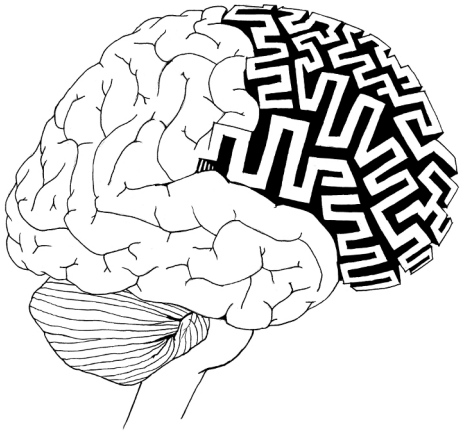
AREADNE 2022

Research in Encoding and Decoding of Neural Ensembles

Nomikos Conference Centre, Santorini, Greece

28 June – 2 July 2022



Conference Information

Schedule and Program

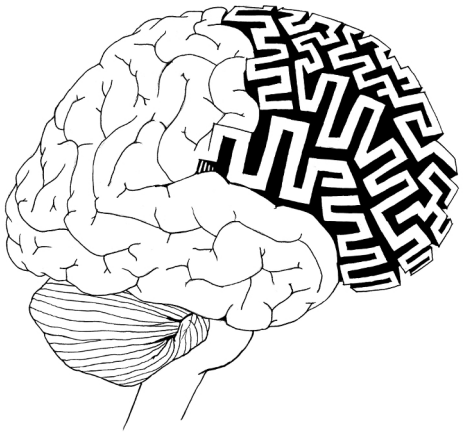
Invited Speaker Abstracts

Poster Abstracts

Attendee and Author Index

AREADNE 2022
Research in Encoding and Decoding of Neural Ensembles
Nomikos Conference Centre, Santorini, Greece, 28 June – 2 July 2022
Nicholas G. Hatsopoulos, John S. Pezaris, editors

Published by The AREADNE Foundation, Inc., Cambridge, Massachusetts, USA, http://areadne.org, info@areadne.org
Single copy price USD 50
ISSN 2154-6819 (on-line)
ISSN 2155-3203 (print)
ISSN 2155-319X (CD-ROM)



FOREWORD

Foreword

Within the range of responsibilities, duties, and tasks in our lives, being co-chairs of AREADNE Conferences and organizing the biennial cycle is among the most satisfying, both professionally and personally. The prospect of resuming an every-other-year pattern has us greatly excited, and the record-breaking interest in this year's meeting suggests we are not alone in looking forward to a return to normalcy.

Like Zorba's telegraphed entreaty to Basil, "Found green stone, the most beautiful, come immediately," [1] Greece is calling us all, urgently, to return to her. We have brought you together for AREADNE to be entranced by the wonders of cutting-edge neuroscience and share that experience with your colleagues, just as Zorba was fascinated by the beauty in his green stone and reached out to share it with his friend. Together, we will celebrate the joy of nature and discovery, as Zorba wished to do with Basil, with "the creative ingeniousness, renewed every morning, to see everything unceasingly for the first time." [1]

The benefits of face-to-face interaction within scientific discourse are clear, as is the role that in-person conferences have to play in the continued advancement of our field. For all of us, our daily lives have shifted between in-office and remote work, often back and forth, but being scientists, we have found ways to continue our investigations despite pandemic-driven restrictions. This conference, our first since the appearance of the virus and its variants, has among the most exciting research submitted to any AREADNE meeting thus far. We, the organizers, take this distinction to be a reflection of our determination as a field to find answers to interesting questions under even challenging circumstances.

We hope that you will enjoy AREADNE 2022, and that the meeting will be productive, inspirational, and perhaps even provocative. Welcome back.

Nicholas G. Hatsopoulos, Ph.D.

John S. Pezaris, Ph.D.

1. Kazantzakis, *Βίος και Πολιτεία του Αλέξι Ζορμπά* (*Life and Times of Alexis Zorbas / Zorba the Greek*), Athens: Dimitrakou, 1946.

WELCOME

Welcome

Welcome to AREADNE 2022, the ninth AREADNE Conference on Research in Encoding and Decoding of Neural Ensembles.

One of the fundamental problems in neuroscience today is to understand how the activation of networks of neurons gives rise to the higher order functions of the brain including learning, memory, cognition, perception, action and ultimately conscious awareness. Electrophysiological recordings in behaving animals for over fifty years have revealed considerable information about what the firing patterns of single neurons encode in isolation, but it remains largely a mystery how collections of neurons interact to perform these functions.

Technological advances have provided a glimpse into the global functioning of the brain. Such tools include functional magnetic resonance imaging, high-density electroencephalography and magnetoencephalography, and, importantly, optical imaging and multi-microelectrode electrophysiology. These methodological advances have expanded our knowledge of brain functioning beyond the single neuron level.

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

Conference Mission Statement

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

Organizing Committee

The AREADNE 2022 conference was organized by Nicholas Hatsopoulos and John Pezaris (Co-Chairs), along with Dora Angelaki, Kenny Blum, Yiota Poirazi, Thanos Siapas, and Andreas Tolias.

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

Sponsors and Support

Our conference is being sponsored with generous gifts from Mrs. Daphne Hatsopoulos through the NIMA Foundation, and The Gatsby Charitable Foundation to the University of Chicago, along with gifts from the Simons Foundation and The William M. Wood Foundation to the Massachusetts General Hospital. We have received generous in-kind support from Foley & Lardner,

LLC, and both the University of Chicago and Massachusetts General Hospital, where the conference is co-administered.

Sarah J. Caddick, Ph.D.
Advisor to Gatsby Charitable Foundation
CEO and Founder, THALAMIC Ltd
sjc@sciencecuratedby.com

Alyssa Picchini Schaffer, Ph.D.
Senior Scientist
Simons Foundation
apschaffer@simonsfoundation.org

Lawrence W. Vernaglia, J.D., M.P.H.
Chair, Health Care Industry Team
Foley & Lardner, LLP
lvernaglia@foley.com

John Maunsell, Ph.D.
Director, Grossman Institute for Neuroscience
Unversity of Chicago
maunsell@uchicago.edu

Bob S. Carter, M.D., Ph.D.
Chief, Neurosurgical Service
Massachusetts General Hospital
bcarter@mgh.harvard.edu

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

The Myth of Ariadne

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

In Greek Mythology, Ariadne was the daughter of Minos, king of Crete. King Minos built a large, intricate maze called the Labyrinth to house the Minotaur, a fearsome creature that was half bull, half human. Any who attempted to face the Minotaur perished, either by becoming lost in the maze or from the Minotaur's vicious attack. When the hero Theseus came from Athens to slay the Minotaur, Ariadne gave him a sword and a ball of silk thread. Theseus tied one end of the thread at the Labyrinth entrance and unwound it as he went along, so that after he had found and slain the Minotaur, he could escape from the maze by following the thread back out.

LOCAL INFORMATION

We have assembled a small selection of local information on Fira and the island of Thera. For more information, select among the many guidebooks written for travel in Santorini.

Restaurant Information

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

Restaurants in Fira and Firostefani

Idol	+30-22860-23292	€ € €	caldera view, wine restaurant
Kapari	+30-22860-21120	€ €	taverna, set back from main road
Koukoumavlos	+30-22860-23807	€ € € €	caldera view, nouvelle cuisine
Mama Thira	+30-22860-22189	€ €	caldera view, taverna
Nick the Grill	+30-22860-23492	€	souvlaki stand, near the main square
Sphinx	+30-22860-71450	€ € € €	caldera view, Greek cuisine
To Ouzeri	+30-22860-21566	€ €	Greek tapas, near main square

Restaurants in Oia

Iliovassilema	+30-22860-71614	€ €	fresh fish
Thalami	+30-22860-71485	€ €	ouzo bar
1800	+30-22860-71485	€ € € €	nouvelle cuisine

Restaurants in Perivolos-Vlychada

Taverna Dimitris	+30-22860-82532	€ €	Greek taverna near the marina
to Psaraki	+30-22869-82783	€ € €	fish tavern overlooking the marina
The Net	+30-22860-82818	€ € € €	fish tavern by the sea, local cuisine

Recommended Activities

Santorini offers not just sweeping vistas, but excellent nightlife, a respectable wine industry, beaches with white, black, or red sand, ancient excavations, and fantastic sunsets. Also, we have optional tours to the Akrotiri archaeological site and to the volcano island at the center of the caldera, although these may not be able to accommodate everyone. Beyond these two excursions (which can be taken on your own, although without the benefit of our invited experts), there are plenty of other activities on the island. A few suggestions to scratch the surface are listed below.

Archaeological Museum at Fira
open 08.00–15.00 (closed Mondays), tel +30-22860-22217, Ypapantis Street, Fira

Museum of Prehistoric Thera
open 08.30–15.30 (closed Tuesdays), tel +30-22860-23217, Mitropoleos Street, Fira

Folk Art Museum
open 10.00–14.00 tel +30-22860-22792, Kondohori, near Fira

Wine Museum
open daily 09.00–19.00, tel +30-22860-31322, located in Vothonas village

Santo Winery
www.santowines.gr, tel +30-22860-22596, located in Pyrgos

Oia at sunset
sunset is at approximately 8 pm in late June; once at Oia, follow the crowds westward

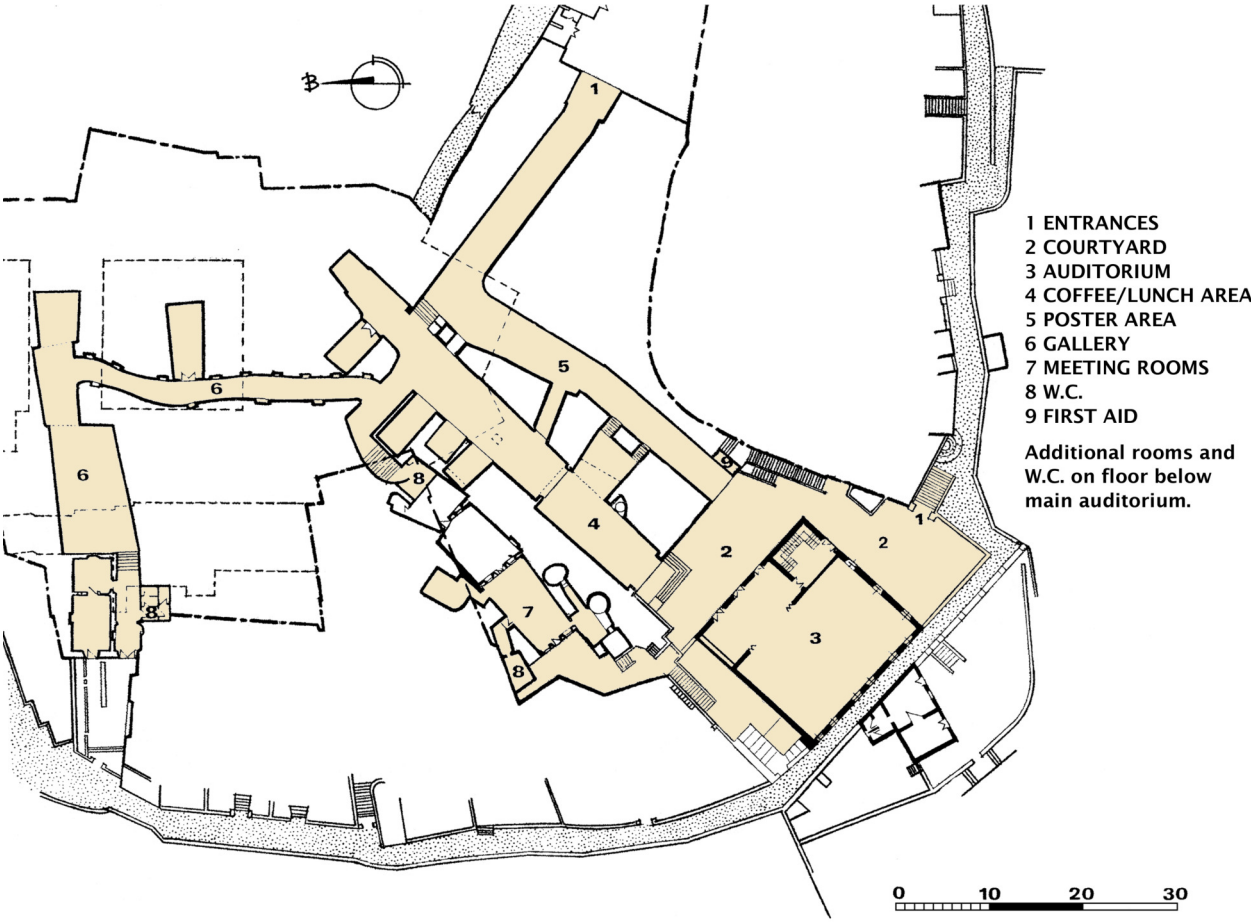
Monastery of Profitis Ilias
in Pyrgos, at the mountain peak; museum open 09.00–20.15; modest dress required

Main Beaches

The beaches on Santorini are beautiful and varied, with white, red, and black sand depending on location. However, swimming must be done with care as the water gets deep quickly and rip currents are not uncommon. Flip-flops are a must as the dark sand can get extremely hot in the sun. SCUBA diving is available with trips to wrecks, the volcano, and the underwater caldera face. Beaches are at Perivolos (13 km from Fira), Perissa (13 km), Vlychada (12 km), and Kamari (10 km).

Conference Centre Map

Oral presentations will be held in the main auditorium of the Nomikos Centre. Coffee breaks will be in the reception area and courtyard. Posters will be hung on the walls of the main tunnel. A first aid station is available off the main tunnel, while restrooms are in the lower level. Please refer to the map below for more details.



DAILY SCHEDULE AND PROGRAM

Overall Schedule

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

Tuesday
19:30–22:00 welcome reception and registration

Wednesday
08:30–09:30 registration
09:30–09:45 opening remarks
09:45–12:30 lectures and coffee break
12:30–14:00 lunch
17:00–21:30 lectures and coffee break, posters

Thursday
09:00–12:30 lectures and coffee break
12:30–14:00 lunch
17:00–21:30 lectures and coffee break, posters

Friday
09:00–13:00 optional excursions (no lunch provided)
17:00–21:30 lectures and coffee break, posters

Saturday
10:00–12:30 lectures and coffee break
12:30–14:00 lunch
17:00–19:00 lectures and coffee break
19:00–19:15 closing remarks
20:30–24:00 banquet dinner at Barolo Restaurant in Fira

TUESDAY, 28 JUNE 2022

19:30–22:00 welcome reception at Nomikos Centre

WEDNESDAY, 29 JUNE 2022

08:30–09:30 registration

09:30–09:45 opening remarks

MORNING SESSION Nicholas Hatsopoulos, moderator

09:45–10:30 **Adam Hantman** (University of North Carolina at Chapel Hill)
Neural basis for skilled movements, 36

10:30–11:00 coffee break

11:00–11:45 **Matt Kaufman** (University of Chicago)
A curved manifold orients rotational dynamics in monkey motor cortex, 38

11:45–12:30 **Claudia Clopath** (Imperial College London)
Sensory feedback can drive adaptation in motor cortex and facilitate generalization, 30

12:30–14:00 lunch

AFTERNOON SESSION David Freedman, moderator

17:00–17:45 **Nachum Ulanovsky** (Weizmann Institute)
Neural codes and replays of natural behaviors in flying bats, 50

17:45–18:15 coffee and light snacks

18:15–19:00 **Cristina Savin** (New York University)
Making sense of neural responses during naturalistic behavior, 46

19:00–19:20 **Desmond Patterson** (University of Texas at Austin)
A question of scale: the Minoan eruption of 1610 BCE and the Hunga eruption (Tonga) of January 2022, 43

19:20–19:40 **Andronike Makres** (Hellenic Education and Research Center)
The (Minoan?) settlement of Akrotiri and the Greek city-state of Ancient Thera, 41

20:00–21:30 posters, presenting author

Ludovica Bachschmid-Romano (Duke University)
Modeling planar traveling waves propagating along specific directions in the motor cortex, 56

Concetta Brusco (Albert Einstein College of Medicine)
Ripples in macaque entorhinal cortex during fixation and image viewing, 60

Spyridon Chavlis (Foundation for Research and Technology, Hellas)
Improving deep learning performance using biological dendrites, 64

Simone Ebert (INRIA Université Coté D'azur)
The role of dynamic inhibitory synapses for coding surprise in the retina, 68

Jiri Hammer (Charles University)
Spectro-temporal characteristics of intracranial EEG recorded from human motor cortex during continuous movements, 76

James Isbister (Blue Brain Project, EPFL)
Evidence of precise time-warped spike timing in vivo *and in silico*, 77

Jean-Nicolas Jérémie (Institut de Neurosciences de la Timone — CNRS)
Ultra-rapid visual search in natural images using active deep learning, 79

Gerick Lee (New York University)
Perceptual and neural representations of texture naturalness in developing monkeys, 86

Nikos Malakasis (Foundation for Research and Technology, Hellas)
Biologically constrained spiking neural network for image classification, 91

Jonathan Mayzel (Weizmann Institute)
Homeostatic synaptic scaling optimizes learning in random projections models of large neural population codes, 92

Fabian Mikulasch (MPI Dynamics and Self-Organization)
Towards hierarchical predictive coding with spiking neurons and dendritic errors, 93

Jorrit Montijn (Netherlands Institute for Neuroscience)
A novel and highly sensitive statistical test for calcium imaging, 95

Dalton Moore (University of Chicago)
Developing a network encoding model for natural behavior in motor cortex of the unconstrained marmoset, 96

THURSDAY, 30 JUNE 2022

MORNING SESSION Barry Richmond, moderator

09:00–09:45 **Laura Colgin** (University of Texas, Austin)
Exploring the relationship between temporal compression of place cell sequences and memory operations, 31

09:45–10:30 **Mark Sheffield** (University of Chicago)
High reward expectation reinforces hippocampal spatial maps through a dopaminergic reward proximity signal, 47

10:30–11:00 coffee break

11:00–11:45 **Stefano Fusi** (Columbia University)
Are place cells just memory cells? Probably yes, 34

11:45–12:30 **Ila Fiete** (MIT)
The emergence and functioning of high-capacity and flexible cognitive codes, 33

12:30–14:00 lunch

AFTERNOON SESSION John Pezaris, moderator

17:00–17:45 **Andreas Tolias** (Baylor College of Medicine)
A digital twin of the brain: engineering a less artificial intelligence, 48

17:45–18:15 coffee and light snacks

18:15–19:00 **Clay Reid** (The Allen Institute for Brain Science)
Large-scale circuit reconstruction in the cerebral cortex, 44

19:00–19:45 **Maria Papadopouli** (Foundation for Research and Technology, Hellas)
Functionally connected neuronal modules in area V1, 42

20:00–21:30 posters, presenting author

Paul Anderson (Medical University of Vienna)
Should I stay or should I go now? Cell-type-specific representations of choice abandonment in orbitofrontal cortex, 54

Alexander Bae (Seoul National University)
Connectivity maps of cortical cells in petascale neural circuit reconstruction, 57

Max Burg (Universität Göttingen)
Digital twin reveals combinatorial code of non-linear computations in the mouse primary visual cortex, 61

FRIDAY, 1 JULY 2022

09:00–13:00 optional excursions (no lunch provided)

AFTERNOON SESSION Ziv Williams, moderator

17:00–17:45 **Sliman Bensmaia** (University of Chicago)
Neural codes and computaions along the primare somatosensory neuraxis, 29

17:45–18:15 coffee and light snacks

18:15–19:00 **Elizabeth Hong** (Caltech)
What are the organizational axes of the olfactory code?, 37

19:00–19:45 **Georg Keller** (FMI)
The significance of self-generated sensory feedback to cortical function, 39

20:00–21:30 posters, presenting author

Alexandra Antoniadou (Foundation for Research and Technology, Hellas)
Encoding and supression of distracting salient stimuli in the prefrontal and parietal cortices, 55

Rune Berg (University of Copenhagen)
A new theory for the neural principles behind generation of movements, 88

Severin Berger (Champalimaud Foundation)
Efficient task representations for habitual and model-based behaviour, 58

Richard Born (Harvard Medical School)
Weak evidence for neural correlates of task-switching in macaque V1, 84

Sophie Caron (University of Utah)
Adaptive traits in the drosophila mushroom body, 63

Eric Denovellis (University of California, San Francisco)
Confidently decoding multiple spatial environments in hippocampal replay, 66

Anna Gillespie (University of California, San Francisco)
Real-time feedback can promote task-relevant memory replay, 72

Gal Goldman (Weizmann Institute)
Reprogramming the topology of the nociceptive circuit in C. elegans reshapes sexual behavior, 73

Ralf Haefner (University of Rochester)
Detecting task-related changes in differential correlations, 53

Ou Zhu (University of Chicago)
Neuronal encoding of rapid categorical decisions across the primate oculomotor network, 120

SATURDAY, 2 JULY 2022

MORNING SESSION Leslie Osborne, moderator

10:00–10:45 **Stefan Treue** (German Primate Center)
Visual cortical area MT — a prototype area for shaping sensation into perception, 49

10:45–11:15 coffee break

11:15–12:00 **John Reynolds** (The Salk Institute for Biological Studies)
Intrinsic travelling waves of neural activity in area MT of the awake, behaving monkey regulate the gain of stimulus-evoked responses and perceptual sensitivity, 45

12:00–12:45 **Christine Constantinople** (New York University)
Orbitofrontal cortex is required to infer hidden task states, 32

12:45–14:00 lunch

AFTERNOON SESSION Georgia Gregoriou, moderator

17:00–17:45 **Roozbeh Kiani** (New York University)
Representational geometry of perceptual decisions, 40

17:45–18:15 coffee and light snacks

18:15–19:00 **Jim Gnadt** (NIH/NINDS)
The NIH BRAIN Initiative and systems neuroscience research, 35

19:00–19:15 closing remarks

20:30–24:00 banquet dinner at Barolo Restaurant in Fira

INVITED SPEAKER ABSTRACTS
(in alphabetical order by speaker)

NEURAL CODES AND COMPUTATIONS ALONG THE PRIMATE SOMATOSENSORY NEURAXIS

Sliman Bensmaia

Dept. Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
Committee on Computational Neuroscience, University of Chicago, Chicago, IL, USA
sliman@uchicago.edu

Texture perception operates over a wide range of spatial scales and occupies a high dimensional space. To sense the texture of a surface, we move our skin across it, which gives rise to two types of skin deformations, each transduced by different tactile nerve fibers. One population of nerve fibers is sensitive to large scale deformations and carries a neural image of a texture's coarse features; another population of nerve fibers responds to skin vibrations by producing precise temporally patterned responses. These two neural codes — spatial and temporal — define a spectrum of neural response properties in somatosensory cortex: Some neurons are sensitive to spatial patterns and encode coarse features, other neurons are sensitive to vibrations and encode fine features. While the texture responses of nerve fibers are dependent on scanning speed, a subset of cortical neurons are less so, giving rise to a speed invariant texture percept.

SENSORY FEEDBACK CAN DRIVE ADAPTATION IN MOTOR CORTEX AND FACILITATE GENERALIZATION

Claudia Clopath

Department of Bioengineering, Imperial College London, London, UK
clopathlab.imperial@gmail.com

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 perturbations (*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: (i) learning generalized to non-learned but similar movements and (ii) followed multiple learning timescales. 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. 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.

EXPLORING THE RELATIONSHIP BETWEEN TEMPORAL COMPRESSION OF PLACE CELL SEQUENCES AND MEMORY OPERATIONS

Laura Lee Colgin

Department of Neuroscience, University of Texas at Austin, Austin, TX, USA
colgin@mail.clm.utexas.edu

The hippocampus is a key brain area for learning and memory. Place cells are neurons in the hippocampus that fire in specific spatial locations and are believed to code the *where* component of episodic memories. Theta rhythms temporally coordinate organized sequences of hippocampal place cells during active behaviors. Sharp wave-ripples coordinate reactivation of place cell sequences during rest and slow wave sleep. Previous work has shown that place cell sequences during active theta-related behaviors develop temporally compressed representations of spatial paths with learning. Prior work has also shown that representations of spatial paths are replayed by place cell sequences in a highly temporally compressed form during sharp wave ripples. Our recent results show that temporal compression of paths represented by place cell sequences during theta rhythms decreased on error trials of a spatial memory task. Preliminary results also suggest that replay events during sharp wave-ripples are less temporally compressed in a rat model of Fragile X syndrome, a genetic disorder that causes learning disabilities, compared to wildtype control rats. The results are consistent with the hypothesis that temporal compression of place cell sequence representations during theta rhythms and sharp wave-ripples is important for successful spatial memory operations.

ORBITOFRONTAL CORTEX IS REQUIRED TO INFER HIDDEN TASK STATES

Shannon Schiereck, Andrew Mah, Christine Constantinople *

Center for Neural Science, New York University, NY, USA
* constantinople@nyu.edu

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 (lOFC) reduces modulation of wait time by block but does not impair modulation of wait time by reward volume. This suggests that lOFC 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 lOFC 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 lOFC is inactivated, but other parameters are not affected. Electrophysiological recordings from lOFC reveal encoding of hidden states (blocks). These data suggest that lOFC promotes the use of a prior that incorporates knowledge of the task structure for inferring partially observable states of the environment.

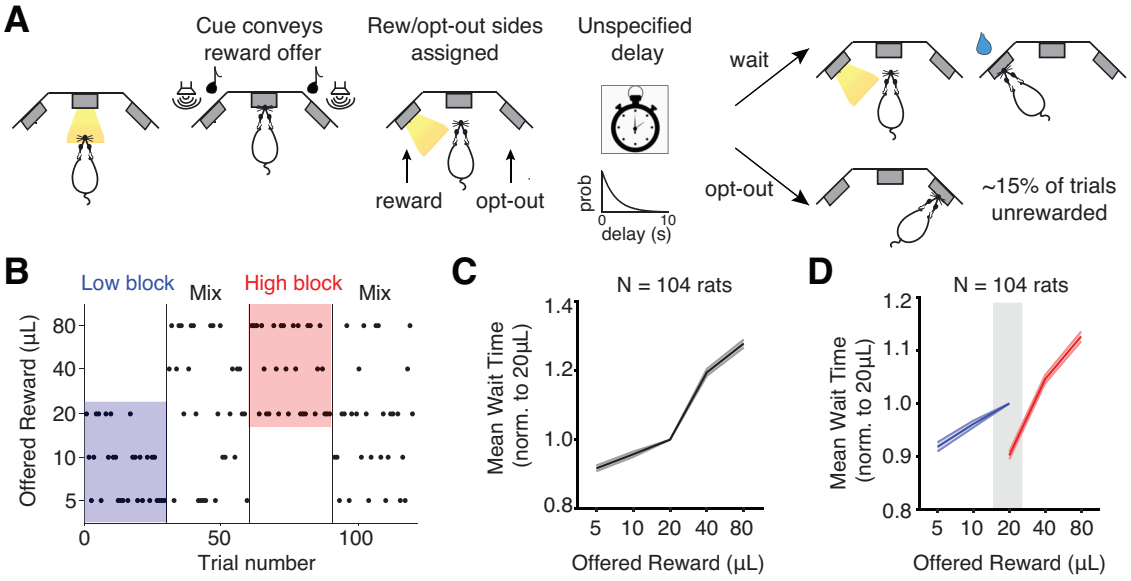


Figure 1. (**A**) Schematic of temporal wagering task. (**B**) Block structure. (**C**) Wait times are sensitive to offered reward volume. (**D**) Wait times are sensitive to current reward block.

References

1. Padoa-Schioppa, Conen, 2017, *Neuron*, 96(4):736–754, 10.1016/j.neuron.2017.09.031
2. Wilson, Takahashi, *et al.*, 2014, *Neuron*, 81(2):267–279, 10.1016/j.neuron.2013.11.005

THE EMERGENCE AND FUNCTIONING OF HIGH-CAPACITY AND FLEXIBLE COGNITIVE CODES

Ila Fiete

Department of Brain and Cognitive Sciences, MIT, Cambridge, MA, USA
fiete@mit.edu

Generalizably solving complex problems involves decomposing them into simpler components and combining these parts in effective ways to solve new instances. The hippocampal complex has been a rich playground for understanding how the brain constructs and combines modular structures for flexible computation. I will describe recent progress in characterizing the rigid and low-dimensional nature of some of these representations, using theoretical approaches including fully unsupervised topological characterization of neural population codes. I will then discuss models of how these rigid and modular circuits can emerge, and how they can generate, with high capacity and high data-efficiency without rewiring recurrent circuitry, cognitive maps across different variables (*e.g.*, spatial and non-spatial) as well as across varied input dimensions. Finally, I will describe how the low-dimensional multi-periodic structure of grid cells serves as a scaffold that visibly undergirds the population-level responses of hippocampal place cells.

ARE PLACE CELLS JUST MEMORY CELLS? PROBABLY YES

Stefano Fusi

Department of Neuroscience, Columbia University, New York, NY, USA
sf2237@columbia.edu

Numerous studies on primates revealed the importance of the hippocampus in memory formation. The rodent literature instead focused on the spatial representations that are observed in navigation experiments. Here, we propose a simple model of the hippocampus that reconciles the main findings of the primate and rodent studies. The model assumes that the hippocampus is a memory system that generates compressed representations of sensory experiences using previously acquired knowledge about the statistics of the world. These experiences can then be memorized more efficiently. The sensory experiences during the exploration of an environment, when compressed by the hippocampus, lead naturally to spatial representations similar to those observed in rodent studies and to the emergence of place cells. We present some preliminary evidence that the predictions of the model are correct in an experiment in which an animal runs in virtual environments that have different levels of compressibility. Work done in collaboration with Marcus Benna, James Priestley, Lorenzo Posani and Attila Losonczy.

THE NIH BRAIN INITIATIVE AND SYSTEMS NEUROSCIENCE RESEARCH

Jim Gnadt

National Institute of Neurological Disorders and Stroke, Bethesda, MD, USA
gnadtjw@mail.nih.gov

The NIH BRAIN Initiative was launched in 2014 with seven priority areas: cell mapping, circuit discovery, neural dynamics, interventional tools, theory and analysis tools, human neuroscience, and integrated approaches — with an emphasis on understanding the normal, healthy brain. Research efforts were parsed into several systematic efforts with differing approaches, including (i) goal-directed cell and circuit mapping across scales from micrometers to centimeters, (ii) systematic optimization and dissemination of cellular and device tool-building, (iii) integrated approaches in investigative systems neuroscience, and (iv) procedural and societal neuroethics. All components have proved highly successful under funding and research review conditions that are partially untethered from traditional NIH funding constraints. The NIH BRAIN Initiative has now achieved a sustaining influence with a budget of over $500M per year. For AREADNE 2022, Jim Gnadt will review the more than 10-fold growth in BRAIN-supported systems neuroscience created uniquely for the initiative (over $200M per year), and document some of the impacts and productivity data in fundamental, disease-agnostic discovery. Innovations include staged support of exploratory and expansive approaches at both single-lab and team-science scales (including international collaborations); incorporation of quantitative and theory-/model-driven approaches at scales from synapses to whole brain networks and from milliseconds to lifetimes; development of data sharing models at scales from inter-lab research to topic domain sharing; and incorporation of human neuroethics, diverse perspectives and within-cycle investigator responses in peer review.

NEURAL BASIS FOR SKILLED MOVEMENTS

Adam Hantman

Dept. Cell Biology and Physiology, Univ. North Carolina at Chapel Hill, Chapel Hill, NC, USA
hantmana@janelia.hhmi.org

Skillful movements contribute to the major functions of the brain, such as perception and manipulation of the world. Skill involves understanding the world, developing appropriate plans, converting those plans into appropriate motor commands, and adaptively reacting to feedback. Considering the range of possible actions and the complexity of musculoskeletal arrangements, skilled motor control is an amazing achievement of the nervous system. The myriad of these underlying operations is likely performed by a diverse set of neural circuits. By combining anatomy, physiology, and specific (genetic and temporal) manipulations, we hope to identify and understand the neural elements responsible for skillful motor control. Currently, we focus on the role of the cortico-cerebellar loop in a learned reach-grab-eat task in the rodent.

WHAT ARE THE ORGANIZATIONAL AXES OF THE OLFACTORY CODE?

