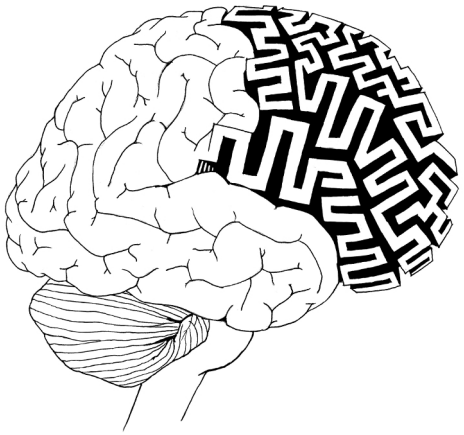
AREADNE 2020

Research in Encoding and Decoding of Neural Ensembles

Nomikos Conference Centre, Santorini, Greece

16-20 June 2020



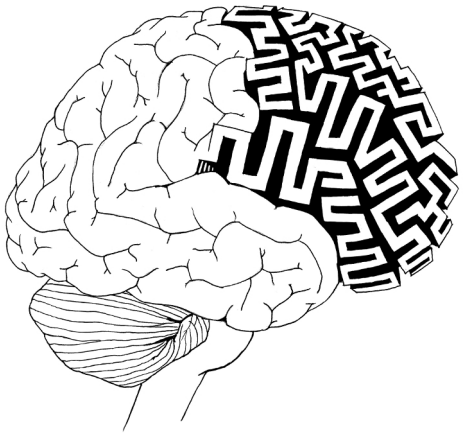
Conference Information

Poster Abstracts

Author Index

AREADNE 2020
Research in Encoding and Decoding of Neural Ensembles
Nomikos Conference Centre, Santorini, Greece, 16-20 June 2020
John S. Pezaris, Nicholas G. Hatsopoulos, 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

There are few things that bring us more pleasure than organizing the AREADNE Conferences. Our efforts have expanded the professional opportunities for many neuroscientists and, now, with over a decade of providing a high-caliber forum for scientific discussion, we have been deeply moved many times by the frequent expressions of appreciation from our participants that accompany each meeting.

We chose, when designing the AREADNE meetings, to highlight the latest, highest-quality research in systems and computational neuroscience, to establish and strengthen long-term professional relationships, and to educate aspiring, young neuroscientists. These goals guide our decisions from large to small, being found in aspects as diverse as the speaker selection process, the location, the daily schedule, the design of the proceedings, and the style of aperitifs during poster sessions. With each choice, we further the goals of intertwining formal interaction with informal discussion, of fostering collaboration, of promoting scientific excellence, of being citizens of the City of Ideas, as the Greek poet Kavafy wrote [1].

When news broke of a new, virulent pathogen that had begun to spread voraciously in East Asia, the co-chairs met to map out contingency plans. We initially anticipated that there might be reduced attendance for the 2020 session, but not a global shutdown. Perhaps we might delay until the fall, we thought, but we would not compromise on the ideals that have made the AREADNE meetings successful.

As time passed, we studied projections, made a few of our own, observed governmental responses, listened to our organizing committee, polled our trusted advisers, and came to a carefully considered decision. While Greece has been spared the ravages suffered by its neighbors as we write this, a meeting where people greet each other warmly, physically, and celebrate the shared, immersive and inspirational experience of being together for four days at the Nomikos Centre cannot happen this year, or perhaps even next. Therefore, we decided to cancel the in-person aspects of AREADNE 2020.

In order to acknowledge the hard work by our contributing authors and organizing committee on the abstract submission and selection process, as well as to provide a means for our authors to be recognized for having their work accepted for presentation at AREADNE 2020, we are publishing this abbreviated program of the poster abstracts. Unlike previous meetings where contributed abstracts are distributed round-robin across the three poster sessions to encourage participation, here, we have organized the submissions by theme, as can be found in the following pages. We hope the reader will find the abstracts as compelling as we have, and will contact authors through their communicating email addresses for additional information and discussion.

John S. Pezaris, Ph.D.
Massachusetts General Hospital
Harvard Medical School

Nicholas G. Hatsopoulos, Ph.D.
University of Chicago

1. Kavafy, *The First Step*, in C. P. Cavafy: Collected Poems, Mendelsohn (tr.).

WELCOME

Welcome

Welcome to AREADNE 2020, the eighth 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 2020 conference was organized by John Pezaris and Nicholas Hatsopoulos (Co-Chairs), along with Dora Angelaki, Kenny Blum, Yiota Poirazi, Thanos Siapas, and Andreas Tolias.

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, and 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 Foundation, 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

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.

SUBMITTED ABSTRACTS

Submitted abstracts are listed by theme, and within each theme, alphabetically by first author. These abstracts were all reviewed and accepted for presentation at AREADNE 2020.

Attention

Decision and Value

Dendritic Computation

Epilepsy

Hippocampus

Learning and Memory

Motor and Sensation

Navigation

Networks

Neural Circuitry

Neural Net Classification

Olfactory Coding

Sequences

Speech

Technique

Timing and Synchronization

Vision

ATTENTION

LFP PHASE AS A REFERENCE FRAME TO REPRESENT THE FOCUS OF ATTENTION

Ehsan Aboutorabi[1], Sonia Baloni Ray[2], Daniel Kaping[3], Farhad Shahbazi[1], Stefan Treue[4], Moein Esghaei[4,]*

[1] Department of Physics, Isfahan University of Technology, Isfahan, Iran
[2] Indraprastha Institute of Information Technology, New Delhi, India
[3] Exzellenzcluster Centre for the Advanced Study of Collective Behaviour, Konstanz, Germany
[4] Cognitive Neuroscience Lab, German Primate Center, Goettingen, Germany
[*] aesghaei@dpz.eu

Selective attention modulates the spike rate of sensory cortical neurons, as well as their activity correlation with other neurons. Using these two types of modulation, attention is hypothesized to improve the encoding of attended stimuli as well as the transmission of the corresponding information to downstream brain areas. Modulation of spike rate and neural activity correlation could be calculated only when a proper history (enough number of previous trials) of neurons is available. Here we suggest a novel mechanism by which the locus of spatial attention could be encoded in the neurons downstream from sensory neurons, using only the instantaneous temporal structure of the neurons' action potentials relative to their neighboring network's activity.

We recorded the extracellular activity from 90 well-isolated direction-selective neurons in visual cortical area MST of two macaque monkeys trained to perform a spatial and feature-based attention task. We recorded action potentials (spikes) and local field potentials (LFP) while the animals performed a change detection task. For each neuron, the spiral motion patterns evoking maximal and minimal response strengths were selected as the preferred and anti-preferred motion patterns, respectively.

We band-pass filtered the LFPs to different frequency bands (4 Hz-wide bands stepped by 1 Hz) and examined the coupling of spikes to the instantaneous phase of the LFPs. Our data show that spikes are preferentially coupled to the phase of LFPs within 16–25 Hz. We further observed that when the animals shifted the focus of attention towards the receptive field (RF) of a neuron (with a preferred stimulus inside the RF), the neuron's spikes shifted towards a different LFP phase, compared to when the animal attended towards the anti-preferred stimulus outside the RF (0.7 rad for neurons with at least 0.1 of spike rate increase with attention; $p<0.05$ paired test on the equality of mean angles & Watson-Williams test). This phase modulation predominantly reflects the shift of the location of attention, rather than the attended visual feature. These results suggest that the attended location relative to a given receptive field is encoded by the LFP's phase where spikes occur preferentially. This opens up a new path towards understanding how the location of attention is encoded, such that it could be decoded by intra-regional and inter-regional neighboring neurons in a history and noise independent manner.

Acknowledgments

This work was supported by the grants of the Deutsche Forschungsgemeinschaft through the Collaborative Research Center 889 "Cellular Mechanisms of Sensory Processing" to S.T. (Project C04) and the Federal Ministry of Education and Research (BMBF) of Germany under grant number 01GQ1005C.

INTERACTIONS BETWEEN VENTROLATERAL PREFRONTAL CORTEX AND VISUAL AREA V4 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

Attention helps filter out stimuli irrelevant to behavior and facilitates processing of stimuli relevant to our current goals. The prefrontal cortex is considered to play a central role in the control of visual attention, however, the mechanism through which distinct prefrontal areas influence processing of visual stimuli remains unclear. Although one prefrontal area, the frontal eye field (FEF), is thought to be a source of spatial attention signals to visual areas, it is largely unknown whether prefrontal regions anterior to the FEF also contribute to this process.

To investigate whether and how the ventrolateral prefrontal cortex (vlPFC) influences processing in visual area V4 we performed simultaneous electrophysiological recordings from the two areas of the macaque brain during a covert attention task. Monkeys were presented with four gratings and were instructed by a spatial cue to attend one of them in order to report its orientation using a joystick.

Firing rates were enhanced in both areas when attention was directed inside the neurons' receptive field and were suppressed when attention was directed outside the receptive field. These spatial attention effects arised significantly earlier in vlPFC compared to V4 neurons. Moreover, an analysis of variance indicated that information about the location of attention reached significance much earlier in vlPFC compared to V4. A prominent enhancement of local field potential (LFP) power was found in gamma (30–70 Hz) frequencies with attention in V4, whereas in vlPFC, the most prominent change was a decrease of LFP power in frequencies between 10 and 30 Hz. Synchronization of activity between vlPFC and V4 was enhanced in theta (4–8 Hz), beta (15–30 Hz) and gamma frequencies with spatial attention with a significant clustering of phases around 230 or -130 degrees in the gamma range. Directed influences estimated by Granger causality analysis revealed that across areas interactions in the theta frequency band originated from vlPFC, whereas interactions in the beta and gamma frequency bands originated from V4. These results suggest frequency specific interactions with spatial attention between vlPFC and V4 and propose a new scheme in frequency-specific long-range communication that involves the prefrontal cortex, distinct from that previously suggested for communication through oscillatory coupling between visual areas.

Acknowledgments

Supported by Research Programs of Excellence IKY-Siemens, and by the project "Advanced Research Activities in Biomedical and Agro alimentary Technologies" (MIS 5002469), which is implemented under the "Action for the Strategic Development on the Research and Technological Sector", funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014–2020) and co-financed by Greece and the European Union (European Regional Development Fund).

LOCALIZED PATTERNS OF SPONTANEOUS POPULATION ACTIVITY IN THE SUPERIOR COLLICULUS

Anton Sumser[†,*], *Wiktor Młynarski*[†], *Maximilian Jösch*

Institute of Science and Technology Austria, Klosterneuburg, Austria
[†] equal contribution
[*] anton.sumser@ist.ac.at

Neural populations typically receive a combination of feed-forward and contextual feedback signals from other brain areas. How the interplay of these internal and external factors shape neural population activity, resulting in perception and behavior, remains a mystery. To explore the relative impact of such internal and sensory inputs on the function of neural populations, we study a behaviorally instructive and highly integrative midbrain region, the superior colliculus (SC) of the mouse. The SC integrates retinal inputs with cortical signals, enabling the detection of objects with immediate behavioral relevance, guiding directed movements and contributing to the allocation of spatial attention. Here we present population activity recordings of the superficial SC acquired by two-photon calcium imaging in behaving animals. Using dimensionality reduction techniques, we demonstrate that SC activity is composed of a small set of distinct neuronal co-activation patterns with varying degrees of anatomical localization: from local hotspots to global activation. Due to the strictly retinotopic organization of SC, local activation can be expected to be triggered by local visual stimuli. However, we find that localized subpopulations regularly dominate the population activity, even when the animal is presented with spatially uniform stimuli. Our results provide preliminary evidence that spontaneously occurring localized activity patterns may reflect top-down processes such as spatial attention.

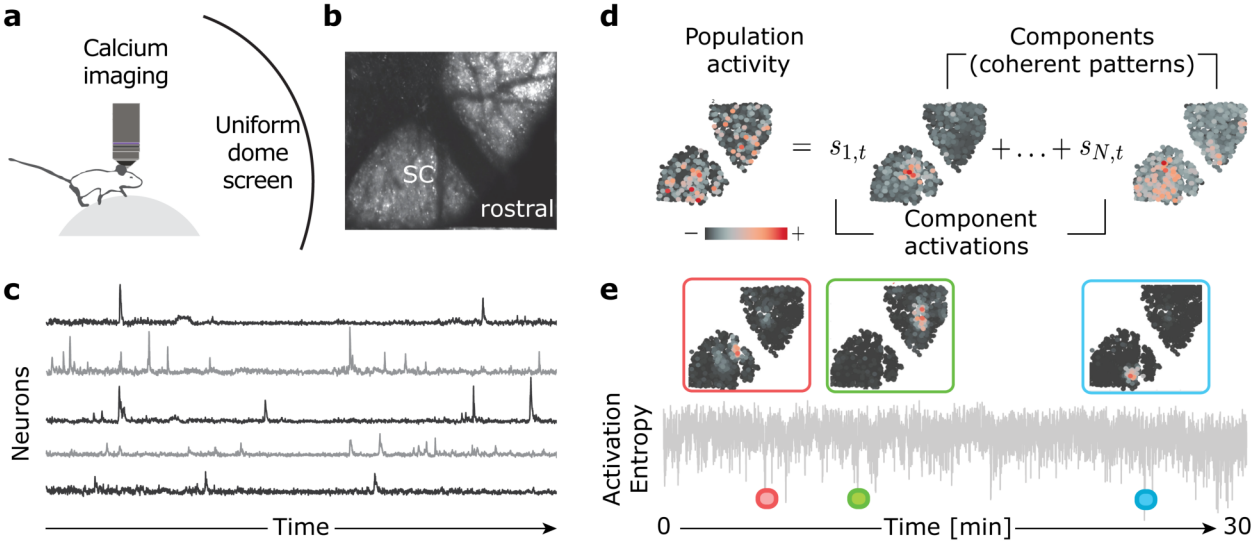


Figure 1. (A) Experimental setup (B) Example frame of the calcium recording (C) Example calcium traces from SC (D) Decomposition of neural population activity into coherent activity patterns with nonnegative matrix factorization (E) Activation entropy (scaled) reflects the number of components active at every time point. Troughs denote intervals when a single pattern dominates population activity. These dominating patterns are frequently localized (colored dots and corresponding insets above).

