chemogenetic inactivation of SC-projecting RSP neurons disrupted single-cell and population encoding of HSA in SC and resulted in inaccurate orientation to shelter during escape. No impairment was observed in sensory-guided orientation nor navigation-to-reward tasks, suggesting that RSP input to SC selectively conveys shelter position, but is not necessary for SC-based motor control. Next, we probed HSA encoding and population dynamics in excitatory and inhibitory SC neurons in response to RSP input using dual-opsin RSP stimulation and optotagging *in vivo*. We found an activity pattern compatible with RSP input mapping HSA onto the SC network using a centre-surround inhibition mechanism, that was modelled using spiking-RNNs constrained by experimental data. Combining molecular, computational and electrophysiological techniques, we identified a circuit-motif through which spatial memories are transmitted to a motor-control area to guide goal-directed behaviour. This cortical-subcortical interface may be a general blueprint for increasing the flexibility of instinctive behaviours.

[1]Vale et al.,2017,Current Biology

1-113. Dendritic integration of thalamic HD signals and retrosplenial input in presubiculum neurons

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The head direction (HD) system functions as the brain's compass system. HD signals are generated based on vestibular inputs that provide information on self-movement. They are combined with signals that permit orientation coding with respect to external landmarks. Lesion studies point to the Presubiculum as a strong candidate for the integration of HD and landmark signals, but the underlying cellular mechanisms remain to be clarified. Here we show that the presubiculum receives HD signals from the anterior thalamic nucleus (ATN) and visual landmark information from the retrosplenial cortex (RSC). We examined the functional convergence of these inputs in the Presubiculum using dual-wavelength optogenetic stimulations in ex vivo brain slices, while recording from layer III pyramidal neurons. Both ATN and RSC projections made mono-synaptic excitatory connections onto single layer

III pyramidal cells, with putative synapses often located close to each other on a same basal dendrite, and more RSC than ATN synapses on the apical tuft. Following photoactivation of Chronos and Chrison, expressed in ATN and RSC respectively, postsynaptic firing was preferentially induced for near-coincident activation, in a short time window of -2 to +5ms. EPSPs induced by ATN and RSC fibers summed in a supralinear fashion. NMDA receptor activation assisted depolarization towards a threshold for the activation of voltage-dependent processes that underly supralinear summation of ATN and RSC inputs. Our data provide initial insights into the integration of landmark and HD inputs in single layer III presubiculum pyramidal cells, potentially including HD cells and also grid cells. Our results suggest that landmarks become associated to HD signals in the presubiculum, where coactive synapses engage dendritic nonlinearities, allowing for rapid updating of the HD attractor.

1-114. Large-scale paired recordings reveal strong and specific connections between retina and midbrain.

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The output of the retina is carried by retinal ganglion cells (RGCs) along parallel functional pathways to multiple areas distributed across the vertebrate brain. The functional organization of the synaptic connections between RGCs and their postsynaptic target neurons is largely unknown. Here, we discovered that high-density Neuropixels probes allow the measurement of large populations of RGC axons where they form synaptic contacts, *in vivo*. The electrophysiological signature of RGC afferent inputs is made of a triphasic waveform composed of the axonal action potential, the axonal terminal response and, finally, the corresponding responses from the synaptically connected dendrites. The signal is spread across multiple recording sites, capturing the axonal synaptic contact field of individual RGCs *in vivo*. Consequently, midbrain neurons can be recorded simultaneously with their presynaptic RGC inputs, at large scales reaching up to 200 functionally connected pairs in individual recordings. Furthermore, we confirmed that these large-scale paired recording are possible in both the mammalian superior colliculus (mouse, *Mus musculus*) and the avian optic tectum (zebra finch, *Taeniopygia guttata*). Using our novel approach to study the spatial organization of retinal axons within the midbrain, we discovered that retinal mosaics are mapped onto the midbrain isomorphically with single cell precision. Functionally, we show that single RGC axons connect to their target neurons with strong and specific connections, i.e., a limited functional convergence and log-normally distributed connection strength. Overall, our results show that high-density electrodes can capture multiple neuronal compartments simultaneously *in vivo*, including afferent axons and their synaptically evoked dendritic responses as well as somatic activity of local neurons; permitting large-scale paired recordings between brain regions. In addition, we conclude that the retinotectal connectivity follows a common organizing principle in mammals and birds that provides a precise and reliable representation of the visual world to neurons in the midbrain.

1-116. Neuromodulatory changes in the efficiency of information transmission at visual synapses

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Neuromodulators adjust sensory processing and synapses are key control sites for such plasticity. Less clear is

how neuromodulation alters the amount of information that synapses transmit through a circuit. To understand the operation of the “vesicle code” the experimenter needs to isolate signals from individual active zones with a resolution of single vesicles while observing or controlling the incoming signal. This has not been possible using electrophysiology but can now be achieved by multiphoton imaging of the glutamate reporter iGluSnFR in the retina of larval zebrafish. This approach reveals that the visual message transmitted from bipolar cells does not use a simple binary code but is instead composed of a number of symbols, composed of one, two, three or more vesicles released as one event. Here we demonstrate that this strategy of coding by amplitude as well as rate is under diurnal control, contributing to a four-fold variation in the Shannon information transmitted at individual active zones. Dopamine contributes to this increase in information transfer by adjusting at least four synaptic properties; the number of vesicles released by a stimulus, spontaneous synaptic noise, the variability of stimulus-driven responses and the balance between univesicular and multivesicular release. By increasing the probability of multivesicular events with larger information content, dopamine also increases the efficiency of transmission quantified as bits per vesicle. The relative contributions of these various mechanisms differs between ON and OFF pathways: reduced variability of synaptic responses and increased emphasis on MVR increased information transfer through the ON pathway without an increase in synaptic gain. This study provides a quantitative understanding of the different mechanisms by which neuromodulators alter the flow of sensory information and highlights the importance of experimental measurements of the statistics of the vesicle code for understanding how information is transferred between neurons.

1-117. Cellular mechanisms of dorsal horn neurons shape the functional states of nociceptive circuits

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Nowadays, 1.5 billion people suffer from chronic pain. Current neuropharmacology and neurostimulation treatments are associated with suboptimal efficacy, due to a lack of understanding of the pain system. A major contributor to many persistent clinical pain states is the phenomenon of central sensitization—a state of hyper-excitability of the pain system resulting from changes in the properties of neurons and circuits within the dorsal horns of the spinal cord. Although spinal cord circuits and their plasticity are challenging to study experimentally, only a handful of computational studies have tried to understand this system with mathematical models. In addition, the high dimensionality of these conductance-based models often limits the possibility to reveal the key mechanisms that modulate the functional state of these nociceptive circuits. As a first step to fill this gap, we built a low-dimensional, integrate-and-fire model of the projection neuron in the dorsal horn. This model aims at capturing the rich dynamical firing activity of the projection neurons: tonic firing, plateau potentials, and endogenous bursting.

This study discusses the importance of regenerative and restorative feedbacks at the cellular level in different time scales. We exploited the time scale separation between the dynamics of the ion channels of these projection neurons. Each type of ion channel is associated with a time scale and with either regenerative or restorative feedback. Then, we use an incremental approach to build our model one time scale at a time to understand their effect separately. We showed that the key mechanisms behind the excitability of dorsal horn neurons rely on a specific balance between regenerative and restorative ion channels spread across four time scales. These results suggest that the excitatory and inhibitory interneurons could control the excitability of projection neurons through metabotropic receptors that can modulate the intrinsic membrane properties of the projection neurons.

1-118. The timescale and magnitude of 1/f aperiodic activity decrease with cortical depth in humans, macaques, and mice

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Cortical dynamics obey a 1/f power law, exhibiting an exponential decay of spectral power with increasing frequency. The slope and offset of this 1/f decay reflect the timescale and magnitude of aperiodic neural activity, respectively. These properties are tightly linked to cellular and circuit mechanisms (e.g. excitation:inhibition balance and firing rates) as well as cognitive processes (e.g. perception, memory, and behavioral state). However, the physiology underlying the 1/f power law in cortical dynamics is not well understood. Here, we compared laminar recordings from human, macaque and mouse cortex to evaluate how 1/f aperiodic dynamics vary across cortical layers and species. We report that 1/f slope is steepest in superficial layers and flattest in deep layers in each species. Additionally, the magnitude of this 1/f decay is greatest in superficial cortex and decreases with depth. We could account for both of these findings with a simple model in which superficial cortical transmembrane currents had longer time constants and greater densities than those in deeper layers. Together, our results provide novel insight into the organization of cortical dynamics, suggesting that the amplitude and time constant of local currents control circuit processing as a function of laminar depth. This may represent a general mechanism to facilitate appropriate integration of fast sensory inputs (infragranular) with slow feedback-type inputs (supragranular) across cortical areas and species.

1-119. Mechanisms of surround facilitation and suppression to holographic perturbations

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Two-photon holographic optogenetic experiments have revealed that excitatory perturbations induce excitation surrounding the perturbed cell on the order of tens of microns, after which the response is suppressive, forming an inhibitory halo. Here we investigated, through a battery of analytical and inference methods, how the strength and spread of the connections between neurons both in cortical space and in feature (preferred orientation) space define the response of the circuit to few-cells perturbations. First, we obtain two analytical expressions, one exact and the other approximate, for the response of linearized models to perturbations as a function of cortical space. We infer parameters from calcium imaging responses to holographic perturbations, and obtain both linear and

nonlinear spatial models that can account for the spatial spread of the responses in the data. We find that linear models cannot explain results from experiments which show that perturbing an ensemble of neurons that are closely clustered causes suppression instead of excitation in nearby cells. Nonlinear models exhibit this compact-ensemble suppression effect because strong perturbations can induce transitions from facilitated to suppressed response in nearby cells, unlike in linear models, where the response to perturbations is always proportional to input strength. Having a nonlinear spatial model that fits different aspects of the spatial response, we expand the model to include feature dependent connectivity. We identified different regimes based on features of the response such as whether the response is positive or negative for nearby neurons and whether there are transitions from facilitating to suppressive response across space and orientation. Finally, we identify a parameter regime in which the response near perturbed cells is positive for co-tuned neurons and negative for orthogonally-tuned neurons, a feature that is observed in experimental data, as we also show.

1-120. An inhibitory network model explains the transient dynamics of hippocampal ripple oscillations

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Hippocampal ripple oscillations (140–220 Hz) have been implicated in important cognitive functions such as memory consolidation (Buzsaki 1989). Their generating mechanism however remains unclear, although various models have been proposed. We suggest that transient features of ripples can guide model selection: So far only the “bifurcation-based” inhibitory network model (Donoso et al. 2018, Brunel and Hakim 1999) could reproduce the experimentally observed intra-ripple frequency accommodation (IFA) — an asymmetry in the instantaneous ripple frequency in response to transient, sharp wave-like (50–100 ms) stimulation (Ponomarenko et al. 2004). This model assumes that the recurrent CA1 PV+ interneuron network generates ripples for strong enough excitatory drive. Here we explain IFA using a theoretical mean-field approach and numerical simulations. In the mean-field limit we describe the density of membrane potentials as a gaussian with time-dependent mean and consider only drift-based spiking. This framework allows us to approximate analytically the frequency and amplitude of the network oscillation as a function of the external drive. Numerical simulations verify that the approximation works in a large parameter regime. We show that for fast changing, sharp wave-like drive the network frequency response is asymmetric due to a speed-dependent hysteresis effect in the oscillation amplitude of the mean membrane potential. We predict that IFA vanishes in the limit of slowly changing transient drive, which can be tested optogenetically. With no further parameter dependencies, IFA is an inherent feature of this model. Conversely, we find that the alternative, “perturbation-based”, inhibitory ripple model (Malerba et al. 2016) cannot exhibit IFA by default. From a theoretical perspective our work introduces a new ansatz to describe strongly nonlinear oscillation dynamics in recurrent spiking networks with interesting links to escape noise formalisms. For experimentalists we provide new evidence to advance the search for the true generating mechanism of ripples.

1-122. Efficient learning of low dimensional latent dynamics in multiscale spiking and LFP population activity

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Learning low dimensional latent dynamics in population spiking and field potential activities together can reveal the relationship between different spatiotemporal scales of population activity and can improve performance of brain-machine interfaces (BMIs). But developing a multiscale learning algorithm is challenging because spikes are discrete-valued signals while field potentials are continuous-valued signals with slower time-scales than spikes. Recently, a multiscale learning method based on expectation maximization was developed (multiscale-EM) for

multimodal discrete-continuous data, which maximizes the joint likelihood of spikes and fields iteratively, thus can be computationally expensive. In some applications, such as tracking neural plasticity in basic science studies or real-time learning in BMIs, a desirable feature for a learning method is computational efficiency. Therefore, it is important to develop a more efficient multiscale learning algorithm than the iterative multiscale-EM. Here, we develop a more efficient multiscale learning algorithm based on subspace identification (multiscale-SID) and validate it using numerical simulations and a non-human primate (NHP) neural dataset during a random target reaching task. We show that multiscale-SID accurately learns multiscale dynamical models for spiking and field potentials and extracts the low dimensional dynamics/modes. Also, multiscale-SID combines information across spiking and field potential population activity, allowing for more accurate identification of dynamics/modes compared to single-scale SID. Critically, we demonstrate that multiscale-SID is much faster than multiscale-EM while having similar or better accuracy when provided with enough training samples. Taken together, multiscale-SID provides a new tool for studying multimodal population dynamics across different spatiotemporal scales and for real-time learning of these dynamics.

1-123. Explainable Machine Learning Approach to Investigating Neural Bases of Brain State Classification

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Identification of mental states in patients based on electrical activity is of interest for clinical neuroscience. While the problem has been successfully addressed for individual patients with multiple (up to 50) states identifiable for the purposes of communication, addressing the problem in a general sense is more difficult, as it requires understanding of the neural bases for successful classification. We used a range of well-established machine learning methods on a two-state classification problem based on EEG data with high success rate (>98%), and then applied Sparse Optimal Scoring (SOS) to reduce the dimensionality of the features, and improve model interpretability for generating an ‘explainable ML’ understanding of the basis for the successful classification. 24-channel EEG data from Deaf signers watching sign language videos and the same videos in reverse (non-comprehensible, but identical in spatiotemporal features) was used to calculate coherence between optical flow in the stimuli and EEG neural response (per video, per participant) using canonical component analysis. Peak correlations for binned frequencies were used as input parameter to machine learning algorithms. Two ensemble classifiers (AdaBoost and Random Forest) achieved 100 percent out-of-sample prediction accuracy on hold-out dataset for the whole brain. Sparse Optimal Scoring (SOS) was then applied to the coherence data to reduce the dimensionality of the features and improve model interpretability. SOS with elastic-net penalty resulted in out-of-sample classification accuracy of 98.89%. The sparsity patterns from the trials using 1 Hz bins consistently indicated frequencies between 0.2-1 Hz were primarily used in the classification. We find that successful classification relies on low (<2 Hz) frequencies of EEG coherence to the input signal. This indicates that the hallmark of communicatively successful brain states is predictive processing for incoming signal.

1-124. Inter-individual alignment and single-trial classification of MEG data using M-CCA

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Neuroscientific studies often involve some form of group analysis over multiple participants. This requires alignment of recordings across participants. A naive solution is to assume that participants' recordings can be aligned anatomically in sensor space. However, this assumption is likely violated due to anatomical and functional differences between individual brains. In magnetoencephalography (MEG) recordings the problem of inter-individual alignment is exacerbated by the susceptibility of MEG to individual cortical folding patterns as well as the inter-individual variability of sensor locations over the brain. Hence, an approach to combine MEG data over individual brains should relax the assumptions that brain anatomy and function are tightly linked and that the same sensors can capture functionally comparable brain activation across individuals. Here we use multiset canonical corre-

tion analysis (M-CCA) to find a common representation of MEG activations recorded from different participants performing a similar task. Our approach applies M-CCA to transform data of multiple participants into a common space with maximum pairwise correlation between participants. Importantly, we derive a method to transform data from a new, previously unseen participant into this common representation. We demonstrate the superiority of the approach over simpler, previously used ones. To this end, we train single-trial inter-individual decoders on the common data representation from one set of participants and test the transfer of the models to data from a new participant who was neither included in finding the common space nor in the training of the decoder. Finally, we show that our approach requires only a small number of labeled data from the new participant. Our work demonstrates that inter-individual alignment via M-CCA has the potential for combining data of different participants and could become helpful in future endeavors on large open datasets. It also has potential applications in reducing training time of online brain-computer interfaces.

1-125. Fast inter-subject alignment method for large datasets shows fine-grained cortical reorganisations

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Between-subject brain variability in shape and function is a major challenge to the definition of accurate brain models [1, 2]. It also obscures the comparison between species. Recently, precision mapping has started to provide data to ground the definition of accurate brain models [3]. Yet technology has been missing to identify correspondences between brains. Leveraging Optimal Transport (OT) methods [5, 6], we derive an algorithm, denoted as unbalanced fused Gromov Wasserstein (UFGW), to compute whole-brain mappings between subjects with minimal anatomical priors, and provide a fast GPU-based Python implementation. We apply it to the Individual Brain Charting dataset - a collection of more than 200 maps of functional activations (contrasts) acquired in 12 human subjects [4]. Our method focuses on building mappings for surface-sampled data. We compare UFGW with its diffeomorphic counterparts (such as Procrustes [12], MSM [7] or spherical daemon [13]). To do so, we systematically evaluate the relevance of derived mappings by (a) quantitatively assessing how well they predict unseen contrasts and (b) qualitatively looking at the cortical reorganisation they induce between subjects through a dedicated web-based interactive visualisation tool. On top of being computationally very efficient and easy to deploy, UFGW outperforms alternatives. Unlike other methods, UFGW doesn't enforce diffeomorphicity between source and target surfaces, but only fosters it. This makes it possible to capture subtle changes between individuals, such as the size and shape of functional areas or their position relative to other areas. Our visualisation tool facilitates exploring these changes. Moreover, as our method is not based on anatomical landmarks, it is particularly suited for cross-species comparisons (e.g. human vs. macaques). We plan to derive these in future work to assess the existence of cortical reorganisations between species, pushing forward recent efforts made in cross-species comparisons [8, 9, 10].

1-126. Approximate gradient descent and the brain: the role of bias and variance

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Gradient descent is a central tool in modern machine learning, largely because it scales well to train large networks on computationally challenging tasks. As such, computational neuroscientists are exploring potential means by which the brain could leverage gradient descent. However, it is unlikely that the brain could implement perfect gradient descent, but instead could rely on using approximations of the true gradient signal. Therefore, it is likely that the gradient estimates used by the brain would have both bias and variance. Here, we use model agnostic mathematical analysis and simulations to understand how bias and variance in gradient approximations affect the learning performance of a system. Our work, supported by experiments involving artificial neural networks trained

on synthetic datasets in a student-teacher setup, demonstrates the distinctive impact of bias and variance on learning performance. Firstly, we find that the effect of bias increases with the gradient norm, and decreases as the network approaches a loss minimum. Secondly, the effect of variance increases when networks are smaller but decreases when network activity is sparser. These results indicate that having good priors over the system's parameters, possibly inherited through evolution, could ameliorate the impact of bias. Additionally, increasing the network size, both depth and width, allows the system to reduce the impact of noise in gradient estimates. Taken together, our findings suggest a normative explanation for the need for good priors over the synaptic connections in the brains to mitigate biased gradient estimates and the need for increased brain size to mitigate noise in gradient estimates. Furthermore, our results can inform the search for algorithms that approximate gradient descent depending on the system characteristics and task complexity. Overall, we believe that our work contributes to developing biologically-plausible learning algorithms for artificial systems as well as the quest to understand learning in the nervous system.

1-127. A new approach to inferring the eigenspectra of high-dimensional neural representations

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The statistical structure of neural population responses is a topic of intense interest in systems neuroscience. The signal eigenspectrum (eigenvalues ordered from high to low) is a fundamental summary statistic that characterizes the dimensionality and efficiency or redundancy of population tuning curves. However, the problem of characterizing signal eigenvalue spectra from limited, noisy neural response data is complicated by two factors. First, noise in the neural responses (aka "noise correlations") can interfere with the estimation of the eigenvalues of the signal distribution. Second, data limitations lead to large discrepancies between the true eigenvalues and those of the sample covariance, a limitation that is especially pronounced in large neural populations where dimensionality is high relative to the number of samples. Here we introduce a new method for estimating eigen-spectra that overcomes these limitations. Our estimator extends recent results from random matrix theory on the unbiased estimation of the moments of the eigenvalue distribution. We show how these moments can be used to infer parametric models, including power laws, of the eigenvalue distribution. We compare our method to cvPCA, a recently proposed estimator that was used to argue that population encoding in mouse visual cortex follows a power law with slope near 1 [Stringer et al, 2019] optimally balancing the efficiency of independent tuning and the robustness of redundant tuning. However, we show that cvPCA can exhibit sizeable biases, which our estimator substantially reduces. We then apply our estimator to the publicly available mouse dataset from Stringer et al, and show that it returns a higher estimate of power law slope, suggesting a more rapid fall-off in tuning with dimension. Our work provides a principled and accurate method for inferring a fundamental characteristic of neural population tuning that we expect to be of wide theoretical and experimental interest.

1-128. Optimal dynamic allocation of finite resources for many-alternatives decision-making

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A fundamental brain computation is to identify the best in a set of noisy or uncertain options, which is required for inference, decision-making, optimization, action selection, consensus, and foraging. To solve these problems, noisy observations need to be integrated over time to evaluate, compare, and choose from them. This process involves allocating attention or other finite neuronal resources dynamically over the alternatives to make the best choice. The problem of allocating finite resources has been recently studied under the context of the so-called breadth-depth (BD) dilemma, but how finite resources should be divided and dynamically allocated over options in an optimal manner is not known. Here, we introduce a novel perspective, designing a recurrent neural network to deal with the BD dilemma from a dynamical point of view. A key hallmark of our model lies in a dynamical noise reduction: during the noisy evidence accumulation, the noise magnitude is regulated by the number of active units, such that less noisy observations result from attending to a lower number of alternatives. This noise reduction embodies the capability of our brain to rearrange its finite attentional or neuronal resources along the

decision processes. The combination of non-linearity, integration, and number-dependent noise reduction results in a close to optimal network performance. We find that it is best to initially divide attention into many alternatives (resembling a form of a pre-attentive mechanism) later followed by a drastic reduction to a handful of attended alternatives (resembling focused attention). Our modelling approach can offer a unifying framework to study the dynamical aspects of attention in many-alternatives decision-making.

1-129. A biophysical counting mechanism for keeping time

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The ability to estimate and produce appropriately timed responses is central to many behaviors including speaking, dancing, and playing a musical instrument. A classical framework for estimating or producing a time interval is the pacemaker-accumulator model in which pulses of a pacemaker are counted and compared to a stored representation. However, the neural mechanisms for how these pulses are counted remain largely unaddressed. We present a biophysical model of how to keep count of cycles of a pacemaker clock. Our model utilizes a system of bistable Wilson-Cowan units asymmetrically connected in a one-dimensional array; all units receive the same input pulses from a central clock but only one unit is active at any point in time. With each pulse from the clock, the position of the activated unit changes thereby encoding the total number of pulses emitted. This neural architecture maps the counting problem into the spatial domain, which in turn translates count to a time estimate thus allowing the mechanism to be used in time interval production and estimation. The encoding of count using discrete states allows our mechanism to overcome sensitivity to two sources of noise: noise internal to the neural units themselves and variability that arises from using a stochastic oscillator as the pacemaker. Furthermore, this discrete representation overcomes the need for the fine-tuning of parameters that is a known criticism of the linear integrator model. Lastly, we extend the model to a hierarchical structure to be able to robustly achieve higher counts using fewer units.

1-130. Encoding of natural movies based on multi-neuron temporal spiking patterns

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The current dogma in neuroscience is that neurons primarily convey stimulus information through their firing rate. However, recent studies suggest a remarkable speed of sensory processing which may be incompatible with traditional rate-coding schemes, and it has been hypothesized that sensory encoding may rely on the spike timing relationships among neurons (Thorpe et al., 2001 and Resulaj et al., 2018). To study multi-neuron spiking patterns, we developed SpikeShip, an unsupervised, linear, geometry-based dissimilarity measure that aligns spikes across pairs of epochs based on optimal transport cost. This method has linear computation cost and is sensitive to higher-order correlations in spike trains. We used both rate and timing codes to find clusters across $N > 8000$ neurons from six visual areas during natural video presentations in 32 mice. We split the video into 30 sub-videos of one second each as in previous studies (Deitch et al., 2021), and compared information content in firing rate population codes and multi-neuron temporal spiking patterns. Using SpikeShip, we show that (1) multi-neuron temporal patterns convey substantially more information about natural movies than population firing rates; (2) multi-neuron temporal patterns show high reliability across presentations, in contrast to firing rate codes; (3) firing rate codes exhibit memory across frames, whereas temporal patterns form a discrete and discontinuous manifold separating different movie frames; (4) the advantage of temporal information becomes larger as the number of neurons grows. These findings reveal the importance of temporal spiking patterns in the encoding of natural visual inputs.

1-131. Awake perception is associated with dedicated neuronal assemblies in cerebral cortex

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Neural activity in sensory cortex combines stimulus responses and ongoing activity, but it remains unclear whether they reflect the same underlying dynamics or separate processes. Here we show that during wakefulness, the neuronal assemblies evoked by sounds in the auditory cortex and thalamus are specific to the stimulus and distinct from the assemblies observed in ongoing activity. In contrast, during anesthesia, evoked assemblies are indistinguishable from ongoing assemblies in the cortex, while they remain distinct in the thalamus. A strong remapping of sensory responses accompanies this dynamical state change produced by anesthesia. Together, these results show that the awake cortex engages dedicated neuronal assemblies in response to sensory inputs, which we suggest is a network correlate of sensory perception.

1-132. Isolated correlates of somatosensory perception in the posterior mouse cortex

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To uncover the neural mechanisms of stimulus perception, experimenters commonly use tasks in which subjects are repeatedly presented with a weak stimulus and instructed to report, via movement, if they perceived the stimulus. The difference in neural activity between reported stimulus (hit) and unreported stimulus (miss) trials is then seen as potentially perception-related. However, recent studies found that activity related to the report spreads throughout the brain, calling into question to what extent such tasks may be conflating activity that is perception-related with activity that is report-related. To isolate perception-related activity, we developed a paradigm in which the same mice were trained on both a regular go/no-go whisker stimulus detection task and a reversed contingencies version, in which they were trained to report the absence of a whisker stimulus. We discovered that isolated perception-related activity appears within a posterio-parietal network of cortical regions contralateral to the stimulus. This perception-related activity was on average an order of magnitude lower than the hit versus miss difference (which mostly consisted of report-related activity) and began just after the low-level stimulus response. In summary, our study revealed for the first time in mice the cortical areas that are associated specifically with the perception of a sensory stimulus and independently of the report.

1-133. Grid cells rapidly integrate novel landmarks

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Successful navigation requires the integration of egocentric (body-centered) and allocentric (world-centered) strategies. Previous studies have shown how these two systems could be integrated by coordinating different functional cell types in the medial entorhinal cortex (MEC): grid cells, which are thought to serve as path integrators encoding egocentric information, and landmark cells, which encode allocentric information [1]. Theoretical work has shown how landmark cells could learn to serve as an error correction mechanism to grid cells via Heb-

bian plasticity, and experiments have found that grid cells deform to match environments over hours or days. But both of these mechanisms require numerous exposures to the environment, and long timescales of learning. In ethological settings, animals must solve navigational tasks from just a single exposure and on rapid timescales.

Here we use Neuropixels recordings to investigate how the neural circuit learns to rapidly integrate visual cues to the grid cell path integrator. Surprisingly, we find that introducing novel landmarks not only stabilizes grid cell spatial firing, but also induces rapid (one-shot) remapping. Upon further analysis, we find that landmark cells also quickly remap to novel landmarks and that they do so in concert with the grid cells. These findings hint at an alternative, rapid mechanism for integrating egocentric and allocentric information.

1-135. Soft-actor-critic for model-free reinforcement learning of eye saccade control

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Saccades are fast eye movements that change gaze direction in a ballistic fashion. Human saccadic behaviour has been studied extensively in neuroscience and several methods have been proposed to model the saccadic system. For example, John et al. (2021) adopted a model-based approach, based on a physical model of the eye plant (eyeball, extraocular muscles, and surrounding tissues). They used feedforward optimal-control principles to replicate human saccadic behaviour. Here, we adopted a model-free approach to study the question: "How to learn saccadic behaviours without prior knowledge of the eye plant?". We addressed saccadic control as a reinforcement learning (RL) problem (Sutton & Barto, 2018). When an agent drives the eyes to a desired gaze direction, it receives a reward signal that accounts for the accuracy in target acquisition (tracking errors are penalized), the saccade duration (the shorter the better), the total movement energy (low energy is better), and the existence of overshoot in the response (exceeding the target angle is penalized). Here, we trained an agent to perform saccades with the soft-actor-critic algorithm (Haarnoja et al., 2019). This algorithm maximizes the expected rewards over time while promoting exploration behaviour. The agent is composed of an actor network that learns the command to drive the eye from the initial to desired orientation, and a critic network that learns to predict the reward of a given command. Both networks interact in the learning process, as the actor network learns to maximize the output of the critic network and the entropy of the command. We validated this approach in a computational simulation of a robotic eye performing horizontal saccades using pulse-step inputs. Results show that the pulse-step parameters leading to saccadic behaviours are compatible with human performance and can be learned with high precision in a few tens of thousands of iterations.

1-136. Neural Representations of Opponent Strategy Support the Adaptive Behavior of Recurrent Actor-Critics in a Competitive Game

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In social interactions, theory of mind (ToM) is postulated as the reason for why humans can successfully interact with novel people, given that everyone has beliefs, desires, and goals. Most ToM studies design explicit models to represent other agents' mental states, using this to inform behavior. However, it is unclear whether or how ToM could emerge through learning to act in a social environment. We sought to identify network mechanisms of ToM in a recurrent neural network trained to play a competitive neuroscience task that requires ToM. The network, trained using deep reinforcement learning, is pitted against a set of opponents who play according to a distribution of algorithmic strategies. Importantly, this network does not have an explicitly hand-crafted ToM mechanism, and thus must learn it in order to perform successfully. Surprisingly, our network plays adaptively against unseen strategies. We hypothesized to observe a structured representation of opponent strategy within

neural activity, which we postulated would be a rudimentary form of ToM. We fit a linear classifier to the network's recurrent activity and found that we could predict the opponent with 96% accuracy, even after a period where the agent played against various randomly-selected opponents. To clarify that this subspace functions as a putative representation, we sought to relate its relationship to behavior. We found that the emergence of adaptive behavior and a robust opponent representation were significantly correlated across training. We subsequently perturbed the neural activity in this subspace from one opponent region to another and found that the reward after perturbation dropped to almost random, indicating that the representation is necessary for adaptive behavior. Our work demonstrates that learning adaptive social behavior is sufficient to develop a basic ToM, and additionally provides an explanation for how neural networks perform ToM which could be utilized to inspire future experiments.

1-138. Cerebellum learns to drive cortical dynamics: a computational lesson

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A recent surge of experimental evidence points towards a significant role of the cerebellum in the development and maintenance of neocortical states through cortico-cerebellar loops. Notably, the resulting positive feedback loop is not limited to the motor domain to which the cerebellum is classically associated but has been shown to extend to various cognitive processes. However, it remains unclear what functional principles may underlie these cerebro-cerebellar loops. Here we model a neocortical area as a recurrent neural network which projects to, and receives from, a cerebellar feedforward network. Neocortical plasticity is modelled with biologically plausible temporal credit assignment, and cerebellar plasticity with a temporal window-specific learning rule used to predict neocortical feedback, in line with recent experimental observations. Our model captures cerebellum-driven cortical dynamics observed experimentally in both motor-based and working memory tasks. In a motor-based task we find that cerebellar feedback consistently improves the rate of learning and mitigates the need for neocortical plasticity. This is due to the predictive learning of our cerebellar model, which triggers a fast and reliable drive of early neocortical states. In working memory tasks, in which maintenance of representation is critical, the model achieves good task performance for all neocortical plasticity assumptions. Overall, we propose the cerebellum is an effective driver of neocortical dynamics with task relevant information, reducing the need for neocortical plasticity in both motor and cognitive domains.

1-139. Modelling Systems Memory Consolidation with neural fields

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Early experiments studying the effects of lesions of the Hippocampus have reported that recent memories are often unavailable to be retrieved, while old memories are successfully reminded. These observations have led to state the theory of Systems Consolidation. This is the process by which the fast-learning Hippocampus replays the encoded memory during sleep and thus consolidates the corresponding memory in the Neocortex [1]. Formation of memory would take longer in the Neocortex because of its much larger spatial scale compared to the Hippocampus, and thus requires axonal growth and synaptogenesis. Finally neurogenesis in the Dentate Gyrus could explain the forgetting in the Hippocampus [2]. In fact newborn neurons alter hippocampal circuits, thus decreasing the probability to retrieve memory and eventually leading to its clearance. We propose here a neural fields model to assess whether the above hypotheses are enough to explain the basis of Systems Memory Consolidation. We considered three 1D connected neural fields, the Neocortex (long-term memory), the areas CA3-CA1 of the Hippocampus (short-term memory) and the Dentate Gyrus, also part of the Hippocampus. We were interested in the formation of connections between two distinct bumps of activity, which represent two distant parts of the memory pattern. Our study suggests that the crucial element for the rate of consolidation would be the initial density of connections between the parts of the pattern. Furthermore the rate of neurogenesis seems to determine the persistence time of a memory in CA3-CA1 before its clearance. We plan in the future to use this study to grasp the origins of dysfunctions of memory consolidation processes.

1-140. A stable memory scaffold with heteroassociative learning produces a content-addressable memory continuum

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Long-term memory is content addressable, in that partial cues are sufficient to drive recognition or recall of complete objects and events. Several content addressable memory (CAM) architectures have been proposed to model long-term memory, including the Hopfield network, several variants of the Hopfield network, and overparametrized autoencoders. However, all of these architectures exhibit a memory cliff, beyond which adding a single pattern leads to catastrophic loss of all patterns. Here we propose a novel and biologically motivated memory architecture, Memory through Scaffolded Heteroassociation (MESH), that generates a CAM continuum: storage of information-dense patterns up to a critical capacity results in complete recovery of all patterns and storage of a larger number of patterns results in partial reconstruction of the stored patterns. This partial reconstruction continues up to an exponentially large number of patterns resulting in correct recognition of each of the stored patterns. Inspired by the entorhinal-hippocampal circuit, MESH contains a bipartite attractor network that stores a large dictionary of well-separated fixed points that serve as a pre-defined “memory scaffold”. Arbitrary dense patterns are then stored by associating them to the pre-defined scaffold states. This novel combination of pre-defined attractor states along with heteroassociative learning that hooks patterns on to scaffolding states results in a biologically plausible CAM continuum, that approaches the theoretical upper-bound on information storage in neural networks. We believe that this is the first model of a content-addressable memory that automatically trades off pattern number and pattern richness; it makes the testable prediction that biological memory systems may exploit pre-existing scaffolds to acquire new memories, potentially consistent with the preplay of hippocampal sequences before they are used for representing new environments.

1-141. A cable-driven robotic eye for the study of oculomotor behaviors

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Human eye movements are controlled by six extraocular muscles. Although the eye socket restricts eye movements to almost pure rotations (3 degrees-of-freedom) the brain seems to control it using only 2 degrees of freedom, keeping the torsional component in a strict relationship with the gaze angles (azimuth and elevation), according to Donders' Law (Tweed et al., 1987). To study the control principles that may lead to such behaviour, we have designed a scaled-up cable-driven robotic eye with six actuators, with cable insertion points closely matching the relative positions of its biological counterpart. Based on this system we have created physical simulation models that allowed us to test several biologically inspired modeling, learning and control methodologies, and compare them on their ability to replicate human behaviour in an artificial system. Our first tests focused on the human saccadic behaviour in head-restrained conditions and fixation at far targets. In these conditions, the eye orientation can be represented by a single-axis rotation between the primary and final gaze orientation. This rotation axis lies in a plane, so-called Listing's plane, where the torsional component is zero. Our results show that an open-loop optimal control law that optimizes duration, accuracy and energy can lead to such behaviour. To the best of our knowledge, this is the first time that compliance to Listing's law is demonstrated in a 6-muscle model of the human eye. Our current efforts are directed towards studying the role of signal-dependent noise both in open-loop and closed-loop optimal control. Previous work (e.g., Shadmehr, 2012) has suggested that signal-dependent noise is instrumental in replicating the eye-saccade velocity profiles, and 1D simulation studies have confirmed that fact. Our full 3D model will allow the validation of these results in a more realistic system reflecting many of the complexities of the human eye mechanics.

1-142. Frontal cortex neural correlations are reduced in the transformation to movement

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Correlated activity between neurons can cause variability in behavior across trials, as trial-by-trial neuronal noise will propagate through the motor system. The extent to which correlated activity affects behavior depends on the properties of its translation into movement. A major hurdle in studying the effect of neural correlations on behavior is the need to assume a model of the relationship between neural activity and behavior. We developed a novel method that estimates the contribution of correlations to behavior, with minimal assumptions. We applied this method to the frontal eye field (FEF) and pursuit eye movements behavior. We defined a distance metric between the behavior on different trials. Based on this metric, we applied a sequence of shuffles to the neuronal responses, allowing trials to be matched with increasingly distant trials. Although correlations were partially explained by behavior, even the most constrained shuffle strongly attenuated the correlations. Thus, only a small fraction of FEF correlations affect the behavior. We used simulations to validate our approach and show that it captures the correlations that affect behavior. The simulations also demonstrate the generalizability of our method over different models. We show that the attenuation of correlated activity through the motor pathway could stem from the interplay between the structure of the correlations and the decoder of FEF activity.

1-144. Engagement of the respiratory CPG for songbird vocalizations

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Complex behaviors are constructed out of simple building blocks. The construction of complex behaviors presents an interesting problem when the behavioral building blocks are driven by independent neural dynamics, as is the case for behaviors that recruit central-pattern generators (CPGs). Breathing is a particularly interesting example since it is vital for sustaining life and yet breathing is integrated into a myriad of other behaviors like speaking, laughing, and coughing. Vocalizations co-opt respiratory machinery for communication. While the generation of vocal motor commands is generally attributed to the midbrain and forebrain, little is known about how these vocal motor commands interact with ongoing respiratory dynamics. Bengalese finch calls provide a unique opportunity to study how vocalizations are integrated with respiratory dynamics since they are produced one at a time, unlike the sequential nature of other well-studied animal vocalizations, like birdsong and rodent ultra-sonic vocalizations. This discrete nature of calls allowed us to study how individual vocal motor commands interact with ongoing respiratory dynamics. First, we found that calls can interrupt and disrupt the respiratory rhythm at any phase, which indicates that call motor commands can override ongoing respiratory dynamics, potentially by directly interacting with the respiratory CPG. Second, we discovered that generation of the call respiratory waveform is dependent on a dynamical system, as unpatterned electrical stimulation of midbrain calling nucleus DM was sufficient to evoke calls. Finally, we found that brief electrical stimulation of the respiratory brainstem itself is sufficient to engage this dynamical system and produce a call-like vocalization. These results show that top-down motor commands generated by the midbrain need not encode moment-by-moment motor commands for vocalizations, but instead can recruit the dynamics of the respiratory CPG to generate calls. Other vocalizations may similarly depend on an interplay between top-down motor commands and local CPG dynamics.

1-145. Cortical adaptation to sound reverberation

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In almost every natural environment, sounds are reflected by nearby objects, producing many delayed and distorted copies of the original sound, known as reverberation. Our brains usually cope well with reverberation, allowing us to recognize sound sources regardless of their environments. In contrast, reverberation can cause severe difficulties for speech recognition algorithms and people with hearing impairments. This study examines how the auditory system copes with reverberation. We trained a linear model to recover a rich set of natural, anechoic sounds from their simulated reverberant counterparts. The model neurons achieved this by extending the inhibitory component of their receptive filters for more reverberant spaces, and did so in a frequency-dependent manner. These predicted effects were observed in the responses of auditory cortical neurons of ferrets in the same simulated reverberant environments. Together, these results* suggest that auditory cortical neurons adapt to reverberation by adjusting their filtering properties in a manner consistent with dereverberation.

1-146. “This Is My Spot!”: Social Determinants Regulate Space Utilization in Macaques.

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Space can be a limited resource. Many species including humans, evolved a compromise regulating space sharing and its occupancy based on social determinants. For example, students in a classroom tend to sit close to their friends, keeping the same spots across days, revealing the social structure in the classroom. This place preference suggests that factors such as social hierarchy and affiliation can shape space utilization; contrasting with classical random walk models of agents moving at random in any given direction. Here, we asked whether spatial occupancy of macaques (*Macaca fascicularis* and *M. mulatta*) within a unisex group, reveals a structured space utilization beyond simple spatial affordance of the finite space. To this end, in two groups of four animals, we analyzed the simultaneously recorded positions of each individual of the group while the group roamed in an enclosure. (1) The identity of each animal could be decoded from its individual pattern of spatial occupancy, revealing that each animal sustained its spatial footprint across multiple days. (2) Average distance between monkeys was a proxy of their social hierarchy, confirming that interpersonal distance is correlated to affiliation and dominance hierarchy. (3) Alternating the social context by removing one of the monkeys revealed that social context influences occupancy. (4) Finally, the distribution of distance between pairs of monkeys was bimodal and was modeled using random walk approach with an additional parameter reflecting propensity to stay in close proximity, which was again related to dominance hierarchy. These analyses reveal the hidden structured nature of space utilization as a function of social determinants in macaques and simple modeling approach to further study group organization in neuro-ethological settings.

1-147. Investigating effort and time sensitivities in rodents performing a treadmill-based foraging task

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Imagine that it's tea time and you'd like to eat a distant cookie. The speed at which you will walk toward this cookie will be modulated by your sensitivities to the energetic cost of movement (e.g., lazy vs. energetic), to

the cost of time (e.g., patient vs. impatient), and to the reward (e.g., hungry vs. sated). How these sensitivities modulate behavior and their neural implementation remain poorly understood. Here, we tackled this question by combining experimental and theoretical approaches. We developed an automated foraging task in which rats have to run back and forth on a treadmill to get rewards. Within each session the probability of getting a reward was alternatively high (90%) and low (10%) in 5 min-long blocks. Across sessions, we manipulated the effort rats had to produce by either modifying the length of the treadmill while its speed remained null, or by manipulating the speed and direction of the treadmill to facilitate or counteract the animals' crossings. We quantified the number of crossings and the running speed. Rats did more crossings when the probability of getting the reward is high, confirming that they are reward and time sensitive (Shadmehr and Ahmed, 2020). Surprisingly, this effect was not paralleled by a modulation of their running speed which was identical in high and low reward blocks, suggesting that the animals display limited effort sensitivity. This asymmetric sensitivity for time and effort was confirmed when we manipulated the treadmill distance and its speed/direction. Interestingly, rats modulate their speed to maintain the same time delay between rewards. We are currently investigating the interindividual variability in effort/time tradeoff using optimal control theory and the potential contribution of the dorsal striatum in controlling this tradeoff.

1-148. Paradoxical effect of exercise on the long-term stability of hippocampal place code

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In addition to maintaining a healthy body, physical activity benefits the brain, improving memory and cognition. While some of the physiological effects of voluntary exercise on the brain are known (e.g., increased hippocampal neurogenesis), little is known about its effects on the neural code. Using longitudinal Ca²⁺ imaging in freely behaving mice and tracking the same neurons over weeks, we studied how voluntary exercise affects the quality and long-term stability of hippocampal place codes. In addition to increasing neurogenesis, we found that running accelerated the emergence of spatial code in novel environments, increased the amount of information that neurons carried about the mouse's position, and increased code stability over timescales of days-weeks. Paradoxically, although running mice demonstrated an overall more stable place code than their sedentary peers, when controlling for code quality, their place code was in fact less stable for any given code quality level. This result suggests that the seemingly increased stability for runners is mediated by the difference in the code quality between the two groups (known as the "Simpson's paradox"). A model-based simulation showed that the combination of both improved code quality and faster representational drift in runners, but neither of these effects alone, could account for our results. Thus, exercise may benefit hippocampal function by inducing faster learning and promoting long-term memory via a more informative place code.

1-149. Data-driven dynamical systems model of epilepsy development simulates intervention strategies

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Much progress has been made in understanding the dynamics of spontaneous epileptic seizures [1], while an understanding of why and how the disease develops (epileptogenesis) remains elusive. Here, we present a first-of-its-kind model of epileptogenesis describing the interactions between neuroinflammation, blood-brain barrier disruption, neuronal death, circuit remodeling, and seizures. The model is formulated as a system of nonlinear differential equations describing processes acting on realistic timescales ranging from seconds to weeks. Math-

ematically, it is characterized by two stable fixed points corresponding to healthy and epileptic conditions divided by a separatrix. The model allows for simulation of epileptogenesis caused by various types of injuries, and captures characteristic injury-specific courses of pathology development. This was tested with data from 3 distinct animal models, in which epilepsy is triggered by neural infection, prolonged seizure (status epilepticus), or blood-brain barrier leakage. In addition, our model captures such features of epileptogenesis as the so-called latent period (time interval between injury onset and first seizure), the emergence of long timescales (up to decades) of pathology development, dose-dependence of epileptogenesis risk and severity on injury intensity, and variability of epileptogenesis outcomes in subjects exposed to identical injury. Furthermore, the model highlights the multicausal nature of epileptogenesis, showing that neuronal death is not necessary for epileptogenesis, while it is alone sufficient to cause disease development. Finally, our model predicts efficient injury-specific therapeutic strategies in the form of specific intervention time windows. In conclusion, our model provides new insights into the multi-causal nature of disease development and generates testable predictions for future experiments and therapeutic interventions.

2-001. Exceptionally large rewards lead to a collapse in neural information about upcoming movements

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Increasing the magnitude of an offered reward for an action can improve performance. However, performance can suffer when the payoff is exceptionally large, a phenomenon dubbed “choking under pressure.” What is the neural basis of choking under pressure, and what are the neural mechanisms whereby potential rewards affect motor performance?

To study the interaction between rewards and movement, we recorded neural population activity in the motor cortex of rhesus monkeys as they performed a challenging delayed-reaching task, in which the reward available for a successful reach was pre-cued. Both animals choked under pressure, showing an “inverted-U” relationship between success rate and reward size.

How does the brain mediate this unintuitive relationship between monotonic reward information and an inverted-U trend in behavioral success? We examined how reward size altered the neural activity before movement onset for different reach directions. We identified three main effects: First, increasing reward yielded a monotonic shift in neural activity along a “reward axis.” Second, we found that this reward axis was nearly orthogonal to the linear 2D projection that best separates neural activity for reach directions (“target plane”). Third, increasing rewards initially drove average preparatory activity for different reach directions farther apart in the target plane, but the highest reward pushed them back together. This expansion-then-contraction of target conditions was sufficient to yield an inverted-U in the accuracy of an offline discriminator of the reach direction as a function of reward.

In summary, increasing reward initially drives motor cortical preparatory activity in a manner that is more informative about the upcoming movement (as measured by decoding accuracy), but then as reward signals grow, less information about target location is present in the population response. In this way, a neural correlate of choking under pressure is evident in the motor cortex.

2-002. State-dependent Reward Encoding in Cortical Activity During Dynamic Foraging

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Multiple brain regions are involved in integrating reward to drive action selection, with rich representations of reward history in the striatum, retrosplenial cortex, and frontal areas. A major challenge in dissecting the circuits that govern reward-guided behavior is the existence of multiple strategies for reward maximization. For instance, in dynamic environments, mice can engage in both model-free behavior, where they update action values from trial to trial, and inference-based learning, where they use an internal model to infer the current world state. These two modes are challenging to distinguish, and can even intermix within training sessions, complicating studies of neural mechanisms that rely on session-averaged activity. Here, we tackled these problems by developing a computational approach to characterize dynamic shifts in behavioral strategies. We first simulated the choice sequences of model-free and inference-based agents, and built decoders of their underlying strategy using features of the choice transition around the block switches. We built on this analysis with a new state-space method, block Hidden Markov Model, which infers the hidden state that governs the behavior in each block of trials. Our analysis revealed a diverse mixture of both model-free and inference-based strategies even in expert animals, with an increased reliance on inference-based behavior with training. We used 1-photon widefield imaging to investigate how mesoscopic cortical activity varies with the inferred hidden state. We found that reward encoding is strongly state-dependent: reward is weakly encoded in the disengaged state, transiently encoded in the model-free state, and persistently encoded in inference-based learning. Activity in diverse cortical regions, including the somatosensory, motor, frontal and visual areas, showed different patterns of correlation with reward in each mode. Our results suggest distinct neural mechanisms that underlie different modes of dynamic foraging, and highlight the importance of hidden states in the dissection of reward circuits.

2-003. Hippocampal representations emerge when training recurrent neural networks on a memory dependent maze navigation task

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Predicting the future outcomes of actions forms the basis for reinforcement learning to shape goal-directed behaviours. Recent work showed that learning based on predicting future sensory experience using the current state and action of an agent leads to representations that resemble those in the brain, for instance place and grid cells of the medial temporal lobe. Here we ask if combining ongoing predictive learning of sensory events and of notional value of actions leading to rewards forms representations that enable more efficient goal-directed learning than reinforcement learning alone. Simulating a simple T-maze environment, we find that once a recurrent network is trained to predict future sensory inputs based on actions, an attractor landscape forms resembling hippocampal place cells. Next, we introduce cued rewards, and train the network to predict state-action Q-values which are used to guide subsequent behaviour. A network previously exposed to the same environment without rewards learns the task faster than a network trained using Q-learning alone, or without previous exposure. Interestingly, this training paradigm causes non-local neural activity to sweep forward in space at decision points, anticipating the future path to a rewarded location. Moreover, prevalent choice and cue-selective neurons form in this network, again recapitulating experimental findings. Together, these results indicate that a simple combination of predictive, unsupervised learning of environment structure and of reinforcers yields efficient representations to support goal-directed behaviour and exhibit dynamics also found experimentally in the hippocampus when learning similar tasks.

2-004. Epiphenomenal representations of abstract rules in a connectionist model of the Delayed Match to Sample task

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In the human brain, some individual neurons respond selectively to abstract variables, invariant to sensory grounding (Mansouri, Freedman, & Buckley, 2020). Similarly tuned units also appear in artificial networks trained on cognitive tasks (Goh et al., 2021). It is often implicitly assumed that the emergence of such interpretable neurons plays a key role in the behavior of the trained network. Here we show that this is not necessarily the case. We train a biologically inspired artificial agent comprising two key components—a recurrent network and an associative memory—on a canonical rule-based neuroscience task (J. Wallis, Anderson, & Miller, 2001), and observe the emergence of brain-like rule representations in the recurrent network. Crucially, however, we find that these representations are not used to guide behavior at test time—ablating these units has minimal impact on performance. However, we find that ablating other units in the recurrent network can severely degrade performance. These results call into question the assumption that observing representations in a brain region along with performance degradation when that region is lesioned is sufficient to infer that those representations cause the animal's behavior in the task. These results point the way toward further modeling and animal experiments that may improve our understanding of epiphenomenality in the brain.

2-005. Learning-to-learn emerges from learning to efficiently reuse neural representations

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Learning-to-learn, a progressive acceleration of learning while solving a series of similar problems, represents a core process of knowledge acquisition. To investigate its underlying brain mechanism, we trained a recurrent neural network (RNN) model on a series of arbitrary sensorimotor mapping problems. The network displayed an exponential speedup in learning across problems. The neural substrate of a sensorimotor task schema emerges as low-dimensional neural representations of task variables that are shared across problems. Its reuse limits the connection weight changes required to learn new problems, thus facilitating their learning. Since the population trajectory of a recurrent network produces behavior, learning is determined by changes in the network's vector field which governs its dynamics. We propose a novel analysis of vector field changes, which showed that novel stimuli in new problems can distort the schema representation. Weight changes eliminate such distortions and improve the invariance of the reused representations in future learning. The accumulation of such weight changes across problems underlies the learning-to-learn dynamics. Taken together, these findings elucidate the neural substrate of a visuomotor mapping schema, why its reuse dramatically improves learning efficiency, and how its progressive refinement gives rise to learning-to-learn. In doing so, they offer experimentally verifiable predictions, and present novel methods to analyze learning in RNNs by linking changes in neural activity and network structure. Therefore, they are of value to a broad audience in neuroscience, cognitive science, and machine learning.

2-006. Capturing the evolution of low-dimensional dynamics in large scale neural recordings with sliceTCA

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A fundamental question in systems neuroscience is how populations of neurons represent sensory, motor, and cognitive variables. Yet how these neural representations evolve over slow timescales is not well understood. Recent work has proposed using tensor decomposition methods to identify low-dimensional latent dynamics without requiring trial-averaging (tensor component analysis; TCA). This approach assumes that the data tensor can be described as a sum of components with fixed neural weights and temporal dynamics that vary over trials only in amplitude. However, recent evidence suggests that the slow timescale evolution of latent variables over trials may instead be characterized by a reorganization of neural encoding weights (“representational drift”), or by shifts in temporal dynamics as in classic reinforcement learning paradigms. To address this, we propose a new dimensionality reduction method (sliceTCA) that extends TCA to identify a broader class of latent low-dimensional dynamics by allowing multilinear dependencies between neural, temporal, or trial factors. We first illustrate the flexibility of this method in a simple linear feedforward model receiving bottom-up sensory and top-down modulatory input in a Go/No-go task. We show that sliceTCA is able to capture the structure of the simulated data tensor with only two components representing the two sources of input. We next apply sliceTCA to a multi-region calcium imaging dataset to determine how the latency of task-related latent dynamics changes over the course of a session. These examples illustrate the ability of sliceTCA to capture interpretable low-dimensional structure that evolves over trials from high-dimensional neural data.

2-007. Disentangling neural dynamics with fluctuating hidden Markov models

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Understanding the neural code depends on capturing latent computational features within the highly complex dynamics of neural activity. While many features of neural dynamics will be relevant for a given computation, other features will not. In contrast with existing methods that describe how latent dynamics depend on experimental variables, we present a model designed to factor out variables that are irrelevant to the latent dynamics. We propose a fluctuating hidden Markov model (FHMM) that simultaneously learns an HMM that captures latent dynamics, and a baseline, dynamic firing rate that captures other drivers of the observed dynamics. We leverage the theory of exponential families to derive a nearly exact implementation of expectation maximization for FHMMs, and to increase model flexibility beyond Poisson spike-counts.

As a demonstration we apply FHMMs to study how the activity of single neurons in macaque primary visual cortex (V1) represent bimodal probability distributions. We first identified images that elicit bimodal response distributions across trials in target neurons (termed ambiguous images). We then studied the within-trial dynamics of responses to ambiguous images, and tested if the neural dynamics stay within a single mode during each individual stimulus presentation (slow sampling), or visit both modes within a presentation (fast sampling). We show that FHMMs learn to correctly factor out onset transients in neural activity, and capture the latent sampling dynamics between the two modes.

We are currently applying FHMMs to systematically assess the role and relative frequency of slow and fast sampling in V1 populations. More generally, our model can be extended to whole neural populations and continuous latent states, and should prove useful to any researchers trying to disentangle relevant computational features from task irrelevant variables or incidental neural dynamics.

2-008. Online neural modeling and Bayesian optimization for closed-loop adaptive experiments

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New recording technologies and population analyses have made it increasingly conceivable to functionally dissect large-scale circuits *in vivo*, causally relating neural activity to behavior. Such direct testing typically relies on hypotheses formulated in advance of the experiment. However, preconceived hypotheses may be restricting our exploration of ever-larger neural systems and more complex behaviors. We propose that adaptive experimental designs give us the statistical efficiency to search large parameter spaces and the flexibility to change our models with evolving dynamics. We thus developed a new method for building models of population-level neural dynamics online, while the experiment is running. Our method combines fast, stable dimensionality reduction with a soft tiling of the resulting neural manifold, allowing dynamics to be approximated as a probability flow between tiles. It can be fit efficiently (rates faster than data acquisition), scales to large populations, and outperforms existing methods when dynamics are noise-dominated or feature multi-modal transition probabilities. We demonstrate its performance on both simulated nonlinear dynamical systems and experimental neural data. Using online modeling, we can also close the loop in visual stimulation experiments performed in larval zebrafish, using real-time interventions to both generate and test hypotheses. While displaying thousands of unique combinations of multidimensional visual stimuli is infeasible, we use ideas from Bayesian optimization to sequentially choose maximally informative stimuli, allowing us to rapidly characterize the preferred stimulus for each neuron. We additionally present a new population optimization method using multi-output Gaussian processes that couples online model fitting and active stimulus selection to acquire data at locations where models are likeliest to be wrong given the data seen so far. These methods, which combine online neural modeling with adaptive intervention, open the door to automated, theory-driven circuit dissection at scale, providing a powerful new means of interrogating neural function.

2-009. Hida-Matern Gaussian Processes

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Bayesian data analysis using probabilistic modeling explicitly utilizes one's a priori scientific beliefs as structured prior distributions. However, scientific inference often requires some of our prior knowledge only be embedded in a 'broad sense', take for example inferring latent dynamics underlying neural population activity; nonparametric approaches such as Gaussian Processes (GPs) are highly flexible, expressive, and allow us to encode broad assumptions such as periodicity, stationarity, and smoothness. Though, these properties make GPs attractive for neural data analysis, their computational overhead, scaling cubically with the number of data points, dilutes their applicability to large scale problems. We introduce the Hida-Matern (HM) kernel, a basis over all stationary GP covariance functions. We show how to leverage the GP state-space model (SSM) representation to achieve fast inference for common probabilistic models in neuroscience that embed prior beliefs via GP priors. We showcase the strengths of the SSM formulation of GPs in latent-variable-modeling (LVM) of neural dynamics, Poisson regression, and intensity estimation of neural point-processes. In addition, we also show how the GP-SSM representation links popular methods such as GPFA and vLGP to linear SSMs; implying limitations in the beliefs about neural dynamics that one can specify with these models *a priori*. Thus, any model specifying latent trajectories under a stationary GP prior is ill suited for inferring neural dynamics that are nonlinear.

2-010. How coding constraints affect the shape of neural manifolds

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While neural population recordings are increasingly high-dimensional, the bulk of recorded activities is usually structured along lower-dimensional manifolds. These manifolds often appear to be nonlinear, so that linear dimensionality reduction methods such as principal component analysis (PCA) yield embedding dimensionalities (ED) that are much higher than the intrinsic dimensionality (ID) of the manifold [Jazayeri, Ostojic, 2021]. Across datasets, the embedding often generates components that resemble higher-order functions of each other, or ‘higher-order components’ (HOCs), thus suggesting some generic, if poorly understood structure of the underlying manifolds. While such manifold structure could reflect underlying mechanisms for information processing, it is unclear why they would yield state-space embeddings with HOCs. Here, we investigate the effect of non-negativity constraints - individual neuronal activity is always non-negative - on neural manifold embeddings, while assuming that intrinsic variables should be read out linearly. We consider both standard network models, which enforce non-negative firing rates through static nonlinearities, and network models in which neuronal activities are solutions to constrained optimization problems [Barrett et al, 2013]. We show in simulations that, when overall population activity is limited in both models, the ED always exceeds the ID. Also, PCA retrieves HOCs that resemble those in data, and we explain this finding geometrically. Furthermore, we show that the combination of homeostatic and non-negativity constraints on optimal neural codes can yield embeddings with increased complexity, in that the ED grows despite a fixed ID. Finally, to test which of the models best describes neural manifolds, we fitted them to real data within a dimensionality reduction setup. While they both outperformed PCA for a given dimensionality, the model with optimal representations outperformed the model with static non-linearities, suggesting that the nonlinearity of neural manifolds may be partly shaped through constrained optimality principles.

2-011. Neuromodulation as a path along the model manifold for spiking networks

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Summary: Modulation of neural activity by hormones, peptides, and other small molecules is known to be required for learning, motor control, and homeostasis, and it can induce similarly structured networks to exhibit different behaviors. Yet, relatively few theoretic studies have attempted to detangle the role and function the various types of modulation play throughout the brain. In particular, it is important to understand how changing neuromodulator concentrations can move a network through its space of possible behaviors. A better understanding of neuromodulatory movement through behavioral space could be applied to pharmacological interventions, allowing a clinician to perturb diseased networks away from pathological activity regimes.

In this work we use techniques from information geometry to define and study the model manifolds of spiking networks. Points on these manifolds correspond to distributions of possible activities of a network as some of its parameters—such as the membrane and synaptic time constants—vary. Neuromodulators can alter physiological parameters like the timescales of a network, so a change in neuromodulator concentration can be viewed as a trajectory along these model manifolds. For exponential families, the model manifold can be characterized by a finite number of coordinates, which are the eigenmodes of a centered distance metric and are physically interpretable relative to the model parameters. We first apply a Gaussian approximation to the membrane potential dynamics of networks of stochastically spiking neurons. This approximation—expected to be valid away from bifurcations in network activity—permits explicit identification of manifold coordinates, estimation of its effective dimensionality, and building of intuition regarding neuromodulatory trajectories across these manifolds.

This information geometric perspective provides a framework for understanding how different activity regimes a network can inhabit are connected by modulation. Further work with this methodology will address neuromodulation in motor network models and extend our approach to networks with non-equilibrium steady states.

2-012. Thalamic head-direction cells are organized irrespective of their inputs

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Continuous attractor networks are believed to support various cognitive functions, from working memory to spatial representations, yet the neuronal dynamics and circuits supporting these dynamics *in vivo* remain unclear. One example of such networks is the head-direction (HD) circuit, a crucial signal for navigation. It is represented by HD cells, which each fire for a specific direction of the animal's head, and is transmitted to the cortex by the anterodorsal nucleus (ADn) of the thalamus where a vast majority of neurons are modulated by HD. ADn HD cells maintain their mutual coordination during sleep, when sensory inputs are virtually absent, supporting the view of an attractor-driven system. The rigid organization of HD cell activity in the ADn begs the question of the origin of these structured patterns. Specifically, it has been proposed that the upstream structure, the lateral mammillary nucleus (LMN), is a central component of the HD signal generator circuit. We thus investigated the organization of LMN ensemble activity across brain states, and its relationship to ADn activity. To this end, we recorded LMN neuronal ensembles during exploration and sleep. The organization of LMN showed two opposite regimes: during Rapid Eye Movement (REM) sleep, when brain's activity is virtually indistinguishable from wake, HD cells in the LMN were coordinated exactly as during exploration - and as in the ADn. In contrast, during non-REM sleep, the coordination of LMN HD cells was reduced while simultaneously recorded ADn neurons maintained the same level of mutual coherence as during wake and REM. The decreased level of correlation in the LMN resulted, at least in part, by a switch to hypersynchronous spiking activity in which neurons co-fired irrespective of their mutual preferred direction. This observation suggests that the HD thalamocortical circuit supports attractor dynamics independent of its inputs.