Jie-Yoon Yang[1], Wei-Mien M. Hsu[2], Tom F. O'Connell[1], Anoop Praturu[2], Matthew S. Bauer[1], Tatyana O. Sharpee[2], Elizabeth J. Hong[1,]*

[1] Division of Biology and Biological Engineering, Caltech, Pasadena, CA, USA
[2] Computational Neurobiology Laboratory, Salk Institute for Biological Sciences, La Jolla, CA, USA
[*] ejhong@caltech.edu

Understanding olfactory coding is challenging due to the complexity of chemical stimuli, which are, by nature, complex, high-dimensional, and not easily organized along any obvious coordinate systems. We investigated this problem in the Drosophila olfactory system, which has a similar core circuit architecture to its vertebrate analogs. Olfactory inputs are randomly expanded onto a large population of third-order, mixed layer neurons, which, in the fly, are the principal neurons of the mushroom body (MB), a major associative olfactory area in the fly brain. Using large-scale calcium imaging in defined olfactory population, we find that MB representations of odor are sparse and structured; odor relationships are reliable and predictable across individual MBs. However, the relationships between odors are unexpectedly remapped between the input odorant receptor layer and the mushroom body layer, in a manner that deviates from the simple predictions of a sparse random expansion of olfactory inputs. We will discuss new analytical approaches towards understanding alternative organizational frameworks by which odor representations are reformatted across successive stages of olfactory processing in the fly brain.

A CURVED MANIFOLD ORIENTS ROTATIONAL DYNAMICS IN MONKEY MOTOR CORTEX

Matthew T. Kaufman[1,2,*], *David A. Sabatini*[1,2]

[1] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[2] Neuroscience Institute, University of Chicago, Chicago, IL, USA
[*] mattkaufman@uchicago.edu

Controlling arm movements requires complex, time-varying patterns of muscle activity. Accordingly, the responses of neurons in motor cortex are complex, time-varying, and heterogeneous during reaching. When examined at the population level, patterns of neural activity evolve over time according to dynamical rules. During reaching, these rules have been argued to be rotational or variants thereof, containing coordinated oscillations in the spike rates of individual neurons. While these models capture key aspects of the neural responses, they fail to capture others, accounting for only 20–50% of the neural response variance. We find that motor cortex dynamics take an unexpected form: there were 3–4 rotations at fixed frequencies in M1 and PMd explaining more than 90% of neural responses, but these rotations occurred in different portions of state space when movements differ. These rotations appear to reflect a curved manifold in state space, with locally rotational dynamics. These fixed-frequency rotations obeyed a simple relationship with movement: the orientation of rotations in motor cortex activity were related almost linearly to the movement the animal made, allowing linear decoding of reach kinematic time-courses on single trials. Like placing a record player in a large bowl, the frequency of activity is fixed, but the location of motor cortex activity on a curved manifold sets the orientation of locally-rotational dynamics. This system simplifies motor control, helps reconcile conflicting frameworks for interpreting motor cortex, and enables greatly improved neural decoding.

THE SIGNIFICANCE OF SELF-GENERATED SENSORY FEEDBACK TO CORTICAL FUNCTION

Georg Keller

Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland
georg.keller@fmi.ch

A defining aspect of our brains interaction with the world is the coupling between movement and the resulting sensory feedback. With experience the brain learns to associate specific movements with their sensory consequences and thus builds an internal model of the world. Based on this we speculate that much of what we perceive is not the result of what our sensory organs transmit to our brains but either the result of what we expect to perceive or the result of a large deviation from these expectations. Our work aims to understand the computational contribution of neocortex to this process. Our research focuses on mouse visual cortex and is guided by the ideas of predictive processing. In visual cortex, visual input is compared to predictions of visual input based on these internal models to compute prediction errors. Experience with self-generated visual feedback establishes a finely tuned circuit in visual cortex capable of computing prediction errors between top-down predictions and bottom-up visual input. Our results describe the cortical microcircuit that implements this computation, as well as contributing to our understanding of the molecular markers of the neurons with defined computational roles. Understanding and manipulating this circuit will be instrumental in advancing our understanding of perceptional disturbances, such as those observed in schizophrenia.

REPRESENTATIONAL GEOMETRY OF PERCEPTUAL DECISIONS

Roozbeh Kiani

Center for Neural Science, New York University, New York, USA
Department of Psychology, New York University, New York, NY, USA
Neuroscience Institute, New York University Langone Medical Center, New York, NY USA
roozbeh@nyu.edu

I will explore two core principles of circuit models for perceptual decisions. In these models, neural ensembles that encode actions compete to form decisions. Consequently, representation and readout of the decision variables (DVs) in these models are implemented similarly for decisions with identical competing actions, irrespective of input and task context differences. Further, DVs are encoded as partially potentiated action plans through balance of activity of action-selective ensembles. I show that the firing rates of neurons in the posterior parietal cortex of monkeys performing motion and face discrimination tasks violate these principles. Instead, neural responses suggest a mechanism in which decisions form along curved population-response manifolds misaligned with action representations. These manifolds rotate in state space for different task contexts, making optimal readout of the DV task dependent. Similar manifolds exist in lateral and medial prefrontal cortex, suggesting common representational geometries across decision-making circuits.

Acknowledgments

The studies were performed by Gouki Okazawa and Christina Hatch in the Kiani lab at NYU in collaboration with Christian Machens and Allan Mancoo from Champalimaud Research. The work was supported by the Simons Collaboration on the Global Brain, McKnight Scholar Award, Pew Scholars Program in the Biomedical Sciences, and National Institute of Mental Health.

THE (MINOAN?) SETTLEMENT OF AKROTIRI AND THE GREEK CITY-STATE OF ANCIENT THERA

Andronike Makres

Hellenic Research and Education Center, Athens, Greece
info@herc.org.gr

Santorini is home to two very important archaeological sites: (*i*) The Bronze Age (possibly Minoan) site of Akrotiri that dates to the 2nd Millennium B.C., and
(*ii*) Ancient Thera, a Greek city-state (polis) that flourished in the 4th and 3rd centuries B.C.

In my presentation I shall discuss these two entirely different ancient societies. The first, Bronze Age Akrotiri, appears exotic because of its extraordinary wall paintings (frescoes) and its well-known climactic end but also because we know very little about it, given the absence of historical texts and writing.

The second settlement, Hellenistic Thera, seems more familiar because it is an ancient Greek city-state, just like Athens and Sparta. The Ancient Greek city-states created cultures and value systems which later became fundamental for modern western civilization: for example, these city-states used the alphabet for the first time, their citizens established the rule of law and enjoyed political freedom. The Greek city-states produced philosophy, geometry, athletics etc. and Athens in particular created the democracy both in theory and in practice, a political system that we still use and value above all others today.

FUNCTIONALLY CONNECTED NEURONAL MODULES IN AREA V1

Maria Papadopouli

Department of Computer Science, University of Crete, Heraklion, Crete, Greece
Institute of Computer Science, FORTH, Heraklion, Crete, Greece
mgp@ics.forth.gr

The rules by which multiple neurons coordinate to represent information about visual stimuli remain elusive. Single neuron responses are both noisy and ambiguous: responses to the same stimulus vary considerably, while multiple different stimuli may elicit the same response. These ambiguities can be resolved at the level of neuronal populations via the coordinated firing of distinct neuronal ensembles, which are also more efficient at relaying shared information downstream [1]. Large field of view, high resolution, 2-photon imaging methods reveal the dynamic patterns of neural activity across large neuronal populations, making it possible to study how large ensembles of neurons coordinate with each other in processing information. Network analysis performed in the absence of sensory stimulation allows us to identify groups of neurons that are connected with each other directly or indirectly, and thus have the potential to coordinate in processing information. It has been suggested that spontaneous activity patterns span a vocabulary space shared with population activity patterns elicited during sensory responses [2,3]. Here we used the Spike Time Tiling Coefficient (STTC) metric of inter-neuronal correlation strength [4] to measure functional connectivity between pairs of neurons firing spontaneously in granular (L4) and supra-granular (L2/3) layers of mouse area V1. We found that about 15–17% inter-neuronal pairs are functionally connected with high statistical significance (z-score above 4). Compared to L2/3, V1 L4 exhibits higher percentage of statistically significant edges, stronger STTC correlation weights, higher normalized degree of connectivity, and higher clustering coefficients. Of particular interest is the group of L4 pyramidal neurons that are functionally connected with a single L2/3 neuron, thereby constituting its putative input set. This talk will also present our main results on the groups of functionally connected neurons in relation to their properties and to the brain state as reflected in modulations of pupil size.

References

1. Smyrnakis, Smirnakis *et al.*, 2013, *Neural Computation* 25:9, 10.1162/NECO_a_00476
2. Palagina, *et al.*, 2019, *J. Neurosci.* 39(25):4931–4944, 10.1523/JNEUROSCI.2275-18.2019
3. Kenet, *et al.*, 2003, *Nature* 425:954–956, 10.1038/nature02078
4. Cutts, Elgen, 2014, *J. Neurosci.* 34(43):14288–14303, 10.1523/JNEUROSCI.2767-14.2014

A QUESTION OF SCALE: THE MINOAN ERUPTION OF 1610 BCE AND THE HUNGA ERUPTION (TONGA) OF JANUARY 2022

Des Patterson

University of Austin at Texas, Austin, Texas, USA
des@helium-labs.com

Volcanic eruptions are ranked from 0 to 8 on the logarithmic Volcanic Explosive Index (VEI). The cataclysmic Minoan eruption of Thera (Santorini) circa 1610 BCE is a 7 with a volume of erupted material about 100 km^3. As such it ranks in the six largest eruptions of the last 10,000 years, and had catastrophic impact on local, regional and global scales — although the timing, details and consequences remain vigorously debated amongst geologists and antiquarians.

There are two reason for this uncertainty: First, after three and a half millennia the curtain of time has fallen — the only human records from Santorini are the ruins and haunting frescoes of Akrotiri. The geological evidence is spectacular but is of necessity incomplete. Second is the scale of the event. Such large eruptions are rare with global return times in excess of 1,000 years. From the human perspective this is fortunate. The most recent VEI 7 eruption comparable to the Minoan was Tambora (Indonesia 1815). This eruption resulted in over 10,000 immediate local fatalities and injected aerosols (including an estimated 60 megatons of SO_2) into the stratosphere causing global cooling of up to 1 C and 1816 is known as The Year Without a Summer. Associated crop failures, famines and malnourishment resulted in a further 80,000 deaths in Indonesia alone — the global death toll is uncertain.

The rarity of these events poses a fortunate but vexing problem; we must extrapolate our understanding of smaller more common events upwards in scale by several orders of magnitude and then attempt to interpret the geological record of events of a scale never witnessed. The recent eruption of the Hunga volcano near Tonga on 15 January 2022 is certainly the largest eruption since the 1981 eruption of Pinatubo (Philippines) and perhaps the largest since Tambora (1815). It caused headlines with spectacular satellite imagery, generated large tsunami, and caused significant devastation to the nearby Kingdom of Tonga. The study of this eruption has already provided insights to long standing questions about tsunami propagation. But it has also posed perplexing questions about the mechanisms involved in the explosions. In the time since the eruption two different expeditions have surveyed and sampled the seabed on and around the volcano. Seafloor mapping using acoustic techniques show the pre-existing submarine caldera floor has deepened from 150 to 800 meters suggesting an eruptive volume of about 10 km^3 and pushing the VEI up from initial estimates of 5 to as much as 6. Although the Hunga eruption is an order of magnitude smaller than the Minoan there are similarities and differences between the two that are illuminating.

Our understanding of the Hunga eruption remains fluid and conclusions preliminary. The Geophysical Journal of the Royal Astronomical Society has called for submissions for a Special Volume. Further expeditions are underway or planned that include the use of robotic vessels. Detailed studies and analyses of the samples collected from the submarine flanks of Hunga during the most recent marine survey have barely begun. In this presentation I aim to provide an up to date summation of what is presently known about the Hunga eruption and how it compares and contrasts with events here on Santorini over 3500 years ago.

LARGE-SCALE CIRCUIT RECONSTRUCTION IN THE CEREBRAL CORTEX

R. Clay Reid[*], *The MICrONS Consortium, Allen Institute Axonal Connectomics Team*

The Allen Institute for Brain Science, Seattle, WA, USA
[*] clayr@alleninstitute.org

Over the past 15 years, new tools have emerged for studying synaptic networks in the brain. EM connectomics (large-scale serial-section electron microscopy) is providing increasingly complete circuit reconstructions in multiple species and brain areas. As part of the IARPA MICrONS project, https://www.microns-explorer.org/, we have recently performed an electron-microscopic reconstruction of a cubic millimeter of mouse visual cortex, encompassing 70,000 neurons and 6×10^8 synapses. I'll discuss the technical challenges in creating, processing, and analyzing this petascale data set, along with results on the highly specific interconnections between distinct cortical cell types.

Finally, I'll discuss a recent movement advocating whole-brain connectomics, in the mouse at the EM/synaptic scale [1, 2] and in non-human primates at the level of projection axons [3] (projectomes). In the past, studies of long-distance projections have been performed sparsely, using targeted injections of anterograde or retrograde tracers. I'll describe our new program to create a dense projectome, using high-throughput light-sheet microscopy of brain regions stained with antibodies that target large axons in the gray and white matter. The long-term goal is to reconstruct the trajectories of many/most projection axons above a given caliber, perhaps 1mm, throughout the brain.

Acknowledgments

Supported by IARPA, NIH, and The Allen Institute

References

1. Abbott, *et al.*, 2020, *Cell*, 182:1372–1376
2. BRAIN CONNECTS: Comprehensive Centers for Mouse Brain
3. BRAIN CONNECTS: Comprehensive Centers for Human and Non-Human Primate Brain

INTRINSIC TRAVELLING WAVES OF NEURAL ACTIVITY IN AREA MT OF THE AWAKE, BEHAVING MONKEY REGULATE THE GAIN OF STIMULUS-EVOKED RESPONSES AND PERCEPTUAL SENSITIVITY

Zachary Davis[1], *Gabriel Benigno*[2], *Alexandra Busch*[2], *Charlee Fletterman*[1], *Theo Desbordes*[1], *Christopher Steward*[2], *Julio Martínez-Trujillo*[3], *Terry Sejnowski*[1], *Lyle Muller*[2], *John Reynolds*[1,*]

[1] The Salk Institute for Biological Studies, La Jolla, CA, USA
[2] Brain and Mind Institute, Western University, London, Ontario, Canada
[3] Robarts Research and Brain and Mind Institute, Western University, London, ON, Canada
[*] reynolds@salk.edu

Perceptual sensitivity varies from moment to moment. One potential source of this variability is spontaneous fluctuations in neural sensitivity. Using newly developed techniques to characterize the moment-to-moment dynamics of noisy multielectrode data, we find that spontaneous cortical activity is organized into traveling waves that traverse visual cortex several times per second. Recording in Area MT of the common marmoset, we find that these *intrinsic traveling waves* (iTWs) regulate both the gain of the stimulus-evoked spiking response and the monkey's perceptual sensitivity. In monkeys trained to detect faint visual targets, the state of spontaneous travelling waves before target onset predicts the magnitude of target-evoked neural response and the likelihood that the monkey will detect the target, as indicated by a saccade to the target location. A large-scale topographic spiking network model with conductance-based synapses recapitulates the properties of iTWs measured *in vivo*. The model shows that large-scale iTWs naturally emerge from the delays that occur as action potentials traverse unmyelinated horizontal fibers. The model predicts iTWs are sparse, in the sense that only a small fraction of the neural population participates in any individual iTW. As a result, iTWs can occur without inducing correlated variability, which we have shown, in separate experiments, can impair sensory discrimination. We thus refer to the model as the sparse-wave model of iTWs in cortex. Further, the model predicts that iTWs fall into feature-selective motifs whose feature selectivity stems from the horizontal fibers that preferentially connect similarly tuned feature domains. Consistent with this prediction, we find clusters of iTW motifs. Individual motifs exhibit characteristic patterns of response modulation across the population, with some motifs modulating the activity of neurons that have similar motion tuning. For example, one motif modulates the activity of neurons that are selective for upward motion, while other motifs modulate subpopulations of neurons with other motion preferences. Further, these feature-selective iTWs modulate perceptual sensitivity to targets whose motion matches the preference of neurons whose activity is modulated by a particular motif. Taken together, these findings lead to the conclusion that feature-selective projection systems endow the visual system with the capacity to organize intrinsic spiking activity into feature-selective iTWs that improve perception. These findings are consistent with studies of iTWs in the motor system, suggesting that iTWs may represent a brain-wide computational principle.

Acknowledgments

The Dan and Martina Lewis Biophotonics Fellowship, Gatsby Charitable Foundation, the Fiona and Sanjay Jha Chair in Neuroscience, the Canadian Institute for Health Research, the Swartz Foundation, BrainsCAN at Western University through the Canada First Research Excellence Fund (CFREF), the Office of Naval Research N00014-16-1-2829, and NIH grants R01-EY028723, U01-NS108683, P30-EY0190005, T32 EY020503-06 and T32 MH020002-16A.

MAKING SENSE OF NEURAL RESPONSES DURING NATURALISTIC BEHAVIOR

Cristina Savin

Center for Neural Science, New York University, New York, NY, USA
Center for Data Science, New York University, New York, NY, USA
csavin@nyu.edu

Modern systems neuroscience is increasingly shifting away from using simple tasks with low-dimensional, well-controlled stimuli towards trying to understand neural activity during naturalistic behavior. However, this shifts bring with it a dramatic increase in number and complexity of task-relevant features, making even standard analyses such as estimating tuning functions or latent dimensionality reduction challenging. Here we present novel data analysis tools designed to address these statistical challenges, and demonstrate their applicability in the context of a dataset involving multi-area recordings from monkeys performing a virtual reality spatial navigation task. First, our Poisson generalized additive model P-GAM [1] framework can be used to map a large number of task variables, the form of discrete events or continuous variables (this could be events within a trial, input stimuli, behavioral outputs, filtered LFP and activity of other neurons) into observed spike counts. The estimator provides marginal confidence bounds for the contribution of each feature to neural responses. This allows us to robustly identify a minimal set of task features that each neuron is responsive to, circumventing computationally demanding model comparison. Second, our probabilistic framework for task aligned manifold extraction TAME-GP allows for interpretable partitioning of population variability within and across areas. TAME-GP extends a probabilistic variant of demixed PCA by (i) explicitly partitioning variability into private and shared sources, (ii) using a Poisson noise model, and (iii) introducing temporal smoothing of latent trajectories in the form of a Gaussian Process prior. This approach allows for robust estimation of axes of task relevant variability in local population responses and shared covariability between areas, with single trial resolution. When applying these analyses to simultaneous recordings from the dorsomedial superior temporal area (MSTd), parietal area 7a, and dorsolateral prefrontal cortex (dlPFC) as monkeys navigate in virtual reality in a firefly catching task [2] reveal mixed selectivity to task variables, with cognitive variables represented even in traditionally sensory areas (MSTd). Strikingly, global encoding profiles and unit-to-unit coupling suggested a functional subnetwork between MSTd and dlPFC, and not between these and 7a, as anatomy would suggest, with intra- and inter-area interactions shaped by the degree of sensory uncertainty. These results highlight the distributed nature of neural coding during closed-loop action-perception naturalistic behaviors and suggest internal models may manifest in structured functional connectivity within parietal and frontal cortices.

Acknowledgments

This work is part of an ongoing collaboration between the Savin and Angelaki labs at NYU, driven by postdocs Edoardo Balzani and Jean Paul Noel.

References

1. Balzani, Lakshminarasimhan, Angelaki, Savin, 2020, *NeurIPS 34*, Vancouver, Canada
2. Noel, Balzani, Avila, *et al.*, 2022, *AREADNE*, Santorini, Greece

HIGH REWARD EXPECTATION REINFORCES HIPPOCAMPAL SPATIAL MAPS THROUGH A DOPAMINERGIC REWARD PROXIMITY SIGNAL

Seetha Krishnan[1,2,†], *Chad Heer*[1,2,†], *Chery Cherian*[1,2], *Mark. E. J. Sheffield*[1,2,*]

[1] Department of Neurobiology, University of Chicago, Chicago, IL, USA
[2] Institute for Neuroscience, University of Chicago, Chicago, IL, USA
[†] equal contribution
[*] sheffield@uchicago.edu

Hippocampal place cells support reward-related spatial memories by forming a cognitive map that over-represents reward locations. The strength of these memories is modulated by the extent of reward expectation during encoding. However, the circuit mechanisms underlying this modulation are unclear. Here we find that when reward expectation is extinguished in mice, they remain engaged with their environment, yet place cell over-representation of rewards vanishes, place field remapping throughout the environment increases, and place field trial-to-trial reliability decreases. Interestingly, Ventral Tegmental Area (VTA) dopaminergic axons in CA1 exhibit a ramping reward-proximity signal that depends on reward expectation and inhibiting VTA dopaminergic neurons mimics the effects of extinguishing reward expectation. We conclude that changing reward expectation rapidly restructures CA1 cognitive maps and determines map reliability by modulating the dopaminergic VTA-CA1 reward-proximity signal. Thus, internal states of high reward expectation enhance encoding of spatial memories by reinforcing hippocampal cognitive maps associated with reward.

A DIGITAL TWIN OF THE BRAIN: ENGINEERING A LESS ARTIFICIAL INTELLIGENCE

Andreas Tolias

Center for Neurosci. and Artificial Intelligence, Baylor College of Medicine, Houston, TX, USA
Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
Department of Electrical and Computer Engineering, Rice University, Houston, TX, USA
atolias@baylor.edu

Despite major advances in artificial intelligence through deep learning methods, computer algorithms remain vastly inferior to mammalian brains: they generalize poorly outside the domain of the data they have been trained on. This results in brittleness (e.g. adversarial attacks) and poor performance in transfer learning, few-shot learning, causal reasoning, and scene understanding, as well as difficultly with lifelong and unsupervised learning — all important hallmarks of natural intelligence. We believe current deep learning architectures are severely under-constrained, lacking key model biases found in the brain that are instantiated by the multitude of cell types, pervasive feedback, innately structured connectivity, specific non-linearities, local learning rules and learning objectives. Therefore, our goal is to learn the brain's model bias in order to engineer less artificial, and more intelligent, neural networks. Using tour-de-force experimental methods, we are collecting a deluge of neural data from the visual cortex, and developed system identification deep learning methods to learn functional digital twins of the cortex. We perform *in silico* experiments in these models to generate hypotheses which we can test back in the brain using inception loops. These models also enable us to learn the brain's model biases.

VISUAL CORTICAL AREA MT — A PROTOTYPE AREA FOR SHAPING SENSATION INTO PERCEPTION

Stefan Treue[1,2,*], *Janina Hüer*[1,3,4], *Vladislav Kozyrev*[1], *Sonia Baloni Ray*[1,5], *Julio C. Martinez-Trujillo*[6], *Moein Esghaei*[1]

[1] German Primate Center, Göttingen, Germany
[2] Leibniz-ScienceCampus Primate Cognition, Göttingen, Germany
[3] Ernst Strüngmann Institute (ESI) for Neuroscience, Frankfurt, Germany
[4] Lab. de Neurosci. Cognitives et Computat., Ecole Norm. Sup., PSL University, Paris, France
[5] Indraprastha Institute of Information Technology, New Delhi, India
[6] Dept. of Physiology and Pharmacology, Western University, London, ON, Canada
[*] treue@gwdg.de

Area MT in primate visual cortex is arguably the best understood area in primate extrastriate visual cortex in terms of its representation of the incoming (bottom-up) sensory information. MT is considered to be of critical importance for our ability to perceive the visual motion patterns in our environment. This level of understanding of the neural representation of sensory information in one cortical area is an excellent basis for investigating the top-down influences exerted by various types of attention onto sensory information processing.

This approach has documented a multitude of attentional effects, ranging from effects of spatial, feature-based and object-based attention on target and distractor encoding, to multiplicative and non-multiplicative modulations of tuning curves and receptive field profiles. The talk will focus on recent and new data on the attentional reshaping of MT population responses at the expense of their sensory accuracy, the source of top-down attention influences on MT responses, and the role of MT in shaping information flow through and beyond extrastriate cortex.

From these investigations a clear pattern emerges that turns MT into a prototype area for the interaction of sensory (bottom-up) signals with cognitive (top-down) modulatory influences that characterizes visual perception. These findings also document how this interaction enables visual cortex to actively generate a neural representation of the environment that combines the high-performance sensory periphery with selective modulatory influences for producing an 'integrated saliency map' of the environment.

Acknowledgments

Supported by grants from the German Research Foundation (DFG), by the Leibniz Association through funding for the Leibniz ScienceCampus Primate Cognition and the German Federal Ministry of Education and Research (BMBF) for the Bernstein Center of Computational Neuroscience.

NEURAL CODES AND REPLAYS OF NATURAL BEHAVIORS IN FLYING BATS

Nachum Ulanovsky

Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel
nachum.ulanovsky@weizmann.ac.il

This talk will focus on the importance of using natural behaviors in neuroscience research — the *Natural Neuroscience* approach. I will illustrate this point by describing studies of neural codes for spatial behaviors and social behaviors, in flying bats — using wireless neurophysiology methods that we developed — and will highlight new neuronal representations that we discovered in animals navigating through 3D spaces, or in very large-scale environments. In particular, I will discuss: (i) A multi-scale neural code for very large environments, which we discovered in the hippocampus of bats flying in a 200-meter long tunnel. This new type of neural code is fundamentally different from spatial codes reported in small environments — and we show theoretically that it is superior for representing very large spaces. (ii) Rapid modulation of *position* × *distance* coding in the hippocampus during collision-avoidance behavior between two bats flying in the long tunnel. This result provides a dramatic illustration of the extreme dynamism of the neural code. (iii) Sequential replay (reactivation) of ultra-long flight trajectories during rest and sleep by ensembles of hippocampal neurons. The lecture will propose that neuroscience experiments — in bats, rodents, monkeys or humans — should be conducted under evermore naturalistic conditions.

POSTER ABSTRACTS

(in alphabetical order by first author)

DETECTING TASK-RELATED CHANGES IN DIFFERENTIAL CORRELATIONS

*Samuel Alvernaz, Anton Pletenev, Richard D. Lange, Ralf M. Haefner**

Department for Brain and Cognitive Science, University of Rochester, Rochester, NY, USA
*ralf.haefner@rochester.edu

Differential correlations reflect the neural variability in the direction defined by the tuning to the task-relevant stimulus, f'. To what degree they are the result of limited input information as originally assumed [1], or the result of task-learning, or task-specific attention [2], and hence feedforward or feedback (FB) in nature, are important open questions. One way to address these questions is by comparing neural covariability across different behavioral states, *e.g.*, task context [3], or attentional states related to the task [2]. However, training animals to switch between different cognitive states is expensive, greatly complicating the interpretation of empirically found noise correlations in the absence of such switches [4].

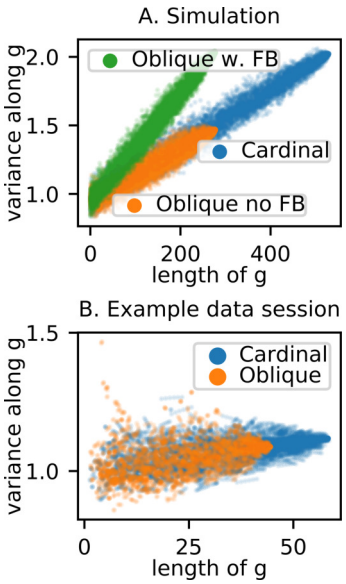


Figure 1. Each point corresponds to a sub-sampled neural population. Naive method: compare response variances in (normalized) directions $\hat{g} = g / ||g||$ over the full set of recorded neurons (rightmost points of each cloud) for different g. We found the magnitude of covariability to be strongly correlated with sensitivity of the (fixed) recorded population in the $\hat{g}$-direction both in simulations (**A**) and data representative for our 78 recording sessions (**B**).

We present a new method for measuring changes in the empirically observed task-specific covariability that does not rely on training an animal on alternative tasks. Our key idea is to infer the degree to which variability along f' is task-specific by comparing it to variability in equivalent neural directions, $\hat{g}$, unrelated to the task actually performed. We validated this comparison method using ground truth simulations, and applied it to neural population responses from two monkeys performing two orientation discrimination tasks, recorded during 78 sessions over the course of learning. Our method succeeds for classic homogeneous population codes, but requires bias-corrections in the case of realistic, heterogeneous, neural populations. The underlying confounds that we have identified — (i) neural sensitivity (length of g), (ii) sparseness of the elements of g, and (iii) the balance of the elements of g — are important beyond our method, and crucial for fairly comparing variability in different directions as is often done, *e.g.*, during PCA. For instance, (i) is often biased due to the practice of optimizing the stimulus to the recorded neural population at hand, while (iii) differs greatly between different tasks, *e.g.*, discrimination (high balance with roughly equal number of neurons preferring either stimulus) versus change-detection tasks (low balance, since most neurons change their firing in the same direction).

Acknowledgments

Supported by NIH/NEI R01EY028811.

References

1. Moreno-Bote *et al.*, 2014, *Nat. Neurosci.*
2. Ni, *et al.*, 2018, *Science*
3. Bondy *et al.*, 2018, *Nat. Neurosci.*
4. Rumyantsev *et al.*, 2020, *Nature*

SHOULD I STAY OR SHOULD I GO NOW? CELL-TYPE-SPECIFIC REPRESENTATIONS OF CHOICE ABANDONMENT IN ORBITOFRONTAL CORTEX

Paul M. Anderson[1,*], *Michael Lagler*[1], *Ben-Orli Nathanson*[1], *Paul Masset*[3,4], *Torben Ott*[5], *Marta Solano Mateos*[1], *Romana Hauer*[1], *Adam Kepecs*[2], *Thomas Klausberger*[1]

[1] Centre for Brain Research, Div. Cognitive Neurobiology, Med. Uni. Vienna, Austria
[2] Department of Neuroscience, Washington University in St. Louis, St. Louis, MO, USA
[3] Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, USA
[4] Center for Brain Science, Harvard University, Cambridge, MA, USA
[5] Bernstein Center for Computational Neuroscience, Humboldt University of Berlin, Germany
[*] paul.anderson@meduniwien.ac.at

Effective decision-making requires not just resolving difficult choices but also knowing when to abandon a failed strategy. The orbitofrontal cortex (OFC) plays a key role in decision-making and has been shown to represent metacognitive computations such as post-decision confidence [1], *i.e.* the evaluation of how successful a decision was. How neural representations of decision confidence drive decisions to abandon a choice commitment is as yet unclear.

Here we examined the activity of neurons in the OFC of rats, while they were performing an auditory choice task with a post-decision time investment option. After making their perceptual decision, animals had to wait for reward delivery delayed by a pseudo-random period. The time animals were willing to invest into waiting for an uncertain reward before abandoning their choice served as a post-decision measure of confidence

We first used a function-first cell-type identification strategy to search for neurons that were specifically active when abandoning a choice commitment. Utilising juxta-cellular recordings in freely-moving animals [2] we searched for specific activity patterns during behaviour and labelled identified neurons with neurobiotin for post-hoc cell-type characterization. We found OFC neurons with distinctive activity profiles that negatively correlated with the reported decision-confidence of a choice and indicated the time when choice commitments were abandoned.

Identified neurons were situated in deep layers of the OFC with unique axonal projection patterns and dendritic arborisation profiles. Further investigations using retrograde viral tracers in conjunction with juxta-cellular recordings as well as projection specific optogenetic activation with high-density silicon probes revealed a selectivity of axonal projections to subcortical areas.

Our results reveal that a subpopulation of OFC neurons that predict choice abandonment corresponds to specific subcortically projecting neuronal populations.

References

1. Masset, Ott, Lak, *et al.*, 2020, *Cell* 182(1):112–126
2. Lagler, Ozdemir, Lagoun, *et al.*, 2016, *Neuron* 91(6):1390–1401, 10.1016/j.neuron.2016.08.010

ENCODING AND SUPRESSION OF DISTRACTING SALIENT STIMULI IN THE PREFRONTAL AND PARIETAL CORTICES

Alexandra Antoniadou[1,*], *Panagiotis Sapountzis*[1], *Georgia G. Gregoriou*[1,2]

[1] Foundation for Research and Technology-Hellas (FORTH), Heraklion, Greece
[2] University of Crete, Faculty of Medicine, Heraklion, Greece
[*] a.antoniadou16@gmail.com

Our ability to focus on behaviorally relevant information is highly dependent on our capacity to ignore distracting, irrelevant stimuli that capture attention by virtue of their physical properties. Previous physiological studies have found that visual salience is represented in several brain areas, including the parietal and prefrontal cortices. Specifically, the lateral intraparietal area (LIP) has been described to elicit stronger responses to salient compared to non-salient stimuli, especially when the salient stimulus is behaviorally relevant. On the other hand, regions in the prefrontal cortex, such as the frontal eye field (FEF), play a key role in the voluntary allocation of visual attention by selecting behaviorally relevant stimuli while at the same time preventing distraction through suppression mechanisms. Although neural correlates of bottom-up and top-down signals have been reported in both the prefrontal and parietal cortices, their distinct contributions to the encoding and suppression of salient stimuli remains unclear.