Acknowledgments

Supported by EMBO, HFSP, ISTPlus and the ERC StG Daphne.

DECISION AND VALUE

ACTIVE MULTI-SENSING ENHANCES PERCEPTUAL DECISION-MAKING VIA BRAIN ENTRIANMENT TO SENSORIMOTOR BEHAVIOR

Ioannis Delis[1,*], *Paul Sajda*[2], *Qi Wang*[2]

[1] School of Biomedical Sciences, University of Leeds, Leeds, UK
[2] Department of Biomedical Engineering, Columbia University, New York, NY, USA
[*] i.delis@leeds.ac.uk

In our daily lives, we make judgments based on noisy or incomplete information that we gather from our environment [1], usually including stimuli from multiple senses [2]. The acquired multi-sensory information crucially depends on our actions — what we see, hear and touch is influenced by our movements — a process known as active sensing [3]. However, multisensory information processing has not been studied so far in an active scenario, where human participants are allowed to implement their own strategy for gathering evidence.

Here we addressed this gap aiming to uncover the neural mechanisms underlying the formation of perceptual decisions via the active acquisition and processing of multisensory information. To achieve this, we capitalized on our previous work probing the neural correlates of active tactile decisions [4] and extended it to a multisensory setting that includes visual and haptic information presented simultaneously or separately. We hypothesized that the neural encoding of active sensory experience would be enhanced when multisensory information was available and that this neural multisensory gain would lead to improvements in decision-making performance.

Human participants were instructed to actively sense to discriminate two texture stimuli using visual or haptic information or the two sensory cues together. To offer a neurocomputational account of active multisensory decision formation, we employed a novel approach assessing the encoding of active sensory experience (scanning patterns) from brain activity (electroencephalography, EEG) in the three sensory conditions. To then understand how the identified brain-sensing couplings influence decisions in the human brain, we employed a popular sequential-sampling model of decision-making, the drift diffusion model (DDM) [5]. To bridge the gap between active evidence acquisition and decision formation, we used the neural correlates of active (multi-)sensing to constrain the DDM. We found a multisensory enhancement of the neural representation of active sensing. We also characterized the neural interactions between the two sensory representations and showed that they predict the dynamics of decision-making behavior.

Acknowledgments

Supported by the European Commission (H2020-MSCA-IF-2018/845884, “NeuCoDe”)

References

1. Juavinett, Erlich, Churchland, 2018, *Curr Opin Neurobiol*, 49:42–50
2. Angelaki, Gu, DeAngelis, *Curr Opin Neurobiol*, 2009. 19(4):452–8
3. Yang, Wolpert, Lengyel, 2016, *Curr Opin in Behav Sci*, 11:100–108
4. Delis, Dmochowski, Sajda *et al.*, 2018, *Neuroimage*, 175:12–21
5. Ratcliff, Smith, Brown, *et al.*, 2016, *Trends in Cogn Sci*, 20(4):260–281

DYNAMICS OF VALUE REPRESENTATION IN THE PREFRONTAL CORTEX

Pierre Enel[1,*], *Joni Wallis*[2], *Erin Rich*[1]

[1] Neuroscience Department, Icahn School of Medicine, New York, NY, USA
[2] Department of Psychology, University of California at Berkeley, Berkeley, CA, USA
[*] pierre.enel@mssm.edu

The ability to associate positive and negative outcomes with predictive stimuli allows us to make optimal decisions. These stimulus-value associations are kept up to date by comparing an expected value with the experienced outcome. When a stimulus and its outcome are separated by a delay, the value associated with the stimulus must be held in mind for such comparisons to be possible, however little is known about the neural mechanisms that hold value representations online across delays. Temporarily remembering task-relevant information has been extensively studied in the context of item-specific working memory, and different hypotheses have suggested this ability requires either persistent [1] or transient neuronal activity [2], with stable or dynamic representations respectively. To test these different hypotheses in the context of value representations, we recorded the spiking activity of neurons in the orbitofrontal and anterior cingulate cortex of two monkeys performing a task in which visual cues predicted a reward delivered after a short delay. We found that features of all hypotheses were simultaneously present in prefrontal activity and therefore no single hypothesis was exclusively supported. Instead, we report mixed dynamics that support robust, time invariant value representations while also encoding the information in a temporally specific manner. We suggest that this hybrid coding is important for optimal behavior and might be a critical mechanism supporting flexible cognitive abilities. To test this hypothesis we are currently developing an artificial neural network model of the prefrontal cortex and its interaction with the basal ganglia that learns to represent value in decision making tasks. We believe that understanding how values are learned and come to be represented in the brain will provide fundamental insight into their representation dynamics. Indeed, recent modeling studies have shown that with the same model architecture learning tasks with higher temporal complexity elicit stronger representations of temporal information [3]. Preliminary results indicate that a network trained only to predict upcoming events and rewards exhibits strong representation of value across cue-outcome delays.

Acknowledgments

This work has been supported by NIH R01 DA19028, R01 MH097990, and K08 DA039051 and the Hilda and Preston Davis Foundation.

References

1. Constantinidis, Funahashi, Lee, *et al.* (2018) *J. Neurosci.* 38:7020–7028
2. Lundqvist, Herman, Miller (2018) *J. Neurosci.* 38:7013–7019
3. Orhan, Ma (2019) *Nat. Neurosci.* 22:275–283, 10.1038/s41593–018-0314-y

ACC SINGLE UNIT AND NEURONAL POPULATION CORRELATES OF RESPONSE CONFLICT VERSUS AND ERROR DETECTION IN A NOVEL RODENT NEAR MISTAKE PARADIGM

Ryo Iwai[1,], Oleg Vinogradov[1,2], Nikos K. Logothetis[1,3], Anna Levina[1,2], Nelson K. Totah[1,4]*

[1] Dept. of Physiol. of Cog. Processes, MPI Biological Cybernetics, Tübingen, Germany
[2] University of Tübingen, Department of Computer Science
[3] Division of Imaging Sci. and Biomed. Eng., University of Manchester, Manchester, UK
[4] Helsinki Institute of Life Science (HiLIFE), University of Helsinki, Helsinki, Finland
[*] ryo.iwai@tuebingen.mpg.de

It is debated whether the anterior cingulate cortex (ACC) detects errors or response conflict because population (EEG) measures support both accounts. One way to disambiguate conflict and errors is to measure *near mistakes* which, in humans, consist of moving but stopping before a threshold (*e.g.*, pressing a key in response to a NoGo stimulus). Near mistake movement magnitude correlates with conflict magnitude; thus, it is a tool for studying neuronal correlates of conflict, which should scale with movement magnitude. Here, we demonstrate near mistakes in head-fixed rats on a treadmill as they discriminate Go and NoGo visual orientation gratings by remaining immobile (NoGo) or running past a distance threshold (Go). Variable near mistake velocities allowed us to study encoding of conflict and errors at the single cell level. We tested the hypothesis that conflict-encoding single units would scale firing rate with conflict magnitude (*i.e.*, near mistake running velocity), but would not respond to error feedback (noise burst).

Preliminary results indicate that conflict-encoding units were 15% of 78 recorded ACC units; such units did not simply encode movement speed. In some units, firing rate scaled inversely with conflict. Error feedback evoked responses in a separate set of units (19%). Finally, 38% of units encoded both conflict and errors, including units that scaled inhibition of spiking with conflict magnitude, but increased spiking after error feedback. We further analyzed the whole population of single units using demixed principal component analysis (dPCA). It decomposed the activity into the condition-dependent components that overall explained about 80% of the variance. The most prominent components were related to encoding of the committed error both during the movement and after error feedback. Other components that explained less variance were related to encoding of movement magnitude and the interaction between movement magnitude and error commission. The dPCA components were distributed across the whole population of neurons.

In summary, our results suggest that separate sets of single units encode conflict and errors, while at the same time, mixed selectivity is observed in many units in the population

Acknowledgments

Supported by Helsinki Institute of Life Science and the Department of Physiology of Cognitive Processes in the Max Planck Institute for Biological Cybernetics. Partly funded by a Sofja Kovalevskaja Award of Humboldt Foundation.

DENDRITIC COMPUTATION

THE BOOLEAN DENDRITE: INTRINSIC COMPUTATION OF WIDE RANGE OF BOOLEAN FUNCTIONS BY DENDRITIC BRANCHES

Sotirios Papadopoulos[1,2,*], *Athanasia Papoutsi*[1], *Albert Gidon*[3], *Matthew E. Larkum*[3,4], *Panayiota Poirazi*[1]

[1] Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[2] Brain and Mind Graduate Program, University of Crete, Heraklion, Greece
[3] Institute for Biology, Humboldt-Universität zu Berlin, Berlin, Germany
[4] NeuroCure Cluster, Charité – Universitätsmedizin, Berlin, Berlin, Germany
[*] sotpapad@protonmail.com

Recent studies investigating the physiology of the human neurons have provided unexpected findings regarding the modus operandi of single neurons [1–3]. One of these studies found calcium mediated dendritic action potentials (dCaAPs) in layer 2/3 pyramidal neurons [2]. Here, we further explore the computational properties of the dCaAPs, using a machine learning approach. Specifically, we used a non-monotonic activation function derived from the properties of the dCaAPs as measured in the experiments; dCaAP's amplitude was zero for subthreshold inputs, maximum [1] at threshold and decayed exponentially with further increasing the input strength (Figure 1). In this study, we show how a single dendritic branch implements all the Boolean functions, including the non-linearly separable XOR and XNOR. We identify the combinations of biologically inspired inputs that solve each of these Boolean functions. This work provides insights into the range of computations a dendrite can perform.

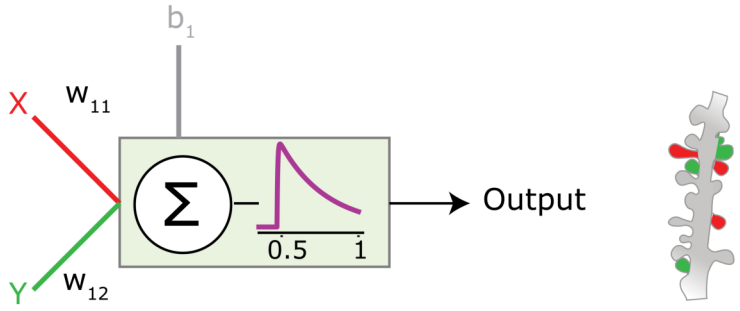


Figure 1. (Left) Artificial dendrite, and the corresponding activation function: b1, bias; X, Y, binary inputs; w11, w12 weights. (Right) Illustration of a dendrite receiving two input pathways (X, red spines; Y, green spines) and background input (grey spines).

References

1. Beaulieu-Laroche, Toloza, *et al.*, 2018, *Cell* 175(3):643–651, 10.1016/j.cell.2018.08.045
2. Gidon, Zolnik, Fidzinski, *et al.*, 2020, *Science* 367(6473):83–87, 10.1126/science.aax6239
3. Eyal, Verhoog, Testa-Silva, *et al.*, 2016, *eLife* 5:e16553, 10.7554/eLife.16553

ORIENTATION PREFERENCE IN DENDRITIC TREES OF L2/3 PYRAMIDAL NEURONS OF THE VISUAL CORTEX

Athanasia Papoutsi[1], *Jiyoung Park*[2,3], *Ryan T. Ash*[2,4,5], *Stelios Smirnakis*[2], *Panayiota Poirazi*[1]

[1] Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[2] Brigham and Women's Hosp. / Jamaica Plain VA Hosp., Harvard Medical School, Boston, USA
[3] Struct. and Comp. Biol. and Mol. Biophys., Baylor College of Medicine, Houston, USA
[4] Department of Neuroscience, Baylor College of Medicine, Houston, USA
[5] Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, USA
[*] athpapoutsi@gmail.com

Cortical pyramidal neurons receive inputs in two anatomically and functionally distinct domains, the apical and the basal tree. Inputs to the basal tree, due to their proximity to the soma, greatly influence neuronal output. The more remote apical tree on the other hand has a smaller potential to influence somatic activity. How these inputs co-operate to form the functional output of neurons, however, is currently unknown. *In vivo* 2-photon dendritic microdissection showed that removal of the whole apical tree does not alter orientation properties of single neurons. Removal of two, but not one, basal dendrites resulted in a small (about 12°) shift in orientation preference. To provide a mechanistic explanation for these experimental findings, we formulated two different hypotheses regarding the underlying input structure to the apical and basal trees. According to the the *shift hypothesis*, the apical and basal trees receive inputs with different orientation preferences, whereas according to the *drift hypothesis* each individual basal dendrite receives differentially tuned inputs (Figure 1).

We implemented the two hypotheses in a biophysical model of a L2/3 V1 pyramidal neuron using the NEURON simulation environment. Using this model neuron we predict that the shift hypothesis could not account for the experimental results, but the drift hypothesis could explain both the apical tree and the basal dendrites ablation data. This prediction for between-branches organization of the basal inputs creates a repository of available orientation preferences in single neurons that can be selectively exploited when adapting a neuron's orientation preference. Overall, model simulations provide new insights regarding the influence of apical versus basal inputs on orientation preference and predict that a distributed, variably tuned input structure along the basal dendrites is optimal for a flexible orientation tuning [1].

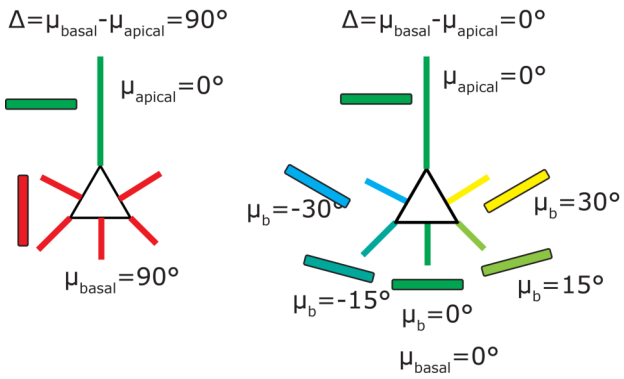


Figure 1. Different inputs arriving in the apical and basal trees (shift hypothesis, left panel) or in the basal dendrites (drift hypothesis, right panel).