2-013. Environment-dependent firing in rigidly organized head-direction cells is stable across weeks

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Primary sensory cortical areas are characterized by low-level representations of sensory inputs, but whether these representations are stable over a long period of time or whether they are continuously renewed is still unclear. The head-direction (HD) signal is essential for the spatial navigation system. In the cortex, it is processed by the postsubiculum (PoSub). HD cells each fire for a specific direction of the head of the animal in the horizontal plane and constitute a vast majority of PoSub principal neurons. To address the question of representational stability, we used one-photon calcium imaging with portable microscopes ('miniscopes') to longitudinally monitor ensembles of HD cells in the PoSub over periods of weeks in freely moving animals visiting several different environments. In the PoSub, the representation of the HD signal was stable at two levels. First, the pairwise offset between HD neurons was preserved for several months, indicating that the subcortical representation of the HD signal is certainly itself stable and that thalamocortical integration is rigid. Second, the orientation of the HD signal at the population level was maintained in a given environment over the same period of time, suggesting that the HD system preserves long-term memories of spatial orientation in different environments. Furthermore, HD neurons in the PoSub participated differently in the HD signal across environments, resulting in environment-specific coding of head direction. Together, these findings shed light on how spatial information is represented over time in the brain's navigation system.

2-014. Goal-directed remapping of enthorhinal cortex neural coding

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The medial enthorhinal cortex (MEC) is a core brain region involved in spatial navigation, and provides navigational information to the downstream hippocampus. Neurons in the MEC respond to an animal's location and

heading direction in an environment, as well as boundaries and an animals' distance from objects. Other studies have demonstrated that MEC neurons respond to more than navigation, illustrating the flexibility of the region in adjusting response profiles in different contexts. However, it remains poorly understood under what conditions and at what time-scale changes in MEC coding occur, or to what extent these changes are indicative of behavior. In the spatial navigation context, this study sought to examine if MEC neurons reflect trial-wise changes in spatial representations, and how these changes relate to behavior. The experimental paradigm required subjects to navigate to a reward location based on a visual-cue while neurons were recorded from the rat MEC. Firing-rate spatial maps were then compared across Cue and Reward conditions for recorded neurons. Spatial remapping is defined by changes in firing-rate or translation of the spatial location in which a neuron is maximally active (measured by spatial correlation). Results of these analyses reveal Cue induced remapping that exceed what can be expected by trial-wise firing-rate fluctuations in the spatial maps. Furthermore, the extent of remapping on a given session strongly correlated with behavioral performance, the greater the remap the better the subject's performance was on the task. Reward-induced remapping was examined by comparing rewarded and unrewarded trials. We find that most neurons remap due to reward, and that remapping strength correlated with performance on the task. We thus demonstrate that trial-wise response profiles of MEC neurons change within the same environment in a behaviorally and context-dependent manner, computations previously thought to be generated within the hippocampus.

2-016. Developmental experience of scarcity affects adult responses to negative outcomes and uncertainty

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Understanding the effects of scarcity and uncertainty on the developing brain and behavior has been a major challenge for neuroscience and evolutionary biology. Currently, over millions of households with children and adolescents worldwide experience insecure and uncertain access to food, a.k.a. food insecurity. The goal of our work is to investigate if transient food insecurity experience during the juvenile-adolescent developmental period has lasting effects in adult learning, decision making, and dopamine system in a mouse model. We manipulated feeding schedules from postnatal day(P)21 to 40 as food insecure (FI) or ad libitum (AL) and returned them back to free access of diet after P41. We found that adult males in the FI and AL group showed significant differences in performance in the reversal phase of a deterministic 4-choice odor-based foraging task (4COF) and differed in 'trials to switch' in a 2-armed bandit task (2ABT) when probability of reward was 65-75% but not 90%. We then applied reinforcement learning models to further investigate how the two groups solved the tasks. The best fit models suggest that P21-40 feeding experience affected sensitivity to negative outcomes in both tasks, but the direction of effect was task specific. In separate cohorts of adult male FI and AL mice, we examined the synaptic plasticity of dopamine neurons in the ventral tegmental area (VTA) in ex vivo slices and evoked striatal dopamine release. We found that AMPAR/NMDAR ratio in the nucleus accumbens (NAc) core-projecting VTA dopamine neurons and dopamine release in the dorsal striatum were significantly decreased in the FI group compared to the AL group. Together, these data show in a rodent model that transient differences in food scarcity and uncertainty in development can have significant impacts on adult learning, decision-making, and dopamine function.

2-017. Indirect-projecting striatal neurons constrain timed action via 'ramping' activity.

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Time represents a fundamental dimension around which all behaviors must be organized. Previous work has shown that dorsal striatal medium spiny neurons (MSNs) encode prospective time via ‘ramping’, progressive linear increases or decreases in firing rate preceding a time at which an animal must act (Emmons et al., 2017; Matell et al., 2003). Furthermore, disruptions to dopamine signaling attenuate this pattern of activity and can bidirectionally modulate performance of timed behaviors (Parker et al., 2015; Soares et al., 2016). Dopamine binds to both D1- and D2-MSNs which play orthogonal roles in movement and reinforcement learning (Kravitz & Kreitzer, 2012). However, the respective roles of D1- and D2-MSNs in timing remain poorly understood. Here, we trained transgenic D1- and D2-cre mice to perform an operant interval timing task which required mice to ‘switch’ response ports after 6 seconds had passed without receiving a reward. In our first experiment, we utilized cell-type specific optogenetics to selectively inhibit either D1- or D2-MSNs and found that D2-MSN inhibition resulted in impaired temporal accuracy. To better understand the in-vivo dynamics underlying this effect, we then recorded from optically tagged D1- and D2-MSNs and observed ‘ramping’ activity amongst a greater proportion of D2-MSNs than D1-MSNs. Finally, we pharmacologically blockaded dopamine binding to either D1- or D2-dopamine receptors with either systemic SCH23390 or sulpiride. Interestingly, we found that D2 receptor blockade, but not D1 receptor blockade, attenuated time-related activity across striatal ensembles although both drugs attenuated movement-associated activity. These results suggest that time-related ramping amongst D2-MSNs may constrain behavior during a timed interval, a process which can be captured by drift-diffusion models. These data are of particular interest for understanding the circuit mechanisms of impaired temporal control of action in disease states involving striatal dysfunction, such as Parkinson’s disease and Huntington’s disease.

2-018. Exploration of learning by dopamine D1 and D2 receptors by a spiking network model of the basal ganglia

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The basal ganglia (BG) play a crucial role in action-selection and reinforcement learning (RL), but how multiple nuclei, transmitters and receptors realize computations for reward-based learning is still unclear. We built a topologically organized spiking BG model. Striatal medium spiny neurons (MSN) were classified based on the expression of dopamine D1 and D2 receptors. We implemented spike-timing dependent plasticity and structural parameters: i) the asymmetry of connections between MSN’s; and ii) the overlap between direct and indirect pathways. In action-selection simulations, we assumed two functional channels representing competitive sensory inputs and actions. We activated two neighboring ensembles of cortical neurons and observed the responses on two adjacent MSN ensembles and downstream nuclei. In RL simulations, we investigated transient increase and decreases of dopamine in a generalization-discrimination task. In generalization-learning (classical conditioning), upon the selection of the preferred channel, reward was delivered as dopamine burst, causing the potentiation of connections to MSN-D1. After several episodes, tests showed the preferred channel selection across both stimuli. In discrimination-learning, the previously learned action-selection upon a non-preferred channel triggered reward omission as dopamine dip, causing the potentiation of cortical synapses to MSN-D2. After several episodes, the prediction was refined, producing the corresponding channel selection for each stimulus. Our simulation results show that discrimination learning, converges faster for higher values of ii). This suggest that overlapping pathways may provide learning advantages, which support the idea of a functional cooperation between direct and indirect pathways. This was possible given a high asymmetry i), with sparse connections from MSN-D1 to MSN-D2. Based on our results, we hypothesize that lateral inhibition from MSN-D2 to other MSN’s increases during dopamine dips, and this modulation is crucial for discrimination learning convergence. In addition, we demonstrate that this model simulation can scales to the size of macaque BG, using the Fugaku supercomputer.

2-019. Learning and expression of dopaminergic reward prediction error via plastic representations of time

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Various models and investigations over the years have attempted to pin down a mechanistic explanation for how dopamine (DA) neurons in the brain can exhibit reward prediction error (RPE), usually through direct analogy to temporal difference (TD) learning. However, there are two key hurdles in imagining how TD could plausibly be implemented in the brain. First, TD models of DA learning frequently require arbitrarily constructed and unrealistic components, such as a temporal chain of feature-specific neurons that uniformly tile the time from stimulus onset to reward arrival. Secondly, various predictions of TD clash with experimental observations of how dopaminergic RPE evolves over learning. Here, we present a biophysically plausible network architecture of spiking neurons, that when coupled with local Hebbian and eligibility trace learning rules, learns RPEs and can replicate results observed from multiple experimental paradigms. The model learns feature specific representations of time, allowing for neural representations of stimuli to adjust their timing and relation to rewards in an online manner. Following learning, our model DA neurons report a distribution of “optimistic” and “pessimistic” RPEs, akin to those seen in distributional reinforcement learning literature. While DA firing in our model reflects an accurate RPE before and after learning, these two quantities are not necessarily synonymous during learning. This separation of DA neuron firing from a strict RPE allows our model to unify seemingly mutually exclusive experimental results, as well as make unique predictions that directly contrast those of TD. One such prediction is that even after overtraining, reward omission will still result in a negative RPE at the time of expected reward, since the model’s representation of the cue-reward delay (and thereby cue-specific suppression of the reward-triggered dopamine) is maintained for timescales longer than the cue-evoked dopamine.

2-020. Learning rules underlying operant matching in *D. melanogaster*

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Foraging animals make decisions based on cues that are unreliable predictors of reward. In these situations, the ratio with which an animal divides its choices between cues matches the ratios with which they provide reward. This operant matching strategy is widespread amongst vertebrates. Performing operant matching requires animals to possess a valuation of available cues, and to update them when cue-reward relationships change. While neurons that represent value information have been found in several brain regions, less is known about how value is updated. Theoretical studies suggest that the underlying learning rule should contain information regarding reward expectation. However, deciphering these rules in the brain has remained a challenge. To address this, we turned to the mushroom body (MB) of *D. melanogaster*. Previous work has assigned this region a key role in learning and identified the underlying synaptic mechanisms. The circuit’s connectome is mapped, and it has a well-studied role in behavioral control. This makes it a promising system to understand the learning rule underlying matching behavior. We designed a dynamic foraging task, and showed for the first time, that flies perform operant matching. Our analyses of behavior in this task suggest that flies rely on reward history over multiple trials when making choices. Further, we developed a model that uses the known architecture of the MB to predict behavior. Consistent with the theoretical predictions, but counter to prior expectations, when this model used a learning rule involving reward expectation, it was able to better fit behavior. To establish how this reward expectation is represented in the MB, we have begun imaging experiments in key candidate neurons. Our findings suggest that a learning rule incorporating reward expectation may be a widespread feature of neural circuits and play an essential role in foraging across disparate species.

2-021. The neurocognitive role of working memory load when motivation affects instrumental learning

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Animals and humans have multiple reinforcement learning (RL) systems, especially a hard-wired Pavlovian system that learns state-outcome associations and promotes an approach to rewards and avoidance of punishment; and an instrumental system that learns values based on state-action-outcome associations. Conflict between the two systems sometimes leads to suboptimal decisions including pathological behaviors but factors that affect the conflict remain largely unclear. Meanwhile, previous findings suggest that taxing cognitive resources alters several decision-making processes and a balance between multiple decision-making systems: under working memory (WM) load, 1) the reliance on computationally cheaper model-free RL increased compared to model-based RL; 2) learning rates in model-free RL decreased; 3) choice consistency decreased. However, the role of WM in the Pavlovian-instrumental conflict remains unknown. Thus, we conducted a functional magnetic resonance imaging (fMRI) study (N=49) in which participants completed a model-free RL task with Pavlovian-instrumental conflict (the orthogonalized go/no-go (GNG) task), and WM load was manipulated with dual-task conditions. The behavioral and computational modeling analysis showed that WM load did not affect the Pavlovian bias, but instead model-free RL by decreasing learning rate and increasing random choice. fMRI analysis showed that striatal reward prediction error signaling increased under WM load. Moreover, under WM load, the striatum showed weakened connectivity with the ventromedial and dorsolateral prefrontal cortex when computing reward expectation. These results suggest that limited cognitive resources do not directly affect the competition between the instrumental and hard-wired Pavlovian systems, but influence model-free RL and action selection through the weakened cooperation for learning between WM and RL.

2-022. Counterfactual outcomes affect reward expectation and prediction errors in macaque frontal cortex

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Identifying situations in which exploration could be beneficial, and learning from such choices, is critical for survival in complex environments. Nonetheless, it is still unclear how animals adapt their choice strategies depending on the potential benefits of exploration and what the neural underpinning of this ability is. We thus adapted a 2-option forced-choice task in which 3 rhesus macaques made choices while the information and the feedback they received was being manipulated: (i) feedback was given about either just the chosen option or both the chosen and unchosen counterfactual options and (ii) feedback could or could not be used to guide future choices. We showed that monkeys chose the least rewarded option more when exploring was beneficial. We also showed that monkeys relied on not just obtained reward but also counterfactual outcomes from the unchosen option to guide their future choices. Using fMRI, we showed that chosen expected reward signals in mid cingulate cortex (MCC) and dorsolateral prefrontal cortex (dIPFC) were modulated by the availability of counterfactual outcomes at the time of choice. Specifically, we showed that when exploration was sensible (because they would only get feedback for the chosen option), MCC and dIPFC activities were negatively modulated with increased chosen expected value. In contrast, when there was no need to explore (complete feedback), MCC and dIPFC were more active with increased chosen expected value. This suggests that the suppressive effect of default actions (choosing the option with higher expected reward) might be specific to environments in which such actions trade-off with the benefits of exploration. We also saw prediction error signals for both obtained and counterfactual outcomes across orbitofrontal cortex (OFC), consistent with the idea of it as a hub for not just experienced but also imagined/ counterfactual values for state value-estimation or credit assignment.

2-023. Optimists and realists: heterogeneous priors in rats performing hidden state inference

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A principle of modern decision theories is reference dependence, in which the subjective value of a reward is computed relative to an internal reference point that is thought to reflect expectations. Previous work often assumes that reference points are retrospective, deriving directly from past experiences. We used behavioral modeling to show that, instead, rats infer underlying task states in order to switch between multiple reference points. We designed a behavioral paradigm with partially observable states – uncued blocks of trials offering only small rewards (low blocks) or large rewards (high blocks). Rats ($n=165$) must determine how long to wait for rewards, providing an explicit behavioral readout of a rat's subjective value of the reward. Rats' wait times are sensitive to the block structure - rats wait longer for the same volume of water in low blocks compared to high blocks. We developed computational models that instantiate retrospective or inferential strategies for computing the reference point, which corresponds to the opportunity cost of time in our task. Model comparison showed that an inferential reference point better describes the rats' behavior, and this model strongly outperformed the retrospective model around block transitions. However, we found that rats exhibited considerable heterogeneity in the quality of their prior over the blocks, where the prior has knowledge of the task structure and transition probabilities. Rats with poorer quality priors were slower to infer switches into low blocks, but not high blocks - a form of "optimism" wherein the rats' priors are biased toward high blocks. These data show that rats perform inference to switch between multiple reference points but vary in their ability to incorporate optimistic versus realistic beliefs about task structure.

2-025. A virtual rodent predicts the structure of neural activity across natural behavior

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In recent years, advances in the fields of computational ethology and neuroscience have enabled detailed modeling of animal behavior and its neural underpinnings. However, these advances have yet to produce normative models of neuromotor control that generate the full diversity of animal behavior. Using recently developed methods in 3D pose estimation and deep reinforcement learning, we trained a latent variable model to control a virtual rodent body to imitate the natural behaviors of real rats in a physics simulator. Once trained, the model faithfully replicated diverse rat behaviors and generalized to unseen examples. We next sought out to quantify the extent to which the model's latent representation of movement resembled that of neural activity in the dorsolateral striatum, a brain region implicated in the control of movement. We compared striatal neural activity recorded during unrestricted behavior in an open field to the model's latent variables when imitating the same behaviors. The structure of neural activity across behavior was better predicted by the latent variable model than any other kinematic or dynamic feature of movement. This motivated us to analyze the ways in which the latent variables affected the model's motor outputs. The model adaptively regulated variability in its motor outputs across behaviors, consistent with the minimum-intervention principle in optimal feedback control. We found that this was mediated by the regulation of latent variability, suggesting a computational mechanism through which the brain can regulate peripheral motor variability to support diverse behavior. These results demonstrate the utility of precise kinematic measurement, physical simulation, and artificial neural networks in modeling animal behavior, predicting the structure of neural activity across behavior, and generating novel hypotheses regarding the computational mechanisms

underlying the neural control of movement.

2-026. A feedback model for predicting targeted perturbations of proprioceptors during fly walking

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Walking is a familiar but complex behavior, requiring the continuous coordination of multiple muscles while integrating proprioceptive feedback to correct for unanticipated disturbances. Although a variety of walking models propose mechanisms for this coordination, the neural computations proposed by these models have yet to be experimentally validated. Two crucial barriers are (1) gaps in modeling approaches that integrate specific neural dynamics with realistic kinematics to connect predictions to observations and (2) the inherent difficulty in perturbing or recording from neurons during walking to validate the underlying neural computations.

We leverage the powerful genetic tools available in the fruit fly *Drosophila melanogaster* to address both challenges. To address the first challenge, we propose a feedback model that integrates a model simulating proprioceptor responses, a state estimator to predict angles based on proprioceptor input, and a neural controller to predict fly actions. After training, our model can reproduce the statistics of natural fly joint angles, generate credible walking kinematics, and provide interpretable intermediate variables. To address the second challenge, we develop an experimental framework to validate our model, combining genetically and spatially targeted optogenetic perturbations with kinematics obtained from markerless 3D tracking. We show that the leg joint kinematics of flies following proprioceptive perturbations qualitatively match those predicted by the model. Thus, our approach integrates proprioceptive feedback with a walking control model in an experimentally verifiable way.

The advances in the experimental and theoretical frameworks proposed here hold great potential for modeling neural systems with tight feedback loops. In ongoing work, we are extending the model to investigate how proprioceptive feedback is modulated by walking speed and to distinguish hypotheses about coordination among multiple legs. This modeling framework may produce new insight into sensorimotor coordination, with applications in legged robotics and treatment of diseases affecting sensorimotor control.

2-027. Sensory feedback can drive adaptation in motor cortex and facilitate generalization

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Experimental and computational studies suggest that motor cortex acts as a feedback controller, allowing for 'on-the-fly' movement corrections in response to afferent sensory feedback. However, it remains unclear whether feedback control relates to longer-term learning, and how this would be implemented in neural circuitry. Here, we tackled these questions by testing how a recurrent neural network (RNN) can use feedback to control its own output, and whether this process can enable learning. We built an RNN that received feedback signaling the error between its intended and observed output. An initial training phase that required producing a broad range of outputs (i.e., 'movements') enabled the model to learn to use this feedback to correct its output on-the-fly. After constructing this RNN, we tested directly whether the feedback signal used for online output correction could enable learning by guiding synaptic plasticity in the recurrent connections within the network. We devised a biologically plausible plasticity rule where the recurrent weight changes were proportional to the error feedback signals received by the postsynaptic neurons. This simple rule allowed the network to adapt to persistent pertur-

bations (e.g., a ‘visuomotor rotation’) by changing its initial output pattern, a process that was mediated through recurrent connectivity changes. Remarkably, the model learned in a way that was similar to adaptation studies in humans [1,2]: i) learning generalized to non-learned but similar movements [1] and ii) followed multiple learning timescales [2]. When we examined the network activity before and after adaptation, we found a signature of our learning rule that was also present in neural population recordings from monkey motor cortex (data from [3]). In short, this work links algorithmic models of motor control and learning to a biologically plausible implementation in neural circuitry, thus offering the potential to guide future experimental studies on the neural basis of motor learning.

2-028. Widespread representations of sensory evidence with distinct temporal dynamics across the sensorimotor axis

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Decisions are often guided by detecting subtle signals in a dynamic sensory environment. Although the brain must track such decision-relevant signals, how they are represented and transformed by neural activity across the sensorimotor axis remains poorly understood. Here, we recorded neural activity with Neuropixels probes across dozens of brain regions while mice performed a visual change-detection task. We trained mice to detect a sustained increase in temporal-frequency (TF) of a drifting grating stimulus, whose speed fluctuates stochastically around the mean of 1Hz. The task requires mice to remain stationary while continuously monitoring the grating with noisy speed which could increase at any moment, thereby allowing us to study the processing of dynamically changing task-relevant sensory evidence (i.e. TF) in the absence of overt movement and prior to the reporting of choice (lick). We find that even transient fluctuations (50 ms) in TF recruit activity in 10-20% neurons across a large number of distributed brain regions in the absence of choice and other movements. Beyond the visual system, we find such representations in posterior parietal cortex, premotor cortex, higher-order thalamus, midbrain, cerebellum and basal ganglia. Strikingly, only brainstem nuclei driving orofacial movements appear to be devoid of such sensory evidence representations. Interestingly, momentary increases in TF caused transient responses in neurons in visual areas (dLGN, V1 and superior colliculus), but more sustained responses in downstream areas previously associated with sensorimotor learning, working memory and motor planning (e.g. frontal-premotor cortex, basal ganglia, cerebellum). These sustained responses allowed for integration of multiple samples of stimulus speed, which could provide a robust neural substrate for better detecting sustained changes in noisy sensory evidence. These findings highlight how sensory evidence is transformed by distributed circuits making it available for computations in the entire sensorimotor axis to guide decisions.

2-029. Auditory cortex represents an abstract sensorimotor rule

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Predicting the sensory consequences of one’s actions is critical to perception and action in dynamically changing environments. For several established sensorimotor behaviours, such as locomotion and vocalizations, neural correlates of this prediction have been reported throughout sensory cortex. Oftentimes, however, the sensory consequences of an action are abstract, context-dependent, and newly learned, such as when one learns to play an instrument. How does cortex represent such complex sensorimotor rules? To investigate this question, we developed a task in which mice manipulated the frequency of an auditory cursor by licking either of two lick ports, in search for a rewarded target frequency. Trained mice monitored the ongoing stream of sounds to adaptively guide their lick behaviour. Using two-photon imaging, we then asked whether auditory cortical responses to tones reflected a representation of this novel, abstract sensorimotor rule, beyond purely sensory or movement-

related effects. If animals did learn to predict the acoustic consequences of their licks, we reasoned that subtle violations of these predictions might modulate sound-evoked neural activity. Indeed, we find that frequency-tuned L2/3 excitatory neurons are sensitive to such violations, both at the level of the population of imaged neurons and at the level of individual neurons, even when matching stimulus history and licking. These effects were more pronounced in higher-order cortical subfield A2 than in the primary subfields A1 and AAF. Linear encoding models confirmed that neural responses to rule violations are better explained by sensorimotor prediction errors than by sensory or reward prediction errors. Together, these findings suggest that the relationship between actions and sensory feedback can shape responses along the sensory cortical hierarchy, even when this relationship is abstract and newly learned. Moreover, the continuous nature of the abstract foraging task presented here opens up new avenues for behavioural paradigms in animal models of cognition.

2-030. Experience early in auditory conditioning impacts across-animal variability in neural tuning

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Perceptual learning has been associated with altered sensory cortical representations in trained animals relative to naive ones. While there is substantial variability across animals in the degree of behavioral learning and the associated changes in neural representations, we lack an account of how experiences during learning may drive these differences. Here we address this question in the context of an auditory learning task, by combining experiments and computational modeling. Mice were progressively trained to classify tones as a single, center frequency or non-center by licking left or right, respectively. In parallel, we used calcium imaging to record from a population of layer 2/3 excitatory neurons in the auditory cortex during learning. Despite similar behavioral performance at the end of training, animals exhibited one of two distinct activity profiles in auditory cortex. Specifically, tuning profiles of excitatory neurons exhibited either a relative enhancement or a suppression of responses at the center frequency. We developed a computational model to explore whether animal-specific choice preferences seen during learning could explain this individual variability in neural tuning. We trained a model neural network using reward-dependent Hebbian learning to perform the task, and examined whether initial choice preferences (rates of licking right and left), and the resulting reward statistics, are related to the learned neural representations. We found that higher rates of reward in trials with non-center frequencies early in learning lead to larger magnitude responses to the center frequency, a relationship which was confirmed in the data. Overall, our results suggest that, through its effects on reward statistics and consequent synaptic plasticity, choice preference during early auditory perceptual learning may play a causal role in producing across-animal variability in learned representations.

2-031. Holographic activation of neural ensembles reveals both space and feature based cortical microcircuitry

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Recent experiments that stimulate a small number of excitatory neurons appear to offer conflicting results regard-

ing the role of recurrent circuitry in the mouse primary visual cortex. Marshel et al. (2019) found that stimulating 20 neurons could drive behavior, suggesting that this circuitry has strong amplifying qualities. However, Chettih and Harvey (2019) show that single-neuron perturbations drive network suppression and feature-specific competition. Here, we attempt to reconcile these results using multiphoton holographic optogenetics and mathematical modeling.

Specifically, we use spatially and temporally precise 3D-SHOT to drive ensembles of ten excitatory neurons in L2/3 of mouse primary visual cortex to spike a total of exactly one hundred times. We find that most ensembles reliably drive significant network suppression. However, we also observe that individual responding neurons may be excited or inhibited depending on their physical proximity to the stimulated ensemble. Furthermore, the selection of which cells make up a stimulated ensemble impacts the inhibition observed. Close together, co-tuned ensembles recruit more inhibition than far apart ensembles.

To explain these results, we create a spiking network model suited to mimicking this insertion of precisely one hundred spikes. While previous models are capable of producing a realistic salt-and-pepper orientation map through the interactions of their feedforward and recurrent connections when they have spatial connectivity rules [3], such models are unable to capture this transition of nearby excitation to nearby suppression observed experimentally. Through the use of a novel remapping algorithm, we add in feature-dependent wiring that maintains the salt-and-pepper map. This biologically-realistic network is able to recapitulate our results, and hence refine our understanding of the cortical microcircuit, reconciling the Hebbian ‘like-to-like’ connectivity, with smooth spatial rules. Further, the model calls attention to the previously undervalued trade-off occurring between the excitatory E->E and suppressive E->I->E recurrent pathways.

2-032. Development of orientation selective receptive fields via Hebbian plasticity

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Orientation selectivity is a key feature of primary visual cortex (V1). Orientation specific receptive fields (OSRFs) appear to arise from specific feedforward connectivity from lateral geniculate nucleus (LGN) to V1 cells. OSRF development has been hypothesized to arise from a competition between ON- and OFF-center LGN cells, if the difference between same-type and opposite-type correlation functions is a non-monotonic, “Mexican hat” function of cell-cell separation. However experiments found this difference decays monotonically. Many models have assumed “Mexican hat” recurrent connectivity (local excitation & lateral inhibition) to develop spatial variation of preferred orientation, but experiments suggest that excitatory projections are longer range than inhibitory.

We have found analytically that OSRFs will develop with a monotonic fall-off of both the correlation difference and intracortical connectivity, provided one or both are sufficiently long-range and homeostatic competition ensures the summed projection strength of each thalamic neuron is conserved. Implementing this in a network model of excitatory and inhibitory cells with plasticity driven by trial-by-trial activities, and a biologically plausible implementation of homeostatic normalisation of the feedforward weights, we find a robust development of OSRFs.

Recent experimental work showed that, within a local cortical region, RFs are anchored by (centered on) subfields of a single type (ON or OFF). We can reproduce this observation by increasing the variance of the anchoring input type. Furthermore the RFs generated in this way tend to match several experimentally measured RF properties.

We conclude that monotonically decaying input correlations together with a competition-based Hebbian plasticity rule and a cortical network layer without recurrent lateral inhibition is sufficient to lead to the emergence of OSRFs with experimentally realistic properties.

2-033. Clustered recurrent connectivity promotes the development of E/I co-tuning via synaptic plasticity

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Experimental studies have shown that cortical neurons often exhibit a co-tuning of their excitatory and inhibitory receptive fields (i.e. correlation of incoming E/I currents for different input signals). Such co-tuning is hypothesised to be important for efficient computations. Theoretical studies have examined how different plasticity mechanisms can create such co-tuning in feedforward settings, where distinct, uncorrelated inputs to a post-synaptic neuron allow the formation of matching excitatory and inhibitory receptive fields. Still, the cortex is characterized by high levels of recurrence which raises the question of the mechanism by which input-driven E/I co-tuning arises. We demonstrate that a possible mechanism of E/I co-tuning in recurrent settings is highly specific recurrent connectivity which produces the necessary statistics for detailed balance to emerge. We first verify that in feedforward networks a combination of triplet STDP on the excitatory synapses and symmetric homeostatic STDP on the inhibitory synapses utilizes inhomogeneities in the pre-synaptic firing rates to create tightly matching excitatory and inhibitory receptive fields. The addition of unstructured recurrent connectivity in the pre-synaptic layer can significantly hamper the ability of STDP to produce co-tuning. We use simulation based inference to uncover possible constraints on the topology of the recurrent connectivity that will allow matching receptive fields to emerge. We find that different levels of clustering within neuron groups can effectively control the statistics of the input the post-synaptic neuron receives and consequently the ability of the STDP to produce co-tuning. Specifically, clustered excitation and global inhibition is particularly beneficial to developing E/I co-tuning. Our results suggest that structured recurrent connectivity can boost information propagation and promote the development of input selectivity in higher brain areas.

2-034. Recurrent suppression in visual cortex explained by a balanced network with sparse synaptic connections

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To support perception, visual cortex transforms sensory-related input to create hierarchical representations. Local recurrent connections between nearby neurons can potentially exert large effects on these transformations, but it has been unclear how recurrent connections influence input-output transformations in the cortex.

Here we study recurrent influences in mouse V1 by experimentally stimulating excitatory neurons. To do this, we selectively express an excitatory opsin (stChrimsonR) in excitatory cells, and record activity using electrophysiology, 2-photon, and widefield calcium imaging. We then use simulations to determine which features of recurrent connectivity can explain the observations.

We find that strong visual stimuli suppress the activity of many neurons, resulting in a salt-and-pepper pattern of neurons with suppressed and elevated firing. Stimulating excitatory cells optogenetically produces a similar salt-and-pepper pattern of suppression. Cells with suppressed firing are distributed across the cortex, though there is a surround region a few hundred microns distant from the stimulation center, where suppressed neurons predominate over excited neurons. A balanced-state cortical model replicates observed firing rate distributions and dynamics – but only when variability in synaptic strengths is large, with sparse strong synapses and many weaker synapses. Thus, sparse, broadly-distributed synaptic connectivity is key to explaining how recurrent connectivity shapes cortical input-output functions.

2-035. Statistics of sub-threshold voltage dynamics in cortical networks

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Temporal irregularity and heterogeneities are key features of neuronal spiking activity in cortical networks. Simplified theoretical models of cortical circuits show that these features can be mechanistically accounted for if cortex operates in a fluctuation-driven regime (FDR). In FDR, excitatory and inhibitory currents are approximately balanced, and activity fluctuations emerge intrinsically from the non-linear network dynamics. However, it is still unclear if cortex operates in this regime. We address this question by analyzing sub-threshold membrane potential of neurons in sensory and frontal cortex recorded in decision-making tasks. Sub-threshold activity is highly heterogeneous across neurons in the same neuronal population. For example, the mean distance to spike threshold of the membrane potential varies substantially across neurons and different neuronal populations. The standard FDR framework accounts for the spiking statistics but fails to capture the heterogeneity in the sub-threshold activity, thus challenging the long-standing view that cortex operates in this regime. We extend the FDR framework by introducing a new phenomenological model of point neurons that mimics dendritic integration, with model parameters estimated from simulations of multicompartment neurons. A network consisting of such 'spatially extended-like' point neurons can account for both sub and supra-threshold statistics. Our model suggests that neurons in frontal cortex are approximately balanced and operate in the FDR. In contrast, excitatory neurons in Layer 4 of the barrel cortex are mean-driven: they are dominated by inhibition and spike in response to occasional synchronous input ('mean-driven'). Our work suggests that different populations in cortex can operate in different dynamical regimes. Cortical excitatory neurons closer to the periphery are mean-driven, firing due to strong and correlated external drive, whereas neurons in other populations hover closer to their thresholds, their currents are approximately balanced, and they are driven by input fluctuations.

2-036. Cortex-wide decision circuits are shaped by distinct classes of excitatory pyramidal neurons

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Understanding how cortical circuits generate complex behavior requires investigating the cell types that comprise them. Here, much effort has been focused on inhibitory neuron types but the functional roles of distinct classes of excitatory pyramidal neurons (PyNs) are less well understood. We, therefore, used widefield imaging to measure the cortex-wide activity of distinct PyN types and investigated their functional role in mice that performed an auditory decision-making task. We used two mouse lines, expressing the calcium indicator GCaMP6s in two major PyN types: FezF2 for pyramidal-tract (PT) and PlexinD1 for intratelencephalic (IT) neurons. Using dimensionality-reduction methods, we isolated cortex-wide activity patterns of PT and IT neurons and compared them to EMX mice with GCaMP6s-expression in all PyNs. We found major PyN-specific differences in complexity and spatial layout of cortical activity patterns, both at the local and mesoscale, suggesting the existence of specialized subcircuits. We also found PyN-specific functional differences during decision-making. Sensory responses were largest in sensory, parietal and frontal cortex but each PyN type showed pronounced differences in cortical localization and spatial specificity. The same was true for choice-related activity: A choice decoder revealed ramping, contralateral choice-selective activity in parts of frontal cortex of EMX and PT mice whereas IT mice showed ipsilateral choice signals. Using an inter-sectional viral strategy, we found that this inverse choice tuning in IT was most pronounced in corticostriatal projection (CStr) neurons. Lastly, we used optogenetic inhibition to causally test the importance of PyN-types for decision-making. Inactivating parietal cortex disrupted sensory processing, with the strongest effect in PT neurons. In frontal cortex all PyN-types reduced animal performance, suggesting that they are equally involved in choice formation and execution. Our work reveals PyN-specific, cortex-wide dynamics and strongly supports the view that local circuits throughout the cortex perform parallel computations, even within the same cortical layer.

2-037. Goal-directed processing flexibly controls the flow of interhemispheric tactile cues

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During behavior, cortical neurons are continuously integrating task-relevant information from the opposite hemisphere. While the importance of bilateral integration to behavior may appear obvious, its underlying neural mechanisms are almost entirely unknown. Naive models of processing often assume that bilateral integration only occurs at higher cortical levels, despite an abundance of interhemispheric (IH) circuits in the primary sensory cortices. However, the basic circuit logic by which the corpus callosum operates remains poorly understood. To reveal the logic of bilateral integration and to dissect the role of its diverse circuitry, we are combining a novel bilateral discrimination behavior with cell-type specific optogenetic silencing, bilateral electrophysiology, and statistical modeling. Initially, mice are trained to discriminate between homotopic (HM, matching) and heterotopic (HT, non-matching) bilateral cues. While mice perform the task, we record high-density electrophysiological activity across both primary somatosensory cortices (S1). We discovered that goal-directed processing flexibly controls the flow of tactile information to favor the reward conditioned bilateral cues. Contrary to expectations, we found interhemispheric facilitation to be the primary driver of the goal-directed bilateral percept. In naive (untrained) mice, S1 neurons were primarily suppressed by ipsilateral input, revealing a default suppressive mode of bilateral integration that is distinct from the goal-directed percepts. Greater synchrony between neurons in opposite hemispheres appears to be a primary mechanism for enhancing goal-directed stimuli. We hypothesize that bilateral synchrony preferentially activates downstream areas involved in action selection. Using latent variables derived from a population of S1 neurons, we show that the goal-directed representation of bilateral space is strongly modulated by behavioral performance. Ultimately, we reveal the contextual flexibility of IH circuits and the spatially-specific transfer of information between hemispheres.

2-038. Dynamics of interhemispheric prefrontal coordination underlying serial dependence in working memory

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Working memory (WM) content is mostly stored in neurons preferring contralateral cues in bilateral prefrontal cortex (PFC) [2], but can travel between hemispheres [3]. This is thought to support full-field spatial WM continuity. Recently, temporal continuity in WM has been linked to activity-silent mechanisms in PFC supporting behavioral serial dependence (SD) between successive trials [1]. Moreover, SD increases when prefrontal activity-silent traces of previous memories are reactivated in the fixation period by either internal or external (e.g. transcranial magnetic stimulation, TMS) inputs [1]. How memory traces and reactivations interact with anatomical lateralization to ensure both WM spatial and temporal continuity is currently unknown. Here, we asked if SD is lateralized and how its mechanisms are propagated between hemispheres. We tested the lateralization of SD using human and monkey behavioral responses and TMS experiments in humans, and we analyzed simultaneous bilateral PFC multiunit recordings in one monkey performing a spatial WM task to assess interhemispheric transfer of fixation-period reactivations. We found that SD for successive stimuli presented across hemifields was diminished compared to within-hemifield sequential stimuli. Furthermore, unilateral TMS in humans showed increased SD for fixation-period TMS pulses in the hemisphere when both stimuli were contralateral to the memorandum, but not for ipsilateral stimuli. This indicates that reactivations of memory traces are constrained to one hemisphere. We then tested the coordination of neural representations across hemispheres. Locations decoded from the

two hemispheres were strongly correlated during the delay but uncorrelated during reactivations, consistent with private reactivations of serial memory traces within each hemisphere. This shows an incomplete spatial continuity of SD in WM. Future computational work will gain understanding on how lateralized activity-silent mechanisms can give rise to this pattern of SD effects, and their implications for combined temporal and spatial continuity in WM.

2-039. Phase dependent maintenance of temporal order in biological and artificial recurrent neural networks

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Spike timing relative to theta phase has been shown to mediate spatial and non-spatial information processing in medial temporal lobe (MTL) regions including hippocampus [1,2,3]. A prominent theory suggests that neural activity at different phases of theta oscillations encodes the serial order of items within short-term memory [4]. Based on recordings of spiking activity and local field potentials (LFPs) of epilepsy patients performing a multi-item sequential memory task, we show phase-dependent spiking during the delay, with preferred phases that were related to stimulus position within the sequence. We also employ Recurrent Neural Network Models (RNNs) trained to perform an analogous task to study neural circuits underlying temporal order memory. Similar to our empirical data, we observe that RNNs contain highly stimulus selective neurons, develop network oscillations and also exhibit phase-dependent activity related to item position. Interestingly, for most units in both recordings and RNNs, the ordering of preferred phases did not reflect the serial order of previously shown items. Our study provides empirical support for spike-phase coding for temporal order memory in humans. Using RNNs, we find that qualitative similarities between neural recordings and network activity, including similar spike-phase dependence on position, emerge simply from task optimization. Thus, our approach provides a generative computational framework to investigate functional interactions between single unit activity and oscillations in neuronal networks in cognitive tasks.

2-040. Can time dependent and invariant decoders co-exist?

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Individual neurons exhibit a rich repertoire of complex dynamical patterns which vary at fast timescales [1]. Despite these fast temporal dynamics, neural circuits are able to maintain stimulus representations over the course of behaviorally relevant timescales that can subsequently be decoded by time-invariant downstream circuits to perform motor actions. Previous studies have proposed that these observations can co-exist due to neural redundancy. Specifically, these frameworks suggest that task relevant information is stably stored in a low dimensional subspace [2][3]. Moreover, time invariant decoders can decode stimulus identity even though neurons exhibit dynamic activity as previously shown in the population of prefrontal cortex neurons while animals perform working memory tasks [4]. We investigated the conditions where stimuli can be decoded by a fixed decoder during a trial when the underlying activity is varying by simulating various neural dynamics. We further probed the existence of an invariant stimulus representation in calcium imaging data collected from the gustatory cortex (GC) as mice performed a cued taste paradigm. GC has been extensively studied for its role in taste representation [5]. Due to the heterogeneous responses observed in the taste evoked mean activity of neurons [6], there has been an

implicit assumption of time varying coding in GC that requires downstream networks to have access to timing information during each trial [7][8][9]. Here, we fit a time varying as well as a fixed linear decoder after reducing the dimensionality of data using PCA or SemiNMF to decode taste identity. We find that we are able to stably decode the taste identity from the neural activity with a fixed decoder over the course of several seconds and the decoding performance is comparable to that of a time varying decoder. This suggests that there exists an invariant linear representation of taste in GC.

2-041. Top-down optimization recovers biological coding principles of single-neuron adaptation in RNNs

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Spike frequency adaptation (SFA) is a well studied physiological mechanism with established computational properties at the single-neuron level, including noise mitigating effects based on efficient coding principles. Network models with adaptive neurons have revealed advantages including modulation of total activity, supporting Bayesian inference, and allowing computations over distributed timescales. Such efforts are bottom-up, modeling adaptive mechanisms from physiology and analyzing their effects. How top-down environmental and functional pressures influence the specificity of adaptation remains largely unexplored. In this work, we use deep learning to uncover optimal adaptation strategies from scratch, in recurrent neural networks (RNNs) performing perceptual tasks. In our RNN, each neuron's activation function (AF) is taken from a parametrized family to allow modulation mimicking SFA. An additional RNN, the adaptation controller, is trained end-to-end to control an AF in real time, based on pre-activation inputs to a neuron. Crucially, each neuron in the network operates with a private copy of this controller, conceptually similar to genetically encoded SFA mechanisms. When trained on temporal perception tasks (sequential MNIST/CIFAR10), our network of adaptive recurrent units (ARU) shows much improved robustness to noise and changes in input statistics. Remarkably, we find that ARUs implement precise SFA mechanisms from biological neurons, including fractional input differentiation. This suggests that even in simplified models, environmental pressures and objective-based optimization are enough for sophisticated biological mechanisms to emerge. We further find that task statistics lead to distinct orders of fractional differentiation in ARUs, prompting experimental predictions that an animal's environment and behavior would selectively influence SFA tuning. While deep networks trained on perceptual tasks have been shown to predict tuning properties of single neurons (e.g. in the visual system) our result is the first, to our knowledge, to show that end-to-end optimization can recover dynamic coding mechanisms from the brain.

2-043. Emergence of convolutional structure in neural circuits

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Exploiting invariances in the inputs is crucial for constructing efficient representations and accurate predictions in neural circuits. In neuroscience, translation invariance is at the heart of models of the visual system, while convolutional neural networks designed to exploit translation invariance triggered the first wave of deep learning successes. While the hallmarks of convolutions, namely localised receptive fields that tile the input space, can be implemented with fully-connected neural networks, learning convolutions directly from inputs in a fully-connected network has so far proven elusive. Whether convolutions can be learnt from scratch has thus been a central problem in neuroscience and machine learning since the seminal work by Olshausen and Field (1996) on unsupervised learning. Here, we show how initially fully-connected neural networks solving a discrimination task can learn a convolutional structure directly from their inputs, resulting in localised, space-tiling receptive fields. By

carefully designing data models for the visual scene, we show that this phenomenon relies on the non-Gaussian, higher-order local structure of the inputs, which has long been recognized as the hallmark of natural images. We provide an analytical and numerical characterisation of receptive field formation, which results in an unexpected link with tensor decomposition of higher-order input correlations. The receptive fields learnt by the fully-connected networks match the filters found by training a convolutional network on the same task. These results provide a new perspective on the development of low-level feature detectors in various sensory modalities, and pave the way for the study of higher-level invariances in cortical processing.

2-044. Feedforward and feedback computations in V1 and V2 in a hierarchical Variational Autoencoder

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A venerable tradition in neuroscience seeks to understand sensory processing, and in particular vision, through unsupervised learning of natural statistics. Generative models have provided invaluable insights into the way neural response statistics of low level vision (including nonlinearities in response means, variability, oscillations) is shaped by probabilistic inference. However, progress has been hampered by the limited capabilities of generative models to learn both nonlinear and hierarchical representations of natural images. Here we harness the inspirations coming from neuroscience to develop a novel flavor of Variational Autoencoders, a class of models that is capable of performing learning and inference, of/in nonlinear generative models. Key to the proposed hierarchical generative model, TD-VAE (Top-Down Variational Autoencoder), is a formulation which builds on the top-down feedback connections between cortical processing stages. We show how inductive biases contribute to shaping the representations emerging in V1 and V2 of the visual cortex, including Gabor-like filters in V1 and texture selectivity in V2 when trained on natural image patches. The model reproduces a number of earlier experimental observations about the interdependence of the activities in V1 and V2. These include progressive compression of images along the hierarchy of the ventral stream, differential sensitivity of V1 and V2 mean responses to the manipulations of high-level statistics. Further, we use TD-VAE to demonstrate that effects that were implicated in top-down influences in V1, such as stimulus-statistics dependent noise correlations and illusory contours, are natural consequences of hierarchical probabilistic inference in TD-VAE. Our study provides a tool that can be used as a starting point for the explorations of the visual cortex through a nonlinear hierarchical generative model for natural images.

2-045. Similar reformatting of object manifolds across rat visual cortex and deep neural networks

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Two very successful solutions exist to the problem of vision: biological brains and convolutional neural networks (CNNs). Despite the inspiration of artificial architectures from their biological counterparts, the extent to which the two solutions are comparable remains unclear, with evidence pointing to both core similarities (e.g., hierarchical learning of feature detectors with increasingly complex tuning) and key differences (e.g., very different sensitivity to pixel-level noise). In our work, we present results that bridge these two worlds, showing that prominent information processing trends previously found in CNNs are also present in visual cortex and vice versa. We took inspiration from two recent studies – one showing that, along the layers of CNNs, the intrinsic dimension (ID) of data manifolds undergoes a sharp initial expansion, followed by a monotonic decrease (Ansuini et al; NeurIPS, 2019); and another one showing that, along the rat homologous of the ventral visual pathway, luminance and contrast information are progressively pruned away from cortical representations (Tafazoli et al, eLife, 2017). In our work, we re-analyzed the neuronal recordings of the latter study to measure the ID of object representations across rat ventral visual areas. Concurrently, we measured how the mutual information between stimulus luminos-

ity (or contrast) and units' activation varied along deep CNNs (AlexNet and VGG-16). We found that the trend of variation of the ID across rat visual cortex displayed the two distinct expansion-contraction phases previously observed in CNNs. In CNNs, we found that luminosity information monotonically decreased across layers, mirroring the increase in ID. Finally, measurements on contrast information revealed how training enhances such information in early CNN layers, while actively discards it afterwards, again in agreement with biological observations. Taken together, these findings suggest a similarly tight relationship between dimensionality expansion/reduction of object representations and reformatting of low-level visual information in CNNs and visual cortex.

2-046. Causal inference can explain hierarchical motion perception and is reflected in neural responses in MT

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Causal inference (CI) has recently been proposed as a universal computational motif in the brain [Shams & Beierholm 2020]. However, how CI is implemented by neural circuits, and its signatures in terms of single neuron responses, are still unclear. We have investigated this question in the context of complex motion processing. Motion perception deviates from retinal motion [Johansson 1973] a computation that can be understood in terms of hierarchical CI over which moving elements to integrate into coherent 'groups' vs segment into different ones [Gershman et al. 2016, Shivkumar et al. 2020]. Yet, most of our understanding of the neural basis of motion processing is in terms of retinal motion, delegating potential CI computations to downstream cortical areas [Rohe et al. 2015, 2019]. Our work makes two contributions: first, we present new psychophysical evidence for the hierarchical nature of this process using a display of hierarchically nested groups of moving dots. Second, we use the hierarchical CI model fit to psychophysical data to derive quantitative neural predictions for neurons representing the variables in our model. At each level, our model contains two types of variables: one that represents the retinal motion predicted by the larger surround, and one that represents the difference between the actual local motion and that predicted from the surround. The predicted neural responses show remarkable similarity to two classes of neurons found in area MT: neurons with suppressing and with reinforcing surrounds [Born & Bradley 2005]. Finally, we present new neurophysiological data from area MT in a macaque monkey where the velocity-dependent pattern of surround suppression of neural responses agreed with that predicted for the relative variable in our CI model. Our results show that signatures of CI are already present at the early stages of sensory processing, and suggest that they may be implemented by local computations.

2-047. Structure in motion: visual motion perception as online hierarchical inference

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Identifying the structure of motion relations in the environment is critical for navigation, tracking, prediction, and pursuit. Yet, little is known about the mental and neural computations that allow the visual system to infer this structure online from a volatile stream of visual information. We propose online hierarchical Bayesian inference as a principled solution for how the brain might solve this complex perceptual task. We derive an online Expectation-Maximization algorithm that continually updates an estimate of a visual scene's underlying structure while using this inferred structure to organize incoming noisy velocity observations into meaningful, stable percepts. We show that the algorithm explains human percepts qualitatively and quantitatively for a diverse set of stimuli, covering classical psychophysics experiments, ambiguous motion scenes, and illusory motion displays. For instance, it quantitatively explains experimental results of human motion structure classification with higher fidelity than a previous ideal observer-based model. Furthermore, we identify normative explanations for the origin of erroneous human perception in motion direction repulsion experiments and make testable predictions for new psychophysics experiments. Finally, the algorithm affords a neural network implementation which shares properties with motion-

sensitive middle temporal area (MT) and dorsal medial superior temporal area (MSTd) and motivates a novel class of neuroscientific experiments to reveal the neural representations of latent structure.

2-048. Learning static and motion cues to material by predicting moving surfaces

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Visually understanding the world requires us to interpret surface properties like shape, depth, and reflectance from retinal images—with little or no access to the ground truth about these properties from which to learn. Previous work showed that perception and misperception of surface reflectance in static images is well predicted by unsupervised learning in a feedforward PixelVAE network. Here we extend into the temporal domain, testing whether learning-by-prediction in a recurrent network discovers the properties of moving surfaces to which humans are sensitive. We rendered 10,000 close-up videos of objects moving with random trajectories, speed, illumination, and reflectance. We trained a four-layer recurrent “PredRNN” network to predict the pixels of the next frame in each video. The network could extrapolate up to ten frames beyond its input data with high quality. Investigating internal representations, we found that over time scenes became strongly clustered according to whether they depicted a matte or mirror-like surface. Material, shape, illumination, texture, and velocity could all be decoded from the network’s internal representations using linear classifiers, with accuracy peaking in different layers and time points for different properties. As well as this population-level information, we found strong selectivity in many individual units for specific properties (e.g. a preference for matte rather than mirrored surfaces). Both static and motion cues contribute to material perception in humans. To compare human and model sensitivity to each cue type, we created test videos depicting either static or moving reflective objects, or moving versions in which reflections were “stuck” to the surface. All had identical static material cues, but differed in motion cues. Model-predicted material agreed with human judgements (N=16) of the relative reflectance of stimuli. Results suggest predictive learning discovers human-relevant material cues, and provides a framework for understanding how brains learn rich scene representations without ground-truth world information.

2-049. Task-dependent contribution of higher-order statistics to natural texture processing

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During natural visual behavior, our visual system extracts multiple features from its inputs and uses them to solve different tasks. Each feature conveys relevant information to different tasks, and for a given task our visual system relies on the relevant features while ignoring others. However, this hypothesis remains largely untested for complex tasks with natural stimuli. Here we compare the role of spectral and higher-order (HOS) texture statistics of the Portilla-Simoncelli model across tasks using natural images, to explain their task-dependent use by humans. Portilla-Simoncelli HOS are important for human texture perception, peripheral vision, and physiology, but they play a much smaller role in texture segmentation. Modeling work suggests this could reflect the redundancy between HOS and spectral statistics (a strong segmentation cue in humans) for natural image segmentation. But the importance of HOS for texture perception suggests that these statistics may be informative for other texture-related tasks. In this work, we test the hypothesis that, in contrast to segmentation, HOS are superior to spectral statistics for natural texture classification. To test this, we trained linear classifiers to solve 4 different natural image classification tasks (classification of physical texture instances, materials, perceptual descriptions, and scenes) across 11 datasets, and compared the performance afforded by HOS and spectral statistics. We find that HOS improved task performance considerably over spectral statistics, unlike what was reported for segmentation. This is compatible with an account of the task-dependent use of these features by humans based on their task-dependent relevance in natural images. Interestingly, we find that the contribution of HOS varies between classification tasks, with larger improvements for instance classification. Future work should test whether the use of HOS by humans follows this finer pattern within classification, and explore the computational underpinnings of the varying HOS contributions.

2-050. Local low dimensionality is all you need

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The efficient coding hypothesis posits that sensory systems are adapted to the statistics of their inputs, capturing essential structure while minimizing the use of resources (neurons, spikes, etc). A variety of formulations have been developed and, differing primarily in their definition of efficiency. For example, Independent Components Analysis [Bell and Sejnowski, 1997] seeks a complete set of axes along which the data distribution is heavy-tailed. Sparse Coding [Olshausen and Field, 1996] learns a set of basis functions that can sparsely reconstruct natural image patches (i.e., using a small subset). And recent work generalizes this to local low dimensionality, by seeking a spatially adaptive set of axes (as opposed to a subset of a fixed basis) in which the data lie [Henaff et al., 2015]. For each of these, the efficiency objective by itself is insufficient – minimization leads to a trivial solution in which all inputs are mapped to zero – and this type of “representational collapse” is typically avoided by imposing a constraint that the signal can be reconstructed from the representation. While this has proven effective from an optimization perspective, there is little evidence to suggest that imagereconstruction occurs in biology, or that such complete information preservation is either necessary or desirable. Here, we develop a novel contrastive objective that avoids the need to reconstruct the input from the representation. Specifically, we minimize the dimensionality of encodings of spatially local image patches relative to their global dimensionality (measured across all image patches). We construct the objective as a continuous relaxation of the discrete dimensionality, allowing for gradient-based optimization, and plausible biological implementation. Although our method does not involve image reconstruction or any other proxy for mutual information between the signal and representation, it is able to generate a rich set of receptive fields that better capture the diversity of tuning properties found in V1 than either Sparse Coding or Independent Components Analysis.

2-051. Initialization choice leads to different solutions in trained RNNs

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Trained artificial neural networks have become essential models in neuroscience. However, the robustness of these models to – seemingly arbitrary – design or initialization choices is currently debated. Some studies reported universality, others variability between solutions found by training. One choice, the magnitude of output weights, has recently received a lot of attention in machine learning, as it induces two very different classes of solutions in feed-forward networks. How this parameter affects solutions in recurrent neural networks (RNNs) trained on neuroscience tasks is not well understood.

We first approached this question with an example: a cycling task inspired by recent experiments. We found two qualitatively different classes of solutions: For large output weights, the internal dynamics were mostly orthogonal to the output weight vector, or oblique. For small output weights, dynamics were instead aligned. Only the oblique solution shared key features with the experimental data.

We developed a theory to understand the different solutions. Our key result is that stability constraints allow for two classes of solutions, distinguished by the correlation between dynamics and output weights: oblique dynamics for large weights, aligned dynamics for small ones. Training RNNs across a variety of neuroscience tasks, we observed the two classes as predicted by our theory. Solutions often differed qualitatively between the classes, and also, for oblique solutions, within. Finally, the two classes differed from those in feed-forward networks, precisely because stability does not play a role there.

Beyond characterizing the effect of a model choice, our results give a new perspective on the relation between internal dynamics and output in the context of learning, and enable a better understanding of the ubiquitous observation of neural dynamics in orthogonal subspaces.

2-052. Beyond accuracy: robustness and generalization properties of biologically plausible learning rules

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Neuroscientists are increasingly turning to the mathematical framework of artificial neural networks (ANNs) training for insights into biological learning mechanisms. This has motivated an influx of biologically plausible learning rules that approximate backpropagation [1-9]. Despite achieving impressive performance quantified by accuracy, these studies have not covered the breadth of solution characteristics found by these rules. In this work, we leverage established theoretical tools from deep learning to investigate the robustness of solutions, and gain insights into generalization properties of biologically relevant learning ingredients. For complex tasks learned by overparameterized neural networks, there typically exists many solutions (loss minima in parameter space) that result in similar accuracy, but can differ drastically in generalization performance and robustness to perturbations. Theoretical work from machine learning establishes that the curvature of such minima matters: flat minima can yield better generalization [10-14]. Leveraging this theory, we ask: how do proposed biologically-motivated gradient approximations affect solution quality. In recurrent networks, we demonstrate that several state-of-the-art biologically plausible learning rules tend to approach high-curvature regions in synaptic weight space which leads to worse generalization properties, compared to their machine learning counterparts. We track loss landscape curvature, as measured by the loss' Hessian eigenspectrum, in numerical experiments, and verify that this curvature informs generalization performance. We derive analytical expressions explaining this phenomenon, which predicts numerical results showing that a large learning rate early in training, followed by gradual decay to avoid instabilities, can facilitate these rules to avoid or escape narrow minima. We discuss how such learning rate regulation could be implemented biologically via neuromodulation [15], and formulate experimental predictions for behaving animal experiments. To our knowledge, our analysis is the first to highlight and study this gap in solution quality between artificial and biological learning rules, thereby motivating further research into how the brain learns robust solutions.

2-053. Supervised learning and interpretation of plasticity rules in spiking neural networks

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Synaptic plasticity is known to be a key player in the brain's life-long learning abilities. However, due to experimental limitations, the nature of the local changes at individual synapses and their link with emerging network-level computations remain unclear. In theoretical work, synaptic plasticity is often modelled with unsupervised local plasticity rules. However, deriving a complete set of functional plasticity rules analytically will require divine intuition and numerous assumptions. Here, we approach the problem numerically. We show how to deduce plasticity rules in silico with supervised (meta-)learning of rules that act on large spiking neural networks solving complex tasks. We discuss how to parameterize, learn, and interpret plasticity rules. Using a rich search space encompassing most rules described in the literature, we employ an evolutionary strategy (CMA-ES) to recover rules that reliably solve the task in a biologically plausible way. We discuss the challenges in designing loss functions that combine performance and biological realism. Once candidate rules are obtained through this framework, we propose to interpret these high-dimensional rules by analyzing the covariance matrix learned along the optimization with CMA-ES. We show an example application of our approach applied to a memory formation and recall task, for which no robust and biologically plausible solutions are known to date. Preliminary analysis revealed that the learned rules used inhibitory plasticity both for stability and computation, and operated mainly via codependent

terms, corroborating recent theoretical work.

2-054. Adversarial learning of plasticity rules

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Understanding synaptic plasticity is critical for elucidating mechanisms for neural development, learning and memory consolidation. Synaptic plasticity is modelled by simulating the activity of interacting neural populations, using hypothesized functions (plasticity rules) that modify the connections between neurons. Plasticity rules are typically hand-crafted from single-synapse experiment data, but have shown limited success in understanding network-level properties.

Recent studies aim to discover rules using supervised learning rather than hand-crafting them. However, these approaches still require hand-crafted loss functions. We here propose to jointly learn the plasticity rule and the loss with an unsupervised approach using generative adversarial networks (GANs). We approximate the plasticity rule ('generator' in GAN parlance) and the loss ('discriminator') with deep neural networks. The inputs to the discriminator are recorded neuron activities and simulated activities from the biological network model with the generator-based plasticity rule. We train the generator and discriminator adversarially: minimizing a cross-entropy loss to train the generator; maximizing it to train the discriminator. At convergence, we expect the generator to have learnt a plasticity rule such that the biological network model produces activity resembling the observed data, and the two are indistinguishable to the discriminator.

We test our set-up on simulated data from a two-layer linear network updated using Oja's rule. We learn plasticity rules that generate qualitatively similar activities to ground-truth data. However, the learnt rules do not resemble Oja's rule. Hence, even in a simple model, a wide variety of update rules could potentially explain the same observed activity. This suggests that shifting focus away from individual plasticity rules to manifolds of rules eliciting similar network dynamics may lead to a better understanding of neural circuits and associated functions. Unsupervised data-driven methods to learn update rules may allow for a more extensive, robust exploration of synaptic plasticity mechanisms.

2-055. Revisiting the flexibility-stability dilemma in recurrent networks using a multiplicative plasticity rule

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Understanding the trade-off between plasticity and stability—how neural networks form new memories while avoiding runaway potentiation or fast overwriting of memories—is a fundamental problem in neuroscience. Previous theoretical studies that relied on non-plausible plasticity rules did not reproduce realistic synaptic weight distributions or neural activity statistics and predicted fast forgetting times. We revisit this problem by investigating the implications of a multiplicative calcium-based plasticity rule in a recurrent network. This rule was recently fitted to experiments done in physiological conditions, and is qualitatively different from classical STDP. We analytically approximate the full distribution of synaptic weight modifications as a function of pre- and postsynaptic firing rates, and temporal correlations. Using mean-field analysis and spiking network simulations, we show that the multiplicative plasticity rule, without fine-tuning, gives a stable, unimodal synaptic weight distribution characterized by a large fraction of strong synapses, as seen in experiments. The strong synapses within this distribution remain stable over long times but do not cause run-away dynamics in recurrent networks, consistent with previous electrophysiological and behavioral studies. Our results provide a mechanistic understanding of how stable learning and memory emerge on the behavioral level from an STDP rule measured in physiological conditions. Furthermore, the plasticity rule we investigate is mathematically equivalent to other learning rules which rely on the statistics of coincidences, so we expect that our formalism will be useful to study other learning processes.

2-056. Efficient inference of synaptic learning rule with Conditional Gaussian Method

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Modification of synaptic connections is thought to be the core mechanism of long-term memory formation. Despite the recent experimental development, there are still challenges inferring the synaptic plasticity rule from the experimental data. Here, we considered a biologically plausible synaptic plasticity model, and explored its key properties that enable efficient inference. As a recent theoretical work suggested the firing rates to be the most critical under in vivo-like conditions, we considered firing-rate dependent plasticity and its matrix representation. To enable efficient recovery under a low sampling ratio, we enforced the smoothness property of the plasticity rule and utilized a Bayesian approach, known as Gaussian process regression.

We first considered in-vitro experiments where the changes of synaptic weights can be measured directly for a few pairs of pre- and post-synaptic rates. We found that this Bayesian method outperforms alternative methods assuming low rankness of the matrix and smoothness utilizing polynomial or Fourier basis functions under variation of learning parameters that generate different plasticity rules. For in-vivo experiments where the direct measurement of synaptic weights is limited, inference of synaptic plasticity rule from changes of network activity with learning could be reformulated as a matrix completion problem with affine constraints. Compared to the previous work showing a partial inference from a single cell recording obtained in vivo, population recording and the Bayesian approach allow the inference of a complete learning rule. Our method performs stably under experimental restrictions such as input noise and missing synaptic connections. Also, we could generalize the method to the case when the change of post-synaptic activity reflects a mixture of different plasticity, such as excitatory and inhibitory plasticity. Overall, we introduced a non-parametric and model-agnostic method for efficient synaptic learning rule inference that can apply to both in-vitro and in-vivo experimental settings.

2-057. Bayesian synaptic plasticity is energy efficient

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Recent work (Aitchison et al. 2021) suggests that synaptic plasticity performs Bayesian inference and that, moreover, variability in synaptic efficacy might reflect uncertainty in the synaptic weight. Here, we consider whether similar phenomena emerge merely from minimizing synapse energetic costs during learning. Following established biophysical principles, we assume that noisy synaptic transmission is energetically cheaper than precise transmission. However, stochastic synapses may be detrimental to performance because noisy transmission adds randomness to a neural network's activity, and so may push the network's input-output function away from its optimum. We explored this dilemma using a combination of analysis of simple models and experiments in artificial neural networks. We found that optimizing a performance-energy trade-off results in low noise for "important" synapses, those for which reliable transmission is crucial to task performance; in contrast greater noise is afforded for less critical synapses. Interestingly, the resulting synaptic noise reflects parameter uncertainty. This implies that energy-efficient synapses should approximate Bayesian inference; we make this connection explicit. In addition, Aitchison et al. (2021) proposed that the learning rate should depend on the Bayesian posterior uncertainty, with more uncertainty leading to faster updates in light of new information. Remarkably, exactly the same phenomenon can be obtained without consideration of Bayesian inference, simply by maximizing performance under assumptions about how quickly the task changes. Jointly maximizing performance and energy efficiency leads to adaptive learning rates and synaptic noise levels, that are dependent on inferred uncertainty.