To address these questions, we performed simultaneous extracellular recordings in area LIP and the FEF of two macaque monkeys performing a visual search task with unconstrained eye movements in the presence or absence of a salient color singleton distractor that was never the target. We examined whether and how competition between the representation of a salient, but behaviorally irrelevant stimulus and its task-relevant suppression is reflected in the activity of FEF and LIP neuronal populations.

We found that a neuronal early firing rate enhancement, as well as a later suppression of a salient distractor was more pronounced in the FEF compared to LIP. However, when choosing sub-populations of selective neurons in the two areas, the relative timing of the early enhancement and late suppression effects were not statistically different between the two regions. These results reaffirm the critical role of prefrontal and parietal cortices in the encoding and suppression of salient distractors, yet suggest a more prominent role of FEF in the representation and suppression of salient information.

Acknowledgments

Work was supported by the Hellenic Foundation for Research and Innovation (HFRI) and the General Secretariat for Research and Technology (GSRT), under grant agreement No 1199.

MODELING PLANAR TRAVELING WAVES PROPAGATING ALONG SPECIFIC DIRECTIONS IN THE MOTOR CORTEX

Ludovica Bachschmid-Romano[1], *Nicholas G. Hatsopoulos*[2], *Nicolas Brunel*[1,3]

[1] Department of Neurobiology, Duke University, Durham, NC, USA
[2] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[3] Department of Physics, Duke University, Durham, NC, USA
[*] ludovica.bachschmid.romano@duke.edu

LFP oscillations in the beta range are known to propagate as traveling waves in the motor cortex of nonhuman primates during movement preparation. In the upper limb area of motor cortex, they have been shown to predominantly take the form of planar waves propagating in the rostro-caudal direction and recent studies have suggested their potential functional interplay with sequential spatiotemporal patterns of excitability involved in movement-initiation, also propagating along the rostro-caudal axis [1].

Here, we investigate the mechanistic origin of cortical traveling waves [2] by using a spatially-extended leaky integrate and fire model to show that LFP oscillations spontaneously propagate in space if the probability of connection decays as a function of the distance between the neurons. Our model reproduces salient features of multielectrode recordings from the primary motor cortex of monkeys during a instructed-delay, reaching task, such as the asynchronous irregular firing dynamics, the population rate dynamics, the typical LFP autocorrelation function, and the LFPs cross-correlation profile as a function of the distance between channels. While a model with isotropic connectivity produces waves that propagate either as planar or radial waves in any direction, after introducing anisotropy in the connectivity we observe predominantly planar waves traveling along a specific direction. Moreover, the zero-lag cross-correlations of LFPs measured from recordings depend not only on the distance between the respective channels on the array, but also on the direction on the cortical sheet along which the distance is computed, supporting our hypothesis that a specific anisotropic pattern of synaptic connectivity underlies motor cortical waves propagating in the rostro-caudal direction, that are a predominant feature of motor preparatory activity.

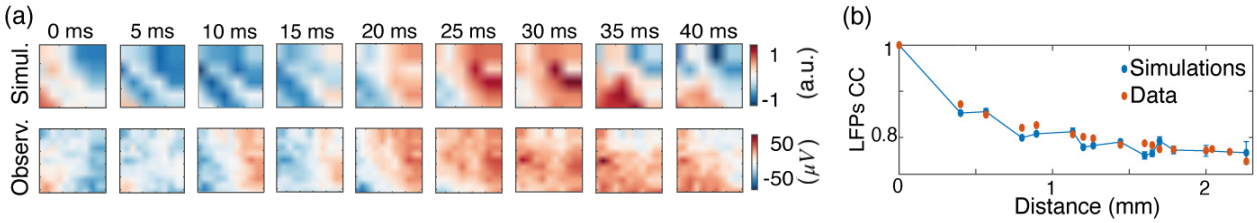


Figure 1. (**a**) LFPs oscillations propagating as traveling waves. Upper panel: LFP amplitude from simulations. Bottom panel: LFP amplitude from recordings. (**b**) Zero-lag cross-correlation between pairs of LFP signals as a function of the distance between the channels.

Acknowledgments

This work has been supported by NIH R01NS104898.

References

1. Balasubramanian, *et al.*, 2020, *Neuron* 106(3):526–536
2. Davis, *et al.*, 2021, *Nat. Comm.* 12(1):1–16

CONNECTIVITY MAPS OF CORTICAL CELLS IN PETASCALE NEURAL CIRCUIT RECONSTRUCTION

J. Alexander Bae[1,*], *Sven Dorkenwald*[1], *Casey M. Schneider-Mizell*[2], *Thomas Macrina*[1], *Shang Mu*[1], *Szi-chieh Yu*[1], *MICrONS Consortium*[1–3], *Jacob Reimer*[3], *Andreas S. Tolias*[3], *R. Clay Reid*[2], *Nuno Macarico da Costa*[2], *Forrest Collman*[2], *H. Sebastian Seung*[1]

[1] Princeton University, Princeton, NJ, USA
[2] Allen Institute for Brain Science, Seattle, WA, USA
[3] Baylor College of Medicine, Houston, Texas, USA
[*] jabae@snu.ac.kr

3D electron microscopy (EM) has set the standard for complete and accurate maps of synaptic connectivity in invertebrate nervous systems. However, 3D EM has suffered from truncation problems when applied for larger mammalian brains. We recently released an automated reconstruction of a cubic millimeter of mouse visual cortex (microns-explorer.org/cortical-mm3), which is large enough to encompass entire dendritic arbors. Thus, after proofreading the cell's axon, we demonstrate our reconstruction can be used to generate a complete spatial map of a cell's probability of synapsing onto target cells in all layers of cortex for cells in primary visual cortex (V1) and higher visual areas (HVA) for both excitatory and inhibitory targets.

Our maps of connection probability between V1 pyramidal cells (PyCs) show L2/3 PyCs target L2/3 and L5 PyCs (Figure 1), consistent with previous optophysiological maps obtained in mouse V1. Notable connectivity from L2/3 to L5 in our excitatory V1 maps corresponds to part of the canonical L4 to L2/3 to L5 pathway reported in mammalian V1 (Figure 1). From the inhibitory connection probability map, it shows L2/3 PyCs target inhibitory cells in L2/3, L4, and L5. Also, the peak value for intralaminar connection probability of PyCs onto inhibitory targets exceed that of PyCs onto PyCs, consistent with previous reports for rodent cortex. These findings validate the proofread reconstruction is accurate and we believe the connectivity maps could aid to understand how neurons interact in the visual cortex.

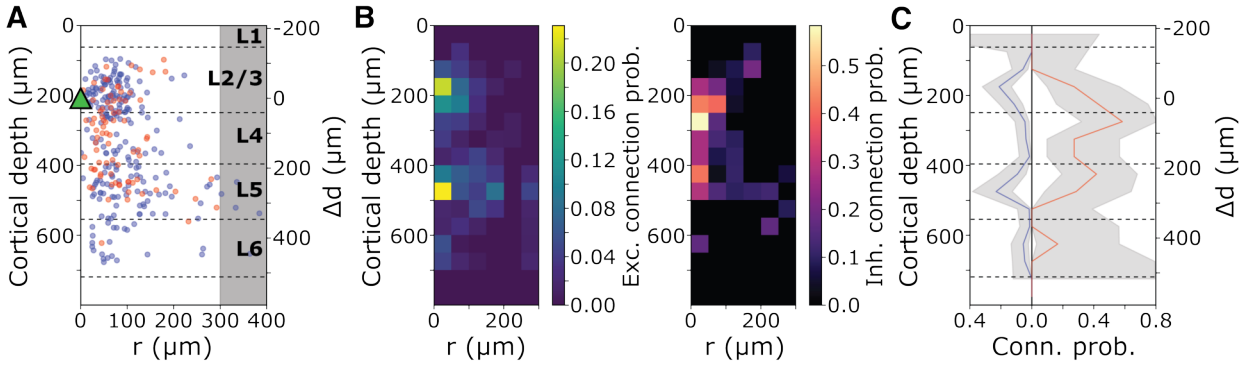


Figure 1. Connectivity maps of L2/3 pyramidal cells in V1. (**A**) Soma locations of excitatory (exc, blue) and inhibitory targets (inh, red) of an example cell (dash: layer boundaries). Right vertical axis indicates relative depth (Δd). (**B**) Exc (left) and inh connection probability map (right). (**C**) Local exc and inh connection probability (shade: 95% confidence interval).

EFFICIENT TASK REPRESENTATIONS FOR HABITUAL AND MODEL-BASED BEHAVIOUR

Severin Berger[*], *Christian Machens*

Champalimaud Research, Champalimaud Foundation, Lisbon, Portugal
[*] severin.berger@neuro.fchampalimaud.org

Higher-order brain activity can be quite complex, switching between fast, stimulus- or motor-driven dynamics, and slower, rising and falling persistent activity. With the advance of high-throughput neuronal recording techniques, we are now getting an increasingly detailed portrait of such activity motifs on a population level, yet how they precisely relate to the task at hand, or indeed, how we can understand their contribution to higher-order brain function, is often unclear.

Many of these activity motifs can be successfully modelled by recurrent neural networks (RNNs) that are trained on specific tasks [1,2]. 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 insights into both the reasons underlying the similarity as well as the rationale of the modelled motifs.

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 and making the learning problem well-posed.

We showcase this approach on a classical working memory task [3]. Formally, we parameterize HA and MBA representations with switching linear dynamical systems regularized by an information bottleneck [4], 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.

References

1. Barak, 2017, *Curr Opin Neurobiol*, 46:1–6, 10.1016/j.conb.2017.06.003
2. Mante, Sussillo, Shenoy, Newsome, 2013, *Nature*, 503(7474):78–84, 10.1038/nature12742
3. Romo, Brody, Hernández, Lemus, 1999, *Nature*, 399(6735):470–473, 10.1038/20939
4. Tishby, Pereira, Bialek, 2000, ArXiv, 10.1108/eb040537

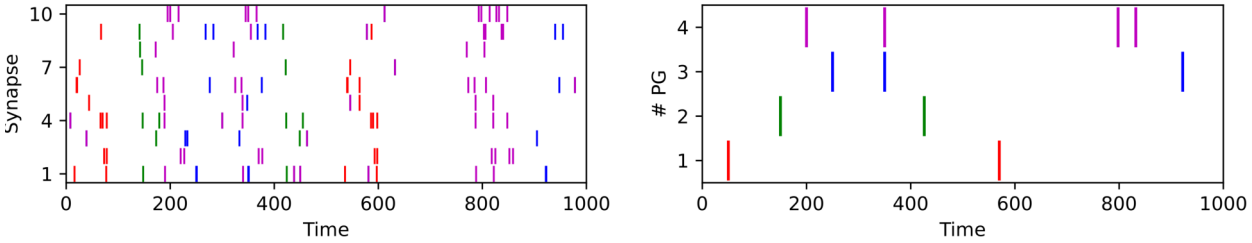
DECODING SPIKING MOTIFS USING NEURONS WITH HETEROSYNAPTIC DELAYS

Camille Besnainou[1], *Antoine Grimaldi*[1], *Hugo J. Ladret*[1,2] *Laurent U. Perrinet*[1,*]

[1] Institut des Neurosciences de la Timone, CNRS and Aix-Marseille Université, Marseille, France
[2] School of Optometry, University of Montreal, Montreal, Canada
[*] laurent.perrinet@univ-amu.fr

The response of a biological neuron depends largely on the precise timing of presynaptic spikes that reach the basal dendritic tree. However, most neuronal models do not take advantage of this minute temporal dimension, especially in exploiting the variety of synaptic delays on the dendritic tree. A notable exception is the polychronization model [1], a recurrent model of spiking neurons including fixed and random heterosynaptic delays and in which the weights are learned using Spike-Time Dependent Plasticity. The output raster plot displays repeated activations of prototypical spiking motifs called *polychronous groups* (PGs). Importantly, these motifs seem to be highly relevant in experimental neuroscience (see for instance [2]). Here, by extending the model of [3], we develop a spiking neural network model for the efficient detection of PGs: By defining the generation of the raster plot as a probabilistic combination of PGs, we build and train the network in order to optimize the inversion of this generative model.

A first result is to show in synthetic data the efficiency of such a scheme in detecting different PGs occurring at specific times. The representational capacity of the PGs is particularly high compared to traditional models of neuronal encoding using spiking frequency like that of [3]. Our second result is to propose a novel method for learning PGs in raster plots in a self-supervised manner. This was validated on synthetic data and we show results of this method when applied to neuronal data acquired in the visual cortex. Of particular relevance is the fact that the learned weights provide with an explainable factor between neural data and the occurrence of specific PGs.



Observed raster plot Raster plot of PGs

An example synthetic raster plot is generated in **(A)** as the combination of PGs whose timing and identity are drawn as a raster plot in **(B)**, here a superposition of 4 PGs projected on the synaptic space of 10 neurons and at an average rate of 3 Hz during 1000 ms. Observing spikes from A, the model decodes the identity and timing of PGs in B, which in turn we may use to color spikes in A with respect to that of the PG that most likely generated them.

References

1. Izhikevich, 2006, *Neural Comput.* 18:245–282, 10.1162/089976606775093882
2. Ikegaya, Aaron, Cossart, *et al.*, 2004, *Science* 32(31), 10.1126/science.1093173
3. Berens, Ecker, Cotton, *et al.*, 2012, *J. Neurosci.* 32(31), 10.1523/jneurosci.1335-12.2012

RIPPLES IN MACAQUE ENTORHINAL CORTEX DURING FIXATION AND IMAGE VIEWING

Concetta Brusco[1,*], *Nathaniel Killian*[1,†], *Elizabeth Buffalo*[2,†]

[1] Dept. of Neurological Surgery, Albert Einstein College of Medicine, New York, USA
[2] Dept. of Physiology & Biophysics, University of Washington, Seattle, USA
[†] equal contribution
[*] concetta.brusco@einsteinmed.edu

Ripples are highly synchronized bursts of activity that originate in hippocampal neural ensembles and spread throughout cortex. They are important for memory consolidation and have been found mainly during resting states such as non-REM sleep. Here we report robust ripples in macaque entorhinal cortex (EC) during an image viewing task.

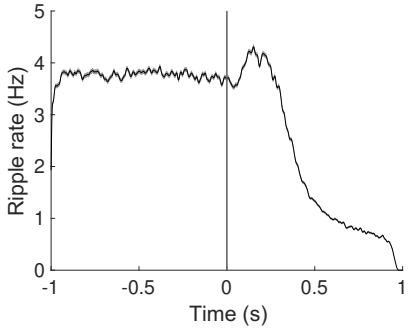


Figure 1. Analysis of ripple rate during fixation and image viewing. Fixation is the 1 second preceding image onset (line at $t = 0$); $n = 247$ channels, 400 trials per channel.

Local field potentials (LFPs) were recorded in the EC of two rhesus macaques using a 12-site linear probe (AXIAL array) while they performed the Visual Preferential Looking Task [1]. The LFPs were transformed to current source density (CSD), then candidate ripple events were identified using a method [1, 2] that parses the CSD into bouts of activity having significantly higher power for at least 5 cycles at frequencies of interest, here, 90–200 Hz. Non-negative matrix factorization was then performed to identify bouts with a unimodal spectral distribution [3]. Bouts that could not be estimated well with 2 factors (signal-to-noise ratio less than 2.5) were eliminated.

The above process identified ripples at a mean rate of 3.71 ripples per electrode per second. The mean ripple duration was 58.9 ± 28.7 ms (mean, std.).

Overall, the ripple rate was higher during the fixation period compared to the image viewing period (Fig. 1, $p < 0.001$), consistent with previous reports of more ripples during off-line or anticipatory phases, potentially consolidating recently viewed images.

We also found a higher ripple rate during novel image viewing compared to repeat images, as well as in strongly encoded images versus weakly encoded ones (defined by the relative viewing times of the novel versus repeat image). However, in order to exclude the possibility of local increases in spiking activity being responsible for these differences, we are currently investigating single unit activity. This will also lead to insight into how individual neurons in the EC contribute to ripples.

References

1. Killian, Jutras, Buffalo, 2012, *Nature* 491(7426):761–4, 10.1038/nature11587
2. Ekstrom, Caplan, Ho, *et al.*, 2005, *Hippocampus* 15(7):881–9, 10.1002/hipo.20109
3. Logothetis, *et al.*, 2012, *Nature* 491(7425):547–53, 10.1038/nature11618

DIGITAL TWIN REVEALS COMBINATORIAL CODE OF NON-LINEAR COMPUTATIONS IN THE MOUSE PRIMARY VISUAL CORTEX

Max F. Burg[1,2,*], *Ivan Ustyuzhaninov*[2], *Santiago A. Cadena*[2], *Jiakun Fu*[3], *Taliah Muhammad*[3], *Kayla Ponder*[3], *Emmanouil Froudarakis*[3], *Zhiwei Ding*[3], *Matthias Bethge*[2], *Andreas S. Tolias*[3], *Alexander S. Ecker*[1]

[1] University of Göttingen, Göttingen, Germany
[2] University of Tübingen, Tübingen, Germany
[3] Baylor College of Medicine, Houston, TX, USA
[*] max.burg@uni-goettingen.de

More than a dozen excitatory cell types have been identified in mouse primary visual cortex (V1) based on transcriptomic, morphological and *in vitro* electrophysiological features [1,2]. However, the functional landscape with respect to neurons responses to visual stimuli is currently unknown. We address two main questions: (*i*) are there distinct discrete functional cell types, each of which implements a specific computation, or rather a continuum of function; and (*ii*) how are previously described nonlinear effects (*e.g.*, phase invariance, surround suppression, etc.) organised at the population level: are they strongly correlated or are they present independently of each other?

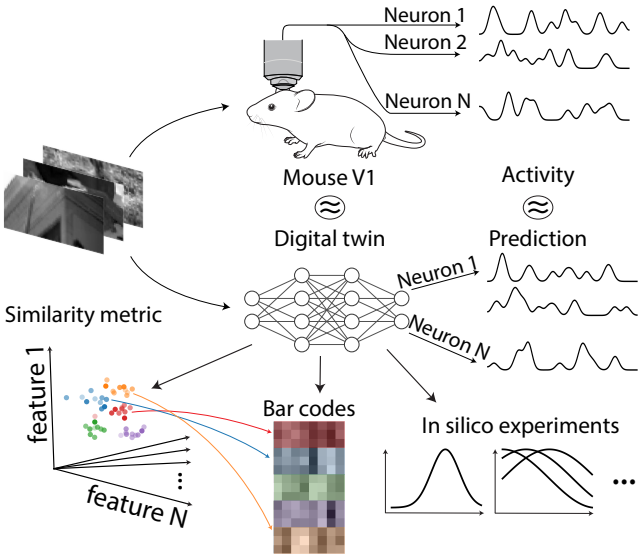


Figure 1. Digital twin of mouse V1 provides a bar code for neurons used for functional clustering and large scale *in silico* experiments.

We combined large-scale population recordings in response to natural stimuli and high-performing predictive deep neural network models to build a digital twin of mouse V1. Our model provides low-dimensional bar codes of neuronal functions which allowed us insight into the above questions. (*i*) We found a non-uniform continuum of functions with a few dozen high-density modes (common neural functions). (*ii*) Classical non-linear properties are expressed independently of each other. For example, knowing the extent of a neuron's non-linearity along the simple-complex cell axis does not provide much information about its degree of surround suppression or cross-orientation inhibition.

Acknowledgments

Supported by BMBF grant FKZ 01IS18039A, DFG grant EC 479/1–1, SFB 1233 (EXC 2064/1, project number 390727645); the National Eye Institute of the National Institutes of Health grants U19MH114830, R01MH109556, P30EY002520, and IARPA contract number D16PC00003.

References

1. Scala, Kobak, Bernabucci, *et al.*, 2021, *Nature* 598, 144–150
2. Gouwens, Sorensen, Baftizadeh, *et al.*, 2020, *Cell* 183(4), 935–953

ANTERIOR CINGULATE NEURONS EVALUATE PERIPHERAL VISION TO GUIDE INFORMATION SAMPLING AND CHOICE

James L Butler[1,*], *Timothy H. Muller*[1], *Sebastijan Veselic*[1], *W. M. Nishantha Malalasekera*[1], *Laurence T. Hunt*[2], *Timothy E. J. Behrens*[2,3], *Steven W. Kennerley*[1]

[1] University College London, London, UK
[2] University of Oxford, Oxford, UK
[3] Sainsbury Wellcome Centre for Neural Circuits and Behaviour, London, UK
[*] james.butler@ucl.ac.uk

We use our eyes to assess the value of objects around us and carefully fixate options that we are about to choose. Neurons in the prefrontal cortex reliably encode the value of fixated options, which is essential for decision making. Yet as a decision unfolds, it remains unclear how prefrontal regions determine which option should be fixated next. Here we show that anterior cingulate cortex (ACC) encodes the value of options in the periphery to guide subsequent fixations during economic choice.

In an economic decision-making task involving four simultaneously presented cues, we found rhesus macaques evaluated cues using their peripheral vision. This served two distinct purposes: subjects were more likely to fixate valuable peripheral cues, and more likely to choose valuable options even if the cues were never fixated. The brain must therefore have been evaluating cues in the peripheral vision (in addition to the fixated cues) to enable this efficient behavior.

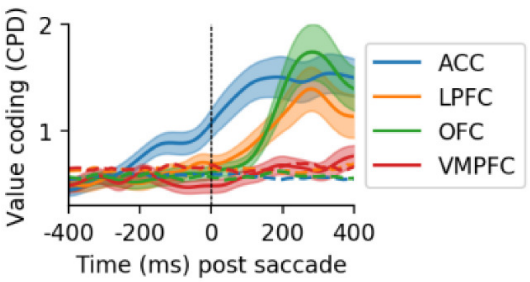


Figure 1. While ACC, LPFC, and OFC neural ensembles all encoded value of the cue after it was fixated, the ACC neural ensemble started encoding the cue's value 200 ms before the saccade occurred.

Neural ensembles recorded from ACC, orbitofrontal cortex, dorsolateral prefrontal cortex, and ventromedial prefrontal cortex all encoded cue value post-fixation. ACC was unique, however, in also encoding the value of cues before fixation (Figure 1), and even cues that were never fixated. Furthermore, this pre-saccadic value encoding by ACC predicted which cue was next fixated during the decision process. ACC therefore conducts simultaneous processing of peripheral information to guide information sampling and choice during decision making.

Acknowledgments

SV was supported by Leverhulme award DS-2017–026. WMNM was supported by funding from the Astor Foundation, Rosetrees Trust and Middlesex Hospital Medical School General Charitable Trust. LTH was supported by a Henry Wellcome Fellowship (098830/Z/12/Z) and Henry Dale Fellowship (208789/Z/17/Z) from the Wellcome Trust. TEJB was supported by a Wellcome Trust Senior Research Fellowship (104765/Z/14/Z) and a Wellcome Trust Principal Research Fellowship (219525/Z/19/Z). SWK was supported by Wellcome Trust Investigator Awards (096689/Z/11/Z and 220296/Z/20/Z).

ADAPTIVE TRAITS IN THE DROSOPHILA MUSHROOM BODY

Sophie J. C. Caron[1,*], *Kaitlyn E. Ellis*[1], *Hayley Smihula*[1], *Ishani Ganguli*[2], *Ashok Litwin-Kumar*[2], *Thomas Auer*[3], *Richard Benton*[3]

[1] School of Biological Sciences, University of Utah, Salt Lake City, USA
[2] Center for Theoretical Neuroscience, Columbia University, New York, USA
[3] Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland
[*] sophie.caron@utah.edu

How the brain adapts in response to changes in the environment remains largely unknown. Thus far, adaptive traits have been primarily identified in sensory systems, suggesting that sensory neurons might be more malleable to evolutionary pressures than neurons embedded in higher brain centers. In Drosophila, comparative studies of closely related species that live in drastically different chemosensory ecology revealed that olfactory sensory neurons can rapidly evolve new detection capabilities. For instance, the obligate noni specialist Drosophila sechellia, a close relative of the generalists *Drosophila melanogaster* and Drosophila simulans, is equipped with olfactory sensory neurons finely tuned to noni volatiles [1]. In this presentation, I will summarize our recent findings showing that adaptive traits can be found in these three species downstream of the olfactory sensory neurons.

We used a neuronal tracing technique to determine how the projection neurons of the olfactory system connect to the Kenyon cell of the mushroom body. We mapped over 2000 projection neuron–Kenyon cell connections in *Drosophila melanogaster*, *Drosophila sechellia* and *Drosophila simulans*. Statistical analyses of these connections revealed global architectural features that are species-specific. Specifically, we found that the projection neurons activated by noni volatiles connect more frequently to Kenyon cells in *Drosophila sechellia* than they do in the generalist species. We also found that this increased connectivity results from a larger number of projection neurons as well as a larger number of pre-synaptic sites formed by these neurons. Finally, we have evidence suggesting that increased connectivity in the mushroom body leads to differences in learning abilities.

Altogether, this study shows that higher brain centers are just as malleable to evolutionary pressures as sensory systems, suggesting that the brain might adapt to novel sensory environments through cellular changes distributed along neuronal circuits.

Acknowledgments

This work has been supported by the National Institute of Health (R01NS106018, R01NS107970) and the National Science Foundation (CAREER Award 2042397).

Reference

1. Auer, Khallaf, Silbering, *et al.*, 2020, *Nature* 579:402–408.

IMPROVING DEEP LEARNING PERFORMANCE USING BIOLOGICAL DENDRITES

Spyridon Chavlis[*], *Panayiota Poirazi*

Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[*]schavlis@imbb.forth.gr

Over the past years, deep learning (DL) algorithms have successfully solved challenging tasks. The backbone of almost all DL architectures are the so-called artificial neural networks (ANNs) and are inspired by biological neuronal networks in our brains. Typical ANNs, consisting of numerous, densely connected nodes that mimic neuronal somata, ignore the nonlinear operations performed by biological dendrites. Biological neuronal dendrites can interact nonlinearly and drive localized regenerative events [1], and these spikes allow the dendrites to perform an array of complex computational tasks [2]. The lack of these critical functions in ANNs comprises their flexibility and energy efficiency [3].

We designed a novel architecture whereby each node consists of one soma with several dendrites. Dendritic nodes are furnished with nonlinear activation functions, the exact form of which could vary across layers. We train the dendritic ANN against benchmark (original and noisy) datasets. Then we compare it to a traditional ANN consisting of dense (all-to-all) layers and the same number of trainable parameters.

Our dendritic ANN outperforms the conventional ANN on all tested classification tasks. At the same time, it achieves a performance very close to the state-of-the-art using an order of magnitude fewer trainable parameters than these DL methods. Our work shows that biological dendrites empower ANNs by enhancing their information processing power and storage capacity.

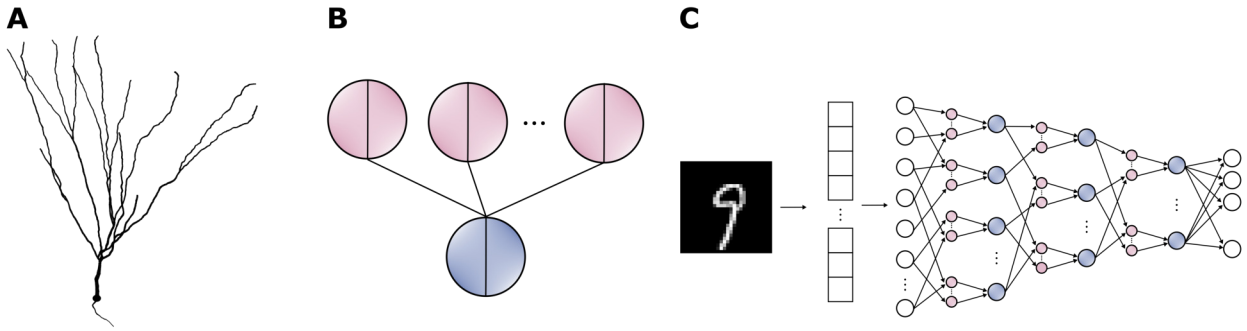


Figure 1. (**A**) A biological neuron. (**B**) Neuronal model with dendrites. (**C**) Dendritic ANN.

Acknowledgments

Supported by NIH grant 1R01MH124867-01.

References

1. Stuart, Spruston, 2015, *Nat. Neurosci.* 18(12):1713–1721, 10.1038/nn.4157
2. Poirazi, Papoutsi, 2020, *Nat. Rev. Neurosci.* 21:303–321, 10.1038/s41583-020-0301-7
3. Chavlis, Poirazi, 2021, *Curr. Opin. Neurobiol.* 70:1–10, 10.1016/j.conb.2021.04.007

DEVELOPMENT OF A CONTROL SYSTEM FOR A NEXT GENERATION HIGH-DENSITY, WIRELESS, BIDIRECTIONAL BRAIN-COMPUTER INTERFACE

R. James Cotton[1,2,*], *Guy Eichler*[3], *Nanyu Zeng*[3], *Taesung Jung*[3], *Mohit Sharma*[3], *Andreas S. Tolias*[4–6], *Ken Shepard*[3]

[1] Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, USA
[2] Shirley Ryan AbilityLab, Chicago, USA
[3] Department of Electrical Engineering, Columbia University, New York City, New York, USA
[4] Center for Neuroscience and Artificial Intelligence, Baylor College of Medicine, Houston, USA
[5] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[6] Department of Electrical and Computer Engineering, Rice University, Houston, TX, USA
[*] rcotton@sralab.org

Brain computer interface (BCI) technologies are advancing rapidly, with cutting edge systems providing thousands of channels that can record and stimulate. For translational applications, a key endpoint, there is a need to make these systems fully portable. Here we describe the development of an embedded, standalone control system for a next generation, wireless, implantable, bidirectional, 65k channel Bioelectric Interfacing to Sensory Cortex (BISC) chip.

The control system is implemented using a Xilinx FPGA with code distributed between an embedded Linux OS and programmable logic (PL). The PL handles the significant data bandwidth and tight latency requirements, ultimately driving the RF frontend to control and receive from the BISC chip wirelessly. The code is structured around a hierarchy of abstractions that start from the low-level BISC opcodes, to a set of register mapped addresses in the PL for higher level functions, such as recording or configuring stimulation. When streaming, the PL handles packetization of the data with accompanying synchronization signals as well as padding any data with invalid error correction codes before streaming it to the application layer via double buffered DMA.

We use PYNQ to provide a higher-level end-user API in python for the Linux layer to access the PL. This allows easy implemention of standalone recording or stimulation applications as experimental needs dictate, such as a fully mobile situation. In addition, we expose an interface to integrate into existing experimental systems in order to enable preclinical evaluation and neuroscience experiments. A server application provides external access to the system via a RESTful API, for example with an endpoint to initiate network streaming of data from a region of the BISC array. A final benefit of this framework is that the BISC chip can also be emulated in the PL, facilitating software development and system integration.

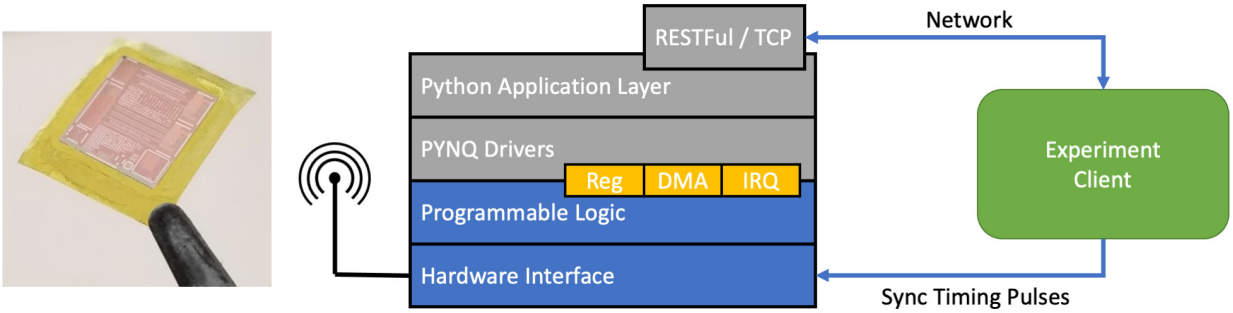


Figure 1. Schematic of control system software stack (middle) connected to the BISC chip (left) and experimental software (right).