Reference

1. Park, Papoutsi, Ash, *et al.* (2019) *Nat Commun* 10:5372, 10.1038/s41467-019-13029-0

EPILEPSY

USING RQA TO IDENTIFY THE STRUCTURE OF 4-AP INDUCED SEIZURE EVENTS

Thomais Asvestopoulou[1,2], Manthos Kampourakis[2], Maria Markaki[2], Joseph Lombardo[3], Ganna Palagina[3], Stelios M. Smirnakis[3], Maria Papadopouli[1,2,]*

[1] Department of Computer Science, University of Crete, Heraklion, Greece
[2] Institute of Computer Science, Foundation for Research and Technology-Hellas, Greece
[3] Dept. Neurol., Brigham Women's Hosp. / JP VA Hosp., Harvard Med. Sch., Boston, MA, USA
[*] mgp@ics.forth.gr

Our understanding of how neurons interact to generate and propagate epileptic seizures is limited. It is important to understand what changes in the cortical circuit allow a highly-correlated firing state to emerge, evolve, and recur after focal-cortical injury. This work aims to measure how cortical neurons are recruited *in vivo* during neocortical focal seizure events in mice. To do so, we employ the 4-aminopyridine (4-AP) model [3]. We perform simultaneous EEG and two photon calcium imaging measurements under three conditions, namely no experimental manipulation, vehicle injection, and 4-AP injection in area V1. Each recording lasts approximately 10 min. Here we report our preliminary analysis on one mouse. To assess the temporal correlation of neuronal activity, we employ the Spike Time Tiling Coefficient (STTC) [1], a metric that accounts for relative time shifts, local fluctuations, and presence of periods without firing events. Two neurons are considered functionally connected and represented by a network edge, if their firing activity has a statistically significant STTC value. Compared to the functional connectivity during spontaneous condition, the functional networks after vehicle and after 4-AP injection are significantly denser (Fig. 1 left)). To identify the dynamical neuronal behavior of ictal phases, we apply Recurrence Quantification Analysis (RQA) [2], a powerful tool based on the analysis of the underlying signal dynamics. RQA specifies the beginning and end of events in the EEG and in the population calcium spike trains (Fig. 1 (right)). The characterization of these events based on neuronal population activity and EEG spectral characteristics is in progress. Our long-term goal is to identify neuronal activity patterns that reliably predict seizure events.

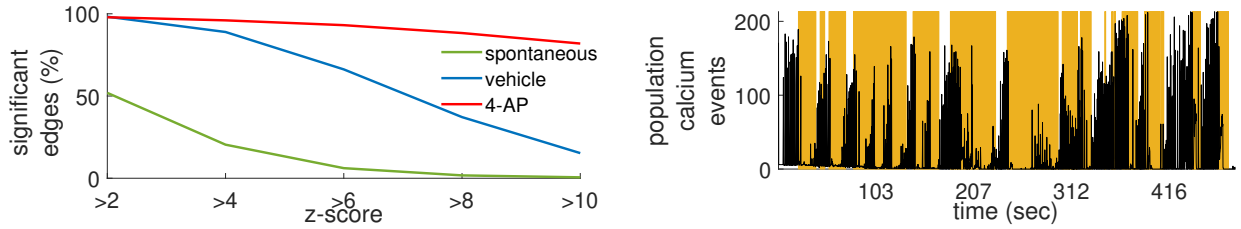


Figure 1. (Left) Significant edges percentage for different z-score thresholds. (Right) Population calcium events; Orange regions mark identified RQA events.

Acknowledgment

Funded by the HFRI and GSRT, Fondation Santé, and NINDS R21.

References

1. Cutts, Eglen, 2014, *J. Neurosci.* 34(43):14288–14303, 10.1523/JNEUROSCI.2767–14.2014
2. Zbilut, Webber, 1992, *Phys. Lett. A* 171(3–4):199–203, 10.1016/0375–9601(92)90426-M
3. Wenzel *et al.*, 2017, *Cell Rep* 19(13): 2681–2693, 10.1016/j.celrep.2017.05.090

USING RQA ANALYSIS TO IDENTIFY AND PROFILE ABSENCE SEIZURES IN STARGAZER MICE

Manthos Kampourakis[1], Elena San Miguel Pérez[2,3], George Tzagkarakis[1], Ganna Palagina[4], Jochen Meyer[5], Stelios M. Smirnakis[4], Maria Papadopouli[1,3,]*

[1] Institute of Computer Science, Foundation for Research and Technology-Hellas, Greece
[2] Facultat d'Informàtica de Barcelona, Universitat Politècnica de Catalunya, Barcelona, Spain
[3] Department of Computer Science, University of Crete, Heraklion, Greece
[4] Dept. Neurol., Brigham and Women's Hosp. / JP Veteran's Admin Hosp., Harvard Medical School, Boston, MA, USA
[5] Department of Neurology, Baylor College of Medicine, Houston, US
[*] mgp@ics.forth.gr

Absence epilepsy [1] interrupts normal cortical processing, producing reversible episodes of altered consciousness. These events can provide unique functional insight into the coupling of human perception and volition. The stargazer model, one of over 20 monogenic mouse mutants with this phenotype [1], displays frequent, recurrent spike-wave seizures with behavioural arrest. We aim to detect neural state changes from the patterns of firing recorded by 2-photon imaging in L2/3 of the stargazer mouse visual cortex. The L2/3 was imaged using the GCamp6 construct in alert awake animals, with simultaneously recorded EEG. For each ROI, we calculate the aggregate number of spikes per consecutive non-overlapping 15-frame windows. Finally, a population spike train is estimated based on neurons that had the maximal discriminability between ictal and non-ictal periods (as marked by the epileptologist reviewing and analyzing the corresponding EEG measurements).

We report our preliminary results on the first mouse using RQA, a powerful nonlinear analysis of time series, which quantifies recurrence structures and detects the critical transitions in the system's dynamics (*e.g.*, deterministic, stochastic) [2]. It can accurately detect the onset and offset of ictal events with high sensitivity above chance. Interestingly, RQA detects substructures within the ictal and interictal periods. We are in the process of characterizing them based on their duration, mean firing rate, number of highly active and quiet neurons. For example, we found that the RQA events that match the ictal onsets are of shorter duration and higher mean firing rate compared to the typical ictal periods. Recently we showed that SVM can accurately classify 1-sec windows as ictal or interictal [3]. Here we identify the seizure onsets and offsets. Our long-term objective is to identify the activity pattern of groups of neurons that can be employed to predict the seizures.

Acknowledgment

Funded by the Hellenic Foundation for Research & Innovation (HFRI) and General Secretariat for Research & Technology (GSRT), the Fondation Sante, and the NINDS R21 NS088457.

References

1. Maheshwari, Noebels, 2014, *Prog Brain Res.*, 213:223–252, 10.1016/B978-0-444-63326-2.00012-0
2. Marwan, *et al.*, 2007, *Physics Reports*, 438(5–6):237–329, 10.1016/j.physrep.2006.11.001
3. Zacharakis, Kampourakis, *et al.*, 2019, *IEEE BIBE*, 783–790, 10.1109/BIBE.2019.00146

HIPPOCAMPUS

COMPLEX INFORMATION DYNAMICS OF CELL ASSEMBLIES IN HIPPOCAMPUS AND ENTHORINAL CORTEX

Wesley Clawson[1], *Nicola Pedreschi*[1,2], *Christophe Bernard*[1], *Pascale Quilichini*[1], *Alain Barrat*[2], *Demian Battaglia*[1,*]

[1] Institut de Neuroscience des Systèmes, UMRS 1106
[2] Centre de Physique Théorique, UMR 7332, Aix-Marseille Université, Marseille, France
[*] demian.battaglia@univ-amu.fr

Neural computation is associated to the emergence, reconfiguration and dissolution of cell assemblies in the context of varying oscillatory states. Here, we describe this complex spatio-temporal dynamics of cell assemblies combining information theoretical analyses with a temporal network formalism.

We use a sliding window approach to extract sequences of information processing profiles from multichannel recordings in hippocampus and enthorinal cortex during anesthesia and sleep. These profiles quantify how much each given neuron is actively maintaining information acting as a buffer (as measured by active information storage), or how much is copying information to other neurons (as measured by information sharing). First, we find that neurons do not a hard-wired information processing profile but change dynamically their involvement in sharing and storage as a function of the current computing state. Second, we find that switching between computing states is neither regular nor random but give rise to non-trivial sequences whose (Kolmogorov-Chaitin) complexity is modulated by global oscillations [1]. We focus then in more detail on the temporal organization of information sharing within cell assemblies, characterized as time-dependent networks of information sharing. We find, that these networks display, at any time, a liquid core-periphery structure. We characterize then the connectivity style of different cells, identifying alternative possible styles of hubness. For instance, some cells may share information with a multitude of other units but only in an intermittent manner, like activists in a flash mob. In contrast, other cells may share information in a steadier manner, more like resolute lobbyists [2]. Altogether, these findings reveal that the storage sharing of information mediated by the intrinsic dynamics of hippocampal and enthorinal cortex cell assemblies have a rich spatiotemporal structure, which could not have been identified by more conventional time- or state-averaged analyses.

Finally, we compare the complexity of information processing dynamics between recordings in control and epileptic mice, identifying a general tendency in epilepsy for randomness replacing complexity.

Acknowledgments

This work was supported by the EU H2020 MSCA ITN project “M-GATE” and by the EU H2020 MSCA-COFUND “Doc2Amu”, cofounded by the Regional Council of Provence-Alpes-Côte d’Azur and the French Investissements d’Avenir project

References

1. Clawson, Vicente, Ferraris, *et al.* (2019) *Sci. Adv.* 5:eaax484. 10.1126/sciadv.aax4843
2. Pedreschi, Clawson, Bernard, *et al.* (2020) BiorXiv, 10.1101/2020.01.17.910315

INTERACTION BETWEEN MEMORY TRACES IN THE HIPPOCAMPAL NETWORK ACTIVITY SPACE

Giuseppe P. Gava[1,2,], Stephen B. McHugh[1], Stéphanie Trouche[1], Mohamady El-Gaby[1], Simon R. Schultz[1,2], David Dupret[1]*

[1] Medical Research Council Brain Network Dynamics Unit, University of Oxford, Oxford, UK
[2] Dept. Bioengineering and Ctr. for Neurotech., Imperial College London, London, UK
[*] gpg12@imperial.ac.uk

The ability to acquire new information and integrate it with previous memories is a fundamental brain mechanism critical to survival. In fact, learning and memory inherently interact together: prior knowledge supports ongoing learning, and new information can retroactively modify previous memories [1, 2]. The hippocampus is a brain region crucial for learning and memory, but its network-level mechanisms that underlie the assimilation of new experiences into memory, separating them as distinct events while allowing their interaction, are unknown.

In this work we display network operations that allow two distinct memories to interact. We monitored electrophysiologically hippocampal CA1 neurons in mice as they explored a familiar environment before and after assimilating a new place-reward memory in a different environment. By embedding co-active principal cells in mathematical graphs, we first found that novel associative learning altered the topology of the neuronal co-firing associations representing the unrelated familiar environment, increasing their spatial information. Moreover, we observed that these co-firing graphs evolved along three functional axes supported by the heterogeneous contributions of high and low activity principal cells. The first axis separated the two spatial environments (the *where*) and was mostly explained by the contribution of high activity cells, the second axis distinguished individual behavioural sessions (the *what*) while low activity cells spanned the third axis by gradually joining co-activation motifs throughout individual experience, revealing cross-memory interaction.

These findings reveal an organizational principle of brain networks where high and low activity cells are differentially recruited into coactivity motifs to enable the flexible integration and interaction between memories.

Acknowledgments

This work has been supported the Engineering and Physical Sciences Research Council UK Centre for Doctoral Training in Neurotechnology (EP/L016737/1), the Biotechnology and Biological Sciences Research Council UK (Award BB/N002547/1) and the Medical Research Council UK (Programme MC_UU_12024/3).

References

1. Dudai, Morris, 2013, *Neuron* 80, 742–750, 10.1016/j.neuron.2013.09.039
2. Schacter, Addis, Buckner, 2007, *Nat. Rev. Neurosci.* 8, 657–661, 10.1038/nrn2213

CONTINUOUS 24-HOUR IMAGING OF HIPPOCAMPAL NEURONAL ACTIVITY IN FREELY MOVING MICE

Walter G. Gonzalez[*], *Carlos Lois*

Biology and Biological Engineering, California Institute of Technology, USA
[*]walterg@caltech.edu

How do CA1 pyramidal neurons in the hippocampus store, recall, and maintain a stable representation of a familiar environment? Understanding how ensemble of neurons in the hippocampus perform this task is essential to deciphering how memories are encoded, decoded, and preserved across time. Using calcium imaging of neuronal activity in freely moving mice we have recently demonstrated that neuronal representations of a familiar environment can be dynamic yet persistent across time and damage [1]. Interestingly, the largest reorganization of these representation occur from one day to the next, regardless of how familiar mice are to the environment (Fig. 1A). These results highlight the potential role of offline neuronal activity in reshaping the memory trace. Here we present ongoing work to investigate the role of offline neuronal activity in reshaping CA1 representations of a familiar environment. We demonstrate the use of sensitive miniscopes able to record hippocampal activity at the single neuron in freely moving mice for continuous 24 hour periods (Fig. 1B). We also present custom circuits allowing simultaneous recording of electrophysiological (Intan headstages) and imaging data (miniscope) in freely moving mice (Fig. 1C). Using these imaging platforms we record neuronal activity in transgenic mice expressing GCaMP6s while traversing a linear track and while performing a delayed alternating task. We further discuss the use of ensemble activity to predict not only behavior but also future reorganization of neuronal activity.