2-058. Turning spikes to space through plastic synaptic dynamics

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Neurons in the brain communicate through action potentials (spikes) that are transmitted through chemical synapses. Throughout the last decades, the question how networks of spiking neurons represent and process information has remained an important challenge. Some progress has resulted from a recent family of supervised learning rules (tempotron) for models of spiking neurons. However, these studies have viewed synaptic transmission as static and characterized synaptic efficacies as scalar quantities that change only on slow time scales of learning across trials but remain fixed on the fast time scales of information processing within a trial. By contrast, signal transduction at chemical synapses in the brain results from complex molecular interactions between multiple biochemical processes whose dynamics result in substantial short-term plasticity of most connections. Here we study the computational capabilities of spiking neurons whose synapses are dynamic and plastic, such that each individual synapse can learn its own dynamics. We derive tempotron learning rules for current based leaky-integrate-and-fire neurons with different types of dynamic synapses. Introducing ordinal synapses whose efficacies depend only on the order of input spikes, we establish an upper capacity bound for spiking neurons with dynamic synapses. We compare this bound to independent synapses, static synapses and to the well established phenomenological Tsodyks-Markram model. We show that synaptic dynamics in principle allow the storage capacity of spiking neurons to scale with the number of input spikes and that this increase in capacity can be traded for greater robustness to input noise, such as spike time jitter. Our work highlights the feasibility of a novel computational paradigm for spiking neural circuits with plastic synaptic dynamics: Rather than being determined by the fixed number of afferents, the dimensionality of a neuron's decision space can be scaled flexibly through the number of input spikes emitted by its input layer.

2-059. Rapid compressed sensing of synaptic circuitry enabled by holographic neural ensemble stimulation

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The ability to efficiently and reliably estimate the presence and magnitude of cortical synapses is critical to understanding how synaptic connectivity relates to neural computation, behaviour, and disease. Two-photon optogenetic stimulation paired with whole-cell electrophysiology allows for potential presynaptic partners to be tested for a given patched cell by measuring optogenetically evoked postsynaptic currents (PSCs). However, existing optogenetic mapping approaches fail to reach their potential for three critical reasons: (1) they rely on stimulating neurons one at a time, (2) they use prolonged interstimulus intervals to allow postsynaptic conditions to return to a baseline, and (3) they typically do not explicitly account for variability in photoactivation and synaptic transmission. Failing to account for such variability introduces systematic biases in connectivity estimates since postsynaptic responses may be incorrectly associated with cells that were stimulated but failed to spike.

Here we develop a high-throughput synaptic mapping system that simultaneously addresses each of these limitations. We combine 3D holographic optogenetics with a temporal demixing neural network and model-based compressed sensing algorithm for rapid learning of synaptic connections. Our holographic system simultaneously stimulates ensembles of neurons, thereby testing for many synaptic partners per trial. Our computational methods provide two key advances. First, our temporal demixing network allows us to stimulate in quick succession with minimal information loss, without having to wait for postsynaptic conditions to return to a baseline before stimulating the next ensemble. Second, our model-based compressed sensing algorithm provides highly scalable parallel inference of synapses while accounting for variability in photoactivation and synaptic transmission. We validate our methods on biological data using paired patch-clamp experiments that provide ground truth presy-

naptic spiking and postsynaptic responses. Together, our mapping system infers synaptic connectivity an order of magnitude faster than previously possible, enabling large-scale *in vivo* experiments where mapping time is highly constrained.

2-060. Real-time neural network denoising of 3D optogenetic connectivity maps

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Mapping the spatial patterns of synaptic connectivity is essential for understanding neural circuit function. Two-photon optogenetics combined with whole-cell patch clamp enable synaptic circuit mapping in mammalian cortex. We consider an experimental set-up in which the experimenter patches a single target cell and uses two-photon optogenetics to stimulate surrounding tissue in a 3-dimensional grid while measuring postsynaptic currents (PSCs). This yields a high resolution spatial map of putative synaptic connections to a single neuron. However, these connectivity maps are noisy due to biological variability and measurement noise. Typical image denoising methods ignore the probabilistic nature of upstream spikes and thus do not capture the full response distribution.

We propose a deep learning framework to overcome this limitation. Our method uses a single Convolutional Neural Network (CNN) to predict the distribution of PSC amplitudes at each stimulated location-power combination. We train the network using a large dataset of simulated experiments built from voxelized electron microscopy (EM) cell reconstructions, in which we have access to the ground truth cell locations, morphologies, and synaptic weights. Our network is trained to output a discretized representation of the response cumulative distribution function (CDF) at each voxel. The CDF, unlike the mean, describes both response reliability and putative connection strength. On data from mouse V1, we show that our method outputs more interpretable response maps than similar denoising methods. Unlike iterative methods, the proposed approach requires only a single forward pass through a neural network, meaning that it can be deployed in real time to guide experiments in progress and scales easily to large tissue samples. Our simulator includes a generative model of upstream spikes and is available as an open-source software library. These tools will allow experimenters to characterize the strength of synaptic connections across space at a level of granularity impossible with prior techniques.

2-062. Unsupervised representation learning of neuron morphologies

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The 3D morphology of cortical neurons is highly complex with widely varying shapes and has long been used to classify neurons into cell types. Classification based on morphology has classically been done by either laborious expert analysis through visual inspection or by computing a set of predefined features that could be quantitatively measured. Both approaches are prone to bias and subjectivity. The classification of neurons by experts was shown to have a high variance, and becomes infeasible with larger datasets. Similarly, the definition of fixed morphological features for classification introduces biases into the classification process by only taking a limited set of features into account. Large-scale datasets of 3D reconstructions have recently become available, enabling unsupervised machine learning methods. Here, we propose a method to learn relevant features from 3D neuron morphologies in a purely data-driven way. We represent neurons as graphs and use a contrastive learning objective similar to recent methods in computer vision to embed them in a latent space. By doing so, we learn a low dimensional representation of the morphology that captures the essence of the 3D shape and enables clustering into cell types. Our approach allows us to differentiate between spiny and aspiny neurons in the mouse visual cor-

tex and clusters the cells with regard to their cortical layer of origin. Furthermore, when clustering the excitatory neurons in latent space, clusters of different cell types emerge, such as L5 thick tufted pyramid cells and stellate cells. We compare our approach to clustering based on expert-defined features and show better predictability of our clusters as well as qualitatively more uniform clusters. Overall, our results suggest that unsupervised representations of 3D morphologies can be learned in a data-driven fashion and could potentially be used to discover novel neuronal cell types.

2-063. Wiring diagram of a central sensory projection revealed by dense Brainbow labeling

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Sensory features are encoded in topographically mapped neuronal populations in the brain. Their fine structure layout is not readily accessible due to their dense wiring and extended volume. To reveal their wiring logic, we combine genetic multicolor labeling of neural cells and large-volume micrometer scale imaging with color multiphoton microscopy. We present an analysis at single neuron resolution of the medial nucleus of the trapezoid body (MNTB), an essential relay for sound localization, which receives inputs from the cochlear nucleus (CN). Multicolor multiphoton microscopy allowed us to acquire continuous images encompassing all ~2500 MNTB neurons and CN-MNTB caliceal synapses. We traced a large portion of these afferent CN axons from their synaptic target toward their origin in the CN, and developed quantitative methods to extract various geometric properties along their trajectory. This analysis defined distinct axon domains and an abrupt transition from a collective, highly correlated and near-unidimensional trajectory to an uncorrelated, wiggly tridimensional layout. We also found that axons in the trapezoid tract were pre-ordered with respect to the arrangement of their synaptic terminals in the MNTB along the anteroposterior axis, unveiling the topographic structuration of the tract along this axis. Furthermore, single cell analysis revealed a subpopulation of caliceal axons that resists developmental synaptic elimination, resulting in convergent CN-MNTB inputs on a fraction of MNTB cells that are evenly distributed throughout most of the nucleus but form a high-density lateral hub. This raises the intriguing possibility that the MNTB may comprise distinct neuronal subpopulations encoding specific sound features or alternatively that convergence may enable to connect two unequal neuronal populations in a "no neuron left behind" model. This work provides a first single-cell resolved structure of a sensory axonal tract revealing axonal topography, trajectory and wiring patterns with individual axon precision over an entire functional area.

2-064. Parallel functional architectures within a single dendritic tree

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The input-output transformation of individual neurons is a key building block of neural circuit dynamics. While previous models of this transformation vary widely in their complexity, they all describe the underlying functional architecture as unitary, performing a single type of elementary computation, either once, or cascaded multiple times. Here, we show that the input-output transformation of CA1 pyramidal cells during phase precession in the ‘theta-state’ is instead best captured by two distinct functional architectures operating in parallel. We use statistically principled methods to fit flexible, yet interpretable cascade models of the transformation of the spatiotemporal patterns of input spikes into the somatic ‘output’ voltage, and to automatically select among alternative functional architectures. For this, we first extend previous methods that only included subunits with static nonlinearities by incorporating subunits expressing arbitrary nonlinear dynamics. Second, we develop methods to fit all the parameters of the model, including those parameterizing the dynamical nonlinearities, as well as the architecture of the model in a data-driven way, with minimal prior assumptions. We find that predicting the contribution of dendritic Na⁺ spikes (v_{Na}) and all other dendritic signals (v_{other}) to the output of the cell requires two, fundamentally distinct functional architectures. Specifically, while v_{other} can be accurately predicted using a single subunit with a static nonlinearity, precisely capturing v_{Na} requires several dendritic subunits equipped with nonlinear dynamics and connected into an architecture that appropriately reflects the clustering of synaptic inputs onto the dendritic tree. Moreover, automatic architecture-discovery reveals that the v_{other} -architecture reflects the somatic distance of synapses, while the v_{Na} -architecture reflects the clustering of synapses on the dendritic tree. The presence of two distinct, parallelized functional architectures within each individual neuron suggests potentially far-reaching consequences for our understanding of the dynamics of cortical circuits.

2-065. Synaptic diversity naturally arises from neural decoding of heterogeneous populations

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Synaptic inputs onto single cortical neurons exhibit substantial diversity in their sensory-driven activity. What this diversity reflects is unclear, and appears counter-productive in generating selective somatic responses to specific stimuli. We propose that synaptic diversity supports computations that most effectively use information from upstream populations. To test this idea, we directly compare *in silico* synaptic weights for probabilistic decoder with *in vivo* synaptic input measurements. We define a decoder for a single sensory variable, orientation, that reads out the stimulus orientation from the responses of a realistic, hypothetical input population of neurons. Decoder synaptic weight variability was higher when upstream input populations consisted of noisy, correlated, and heterogeneous neurons, as is typically found *in vivo*. In addition, *in silico* weight diversity was necessary to accurately decode orientation. We then provide a straightforward mapping from the decoder weights to real excitatory synapses and found the diversity of decoder weights well-matched the functional heterogeneity of dendritic spine orientation tuning *in vivo*. Our results indicate that synaptic weight diversity is a necessary component of information transmission and reframes studies of connectivity through the lens of probabilistic population codes. These results suggest that the mapping from synaptic input tuning to somatic selectivity may not be directly interpretable without considering input covariance and highlights the importance of population codes in pursuit of the cortical connectome.

2-066. Random compressed coding with neurons

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According to the efficient coding hypothesis, neural responses represent information so as to enable the most accurate readout possible, constrained by neuronal resources and neuronal noise. To date, much of the theoretical work on efficient neural coding has focused on relatively simple models of neural activity, characterized by smooth, often unimodal tuning curves. Real neurons, however, often exhibit more complex tuning curves. For instance, in the entorhinal cortex, the periodicity of grid cell tuning curves, as well as their functional organization in modules, imparts the population code with an exponentially large dynamic range, defined as the ratio between the range of represented stimuli and resolution. Recently, multiple other examples of neurons with complex, but unstructured tuning curves have been identified. These findings lead us to ask whether highly efficient neural codes require fine organization, as in grid cells, or whether they can be realized with more complex and irregular tuning curves. We approached this question with a benchmark model: a shallow neural network in which irregular tuning curves emerge due to random synaptic weights. The synapses project from a large population of sensory neurons with unimodal tuning curves in response to a one-dimensional stimulus onto a smaller neural population. A trade-off is observed between two qualitatively different types of readout errors: 'local' errors whereby two nearby stimuli are confused, and 'global' errors causing complete loss of information about the stimulus. When balancing the two error rates, we obtain an optimal solution in which a population code with irregular tuning curves achieves exponentially large dynamic range. We argue that compression balancing local and global errors takes place in the motor cortex, based on primate cortex recordings. Our results show that highly efficient codes do not require finely tuned response properties, and can emerge even in the presence of random synaptic connectivity.

2-067. Diverse covariates modulate neural variability: a widespread (sub)cortical phenomenon

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Neural responses are variable: even under identical experimental conditions, single neuron and population responses typically differ from trial to trial and across time. Recent work demonstrated that this variability can be modulated by specific stimulus features, most prominently quenched by stimulus onset. However, it is unknown how ubiquitous this effect is across stimulus features, and indeed whether it exists in brain areas to which classical neural coding approaches cannot be applied due to the lack of trials with repeatable experimental stimuli. To address these questions, we develop a universal probabilistic spike count model that builds on sparse Gaussian processes and can model arbitrary spike count distributions (SCDs) with flexible dependence on observed covariates. Without requiring repeatable trials, our method can flexibly capture covariate-dependent joint SCDs, and thus provide a characterisation of neural variability and its modulation by a set of covariates. We apply the model to recordings from four different cortical and subcortical areas, including non-sensory neural populations: V1 (both mouse and monkey), head direction cells in the anterodorsal thalamic nucleus (ADn), hippocampal place cells, and entorhinal grid cells. We find that variability across brain areas defies a simple parametric relationship with mean spike count as assumed in standard models, and its modulation by a diverse set of external covariates can be comparably strong to that of the mean firing rate. These results demonstrate that the modulation of variability is a widespread phenomenon across the brain, with a diverse set of covariates contributing to it.

2-068. Relating Divisive Normalization to Modulation of Correlated Variability in Primary Visual Cortex

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Correlated fluctuations of neural activity, termed noise correlations (NCs), are widespread in cortex and affected by sensory and non-sensory variables. Past work suggests that divisive normalization (DN), a cortical computation responsible for coordinating neural activity, could explain those modulations of neuronal covariability. However, quantifying the relation between DN and NCs remains challenging, as most successful descriptive models of neural variability do not account for DN. We propose a pairwise stochastic DN model that accounts for the effect of DN on covariability. In the model, the numerators (representing excitatory input drive) and denominators (normalization signals) of two neurons are correlated random variables. Therefore, the model partitions NCs into two main sources of correlated fluctuations. We show analytically and with simulations that the effects of DN on NCs depends qualitatively on whether normalization signals are correlated, highlighting the importance of understanding the sharing of normalization between neurons to fully understand DN's influences on covariability. By fitting the model to simulated pairwise responses, we study the regimes of parameter identifiability: importantly, the denominators' correlation parameter is best recovered when the numerators contribution to NCs is small. Furthermore, we find that the pairwise model can improve both predictive power and inference of single-trial normalization strength, relative to independent stochastic DN. Lastly, we demonstrate that the model fits accurately Ca²⁺ imaging data in mouse primary visual cortex (V1) and captures the modulation of NCs by contrast. Our descriptive model can be used to characterize NCs in neural data and quantitatively measure the modulation of NCs by stimulus and state variables. This will enable researchers to study mechanisms underlying DN, test predictions made by normative models about how the structure of population variability affects information coding, and quantify the effects of DN and neural variability on behavior.

2-069. Electrical but not optogenetic stimulation drives nonlinear contraction of neural states

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Substantial progress towards understanding neural computation has been made by studying the dynamical systems that govern neural population activity. Because dynamical models make predictions about the temporal evolution of neural states, perturbations of neural activity are a powerful tool to evaluate and refine these models. Here, using electrodes and Neuropixels in the motor cortices of macaques engaged in a reaching task, we probed how local population dynamics are affected by two perturbation modalities: optogenetic excitation and electrical intracortical microstimulation (ICMS).

Both stimulation modalities drove strong, transient changes in nearby neurons' firing rates, causing a large displacement of the neural state. To study the interaction of perturbation with task-related activity, we stimulated at one of multiple timepoints on randomly interleaved trials. We developed a latent variable model similar to GPFA, that incorporates an additive, low-rank perturbation term and a rectified-Poisson observation model. This approach revealed that optogenetic stimulation was adequately described as additive, simply translating the neural state. While neural activity during ICMS also contained this additive component, neural states across different reach conditions contracted together during stimulation. Strikingly, the amount of this stimulation-induced contraction correlated with the magnitude of the evoked displacement of hand velocity.

Our findings reveal a difference in engagement of cortical dynamics under optogenetic excitation and ICMS. While large additive transients dominate stimulation responses of both modalities, the additive transient alone was in-

sufficient to produce kinematic effects. We hypothesize that additive perturbations may produce strong behavioral effects when specifically targeted to the low-dimensional subspaces that govern population dynamics and behavior. Perturbations that engage neural dynamics nonlinearly—in this case, by contracting neural states—can readily impact population activity and behavior without special targeting approaches. Ultimately, combining perturbations with simultaneous observation of neural responses will yield new insights into the mechanisms of neural computation and inform effective therapeutic interventions.

2-070. Disrupting periodic neuronal synchrony with closed-loop stimulation in vitro

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Neurological disorders, such as Parkinson's disease, epilepsy and dystonia, are associated with excessive neuronal activity synchrony that overshadows normal brain activity. To disrupt these pathological occurrences, implantable brain stimulators apply electrical stimulation continuously, in an open-loop setting. However, stimulation should ideally be provided only when needed, guided by a closed-loop control system. Computational studies have focused on developing closed-loop stimulation protocols to counteract excessive neuronal synchronization. Delayed feedback control (DFC) is a method known to control chaotic systems and has been extensively explored to desynchronize neuronal networks in silico. Briefly, DFC theoretically disrupts synchronization by perturbing the system in its anti-phase periods using actuation signal intensity proportional to the synchrony level of the previous synchronous event. Despite its multiple applications in computational studies, there is still controversy in the literature regarding its efficacy, with reports suggesting that synchronization may actually be amplified under certain conditions. Here, we present the first implementation of DFC to disrupt periodic synchronization in biological neuronal networks. We used hippocampal neurons cultured on microelectrode arrays that, after several days in vitro, exhibit periodic synchronous bursts (periodicity in seconds range). We developed an algorithm to modulate the neuronal activity in real-time (latencies below 40 ms) using two different versions of DFC. We show that the version proposed in the literature cannot disrupt the synchronization cycle of dissociated networks in vitro but rather promotes a new oscillatory period. We present a new version of DFC - adaptive delayed feedback control (aDFC) - that automatically adapts to the changing oscillatory bursting activity, successfully disrupting it with precisely timed electrical stimuli. Our results show that the control outcome is dependent on the basal network dynamics. We support these results with in silico simulations where we compare the efficacy of non-adaptive DFC and aDFC to control networks displaying different temporal dynamics.

2-071. Hierarchy of brain oscillations emerges from recurrent error correction

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Neuronal processing in the brain occurs rhythmically across a set of discrete frequency bands, spanning over two orders of magnitude. The origin of these rhythms remains a matter of debate, as well as why activity appears to be organized in canonical bands. Here we demonstrate that the relative distribution of frequency bands emerges from the dynamics of recurrent neural networks (RNNs) performing error correction. These networks achieve best performance when processing pulsed inputs with noise levels proportional to those observed in cortical networks. In this optimal regime, the performance timescale is $T_0 \approx 2.16 * \tau$, where τ denotes the integration time constant for network nodes. A minimal timescale T_0 can be obtained for recurrent networks composed of individual neurons. Longer timescales T_n are sequentially derived when the outputs of individual RNNs become the nodes of a higher order recurrent network of their own, where $T_n = T_0 * (T_0/\tau)(n - 1)$. We show that this pattern of timescales reproduces the canonical oscillatory bands seen in neural data. The intrinsic timescale T_0

can be reduced by increasing the gain of individual nodes. This could allow neuromodulatory or attentional gain mechanisms to modulate the processing speed of salient signals. Successful error correction can be achieved in small networks with several neurons, with no substantial benefit of using larger networks. These results describe a mechanism through which the empirically observed discrete set of frequency bands can emerge through hierarchically organized RNNs.

2-072. How spiking neural networks can flexibly trade off performance and energy use

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Many engineered and biological systems must trade off performance and energy use, and the brain is no exception. Over long time-scales, evidence suggests that energy use is kept approximately stable by homeostatic firing-rate set-points, resulting in stable average performance levels. On shorter timescales, however, this stability can and should be deviated from, such as during attention when both neural activity and performance often increase (e.g., in predator situations, or when attending to small sensory details). It remains unclear how this fundamental performance-energy trade-off can be achieved in neural circuits of the brain. Here we show that any spiking network with linear readouts is subject to a trade-off between total spike count (energy use), and decoded signal error (performance). However, standard network models have no control over this trade-off as energy use varies, e.g., with input strength, and precision typically remains fixed. To remedy this, we first formulate a cost function which explicitly trades off performance and energy use on different neural and temporal scales. We then derive a spiking network model from this cost function, and show that it adaptively controls target activity levels. The network utilizes several known activity control mechanisms for this — threshold adaptation and feedback inhibition — and elucidates their potential function within neural circuits. Finally, using geometric intuition, we demonstrate how these mechanisms in turn regulate coding precision, and thereby performance. Overall, this work addresses a key energy-coding trade-off which is often overlooked in network studies, and unifies work on homeostatic set points, attentional signals, and inhibitory feedback.

2-073. Optimal Multimodal Integration Supports Course Control Under Uncertainty in Walking Drosophila

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Sensorimotor systems are inherently uncertain, either because of the physical nature of the sensory stimulus or because of noise within neural circuits. To curtail such limitations, sensorimotor systems combine information about the same event across different sensory sources to create robust internal representations for behavioral performance. Here we show that congruent multimodal self-movement signals are consistently found throughout populations of visual neurons, the lobula plate tangential cells (LPTCs). LPTCs monitor head and/or body rotations to support steering during locomotion1-3. We investigated the computational purpose of this congruent interaction by contrasting activity in LPTCs in walking flies with the predictions from Bayesian integration of independent inputs4. Under varying sensory reliability and in the presence of perturbations, we found that multimodal signals within LPTCs are compatible with the predicted weighting of unimodal signals based on their reliability. The precision of self-motion estimation by LPTCs faithfully follows the predicted precision from optimal integration of the unimodal inputs. Furthermore, we found a signature of normalization within the activity of these cells, a canonical computation generally considered to increase the regime for optimal operation of neurons. To examine the role of this optimal integration on behavior, we developed artificial agents following the behavior of an exploratory walking fly. Exploratory flies change their ability to walk straight as a function of the visual reliability of the environ-

ment. This relationship is mimicked by artificial agents employing the measured multimodal integration rules even under perturbation conditions. Altogether, our findings demonstrate that the LPTC network optimally combines multimodal information to infer self-motion robustly and support steering under natural uncertainty. Our results further open the possibility to mechanistically study the neural implementation of general computations such as Bayesian inference and normalization during a continuous and dynamically changing behavior in a compact and genetically tractable system.

2-074. Sensory tuning in neuronal movement commands

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Movement control is critical for successful interaction with our environment. However, movement does not occur in complete isolation of sensation, and this is particularly true of eye movements. Here, the superior colliculus (SC) plays a fundamental role, issuing saccade motor commands in the form of strong peri-movement bursts that are very widely believed to specify both saccade metrics (direction and amplitude) and kinematics (speed). However, practically all models of saccade control by the SC rely on observations with small light spots as saccade targets. Instead, we asked monkeys to “look” at images, akin to natural behavior. We tested gratings of different contrasts, spatial frequencies, and orientations; images of animate and inanimate objects; and black versus white stimuli. Despite matched saccade properties across trials within a given image manipulation, SC motor bursts were strongly different for different images. Such sensory tuning in the SC movement commands was even sharper than that in passive visual responses: the difference in movement burst strength between the most and least preferred image features (for the same saccade vector) was larger than that in visual bursts, consistent with known pre-saccadic enhancement of perception. Most intriguingly, even purely motor neurons exhibited strong sensory tuning in their saccade-related bursts. Since SC motor bursts are relayed virtually unchanged to the cortex (Sommer & Wurtz, 2004), one implication of our results is that the visual system is primed not only about the sizes and directions of upcoming saccades, as is traditionally believed, but also about the movement targets’ visual sensory properties. Consistent with this, we additionally found that saccade-target visual features significantly modulate two highly classic peri-saccadic perceptual phenomena: suppression and mislocalization. Our results provide novel insights about the functional role of SC motor commands, and they motivate extending theoretical accounts of corollary discharge beyond just spatial movement-related reference frames.

2-075. Movement and stimuli are differentially encoded in on- or off-manifold dimensions revealed by sleep

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Recent work has shown that spontaneous movements are represented throughout the brain, even in sensory areas such as primary visual cortex (V1). Interference between visual stimuli and movement is minimized in V1 because they are encoded in orthogonal subspaces, but it is not known how these subspaces are formed. Here, we report that Neuropixels recordings in mouse V1 during slow-wave sleep (SWS) reveal internally generated low-dimensional manifold structure that is mostly preserved in the awake state. However, the awake state has more variance in “off-manifold” dimensions, defined as those exhibiting less variance during SWS than expected by chance. Spontaneous movements are encoded in “on-manifold” dimensions, which during SWS account for more variance than chance and exhibit multi-region coordination strikingly similar to during movement. Surprisingly, we found that natural visual scenes are encoded in both on-manifold dimensions and off-manifold dimensions.

Off-manifold dimensions are underrepresented in spontaneous activity because they comprise sparse activation of neurons that are statistically unlikely to fire sparsely due to their strong coupling to the overall population. Internally-generated low-dimensional structure in V1 thus creates both a dense on-manifold subspace encoding movements and a sparse off-manifold subspace encoding stimulus features. These results reveal an unexpected link between dimensionality and sparse coding and also shed light on a simple yet overlooked mechanism by which brainwide representations of movement can coexist peacefully with local representations of task-related variables.

2-076. A control space for muscle state-dependent cortical influence during naturalistic motor behavior

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A prevailing view of the role motor cortex plays in movement execution is that it's limited to certain tasks, such as those involving novel muscle activation-patterns. Yet the relevant experimental support remains tenuous and the specific movement features that necessitate motor cortical involvement remain unclear. Classical studies often limited motor cortical function characterization to only a small number of qualitatively-defined movement types. Certain results suggest a broad motor cortical involvement in ensuring the smoothness/agility of many or all movements. Recent studies have raised the possibility that the involvement of motor cortical output may change as movements are repeatedly practiced, calling into question the generalization of findings from well-trained, stereotyped movements. To address this persistent ambiguity regarding motor cortical influence, we combined a new naturalistic climbing paradigm, rapid optogenetic silencing, forelimb electromyography, large-scale multielectrode array recording, and dimensionality-reduction-based analyses. To overcome the lack of trial structure during self-driven-climbing and achieve statistical power, muscle activity-states were embedded on a low-dimensional map via UMAP (Uniform Manifold Approximation and Projection). Rapid optogenetic silencing of the caudal forelimb area (CFA; forelimb M1) throughout climbing was used to characterize the direct influence of motor cortical output across these maps ('inactivation mapping'). Visualization of the map-regions showing significant CFA influence on each of four limb-muscles revealed that influence varied greatly across muscle-states. By aligning CFA neural activity with inactivation maps and developing methodology based on singular vector canonical correlation analysis (SVCCA), we found that neural activity within a low-dimensional subspace could almost perfectly predict inactivation effects. It thus appears that activity within this subspace steers climbing in a movement-specific manner. What emerges is a picture in which motor cortical output contributes to particular forms of muscle output that can be deployed throughout naturalistic movement, with influence on each muscle defined by activity variation within a low-dimensional subspace.

2-077. Stabilizing brain-computer interfaces through nonlinear manifold alignment with dynamics

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Intracortical brain-computer interfaces (iBCIs) can restore voluntary movement to people with paralysis by translating their brain activity into a control signal for an external device. Maintaining stable iBCI performance is chal-

lenging due to instabilities at the neural interface, such as shifts in electrode position in the brain or malfunctions of electrodes. Such instabilities result in a degradation of decoding performance, requiring that device use be interrupted to allow for the collection of recalibration data for the iBCI decoder. To address this challenge, an emerging class of methods leverages population-level latent manifold structure, thought to provide a more stable mapping between brain activity and behavior. In recent demonstrations, unsupervised manifold alignment achieved stable decoding performance without supervised recalibration. However, these methods do not incorporate dynamics models, which achieve higher initial iBCI decoding performance than models lacking dynamics. Thus, we developed a platform for nonlinear manifold alignment with dynamics (NoMAD) that stabilizes iBCI decoding. In NoMAD, manifold discovery is performed by latent factor analysis via dynamical systems (LFADS), a deep learning approach that uncovers dynamical structure underlying population activity. NoMAD combines LFADS with unsupervised distribution alignment to produce consistent manifold estimates that are robust to changes in the recorded neurons. We tested whether NoMAD could improve the stability of offline decoding from the motor cortex as a monkey performed an isometric wrist force task. NoMAD achieved stable, high-performance decoding of the monkey's exerted force throughout 20 sessions spanning over three months without supervised recalibration.

2-078. Multitask computation in recurrent networks utilizes shared dynamical motifs

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Flexible computation is a hallmark of intelligent behavior. Yet, little is known about how recurrently connected circuits contextually reconfigure for different computations. Neuronal activity is primarily studied during the performance of a single task due to difficulty of animal training. To investigate neural network flexibility for multiple computations, we trained recurrent neural networks (RNNs) to perform a set of sensori-motor and cognitive tasks. We examined networks through the lens of dynamical systems, where the evolution of population activity is dependent on activity in the previous timestep and on inputs to the system. Population activity was organized such that similar task computations operated in nearby parts of state space, sharing the same dynamical landscape. For example, a ring attractor was reused across tasks that required memory of the same circular variable input. We refer to shared point attractors, ring attractors and decision boundaries as dynamical motifs. Using fixed point analysis and analysis of population variance, we found that individual dynamical motifs were implemented by clusters of units. Cluster lesions resulted in modular effects on network performance: lesioning one dynamical motif had little to no effect on other dynamical motifs. These results are due to the orthogonal organization of motifs, which allows for compositionality. Finally, modular dynamical motifs could be reconfigured for fast transfer learning without catastrophic forgetting. After slow initial learning of dynamical motifs, a subsequent faster stage of learning reconfigures motifs to perform novel tasks. Overall, our work provides a framework to understand flexible computation in recurrently connected circuits. Our lesion studies make direct hypotheses that could be tested experimentally, and many of our analyses could be applied to neural population recordings. As more neuronal data is collected from multiple brain regions simultaneously and chronically, we hypothesize that modular dynamical motifs will provide a theoretical framework to understand these data.

2-079. Reduced dynamics - a tool for describing RNNs activity as a directed graph

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Dynamical systems are a contemporary and promising approach to model the computation carried out by neural populations. This perspective hypothesizes that certain dynamical features underlie the computations performed by the system, and characterizing them enables an intuitive understanding of the system. One central feature is the fixed (or slow) point: the fixed points of the system and the linearized dynamics around them can explain important aspects of the computation that is being performed. While successful in many cases, fixed-points analysis has limitations. Finding fixed points is generally hard, and requires knowledge of the full synaptic connectivity. Furthermore, many computations have a transient nature and might be subserved by other dynamical objects. Our goal in this work is to complement fixed-point analysis by providing a general tool for describing the computa-

tion performed by a dynamical system during a wide range of controlled tasks. This tool receives as inputs a set of neural trajectories from several trials and produces a directed graph that captures the essence of the calculation, which we call reduced dynamics. The process has two steps: identification of converging trajectories, and rule-based graph compression. In the first step, the algorithm identifies and merges converging trajectories. The second stage accepts a set of criteria from the user that compress the graph to remove redundant information. For instance, different trajectories that lead to the same output might be joined to reflect the final output of the network. A different setting could maintain the duration of these trajectories to allow visualization of delays in the dynamics. This stage is done via an iterative contraction of nodes using the chosen criteria. This tool provides an alternative way to explain task-related computations. Furthermore, the compact and graph-based representations can be used to compare networks one to another and thus allow clustering and other data analyses to be performed on sets of networks.

2-080. Gaussian Partial Information Decomposition: Quantifying Inter-area Interactions in High-Dimensional Neural Data

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A fundamental problem in neuroscience is to understand the different ways in which brain areas can interact to encode information. When two brain areas interact with a third, what fraction of the mutual information between the former and the latter can be attributed uniquely to each of the former? What fraction is redundant between them, and what fraction is synergistic? These “partial information” components quantify how different brain areas interact, which can help us understand the efficiency of various neural coding or communication schemes. Information-theoretic measures called partial information decompositions (PIDs) have previously been used to quantify partial information components. However, the practical application of PID methods has faced challenges: measures that capture uniqueness, redundancy and synergy precisely require a complex optimization, and do not scale to high-dimensional neural data, while measures that do scale are often less precise and tend to conflate two or more partial information terms. Here, we present the Gaussian Partial Information Decomposition (GPID): starting with a non-conflationary PID measure, we approximate it under a Gaussian parameterization. The parameterization exponentially reduces the space of the optimization, while the approximation makes it a convex problem—allowing for a more precise PID estimator that scales to high dimensions. We first validate GPID on simulated neural data, through comparisons with alternative estimators at lower dimensions, and observing intuitive trends at higher dimensions. We also apply GPID to high-dimensional spiking data from mouse visual cortex and thalamus recorded using Neuropixels probes, from the Allen Brain Observatory. GPID reveals differences in how cortico-thalamic regions share information, relative to cortico-cortical regions, and provides a new approach: using simulations, we can map different computational motifs to specific PID profiles. By comparing these to PID profiles estimated from data, we can formulate hypotheses about how different regions compute or communicate.

2-081. Towards hierarchical predictive coding with spiking neurons and dendritic errors

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Hierarchical predictive coding (hPC) is one of the major theories of sensory processing and cortical computation.

It provides a comprehensive explanation of the role of top-down connections in cortex, by proposing how they can guide sensory processing, and has inspired many experimental studies, ranging from electrophysiological studies of individual neurons to high-level studies of cognitive computation. Still, after twenty years of research, important questions remain open: Experimental evidence for error units, which are central to the theory, is inconclusive, and little theoretical work exists that demonstrates how hPC and learning can be implemented in biologically plausible neural circuits. At the same time, recent work showed how spiking neurons can very efficiently encode information, by relying on the principles of tight excitation-inhibition (EI) balance and plastic lateral inhibition. We propose to combine these two branches of research, and show that a functionally equivalent formulation of hPC is possible without error units, using an architecture that exploits a tight EI balance on neural dendrites. This interpretation of hPC naturally leads to a biologically plausible implementation of hPC with spiking neurons, and provides promising alternative explanations for existing empirical results on predictive coding, as well as cortical connectivity and dynamics. Most centrally, we propose a purpose for the localized voltage (and inhibition) dependence of synaptic plasticity, and we demonstrate how mismatch responses to unexpected optic flow arise in a model of V1 that only contains prediction neurons. Our results promote a theory of cortical computation, where errors are computed not in distinct neural populations, but in separate dendritic compartments.

2-082. Self-supervised learning in neocortical layers: how the present teaches the past

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In the canonical view of the neocortical microcircuit, first-order thalamic projections target layer 4 (L4), which in turn projects onto layer 2/3 (L2/3) pyramidal cells (PCs) and then finally onto layer 5 (L5) PCs. Although this is a motif found throughout the neocortex, the functional role of this architecture has remained unclear. Here, inspired by recent observations showing that first-order thalamic input also targets L5 pyramidal cells, we propose that the canonical microcircuit enables the brain to learn through temporal self-supervision. In our model, L2/3 PCs learn to predict thalamic inputs by comparing past sensory information originating from L4 with the current thalamic input received by L5 PCs. First, we tested our model in a simple sensorimotor task, in which visual flow must be associated with motor speed signals. Our model can successfully learn to predict visual flow through local L2/3-L5 self-supervised learning and visuomotor interactions through cortico-cortical learning. When halting the visual input after training, it generates prediction error signals with positive and negative error signals dominating L2/3 and L5, respectively, in line with recent experimental findings. Next, we used the prediction errors generated by L2/3-L5 interactions as intrinsic reward (i.e. surprise) to guide exploration in a reinforcement learning control task. Our results show that agents trained with this form of learning develop a diversity of task-relevant behaviours. Overall, our work proposes that the classical L4->L2/3->L5 motif underlies a form of self-supervised learning in the brain with important functional implications.

2-083. Multiscale encodings of memories in hippocampal and artificial networks

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The hippocampal subfield CA3 is thought to function as an autoassociative network that stores sensory information as memories. This information arrives via the entorhinal cortex (EC), which projects to CA3 directly as well as indirectly through the dentate gyrus (DG). DG sparsifies and decorrelates the information before also projecting to CA3. The computational purpose for receiving two encodings of the same sensory information has not been firmly established. We model CA3 as a Hopfield-like network that stores both sparse and dense encodings and retrieves them at high and low inhibitory tone, respectively. As more memories are stored, the dense, correlated encodings merge into clusters while the sparse, decorrelated encodings remain distinct. In this way, the model learns to transition between concept and example representations by controlling inhibitory tone. To experimentally test for the presence of these complementary encodings, we analyze the theta-modulated tuning

of phase-precessing place cells in rat CA3. In accordance with our model's prediction, these neurons exhibit sharper, more distinct spatial tuning during theta phases with sparser activity. Finally, we generalize the model beyond hippocampal architecture and find that feedforward neural networks trained in multitask learning benefit from a novel loss term that promotes hybrid encoding using correlated and decorrelated representations. Thus, the complementary encodings that we have found in CA3 can provide broad computational advantages for solving complex tasks.

2-084. A GABAergic plasticity mechanism for world structure inference by CA3

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The hippocampus reinstates learned sequences in temporally compressed "replay" epochs inside sharp-wave ripples (SWRs), which occur while an animal is at rest. Replay is required for the long-term consolidation of memories. However, the content of these replay episodes, and in particular whether specific experiences or a task-optimized representation of the world are consolidated, remains controversial. Using two-photon calcium imaging of CA3 outputs combined with simultaneous local field potential (LFP) recordings, our group has shown that the statistics of replay deviate significantly from those of experience: environmental features which are highly salient in experience may be either selected or suppressed in replay depending on their behavioral importance. We propose a parsimonious novel mechanism for this phenomenon: the reuse of the symmetric spike-time dependent plasticity rule (sSTDP), previously reported at CA3 excitatory synapses, to remodel inhibitory synapses as well. We show using three levels of modeling—spiking network, detailed biophysical, and abstract normative—that this mechanism enables efficient inference of the latent statistical structure of the world given noisy observations. We develop a mathematical theory of how sSTDP shapes sequence dynamics in a recurrent network, and prove that replay, viewed as a statistical estimator of a latent sequence, converges asymptotically to the true sequence. Finally, we make a number of predictions illustrating the power of inhibitory plasticity as a conceptual advance in our understanding of hippocampal dynamics and memory consolidation, foremost that CA3 replay consolidates "world structure" rather than specific experience. Our experimental and theoretical work here outlines a potential direct link between the synaptic and cognitive levels of memory consolidation.

2-085. Experience-Driven Rate Modulation is Reinstated During Hippocampal Replay

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Replay, the sequential reactivation of a neuronal ensemble, is thought to play a central role in the hippocampus during the consolidation of a recent experience into a long-term memory. Following a contextual change (e.g. entering a novel environment), hippocampal place cells typically modulate their in-field firing rate and shift the position of their place field, providing a rate and place representation for the behavioral episode, respectively. However, replay has been largely defined by only the latter- based on the fidelity of sequential activity across neighboring place fields. Here we show that dorsal CA1 place cells in rats can modulate their firing rate between the replay of two different contexts, mirroring the same pattern of rate modulation observed during behavior. This context-driven rate modulation within replay events was experience-dependent, observable during both behavioral episodes and throughout the subsequent rest period, but not prior to experience. Furthermore, we demonstrate that both the temporal order and firing rate of place cells can independently be used to decode contextual information within a replay event, revealing the existence of two separable but complementary neural representations

available for memory consolidation processes.

2-086. The anterior thalamus drives hippocampal replay following spatial learning

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During sleep, spontaneous neuronal activity in the spatial navigation system recapitulates previous wake experiences, and this phenomenon is instrumental for learning and memory. Specifically, in the hippocampus, place cell ensembles are spontaneously replayed in sequences corresponding to trajectories of the animal in previously visited environments¹. In parallel, head-direction cells of the anterodorsal thalamic nucleus which fire for a specific direction of the animal's head, remain coordinated during sleep. The HD signal is crucial for spatial navigation and the anterior thalamus is necessary for spatial memory, yet whether thalamic HD cells and hippocampal activity are coordinated during sleep and how much this coordination depends on learning remain unknown. To address this question, we recorded neuronal ensembles of HD cells and hippocampal place cells in freely moving mice performing a spatial memory task. Animals were trained on a forced alternation task on a Y-maze, during which they had only one path to take on each trial. On the day of the recording, after the forced choice task, the animal performed a free alternation task in which it was free to choose either one of the two arms and spontaneously alternated between them. Sleep was recorded before and after each task. HD cells fired systematically 50-100 ms before hippocampal neurons. We observed mild reactivation in the hippocampus in the two sleep sessions following the tasks, as expected in a highly familiar environment. HD cells showed no reactivation after the forced alternation but interestingly, showed strong reactivation after the free alternation task. Furthermore, HD and hippocampal ensembles reactivated together after the free alternation task. Hence, during sleep following exposure to a familiar context, the hippocampus potentially reactivates independently of other structures, and spatial learning recruits large scale thalamocortical networks upstream of the hippocampus. These findings shed a new light on the mechanisms of sleep-dependent learning.

2-087. Hippocampal Neocortical Coupling Varies as a Function of Depth of NREM Sleep

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During NREM sleep, the brain is in a self-organized regime in which alternations between spiking and near cessation of spiking propagate along the forebrain, termed slow oscillations (SOs) in the neocortex and SPW-Rs in the hippocampus. Both gain and loss of function studies have demonstrated the importance of tight temporal coordination between SOs and SPW-Rs for systems consolidation, and this temporal coupling has been observed across pairs of regions many synapses removed from one another. However, the spatial extent to which coupling between SPW-Rs and SOs occurs across regions at any one time is unknown, and is of great interest given the multi-modal nature of memories. Taking advantage of the spatial resolution of widefield calcium imaging and temporal resolution of extracellular recordings, we developed a novel chronic preparation in mice that allows simultaneous imaging of all of dorsal neocortex with high-density ipsilateral silicon probe recordings of the hippocampus and retrosplenial cortex, allowing us to monitor multi-scale interaction between regions during sleep. We find interaction between neocortex and hippocampus occurs in three phases, or a neocortical-hippocampal-neocortical loop, with topographic specificity. First, hippocampal SPW-Rs are preceded by increased fluorescence in mouse visual and association cortices, or mouse default mode network (DMN). The number of cortical regions active preceding the SPW-R predicts the magnitude of sharp wave associated with the ripple, which is thought to reflect the degree of input to the region. The greater the magnitude of input, the larger the amplitude of the evoked ripple, and the larger the DOWN state evoked in the DMN. This evoked DOWN state is most likely to occur in retrosplenial cortex, and the extent to which it propagates down the cortical hierarchy varies as a function of the depth of NREM.

2-088. Conjunctive theta- and ripple-frequency oscillations across hippocampal strata of foraging rats

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Brain rhythms have been postulated to play central roles in animal cognition. A prominently reported dichotomy of hippocampal rhythms exclusively assigns occurrences of theta-frequency (4–12 Hz) oscillations to exploratory behavior and rapid eye movement (REM) sleep, and of ripple-frequency (120–250 Hz) oscillations to wakeful rest and non-REM sleep. However, due to their differential expression across hippocampal strata, reports of such exclusivity demand validation through simultaneous multi-strata recordings. Here, we assessed co-occurrence of the two oscillations in multi-channel recordings of extracellular potentials across hippocampal strata from rats foraging an open-field arena. We detected all ripple events from an identified stratum pyramidale (SP) channel based on rigorous thresholds relating to the spectro-temporal and spatial characteristics of ripples. We then defined Θ epochs based on theta oscillations detected from each of the different channels spanning the SP to the stratum lacunosum moleculare (SLM) through the stratum radiatum (SR). Across rats, we found 10–20% of ripple events to co-occur with Θ epochs identified from SR/SLM channels, defined here as Θ -ripples. Strikingly, when Θ epochs were identified from the SP channel, there was no such co-occurrence, emphasizing that the reported behavioral dichotomy is merely a reflection of conclusions from single-channel recordings targeting the SP. We assessed the behavioral state of rats during ripple events and found a distribution of ripple kinds: e- Θ , i- Θ , e-Non Θ , and i-Non Θ (e/i: exploratory vs. immobile behavior; Θ /Non Θ : co-occurring theta oscillations detected vs. not detected in SR/SLM), with i-Non Θ ripples showing the highest detection frequency. Finally, we found a strong Θ -phase preference of Θ -ripples within the third quadrant [$3\pi/2^{\circ}$ – 2π]. Together, our analyses provide direct quantitative evidence for the occurrence of ripple events nested within Θ oscillations. Given the established roles of these oscillations, our analyses suggest concomitant encoding and consolidation processes during different behavioral states.

2-089. Comparable theta phase coding dynamics along the CA1 transverse axis

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Topographical projection patterns from the entorhinal cortex (EC) to the CA1 region of the hippocampus have led to a hypothesis that the proximal pole of CA1 (pCA1) is spatially more selective than the distal pole of CA1 (dCA1). While earlier studies (Henriksen et al., 2010; Oliva et al., 2016) have shown evidence supporting this hypothesis, a recent study (Deshmukh, 2021) showed that this difference does not hold true under all experimental conditions. In a complex environment with distinct local texture cues on a circular track and global visual cues, pCA1 and dCA1 display comparable spatial selectivity. Correlated with the spatial selectivity differences, the earlier studies also showed differences in theta phase coding dynamics (theta phase precession and theta modulation) between pCA1 and dCA1 neurons. In this study, we show that there are no differences in theta phase coding dynamics between neurons in these two regions under the experimental conditions where pCA1 and dCA1 neurons are equally spatially selective. We also show that dCA1 local field potentials (LFPs) show higher power in the theta range compared to pCA1 LFPs. These findings challenge the established notion of dCA1 being inherently less spatially selective and theta modulated than pCA1 and suggest that theta-mediated activation of the CA1 sub-networks to represent space is more task-dependent than being primarily driven by EC inputs. We are building leaky integrate-and-fire models to test if non-theta and non-spatially modulated inputs can contribute to the enhanced theta phase coding dynamics of a neuron that primarily receives spatially tuned excitation and theta oscillatory inhibition.

2-090. Acetylcholine in amygdala does not encode outcome uncertainty

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Animals must continually assess their uncertainty about their environment and future events in order to drive choice behavior and learning. Because uncertainty is a key decision variable for myriad behaviors (e.g. curiosity, attention), neuromodulatory systems, which engage and regulate diverse brain regions and brain states, are ideally suited to subserve uncertainty-guided modulation of local brain computations. Theoretical studies have hypothesized that the neuromodulator acetylcholine is responsible for encoding “expected uncertainty” in the brain (i.e., learned unreliability of predictive cues) (Yu & Dayan, 2005), but direct experimental evidence is scarce. To address this, we used a recently developed acetylcholine sensor (Jing et al., 2020) to monitor acetylcholine release in the basolateral amygdala during behavior. To study outcome uncertainty, we trained mice to associate 3 different odors with distinct probabilistic outcomes, each odor being assigned a 75, 50 or 25% reward probability. Hence, whereas the value associated with each odor increased with the reward probability, the uncertainty was maximum for the odor with a 50% chance of reward. Initially, reward delivery triggered acetylcholine release. After training, as previously reported, reward-related acetylcholine transients were greatly diminished (Sturgill et al., 2020). Further, acetylcholine release was rapidly triggered by the presentation of predictive cues. Remarkably, these cue responses increased with cue value but not uncertainty. The cholinergic sensor also revealed rapid responses, reminiscent of quantal release. To quantify these transients, we developed an event detection algorithm enabling us to assess the latency and amplitude of cholinergic release events across learning. We found that high-value cues elicited lower latency and larger magnitude acetylcholine transients compared to low-value cues. Neither of these metrics scaled with uncertainty during or after cue presentation. Our data supports the idea that acetylcholine release scales with reward prediction rather than uncertainty as previously hypothesized in theoretical models of reinforcement learning.

2-091. Universality of modular correlated networks across the developing neocortex

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Columnar organization is the hallmark of mature visual cortex in primates and carnivores, and is often assumed to be unique to those areas. Such an organization is already evident in the developing visual cortex (V1) well before eye-opening, where correlated modular spontaneous activity predicts future sensory-evoked representations. The multiple computational models proposed to account for this modular activity suggest several biologically plausible regimes which can produce modular activity and long-range correlations. Notably, these potential mechanisms are highly unlikely to be specific in early development to primary visual cortex, raising the question of whether modular and correlated networks exist beyond V1. Here we demonstrate that highly organized, modular, and well correlated network structure is a universal feature of the early developing cortex in a species with a columnar V1. Using a combination of wide-field and multi-photon calcium imaging of spontaneous activity in the ferret prior to eye-opening, we find that both primary sensory cortices (V1, auditory [A1], and somatosensory [S1]) as well as association cortices (prefrontal [PFC] and posterior parietal [PPC]), all exhibit similar modular patterns of low dimensional neural activity with robust correlations across millimeters. Moreover, we find that while both the degree of modularity and the strength of long-range correlations declines with age, spontaneous activity remains predominantly modular at the cellular level across areas. Notably, activity becomes increasingly sparse and higher

dimensional, suggesting an improved representational capacity with increasing maturity. Furthermore, similar to published reports in V1, sensory evoked activity in A1 exhibits strongly modular responses with significant statistical similarity to spontaneous activity, suggesting that early spontaneous networks seed developing cortical representations in sensory areas and raising the possibility of a similar relationship in higher association areas such as PFC. Together, our findings suggest that the diverse representations found across neocortex may arise from a common developmental origin.

2-092. Environmental Statistics of Temporally Ordered Stimuli Modify Activity in the Primary Visual Cortex

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Neural representations of statistical probability and uncertainty are critical for brain function and behavior (Ma and Jazayeri 2014), and it is particularly important that the brain learn temporal relationships since they can infer causation and allow predictions about future events. Influential models assume this information is available in the brain, but many details are speculative and direct evidence remains elusive. Multiple labs (Bear, Berry, Buonomano, Buschman, Carandini, Fiser, Gavornik, Hawkins, Keller, Mrsic-Flogel, Hussain Shuler, Shouval) have demonstrated that primary visual cortex (V1) circuits are capable of reporting and predicting temporal relationships, though the degree to which statistical predictability in the environment shapes these responses is unclear. To address this issue we recorded visually-evoked activity in mouse V1 during exposure to sequences of visual stimuli presented with specific transition probabilities. Using local field potentials in layer 4 and two-photon calcium imaging in layer 2/3, we found that unexpected transitions drive prediction-error (PE) responses coding for stimulus identity and event likelihood conditioned on the recent past. We describe the speed at which PEs emerge within V1 and show that PEs, reflected in firing rates and population size, scale with the degree of uncertainty and over a wide range of probabilities. The findings demonstrate that cortical circuits rapidly encode information similar to a Bayesian prior, and may be useful for guiding the development and refinement of predictive coding theories by describing how neural activity adapts to reflect specific elements of observed statistics in the environment.

2-093. State Prediction in Primary Olfactory Cortex

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Activity in primary sensory areas is robustly driven by signals from their respective sensory inputs. However, both theory and experiment suggest that the same cortices are modulated by context-dependent internally generated activity. Predictive coding theories propose that generative models formed through learning modulate primary sensory responses on a moment-to-moment basis according to how well incoming signals conform to the animal's predictions. Experimental data has shown that prediction errors can alter neural responses, even in the absence of behavioral relevance. Yet several aspects of how sensory expectation is expressed in primary sensory areas remain unclear. A fundamental question is whether sensory predictions only modulate responses to incoming sensory signals, or if they also reactivate responses based on mnemonic context. Hippocampal populations express past and future events through pre- and replay events, but we are unaware of any work showing such 'phantasmal' representations in primary sensory areas. To address this, we chronically recorded neural populations in the primary olfactory cortex during presentation of odor pairs without reinforcement. 12 odors were systematically paired to establish stimulus-specific sensory predictions. In 1/6th of the trials, the second odor was either presented alone (unpredicted) or omitted. We observed changes in the correlation structure and decodability of the odor responses during learning. Surprisingly, we observed that phantasmal representation—the ability to decode an odor in absence of actual odor stimuli—developed after just one session for the predicted odor on omission trials. Further, predicted second odor responses were decodable in the population preceding the odor onset. While the source of the mnemonic information—local or from higher areas—is unknown, this data

strongly suggests that it provides a complete prediction of the sensory response, as proposed by the theory of predictive coding or in the form of a prior as proposed by Bayesian models.

2-094. Shared representational features in *Drosophila* olfactory centers

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The peripheral olfactory system analyses odorants through a large number of genetically defined information channels in the antennal lobe (AL), each associated to an olfactory receptor (OR) type. In *Drosophila*, these channels are combined in two major downstream areas - the mushroom body (MB) and lateral horn (LH). These areas are thought to support different aspects of olfactory information processing: the MB supports ongoing learning, while the LH mediates innate behavioral responses. Here, we provide a geometric analysis of representations in these different areas. We model odorant representations in each area by projecting affinity patterns for a panel of odorants onto the spaces spanned by LH and MB connectivity matrices. To compare these representations, we first perform an analysis of the intrinsic and shared dimensionalities between the two areas, using a novel method for measuring the shared dimensionality between two datasets based on a generalization of the participation ratio. We show that structure in MB is consistent with nearly random connectivity, as expected for an associative learning center, and that the LH displayed detailed structure shaping on odor representations. We also find that the structure contained in the MB overlaps with structure in the LH, suggesting some role for shared representations between MB and LH. For example, MB may also play a role in mediating innate behaviors. We then perform a clique topology analysis to understand the geometry of both representations. Our results indicate similar geometry in both areas, i.e. three-dimensional hyperbolic. Zhou et al. (2018) arrived at a similar result using perceptual data; our work suggests that this structure may also be present in the fly and may emerge as early as the LH and MB. Altogether, our results are in line with previous experimental results on the structure and function of representations in both olfactory areas.

2-095. High-level prediction signals cascade through the macaque face-processing hierarchy

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We live in highly structured environments where patterns often repeat. Our brain forms internal models of the world by extracting the regularities. Such models are utilised to form predictions about future events and incoming information. Predictions lead to efficient neural processing of incoming stimuli and hence facilitate perception. Although the existence of prediction signals is known, much less is known about the neural mechanisms underlying the propagation of prediction signals, especially in higher-vision. Predictive processing theories propose that in cortical hierarchies, high-level prediction signals are sent to lower regions via feedback pathways, where they are compared against its input to compute a prediction error. In this study we investigate neural mechanisms underlying communication of sensory predictions using functional neuroimaging. To this end, we leverage the macaque face-processing network, a three-level hierarchical system in the ventral-visual pathway where face representation becomes more view-invariant as information goes up the hierarchy. We test the role of feedback pathways in sending predictions by investigating how expectations affect neural representations. We hypothesized that expectations lead to higher-order area sending predictions, such that the lower-areas inherit the tuning properties of the areas from which they receive feedback. By conducting representational similarity analyses, we show that after statistical learning of arbitrary face-pair sequences, expectations lead to view-invariant representations in lower face-areas. Rather than their own view-specific feedforward tuning properties, these lower areas now exhibit view-invariant abstract representations of higher face-areas. This cascading-down of high-level prediction signals in the entire face-processing network suggests a functional role of feedback connections in signaling predictions, which is in-line with predictive processing theories. By showing how the top-down information flow of predictions and previous experience affects face-processing, this work contributes to a revision of currently dominant theories

that view face perception and generally, object recognition through the lens of pure feedforward architectures.

2-096. Neural network mechanisms underlying post-decision biases

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Perception is influenced by past choices. In combined discrimination-estimation experiments a categorical choice leads to two biases: (i) a choice-dependent confirmation bias in the continuous estimate of the stimulus average, and (ii) an overall decrease in the sensitivity to subsequent sensory evidence. It remains unknown what neural mechanisms give rise to these post-decision biases and whether continuous estimates and categorical choices are computed in a common cortical circuit. Here, we develop a neural network model that addresses these questions. We study the integration of continuous sensory evidence in a bump attractor network. We find that modulating the amplitude of the bump (by changing the global excitatory input to the network) leads to qualitatively distinct temporal integration regimes (early, uniform and late temporal weighting). We embed this integration circuit in a hierarchical three-area network such that it receives stimulus information through a low-level sensory circuit and sends integrated stimulus evidence to a top-level decision circuit. Both the categorical choice as well as the stimulus estimate rely on the accumulated evidence in the integration circuit. To model post-decision biases, we include top-down feedback signals from the decision circuit. The feedback to the integration circuit is non-specific and reduces the sensitivity to subsequent stimuli by increasing the bump amplitude as described above. The feedback to the sensory circuit is selective, like feature-based attention, and gives rise to a confirmation bias through a choice-dependent modulation of the sensory inputs. Our network model provides a comprehensive and experimentally testable computational framework to study the neural mechanisms underlying stimulus estimation and perceptual categorization and their interaction.

2-097. The interplay between prediction and integration processes in human perception

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According to the Accumulation of Evidence (AE) framework, reliable perceptual decisions are forged by integrating the evidence provided by each sensory sample independently of other samples. However, that framework, grounded on the mathematical formulation of the Sequential Ratio Probability Test (SPRT), does not consider that sensory samples can be conditionally dependent (i.e. partially redundant). Partial redundancies are ubiquitous in naturalistic environments. In such case, the normative framework is what we call the Accumulation of Unpredicted Evidence (AUE). In AUE, the current belief is updated with the part of the stimulus evidence not predicted by previous samples (unpredicted evidence) and not the raw stimulus evidence. We tested the AUE model in an auditory accumulation reaction-time task in humans where we introduced sequential correlations between pairs of successive tones within each stimulus sequence. The AE model predicts that first and second tones in a pair (unpredictable and predictable tones, UT and PT) should have equal impact on perception. By contrast, in AUE, PTs impact on current belief is smaller, because part of PT evidence can be predicted from the previous tone. Participants reaction time distributions revealed that the decision threshold was more frequently reached after an UT rather than PT presentation, in agreement with AUE. Moreover, a late central positivity EEG signal, previously associated with evidence integration, showed a much stronger response to evidence in UTs than in PTs, a clear indication that the brain accumulates Unpredicted Evidence. On the other hand, an earlier component corresponding to the Mismatch Negativity (MMN) encoded the sensory surprise associated with each tone, irrespective of its behavioral relevance. Overall, participants' behaviour and neural activations confirm that human perception relies on the accumulation of unpredicted evidence, where predictive processes interact with classical temporal integration. This shows that the brain tracks complex statistical regularities to guide behavior.

2-098. Tracking human skill learning with a hierarchical Bayesian sequence model

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Perceptuo-motor sequences that underlie our everyday skills from walking to language have higher-order dependencies such that the statistics of one sequence element depend on a variably deep window of past elements. We used a non-parametric, hierarchical, forgetful, Bayesian sequence model to characterize the multi-day evolution of human participants' implicit representation of a serial reaction time task sequence with higher-order dependencies. The model updates trial-by-trial, and seamlessly combines predictive information from shorter and longer windows onto past events, weighting the windows proportionally to their predictive power. We fitted the model to participants' response times (RTs), assuming that faster responses reflected more certain predictions of the upcoming elements. Already in the first session, the model fit showed that participants had begun to rely on two previous elements (i.e., trigrams) for prediction, thereby successfully adapting to the higher-order task structure. However, at this early stage, local histories influenced their responses, correctly captured by forgetting in the model. With training, forgetting of trigrams was reduced, so that RTs were more robust to local statistical fluctuations – evidence of skilled performance. However, error responses still reflected forgetting-induced volatility of the internal model. By the last training session, a subset of participants shifted their prior further to consider a context even deeper than just two previous elements. Our model was able to predict the degree to which individuals enriched their internal model to represent dependencies of increasing orders.

2-099. Dynamic and structured action bias masks learned task contingencies early in learning

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Learning is not only the acquisition of knowledge, but also the ability to express that knowledge when needed. Previous work using non-reinforced probe trials showed that animals exhibit complete acquisition of stimulus-action associations far before they express them under reinforcement. Why do animals exhibit this gap in performance between acquisition and expression despite already acquiring the stimulus-action associations? Early in learning, animals may (1) exhibit motor biases that they slowly learn to suppress, (2) continue to explore different choice alternatives, or (3) base decisions on recent trial history, including choice and reward, rather than current stimuli. To test between these and other potential drivers, we trained mice on a balanced, two-alternative forced choice auditory task. During probe trials, animals exhibited surprisingly high accuracy early in learning even when performance in reinforced trials was near chance levels. In addition, animals exhibited less directional biases in choices during probe comparing to reinforced trials early in learning. We investigated the nature of this directional bias further using a generalized linear model to separate the influence of action bias and trial history. The full model fit individual learning curves well; action bias, but not trial history, emerged as the most important contributor. Removing both factors from the model 'rescued' behavioral performance and bridged the gap between reinforced and probe trials. The action bias itself was itself dynamic – animals would execute blocks of right or left choices with rapid transitions between the two, reflecting a potential sampling strategy rather than a motor bias. Choices during biased blocks were also faster and less deliberative. Together, our results suggest that behavioral expression reflects a potential exploratory process unique to individual animals that is uncoupled from the acquisition of the core task knowledge.

2-100. Selection from working memory can lead to catastrophic misbinding errors

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When making decisions in a cluttered world, humans and other animals often have to hold multiple items in memory at once – for instance, remembering the different items on a shopping list. Interestingly, psychophysical experiments in humans and other animals have shown that sometimes the remembered stimuli become confused; that is, instead of reporting a stimulus that was actually present, the participant will occasionally report a chimeric stimulus, composed of feature values that were present but bound together in combinations that were not (e.g., setting out to buy a green apple and red pear, but ending up with a red apple and green pear). These errors are referred to as swap, or misbinding, errors – and while they have been described behaviorally, their neural mechanisms are, to our knowledge, unknown. We show how these swap errors manifest in neural activity from both posterior and frontal brain regions while monkeys perform a multi-stimulus working memory task. In the task, the monkeys must remember the color and location of two stimuli. After a delay, a learned cue indicates which location held the target color. After a second delay, the animal reports the target color on a continuous color wheel. We use a behavioral model to infer the likelihood that each response is a swap error, and combine this with a model of the neural activity that reflects different hypotheses about how representations change during swap errors relative to correct responses. Surprisingly, we find that swap errors are associated with a misbinding of color to location during the selection process, rather than with a misinterpretation of the cue, or an error encoding the stimuli. More broadly, these results suggest that selection from working memory may be key source of catastrophic behavioral errors, indicating a potentially fruitful focus for future research.