CONFIDENTLY DECODING MULTIPLE SPATIAL ENVIRONMENTS IN HIPPOCAMPAL REPLAY

Eric L. Denovellis[1–3], *Loren M. Frank*[1–3,*]

[1] Howard Hughes Medical Institute (HHMI), UCSF, San Francisco, USA
[2] Departments of Physiology and Psychiatry, UCSF, San Francisco, USA
[3] Kavli Institute for Fundamental Neuroscience, UCSF, San Francisco, USA
[*] loren@phy.ucsf.edu

Hippocampal replay, a phenomenon whereby cells in the hippocampus appear to recapitulate previously experienced spatial trajectories in a given environment, is thought to be crucial for the storage and consolidation of spatial memories. This phenomenon is commonly studied with respect to a single spatial environment. For example, studies have shown that sleeping rats can replay trajectories of the spatial environment they previously experienced and awake rats can replay spatial trajectories of the current spatial environment they are in. However, an important study by Karlsson and Frank [1] established that awake rats can replay both the current spatial environment they are in as well as a previously experienced environment.

This means that care is needed in interpreting replay, as it may represent a replay of the current environment or another environment the animal has experienced. It is possible that replays that experimenters previously thought were not interpretable are actually coherent replays of some other experience. More broadly, experiences often occur across many different environments, and how the hippocampus might multiplex the replay of those different experiences remains unknown.

Therefore, in order to accurately characterize hippocampal replay, it is important to establish decoding methods that take into account multiple spatial environments and tell us with statistical confidence which environment the animal is replaying as well as the trajectory represented in that environment. Here, we show how our previous work on hybrid point process state space models [2], which use discrete and continuous latent states, can be extended to construct such a model by leveraging the hippocampal cell spatial rate maps in each environment as well as our prior knowledge about the spatial structure of each environment. This model is flexible, in that it can decode activity patterns associated with an arbitrary number of environments.

We show on simulated data how this model can turn noisy spatial trajectories decodings based on considering only one environment, into interpretable trajectories in another environment. We then show on real data that we can decode three environments when the animal is asleep as well as replicate the result of Karlsson and Frank of replaying two environments when the animal is awake. We believe this state space model will be important for understanding how the brain's storage and consolidation mechanisms work in the context of more complex, real-world experiences.

Acknowledgments

This work was supported by Simons Foundation Grant 542981 and HHMI.

References

1. Karlsson, Frank, 2009, *Nat. Neurosci.* 12(7):913–918, 10.1038/nn.2344
2. Denovellis, Gillespie, Coulter, *et al.*, 2021, *eLife* 10:e64505, 10.7554/eLife.6450

FUNCTIONAL CONNECTOMICS OF MOUSE VISUAL CORTEX REVEALS ORGANIZATION OF SYNAPTIC CONNECTIONS

Zhuokun Ding[1,*], *Paul G. Fahey*[1], *Stelios Papadopoulos*[1], *Eric Wang*[1], *Christos Papadopoulos*[1], *Anthony Ramos*[1], *MICrONS Consortium*[1,3,4], *H. Sebastian Seung*[4], *Forrest Collman*[3], *Nuno Macarico da Costa*[3], *R. Clay Reid*[3], *Xaq Pitkow*[1,2], *Edgar Y. Walker*[5,6], *Jacob Reimer*[1], *Andreas S. Tolias*[1,2]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[2] Department of Electrical and Computer Engineering, Rice University, Houston, TX, USA
[3] Allen Institute for Brain Science, Seattle, WA, USA
[4] Princeton Neuroscience Institute, Princeton University, Princeton, NJ, USA
[5] Department of Physiology and Biophysics, University of Washington, Seattle, WA, USA
[6] UW Computational Neuroscience Center, University of Washington, Seattle, WA, USA
[*] zhuokund@bcm.edu

The neocortex is a densely-connected network of neurons, endowing mammals with astonishing perceptual, cognitive, and motor capabilities. Deciphering how neural connectivity governs function is a prerequisite towards a circuit level mechanistic dissection of behavior. Previous studies found *like-to-like* connectivity [1, 2], where neurons with similar tuning preferentially connect to each other. However, existing investigations of the neocortex have been limited to small populations of dozens of neurons restricted to small volumes in the primary visual cortex (V1) due to technical challenges inherent to the minute anatomical scale of tracing connections, the massive network complexity, and integration of functional and microconnectivity measurements. To unravel the structure-function wiring principles across brain areas, layers, and cell types, a much larger and more comprehensive dataset is required.

To this end, we analyzed a subset of the MICrONS multi-area functional connectomics dataset, which covers over 10,000 synaptic connections among 6000 neurons from visual areas V1, RL and LM, spanning layer 2 through layer 5. In agreement with prior V1 studies [1,2], we found that pyramidal neurons selectively formed synapses with neurons tuned to similar orientation. However, this like-to-like orientation tuning based rule did not generalize to other connections across visual areas and between cortical layers.

To explore the relationship between synaptic connections and more complex tuning features, we used deep learning models to accurately predict the responses of neurons to arbitrary visual stimuli and extract functional barcodes to characterize the high dimensional non-linear tuning of neurons. These barcodes predicted the wiring of excitatory neurons within and across visual cortical areas, including feedback connections, significantly better than wiring predictions from response correlations and orientation tuning. Our results suggest that the cell-type specific rules that wire cortical circuits incorporate non-linear pairwise functional relationships beyond signal correlations as Hebb's rule "cells that fire together, wire together" predicts.

Acknowledgments

Supported by the Intelligence Advanced Research Projects Activity (IARPA) via Department of Interior/Interior Business Center (DoI/IBC) contract number D16PC00003.

References

1. Ko, Hofer, Pichler, *et al.*, 2011, *Nature* 473(7345):87–91, 10.1038/nature09880
2. Lee, Bonin, Reed, *et al.*, 2016, *Nature* 532(7599):370–374, 10.1038/nature17192

THE ROLE OF DYNAMIC INHIBITORY SYNAPSES FOR CODING SURPRISE IN THE RETINA

Simone Ebert[1,*], *Thomas Buffet*[2], *Semihchan Sermet*[2], *Olivier Marre*[2], *Bruno Cessac*[1]

[1] Biovision and Neuromod Insitute, Université Côte d'Azur, Sophia Antipolis, France
[2] Institut de la Vision, Sorbonne Université, Paris, France
[*] simone.ebert@inria.fr

The retina is the first stage of visual processing, it compresses relevant visual information before sending it to the brain. To this end, a long standing hypothesis is that retinal ganglion cells, the retinal output, do not signal the visual scene per se, but rather surprising events, eg. mismatches between observation and expectation formed by previous inputs [1]. A striking example of this is the Omitted Stimulus Response (OSR) [2]: when a regular sequence of flashes suddenly ends, the retina emits a large response signaling the missing stimulus, and the latency of this response scales with the period of the flash sequence (Figure 1). The mechanisms behind this behavior remain unclear so far. Here we show that a retinal circuit can generate this OSR by an interaction between excitatory and inhibitory neurons, where dynamical synapses play a key role in shaping the surprise signal.

The retina processes information via an excitatory feed-forward pathway that is substantially modulated by inhibitory interneurons such as amacrine cells. Combining electrophysiological experiments and biophysical modeling, we show that depressing inhibitory synapses from amacrine to ganglion cells can explain the OSR with its predictive latency tuning. By recording the OSR with a multi-electrode array while blocking specific types of inhibitory amacrine cells with pharmacological compounds, we show that inhibitory transmission via amacrine cells is necessary to maintain the predictive timing of the OSR (Figure 1).

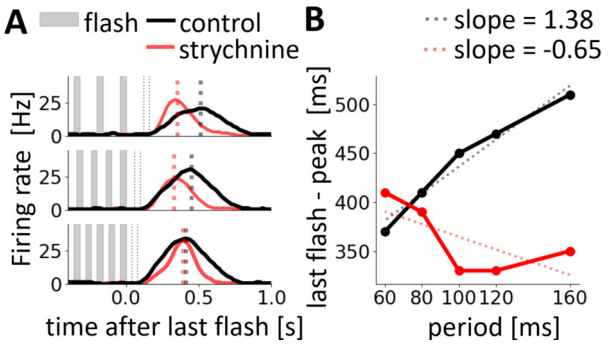


Figure 1. **A**. Experimental recording of the OSR in control conditions (black) and blocked anmacrine transmission using the glycine receptor antagonist strychnine (red). The peak time-point (dotted lines) changes significantly. **B**. Peak time-point increases linearly with stimulus period in control conditions but not without amacrine inhibition.

We propose a network model where inhibitory amacrine cells impact ganglion cells through depressing synapses, where the strength of inhibition adapts to previous stimulation via short-term plasticity and thereby determines the timing of the response. We then use this model to explore more generally the potential effect of short-term plasticity on retinal responses.

Acknowledgments

This work has been funded by the Neuromod Institute, Université Côte d'Azur.

References

1. Hosoya, Baccus, Meister, 2005, *Nature*, 436(7047):71–77, 10.1038/nature03689
2. Schwartz, Harris, Berry, *et al.*, 2007, *Nat. Neurosci.*, 10(5):552–554, 10.1038/nn1887

CELL ASSEMBLIES AND CALCIUM-BASED PLASTICITY IN A DETAILED, LARGE-SCALE CORTICAL MODEL IN IN-VIVO-LIKE STATE

András Ecker[*], *Daniela Egas Santander, Michael W. Reimann*

Blue Brain Project, École Polytechnique Fédérale de Lausanne, Geneva, Switzerland
[*] andras.ecker@epfl.ch

The rapid rise in experimental techniques have enabled simultaneous recordings of thousands of neurons. In particular, these techniques have made it possible to study the formation of functional cell assemblies. However, characterizing the evolution of synaptic connections and their plasticity within such assemblies remains challenging. To surmount this challenge, we developed a complementary, simulation-based approach of a biologically detailed cortical network model (an improved version of the Markram model [1] with 212,000 neurons) equipped with a calcium-based, functional plasticity of the synapses between excitatory cells.

To this end, we detected functional cell assemblies from the stimulus-evoked spiking activity of 185,000 excitatory cells with a combination of recently published methods [2,3]. Significant time bins (20 ms binning) are detected and clustered based on their cosine similarity as described by Carillo-Reid and colleagues [2]. Neurons firing in these time bins are grouped to form cell assemblies with a pairwise correlation-based method [3]. Then, using algebraic topology (counting directed simplices [4]) we show, that their connectivity is enriched with structural circuit motifs, thus link their underlying structure to the assemblies' co-firing function.

By analyzing the evolution of the 320 million plastic synapses over 10 minutes of biological time, we found that while the overall strength increased by 15 pS, a higher number of synapses (19.5%) depressed and 66.5% of the synapses remained unchanged. The strong but rare potentiation reorganized the network dynamics, while the more frequent but weaker depression kept in stable without the addition of homeostatic mechanisms. Significantly more synapses potentiated between (temporally ordered) assemblies then within them and depression within assemblies was higher than average, consistent with the experimental observation that stable structures cannot be potentiated further. In summary, we predict a highly organized structural connectivity underlying functional assemblies, small but frequent weakening of these synapses and strengthening the ones that are connecting these assemblies to each other.

References

1. Markram, Muller, Ramaswamy, *et al.*, 2015, *Cell* 163(2):456–492, 10.1016/j.cell.2015.09.029
2. Carillo-Reid, *et al.*, 2015, *J. Neurosci.* 35(23):8813–8828, 10.1523/JNEUROSCI.5214-14.2015
3. Herzog, *et al.*, 2021, *PLoS ONE* 16(7):e0251647, 10.1371/journal.pone.0251647
4. Reimann, Nolte, *et al.*, 2017, *Front. Comput. Neurosci.* 11(48), 10.3389/fncom.2017.00048

A LIGHT CONVOLUTIONAL NEURAL NETWORK TO DECODE NEURAL DYNAMICS OF REACHING MOVEMENTS FROM THE MACAQUE POSTERIOR PARIETAL CORTEX

Matteo Filippini[1,*], *Davide Borra*[2], *Mauro Ursino*[2,3], *Elisa Magosso*[2,3], *Patrizia Fattori*[1,3]

[1] University of Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy
[2] Univ. Bologna, Dept. Elect., Electronic and Inf. Eng. "Guglielmo Marconi", Cesena, Italy
[3] Alma Mater Research Institute for Human-Centered Artificial Intelligence, Bologna, Italy
[*] matteo.filippini7@unibo.it

To convert neural signals into signals suitable for controlling prosthetics or electro myo-stimulation devices, brain-computer interfaces rely on decoding algorithms. Decoders based on neural networks are gaining popularity because they can model the intrinsic non-linearity of the activity of neurons and achieve performance superior to traditional algorithms [1]. In this study we propose a neural decoder based on a convolutional neural network designed to be able to catch the temporal encoding dynamics present in the posterior parietal cortex of macaque [2], while at the same time maintaining a light architecture. For this purpose, we trained two macaques to perform a 3D reach-to-point task toward 9 targets arranged in the monkey's peripersonal space. We recorded 613 neurons across the medial posterior parietal cortex of macaque and the neurons' activity was given as input to a convolutional neural network, whose design was selected by using Bayesian optimization, to classify the 9 spatial positions or reconstruct the trajectories of reaching. We found that our algorithm classified the target reached by the monkeys with accuracies over 80% and faithfully reconstructed the 3D movement trajectory (R-squared around 0.7), outperforming a classic linear algorithm. In addition, the time course of decoding accuracies reflected a sensory to somatomotor transformations happening in the tested reaching brain network. Overall, the present study validated a novel neural decoder that is based on a convolutional neural network and that can both get a better understanding of how the brain dynamically transforms information and, in perspective, find applicability in BCI systems.

Acknowledgments

Supported by Horizon 2020 MAIA G.A. n. 951910.

References

1. Glaser, *et al.*, 2020, *eNeuro* 7(4), 10.1523/ENEURO.0506-19.2020
2. Filippini, *et al.*, 2020, *J. Neural Eng.* 10.1088/1741-2552/aba87e

DEEP LEARNING DIGITAL TWIN MODELS REVEAL CONGRUENT CENTER-SURROUND INTERACTIONS IN MOUSE VISUAL CORTEX

Jiakun Fu[1,*], *Kayla Ponder*[1], *Taliah Muhammad*[1], *Xaq Pitkow*[1], *Alexander S. Ecker*[2], *Andreas S. Tolias*[1]

[1] Baylor College of Medicine, Houston, USA
[2] University of Göttingen, Germany
[*] jiakunf@bcm.edu

A primary role of visual processing is integrating information across space. To this end, center-surround modulation describe changes in neural activity resulting from interactions of stimuli presented in the classical receptive field (RF) with those in the surround. These contextual interactions are hypothesized to play a critical role in perceptual inference. They have been mostly studied in V1 of primates with respect to orientation tuning, where the surround stimuli are configured based on the orientation preference of the RF. Studying center-surround interactions in mice is ideally suited to dissect the circuit level mechanisms of contextual computations. However, recent work has shown that the optimal stimuli for neurons in mouse V1 exhibit complex spatial structures deviating from Gabor-like filters [1]. Moreover, surround modulation probed with orientated stimuli shows non-consistent effects across cells making it hard to extract computational principles in mouse visual cortex [2]. Therefore, orientation tuning alone is not adequate to comprehensively study center-surround interactions and decipher the rules that govern contextual modulation.

To systematically study contextual modulations in mice we used an unbiased data-driven approach. Specifically, we used large-scale functional imaging to build deep learning neural predictive models of the mouse visual cortex. These digital twin models accurately predicted the responses of neurons to contextual spatial interactions in natural images. We adapted the Most Exciting Images (MEIs) optimization method [1] to generate highly excitatory and inhibitory surrounding stimuli, conditioned on optimal stimuli in the center. Using inception loops these stimuli were verified *in vivo*, confirming the predictions of the digital twin models.

Surprisingly, in contrast to studies from macaque V1, the most excitatory surround stimuli were spatially congruent with the MEIs patterns in the center. In contrast, the most inhibitory surround were incongruent with the MEIs. We quantified this perceptual effects showing that the congruent excitatory surround-MEI pair occurred much more frequently in natural image patches than the incongruent inhibitory surround-MEI pair. Our work is the first data-driven approach to study center-surround processing showing that surround stimuli that are congruent with the center enhance the responses of neurons, consistent with the theory of Bayesian inference for cortical computation.

Acknowledgments

This work was supported by IARPA contract D16PC00003, and DARPA contract N66001-19-C-4020.

References

1. Walker, *et al.*, 2019, *Nat. Neurosci.* 592(22):2060–2065, 10.1038/s41593-019-0517-x
2. Samonds, *et al.*, 2017, *J. Neurophysiol.* 118(6):3282–3292, 10.1152/jn.00172.2017

REAL-TIME FEEDBACK CAN PROMOTE TASK-RELEVANT MEMORY REPLAY

Anna K. Gillespie[1,*], *Daniela A. Astudillo Maya*[1], *Eric L. Denovellis*[1], *Sachi Desse*[1], *Uri T. Eden*[3], *Loren M. Frank*[1,2]

[1] Kavli Institute for Fundamental Neuroscience, UCSF, San Francisco, CA, USA
[2] Howard Hughes Medical Institute, San Francisco, CA, USA
[3] Department of Mathematics and Statistics, Boston University, Boston, MA, USA
[*] anna.gillespie@ucsf.edu

The ability to generate representations of past experiences is central to a set of cognitive functions that include memory retrieval and planning. Hippocampal sharp-wave ripple (SWR) events are associated with the time-compressed replay of representations of past experience, and multiple correlative and causal studies have demonstrated that SWRs critically contribute to these cognitive functions. Further, reductions in SWRs have been reported in multiple rodent models of memory impairment. To provide a potentially therapeutic intervention to rescue SWRs in disease states, we developed a neurofeedback paradigm in which real-time detection of SWRs triggers positive reinforcement (food reward) to food-restricted rats. Training in this task paradigm results in an approximately two-fold increase in SWR rate in a task-phase-specific manner. The efficacy of this manipulation demonstrates that subjects can learn to use rapid, salient feedback triggered by spontaneous SWRs to modulate physiologically relevant patterns of hippocampal network activity.

This manipulation takes place in the context of a dynamic spatial memory task, allowing us to ask whether enhancing SWR activity altered replay content or affected task performance. To assess the replay content, we apply a marked point process clusterless decoding algorithm [1] and a state-space movement classifier that captures the spatiotemporal structure of replay [2]. In unmanipulated subjects, we previously observed biases toward replay of past goal locations rather than upcoming trajectories, suggesting that replay serves to store past experience rather than plan future choices [3]. We observe very similar patterns of replay content after neurofeedback training, indicating that only the amount, but not the content, of replay is altered by the paradigm. Further, the increase in replay did not improve performance of the task on a trial-by-trial basis, providing additional evidence that replay does not guide immediately subsequent choices. Future work will assess the impact of promoting SWR activity on long term, rather than short term, behavioral performance and establish whether this approach can rescue SWR and behavioral impairments in disease models.

Acknowledgments

This work has been funded by HHMI, NIH MH105174 to LMF, and Simons Foundation Postdoctoral Fellowship 500639 to AKG.

References

1. Deng, Liu, Karlsson, Frank, Eden, 2016, *J. Neurophysiol.* 116(5):2221–2235
2. Denovellis, Gillespie, Coulter, *et al.*, 2021, *eLife* 10e64505
3. Gillespie, Astudillo Maya, Denovellis, *et al.*, 2021, *Neuron* 109:3149–3163

REPROGRAMMING THE TOPOLOGY OF THE NOCICEPTIVE CIRCUIT IN C. ELEGANS RESHAPES SEXUAL BEHAVIOR

Gal Goldman[*], *Vladyslava Pechuk, Yehuda Salzberg, Meital Oren-Suissa, Elad Schneidman*

Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel
[*] gal.goldman@weizmann.ac.il

How the topology of neural circuits affects their function and the resulting behavior is a key question in neuroscience. *C. elegans* is a particularly accessible system to explore these relations, thanks to its relative simplicity, the reconstruction of its connectome [1], and the range of molecular, imaging, and behavioral tools for studying it. Here, we study the circuit for nociception that is composed of the same set of neurons in the two sexes of *C. elegans*, and are connected in a sex-dependent topology (Fig. 1A). As the two sexes demonstrate dimorphic behavioral response to aversive stimuli (Fig. 1B), we ask whether the distinct topologies are sufficient to explain these differences.

We show, experimentally, that the sensory transduction is similar in the two sexes, and then explore the role of network connectivity as the source of behavioral dimorphism — by simulating the dynamics of the nociceptive circuits. Since the biophysical parameters of circuits that perform the same function might differ between animals [2], we explore a wide range of realistic values. The overlapping parameter sets for the two sexes is relatively small, and, importantly, reproduce the experimental behavioral differences.

We then use our simulated model to identify critical potential rewiring of the networks that would switch behavior between sexes. Our model predictions were validated experimentally: the male's network can be simply rewired to generate the responses of the opposite sex, whereas the hermaphrodite's network is more robust (Fig. 1C). Behavioral assays of the rewired males suggest that a topology that enables efficient avoidance of a noxious cue may have a cost in terms of finding a mate. We conclude that sexual identity sculpts neuronal circuits to fit sex-specific needs and present an example of behavioral reprogramming by simple connectomic editing.

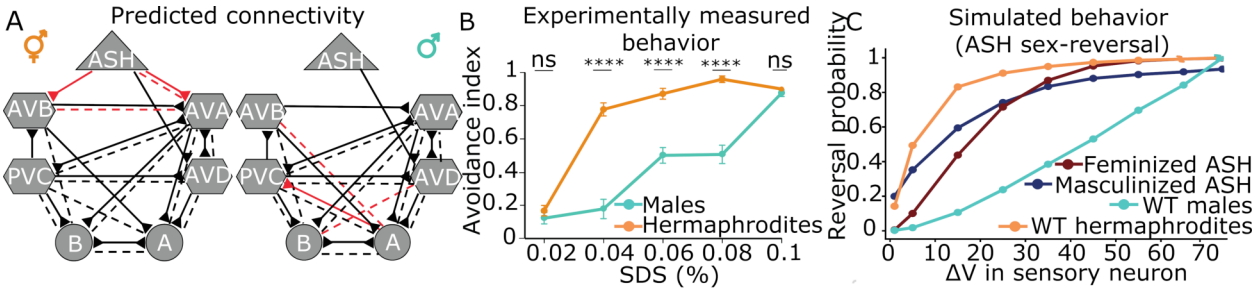


Figure 1. (**A**) Nociceptive circuit connectivity in *C. elegans*, sex-specific connections in red. (**B**) Sexually-dimorphic dose-dependent escape responses to SDS in tail drop assay. (**C**) Model predictions of the responses in WT worms and worms with sex-reversed ASH.

References

1. Cook, Jarrell, Brittin, *et al.*, 2019, *Nature* 571(7763):63–71
2. Prinz, Bucher, Marder, 2004, *Nat. Neurosci.* 7(12), 1345–1352

DALEIAN SPIKING NEURAL NETWORKS ARE MORE INFORMATIVE, ROBUST, AND COMPUTATIONALLY RICHER THAN NON-DALE ONES

Adam Haber[*], *Elad Schneidman*

Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel
[*]adamhaber@weizmann.ac.il

The structural connectivity of neurons in the brain is constrained by a variety of physical, chemical, and biological factors. These constraints shape the map of synaptic connections between neurons, and therefore the patterns of neural activity in these circuits, and the computations they can perform. Specifically, the identity of neurons as either excitatory or inhibitory, a corollary of Dale's principle, represents an especially stringent structural and combinatorial constraint. While Dale's principle has clear structural and assembly benefits, little is known about its computational implications for neural circuits.

Here, we study the functional differences between 'Daleian' and 'non-Daleian' networks, by simulating the response of large ensembles of networks to a wide range of stimuli, and comparing the responses of Daleian and non-Daleian network, to each stimulus. We find that the computations implemented by each of the non-Dale (unconstrained) networks can be implemented nearly as well by a Daleian (constrained) one (Fig. 1a-b). Moreover, we find that Daleian networks are more robust to synaptic noise. Importantly, this robustness does not hinder the learning ability of these networks, which can be efficiently achieved by tuning synaptic weights and neuronal spiking thresholds together. We further show that the class of Daleian networks spans a wider range of population responses, and they carry more information about their stimuli than non-Daleian networks.

Our results suggest that the structural benefits of Dale's principle do not inflict strong functional constraints on the computational capacity of neural circuits. Moreover, they might confer significant computational benefits, allowing learning trajectories to explore areas of the space of neural responses that are highly improbable for random topologies.

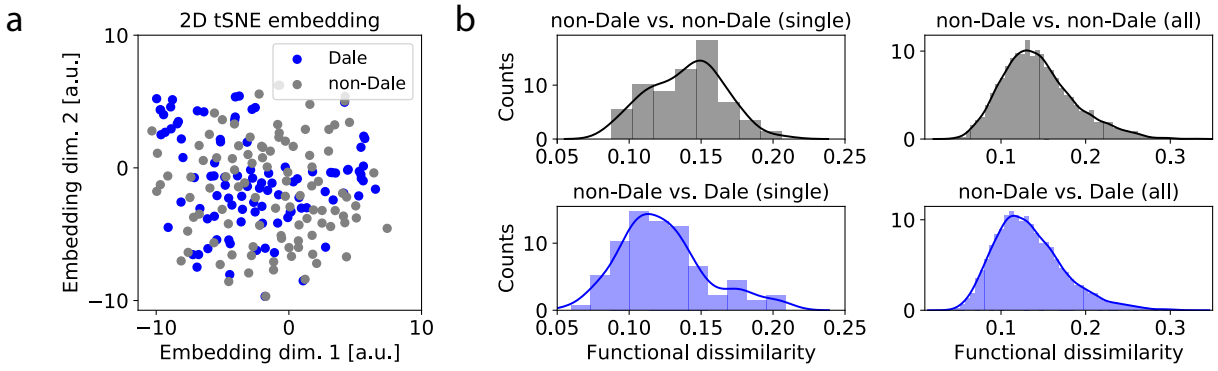


Figure 1. (**a**) 2D tSNE embedding of individual Dale and non-Dale networks, based on their functional similarity. (**b**) Left: An example of the distribution of distances between one non-Dale network and all other non-Dale networks, which is similar to its distances to all Dale networks. Right: distribution of distances for the whole ensemble.

ANTERIOR-POSTERIOR GRADIENT IN THE JOINT PROCESSING OF ARM MOVEMENT DIRECTION AND DEPTH IN PRIMATE PARIETAL CORTEX

Kostas Hadjidimitrakis[*], *Marina De Vitis, Matteo Filippini, Patrizia Fattori*

Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[*]kon.chatzidimitrakis@unibo.it

Accurate performance of arm movements depends on the integrity of a network of areas located in the parietal cortex that integrate visual information about the location of objects in space with visual and proprioceptive information about hand position, to guide arm movements. Although every arm movement happens in 3D space, it has become traditional among researchers to make a distinction between the direction of a movement and its depth. Psychophysical evidence suggests that the direction and distance of reaching movements are likely to be specified independently, however there is no clear physiological evidence of this segregation.

Neural activity was recorded from three different parietal cortex areas in *M. fascicularis* during an arm reaching task with targets presented at varying distances and directions from the body. We used information theory, singular value decomposition and dimensionality reduction methods and compared reach direction and depth strength and convergence within and across the three parietal areas.

We found two major classes of cells: (a) neurons that encoded both distance and direction information, and (b) cells encoding only one type of signal. While direction effect was stronger than depth during early planning, depth signals became dominant towards movement execution. Going from anterior to posterior regions, cells that processed both signals consistently increased. These findings suggest a significant degree of sequential direction and depth processing that supports behavioral evidence. In addition, they reveal a gradient-like organization of joint versus independent control of reach parameters in parietal cortex that could be viewed in light of its role in visuo-motor transformations during actions.

Acknowledgments

Supported by H2020-EIC-FETPROACT-2019-951910-MAIA, and PRIN-2017KZNZLN.

SPECTRO-TEMPORAL CHARACTERISTICS OF INTRACRANIAL EEG RECORDED FROM HUMAN MOTOR CORTEX DURING CONTINUOUS MOVEMENTS

Jiri Hammer[1,2,*], *Petr Marusic*[2], *Tonio Ball*[1]

[1] Department of Neurosurgery, University of Freiburg, Freiburg, Germany
[2] Department of Neurology, Charles University, Prague, Czech Republic
[*] hammer@bcf.uni-freiburg.de

Research of functional properties of neurons in motor cortex has brought many important insights into the representation of movements in the human brain. Among the seminal findings is the directional selectivity of single unit activity (SUA) in primary motor cortex (M1) — the so-called directional tuning [1]. Other studies showed that the neurons in M1 did not code only for a single movement parameter, but that the tuning characteristics of a single neuron changed in time, for example from position to velocity tuning [2]. However, much less is known about the temporal profile of encoded information in M1 during movements in large-scale neuronal populations, such as those measured by EEG in humans.

To bridge the gap between SUA and EEG, we measured the intracranial EEG (iEEG), an intermediate between the micro-scale SUA and macro-scale EEG, and analyzed the high-gamma band (HGB) activity (above 60 Hz), which is assumed to closely correlate to the firing rate of the underlying neuronal population [3].

We observed a robust representation of two kinematic parameters: movement speed (defined as the magnitude of the velocity vector) and distance (magnitude of the position vector) in the HGB of iEEG. Surprisingly, there was a consistent temporal structure, in which the distance-tuning preceded the speed-tuning.

The presented results demonstrate that there is also a clear pattern of spectro-temporal tuning properties at the level of iEEG. This pattern is different from that at the level of SUA and shows a selectivity of neuronal population signals to non-directional movement parameters [4]. These results may have profound implications for the design of EEG-controlled brain-machine interfaces.

Acknowledgments

This work has been supported by BMBF 01IS19077C and GACR 20–21339S.

References

1. Georgopoulos, *et al.*, 1982, *J. Neurosci.* 2:1527–37, 10.1523/JNEUROSCI.02-11-01527.1982
2. Hatsopoulos, *et al.*, 2007, *J. Neurosci.* 27(19):5105–14, 10.1523/JNEUROSCI.3570-06.2007
3. Ray, Maunsell, 2011, *PLoS Biol.* 9:e1000610, 10.1371/journal.pbio.1000610
4. Hammer, Pistohl, Fischer, *et al.*, 2016, *Cereb. Cortex* 26(6):2863–81, 10.1093/cercor/bhw033

EVIDENCE OF PRECISE TIME-WARPED SPIKE TIMING IN VIVO AND IN SILICO

James B. Isbister[1,2,*], *Michael Reimann*[1]

[1] The Blue Brain Project, EPFL, Lausanne, Switzerland
[2] Department of Experimental Psychology, University of Oxford, Oxford, UK
[*] james.isbister@epfl.ch

Precise and reliable spike time patterns are rarely reported in the cortex, classically supporting the spike count view. The sensitivity of neural integration, and the potential speed and efficiency of a spike time code, maintains the appeal of spike time coding, however. It is known that spike counts and trajectories in low-dimensional manifolds depend on the state (*i.e.* excitability) of the cortex on single trials. How then, does the state of the cortex on single trials affect spike time representations?

To answer this question *in vivo*, we studied stimulus-evoked patterns in which each neuron spikes once (multi-neuron single spike patterns). Recent research implicates such patterns as a fundamental form of representation. We previously showed that spike times within a sequence depended on single trial cortical excitability [1]. When the cortex was more excited, a spike sequence was compressed: evolving quickly in time. When the cortex was less excited, the spike sequence was stretched: evolving slowly in time. Moreover, relative differences between the timings of spikes, which can be decoded by downstream neurons, depended on cortical excitability.

This compression and stretching of spike sequences in time was referred to as *time-warping* and may explain why reliable and precise spike sequences are rarely reported. Modulation of spike times for neurons separated over layers and columns of cortex, introduced the possibility that decoding neurons are modulated by the same changes in excitability and could respond in an excitability-dependent manner. This would confer a higher potential coding capacity for relative spike time differences.