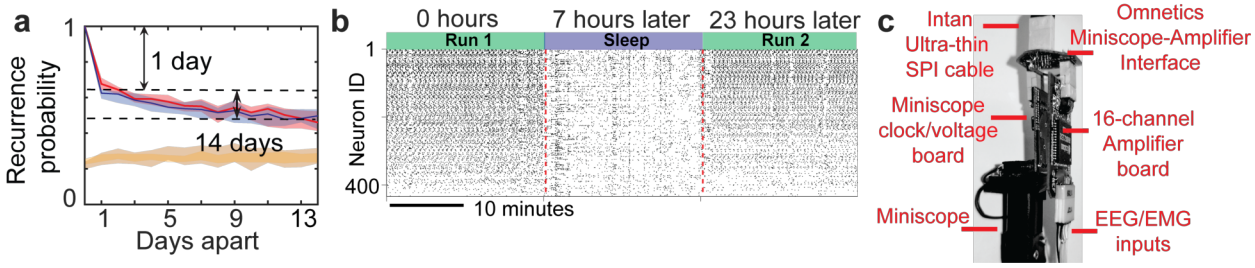


Figure 1. Continuous imaging in mice. (A) A large fraction of place cells change their spatial tuning after a single day. (B) Ten minutes of hippocampal activity during two consecutive exposures to the linear track separated by 23 hours under continuous imaging. A representative 10-minute period of sleep is shown. (C) Custom miniscope-amplifier system developed in our laboratory to perform simultaneous calcium imaging and EEG/EMG recording in freely behaving mice. The complete system weighs a total of 3.8 grams.

Acknowledgments

Supported by Burroughs Wellcome Fund, the American Heart Association, and the National Institute of Neurological Disorders and Stroke.

Reference

1. Gonzalez, Zhang, *et al.*, (2019) *Science* 365(6455):821–825, 10.1126/science.aav9199

LEARNING AND MEMORY

THE FUNCTIONAL INTERCONNECTIVITY OF THE NUCLEUS BASALIS AND DORSOLATERAL PREFRONTAL CORTEX DURING ASSOCIATIVE LEARNING

Edward R. Bader[*]*, Emad Eskandar, Nathaniel Killian*

Department of Neurosurgery, Albert Einstein College of Medicine, New York, USA
[*]edward.bader@einsteinmed.org

The nucleus basalis of Meynert (NBM) lies within the basal forebrain and provides cholinergic innervation to the entire cortex, including the dorsolateral prefrontal cortex (DLPFC). It has been implicated in numerous cognitive processes [1] and dysfunction of the NBM occurs early in Alzheimer's Disease, underscoring its importance [2]. Here, we demonstrate that NBM and DLPFC are functionally interconnected by way of distinct oscillatory frequencies that change as associations are learned. We also demonstrate that greater NBM-DLPFC beta synchrony is correlated with greater peak saccade velocity, which is in turn associated with higher task performance.

To study NBM-DLPFC interconnectivity, we applied (GC) analysis to simultaneously recorded local field potentials (LFPs) in two non-human primates (Macaca mulatta) performing a visual-motor associative learning task (N = 26 recorded pairs). Power transfer between the NBM and DLPFC occurred over two distinct oscillatory bands. Early in learning, while monkeys were still learning associations, NBM drove beta power (peak 14 Hz) in DLPFC. The beta drive disappeared late in learning (when associations had been well-learned), during which the DLPFC drove gamma power (peak 49 Hz) in the NBM. Using Spearman's rank correlation coefficient, we found that increased GC beta-synchrony was correlated with increased peak saccade velocity across trials. Saccade velocity was further correlated with greater trial performance.

These novel findings may indicate that the NBM coordinates cortex during attention-heavy processes. Beta synchrony has been suggested to allow the formation of neural ensembles during computationally intense activities in forebrain areas [3]. Correlation with saccade velocity may also indicate that NBM-DLPFC beta synchrony is a substrate of arousal, in keeping with prior literature [4]. These results may also indicate that DLPFC can provide feedback to NBM that inhibits the beta-band drive. Reciprocal NBM-DLPFC functional connectivity is noteworthy as, to the best of our knowledge, there are no known anatomical connections from DLPFC to NBM. Further elucidating these mechanisms would be meaningful to provide a fuller understanding of the NBM.

Acknowledgments

A. Paulk and C. Martinez-Rubio provided the data used in these analyses (Martinez-Rubio *et al.*, *J. Neurosci.*, 2018). This work was supported by NIH MH086400, DA026297, and EY017658 to E. Eskandar.

References

1. Mesulam, *et al.*, 1983, *J Comp Neurol*
2. Grothe, *et al.*, 2016, *Cereb Cortex*
3. Stanley, *et al.*, 2018, *Cereb Cortex*
4. Di Stasi, *et al.*, 2013, *Neurosci Biobehav Rev*

REVERSAL LEARNING WITH VALUE BACKPROPAGATION FROM LATERAL ORBITOFRONTAL TO SENSORY CORTEX

Abhishek Banerjee[1,3,†,*], *Matthias C. Tsai*[2,†], *Giuseppe Parente*[1], *Willem A.M. Wybo*[2], *Jasper Teutsch*[1,3], *Fritjof Helmchen*[1,†], *Walter Senn*[2,†]

[1] Brain Research Institute, University of Zürich, Zürich, Switzerland
[2] Department of Physiology, University of Bern, Bern, Switzerland
[3] Biosciences Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom
[†] Equal contribution
[*] abhi.banerjee@newcastle.ac.uk

Flexible decision-making in response to changing reward contingencies is crucial for adaptive behaviour. From a computational perspective, non-stationary environments can however be difficult to cope with. The standard way to approach them is with online reinforcement learning methods, but those can be very inefficient in quickly changing environments and could benefit from inspiration from biological systems. In mammals, value-guided behaviour relies largely on frontal cortex, and specifically, the orbitofrontal cortex (OFC). How OFC neurons encode decision variables and hierarchically instruct sensory areas to guide adaptive behaviour is still an open question. We developed a reversal learning task for head-fixed mice together with two-photon calcium imaging to monitor the activity of lateral OFC neural populations and investigate their dynamic interactions with primary somatosensory cortex (S1). Mice trained on this task learned to discriminate tactile cues and to adapt their behaviour upon changes in stimulus-reward contingencies (rule-switch). By imaging neurons longitudinally at cellular resolution, we found distinct engagement of S1 and lateral OFC neurons: S1 activity reflects task learning, whereas neurons in the mouse lateral OFC saliently and transiently responded to the rule-switch. A subset of outcome-selective OFC neurons conveys this rule-related signal via feedback projections to S1.

To elucidate the computational nature of the OFC responses and the OFC-driven feedback to S1, we implemented a reinforcement learning (RL) model of the involved circuitry. We conceptualized the learning task as learning to predict outcomes based on tactile cues. The outcomes are assigned values, and after reversal, the previous outcome predictions are discarded and eventually reversed. In our model, OFC neurons respond to unfulfilled predictions. They encode the error (the unfulfilled-prediction error, UPE) arising from the lack of reward or punishment, when it is expected. The UPE matches the *in vivo* OFC activation and explains the OFC response selectivity. Feeding the values back to S1 yields the experimentally observed shift in S1 outcome-selectivity upon reversal. We believe that this feedback signal crucially induces outcome-dependent remapping in S1 that further stabilizes reversal learning, akin to learning in deep networks where early processing layers show a delayed adaptation to support the correct network output.

Acknowledgments

Supported by the Brain & Behavior Research Foundation (AB), Marie Skłodowska-Curie Fellowship (AB), European Research Council (FH), and Swiss National Science Foundation (WS and FH).

MNEMONIC STRATEGIES CREATE DISTRIBUTED POPULATION CODES FOR WORKING MEMORY IN LATERAL PREFRONTAL CORTEX

Feng-Kuei Chiang[1], *Joni D. Wallis*[2], *Erin L. Rich*[1,*]

[1] Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, USA
[2] Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, USA
[*] erin.rich@mssm.edu

Working memory (WM) is a key cognitive ability with limited capacity, estimated to be about 4 items [1]. The use of mnemonic strategies allows us to overcome this capacity constraint, however the neural basis of such strategies remains unclear. A recent study found that monkeys spontaneously adopt WM strategies in a self-ordered target-selection task [2], for example selecting targets in stereotyped sequences. As sequencing increased, WM performance improved, but tuning for selected targets decreased in lateral prefrontal cortex (LFPC) neurons. Using this data set, we assessed how sequencing strategies changed population codes for information held in WM.

In the task, monkeys were shown 6 identical visual targets and required to saccade to each, one at a time in any order, returning their gaze to the center point between selections. Juice reward was delivered upon selection of a new target, but not if the target was previously visited in that trial. Thus, subjects had to use WM to track visited targets. Target configurations were consistent for blocks of 40 trials, and the reliability with which monkeys followed self-generated sequences was quantified [2].

We first assessed information in LFPC ensembles using simple linear classifiers to decode target identities (defined by spatial locations) or saccade number. Counterintuitively, decoding improved when monkey behavior was more sequenced, despite decreased tuning among individual neurons. To explore this, we quantified each neuron's contribution to the classifier, and found that contribution variance decreased with more sequencing, as did the mean contributions. Thus, sequencing corresponded to more homogenous population codes with less information in individual neurons. In addition, optimal decoding could be achieved by subsamples of the full ensemble. Optimal ensemble sizes increased with more stereotyped behavior, so that more neurons were required to accurately decode task information when sequencing strategies were used. Overall, sequencing resulted in a greater distribution of WM information in LPFC, with more information in the overall population, but less information per neuron. In contrast, more flexible behaviors corresponded to a smaller number of neurons carrying more task-relevant information.

Acknowledgments

Supported by The Whitehall Foundation (ELR), R01MH097990 (JDW), and Taiwan Top University Strategic Alliance Graduate Fellowship USA-UCB-100-S01 (FKC).

References

1. Cowan (2001) *Behav Brain Sci*, 24:87–114, 10.1017/s0140525x01003922 2. Chiang, Wallis (2018) *PNAS*, 38:7013–7019, 10.1073/PNAS.1805044115

REAL-TIME FEEDBACK CAN PROMOTE TASK-RELEVANT MEMORY REPLAY

Anna K. Gillespie[1,], Daniela A. Astudillo Maya[1], Daniel F. Liu[1], Eric L. Denovellis[1], Michael E. Coulter[1], Sachi Desse[1], Demetris Roumis[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
[3] Department of Mathematics and Statistics, Boston University, Boston, MA, USA
[*] anna.gillespie@ucsf.edu

The ability to generate representations of past or potential future 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 or potential future experience, and multiple correlative and causal studies have demonstrated that SWRs critically contribute to these cognitive functions. Further, impaired SWRs and replay have been reported in multiple rodent models of memory impairment. However, the specific role of SWRs and replay in memory and planning processes remains unclear. To test hypotheses about the role of SWRs and provide a potentially therapeutic intervention to modulate these processes in disease, we therefore developed an operant conditioning paradigm in which real-time feedback triggered by online detection of SWRs reinforces hippocampal replay. Training of rats 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 in order to modulate physiologically relevant patterns of hippocampal network activity.

This manipulation took place in the context of a dynamic spatial task, allowing us to ask whether enhancing SWR activity improved performance on individual trials and to relate replay content with specific decisions. To assess the replay content of conditioned SWRs, we apply a marked point process clusterless decoding algorithm [1] and a novel state-space movement classifier that captures the spatiotemporal structure of replay. We find that conditioned events contain indistinguishable replay content compared to control events, including frequent expression of task-relevant spatial trajectories. However, replay did not reliably predict the rat's upcoming or immediate previous destination, and further, the increase in replay did not improve performance of the task. These findings are inconsistent with a common interpretation of replay as a direct planning or deliberation signal, and instead suggest a more complex role for replay in this spatial memory task. Future work will assess the effect of promoting SWR activity during task learning and in disease models.

Acknowledgments

This work has been funded by the Howard Hughes Medical Institute, NIH MH105174, and a Simons Foundation Postdoctoral Fellowship to AKG.

Reference

1. Deng, Liu, Karlsson, *et al.*, 2016, *J. Neurophysiol.*, 116(5):2221–2235

BEHAVIORAL AND NEURAL CORRELATES OF EPISODIC MEMORY CONFIDENCE IN RAT

Hannah R. Joo[1,], Hexin Liang[2], Jason E. Chung[1], Charlotte Geaghan-Breiner[2], Jiang Lan Fan[2], Adam Kepecs[3], Loren M. Frank[2]*

[1] Medical Scientist Training Program and Neuroscience Graduate Program, UCSF, CA, USA
[2] Kavli Institute for Fundamental Neuroscience, CIN, and Physiology Dept., UCSF, CA, USA
[3] Washington University School of Medicine, St. Louis, MO, USA
[*] hannah.joo@ucsf.edu

Memory is unreliable. It fades and loses fidelity, and can lead us to make incorrect choices. To mitigate these possible errors, we can ask: *is what I remember what really happened?* Such an introspective assessment of memory confidence is indispensable in deciding what to do.

It is well established that perception follows probabilistic principles and that brains are able to compute and use sensory uncertainty [1]. Whether this is also true for information retrieved from memory is less established. While recent studies have reported correlates of memory confidence in visual tasks [2, 3], the neurophysiology of confidence in episodic memories (with features *where*, *when*, and *what*) is not understood. Moreover, whether non-primate species use memory confidence is not known. To address these questions, we developed a novel spatial sequence memory task in the rat. On a large maze with six radially located choice ports, two ports are cued with a light on each trial. The rat must visit the one that was last visited further in the past, then invest a variable time at the port. For correct choices only, a reward amount proportional to the invested time is delivered. This allows the rat to maximize overall reward by investing more time for those choices that are based on more accurate memory recall. We found that, indeed, rats invested more time preceding correct outcomes relative to errors, and did so in a graded fashion consistent with an ability to compute episodic memory confidence. This reveals that rats have metacognitive memory recall, opening the door to a mechanistic understanding of the underlying neural processes.

To begin investigation of this neural activity, we focused on three interconnected brain areas: the dorsal hippocampus (HPC), for its representation of spatial memory; the orbitofrontal cortex (OFC), where firing rates are correlated with decision confidence in rodent perceptual discrimination tasks [4]; and the nucleus accumbens (NAc), which receives inputs from both HPC and OFC. We recorded single unit spiking in all three areas simultaneously, using tetrodes in HPC and polymer electrode arrays in OFC and NAc in a single implant (288 channels), in rats performing the episodic confidence task. We are currently investigating the activity in these areas, and the coordination between them, that may support episodic memory confidence.