2-101. One-shot learning of paired associations by a reservoir computing model with Hebbian plasticity

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One-shot learning can be achieved by animals and algorithms, but how animals do it is poorly understood as most of the algorithms are not biologically plausible. Experiments studying one-shot learning in rodents have shown that after initial gradual learning of associations between cues and locations, new associations can be learned with just a single exposure to each new cue-location pair. Foster, Morris and Dayan (2000) developed a neuro-symbolic actor-critic and coordinate learning agent that exhibited one-shot learning to displaced single locations in an open field maze using dead reckoning. While the temporal difference rule for learning the agent's coordinates was biologically plausible, the agent's memory mechanism for learning target coordinates was not, nor did they address one-shot learning of multiple cue-location pairs that rodents are also capable of (Tse et al., 2007). Here we extend the biological plausibility of that agent by replacing the symbolic memory mechanism with a reservoir of recurrently connected neurons resembling cortical microcircuitry. Biologically plausible learning of goal coordinates was achieved by subjecting the reservoir's output weights to synaptic plasticity governed by a novel 4-factor variant of the exploratory Hebbian (EH) rule gated by reward. The agent's current coordinates and goal coordinates were passed to a pretrained neural network that performed vector subtraction and selected the direction of movement towards the target. Our fully neural agent trained by Hebbian plasticity combines functions thought to involve the hippocampus and prefrontal cortex such that the memory system can store in one shot goal coordinates that can be recalled when a relevant cue is presented, while the coordinate system acts as a cognitive map encoding relational information for goal directed dead reckoning. As with rodents, the biologically plausible agent exhibited one-shot learning in the multiple cue-location paired associations task of Tse and colleagues.

2-102. The role of hippocampal CA1 in relational learning in miceSvenja Nierwetberg^{1,2}David Orme¹Karel Kieslich¹Andrew MacAskill¹

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Learning relationships between cues in our environment enables us to recognise common underlying structures of events and is thought to form the basis of episodic memory. This type of learning - often called relational, hierarchical or structured learning - requires retaining both the stimulus identity as well as its relation to other cues, for example their relative order in time or location in space. Despite being essential for many of our everyday decisions, relational learning cannot be performed by classic reinforcement learning algorithms, and there is limited insight into how it is achieved within the brain.

One area implicated in relational learning is the hippocampus. Specifically, neurons in the CA1 area of the hippocampus have been shown to represent variables that are essential for constructing a relational structure of the environment, such as cue configurations, the value of such configurations and their order in space and time.

To investigate the neural mechanisms of relational learning, we designed an odour sequence task for mice that requires subjects to learn about both the identity of an odour and its temporal position within a sequence. Importantly, the task design allows for manipulation of the temporal structure and value of cues separately. Using this ability allowed us to probe generalisation to novel cues in the same temporal structure, and the ability to rapidly update the value associated with learnt relational structure.

We found that mice quickly learnt this task and, in line with a key role for hippocampal circuitry, optogenetic inactivation of CA1 markedly impaired task performance. In addition, we found that after initial learning, mice could rapidly adapt to manipulations of cue value and identity, suggesting flexible use of previously learnt relational structures.

Ongoing work aims to understand how the role of CA1 in these computations differs along the dorso-ventral axis of the hippocampus.

2-103. Internally Organized Abstract Task Maps in the Mouse Medial Frontal CortexMohamady El-Gaby^{1,2}Adam Harris^{1,3}James Whittington⁴Mark Walton¹Thomas Akam^{1,3}Timothy Behrens¹

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New tasks are often similar in structure to old ones. Animals that take advantage of such conserved or “abstract” task structures can master new tasks with minimal training. To understand the neural basis of this abstraction, we developed a novel behavioural paradigm for mice and recorded from their medial frontal neurons as they learned. Freely moving mice learned multiple tasks where they had to visit 4 rewarded locations in sequence (ABCD) on a 3x3 spatial maze. Tasks shared the same circular transition structure (... ABCDABCD ...) but differed in the locations and geometric arrangement of rewards. As well as improving across tasks, mice inferred that A followed D (i.e. completed the loop) on the very first trial of a new task. This “zero-shot inference” is only possible if animals had learned the abstract structure of the task. Medial frontal cortex (mFC) neurons showed several signatures of internally organized tuning to abstract task-space. Firstly, the majority of state-tuned neurons in the mFC responded to the mouse’s “location” in abstract task space, conserving their state tuning across distinct tasks. Secondly, we found robust, task-stage modulated offline replay of activity in task-space during sleep. Thirdly, a minority of state-tuned neurons remapped across tasks. Preliminary evidence suggests that such remapping is quasi-coherent across neurons, consistent with the existence of task-space modules analogous to modules of grid-cells that coherently remap in physical space. These findings point to separable neuronal substrates for internally organised representations of task structure that may guide abstraction in the mammalian brain.

2-104. Mice identify subgoal locations through an action-driven mapping process

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Mammals instinctively explore and form mental maps of their spatial environments. Models of cognitive mapping in neuroscience tend to depict map-learning as a process of random or biased diffusion; however, in practice, animals explore spaces using structured, purposeful, sensory-guided actions. A promising model system for probing the relationship between spontaneous exploration and spatial cognition is threat-evoked escape behavior in mice. Notably, Shamash et al. 2021 examined how mice learn routes to a shelter when the direct path is blocked by an obstacle. They found that during a 20-min free exploration period, mice memorized allocentric subgoal locations at the obstacle edges, helping them to perform efficient two-step escape routes past the obstacle. Here we demonstrate that a particular class of movements - runs targeting an obstacle edge during exploration - plays a causal role in triggering subgoal memorization. We used closed-loop neural manipulations to interrupt running movements during exploration. Blocking edge-directed runs abolished subgoal learning. In contrast, three similar stimulation protocols that spared edge-directed runs had no such effect. We next examined the distribution of locations from which mice executed subgoal escapes. This revealed that the decision of whether to pursue a subgoal incorporates information about the mouse's position relative to the environment's layout. Thus, mice use an action-driven learning process to identify subgoals, and these subgoals are then integrated into a map-based planning process. From a reinforcement-learning perspective, this process fits with a model-free/model-based hybrid called the successor representation (Dayan 1993), albeit with several modifications. From a cognitive-science perspective, it matches the sensorimotor enactivism framework Clark 1999; Ballard et al. 1997). Overall, our results indicate that action-driven mapping may be an important component of gaining useful information about the environment and suggest the possibility of a tight link between the hippocampal mapping network and the cortico-striatal action-learning circuit.

2-105. Automatic Task Decomposition using Compositional Reinforcement Learning

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Decomposing complex tasks into their simpler components is often the only way for animals to make any meaningful progress at all. We show that reusing the traditional reward prediction error machinery at multiple hierarchical levels allows complex tasks to be automatically decomposed in a compositional manner, leading to fast and flexible reinforcement learning. In this compositional reinforcement learning (CRL) framework, the agent computes a set of predictions for each state in the form of hierarchically organized general value functions (GVFs). Level 0 GVF predict whether continuing straight along cardinal directions in the state space will lead to a rewarded location; while a level P GVF predicts whether the same simple straight ahead policy leads to any location with a high value in any of the level P-1 GVFs. Learning involves two steps: (1) learning the mapping from state to GVFs and (2) learning the policy from the GVFs. These steps are fast in environments with natural cardinal directions and strong compositional structure. Learning the mapping from states to the GVFs with TD learning is fast because it involves simple policies which have low entropy in their outcomes and are able to efficiently explore the state space; while learning the mapping from GVFs to policy is greatly simplified by the compositional structure of the GVFs and the simple mapping from the cardinal directions to available actions. In rapidly changing environments, as is typical for the real world, CRL leads to remarkably fast learning. For instance, CRL vastly outperforms traditional approaches in a maze task in which the maze changes frequently, or when learning to reach for an object, whose location varies over trials, with a robotic arm. This work provides a biologically plausible framework to study task decomposition in animals confronted with rapidly changing environments.

2-106. Environmental complexity modulates the arbitration between deliberative and habitual decision-making

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Research into decision-making suggest that the brain contains multiple systems for generating adaptive strategies. The usual explanation is that each strategy is optimized for different environmental conditions. Neurophysiologically, current theories suggest that habitual control requires dorsolateral striatal (DLS) networks, while deliberative control depends on hippocampus (HC) and medial prefrontal cortex (mPFC). Within mPFC, manipulation studies and prior research suggest that prelimbic cortex (PL) contains strategy representations making it especially important for this interaction. To examine the role of environmental structure on the arbitration between decision-making systems, we first re-analyzed behavior and recordings from HC and DLS during a contingency-switching task in the light of a novel graph-theoretic measure of maze complexity. Second, we chemogenetically disrupted PL while explicitly controlling for maze complexity. In HC, both the duration of the ascending phase of the theta cycles—hypothesized to contain more nonlocal representations—and overall rate and duration of sharp wave ripple events increased with environmental complexity. In DLS, the development of the preferential firing at the start and end of a lap—task-bracketing—increased with environmental simplicity. PL inactivation reduced deliberation and led to deficits in performance, particularly in complex environments. Furthermore, it resulted in an increase in behavioral stereotypy and a decrease in spatial exploration, but again, only in complex environments. Conversely, in simple environments, we found no significant difference in the durations of the decision-making mode or overall exploration. This data suggests that mPFC engagement—hypothesized to be important for both strategy-setting and the initiation of deliberative sequences—may be particularly crucial in complex environments. Consistent with current theories, more complex environments likely require a higher cognitive memory load resulting in slower automation. PFC disruption may cause working memory disruptions that were consequential for performance in complex environments in which deliberation is necessary.

2-107. The rodent medial prefrontal cortex is composed of functionally distinct subregions

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The rodent medial prefrontal cortex (mPFC) is considered central in executive functioning and decision making, and from an anatomical perspective there is consensus that the mPFC is not a single homogenous structure. However, the nature of mPFC is more contentious in the functional domain, with disagreement as to whether mPFC is homogenous, or instead composed of multiple distinct subregions with distinct roles. To answer this question it is necessary to monitor activity across a wide swath of mPFC as rats actively engage prefrontal processing, and critically, to precisely identify the anatomical location of these recordings. To meet this objective, we recorded neural activity using linear silicon probes placed along the dorso-ventral axis of the mPFC as rats performed an economic decision task. We then identified the precise location of each recorded cell to relate functional activity to decision behavior. Examination of information flow between mPFC cells, measured via transfer entropy (TE), provided critical insight into the nature of mPFC. Leveraging our cell localizations, we performed a novel analysis where we evaluated TE as a function of anatomical position and found four distinct areas of elevated information flow, reflecting distinct processing units within mPFC. Crucially, the locations of these areas closely matched anatomical boundaries (ACC, dPL, vPL, IL), providing clear correspondence between function and anatomy. Further analysis of subregional responses revealed that dorsal areas (ACC & dPL) were engaged during decision processing, IL was involved in maintaining representations of the current task state, and vPL occupied a middle ground between these functions. Our work demonstrates that mPFC is composed of four functionally distinct subregions and suggests how these four areas work together to support decision making. These findings provide future research with an updated conceptual framework of mPFC functioning, and a deeper understanding of network processing in this critical brain area.

2-108. Defining the role of a locus coeruleus-orbitofrontal cortex circuit in behavioral flexibility

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To flexibly update behavior in response to a sudden change in outcome of previously learned cues and actions, neural activity in the orbitofrontal cortex (OFC) must be updated. Novelty activates the locus coeruleus (LC), a group of cells in the brainstem that release the neurotransmitter norepinephrine (NE) throughout the brain. NE release may drive behavioral flexibility by facilitating the reorganization of neural activity in target brain areas, including the OFC. To test this hypothesis, mice were assessed in a T-maze reversal learning task, which requires subjects to reverse a previously learned strategy to succeed. During this task, neural activity in the OFC was recorded via miniendoscopic calcium imaging, which allows us to observe populations of neurons over multiple days. During reversal, the LC was either excited or inhibited using chemogenetic, pharmacological, or optogenetic manipulation. We find an inverse-U-shaped effect of NE on behavioral flexibility, with a sustained increase or decrease in LC activity during the task decreasing reversal performance. In the OFC, we observe that different patterns of neural activity underlie behavioral deficits caused by too little or too much NE. Inhibiting the LC impairs reorganization of OFC neural activity, with a higher proportion of cells continuing to respond to the previously rewarded side of the maze. Exciting the LC increases the proportion of OFC cells responding to both sides of the maze, potentially decreasing the signal to noise ratio of the system. These experiments investigate an important brain circuit from the level of individual cells to modulation of behavior. The study provides important insights into population-level OFC neural activity during learning and reversal and how LC-mediated NE signaling modulates this OFC activity and reversal learning. The knowledge gained through this study may also provide scientific rationale for targeting circuit-specific deficits in neurological disorders where behavioral flexibility is impaired.

2-109. Input-specific regulation of locus coeruleus activity for mouse maternal behavior

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The locus coeruleus (LC) is a small brainstem nucleus that provides the forebrain with the primary source of noradrenaline (NA), a neuromodulator important for a range of core behavioral and physiological functions (Aston-Jones & Cohen, 2005; Martins & Froemke, 2015; Poe et al., 2020). While early theories described the LC as a homogeneous structure whose neurons release NA uniformly to broadly coordinate brain states, recent studies have begun to reveal that complex behavioral contexts can lead to engagement of specific subpopulations of LC neurons depending on their inputs, outputs, and molecular properties (Aston-Jones & Cohen, 2005; Schwarz et al., 2015; Uematsu et al., 2017). Maternal care involves a complex set of behaviors requiring noradrenaline, but whose regulation by LC circuits is unknown (Thomas & Palmiter, 1997). Here we show that LC-NA activity is required for pup retrieval, a rodent parental behavior wherein experienced caretakers retrieve isolated pups back to the nest (Carcea et al., 2021). We demonstrate that pup cues activate LC neurons in maternal female mice—electrophysiological recordings showed that ultrasonic pup vocalizations increased LC firing, and fiber photometry showed that pup contact produced phasic increases in LC-NA activity during retrieval. We then investigated what inputs drive LC activity during maternal behavior, finding a role for a corticotropin-releasing factor (CRF)-positive projection from the central amygdala (CeA) in modulating retrieval. Selective suppression of CeA inputs impaired different facets of retrieval compared to global inhibition of LC-NA neurons. Collectively, our results indicate that input-specific subpopulations of LC neurons coordinate different aspects of neural and behavioral responses for maternal care.

2-110. Mechanisms of plasticity for pup call sounds in the maternal auditory cortex

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Distress calls of mice pups outside their nest elicit reliable pup retrieval in maternal female mice but not in their virgin ('naive') conspecifics. However, when co-housed with maternal mice, naive mice become 'experienced' and learn to reliably perform pup retrieval. This process correlates with neuronal changes in the primary auditory cortex (A1): While excitatory (E) neuron responses are sharply tuned to a certain inter-pup-call interval and inhibitory (I) neuron responses are broadly tuned in naive mice, the two neuron types are co-tuned in experienced mice. This change in behavior and tuning is mediated by oxytocin (Marlin et al., 2015; Schiavo et al., 2020). Here, we aim to dissect the underlying mechanisms behind the behaviorally-relevant changes in tuning of excitatory and inhibitory neurons from naive to experienced mice by combining computational modeling and in-vitro experiments. Using optogenetic targeting of somatostatin-positive (SST) or parvalbumin-positive (PV) inhibitory neurons, we quantified short-term plasticity (STP) at SST-to-E and PV-to-E connections. Furthermore, pairing experiments reveal sufficient long-term plasticity at SST-to-E but not PV-to-E connections. Using a model, we study the interaction of three neuron populations (E, SST, and PV) with synapses experiencing experimentally-identified short- and long-term plasticity. We show that 1) short-term plasticity leads to the tuning of excitatory and inhibitory neurons to specific inter-stimulus intervals (ISIs), and 2) oxytocin-gated long-term plasticity of E-to-E and SST-to-E connections leads to experience-dependent changes in the tuning properties from naive to experienced mice. Furthermore, 3) short-term plasticity at SST-to-E and PV-to-E synapses can control the excitatory signal amplitude without changing the tuning properties. Our results reveal that short- and long-term plasticity cooperate to generate tuning of excitatory and inhibitory neurons in local microcircuits and have important implications for maternal behavior.

2-111. Emergence of functional circuits in the absence of neural activity

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During development, the complex neuronal circuitry of the brain emerges from limited information contained in the genome. After the genetic code instructs the birth of neurons, the emergence of brain regions, and the formation of axon tracts, it is believed that neural activity plays a critical role in shaping neural circuits for behavior. Current AI techniques are modeled after the same principle: connections in an initial weight matrix are pruned and strengthened by activity-dependent signals until the network can sufficiently generalize a set of inputs into outputs. Here, we challenge these learning-dominated assumptions by quantifying neuronal activity contribution to the emergence of the OptoMotor Response (OMR), a complex, visually guided swimming behavior in larval zebrafish that involves the whole nervous system, from sensory input to motor output. Dark-rearing zebrafish revealed that visual experience plays no effect on the emergence of the OMR behavior. We then raised zebrafish under continuous anesthesia in complete darkness, such that from fertilization onward, they were deprived entirely of both sensory experience and neuronal activity. Strikingly, these animals could immediately perform swim bouts and respond to visual stimuli with 75% accuracy in the OMR paradigm. Shorter periods of anesthesia and dark-rearing during development did not reduce OMR performance below 90% accuracy, calling into question classical critical periods for visual development. Thus, contrary to what you learn on your mother's knee, the OMR in larval zebrafish is wired up by largely activity-independent developmental mechanisms, whereas neuronal activity plays only a minor role in refining the circuit.

2-112. Social cues modulate circuit dynamics to control the choice between communication signals in flies

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Communication is multi-modal - when we interact, we speak, gesticulate, and touch. However, the neural computations and circuits that choose these different communication signals are unclear. We address this issue in *Drosophila* which thanks to its complex social behavior and genetic toolbox is ideal for dissecting the neural basis of communication. During courtship, male flies produce two types of communication signals to woo the female: air-borne song is produced by wing movement, while substrate-borne vibrations are transmitted via the legs. Using statistical modelling of pose tracking data alongside recordings of the song and vibration during courtship, we identified the behavioral contexts in which each signal is produced. We found that female locomotion controls the choice between song and vibration: When the female moves, the male sings, when she is stationary, he vibrates. Optogenetic control of female locomotion confirms the model results. Combining optogenetics and network models, we elucidate the circuit mechanisms underlying this choice. Two groups of sexually dimorphic neurons, “P1a” and “pC2”, drive both signals with complex dynamics: While optogenetic activation of P1a in a solitary males primarily drives persistent vibrations, pC2 induces a sequence of first song and then vibrations. A circuit model reveals that these complex dynamics emerge from a combination of recurrence and mutual inhibition. Lastly, we show how sensory cues modify the intrinsic dynamics to support context-dependent signaling: Female movement affects male signal choice not via visual motion cues but by changing the males locomotor state, which we demonstrate by controlling the male movement and visual inputs during optogenetic stimulation. Overall, by combining behavioral and neural circuit modelling, we show how intrinsic circuit dynamics are modified by sensory cues to produce context-dependent signals during social interactions.

2-113. Flexible circuit mechanisms for context-dependent song sequencing

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Sequenced behaviors, including locomotion, reaching, and vocalization, are patterned differently in different contexts, enabling animals to adjust to their current environments. However, how contextual information shapes neural activity to flexibly alter action patterning is not yet understood. Prior work indicates such flexibility could be achieved via parallel motor circuits, with differing sensitivities to sensory context; instead we demonstrate here how a single neural pathway operates in two different regimes dependent on recent sensory history. We leverage the *Drosophila* song production system to investigate the neural mechanisms that support male song sequence generation in two contexts: near versus far from the female. While previous studies identified several song production neurons, how these neurons are organized to mediate song patterning was unknown. We find that male flies sing ‘simple’ trains of only one mode far from the female but complex song sequences comprising alternations between modes when near her. We characterize the male song circuit from brain to ventral nerve cord (VNC), and find that the VNC song pre-motor circuit is shaped by two key computations: mutual inhibition and rebound excitability between nodes driving the two modes of song. Weak sensory input to a direct brain-to-VNC excitatory pathway drives simple song far from the female. Strong sensory input to the same pathway enables complex song production via simultaneous recruitment of brain-mediated disinhibition of the VNC song pre-motor circuit. Thus, proximity to the female effectively unlocks motor circuit dynamics in the correct sensory context. We construct a compact circuit model to demonstrate that these few computations are sufficient to replicate natural context-dependent song dynamics. These results have broad implications for neural population-level models of context-dependent behavior and highlight that canonical circuit motifs can be combined in novel ways to enable circuit flexibility required for dynamic communication.

2-114. Modeling tutor-directed dynamics in zebra finch song learning

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Just as humans often follow the instructions of a tutor to learn new skills, juvenile male zebra finches learn to sing by copying the song of an adult tutor, providing a powerful system for analyzing tutor-driven learning from both behavioral and neurobiological perspectives. Decades of work have characterized the general trajectory of this learning process [1,2], but recent work using generative modeling methods like Variational Autoencoders (VAEs) has opened entirely new avenues for analyzing song learning [3,4]. While it is generally agreed that juveniles learn to sing by using auditory feedback to evaluate their own songs in reference to a memorized model of the tutor song [5,6], the actual dynamics of juvenile song copying remain unexplained. Specifically, it is unclear how juvenile zebra finches direct their vocal exploration on a rendition-by-rendition basis toward the tutor song. We characterized changes in vocal exploration across development, examining differences between renditions. We used VAEs to create low-dimensional representations of birdsong over the course of vocal learning—from just after tutor exposure to song crystallization. We modeled vocalizations as trajectories within these low-dimensional representations using Langevin dynamics with a learned drift term and temporally autocorrelated noise. The model recapitulated prior findings in juvenile song development [1] and demonstrated that the balance between stochastic vocal exploration and exploitation of learned vocalizations changes based on both developmental age and millisecond-level variation in vocalization. We found that pupil song becomes more deterministic as syllables consolidate closer to the tutor song (as measured by distance in latent space). Moreover, even at a young age, vocalizations that more closely resemble the final, crystallized song are less variable than those farther away. This model of directed exploration thus makes possible future experiments in which neural activity can be related to local measures of tutor-referenced maturity in developing birdsong.

2-115. Many, but not all, deep neural network audio models predict auditory cortex responses and exhibit hierarchical layer-region correspondence

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Deep neural networks are commonly used as models of the ventral visual stream, but are less explored in audition. Prior work provided examples of audio-trained neural networks that produce good predictions of fMRI responses in auditory cortex, and exhibit correspondence between model stages and brain regions, but left it unclear the extent to which these results would generalize to other audio neural network models. We evaluated brain-model correspondence for a wide range of publicly available high-performing audio neural network models along with a set of models that we trained on four different tasks. We used two different fMRI datasets of responses to natural sounds to assess replicability. We found that most tested models out-predicted previous “shallow” spectrotemporal filter models of auditory cortex, and exhibited a systematic layer-region correspondence, with middle layers best predicting primary auditory cortex and deep layers best predicting non-primary cortex. However, some state-of-the-art models produced notably worse brain predictions, including recent speech-to-text and audio captioning systems developed for engineering purposes. The results support the hypothesis that hierarchical models optimized for auditory tasks often learn representational transformations that coarsely resemble those in auditory cortex, but indicate that models derived for engineering purposes can deviate substantially from biological systems.

2-116. Identifying and adaptively perturbing compact deep neural network models of visual cortex

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The best current models of visual cortical neural responses rely on internal representations of large deep neural networks (DNNs) trained for object recognition. However, the inner workings of these DNN models are mostly uninterpretable due to their massive size—tens of millions of parameters. Do we need such large models in the first place? In this work, we focused on modeling visual cortical neurons in macaque mid-level visual area V4. We used ensemble learning and closed-loop experiments with active learning to train a DNN model to accurately predict V4 responses. However, our model had 90 million parameters—too many to interpret. We then leveraged machine learning techniques of distillation and pruning to identify compact models that were 1,000x smaller than the large model but still as predictive. We causally tested our compact models by using them (1) to adaptively synthesize images to maximize V4 responses and (2) to slightly perturb images to yield large changes in V4 responses (i.e., adversarial images). We found that the compact models preferred a large variety of oriented edges, curves, textures, and colors. One prominent preference was for small dots; we ran additional experiments to probe the properties of these “dot detectors” in V4. We then analyzed the compact “dot detector” model to uncover the necessary and sufficient computations needed to build such a detector. Overall, we propose a general approach to identify highly-predictive, interpretable models; we used this approach to find compact models of V4 neurons whose size is substantially smaller than previously thought.

2-117. Mind the gradient: context-dependent selectivity to natural images in the retina revealed with a novel perturbative approach

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Understanding how sensory neurons extract relevant information from natural scenes is a major challenge in neuroscience. Probing sensory systems with simple stimuli give limited insights on natural scene processing, and probing selectivity during natural scene stimulation is difficult. Even in the retina, it is not clear how Retinal ganglion cells (RGC) extract specific features from natural scenes and send this information to the brain. Many studies using simple, artificial stimuli have shown responses to local light increase (ON-responses), and/or decrease (OFF), but it is unclear if this selectivity is maintained when processing natural stimuli. Other works tried learning non-linear models to predict RGC responses to natural stimuli, but are hard to interpret. Here we address these issues using a novel perturbative approach that takes the best of these two strategies by probing selectivity with perturbations added to natural scenes. We stimulated mouse and axolotl RGCs with natural images, adding small checkerboard-like perturbations on top. We found that single RGC can be selective to light increments for a perturbed natural image, and to light decrements when the same perturbations are added to another. RGCs can thus switch selectivity from ON to OFF depending on the natural context. We designed a convolutional neural network model to explain these changes, and mapped it to specific retinal circuits. Pharmacological experiments and modeling showed that ON/OFF selectivity changes were due to the non-linear combination of different retinal pathways. Finally, using dimensionality reduction and gradient field representations, we demonstrated that this strong context dependence is compatible with a robust computation of a more abstract feature: contrast. Our

perturbative approach thus uncovers neuronal selectivity to more complex features than initially thought during natural scene stimulation and could be applied in other sensory systems to refine models or test hypotheses about what features are extracted from the sensory input.

2-118. Divergence of chromatic information in GABAergic amacrine cells in the retina

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Along with other visual features, chromatic information is extracted by the retina. The excitatory, feedforward pathways of chromatic signals in the mouse retina have recently been investigated (Szatko et al., 2020), but it is unclear how inhibitory cell types contribute. In particular, a systematic characterization of chromatic responses in amacrine cells (ACs), the largest and most diverse retinal class of inhibitory neurons, is missing, and the ACs' role in color processing remains unknown. One challenge in studying AC responses is the fact that most of them lack axons and signal primarily through their dendrites; thus recordings of their somatic activity do not necessarily capture their many functional roles (Diamond, 2017). To overcome this challenge, we performed a comprehensive survey of chromatic responses in GABAergic AC processes using 2-photon calcium imaging in mouse retina. We presented color noise stimuli calibrated to green- and UV-sensitive mouse photoreceptors to obtain chromatic receptive fields of individual subcellular regions of interest. We clustered AC chromatic receptive fields using Gaussian mixture models and identified functional groups with diverse color preferences and response polarities. These preliminary data suggest that ACs play an important role in diversifying the representation of chromatic information in the inner retina. Currently, we are extending a circuit model of the inner retina with biophysical constraints (Schroder et al., 2020) to assess the interplay of excitatory and inhibitory interneurons in chromatic processing. Diamond JS (2017) Inhibitory Interneurons in the Retina: Types, Circuitry, and Function. Annu Rev Vis Sci 3:1–24. Schroder C, Klindt D, et al. (2020) System Identification with Biophysical Constraints: A Circuit Model of the Inner Retina. NeurIPS. Szatko KP, Korympidou MM, et al. (2020) Neural circuits in the mouse retina support color vision in the upper visual field. Nat Commun 11:3481.

2-120. Organization of local directionally selective neurons informs global motion vision encoding

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The apparent motion of features in a visual scene — optic flow — provides rich information about the animal's self-motion and its environment [Gibson 1950]. An animal estimates the optic flow with motion sensitive neurons. In flies, the T4/T5 neurons encode small-field directional motion signals by sampling neighboring eye facets. The signals are then integrated by large-field neurons, which are tuned to complex global patterns of optic flow. Are these patterns simply inherited from their T4/5 inputs or synthesized by a more complex computation? Near the center of the eye, the 4 T4 subtypes have been shown to encode motion along the 4 cardinal directions — forward, backward, up and down [Maisak, et al 2013; Takemura, et al 2013]. In this case, a simple summation would generate a translational flow pattern. However, it's not possible for all T4's locally preferred direction (LPD) to follow the cardinal directions across the eye while maintaining a uniform sampling of the eye's hexagonal grid.

We set out to systematically describe, for the first time, the global organization of the local directionally selective neurons using computational neuroanatomy of the FAFB EM data set [Zhang, et al 2017]. We reconstructed hundreds of T4 neurons and determined their dendritic orientation (proxy for LPD). To compare the organization of LPDs to the eye structure and to global optic flow fields, we developed an “eye map” using uCT of an entire fly head to register the neuronal coordinates of the EM reconstructions into eye coordinates. We found that T4 neurons are mostly aligned to the local hexagonal grid, but this grid maps onto the eye with systematic spatial variations. This mapping has pronounced effects on the local motion sensitivity and subsequently the global motion pattern encoding. Our results demonstrate that the organization of the sensory apparatus substantially informs neural computations.

2-121. Evaluating Noise Tolerance in *Drosophila* Vision

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High noise tolerance is a hallmark of sensory systems as external stimuli are intrinsically noisy. However, the neural mechanisms underlying the noise tolerance are not clearly understood. In *Drosophila* vision, we evaluated behavioral and physiological changes in visual responses to simple visual patterns—translating bars, gratings, spots, and looming objects—overlaid with varying levels of salt-and-pepper noise. In tethered, flying *Drosophila*, we found that the noise tolerance, evaluated by changes in visually evoked wingbeat responses, depends on the pattern. Namely, the noise tolerance was highest for the grating patterns, medium for the bar and the looming disc patterns, and lowest for the spot patterns. Furthermore, we found that wing response latencies increased significantly for increasing noise levels for the spot and loom patterns, but not for the grating and bar patterns, suggesting distinct neural pathways associated with these visual patterns. To evaluate the noise tolerance at the neuronal level, we genetically silenced a group of visual neurons known to be associated with these visual patterns as well as two neuromodulatory neurons. We found the largest reduction in wing responses to the loom pattern when either a specific group of visual projection neurons (LPLC2) or octopaminergic neurons were silenced. To a noiseless loom pattern, however, silencing of either LPLC2 or octopaminergic neurons had little, if any, effect on the wing responses, suggesting the role of these neurons in noise suppression. Finally, we measured physiological responses of the visual neurons via calcium imaging and found that the noise tolerance of individual cell types was consistently lower than that of behavioral responses, suggesting further noise suppression in the downstream circuits. This work will lead to the understanding of the neural mechanisms by which sensory systems extract salient stimulus features in a noisy environment.

2-122. Affine models explain tuning-dependent correlated variability within and between V1 and V2

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Sensory cortex exhibits highly variable responses to the same stimulus across trials. This variability is correlated across neurons. The pattern of correlated variability is important because it informs us about stimulus encoding and the underlying structural connectivity. In visual areas, it has been shown that correlated variability depends on orientation tuning. However, it is challenging to interpret this tuning dependence when the spikes are generated from a doubly stochastic Poisson process, which is commonly assumed. In this case, spikes can exhibit tuning-dependent noise correlation, even if the noise correlation of the underlying firing rate is tuning-independent. Furthermore, a diverse set of tuning-dependent patterns can be explained by adjusting tuning-independent multiplicative and additive noise in the firing rates. We investigated how noise correlation and covariance of simultaneously recorded spikes from V1 and V2 depend on orientation tuning. Affine models with tuning-independent multiplicative and additive noise fit separately to V1 and V2 capture the observed tuning dependence of the correlations both within and between areas. Moreover, we carry out a simple derivation of noise correlation that provides an intuition for the observed patterns. We show that the additive noise within V1 is not correlated with the additive noise within V2, whereas the multiplicative noise is correlated across areas. To investigate the underlying circuit mechanisms, we simulated a stabilized supralinear network with a ring architecture representing a single area, receiving external input. We find that both multiplicative and additive noise emerge in the network when the neurons only receive additive noise in the input. Interestingly, only the additive, but not the multiplicative, noise is

correlated with the input noise. Our results demonstrate that tuning-independent multiplicative and additive noise are sufficient to explain the tuning-dependent correlated variability within and between V1 and V2.

2-123. Disentangling Fast Representational Drift in Mouse Visual Cortex

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In the mouse visual cortex, neural representations of stimuli fluctuate across repetitions (Scholvinck et al. 2015, Deitch et al. 2021). The single-trial dynamics, often termed as representational drift, were also found in other cortical structures (Rokni et al. 2007, Low et al. 2021, Schoonover et al. 2021). However, most of these studies focused on slow drift over days. Here, we demonstrated that representational drift occurs at a fast timescale of several minutes and is prevalent regardless of stimulus type and independent of behavioral state. Within sessions of the same day, repeats of the same stimulus in different blocks were separated in the low-dimensional neural manifold, indicating larger changes in neural activity across blocks than within blocks. The trial-by-trial variability was partially associated with behavior variables but did not account for fast drift. It suggests that the fast representational drift was more than just fluctuations in behavioral state. Moreover, in line with previous work (Xia et al. 2021), we found that decoding remained stable despite representational drift, indicating that fast drift is restricted to a coding subspace orthogonal to the stimulus dimension. To disentangle the representational drift component from behavior-relevant variability, we adopted an unsupervised dimensionality reduction method called Tensor Component Analysis (TCA) to identify underlying factors. TCA decomposed the trial-by-trial variability into behavior-related and fast drift components. Furthermore, we found that subcortical areas also displayed representational drift across blocks. Canonical Correlation Analysis (CCA) showed a strong correlation in drift between brain structures. Using a generative model called Inter-Battery Factor Analysis (IBFA), we identified components that were shared between visual cortex and hippocampus. The shared drift factors were highly correlated with the disentangled tensor components, indicating that the fast representational drift signal is propagated among different brain structures.

2-124. A brain-computer interface in prefrontal cortex that suppresses neural variability

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When presented with identical task conditions across multiple trials, the brain produces variable patterns of neural activity. This neural variability stems from many sources, one of which is fluctuations in internal states (e.g., arousal, attention, and motivation). Neural variability may reflect changes in these internal cognitive factors and can influence our perceptual and decision-making abilities. For instance, when tasked with shooting consecutive free throws on a basketball court, we may experience changes in our arousal, and our minds might wander. Such trial-to-trial variability can detrimentally impact our task performance by limiting information encoding in our brains. Also, deficits in regulating neural variability have been linked to neuropsychiatric disorders. Being able to reduce neural variability thus has implications in enhancing and restoring the brain's cognitive capabilities. However, the extent to which neural variability is under volitional control is unclear. We designed a prefrontal cortex (PFC) brain-computer interface (BCI) to assess whether a macaque could use moment-to-moment visual feedback to stabilize its neural activity. We challenged the subjects to use the BCI to keep their neural activity as close as possible to a baseline neural state observed at the beginning of each session. We discovered that subjects successfully used the moment-to-moment visual feedback to produce neural activity similar to baseline activity. Throughout the session, we observed that the neural activity gradually moved away from the initial baseline state. While non-BCI trials exhibited these slow fluctuations in neural activity, we found that BCI trials suppressed these slow changes. Overall, our results demonstrate that subjects could suppress neural variability using our novel neurofeedback paradigm. Furthermore, these findings can inform the development of clinical BCIs that treat cognitive disorders.

2-125. Behavior measures are predicted by how information is encoded in an individual's brain

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Understanding the brain-behavior relationship is a central goal in neuroscience. Recent neuroimaging studies have demonstrated that individual differences in both brain anatomy and the connectivity between regions are predictive of behavior. We hypothesize that behavior can also be predicted by how the same brain region, in different individuals, encodes information. As an analogy, athletic ability is not only related to the size of the components of the cardiovascular and musculoskeletal systems or the strength of the connections between components, it is also related to the proficiency of the individual components.

Here we propose a framework, built on encoding-models, to evaluate our hypothesis that individual differences in how information is encoded in the brain can predict behavior measures. We evaluate our framework on fMRI data collected when 90 participants from the Human Connectome Project (HCP) watched naturalistic video clips, and when they performed a tightly controlled motor task. We find that individual differences exist in where and what stimulus information is encoded in the brain, and that these differences are predictive of variability in cognitive behavior. Given what is expected in predicting behavior from fMRI data, our results argue that encoding-models are a powerful tool for studying the brain-behavior relationship. Crucially, our results also reveal that the ability to predict different behavior measures depends on the choice of task and encoding-model.

These findings open the door for neuroimaging studies to increase our understanding of the brain-behavior relationship by investigating the relationship between individual differences in brain encoding and behavior. Further, the task/encoding-model specificity suggests that experimenters interested in predicting behavior should tailor their choice of task and encoding-model to the behavior of interest.

2-126. Fast ACh signals and the optimal control of attention in a detection task

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Understanding how the brain represents, updates, and accommodates uncertainty is a key challenge for computational neuroscience. Neuromodulators such as acetylcholine (ACh) have been suggested as playing important roles over multiple timescales, regulating excitability and plasticity to mediate various effects of uncertainty on inference and learning. While these influences are consistent with ACh's long-standing association with general functions of attention and arousal, recent studies using novel techniques to measure and manipulate this system with increasing exactitude have revealed intriguing patterns of activity at fast timescales. Notably, Sarter and colleagues used ACh amperometry (Howe et al., 2013, J.Neurosci., 33(20):8742-8752) and optogenetics (Gritton et al., 2016, PNAS, 113(8):E1089-E1097) as rodents performed a challenging signal detection task; they reported effects such as a serial dependency over multiple trials as to whether ACh is released, and increased false alarm rates when optogenetic stimulation is applied during non-signal trials. Inspired by their task and findings, we construct an abstract detection task, and consider how attentional state might be optimally controlled over each trial, assuming that more focused attention improves sensory information but incurs costs. We show similarities between the resulting attentional dynamics and task performance in the model and experimental results.

2-127. Perceptography: Reconstruction of visual percepts induced by brain stimulation

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Local stimulation in high-level cortical visual areas perturbs the contents of visual perception. Understanding how the contents of perception are altered by cortical stimulation is necessary for characterizing visual hallucinations in mental disorders and developing visual prosthetics. Anecdotal verbal reports by human patients constitute the main body of evidence in this area of research. The absence of speaking ability in nonhuman primates severely limits the systematic and high-throughput study of stimulation-induced perceptual events. Here we introduce a novel methodology, perceptography, that allows taking pictures of complex visual events induced by optogenetic stimulation of macaque inferior temporal (IT) cortex. The animals started each trial by fixating on a computer-generated image. Halfway through the 1-second image presentation, we altered the image features for 200ms. A ~1x1mm area of the IT cortex was optogenetically stimulated in half of the trials at random for 200ms using an implanted LED array. The animals were rewarded for successful detection of stimulation trials by looking at one of the two subsequently presented targets. We hypothesized that image alterations that share common features with the stimulation-induced perceptual event increase the chance of false alarms (FA) by the animal. Under the hood, two learning systems were deployed to increase the probability of FA. Ahab, our feature extraction deep network, used the animals' behavioral responses to guide DaVinci (a generative adversarial network) to achieve this goal. This closed-loop system created altered images that induced 55-85% FA rate, dramatically higher than the baseline 3-7% (cross-validated, $p < 0.01$). We would like to name these images Perceptograms, given that the state of perceiving them is difficult for the animals to discriminate from the state of their IT cortex being stimulated. We have also shown that higher cortical illumination leads to more pronounced alterations in the resulting perceptograms.

2-128. Using 1D-convolutional neural networks to detect and interpret sharp-wave ripples

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Sharp-wave ripples (SWR) are high frequency events recorded in the local field potential (LFP) of the hippocampus of rodents and humans. During SWR, the sequential firing of ensembles of neurons act to reactivate memory traces of previously encoded experience. SWR-related interventions can influence hippocampal-dependent cognitive function, making their real-time detection crucial to understand underlying mechanisms. However, existing SWR identification tools mostly rely on using spectral methods, which remain suboptimal.

Here, we introduce a 1D convolutional neural network (CNN) operating over high-density LFP recordings to detect hippocampal SWR both offline and on-line. The adapted architecture included seven convolutional layers composed of different kernels to process 8-channel LFP inputs in increasing hierarchical complexity and one output layer delivering the probability of an occurring SWR. We report offline performance on several types of recordings (e.g. linear arrays, high-density probes, ultradense Neuropixels) as well as on open databases that were not used for training. By saturating the operation of different kernels, we examine and interpret their optimal behaviour associated to the ground truth versus a random selection. We then use dimensionality reduction techniques to visualize how the network processes information across layers. Finally, we show how by building a plug-in for a widely used open system such Open Ephys, our method detects SWRs in real time. We conclude with discussion on how this approach can be used as a discovery tool for better understanding the dynamics of SWR.

2-129. Cross-Frequency Coupling Increases Memory Capacity in Oscillatory Neural Networks

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An open problem in neuroscience is to explain the functional role of oscillations in neural networks, contributing, for

example, to perception, attention, and memory. Cross-frequency coupling (CFC) is associated with information integration across populations of neurons [1]. Impaired CFC is linked to neurological disease [2]. It is unclear what role CFC has in information processing and brain functional connectivity. We construct a model of CFC which predicts a computational role for observed $\theta - \gamma$ oscillatory circuits in the hippocampus and cortex [3]. Our model predicts that the complex dynamics in recurrent and feedforward networks of coupled oscillators performs robust information storage and pattern retrieval. Based on phasor associative memories (PAM) [4], we present a novel oscillator neural network (ONN) model [5] that includes subharmonic injection locking (SHIL) [6] and which reproduces experimental observations of CFC. We show that the presence of CFC increases the memory capacity of a population of neurons connected by plastic synapses. CFC enables error-free pattern retrieval whereas pattern retrieval fails without CFC. In addition, the trade-offs between sparse connectivity, capacity, and information per connection are identified. The associative memory is based on a complex-valued neural network, or phasor neural network (PNN). To our knowledge, this is the first work to validate the capacity analysis of Q -state PAM networks [7] through simulation and provide a model of how to implement such a memory on a physical system. We show that for values of Q which are the same as the ratio of γ to θ oscillations observed in the hippocampus and the cortex, the associative memory achieves greater capacity and information storage than previous models. The novel contributions of this work are providing a computational framework based on oscillator dynamics which predicts the functional role of neural oscillations and connecting concepts in neural network theory and dynamical system theory.

2-130. Intrinsic neural excitability induces time-dependent overlap of memory engrams

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Memories are thought to be stored in neural ensembles known as engrams that are specifically reactivated during memory recall. According to recent studies, memory engrams of two events that happened close in time tend to overlap in the hippocampus and the amygdala, and this overlap has been shown to support memory linking. It has been hypothesised that these overlaps arise from the mechanisms that regulate memory allocation itself, involving neural excitability, but the exact process remains unclear. Indeed, most theoretical studies focus on synaptic plasticity and little is known about the role of intrinsic plasticity, which could be mediated by neural excitability and serve as a complementary mechanism for forming memory engrams. Here, we developed a rate-based model that includes neural excitability as a variable threshold of the firing rate input-output function. We obtained overlapping memory engrams for contexts that are presented close in time, consistent with experimental studies. Moreover, we showed that increasing the initial excitability of a subset of neurons just before presenting a context biases the memory allocation to these neurons. We then explored the role of global inhibition as a way of controlling competition between neurons from two ensembles. These results have identified the possible mechanisms underlying the role of intrinsic excitability in memory allocation and linking, and now allow for predictions regarding the dynamics of memory engrams.

2-131. Dynamic and selective engrams emerge with memory consolidation

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Episodic memories are encoded by sparse populations of neurons activated during an experience. These neural ensembles constitute memory engrams that are both necessary and sufficient for inducing recall even long after memory acquisition. This suggests that following encoding, engrams are stabilized to support reliable memory retrieval. However, little is known about the temporal evolution of engrams over the course of memory consolidation or how it impacts mnemonic properties. Here we employed computational and experimental approaches

to examine how the composition and selectivity of engrams change with memory consolidation. We modeled engram cells using a biologically-plausible spiking recurrent neural network that yielded three testable predictions: memories transition from unselective to selective as neurons are removed from and added to the engram, blocking inhibitory neurons during recall disrupts memory selectivity, and blocking inhibitory synaptic plasticity during memory consolidation prevents engrams from becoming selective. By tagging activated neurons *in vivo* with high spatiotemporal precision as well as using optogenetic and chemogenetic techniques, we conducted contextual fear conditioning experiments that supported each of our model's predictions. Our results reveal that engrams are dynamic even within hours of memory consolidation and that changes in engram composition mediated by inhibitory synaptic plasticity are crucial for the emergence of memory selectivity. These findings challenge classical theories of stable memory traces and point to a close link between engram state and memory expression.

2-132. Mice can do complex visual tasks

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Humans and other primates possess a wide range of complex visual functions ranging from invariant object recognition to fine pattern discrimination, visual memory, spatial reasoning etc. We would ideally like to study the neural basis of such visual computations in lower animal models like the mouse, which are amenable to modern neuroscience techniques. However, it is not known if mice can perform interesting visual computations, and are notoriously known as "non-visual" animals. Here we demonstrate advanced visual functions in mice navigating and foraging in an immersive virtual reality while headfixed on an air-floating ball. The mice demonstrate: 1) visual generalization of texture class, 2) fine discrimination within a texture class, 3) visual reasoning about task rules and 4) high-capacity visual memory. While the mice were engaging in these tasks, we recorded up to 70,000 neurons simultaneously from multiple visual and non-visual cortical areas, using mesoscopic two-photon calcium imaging. We developed new analysis and visualization tools, and used them to identify several neural populations involved in these visual tasks. Our results pave the way for a new generation of high-powered visual neuroscience studies in mice.

2-133. 'Silent' olfactory bulb mitral cells emerge from common feature subtraction.

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Recordings from neural populations can be biased towards cells that are spontaneously active, and it is often implicitly assumed that stimulus responses will be unrelated to spontaneous activity. To avoid such biases [1] performed blind whole-cell patch clamp recordings of olfactory bulb mitral cells. Intriguingly, these recordings revealed an inverse relationship between spontaneous and odor-evoked activity: cells that were highly active at baseline were often quiet during odor presentation, while conversely, 'silent' cells, quiet at baseline, dominated odor responses. In this study we use a probabilistic model of early olfactory processing to show how such an inverse relationship between baseline and odor-evoked activity can emerge through an odor-triggered variant of olfactory background subtraction we call 'common feature subtraction.' In this computation, the olfactory system subtracts features common to recently encountered odors to preferentially infer the features unique to each odor. We suggest that the common features are not modeled directly, but are accounted for through the negative of their expected effects on receptor inputs. In a neural implementation of our probabilistic model we show that adjusting the background activation of mitral cells towards the negative of their recent activity results in their background rates reflecting the negative of the expected effect of the common features on receptor inputs. This negative expectation cancels the contribution of common features when odors are present, allowing preferential inference of odor-specific features by downstream neurons. Our model qualitatively reproduces the experimentally observed relationship between baseline and odor-evoked responses of mitral cells in [1] and provides a normative explanation for them. It is also readily testable through the direct link it predicts between baseline responses and the common features of recent odors.

2-134. A neural mechanism for the termination of perceptual decisions in the primate superior colliculus

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In the study of decision making, neuroscientists have largely focused on how the brain accumulates evidence during the formation of decisions. Less is known about how the accumulation of evidence is terminated. When decisions are communicated with an eye movement, neurons in the lateral intraparietal area (LIP) represent the accumulation of evidence. It has long been hypothesized that downstream areas terminate the decision process when LIP reaches a threshold level of activity. We recorded from neurons in the superior colliculus (SC), a primary downstream target of LIP, as a monkey performed a reaction-time, motion discrimination task. Simultaneously, we recorded from 80-250 LIP neurons using prototype, macaque neuropixels probes. Among these neurons, we identified subpopulations with response fields aligned to those of the SC neurons, allowing access on single trials to the putative LIP input to the SC population. Single-trial activity in LIP displayed drift-diffusion dynamics, as previously inferred. In contrast, single-trial dynamics in SC manifested as quiescence and bursts—one immediately before the saccade, sometimes preceded by smaller, non-saccadic bursts. Saccadic bursts were predicted by a distinct signal in LIP involving the derivative and magnitude of LIP responses. We hypothesized that the bursting dynamics in SC are the product of a threshold mechanism important for terminating the decision. Consistent with this, focal SC inactivation caused (i) an ipsiversive bias; (ii) longer contraversive reaction-times; and (iii) increased overall sensitivity. The combination of these effects is diagnostic of an increased decision threshold for contraversive choices. Simultaneous recordings in LIP showed a prolonged build-up of activity, further suggesting that SC inactivation caused an increase in the decision threshold. Together, the results shed light on the neural mechanism of a fundamental cognitive process—the transformation from deliberation to commitment.

2-135. Serotonergic Control of Model-based Decision Making

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Serotonin (5-HT) is an essential neuromodulator affecting behavioral, affective, and cognitive functions. Recent studies by tryptophan depletion in humans and devaluation paradigm in mice suggest that 5-HT promotes model-based decision making. However, the influence of 5-HT on such decision making remains poorly understood. Recent development of rodent two-step decision making tasks enables us to examine the effect of 5-HT manipulations in situations where rewards do not simply reinforce previous choices but rather interact with task structure to influence policy. Here we took a two-step decision making task and tested the effect of optogenetic inhibition of 5-HT neurons using Tph2-ArchT transgenic mice. We implanted an optic probe above the dorsal raphe nucleus (DRN) and applied photoinhibition by yellow light from outcome delivery to first-step choice at the next trial. In control trials, blue light stimulation was applied. Mice showed choice behavior using model-based controls. The photoinhibition shortened the time to make first-step choices, possibly due to disrupted deliberative model-based decision making process. Furthermore, fitting model-free/model-based hybrid reinforcement learning model suggested that photoinhibition decreased the reliance on model-based decision making. These results revealed the computational role of DRN 5-HT neurons in model-based decision making in dynamic environments.

2-136. Dopamine and norepinephrine signaling differentially mediate the exploration-exploitation tradeoff

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In an uncertain world, we balance two goals: exploiting rewarding options when they are available, and exploring potentially better alternatives. One neuromodulatory system that has been implicated in mediating the transition between exploration and exploitation is the catecholamine system, in particular, norepinephrine (NE) and dopamine (DA). Although both molecules have been implicated in decision making, their contributions have not been directly compared. When each neuromodulatory system is examined in isolation, they have been assigned similar roles in the latent cognitive processes that mediate exploration and exploitation. To understand the differences and overlaps of the role of these two catecholamine systems in regulating exploration and exploitation, a direct comparison using the same dynamic decision making task is needed. Here, we ran mice in a restless two-armed bandit task, which encourages both exploration and exploitation. We systemically administered a NE beta-receptor antagonist (propranolol), NE beta-receptor agonist (isoproterenol), a nonselective DA receptor antagonist (flupenthixol), and a nonselective DA receptor agonist (apomorphine) within subjects across sessions and examined changes in exploration. We found that modulating NE and DA receptor function had opposing effects on exploration - decreasing NE beta receptor activity or increasing DA receptor activity decreased exploration and resulted in stickier behaviors. Fitting a reinforcement learning model revealed that changes in exploration through manipulating NE and DA were due to changes in different latent processes - decreasing NE receptor activity decreased decision noise and increasing DA receptor activity decreased both learning rate and decision noise. Together, these findings suggested that the mechanisms that govern the transition between exploration and exploitation are sensitive to changes in both catecholamine functions and revealed differential roles for NE and DA in regulating exploration.

2-137. Multimodal cues displayed by submissive rats facilitate prosocial choices by dominants

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Animals often display prosocial behaviours, actions that benefit others, which are essential for social bonding and cooperation. Most studies on prosociality come from the Primate Order and have highlighted how features of the social context influence the expression of prosocial behavior, contributing to intraspecific and interspecific variation. However, less effort has been devoted to the detailed investigation of the behaviours of subjects, which is necessary to determine the proximate mechanisms through which the social context influences prosociality, across different species. To address this point, we tested pair of rats in a prosocial choice task and studied how social relationships, including sex, degree of familiarity and dominance status, modulate the emergence of prosocial choices. Here, a decision-maker rat can choose on each trial between providing food to itself only (selfish choice) or to itself and a partner rat, recipient of help (prosocial choice). While sex and familiarity did not affect prosociality, dominance status revealed to be a potent modulator. We found faster emergence and higher levels of prosocial choices in pair of rats where the decision-maker was dominant and the recipient submissive. To get insights into the proximate mechanisms driving this effect, we quantified multimodal interactions during decision-making. Dynamics of nose position, movement and head orientation revealed that the more prosocial pairs showed interactions indicative of increased social attention. These interactions were mainly driven by submissive recipients when dominant decision-makers were behaving selfishly. Moreover, call rate of submissive recipients was positively correlated with the emergence of prosocial choices. We propose that multimodal cues displayed by

submissive recipients may enhance the social salience of signalling need, facilitating the emergence of prosocial choices by dominant rats. Our work demonstrates how the study of behavioural dynamics can generate novel insights into how rats navigate social decision-making, where dominance status is an important factor.

2-138. Confidence-guided waiting as an evidence accumulation process

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When making decisions, combining multiple pieces of information can increase the probability of making the right choice. A decision maker's estimate of this probability, referred to as decision confidence (Hangya et al., 2016), is useful for guiding subsequent actions and learning improvements in the decision policy (Drugowitsch et al., 2019). But studies of the neural computations that give rise to confidence have been limited by the difficulty of measuring confidence in animal subjects. One promising approach uses willingness to wait for reward after choice as a proxy for confidence (Lak, 2014). While rats can learn to modulate wait time as a function of the probability that they've chosen correctly (Lak et al., 2014; Joo et al., 2021), it is unclear how subjects transform confidence into wait time. Here, we show that a drift diffusion to bound model can generate optimal wait times using a tractable update rule to a confidence variable whose initial value is set by the choice process. In this model, each time step that elapses without reward is treated as evidence that reward will not be delivered on that trial. Correspondingly, confidence decreases with time until the expected value of waiting falls to the expected value of starting a new trial. We trained rats to wait for randomly delayed rewards after trials of an auditory evidence accumulation task (Brunton et al., 2013). We used an extensively studied model of the choice process (Brunton et al., 2013; Piet et al., 2018) as the initial point of a drift diffusion process controlling the wait time decision. Fitting the parameters of the wait time model, we find that rats can learn the optimal drift rate for the wait time decision process, but that not all do. Our model offers a strategy for performing this task, unifying the side choice and wait time decisions into a single process and producing a dynamic view of decision confidence.

2-139. Rats employ a task general strategy to report calibrated confidence during learning

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Humans can flexibly monitor their own data processing, and unlike modern AI algorithms appropriately adjust their confidence estimates for decisions in new contexts. Here, we develop a behavioral task to evaluate whether rats, like humans, can calibrate their confidence reports while learning new stimuli-response associations. We compare rat behavior to a self-reflective (metacognitive) model that uses statistical inference to produce calibrated confidence reports. Consistent with model predictions, the variance and calibration of rat confidence increases as their behavioral performance improves. These results suggested rats might employ a flexible, task general second stage of processing – e.g. metacognitive to generate confidence reports. Consistent with this conclusion, Orbitofrontal Cortex (OFC) confidence-encoding neurons were stable across novel stimulus learning. These behavioral and neural correlates of confidence reports support the conclusion that the sense of confidence in rats is a separable metacognitive module that can be flexibly applied in novel situations.

2-140. An Analytical Theory of Curriculum Learning

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In animals and humans, curriculum learning—presenting data in a curated order—is critical to rapid learning and effective pedagogy. A long history of experiments has demonstrated the impact of curricula in a variety of animals—including rats, mice, dogs, pigeons and humans—but, despite its ubiquitous presence, a theoretical understanding of the phenomenon is still lacking. Surprisingly, in contrast to animal learning, curricula strategies are rarely used in machine learning and recent simulation studies conclude that curricula are moderately effective or ineffective in most cases. This stark difference raises a fundamental theoretical question: when and why does curriculum learning help?

In this work, we analyse a prototypical model of curriculum learning in the high-dimensional limit, employing statistical physics methods. We study a task in which a set of informative features are embedded amidst a large set of noisy features. We analytically derive average learning trajectories for simple neural networks on this task, which establish a clear speed benefit for curriculum learning in the online setting. However, when training experiences can be stored and replayed (for instance, during sleep), the advantage of curriculum in standard neural networks disappears, in line with observations from “batch” training in the deep learning literature.

Inspired by synaptic consolidation techniques developed to combat catastrophic forgetting, we investigate whether consolidating synapses at curriculum change points can boost the benefits of curricula. We derive generalization performance as a function of consolidation strength (implemented as Gaussian priors connecting learning phases), and show that this consolidation mechanism can yield large improvements in test performance.

Taken together, our analytical descriptions help reconcile apparently conflicting empirical results, trace regimes where curriculum learning yields the largest gains, and provide experimentally-accessible predictions for the impact of task parameters on curriculum benefits. More broadly, our results suggest that fully exploiting a curriculum may require explicit consolidation at curriculum boundaries.

2-141. SemiMultiPose: A Semi-supervised Multi-animal Pose Estimation Framework

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Multi-animal pose estimation is essential for studying animals' social behaviors in neuroscience and neuroethology. Advanced approaches have been proposed to support multi-animal estimation and achieve state-of-the-art performance. However, these models rarely exploit unlabeled data during training even though real-world applications have exponentially more unlabeled frames than labeled frames. Manually adding dense annotations for a large number of images is costly and labor-intensive, especially for multiple instances. To reduce the need for laborious human labeling, we propose a semi-supervised framework for multi-animal pose estimation which is critical for sparsely-labeled problems. The proposed work is an extension of a semi-supervised single-animal pose estimation method, DeepGraphPose [1], to the multi-animal scenario in a non-trivial fashion. DeepGraphPose leverages the abundant spatiotemporal structures pervasive in unlabeled frames in behavior videos to enhance training, particularly in the regime of few training labels. However, it heavily relies on a uni-modal assumption on the output tensor of the neural network to predict poses for single animals. In order to construct the loss term for unlabeled frames, the model needs to read out differentiable pseudo pose locations from the uni-modal output, which cannot be easily achieved in the multi-animal setting. We propose to resolve the issue by introducing a separate network branch to generate differentiable pseudo pose locations, instead of reading directly from the output multi-modal tensor. The resulting algorithm provides superior multi-animal pose estimation results on three animal experiments compared to the state-of-the-art baselines and exhibits more predictive power in sparsely-labeled data regimes.

2-142. Attractor neural networks with metastable synapses

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It is widely believed that storing and maintaining memories on long-time scales depends on modifying synapses in the brain in an activity-dependent way. Classical studies of learning and memory in neural networks model synaptic efficacy as a continuous or discrete scalar value [1–3]. Theoretical work has shown such models have a reasonably large capacity, especially in the biologically relevant sparse coding limit [4]. However, multiple recent results suggest an intermediate scenario in which synaptic efficacy can be described by a continuous variable, but whose distribution is peaked around a small set of discrete values [5,6]. Motivated by these results, we explored a model in which synapses are described by a continuous variable that evolves in a potential with multiple minima. External inputs to the network can switch synapses between different potential wells. This model can interpolate between models with discrete synapses in which synapses have a deep potential, and models with continuous synapses in which synapses have a flat potential. Our results show that the model with metastable synapses is more robust with respect to the noise compared to models with continuous synapses, and has an enhanced capacity compared to models with discrete synapses. Our results indicate that metastable synapses are critical for the neural network to maintain a large and robust storage capacity.

2-143. Activity-dependent dendrite growth through formation and removal of synapses

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Neurons execute diverse computations that are constrained by the branching of their dendrites and the synapses they form with other neurons. During brain development, many dendrites grow simultaneously and become integrated into multiple networks. Extensive experimental data has demonstrated the role of synapse formation and neural activity on dendrite growth. Yet, computational models of dendrite growth mostly assume random branching, implement activity-independent growth cones or generate dendrite morphologies based on abstract mathematical constraints. While these approaches achieve highly accurate dendritic morphologies and capture the dendrite's developmental stages, they lack mechanistic insight into how changes in morphology influence and constrain the emergence of function and vice versa. Consequently, they fail to elucidate the link between morphological variability and electrophysiological or functional properties.

Here, we propose a model in which dendrite growth and retraction stem from combining activity-dependent and -independent cues from potential synaptic partners. A newly formed synaptic contact is either stabilized or removed according to a local plasticity rule for synaptic organization. Consistent with experiments, three sequential phases (overshoot, pruning, and stabilization) emerge naturally in this model. Furthermore, growth is perturbed in a biologically-plausible fashion when the local plasticity is perturbed. Since input correlations determine synaptic stability, dendrites achieve selectivity to correlated inputs by pruning uncorrelated inputs. In our model, this selectivity of individual dendrites leads to competition for appropriate synaptic input between nearby dendrites and affects dendrite morphology in an experimentally-testable way. Furthermore, dendrites acquire diverse morphologies despite nearly identical initial conditions, highlighting how early developmental variability affects mature morphology. Since proximity to potential synaptic partners controls dendritic outgrowth in the model, dendrites approximate optimal wiring length but overshoot it slightly. In summary, our mechanistic model captures diverse phenomena related to dendrite growth and suggests specific ways in which synaptic formation and removal control both form and function.

2-144. Faithful encoding of interlimb coordination by individual Purkinje cells during locomotion

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Whole-body movements like locomotion require timely and precise coordination of multiple effectors. Moreover, control needs to be robust and flexible to changes in the state of the body and environment. How is such a complex control problem solved by the brain? The cerebellum is critical for coordinating movement; during locomotion it is particularly important for interlimb and whole-body coordination. Decades of recordings have consistently shown that Purkinje cell modulation (the sole output of the cerebellar cortex) is broadly correlated with the locomotor stride cycle. However, much of the firing rate variability has remained unexplained; moreover, previous analyses do not provide a clear model for how Purkinje cell activity could be read out to control coordination. Here we performed cell-attached recordings from individual Purkinje cells in head-fixed mice during locomotion, along with continuous, high-speed tracking of limb and body kinematics. We find that beyond representing the locomotor stride cycle, Purkinje cells are exquisitely sensitive to stride-to-stride kinematic variation. Further, analyzing responses with respect to movements across the body reveals that many individual Purkinje cells respond to multiple behavioral events, including movements of multiple limbs. To disentangle the contribution of individual limbs in light of the high degree of correlation imposed by the locomotor pattern, we used Generalized Additive Models (GAMs). GAMs allow us to simultaneously approximate even highly non-linear contributions of multiple body parts to the overall activity of individual neurons. This modeling reveals that a substantial proportion of Purkinje cells simultaneously encode movements of multiple limbs and body parts to provide precise representations of temporal coordination across diverse combinations of behavioral events. High prevalence of this non-linear mixed selectivity across the Purkinje cell population resolves long-standing controversies surrounding the role of Purkinje cells in locomotor control and could allow for efficient readouts of whole-body coordination by a simple linear decoder.

2-145. Neural Representation of Hand Gestures in Human Premotor Cortex

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High-resolution neuroprosthetic decoding of finger movements and hand gestures could greatly improve the usability of robotic limbs and enable new communication methods such as typewriting. Here, we aimed to understand the motor cortical neural activity during naturalistic hand gestures, to guide the design of hand motion neuroprostheses.