We present new visualisations of time-warped multi-neuron single spike patterns (for up to 12 neurons), which could be a fundamental form of representation. We show that trial-to-trial changes in shared excitability are low-dimensional, increasing the possibility of modulation of decoding neurons. We present improved estimates of single trial cortical state from spike times, and an increased potential coding capacity under a possible excitability-dependent coding scheme. We present *in silico* results, exploring the time-warped phenomenon in a large-scale biophysical cortical model.

Acknowledgments

This study was supported by funding to the Blue Brain Project, a research center of the École Polytechnique Fédérale de Lausanne (EPFL), from the Swiss government's ETH Board of the Swiss Federal Institutes of Technology.

Reference

1. Isbister, Reyes-Puerta, Sun, *et al.*, 2021, *Sci. Rep.* 11(1):1–20

SINGLE-CELLULAR REPRESENTATIONS OF SEMANTIC CONTENT IN HUMAN PREFRONTAL CORTEX DURING LANGUAGE COMPREHENSION

Mohsen Jamali[1,2,*], *Benjamin Grannan*[1,2], *Jing Cai*[1,2], *Arjun R. Khanna*[1,2], *Ziv Williams*[1,2]

[1] Department of Neurosurgery, Massachusetts General Hospital, Boston, USA
[2] Department of Neurosurgery, Harvard Medical School, Boston, USA
[*] mjamali@mgh.harvard.edu

Humans are capable of communicating exceptionally diverse and complex meanings through language. Yet despite a growing understanding of the frontotemporal network of brain areas that supports semantic processing, the precise derivation of linguistic meaning in neural tissue at the cellular level and over the temporal scales of action potentials remains largely unknown. Here, through acute single unit recordings from the posterior middle frontal gyrus of the prefrontal cortex in patients undergoing awake neurosurgery and by employing a modeling-and-decoding approach on both single- and population-level neuronal data we aim to (i) examine whether individual prefrontal neurons encode semantic content and whether/how they may reflect the real-time context-dependent inferred meaning of individual words, (ii) investigate the degree to which these encoding dynamics are robust and generalizable across linguistic materials and participants, and (iii) assess whether and how the ensemble activities of neuronal population reflect the hierarchical organization of meaning representations.

To this end, acute neuronal recordings were performed as participants listened to prerecorded 8-word sentences and non-ordered word lists that were designed to sample broadly across different semantic themes. All unique words were then clustered into nine different groups based on semantic similarities using a word embedding (*i.e.*, word2vec) and spherical clustering approach. Of 220 neurons across 10 participants, 48 (21.8%) of neurons displayed significantly differential firing rate to at least one semantic domain ($p < 0.025$, false-discovery correction) during sentence comprehension. These neurons exhibited responses selective to specific semantic domain(s) during sentence comprehension compared to when presented with non-ordered word lists or homonym words with identical phonetics but different semantic meanings; *e.g.*, the average selectivity index (SI) dropped from 0.35 during the sentences to 0.18 during the word lists, $p = 0.0006$. This suggests a context-dependent prefrontal activation rather than lower-level linguistic characteristics such as lexical or phonetic representations.

Building support vector classifiers that randomly sampled words from 60% of the sentences and used the remaining 40% for validation across 1000 iterations, we further found that the ensemble neuronal activities could predict the semantic domains with significant accuracy (488% s.d. vs. 11.1% chance, $p < 0.001$). The selectivity and decoding results were consistent across subjects and different embedding models (*e.g.*, GloVe) indicating the generalizability and robustness of our analysis. Finally, using an agglomerative hierarchical clustering procedure, we found that differences in the firing activities of semantically selective neurons were significantly correlated with the cophenetic distances between word pairs in the word embedding space ($r = 0.22$, $p < 0.001$). In conclusion, these findings reveal a remarkably detailed organization and segmentation of semantic information by neurons in the language-dominant prefrontal cortex and begin to illuminate the cellular-level processing of linguistic meaning during language comprehension.

Acknowledgments

Supported by NARSAD, CIHR, and Foundations of Human Behavior.

ULTRA-RAPID VISUAL SEARCH IN NATURAL IMAGES USING ACTIVE DEEP LEARNING

Jean-Nicolas Jérémie[1,*], *Emmanuel Daucé*[1,2], *Laurent Perrinet*[1]

[1] Institut de Neurosciences de la Timone, CNRS/Aix-Marseille Univ, France
[2] École Centrale, Marseille, France
[*] jean-nicolas.jeremie@etu.univ-amu.fr

Visual search, that is, the simultaneous localization and detection of a visual target of interest, is a vital task. Applied to the case of natural scenes, searching for example to an animal (either a prey, a predator or a partner) constitutes a challenging problem due to large variability over numerous visual dimensions such as shape, pose, size, texture or position. Yet, biological visual systems are able to perform such detection efficiently in briefly flashed scenes and in a very short amount of time [1].Deep convolutional neuronal networks (CNNs) were shown to be well fitted to the image classification task, providing with human (or even super-human) performance. Previous models also managed to solve the visual search task, by roughly dividing the image into sub-areas. This is at the cost, however, of computer-intensive parallel processing on relatively low-resolution image samples. Taking inspiration from natural vision systems, we develop here a model that builds over the anatomical visual processing pathways observed in mammals, namely the What and the Where pathways [2]. It operates in two steps, one by selecting regions of interest, before knowing their actual visual content, through an ultra-fast/low resolution analysis of the full visual field, and the second providing a detailed categorization over the detailed foveal selected region attained with a saccade.

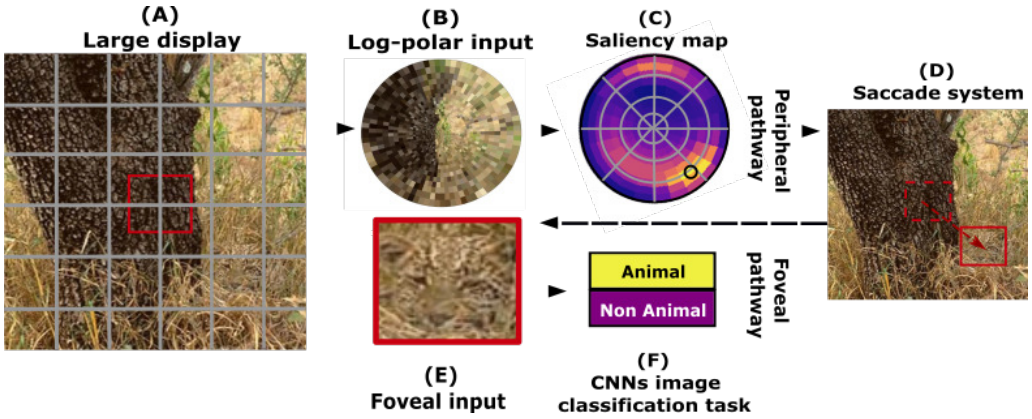


Figure 1. The peripheral pathway (top row) is applied to a large display from a natural scene (**A**). It is first transformed into a retinotopic log-polar input (**B**) and we then learn to return a saliency map (**C**). The latter infers, for different positions in the target, the predicted accuracy value that can be reached by the foveal pathway, mimicking the Where pathway used for global localization. The position with the best accuracy feeds a saccade system (**D**), adjusting the fixation point at the input of the foveal pathway (bottom row). The subsample (**E**) of the large display, is fed to a categorization (**F**), mimicking the What pathway.

Our dual-pathways architecture creates an efficient model of visual search as active vision. In particular it allows to fill the gap with the shortcomings of CNNs with respect to physiological performances. In the future, we expect to apply this model to better understand visual pathologies in which there would exist a deficiency of one of the two pathways.

References

1. Thorpe, Fize, Marlot, 1996, *Nature*, 381(6582):520–522, 10.1038/381520a0
2. Dauce, Perrinet, 2020, *J. Vision* 1326:165–178, 10.1007/978-3-030-64919-7_17

MODELLING CONTINOUS LEARNING AND ADAPTIVE BEHAVIOR IN DROSOPHILA LARVA

Anna-Maria Jürgensen[*], *Panagiotis Sakagiannis, Martin P. Nawrot*

Computational Systems Neuroscience, University of Cologne, Cologne, Germany
[*] a.juergensen@uni-koeln.de

Predicting positive or negative rewards from environmental clues is highly relevant to guide decision making and goal-directed behavior in vertebrates and invertebrates alike. In our model of the Drosophila mushroom body (MB) we test the capacity of prediction error coding to explain larval behavior in associative learning experiments. The theory of prediction error coding assumes that associative learning about stimulus A is proportional to the difference between the reinforcement currently received with A minus the reinforcement predicted by A, which is based on prior experience [1].

In our spiking model synapses between Kenyon cells (KC) and MB output neurons (MBON) are the site of plasticity. Modulation of synaptic strength during learning leads to an imbalance in MBON activity hat represents the association of odors with rewards or punishments (behavioral bias). We use real-time replications of larval learning experiments to produce the time resolved dynamics of the behavioral bias and apply our locomotory model of Drosophila larva to simulate movement towards or away from odor sources. The directness of this movement, defined by the frequency of bending and turning is simulated based on the behavioral bias. We show that our implementation of prediction error can account for experimentally observed saturation of learning curves, extinction learning and the influence of reward magnitude.

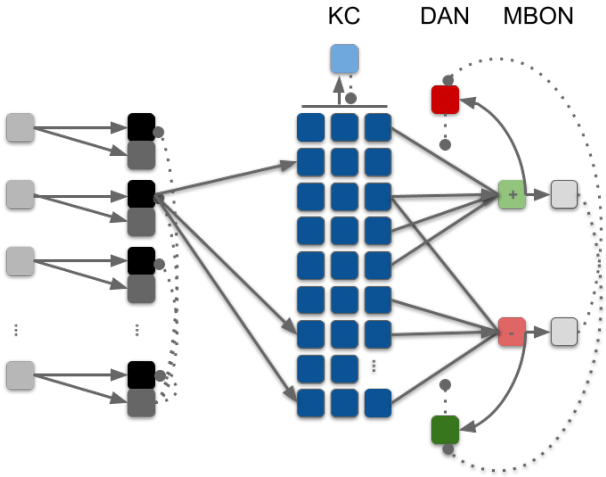


Figure 1. Network model of the Drosophila larva olfactory system including all neurons and connections modeled between Kenyon cells (KC), output neurons of the mushroom body (MBON) and dopaminergic neurons encoding reward and punishment (DAN). Plasticity is implemented at KC::MBON synapses and the MBON::DAN feedback encodes prediction error.

Acknowledgments

Funded by the German Research Foundation (DFG), grant no. 403329959.

Reference

1. Rescorla, 1972, Informational variables in Pavlovian conditioning, in *Psychology of Learning and Motivation*, ed. G. H. Bower (New York, NY: Academic Press)

NEURAL STABILITY IN THE STRIATUM AND MOTOR CORTEX OF RATS DURING ACQUISITION AND PERFORMANCE OF MOTOR SEQUENCES

Naama Kadmon Harpaz[1,2,*], *Kristopher T. Jensen*[3], *Steffen B.E. Wolff*[4], *Bence P. Ölveczky*[1,2]

[1] Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, MA, USA
[2] Center for Brain Science, Harvard University, Cambridge, MA, USA
[3] Department of Engineering, University of Cambridge, Cambridge, UK
[4] Department of Pharmacology, University of Maryland, Baltimore MD, USA
[*] naama_kadmon@fas.harvard.edu

Our nervous system's ability to acquire new actions allows us to gradually broaden our pool of motor expertise. From using utensils to writing the alphabet, mastering multiple skills requires the acquisition of new task-specific motor sequences without overriding previously learned ones. Through practice, these learned skills are stabilized and remain so thereafter, even if not practiced for months and years. Such stable performance implies that the neural dynamics that generate a learned motor sequence are robust and resistant to interference. Yet how the brain can maintain a stable motor memory while also learning new skills is far from understood.

To study the neural dynamics underlying the learning and stable performance of motor sequences we tracked the behavior of rats as they practiced a motor skill over several months. Simultaneously, we recorded the activity of the same neurons in motor cortex and dorsolateral striatum (DLS) continuously over days. First, we examined the neural activity in expert rats performing a single stereotyped motor sequence following months of training. We found that single neuron activity in both regions was highly stable over weeks of expert performance. A small drift observed over time could be largely explained by a concomitant slow drift in the motor output in directions orthogonal to task performance, emphasizing the need for careful assessment of behavioral readouts. These findings suggest that stereotyped motor sequences are indeed stored and generated in highly stable neural circuits.

Next, we asked whether the activity observed in the motor cortex and DLS will be destabilized by the acquisition of a new motor sequence, or whether it is robust to learning new skills. To this end, we developed a continual learning paradigm and trained rats on two distinct motor sequences, while tracking single neurons continuously throughout learning. Our preliminary findings show that rats had no problem recalling the first learned sequence after acquiring a new sequence and performed both sequences subsequently in a highly stereotypical manner, demonstrating robust performance of multiple sequences. Analysis of the underlying neural activity is currently in progress. Understanding whether and how neural activity of a previously learned motor sequence changes when learning a new skill will help decipher the physiological mechanisms underlying robust and flexible motor learning.

ADVANCEMENTS IN HUMAN SINGLE-NEURON LARGE-SCALE CORTICAL RECORDINGS

Yoav Kfir[1,2,*], *Angelique C. Paulk*[2], *Sydney S. Cash*[1,3], *Ziv M. Williams*[1,2]

[1] Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA
[2] Department of Neurosurgery, Harvard Medical School, Boston, MA, USA
[3] Department of Neurology, Harvard Medical School, Boston, MA, USA
[*] ykfir@mgh.harvard.edu

Recording single neurons activity is one of the fundamental methods being used to decipher the computation underlying any function of our brain. The number of recorded neurons in animal research is constantly increasing, and the current technology advances allow us to record from hundreds and even thousands of neurons simultaneously. Animal research provided many important insights on brain functions and computation, however, to fully understand high cognitive processes, such as language, we require also to translate these abilities to humans. Here, we used a rare opportunity to record from awake patients with a novel multi-contact probe, the Neuropixels probe, during intraoperative neurosurgical procedures. The Neuropixels probe can record from up to 384 channels with 20 μm spatial resolution and allowed us to capture over 200 separable units simultaneously. Taking advantage of the high spatiotemporal information of the Neuropixels recordings, we characterized the diversity of neurons in the human dlPFC [1] and observed eight distinct classes of cells that differ in location across the probe and in their firing patterns.

Although the Neuropixels probe quickly gained popularity for animal use, adapting it for human research introduced new challenges and required adjustments for safe and reliable recordings. To that end, we used a thicker variant of the probe, and adapted our methods for sterilization and electrical isolation in the operating room. The high spatial resolution of the neuropixels probe revealed a major challenge in acute human electrophysiology, while the probe is held fixed against a frame and/or skull, the brain tissue is constantly moving rhythmically with heart pulsation and breathing. This motion artifact is not specific to humans or the Neuropixels probe, however, due to the high spatial resolution of this probe, we could observe and quantify it across multiple patients. We introduce here a method for correcting the motion artifacts based on the low-frequency voltage information (LFP). This method exceeds the performance of available action-potential-based algorithms. We adapted a registration algorithm [2] and modified it to use LFP information. This allows us to register and correct for the motion artifacts with greater temporal precision than possible with point processes like spikes. The current method can potentially be used for online spike registration and detection without the need for robust mechanical stabilization.

Overall, translating the ability to record from a large scale of neurons simultaneously opens a window of opportunities to further expand our knowledge and understating human cortical computation underlying complex cognitive processes.

References

1. Lee, *et al.*, 2021, *eLife* 10:e67490, 10.7554/eLife.67490
2. Varol, *et al.*, 2021, ICASSP, 10.1109/ICASSP39728.2021.9414145

A RESILIENT NEURAL CODE IN V1 TO PROCESS NATURAL IMAGES

Hugo J. Ladret[1,2,*], *Laurent U. Perrinet*[1]

[1] Institut des Neurosciences de la Timone, CNRS and Aix-Marseille Université, Marseille, France
[2] School of Optometry, University of Montreal, Montreal, Canada
[*] hugo.ladret@univ-amu.fr

On a daily basis, the primary visual cortex (V1) detects oriented elements from sensory inputs made of orientation distributions. To remain selective to a large variety of possible input configurations, V1 has to account for the precision of these inputs [1]. Here, we decode the population activity of V1 to uncover a neural code which achieves invariance to input precision.

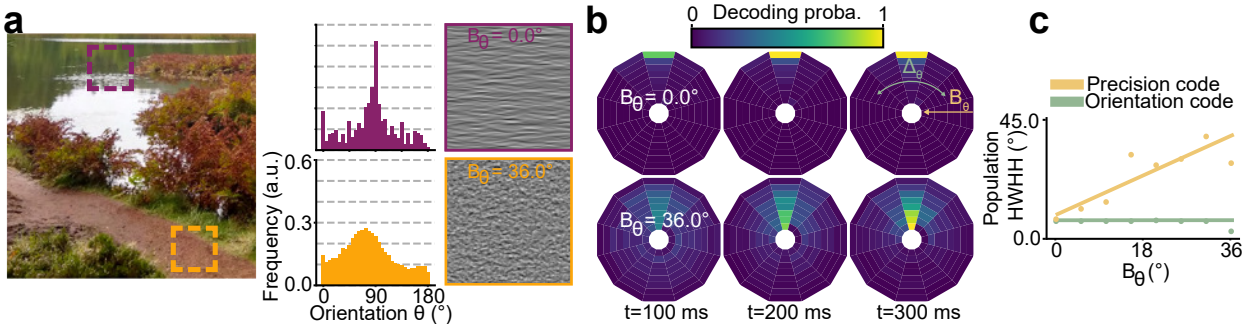


Figure 1. (**a**) Example natural scene with multiple textures used to create two example oriented naturalistic textures with similar orientation but different precision. (**b**) Encoding of orientation and precision by two example neurons. (**c**) Population-derived orientation and precision representation.

Extracellular recordings were made from 247 V1 neurons in anesthetized cats in response to visually presented naturalistic textures (Fig. 1a). These textures were generated from two parameters: orientation θ and orientation precision B_θ. Using multinomial logistic regression [2], we were able to recover these two parameters from the population activity.

We report two previously unknown types of neurons in V1: predominantly infragranular neurons that encode solely orientation, and predominantly supragranular neurons which co-encode both orientation and its precision. Using a simple mean-rate population model, we observed that recurrent cortical inhibition can single-handedly account for the existence of these two types of neurons. At the overall population level, the structure of the neural code shows that the orientation error Δ_θ (Fig. 1b) is invariant to precision B_θ. This results in V1 achieving robust orientation selectivity to all possible configurations of oriented inputs (Fig. 1c). Furthermore, we found that precision dictates the temporality of the response, with lower precision textures eliciting slower responses in V1, which can explain the non-canonical dynamics elicited by natural images in V1 [3]. Overall, these results shed additional light not only on the processing of natural images, but also on Bayesian processing in the brain, in which precision modulates prior/posterior integration [4].

References

1. Simoncelli, Olshausen, 2001, *Ann. Rev. Neuro.* 24(1):1193,10.1146/annurev.neuro.24.1.1193
2. Berens, Ecker, Cotton, *et al.*, 2012, *J. Neurosci.* 32(31), 10.1523/jneurosci.1335-12.2012
3. Yoshida, Ohki, 2020, *Nat. Comm.* 11(1):1–19, 10.1038/s41467-020-14645-x
4. Friston, 2010, *Nat. Rev. Neurosci.* 11(2):127–138, 10.1038/nrn2787

WEAK EVIDENCE FOR NEURAL CORRELATES OF TASK-SWITCHING IN MACAQUE V1

Richard D. Lange[1], *Camille Gomez-Laberge*[2], *Anton Pletenev*[1], *Ariana Sherdil*[2], *Till Hartmann*[2], *Richard T. Born*[2,†], *Ralf M. Haefner*[1,†,*]

[1] Department for Brain and Cognitive Science, University of Rochester, Rochester, NY, USA
[2] Department of Neurobiology, Harvard Medical School, Boston, MA, USA
[†] equal contribution
[*] ralf.haefner@rochester.edu

A central goal of systems neuroscience is to understand how populations of noisy sensory neurons encode and relay information to the rest of the brain. Key quantities of interest are (i) how mean neural activity depends on the stimulus (sensitivity), (ii) how neural activity (co)varies around the mean (noise correlations), and (iii) how predictive these variations are of the subject's behavior (choice probability). Previous empirical work suggests that both choice probability and noise correlations are affected by task training [1], with decision-related information fed back to sensory areas [2] and aligned to neural sensitivity on a task-by-task basis [3].

We used Utah arrays to record activity from populations of V1 neurons from two macaque monkeys who were trained to switch between two coarse orientation-discrimination tasks. We set out to replicate and extend previous work [1–3] by tracking the emergence of decision-related signals and task-specific covariability over the course of training. First, each monkey was trained on a single task for several weeks, then the other task for several weeks, finally performing each task randomly interleaved, cued at the beginning of each trial. Both monkeys became proficient in each task, and we confirmed through reverse correlation that they switched their decision-strategy from trial to trial as expected during the interleaved epochs. Surprisingly, we find no evidence for significant trial-by-trial changes in noise covariance between tasks, nor do we find a consistent relationship between neural sensitivity and choice probability, despite recording from well-tuned task-sensitive neurons, many of which were histologically confirmed to be in supragranular V1, and despite behavioral evidence that the monkeys switched their strategy between tasks. Our work includes a number of methodological developments designed to minimize potential confounds, such as whitening raw voltages to reduce spurious shared spike events across channels, and accounting for the non-independence of chronically recorded neural data over many days. Compared to nominally similar previous studies, differences in task training, stimulus design, recording and analysis techniques therefore provide insights into the robustness and ubiquity of choice-related signals and task-dependent noise correlations, and constrains future models of how they arise. Our results raise the intriguing possibility that choice-related signals in early sensory areas are less indicative of task learning and instead more closely related to perceptual learning that occurs in highly over-trained subjects.

Acknowledgments

Supported by NIH/NEI R01EY028811.

References

1. Law, Gold, 2006, *Nat. Neurosci.*, 11:505–513, 10.1038/nn2070
2. Nienborg, Cumming, 2009, *Nature*, 459:89–92, 10.1038/nature07821
3. Bondy, Haefner, Cumming, 2018, *Nat. Neurosci.*, 21:598–606, 10.1038/s41593-018-0089-1

STABILITY AND PLASTICITY OF POPULATION ACTIVITY IN PERIRHINAL CORTEX DURING ABSTRACT LEARNING

David G. Lee[1,*], *Caroline McLachlan*[2], *Danielle LaMay*[2], *Jerry L. Chen*[1,2]

[1] Department of Biomedical Engineering, Boston University, Boston, MA, US
[2] Department of Biology, Boston University, Boston, MA, US
[*] dglee3@bu.edu

In order to interpret the environment, sensory information must be unitized, associated with behavioral outcomes, and stored in long-term memory for future recall. The perirhinal cortex (Prh) is a zone of convergence between sensory neocortex and hippocampus that encodes complex, experience-dependent sensory features and their associative relations. Anatomical tracing shows reciprocal connections between Prh and somatosensory cortices. We sought to investigate how Prh participates in goal-directed learning of abstract tactile representations.

Head-fixed mice (n = 7) were trained to perform a whisker-based, go-no go, delayed non-match-to-sample task (Fig. 1A). Using two-photon calcium imaging in animals implanted with microprisms over Prh, we chronically monitored populations of layer 2/3 neurons (200–500 neurons per animal) across the entirety of task learning (26–68 sessions). Task training proceeded in successive stages that enabled neuronal activity related to instrumental learning (T1–T2), rule generalization (T3), and working memory (T4–T5) to be investigated.

Single-cell and population activity was decoded using generalized linear models and support vector machines, respectively. On a single-cell level, task learning modified sensory representations by binding related features and untangling irrelevant features. At a population level, neuronal dynamics formed sequences that became less stimulus-locked and more associated with network states linking reward prediction with outcome. Representations of reward prediction were unstable and varied from session to session. In contrast, representations of reward outcome stabilized with learning (Fig. 1B). Stimulus reward associations emerged from reward outcome in a retrograde manner and generalized across stimulus conditions (Fig. 1C). Our results suggest that neural dynamics linking reward prediction and outcome provide an algorithmic scaffold that supports abstract sensory learning.

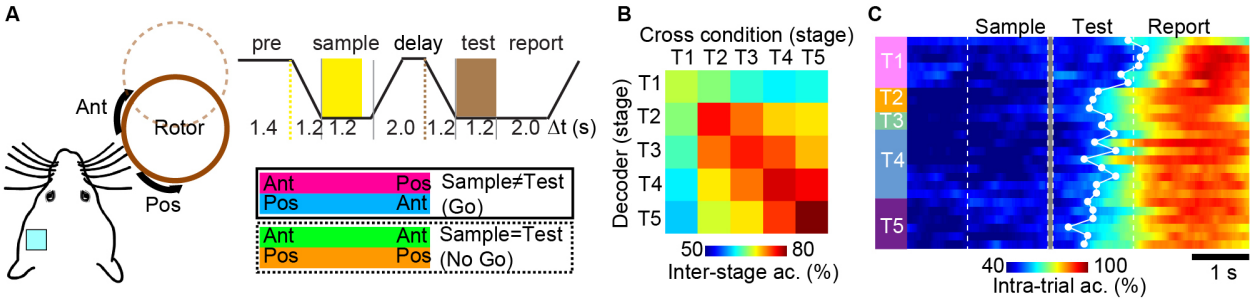


Figure 1. (**A**) Schematic of task design. (**B**) Stability of reward outcome representations across training stages. (**C**) Over training sessions, decoding of stimulus reward association emerges retrogradely from reward outcome.

PERCEPTUAL AND NEURAL REPRESENTATIONS OF TEXTURE NATURALNESS IN DEVELOPING MONKEYS

Gerick M. Lee, Carla L. Rodriguez-Deliz, Najib J. Majaj, J. Anthony Movshon, Lynne Kiorpes[*]

Center for Neural Science, New York University, New York, USA
[*]lk6@nyu.edu

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 oddity 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 analyzed the responses of these neural populations with suitable classifier-based decoding methods (we applied a linear discriminant to a low-dimensional projection of each population), and used these to derive population measures of neural naturalness sensitivity analogous to the sensitivities we measured behaviorally.

We found a robust increase in behavioral naturalness sensitivity across the ages tested. In contrast to the behavioral data, neural naturalness sensitivity did not change consistently with age, though sensitivities were greater in V4 than in V1 or V2, at both the unit and population levels.

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.

Our longitudinal data suggest that developmental performance improves at least in part as a result of changes downstream of V2 and V4. Our analysis of response dynamics suggests that naturalness sensitivity in the ventral visual stream may emerge first in V4 before being fed back to earlier areas.

SPATIO-TEMPORAL PATTERNS IN THE PRIMARY MOTOR CORTEX ENCODE KINEMATICS

Wei Liang[1,2,*], *Karthikeyan Balasubramanian*[2], *Vasileios Papadourakis*[2], *Nicholas Hatsopoulos*[1,2]

[1] Committee on Computational Neuroscience, University of Chicago, Chicago, IL, USA
[2] Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[*] weiliang@uchicago.edu

The primary motor cortex (M1) is known for its general static correspondence between body parts and clustered sites on the physical cortical sheet — the somatotopic map. However, it is largely unknown whether there exists any interplay between physical space and time that might account for finer movement execution.

In search of potential M1 spatio-temporal patterns that might be important during movement execution, we investigated the high gamma band (200–400 Hz) envelope in the local field potential, as a proxy of multi-unit activities. We recorded from two male rhesus macaques with implants in M1, while they performed a constrained reach task in different directions (Fig. 1A). To cleanup noisy single-trial signals, we denoised the single-trial envelopes primarily by using a contractive autoencoder. The high gamma amplitude envelopes from different electrode locations tended to amplify around movement initiation at slightly different times but in a spatially organized fashion forming a propagating pattern, which could be characterized by a few parameters from a planar fit. We found that for both monkeys the exact direction of this propagating pattern varied according to initial reach directions (Fig. 1B and C show results from one monkey), indicating that these spatiotemporal patterns encode movement execution. Next, we found that parameters characterizing these propagating patterns alone could predict movement kinematics. Furthermore, those spatio-temporal patterns provided additional prediction boosts on top of the information-rich high Gamma envelopes themselves. Together we show that the spatio-temporal patterns encode important details regarding movement execution.

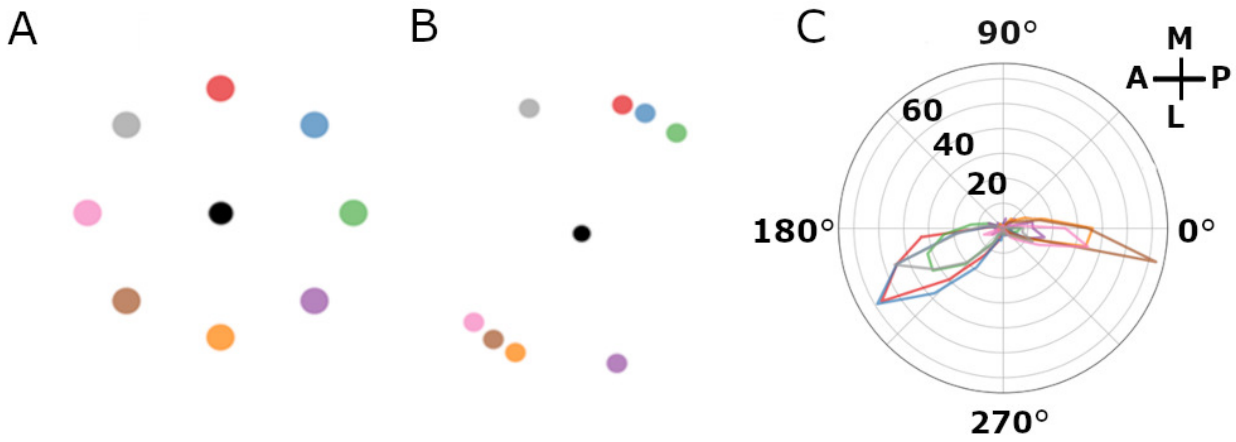


Figure 1. (**A**) Target directions. (**B**) Actual initial movement directions. (**C**) Distributions of propagating directions for corresponding reach directions (counts on the radius).

Acknowledgments

Supported by NIH R01 NS111982.

A NEW THEORY FOR THE NEURAL PRINCIPLES BEHIND GENERATION OF MOVEMENTS

Henrik Lindén, Peter Petersen, Mikkel Vestergaard, Rune W. Berg *

Department of Neuroscience, University of Copenhagen, Copenhagen, Denmark
* runeb@sund.ku.dk

While the orchestration of movements is accomplished by motor cortex and the brainstem, networks in the spinal cord are responsible for the detailed muscle commands, including the generation of rhythmic movements such as locomotion. Although spinal neurons are well characterized at the cellular level, the mechanisms underlying rhythmic generation is largely unknown. It is known that the motor cortex exhibits rotational dynamics associated with certain types of movements [1] *i.e.* the neural populations follow a rotating trajectory through their state space, but it is unknown whether the spinal cord has similar dynamics. To investigate this issue, we analyzed simultaneous multi-electrode recordings from the spinal cord of hundreds of neurons and discovered similar low-dimensional rotational dynamics characterized by a wide phase distribution in relation to the muscle activation. This is in opposition to the assumed alternation, which is predicted by the half-center theory. To further appreciate how such slow population dynamics can yield rotational dynamics in the spinal cord, we develop a new theory, briefly involving firing rate dynamics of networks of recurrently connected excitatory and inhibitory spinal interneurons. By analyzing the spectrum of the linearized effective coupling matrix of the rate dynamics we illustrate how a tonic supraspinal drive can induce rhythmic network activity if two conditions are met: (i) the real part of the maximum eigenvalue of the effective coupling matrix is larger than a critical value, and (ii) this eigenvalue has a non-zero imaginary part. Using numerical simulations of networks fulfilling these two conditions we show that the resulting population activity is largely determined by the eigenvector corresponding to the largest eigenvalue, displaying rotational dynamics with wide phase distributions consistent with the experimental data. Finally, we demonstrate how such population states can be flexibly modulated via a selective drive to allow multi-functional motor output patterns including multiple gaits.

Acknowledgments

Supported by The Independent Research Fund Denmark, The Lundbeck Foundation, and the Carlsberg Foundation.