Acknowledgments

NIMH F30MH115582 (H.J.), F30MH109292 (J.C.), U01 NS107667 (L.F.), U01 NS094288 (L.F., A.K.); NIGMS MSTP T32GM007618 (J.C., H.J.); Howard Hughes Medical Institute (L.F.).

References

1. Pouget, Drugowitsch, Kepecs, 2016, *Nat. Neurosci.*, 19(3):366–374
2. Rutishauser, Ye, *et al.*, 2015. *Nat. Neurosci.*, 18(7):1041–1050
3. Miyamoto, Osada, Setsuie, *et al.*, 2017, *Science*, 355(6321):188–193
4. Lak, Costa, *et al.*, 2014, *Neuron*, 84(1):190–201

MAINTENANCE OF VISUAL WORKING MEMORY BY A CORTICOCORTICAL LOOP

Ivan Voitov[*], *Thomas Mrsic-Flogel*

Sainsbury Wellcome Centre, University College London, London, UK
[*]i.voitov@ucl.ac.uk

Connections between cortical areas are almost always reciprocal. Theories of perception-as-inference have stressed the interdependent nature of feedback and feedforward representations in generating behaviorally relevant perceptual models. We therefore hypothesized that task-dependent, internally generated cortical feedback representations will be sensitive to simultaneously ongoing feedforward activity.

We examined this hypothesis in a novel visual working memory paradigm using head-fixed mice, in which animals alternated performing blocks of a delayed (non-)match-to-sample task and a simple Pavlovian discrimination task. Critically, the two tasks did not differ in stimuli, reward, or movement, such that we could experimentally isolate the internal representations of visual working memory in our neural recordings. Using optogenetic silencing we examined the contributions to visual working memory of several cortical regions in different phases of each trial, and identified a highly distributed role of the neocortex in supporting working memory at the start of the inter-stimulus delay periods.

We next investigated neural activity in higher visual area AM and premotor area M2, which are reciprocally connected, and found robust population representations of task variables, including working memory engagement and strength. As a more direct test for the instantaneous necessity of this cortical loop for memory maintenance, we transiently silenced either area AM or M2 (feedforward) while imaging incoming axons from the reciprocally connected area (feedback) at the onset of the delay. While the magnitude of this optogenetic perturbation on neural activity of either projection was similar between the two tasks, the population representation of working memory was selectively disrupted. This effect was specific to the memory-dependent task and persisted until the end of the delay. Our results therefore support the role of reciprocal cortical interactions in maintaining distributed cognitive representations during visual working memory.

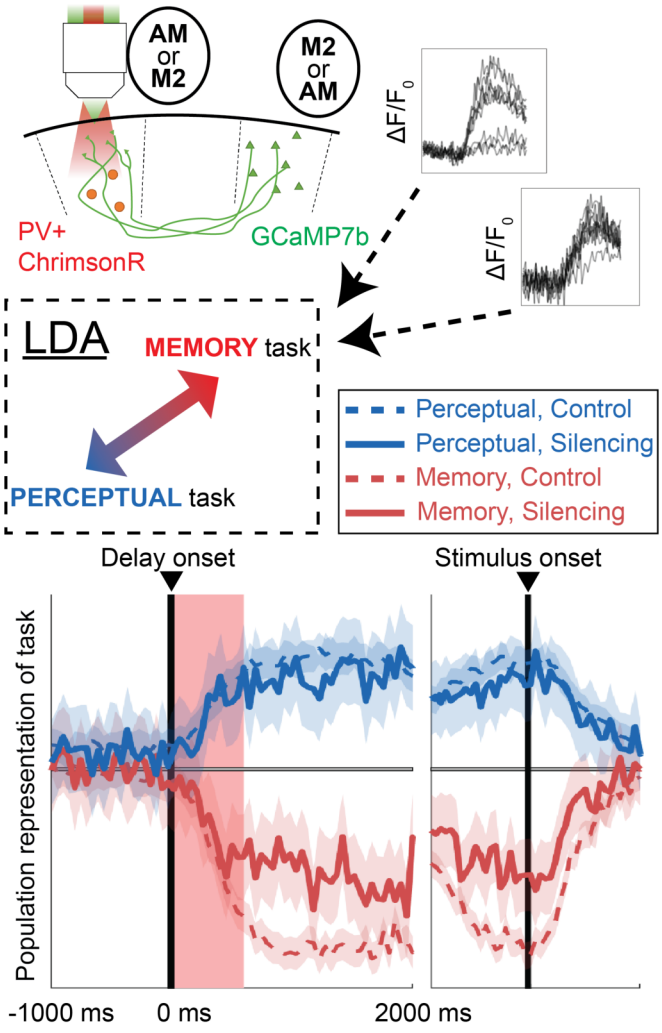


Figure 1.

REORGANIZATION OF NEURONAL POPULATION CODES IN THE ACC UNDERLIES LONG-TERM MEMORY RETRIEVAL

Meytar Zemer[*]*, Noa Brande-Eilat, Liron Sheintuch, Alon Rubin, Ofer Yizhar, Yaniv Ziv*

Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel
[*]meytar.zemer@weizmann.ac.il

The contribution of prefrontal circuits to episodic memory retrieval increases with time following learning, suggesting that in these circuits, memory representations evolve in a way that benefit retrieval [1–3]. How memory representations in the prefrontal cortex evolve with time and what aspects of this evolution contribute to remote memory retrieval remain unknown.

We used Ca^{++} imaging with miniature microscopes to longitudinally record from hundreds of neurons in the anterior cingulate cortex (ACC; part of the medial prefrontal cortex) of freely behaving mice [4]. The experiment consisted of eight recording days. During the first four days, mice explored two novel neutral environments. On the fifth session, mice underwent contextual fear conditioning in a new context, and were placed in the same context after two days (recent recall group, $n = 7$) or 35 days (remote recall group, $n = 9$). On the two following days mice were re-exposed to the same neutral environments they explored on days 1–4.

We found that neuronal activity in the ACC discriminates between different spatial contexts. Contrary to predictions made by recent studies that tagged active neurons using immediate-early genes, we found no differences in the number of active neurons or their firing rates between recent and remote recall sessions. However, during remote recall, ACC neurons exhibited higher pairwise correlation than during recent recall. The increased pairwise correlation during remote recall was specific to the fear conditioning context and was not observed during exploration of the neutral environments, suggesting the observed time-dependent changes in population activity were specific to the learned information. Finally, we found that population activity in the ACC better differentiated between the fear conditioning context and a neutral context during remote recall, relative to recent recall, and that the difference between these contextual representations correlated with the amount of time spent freezing during remote recall. Taken together, our results suggest that population activity in the ACC becomes more organized and more contextually informative with time following learning, pointing to specific aspects of the neural code that may underlie the emergent time-dependent involvement of prefrontal circuits in memory retrieval.

References

1. Frankland, Bontempi, *et al.* (2004) *Science* 304(5672):881–3, 10.1126/science.1094804
2. Maviel, Durkin, Menzaghi, *et al.* (2004) *Science* 305(5680): 96–99, 10.1126/science.1098180
3. Ding, Teixeira, Frankland (2008) *Learn. Mem.* 15(5):290–293, 10.1101/lm.905008
4. Sheintuch, Rubin, *et al.* (2017) *Cell Reports* 21(4):1102–1115, 10.1016/j.celrep.2017.10.013

NEURONAL SIGNATURE FOR TEMPORAL-ORDER MEMORY AND TEMPORAL CONTEXT IN MACAQUE MEDIO-POSTERIOR PARIETAL CORTEX

Shuzhen Zuo[1], Lei Wang[1], Zhiyong Jin[1], Makoto Kusunoki[2], Yong-di Zhou[3], Sze Chai Kwok[1,]*

[1] School of Psychology and Cognitive Science, East China Normal University, China
[2] Department of Experimental Psychology, University of Oxford, Oxford, UK
[3] School of Psychology, Shenzhen University, Shenzhen, China
[*] sk5899@nyu.edu

Humans and rodents recall the past by replaying fragments of events temporally. Our recent study also demonstrated that macaque monkeys apply a non-linear forward, time-compressed replay mechanism during temporal-order judgement with naturalistic material (Zuo, Wang *et al.*, bioRxiv, 2020). However, the neuronal correlates of memory replay and temporal context in the macaques remains understudied. To elucidate these issues, we recorded multi-unit activities simultaneously with 32 independently movable microelectrodes in the dorsal-medial posterior parietal cortex on two monkeys, while they performed a temporal order judgement (TOJ) task between two frames extracted from videos they had watched and encoded.

We first clarified that these neurons and their firing patterns are implicated during the memory processes. We showed that the firing patterns during TOJ are more similar to the segment(s) in the video from where the video frames were extracted (*i.e.*, the moment in which probe frames occurred in the encoding phase) than other segments (*i.e.*, where probe frames were not contained in the encoding phase) and inter-trial intervals (as control condition), providing evidence that the firing activity during encoding is related to their subsequent memory judgement. Moreover, these correlations are significantly stronger for correct trials than for incorrect trials, suggesting the firing similarity between encoding and retrieval is important for memory performance.

However, this effect could be attributed to recognition memory rather than memory replay of the material. We therefore looked specifically into the time-series of each phase by finely dividing the encoding phase and retrieval phase into eighty 100-ms bins and computed the pair-wise Pearson correlation between firing rates for all neurons in each temporal bin of the retrieval phase with each temporal bin of the encoding phase. The results show that the firings for the initial phase of TOJ are more significantly correlated with the encoding phase as compared to the latter phase of TOJ, revealing some fine-tuned temporal dynamics during TOJ which is consistent with our behavioral RT findings. It is thus possible to decode the temporal location of chosen frame (*i.e.*, the location of frame in the video that the monkey chose during TOJ). In addition, we also tapped into the population signals in the encoding stage to look for correlates for contextual representation of the dynamic videos. We used the neuronal patterns to track the changing temporal context across the encoding stage and found that neurons fire more similarly for events that occurred closer in time as compared with events that occurred farther apart in time (Mahalanobis distance for temporally close vs. far events: All $P < 0.001$, except one session $P = 0.015$). Altogether, these findings help delineate the neuronal signature for temporal-order judgement and temporal-context for dynamic cinematic information in the macaque parietal cortex.

MOTOR AND SENSATION

MODELING DIRECTION SELECTIVITY DURING MOVEMENT PREPARATION AND EXECUTION IN THE MOTOR CORTEX

Ludovica Bachschmid-Romano[1,*], *Jason MacLean*[2–4], *Nicholas G. Hatsopoulos*[2,4,5], *Nicolas Brunel*[1,6]

[1] Department of Neurobiology, Duke University, Durham, NC, USA
[2] Committee on Computational Neuroscience, University of Chicago, Chicago, IL, USA
[3] Department of Neurobiology, University of Chicago, Chicago, IL, USA
[4] Grossman Inst. for Neurosci., Quant. Biol. and Human Behav., U. Chicago, Chicago, IL, USA
[5] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[6] Department of Physics, Duke University, Durham, NC, USA
[*] ludovica.bachschmid.romano@duke.edu

The role of the motor cortex's activity in the stages that precede motor action is a central question in understanding the neural substrate of motor control. Recent studies suggest that the same preparatory process that is displayed in a delayed-reaching task appears also before non-delayed movements [1] and it is also involved in reach correction [2]. It has been suggested that the preparatory activity serves to settle the initial state of a dynamical system whose evolution will give rise to future movements [1, 2], yet it is still poorly understood how such computation can be implemented at the level of the network population dynamics. We propose a simple rate network model that encodes movement direction during both preparation and execution, where single neurons can display different tuning properties in the two epochs. Neurons receive both input currents from outside of the network and recurrent inputs mediated by direction-specific cortical interactions. A mean-field formalism allows us to describe the system dynamics by a few global measures of the tuning properties of the neurons. We show that our model can reproduce the time evolution of the population responses recorded in the Hatsopoulos Laboratory from the primary motor cortex of a macaque monkey during an instructed-delay reaching task [3]. We also show that the strength of external input required for the network to sustain the observed activity is minimal if the external input is weakly anisotropic and recurrent connections depend on the tuning properties of the neurons.

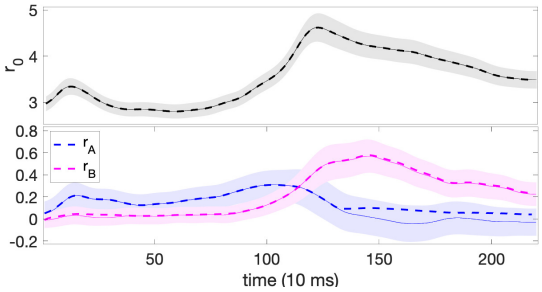


Figure 1. Dynamics of the order parmeters. r_0 measures the average network activity; r_A and r_B measure the spatial modulation of the activity profile during preparation and execution, respectively. Solid lines: order parameters computed from data. Dashed line: mean-field prediction.

Acknowledgments

This work has been supported by NIH R01NS104898.

References

1. Lara, Elsayed, Zimnik, Cunningham, Churchland. *Elife* 7 (2018):e31826
2. Ames, Ryu, Shenoy, 2019, *Nat Comms* 10.1:2718
3. Rubino, Robbins, Hatsopoulos, 2006, *Nat Neurosci* 9.12:1549

STABILITY AND DYNAMICS OF FUNCTIONAL NETWORKS IN MARMOSET MOTOR CORTEX DURING UNCONSTRAINED, VOLUNTARY MOTOR TASKS

Marina Sundiang[1,2,*], *Jeff D. Walker*[2], *Dalton D. Moore*[1,2], *Jason N. MacLean*[1–3], *Nicholas G. Hatsopoulos*[1–3]

[1] Committee in Computational Neuroscience, University of Chicago, Chicago, IL, USA
[2] Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[3] Grossman Institute, University of Chicago, Chicago, IL, USA
[*] sundiang@uchicago.edu

Individual neurons do not function in isolation; Networks of interconnected neurons are required to propagate information between and within different brain areas to carry out different behaviors. Thus, in order to gain insight on how the motor cortex drives voluntary behaviors and facilitates the learning of new motor skills, it is important to describe single neuron activity relative to movement and also neuronal activity relative to other neurons; *i.e.* the circuit. Moreover, investigating unconstrained ethologically relevant behaviors may reveal richer dynamics of these neural populations that may not be salient during more constrained tasks. Here, we present an experimental paradigm to simultaneously record large-scale neural and behavioral data from unconstrained, freely behaving marmosets while they voluntarily engaged in a visually cued reaching task.