Simultaneous neural population activity was recorded from two intracortical Utah arrays (192 channels) in the ‘hand knob’ area of left premotor cortex of a participant with tetraplegia (‘T5’) while he attempted different hand gestures. Trials varied across laterality (left/right hand) and palm position (up/down/sideways). Trials started from a neutral resting position and requested attempting to move (‘move’) to either a natural gesture from sign language or one of 81 different combinations of three movements (flex/extend/idle for four finger groups (ring and little fingers had the same movement)).

For the same single finger movement (flexion/extension), changing the hand laterality (left/right) or the hand pose (up/down/sideways) caused neural activity patterns to be largely transformed by a uniform, time-independent shift for the entire duration of the trial. For single finger movements, nearby fingers had similar representation, reflecting the biomechanical constraints of an able-bodied hand. While various gestures with simultaneous finger movements are distinctly represented in the neural activity, we found that the neural representation for individual fingers rotated significantly based on the movement of other fingers. To compensate for these non-linearities, an RNN was trained to decode continuous finger movements, enabling T5 to perform a “center-out” task with

independent targets for two finger groups.

Overall, insights about the neural activity corresponding to individual and simultaneous movements of multiple effectors would enable neuroprosthetic control of other complex movements that are uniquely human.

2-146. Time-warped state space models for distinguishing movement type and vigor

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Quantitative methods that cluster videos of animal behavior into repeated syllables (sometimes called “motifs”) have become fundamental tools for systems neuroscientists and neuroethologists. A popular approach is to use autoregressive hidden Markov models (ARHMMs) to identify behavioral syllables in the absence of labeled training data. This model, called MoSeq, has been shown to successfully segment depth-camera videos of mouse behavior into syllables that are familiar to a human observer. However, one issue with MoSeq is that it sorts behaviors which appear very similar to the human eye (e.g. rears occurring at different speeds) into distinct syllables. These duplicated clusters complicate downstream analysis, and encourage ad hoc post-processing steps such as manually merging visually similar clusters. Here, we extend the MoSeq model by incorporating a time-varying “vigor” parameter, which is decoupled from syllable identity. That is, each frame of the video is assigned not only a behavioral syllable but also a time constant which represents the relative vigor at which the syllable occurs. The addition of this time constant allows similar actions performed at different vigors to be grouped under the same syllable. We then show that our “time-warped” MoSeq achieves similar performance to standard MoSeq on mouse depth-camera data while using fewer behavioral syllables. Finally, we compare the time-warped MoSeq results of mice treated with saline and amphetamine to show the utility of the time constant parameter.

3-001. Biological learning in key-value memory networks

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In neuroscience, classical Hopfield networks are the standard biologically plausible model of long-term memory, relying on Hebbian plasticity for storage and attractor dynamics for recall. In contrast, memory-augmented neural networks in machine learning commonly use a key-value mechanism to store and read out memories in a single step. Such augmented networks achieve impressive feats of memory compared to traditional variants, yet it remains unclear whether they can be implemented by biological systems. In our work, we bridge this gap by proposing a set of biologically plausible three-factor plasticity rules for a basic feedforward key-value memory network. Keys are stored in the input-to-hidden synaptic weights by a “non-Hebbian” rule, controlled only by pre-synaptic activity, and modulated by local third factors which represent dendritic spikes. Values are stored in the hidden-to-output weights by a Hebbian rule, with the pre-synaptic neuron selected through softmax attention which represents recurrent inhibition. The same rules are recovered when network parameters are meta-learned. Our network performs on par with classical Hopfield networks on autoassociative memory tasks and can be naturally

extended to correlated inputs, continual recall, heteroassociative memory, and sequence learning. Importantly, since memories are stored in slots indexed by hidden layer neurons, unlike the fully distributed representation in the classical Hopfield network, they can be individually selected for extended storage or rapid decay. Finally, our memory network can easily be incorporated into a larger neural system, either as a memory bank for an external controller, or as a fast learning system used in conjunction with a slow one. Overall, our results suggest a compelling alternative to the classical Hopfield network as a model of biological long-term memory.

3-002. Local dendritic balance enables the learning of efficient representations in networks of spiking neurons

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How can neural networks learn to efficiently represent complex and high-dimensional inputs via local plasticity mechanisms? Classical models of representation learning assume that feedforward weights are learned via pairwise Hebbian-like plasticity. Here, we show that pairwise Hebbian-like plasticity only works under unrealistic requirements on neural dynamics and input statistics. To overcome these limitations, we derive from first principles a learning scheme based on voltage-dependent synaptic plasticity rules. Here, recurrent connections learn to locally balance feedforward input in individual dendritic compartments, and thereby can modulate synaptic plasticity to learn efficient representations. We demonstrate in simulations that this learning scheme works robustly even for complex high-dimensional inputs, and with inhibitory transmission delays, where Hebbian-like plasticity fails. Our results draw a direct connection between dendritic excitatory-inhibitory balance and voltage-dependent synaptic plasticity as observed in vivo, and suggest that both are crucial for representation learning.

3-003. A Theory of Coupled Neuronal-Synaptic Dynamics

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In recurrent circuits, neurons and synapses are coupled in an intricate dance: neurons influence synapses through activity-dependent plasticity, and synapses influence neurons by shaping network dynamics. While previous studies have analyzed recurrent circuits with static synapses, or synapses displaying short-term facilitation and depression, the impact of ongoing Hebbian plasticity on network behavior is not well elucidated. Such an understanding is required to map the full landscape of neural-circuit dynamics and to probe computational roles of dynamic synapses. To address this knowledge gap, we developed a dynamical mean-field theory for a model of coupled neuronal-synaptic dynamics. In this model, neuronal rates follow recurrent dynamics shaped by time-dependent synaptic weights that are modulated, in turn, by pre- and postsynaptic neuronal rates. We assumed that plasticity modulates each synapse about a random baseline strength. We show that neuronal-synaptic dynamics are much richer than neuronal dynamics alone. Hebbian plasticity generates slow chaos, while anti-Hebbian plasticity generates fast chaos with an oscillatory component. Studying the spectrum of the joint neuronal-synaptic Jacobian revealed that these behaviors manifest as differential effects of eigenvalue repulsion. Hebbian plasticity can generate chaos in a circuit that, without plasticity, would be quiescent. When Hebbian plasticity is sufficiently strong, a chaotic state coexists with stable nonzero fixed points. Finally, in the chaotic regime, halting plasticity can leave a stable fixed point of the neuronal dynamics, freezing the chaotic state. This phase of freezable chaos provides a natural mechanism for keeping a running copy of the instantaneous neuronal state and could shed light on features of general anesthesia. Overall, our work presents a theoretical framework for studying circuits in which synapses are dynamical variables on equal footing with neurons and elucidates several surprising dynamical characteristics of such circuits.

3-004. Top-down modulation in canonical cortical circuits with inhibitory short-term plasticity

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Inhibitory neurons in the cortex are highly diverse in terms of anatomy, electrophysiology and functions. In the mouse cortex, three major classes of interneurons expressing parvalbumin (PV), somatostatin (SST) and vasoactive intestinal peptide (VIP) constitute more than 80% of GABAergic interneurons. Together with excitatory (E) neurons, they form a canonical microcircuit relevant for cortical computations. Multiple experimental studies have revealed that this canonical microcircuit can exhibit counterintuitive nonlinear behavior. More specifically, the circuit can perform response reversal whereby depending on the presence of visual input, top-down modulation via VIP affects SST response oppositely (Fu et al., 2014; Pakan et al., 2016). Recent computational work has showed that static networks with nonlinear neuronal input-output functions can generate response reversal (del Molino et al., 2017). Yet, whether neuronal nonlinearities underlie these computations in the cortex is contentious (van Vreeswijk and Sompolinsky, 1998; Ahmadian and Miller, 2021). In contrast to static synapses widely assumed in computational studies, synapses in the brain are subject to short-term plasticity (STP) on a time scale of milliseconds to seconds. In particular, inhibitory synapses exhibit more pronounced short-term dynamics than excitatory synapses (Campagnola et al., 2021). How these experimentally identified short-term plasticity mechanisms shape network dynamics and the above mentioned computations is largely unknown. Here, we demonstrate that inhibitory short-term plasticity enables response reversal without the requirement for neuronal nonlinearities. We further identified that PV-to-E short-term depression provides the dominant influence on response reversal over other STP mechanisms. By examining the relationship between response reversal and inhibition stabilization, we found that PV stabilization is neither a necessary nor sufficient condition to have response reversal, whereas SST stabilization is a necessary but not sufficient condition to have response reversal. In summary, inhibitory short-term plasticity enables the network to perform nonlinear computations, allowing us to make experimentally testable predictions.

3-005. Linking neural dynamics across macaque V4, IT, and PFC to trial-by-trial object recognition behavior

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Primates exhibit a remarkable ability to rapidly and accurately recognize visual objects in their central field of view. Based on accurate estimates of object identity from neural population activity and the object-specific behavioral deficits observed after cortical perturbation, previous work has identified the primate ventral visual cortex as a critical brain circuit for core object recognition. In addition, our recent work has demonstrated that the ventrolateral prefrontal cortex (vlPFC; recurrently connected to the ventral stream) is also critical for robust object recognition. In this study, we ask: is there a common neuronal basis (e.g., in vlPFC? in IT cortex?), and a simple (e.g., linear) transformation that can account for various levels of behavioral measurements? We performed large-scale (multi-electrode) recordings in areas V4, IT, and vlPFC while monkeys performed a battery of binary object discrimination tasks. We tested ~10,000 neural linking models (hypotheses) that comprised various spatial (brain areas: V4, IT, vlPFC) and temporal (integration windows) pooling algorithms. We then determined how accurately those models predict macaque behavior at the level of overall performance, object-level confusions, image-level difficulty, and trial-by-trial choices. We observed that a specific subset of IT-based linking models that integrate weighted summations of neural activity exhibited significantly higher trial-by-trial choice consistencies (our finest-grained behavioral measurements) with the monkeys' behavior than those constructed from V4, or vlPFC responses. Therefore, despite being downstream of the IT cortex, our results provide evidence against a vlPFC readout model. Together with prior work, we speculate that, vlPFC might be part of a specialized circuitry (including the ventral stream) to enable more robust recognition while the behavioral read-out is primarily IT-based. Apart from shedding light on the neural underpinnings of primate visual object recognition, our results provide algorithmic guidance to improve current computer vision models that are typically less robust and outperformed by humans.

3-006. Selective signal processing by spontaneous synchronization

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Neural information processing in dynamic, natural environments requires the brain to flexibly allocate limited computational resources to varying task demands. One example is selective attention in the visual system, which allows to preferentially route signals from behaviourally relevant stimuli to downstream visual areas, while suppressing irrelevant visual information. It is an open question which neural mechanisms realize selective routing, and how this process is controlled. Here we propose that spontaneous synchronization in recurrent networks is the key mechanism for selective processing. We study a hierarchical network consisting of recurrently coupled populations of spiking neurons which send activation to a common receiver/output population. The network is driven by two external signals of which one has to be routed to the output, while the other signal has to be ignored. Communication takes place via propagation of spike avalanches between sending and receiver populations. Routing is established by releasing inhibition from control populations which enhance avalanche generation and increase sizes of synchronous events carrying the information from the attended stimulus. Our framework provides a unifying account for selective information transfer through the visual hierarchy while reproducing a series of key experimental observations, such as typical rate modulations induced by attention in different visual areas, and the emergence of gamma oscillations and inter-areal phase synchronization. In contrast to previously proposed routing schemes based on oscillatory dynamics such as Communication-through-Coherence, selective routing can be established quickly since it does not need an intricate control scheme organizing the phase relationship between different oscillatory units. In addition, it proposes a simple and biophysically plausible control mechanism in form of a population with a critical dynamics, which becomes engaged by attention and then boosts generation of synchronous events for enhancing signal transfer.

3-007. Learning accurate path integration in ring attractor models of the head direction system

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Head direction (HD) cells track an animal's head direction in darkness by integrating angular velocity signals, a phenomenon called path integration (PI). Ring attractor models for angular PI have received strong experimental support. To function as integrators, HD circuits require precisely tuned connectivity, which is costly to pass down genetically. This suggests that synaptic plasticity is crucial in setting up these circuits.

We propose a network model in which a local, biologically plausible learning rule adjusts synaptic efficacies during development, guided by supervisory allothetic cues. The learning rule is inspired by layer-5 pyramidal neurons assumed to be the fundamental associative unit in the cortex, where backpropagating action potentials implement coincidence detection. The learning rule contains an anti-Hebbian component which performs predictive coding, whereby idiothetic inputs get associated with allothetic inputs that arrive at another compartment, so that the former can predict the latter. Applied to the *Drosophila* HD system, where such a segregation of inputs exists, the model learns to path-integrate accurately for the full range of angular velocities that the fly displays, and develops a connectivity strikingly similar to the one reported in experiments. The mature network is a quasi-continuous attractor (CAN), and reproduces key experiments in which optogenetic stimulation controls the internal representation of heading, and where the network quickly remaps to integrate with different gains akin to experiments conducted in augmented reality in rodents.

Our model proposes a general framework to learn gain-1 PI, even in architectures that lack the physical topography of a ring, like the HD system in mammals. Finally, we develop a tractable reduced model that exploits circular symmetries present in the full network, explains how the latter solves credit assignment, and offers a rigorous mathematical framework to study the self-organization of CANs for angular PI in general.

3-008. Neural Circuit Architectural Priors for Motor Control

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Artificial neural networks (ANNs) for simulated motor control and robotics often adopt generic architectures like fully connected multi-layer perceptrons (MLPs) and randomly connected recurrent neural networks (RNNs). While general, these tabula rasa architectures rely on large amounts of experience to learn, and their internal dynamics are difficult to interpret. In nature, animals are born with highly structured connectivity in their nervous systems shaped by evolution; this innate circuitry acts synergistically with learning mechanisms to provide inductive biases that enable most animals to function well soon after birth and improve abilities efficiently. Convolutional networks inspired by visual circuitry encode the inductive biases of spatial locality and weight sharing to improve data and parameter efficiency for vision. It is unknown the extent to which ANN architectures inspired by neural circuitry can yield useful inductive biases for other domains.

We asked what advantages biologically inspired network architecture can provide in the context of motor control. Specifically, we translate *C. elegans* circuits for locomotion into an ANN model applied to a simulated Swimmer agent. In contrast to previous work on neuromechanical models of movement, our model is designed within the abstract discrete-time ANN framework and is fully differentiable, enabling parameters to be trained with reinforcement learning (RL) and evolution strategies (ES) just like standard MLPs. Further, our model controls a body significantly different from the original.

On a locomotion task, our architecture achieves good initial performance and asymptotic performance comparable with MLPs, while dramatically improving data efficiency and requiring orders of magnitude fewer parameters. Our architecture is more interpretable and generalizable to new body designs. An ablation analysis shows that principled excitation/inhibition significantly contributes to learning. Our work demonstrates several advantages of and design principles for ANN architectures inspired by systems neuroscience and suggests a path towards modeling more complex animals.

3-009. Hebbian plasticity with a predictive component enables local learning in deep networks

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Learning in the brain is thought to be largely unsupervised since the bulk of an animal's natural experience arrives neither with associated reinforcement signals nor explicit supervisory signals. A compelling account of unsupervised learning in animals is provided by the notion that the brain learns by trying to predict the future, thereby identifying statistical redundancies in sensory inputs over time. Based on this principle, self-supervised learning (SSL) techniques have enabled deep artificial neural networks (ANNs) to achieve competitive results on challenging perceptual tasks. SSL attempts to minimize the representational distance between inputs that are semantically related or temporally adjacent, while maximizing the distance between inputs that are not (negative samples). Importantly, this objective enables learning even when applied in a layer-local manner, suggesting that local learning rules derived from SSL objectives could provide a novel approach for understanding unsupervised learning in the brain. However, a central problem with this interpretation is the difficulty of envisioning how biological systems could access negative samples, without which current SSL methods suffer from representational collapse, wherein ANNs learn a trivial mapping from every input to a single representation vector.

Here, we address this issue by developing negative-sample-free SSL objectives that remain amenable to optimization through local learning rules. Moreover, we show that the resulting learning rules are closely related to classical Hebbian plasticity, and primarily differ in the additional predictive term. We demonstrate through a series of tasks that the predictive term steers learning towards prioritizing slow, predictive features whereas the Hebbian term prevents collapse. Furthermore, we show that this mechanism is crucial for learning complex features in deep ANNs. In summary, we develop learning rules for non-contrastive SSL that are largely consistent with Hebbian plasticity, with key differences which indicate novel mechanisms that might be crucial for functional representation learning in the brain.

3-010. Meta-learning biologically plausible feedback learning rules

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Learning in cortical multi-layer networks is thought to occur through spatially and temporally local synaptic plasticity aided by ubiquitous feedback connections from upper layers. However, the known biologically plausible learning rules for such networks are yet to reach the high performance of the machine learning algorithms, such as backpropagation [1], on difficult tasks that the brain is capable of solving. It has been shown that one of the obstacles to backpropagation-like algorithm implementation in the brain, the ‘weight transport’ problem, can be overcome with initially random feedback connections [2] undergoing local synaptic plasticity [3,4]. Nevertheless, the gap in performance still remains [4,5]. Here, we use the optimization framework to further explore the space of effective biologically plausible feedback learning rules. More precisely, we meta-learn a parametric function defining the learning rule using gradient descent, building upon previous work with forward learning rules [6,7,8,9]. First, we show that we can rediscover a simpler variant of a previously proposed feedback learning rule [4]. We then extend our approach to learning rules that can encompass previously unexplored terms as well as increased biological realism, such as coupled forward and feedback computation. In summary, we show that meta-learning of learning rules can also be applied to the plasticity of feedback connections and provide insights on how multi-layer learning may be orchestrated in the brain.

3-011. Cerebro-cerebellar networks facilitate learning through feedback decoupling

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Behavioural feedback is critical for learning in the cerebral cortex, but such feedback is often not readily available which slows down learning. Inspired by deep learning algorithms, we introduce a systems-level computational model of cerebro-cerebellar interactions in which a cerebral recurrent network receives continuous cerebral feedback predictions from a cerebellar network, thereby decoupling learning in cerebral networks from future feedback. When trained in a simple sensorimotor task the model shows faster learning and reduced ataxia-like behaviours, in line with experimental observations. Next, we demonstrate that these results generalise to a range of more complex motor and cognitive tasks. Finally, we highlight a number of experimentally testable predictions regarding (1) how cerebral and cerebellar representations develop over learning, (2) how cerebral and task feedback properties shape the need for cerebellar predictions and (3) the differential impact of lesions of the cerebellar output and inferior olive. Overall, our work offers a novel theoretical framework of cerebro-cerebellar networks as feedback decoupling machines.

3-012. Subcortical modulation of cortical dynamics for motor planning: a computational framework

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Planning, a prospective form of short-term memory, is a cognitive function that has been predominantly attributed to the cortex. Recent experiments, however, have concluded that the thalamus and other subcortical structures participate in this function. A comprehensive computational framework to link neural dynamics and cognition in

the context of large-scale subcortical-cortical circuits is lacking.

In this computational study, we elucidated the dynamical mechanisms by which the cortex, thalamus and other subcortical structures jointly contribute to planning. Recurrent circuitry in the cortex generates stimulus-selective activity patterns, which are maintained by reciprocal corticothalamic projections across a memory epoch. Subcortical signals are routed through the thalamus to selectively modify these patterns, for example enabling execution after planning. We refer to this dynamical process as subcortex control of activity modes, as the cortical activity patterns ('activity modes') are low-dimensional in comparison to the number of neurons that are modulated by the task.

We evaluated the implications of subcortex control by simulating networks of interconnected thalamic and cortical 'rate' units in the context of a motor planning task. In tight link with electrophysiological data from mice, we identified subcortical excitatory and inhibitory contributions to the planning computations during the memory epoch. Our model predicts that the distinct computational roles of the pars reticulata (SNr) and thalamic reticular nucleus (TRN) during planning (Wang et al., 2021) are a result of their specific selectivity-dependent connectivity patterns with the thalamus. Moreover, the 'switch' from movement planning to execution (Inagaki et al., 2021) is instantiated by a midbrain-mediated thalamic burst, which uncovers a latent motor instruction that is stored in deep cortical layers during the memory epoch. Overall, we propose a novel framework to analyze planning computations in terms of cortical activity modes, which are shaped by subcortical structures via the thalamus based on task demands.

3-013. Contextual modulation of mesoscale functional connectivity

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Cognitive flexibility involves adapting behaviour to changing rules or contexts by modifying input-output mappings of brain-wide networks to achieve context-appropriate behaviour. This process relies on distinct neural representations of different rules or contexts in multiple brain regions, as well as changes in functional connectivity across brain regions. While context-dependent changes in neural responses have been studied locally in various brain regions, it is not clear to what extent different contexts lead to changes in functional connectivity between brain regions. We imaged widefield calcium activity from the entire dorsal cortex of mice as they switched between two distinct contexts in an attention-switching task. Different task contexts were distinctly represented across multiple cortical areas with both increases and decreases in average activity levels, which could not be accounted for by overt movements. These average activity changes were observed in both sensory and motor areas and were present both during baseline and stimulus-evoked periods. We performed locally selective spectral clustering to segment the cortex into functional parcels and used correlations in activity between these functionally defined regions to obtain measures of cortex-wide functional connectivity. Different task contexts were associated with widespread, systematic changes in functional connectivity. While some regions showed uniform, cortex-wide changes in functional connectivity, the majority of regions showed a heterogeneous distribution of increased and decreased functional connectivity distributed across different brain regions. Interestingly, during visual attention, visual and retrosplenial cortex showed the greatest increase in functional coupling to most other regions of the brain. These results demonstrate that changes in mesoscale functional connectivity provide a substrate for flexibly rerouting information across brain-wide networks with changing contextual demands.

3-014. Multi-region Poisson GPFA isolates shared and independent latent structure in sensorimotor tasks

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Identifying how brain regions work together to process inputs and generate behavior is a central goal in systems neuroscience. Recently, there has been a surge of interest in characterizing communication between brain regions and shared variability in multi-region neural recordings. In this work, we use a multi-region latent variable model (LVM) to identify computations shared-across and independent-to-specific brain regions in spiking neural population data from two different animals. Here, we use a multi-region latent variable model (LVM) to identify computations shared-across and independent-to-specific brain regions in spiking neural population data from two different animals. Our model is an extension of Gaussian Process Factor Analysis with Poisson observations (PGPFA) that separates per-trial neural activity into shared and independent components via a partitioned linear mapping. This model is distinct from previous approaches in that it is 1) not directional, i.e. there is no regression or delay across regions, 2) it uses an appropriate likelihood for spiking data (Poisson), and 3) it does not make strong assumptions about the latent state such as linear dynamics. Rather, it characterizes region-specific and global variability based on latent functions characterized only by their smoothness. We use this multi-region PGPFA model to understand shared and independent latent structure during sensorimotor tasks across two neural datasets: one, lateral intra-parietal area (LIP) and frontal eye field (FEF) electrophysiological recordings during a delayed target visual task in macaques, and the second, silicon probe (Neuropixels) recordings from anterior and posterior striatum during an evidence accumulation task in rats. We find that our model is able to simultaneously uncover both ramping-like structure in per region latents, and rotational dynamics in latents shared across regions. We also find that error signals are more prominently seen in shared structure, whereas stimulus preference is transient in shared structure, but sustained in specific brain regions.

3-015. Flexible inter-areal computations through low-rank communication subspaces

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Neural computations underlying complex behavior implicate multiple brain regions and large-scale, multi-site recordings from behaving animals are becoming increasingly common. Based on simultaneous recordings across the visual cortex (V1, V2, and V4), a recent hypothesis posits that brain regions communicate through low-dimensional subspaces [Semedo et al. (2019, 2021)]. In particular, it was found that these communication subspaces are not fully aligned with the internal variability of individual areas, with some information remaining in a private subspace and the rest being communicated through a shared subspace. Most theoretical works, however, focus on modeling individual regions, with multi-area interactions only starting to be explored [e.g. Perich & Rajan (2020)]. Due to the lack of theoretical frameworks, the dynamical mechanisms governing communication through subspaces and their implications for behaviorally meaningful computations are still unclear.

Here we present a mechanistic model of the communication subspace hypothesis based on low-rank recurrent neural networks [Mastrogiovanni & Ostojevic (2018)]. Concretely, we focus on a two-area network (representing A1 and PFC) that implements a context-dependent decision-making task, similar to experiments with rats [Rodgers & deWeese (2014)]. Considered in isolation, the A1 network represents incoming stimuli, while the PFC network generates a sustained representation of context. Task-solving computations emerge only when the two networks are connected through low-rank subspaces. Specifically, context information was shared through a PFC→A1 communication subspace and led to the computation of a context-dependent decision in A1 that was propagated through an orthogonal A1→PFC subspace. In contrast, stimuli information remained in a private subspace of A1, similar to what we found in single-unit recordings from rat's A1. Altogether, our model offers a mechanistic implementation of the communication subspace hypothesis, which provides a test-bed for statistical inference of multi-area interactions and derives specific predictions for analyses of multi-region recordings.

3-016. Neuronal implementation of the representational geometry in prefrontal working memory

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Representational geometry is a prevalent approach to abstract and investigate population coding derived from the activities of individual neurons. However, the same representational geometry can be implemented by neurons in different ways, which implies different potential readout mechanisms. Leveraging the biological constraint

of sparsity of readout synapses, we identified the biologically meaningful sparse components that express the geometry of working memory representations in primate prefrontal cortex (PFC). The dominant neuron groups corresponding to each component had distinct electrophysiological properties. We found that memorized information was represented in a sequential manner by these neuron groups that followed the task requirements. A recurrent neural network (RNN) model was trained to reproduce the firing rates in the PFC population. The RNN's accuracy dropped when the sequential sparse implementation in the data was destroyed, suggesting the necessity of this specific implementation to the observed activity in PFC. This study provides the perspective of neuronal implementation as an important complement to representational geometry, which helps bridge the gap between single-neuron activity and population-level dynamics.

3-017. Learning generalised representations of behaviour within the hippocampal-entorhinal-prefrontal system

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Recent theoretical work has proposed that hippocampus acts as a binding site for sensory stimuli and a task coordinate system, each represented in the entorhinal cortex. Since this coordinate system path-integrates, incoming sensory observations can be inferred rather than learned. Here, we show that (1) a similar mechanism can learn representations that predict actions rather than stimuli. This mechanism supports zero-shot action prediction – a significant departure from current theoretical frameworks for action-learning. (2) The learned representations resemble object-vector and landmark cells observed in the brain. (3) These representations can be controlled by simply gating memories, providing a potential mechanism for prefrontal cortex to select between goals. To achieve this, we extend the Tolman-Eichenbaum Machine (TEM) to include representations that both path-integrate and predict actions. In TEM, position representations are bound to sensory representations via hippocampal memories, with these memories retrievable via attractor dynamics. Here, we play the same trick but with position and action-predictive representations bound in hippocampus, meaning that action-predictive and position representations are arbitrarily composable. Now, 1) the same action-predictive representations can be learned, reused, and recombined at any position in space, thus actions can be predicted (and good behaviours taken!) in novel environments and contexts. 2) Memory retrieval can be modulated from prefrontal contextual signals, meaning the same action representation can be active in different positions depending on context. This allows different goals to be attended to within the same environment. In sum, we provide a mechanistic understanding of how action-predictive representations can be learned within the hippocampal-entorhinal system and controlled by prefrontal input. A companion paper shows that, once learned, these representations can be used to zero-shot optimal actions in complex structured environments. Together, these papers provide a theoretical foundation for the flexible context-dependent behaviour that is characteristic of animals but evades classical Reinforcement Learning algorithms.

3-018. Efficient task representations for habitual and model-based behaviour

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Higher-order brain activity can be quite complex, switching between fast, stimulus- or motor-driven dynamics, and slower, rising and falling persistent activity. Many of these activity motifs can be successfully modelled by recurrent neural networks (RNNs) that are trained on specific tasks. However, the training of RNNs is usually an ill-posed problem so that, at least in principle, multiple solutions exist for any particular task. Accordingly, a specific match of a trained RNN to data can be serendipitous, providing only limited insight into the reasons underlying the similarity. Here we take a normative approach by first stating the goal of an agent's internal task representation. We distinguish two goals: The goal of a 'habitual agent' (HA) is to take correct actions, while the goal of a 'model-based agent' (MBA) is to predict all ethologically relevant observations. We define these two

behavioural strategies within the framework of partially observable reinforcement learning. Each strategy imposes different constraints on the representation of task variables. Our main contribution here is to show how to find, among all representations consistent with the agent's goals, the one that eliminates all irrelevant information, thereby following the efficient coding hypothesis. We showcase this approach on a classical working memory task. Formally, we parameterize HA and MBA representations with switching linear dynamical systems regularized by an information bottleneck, which squeezes out all the information in the representation that is not needed to achieve the behavioural goal. In both agents, we find that efficient representations reproduce the key features of population activities recorded from the prefrontal cortex (PFC). However, only the MBA closely reproduces the persistent delay dynamics. In either case, the representational motifs are directly interpretable in terms of the goal they serve, thus yielding potential insights into the goals underlying higher-order brain representations.

3-019. Arithmetic value representation for hierarchical behavior composition

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The ability to compose new skills from a pre-acquired behavior repertoire is a hallmark of intelligence in humans and other animals. In deep reinforcement learning (RL), artificial agents can extract re-usable skills from past experience and recombine them in a hierarchical manner. It remains largely unknown, however, whether the brain similarly composes a novel behavior. Here we trained deep RL agents with the soft actor-critic (SAC) algorithm and studied their representation of RL variables during hierarchical learning. The objective of SAC is to maximize future cumulative rewards and policy entropy, which confer artificial agents with flexibility and robustness to perturbation. We demonstrate that the agents learned to solve a novel composite task by additively combining representations of previously learned values of actions from constituent subtasks. Sample efficiency in the composite task was further augmented by the introduction of a stochastic policy in the subtask, which endowed the agents with a wide range of action representations. These theoretical predictions were empirically tested in mice trained in the same behavior paradigm, where mice with prior subtask training rapidly learned the composite task. Cortex-wide two-photon calcium imaging across the subtasks and composite task revealed neural representations of combined action values analogous to those observed in the deep RL agents. These mixed representations of subtask action values in single neurons of mice were not observed in the agents when a new value function was constructed by taking the maximum of the subtask-related action values, highlighting the specificity of the additive operation. As in the case of the deep RL agents, learning efficiency in mice was enhanced when the subtask policy was made more stochastic. Together, these results suggest that the brain composes a novel behavior with a simple arithmetic operation of pre-acquired action-value representations with a stochastic policy.

3-020. Understanding rat behavior in a complex task via non-deterministic policies

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We trained five rats to perform a complex auditory-guided task in a large environment (diameter 160 cm) with twelve nose-poke ports. To obtain rewards, rats had to position themselves at specific locations indicated by sounds. Despite the nontrivial task, rats reached high success rates within two 70-minute sessions. We modeled the task as a Markov Decision Process. Observed rat trajectories resembled the model's optimal policies. However, while optimal policies were deterministic, observed behavior was non-deterministic. We introduced non-deterministic, information-limited policies that realize optimal reward rates under constraints on the Kullback-Leibler divergence from a default, non-informative policy (Tishby's complexity, TC). We estimated the TC of rat movement and nose-poking over more than 10 months by comparing observed behavior with TC-limited policies. Our model revealed a prolonged, large increase in the TC over time. Significantly, this prolonged behavioral refinement was not discernible via reward rates, and to our knowledge has not been described previously. The model also captured individual propensities for preferring some foraging strategies over others. Specifically, one strategy

required sharp-angled body-turns. By transiently altering the task structure, we successfully encouraged rats to increase their preference for that strategy. Concurrently, our model uncovered a permanent decrease in body-turn cost in every rat, with new costs that differed between rats but were constant over time within rat. Recording with chronically implanted silicon probes from the left insular cortex, we found that in many neurons, firing rates (averaged over ten minutes) strongly correlated with TC, computed in the same time periods. Significantly, our model is based on first principles of information theory, and does not employ ad-hoc measures of behavior. Thus, we present here novel insights into rat behavioral refinement over very long time scales, and introduce TC as a regressor for cortical activity.

3-021. Inferring implicit sensorimotor costs by inverse optimal control with signal dependent noise

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Normative computational models of sensorimotor behavior based on optimal feedback control with signal-dependent noise (Todorov, 2005) have been able to account for many phenomena including online corrections, redundancy, synergies, and uncontrolled manifolds of movements. In past research, a cost function needed to be assumed for the respective task, and agreement between the predictions of optimal behavior by the model and empirical movement trajectories had to be assessed. However, not all behavioral goals may be known *a priori* and costs internal to the subject such as biomechanical or subjective cognitive costs including effort are generally hard to measure independently. Thus, relating neuronal activities to sensorimotor behavior may miss crucial components.

Here, we show how a recently developed algorithm for inverse optimal control with signal-dependent noise allows inferring the cost function underlying behavior from observed trajectories. We use a formalization of sequential sensorimotor behavior as a partially observable Markov decision process and distinguish between the subject's and the experimenter's inference problems. Specifically, we employ a probabilistic formulation of the evolution of states and belief states and an approximation to the propagation equation in the linear-quadratic Gaussian problem with signal-dependent noise. We extend the model to the case of partial observability from the experimenter's point of view, in which internal states of the subject are unobserved by the experimenter.

First, we validate the algorithm using synthetic data of eye and reaching movements. Then, we apply this framework to experimental reaching data to infer the cost functions implicit in the subject's behavior. Additionally, we show how the subject's dynamic perceptual belief throughout the experiment can be inferred. Taken together, our approach enables recovering the costs and rewards implicit in sequential sensorimotor behavior, thereby reconciling normative and descriptive approaches in a computational framework, which should be of great value to researchers in sensorimotor neuroscience.

3-022. In silico manipulation of cortical computation underlying goal-directed learning

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While simple value-based learning efficiently predicts an outcome in a stable environment, goal-directed learning can deal with dynamic and uncertain environments¹. It is this complex nature that poses a challenge for experimental design to investigate such learning processes. For example, it is hard to predict how task manipulations affect the latent process of goal-directed learning. Here we present a computational framework of goal-directed task control to guide goal-directed learning. The proposed framework is based on an asymmetric two-player game setting: while a computational model of human RL (called a cognitive model) performs a goal-conditioned two-stage Markov decision task, an RL algorithm (called a task controller) learns a behavioral policy to drive the key variable (i.e., state prediction error) of the cognitive model to the arbitrarily chosen state, by manipulating the task parameters (i.e., state-action-state transition uncertainty and goal conditions) on a trial-by-trial basis. We fitted

the cognitive models individually to 82 human subjects' data, and subsequently used them to train the task controller in two different scenarios, minimizing and maximizing state prediction error, each intended to improve and reduce the motivation for goal-directed learning, respectively. The model permutation analysis revealed a subject-independent task control policy, suggesting that the task controller pre-trained with cognitive models could generalize to actual human subjects without further training. To directly test the efficacy of our framework, we ran fMRI experiments on another 21 human subjects. We confirmed the task controller successfully manipulates human goal-directed behavior. Notably, we found neural effects of the task control on the insular and lateral prefrontal cortex, the cortical regions known to encode state prediction error during goal-directed learning^{2,3}. Our work not only advances recent task optimization confined to simple decision-making tasks^{4,5} but also demonstrates the control effect at the behavioral and neural levels.

3-023. Identifying the control strategies of monkeys and humans in a virtual balancing task

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Primate neurophysiology has provided numerous insights into the neural mechanisms of short and stereotypical movements, such as center-out reaching, which are mainly guided by feedforward control. However, to understand highly interactive and feedback-driven behaviors, experimental paradigms are needed that involve continuous interactions with the world. One example of such paradigms is stick-balancing which requires constant integration of feedback for successful control. Recently, a simplified virtual implementation of the stick-balancing task was developed as the Critical Stability Task (CST), where monkeys and humans learned to balance an unstable system in a virtual environment. However, the control strategies to accomplish the task, as well as its neural underpinnings, remains to be examined. In theory, the task could be performed based on various control policies by prioritizing either the control of position or velocity of the system. This distinction, however, is particularly challenging to identify in the data as the unstable nature of the task leads to unique behavior at each attempt, with potentially different control policies at different trials. These variations render trial-averaging methods unsuitable as they fail to capture trial-specific control strategies. Here, we propose a generative-model approach at the level of behavior that successfully accounts for the behavioral features of monkeys and humans who performed the task under matching conditions. The model makes further predictions about the effect of different control strategies on how the task could be accomplished. These predictions were used to identify, at the single-trial level, the control priorities most likely used by monkeys and humans in each trial. These results provide a critical step towards understanding the neural activity associated with highly interactive sensorimotor behavior, and how such activity might represent different control priorities in the motor system.

3-024. Identifying changes in behavioral strategy from neural responses during evidence accumulation

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Recent studies in flies and rodents have shown that animals switch between a small number of 'behavioral states' during decision-making. However, the majority of studies infer these state switches only from behavioral measurements such as choices or movements. To provide greater insight into the internal processes that guide these switches, we developed a method for identifying state changes from behavioral measurements and neural responses. We applied this method to an evidence accumulation task studied in rats. Our method models trial-to-trial state switches with a hidden Markov model (HMM) and within-trial latent dynamics with a drift-diffusion model (DDM). The resulting model provides a 'DDM-HMM' account of state-dependent neural activity and behavior. We

applied this model to neural recordings in two brain regions, anterodorsal striatum and posterior parietal cortex, and found strong support for the hypothesis that neural responses switch states on a trial-to-trial basis and that these switches are informative about behavior. Parameters of the fitted model indicated that the accumulation dynamics underlying neural activity differed strongly between two different states. The model identified a low-noise ‘early-weighting’ state, where early stimuli were weighted more strongly than late stimuli, and a high-noise ‘leaky’ state, where stimulus information decayed during each trial. On trials in the low-noise state, neurons more strongly reflected accumulated evidence and task performance was better. Moreover, choice could be decoded accurately from neural activity in this state, while neural activity in high-noise state trials carried virtually no choice information. These findings suggest that rodents switch between behavioral strategies during decision-making, that a signature of these switches can be identified in neural responses, and that switches correspond to changes in specific cognitive ‘strategies’ for this task. Previous analyses of decision-making dynamics in well-trained animals have largely assumed a stationary brain state, an assumption that our results strongly call into question.

3-025. Divisive normalization shapes evidence accumulation during dynamic decision-making

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Perceptual decisions are ubiquitous and essential in life, and even in their simplest forms open a window into the neural mechanisms underlying cognition. However, the properties of decision mechanisms inferred in simple behavioral paradigms are not independent of the properties of employed stimuli and task. One key task property is the type of information provided by a single stimulus, which can be either stationary or dynamic. Stationary paradigms are based on evidence with fixed central tendency, often obscured by noise, whereas in dynamic paradigms the mean of the evidence can vary within the duration of the stimulus. Both types of evidence can be mapped on specific settings occurring in nature, but in scientific studies stationary paradigms have dominated. Here we introduce a novel dynamic, motion-direction discrimination task based on stimuli with rich, but controlled structure, which are well suited to characterize the dynamics of a decision process at fine timescales. Human participants were asked to report the prevalent direction of motion in a stimulus consisting of a random sequence of motion pulses (left or right) interleaved with static periods. We find that traditional models of evidence accumulation, although validated by decades of research with stationary paradigms, do not account for behavior in our task, even when augmented with non-linear mechanisms like boundaries, leakiness, or sensory adaptation. The key shortcoming of these models lies not in the nature of the accumulation process, but of the underlying evidence—only an accumulation process acting on a form of “relative” evidence, computed through a step of divisive normalization operating over time, closely captures the behavior, and explains otherwise puzzling, striking deviations from perfect accumulation. These findings point to a prominent, previously unrecognized, role for divisive normalization in evidence accumulation, which may prompt a re-interpretation of the mechanism of decision-making in stationary and dynamic paradigms.

3-026. How cerebellar architecture facilitates rapid online learning

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The cerebellum is critically involved in motor control, refining trajectories as movements are being executed. This requires fast, online learning. What features of cerebellar circuit structure make it particularly suited to online learning? The cerebellum has a distinctive circuit architecture in which each mossy fibre input typically projects to 250 granule cells, a population that comprises more than half of the neurons in the brain. Each granule cell forms ~4 synapses with mossy fibres. The main hypotheses for this sparse input expansion are that it facilitates pattern separation¹ and smooth function approximation. However, we currently lack a theory that explains why this architecture is suited to online motor learning. We show that the large input expansion effectively trades time for space, allowing rapid and accurate learning in an online context. We consider a cerebellar-like network tasked with simultaneously learning an internal model of a motor system, and using this model to better control motor output. Learning online introduces a narrow time window that severely limits the information available for synaptic plasticity mechanisms to appropriately adjust synaptic weights. We find that the effect of having limited information depends on the spread of the eigenvalues Hessian of the task error. As the input expansion

increases, the geometry of the error surface becomes more favourable for online learning, diminishing the effect of information error and allowing for faster learning. This suggests that the large energy cost associated with maintaining the majority of the brain's neurons might be an inevitable cost of precise, fast, motor learning. In contrast to existing theories that argue for a role of dimensionality expansions in pattern separation, we account for a role in online learning. We provide a new framework for computing the algorithmic error introduced in online learning and show how it can be mitigated by redundant connectivity.

3-027. Synaptic and mesoscale plasticity in auditory cortex of rats with cochlear implants

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Cochlear implants (CI) are neuroprostheses that restore hearing for deaf humans by delivering patterned pulses of current to the auditory nerve, bypassing the damaged sensory epithelium of the inner ear. Almost all CI users require adaptation periods to attain speech comprehension, which improves most rapidly in the first weeks to 6 months following CI activation [1]. In CI studies of deafened animals, training induces cortical map plasticity in primary auditory cortex (A1) of task-relevant stimuli [2, 3]. It remains unclear whether observed CI training-induced cortical plasticity in animal models relate to early adaptations in human CI users. To connect human and non-human studies of CI use, our experimental framework focuses on plasticity that may generalize to a broad range of auditory stimuli. First, we developed a 2-alternative forced choice (2AFC) task for sound frequency discrimination in both rats and humans. Rats completed the 2AFC task with high discrimination ($d' > 1$) after 2-3 weeks of acoustic (N=18) or CI training (N=5). Discrimination performance of human CI users (N=2) were similar to rats. Next, we performed whole-cell recordings from rat A1 neurons and measured excitatory and inhibitory postsynaptic currents (EPSCs) evoked by CI stimulation in untrained vs trained animals. Synaptic responses were highly irregular and long latency in untrained animals, resulting in poor excitatory-inhibitory correlation; in contrast, animals trained on the 2AFC task had A1 neurons with high excitatory-inhibitory correlation values. Lastly, we performed micro-electrocorticography (μ ECoG) recordings across A1. Using a supervised linear classifier, we found better classification of acoustic tones than CI stimuli. Chronic μ ECoG recordings over CI training showed increased heterogeneity in topographical representation of CI-evoked stimuli. Taken together, we have identified potential neural correlates that may underlie more generalized adaptations for improved encoding of CI stimulation following initial activation.

3-028. Reward modulates visual responses in mouse superior colliculus independently of arousal

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The superior colliculus (SC) is a major recipient of visual input in the mouse and controls innate approach and avoidance behaviours. Neurons in the superficial SC (sSC), which receives direct input from the retina, do not only process visual stimuli, but are also modulated by the animal's running speed and pupil-linked arousal, similar to modulations observed in the primary visual cortex. While these observations were made during passive viewing of visual stimuli, a major purpose of vision is to guide behaviour. We therefore asked whether, in the context of a behavioural task, visual activity in the sSC is modulated by states or variables other than pupil-linked arousal. We trained mice to perform a visual detection task, where they needed to detect a stimulus of varying contrast in the left or right visual field and then interactively move the stimulus towards the centre of the visual field. If no stimulus was presented, the mice had to refrain from moving the stimulus. After correct choices, the mice received water reward; after incorrect choices, auditory white noise was played instead. We expressed GCaMP6f in sSC neurons and used two-photon imaging to record neural activity in trained mice performing the task. Simultaneously, we monitored the mouse's pupil size. Similar to previous studies, we found that pupil-linked arousal modulated the visual responses of sSC neurons. Additionally and independently of this modulation, previous reward strongly increased the subsequent visual responses, while negative feedback was followed by weaker visual responses.

This modulation by previous feedback could not be explained by licking. Our findings show that visual responses of sSC neurons are strongly influenced by two independent state variables: pupil-linked arousal and previous reward. Future studies may reveal how these non-visual modulations help downstream processes in guiding behaviour.

3-029. VIP interneuron-mediated disinhibition does not interact with endogenous attention modulation in V1

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When animals attend to visual stimuli, neural responses in visual cortex show increased stimulus selectivity compared to viewing the same stimuli without attending. This increased stimulus selectivity is believed to underlie the improved behavioural detection and discrimination of attended stimuli and is a key neural correlate of cognitive control. However, the neural circuit mechanisms of attentional modulation are poorly understood. While GABAergic inhibitory circuits can strongly modulate cortical neural activity, it is unknown whether these circuits implement the attentional modulation observed in visual cortex. Vasoactive intestinal peptide (VIP) expressing interneurons in primary visual cortex (V1) receive top-down inputs from prefrontal cortex and exert disinhibitory control over pyramidal neurons by inhibiting somatostatin (SOM) expressing interneurons. We hypothesised that VIP expressing interneurons are involved in the endogenous attentional modulation of V1 stimulus responses. We performed chronic *in vivo* two-photon calcium imaging of neurons in layer 2/3 of V1 in mice performing an attention switching task. VIP cells in V1 were either optogenetically activated or inhibited, while simultaneously imaging the calcium activity of the network. Attention produced a robust increase in neural response selectivity, through a combination of boosting and suppression of responses. Activation of VIP cells produced a strong additive modulation of pyramidal neurons both during passive viewing of visual stimuli, and during active visual discrimination. However, the VIP-induced modulation did not interact with the attentional modulation of firing rates. Similarly, inhibition of VIP cells during the task did not affect the attentional modulation of pyramidal neuron responses. These results show that VIP interneurons play a minor role, if any, in producing attentional modulation, and suggest a re-evaluation of existing models of top-down response modulation in visual cortex.

3-030. A parallel channel of state-dependent sensory signaling by the cholinergic basal forebrain

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Cholinergic activity is thought to play an important role in learning and the control of brain state. Multiple studies have shown that pairing external phasic stimulation of the cholinergic basal forebrain (CBF) with a sensory stimulus drives long-lasting sensory cortical plasticity, implicating the CBF as a potential substrate for associative learning. For this to be ecologically valid, we hypothesized that CBF projections to the sensory cortex should exhibit phasic signaling that is temporally-synchronous with sensory-evoked responses in cortical neurons. Intrinsic sensory-evoked responses have previously been observed in CBF neurons but their spatiotemporal dynamics in downstream regions (i.e. sensory cortex) have not been systematically characterized. Here, we used simultaneous two-channel, two-photon imaging to examine sensory-evoked responses of CBF axon projections and cortical neurons in the ACx in mice passively listening to auditory stimuli. We observed striking, non-habituating, phasic axonal responses to neutral auditory stimuli that display an inverted-U-shaped relationship with tonic cholinergic activity – a known neural correlate of brain state. Interestingly, individual axon segments exhibited heterogeneous tuning, allowing tone frequency to be decoded from population activity. However, despite this microscopic heterogeneity, we observed no evidence of mesoscopic tonotopy in CBF axons. Furthermore, our two-color imaging approach revealed that the tuning of cortical neurons and nearby axonal segments was uncoupled, suggesting that the ACx receives de-correlated auditory signals from the feedforward auditory pathway and the CBF. Finally, we demonstrated that chemogenetic inactivation of the auditory thalamus abolished the frequency tuning of CBF axons. Our work proposes a novel, non-canonical function of the CBF in which it receives input from the auditory

thalamus, modulates these signals based on brain state, and then projects the multiplexed signal to the ACx. These signals are temporally-synchronous with cortical responses but differ in their tuning, providing a potential mechanism to influence cortical sensory representations during learning.

3-031. A biophysical account of multiplication by a single neuron

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Nonlinear, multiplication-like operations carried out by individual nerve cells greatly enhance the computational power of a neural system, but our understanding of their biophysical nature is scant. We pursue this problem in the Drosophila ON motion vision circuit, where we record the membrane potentials of direction-selective T4 neurons and of all their columnar input elements in response to visual and pharmacological stimuli *in vivo*. Our electrophysiological measurements and conductance-based simulations suggest a passive supralinear interaction between two distinct types of synapse on T4 dendrites. We show that this multiplication-like operation arises from the coincidence of cholinergic excitation and release from glutamatergic inhibition. The latter depends on the expression of the glutamate-gated chloride channel *GluCl α* in T4 neurons, which sharpens the cells' directional tuning and shapes the animals' optomotor behaviour. Interacting pairs of shunting inhibitory and excitatory synapses have long been postulated as a way of implementing an analogue version of a logic AND gate, which is integral to theories of motion detection, sound localization, and sensorimotor control.

3-032. Characterization of neuronal resonance and inter-areal transfer using optogenetics

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Neural computation depends on inter-areal signal transformations, which are determined by the input-output (I/O) functions of individual and networks of neurons. Due to intrinsic neuronal properties and inter-neuronal interactions, networks can show preferences for synaptic inputs in certain frequencies, e.g. in the form of lowpass filtering or resonance [Izhikevich 2003, Cardin et al 2009, Lewis et al 2021, Pike et al 2000]. High-density silicon-probe recordings were made from area V1 and V2 in awake mice. We used optogenetic stimulation (continuous (1s), pulses (5ms), sinusoids) with an opsin having fast kinetics (Chronos) to gain precise temporal control over specific cell populations and to study the I/O functions of (1) V1 neurons expressing the opsin, (2) excitatory and inhibitory V1 and V2 neurons not expressing the opsin. We determined the dependence of firing rates, phase-locking, coherence and power on stimulation frequency. Spike-laser phase-locking increased steeply towards higher frequencies, indicating that opto-tagged excitatory neurons high-pass filtered optogenetic inputs. This was explained by the narrowing of phase distributions with frequency, suggesting a non-linear I/O transformation. Fast-spiking interneurons closely followed the phase-locking of excitatory neurons without exhibiting resonance. Surprisingly, non-opto-tagged excitatory neurons, both in V1 and V2, phase-locked predominantly to low-frequency optogenetic inputs. Next, we compared different measures of I/O transformations. Strikingly, opto-tagged excitatory neurons responded with similar firing rates to all optogenetic input frequencies. Likewise, spike-field coherence was relatively flat, indicating optogenetic inputs were reliably encoded at all frequencies. Thus, in the absence of synaptic filtering, neurons encode and respond to different frequencies very similarly, despite being more phase-locked to high frequencies. Together, these findings indicate a major difference between the filtering of synaptic and optogenetically-induced inputs. They further suggest that area V1 does not exhibit band-pass resonance and that local as well as inter-areal synaptic communication is most effective at low frequencies.

3-033. Cortical inhibitory tuning reflects the Fourier components of locally encoded features

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Inhibition plays an important role in shaping neural representations. Still, it is unclear whether inhibitory neurons merely refine the tuning of excitatory (EX) neurons or encode a parallel neural representation. We aimed to uncover the principles of inhibitory tuning in the cortex, using a simple system encoding a 1-dimensional sensory signal - the head-direction (HD) system. To this end, we recorded populations of neurons in the postsubiculum (PoSub), the primary cortical hub of the HD system. While excitatory HD cells had narrow receptive fields, fast-spiking (FS) interneurons had broad and multi-modal tuning curves. FS cell receptive fields rotated in concert with HD cells during environmental manipulation and their temporal coordination with HD cells during sleep was similar to wakefulness, indicating that they are functionally integrated into the HD circuit. On average, their tuning showed the same Fourier spectrum as HD cells, with the power centered in the first three components. However, while the average FS cell spectrum reflected the HD cell spectrum, individual spectra were heterogeneous. To determine the origin of FS tuning, we performed selective disinhibition of thalamic input to PoSub. We observed exclusively multiplicative gain in HD cell tuning and exclusively additive gain in FS cell tuning, indicating that FS cells receive homogenous HD input from the thalamus. These findings suggest that tuning of FS cells is a Fourier transformation of the signal encoded by EX cells and provides new constraints on biologically plausible neural network models involving inhibition.

3-034. Inception loops reveal novel spatially-localized phase invariance in mouse primary visual cortex

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To decipher the algorithm of perception, it is important to characterize neural tuning functions and identify the directions of maximal sensitivity and invariance to stimulus features. To this end, parametric stimuli are typically used, but they make strong assumptions about the stimulus features to which neurons are selective and invariant. Recently, the “inception loop” paradigm was developed, which combines large-scale neuronal recordings with deep learning system identification models which are trained to predict the responses of neurons to arbitrary stimuli. Inception loops have been used to find and verify the most exciting inputs of neurons (MEIs) in mouse primary visual cortex (V1). The MEIs exhibited complex spatial features deviating strikingly from the textbook Gabor-like optimal stimuli for V1, challenging decades-old dogma of V1 representations. Here, we extend these deep learning imaging synthesis methods to study neural tuning invariance. The progressive increase in invariance of neuronal responses to nuisance transformations of visual features is a hallmark of hierarchical visual processing. However, a systematic characterization of neural tuning invariance across sensory systems is currently missing. We introduce “diverse exciting inputs” (DEIs), a synthesized set of diverse images that strongly excite neurons, and verify the high activation of these diverse images *in vivo*. We found that the DEIs of many neurons in mouse V1 exhibit novel types of invariances. Empirically, these tuning invariance can be mostly char-

acterized by phase shifts within a spatially localized region, a property that cannot be explained by the canonical Hubel & Wiesel simple-complex cell model. Thus, we propose a localized-phase-invariant model to explain these observed single-neuron invariances in mouse V1. Taken together, we introduce a novel framework to study sensory processing using deep learning and discover a novel type of single-neuron invariance in mouse primary visual cortex.

3-035. Learning to combine sensory evidence and contextual priors under ambiguity

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The neocortex is composed of a hierarchy of regions and is thought to perform sensory inference by combining two complementary information streams: 1) a feedforward stream propagating bottom-up in the hierarchy, representing sensory information, and 2) a feedback stream propagating top-down, representing expectations or priors derived from contextual information integrated in higher-order associative regions. Within a cortical region, pyramidal neurons in layers 2 & 3 are a key cellular component of the feedforward pathway which integrate these two streams at their basal and apical dendrites, respectively. How they combine these two streams to update feedforward representations based on contextual priors is unknown. Here we propose a functional model of integration of these two streams at basal and apical compartments of pyramidal cells based on known physiological principles. We developed an ambiguous MNIST dataset that implements parameterized ambiguity between digits by conditional generation, and trained the feedback projection onto apical dendrites in our model by gradient descent to complement the sensory representation at the basal dendrites and resolve ambiguity. Specifically, when input stimuli are ambiguous, contextual priors arriving at the apical dendrites are integrated in the sensory representation to rescue classification performance. Importantly, when stimuli are unambiguous, contextual priors which oppose sensory evidence are appropriately ignored. Our proposed model allows analysis of candidate local learning rules that could support learning of such models, and provides insight into how pyramidal neurons and neocortical circuitry could integrate sensory and contextual information to learn predictive models of the world.

3-036. Predictability in the spiking activity of mouse visual cortex decreases along the processing hierarchy

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Understanding neural information processing is extremely challenging. This is because often, it is not even clear what information neurons are really processing. However, we can access the dynamic fingerprint of the processing with information-theoretic and statistical methods. Recent work has thus focused on the autocorrelation time of neural activity, also termed intrinsic timescale, which serves as a proxy for how long information is stored in the activity of the network. This work revealed a hierarchy of intrinsic timescales, which suggests that along the processing hierarchy, the brain forms higher-level representations through an enhanced and long-lasting integration or maintenance of past information. Intuitively, one could expect that an enhanced integration of past information does not only affect the timescale, but also increases the "predictability", i.e. the proportion of predictable information in neural spiking. To test this hypothesis, we estimated predictable information in highly parallel electrophysiological recordings of the mouse visual cortex. We could recover the result that the intrinsic timescale (measured both in terms of the autocorrelation time and as generalized timescale of predictable information) increases for higher cortical areas. Surprisingly, however, we found that the predictability decreases along the cortical hierarchy. Although surprising at first, this decrease in predictable information is in line with hierarchical

predictive coding, where, at each processing stage, predictable information is cancelled by internal predictions. Thus, our results provide a new perspective on hierarchical processing in mouse visual cortex, where higher-level representations of inputs are formed through an enhanced and long-lasting integration of past information, which is accompanied by a predictive coding scheme to implement inference in a hierarchical internal model.

3-037. Mechanistic modeling of *Drosophila* neural population codes in natural social communication

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Naturalistic animal behavior can now be efficiently collected and annotated, but understanding brain function in natural settings remains challenging. It is difficult to record neural activity in freely moving animals, and complex statistics and lack of stimulus repeats preclude traditional analyses. While a popular approach is to first identify reduced, data-driven behavioral variables prior to seeking neural correlates, we propose a complementary approach: comparing a suite of mechanistic models, directly fit to behavior, that embody competing hypotheses about single-cell or population neural codes. Using recordings from a large set of fly auditory neurons to design several such models, we in turn fit these to a separate, naturalistic fly courtship dataset. In doing so we find that female locomotion is best predicted by a distributed population representation of the male's complex and hallmark courtship song. This best-fit population code requires multiplicative adaptation and heterogeneous timescales across the population, predicting female motor output far better than the best single-neuron code. Moreover, we find the behaviorally predictive axis to be nearly orthogonal to the dominant axes of neural variability, suggesting behavior may be modulated largely by deviations around larger ongoing neural fluctuations. This work establishes invertebrate brains as a potentially rich system for studying distributed processing of temporally complex communication signals and illuminates a viable approach for gaining insight into neural population codes from pure natural behavior data.

3-038. Unsupervised sparse deconvolutional learning of features driving neural activity

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Understanding the activity of single neurons in relation to features in the environment is the first step in many neuroscience studies. We propose a method using algorithm unrolling, an emerging technique in interpretable deep learning, to deconvolve single-trial neuronal activity into interpretable components. Specifically, we model the firing rates of single neurons using a set of kernels characterizing neurons' responses to time-sensitive sparse events/stimuli. The kernels can be either unique or shared across the population and are weighted by codes whose amplitude and timing are trial-specific. Our inference results in a deep sparse deconvolutional encoder and, unlike sequential deep encoder approaches, is based on a generative model; hence, the learned parameters and encoding are directly interpretable. First, we characterize the performance regime of our method; this guides end users to understand the model's accuracy and limitations. Second, we apply our method to deconvolve overlapping signals in the response of dopaminergic neurons to rewards of varying size. Previous studies have suggested that reward prediction error responses of dopaminergic neurons are modulated by two components: salience and value. However, this multiplexing is often ignored or analyzed using ad-hoc windows to estimate the two contributions. Here, we deconvolve the two factors in an unsupervised manner; one kernel corresponds to salience whose code is common across reward sizes and another to value whose code changes as a function of reward amount. We show that the inferred codes are more informative than firing rates estimated using ad-hoc

windows. Third, we study the response of piriform cortex neurons to brief odor pulses delivered at random time across trials. Based on the learned neural impulse responses, we uncover 3 clusters of response types across the population. Overall, we propose a novel method to deconvolve into interpretable components the factors driving neural activity in single trials.

3-039. An interpretable dynamic population-rate equation for adapting non-linear spiking neural populations

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Recently, the field of computational neuroscience has seen an explosion of the use of trained neural networks (NNs) to model patterns of neural activity. These NN models are typically characterized by tuned interactions between rate 'units' whose dynamics are governed by smooth, continuous differential equations. However, the response of biological single neurons is better described by all-or-none events - spikes - that are triggered in response to the processing of their synaptic input by the complex dynamics of their membrane. One line of research has attempted to resolve this discrepancy by linking the average firing probability of a population of simplified spiking neuron models to rate dynamics similar to those used for NN units. However, challenges remain to account for complex temporal dependencies in the biological single neuron response and for the heterogeneity of synaptic input across the population. Here, we make progress by showing how to derive dynamic rate equations for a population of spiking neurons with multi-timescale adaptation properties - as this was shown to accurately model the response of biological neurons - while they receive time-varying inputs, leading to plausible asynchronous activity in the network. The resulting rate equations yield an insightful segregation of the population's response dynamics into those driven by the mean signal received by the neural population, and those driven by the variance of the input across neurons, with respective timescales that are in agreement with slice experiments. Further, these equations explain how input variability can shape log-normal instantaneous rate distributions across neurons, as observed *in vivo*. Therefore, we have derived rate equations that explain how single neuron properties shape rich population dynamics. This opens the way to investigating whether this increased complexity relative to vanilla rate equations could provide useful inductive biases when used in NN models trained to solve specific tasks.

3-040. Reduced stochastic models reveal the mechanisms underlying drifting cell assemblies

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In a standard model, associative memories are represented by assemblies of strongly interconnected neurons. It has recently been proposed that these assemblies are not static but drift freely in neural circuits. This explains experimental findings of changing memory representations. On the level of single neurons, assembly drift is reflected by characteristic dynamics: relatively long times of stable assembly membership interspersed with fast transitions. How can we mechanistically understand these dynamics? Here we answer this question by proposing simplified, reduced models. We first construct a random walk model for neuron transitions between assemblies based on the statistics of synaptic weight changes measured in simulations of spiking neural networks exhibiting assembly drift. It shows that neuron transitions between assemblies can be understood as noise-activated switching between metastable states. The random walk's potential landscape and inhomogeneous noise strength induce metastability and thus support assembly maintenance in the presence of ongoing fluctuations. In a second step, we derive an effective random walk model from first principles. In this model, a neuron spikes at a fixed background rate and with an input weight-dependent probability when its current or another assembly reactivates. The model generates neuron transitions between assemblies as well as potentials and inhomogeneous noise similar to spiking networks. The approach can be applied generally to networks of drifting assemblies, irrespective of the employed neuron and synapse models.

3-041. Frustrated synchronization and excitability in hierarchical-modular brain networks

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Brain waves are one of the most important features of brain dynamics. Waves at a large scale are a direct consequence of the microscopic synchronization of neuronal populations. For this reason, simple models of coupled oscillators are widely used tools to analyse whole-brain dynamics, both in computational and data-driven studies. Experimental evidence suggests that, at this description level, large neuronal regions work close to the edge-of-synchronization, which according to theoretical models would confer optimal capabilities for information processing and computation.

However, how this critical state emerges is yet unclear. Different hypotheses have pointed out the hierarchical-modular structural organization of the brain as a relevant piece of the puzzle: on one hand, this structure can produce Griffiths' phases, i.e., large regions in parameter space that present critical-like properties. On the other hand, a core-periphery hierarchical structure has been identified as an optimal structure to balance segregation and integration of information, which could enhance the network computational capabilities. The topological structure is deeply entwined with oscillatory behaviour: in low dimensions, oscillator models display topological defects which manifest as time-dependent, rich activity patterns.

In this context, we address two different issues that fill a gap in the literature: first, we study the behaviour of non-linear excitable oscillators. Neuronal tissue is known to be excitable, an ingredient that strikingly changes the macroscopic collective behaviour of the system, leading to complex dynamics in realistic connectivities. Second, we provide insights linking oscillator frustration and the segregation-and-integration balance view, by studying synchronization models with core-periphery synthetic networks for the first time. We present a unifying view, comparing the differences among different dynamical models and structural topologies, thus paving the way for future theoretical and data-driven studies based on oscillator models.