References

1. Churchland, *et al.*, 2012, *Nature*, 10.1038/nature11129

SPATIO-TEMPORAL DYNAMICS OF NEURONAL ENGAGEMENT TO THE MICRO-PROGRESSION OF ACUTE SEIZURES IN MOUSE CORTICAL CIRCUITS

Joseph Lombardo[1,2], *Maria Markaki*[3], *Maria Papadopouli*[3,4,*], *Stelios M. Smirnakis*[1,2,*]

[1] Dept. Neurol., Brigham and Women's & Jamaica Plain VA Hospitals, Boston, MA, USA
[2] Dept. Neurol., Harvard Medical School, Boston, MA, USA
[3] ICS, Foundation for Research & Technology-Hellas, Heraklion, Greece
[4] Dept. of Computer Science, University of Crete, Heraklion, Greece
[*] maria@csd.uoc.gr, smsmirnakis@bwh.harvard.edu

Epilepsy is a common neurological disorder with poorly understood circuit mechanisms [1]. Focal injury in acquired forms of epilepsy is thought to induce an abnormal balance between excitation and inhibition that drives neuronal networks into self-perpetuating oscillatory activity states [2] (seizure). A major unsolved question is how neurons get recruited, *in vivo*, during the evolution of seizure events. Specifically, it is not known whether neurons fire in a stereotyped pattern or sequence per seizure event, whether this happens reliably, and how it depends on neuronal type. To study the recruitment of cortical neurons to acute seizures, we injected the chemoconvulsant 4-aminopyridine (4-AP) in the mature neocortex (layer V) and performed *in vivo* 2P calcium imaging in the primary visual cortex (V1) of awake mice. In each neuron, we defined *local plateaus* as periods of abnormally increased and prolonged calcium activity based on thresholds derived from recordings prior to 4-AP injection, and *bursts* as periods when at least 2% of neurons showed local plateaus simultaneously. Neurons were then divided in temporal quartiles based on the time-intercept of the tangent at the half maximum of the sigmoidal fit of their local plateaus. Acute seizure micro-progression was characterized by a cyclical alternation of spatial expansion and contraction in the engagement of neuronal ensembles starting from the injection site. This spatio-temporally organized pattern is repeated until the organization fades away and only few and sparse neurons are engaged.

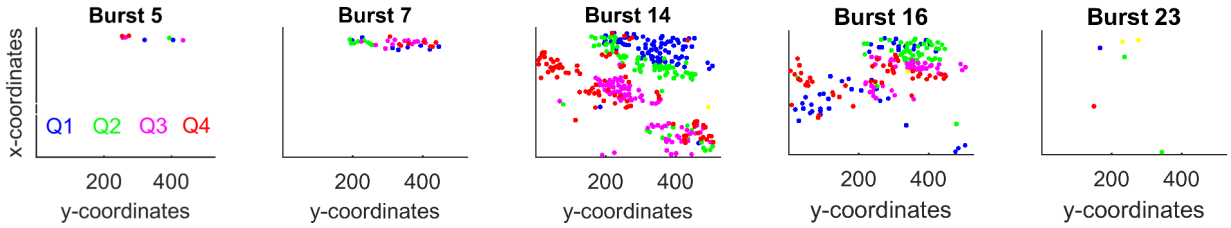


Figure 1. Spatio-temporal dynamics of representative bursts of a mouse; color indicates quartile of lags of local plateaus relative to the start of bursts; coordinates in pixels.

Acknowledgments

Funded by the HFRI/GSRT 2285, MC-RISE GA101007926, and NINDS R21 NS088457.

References

1. Hirtz, *et al.*, 2007, *Neurol.* 68(5):326–337
2. Sisodiya, Mefford, 2011, *Curr. Opin. Neurol.* 24(2):140–145

INFORMATION-THEORETIC EVALUATION OF NEURAL PREDICTION MODELS

Konstantin K. Lurz[1,2,†], *Mohammad Bashiri*[1,2,†], *Edgar Y. Walker*[3], *Fabian H. Sinz*[2,*]

[1] University of Tübingen, Tübingen, Germany
[2] University of Göttingen, Göttingen, Germany
[3] University of Washington, Seattle, WA, USA
[†] equal contribution
[*] sinz@cs.uni-goettingen.de

Recently, significant progress has been made in modeling neural responses to arbitrary sensory stimuli. These models are often trained by maximizing the likelihood of a parametric probability distribution. The predictive performance is then commonly evaluated and reported using correlation which is intuitive, convenient to compute, and can be put into the context of trial-to-trial fluctuations using upper bounds like the oracle estimator [1]. In this work, we provide two reasons to advocate for using a likelihood-based measure instead of correlation. We then propose a method to compute a likelihood-based upper bound estimator.

The first reason is that training via likelihood and evaluating via correlation implicitly assumes that the optima under both measures coincide. We show experimentally and theoretically that this assumption does not hold when the objective function is not chosen from the exponential family with the mean as a sufficient statistic. With increasing adoption of complex distributions to model neural responses, this discrepancy can result in a misleading estimation of model performance. The second reason is that a likelihood-based measure allows for model evaluation based on the full distribution, as opposed to correlation which is only sensitive to the mean.

To contextualize the likelihood-based metric in the presence of trial-to-trial fluctuations, there is a need for an upper bound estimator [2]. However, to the best of our knowledge, such an estimator has not been proposed for neural likelihood models. To this end, we propose a Bayesian approach to compute a probabilistic upper bound estimator of the response distribution in a target trial given the responses in other trials. The model likelihood is then reported relative to the upper bound and a simple lower bound, resulting in an interpretable and intuitive measure of how well the model captures the distribution of neural responses.

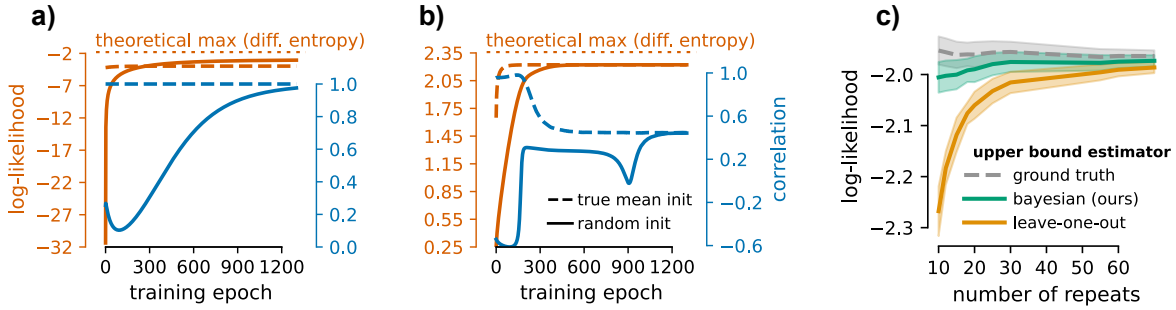


Figure 1. Comparison of log-likelihood and correlation during training via maximum likelihood. **(A)** When the mean is a sufficient statistic, even though they coincide at their optima, their trajectory can be different. **(B)** When the mean is not a sufficient statistic, the optimal log-likelihood does not yield an optimal correlation. **(C)** Performance of the upper bound estimator of the likelihood as a function of the number of repeats. In the low-data regime, our bayesian estimator outperforms a naive leave-one-out estimator.

References

1. Sinz, Ecker, Fahey, *et al.*, 2018, *NeurIPS*
2. Kuemmerer, Wallis, Bethge, 2015, *PNAS* 112(52):16054–16059

BIOLOGICALLY CONSTRAINED SPIKING NEURAL NETWORK FOR IMAGE CLASSIFICATION

Nikos Malakasis[1,*], *Spyridon Chavlis*[2], *Panayiota Poirazi*[2]

[1] School of Medicine, University of Crete, Heraklion, Greece
[2] Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[*] malakasisnikos@gmail.com

Artificial neural networks are widely used at the core of smart software applications in machine learning and artificial intelligence. Even though these networks are inspired by neurobiology, they lack features that neuronal circuits utilize to facilitate learning. More specifically, they employ learning algorithms which are not yet proven biologically plausible.

Here, we hypothesize that a biologically constrained spiking neural network can perform image classification by utilizing network mechanisms and plasticity rules employed in the brain during learning. We built a network of cells consisting of two layers, a hidden and an input layer. The hidden layer includes 120 multi-compartmental excitatory and inhibitory neurons with active dendrites, whereas the input layer consists of artificial cells represented by spike trains. The input spike trains are Poisson-distributed, with their average firing rate positively correlated to the pixel intensity. Learning occurs by utilizing a class-specific teaching signal and a synaptic tag-and-capture plasticity rule [1].

We show that the network can perform binary classification using a set of biological mechanisms. In particular, structural plasticity via synaptic turnover and a neuro-inspired adaptive learning rate improve its performance significantly by optimizing the utilization of learnable parameters. This model can also serve as a template to test the advantages of biologically inspired architectures and learning rules compared to traditional deep learning models.

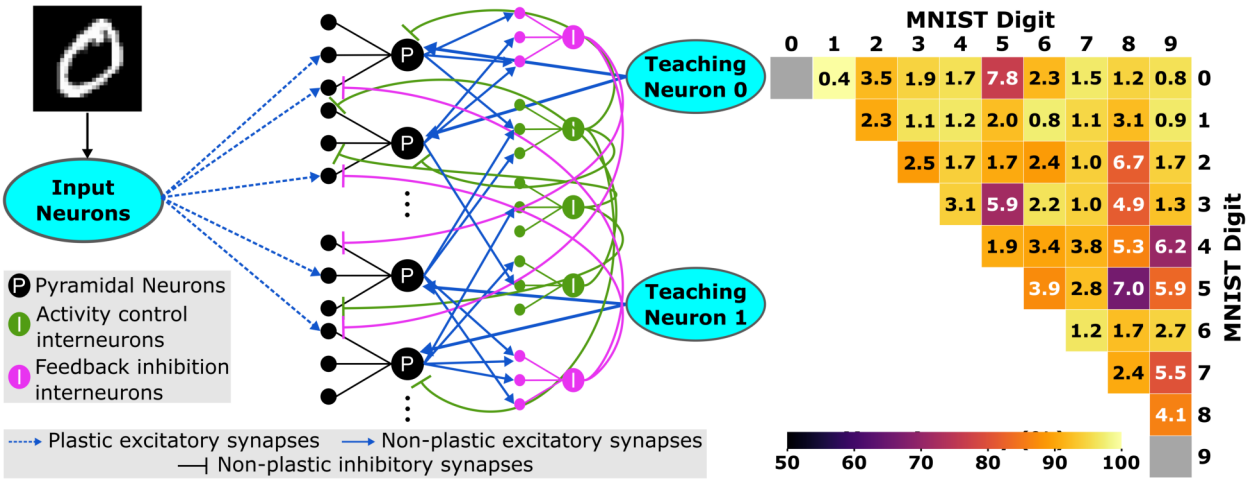


Figure 1. (**Left**) The Spiking Neural Network. (**Right**) Mean accuracy for all pairs of digits. Colormap denotes the mean value and text in each box the std across 10 trials.

Reference

1. Kastellakis, Silva, Poirazi, 2016, *Cell Rep.* 17(6):1491–1504

HOMEOSTATIC SYNAPTIC SCALING OPTIMIZES LEARNING IN RANDOM PROJECTIONS MODELS OF LARGE NEURAL POPULATION CODES

Jonathan Mayzel[*], *Elad Schneidman*

Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel
[*]jonathan.mayzel@weizmann.ac.il

Studying and understanding the code of large neural populations hinge on learning accurate statistical models of population activity. For small groups of neurons, the minimal models that use pairwise relations between neurons or a small set of higher-order features, proved to be surprisingly accurate. It has been unclear, however, how to scale such models to larger populations. Recently, a new class of models, based on sparse nonlinear random projections of the population (RP) [1], was shown to be highly accurate, efficient, and scalable. Interestingly, these models can be implemented by a simple biologically plausible shallow neural circuit. Moreover, adding biologically inspired mechanisms to these models makes them even more accurate and efficient. We therefore ask whether RP models can be further improved by copying more biological mechanisms or characteristics.

We present a new class of models for the spiking patterns of large neural populations, extending the RP models by optimizing or "reshaping" the randomly selected sparse projections (Fig. 1A). This reshaping of projections is akin to changing synaptic connections in the shallow neural network that can implement this model. Applied to recordings of tens of cortical neurons from behaving monkeys, we show these Reshaped Random Projections models to be more accurate and efficient than state-of-the-art RP models (Fig. 1B). We then show that adding biological constraints to the learning process further improves the Reshaped RP models. Specifically, we show that bounding synaptic weights results in poor performance of these models, but, surprisingly, learning reshaped models with homeostatic synaptic scaling (inspired by Turrigiano's work [2]), result in highly efficient and accurate models, surpassing even unconstrained reshaping (Fig. 1B). Thus, our results present a new class of biologically-inspired accurate, scalable, and efficient models for large neural population activity and suggest a key functional role for homeostatic scaling in neural circuits: optimizing performance and minimizing synaptic costs.

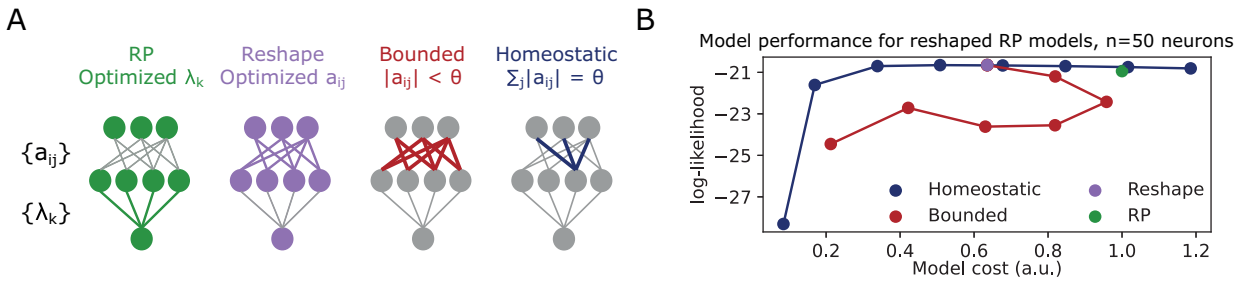


Figure 1. (**A**) Schematics of the shallow network implementations of the RP and Reshaped RP models, and the features or parameters of the models that are learned in each case. (**B**) Average performance of RP and the different RP models over many groups of 50 neurons, using test data of prefrontal cortex neurons, is shown as a function of models cost in terms of total synaptic weights $\sum_{ij}|a_{ij}|$. Homeostatic models are the most accurate and most efficient ones.

References

1. Maoz, Tkaèik, Esteki, *et al.*, 2020, *PNAS* 117(40):25066–73
2. Turrigiano, 2008, *Cell* 135(3):422–35

TOWARDS HIERARCHICAL PREDICTIVE CODING WITH SPIKING NEURONS AND DENDRITIC ERRORS

Fabian A. Mikulasch[1,*], *Lucas Rudelt*[1], *Michael Wibral*[2], *Viola Priesemann*[1,3]

[1] Max-Planck-Institute for Dynamics and Self-Organization, Goettingen, Germany
[2] Georg-August University, Goettingen, Germany
[3] Bernstein Center for Computational Neuroscience (BCCN), Goettingen, Germany
[*] fabian.mikulasch@ds.mpg.de

Cortical feedback connections guide sensory processing by providing top-down expectations. An open question is how these computations are implemented by cortical spiking neurons. Here, we derived a new model of hierarchical predictive coding (hPC) in cortex, which builds on the computation of prediction errors in dendrites of spiking neurons [1,2] (A). Our model connects ideas from hPC [3] to models of efficient spike coding and neural sampling [1], and is consistent with many aspects of cortical connectivity, dynamics and plasticity.

An important question for our model is how it can explain observations of mismatch responses in cortex [4] (B,C,D). In hPC these typically have been explained with specialized error neurons [4], which are not present in our model. In simulations we show that mismatch responses arise in the prediction neurons of our model, when multiple populations learn to encode the same signal, *i.e.* due to *explaining away* (D). Our results suggest that V1 optic flow mismatch responses [4] are not error signals, but represent aspects of sensory data that are independent of a subjects own actions; *i.e.* mismatch responses encode the motion of objects that are independent of the egomotion of the subject. This can be tested directly, by disabling the influence of higher-level visual areas on V1, as these areas are expected to have opposite impacts on error or prediction neurons. Overall, our model connects high-level hierarchical computations in cortex to microscopic voltage dynamics and plasticity in individual dendrites.

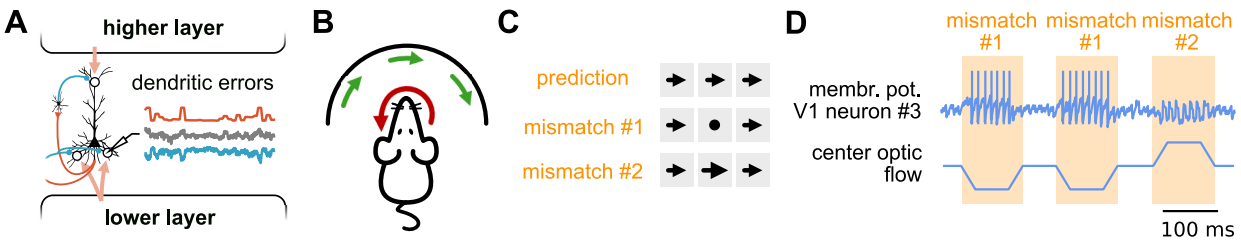


Figure 1. (**A**) Proposed hierarchical coding model where errors are computed at neural apical and basal dendrites via a balance of excitatory and inhibitory currents. (**B**) Experimental setup in [4]. A mouse moves freely in a virtual environment. (**C**) Egomotion of the mouse predicts a specific optic flow pattern, which can be conflicting with the displayed optic flow. (**D**) In V1 pyramidal cells mismatch responses can be observed, which signal the deviation of observation from prediction [4]. In our model we can reproduce this effect (depicted here), when V1 neurons learn to encode a residual signal that is not predicted from egomotion.

References

1. Mikulasch, Rudelt, Priesemann, 2021, *PNAS*, 118(50)
2. Urbanczik, Senn, 2014, *Neuron*, 81(3):521–528
3. Rao, Ballard, 1999, *Nat. Neurosci.*, 2(1):79–87
4. Jordan, Keller, 2020, *Neuron*, 108(6):1194–1206

THE ROLE OF MOTOR CORTEX IN MOTOR SEQUENCE EXECUTION DEPENDS ON DEMANDS FOR FLEXIBILITY

Kevin G. C. Mizes[1,*], *Bence P. Ölveczky*[2]

[1] Biophysics, Harvard University, Cambridge, USA
[2] Organismic and Evolutionary Biology, Harvard University, Cambridge, USA
[*] kmizes@g.harvard.edu

Our ability to flexibly combine elementary movements into complex sequences enables our rich behavioral repertoire. For example, a concert pianist can play a never-before-seen sonata from 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 and robust to mistakes. The neural circuits underlying automatic motor sequences are thought to differ from those underlying flexible ones, but this distinction is poorly understood.

In particular, motor cortex is widely believed to play a central role in the acquisition and execution motor sequences, but its exact role is much debated. In one hypothesis, motor cortex develops sequence specificity following extensive practice [1], where neurons activate for motor elements only when executed as part of an automatized sequence, and not when performed flexibly or in isolation. Alternatively, complex sequences may be organized elsewhere, and motor cortex executes only the motor elements, regardless of the sequence or context [2,3]. Further confusion stems from experiments that found motor cortex is completely disposable for the execution of a well-practiced skill [4], suggesting these encoding schemes become redundant following automatization.

To address this, we trained rats to execute sequences of three lever presses in both flexible sessions, where cues instruct the sequence order, and automatic ones, where a single uncued sequence is repeated. Many single neurons in motor cortex exhibited differential activity across flexible and automatic execution. However, this difference was encoded primarily in the gain, and firing patterns were still tightly locked to particular phases of the motor sequence, irrespective of the execution context. Population activity was thus highly correlated across flexible and automatic execution. Across the different flexible sequences, we found neurons that encoded individual motor elements, but this representation generalized across sequences, inconsistent with expectations from sequence selectivity.

To test the causal role of motor cortex in flexible and automatic movements, we performed excitotoxic lesions in expert rats. Lesions disrupted flexible execution, indicating motor cortex's vital role in sequencing motor elements. Intriguingly, automatic motor sequences were also affected by motor cortex lesions, inconsistent with a previous result [4]. As a control, we trained a separate cohort of rats to only perform the well-practiced movement, with no demands for flexibility. Remarkably, this cohort was more resilient to motor cortex lesions. Together, these results suggest that flexible performance can interfere with subcortical consolidation of an automatic movement and render it vulnerable to motor cortex lesions.

References

1. Karni, Meye, Jezzard, *et al.*, 1995, *Nature* 377(6545):155–8, 10.1038/377155a0
2. Mushiake, Inase, Tanji, 1991, *J. Neurophysiol.* 66(3):705–18, 10.1152/jn.1991.66.3.705
3. Zimnik, Churchland, 2021, *Nat. Neurosci.* 24(3):412–424, 10.1038/s41593-021-00798-5
4. Kawai, Markman, Poddar, *et al.*, 2015, *Neuron* 86(3):800–12, 10.1016/j.neuron.2015.03.024

A NOVEL AND HIGHLY SENSITIVE STATISTICAL TEST FOR CALCIUM IMAGING

Jorrit S. Montijn[*], *J. Alexander Heimel*

CSF group, Netherlands Institute for Neuroscience, Amsterdam, The Netherlands
[*]j.montijn@nin.knaw.nl

Neurophysiological studies depend on a reliable quantification of whether and when a neuron responds to stimulation. In calcium imaging data, a standard approach is to test all cells for stimulus responsiveness and include only those that are significantly modulated. New recording techniques, such as wide-field and multi-plane imaging, yield increasingly large numbers of cells, and such data sets may benefit from a test for neuronal responsiveness that requires no arbitrary parameters, binning, or manual curation. We recently proposed a novel statistical test for electrophysiological spiking data: the ZETA-test [1]. While this test works well for spiking data and outperforms model-based approaches, *t*-tests, and ANOVAs, it can only be applied to point events, such as spike times.

Building on this prior work, we present a new method that solves this drawback and can be applied to time-series data, such as calcium imaging dF/F0 traces: the time-series (TS)-ZETA test. To summarize the method, we take the following steps. (*i*) We have to ensure that time is contiguous [1], so we create a pseudo data set by stitching the end of one trial to the beginning of the next trial. (*ii*) We construct a reference time vector over the window of interest (*e.g.*, −3 to +3 seconds after stimulus onset), using across-trial delay differences to achieve a higher temporal resolution. For each trial, we interpolate the values to this reference vector. (*iii*) We take the average across all trials, and calculate the cumulative sum of average dF/F0 values. Then we subtract from this cumulative sum a linear curve (representing dF/F0 values that are static over time), which gives us a deviation from a null-hypothesis curve. (*iv*) We jitter the stimulus onsets and repeat step three 250 times to obtain a sample of null-hypothesis deviation curves under the assumption that the neuron's dF/F0 values are not temporally modulated by the stimulus. (*v*) For each deviation curve, we take the maximum absolute value, and compare the real absolute deviation to those obtained after jittering using extreme value theory. Quantifying the sensitivity of the TS-ZETA test, we found it performs significantly better than alternative, commonly used approaches, such as *t*-tests (Fig. 1).

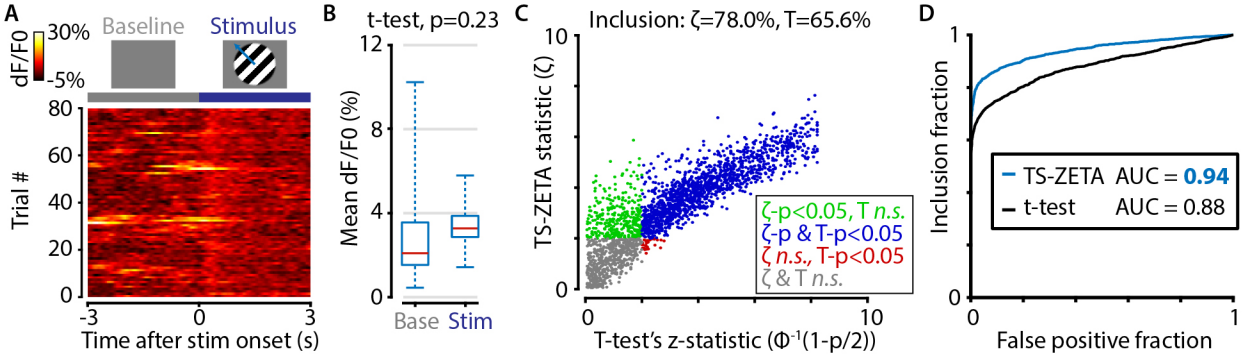


Figure 1. Overview of the TS-ZETA test. (**A**) An example cell's activity recorded in response to drifting gratings; it shows a clear response, but also variable spontaneous activity. (**B**) Spontaneous activity leads a *t*-test to erroneously classify this cell as non-responsive. (**C–D**) Benchmarking the performance of our TS-ZETA test on 2430 cells, we found it includes more cells than a *t*-test at a similar false positive rate (TS-ZETA, AUC = 0.94; *t*-test, AUC = 0.88).

Reference

1. Montijn, Seignette, Howlett, *et al.*, 2021, *eLife*, 10, e71969

DEVELOPING A NETWORK ENCODING MODEL FOR NATURAL BEHAVIOR IN MOTOR CORTEX OF THE UNCONSTRAINED MARMOSET

Dalton D. Moore[1,*], *Jeffrey D. Walker*[2], *Paul Aparicio*[2], *Jason N. MacLean*[1,3,4], *Nicholas G. Hatsopoulos*[1,2,4]

[1] Committee on Computational Neuroscience, University of Chicago, Chicago, USA
[2] Dept. of Organismal Biology and Anatomy, University of Chicago, Chicago, USA
[3] Department of Neurobiology, University of Chicago, Chicago, USA
[4] University of Chicago Neuroscience Institute, Chicago, USA
[*] daltonm@uchicago.edu

Neural control of reaching has been studied through both single neuron activity and population dynamics. While studies of single neurons often miss broader activity patterns across a population, studies of population dynamics struggle to explain the role of individual neurons in producing such patterns. Here, we combine a temporally extended single neuron kinematic encoding model with a functional network approach to place single neuron properties in the context of population dynamics.

Two common marmosets (1 male and 1 female) were chronically implanted with one multi-electrode array each (one 96-channel Utah array and one 96-channel N-Form array) and equipped with a custom headstage assembly for wireless neural recordings [1]. The marmosets engaged in foraging or prey capture as synchronized neural and video data were collected. DeepLabCut with Anipose was used to track the marmoset forelimb and perform 3D pose estimation [2,3].

To model the encoding properties of individual neurons as a function of hand trajectories, we built a generalized linear model (GLM). Preliminary findings on a small neural population show that this trajectory-based model outperforms a direction-tuning model on held-out test data, confirming past results [4]. We will extend these results to a dataset of >130 single units recorded from sensorimotor cortex with the Utah array and to a second dataset from the N-Form array that will provide recordings from both superficial and deep layers of primary motor cortex. We will then incorporate network activity in the model by adding functionally connected neurons as covariates, with interaction weights taken from a computed functional network [5]. Finally, we will use a leave-one-out approach to probe the effects of kinematics and network interactions on singe neuron encoding. This work places single neuron encoding properties in the context of broader population activity patterns.

Acknowledgments

This work has been supported by NIH R01NS104898, and NIH F31NS118950.

References

1. Walker, Pirschel, *et al.*, 2021, *Cell Rep.* 36(2), 10.1016/j.celrep.2021.109379
2. Mathis, Mamidanna, *et al.*, 2018, *Nat. Neurosci.* 21, 10.1038/s41593-018-0209-y
3. Karashchuk, Rupp, *et al.*, 2021, *Cell Rep.* 36(13), 10.1016/j.celrep.2021.109730
4. Hatsopoulos, Xu, Amit, 2007, *J. Neurosci.* 27(19), 10.1523/JNEUROSCI.3570-06.2007
5. Kotekal, MacLean, 2020, *PLoS Comput. Biol.* 16(1), p.e1007591

DIFFERENT CORTICAL STATES EMERGE AROUND SPONTANEOUS ACTIVATIONS OF DISTINCT LOCUS COERULEUS ENSEMBLES

Shahryar Noei[1,2], *Ioannis S. Zouridis*[3], *Nikos K. Logothetis*[3,4], *Stefano Panzeri*[1,5,*], *Nelson K. Totah*[3,6,*]

[1] Neural Computation Laboratory, Istituto Italiano di Tecnologia, Rovereto, Italy
[2] Center for Mind/Brain Sciences, Università di Trento, Rovereto, Italy
[3] Dept. of Physiol. of Cog. Processes, MPI Biological Cybernetics, Tübingen, Germany
[4] Cntr. for Excellence in Brain Science and Intelligence Technology, Shanghai, China
[5] Dept. of Excellence for Neural Information Processing, UKE, Hamburg, Germany
[6] Helsinki Institute of Life Science (HiLIFE), University of Helsinki, Helsinki, Finland
[*] nelson.totah@helsinki.fi, s.panzeri@uke.de

Various states of wakefulness, perceptual ability, and locomotor activity are associated with different cortical states defined by local field potential (LFP) oscillatory content. The brainstem nucleus, Locus Coeruleus (LC), contributes to cortical state via noradrenergic projections to nearly the entire central nervous system. Electrical or optogenetic LC stimulation evokes increased high-frequency (HF, >20 Hz) cortical LFP oscillations and decreased low-frequency (LF, <12 Hz) oscillations in anesthetized and non-anesthetized experiments and evokes awakening in sleeping mice. The LC stimulation-evoked cortical state is due to highly synchronous whole-LC neuronal activation because about 1600 neurons are densely packed into only about $200 \times 500 \times 1000\mu$m (in rats) and stimulation even at the lower end of the current range used in these studies (30–50μA) evokes spikes 400um from the stimulation site. These studies established the conceptual model that LC generates a single aroused cortical state.

Recently, however, recordings of spontaneous LC single unit spiking demonstrated that pairs of LC neurons have sparse, yet structured time-averaged cross-correlations that are uncharacteristic of the en masse population event elicited by LC stimulation. It remains unknown whether spontaneous LC population activity consists of multi-cell ensembles or how LC ensemble activity evolves over time. Here, we used non-negative matrix factorization (NMF) to analyze large populations of simultaneously recorded LC single units in the urethane anesthetized rat. NMF, unlike traditional time-averaged pairwise correlations, detects the precise neuronal composition of LC ensembles and the evolution of their activity over time. We found that LC population dynamics consists of ensembles of co-active neurons with largely non-overlapping activation dynamics.

We then characterized the relationship between LC ensemble activation dynamics and cortical state. We calculated cortical LFP (area 24a) band-limited power and spectrograms aligned to spontaneous activations of LC ensembles. Spontaneous activation of distinct LC ensembles was associated with a diverse pool of cortical states. Depending on which LC ensemble fired, we observed a diverse state space of increased HF and LF, decreased HF and LF, and opposing HF and LF power. Thus, LC is not simply a switch controlling a single arousal-associated cortical state.

Acknowledgments

Supported by Univ. of Helsinki and Dept. of Physiol. Of Cog. Processes, MPI-Biol. Cyb.

FLEXIBLE NEURAL CODING IN SENSORY, PARIETAL, AND FRONTAL CORTICES DURING GOAL-DIRECTED VIRTUAL NAVIGATION

Jean-Paul Noel[1,*], *Edoardo Balzani*[1], *Eric Avila*[1], *Kaushik Lakshminarasimhan*[2], *Stefania Bruni*[1], *Panos Alefantis*[1], *Cristina Savin*[1], *Dora E. Angelaki*[1]

[1] Center for Neural Science, New York University, New York City, USA
[2] Center for Theoretical Neuroscience, Columbia University, New York City, USA
[*] jpn5@nyu.edu

The complex behaviors we ultimately wish to understand are far from those most often studied in systems neuroscience. A major differentiator between laboratory tasks and real-world cognition is the presence of closed action-perception loops in the latter and not the former.

Accordingly, we have developed a *firefly task*, wherein macaques must memorize the location of a briefly presented target that appears much like the flash of a firefly, and then use a joystick controlling linear and angular velocity in virtual reality to actively path integrate to the location of the target, metaphorically catching the no longer visible firefly. We have shown that within this closed-loop setting with intuitive physics, animals naturally develop intelligent task strategies [1] and are able to generalize to variants of the task with different sensorimotor contingencies, as well as demonstrate decision-making and inference [2]. Here, we present the first neural results from this firefly task.