We took advantage of the marmosets' natural tendency to forage for food and developed a motor task to allow marmosets to learn new prey hunting strategies. To do so, we simulated movement of the Tenebrio molitor beetle, a prey target of the marmoset in the wild, by parameterizing a correlated random walk. A moving target follows the generated beetle trajectory and is presented to the marmoset via a touchscreen. Marmosets self-trained in this platform throughout the day, and demonstrated learning by increasing successful captures, and decreasing their time to capture the prey. Using DeepLabCut, a pose estimation toolbox, we were able to track upper limb kinematics, comparing joint angles from trial to trial, and session to session, in order to assess motor learning. Additionally, we used a wireless recording platform to record from a multi-electrode array in marmoset primary motor cortex and neighboring cortical areas, recording activity from a population of cells while the marmosets engaged in the task.

We then employed an analytical framework that relates reach similarity to functional networks which summarize pairwise correlations between neurons. In preliminary results using macaque motor cortical data during a reaching task, we constructed functional networks by measuring the estimated the mutual information between spike trains during different reach directions and found that the similarity of these dynamically reorganized circuits is related to the similarity of the reach. This result suggests that pairwise correlations across the recorded population are modulated by the specifics of each reach which in turn argues in favor of a network perspective when evaluating multi-neuronal recordings.

Acknowledgments

Supported by NIH R01 104898–01.

TACTILE CODING IN CUNEATE NUCLEUS

Aneesha K. Suresh[1,], Qinpu He[1], Lee E. Miller[2], Sliman J. Bensmaia[3]*

[1] Committee on Computational Neuroscience, University of Chicago, Chicago, IL, USA
[2] Department of Physiology, Northwestern University, Chicago, IL, USA
[3] Department of Organismal Biology and Anatomy, University of Chicago, Chicago IL,
[*] aneesha@uchicago.edu

The coding of tactile information has been extensively studied in the nerves and in the primary somatosensory cortex (S1 or Area 3b) of non-human primates. One of the themes to emerge from this work is that sensory representations in S1 differ from those at the periphery in two important ways. First, while cutaneous nerve fibers can be classified into a small number of submodalities, each responding to a different aspect of skin stimulation, individual S1 neurons integrate sensory signals from multiple submodalities and exhibit a wide range of response properties [1, 2]. Second, the responses of cortical neurons reflect computations on their inputs — temporal and spatial differentiation — which lead to give rise to explicit representations of behaviorally relevant stimulus features, such as edge orientation or motion direction [3, 4]. The degree to which these properties of S1 responses begin to emerge in the two intervening structures along the medial lemniscal pathway, namely the cuneate nucleus (CN) and the ventroposterior nucleus of the thalamus, is unknown.

In these studies, we investigated the extent to which the elaboration of tactile representations occurs at the CN. To this end, we record the response of CN neurons to stimuli that have been used to characterize responses both in the nerve and in the cortex, including skin indentations, vibrations, and scanned edges and dot patterns. We then characterize the response properties of CN neurons and compare them to their peripheral and cortical counterparts. We find that that individual CN neurons exhibit properties that are indicative of convergent input from multiple cutaneous submodalities and perform computations that form the basis of those observed in cortex. We conclude that the CN is not a simple relay station for tactile information, but rather plays a critical role in processing tactile signals and modulating them depending on the behavioral state of the animal.

Acknowledgments

This work was supported by NIH NINDS Grants NS-095162 (S. J. Bensmaia and L. E. Miller) and F31 NS-096952 (A. K. Suresh).

References

1. Prud'homme, Kalaska, 1994, *J Neurophysiol*, 72(5)
2. Saal, Bensmaia, 2014, *Trends Neurosci*, 37(12):689–697
3. Bensmaia, Denchev, Dammann, Craig, Hsiao, 2008, *J. Neurosci.*, 28(3):776–786
4. Harvey, Saal, Dammann 3rd, Bensmaia, 2013, *PLoS Biol*, 11(5):e1001558

LAYER 2/3-DOMINANT DYNAMIC REORGANIZATION OF MOTOR CORTICAL CIRCUITS DURING MOTOR SKILL LEARNING

Yuanlei Yue[1,2], Pan Xu[1,2], Zhichao Liu[3], Hongfei Du[6], Zekai Chen[1], Juntao Su[1], Ryan T. Ash[5], Emre Barut[6], Stelios M. Smirnakis[5], Chen Zeng[3], Hui Lu[1,2,]*

[1] GW Institute for Neuroscience, The George Washington University, Washington, DC, USA
[2] Dept. Pharmacol. Physiol., Sch. of Med. Health Sci., George Wash. Univ., Washington, DC, USA
[3] Dept. Physics, Columbia College of Art and Sci., George Wash. Univ., Washington, DC, USA
[4] Dept. Psychiatry, Stanford University, Palo Alto, CA, USA
[5] Dept. Neurol., Brigham and Women's Hosp., JP VA Hosp., Harvard Med. Sch., Boston, MA, USA
[6] Dept. Statistics, Columbia College of Art and Sci., George Wash. Univ., Washington, DC, USA
[*] huilu@email.gwu.edu

All brain activity involves neurons generating fast-propagating spikes to encode and relay information within dynamic neural networks, whose workings can be deciphered using optical and computational tools. The primary motor cortex (area M1) is known to enable normal motor skill learning. It is not yet well understood how a given network changes through the process of learning a skill.

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, we found that a consistent proportion of M1 neurons dynamically encoded the running speed during the whole learning process although the overall circuit underwent a spatiotemporal reorganization to accommodate motor learning. Motor learning induced circuit reorganization in the superficial but not deep layer of the motor cortex while mice learned to run on this speed-controlled treadmill. We then compared motor learning in wild-type mice and mice with a deficit in motor learning. The results revealed that mice lacking Methyl-CpG-binding protein (MeCP2), an animal model for Rett Syndrome, exhibited impaired both motor skill learning and dynamic circuit reorganization in layer 2/3, but not layer 5a.

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 study neurodevelopmental disorders with motor problems.

Acknowledgments

Supported by NINDS and the March of Dimes Foundation.

NAVIGATION

BEHAVIORAL AND NEURAL EVIDENCE FOR OPTIC FLOW INTEGRATION IN AN ACTIVE NAVIGATION TASK

Panos Alefantis[1,*], *Kaushik J. Lakshminarasimhan*[1], *Xaq Pitkow*[2], *Dora E. Angelaki*[1–3]

[1] Center for Neural Science, New York University, New York City, NY, USA
[2] Department of Neuroscience, Baylor College of Medicine, Houston Texas, USA
[3] Tandon School of Engineering, New York University, New York City, NY, USA
[*] pa77@nyu.edu

Evidence integration is a fundamental hallmark of mammalian intelligence. Yet insights about how the brain integrates inputs come largely from simple laboratory tasks in which sensory cues are discrete (*e.g.*, auditory clicks) and/or have statistics that remain stationary over time (*e.g.*, random dot coherograms). Here we use a naturalistic task in which subjects navigate by temporally integrating momentary evidence about self-motion available from an ethologically-relevant, continuous-valued, dynamical sensory input in the form of optic flow.

In this experiment, monkeys used a joystick to control their linear and angular speeds in a virtual environment and received juice reward for successfully navigating to a goal that was a circular target. The target only appeared briefly (about 300 ms) and the virtual world comprised a ground plane whose texture elements were continually repositioned and reoriented, making it impossible to use them as landmarks. Consequently, subjects had to rely on a learned model of the controller (joystick), combine this knowledge with time-varying sensory input (optic flow) to estimate self-motion, and then integrate this estimate to navigate to the remembered goal location. We used three different variations of this task that provide converging lines of evidence that monkeys do integrate optic flow over time in order to navigate. First, we used transient optic flow perturbations of unpredictable magnitude and timing to dislocate monkeys from their intended trajectory. Although these perturbations reduced the precision of the response, the reduction was much less than that expected by chance implying that monkeys dynamically compensated for such perturbations. Second, reducing the reliability of optic flow by varying the density of the ground plane elements compromised behavioral performance, implying that subjects' self-motion estimates are affected by noise in optic flow measurements and these effects propagate to behavior via temporal integration. Finally, we manipulated the gain of the joystick controller to alter the sensorimotor mapping learned by the monkeys and found that they rapidly adapted to the different gain values by adjusting their travel duration. We also recorded neural activity from neurons in PPC while the animals performed the task. We found sequential neural dynamics, neurons were activated at different points of the trajectory as the animal moved towards the goal, constituting a sequence. This sequence was robust to precise goal location and is a signature of sensory integration implemented by neural circuits.

These results suggest that the monkeys can navigate by integrating optic flow in an active sensorimotor paradigm and this computation is reflected at the neural sequential activity observed in PPC neurons.

Acknowledgments

This work has been supported by grants EY825538 and R01DC014678.

INFLUENCE OF SENSORY MODALITY AND CONTROL DYNAMICS ON HUMAN PATH INTEGRATION IN VIRTUAL REALITY

Akis Stavropoulos[1,*], *Kaushik J. Lakshminarasimhan*[1], *Jean Laurens*[2], *Xaq Pitkow*[2], *Dora E. Angelaki*[1–3]

[1] Center for Neural Science, New York University, New York City, NY, USA
[2] Department of Neuroscience, Baylor College of Medicine, Houston Texas, USA
[3] Tandon School of Engineering, New York University, New York City, NY, USA
[*] ges6@nyu.edu

Path integration is a dynamic, naturalistic, sensorimotor task of sensory evidence accumulation in an active sensing framework where perception and action are not artificially segregated as in most laboratory behaviors. Using a motion-cueing algorithm that links joystick movement to both optic flow and inertial accelerations of a motion platform, we studied active, multisensory navigation in a continuous and dynamic behavioral task, where subjects steer to a remembered target location on a ground plane without landmarks.

We varied both the sensory cues (vestibular, optic flow, and multisensory) and control dynamics (joystick position coupled to varying degrees of self-motion velocity/acceleration) on a trial-by-trial basis. We found that subjects' performance was biased, especially for the vestibular condition, and this bias depended on control dynamics. A Bayesian estimator attributed these results to biased internal estimates of joystick dynamics: subjects depended more on the prior and less on the trial-by-trial sensory measurements in the vestibular than in optic flow/multisensory conditions. We also found that eye movements systematically tracked the latent variable (self-distance to target) in each trial, revealing correlations between eye tracking and steering precision, even in the absence of optic flow (vestibular condition). Eye movements were also influenced by the varying control dynamics, similarly to the subjects' steering.

These results suggest that the brain can infer latent structures that govern the dynamics of the world and that the eyes are tracking these internal beliefs dynamically over time, regardless of the sensory source of those beliefs. Thus, eye movements are an integral component of navigation behaviors, a fact that may explain the growing evidence of oculomotor signals in the navigation neural circuit. Future recordings in oculomotor areas during active sensing tasks could shed light on the role eye movements play in action selection during navigation.

Acknowledgments

This work has been supported by grants EY825538 and R01DC014678.

NETWORKS

A MULTIVARIATE APPROACH TO DECODING CORTICAL NEURAL ACTIVITY THROUGHOUT MULTIPLE STATES OF CONSCIOUSNESS

Lindsey M. Brier[1,], Xiaohui Zhang[2], Eric C. Landsness[3], Jin-Moo Lee[3], Mark Anastasio[2], Joseph P. Culver[1]*

[1] Department of Radiology, Washington University in St. Louis, St. Louis, MO, USA
[2] Department of Bioengineering, University of Illinois, Urbana, IL, USA
[3] Department of Neurology, Washington University in St. Louis, St. Louis, MO, USA
[*] brierl@wustl.edu

Correlation analysis of spontaneous brain activity (*e.g.*, functional connectivity) has provided many breakthroughs in understanding cognitive neuroscience. However, a multivariate approach to decoding individual neural networks from spontaneous neuroimaging data could be influential in understanding how distinct neural ensembles form larger connectivity structures. For instance, network analysis could be used to determine if and how accurately specific brain regions predict activity in other brain regions, thereby creating a hierarchical organization of the cerebral cortex. Further, it is well known that global modulation of brain activity, *e.g.*, by sleep, superficially alters correlation structures [1], however, it is unknown if a more involved multivariate approach to calculating connectivity can circumvent global state-dependent changes.

In order to study specific neural networks, we performed calcium imaging of mice ($n = 5$) expressing the genetically encoded fluorescent indicator GCaMP6f under the excitatory neural promoter Thy1. Mice were imaged while awake, naturally sleeping (NREM), and under ketamine/xylazine anesthesia (K/X). Linear support vector regression (SVR) was used to predict spontaneous neural activity in a specific parcel (parcels as defined in White *et al.* [2]) as a function of activity in other brain parcels. A non-parametric framework [3] was used to evaluate the effectiveness of the model.

The accuracy and reproducibility of each predicted time series was compared to a null distribution created by a 1-D time series wavestrapping procedure [4]. Not only did the prediction accuracy and reproducibility significantly outperform the null distribution (>500%), but the spatial distribution of regions highly contributing to the prediction accuracy of a given parcel resembled seed based Pearson correlation analysis (*i.e.* functional connectivity). Further, these prediction maps were consistent across wake, sleep, and anesthesia. Interestingly, regions proximal to a predicted parcel contributed more than the same parcel in the contralateral hemisphere. This finding could be instrumental in targeting accessory brain regions to aid recovery after stroke.

Acknowledgments

This work has been supported by NINDS R01NS078223 and NIA F30AG061932.