3-042. Towards using small topologically constrained networks in-vitro in combination with in-silico models

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Understanding how the brain can store and process information is one of the biggest challenges we are currently facing in the field of neuroscience. It is possible to study the brain as a whole. However, such approaches tend to only recover neural activity from a sparse subset. To counteract this problem, we are using a bottom-up neuroscience paradigm, where neurons are cultured on top of a multi-electrode array (MEA). The MEA can be used to stimulate and record neural activity. To further reduce the complexity, we culture neurons inside of a polydimethylsiloxane (PDMS) microstructure, which ensures that the somas are confined to predefined locations (nodes) while at the same time guiding the growth of the neurites by physically constraining them. With such PDMS microstructures it is possible to create small circular neural networks consisting of 4 nodes, where the

axons of one node predominately connect with other nodes in a clock-wise fashion. Hence, we can put constraints on the topology of such networks. It is possible to apply complex stimulation patterns to such a circular network through the MEA that consist of multiple electrical pulses. In this work we investigated the effect of 125 unique stimulation patterns on the network response. We found out that the network response to each stimulation pattern stays constant for multiple hours. Furthermore, the responses are unique for different stimulation patterns. Yet, similar stimuli elicit similar responses. We believe that given the relative ease of creating such circular networks and their corresponding spiking responses to a wide set of different stimulation patterns, the here proposed platform is a promising candidate for validating both simulated neuronal networks and tools that can reconstruct the topology of a network such as generalized linear models. In the future, we will be working on achieving both of these goals.

3-043. Emergence of modular patterned activity in developing cortex through intracortical network interactions

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Modular (columnar) activity is a fundamental mode of neural activity in the cortex of primates and carnivores. Work in ferret visual cortex has shown that already prior to visual experience, early spontaneous activity is modular, revealing large-scale correlated networks that are predictive of future functional networks representing stimulus orientation. However, the origin of modular activity in the early cortex is unclear at present. Computational models predict a striking ability of developing intracortical circuits to self-organize into modular, coordinated patterns of activity which reflect the spatial statistics of *in vivo* spontaneous activity. However, this prediction has not yet been tested *in vivo* during early development. Here, we combine widefield epifluorescence calcium imaging with excitatory optogenetics to simultaneously image and stimulate pyramidal neurons in layer 2/3 of developing ferret visual cortex (postnatal day 24-29, before eye opening). We found that optogenetic stimulation of the cortex with a large (~3 mm) spatially uniform stimulus led to the rapid emergence of non-uniform, modular neural activity, consistent with the predictions of the model. The proportion of strongly modular patterns increased with optogenetic light intensity, suggesting a network activity threshold to generate structured activity from this spatially uniform input. Repeated stimulations lead to a variety of spatial patterns, and opto-evoked activity resided in a moderately low-dimensional subspace that it appeared to share with ongoing spontaneous activity. Notably, these modular opto-evoked events resembled spontaneous activity in their spatial structure and revealed highly similar large-scale correlated networks. As predicted by the computational model, we found that the presence of modularity in opto-evoked events required activity propagating through local intracortical synapses to emerge, and that modularity persisted even in the absence of feedforward input from the LGN. Together, this provides strong evidence that modular patterned activity is an emergent property from intracortical interactions through a self-organizing network.

3-044. Reduction of entropy specific to cortical outputs during anesthetic-induced loss of consciousness

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Understanding the circuit mechanisms underlying the loss of consciousness during general anesthesia is a long-standing question. Activity within cortex drives conscious perception and, hence, the loss of consciousness is thought to result from the disconnection of cortex from subcortex. Here, we identify a change in the correlation structure of neuronal activity during general anesthesia, specific to the primary population of cortical output neurons. We demonstrate that this increased correlation reduces the information output from cortex, suggesting a mechanism for the loss of consciousness.

In detail, across different general anesthetics with diverse molecular modes of action, we found that spontaneous activity across the population of layer 5 pyramidal neurons increased in correlation, resulting in an aperiodic alignment of activity (termed “neuronal synchrony”). During transitions to and from anesthesia, the change in synchrony within layer 5 coincides with the loss and recovery of consciousness. Synchronous layer 5 activity extended spatially both within individual cortical areas and between different cortical areas, resulting in a global synchrony across cortex. In contrast, all other cortical cell types, across other cortical layers, did not show a consistent change in synchrony across anesthetics.

Layer 5 pyramidal neurons constitute a primary output circuit of cortex. Quantifying the decrease in the variability of activity across layer 5 pyramidal neurons during unconsciousness, we observed a decrease in the information entropy across the population, with the entire population acting as a single effective unit. In contrast, the aperiodic activity of each neuron showed no significant change during anesthesia. Hence, our results show that cortex shifts from a mode characterized by spatially asynchronous outputs transmitting high information, to a mode characterized by spatially synchronous outputs, transmitting low information. This reduction in information output disconnects cortex from sub-cortical structures and, thereby, provides a possible mechanism for the loss of consciousness.

3-045. A manifold of heterogeneous vigilance states across cortical areas

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Brain states are conventionally divided into wake, slow wave sleep (SWS) and rapid eye movement (REM) sleep based on distinct patterns of neural activity and muscle tone. However, recently available large-scale recordings indicate that this conventional division of brain states is insufficient to account for rich heterogeneity of neural dynamics on the global scale. During sleep, neural activity in some brain regions can exhibit awake signatures and vice versa [1,2]. While brain states provide the backdrop for any activity underlying behavioral functions, the spatiotemporal structure of multi-regional brain states remains unexplored. We simultaneously recorded electromyogram (EMG) and local field potentials (LFP) at 14 sites across the mouse cortex during the natural variation of sleep and wake cycles continuously over multiple days. To characterize the heterogeneity of brain states in these multi-regional recordings, we developed an approach to uncover a low-dimensional manifold on which these states evolve. We use unsupervised dimensionality reduction based on a variational autoencoder (VAE) that predicts the next point in time. We trained the model on activity from an individual channel to uncover a local characterization of brain states. For single channels, the inferred manifold revealed three major clusters corresponding with human-expert labels of the basic wake, SWS, and REM states. Classical frequency bands, such as alpha, beta, and gamma, contributed nonlinearly to the inferred manifold. Applying the model to other electrodes, we found profound differences in the expression of states across cortical areas, particularly, the lack of REM-like activity in the lateral somatosensory cortex. We found that heterogeneity of states largely appears during transition periods between primary states, suggesting a more continuous global manifold. Our work provides a framework for quantifying heterogeneous brains states and shows that the regional co-existence of wake and sleep states is a common feature of global brain activity.

3-046. Walking elicits global brain activity in adult Drosophila

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Motor activity including locomotion and other movement types influence neuronal activity in many brain areas across animal species, including worms, flies, and mice. Yet the origin of these neural representations of ongoing behavior remain elusive. We posit that in extreme cases, activity could arise from two opposite sources: neural activity could originate in superior decision-making areas and then spread across the brain (“top-down”). Alternatively, neural activity could be initiated by motor activity and proprioception, and then distributed to higher brain areas (“bottom-up”). To distinguish between these two informational flows, we used fast, *in vivo* light field microscopy to image whole brain activity of head-fixed flies during spontaneous and forced behavior. We used unsupervised methods (PCA and ICA) to generate activity maps and obtain functional associated with locomotor activity. We assigned neuronal activities to different brain regions or neuron types by aligning activity maps to a comprehensive set of anatomical images widely available within the *Drosophila* community. We found that walking elicits global activity across the brain, regardless of whether flies were spontaneously walking or forced to walk. Furthermore, this global neural activity is not due to disinhibition of specific motor pathways, since excitatory and inhibitory neurons were both activated during behavior. In addition, neuromodulatory neurons (i.e. dopamine, serotonin and octopamine) differentially encode walk. Lastly, activity signatures of walking are different from those of grooming or flailing, indicating that the observed global upregulation of neuronal activity is not simply due to leg movements. We propose that specific locomotion patterns activates the brain by sending proprioceptive information to the base of the brain, from where it spreads over all brain regions. Ascending neurons, which carry information from the motor to higher brain centers, are promising candidates involved in this global activity upregulation.

3-047. How neuronal axons get from here to there using gene-expression maps derived from their family trees

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During brain development, billions of axons navigate over multiple spatial scales to reach specific targets, and so form functional circuits. However, the limited information capacity of the zygotic genome puts a strong constraint on how, and which, axonal routes can be encoded. We propose and validate a mechanism of development that can provide an efficient encoding of this global wiring task. The key principle is that successive mitoses of the neural stem cells induce a hierarchical organization of gene expression patterns in global high dimensional expression space. Provided that mitotic daughters do not stray too far from one another, this hierarchy of gene expression is embedded (with some loss) in 3-dimensional brain space. However, it is sufficiently well embedded to provide a multi-scale map over the final neuronal progeny of development. Thus, a traversal of the gene expression hierarchy has in many instances a dual traversal of brain space and so offers systematic sequences of expression profiles able to guide a growth cone from its source neuron to a collection of remote target neurons. We explain this principle mathematically, and confirm its operation through simulation. Furthermore, we have analyzed gene expression data of developing and adult mouse brains, published by the Allen Institute for Brain Science, and found them consistent with our simulations: gene expression indeed partitions the brain into a global spatial hierarchy of nested contiguous regions that is stable over pre- and postnatal time. We use this experimental data to demonstrate that our axonal guidance algorithm is able to robustly extend arbors over long distances to specific targets, and that these connections result in a qualitatively plausible connectome.

3-048. Self-assembly of the mammalian neocortex, from mouse to macaque

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During mammalian neural development, mitotic cells sense local cues and morphogenic gradients to form complex and coherent processing systems, such as the cerebral cortex, that contains billions of neurons classified into different cell types. We use agent-based simulations of cellular growth and differentiation to explore and understand the regulatory principles governing cortical development in mouse and macaque. We use the Java platform Cx3D, which provides methods for detailed simulations of genetic networks and also physical cellular processes in a 3-D space. First, we derive an artificial gene regulatory network (GRN) consisting of only 36 genes from experimental lineage and phenotypic data of mouse corticogenesis. Then, in Cx3D, a small group of precursor cells loaded with this GRN develop through mitosis, into a portion of the six-layered mouse neocortex with the correct quantitative and dynamical measurements observed experimentally for the primary somatosensory area (S1). One line of investigation explores the control of cortical lamination. In this regard, we find that modulation of one gene in the model GRN distinguishes the specification of the primary motor area (M1), suggesting that key genetic control points are able to shift developmental programs. This observation raises the question whether small changes in the GRN could also account for species specific differences of primate neocortex. We find that adding a state node to the mouse GRN resulted in a new precursor pool that following differentiation resembled the stereotypical macaque primary visual cortex (V1). Our models show how autonomous mitotic cells, which have a restricted repertoire of only local and simple actions, develop into the six-layered murine neocortex. Simple changes to the murine GRN give rise to a very different macaque neocortex, which follows nearly identical self-assembling principles.

3-049. Emergence of an orientation map in the mouse superior colliculus from stage III retinal waves

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The upper visual layers of the mouse superior colliculus (SC) exhibit an orientation preference map (OPM) with a retinotopy-based concentric pattern (Ahmadlou and Heimel, 2015; Feinberg and Meister, 2015; but see Chen et al., 2020). The underlying developmental mechanisms that give rise to this concentric OPM in the mouse SC are still unclear. During visual system development, the stage III (S3) retinal waves are known to play important roles in circuit formation. Specifically, the S3 waves that tend to propagate towards the caudal direction (Gribizis et al., 2019) have impacts on the direction selectivity of the SC neurons (Ge et al., 2021). In addition, the OFF retinal ganglion cells (RGCs) are recruited with a time-delay relative to ON RGCs during S3 waves (Kerschensteiner and Wong, 2008). Here, we propose that these S3 wave directionality biases, together with the OFF-ON delay, play an instructive role in establishing the OPM during development. To test this hypothesis, we built a model that incorporates the above-mentioned S3 wave features to predict the properties of the established OPM. The Hebbian mechanism was used to refine the RGC-SC connections during S3 waves to show that the OFF delays can segregate the ON- and OFF-RGC connections to individual SC neurons, which locally give rise to the orientation preference. Furthermore, we show that the biases in S3 wave directionality can mediate the formation of a concentric OPM. In summary, our model suggests that OFF delay of S3 waves can mediate local microscopic segregation of the ON-OFF subfields of the postsynaptic SC neurons, whereas the biases in the wave propagat-

ing direction determine the overall macroscopic organization of the OPM. Taken together, these findings suggest that the S3 waves could instruct the formation of the OPM in the mouse SC by fine-tuning the receptive fields of the postsynaptic SC neurons.

3-050. Natural scene expectation shapes the structure of trial to trial variability in mid-level visual cortex

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What we expect to see can greatly affect what we perceive. How does expectation influence local circuitry among visual cortical neurons to allow for perceptual discrimination in the context of rich natural inputs? Little work has sought to understand how populations of sensory cortical neurons change their responses with expectation, and the majority of studies manipulate expectation in a task-irrelevant way, disallowing for comparisons of changes in neural activity with behavioral performance. Theoretical and experimental work indicates that changes at the population level, in particular those related to the variability in neural responses, greatly impact stimulus encoding. Therefore, we sought to investigate whether changes in the structure of neural population activity in mid-level visual cortex might underlie the behavioral advantages conferred by forming an expectation. We recorded from populations of visual cortical area V4 neurons using implanted 96-electrode arrays in macaques engaged in a natural scene change detection task in which we modulated image expectation. During high expectation blocks, the same image (e.g. image A) was used on every trial. During low expectation blocks, a random image (from 10 possible images, including image A) was chosen for each trial, thereby reducing the expectation that image A would be selected for a given trial. Comparisons were made for image A during high and low expectation blocks. Data from 2 monkeys showed a robust improvement in behavioral performance when the image was expected. Our recordings showed that expectation decreased neural responses and modulated noise correlations. Using dimensionality reduction methods, we found a decrease in shared variability and increase in dimensionality with high expectation. Our results support the idea that expectation is built through the interactions among populations of neurons relatively early in the visual system, enabling it to be flexible for arbitrary visual scenes and objects.

3-051. Sensory specific modulation of neural variability facilitates perceptual inference

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Perception is not a faithful representation of the sensory world; rather, it is an inference of the most likely explanation given sensory evidence. Illusions arise due to rational mistakes in perceptual inference, exemplifying the dichotomy between faithful representation and inferred representation. We utilized illusory contours to ask how and where perceptual inference is encoded in the mouse visual cortex. In illusory contour perception, the perceived whole is greater than the sum of its parts. As such, we hypothesized that brain regions encoding perceptual inference would show enhanced neural activity specific to illusory contours. We employed mesoscale two-photon microscopy to record visual responses from thousands of excitatory neurons across 6 visual areas of the mouse neocortex simultaneously. Contrary to our initial hypothesis, the average neural population activity did not show illusory contour specific enhancement, in neither primary visual cortex (V1) nor any of the higher visual areas (LM, RL, AL, PM, AM). Subsequently, we tested the alternative hypothesis that the inferred illusory contour is represented in the specific pattern of neural activity. To this end, we employed machine learning to decode visual stimulus from visually evoked neural activity (support vector machines, SVM, and artificial neural networks, ANN). Across decoders, the inferred illusory contour was consistently represented in V1 and LM, but not PM. Next, we leveraged our decoding approach to ask how trial-by-trial variability influences perceptual inference. We found that neurons responded with the lowest variability (Fano factor) to visual stimuli that evoked the strongest activity. This sensory specific neural variability facilitated the capacity for inference contained in the neural activity pattern, despite degrading the capacity for faithful discrimination. Such tradeoff between perceptual inference and faithful representation has profound implications for interpreting the neural code.

3-052. Processing of visual textures in the mouse visual cortex

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Visual textures efficiently represent real-world information that is essential for perceptual tasks like pattern detection, object segmentation and classification. This information appears to be encoded in intermediate areas along the primate ventral visual stream (areas V2-V4), but how textural selectivity emerges at the circuit level, and whether the neural architectures that support texture processing are shared across mammalian species is currently unknown. We addressed these questions in the mouse by first examining the mouse's perceptual ability to discriminate higher order texture statistics, and then by studying the neural substrate of texture processing along the ventral visual stream. We employed a new model to synthesize textures using convolutional neural networks pretrained for object recognition, and in addition we generated spectrally matched stimuli (scrambles) which shared the same low-order features as the textures. Mice could be trained to behaviorally discriminate textures from scrambles across different texture families. We then studied the neural underpinning of texture encoding in primary (V1) and secondary (LM) visual cortices by performing widefield and 2-photon GCaMP imaging. Both at the population and single cell level we observed that V1 and LM differentially responded to the textures compared to the scrambles, with response modulation in LM being higher than in V1. To examine whether these area differences were driven by the higher-order statistical features of texture stimuli, we trained a linear encoder model to predict responses of individual cells using the texture statistics as features. Overall, the model better captured the neural responses in LM than in V1, with larger weights associated with higher-order image statistics in area LM. In summary, our results provide evidence for texture vision in the mouse with a neural underpinning sharing encoding characteristics with the primate ventral visual stream, thus suggesting preserved neural principles for texture processing across mammalian species.

3-053. The geometry of cortical representations of touch in rodents

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Neural responses are often highly heterogeneous non-linear functions of multiple task variables, a signature of a high-dimensional geometry of the neural representations. We studied the representational geometry in the somatosensory cortex of mice trained to report the curvature of objects using their whiskers. High-speed videos of the whisker movements revealed that the task can be solved by linearly integrating multiple whisker contacts over time. However, the neural activity in somatosensory cortex reflects a process of non-linear integration of spatio-temporal features of the sensory inputs. Although the responses at first appear disorganized, we could identify an interesting structure in the representational geometry: different whisker contacts are disentangled variables represented in approximately, but not fully, orthogonal subspaces of the neural activity space. The observed geometry allows linear readouts to perform a broad class of tasks of different complexities without compromising the ability to generalize to novel situations.

3-054. Nonlinear manifolds underlie neural population activity during behaviour

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The activity of neural populations can be well-described by relatively few population-wide activity patterns spanning a “neural manifold”. Virtually all these studies have analysed flat neural manifolds to understand how the brain controls behaviour. We hypothesised that since neurons have nonlinear responses and make thousands of recurrent connections that may enhance this nonlinearity, nonlinear manifolds should capture the neural population activity better than flat manifolds. Analysis of a centre-out reaching task in monkeys confirmed that, even during a relatively simple behaviour, motor cortical (MC) population activity is best captured by a nonlinear manifold. To investigate if manifold nonlinearity arises due to the dense connectivity patterns of brain circuits, we trained neural networks with different degrees of recurrent connectivity to perform this task. Indeed, manifold nonlinearity increased monotonically with the number of recurrent connections. To test *in vivo* this presumed influence of circuit connectivity on manifold nonlinearity, we compared neural manifolds from two anatomically distinct motor regions –MC and striatum– using simultaneous recordings from mice performing a grasping and pulling task. Manifold nonlinearity was strongly region-dependent: Striatal manifolds were consistently more nonlinear than MC manifolds. Besides circuit connectivity, we also expected task complexity to influence manifold nonlinearity. We hypothesised that if manifolds are nonlinear, more varied tasks requiring a richer set of neural activity patterns should reveal greater nonlinearities. We confirmed this prediction using neural population recordings from human MC during attempted handwriting. Drawing lines of varying length across 16 directions and writing all the letters in the English alphabet had more nonlinear manifolds than the simpler tasks of drawing lines in one direction or writing a handful of morphologically similar letters, respectively. Thus, manifolds underlying neural population activity during behaviour are nonlinear, their degree of nonlinearity depends on the connectivity of the brain region, and increases during more complex tasks.

3-055. Dissecting emergent network noise compensation mechanisms in working memory tasks

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In *vivo*, single neurons have high trial-to-trial variability in their information transmission, which presents a challenge for networks whose outputs must be consistent for high task performance. Reliability becomes increasingly difficult to attain for working memory tasks where information must be preserved for extended periods of time. This implies that relative to systems without noise, the brain must have mechanisms dedicated to compensating for unreliability in neuron activity. How trained networks mitigate the effects of noise while completing working memory tasks remains largely unexplored, primarily due to the lack of a theoretical framework for quantifying and analyzing noise compensation in neural networks. We take a step in this direction by analyzing noisy recurrent neural networks (RNNs) trained to perform a delayed replication task, where noisy neurons hold inputs in memory for several time steps before outputting the same signal. Noise makes this task increasingly difficult, because information becomes progressively corrupted throughout time. We develop a principled method to quantify noise

compensation across temporal trajectories, and show that trained networks reduce noise within a low-dimensional ‘mechanistic’ activity space by maximizing the signal-to-noise ratio for highly probable inputs, and quenching low probability inputs, which are likely due to noise. Further, we show that this compensation phenomenon can be understood in terms of the implicit regularization introduced by training a system under noise, as it does not exist in networks that are trained without noise. From this simple example, our analysis suggests a more general framework for exploring the noise compensation properties of neural networks engaged in working memory tasks, which require holding information in memory for extended periods of time.

3-056. A genetic algorithm to uncover internal representations in biological and artificial brains

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Diverse methods have been developed to visualize the representations learnt by artificial neural networks. Such visualization methods however are not easily adapted to biological systems. This prevents direct comparisons between the internal representations of artificial and biological neural systems. One promising approach to visualize sensory representations in biological systems is reverse correlation. Behavioural reverse correlation experiments leverage pareidolia, our tendency to detect spurious signals in noise, such as seeing shapes, objects, or faces in clouds. In these experiments, observers report whether they detect a signal—e.g., the letter “s”—in noise. Just as some clouds happen to resemble known shapes, some noise samples resemble the signal an observer has in mind. Averaging over noise samples in which an observer spuriously detected a signal yields a “classification image”—a visualisation of their representation of the signal. Averaging noise however has several drawbacks: the method is slow to converge, produces blurred reconstructions, and cannot tease apart competing representations. We present a genetic algorithm approach that addresses these issues. We generate image populations by crossbreeding noise samples in which observers detect a signal. This approach converges faster and yields sharper reconstructions than reverse correlation, and is able to recover competing internal representations. Deep neural network image classifiers are able to correctly interpret the classification images generated by human observers, allowing us to “mind-read” which numerical digits observers are thinking of. This method could potentially recover—using equivalent stimuli and procedures—the internal representations of behaving organisms, neurons or neural populations, and units in neural network models, thus providing a powerful tool for comparing neural computations across biological and artificial brains.

3-057. How many objects can be recognized under all possible views?

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The brain must recognize objects in the face of identity-preserving transformations such as changes in lighting, position, and orientation. However, to achieve general purpose geometric reasoning these view transformations should also be represented in neural codes. A natural strategy to encode both the identity of an object and its view is to utilize an equivariant code, where the neural representation transforms in a manner consistent with the transformations to the inputs, and consistent across objects. A classic example of such a code is given by an intermediate layer of a convolutional network, which is equivariant to spatial translations of the inputs. A fundamental and unanswered question is how equivariant structure in a code alters the number of objects that can be expressed (capacity). To address this, we derive a complete theory of perceptron capacity, which measures the number of objects that can be linearly separated under all possible labelings, for equivariant neural codes and apply this theory to models of vision. We show that our theory accurately predicts the capacity of simple models of visual cortex and convolutional networks, showing that capacity scales not with the number of neurons in the circuit but rather with the number of trivial irreps of the representation. These results constitute an advance in the

theory of the expressivity of learning systems under the natural condition of equivariance.

3-058. Map Induction: Compositional spatial submap learning for efficient exploration in novel environments

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Humans efficiently reason about space to navigate and forage in new environments, which may, at least in part, depend on an ability to generalize across tasks and organize observations into patterns that can be re-used. Generalization and transfer learning in spatial domains is evident in mirror-invariant neural scene representations, and in the reuse of reference frames and representations across similar environments. Shared reference frames appear in other mammals as well, as, for example, in rodents reusing grid-cell maps for different but perceptually similar environments. However, the field lacks conceptual and quantitative models of how the spatial system might discover patterns during spatial exploration, how seen patterns might be compositionally combined to represent complex spaces, or how they might be leveraged to represent and navigate through new spaces through reuse. Here we introduce a computational model of “Map Induction”, which involves the compositional formation of proposed maps of complex spaces based on already seen spaces through program induction in a Hierarchical Bayesian framework. The model thus explicitly reasons about unseen spaces through a distribution of strong spatial priors. We introduce a new behavioral Map Induction Task (MIT), and compare human performance with that of state-of-the-art Partially Observable Monte Carlo panning models as well as our Map Induction framework. We show that our computational framework better predicts human exploration behavior than non-inductive models. Understanding the computational mechanisms that support such map learning can generate hypotheses for circuit-level neural representations and dynamics, advance the study of the human mind, as well as support more efficient exploration algorithms.

3-059. Occam's razor guides intuitive human inference

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Occam's razor is the principle stating that, all else being equal, simpler explanations for a set of observations are to be preferred to more complex ones. This idea can be made precise in the context of statistical inference, where a geometrical characterization of statistical model complexity emerges naturally from an approach based on Bayesian model selection. The broad applicability of this formulation suggests a normative reference point for decision making under uncertainty. However, little is known about if and how humans intuitively quantify the complexity of competing interpretations of noisy data. In this work, we: 1) extend an existing geometrical characterization of model complexity to apply to models with bounded parameters; 2) measure the sensitivity of naive human subjects to statistical model complexity; and 3) introduce a deep neural network architecture for statistical model selection. Our data shows that human subjects bias their decisions in favor of simple explanations based not only on the dimensionality of the alternatives (number of model parameters), but also on finer-grained aspects of their geometry, such as volume, curvature, and presence of prominent boundaries. We conclude by studying the behavior and learned representations of our deep network architecture when trained on the same task as the human subjects. Overall, our results imply that principled notions of statistical model complexity have direct quantitative relevance to human decision making.

3-060. A high-throughput pipeline for evaluating recurrent neural networks on multiple datasets

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Neural networks are now widely used for modeling neural activity in the brain. They have been particularly successful in modeling the visual system, using mostly feedforward networks and leveraging community-wide efforts centered around benchmarks to both improve model architectures and evaluate model fits to data. Now that recurrent neural networks (RNNs) are also used to model a larger variety of brain functions, there is a similar need for developing appropriate metrics to compare these models. Towards this goal, we have built a high-throughput pipeline for training different RNN models on a wide range of tasks and comparing them to many experimental datasets through a variety of analysis methods. To ensure the reliability of results generated by these methods we evaluate a set of model-data similarity measures based on several criteria: 1) robustness to noise, 2) higher similarity scores for comparisons between models of the same structure versus models of different structures, and 3) rise in similarity scores between models and data after training. We found that the similarity of models to datasets rises after training for all the methods. Centered kernel alignment (CKA) is less sensitive to noise and better identifies models of the same structure compared to methods based on canonical correlation analysis (CCA). Our framework provides the flexibility to add models, datasets and analysis methods, serving as a basis for further refinement and testing of RNN models by evaluating them against multiple datasets.

3-061. An adaptive analysis pipeline for automated denoising and evaluation of high-density electrophysiological recordings

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The availability of high-density electrophysiology is transforming systems neuroscience and enables virtually any experimental lab to simultaneously acquire activity from hundreds of neurons throughout the brain. However, extracting single-cell activity from the resulting large datasets remains a major challenge: different experimental settings introduce various sources of contaminating noise, and even optimized spike-sorting algorithms still require manual evaluation of the resulting spike clusters. Establishing a pre-processing pipeline and manual evaluation requires expert knowledge and is often extremely labor-intensive, presenting a major roadblock, particularly for experimental labs with little programming experience. To evaluate and improve the performance of automated preprocessing pipelines, we, therefore, used Neuropixels probes to collect various datasets, including high- and low-quality recordings from multiple setups, and combined recordings with optogenetic stimulation or functional imaging. We then tested different preprocessing methods and hand-labeled the resulting spiking clusters to characterize the impact of preprocessing on cluster quality. Different analyses, such as rescaled median subtraction and automated channel rejection, significantly reduced the number of noise clusters but, importantly, even high-quality datasets still contained a large amount of non-neuronal noise clusters. We, therefore, established a set of noise-predictive quality metrics, such as hyper-synchronous spiking across clusters, and used supervised UMAP analysis and an SVM classifier to automatically identify noise clusters. The classifier detected hand-labeled noise clusters in unseen datasets significantly better than existing methods (84% versus 62% cross-validated accuracy)

and generalized well across all dataset types. A similar approach isolated single-unit clusters and we created a fast and simple interface for efficient evaluation of cluster quality. We demonstrate the importance of evaluating high-density spike sorting outputs and offer an automated processing pipeline, including novel methods for data denoising and classification. The pipeline is very user-friendly and extendable with additional metrics, thus providing a powerful tool to efficiently isolate single-cell activity from large datasets.

3-062. Automated processing of calcium imaging videos for densely labeled dendritic and somatic ROIs

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Non-linear dendritic input integration can greatly boost the computational power of individual neurons. Investigating dendritic population dynamics in regions with sparsely active neurons such as hippocampus using *in vivo* 2-photon requires calcium imaging of densely labeled preparations. However, current analysis methods face limitations in processing densely labeled dendritic preparations because identification of regions of interest (ROIs) corresponding to individual dendrites and extracting temporal components from overlapping ROIs is difficult. Here we present a method for automatic identification of dendritic ROIs in dense samples, as well as a measure to validate significant calcium transients in detected ROIs.

Sparse constrained non-negative matrix factorization (sCNMF) has been used to identify and de-mix dendritic ROIs in dense fields of view, but this requires random initialization and the results can be difficult to map to individual neurons. We modified sCNMF to initialize with regions of contiguous simultaneously active pixels and maintain contiguous ROIs throughout the procedure. This results in deterministic ROIs that are traceable to the parent soma, with efficient time and memory requirements.

Given a complete set of ROIs, CNMF extracts accurate temporal signals from overlapping segments. But complete labeling is not guaranteed in dense datasets, which can lead to misattributed activity and corrupted tuning properties. To address this, we define a “fitness trace” of an ROI, reflecting the completeness of ROI activation for each frame. Using this, we automatically identify and discard false calcium transients from overlapping ROIs, saving hours of manual proof-reading time. We integrate these methods into existing imaging pipelines such as CalmAn, automating easy and robust processing of dendritic data in an accessible, open-source manner. We are optimistic that this will pave the way for more studies of dendritic function using increasingly dense fields of view, which will accelerate the field’s understanding of the importance and utility of dendritic activity.

3-063. Bias-free estimation of information content in temporally sparse neuronal activity

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Applying information theoretic measures to neuronal activity data enables the quantification of neuronal encoding quality. However, when the sample size is limited, a naive estimation of information typically contains an upward bias, which may lead to misinterpretation of coding characteristics. This bias is exacerbated in Ca₂₊ imaging because of the temporal sparsity of detected Ca₂₊ signals. Here, we introduce methods to correct the bias in the naive estimation of information from limited sample sizes and temporally sparse activity. We demonstrate the higher accuracy of our methods over previous ones, when applied to Ca₂₊ imaging data recorded from the mouse hippocampus and primary visual cortex, and to simulated data with matching tuning properties and firing statistics. Our bias-correction methods allowed an accurate estimation of the spatial information carried by place cells and revealed the spatial resolution of the hippocampal code. Furthermore, using our methods, we found that cells with higher within-field firing rates carry higher information per spike, and exposed the long-term evolution of the spatial

code across distinct hippocampal subfields. Overall, a bias-free estimation of information can uncover properties of the neural code that could be masked by the bias when applying the commonly used naive calculation of information.

3-064. Single cell measures of tuning to imagined position during replay show preserved spatial tuning but quenched neural variability in place cells.

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Hippocampal cells show precise spatial tuning to the animal's position during behavior. During stopping periods, the hippocampus encodes spatially coherent trajectories through the environment called replays that resemble the animal's behavior. Replay has been proposed as a form of virtual experience that supplements real experience for the purposes of learning and planning. However, it is unknown whether the precise spatial tuning of place cells as a function of animal position is preserved as a function of encoded replay position, independent of the animal's location. This is far from obvious, given that replay unfolds at much higher speeds and is likely to involve different mechanisms and circuits. We show that in a 2D environment, spatial tuning is preserved as a function of the encoded position during replay (its "replay field"), using a leave-one-out analysis that removes the cell's contribution to replay before evaluating its replay field. Replay fields are shown to match place fields on both coarse- and fine-grained measures, including spatial information, field shape and skewness, as well as in the relative positions and peak rates of the primary and secondary fields. Crucially, however, we show that spiking variability during replay is quenched (sub-Poisson) and thus does not exhibit the overdispersion or excess temporal variance that is characteristic of passes through place fields, suggesting that firing patterns during replay are less subject to covert shifts in attention and context as during behavior. Spiking reliability is typically only observed in sensory areas where stimulus sensitivities are well characterized, indicating that replay may be the equivalent of an idealized stimulus for the hippocampus. Lastly, we demonstrate that sub-Poisson spiking variability naturally emerges from a prominent, though largely untested, model of replay whereby spike frequency adaptation drives movement of a bump in a continuous attractor network.

3-065. Neural adaptation in attractor networks implements replay trajectories in the hippocampus

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Sequential reactivation (replay) of neurons in the hippocampus has been widely observed in sharp wave ripple events (SWRs) during awake and sleep periods, and they are associated with mnemonic processes, such as memory retrieval, consolidation, future planning and decision making. Previous studies have shown that the replay trajectories in the rat hippocampus are rather random, which resemble at least two different types of stochastic process, one corresponding to Brownian diffusion discovered during sleep SWRs and the other Levy superdiffusion discovered during awake SWRs. The underlying mechanism of generating these different types of replay trajectory remains, however, obscure. In this study, we build a continuous attractor neural network (CANN) for encoding spatial information in the hippocampal circuit, and show that neural adaptation, exemplified by spike frequency adaptation (SFA) here, can serve as a general mechanism to implement the two types of replay trajectories. In our model, the role of SFA is to induce a negative feedback to neuronal responses, which destabilizes the bump-like network state. Specifically, when the SFA strength is sufficiently large, it induces a travelling wave state of the bump, i.e., the bump moves spontaneously in the attractor space. Thus, by modulating the SFA strength, we can observe two different stochastic processes of the bump movement. When the SFA strength is small, the bump movement is mainly driven by noise fluctuations, and its trajectory displays Brownian motion; while when the SFA strength is large, the bump movement is driven by both noise fluctuations and the intrinsic mobility (travelling wave) induced by SFA, and its trajectory displays Levy superdiffusion. We carry out theoretical analyses and simulations to demonstrate that our model reproduce various experimental findings, including the Brownian motion in sleep SWRs, the Levy motion in awake SWRs, and the anti-phase locking between neural

activities and long-jump motions in the awake replay trajectories. We hope that this study helps us to understand the neural mechanism for generating rich dynamics in the hippocampus.

3-066. Multiple bumps can enhance robustness to noise in continuous attractor networks

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A central function of continuous attractor networks is encoding coordinates and accurately updating their values through path integration. To do so, these networks produce localized bumps of activity that move coherently in response to velocity inputs. In the brain, continuous attractors are believed to underlie grid cells and head direction cells that maintain periodic representations of position and orientation, respectively. However, these representations can be achieved with any number of activity bumps, and the consequences of having more or fewer bumps are unclear. We construct 1D ring attractor networks with different bump numbers and characterize their responses to three types of noise: fluctuating inputs at each timestep, spiking noise, and deviations in connectivity away from ideal attractor configurations. Across all these types, networks with more bumps experience less noise-driven deviations in bump motion. This translates to more robust encodings of linear coordinates such as position, assuming that each neuron represents a fixed length no matter the bump number. Alternatively, we consider that the network encodes a circular coordinate such as orientation, where the network distance between adjacent bumps always maps onto 360 degrees. Under this mapping, the coordinate readout generally exhibits less noise-driven error in networks with fewer attractor bumps. We have developed a mathematical theory that quantitatively explains these results. Thus, to suppress the effects of biologically relevant noise, continuous attractor networks should employ more bumps when encoding linear coordinates and fewer bumps when encoding circular coordinates. Our findings provide motivation for the presence of multiple bumps in the mammalian grid network and a single bump in the Drosophila head direction network.

3-067. Long-term motor learning creates structure within neural space that shapes motor adaptation

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Motor adaptation is a widely-used paradigm for understanding short-term learning. However, it is unknown how existing skillsets acquired through the long-term learning process that begins in utero can affect motor adaptation. Long-term learning likely causes changes in neural connectivity, which may shape the neural dynamics that can be produced. To understand the interaction between circuit connectivity constraints and a neural population's ability to change its activity patterns, we modeled the neural dynamics of the motor cortex during skill learning and subsequent adaptation using a recurrent neural network. We trained the network on different skillsets with varying numbers of movements. We hypothesized that having a larger repertoire of movements would facilitate short-term adaptation since the activity is already primed to explore a larger range of possible activity states.

Indeed, we found that larger skillset networks can adapt to perturbations more easily. In particular, multi-movement networks performed significantly better than single-movement networks. To understand how learning multiple movements impacts the underlying network dynamics, we examined the differences between networks initially trained on one or two movements. The dynamics of two-movement networks were more constrained, without leading to constraints in the output: two-movement networks had less variance in unit and population latent activity, but greater variance in motor output. They also had more predictable neural trajectories, suggesting that their dynamics have more organizational structure mapping motor output. When we reduced the structure with uninformative inputs, the differences in adaptation between multi-movement networks disappeared, showing that

the structure facilitates adaptation. However, structure can also harm adaptation: networks with larger skillsets performed worse with larger perturbations and faster learning rates.

Thus, learning multiple movements creates structure in neural space and highlights an inherent trade-off in skill acquisition: more structure facilitates adaptation requiring small changes in motor output, but can harm adaptation that requires large changes.

3-068. Coordinated cortico-cerebellar neural dynamics underlying neuroprosthetic learning

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Brain-machine interfaces (BMIs) or neuroprosthetics allow neural control over assistive devices. They also provide an important framework for studying neural plasticity. It has been suggested that learning is essential for robust neuroprosthetic control. However, little is known about neural processes in subcortical regions that support learning a neuroprosthetic skill. Recently, cortico-striatal interactions during neuroprosthetic learning have been explored⁵ but what are the emergent cerebellar dynamics with cortical neuroprosthetic control is unknown. We performed simultaneous electrophysiologic recordings in the motor cortex (M1) and the cerebellum (Cb) of rats while they used M1 activity for direct neuroprosthetic control on the angular velocity of a feeding tube. We analyzed how the activity of M1 'direct' neurons controlling the tube, as well as other recorded 'indirect' neurons in M1 and Cb changed while learning the neuroprosthetic task. We also analyzed band-limited activity in local-field potentials (LFPs) in both regions. Furthermore, we performed optogenetic silencing of Cb, by injecting red-shifted halorhodopsin (Jaws), while rats performed the neuroprosthetic task and analyzed how cerebellar silencing affected the M1 activity and neuroprosthetic learning. We found that learning successful BMI control was associated with robust modulation of 'direct' neurons in M1 along with robust 'indirect' modulation in M1 and Cb. Furthermore, we observed the emergence of task-related 3-6 Hz synchronous activity in cortico-cerebellar LFPs. We found that these trends emerged late in learning once skillful BMI control was learned. Furthermore, Cb inhibition led to poor performance and weak M1 activity, causally demonstrating the necessity of Cb for skillful BMI control. Our work has identified neural mechanisms in M1 and Cb which are associated with learning of a cortically controlled neuroprosthetic task. This underscores the importance of optimal engagement of neural learning mechanisms in an offsite motor region- the cerebellum, for successful learning of M1-controlled neuroprosthetic task.

3-069. Regionally distinct striatal circuits support broadly opponent aspects of action suppression and production

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The direct and indirect pathways of the basal ganglia (BG) are classically thought to promote and suppress action, respectively. However, observed coactivation of neurons initiating the two pathways, striatal direct (dMSNs) and indirect (iMSNs) medium spiny neurons, has called this view into question. Here we study these circuits in mice performing an interval categorization task that requires a series of self-initiated and cued actions, and critically, a sustained period of dynamic action suppression. While movement produced similar activation of iMSNs and dMSNs in sensorimotor, dorsolateral striatum (DLS), proactive suppression of action revealed clear signatures of functional opponency between the two pathways as assessed using fiber photometry and photo-identified electrophysiological recordings. Surprisingly, both neural signals and effects of optogenetic inhibition demonstrated that

DLS circuits overall were engaged to suppress actions, and not to promote them. Specifically, iMSNs on a given hemisphere were dynamically engaged to suppress contralateral action when that action was tempting. In other words, DLS appeared to support the suppressive complement to an action-promoting policy located elsewhere. To understand how such regionally specific circuit function arose, we constructed a computational reinforcement learning model that reproduced key features of behavior, neural activity, and optogenetic inhibition. The model predicted that parallel striatal circuits not in DLS learned the action-promoting functions that comprise the temptation to act. Consistent with this, optogenetic inhibition in dorsomedial striatum (DMS) indicated that dMSNs there, in contrast to those in DLS, contributed to the promotion of contralateral actions. These data highlight how opponent interaction between multiple circuit- and region-specific BG processes can lead to behavioral control, highlight an underappreciated mode of operation for parallel basal ganglia circuitry, and establish a critical role for the sensorimotor indirect pathway for the proactive suppression of tempting actions.

3-070. Distinct aversive states in the mouse medial prefrontal cortex.

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It was recently shown that glutamatergic neurons in the lateral hypothalamus (LHA) projecting to the lateral habenula (LH) encode negative value. However, it is still unclear how such aversive neuronal pathways located in subcortical neuronal populations affect the activity of the rest of the brain. We report here how the neuronal activity in an integrative cortical area previously reported to be involved in aversion, the medial prefrontal cortex (mPFC), is modulated when an internal aversive signal is emitted in the hypothalamic-habenula (LHA-LH) pathway. We have used a transgenic mouse line (VGAT2-cre) to determine the role of the LHA-LH pathway in signaling the aversive state in (mPFC). We recorded from 2569 single units using dense extracellular recordings (Neuropixels) in combination with optogenetic activation to determine the neural signature across prefrontal subregions (anterior cingulate area, dorsal part (ACAd), prelimbic area (PL), infralimbic area (ILA), and orbitofrontal area, medial part (ORBm)). We found that the specific activation of the aversive LHA-LH pathway elicited distinct activity signatures in the mPFC, suggesting a central role of the PL in response to internal aversive signals. Interestingly, the induced activity dynamics showed region-specific patterns that were decodable from the spontaneous spiking activity, supporting that the PL and the ORBm carry distinct signatures of the aversive state.

3-071. Dentate gyrus inhibitory microcircuit promotes network mechanisms underlying memory consolidation

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The hippocampal dentate gyrus (DG) to CA3 pathway plays a key role in encoding new experiences that are ultimately consolidated in the anterior cingulate cortex (ACC). Experience-dependent changes among excitatory neurons in the DG – CA3 circuit have been intensely studied. However, DG cell axons innervate not only CA3 pyramidal neurons but also inhibitory, parvalbumin positive interneurons (PV IN) to provide strong feed-forward inhibition (FFI) onto CA3 pyramidal neurons. Following learning, FFI onto CA3 is temporarily increased which may be a key element for consolidation and long-term memory storage in hippocampal – cortical networks^{1, 2}. Computationally, feed-forward inhibition has been suggested to support spike-timing fidelity and regulate bursting activity. However, the underlying mechanisms through which this inhibitory microcircuit mediates memory consolidation in hippocampal – cortical networks are not well understood. Here, we harnessed a molecular tool² to investigate

how increased FFI in this microcircuit affects downstream neuronal ensembles and network oscillations during memory consolidation. We performed longitudinal *in vivo* calcium imaging in CA1 and ACC during contextual fear learning in mice with virally enhanced FFI in the DG – CA3 circuit. We found that selectively increasing FFI onto CA3 facilitated formation and maintenance of neuronal representation, in form of context-associated neuronal ensembles, in both brain regions as it prevented a time-dependent decay of neuronal representations. Furthermore, the specificity of neuronal ensembles was increased in a time-dependent manner in ACC. Simultaneous recordings of local field potentials (LFPs) in CA1 and ACC revealed that virally enhanced FFI in DG – CA3 increased coupling of CA1 sharp-wave ripples and ACC spindles, a mechanism for hippocampal – cortical communication during memory consolidation³. This study links a defined synaptic mechanism in a DG – CA3 inhibitory microcircuit with ensemble dynamics and network oscillations and provides direct evidence for its role in memory consolidation.

3-072. Neuromodulation of synaptic plasticity rules avoids homeostatic reset of synaptic weights during switches in brain states

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Brain information processing is shaped by fluctuations in neuronal rhythmic activities, each defining distinctive brain states. Switches in brain states during wake-sleep cycle are described at the network level, by a neuronal population shift from active to oscillatory state. At the cellular level, neurons switch from tonic to burst. This switch is organized thanks to neuromodulators. They refer to signaling molecules that induce reversible changes in functional properties of neurons or synapses. Simultaneously, learning and memory are attributed to the ability of neurons to modify their connections based on experience, a property called synaptic plasticity. It exploits the correlation level in the activity of connected neurons. Altogether, sleep contributes to memory, a phenomenon called sleep-dependent memory consolidation. Experimental results show a down-selection mechanism i.e., strong (resp. weak) connections established during wakefulness are preserved (resp. decreased) during sleep. However, little is known about its underlying physiological processes. This research leads the way to uncover biological explanations.

Using a conductance-based model robust to neuromodulation and synaptic plasticity, we built a cortical network to study the evolution of synaptic weights during switches in brain states. We tested several types of synaptic plasticity rules such as triplet and calcium-dependent models. We reproduced experimental data acquired in wakefulness. Then, switching the network from tonic to burst without any modification of the synaptic rule leads to a homeostatic reset. All synaptic weights converge towards the same basal value whatever the rule due to neuromodulation of neuronal activity.

We showed that neuromodulation of synaptic rules is necessary to overcome this reset. For triplet models, the spike-time dependent curve is deformed as demonstrated in [Gonzalez-Ruedas,2018]. For calcium-based models, calcium thresholds are neuromodulated or the potentiation level is weight-dependent due to neuromodulatory markers. The neuromodulated-synaptic rules are shown to support the down-selection mechanism during sleep, avoiding the homeostatic reset.

3-073. A synaptic plasticity rule based on presynaptic variance to infer input reliability

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The response of sensory neurons to different stimuli are largely characterized by tuning curves, with a peak of activity at a preferred stimulus. Tuning curves are thought to be shaped by Hebbian plasticity during development through the strengthening of synapses between neurons with similar functional preferences. This raises the hypothesis that the strength of synapses should correlate with the difference in functional preference between pre- and postsynaptic activity. A recent study, however, found that the functional preference of cortical neurons was correlated with the number of spines activated by a given stimulus, rather than with their strength [1]. Furthermore, they found that synaptic strength actually correlated with spine selectivity. Here, we study what type of plasticity rule could lead to the emergence of such connectivity pattern and what are the functional implications in a sensory

circuit. We use a rate model to simulate a single neuron receiving input from multiple presynaptic sources with different preferred stimuli and different selectivity. We find that a plasticity rule based on presynaptic activity only, more specifically the variance of presynaptic activity, leads to the formation of a feed-forward circuit where the strength of individual synapses is correlated with presynaptic selectivity, but independent of the presynaptic preferred stimulus. Assuming selectivity to be a measure of input signal reliability, we further explore how the correlation between synaptic weight and presynaptic selectivity could be relevant in the context of Bayesian cue integration. Our results suggest a model of sensory cortex where the number of spines defines preferred stimulus, while the strength of individual synapses can be used as a measure of input reliability.

3-074. An anatomically accurate circuit for short- and long-term motivational learning in fruit flies

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Many proposed neural circuits for learning are theoretically well-grounded but have limited biological evidence to support them. Emerging anatomical and functional data from neurons in the fruit fly brain allows us to identify interconnections in the mushroom body neuropil that form an 'incentive circuit', supporting rich dynamics of memory acquisition, consolidation and forgetting. In addition, new insights into dopamine function in the fruit fly brain motivate a novel 'dopaminergic plasticity rule' that alters the weights between input sensory patterns and output neurons of the mushroom body. Three output neurons and three dopaminergic neurons for each valence (i.e. attraction or avoidance) allow the flexible formation of short-term memories, transfer to long-term memory, and balancing between opposing valences for similar stimuli, resulting in an effective exploration-exploitation trade-off. Each element of the proposed circuit is mapped to identified neurons in the fruit fly brain, and we show that the simulated responses produced by modelling this circuit and plasticity rule closely replicate experimental data recorded in these neurons, while a reward prediction error rule causes catastrophic forgetting. By testing our model in 92 olfactory conditioning paradigms collected from previous studies, we show a strong correlation to the resulting behaviour. Finally, when this circuit is used for controlling the behaviour of simulated flies, it replicates many features of fly behaviour such as the differential acquisition of aversive and attractive memories despite symmetry in the neural circuitry. This provides new insight into the underlying mechanisms of associative learning that might generalise beyond the fruit fly brain.

3-075. One engram, two ways to recall it

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Animals learn when punishment or reward is predicted by neutral stimuli like tones or odors. Synaptic plasticity maps the predictor to the appropriate behavioral drive, forming a memory trace. But if the predictor is presented as one of two options, the optimal response is uncertain and depends on the alternative. Can a single memory trace evoke different behaviors, depending on stimulus context? We used optogenetics in Drosophila to form an odor-punishment association restricted to a single set of synapses, ie. a single memory trace. These flies showed flexible behavioral responses to a given odor stimulus. Depending on the choice, flies either generalized the association from the learned odor (A) to an unreinforced, similar odor (A'), or discriminated between them. We measured neuronal activity in the fly memory circuit, the mushroom body. The mushroom body output neuron (MBON) downstream of the memory trace had indistinguishable responses to single pulses of odors A and A' - generalizing across them. But if odors were presented as transitions from A to A', mimicking the fly crossing an odor boundary, MBON responses to A' were dramatically altered, allowing discrimination. Receiving odors in a specific sequence caused the MB circuit to alter the output of the memory trace. We tested this behaviorally. When odors were presented singly, flies responded to the punished odor, A and A' indistinguishably. Only when A transitioned into A', fly behavior switched and they were attracted to A'. An association assigns valence or meaning to a stimulus. But valence is subjective and ever-changing, depending on ongoing events in the environment. Our study reveals a novel way for animals to modulate how a test stimulus evokes behavior, based on ongoing stimulus

dynamics. This is an important step to move beyond a plasticity-centric view of memory recall.

3-076. Stimulus-specific olfactory processing via nonlinear transient dynamics

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Olfactory Receptor Neurons (ORNs) in insects are tightly packed into sensory hairs (sensilla), where they are electrically coupled. This organization is highly stereotyped and genetically determined. Electrical ('ephaptic') coupling between neurons within the same hair results in strong lateral inhibition, posing questions about the functional significance of the stereotyped organization. We developed a phenomenological model of coupled ORNs responding to odor mixture stimuli. Our model includes two forms of nonlinearity, essential to capture the nature of the coupling. First, ephaptic interaction depends on the activation level of both neurons, unlike 'regular' synaptic coupling. Second, the interaction is strong only if the activity of either ORN exceeds a threshold. We derived a complete analytical solution for the transient and steady-state dynamics of the model, and used it to fit the model parameters to electrophysiological measurements from one sensillum-type. Our fit results are consistent with independent morphometric measurements of the same sensillum. A detailed analysis of model dynamics suggests that electrical coupling can extract the valence of odor mixtures via transient signal amplification. Extracting a valence signal may allow for efficient initiation of some behaviors, bypassing the need for odor identification. Beyond valence computations, our theory suggests that the conserved asymmetries of coupling strength sensitize the ORN array to specific odor mixtures which are hard-coded in the morphometry of sensilla. Combining our theory with recently published fruitfly connectomes will make experimentally testable predictions for both electrophysiological and behavioral experiments in flies responding to natural odor mixtures in realistic settings.

3-077. Inferring olfactory space from glomerular response data

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Sensory coding in olfaction remains poorly understood. Unlike in vision, where the stimulus space is well-characterized, the complexity of the "odor space" and the complexity of the olfactory receptor (OR) repertoire has hindered our understanding of odor coding and processing. There is no consensus on key defining features of odor sensation, such as the dimensionality of odor perceptual or odor receptor space. It is commonly conjectured that the ORs transform the high-dimensional "chemical space" to a relatively low-dimensional space of neuronal representations.

We developed a novel method for the inference of a stimulus space from neural activity. This method makes no assumptions on the underlying stimulus space; instead it assumes that the receptive fields are half-spaces in some natural coordinate system in the underlying olfactory space. A key feature of this method is that it is insensitive to the inherent (and unknown) monotone non-linearities of neuronal responses.

It turns out that it is possible to infer the stimulus space from the noisy and sparse data that is available for the activity of olfactory receptors in flies and mice. Our method converts the activity of each OR into a combinatorial summary that records relative rankings of neuronal responses; we then construct the stimulus space based on these rankings. We found that the olfactory space constructed with our method has several desired properties: the space is consistent between individual mice, odorants from the same chemical classes are roughly clustered together, and the space cleanly captures the effect of changing odorant concentration.

3-078. Exploiting color space geometry for visual stimulus design across animalsMatthias Christenson^{1,2}S Navid Mousavi¹Rudy Behnia¹¹Columbia University²Neuroscience

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Color vision represents a vital aspect of perception that ultimately enables a wide variety of species to thrive in the natural world. For humans, a suite of color management tools, developed since the early 20th century and used in our everyday devices, allow for a straightforward investigation of human color vision. However, unified methods for constructing chromatic visual stimuli in a laboratory setting for other animals are lacking. This has limited the study of visual perception in animals, where the spatiotemporal and chromatic components of vision are often treated separately, and results are difficult to compare across different hardware setups. We have developed stimulus design methods and an accompanying programming package to efficiently probe the color space of any species in which the photoreceptor spectral sensitivities are known. Our hardware-agnostic approach incorporates photoreceptor models within the framework of the principle of univariance. These models inherently represent the spectral distribution of light as a low-dimensional vector, similar to the tristimulus codes used to represent human colors. Using constrained fitting procedures, experimenters will be able to identify the most effective way to combine multiple light sources to create desired distributions of light, and thus easily reconstruct relevant stimuli for mapping the color space of an organism. We include methodology to transfer color stimuli between devices with different light sources. We also show how to incorporate uncertainty of photoreceptor spectral sensitivities as well as how to reconstruct natural scenes in the spatial and spectral domain using our approach and recent hardware advances. Our methods support broad applications in color vision science and provide a color management tool for uniform stimulus designs across experimental systems. More generally, our fitting procedures can also be applied to design stimuli for other sensory organs with a diverse set of filters.

3-079. Photoreceptor dynamics in the context of optimal chromatic codificationLuisa Ramirez^{1,2}Ronald Dickman¹

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The functional properties of the outermost retinal circuits involved in color discrimination are not well understood across species. Recent experimental work on zebrafish has elucidated the in-vivo activity of photoreceptors and horizontal cells as a function of the stimulus spectrum, highlighting the appearance of chromatic-opponent signals at the first synaptic connection between cones and horizontal cells. These findings, altogether with the observed lack of gap junctions, suggest that the primary mechanism yielding early color opponency in zebrafish is a dominant inhibitory feedback. The relevance of the observed neuronal activity is discussed in the context of efficient codification of chromatic information, hypothesizing that opponent chromatic signals provide an optimal codification minimizing signal redundancy. We examine whether these functional properties are general across species by studying the dynamical properties of dichromatic and trichromatic outermost retinal networks. Our findings show that dominant inhibitory feedback mechanisms provide an unambiguous codification of chromatic stimuli, which is not guaranteed in networks with strong excitatory feedback, via gap junctions. This provides a plausible explanation for the absence of gap junctions observed in zebrafish outermost retinal layers. In addition, our model suggests that in zebrafish retinas, the simplest network with dominant inhibitory feedback capable of optimally codifying chromatic information requires at least two successive inhibitory feedback mechanisms. Finally, we contrast the chromatic codification performance of zebrafish-inspired retinal networks with networks having different opsin combinations. We find that optimal combinations might lead to a chromatic codification improvement of only a 13% compared with zebrafish opsins. This suggests that zebrafish retinas are near to optimal codification of environmental chromatic information.

3-080. The smart image compression algorithm in the retina: recoding inputs in neural circuits

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Sensory neural circuits rely on a common set of motifs to process inputs, including convergence of multiple inputs to a single neuron, divergence of inputs into parallel pathways, and nonlinearities that are selective for some inputs over others. Past work has detailed how optimized response nonlinearities and synaptic weights can maximize encoded information, but these solutions depend on tightly tuned response functions and connectivities. Our study found that incorporating generic, non-invertible, selectivity-inducing nonlinearities into a circuit with divergent and convergent structure can enhance encoded information despite the information loss induced by the convergence of inputs and the nonlinearities when considered separately. This study extends a broad literature on efficient coding in single neurons to more complex circuits. Our study shows how neural circuits may combine selectivity at the single neuron level with convergent and divergent circuit architectures to flexibly maximize encoded information.

3-081. Localized balance of excitation and inhibition leads to normalization

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Excitatory and inhibitory inputs to cortical neurons remain balanced across different conditions. The balanced network model (Van Vreeswijk & Sompolinsky 1998) provides a self-consistent account of this observation: under mild inequality conditions on connectivity parameters, population rates dynamically adjust to yield a state in which inputs to all neurons are tightly balanced, keeping all populations active at biological levels. Global tight balance, however, predicts a linear stimulus-dependence for population responses and cannot explain systematic cortical response nonlinearities such as divisive normalization, a form of sublinear integration and a canonical brain computation (Carandini & Heeger 2012). Nevertheless, when necessary connectivity conditions for global balance fail, states arise in which only a subset of neurons are active and have balanced inputs. While such localized balance states open the door to nonlinear behavior (Baker et al. 2020), it is unknown if they yield sublinear integration. Here we show that in networks of neurons with different stimulus preferences, localized balance robustly leads to sublinear integration, including normalization and winner-take-all behavior. We analytically quantify these effects and derive inequality conditions for their emergence. An alternative model that exhibits normalization is the stabilized supralinear network (SSN), which predicts a regime of loose, rather than tight, excitatory-inhibitory balance (Ahmadian & Miller 2021). However, an understanding of the causal relationship between excitatory-inhibitory balance and normalization in SSN and conditions under which SSN yields significant sublinear integration are lacking. For weak inputs, SSN integrates inputs supralinearly, while for very strong inputs it approaches a regime of tight balance. We show that when this latter regime is globally balanced, SSN cannot exhibit strong normalization for any input strength; thus, in SSN too, significant normalization requires localized balance. In summary, we causally and quantitatively connect a fundamental feature of the dynamics of cortical excitation and inhibition with a canonical brain computation.

3-082. Normative Network Regularization for Neural System Identification

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Neural system identification aims at learning the response function of neurons to arbitrary stimuli by incorporating the right assumptions into the model that facilitate generalization beyond the particular stimuli used during training [1]. Here, we present normative network regularization as a novel regularization tool that allows to flexibly impose prior assumptions into the model training. In particular, we use this approach to incorporate the efficient coding hypothesis as a regularizer which states that neural response properties of sensory representations are strongly shaped by the need to preserve most of the stimulus information with limited resources [2]. Using this approach we explore if natural input statistics could help to improve predictive performance of neural responses. To this end, we regularized the filters of a system identification model with a normative efficient coding model, to predict the responses of retinal neurons to noise stimuli. By forcing both models to share convolutional filters, we found a synergy between neural system identification and efficient coding. As a result, the normative regularization approach did not only yield a higher performance than the “stand-alone” system identification model, it also produced more biologically-plausible filters. We found these results to be consistent for different stimuli and across model architectures. Moreover, our normatively regularized models performed particularly well in predicting responses of direction-of-motion sensitive retinal neurons. In summary, our results demonstrate how the efficient coding hypothesis can be successfully leveraged as normative regularization for the identification of neural response properties.

3-083. Bayesian active learning for closed-loop synaptic characterization

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Model fitting methods have been widely used in neuroscience to infer the parameters of a biophysical system from its responses to experimental stimulations. For instance, the parameters of a chemical synapse (e.g. the number of presynaptic vesicles, or its depression time constant) can be estimated from its postsynaptic responses to evoked stimuli. However, these estimates critically depend on the stimulation protocol being used. Experiments are often conducted with non-adaptive stimulation protocols that may not yield enough information about these parameters. Here, we propose using Bayesian active learning (BAL) for synaptic characterization, and to choose the most informative stimuli by maximizing the mutual information between the data and the unknown parameters. This requires performing high-dimensional integration and optimization in real time. Current methods are either too time consuming, or only applicable to specific models. We build on recent developments in non-linear filtering and parallel computing to provide a general framework for online BAL, which is fast enough to be used in real-time biological experiments and can be applied to a wide range of statistical models. Using synthetic data, we show that our method has the potential to significantly improve the precision of inferred synaptic parameters. Finally, we explore the situation where the constraint is not given by the total number of observations but by the duration of the experiment.

3-084. AutSim: Principled, data driven model development and abstraction for signaling in synaptic protein synthesis in Fragile X Syndrome (FXS) and healthy control.

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Data provenance and model complexity are recurring challenges when simulating neural function, particularly signaling, at the level of detail needed to address disease conditions. Here we report a data-driven modeling and model abstraction framework applied to ~40 signaling pathways involved in translation and FXS. FXS is an X-linked neurodevelopmental disorder caused by the loss of FMRP which is an essential regulator for local translation at synapses. Bowling et al., 2019 had suggested that the de-novo translation profiles tend to differ in FXS mouse at steady-state and in the presence of mGluR5 agonist. Thus, we wanted to study how the mGluR5 signaling cascade is affected in FXS using an in-silico model of rodent dendritic spine. We used detailed biochemical (Mass-action+ODE) modeling to study synaptic translation in FXS neurons. We drew on ~320 published experiments, spanning measurements from receptors such as mGluR1/5, TrkB, EGFR and b2AR, to intervening kinases, to protein synthesis. The resultant model has ~250 reactions and 350 protein pools, making it difficult

to parameterize. Therefore, we developed a pipeline to hierarchically optimize the model to fit experiments and score subsections of the model, based on how closely the model outcome matches experiments. To anchor this enormous parameter fitting process, we built abstract models with all major nodes of the detailed model using the HillTau formulation (Bhalla, 2020 bioRxiv) but with a much reduced parameter space of ~180 parameters. These abstract models were used to synthesize experiments to provide a scaffold of input-output properties that the detailed model subsets must fit. The resulting models will be used to understand how different signalling cascades are affected in a FXS neuron. In summary, we have developed a principled, hierarchical methodology to use experiments to generate both detailed and abstract models of complex cellular signaling, which are all valuable resources for the field.

3-085. Semi-supervised sequence modeling for improved behavior segmentation

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A popular approach to quantifying animal behavior from video data is through behavioral segmentation, wherein video frames are labeled as containing one or more discrete behavior classes, such as grooming or rearing. These behaviors are often manually labeled, which is time consuming and error prone. An alternative approach is to train a sequence model which learns to map behavioral features extracted from video frames to discrete behaviors, although supervised models still require manually labeled examples to learn from. In order to reduce the need for expensive manual labels in this supervised setting, we introduce a semi-supervised approach that takes advantage of the rich spatiotemporal structure in unlabeled frames to learn a stronger sequence model. This approach constructs a sequence model loss function with three terms: (1) a standard supervised loss that classifies a sparse set of hand labels; (2) a weakly supervised loss that classifies a set of easy-to-compute heuristic labels; and (3) a self-supervised loss that predicts the evolution of the behavioral features. We show how this approach can effectively leverage a large number of unlabeled frames to outperform fully supervised segmentation with fewer labeled frames across a variety of species, behaviors, and experimental paradigms: a head-fixed and spontaneously behaving fly; a head-fixed mouse performing a perceptual decision-making task from the International Brain Laboratory; a freely moving mouse in an open field arena; and two mice in a resident-intruder assay. Our approach thus provides a frame-by-frame estimate of an animal's behavior, which can be crucial for understanding the effects of experimental and environmental manipulations, with less manual labeling effort.