We recorded single units simultaneously from dorsomedial superior temporal area (MSTd), parietal area 7a, and dorsomedial prefrontal cortex (dlPFC) as monkeys performed the task. We observed mixed selectivity in all areas, with even MSTd tracking latent variables (*e.g.*, distance to target). Strikingly, global encoding profiles and unit-to-unit coupling suggested a functional subnetwork between MSTd and dlPFC, and not between these areas and parietal area 7a, as anatomy and traditional laboratory tasks would suggest. When sensory evidence was rendered scarce, arguably requiring animals to further rely on their internal models rather than incoming sensory evidence, lateral connectivity within MSTd strengthened but its pattern remained fixed. Instead, neuronal coupling adaptively remapped within 7a and dlPFC. The larger the remapping in 7a/dlPFC and the greater the stability within MSTd, the less behavior was impacted by loss of available sensory evidence.

Overall, our results highlight the distributed nature of neural coding during closed-loop action-perception and suggest that internal models may be housed in the pattern of fine-grain lateral connectivity within parietal and frontal cortices. In ongoing work, we are examining how fine-grain patterns of lateral connectivity drive population dynamics within this active sensing framework.

References

1. Lakshminarasimhan, Avila, Neyhart, *et al.*, 2020, *Neuron*, 10.1016/j.neuron.2020.02.023
2. Noel, Caziot, Bruni, *et al.*, 2021, *Prog. Neurobiol.*, 10.1016/j.pneurobio.2021.101996

RIVAL NETWORKS: CORTICAL CIRCUIT OF BI-STABLE VISUAL PERCEPTION

Ganna Palagina[1–3,*], *Daria Bogatova*[1], *Stelios M. Smirnakis*[1–3]

[1] Brigham and Women's Hospital, Boston, MA, USA
[2] Harvard Medical School, Boston, MA, USA
[3] Jamaica Plain VA Hospital, Jamaica Plain, MA, USA
[*] gpalagina@bwh.harvard.edu

Sensory stimuli are inherently ambiguous, and their perception is a probabilistic process reflecting the most likely interpretation of the inputs. Understanding how the brain selects the correct interpretation to guide the behavior and then maintains this interpretation across environmental changes is central to our understanding of the brain as a decision-making machine. Bistable visual perception, when unchanging visual stimulus results in subjective perception vacillating between two mutually exclusive interpretations of the input, offers a well-controlled model for the study of percept formation and maintenance. At this moment we lack precise mechanistic understanding of the canonical computations that underlie perceptual transitions and percept maintenance.

We set out to bridge this gap starting with identification of large-scale distributed motifs of cortical neuronal population activity during bistable visual perception and deciphering the circuit structure that generates these motifs at single cell resolution. For this approach, we developed a bi-stable perception task in the mouse, based on plaid patterns consisting of two transparent gratings drifting at an angle of 120° relative to each other [1]. These stimuli result in the spontaneous reversals of the visual percept between pattern motion (a *coherent* percept) and component grating motion (a *transparent* percept). An advantage of this paradigm is that it is robust and does not depend on the explicit report of the mouse, as the direction of the nystagmus (rapid eye movements elicited by following pattern or component motion) is used to infer the dominant percept.We combined this paradigm with mesoscopic single-cell resolution 2-photon imaging of the cortical hemisphere [2], simultaneously following the neurons of the visual cortical hierarchy (V1, visuomotor and visual association areas VRL and VA), retrosplenial cortex, motor cortex (M1) and secondary motor area MOs.

We found two distinct distributed subnetworks of neurons: (i) stimulus interpretation-selective subnetworks, predominantly located in V1 and secondary visual areas, and (ii) perceptual reversal-locked cortex-wide subnetwork, comprised of diverse interneurons (SST+ cells, layer 1 cells) and pyramidal cells, distributed across both visual and higher-order areas such as retrosplenial cortex and MOs. Up to approximately 30% of neurons are reversal-yoked, ramping up their response as early as 10 seconds before the reversal, peaking just prior to or during the reversal saccade. We propose that the reversal is initiated by periodic activation of reversal subnetwork and is passed down from higher-order areas to sensory areas' local circuits via long-range feedback and area-wide coupling of SST+ interneurons.

Acknowledgments

Supported by NEI-NIH R21 EY031537.

References

1.Palagina, *et al.*, 2017, *J. Neurosci.*, 37:164–183
2.Sofroniew, *et al.*, 2016, *eLife*, 5:e14472.

PREFRONTAL THETA OSCILLATIONS SHAPE V4 GAMMA MODULATION DURING SPATIAL ATTENTION

Sofia Paneri[1,2,*], *Panagiotis Sapountzis*[2], *Georgia G. Gregoriou*[1,2]

[1] Faculty of Medicine, University of Crete, Heraklion, Greece
[2] Foundation for Research and Technology-Hellas (FORTH), Heraklion, Greece
[*] s.paneri@med.uoc.gr

Selective attention is central to cognition and adaptive behavior. Numerous studies have shown that attention has a profound influence on the representation of stimuli in the brain by selectively enhancing the representation of behaviorally relevant stimuli and suppressing the representation of distracting stimuli. The prefrontal cortex is considered to play a central role in this process with the frontal eye field (FEF) being a source of spatial attention signals that bias activity in visual areas in favor of attended stimuli. However, it is largely unknown whether prefrontal regions anterior to the FEF contribute to this process and through which mechanism.

To examine the role of ventrolateral prefrontal cortex (vlPFC) in spatial attention, we performed simultaneous extracellular recordings with multiple electrodes from vlPFC and V4 in two macaques engaged in a covert spatial attention task. Monkeys were presented with an array of four gratings and were subsequently instructed by a central spatial cue to covertly attend to one of them and report its orientation using a joystick. We recorded both spikes and local field potentials (LFPs).

Spiking activity was modulated by spatial attention in both areas but attention effects emerged significantly earlier in vlPFC compared to V4. Moreover, within V4, LFP power and spike-LFP coherence were significantly enhanced by spatial attention in gamma frequencies (above 30 Hz) and they were reduced in low frequencies (4–30 Hz). Within vlPFC, theta power and coherence (4–8 Hz) were significantly enhanced with attention. Across the two areas, phase coupling was found both in the theta and gamma bands with attention. Results from spike-LFP coherence between V4 and vlPFC and a Granger causality analysis between LFPs indicated a vlPFC origin for theta interactions and a V4 origin for gamma interactions. Notably, attentional effects in theta and gamma V4-vlPFC coherence showed a significant positive correlation indicating a theta-gamma band interdependence. Effects in theta band coherence emerged significantly earlier compared to gamma band coherence. Within V4, theta-gamma phase-amplitude coupling was stronger with attention outside the receptive field suggesting a mechanism that mediates the filtering of unattended stimuli. These results indicate that vlPFC originating coupling in theta frequencies with V4 provides a possible mechanism for the attentional modulation of gamma synchrony in V4.

Acknowledgments

This research was co-financed by Greece and the European Union (European Regional Development Fund) through the Operational Programme “Competitiveness Entrepreneurship Innovation 2014–2020” in the context of project MIS 5070462.

EMPIRICAL ABSENCE OF SHORT CYCLIC MOTIFS IN THE HUMAN CORTICAL MICROCIRCUIT AND ITS COMPUTATIONAL IMPLICATIONS

Yangfan Peng[1], *Antje Bjelde*[1], *Pau Vilimelis Aceituno*[2,*], *Benjamin Grewe*[2], *Jörg Geiger*[1],

[1] Charité-Universitätsmedizin Berlin, Institut für Neurophysiologie, Berlin, Germany
[2] Institute of Neuroinformatics, University of Zürich and ETH Zürich, Zürich, Switzerland
[*] pau@ini.uzh.ch

We explore the network architecture of the human cortex, where we find a significant under-representation of cycles. Similarly to previous works that relate network motifs to activity dimensionality [1], here show that this almost acyclic architecture can increase the entropy of the neural activity in a recurrent neural network model and lead to improved task performance in a speech recognition task.

We study the microcircuit-level synaptic network in the layer 2/3 of medial temporal lobe of human cortex by probing synaptic connections between pyramidal neurons from human tissue. We compare the networks obtained to various random network models by studying their motifs [2]. We find that we can account for most motif abundances, except for an under-representation of short cyclic motifs.

We investigate the computational effects of this absence of cycles by using a recurrent neural network model. The absence of cycles alters the eigenvalues of the adjacency matrix [3], increasing the entropy of the state space of the neural activity. For a practical interpretation of this result, we use a reservoir computing set-up to show that this increase in entropy improves the performance of a neural network in speech recognition [4]. This same architecture has no effect in low-dimensional tasks (chaos forecasting), hence it seems to be important mostly for tasks requiring rich information content.

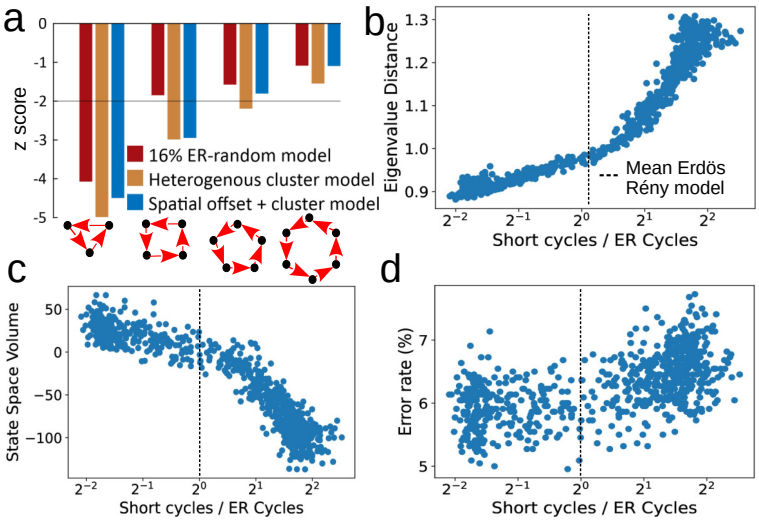


Figure 1. (**A**) difference between the circulant motifs found in the data vs those expected in three different network models. (**B**, **C**, **D**) we plot different metrics vs the number of short cycles divided by those expected in an Erdös Rény graph.

Acknowledgments

PVA is supported by an ETH Postdoctoral fellowship, YP is supported by the DFG Walter Benjamin Fellowship.

References

1. Recanatesi, Ocker, Buice, Shea-Brown, 2019, *PLoS Comput. Biol.*, 15(7), e1006446
2. Song, Sjöström, Reigl, *et al.*, 2005, *PLoS Biol.*
3. Vilimelis Aceituno, Rogers Schomerus, 2019, *Phys. Rev. E* 100.1
4. Vilimelis Aceituno, Gang, Liu, 2020, *Science* 23.9

UNSUPERVISED INFERENCE OF BRAIN-WIDE FUNCTIONAL MOTIFS UNDERLYING BEHAVIORAL STATE TRANSITIONS

Matthew G. Perich[1,2,*], *Tyler Benster*[3], *Aaron Andalman*[3], *Eugene Carter*[1], *Kanaka Rajan*[1], *Karl Deisseroth*[3]

[1] Icahn School of Medicine at Mount Sinai, New York, NY, USA
[2] Université de Montréal, Montréal, Canada
[3] Stanford University, Stanford, CA, USA
[*] matthew.perich@umontreal.ca

The neural control of behavior is distributed across many functionally and anatomically distinct regions of the brain. While classical neuroscience models treated these regions as a set of hierarchically isolated nodes, the brain comprises a recurrently interconnected network in which each region is intimately modulated by many others. Modern experimental techniques allow access to large neural populations from many brain regions simultaneously, yet harnessing these large-scale datasets requires new theoretical approaches. Here, we present a unique, unsupervised pipeline to parcellate multi-region recordings, even brain-wide, and identify interpretable latent structure.

We applied our method to longitudinal, whole-brain, cellular-resolution neural recordings from larval zebrafish in the face of persistent, inescapable stress [1]. The animals underwent behavioral state transitions from active to passive coping strategies to manage effort expenditure. We applied our method to disentangle both the spatial and temporal dependencies of the neural mechanisms driving behavioral state transitions using computational models directly constrained by the recorded neural data. In brief, 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 and inter-region currents [1] with tensor decomposition 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 [2] — 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 numerous other regions, including dorsal thalamus and telencephalon, to drive the transition from active to passive coping.

This method provides an unbiased mechanistic framework to disentangle the simultaneous encoding of behaviorally-relevant signals across interacting regions brain-wide. Our results demonstrate that behavioral state transitions require simultaneous integration of inputs from distinct networks over slow timescales.

References

1. Andalman, *et al.*, 2019, *Cell* 177(4):970–985, 10.1016/j.cell.2019.02.037
2. Dolzani, *et al.*, 2016, *eNeuro* 3(5), 10.1523/ENEURO.0229-16.2016

ABSTRACT CATEGORY ENCODING IN PRIMATE OCULOMOTOR CIRCUITS: A NOVEL ROLE OF THE SUPERIOR COLLICULUS IN HIGHER-ORDER COGNITION

Barbara Peysakhovich[*], *Stephanie Tetrick, Ou Zhu, Guilhem Ibos, W. Jeffrey Johnston, David J. Freedman*

Department of Neurobiology, University of Chicago, Chicago, IL, USA
[*]bpeysakhovich@uchicago.edu

Animals have a remarkable ability to categorize complex stimuli into behaviorally meaningful groups. Investigations of visual categorization in primates have focused on a hierarchy of cortical areas that transform 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 cognition. One candidate structure is the superior colliculus (SC), a brainstem region that is evolutionarily conserved across vertebrates. Although traditionally thought to mediate reflexive orienting behaviors such as eye movements [1], the SC is also involved in cognitive tasks that require spatial orienting [2,3]. However, the role of the SC in non-spatial cognitive functions is unknown. Here, we show that the primate SC robustly encodes learned categories during a non-spatial visual categorization task, suggesting that the SC plays an unexpected key role in higher-order cognition.

We trained two monkeys to perform a visual categorization task and compared neuronal population activity in the SC and the lateral intraparietal area (LIP), a cortical region previously shown to causally contribute to categorical decisions [4]. Monkeys learned to group dot motion stimuli into two categories defined by an arbitrary rule. The task required monkeys to maintain fixation on a central cue and to report their decisions with a hand movement. We show that single neurons and neural populations in the SC strongly encode monkeys' categorical decisions. This category encoding in the SC arises with a similar latency to the LIP, is evident during both stimulus viewing and a memory delay period, and is independent of the actions monkeys used to report their decisions.

Our results extend SC's well-established role in spatial orienting functions to abstract, non-spatial cognitive processing, and provide a novel perspective on subcortical contributions to primate cognition. In ongoing experiments, we are reversibly inactivating the SC while simultaneously recording in the LIP to investigate the causal contribution of the SC to categorical decisions and to cortical category encoding.

Acknowledgments

This work has been supported by NIH R01EY019041, NIH F31MH124395, and NIH 5U19NS107609.

References

1. Wurtz, Goldberg, 1971, *Science* 171(3966):82–84, 10.1126/science.171.3966.82
2. Lovejoy, Krauzlis, 2009, *Nat. Neurosci.*, 13(2):261–266, 10.1038/nn.2470
3. Jun, Bautista, Nunez, *et al.*, 2021, *Nat. Neurosci.*, 24(8):1–11, 10.1038/s41593-021
4. Zhou, Freedman, 2019, *Science*, 365(6449):180–185, 10.1126/science.aaw8347

PITFALLS OF INTERPRETING DYNAMICS OF NEURAL ACTIVITY AFTER DIMENSIONALITY REDUCTION

Timothée Proix[1,*], *Matthew G. Perich*[2], *Tomislav Milekovic*[1,3,4]

[1] Dept. Fundamental Neurosci., Faculty of Medicine, Univ. of Geneva, Geneva, Switzerland
[2] Department of Neuroscience, Université de Montréal, Montréal, Canada
[3] Defitech Center for Interventional Neurotherapies, Lausanne, Switzerland
[4] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
[*] timothee.proix@unige.ch

Modern experimental techniques allow researchers to monitor the activity of hundreds to thousands of neurons simultaneously. Analyzing such high-dimensional neural activity is challenging. Dimensionality reduction methods are commonly used to simplify interpretation of this activity. Consistent oscillatory structure in the obtained trajectories is often identified as signatures of the existence of latent oscillatory dynamical systems in the recorded neural population [1]. However, oscillatory structure emerge when applying dimensioxnality reduction methods to data exhibiting continuous variations in time [2], regardless of whether the data incorporates latent oscillatory dynamics or not.

Here, we show that this relationship between the continuous variation in time and low-dimensional oscillatory trajectories can also apply to neural population recordings. We used two datasets recorded with microelectrode arrays in the motor and visual cortex of non-human primates during reaching and visual stimulation tasks respectively. In both datasets, continuous variation in time of the recorded neural activity led to emergence of oscillatory trajectories when analyzed by principal component analysis. To illustrate that oscillatory trajectories are not necessarily a signature of latent oscillatory dynamics, we designed models of neural activity for those experimental tasks. In these models, firing rates exhibited continuous variations in time, but without incorporating any latent oscillatory dynamics. Each model showed high correlation with recorded data, both for the temporal covariance matrices and the latent oscillatory trajectories.

Rather than demonstrating the absence of the latent oscillatory dynamics in the analyzed neural data, our analysis shows that oscillatory trajectories obtained by applying dimensionality reduction techniques cannot be used as evidence of the underlying oscillatory dynamics. Therefore, our results provide a cautionary tale on the risks of overinterpreting observed oscillatory structure.

Acknowledgments

Supported by Whitaker International Scholars Program, Wyss Center for Bio and Neuroengineering, and Swiss National Science, Bertarelli, and Defitech Foundations.

References

1. Churchland, *et al.*, 2012, *Nature*, 487(7405):51–56, 10.1038/nature11129
2. Novembre, Stephens, 2008, *Nat. Genet.*, 40(5):646–649, 10.1038/ng.139

TRACKING NONSTATIONARITY IN MULTI-DAY INTRACORTICAL NEURAL RECORDINGS DURING iBCI USE BY A PERSON WITH TETRAPLEGIA

Tsam Kiu Pun[1,2,*], *Tommy Hosman*[1,2,5], *Anastasia Kapitonava*[6], *Carlos E. Vargas-Irwin*[2,3,5], *John D. Simeral*[1,2,5], *Matthew T. Harrison*[4], *Leigh R. Hochberg*[1,2,5–7]

[1] School of Engineering, Brown University, Providence, RI, USA
[2] Carney Institute for Brain Science, Brown University, Providence, RI, USA
[3] Dept. of Neuroscience, Brown University, Providence, RI, USA
[4] Div. of Applied Math, Brown University, Providence, RI, USA
[5] VA RR&D Ctr. for Neurorestoration and Neurotech., Dept. VA Med. Ctr., Providence, RI, USA
[6] Ctr. for Neurotechnology and Neurorecovery, Dept. of Neurology, MGH, Boston, MA, USA
[7] Dept. of Neurology, Harvard Medical School, Boston, MA, USA
[*] tsam_kiu_pun@brown.edu

Intracortical brain-computer interface (iBCI) has enabled individuals with tetraplegia to control external devices via decoding movement intentions from neural recordings. However, neural activity underlying consistent motor intentions varies over time due to changes in recording conditions, cognitive states, etc. Within- and across-day nonstationarity in the relationship between neural activity and intended movements can lead to a drop in performance if the decoder is fixed or not robust against such changes. To translate iBCIs for practical everyday use, we demonstrate a robust online long-short term memory (LSTM) decoder for human iBCI use for over three months. We also propose a statistical method to predict when the decoder should be updated solely based on neural activities and decoder outputs, agnostic to the decoder performance.

Neural activity was recorded with two Blackrock Utah microelectrode arrays from the hand-arm area of the precentral gyrus of a participant, T11, who is a 37-year-old male with C4 AIS-B spinal cord injury. Threshold crossing and spike power were extracted per electrode. We trained a LSTM model with recordings from 20 prior sessions of T11 completing point-and-select tasks (trial days 576–646). We analyzed 1832 trials in a closed-loop radial-8 task in 15 sessions (trial days 658–800). The same decoder achieved a mean 93.8% success rate in the first 11 sessions without parameter updates, but subsequently to 33.1% in later sessions. In addition, Bhattacharyya distance and Kullback-Leibler divergence on sampled neural features and decoder outputs are highly correlated with the online cursor angular error ($r = 0.951$, Pearson's coefficient). This suggests that they are sensitive to changes that affect decoder performance, and sufficiently specific to ignore changes that the decoder does not concern. These metrics may be effective to track nonstationarity online and be useful for triggering either a user-engaged or background update for the decoder prior to its anticipated degradation.

Acknowledgments

Research supported by the Office of Research and Development, Rehabilitation R&D Service, Dept of Veterans Affairs (N2864C, A2295R), NIH NIMH (T32MH115895), and the Croucher Foundation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, Dept of VA or the US Gov.

EMERGENCE OF SPARSE UNIT-LEVEL REPRESENTATIONS YET INCREASED POPULATION DIMENSIONALITY IN BRAIN COMPUTER INTERFACE LEARNING

Pavithra Rajeswaran[1,*], *Alexandre Payeur*[2], *Jose M. Carmena*[3], *Guillaume Lajoie*[2], *Amy L. Orsborn*[1,4,5]

[1] Dept. Bioengineering, University of Washington, Seattle, WA, USA
[2] Dept. Math. and Statistics, Université de Montréal, Mila – Québec AI Institute, Montreal, Canada
[3] Dept. Electrical Engineering and Computer Science, University of California, Berkeley, CA, USA
[4] Dept. Electrical and Computer Engineering, University of Washington, Seattle, WA, USA
[5] Washington National Primate Research Center, Seattle, WA, USA
[*] pavir@uw.edu

Brain-Computer Interfaces map recorded neural activity (readouts) to behavior through an experimenter-defined transformation (decoder). Studies using fixed decoder mappings show differential modulation of readout neurons relative to non-readout neurons with learning, suggesting neural populations perform a form of credit assignment during learning. Credit assignment has primarily been studied via single-unit encoding analyses [1]. Here, we ask how single-unit changes in task participation influence population dynamics by quantifying BCI credit assignment learning at both the single unit and population level.

We analyzed neural activity as a monkey learned to control a 2D BCI cursor across 16 days [2]. The decoder was intermittently modified during training with closed-loop decoder adaptation (CLDA) [2]. 78 motor cortex multi-units were recorded, from which 20 readout units were used for cursor control. We analyzed single-unit changes in task representations using a multi-class logistic regression model. Population dynamics were quantified by computing the neural ensemble dimensionality using participation ratio [3].

Single-unit analyses replicated past findings, with readout units becoming more predictive with learning (Prediction accuracy on Day 16 (readout, non-readout): $89.34 \pm 3.6\%$, $52.22 \pm 9.8\%$; Day 2: $56.69 \pm 3.9\%$, $52.99 \pm 9.4\%$). Indeed, single-unit analyses show an emergence of sparse control strategies (fewer neurons required to achieve 80% normalized prediction accuracy, Day 2 vs Day 16, paired t-test, $p = 0.007$). Despite a reduction in units with task-relevant information, population dimensionality increased within readout ensembles across days for all targets.

Our results show the brain learns stable representations specific to readout ensembles, even in the presence of decoder adaptation. Single-unit dynamics show sparse BCI control strategies within the readout ensemble. Surprisingly, population dimensionality increases. We propose this may indicate that BCI task requirements shape population responses so that neural activity associated with distinct targets becomes more separable. This suggests an important strategy emerging from learning dynamics, whereby activity subspaces are factorized along neural coordinates.

Acknowledgments

Supported by Accelnet INBIC Fellowship funding.

References

1. Gulati, 2017, *Nat. Neurosci.*
2. Orsborn, 2014, *Neuron*
3. Recanatesi, 2019, *PLoS Comput Biol.*

WHICH SPARSITY PROBLEM DOES THE BRAIN SOLVE?

Ilias Rentzeperis[1,*], *Luca Calatroni*[2], *Laurent Perrinet*[3], *Dario Prandi*[1]

[1] Université Paris-Saclay, CNRS, CentraleSupélec, Laboratoire des Signaux et Systèmes
[2] UCA, CNRS, INRIA, Laboratoire d'Informatique, Signaux et Systèmes de Sophia Antipolis
[3] Aix Marseille Univ, CNRS, INT, Inst Neurosci Timone, Marseille, France
[*] ilias.rentzeperis@centralesupelec.fr

Experimental evidence suggests that activity in sensory cortices is sparse in that only few neurons, out of a large pool that could respond to sensed stimuli, are active at a time. Generative learning models that aim to replicate sensory systems could deviate from sparse activity patterns when representing noisy signals. We ask: are there biologically plausible implementations that will maintain sparse activations for different levels of noise while representing the underlying signal? A family of generative algorithms modelling sensory systems represent a stimulus as a linear sum of an overcomplete dictionary of vectors with their corresponding coefficients taking the role of activations. Olshausen and Field [1] showed that a learning algorithm that is set to reconstruct natural images with sparse activations develops vectors with properties, found in the receptive fields of neurons in V1, *i.e.* they are localized, bandpass, and oriented (Fig. 1).

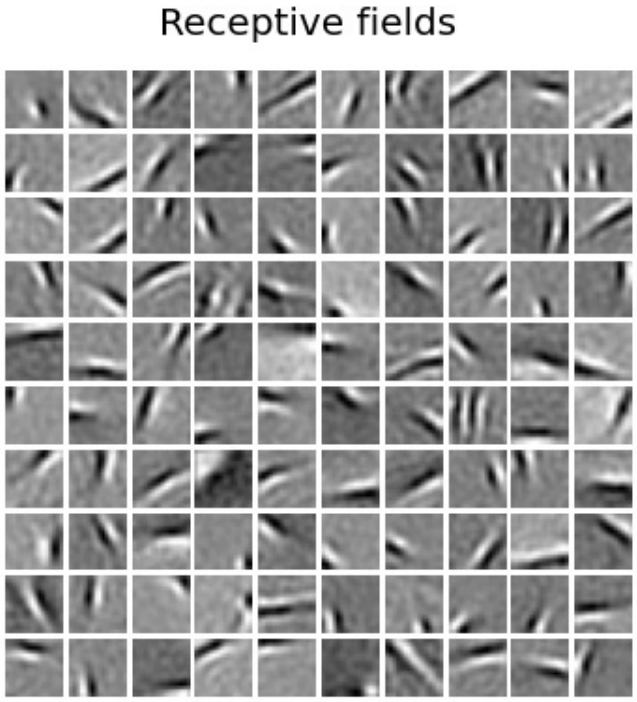


Figure 1. Feature vectors generated with sparse codes are similar to the receptive fields of V1 cells.

The properties emerge by solving an optimization problem which aims to minimize the square error between the actual image and the reconstructed one while keeping the sum of the activities (L1 norm) as small as possible (with the relative weight of the two tasks being controlled by a trade-off parameter). Traditionally, to keep this kind of problems convex we minimize the summation of activations; but an ideal sparsity promoting penalty term would be the minimization of the number of nonzero activations (L0 norm), a change that turns the problem into a nonconvex one. Moreover, when fixed the trade off parameter cannot accommodate the same sparsity for a wide range of noise levels. To remedy these effects we use an adaptable trade-off parameter and an L_p norm with $0 < p < 1$. We discuss possible connections of these tools with brain mechanisms, and assess their effectiveness via various metrics, both at the activation level and at the signal level. In the latter case, we use methods, such as Structural Similarity (SSIM), that take into consideration the perceived visual quality.

Reference

1. Olshausen, *et al.*, 1996, *Nature* 381.

RAPID LEARNING WITH HYPER-LOCALIZED SYNAPTIC PLASTICITY

Matthew C. Rosen[1,†,*], *Nicolas Y. Masse*[1,†], *Doris Y. Tsao*[3,4,5], *David J. Freedman*[1,2]

[1] Department of Neurobiology, University of Chicago, Chicago, IL, USA
[2] Grossman Inst. for Neurosci., Quant. Biology, and Human Behav., U. Chicago, Chicago, IL, USA
[3] Department of Molecular and Cellular Biology, University of California, Berkeley, CA, USA
[4] Helen Wills Neuroscience Institute, University of California, Berkeley, CA, USA
[5] Howard Hughes Medical Institute
[†] equal contribution
[*] mattrosen@uchicago.edu

The brains of all animals are plastic, a feature critical for forming new memories, adaptating to new environments, and learning new tasks. However, plasticity, particularly of synaptic connections, is highly energetically expensive [1] and can overwrite or interfere with prior knowledge [2]. These costs can be mitigated by limiting the scope of synaptic plasticity within a neural network, as in reservoir computing, which employs large, fixed recurrent networks with plastic readout synapses. But reservoir approaches struggle to learn and flexibly switch between complex tasks. We are thus interested in understanding the tradeoffs between rigidity and plasticity in neural networks, and how compartmentalized plasticity can promote context-dependent learning and behavior.

Here, we use biologically-inspired recurrent neural network (RNN) models obeying Dale's principle to show that sparse, localized plasticity (below 0.5% of a network's synapses) can support rapid multitask learning (fewer than 6,000 gradient updates per task). This learning requires highly specific combinations of network properties, such as topology, normalization, and reciprocal connection strength: for networks with 2,500 units, 26 of the hyperparameter combinations we tested ($n \approx 2 \times 10^5$) reached 85% accuracy across all 8 tasks (chance being 12.5%).

Analysis of network activity dynamics suggests that this multi-task learning occurs through a mechanism of error-driven subspace capture. Initially, network activity across all tasks occupies a common, overlapping subspace, precluding context-dependent behaviors. As learning proceeds, activity during each task is progressively sequestered into its own low (below 10) dimensional subspace of network activity, diminishing between-task interference and facilitating reliable, context-dependent readout of different decisions about a single set of stimuli. Importantly, the arrangement of task subspaces reflects both task epoch and task-task similarity. This work suggests that rapid learning in artificial (and potentially biological) agents can be accomplished using localized, highly-constrained synaptic plasticity.

References

1. Li, Van Rossum, 2020, *eLife* 9:e50804
2. Masse, Grant, Freedman, 2018, *PNAS* 115(44), E10467-E10475

FUNCTIONAL SPECIALIZATION AND ADAPTIVE CODING OF TASK RELEVANT ATTRIBUTES IN THE PREFRONTAL CORTEX

Panagiotis Sapountzis[1,*], *Sofia Paneri*[1,2], *Sotirios Papadopoulos*[2,3], *Georgia G. Gregoriou*[1,2]

[1] Foundation for Research and Technology-Hellas (FORTH), Heraklion, Greece
[2] University of Crete, Faculty of Medicine, Heraklion, Greece
[3] Lyon Neuroscience Research Center, Lyon, France
[*] pasapoyn@iacm.forth.gr

Despite the indisputable role of the prefrontal cortex (PFC) in the encoding of task relevant information, it remains unclear how stimulus attributes are encoded across different PFC regions. The prevailing view postulates that PFC neurons are not inherently feature selective, but rather represent task relevant parameters in an adaptive way according to behavioral demands. The degree to which this adaptive processing is constrained by anatomy, however, remains unknown. Moreover, the temporal dynamics of the neural population code during the encoding and maintenance of spatial and non-spatial features have yet to be explored.

To examine how population activity patterns in distinct PFC regions encode task relevant attributes, we performed simultaneous extracellular recordings in two prefrontal areas, the frontal eye field (FEF) and the ventrolateral PFC (vlPFC) in a cued attention task with either a spatial or a color cue. We employed multivariate pattern-classification approaches using spiking and LFP signals, to assess whether encoding of color and spatial information differs within the same and across PFC regions during cue presentation and maintenance of cue information in working memory.

We found that neural ensembles in PFC encode and retain information about the location and the color of a future target in an anatomically specific manner. Specifically, spatial information was decoded from both FEF and vlPFC but with higher accuracy from the FEF population, whereas color information was decoded robustly only from vlPFC during the stimulus presentation and delay periods. Moreover, the population code for color identity was highly dynamic during the delay period in vlPFC whereas the code for location was relatively stable. These results suggest that adaptive coding in PFC is shaped by functional selectivity and can be implemented by different mechanisms for different features even within the same area.

Acknowledgments

This work was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the “1st Call for H.F.R.I. Research Projects to support Faculty Members & Researchers” (Project Number: 41).