References

1. Brier, Landsness, Snyder, *et al.*, 2019, Neurophotonics, 6(3), 035002
2. White, Bauer, Snyder, *et al.*, 2011, *PLoS ONE*, 6(1):e16322
3. Craddock, Milham, LaConte, 2013, *Neuroimage*, 15;82:127–36
4. Bullmore, Long, Suckling, *et al.*, 2001, *Hum Brain Mapp*, 12(2):61–78

MODULATION OF SENSORIMOTOR CORTICAL ACTIVITY AT MULTIPLE SCALES BY VALENCE EXPECTATION AND MOTIVATION

Joseph T. Francis[1,2,*], *Nivas Kumar*[1], *Yao Zhao*[3]

[1] Dept. of Biomedical Engineering, University of Houston, Houston, Texas, USA
[2] Dept. of Electrical and Computer Engineering, University of Houston, Houston, Texas, USA
[3] Dept. of Physiology and Pharmocology, SUNY Downstate, NY, NY, USA
[*] jtfrancis@uh.edu

When planning and executing movements animals are rarely in the same affective/emotional state. Whether one is motivated by the expectation of reward or punishment can have an influence that is clear from personal experience. Currently we have the ability to record from hundreds of electrodes within several brain regions in non-human primates (NHPs) simultaneously, and as NHPs have similar affective neural structures as humans, we can ask questions about how the affective state of a subject influences neural dynamics that have been considered necessary for movement production and planning. We have started testing these concepts while tracking the neural state and dynamics of the cortex when NHPs either make reaching or grasping movements, observe such movements, or control such movements via a BMI, while we influence their affective state by cuing the possible reward level to be gained on a trial if successful, or the amount of timeout punishment if unsuccessful.

We recorded single-, multi-unit and local field potentials (LFPs) simultaneously from 384 electrodes implanted in M1, S1 and PMd of 4 non-human primates (NHPs), while the NHPs conducted the above stated tasks. We utilized multiple levels of analysis from single unit (divisive normalization models), populations of units (Tensor Component analysis, TCA; noise correlation, jPCA), and cross-level analysis (Spike-field Coherence and Phase-Amplitude Coupling). We found at all levels of analysis there is a clear influence of valence and motivation in each brain region (M1, S1 and PMd). We have found clear results utilizing divisive normalization models where the brain regions population activity acts as the divisive term normalizing individual units. With this analysis we found that the neural population represents both valence and motivational intensity and will present results on the distribution of such representations within the three brain regions. We have also found changes in noise correlation within the neural populations as well as changes in the strength of Spike-field coherence and phase amplitude coupling when looking at the LFPs alone. Finally, we have found support for learning dynamics within M1 reflecting a reinforcement learning process as the NHPs tracking and learn the state values associated with conditioned stimuli within a task. We found that this state-value representation is clear even when there is no explicit cue of a trial's valence as long as the state-valence is predictable based on a temporal sequence.

Acknowledgments

This work has been supported by NIH 1R01NS092894-01, NSF IIS-1527558, NYS SCIRB C30600GG C030838GG and C32250GG, DARPA N66001-10-C-2008.

ON THE FUNCTIONAL ORGANIZATION OF THE SPACE OF NEURONAL NETWORKS AND THE COMPUTATIONAL IMPLICATIONS OF DALE'S PRINCIPLE

Adam Haber[*], *Elad Schneidman*

Neurobiology Department, Weizmann Institute of Science, Rehovot, Israel
[*]adam.haber@weizmann.ac.il

The nature of connectivity between neurons in a network shapes the dynamics, learning processes, and function of the network. Typically, this connectivity is highly non-random, governed by spatial and physical constraints, wiring cost and accuracy, and biochemical limitations. These structural constrains, in turn, must reflect on the function of neural circuits.

One obvious structural constraint is that all outgoing synapses of a neuron are either excitatory or inhibitory, also known as Dale's principle. The interplay between excitation and inhibition in the brain has been studied widely, experimentally and theoretically, yet little is known about the implications of Dale's rule on the computational capacity of neural circuits.

Here we study the *functional* differences between Daleian and non-Daleian networks, using simulated networks of spiking neurons. We presented large ensembles of networks of integrate and fire neurons with a wide range of stimuli, and computed the pairwise similarity between networks, based on their spiking patterns in response to the same stimulus. Importantly, each ensemble was made of many networks of the same size, each with a different topology - including thousands of networks that obeyed Dale's rule and thousands that did not. The pairwise distances define a metric on the space of networks. We asked where are Daleian and non-Daleian networks in this space, and how do they relate to one another.

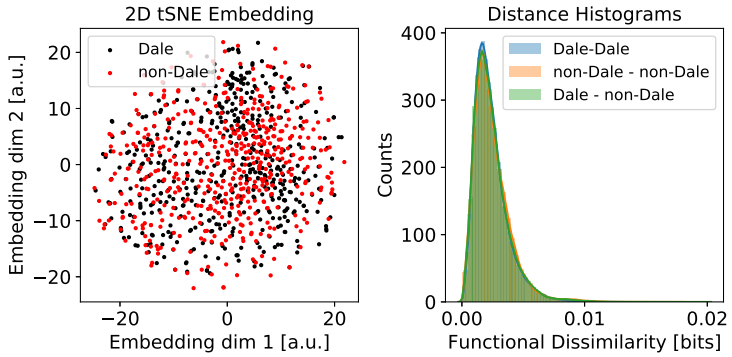


Figure 1. (left) 2D-tSNE embedding of a sample of 1000 networks of 10 neurons, based on the similarity of their responses to Poisson inputs. Daleian network were uniformly distributed among non-Dale ones. (right) Histograms of pairwise distances between different types of networks show high overlap, reflecting the uniform coverage of the space of networks.

We find that over a wide range of stimuli, and ensembles ranging from networks of 4 neurons to 100 neurons, almost all non-Daleian networks had a close Daleian neighbor (see Fig. 1). Thus, the input-output functions implemented by unconstrained networks can be implemented as well by constrained networks. Since Daleian networks have clear structural and assembly benefits, our results suggest a new design principle and a novel framework for studying the computational design of neural circuits.

MULTI-REGION NETWORK MODELS OF BRAIN-WIDE INTERACTIONS DURING ADAPTIVE AND MALADAPTIVE STATE TRANSITIONS

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

[1] Icahn School of Medicine at Mount Sinai, New York, NY, USA
[2] Stanford University, Stanford, CA, USA
[*] matthew.perich@mssm.edu

During prolonged periods of stress, animals can switch from active to passive coping strategies to manage effort-expenditure. Such normally adaptive behavioral state transitions can become maladaptive in disorders such as depression. Here, we studied the neural mechanisms underlying behavioral state transitions using whole-brain neural recordings during maladaptive passivity induced by inescapable stress [1]. Larval zebrafish expressing nucleus-localized GCaMP6s were exposed to a behavioral challenge protocol with repeated electric shocks. Initially, the fish showed vigorous tail movements, indicating an active coping (adaptive) strategy. The fish reduced movements as the shocks persisted, entering into a passive coping (maladaptive) state. We imaged whole-brain neural activity using two-photon (2P) microscopy and developed multi-region recurrent neural network (RNN) models to infer brain-wide directed interactions driving such maladaptive behavior. The models were trained to match experimental data across two levels simultaneously [2]: brain-wide neural dynamics from 10,000 neurons and the behavior of the fish. Analysis of the trained RNN models revealed a specific change in directed interactions between the habenula (Hb) and raphe nucleus during the transition into passivity [1].

Using the directed interaction weights derived from the RNN models, we then calculated the input currents from different brain regions to each Hb neuron. We computed neural manifolds [3] spanning these input currents across all Hb neurons to define subspaces within the Hb activity that independently captured the communication between other individual brain regions. At the onset of stress, there was an immediate response within the Hb/raphe subspace alone. However, RNN models identified no similarly rapid change in the directed interactions between these regions. As the animal lapsed into passivity, responses within the Hb/raphe subspace decreased, with a concomitant change in the interactions between the raphe and Hb inferred from the RNN weights. This innovative combination of network modeling and neural dynamics analysis points to dual mechanisms with distinct timescales driving the behavioral state transition: early response to stress is mediated by reshaping the neural dynamics within a preserved network architecture, while long-term state changes correspond to altered directed interactions between neural ensembles in distinct brain regions.

References

1. Andalman, Burns, Lovett-Baron, *et al.*, 2019, *Cell* 177:1–16, 10.1016/j.cell.2019.02.037
2. Rajan, Harvey, Tank, 2016, *Neuron* 9(1):128–142, 10.1016/j.neuron.2016.02.009
3. Gallego, Perich, Miller, Solla, 2017, *Neuron* 94(5):978–984, 10.1016/j.neuron.2017.05.025

NEURAL CIRCUITRY

FUNCTIONALLY DISTINCT COORDINATED NEURONAL ENSEMBLES IN THE AUDITORY THALAMOCORTICAL SYSTEM

Congcong Hu[*]*, Jermyn Z. See, Christoph E.Schreiner*

University of California San Francisco, San Francisco, California, USA
[*]congcong.hu@ucsf.edu

The highly interconnected neurons in the auditory thalamocortical system are responsible for auditory information processing. It has long been proposed that signal processing in sensory systems requires temporally precise neuronal coordination [1]. Previous studies on coordinated neuronal ensembles (cNEs), defined as groups of neurons with reliable synchronous activity, within primary auditory cortex (A1) have demonstrated cNEs as local network configurations with enhanced information encoding properties [2]. However, the functional properties of cNEs in relation to their contributing neurons are not well understood. Also, whether cNEs are unique to cortical local networks or exist in neuronal populations across brain regions remains unknown.

To better understand the biological relevance of cNEs, we recorded neuronal activities in medial geniculate body (MGB) and A1 using multi-channel probes and identified cNEs using dimensionality reduction techniques. cNE events were isolated to assess spectro-temporal receptive field (STRF) properties. We found there were two main types of cNEs: those with high STRF reliability over member neurons, and those that do not reflect explicit auditory features and might reflect the convergence of top-down inputs. Individual neurons participating in multiple cNEs show that their spike train is a multiplexed representation of different sensory information. Recording simultaneously in the auditory thalamus and A1 revealed that cNEs are functional units that link several levels in thalamocortical system. These properties of cNEs demonstrate their diverse function and benefits and suggest that they manifest general principles of neural computation.

References

1. Zandvakili, Kohn (2015) *Neuron* 87(4):827–39, 10.1016/j.neuron.2015.07.026
2. See, Atencio, Sohal, *et al.* (2018) *eLife* 7:e35587, 10.7554/eLife.35587

INTER-LAYER TEMPORAL CORRELATION MEASUREMENTS REVEAL CONNECTIVITY FIELDS

Georgios Loupas[1], *Epistimi-Anna Makedona*[1], *Ganna Palagina*[3], *Stelios M. Smirnakis*[3], *Maria Papadopouli*[1,2,*]

[1] Institute of Computer Science, Foundation for Research and Technology-Hellas, Greece
[2] Department of Computer Science, University of Crete, Greece
[3] Department of Neurology, BandW/JP Hospitals, Harvard Medical School, Boston MA, USA
[*] mgp@ics.forth.gr

Inter-layer functional connectivity analysis has the potential to uncover input output relationships across layers. To examine the functional connectivity, we estimate the temporal correlation based on an extension of the Spike Time Tiling Coefficient [1], a metric superior to commonly-used measures, as it accounts for relative time shifts, local fluctuations of neural activity or noise, and presence of periods without firing events. Two neurons are functionally connected (*i.e.*, linked by an edge), if their firing activity has a statistically significant temporal correlation compared to a circularly shuffled null distribution of STTC values (control). The firing of neurons located in different layers present substantial temporal correlation (*e.g.*, Fig. 1, left). For each neuron of L2/3 and L5 (reference neuron), we identify the group of neurons in L4 with which it has significant pairwise temporal correlations (*putative connectivity input field* of the reference neuron). Both L2/3 and L5 neurons have multiple significant STTC connections with neurons residing in L4. Furthermore, the probability of firing of both L2/3 and L5 neurons rises sharply as a function of the aggregate number of firing events noted in their corresponding putative connectivity input fields. This probability can be modeled using a sigmoid function. Note that the corresponding relation to the aggregate firing of a control set of L4 neurons remains flat. We comparatively analyze the functional intra- vs. inter-layer architectures and how the identified connectivity fields relate to neuronal response properties.

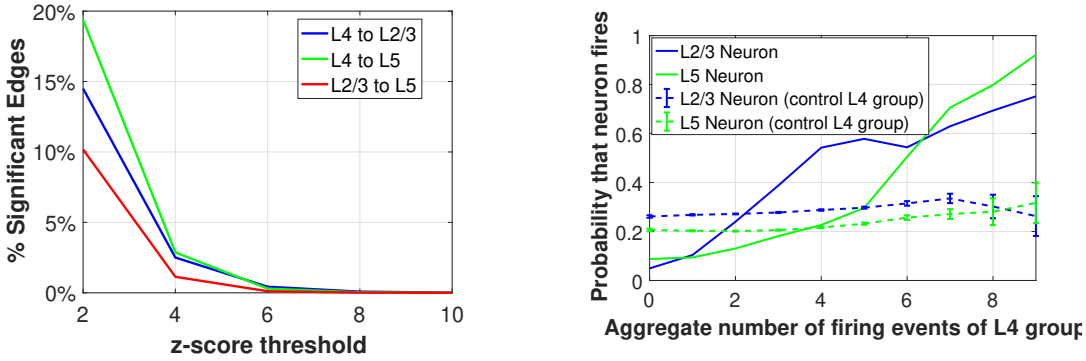


Figure 1. (Left) Significant interlayer edges at different z-score thresholds. (Right) Errorbars refer to 95% confidence interval of the mean. L2/3 and L5 neurons have firing rate of 1.74 and 1.31 Hz, respectively.

Acknowledgment

Funded by the HFRI and GSRT, and NINDS R21.

Reference

1. Cutts, Eglen, 2014, *J. Neurosci.* 34(43):14288–14303, 10.1523/jneurosci.2767-14.2014

PREDICTING OPTOGENETIC RESPONSES THROUGH FULL-DIMENSIONAL MODELS OF INTERNEURONAL CIRCUITRY

Agostina Palmigiano[1,*], *Francesco Fumarola*[2], *Kenneth D. Miller*[1]

[1] Center for Theoretical Neuroscience, Columbia University, New York, USA
[2] RIKEN Brain Science Institute, Saitama, Japan
[*] ap3676@columbia.edu

Optogenetic perturbation of *in vivo* cortical circuits offers a novel angle to characterize the operating regime of cortex. Experiments in mouse [1] show that weak optogenetic perturbation to inhibitory populations decreases both the mean excitatory and, paradoxically [2], the mean inhibitory activity, consistently with inhibition-stabilized-network paradigms. Single-cell stimulation produces a spatially structured inhibitory halo around a local excitatory blob [3]. There is currently no understanding of these results given the presence of multiple inhibitory cell-types, and no model for the structure of inhibitory stabilization within multiple inhibitory populations. Also lacking is the fundamental link between low-dimensional (LD) population-rate models yielding those predictions, and the high-dimensional (HD) models incorporating the full population of each cell-type.