3-086. Visual association cortex immediately reactivates sensory experiences

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How do we learn about experiences while being removed from the experience itself? One solution involves offline learning via reactivations. Sensory reactivation involves the recurrence of a pattern of neural activity during sleep or quiet waking that previously occurred during a sensory experience. Historically, reactivations have been studied in the hippocampus. However, whether reactivations in sensory cortex depend on local activation of neurons during prior experience is not well understood. We hypothesize that such reactivations in sensory association

cortex could be important for learning. To study reactivations in mouse visual cortex, we used a simple paradigm and presented two different 2-s visual cues, each followed by a 60-s inter-trial-interval to assess reactivations. We imaged calcium activity simultaneously in thousands of layer 2/3 excitatory neurons in lateral visual association cortex using jGCaMP7s. Our preliminary studies suggest that offline cue reactivations decrease across time within individual inter-trial intervals, and within each two-hour long session. Strikingly, the content of cue reactivations were 2-3 times more likely to reflect the most recently presented cue. The network responses to the two cues gradually became more distinct across trials, which correlated with the time-varying rates of cue reactivations. To determine whether activity in lateral visual association cortex is necessary to produce biased cue reactivations, we silenced cue-evoked responses unilaterally in lateral visual cortex by activating PV+ interneurons with Chrimson while concurrently imaging calcium activity. We found that both the rate of cue reactivations and the bias in reactivations to the most recent cue dramatically decreased, suggesting that lateral visual association cortex is necessary for generating the post-cue enhancement in cue reactivation rate. These results provide evidence of pronounced and widespread reactivations in visual association cortex during offline periods between cue presentations. We suggest that these reactivations provide a unique means for distributed sensory and associative learning.

3-087. Abstract cognitive encoding in the primate superior colliculus

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Animals are remarkably adept at recognizing the categorical significance of stimuli and using this information to guide behavior. Investigations of visual categorization in primates have focused on a hierarchy of cortical areas that transform veridical sensory information into abstract categorical representations. However, categorical behaviors are evident throughout the animal kingdom, including in species without a neocortex, raising a question about the contributions of subcortical regions to primate categorization. One candidate structure is the superior colliculus (SC), a midbrain sensorimotor region that is evolutionarily conserved across vertebrates. Previous studies have shown that the primate SC is involved in cognitive tasks that involve spatial orienting, but its role in non-spatial cognitive functions is not well understood.

We trained monkeys to perform a visual categorization task and recorded activity in the SC and the lateral intraparietal area (LIP), a cortical region previously shown to be causally involved in categorical decisions. The task required monkeys to maintain fixation on a central cue and to report their decisions with a lever release. We show that the SC exhibits categorical encoding that is stronger and arises with a shorter latency than in the LIP, is evident during both stimulus viewing and a memory delay period, and is independent of the actions that monkeys used to report their decisions. This suggests that the primate SC is involved in abstract cognition, even in tasks that involve neither saccadic eye movements nor explicit manipulation of spatial attention. These results provide a novel perspective on subcortical contributions to cognition in primates, and have significant implications for models of high-level visual processing in the primate brain.

3-088. Hippocampal spatio-temporal cognitive maps adaptively guide reward generalization

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The brain forms cognitive maps of relational knowledge, an organizing principle thought to underlie our ability to generalize and make inferences. Such map-like representations may facilitate goal-directed behavior by enabling generalization of information across related states. However, it is not fully understood what neural and com-

putational mechanisms give rise to map-based generalization, nor how a relevant map may be selected when a stimulus is embedded in multiple relational structures. Here, we find that both spatial and temporal cognitive maps influence reward generalization in a choice task, where spatial location determines reward magnitude. Employing Gaussian Process regression to model reward generalization, we find corresponding hippocampal map representations of not only spatial relationships, but of temporal relationships as well, providing novel neural evidence for hippocampal map-based reward generalization. As the task progresses, we observe a strengthening of the spatial map and a weakening of the temporal map in the hippocampus, which is reflected behaviorally in participants' choices becoming more influenced by the spatial map over time. We find that this change in both behavior and neural representations are driven by a signal in orbitofrontal cortex (OFC) which represents the degree to which an observed reward is consistent with the spatial rather than the temporal map, and which updates hippocampal representations accordingly. In the end, the participants whose decisions become more influenced by the spatial map as the task progresses display the largest increase in the strength of the spatial map representation in the hippocampus from before to after the choice task, an effect which is mediated by the signal in OFC. Overall, our work demonstrates computationally and neurally how hippocampal cognitive maps, in conjunction with a signal from OFC, are used and updated flexibly for inference and reward generalization.

3-089. Modeling Hippocampal Spatial Learning Through a Valence-based Interplay of Dopamine and Serotonin

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Hedonic or valence-based learning by valence is inherent to cognition. From a neuroethological perspective, value-assignment requires emotional or volitional characteristics that improve the representation of the environment. Such processing is especially relevant in functions involving episodic memory such as spatial learning, in which navigation may be enhanced by associating states with hedonic values – e.g., the poisonous plant near the river is aversive, and the prey inside a cave is attractive.

In this context, dopamine (DA) and serotonin (5-HT) have been studied in their encoding of oppositional valence, whereby DA is driven by positive or appetite-driven rewards and 5-HT acts for negative or aversive stimuli. Both neuromodulators are known to be involved in hippocampal synaptic plasticity and, under certain conditions, DA and 5-HT produce, respectively, long-term potentiation (LTP) and depression (LTD).

Here, we examine an antagonistic interplay of these modulators in a navigational model. We compare two reward-modulated spike time-dependent plasticity (R-STDP) learning rules to describe the action of DA and 5-HT. Our results show that modeling the balance between DA and 5-HT as a compensatory mechanism matches the improvement of spatial learning performance observed experimentally in the Morris water maze (MWM) task. We also analyze how the timing assumptions underpinning each rule account for the value description of the environment. Furthermore, this system allows us to predict spatial reversal learning in an open field (OF).

3-090. The role of inhibition in shaping memory-encoding hippocampal sequences

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Hippocampal networks link temporally contiguous memories through spiking sequences that encode sensory cues (external world) and time between them (internal representations), constructing 'memory-maps' of related

experiences. It was recently shown that such sequences combine particularly stable representations of sensory cues with highly dynamic, learning-dependent temporal-codes. This combination of stability and flexibility allows linking fixed elements of the external world across variable time intervals. But how does feedback inhibition by parvalbumin- (PV) and somatostatin-expressing (SOM) interneurons (INs) control the shaping and stability of these multi-modal representations? First, we employed two-photon calcium imaging *in vivo* in the CA1 area of head-fixed mice, to track the activity of non-specific GABAergic INs across days, while mice learned and performed an olfactory delayed non-match-to-sample task (DNMS) requiring working memory. We found that a subset of INs yielded significant odor- and time-fields, collectively forming odor-specific sequences. These ‘odor-INs’ and ‘time-INs’ had lower odor-selectivity and noisier activation than pyramidal cells (PY), yielding poor cue-decoding performance. Moreover, odor-IN had more stable fields than time-IN, but overall, much more unstable ones than PY fields across days. Importantly, unlike PYs, the number of time-cell INs did not increase during learning of the task. Secondly, through ultra-fast, voltage imaging *in vivo* on transgenic mice, we recorded single action potentials and subthreshold membrane dynamics from multiple PV and SOM INs during DNMS performance. We followed the same cells across multiple days, before and after DNMS training. We confirmed that both PV and SOM INs yielded odor-fields with reduced odor-specificity. Moreover, increased spiking during odor-presentation was accompanied by an increase in intracellular theta and beta oscillations in subthreshold traces, which was stronger for PV than SOM INs. Therefore, PV and SOM IN ensembles provide timed but not cue-specific inhibition. They thus increase the signal-to-noise-ratio of PY sequences by silencing the non-cue-specific PY population.

3-091. Probing neural value computations in the nucleus accumbens dopamine signal

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Dopamine (DA) in the nucleus accumbens (NAc) is a critical signal for both learning and motivation. While DA release dynamics are often associated with reward prediction errors, they also scale remarkably well with a state-value signal – expectations of reward from an animal’s current state. However, computing value in real-world environments poses a substantial computational problem. Expectations of future rewards from a given state depend on future actions and their reward likelihood. Computing state value, therefore, necessitates assumptions about future navigational choices. Furthermore, values could be cached for quick access during behavior, or they could be computed on-the-fly to flexibly evaluate options. We investigated what strategy the brain uses to compute value in the NAc DA signal. We measured DA release dynamics in the NAc using the fluorescent biosensor dLight1.3b in Long-Evans rats ($n=7$) as they foraged for reward in a novel naturalistic decision-making task, the Triangle Maze. As in real-world environments, the Triangle Maze requires rats to evaluate navigational options to pursue probabilistic reward, while movable barriers periodically alter path structures. We first confirmed that spatial-state-value estimates significantly explain NAc DA dynamics during navigation. We then leveraged this relationship to test how NAc DA was estimating value. Prior to a navigational choice point, NAc DA scaled with expectations about the subsequently taken navigational trajectory, reflecting realistic assumptions about future behavior. Finally, we found evidence suggesting that NAc DA is computed on-the-fly when navigational decisions require planning. NAc DA was released to a greater degree during flexible versus stereotyped periods of behavior, especially following changes in state-transition matrix structure. Insights into how the brain computes value will help inform our current models of decision making, including the assumptions we build into artificial agents.

3-092. VTA dopamine neurons signal phasic and ramping reward prediction error in goal-directed navigation

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The predominant theory of ventral tegmental area (VTA) dopamine neuron function is that they signal reward prediction error (RPE) in their phasic activity. Some recent studies have observed ramping dopamine neuron activity, but its relationship to RPE signalling is currently under debate. We set out to explain the function of this ramp and its relationship to phasic RPEs, using both experimental and theoretical methods. We chose to examine goal-directed navigation, as it requires learning to accurately estimate location and select optimal actions in each location. Given that VTA dopamine neurons are involved in value learning, action selection, and reward location learning, they are ideally placed to provide teaching signals for goal-directed navigation. We characterised VTA dopamine neuron activity by performing calcium imaging using a Miniscope as mice learned to navigate in a closed-loop virtual reality corridor and lick to report a reward location. Across learning, phasic responses resembling RPEs developed, as well as a slow pre-reward ramp in activity. The slope of this ramp was modulated by both learning stage and task engagement. The ramp slope was inversely correlated with locomotor speed, indicating that the ramp did not reflect motor vigour, contradicting previous studies. We considered whether ramping VTA dopamine neuron activity could represent a form of RPE. We devised a Q-learning model that incorporated noisy state inference and an eligibility trace. This model recapitulated our behavioural findings and produced simultaneous phasic and ramping prediction error. The model predicted that a ramp should improve task performance, which we confirmed in our experimental data, indicating that the ramp played a teaching role in the selection of accurate location-specific action during navigation. Our findings provide neural evidence and a theoretical framework to explain ramping dopamine neuron activity as a form of RPE that improves goal-directed navigation.

3-093. Neurons in dlPFC signal unsigned reward prediction error independently from value

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Signaling that an expectation has been violated is a central function of the nervous system. This signal may come in the form of a reward prediction error, which can either be signed, reflecting the value of an unexpected outcome, or unsigned, reflecting the capture of attention. The role of dorsolateral prefrontal cortex (dlPFC), known to carry both value and attention related signals, in communicating when expectations are violated is not well understood [1,2]. How are unexpected outcomes signaled in dlPFC? To address this question, we trained macaque monkeys to view displays consisting of two cues presented in a predictive sequence while recording from small populations of neurons in dlPFC. The second cue in the sequence usually confirmed, but occasionally violated, the expectation set by the first cue. At the end of each sequence, either a small or a large reward was delivered to the monkey, based on the identity of the second cue. This paradigm allowed us to analyze neuronal sensitivity to both value as well as to unexpected events. We report three main effects. First, we found that, in addition to signaling value, activity in dlPFC was enhanced to cues that violated rather than confirmed an expectation. This enhancement took the form of an unsigned reward prediction error, occurring both when the unexpected outcome was better and worse than expected. Second, we found pairwise correlations were reduced to cues that violated rather than confirmed an expectation. Lastly, we found the reward prediction error signal was dissociable from the value signal across the neuronal population. We conclude that dlPFC carries an unsigned reward prediction error signal in response to unexpected outcomes, which is separable from its value signal. This pattern is consistent with the interpretation that unexpected events, regardless of their valence, enhance dlPFC response strength by capturing attention.

3-094. Irrational choice via curvilinear value geometry in ventromedial pre-frontal cortex

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Converging evidence suggests that we make decisions by comparing the value of the options in front of us, but how are these values represented in the brain? Many models assume that the representational geometry of value is linear, and this shape could be important for generating rational economic decisions. However, in part due to historical focus on noisy single neurons, rather than neural populations, the linearity hypothesis has not been rigorously tested. Here, we examined the representational geometry of value in populations of neurons recorded in the ventromedial prefrontal cortex (vmPFC), a part of the prefrontal cortex closely linked to economic decision-making. Monkeys performed a “menu search” task in which they chose between a set of reward cues associated with different volumes of juice. Although the average neuronal response to offer values was essentially linear, at the population level, multiple converging analyses suggested that offer values were encoded along a curved manifold in vmPFC. The curvilinear geometry predicted a specific violation of one of the axioms of rational decision-making, which posits that the preference between high-value options should not depend on adding irrelevant, low-value alternatives to the set. Instead, when the representation of values is curved, the upper bound on the accuracy of decoding high-value offers changes systematically with the value of the worst option in the set. Critically, monkeys exhibited exactly the paradoxical pattern of irrational choices predicted by the curvilinear manifold: the worse the irrelevant offer was, the more likely they were to confuse two good options. Together, these results suggest that neural representation of values may not be linear, as is generally assumed, but instead traces a curvilinear manifold, at least in vmPFC. This nonlinearity could be one cause of the systematic patterns of irrational economic decisions that appear in humans and other animals.

3-095. Imagining what was there: looking at an absent offer location modulates neural responses in OFC

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When making choices, we allocate our fixations to each contemplated option, and tend to look longer at more valued ones (1-5). The purpose of fixation during choice remains unknown. Here we examined behavioral and neural activity of rhesus macaques (*Macaca mulatta*) performing a two-options risky choice task in which offers occurred in sequence, each followed by a long (600 ms) blank screen delay period. As expected, we found that subjects allocated their gaze towards offer presentation locations and spent more time looking at most valuable offers; after factoring out value, we found that more looking time was devoted to the chosen offer. Surprisingly, we found the same pattern before choice execution when the screen was blank: subjects spent more time fixating the locations where valuable offers had occurred. Moreover, we found that neural encoding of the offers’ expected values in orbitofrontal cortex (OFC) is modulated by eye position even when the screen is blank. Specifically, when gaze is directed to a former offer location, its value is more strongly encoded in OFC, while the encoding of the alternative offer value is suppressed. The same modulatory effects by gaze on value encoding are observed later in the trial when monkeys were supposed to report their choice while both offers were presented simultaneously. Our results provide evidence that eye position reflects and internal deliberation process that modulates the encoding of imagined content, providing a new window to study the hidden dynamics of decision making. (1) Krajbich, I., Armel, C. and Rangel, A., 2010. *Nat. Neuroscience*, 13(10), pp.1292-1298; (2) McGinty, V.B., Rangel, A. and Newsome, W.T., 2016. *Neuron*, 90(6), pp.1299-1311. (3) Padoa-Schioppa, C. and Assad, J.A., 2006. *Nature*, 441(7090), pp.223-226; (4) Strait, C.E., Blanchard, T.C. and Hayden, B.Y., 2014. *Neuron*, 82(6), pp.1357-1366; (5) Rich, E.L. and Wallis, J.D., 2016. *Nat. Neuroscience*, 19(7), pp.973-980.

3-096. How does the dorsal striatum contribute to active choice rejection?

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Choice rejection is an important part of decision making with high clinical relevance for addiction. Our goal is to understand how neural circuits are engaged during active rejection. This question is largely understudied due to a focus on choice omission, freezing, or stopping in animal studies of behavioral control. Similarly, two-alternative forced choice studies of decision making also fail to isolate active rejection from acceptance since these two aspects of decision making occur in parallel in these tasks. To better isolate active rejection, we adapted a serial decision-making task, Restaurant Row, in which mice decide to either accept or reject reward offers as they traverse four interconnected T-mazes. Mice report accept choices by turning right for an opportunity to receive a food pellet or turn left to actively reject an offer and continue to the next T-junction. Fiber photometry recordings were used to compare dSPN or iSPN activity preceding reject choices at each T-junction in Restaurant Row. We also recorded from these same mice in a two-arm bandit (2ABT) task.

3-097. Balancing safety and efficiency in human decision-making.

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Across species, survival depends on harvesting essential rewards such as food in the face of potential, occasionally catastrophic, dangers (such as serious injuries). This presents the challenge as to how to remain as efficient as possible when it comes to reward acquisition, whilst avoiding accrual of damage, especially during early exploration of new environments. This safety-efficiency dilemma is a special case of the exploration-exploitation dilemma, which typically collapses punishment and reward into a single scalar signal, whereby early losses can be overcome by later gains. However, the agent might want to consider losses separately in scenarios where damage can accrue and potentially lead to death. One approach is to keep value learning systems for reward and punishment separate, and only integrate them to make choices. Indeed the brain appears to adopt this strategy by overlaying a Pavlovian fear system atop an instrumental reward system. In a series of grid-world simulations, we show here how this emulates a multi-attribute reinforcement learning system that promotes safe learning, especially in early exploration. But it also introduces the problem of how to arbitrate when Pavlovian avoidance actions do not align with that of the reward-oriented instrumental system. Indeed we show that different learning environments may require a different balance of rewards and punishment, which implies the best strategy is to have a flexible Pavlovian fear commissioning scheme. We propose a model for doing this in which Pavlovian ‘fear’ actions are gated by uncertainty: and show that this enhances safety in early exploration and hence improves safety-efficiency trade-offs. In conclusion, our work shows how safe exploration can be achieved by a flexible Pavlovian fear system without too much cost to efficiency. One implication of this is that inflexibility of the fear commissioning parameter could lead to maladaptive anxiety, depression and chronic pain.

3-098. Dual pathway architecture in songbirds boosts sensorimotor learning

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Juvenile songbirds learn to imitate adult vocalizations. Song acquisition and production is governed by a dedicated neural circuitry that involves two parallel pathways: a cortical pathway required for production and a basal ganglia-thalamo-cortical (BG) pathway necessary for plasticity. The BG pathway induces variability in production during vocal exploration, receives a performance signal via midbrain dopaminergic projections and drives a motor bias that corrects vocal errors. This dopamine-modulated change in vocal output, induced by the BG is gradually consolidated within the cortical pathway. Reinforcement learning (RL) has been widely hypothesized to underlie sensorimotor learning, including song learning. However, pure RL approaches may result in non-optimal solutions under uneven reward contours in a continuous action space. We propose to re-interpret the role of the dual pathway architecture in songbirds and to help overcome these limitations. We posit that the BG pathway conducts daily exploration by inducing large jumps in the vocal exploration. BG-driven vocal exploration is modulated over both the daily and weekly timescales, as the cortical pathway matures. The cortical pathway gradually consolidates BG reward-modulated exploration with Hebbian learning. We demonstrate how this process essentially implements simulated annealing. In an artificial reward landscape, the dual pathway network can reach the global optimum in a number of trials, comparable with the learning period of songbirds (60 days of learning, 500 trials per day). We further emulate an experimental protocol to induce plasticity in adult birds by locally modulating the reward profile around the global optimum after convergence. As observed experimentally, our model network adapts to this change in reward profile and modifies its vocal exploration profile. To further test this interpretation, we shall contrast with ongoing electrophysiological investigations in the output nuclei of these two pathways in zebra finches, subjected to a distorted feedback protocol.

3-099. Contextual motor learning in birdsong reflects two distinct neural processes

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Optimal motor performance requires flexible adjustments to behavior depending on different contexts. This idea has gained wide support from behavioral and computational studies, but remains poorly understood at the neural level. Bengalese finch (*Lonchura striata*) song is a learned motor sequence composed of discrete elements, or syllables. Adult finches can learn to modify the pitch of individual syllables in a gradual way, supported by a well-understood cortical-basal ganglia circuit, the AFP (anterior forebrain pathway). We here tested whether adult finches can use arbitrary contextual cues to flexibly and immediately switch between different modifications of the pitch of a target syllable. We paired opposite directions of pitch reinforcement for the same syllable with different colors of cage illumination, e.g., reinforcing upward pitch shifts in orange light and downward pitch shifts in green light. After training, light switches elicited immediate adaptive changes to song that minimized aversive feedback in each context. At the behavioral level, we could dissociate two processes, an immediate cue-dependent pitch shift at the beginning of new context blocks, and a gradual reinforcement-dependent pitch adaptation within context blocks. At the neural level, we show that immediate cue-dependent pitch shifts are independent of the AFP, while lesions of this circuit abolished gradual pitch adaptation, consistent with prior studies. This indicates that rapid sensory context-dependent pitch shifts are mediated by different mechanisms than gradual pitch adjustments. Prevailing models of contextual motor adaptation argue for at least two parallel processes: one that is flexible, and sensitive to contextual information, and a second that cannot readily be associated with contextual cues and is gradually updated during motor adaptation. Our results indicate that context-dependent pitch learning in birdsong likewise involves two dissociable processes, based on different neuronal circuits. This provides a window to understand one neural implementation of dual process models in motor adaptation.

3-100. Saccade preparation does not benefit visual change detection

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Saccades enable primates to sample their visual environments at high resolution. Yet, even before the saccade occurs, visual discrimination sensitivity increases at the saccade target location. Does this benefit occur in all scenarios? To address this question, we designed a dual-task paradigm involving visual change detection. On each trial, participants ($n=10$) prepared and executed a saccade to one (cued) of four grating locations while concurrently localizing a change in grating orientation that immediately preceded the saccade. Surprisingly, we found no improvement in orientation change detection sensitivity at the saccade target (ST) location relative to the other locations: while the proportion of hits increased marginally, the proportion of false-alarm increased significantly. To investigate this result further, we performed another experiment in which participants ($n=10$), presaccadically, estimated the precise orientation of one of four gratings. Here, presaccadic precision of orientation estimates was indeed higher for ST gratings, as expected. Yet, when a second set of gratings – oriented completely differently – was flashed immediately after the first set, the benefit in presaccadic precision shifted to the more recent (second) set and, surprisingly, vanished for the original (first) set. We modeled these behavioral findings with a Bayesian ideal observer model: the variable precision (VP) model. Change detection behavior was best fit by a VP model that accounted not only for differences in precision across locations but, interestingly, also incorporated a different (lower) detection criterion at the ST location. In summary, presaccadic benefits on sensory precision occurred only for the most recent of multiple, sequential stimuli, suggesting that resource-limited neural populations encode precision dynamically at the prioritized saccade target location. Moreover, saccade preparation lowered change detection criteria and increased false-alarms at the saccade target location. Our results show, for the first time, that presaccadic benefits do not extend to visual change detection scenarios.

3-101. Associative memory of structured knowledge

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Humans can robustly store and retrieve information with complex and hierarchical structure. Some examples are temporal sequences, where each event is associated to a particular time, episodic memories where each event is associated with a particular context, cognitive maps representing spatial environments through landmarks associated with relative locations, and semantic structures in language in which meaning is conveyed through both the identity of individual words and their role in the sentence. While working memory tasks typically process one structure at a time, a long-term associative memory network must store multiple structures in a manner that allows them to be used upon retrieval for a variety of higher cognitive tasks. In this work, we specifically ask how Hopfield type networks can store and retrieve multiple knowledge structures. We model each structure as a set of binary relations between events and attributes (attributes may represent e.g., temporal order, spatial location, role in semantic structure). We use binarized holographic reduced representation (HRR) to map structures to distributed neuronal activity patterns (Plate, 1994; Eliasmith, 2013). We then use associative memory plasticity rules to store these activity patterns as fixed points in a recurrent network. By a combination of signal-to-noise analysis and numerical simulations, we demonstrate that our model allows for efficient storage of these knowledge structures, so that memorized structures and their individual building blocks (e.g., events and attributes) can be subsequently retrieved, from partial retrieving cues. We show that long-term memory of structured knowledge relies on a new principle of computation beyond the memory basins. Our model can also be extended to store sequences of memories as single attractors.

3-102. Learning sequences with fast and slow parts

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Sequential neural activity is hypothesized to underlie driven motor actions, memories of linked sequences of causal relationships, planning and reflection on navigation through environments, and the tracking of the passage of time, among other brain functions. Sequences arise in recurrent networks with asymmetric connectivity structures [1]. These models are of particular interest because they can be learned with biologically plausible temporal asymmetric Hebbian learning (TAH) rules, providing a foundation for modeling of sequential activity in neural circuits. In existing models, the time interval between each part of the sequence is constant, which does not reflect the reality of behaviorally relevant sequences which may have fast and slow parts. Starting from a mathematical framework derived in [2], we show that the addition of a temporal symmetric Hebbian associative memory term

allows for the modulation of the propagation speed of the sequences. By selectively strengthening and weakening the symmetric term corresponding to particular elements of the sequence, we show that the propagation speed can be modulated to be faster and slower at different parts of the sequence. This provides an answer to a key mystery: how can the brain learn sequences with fast and slow parts?

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3-103. Phase precession and theta sequences in the hippocampus are spatially and temporally segregated

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Two aspects of hippocampal temporal coding during behaviour have come to dominate theories of hippocampal function: phase precession at the single-cell level, and theta sequences at the population level. Both their significance for memory functions as much as their connection to specific network dynamics and to each other, remain matter for speculation. Here we address these questions by taking advantage of simultaneous recordings of population activity and layer-specific LFP dynamics in the CA1 region. What we find is that these two phenomena are largely segregated both at the spatial and at the temporal level. Phase precession appears only in a subset of place fields. Moreover, even for these fields, phase-location correlation only emerges in coincidence with a strong presence of medium gamma in the network. Finally, the effects of phase precession are mostly felt in the early portions of the theta cycle. At the same time, the emergence of theta sequences appears to follow an almost completely complementary pattern. Cells exhibiting stronger phase locking of spikes are more likely to be involved in the sequential encoding of spatial locations, and more strongly so in coincidence with periods dominated by slow gamma oscillations. And as a further demonstration of their separation at a finer temporal scale, theta sequences are more likely expressed in the later portion of the theta cycle. While there has been much debate about the direction of dependency between phase precession and theta sequences, and about which of the two is the most fundamental for hippocampal computations, our results point to a radically different scenario, in which these two aspects of temporal coding are largely independent, if not downright complementary. Indeed, we argue that phase precession might have very little involvement in sequential coding and could be better understood as relevant for modulating plasticity of CA1 pyramidal cells.

3-104. Long-term dynamics of the entorhinal grid code

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The hippocampus and entorhinal cortex form an "information loop": The superficial layers of the entorhinal cortex provide the majority of excitatory input to the dorsal hippocampus, whereas the deep layers of the entorhinal cortex receive most of their input from the hippocampus. The medial entorhinal cortex (MEC) is crucial for the formation of spatial memory, and its inactivation impairs both recent and remote memory retrieval during spatial navigation tasks- indicating a key role for entorhinal neural codes in long term memory. Recent studies have found that hippocampal place codes gradually change over days and weeks when the animal repeatedly visits a fixed familiar environment. However, the long-term dynamics of entorhinal spatial codes have remained unexplored. Here, we developed a novel imaging preparation that enables simultaneous imaging from > 1,000 MEC cells in freely behaving mice. Unsupervised learning extracted hundreds of grid cells from up to four different modules within a single field of view. By tracking the same neurons over weeks, we longitudinally analyzed the long-term stability of grid cells, and compared it to that of hippocampal CA1 place cells. We found that over days entorhinal grid cells gradually changed their tuning while maintaining similar activity rates. Conversely, hippocampal place cells displayed gradual changes in cell activity rates, but their tuning changed to a lesser extent. We found similar differences between MEC grid cells and CA1 place cells when examining drift on shorter timescales (within a session). Overall, we found a double dissociation between MEC grid cells and CA1 place cells with respect to

properties of neural code stability, suggesting that different mechanisms may govern representational drift in these circuits. Moreover, our results suggest that stable grid fields are not a prerequisite for stable place fields.

3-105. Object × position coding in the entorhinal cortex of flying bats

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Successful navigation requires knowledge of the specific locations of different objects. However, currently only an object-invariant signal was discovered, marking all objects at all locations (carried by object-vector cells in the superficial layers of the medial entorhinal cortex (MEC)). It is thus unknown where and if this general object signal is crossed with a signal for a specific location (as is carried by place cells in the hippocampus), and whether these two variables are encoded conjunctively. We hypothesized that if indeed the brain represents object × position in a conjunctive manner, such encoding will be found at the “end” of the MEC-hippocampal-MEC loop – the deep layers of MEC – where all-object information from MEC converges with location-specific information from hippocampal place-cells and is sent to the neocortex. Here we recorded from MEC of flying bats as they foraged for food in a large flight-room where 6–11 identical rest-objects were placed at various heights and locations. We found that a substantial fraction of cells in the deep layers of MEC (but not superficial layers) fired at the vicinity of specific rest-objects at specific locations. These cells fired near the rest-object when the bat flew from or to the object, but not when it flew through the same location without object-engagement – thus encoding object × position. Our results suggest a broader prevalence than currently thought for conjunctive-coding of navigational variables – including the encoding of objects, which are crucially important for navigation.

3-106. Hippocampal representations during natural social behaviors in a bat colony

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Highly-social animals, like humans, live with many individuals, and interact with each other at times, locations and manner of their choosing. However, neurophysiological investigations of social responses are rarely conducted in such rich settings. To determine how the brain represents social information in a naturalistic setting – when the animals’ behavior is not experimentally constrained to a particular task – we constructed a bat cave for a colony of 5–10 bats of both sexes. The bats lived there 24×7, free to engage in any behaviors. Every day we conducted a ~3 hour experimental session, in which we tracked the bats’ identities, their 3D positions and their social interactions while recording from their dorsal CA1 hippocampal neurons. Based on behavioral data analysis, we found that sessions could be divided into three distinct and interleaved phases: (1) Social Interaction phase, (2) Flight phase, and (3) Sedentary phase. Preliminary results indicate that when bats interacted with each other, hippocampal neurons represented specific social events. During flight, we found social regulation of spatial representations – where the place-tuning of neurons was modulated by whether conspecifics were present at take-off or landing locations. During the sedentary phase on their roosts, we reasoned that the neurons could potentially track three broad categories of information: (i) self-position or head direction, (ii) allocentric locations of other bats, or (iii) egocentric information of direction and distance to other bats. We used generalized additive models (GAMs) to elucidate the contribution of these factors to neural spiking. Preliminary findings indicate that single neurons merge several streams of information, and often combine factors related to both self and others. Overall, we found that dorsal CA1 neurons combine complex social and spatial information to form an abstract representation of the natural world.

3-107. The representational geometry of social memory in the hippocampusLorenzo Posani^{1,2}

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The ability to remember and recognize other individuals is crucial for complex social behaviors. Although the hippocampus is known to be fundamental for social memory (Hitti & Siegelbaum, 2014), how this region represents and supports the two processes of social recognition - familiarity and recollection - remains unknown. We used microendoscopic calcium imaging to measure the activity of hippocampal dorsal CA2 pyramidal neurons (dCA2) - a region known for its importance in social memory - in mice interacting with novel and familiar conspecifics in different spatial contexts. Through a decoding analysis, we reconstructed the representational geometry of social and spatial variables in a series of social interaction experiments. We found that both social (familiarity and individual identity of the encountered mouse) and spatial (position of the encounter) variables are decodable from CA2 activity, and that the decoding performance for familiarity positively correlates with behavioral preference for novel animals. Importantly, CA2 represents familiarity as an abstract variable, suggesting that representations of novel and familiar individuals lie on distinct but parallel manifolds in the neural activity space. By comparing the representations of familiar and novel animals, we found that familiarity distorts the representational geometry by increasing its dimensionality, enhancing social-spatial discrimination at the expense of generalization. Finally, we confirmed our geometrical interpretation by showing that a statistical model based on geometrical reasoning is able to reproduce the experimental results. Thus, dCA2 population activity supports social recognition memory through an abstract representation of familiarity and a change in the geometrical properties of recollected social identities.

3-108. Using navigational information to learn visual representationsLizhen Zhu^{1,2}

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Children learn to build a visual representation of the world from unsupervised exploration and we hypothesize that a key part of this learning ability is the use of self-generated navigational information as a similarity label to drive a learning objective for self-supervised learning. The goal of this work is to exploit navigational information in a visual environment to provide performance in training that exceeds the state-of-the-art self-supervised training. Here, we show that using spatial and temporal information in the pretraining stage of contrastive learning can improve the performance of downstream classification relative to conventional contrastive learning approaches that use instance discrimination to discriminate between two alterations of the same image or two different images. We designed a pipeline to generate egocentric-vision images from a photorealistic ray-tracing environment (ThreeDWorld) and record relevant navigational information for each image. Modifying the Momentum Contrast (MoCo) model, we introduced spatial and temporal information to evaluate the similarity of two views in the pre-training stage instead of instance discrimination. This work reveals the effectiveness and efficiency of contextual information for improving representation learning. The work informs our understanding of the means by which children might learn to see the world without external supervision.

3-109. Talking Nets: Neural Networks Trained to Understand and Communicate Task InstructionsReidar Riveland^{1,2}

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One of humans' most astonishing cognitive feats is the dual ability to interpret linguistic instructions to perform novel tasks in very few practice trials and conversely produce a linguistic description for a task once it has been

learned. In contrast, it typically takes thousands of trials for animals to learn even the simplest behavioral tasks. To explore the neural mechanisms that underpin these remarkable abilities, we trained recurrent neural networks to perform a set of common psychophysical tasks simultaneously with task type information provided by the output of a pre-trained transformer architecture processing natural language instructions. To test the extent to which these models can use language to generalize performance to unseen tasks, we trained models on 14 tasks and tested on 2 held out tasks. The key question is whether the networks exhibit 0-shot learning, i.e., the ability to perform the held out tasks solely by being told what to do. We found that this architecture achieves 0-shot performance of 80% correct (and 90% 3-shot) using S-BERT compared to 27% performance for a model that encodes tasks with orthogonal rule vectors. Examining the first 2 PCs of sensorimotor activity across tasks revealed a highly structured representation aligned along task defined axis, even for previously unseen tasks. Finally, if we allow a network to learn through trial and error, without linguistics instructions, we can invert the network's language comprehension and train a decoder to produce a linguistic description of how it solved the task. Strikingly, when produced instructions are provided to a second network trained to perform all tasks with instructions, the second network achieves near perfect performance (97% on average). To our knowledge, this is the first neural model demonstrating how the compositional nature of language leads to strong 0-shot generalization in sensorimotor networks.

3-110. Covert reinstatement predicts recall initiation

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Scholars have long theorized a role for reactivation and rehearsal in maintaining items in memory. Recent evidence suggests that reactivation during awake rest or sleep predicts subsequent recognition and cued recall performance. In a free recall task however, the relationship between covert reinstatement and recall may be more complex because the memory cues must be self-generated and retrieval depends strongly on what has previously been retrieved. Retrieved context theories suggest that covert retrievals during a delay interval should specifically predict the initiation of recall. To test this hypothesis, we analyzed electrophysiological recordings from 116 neurosurgical patients performing a categorized free-recall task. Lists comprised 12 words (four exemplars from each of three taxonomic categories, drawn from a set of 25 categories), and subjects freely recalled these words following an arithmetic distractor task – a time period during which covert reactivation may occur, and in turn support subsequent recall. We trained an encoding model, using regularized regression, to predict oscillatory neural signals during the study period from the semantic (word2vec) representation of the category associated with each word. We validated our model by demonstrating that, during the encoding period on heldout lists, neural activity during word presentation is more similar to the model's prediction for the word's associated category than categories of other words on the list. We then compared model predictions for each category to neural activity during the arithmetic distractor task as a measure of neural reinstatement. We find that distractor activity was more similar to the model predictions for the first recalled category than others on the list and more similar to predictions for categories on the list than those not on the list, confirming the prediction from retrieved context models that reactivation would predict recall initiation.

3-111. You don't always forget: Mechanisms underlying working memory lapses.

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Working memory (WM) is central for cognition and is impaired in many brain disorders including those hypo-

thetically mediated by NMDA receptor (NMDAR) hypofunction. Evidence suggests that network attractor states underlie WM maintenance and that failures are mostly caused by fluctuation-driven transitions, but direct evidence for this is still lacking. To investigate what makes WM fail we used a simple two-alternative delayed response task in which mice listen to a lateralized auditory stimulus and, after a variable delay (duration D=0-10 s), they have to lick the associated lateral port. Mice accuracy decreased with delay showing that there were forgetting errors. They also showed a repeating bias, i.e. a tendency to repeat the previous choice, which was however independent of delay. Inactivation of NMDAR caused a decrease in accuracy and an increase of the repeating bias, but critically did not affect the forgetting rate, i.e. the decay of accuracy with delay. We recapitulate these findings using a hidden Markov Model that switches between (1) a WM state describing a stimulus-based strategy that requires memory maintenance, and (2) a history-based state (HB) which elicits lapse responses determined by previous choices. A shift in the transition probabilities towards the HB-state reproduces the effect of NMDAR blockade. Electrophysiological recordings in the anterolateral motor cortex (ALM) supported our model by showing that the encoding of the stimulus differs between inferred HB-state and WM-state trials: neurons showed similar encoding during the stimulus presentation, but only in the WM-state the encoding persisted during the delay period. Our results show that task performance is heavily limited by lapse epochs in which subjects stop using WM and suggest that deficits caused by NMDAR hypofunction could be related to an increased sensitivity to the cognitive effort associated with WM rather than by a decrease in its stability.

3-112. Predictive coding of global sequence violation in the mouse auditory cortex

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The ability to extract temporal regularities at different time scales in sensory inputs and detect unexpected deviations from these regularities is a key cognitive ability. The classical auditory oddball paradigm shows that the brain responds to sequence violations at a local time scale, but such responses also occur under anesthesia and therefore seem pre-attentive. In contrast, recent studies in humans and monkeys suggest that when the violation concerns regularities occurring over longer time scales, responses to the violation appear only in conscious, attentive subjects. To investigate whether local and global sequence violation responses exist in the mouse, we recorded from layer 1 to 5 of the auditory cortex using two-photon calcium imaging while mice passively listened to repetitions of 1s-long sequences of five tones. The repeated short sequence contained either a single tone (AAAAAA) or a local violation at its end (AAAAB). Purely global violations could be generated by presenting occasionally the AAAA sequence in a block where AAAAB is repeated. We found that a population of neurons in the auditory cortex specifically responds to such purely global violations at the end of the AAAA sequence. Although small, this population contained enough information to predict violations on single trials. A larger fraction of neurons boosted their responses to combinations of local and global violations (AAAAB presented in an AAAAA block). These global responses were resistant to a wide increase of inter-sequence interval (1.5s - 25s) ruling out that short-term adaptation causes these responses. However, global responses vanished when the difference between A and B sounds is less salient to the mouse. These results establish that the mouse brain is able to detect global violations in sound sequences in a subgroup of auditory cortex neurons, paving the way for the study of circuit mechanisms underlying long-term temporal regularity detection.

3-113. Clear evidence in favor of adaptation and against temporally specific predictive suppression in monkey primary auditory cortex

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The attenuation of neural responses to repeated stimuli (response attenuation) is often attributed to either adaptation or predictive suppression. While the two mechanisms differ dramatically in their theoretical underpinnings and computational complexity, they have been difficult to separate experimentally, because they make rather similar prediction in many commonly used paradigms. To that aim we developed a new experimental paradigm that leverages the time-course of response attenuation to arbitrate between the two theories. If response attenuation

is mediated by adaptation, we expect the strongest attenuation for stimuli presented with short delays to previous sounds, and a monotonic recovery of responses for increasingly longer delays. If, however, response attenuation is mediated by predictive suppression, we expect the strongest attenuation for stimuli presented at the most likely delay, and weaker attenuation for stimuli presented either at shorter or longer delays. To quantify the temporal specificity of response attenuation, we studied auditory evoked EEG and multi-unit responses of macaque monkeys to pure tone pips presented either in 1) highly regular contexts with predominantly predictable timing and identity, or 2) in random contexts with mostly unpredictable timing and identity. In line with the adaptation theory, we found that neural responses were most strongly attenuated if tones were presented at short delays rather than the most likely delay. Furthermore, attenuation was not modulated by the degree of confidence in the upcoming delay or tone identity. In summary, the data strongly support the notion that response attenuation in monkey primary auditory cortex is mediated by adaptation, not predictive suppression. It is possible that monkeys either do not form the necessary temporal predictions, or that they are not fed back all the way to primary auditory cortex.

3-114. The role of temporal coding in everyday hearing: evidence from deep neural networks

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The auditory nerve encodes sound with spike-timing that is phase locked to the fine-grained temporal structure of sound. The precision of this coding substantially exceeds that of any other sensory modality, but its role in hearing remains controversial because physiological mechanisms for extracting information from the spike timing have proven elusive. We investigated the perceptual role of auditory nerve phase locking using deep artificial neural networks in the spirit of ideal observer analysis. Neural networks took input from a simulated cochlea and were optimized for natural tasks. We examined whether phase locking in a network's cochlear input was necessary to obtain human-like behavior. We trained networks to recognize and localize words, voices, and environmental sounds using simulated auditory nerve representations of naturalistic auditory scenes. We manipulated the upper limit of phase locking via the lowpass cutoff in simulated inner hair cells. Networks using high-frequency phase locking replicated key aspects of human auditory behavior: task performance was robust to sound level and background noise. Degrading phase locking impaired performance, but much more so on some tasks than others, substantially impairing voice recognition and sound localization while leaving word recognition largely intact. The results suggest that auditory nerve phase locking is critical for accurate sound localization, for voice recognition in noise, and for level-invariant hearing. These findings may clarify conditions in which prostheses that fail to restore high-fidelity temporal coding (e.g., contemporary cochlear implants) should and should not be expected to restore near-normal hearing.

3-115. An insect vision-based flight control model with a plastic efference copy

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Flying insects can process multiple visual features in parallel neural circuits and generate an appropriate action. Neural processing of singly presented visual patterns has been studied intensively in *Drosophila* for the past few decades. How do parallel visual circuits responding to different features, presented in a single visual scene, are integrated to control a shared motor circuit? An influential theory proposed for combining multiple sensorimotor circuits is an efference copy mechanism, in which an intended action offsets other sensory circuits to prevent them from responding to reafferent sensory inputs caused by the action. Recent studies in *Drosophila* have identified efference copy-like signals in an array of motion-sensitive visual neurons that mediate visual stability reflexes. Using a dynamical systems approach, we implemented two computational models that combine the stability reflex with spontaneous or other visually evoked flight controls such as object tracking and avoidance. The model demonstrates that the visual stability reflex dampens spontaneous as well as visual object-induced flight turns when combined additively and that the modulation of the stability reflex by an efference copy permits

undamped, concurrent operation of multiple visual behaviors. Finally, we show that a simple supervised learning model can adjust its efference copy to match variations in sensory feedback associated with changes in internal or environmental variables. Our study provides an integrative model of vision-based flight control when multiple visual features are presented simultaneously and may be extended to an adaptive flight control mechanism for artificial flying agents such as drones.

3-116. Multiple stimulus features are encoded by single mechanosensory neurons in insect wings

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Animals rely on sensory feedback to achieve flexible coordinated movements, such as walking on rough terrain or grasping an object with appropriate force. Mechanosensory feedback is especially critical, as it operates with remarkable speed and sensitivity. One challenge in understanding these systems is the fact that mechanosensory inputs are transformed by the body structures in which sensory receptors are embedded. This transformation is particularly complex in the case of insect flight, where applied forces and torques are transformed by wing structural mechanics into complex spatiotemporal patterns of wing bending. Information about these dynamic shape changes is encoded by strain-sensitive neurons embedded in the wings, but it remains unclear which features of wing bending drive neural responses. Here we elucidate this feature space, which is essential to understanding the sensory information available to the animal during flight and to explore hypotheses for processing by downstream circuits. We record from primary mechanosensory neurons as the wing is driven through a range of motions and use simultaneous measurements of wing position to reconstruct the full wing shape over time. We then characterize the temporal features encoded by individual neurons using several analyses, including reverse correlation, covariance analysis, and maximally informative dimensions. Our results show that a diversity of features are encoded by this population and that single neurons are selective for multiple distinct features, suggesting a richer feature space is encoded by these neurons than previously known.

3-117. A visuomotor pathway underlies small object avoidance in flying Drosophila

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Animals use their vision to detect objects in their environment and thereby guide their behavior. In particular, flying insects show behavioral responses to small moving visual objects, but neural circuits underlying such visuomotor reflexes are not clearly understood. We identified a neural pathway underlying small object avoidance in flying Drosophila. We first screened various types of visual projection neurons (VPNs) and descending neurons (DNs) by unilaterally stimulating their dendritic processes using optogenetics. We found 5 types of VPNs and 2 types of DNs that caused flies to turn away from the stimulated side. To test whether these neurons are required for small object avoidance, we reversibly blocked synaptic transmission of these neurons using thermogenetics while presenting a small moving object. We found that the amplitude of wing responses decreased significantly for 1 type of VPNs (LPLC2) and 2 types of DNs (DNp03, DNp06). From the hemibrain connectome, we found that LPLC2 and DNp06 form strong synaptic connections, likely to mediate the small object avoidance. To further substantiate this, we measured calcium responses of LPLC2 neurons using genetically encoded calcium sensors and found that they indeed responded to a small moving object. Since these neurons were previously reported to respond to a looming visual pattern, we further investigated how these neurons respond to both looming and translating visual objects. We abolished the loom response of these neurons by blocking T4/T5 cells, elementary motion detector neurons known to provide major visual inputs for the looming visual pattern. Surprisingly, their calcium response to a small translating object was only mildly affected by this genetic silencing, suggesting the existence of presynaptic visual neurons other than T4/T5 cells that provide inputs to LPLC2 neurons for small moving objects. Together, our study delineates a neural circuit underlying small object avoidance in flying Drosophila.

3-118. Feedforward thalamocortical inputs to primary visual cortex are OFF dominant

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The responses of mammalian visual system to the increment (ON) and decrement (OFF) of light are asymmetrical. Previous studies have shown that the OFF responses in early visual systems of higher mammals are dominant. Recently, the OFF dominance had been shown in mouse primary visual cortex (V1), but it is unclear whether the feedforward inputs from dorsal lateral geniculate nucleus (dLGN) to V1 in mouse are OFF dominant. Here, we labeled thalamocortical projecting cells in dLGN with calcium indicator and imaged their axonal bouton activity at different depths in V1. By using locally sparse noise stimuli to map the ON and OFF receptive fields (RFs) of these boutons in awake head-fixed mice, we found that the OFF boutons were more numerous and had larger response amplitude across all cortical depths recorded (layer 1 through layer 4). To quantify the retinotopic scatter, we measured the difference between the bouton's RF center and its retinotopic location in visual space. We found that the OFF boutons showed significantly less retinotopic scatter than the ON boutons across cortical depth. This difference was still significant even after the count bias of OFF boutons was controlled by bootstrapping. Finally, pairwise RF distance distributions were plotted to quantify 2D RF distribution. OFF-to-OFF pairs had significantly higher pairwise RF distance than ON-to-ON pairs, indicating OFF RFs formed better mosaic tiling and ON RFs formed randomized clusters. A Monte Carlo simulation of RF distribution in visual space with grid irregularity (gaussian noise, σ) and cluster spread (exponential decay, τ), showed that low irregularity and high spread mimicked the OFF-to-OFF distribution while high irregularity and low spread recapitulated the ON-to-ON distribution. Overall, our results showed the OFF dominance of thalamocortical boutons in counts, response amplitude, retinotopy, and mosaic tiling.

3-119. Sparse coding predicts a spectral bias in the development of V1 receptive fields

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It is well known that sparse coding models trained on natural images learn basis functions whose shapes resemble the receptive fields (RFs) of simple cells in the primary visual cortex (V1). However, few studies have considered how these basis functions develop during training. In particular, it is unclear whether certain types of basis functions emerge more quickly than others, or whether they develop simultaneously. In this work, we train an overcomplete sparse coding model (Sparsenet) on natural images and find that there is indeed order in the development of its basis functions, with lower spatial frequency basis functions emerging earlier and higher spatial frequency basis functions emerging later. We observe the same trend in a biologically plausible sparse coding model (SAILnet) that uses leaky integrate-and-fire neurons and synaptically local learning rules, suggesting that this result is a general feature of sparse coding. Our results are consistent with recent experimental evidence that the distribution of optimal stimuli shifts towards higher frequencies during normal development in mouse V1. Our analysis of sparse coding models during training yields an experimentally testable prediction for V1 development that this shift may be due in part to higher spatial frequency RFs emerging later, as opposed to a global shift towards higher frequencies across all RFs, which may also play a role. We also find that at least two explanations could account for the order of RF development: 1) high frequency RFs require more information to be specified accurately, and thus may require more training data to learn, and 2) early development of low frequency RFs improves the sparseness and fidelity of the representation more than early development of high frequency RFs.

3-120. Do better object recognition models improve the generalization gap in neural predictivity?

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The internal activations of particular deep neural networks (DNNs) are remarkably similar to the neuronal population responses along the ventral visual cortex in primates. Nevertheless, the similarities between the two are often investigated through stimulus sets consisting of everyday objects under naturalistic settings. Recent work has revealed a gap in generalization ability of these models in predicting neuronal responses to out-of-distribution (OOD) samples (i.e. samples that are not regarded as natural photos) .

Here, we investigated how the recent progress in improving DNNs' object recognition generalization have impacted the generalization gap in neural predictivity. We quantified each model's neural prediction generalization in terms of its OOD neural prediction accuracy and generalization gap (difference between In-Distribution (ID) and OOD neural prediction accuracy). To study what factors contribute to such generalization capacity, we performed experiments on a wide range of DNNs and investigated how various DNN design choices that were shown to improve object-recognition generalization behavior in these models affect their neural prediction generalization capacity.

We found that: 1) Increasing the network depth or width does not consistently improve the generalization gap or the OOD prediction accuracy ; 2) Comparing between supervised and unsupervised learning algorithms, we found that a particular unsupervised learning algorithm (Momentum Contrast) can significantly improve the neural prediction generalization ; 3) While adversarially robust models show consistently lower neural prediction accuracy on both ID and OOD samples, compared to other baselines, they achieve a smaller generalization gap compared to regular models; 4) The neural prediction generalization gap is significantly correlated with adversarial robustness gap while surprisingly, it is not significantly correlated with OOD object recognition generalization gap. Together, our results suggest that unsupervised and robust DNNs may lead to more general models of neuronal responses in the visual cortex.

3-121. Energy efficient reinforcement learning as a matter of life and death

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Synaptic plasticity allows animals to adapt to the environment. However, making permanent synaptic changes requires a significant amount of metabolic energy. This cost is so high that learning reduces the lifespan of fruit flies by 20% when feeding is stopped (Mery and Kawecki, 2005). Thus the brain should carefully regulate learning. For instance, flies stop some forms of memory formation to survive upon starvation (Placais and Preat, 2013). To examine when it is best to halt energy-costly learning, we used a computational reinforcement learning model which takes the animal's energy budget into account. In the model, flies should learn to avoid the hazard from aversive stimuli. However, this consumes energy and exposes them to starvation hazard. We implemented a high-cost long-term memory (LTM) pathway and a low-cost, but less persistent, anesthesia-resistant memory (ARM) pathway, and find an energy efficient learning policy by exploring how the brain switches memory pathways to maximize survival. Consistent with experimental results (Placais and Preat, 2013), the lifespan in our model is prolonged when LTM is gated by energy reserve. Moreover, we find that it is more energy efficient to learn by depressing the weight inducing the unwanted action than by potentiating the weight of the desired action, again consistent with experiments (Perisse et al., 2016). We propose that energy considerations pervade learning and memory across species.

3-122. A Model for Representational Drift: Implications for the Olfactory System

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Representational drift has been observed in different parts of the nervous system. Nevertheless a complete mechanistic understanding about it is missing. In a recent experimental study in the olfactory system, recordings from the piriform cortex demonstrate drift in the representation of a single olfactory stimulus, despite apparently stable odor identification. Such drift is characterized by a decay in the self-similarity of the stimulus representation vector as a function of the time between the recordings. Additionally, the rate of the decay was shown to be smaller for more frequent stimuli. In this work, we study whether a diffusion process driven by noise during learning can

explain some or all of the features observed in the experiments.

We first show that a constrained diffusion process could explain the decay in the representation self-similarity. Next, we demonstrate how such process could occur as a result of noisy learning in a simple biologically relevant model of two-layer linear neural network, with the constraint being determined by the manifold of solution. We analytically derive the diffusion tensor on the manifold for the high-dimensional representation due to both online learning stochasticity and synaptic noise. Finally, using the current assumptions in the model, we quantify the change in the diffusion due to the application of a frequently applied stimulus.

3-123. Stable memories without reactivation

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Memories are known to reactivate during sleep. A recent modelling study (Fauth & van Rossum, eLife, 2019) could reproduce this based on self-reactivations of heavily interconnected cell assemblies and showcased its beneficial consequences for memories. However, to be maintained, the memories needed frequent reactivations such that the weights within the assemblies remain at a high level. In this work, we extend the model such that memories are maintained independently of reactivations. We suggest that long-term memories are mainly represented by the number of connections between assembly neurons, and less dependent on the actual weight of these connections. We test this with simulations and (mean-field) analyses in recurrent networks, in which connections are subject to (1) structural plasticity, which creates and removes connections via stochastic processes, (2) synaptic plasticity adapting the synaptic weights according to neural activity and (3) a biologically inspired spontaneous dynamics of the synaptic weight. We show that, after extended periods without reactivations, memories can have three different states depending on their connectivity: At relatively high degrees of connectivity, memories can reactivate themselves. At slightly lower degrees of connectivity, memories can only be reactivated by external stimuli but may self-reactivate in a short time span afterwards. At even lower degrees of connectivity, memories cannot be reactivated by external stimuli at all. In this case, the structural connections of the memory still exist for extended periods and can be used to relearn the pre-existing memory very fast. This provides a possible explanation for Ebbinghaus' savings effect. Hereby the connectivity of newly learned assemblies relies mainly on strong synaptic weights, whereas older assemblies rely on a large number of synapses. Thus, interference with the reactivations (i.e. sleep deprivation), existing synapses, or synaptogenesis will impact new memories more severely than older ones, which may explain the gradedness of retrograde amnesia.

3-124. Sharing weights with noise-canceling anti-Hebbian plasticity

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Weight sharing among neurons is widely used in deep learning: convolutional networks are an obvious example, but in addition transformers need it for matrix-matrix multiplications. Without weight sharing, deep networks perform badly on hard tasks. This is potentially problematic for the brain, since weight sharing is biologically implausible - a fact that is ignored in deep learning models of brain activity, especially of visual processing, which are becoming widely used. Recently it was shown that partial weight sharing can be implemented with a "sleep phase", in which plasticity is anti-Hebbian. While the sleep phase significantly increases the performance of networks without explicit weight sharing, it has to be done often, and requires precise lateral connectivity in every layer. In this work, we propose a method for inducing weight sharing continuously during training, through noise-canceling anti-Hebbian plasticity. We find that for a common type of deep learning architecture, it's enough to share weights in a subset of the layers. Our model, which implements a form of homeostatic plasticity, makes several experimentally testable predictions.

3-125. Relating local connectivity and global dynamics in excitatory-inhibitory networksYuxiu Shao^{1,2}Srdjan Ostojic¹¹Ecole Normale Supérieure²Group for Neural Theory

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One of the key questions in neuroscience is how the connectivity structure of cortical networks determines the collective dynamics of neural activity. Two complementary approaches have been developed to address this question: (i) specifying connectivity in terms of local statistics of excitatory-inhibitory motifs [Trousdale et al. 2012, Aljadeff et al. 2015]; (ii) specifying connectivity through a global low-rank structure that determines the low-dimensional dynamics [Mastrogiosseppe and Ostojic 2018, Beiran et al. 2021, Dubreuil et al. 2020]. It is however currently unclear how local connectivity statistics are related to the global structure and shape the low-dimensional activity. To bridge this gap, here we map local EI statistics onto global statistics of low-rank connectivity and examine the emerging dynamics. We consider a randomly connected, block-like network composed of excitatory and inhibitory subpopulations. Connections in each block are specified by cell-type-dependent statistics and consist of independent and reciprocal parts. We first determine the dominant eigenvalues and eigenvectors of the resulting connectivity matrix, and show that the statistics of their entries universally obey a mixture of Gaussian distribution. We then exploit this result to approximate random EI networks by Gaussian-mixture low-rank networks [Beiran et al. 2021]. Comparing the parameters of local connectivity to the emerging low-rank structure, we show that mean cell-type connectivity determines the dominant low-rank structure, but the reciprocal motifs further modify it by modulating the dominant eigenvalue. Comparing the dynamics in the original EI network and their low-rank approximations, we find that the mean and variance of population activity closely match. In both cases, reciprocal motifs enhance positive feedback and induce bistable dynamics. Altogether, our analytical mapping of the local EI statistics to low-rank description provides an intuitive picture of how local connectivity statistics determine global low-dimensional dynamics and resulting computations.

3-126. A White Matter Ephaptic Coupling Model for 1/f Spectral DensitiesPamela Douglas^{1,2}Garrett Blair³Jack Vice^{4,5}¹UCLA; UCF²Psychiatry & Computer Science³UCLA⁴University of Central Florida⁵Computer Science

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Log-linear 1/f spectral densities are widely observed in the brain - across multiple species and at many levels of abstraction. However, the intrinsic relationship between the structural attributes of the brain and 1/f biorhythms remains largely unclear. Here, we explore a novel theoretical and generative framework, the white matter ephaptic coupling model (WMEC), and test its ability to explain the relationship between white matter morphology, spike propagation dynamics, and log-linear spectral densities observed in brain activity data.

3-127. Deep Reinforcement Learning mimics Neural Strategies for Limb MovementsMuhammad Noman Almani^{1,2}Shreya Saxena^{1,2}

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How does the motor cortex achieve generalizable and purposeful movements from the complex, nonlinear musculoskeletal system? Previous research in this field has focused on developing dimensionality reduction and modeling techniques to elucidate the structure in high-dimensional neural activity, and relate this directly to kinematic outcomes. However, these models typically do not consider the biophysical underpinnings of the musculoskeletal system, nor do they allow us to understand the role of sensory feedback in motor control. These models thus fail to elucidate the computational role of neural activity in driving the musculoskeletal system such that the body

reaches a desired state. Recent advances have led to vast improvements in powerful physics-based engines for efficient rigid body simulations, allowing us to efficiently simulate and analyze musculoskeletal motion. However, these techniques do not allow any insight into the neural strategies that underlie motor control, nor allow for prediction of neural strategies in novel environments. Here, we develop a neuromechanical control model using deep reinforcement learning (DRL) for a monkey limb model. We adapted an established 39-muscle anatomically accurate monkey limb model for DRL-applications and designed a maximum-entropy based actor-critic algorithm with the goal of tracking a rotating target by issuing appropriate muscle signals, resulting in the cycling motion of the limb model at different speeds. We analyzed the trained actor-network's activity and observed high correlations and consistency with the recorded motor cortex (M1) data. Moreover, perturbations in the muscle and kinematic space led to the accurate generalization of the observed response to novel movements, and produced accurate and reasonable responses in unobserved conditions. Thus, the DRL framework for anatomically accurate limb models can mimic biologically observed neural strategies, and enables hypothesis generation for prediction and analysis of novel movements and neural strategies.

3-128. A novel experimental framework for simultaneous measurement of excitatory and inhibitory conductances

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The activity of neurons throughout the brain is determined by the precise relationship between excitatory and inhibitory inputs and disruption of this relationship underlies many psychiatric diseases. Whether these inputs covary over time or between repeated stimuli remains unclear due to the lack of experimental methods for measuring both inputs simultaneously. We developed a new analytical framework for simultaneous measurement of both the excitatory and inhibitory neuronal inputs during a single trial of a current clamp recording. This can be achieved by injecting a current composed of two high frequency sinusoidal components followed by analytical extraction of the conductances. We demonstrate the ability of this method to measure both inputs in a single trial under realistic recording constraints and from morphologically realistic CA1 pyramidal model cells. We next applied the method to in-vitro electrophysiological recordings, using optogenetics to evoke mixed inhibitory and excitatory synaptic responses, and achieved high resolution extraction of both excitatory and inhibitory conductances in a single trial. Importantly, these conductances were similar both in amplitude and time course to the conductances that we measured from the same cells using classical voltage clamp recordings - fully validating our new method. We present this method as a new experimental tool, which will facilitate our understanding of fundamental questions in neuroscience, in both health and disease.

3-129. A latent model of calcium activity outperforms alternatives at removing behavioral artifacts in two-channel calcium imaging

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A fundamental goal in neuroscience is to connect an animal's behavior to its neural activity. However, imaging neural activity in a behaving animal presents unique challenges because the animal's movements create motion artifacts that, in the worst cases, cannot be distinguished from neural signals of interest. One approach to mitigating motion artifacts is to image two channels simultaneously: one that captures a calcium sensitive fluorophore, such as GCaMP, and another that captures a calcium insensitive fluorophore such as RFP. In principle, because

the calcium insensitive channel contains the same motion artifacts as the calcium sensitive channel, but no neural signals, it can be used to correct for motion artifacts. In practice, existing approaches such as taking the ratio of the two channels do not satisfactorily mitigate all motion artifacts. Moreover, no systematic comparison has been made of existing approaches that utilize two-channel signals. Here, we construct a generative model of the fluorescence of the two channels as a function of motion, neural activity, and noise. We then use Bayesian inference to infer the latent neural activity, uncontaminated by motion artifact. We further present a novel method for evaluating ground-truth performance by attempting to decode behavior from calcium recordings in moving animals. We compare recordings of freely moving *C. elegans* that express GCaMP to that of control animals that lack GCaMP. Our insight is that a successful method should not only decode neural signals well, but should also eliminate decodable motion artifacts from recordings that have no neural activity. We use this method to systematically compare five models for removing motion artifacts and find that our model decodes locomotion from a GCaMP expressing animal 12x more accurately than from control, outperforming all other methods tested by a factor of 4.