TRANSFORMATION OF POPULATION ENCODING IN PREFRONTAL CORTEX AND HIPPOCAMPUS DURING THE LEARNING-TO-LEARN PROCESS

Vinay Shirhatti[1], *Barbara Peysakhovich*[1], *Rheza Budiono*[1], *Vishwa Goudar*[2], *Xiao-Jing Wang*[2], *Elizabeth Buffalo*[3], *David J. Freedman*[1,*]

[1] Department of Neurobiology, University of Chicago, Chicago, USA
[2] Swartz Center for Theoretical Neuroscience, New York University, New York, USA
[3] Department of Physiology and Biophysics, University of Washington, Seattle, USA
[*] dfreedman@uchicago.edu

Humans and other animals have a remarkable ability to explore and learn a new concept, and progressively improve at it through repetition or practice. This process of learning to learn (LTL) can be thought of as a progressive generalization across tasks with common structure and rules but different sensory elements. LTL consolidates the understanding of abstract structures and rules and helps to solve similar problems more efficiently. We studied this phenomenon in a monkey in the context of visual association learning, while recording from populations of neurons in the prefrontal cortex (PFC) and hippocampus (HPC) to understand their role in this process.

One monkey was trained on an image-pattern association (IPA) task, in which she learned arbitrary pair-associations between two images and two pattern targets, such that each image was associated with one of the targets. After fixating on a central fixation cue, a sample image was presented foveally for 500 ms, followed by presentation of two pattern targets. 200 ms after target presentation, the central fixation and sample disappeared, and the monkey had to saccade to the sample-associated target to receive a reward. After the monkey reached a learning criterion (90% accuracy on 200 consecutive trials) for an image pair (or problem), the images were replaced with two novel images. The monkey reached criterion on 24 problems over the course of 60 sessions and exhibited characteristics of LTL as the number of trials to criterion decayed exponentially with problem number.

We used two semi-chronic Gray Matter Research (GMR, LLC.) arrays to record single-units and local field potentials (LFPs) simultaneously from PFC (96 channels) and HPC (124 channels) throughout IPA-task training. This enabled recording on each session from approximately 100 single/multi units and approximately 90 LFP sites. We recorded from the same neurons during two consecutive problems in every session to understand how knowledge from one task is generalized to the other. Dimensionality reduction analyses of the population responses revealed clear representations of task parameters — sample stimuli, decision, saccade direction and reward outcome — which progressively transformed across problem sets. Additionally, we identified signatures of performance monitoring or reward expectancy in population LFP responses in PFC and HPC that developed gradually during a problem set, as it was learned. Importantly, this build-up accelerated for later problems, during which the monkeys also showed accelerated behavioral learning. We suggest that this is a likely neuronal correlate of the process of learning to learn. Our findings suggest the formation of a learning schema that develops gradually across multiple brain regions during learning set acquisition.

Acknowledgments

NIH U19NS107609, NIH T32GM007281, DOD VBFF, NIH F31MH124395.

FITTING NORMATIVE NEURAL SAMPLING MODELS TO NEURONAL RESPONSE DATA

Suhas Shrinivasan[1,*], *Edgar Y. Walker*[2,†], *Fabian H. Sinz*[1,†]

[1] Universtät Göttingen, Göttingen, Germany
[2] University of Washington, Seattle, USA
[†] equal contribution
[*] shrinivasan@cs.uni-goettingen.de

Our environment is riddled with sensory stimuli that are noisy, ambiguous and often incomplete, necessitating perceptual systems to handle uncertainty. To this end, the Bayesian Brain Hypothesis (BBH) posits that the brain maintains a generative model of stimulus, which upon receiving some stimulus, inverts the generative model (Bayes' rule) obtaining the posterior distribution to infer the latent cause of the stimulus. A prominent instance of BBH — the Neural Sampling Hypothesis (NSH) — provides a neural basis of probabilistic inference by postulating that sensory neuronal responses (*e.g.* from V1) to a stimulus represent samples from the said posterior distribution over latent causes given the stimulus.

Despite its theoretical elegance, providing strong experimental evidence for NSH has been challenging. Supporting evidence has mostly been qualitative in nature and no work exists that directly fit NSH models against recorded neuronal responses to provide experimentally-verifiable, neuron-specific predictions. Furthermore, NSH models have been typically simple and hand-crafted, with limited expressivity. In contrast to that, recent advances in deep-learning based system identification have set new standards in providing expressive models that can faithfully predict neural population responses to arbitrary stimuli.

We propose a novel theoretical formulation for NSH that enables us to directly fit NSH models to recorded stimulus-response data. This, in turn, allows us to quantitatively compare different normative assumptions based on the predictive performance (likelihood). Crucially, we formalize NSH as positing *a functional equivalence between the distribution of stimulus conditioned responses and stimulus conditioned latent causes (the posterior)*. Rigorously abiding by this novel formulation, we can straightforwardly fit any generative model under NSH to pairs of recorded neuronal responses and stimuli. Using our formulation, we demonstrate successful fitting of several prominent NSH models, such as the Hoyer and Hyvärinen model and the Olshausen and Field model, to simulated neuronal responses and stimuli.

However, all existing NSH models share the common restriction of working with specific parameterized generative models, *e.g.*, with prior and conditional distributions from pre-specified distributional families. In other words, there is little room for the generative model to be informed or learned from the data. To this end, we combine recent advances in generative modeling in machine learning with our method to devise a flexible normalizing flow-based neural network model that can *learn* the generative model directly from pairs of responses and stimuli. We show that our flexible NSH model can fit to neuronal responses simulated under NSH with various generative models, significantly outperforming the fit of mismatched generative models.

We believe that this is an important step towards a more quantitative evaluation of NSH: Our learned generative model has the ability to yield new experimental predictions to quantitatively and experimentally assess the normative theory and will help get us closer to an understanding of neuronal computation and behavior from first principles.

CORRELATING EXTRACELLULAR SPIKE SHAPE AND NEURONAL RESPONSES IN THE LATERAL GENICULATE NUCLEUS OF AWAKE MACAQUES

Shi Hai Sun[1,2,*], *Nathan J. Killian*[3], *John S. Pezaris*[1,2]

[1] Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA
[2] Department of Neurosurgery, Harvard Medical School, Boston, MA, USA
[3] Department of Neurological Surgery, Albert Einstein College of Medicine, Bronx, NY, USA
[*] shsun@mgh.harvard.edu

Have we identified all cell types in the lateral geniculate nucleus (LGN)? Of retinal cells projecting to LGN, only 80% carry signals associated with classic thalamic responses [1], and we want to identify the missing 20% through rigorous analysis in the LGN of awake monkeys. With the development of multiple-electrode arrays and sophisticated spike-sorting algorithms, we can now simultaneously sample the brain with detailed identification of extracellular signals, which may reveal previously overlooked signals. Using these tools, we attempt to characterise the full range of neuronal responses in the LGN of awake monkeys.

We recorded from 255 single units in the LGN of three macaques using 16-channel electrode arrays and found three distinct classes of extracellular spike waveForms (Fig. 1, left and middle insets): the commonly reported negative-dominant waveforms (64%, blue); triphasic waveforms (13%, purple) that are also negative but have three phases; and positive-dominant waveforms (23%, black) that are not often reported in the literature. All units were stimulated with high-resolution visual noise, with 71% having their receptive field (RF) successfully mapped (Fig. 1, right inset). We correlated the spike classes against their RF and response characteristics to identify any relationships between spike shape and neuronal class (magnocellular, parvocellular, koniocellular or, importantly, other). Out of the remaining LGN cells for which an RF could not be found, 77% responded significantly to the mapping stimulus. Our observations suggest that the population of LGN cells may be broader than traditionally thought and includes cells that are visually responsive in unusual ways, in addition to non-visual cells. Understanding these often-ignored cells may help identify the previously missing retinothalamic projections.

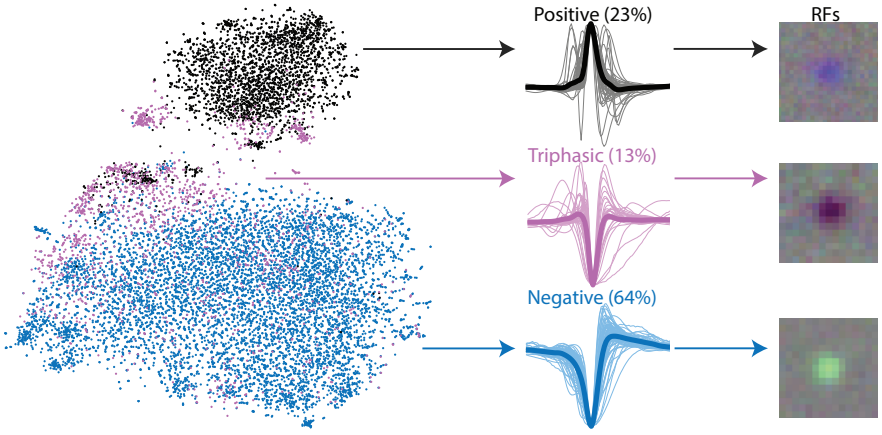


Figure 1. TSNE projected spikes from LGN neurons classified by spike shape into Positive (black), Triphasic (purple), and Negative (blue), along with typical response fields.

Reference

1. Dacey, 2004, Origins of perception: Retinal Ganglion Cell Diversity and the Creation of Parallel Visual Pathways. In *Sensory Systems* (pp. 281–301).

A CELLULAR-LEVEL ACCOUNT OF CLASSICAL CONDITIONING

Pantelis Vafidis[1,*], *Antonio Rangel*[1,2]

[1] Computation and Neural Systems, Caltech, Pasadena, CA, USA
[2] Division of Humanities and Social Sciences, Caltech, Pasadena, CA, USA
[*] pvafeidi@caltech.edu

Animals learn from experience the value of environmental stimuli to guide their behavior. This requires the capacity to associate the neural activity patterns induced by unconditioned stimuli (*US*) with the patterns produced by conditioned stimuli (*CS*). Existing models of reward-modulated synaptic plasticity have been able to explain conditioning when the neural representations of behavioral stimuli are unmixed [1], but not when they are mixed. This is a problem because the relevant frontal cortical neurons typically display mixed selectivity [2].

We propose a computational model that learns *US*-*CS* associations with mixed representations, which is inspired by experimental findings on the associative power of single cortical pyramidal neurons [3]. The model uses a local learning rule operating in compartmentalized neurons, which mirrors the capacity of cortical pyramidal neurons to implement predictive learning through coincidence detection [4]. This allows L5 feedforward (external) *US* inputs to be separated from L1 feedback (contextual) *CS* information and compared within the same neuron via backpropagating action potentials, which drives learning. We model a primary reinforcer area (*e.g.*, orbitofrontal cortex) with a population of such neurons and find that, over time, the population response to the *CS* resembles that to the *US*, thus implementing the psychological process of stimulus substitution. Importantly, after learning, downstream decoding units can predict the *US* when only the *CS* has been presented and guide behavior in advance.

We show that adding global gating from reward prediction errors allows the model to account for a wide gamut of conditioning phenomena, including S-shaped acquisition, interstimulus interval effects, blocking, overshadowing, salience effects and overexpectation. Moreover, we find that the model offers a reductionist mechanism for causal inference by resolving the *post hoc* fallacy, which states that when event Y occurs after event X, then X is considered its cause.

The model makes testable predictions about the evolution of neural mixed representations during canonical conditioning experiments that we hope will be useful to understand existing datasets and guide future experiments. Other potential applications include decoding evolving beliefs in real time, validating conditioning models and investigating how it can go awry in brain disorder. We believe that pyramidal neurons are not by chance the most populous in the mammalian cortex; once discovered by evolution, this structure might have been favoured for its ability to accomplish one of the feats of organized life: predicting external contingencies.

Acknowledgments

Supported by NOMIS Distinguished Scientist Award and Onassis Foundation Scholarship.

References

1. Izhikevich, 2007, *Cereb. Cortex* 17(10):2443–2452, 10.1093/cercor/bhl152
2. Rigotti, Barak, Warden, *et al.*, 2013, *Nature* 497(7451):585–590, 10.1038/nature12160
3. Doron, Shin, Takahashi, *et al.*, 2020, *Science* 370(6523):eaaz3136, 10.1126/science.aaz3136
4. Urbanczik, Senn, 2014, *Neuron* 81(3):521–528, 10.1016/j.neuron.2013.11.030

DECODING MOVEMENT ACTIONS AND INTENTIONS IN SIMPLE REACHES AND REACH-TO-GRASPS USING WAVELET SCATTERED LOCAL FIELD POTENTIALS

Fabio Vallone[1,†,*], *Reyhaneh Boroughani*[1,†], *Matteo Filippini*[2], *Patrizia Fattori*[2,3], *Silvestro Micera*[1,4]

[1] Dept. Excellence in Robotics and Artificial Intelligence, Scuola Superiore Sant'Anna, Pisa, Italy
[2] Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[3] Alma Mater Res. Inst. Human-Centered Artificial Intelligence, Univ. Bologna, Bologna, Italy
[4] Ctr. for Neuroprosth., École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland
[†] equal contribution
[*] fabio.vallone@santannapisa.it

Decoding algorithms are a crucial step to provide proper translation of neural signals into suitable instructions for brain machine interfaces (BMIs). Here, we implemented an advanced decoding algorithm to decode distinct phases of movement in two instructed-delayed tasks: a reach-to-grasp (Task 1) and a reach-to-point task (Task 2) performed by a non-human primate [1,2]. We were interested in decoding four distinct temporal epochs: *Free*, the monkey was not engaged in the task, *Obj-Vis*, early vision of the target, *Delay*, a waiting time that also included the preparation of the movement, and *Mov*, the actual movement time. Task 1 was tested over two environment conditions, in the light condition, the animal could see the object to grasp all the time during the task, whereas in the dark condition the object was visible only for a short period at the beginning. Neural signals were acquired using a multielectrode array simultaneously recording up to 32 channels implanted in the primary motor cortex of a *M. fascicularis*. We proposed a novel approach to BMI studies decoding scheme by processing Local Field Potentials using wavelet scattering transform [3], principal component analysis, and support vector machines. We obtained a reliable decoding of the four epochs with accuracy values of 82% and 83% in the light and dark conditions for Task 1, respectively. In Task 2, we obtained an accuracy of 85%, indicating an overall robustness of the decoding algorithm across tasks. Our results could represent an important step toward the development of BMIs that relies on (i) the detection of movement actions and intentions, (ii) population signals that are more robust than recording units typical of intracortical implants.

Acknowledgments

Supported by Bertarelli Foundation, Swiss National Science Foundation-REGRASP project, and European Union's Horizon 2020-MAIA project (No. 951910).

References

1. Filippini, *et al.*, 2017, *J. Neurosci.* 37(16) 4311–4322, 10.1523/JNEUROSCI.3077-16.2017
2. Filippini, *et al.*, 2018, *Cell Rep.* 23(3), 725–732, 10.1016/j.celrep.2018.03.090
3. Andén, Mallat, 2014, *IEEE Trans. Signal Process*, 62(16) 4114–4128, 10.1109/TSP.2014.2326991

ACC NEURONS RESPOND BOTH DURING AND AFTER RESPONSE CONFLICT

Dmitrii Vasilev[1,2], *Oleg Vinogradov*[2,3], *Anna Levina*[2,3], *Nelson K. Totah*[1,2,*]

[1] Helsinki Institute of Life Science (HiLIFE), University of Helsinki, Helsinki, Finland
[2] MPI Biological Cybernetics, Tübingen, Germany
[3] University of Tübingen, Tübingen, Germany
[*] nelson.totah@helsinki.fi

The anterior cingulate cortex (ACC) plays a central role in monitoring ongoing behavioral performance, for example by activating during tasks that evoke response conflict (*i.e.*, the simultaneous engagement of two incompatible actions, such as going and stopping). This has been classically studied using the stop signal task in which an external cue instructs the subject to stop ongoing movement preparation. However, in this task, there is no observable behavioral event demarcating the occurrence of response conflict because the subject never actually moves. Thus, it is unknown precisely when and how ACC neuronal activity changes during response conflict, but the predominant view is that ACC neurons respond only after conflict occurs.

Here, we introduce a new paradigm to observe response conflict with precise timing in head-fixed rats on a treadmill. Rats learned that when presented a NoGo stimulus, the correct response was to remain immobile, but if they released a pre-potent running response, they could still correctly respond by stopping before crossing a distance threshold. On a subset of trials, rats committed these *near-mistake* (NM) movements. At the peak velocity of the NM movement, competing Go and NoGo actions were simultaneously engaged; thus, peak velocity provides an unambiguous time on each trial to mark the maximal conflict for neuronal activity alignment. Moreover, peak velocity can be used as a proxy for conflict magnitude on each trial because a larger incorrect movement needs more conflicting response to stop.

We recorded 478 ACC single units from 3 rats and assessed neuronal activity changes in a 400 ms to 1400 ms window around NM peak velocity. Trials were divided into tertiles of peak velocities representing none-to-low, medium, or large conflict. Out of 478 units, 209 significantly scaled their firing rate with NM movement size (31% significantly positively correlated and 18% negatively with movement size). These units did not scale firing rate during running to a Go stimulus (when there is no conflict) and are therefore not simply correlated with speed. We also characterized population responses with demixed PCA using conflict magnitudes as conditions. The method isolates the components of the population activity that specifically scale with conflict. We again observed scaling with NM magnitude. The scaling is detectable as early as 400 ms before velocity peak and persisting until after conflict was resolved (1400 ms after velocity peak when the rat had stopped). Our findings provide strong evidence for ACC activity correlating with the degree to which incompatible actions compete. In contrast to current thinking that ACC only monitors past performance, we show that ACC neurons respond during conflict resolution and may inhibit actions.

Acknowledgments

Supported by Acad. of Finland (NT), S. Juselius Foundation (NT), Univ. Helsinki (NT), MPI-Biol. Cyb. (NT, AL), Joachim Herz Foundation (OV), and AvH (AL).

DIGITAL TWIN FOR IMMORTALIZING NEURONAL FUNCTION OF MOUSE VISUAL CORTEX

Eric Wang[1,*], *Paul Fahey*[1], *Kayla Ponder*[1], *Fabian Sinz*[3], *Xaq Pitkow*[1,2], *Jacob Reimer*[1], *Andreas S. Tolias*[1,2]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[2] Department of Electrical and Computer Engineering, Rice University, Houston, TX, USA
[3] Institute of Computer Science, Univerity of Gottingen, Gottigen, Germany
[*] eric.wang2@bcm.edu

To mechanistically understand complex biological systems such as the brain, we must link function, structure, and molecular architectures. Functional studies of the brain involve recording and manipulating activity of neurons across different behaviors and environments *in vivo*. In contrast, high-resolution structural and molecular studies require tissue-destructive methods such as electron microscopy, transcriptomics, and immunohistochemistry. Therefore, studies that bridge these levels of analysis are limited by the number of *in vivo* experiments that can be performed before tissue is damaged. This only partially captures the large diversity of behaviors and environments, rendering functional characterization incomplete. Here we address this problem by using limited data to build digital twins that accurately reproduce the dynamical functional response properties of neuronal populations. Digital twins can then be probed with unlimited experiments. We combined *in vivo* recordings from large populations of neurons in the mouse visual cortex (more than 200,000 neurons) with an artificial neural network to predict responses to visual stimuli. We used a bio-inspired deep recurrent architecture with lateral and feedback connections, inferred visual perspective with eye tracking, combined data from multiple subjects to learn a common latent representation, and incorporated behavioral information to modulate neural responses. This model accurately predicted dynamic neural responses not only to novel natural movies but also to unseen stimulus domains. Our *in silico* modeling approach enables rapid, exhaustive, and adaptable exploration of how neurons function in natural environments, extending the lifespan of functional studies indefinitely beyond *in vivo* constraints.

Acknowledgments

Supported by the Intelligence Advanced Research Projects Activity (IARPA) via Department of Interior/Interior Business Center (DoI/IBC) contract number D16PC00003.

BEHAVIORAL STATE TUNES MOUSE VISION TO ETHOLOGICAL FEATURES THROUGH PUPIL DILATION

Konstantin F. Willeke[1,†], *Katrin Franke*[2,†], *Kayla Ponder*[3], *Mario Galdamez*[3], *Saumil Patel*[3], *Emmanouil Froudarakis*[3,4], *Jacob Reimer*[3], *Fabian Sinz*[1,3,‡,*], *Andreas Tolias*[3,‡,*]

[1] Georg-August University Göttingen, Göttingen, Germany
[2] Institute for Ophthalmic Research, Tübingen University, Tübingen, Germany
[3] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[4] Institute of Molecular Biology and Biotechnology, Hellas, Heraklion, Greece
[†] equal contribution
[‡] equal contribution
[*] sinz@cs.uni-goettingen.de, astolias@bcm.edu

In the visual cortex, active behavioral states enhance sensory responses but typically leave the preferred stimuli unchanged. Here, we find that behavioral state does modulate stimulus selectivity in mouse primary visual cortex. Using population imaging, behavior, and deep neural networks, we identified a shift of color selectivity towards ultraviolet stimuli during active behavioral states. By pharmacological manipulations of the pupil, we showed that pupil dilation is causing a dynamic switch from rod to cone photoreceptors, extending their role beyond day and night vision. This change in tuning selectivity facilitated the detection of ethological stimuli, such as aerial predators against the twilight sky.

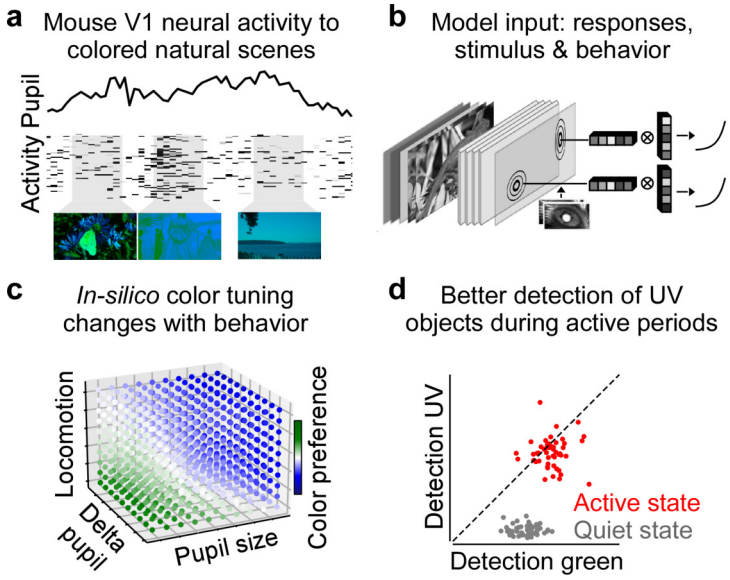


Figure 1. (**a**) Calcium activity of example neurons recorded in V1 of awake mice in response to colored natural scenes and simultaneously recorded pupil size. (**b**) Schematic illustrating model architecture. Model input consists of two image channels and three behavior channels. (**c**) *In silico* characterization of color preference for different behavioral states for one example neuron. (**d**) Detection (bits) of objects in UV versus green image channel based on recorded neural activity for a quiet and active behavioral state.

Our study challenges the belief that state-dependent pupil dilation is an epiphenomenon of brain state and does not causally affect information processing itself. Given that changes in pupil dilation with arousal and attention is ubiquitous across vertebrate species including humans, our work opens up a host of new research questions about how state-dependent changes in pupil size affect visual information processing, potentially adapting vision to different ethological demands during periods of increased sympathetic tone. Importantly, this discovery relied on an approach we refer to as digital twin, mimicking the responses of large neural populations recorded from visual cortex with deep neural networks. This enabled us to loop between *in silico* experiments and targeted *in vivo* verification experiments, which we believe has enormous potential in order to turn large scale data that is now commonplace in biology and beyond into fundamental scientific insights.

ENGINEERING BRAIN ACTIVITY PATTERNS FOR THERAPEUTICS

M. Fatih Yanik[*], *Mostafa G Rezaie, T. Baran Yasar, Peter Gombkoto, Alexei Vyssotski, Paul Johnson, Mehmet S Ozdas, Aagam Shah, Markus Marks, Wolfger v.d. Behrens*

Institute of Neuroinformatics, ETH, Zurich, Switzerland
[*]yanik@ethz.ch

Brain networks are disrupted in numerous disorders. Existing treatments often cannot address such complex dysfunctions. We first show that the aberrant brain-wide activity and functional connectivity patterns can be completely corrected by targeting distinct network motifs with multiple neuromodulators using a vertebrate model of human epilepsy and autism [1]. Our systematic approach rescues behaviour unlike any other treatment as verified by ML-based deep behavioural analysis.

We next ask and determine what are the essential measurements and criteria for accurately calculating inter-areal functional brain connectivity patterns, such that they are also predictive of the most accurate treatment vectors and behavioural outcomes. We show that such functional connectivity analysis requires single-neuron multi-areal ensemble measurements. In particular, we identify the number of single units per area necessary to be recorded, the number of brain areas necessary to be recorded, and the type of functional connectivity metric that works best, using behavioural improvement as a direct causal readout of the performance of the measurement and analysis. These criteria are also predictive of the performance of BMI tasks in primates. We next present a technology to perform such single-neuron ensemble measurements simultaneously across dozens of cortical areas using penetrating ultrasoft electrodes. This technology allows year-long stable single-unit ensemble recordings in rodents without spike-shape drift, and post-mortem analysis shows absence of neuroinflammatory markers surrounding electrode implantation sites. The minimal invasiveness of this technology opens the possibility to perform such network functional connectivity measurements in primates involving several cortical areas.

Finally, we show how specific inter-areal functional connectivity patterns can be precisely and selectively modulated by targeting focal brain areas with a non-invasive cell-type-specific spatially precise technology (using ultrasound aggregation and uncaging of drugs) with down to 2–3mm resolution [2] and how subsequent behavioural perturbations can be analysed using a new deep-learning based approach that works in highly complex environments and for social interactions [3].

Acknowledgments

Supported by NIH DP1/2, NIH Transformative R01, ERC Consolidator Awards.

References

1. Rezaie, et al., 2019, *Nat. Comm.*
2. Ozdas, et al., 2020, *Nat. Comm.*
3. Markus, et al., 2022, *Nat. Mach. Intell.*

MOTOR SKILL LEARNING STABILIZES THE SPEED CODING OF L2/3 NEURONS IN THE MOTOR CORTEX

Yuanlei Yue[1], Ryan T. Ash[2], Stelios M. Smirnakis[3,4], Chen Zeng[5], Hui Lu[1,]*

[1] Dept. Pharmacology and Physiology, George Washington University, Washington, DC, USA
[2] Dept. Psychiatry, Stanford University, Palo Alto, CA, USA
[3] Dept. Neurology, Brigham and Women's Hospital, Jamaica Plain VA Hospital, Boston, MA, USA
[4] Dept. Neurology, Harvard Medical School, Boston, MA, USA
[5] Dept. Physics, George Washington University, Washington, DC, USA
[*] huilu@gwu.edu

Experience tells us that we develop a skill by repeated efforts at a particular outcome, whether the task is cognitive, physical, or both. Even a relatively simple task such as walking involves a combination of both hardwired abilities and plasticity for adapting basic movements to different environmental demands while achieving reliable outcomes. The neurons in the motor cortex are known to be modulated while skills are needed during walking, such as placing the feet on the rungs of a ladder or accurately in complex terrain. It is not yet well understood how the neural network dynamics in the motor cortex evolves through the process of developing skilled walking.

We employed a computerized treadmill approach that forces the animal to acquire the skill to perform speed-matching locomotion on the treadmill running at different speeds without food/water restriction. Using chronic *in vivo* 2-photon Ca^{++} imaging over the forelimb region of area M1 of head-fixed mice performing this motor skill acquisition task. Mice were trained daily for two weeks to develop skills to better adapt to the changing speed. We found most layer 2/3 neurons tuned their firing rate to specific speeds in a highly dynamic manner. Some neurons increased their firing activity with increasing locomotion speed, while other neurons decreased their firing during locomotion. Moreover, a subset of neurons was specifically tuned to a specific locomotion speed. Overall, neurons with the activity that was negatively correlated with running speed cast little contribution to the speed coding both before and after motor skill learning. Motor training reduced the variation of activity pattern that encodes the running speeds at both cellular and population level. These results shine a light on how the motor cortical neurons store the information of the skills required for adaptation to different running speeds.

In summary, these results identify potential circuit mechanisms underlying motor skill learning and will shed light on long-standing questions about neural network organization and dynamics. These approaches and outcomes of the current work are broadly applicable to studying neurodevelopmental disorders with motor problems.

Acknowledgments

Supported by NINDS and March of Dimes Foundation.

NEURONAL ENCODING OF RAPID CATEGORICAL DECISIONS ACROSS THE PRIMATE OCULOMOTOR NETWORK

Ou Zhu[*], *Vinay Shirhatti, Samuel David, Suha Chang, Alexander Medoff, David J. Freedman*

Department of Neurobiology, University of Chicago, Chicago, IL, USA
[*]zhuou@uchicago.edu

Our ability to rapidly categorize incoming stimuli is an essential cognitive process that imbues our world with meaning and guides our behavior. Previous studies have examined the oculomotor system's role in categorical decisions, but few have explored this process when ongoing motor plans are rapidly modulated and updated by incoming sensory information. In this study, we designed an urgent saccade-based, motion categorization task that utilizes a compelled-saccade paradigm to systematically limit the viewing time of the motion stimuli [1]. This task structure exploits the animal's natural variability in reaction times across trials to quantify the psychophysical impact of categorical information towards ongoing motor plans with millisecond resolution.

During task performance, we recorded populations of neurons using up to six linear microelectrode arrays (Plexon V-Probes) simultaneously targeting the lateral intraparietal area (LIP), frontal eye field (FEF), and superior colliculus (SC). On average, each session yielded around 50 well-isolated single units simultaneously recorded from each area. We quantified category selectivity in each area using linear support vector machine (SVM) classifiers trained using the activity of simultaneously recorded units from each area in individual sessions and found that SVMs for each area achieved above 90% decoding accuracies and, on average, exhibited latencies that were not significantly different from each other (about 120 ms after stimulus onset; $p > 0.05$, Student's t-test). We also quantified the saccade selectivity of each area with linear SVMs and found that all areas achieved above 95% decoding accuracies, though FEF and SC exhibited significantly shorter latencies than LIP ($p < 0.05$, Student's t-test). The similar latencies and clear selectivities present in each area support a distributed model of categorical decision making in which brain areas operate as a collective network rather than discrete modules for perception and motor control. Our results also demonstrate that SC is engaged in cognitive functions such as categorization and decision making beyond its traditionally understood role in saccade execution and orienting behaviors. Ongoing experiments will reversibly inactivate each area individually while simultaneously recording the other areas to investigate the causal relationships between brain areas during rapid categorical decision making.

Acknowledgments

This work has been supported by NIH R01EY019041, NIH-NINDS U19NS107609–03, DOD VBFF, NIH T32GM007281, and NIH F30EY033648.

Reference

1. Stanford, Shankar, Massoglia, *et al.*, 2010, *Nat. Neurosci.* 13(3):379–385, 10.1038/nn.2485

ATTENDEE AND AUTHOR INDEX

Entries for attendees are listed with last name, first name, affiliation, and email. Page numbers in bold (**00**) indicate presenting authorship, in italics (*00*) indicate session moderation, underlined (<u>00</u>) indicate organizing committee reference, and in normal typeface (00) indicate non-presenting authorship or other reference in the program text.

TZIAMPIRI, Olympia (Hellenic Education and Research Center, AREADNE Staff) olympia.tziampiri@gmail.com, 7
ULANOVSKY, Nachum (Weizmann Institute) nachum.ulanovsky@weizmann.ac.il, **50**
VAFIDIS, Pantelis (Caltech) pvafeidi@caltech.edu, **113**
VALLONE, Fabio (School of Advanced Studies Sant'Anna) fabio.vallone@santannapisa.it, **114**
VASILEV, Dmitrii (University of Helsinki) dmitrii.vasilev@helsinki.fi, **115**
VILIMELIS ACEITUNO, Pau (Institute of Neuroinformatics UZH/ETH) pau@ini.uzh.ch, **101**
WILLEKE, Konstantin (University of Tübingen) konstantin.willeke@gmail.com, **117**
WILLIAMS, Ziv (Massachusetts General Hospital) zwilliams@mgh.harvard.edu, *22*, 78, **82**
WOODHALL, Gavin (Aston University) g.l.woodhall@aston.ac.uk
YANIK, Mehmet Fatih (ETH Zürich) yanik@ethz.ch, **118**
ZHU, Ou (University of Chicago) zhuou@uchicago.edu, 103, **120**