3-130. Emergent behavior and neural dynamics in artificial agents tracking turbulent plumes

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Tracking a turbulent plume to locate its source is a complex control problem requiring robust multi-sensory integration in the face of intermittent odors, changing wind direction, and variable plume shape. This task is routinely performed by flying insects, often over long distances, in pursuit of food or mates. Several aspects of this remarkable behavior have been studied in detail in many experimental studies. Here, we take a complementary *in silico* approach, using artificial agents trained with reinforcement learning to develop an integrated understanding of the behaviors and neural computations that support plume tracking. Specifically, we use Deep Reinforcement Learning (DRL) to train Recurrent Neural Network (RNN) based agents to locate the source of simulated turbulent plumes. Interestingly, the agents' emergent behaviors resemble those of flying insects, and the RNNs learn to represent task-relevant variables, such as head direction and time since last odor encounter. Our analyses suggest an intriguing experimentally testable hypothesis for tracking plumes in changing wind direction—that agents follow local plume shape rather than the current wind direction. While reflexive short-memory behaviors are sufficient for tracking plumes in constant wind, longer timescales of memory are essential for tracking plumes that switch direction. At the level of neural dynamics, the RNNs' population activity is low-dimensional and organized into distinct dynamical structures, with some correspondence to the uncovered behavioral modules. Our *in silico* approach provides key intuitions for turbulent plume tracking strategies and motivates future targeted experimental and theoretical developments.

3-131. Optimization of error distributions as a design principle for neural representations

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Neural circuits encode and transmit information to support a diversity of tasks. Such neural coding is corrupted by noise and uncertainty, which in turn results in different magnitudes of error in the signals that are received by downstream regions. Therefore, even in the same task and given a fixed distribution of input signals, the performance of a neural code is characterized by a distribution of errors. Different task demands might necessitate distributions with different properties; for example, a task that requires avoiding failure at all costs might necessitate coding schemes that minimize the maximum possible error value.

Despite the importance of error distributions, current theories of neural coding focus predominantly on optimizing average performance. Here, we generalize this approach to optimize full error distributions. We do so by interpreting error as a random variable whose statistics depend on the input distribution and the system parameters.

We show that optimizing for different target error distributions yields different coding schemes and performance tradeoffs.

To demonstrate the relevance of this approach, we consider a simple model of decoding escape direction from a neural command signal. In the fly, this computation is performed by two parallel pathways: Descending Neurons, which control a slower but higher-precision escape, and the Giant Fiber, which triggers a rapid but lower-precision escape. We postulate that a rapid escape might require minimizing the probability of exceeding a critical error threshold, and we demonstrate that such a coding scheme differs from one that minimizes average error. We further show that dynamically adapting the code to switch between these schemes would be costly and error prone. Our theory thus provides a candidate explanation as to why escape behavior in the fly is controlled by two parallel pathways that yield different performance characteristics.

3-132. Uncertainty-weighted prediction errors (UPEs) in cortical microcircuits

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The brain learns an internal model of the world by making predictions about upcoming inputs and comparing its predictions with actual incoming sensory information. Prediction errors are essential for learning an accurate internal representation of the world because they indicate where the internal representation needs to be improved to make a better prediction in the future. Promisingly, a neural correlate for prediction errors has been found in the activity of pyramidal neurons in layer 2/3 of diverse cortical areas. To make contextually appropriate predictions in a stochastic environment, the brain needs to take uncertainty into account. How uncertainty modulates prediction errors and hence learning is, however, unclear. Here, we use a normative approach to derive how prediction errors should be modulated by uncertainty and postulate that such uncertainty-weighted prediction errors (UPE) are represented by layer 2/3 pyramidal neurons. We then implement the calculation of the UPEs in a biologically plausible microcircuit model of layer 2/3. In particular, in our theory, the UPE reflects the optimal update of the prediction that maximises the likelihood of the incoming sensory inputs given the prediction. The optimal update is the difference between the predicted mean and the sensory input scaled inversely by the uncertainty. Interestingly, pyramidal cells are modulated by both subtractive and divisive inhibition from somatostatin (SST) and parvalbumin (PV) interneurons, respectively. We, therefore, hypothesise that the layer 2/3 circuit calculates the UPE through the subtractive inhibition by SSTs and the divisive inhibition by PVs. We show that (1) PVs can learn to represent the uncertainty in both positive and negative prediction error circuits with a biologically plausible plasticity rule, (2) the inhibitory connections from SSTs to PVs are essential for estimating the uncertainty, and (3) the resulting UPE can be used to update the internal representation of the predicted mean.

3-133. Inference of the time-varying relationship between spike trains and a latent decision variable

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Drift-diffusion models have been widely used to study the neural mechanisms of decisions guided by noisy stimuli. In this framework, momentary evidence is integrated through a scalar decision variable, which has been found to correlate with spike rates in many brain areas. However, the relationship between the decision variable (i.e., accumulated evidence) and spike rate is widely assumed to be fixed over the course of a single trial, even though sensory and motor weights on spiking activity vary over time. Allowing the weight of the decision variable to be temporally inhomogeneous may capture the decision process more accurately. Therefore, we incorporated hidden-Markov generalized linear models of spike trains into a drift-diffusion model, resulting in two independent Markov chains, one of the decision variable and the other of a coupling variable controlling the weight of the decision variable. In the resulting factorial hidden Markov drift diffusion model (FHMDDM), the spike rate is a nonlinear output of the weighted sum of inputs including the decision variable, spike history, and timing of

task events, with the weight of the decision variable dependent on the coupling variable. Fitting FHMDMM to Neuropixels recordings from dorsomedial frontal cortex (dmFC) of rats discriminating between auditory click trains and to their behavioral choices, we found that compared to a model with temporally fixed weights, FHMDMM captures both the spike trains and choices more accurately. The posterior estimate of the coupling variable reveals that the weights of the decision variable on dmFC spiking are strongest at the beginning of a decision and decrease over deliberation. These results suggest that decision formation can be more accurately characterized by a time-varying relationship between the decision variable and spike trains and that processes separate from decision formation such as motor preparation have sizable influence over late dmFC spiking.

3-134. Mutual gaze with a robot influences social decision-making

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Human decisions are often made in a social context, thereby relying on the ability to anticipate and predict others' behavior. In such contexts, gaze is an important communicative signal which can inform individuals about others' intentions, goals and upcoming decisions. Gaze has been shown to affect various cognitive processes and states in human interactions. Nevertheless, the effect of gaze on social decision-making is still understudied. Here, we investigated the effect of mutual gaze exhibited by a humanoid agent in an interactive setup. Participants (N=40) played a strategic game against the robot iCub while we measured their behavior and neural (EEG) activity. Critically, participants were instructed to look at the robot before choosing their next move. During that time period, we manipulated the iCub's behavior to either establish eye contact (mutual gaze) or avoid eye contact (averted gaze) with them. This manipulation was orthogonal to the robot's choices. Participants were assigned either to a group with 70% instances of mutual gaze or 70% of instances of averted gaze. As a result, participants were slower to respond in the mutual gaze condition, relative to averted gaze. Based on the drift diffusion model, we found that this delay was driven by an increase of the decision threshold. This behavioral effect was paralleled by higher alpha synchronization during mutual gaze, suggesting a stronger need to suppress the distracting gaze signal. Overall, our results indicate that mutual gaze engages brain resources for managing social signals. Even when this social signal is irrelevant to the decisions to be made, its processing can influence decision time, neural synchronization, choice strategies and sensitivity to outcomes. These findings underline how communicative behaviors can be impactful in real-world decision-making.

3-135. Near-optimal time investments under uncertainty in humans, rats, and mice

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Our scarcest resource is time. Humans and other animals allocate their time on a vast number of different activities – from reading a paper, pursuing a degree, or foraging for food. Optimal, reward-maximizing, behavioral strategies must balance expected future gains with irrecoverable time investment. However, humans and other animals often succumb to cognitive biases that lead to suboptimal payoffs such as considering sunk costs when investing time to obtain future payoffs. Here we argue that humans, rats, and mice invest time according to op-

timal predictions given available evidence and subjective time preferences. First, we argue that previous data showing apparent sunk cost sensitivity (1) can be explained by an attrition bias when analyzing variable choice behavior of rational agents. Second, we behaviorally tested the optimality of time investments in humans, rats, and mice. Across trials we varied subjects' uncertainty in obtaining rewards, enabling us to evaluate whether subjects invested time in proportion to their confidence about successful outcomes. Human or animal subjects committed to one of two choice alternatives with ambiguous sensory evidence, which determined the subjects' confidence in making a correct choice. After making a choice, subjects invested time in their decision by waiting for randomly delayed reward for correct choices. We developed a statistical approach to non-parametrically estimate the optimal (reward-maximizing) time investment given the evidence and their overall time preference. Crucially, this approach allowed us to isolate the contribution of confidence to investment behavior irrespective of individuals' subjective assessment of the costs and benefits of waiting. We found that all species invested time close to optimal model predictions, i.e., with low confidence noise, demonstrating that all species appropriately use sensory evidence to adjust investments. Our analyses reveal that humans, rats, and mice can be efficient economic agents, who appropriately allocate investment decisions in uncertain environments.

3-136. Optimal search strategies under energetic constraints

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To successfully forage for food, animals much balance the energetic cost of searching for and traveling between food sources with the energetic benefit of exploiting those sources. The Marginal Value Theorem (MVT) provides one normative account of this balance by specifying that a forager should leave a food patch when its energetic yield falls below the average yield of other patches in the environment. This framework and its extensions treat the decision of when and how fast to leave a patch under the assumption that other patches exist and are readily reachable. However, in natural settings, a forager does not know whether it will encounter additional food patches, and must balance potential energetic costs and benefits accordingly.

Here, we explore how a forager should structure its search for new food patches when (i) the existence of those patches is not known, and (ii) searching for those patches requires energy that can only be harvested from a single known food patch. Because the forager faces the possibility that there will not be any food patches nearby, we assume that it structures its search in a series of outbound and inbound trips to ensure that it returns to the known food patch if it fails to find a second patch. We identify conditions under which it is more favorable to explore the environment in several successive trips rather than one long exploration, and we show how the optimal sequence of trips depends on the forager's beliefs about the distribution and utility of food patches in the environment. Finally, we derive a local decision rule for structuring this search, and we show that this local rule can achieve near-optimal performance and be implemented by a simple neural circuit architecture. Together, this work highlights how energetic constraints shape optimal foraging strategies.

3-137. Pupil size anticipates exploration and predicts disorganization in pre-frontal cortex

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In uncertain environments, we balance exploitation and exploration: we generally exploit rewarding opportunities, but sometimes explore uncertain alternatives that could be even better. Exploration is associated with a sudden disorganization of neuronal activity patterns in the prefrontal cortex, which could be a powerful way to promote discovery and learning. Although the mechanisms behind this disorganization remain unknown, one possibility is pupil-linked neuromodulatory systems. However, it is not clear whether pupil size predicts the neural signatures of exploration, much less the sudden transitions that occur at the onset of exploration. Here, we simultaneously measured pupil size and neuronal activity in the prefrontal cortex while two rhesus macaques made decisions in a dynamic environment that encouraged both exploration and exploitation. Consistent with our expectations

from previous studies, we found that pupil size was larger during exploration than exploitation. Pupil size also predicted disorganized patterns of prefrontal activity in both single neurons and the population. This was true even within periods of exploitation. The pupil also exhibited surprising trial-by-trial dynamics: it grew larger across trials before exploration, then abruptly decreased to below-baseline levels. Because pupil size began decreasing immediately after the first explore trial, pupil-linked mechanisms may anticipate the start of exploration, without being sustained throughout periods of exploration. Indeed, before the onset of exploration, we observed a general slowing of both response time and neural activity, consistent with the idea that the onset of exploration represents a critical “tipping point” in prefrontal dynamics. Pupil size, in turn, predicted this slowing. In sum, we found that pupil size tracked both exploratory behavior and its neural correlates, supporting models that connect pupil-linked mechanisms in these phenomena. However, the trial-by-trial dynamics of these effects specifically implicate pupil-linked mechanisms in the critical transition at the onset of exploration, rather than in sustaining exploration over time.

3-138. Exploring too much? The role of exploration in impulsivity

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Deciding whether to forgo a good choice in favour of exploring a potentially more rewarding alternative is one of the most challenging arbitrations both in human reasoning and in artificial intelligence. Humans show substantial variability in their exploration, and theoretical but only limited empirical work has suggested that excessive exploration is a critical mechanism underlying the psychiatric dimension of impulsivity. We put these theories to test using a large online sample (N=580 healthy adults), dimensional analyses, and computational modelling in a pre-registered study. Capitalising on recent advances in disentangling distinct human exploration strategies, we demonstrate that impulsivity is associated with a specific form of exploration, value-free random exploration, a computationally light exploration heuristic. Our results not only demonstrate this specific association with impulsivity, but also explore links between exploration and other psychiatric dimensions.

3-139. Theories of surprise: definitions and predictions

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‘Surprise’ is used in the neurosciences to explain a multitude of phenomena: from memory-modification and adaptive learning to attentional shift and exploration. However, different studies refer to different definitions of ‘surprise’, and it remains unclear how these different definitions relate (1) to each other and (2) to different phenomena attributed to surprise.

To address the 1st issue, we identify 10 mathematical definitions of surprise in a unifying framework and show how they relate to each other. Importantly, we classify these definitions into four main categories: (i) ‘prediction surprise’ measures a mismatch between a prediction and an observation; (ii) ‘change-point detection surprise’ measures the probability of a change in the environment; (iii) ‘confidence-corrected surprise’ explicitly accounts for the effect of confidence; and (iv) ‘information gain surprise’ measures the belief-update upon a new observation. To address the 2nd issue, we focus on surprise-modulated adaptive learning and surprise-seeking exploration. We propose two experimental paradigms where different categories (i-iv) make different predictions: an association learning task in volatile environments and a model-building task in reward-free bandits. In these two paradigms, modeling shows that surprise-modulation of the speed of learning leads to sensible adaptive behavior only for change-point detection surprise whereas surprise-seeking leads to sensible exploration strategies only for information gain surprise. We, therefore, conclude that there cannot be a single surprise measure with all functions and properties previously attributed to surprise.

Overall, our results unify multiple theories of surprise and propose a theory-driven approach to design experiments on the physiological signatures and functional roles of surprise in the brain.

3-140. Spontaneous emergence of magnitude comparison units in untrained deep neural networks

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The ability to compare two magnitudes is observed in naive animals in the absence of learning (Rugani 2016; McCrink 2007), but how this cognitive function emerges without training remains elusive. In monkeys, neurons in the prefrontal and parietal cortex were observed to respond selectively to the proportion between two magnitudes (Vallentin 2008, 2010), suggesting these units could be fundamental for innate magnitude comparisons. However, details of how these comparison units emerge without any learning also remain unclear. Here, we show that magnitude comparison units can arise spontaneously even in completely untrained deep neural networks. We hypothesized that comparisons on a relative or absolute scale are two main means of magnitude comparison. Thus, we designed a set of images in which the number of white and black dots represents a proportion or difference. We fed these images into a randomly initialized AlexNet and found distinct populations of units responding selectively to a specific proportion or difference, regardless of the total number of dots. We confirmed that these units respond to abstract proportions or differences irrespective of the total area and/or the total number of dots, thus enabling the network to compare the two magnitudes. Next, based on the summation coding model, we hypothesized that a combination of monotonically increasing responses according to the number of white or black dots, observed in a previous layer, can generate proportion and difference units. We found that both types of comparison units can emerge when the observed increasing responses are connected with random weights, implying that distinct functional units may share a qualitatively identical developmental mechanism. Furthermore, using a theoretical model, we found that differences in the shape and concavity of response patterns can determine the proportion or difference selectivity. Our findings suggest that statistical variations of feedforward projections can induce diverse innate cognitive functions.

3-141. Dissecting the Factors of Metaplasticity with Meta-Continual Learning

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Metaplasticity is the change in plasticity of a synapse, and an important mechanism for resolving the stability-plasticity dilemma. However, the exact synaptic or neuron properties that modulate metaplasticity still remains unclear.

In this work we use meta-continual learning to discover the importance of factors that contribute to metaplasticity. We use a linear model to assign the relative contribution of four commonly used synaptic properties to metaplasticity: the Hessian, gradient, magnitude of the weights, and activity of the post-synaptic neuron. The coefficients of the linear model are meta-optimized jointly with the neural network on multiple tasks of the Om?niglot dataset continuously with a retained accuracy meta-objective.

We find that the weight and activity make the most significant contributions to metaplasticity, while the Hessian and gradient are unimportant. We also find that metaplasticity is required to overcome catastrophic forgetting, as opposed to fixed plasticity. It has superior retained accuracy than other continual learning methods, with at most 39.3% improvements. These results suggests that simple activity-based mechanisms of meta?plasticity may be sufficient and cast doubt over the relevance of gradient-based and Hessian-based ones.

3-142. Modeling and optimization for neuromodulation in spinal cord stimulation

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Spinal cord stimulation is a promising therapy for the recovery after spinal cord injury and control of movement. However, the complex interaction between electrodes and neural reaction impedes more effective neuromodula-

tion. Empirical knowledge and manual adjustment are playing dominant role for the tuning of neuromodulation parameters. The growth of electrode array's complexity also brings new challenges to find optimal stimulating configurations. Developing a more efficient way to predict the stimulation results and explore the optimal therapy is necessary for the tuning of sensitive neural circuits in spinal cord. We developed a hybrid computational model of human spinal cord and stimulating electrode array to simulate the effect of spinal cord stimulation. The high-precision finite element model of the spinal cord we built matches the anatomical size and segmental innervation of human spinal cord. Biophysical neuron models were embedded into the finite element model. Based on the results of simulation, we analyzed the selectivity of neural stimulation for different muscles. The influence of arrangement and size of the neural electrodes was calculated to provide information for the design of electrode arrays. The polarity configuration and implanting position of the multiple-contact electrode were also considered. We developed Bayesian optimization method to explore the optimal configuration of polarity based on our hybrid model. Our method can efficiently optimize stimulating parameters from a large input space. These results provide effective guidance for electrode design, surgical implantation and neuromodulation therapies for spinal cord stimulation. The optimization result for configuration of polarity shows the potential of using Bayesian optimization in clinical practice. Analysis based on our simulation also contributes to the quantitative understanding of the mechanism of spinal cord stimulation.

3-143. Flexible cue anchoring strategies enable stable head direction coding in blind animals

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Vision plays a crucial role in instructing the brain's spatial navigation systems. In the absence of vision, the remaining sensory systems attempt to fill in the previously dominated role of vision. However, how the brain's navigational system is affected, as well as the strategies it adapts to facilitate spatial awareness following vision loss remains an open question. To explore this, we recorded from head direction (HD) cells in the anterior dorsal nucleus (ADn) of the thalamus in freely moving sighted and blind animals. First, we found that both congenitally blind and late-onset blind animals exhibit stable and robust HD tuning. In contrast, placing sighted animals in darkness impaired their HD cell tuning. The timing of vision loss affected the stability of HD cell tuning, with congenitally blind mice exhibiting less refined tuning compared to late-onset blind mice who had vision at eye opening. Additionally, we observed that HD cells in blind animals are primarily anchored to floor olfactory cues. By ablating olfactory sensory neurons, we got rid of the stable HD tuning in blind animals. Interestingly, without both visual and olfactory cues, the ring attractor in ADn remains intact but continuously drifts. We thus demonstrate remarkable flexibility in how the brain uses sensory information to generate a stable directional representation of space.

3-144. Task demands drive choice of navigation strategy and distinct types of spatial representations

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Navigation is a complex process that involves several interacting brain regions and has been the subject of intense research for several decades. In general, spatial navigation involves strategies using one of two reference frames: egocentric and allocentric. However, it remains unclear why a particular strategy is chosen over another, and how the neural spatial representations should be related to the chosen strategy. Here, we use a deep reinforcement learning model to investigate whether a navigation strategy could arise spontaneously during spatial learning without imposing a bias onto the model. We then examine the spatial representations that emerge in the network to support different navigational strategies. To this end, we study two ethologically valid tasks, which we refer to as guidance and aiming, respectively. In guidance, the agent navigates to a goal location fixed in allocentric space from different start locations in an environment with stable external landmarks. In aiming, the goal is marked by a visible cue, which is shifted to a different position in each trial. We find that when both strategies are available to the agent, the solutions it develops for guidance and aiming are heavily biased towards the allocentric or the egocentric strategy, respectively, as one would expect. Nevertheless, the agent is able to learn both tasks

using either strategy in principle, although learning efficiency is higher for the preferred strategy. Furthermore, we find that place-cell-like allocentric representations emerge preferentially in guidance when using an allocentric strategy, whereas egocentric vector representations emerge when using an egocentric strategy in aiming. We thus find that alongside strategy, the nature of the task plays a pivotal role in the type of spatial representations that emerge.

3-145. The role of prior experience in the replay of both novel and familiar contexts

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Hippocampal replay, the sequential reactivation of place cells, is postulated to be a mechanism central to memory consolidation. Commonly studied using highly repeated stereotyped behaviours (e.g. running back and forth on a linear track), we don't understand how such memories are formed in more naturalistic settings, with a single or limited exposure, and the effect on subsequent replay. To further investigate this, we trained rats to run back on forth on two novel linear tracks each day, each track limited to a fixed but different number of laps. Following a post-behaviour sleep session, rats were re-exposed to both tracks again, but this time ran an equal amount of time on each track, followed by a second sleep session. This approach allowed us to (1) study sleep replay arising from differences in the amount of exposure to a novel environment [post first exposure], and (2) simultaneously examine how different degrees of familiarity influenced replay when the duration of the most recent exposure was similar [post re-exposure]. We found that as the rat ran additional laps along the novel track, the levels of sleep replay for that experience increased. However, when the rat was re-exposed to both tracks (for an equal amount of time), replay events were more prevalent for the track in which the rat had less experience on the initial exposure (less familiar). While theta sequences are postulated to be a central mechanism required for offline replay, we unexpectedly observed that the amount of awake replay during the most recent behavioural episode was the most accurate predictor of how much offline replay occurred during the subsequent sleep session. These results further our understanding of how experience shapes the encoding of different spatial trajectories, and the mechanisms modulating offline replay during the subsequent sleep memory consolidation.

3-146. Orienting eye movements during REM sleep

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REM sleep is characterized by rapid eye movements, from which it gets its acronym, and is often accompanied by vivid visual dreams. Rapid eye movements occurring during REM sleep are proposed to represent gaze shifts in the virtual environment of dreams, while other studies suggest that they simply reflect random brainstem activity. In order to address this issue, we recorded from head direction (HD) cells in the anterodorsal nucleus of the thalamus (ADN), a population of neurons whose activity reports heading of the animal. Previous work has shown that during REM sleep, the population activity of HD cells is similar to that during actual navigation, in that it maintains a coherent representation of heading, i.e. a "virtual heading". Because fast saccade-like eye movements are coupled to head movements during gaze shifts in awake freely-moving animals, we hypothesized that during REM sleep rapid eye movements may predict changes in virtual heading. To this end, we monitored eye movements during REM sleep while recording ensembles of HD cells from the ADN. We discovered that, during REM sleep, the direction of eye movements predicted the direction of the changes in virtual heading. Furthermore, the amplitude of rapid eye movements correlated with amplitude of changes in virtual heading. Importantly, such correlation between rapid eye movements and virtual heading was analogous to the relationship between fast saccade-like eye movements and the representation of heading in the ADN of awake mice. In conclusion, this study provides direct physiological evidence that rapid eye movements are coordinated with virtual heading during REM sleep, supporting the hypothesis that rapid eye movements represent gaze shifts in the virtual world of dreams during REM sleep. Furthermore, this study will facilitate future studies to elucidate the organization of the generative model during REM sleep, using rapid eye movements as its readout.

3-147. Integration of infant sensory cues and internal states for maternal motivated behaviors

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Maternal motivation enables heightened responsivity of mothers towards offspring. While this motivational state is critical to infant survival, little is known about its regulation. Previous work in maternal rodents demonstrates that lesioning ventral tegmental area (VTA) neurons disrupts maternal motivated behaviors; and that these behaviors are restored by manipulating pup sensory salience (i.e., by increasing pup cries) and maternal states (Hansen 1994 *Physiol Behav*). Additionally, the neurohormone oxytocin is known to promote VTA-mediated maternal behaviors including infant approach and nursing (Pedersen et al., 1994 *Behav Neurosci*). What remains unclear is how information about infant needs and internal states of the mother are integrated in the VTA to determine the overall levels of maternal motivation that drive context-specific offspring care. Here, we show that infant cues are signaled to the VTA by oxytocin and that this sensory input, along with internal state, modulates maternal motivation. We used a combination of anatomical tracings and recordings in brain slices to identify a noncanonical auditory pathway relaying acoustic information about infant cries via the posterior intralaminar thalamus (PIL) to hypothalamic oxytocin neurons. We performed fiber photometry from oxytocin neurons in awake maternal mice (dams), and found that these cells are activated by pup distress vocalizations. The thalamus-hypothalamus auditory pathway gates oxytocin release in the VTA and maternal behavior in response to calls. We further show that internal states regulate maternal motivation by exploring the effect on pup-oriented behaviors of dams which were temporarily separated from their litters. Our results provide a mechanism for the transformation of sensory cues from the offspring into hormonal output in maternal motivational networks which, together with the contribution of internal states, sustain maternal arousal and pup-oriented behaviors.

Author Index

- Abbasi A., 223
Abbott L., 76, 100, 190
Abdeladim L., 148
Abe E., 33
Adesnik H., 105, 132, 146, 147, 151, 214
Afraz A., 179
Agnes E. J., 143
Aguiar A. P., 152
Aguiar P., 152
Ahmadian Y., 229
Ahmadipour P., 106
Ahn W., 128
Aimon S., 212
Aitchison L., 145
Akam T., 168, 183
Akhlaghpour H., 101
Albanna B., 47
Aldarondo D., 129
Ali Y. H., 155
Aliyari E., 97
Alizadeh K., 173
Aljadeff J., 144, 227
AlKhamissi B., 120
Alleman M., 167
Almani M. N., 250
Amaducci R., 180
Amematsro E., 97
Amemiya S., 170
Ames B., 107
Amsalem O., 134
Amvrosiadis T., 150
An S. J., 93
An X., 135
Anastasiades P., 158
Andalman A., 81
Andermann M., 231
Anderson D., 36
Andrianarivelo A., 45
Angeles Duran S., 160
Antin B., 147
Aoi M., 164
Apps R., 194
Aragon M., 173
Arganda-Carerras I., 148
Arkhipov A., 62
Aronov D., 73
Arora A., 91
Aroso M., 152
Ashwood Z. C., 58, 59
Aso Y., 74, 226
Asumbisa K., 258
Auksztulewicz R., 83
Avansino D., 188
Azeredo da Silveira R., 150
Azizpourlindi S., 38

B Grayden D., 152
Ba D., 207
Bagur S., 83
Bai Reddy C., 63
Bair-Marshall C., 171
Baker C., 207
Bakermans J., 37, 94, 197
Balasubramanian H., 103
Balasubramanian V., 218
Ballesta S., 116
Barabasi D., 172
Barak O., 142, 156
Baram A., 37
Barbosa J., 136, 196
Barnes W., 68
Barron H., 37
Barry C., 73
Barson D., 60
Baruchin L. J., 202
Basak R., 161
Bashivan P., 247
Basnak M., 42
Bastos A. M., 72
Basu J., 160, 220
Bateup H., 125
Bathellier B., 83, 111, 244
Batifol C., 45
Batista A., 118, 200
Batista-Brito R., 39, 154
Battaglia F., 82, 110, 240
Batulin D., 117
Bauer Y., 66
Baumann M., 154
Bazzi S., 200
Beaurepaire E., 148
Beck H., 251
Behnia R., 100, 228
Behrens T., 37, 94, 168, 197
Belkaid M., 254
Bellec G., 60
Belsten A., 180
Bemelmans A., 148
Bendesky A., 186
Bendor D., 159, 259
Benichou A., 79
Benichov J., 103
Benisty H., 60
Bennasar-Vazquez J., 216
Benster T., 81
Benucci A., 215
Berchenko-Kogan Y., 227
Berens P., 66, 176
Bergaoui K., 83
Berger S., 197
Berke J., 234
Bernardino A., 112, 114
Berry H., 113
Bethge M., 229
Betizeau M., 213
Bhalla U., 230

- Bharioke A., 210
 Bhattachari N., 193
 Bi C., 136
 Bicknell B., 50
 Bill J., 140
 Binshtok A., 251
 Bishnoi A., 161
 Bishop W., 61, 118
 Bisi A., 98
 Biswas T., 77
 Blair G., 250
 Blanco Malerba S., 150
 Blanco-Arnau P., 165
 Blau A., 186
 Blum Moyse L., 113
 Boato F., 148
 Bodkin K., 155
 Boebinger D., 174
 Bogacz R., 90
 Bogadhi A. R., 154
 Bolanos F., 215
 Bolkan S. S., 96
 Bolton A., 172
 Bondy A., 195
 Boorman E., 51
 Bordelon B., 217
 Borneman S., 107
 Borst A., 204
 Bortolozzo Gleich M. H., 184
 Bosc M., 254
 Bose A., 110
 Bosman C. A., 72
 Botvinick M., 129
 Bouchard K., 58
 Bounds H., 151
 Boundy-Singer Z., 71
 Bouret S., 128
 Bourg J., 83
 Bourien J., 83
 Boven E., 194
 Bowes B., 86
 Bowler J., 48
 Boyd-Meredith T., 185
 Boyle L., 242
 Bozic T., 131
 Bradley J., 148
 Brainard M., 115, 238
 Bramel M., 231
 Branco T., 102, 169
 Brea J., 256
 Bredenberg C., 65, 132, 216
 Breton-Provencher V., 81
 Brignall A., 210
 Brinkman B., 123
 Brody C. D., 59, 96, 185, 195, 200, 253
 Bromberg-Martin E., 45
 Brown E., 205
 Brown L., 96
 Bruce R., 125
 Brudner S., 174
 Brunel N., 187
 Bruno R. M., 215
 Brunton B., 130, 246, 252
 Buchanan K., 231
 Buendia V., 209
 Buffalo E. A., 120
 Bugeon S., 63
 Burak Y., 150
 Burgess N., 95
 Burioni R., 209
 Buschman T. J., 167
 Busse L., 66, 229
 Butts D., 136
 Buzsaki G., 160
 Bybee C., 180
 Cadena S., 205
 Cagnan H., 72
 Cain N., 84
 Calaim N., 153
 Calhoun A., 46
 Calvignoni D., 224
 Campagner D., 102
 Canatar A., 52
 Canelo A., 245
 Cang J., 85
 Cappotto D., 83
 Carandini M., 63
 Cardin J., 60
 Caref K., 184
 Carey M., 188
 Carlen M., 224
 Carrillo E., 243
 Carter E., 81
 Cash S., 105
 Cash-Padgett T., 236
 Castelhanito P., 188
 Cayco Gajic N. A., 45, 121
 Cazettes F., 98
 Chadderton P., 194
 Chandra S., 99, 114
 Chang J., 222
 Chase S., 118
 Chau H. Y., 105
 Chauvette S., 211
 Chebolu S., 179
 Chen C., 184, 231
 Chen H., 85, 97
 Chen K., 137, 251
 Chen S., 145
 Cheng K., 212
 Cheng S., 258
 Chessel A., 148
 Chettih S., 73
 Chevy Q., 162
 Cheyne J., 64
 Chiappa A., 98
 Chiappe E., 32, 153
 Chintaluri C., 97
 Chklovskii D., 56, 68, 220
 Cho J. R., 96
 Choi H., 84
 Choi W., 257
 Choo-Choy J., 61
 Chowdhury R., 200
 Christensen A., 185
 Christenson M., 100, 228
 Chu T., 221
 Churchland A., 135
 Churchland M., 97
 Ciocchi S., 50
 Cisek P., 91

- Clark D., 47, 87, 190
Claudi F., 102
Clemens J., 173
Cloos N., 219
Clopah C., 62, 127, 130, 181, 194, 222, 225, 233
Cobos E., 205
Cocco S., 77
Codrington N., 220
Coen-Cagli R., 121, 141, 151
Cohen M., 86
Cohen Y., 35
Coifman R., 60
Cole N., 89
Compte A., 31, 136, 243
Comrie A., 234
Cone I., 127
Confavreux B., 143, 144
Constantinople C., 44, 129
Conzelmann K., 210
Cook M., 33
Cornelisse D., 81
Cortez M., 162
Costa R. P., 44, 50, 53, 113, 158, 194
Costacurta J., 189
Cowley B., 46, 175
Creamer M., 251
Crochet S., 60
Crombie D., 66
Crosser J., 123
Cruz B., 223
Cruz T., 153
Csikor F., 139
Cueva C. J., 219
Cunningham P. J., 170
Curtis A., 218
- D'Albis T., 192
Dahan J., 162
Dahmen J., 131
Daie K., 41
Dallmann C., 130
Dalmau J., 243
Damiani F., 109
Dan O., 94
Daniel T., 246
Danielsen N., 223
Darshan R., 41, 127, 134
Datta S. R., 29, 189
Daw N., 234
Dayan P., 166, 169, 179
de Cothi W., 73
de la Rocha J., 243
De Martino B., 93
de Tommasao D., 254
De Worm A., 104
DeAngelis G., 140
Debregeas G., 77
Dehaene S., 108, 244
Dehay C., 213
Dehghani Habibabadi M., 75
Deisseroth K., 81
Delamare G., 181
Denninger A., 154
DePasquale B., 47, 200, 253
Deshmukh S., 161
Destexhe A., 111
- Deutsch D., 87
Devinsky O., 105
DeWeese M., 247
DeWitt E., 163
Dhingra S., 86
Di Santo S., 65
Diamanti E., 59
Dias B., 114
DiCarlo J., 191
Dickman R., 228
Diehl G., 170
Dimitrov M., 50
Ding J., 37
Ding Z., 205
Dipoppa M., 63, 65
Doeller C., 232
Doerenkamp K., 219
Doh H., 128
Doiron B., 132
Dong L. L., 189
Dong X., 221
Donner T., 165
Dotson N., 101
Douglas P., 31, 250
Douglas R., 212, 213
Dowling M., 122
Doya K., 126, 183
Doyle W., 105
Draelos A., 122
Drammis S., 51
Drieu C., 82, 166
Drion G., 225
Driscoll L., 156
Drugowitsch J., 42, 90, 140
Drummond G., 81
Dubois M., 256
Dudman J., 216
Duffield J., 63
Duhamel J., 116
Dumas L., 148
Duncker L., 151
Dunn T., 61
Duong L., 65
Duru J., 209
Duszkiewicz A., 205
Dvali S., 41
- Ebitz B., 184, 235, 255
Ecker A., 147, 175, 205
Eizinger M. F., 210
El-Gaby M., 168
Ellenberger B., 53
ElNokrashy M., 120
Elnozahy S., 82, 203
Eloy C., 116
Elpelt J., 162
Elteto N., 166
Elum J., 34
Elyasaf G., 251
Emerson J., 71
Emonet T., 47
Engel T., 193, 211
Engelken R., 76, 216
Engert F., 172
Ernst U., 192
Eross L., 105

- Escola S., 97, 99, 208
 Esnaola-Acebes J. M., 165
 Essig J., 237
 Esteve Agraz J. A., 184
 Etter G., 206
 Euler L., 187
 Euler T., 176, 229
- F Grewe B., 56
 Fabo D., 105
 Fadaei S., 47
 Fairhall A., 157
 Fang C., 189
 Farashahi S., 56
 Fardet T., 79
 Farrell K., 234
 Farrell M., 217, 239
 Fauth M., 249
 Fealy A., 223
 Feather J., 174
 Fedele T., 37
 Feitosa Tome D., 181
 Felder T., 209
 Feng Y., 45, 187
 Fenton A., 30
 Fermino de Oliveira E., 154
 Fernando J., 231
 Ferrari U., 175
 Ferro D., 236
 Feulner B., 130
 Field G., 67
 Fiete I. R., 64, 99, 114, 218
 Filipchuk A., 111
 Filipovica M., 44
 Finkelstein A., 41
 Fitzgerald J., 77, 127
 Fleming R., 141, 217
 Flynn M., 176
 Fontanini A., 137
 Ford K., 107
 Forrest H., 63
 Forro C., 209
 Fortunato C., 216
 Foster D., 221
 Fox L., 94
 Frank L., 234
 Franke K., 176
 Franks H., 171
 Freedman D., 120, 232
 Fricker D., 102
 Friedrich J., 56
 Fries P., 68, 72
 Friston K. J., 72
 Froemke R., 47, 132, 171, 172, 202, 260
 Fujiwara T., 153
 Fuller K., 82
 Fumarola F., 133
 Fusi S., 48, 215, 242
 Fuzik J., 224
- Gabillet J., 45
 Gachomba M., 184
 Gajowa M., 146, 147
 Galarce E., 125
 Gallego J., 216, 222
 Gallego J. A., 130
- Gallinaro J., 225
 Ganguli S., 111
 Ganguly I., 100
 Gardner J. L., 215
 Garrett M., 62, 84
 Garvert M., 232
 Gavornik J., 163
 Geadah V., 138
 Gebhardt C., 186
 Gehr C., 103
 Gellis A., 129
 Genkin A., 56, 68
 George T., 73
 Gershman S. J., 140
 Gerstner W., 60, 208, 256
 Geva N., 49
 Ghosh A., 108
 Giaffar H., 164
 Giannakakis E., 133
 Gillis W., 189
 Gilra A., 89
 Ginosar G., 241
 Giocomo L., 37, 72, 111, 124
 Girard B., 126
 Girardin S., 209
 Gjorgjieva J., 40, 64, 172, 187, 191, 212
 Gkanias E., 226
 Glennon E., 202
 Gluf S., 135
 Goedeke S., 76, 208
 Gold J., 218
 Goldbach H., 134
 Goldin M., 175
 Goldman G., 80
 Goldman M. S., 96
 Goldt S., 138
 Golkar S., 56
 Gollisch T., 67
 Golshani P., 233
 Goncalves A., 188
 Gontier C., 230
 Gonzalez A., 124
 Gonzalez Marx D., 206
 Goris R., 71
 Gosselin E., 83
 Goudar V., 120
 Gouvea T., 91, 254
 Graff S., 219
 Granado H., 112
 Graupner M., 45
 Greedy W., 44, 53
 Green R., 191
 Grissom N., 184
 Groblewski P., 62
 Groh J., 86
 Grohn J., 128
 Groschner L., 204
 Gross-Scherf B., 210
 Grun S., 219
 Grunwald Kadow I., 212
 Guardamagna M., 240
 Guiomar G., 223
 Guirguis M., 148
 Gulati T., 223
 Guo Y., 83, 255
 Gupta D., 40

- Gupta P., 122, 238
Gupta T., 47
Gurbuz T., 206
Gutierrez C. E., 126
Gutierrez G., 229
Gutig R., 146

Hadjiabadi D., 159
Haefner R., 140
Hafed Z. M., 154
Haider P., 53
Haimerl C., 54
Halassa M., 51
Halgren E., 105
Halgren M., 105
Halpern D., 243
Handy G., 132
Hansclever L., 129
Hardcastle K., 46
Harnett M. T., 105
Harper N., 115
Harris A., 168
Harris K. D., 63
Hart E., 195
Harvey M., 89, 195
Hauri A., 213
Hauser T., 256
Hausser M., 50
Hayden B., 235, 236
Heeger D., 65
Hein B., 133, 162
Henderson* J., 188
Hendricks W., 105, 132
Hengsteler J., 209
Hennequin G., 57
Hennig M., 119
Hermundstad A., 31, 252, 255
Herrera D., 141
Hertag L., 62
Herweg N. A., 48, 73
Hige T., 74
Hight A. E., 202
Higley M., 60
Hillier D., 210
Hiratani N., 70
Histed M., 134
Hochberg L., 188
Hofer S. B., 42
Hoffman S., 170
Holmes C., 76
Hong T., 92
Horoi S., 138
Houghton C., 145
Huang Z., 66
Huelin Gorriz M., 159, 259
Huk A., 195
Hummos A., 51
Hyafil A., 165
Hyseni F., 96

Ibos G., 232
Ihle S., 209
Illing B., 54
Imbach L., 37
Inagaki H., 134
Inati S., 95

Indiveri G., 33
Ingrosso A., 76, 138
Insanally M., 47
International Brain Laboratory T., 231
Iordanidou P., 102
Ireland E., 173
Irfan S., 242
Ishiwaka Y., 126
Islah N., 206
Isogai Y., 63
Issa H., 260
Istrate N., 43
Ito T., 52
Itskov V., 227
Ivanov A., 115
Iyer N., 176

Jacob S., 196
Jacobs W., 61
Jacquerie K., 225
Jagadeesh A. V., 215
Jahn C., 128
Jain A., 219
Jamali S., 244
James B., 103
Janacek K., 166
Jankowski M. M., 93, 198
Jaramillo J., 194
Javadzadeh M., 42
Javanmard R., 112, 114
Jedlicka P., 117
Jeffery K., 32
Jensen K., 57
Jeurissen D., 183
Jha A., 58
Ji Z., 221
Ji-An L., 55
Jiang J., 248
John A., 112, 114
Johnston W. J., 167, 232
Jordan J., 53, 54
Josch M., 40
Joshua M., 115
Jude J., 119
Jun N. Y., 67, 86, 122
Jung F., 224
Jung K., 260
Jurado-Parras T., 180
Jurewicz K., 235, 255

Kadakia N., 47
Kaganovsky K., 37
Kahana M., 48, 73, 243
Kaleb K., 194
Kalle Kossio F. Y., 208
Kamdar F., 188
Kampa B., 219
Kang H., 83
Kang L., 158, 222
Kang R., 105
Kao J. C., 57
Kao T., 57
Kar K., 191
Karamanlis D., 67
Karashchuk P., 130
Karigo T., 36

- Karniol-Tambour O., 59
 Karpowicz B., 155
 Kasavica S., 253
 Kaschube M., 162, 210
 Katsanevaki C., 72
 Katz Y., 251
 Kazakov A., 93, 198
 Keeley S., 195
 Keemink S., 153
 Keijser J., 42
 Keller A., 65
 Kempf A., 83
 Kempter R., 106, 192
 Kennedy A., 36
 Kennedy H., 213
 Kepecs A., 91, 162, 185, 254
 Kerg G., 138
 Keri H., 136
 Kermani Nejad K., 158
 Kerstjens S., 212
 Keshavarzi S., 102
 Keshtkaran M. R., 155
 Ketkar M., 40
 Khajeh R., 76
 Khalili A., 173
 Khan A., 89, 195, 203
 Khilkevich A., 131
 Khona M., 99
 Khosla M., 69
 Ki C., 178
 Kieslich K., 168
 Kim A., 177, 245, 246
 Kim H., 177, 246
 Kim M. J., 224
 Kim S., 154, 245
 Kim T., 253
 Kim Y. J., 149
 King A., 115, 131
 Kiorpes L., 85
 Kirchner J. H., 64, 187
 Kish E., 115
 Klee J., 82
 Kleinjohann A., 219
 Kleinman M., 221
 Klibaite U., 129
 Klindt D., 229
 Klon-Lipok J., 68
 Klos C., 208
 Knep E., 184
 Knudstrup S., 163
 Koay S. A., 96
 Koch C., 157
 Kogan J., 137
 Koh N., 155
 Kolling N., 128
 Kollo M., 182
 Kompatsiari K., 254
 Kong D., 162
 Konkle T., 99
 Kononowicz T., 116
 Kording K., 108
 Korympidou* M. M., 176
 Kosche G., 210
 Kosillo P., 125
 Kotkat A. H., 66
 Koulakov A., 248
 Kramer L., 86
 Krause R., 33
 Krausz T., 234
 Kreiman G., 36
 Kremkow J., 103, 213
 Kriener L., 53
 Kristl A., 155
 Kryven M., 218
 Kuchibhotla K., 82, 166, 203
 Kuczala A., 152
 Kukovska L., 159
 Kumar A., 89
 Kumar M. G., 167
 Kurth-Nelson Z., 120
 Kutschireiter A., 42
 Kwapičh R., 211
 Kwon H., 260
 LaFosse P., 134
 Lagnado L., 103
 Lagzi F., 117
 Laiò A., 139
 Lajoie G., 91, 138, 143, 216
 Lak A., 234
 Lambus T., 77
 Lammel S., 125
 Lampl I., 111, 251
 Lansdell B., 171
 Laplagne D. A., 184
 Larry N., 115
 Larsen R., 84
 Las L., 241
 Latham P., 70, 92, 249
 Laughland C., 176
 Lavian H., 43
 Lawlor J., 203
 Lazar A., 68
 Lazar A. A., 80
 Le Goc G., 77
 Le Merre P., 224
 Leblois A., 38, 96, 237
 Lecoq J., 84
 Ledergerber D., 37
 Ledergerber N., 210
 Lee G. M., 85
 Lee H., 257
 Lee J., 246
 Lee J. H., 199
 Lee S. W., 93, 199, 237
 Lefebvre B., 175
 Lei J., 132
 Leifer A. M., 41, 251
 Leite de Castro D., 152
 Lengyel G., 140
 Lengyel M., 77, 149, 150
 Leonard E., 33
 Levina A., 79, 133
 Li A., 134
 Li C., 36, 243
 Li H., 257
 Li J., 88
 Li K., 83
 Li M., 219
 Li X., 173
 Liang K., 57
 Liao Z., 159

- Libedinsky C., 167
 Lichtman J., 148
 Liebe S., 137
 Lienard J., 126
 Ligeralde A., 247
 Lillicrap T., 143
 Lim S., 145
 Lin D., 49
 Lin M., 233
 Lin W. C., 125
 Lin X., 196
 Linderman S., 72, 189
 Lindner B., 106
 Lindsey J., 74, 99
 Lippl S., 131
 Liston C., 38
 Litwin-Kumar A., 74, 78
 Liu C., 125
 Liu D., 150
 Liu J., 178
 Liu S., 218
 Liu Y. H., 143
 Liu Z., 64
 Livet J., 148
 Lloyd K., 179
 Loewenstein Y., 94
 Logiaco L., 208
 Lohani S., 60
 Lohmann C., 64
 Lohse M., 131
 Long M., 29
 Long W., 32
 Lonsdale R., 66
 Loring M., 61, 122
 Losonczy A., 48, 159
 Loughlin P., 200
 Low I., 72
 Lowe A. T., 55
 Lowet A., 90
 Luddecke T., 147
 Ludwig H., 176
 Lui H. W., 257
 Luo T., 253
 Lupashina T., 103
 Lutas A., 231
 Lynn C., 76
 Ma T., 179
 Ma X., 155
 Ma Z., 155
 MacAskill A., 34, 168
 Mace E., 210
 Machens C., 30, 50, 123, 153, 197, 223
 Macke J., 137, 144
 Madruga B., 233
 Madsen J., 105
 Mah A., 44, 129
 Mahajan P., 237
 Mahou P., 148
 Maiello G., 217
 Maigre L., 116
 Maimon G., 101
 Mainen Z., 98, 163
 Majaj N. J., 85
 Makino H., 198
 Malagon-Vina H., 50
 Malaia E., 107
 Malis J., 204
 Malkin J., 145
 Mancoo A., 123
 Mante V., 29, 33, 201
 Manz P., 75
 Margrie T., 102
 Marin Vargas A., 98
 Marino P., 118
 Markowitz J., 189
 Marques A., 153
 Marques H., 188
 Marquez C., 184
 Marre O., 175
 Marrocco G., 255
 Marshall J., 46, 129
 Marshall N., 97
 Martin K., 132, 260
 Martinez M., 174
 Martins D., 33
 Masset P., 78, 207, 254
 Masson J., 79
 Mastrogiossepe F., 70, 142
 Mathis A., 98
 Matho K., 148
 Matias S., 90
 Mattar M. G., 55
 Maurer B., 209
 Mazzucato L., 39, 43, 82, 84
 McCaffary D., 197
 McDermott J., 174, 245
 McPherson T., 152
 Mehta M., 86
 Mehta P., 235
 Meletis K., 89, 224
 Melloni L., 83
 Mellor J., 53
 Memmesheimer R. M., 75, 208
 Menendez de la Prada L., 180
 Meng R., 58
 Merel J., 129
 Meszena B., 139
 Meulemans A., 56
 Meyerolbersleben L., 66
 Michalke L., 107
 Michel G., 212, 213
 Miehl C., 172
 Mihalas S., 62, 157
 Mikulasch F., 157, 190
 Miller K., 177
 Miller K. D., 65, 105, 133
 Miller L. E., 98, 130, 155, 216, 222
 Millidge B., 90
 Minai Y., 61
 Minh Le N., 119
 Minne C., 225
 Miri A., 155
 Mishchanchuk K., 34
 Mishne G., 60
 Mishra N., 231
 Mizes K., 99
 Mlynarski W., 40, 252
 Moberly A., 60
 Modi M., 226
 Modirshanechi A., 256
 Mohammadi Z., 59

- Mohan H., 135
 Mohinta S., 50
 Monasson R., 77
 Monosov I., 45
 Mooney R., 174
 Moore J., 220
 Moore T., 255
 Mora T., 175
 Moreno Bote R., 109, 236
 Mormann F., 137
 Morrison A., 54
 Morvan T., 116
 Motiwala A., 223
 Mou D., 148
 Mousavi S. N., 228
 Movshon J. A., 85
 Moya-Diaz J., 103
 Mrsic-Flogel T., 131
 Mugan U., 170
 Muhammad T., 205
 Muhle-Karbe P. S., 55
 Mulholland H., 162, 210
 Muller A., 83
 Muller E., 206
 Muller-Komorowska D., 251
 Munoz M. A., 209
 Munz M., 210
 Muratore P., 139
 Murray J. D., 52
 Murthy M., 46, 87, 88, 173, 207
 Musall S., 135, 219
 Muscinelli S., 78
 Myers-Joseph D., 89, 203
 N Murthy V., 78, 207
 Nair A., 36
 Najafi F., 62
 Narayanan N., 125
 Narayanan R., 161
 Nassar M., 102
 Naumann E., 61, 122
 Naumann L. B., 42
 Navas Olive A., 180
 Neftci E., 257
 Nelken I., 93, 198
 Nemeth D., 166
 Nern A., 176
 Neuhofer J., 249
 Nguyen N., 231
 Nicholson D. A., 35
 Nicoloutsopoulos D., 63
 Niculescu D., 148
 Niediek J., 93, 137, 198
 Nieh E. H., 96
 Niell C., 33
 Niemeyer J., 38
 Nierwetberg S., 168
 Nigam T., 164
 Nikitchenko M., 61, 122
 Noble C., 38
 Nogueria R., 215
 Nolen H., 171
 Normand E., 87
 O'Donnell C., 145
 O'Leary T., 201
 O'Rawe J., 134
 O'Reilly R., 51
 O'Shea D., 151
 Oby E., 118
 Ogasawara T., 45
 Ogg C., 171
 Oldenburg I., 105, 132
 Olman C., 71
 Olsen S., 62, 157
 Olson C., 235
 Olveczky B., 46, 99
 olveczky B., 129
 Ona Jodar T., 243
 Onorato I., 204
 Orban G., 139
 Oren-Suissa M., 80
 Orhan P., 205
 Orlandi J. G., 215
 Orme D., 63, 168
 Orsolic I., 131
 Oryshchuk A., 60
 Ostojic S., 142, 196, 250
 Ostrow M., 112
 Ott T., 91, 185, 254
 Ouellette N., 247
 Owald D., 192
 Owczarek E., 205
 Pacheco D., 173, 207
 Pachitariu M., 32, 182
 Pagliaro A., 88
 Paik S., 257
 Palacios Munoz A., 173
 Palmer S., 76
 Palmigiano A., 105
 Pals M., 137
 Pandarinath C., 155
 Pang R., 173, 207
 Panichello M. F., 167
 Paninski L., 146, 147, 186, 231
 Papadopoulos L., 39
 Park H., 128, 136, 246
 Park J., 216
 Park M., 122, 137
 Park S., 51
 Parker P., 33
 Pasarkar A., 147
 Pashakhanloo F., 248
 Paton J. J., 223
 Pattadkal J. J., 64
 Patwa M., 163
 Pavlovsky N., 118
 Pavon Arcas O., 102
 Pawelzik K., 75
 Pearson J., 67, 122, 174
 Pechuk V., 80
 Pedamonti D., 50, 158
 Pede L., 147
 Pehlevan C., 52, 78, 217, 239
 Pellegrino A., 121
 Pemberton J., 113, 194
 Peng H., 63
 Pereira T., 87, 88
 Pereira U., 194
 Perez Rotondo A., 201
 Perich M., 81, 216, 222

- Perich M. G., 130
Peter A., 68
Petersen C., 60
Petersen R. S., 102
Petrovici M. A., 53
Petrucco L., 43
Peyrache A., 124, 154, 160, 205, 258
Peysakhovich B., 120, 232
Pfister J., 230
Pfister S., 213
Phan M. S., 148
Piasini E., 218
Picard S., 131
Pieropan M., 150
Piet A., 62, 185
Pillow J., 46, 58, 59, 88, 109, 175, 195, 200, 207, 251
Pinto L., 59
Pitkow X., 205
Pleger B., 51
Plitt M., 37
Pluta S., 136
Podlaski W., 50, 153
Pogodin R., 249
Polterovich A., 93, 198
Ponder K., 205
Portugues R., 43
Posani L., 242
Pospisil D., 109
Pouget A., 92, 169, 242
Powell N., 162
Prankerd I., 63
Prat-Ortega G., 243
Priebe N., 64
Priesemann V., 157, 190, 206
Priestley J., 48
Puel J. L., 83
Puelma Touzel M., 91, 216
Purandare C., 86
Puri P., 227

Qiu T., 154
Qiu Y., 229
Qu A. J., 237
Quintus A., 217

R Cervera M., 56
R Sebastian E., 180
Rajagopalan A., 127, 226
Rajan K., 47, 81
Rajasethupathy P., 38
Raltchev C., 253
Raman D., 201
Ramanathan S., 36
Ramesh P., 144
Ramirez L., 228
Ramirez* J., 188
Randi F., 41
Rangarajan N., 46, 87
Rao R. P., 252
Rapela J., 42
Rashid S. K., 220
Ratliff J., 39
Ravindranath S., 88
Ray S., 241
Rechavi Y., 117
Redish A. D., 170

Regier P. S., 170
Reid R. C., 247
Reiser M., 176
Ren S., 91
Ren Y., 247
Renart A., 98
Reneaux M., 233
Renner S., 66
Richards B., 49, 108
Richevaux L., 102
Rieger J., 107
Rieke F., 229
Rife Mata A., 236
Rinzel J., 110
Ritoux A., 63
Ritter S., 120
Riveland R., 242
Robbe D., 116
Roche M., 148
Rochefort N., 150
Rodgers C. C., 215
Rodriguez-Deliz C. L., 85
Roemschied F., 173
Roese R., 68
Rogers E., 176
Rolando F., 116
Rolls A., 31
Rolotti S., 48
Romero Pinto S., 35
Roska B., 210
Roth A., 50
Roth M., 65
Rothkopf C., 199
Rouault H., 226
Rougier N. P., 96, 237
Roxin A., 165
Roy D., 181
Rubin A., 49, 117, 220, 240
Rudelt L., 157, 190, 206
Rudoler J., 73
Ruff D., 86
Ruff T., 209
Rullan C., 164
Rupert D., 88
Russek E., 95
Russell L., 50
Russin J., 51
Ryu S., 185

Saanum T., 232
Sacadura F., 97
Sachidanandam S. B., 253
Sacramento J., 56
Sacre P., 104
Sadahiro M., 147
Saddler M., 245
Sadeghi M., 200
Sadeh N., 240
Sadeh S., 181
Saglietti L., 186
Sahani M., 42, 151
Sahay A., 224
Saleem A., 234
Sallet J., 128
Sanders J. I., 254
Sani O., 106

- Sankar R., 237
Sanz Maroto A., 184
Sarao Mannelli S., 186
Sarno S., 116
Sarnthein J., 37
Sarup A., 155
Savin C., 54, 132
Saxe A., 55, 186
Saxena S., 250
Scanziani M., 65, 259
Schaefer A., 182
Schaffer E., 231
Schamburg G., 157
Scheirer W., 179
Schieferstein N., 106
Schiereck S., 44
Schimel M., 57
Schmors L., 66
Schneidman E., 80
Schnupp J., 83
Scholl B., 149
Schottdorf M., 96
Schreiber S., 30
Schroeder S., 202
Schubert T., 176
Schuck N. W., 55, 232
Schuessler F., 142
Schuhknecht G., 172
Schultheis M., 199
Schulz E., 232
Schunemann M., 192
Schwalger T., 106
Schwarz L., 171
Schwiedrzik C. M., 164
Sederberg A., 71
Sedler A. R., 155
Seenivasan P., 161
Sengupta A., 56
Senn W., 53, 54, 253
Senzai Y., 259
Seo H., 112
Seymour B., 237
Shadlen M., 97, 183
Shah N., 188
Shahbazi E., 179
Shamash P., 169
Shanechi M., 106
Shao S., 40
Shao Y., 250
Shapcott K. A., 68
Sharif Razavian R., 200
Sharma A., 41
Sharma S., 114, 218
Sharpee T., 152
Shavina V., 201
Shea S. D., 88
Shea-Brown E., 229
Sheffer B., 189
Sheintuch L., 220
Shenoy K., 151, 156, 188
Shin H., 214
Shin J. H., 199
Shinn M., 63
Shirinifard A., 171
Shivkumar S., 140
Shourkeshti A., 255
Shouval H., 127
Shpektor A., 37
Shteyn M., 235
Sibile J., 103, 213
Siegelbaum S. A., 242
Silies M., 40
Silva Simoes L., 92
Silveira Broggi A. C., 204
Simoncelli E., 54, 65, 132, 142
Singer W., 68
Singh S. H., 252
Sirigu A., 116
Sjulson L., 154
Skromne Carrasco S., 124, 205
Skyberg R., 85
Slashcheva M., 224
Sleizer B., 235
Smith G., 162, 210
Smith M., 61, 136, 175, 178, 214
Smoulder A., 118
Snyder S., 118
Soares S., 223
Sokol P., 122
Sokoletsky M., 111
Sokoloski S., 66, 121
Sol-Foulon N., 102
Soldado Magraner J., 61
Soltész I., 159
Sommer F., 180
Sompolinsky H., 146, 239
Song S., 172
Soo W. M. W., 77
Sorscher B., 111
Sotomayor B., 110
Sourmpis C., 60
Souza B., 82
Sprekeler H., 42
Sreekumar V., 95
Sridharan D., 238
Srinath Halvagal M., 193
Sriworarat C., 122
Stachenfeld K., 73
Stan P., 175, 214
Stauffer W., 92
Stein H., 45, 121
Steinberg J., 239
Steinfath E., 173
Steininger V., 224
Stella F., 240
Stempel A. V., 102
Stensola H., 163
Stensola T., 163
Stern M., 43
Sternad D., 200
Stih V., 43
Stine G. M., 183
Storrs K., 141, 217
Straub D., 199
Strauss S., 176
Stringer C., 32, 182
Sturgill F., 162
Su C., 227
Su S., 100
Sudhof T., 37
Sugihara H., 119
Sui Y., 257

- Summerfield C., 55
Sun X., 151
Sun X. R., 135
Supatto W., 148
Sur M., 81, 119
Surace S. C., 230
Sussillo D., 156
Svara F., 43
Svirsky M. A., 202
Svoboda K., 41, 134, 194
Swanson R., 160
Syeda A., 32
Symonova O., 40
Szatko K., 229

Tafazoli S., 139
Tai L., 125, 237
Taira M., 183
Takigawa M., 159
Talluri B. C., 165
Tan A., 167
Tan C., 167
Tan H., 95
Tan Y. L., 102
Tanabe S., 85
Tanaka R., 87
Tank D. W., 59, 96
Tano P., 169
Tarpin T., 83
Tassa Y., 129
Taxidis J., 233
Tchumatchenko T., 233
Teh K. L., 103, 213
Teichert T., 244
Tenenbaum J., 218
Terada S., 159
Terceros A., 38
Tesileanu T., 68
Tetrick S., 232
Tetzlaff C., 249
Thirion B., 108
Thomson A., 176
Thual A., 108
Tian L., 238
Timofeev I., 211
Tirole M., 159
Title B., 251
Tokdar S., 86
Tolias A., 205
Tolooshams B., 207
Tong A. P., 95
Tootoonian S., 182
Toth J., 47
Touzo L., 55
Toyoizumi T., 158
Tran D., 205
Tran H., 108
Trautmann E., 97, 183
Trenholm S., 258
Triesch J., 117
Triplett M., 146, 147
Tristany Farinha M., 56
Trivedi S., 217
Tsai M., 54
Tschiersch M., 136
Tsodyks M., 146

Tuckute G., 174
Tung R., 32
Turkcan M., 80
Turner E., 156
Turner G., 127, 226
Tuthill J., 130
Twarkowski H., 224
Tyulmankov D., 189
Tzanou A., 204

Uchida N., 35, 90, 207
Ujfalussy B., 149
Ulanovsky N., 241
Ulbert I., 105
Umakantha A., 136, 178
Ungarish D., 111
Urakubo H., 126
Uran C., 68, 204

Vadaparty A., 189
Vafidis P., 192
Vale R., 102
Vallentin D., 103
Valley M., 84
Valtcheva S., 202, 260
van Breugel F., 252
van Kerkoerle T., 244
Van Opstal J., 112, 114
van Rossum M., 248
Varela N., 153
Vega V., 91
Veit L., 238
Venkatesh P., 157
Vermani A., 137
Versteeg C., 98
Vestergaard C. L., 79
Vezzani A., 117
Vice J., 250
Victor J., 38
Viduolyte A., 63
Viejo G., 124
Vijayabaskaran S., 258
Vikbladh O., 95
Villegas A., 231
Villegas P., 209
Vinck M., 68, 110, 178, 204
Vinogradov O., 133
Virgili S., 175
Viswan N., 230
Vlasits A. L., 176
Vogels T., 66, 97, 143, 144
Volkman R., 125
von Hagel A., 246
Voros J., 209
Voytek B., 105
Vuillemin N., 148
Vulić K., 209
Vyas S., 151

Wachowiak M., 227
Wagner M., 78
Waitzmann F., 191
Walker K., 115
Walling-Bell S., 130
Walton M., 90, 128, 168, 183
Wang A., 82

- Wang B., 51, 144
 Wang J., 88, 211, 242
 Wang M., 87
 Wang R., 222
 Wang X., 120, 194
 Wang Y., 119
 Warnberg E., 89
 Warren J., 94, 197
 Wayne G., 129
 Weaver S., 209
 Webb B., 226
 Weber A., 246
 Wehbe L., 69, 179
 Wehr M., 39
 Weinreb C., 189
 Weis M. A., 147
 Weisman J., 101
 Weiss O., 151
 Weissenberger Y., 131
 Wen J., 111
 Wenliang L., 70
 Wert Carvajal C., 233
 White J. K., 45
 Whiteway M., 231
 Whittington J., 94, 168, 197
 Wibral M., 157
 Widłoski J., 221
 Wilbrecht L., 125, 237
 Willett F., 188
 Williams A., 72, 189
 Williams J., 179
 Williamson R., 178
 Willmore B., 115
 Wilmes K., 253
 Wilson R., 42
 Wimalasena L. N., 155
 Wimmer K., 165
 Wirth S., 116
 Witten I. B., 96
 Wittner L., 105
 Wolf G., 138
 Wolf S., 77
 Wolpert D., 97
 Wood E., 205
 Woolrich M., 95
 Wu A., 186, 231
 Wu H., 207
 Wu M., 227
 Wu S., 221, 227
 Wu Y. K., 43, 191
 Wyble B., 242
 Wybo W., 54
 Wykowska A., 254
 Wyrick D., 84

 Xia J., 177
 Xie M., 78
 Xu Z., 140

 Yackle K., 115
 Yadav N., 38
 Yamada D., 74
 Yancy G., 195
 Yang B., 36
 Yang G. R., 112, 189, 219
 Yang Q., 145