Here we bridge the gap between LD models of V1 circuitry and HD networks of multiple interneuronal types. Incorporating the precisely sculpted architecture of GABAergic connectivity [4], we find that LD circuit response to perturbation possesses several parameter-independent invariants; this is moreover tightly linked to the stability of network sub-circuits. To investigate the robustness of these results, we map an LD circuit to an HD one with log-normally distributed synaptic weights whose means are the LD inter-population weights. Relying on field-theoretical methods for the analysis of such matrix ensembles, we calculate the response of the HD circuit to optogenetic perturbations affecting arbitrary fractions of any cell-type population. The final results reveal that: (*i*) LD and HD circuit responses are intuitively linked only for full-population perturbations unlikely to occur in current experimental setups; (*ii*) partial perturbations, surprisingly, give rise to a bimodal distribution of responses; (*iii*) the fraction of paradoxical responses is in fact a nonlinear function of the fraction of optogenetically stimulated cells. We then proceed to study the extension of the theory to space-dependent synapses, and recover the specific profile of the inhibitory response halo found in the data [3].

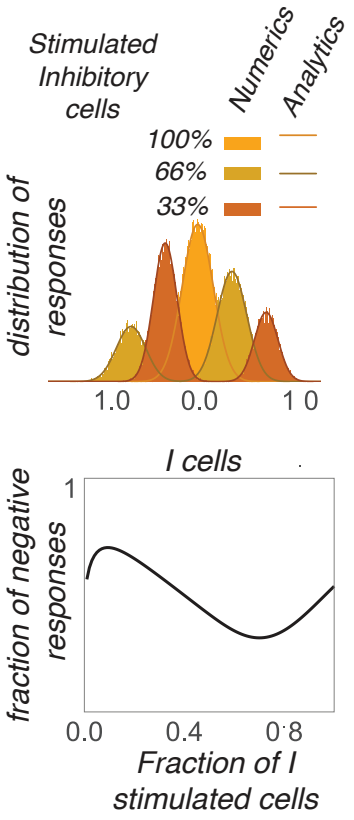


Figure 1. Perturbation to a fraction of neurons gives rise to bimodal distributions, given by a mixture of gaussians that can be computed exactly. The fraction of negative I responses (the fraction of I neurons that exhibit a paradoxical effect) is nonlinear with respect to the fraction of stimulated cells.

References

1. Sanzeni, *et al.*, 2019, *bioRxiv*, 656710
2. Tsodyks, *et al.*, 1997, *J Neurosci*, 17(11):4382–4388
3. Chettih, *et al.*, 2019, *Nature*, 567(7748):334–340
4. Pfeffer, *et al.*, 2013, *Nat Neurosci*, 16(8): 1068–76

INDIVIDUALIZED RT-FMRI NEUROFEEDBACK INDUCES BILATERAL DYNAMIC REORGANIZATION TO FRONTOPARIETAL, INSULAR, CEREBELLAR NETWORKS

T. Dorina Papageorgiou[1,2,], Rasoul Hekmati[1], Duong Huynh[1], Emmanouil Froudarakis[2], Michael Scheurer[3]*

[1] Departments of Psychiatry, Baylor College of Medicine, Houston, USA
[2] Department of Neuroscience, Baylor College of Medicine, Houston, USA
[3] Department of Hematology & Oncology, Baylor College of Medicine, Houston, USA
[*] papageor@bcm.edu

Cranial nerve (CN) IX and XII injuries can result in neuropathic tongue pain, swallowing, mastication, and speech impairment following stroke, head and neck tumors. CN IX and XII nerves receive projections from somato-sensory and -motor areas. We developed a closed loop fMRI-based brain computer interface to enhance voluntary and consistent tongue movement (TM) selectivity in 4 directions, and to elucidate the mechanisms that guide induced control of TM. We induced upregulation of the BOLD via individualized real-time functional MRI neurofeedback (iRTfMRI nFb) by delineating unique networks for each of the 30 subjects we enrolled 30 subjects in a two-day study.

We hypothesized that nFb in comparison to no-nFb will: (i) increase the consistency of decoded spatial patterns that control TM; (ii) increase the area under the curve (AUC), generated by the BOLD's signal intensity in somatomotor and attention areas for each TM direction selectivity, (iii) decrease the BOLD variance in these decoded networks; and iv. decrease the diffusivity of these decoded networks' spatial expansion (reduced number of voxels activated). Our findings delineate the spatiotemporal patterns that characterize direction selectivity induced by iRTfMRI nFb: a bilateral frontoparietal, insular, and cerebellar network, as denoted by increased d-prime and percent increase in the AUC (24–50%). SVM nFb-generated increased classification accuracies for the consistency of the decoded spatial patterns compared to the control-no nFb. The Euclidian distance for the nFb-induced networks shows a decrease in variance compared to the no-nFb (35–86%), visualized using t-SNEs as a function of time. We also show a decrease in the spatial extents, diffusivity of these networks, which denotes that iRTfMRI nFb increases the signal to noise ratio.

We also present findings of a patient with neonatal CNIX and CNXII injuries who underwent longitudinal iRTFMRI nFb. The data shows an increase in speech intelligibility, an increase in the consistency of the networks' patterns shown by support vector machine classification accuracies, an increase in BOLD signal intensity and a decrease in the networks' spatial extents induced iRTfMRI nFb.

This study suggests that the purposeful induction of neuromodulation via iRTfMRI nFb can enhance control of voluntary TM by increasing the consistency and magnitude and decreasing the variance of the BOLD signal across each direction. These findings can lead to the neuro-rehabilitation to patients who have sustained LC IX and XII injuries.

Acknowledgments

Supported by grants to T.D. Papageorgiou: McNair Medical Institute, Robert and Janice McNair Foundation, TIRR/Mission Connect, Junior Faculty Award, NIH-T32.

LOW-DIMENSIONAL DYNAMICS OF SPIKING NEURON NETWORKS

Gianni Valerio Vinci[1,2,*], *Maurizio Mattia*[1]

[1] Istituto Superiore Sanità, Rome, Italy
[2] "Tor Vergata" University of Rome, Rome, Italy
[*] gianni.vinci@iss.it

The collective dynamics of neuronal networks can be complex even when simplified one-compartment spiking (integrate-and-fire, IF) neurons are considered for modeling, due to the high-dimensionality of the system and the quenched randomness in the synaptic couplings. Despite several decades of efforts, a general expression for the dynamics of the population firing rate $\nu(t)$ independent from neuronal models and dynamical regimes expressed is still lacking [1–3]. Here, we contribute to solve this issue by deriving a low-dimensional mean-field dynamics of $\nu(t)$ (*i.e.*, the network activity) valid for a wide class of IF neurons and outside equilibrium. To this purpose we focused on the evolution of the population density of neuron membrane potentials which in these networks is fully captured by a Fokker-Plank (FP) equation [1]. Relying on the first modes in the state-dependent spectral expansion of the FP operator, we derive the 2nd-order ODE $\tau_\nu^2\,\ddot{\nu} + 2\tau_\nu\,\dot{\nu} = (1+\tau_\nu^2\,\omega_\nu^2)(\Phi-\nu)$, with ν-dependent input-output gain function Φ, relaxation time τ_ν and angular frequency ω_ν. In this framework the $\nu(t)$ dynamics naturally incorporates the strength of the synaptic couplings and synaptic delays. The agreement between theory and simulations is shown both under noise- and drift-dominate regimes in networks of LIF neurons for which we explicitly derive both τ_ν and ω_ν (Figure 1).

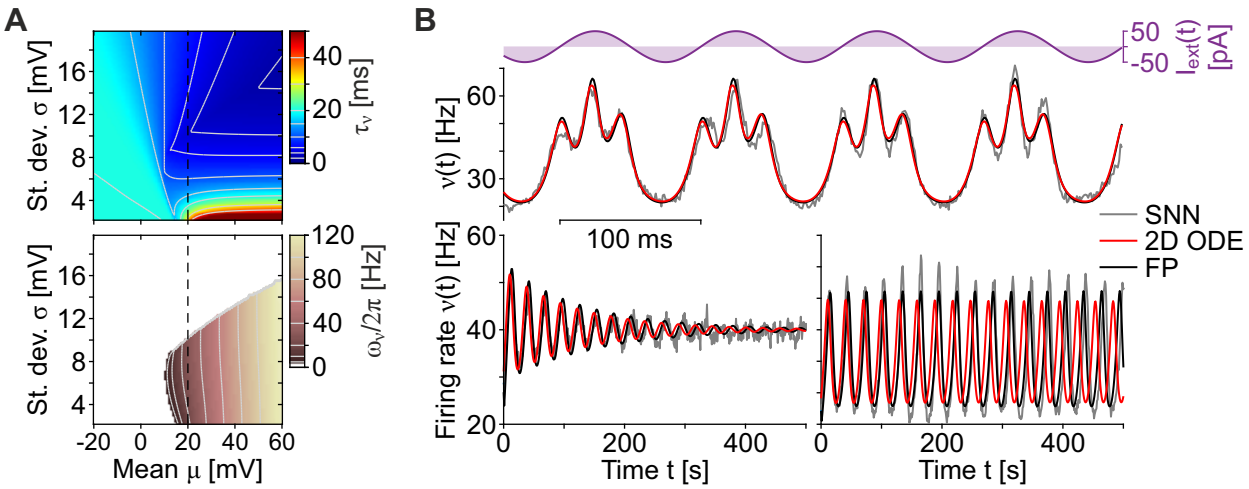


Figure 1. Dynamics of example leaky IF (LIF) neuron networks. (A) Relaxation time τ_ν and angular frequency ω_ν *versus* mean μ and variance ς^2 of the input synaptic current. (B) Match between spiking neuron network (SNN) simulations, numerical integrations of the related FP equation and the derived $\nu(t)$ 2nd-order ODE for an excitatory network stimulated with a sinusoidal input (top), relaxing to an asynchronous state and to a limit cycle (bottom left and right, respectively).

References

1. Mattia, Del Giudice, 2002, *Phys. Rev. E* 66: 051917, 10.1103/PhysRevE.66.051917
2. Schaffer, Ostojic, Abbott, 2013, *PLoS Comput Biol* 9:e1003301 10.1371/journal.pcbi.1003301
3. Montbrió, Pazó, Roxin, 2015, *Phys. Rev. X* 5: 021028, 10.1103/PhysRevX.5.021028

INFORMATION DYNAMIC METRICS TRACK THE EMERGENCE OF COGNITIVE INFORMATION PROCESSING FROM NEURAL CIRCUIT DYNAMICS

Nicole Voges[1,*], *Andrea Brovelli*[1], *Demian Battaglia*[2]

[1] Inst. Neurosci. de la Timone, UMR 7289, Aix-Marseille Université/CNRS, Marseille, France
[2] Inst. Neurosci. des Systèmes, UMRS 1106, Aix-Marseille Université/INSERM, Marseille, France
[*] nicole.voges@univ-amu.fr

Cognitive function arises from the coordinated activity of neural populations distributed over large-scale brain networks. However, it is challenging to understand how specific aspects of neural dynamics translate into operations of information processing, and, ultimately, cognitive functions. To address this question, we combine novel approaches from information theory with computational simulations of canonical neural circuits, emulating well-defined cognitive functions. Specifically, we simulate circuits composed of one or multiple brain areas, each modeled as a 1D ring network of simple rate units. Despite its simplicity, such model can give rise to rich neuronal dynamics [1]. These models can be used to reproduce functions such bottom-up transfer of stimuli, working memory and even top-down attentional modulation [2].

We then apply recent tools from the Information Dynamics framework to simulated data. Information Dynamics is a novel theoretical approach that formalize the decomposition of generic information processing into primitive operations of active storage, transfer and modification of information [3]. In particular, we analyze simulated recordings from our models, quantifying how its nonlinear dynamics implement specific mix of these different primitive processing operations, varying depending on the emulated cognitive function. For instance, we show that the neuronal subsets maintaining sensory representations in working memory (via reverberant self-sustained activity) can be revealed by high values of the active Information Storage metric. Or, the integration of top-down signals (mediated by nonlinear interactions between active sub-populations) is detected by increased values of information modification.

Our models thus highlight transparently the capacity of information dynamics metrics to characterize which network units participate to cognition-related information processing, and how they do it. Such capability can be exploited for the analysis of actual human MEG datasets.

Acknowledgments

This work has been supported by a postdoctoral grant to NV from the Institute of Language, Communication and the Brain (ILCB).

References

1. Roxin, Brunel, Hansel, 2005, *Phys Rev Let* 94(23):238103
2. Ardid, Wang, Compte, 2007, *J Neurosci* 27(32):222
3. Wibral, Priesemann, Kay, *et al.*, (2017) *Brain Cogn* 112:25

NEURAL NET CLASSIFICATION

A DEEP LEARNING FRAMEWORK TO DISCOVER FUNCTIONAL CELL TYPES

Mohammad Bashiri[1], Konstantin-Klemens Lurz[1], Edgar Y. Walker[1–3], Taliah Muhammad[2,3], Erick Cobos[2,4], Alexander S. Ecker[3,5], Andreas S. Tolias[2,3], Fabian H. Sinz[1–4,]*

[1] Institute for Biomedical Informatics, University of Tübingen, Tübingen, Germany
[2] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[3] Center for Neuroscience and Artificial Intelligence, Baylor College of Medicine, Houston, USA
[4] Bernstein Center for Computational Neuroscience, Tübingen, Germany
[5] Department of Computer Science, University of Göttingen, Germany
[*] fabian.sinz@uni-tuebingen.de

Our current understanding of visual system is based on the idea that neurons encode similar features (*e.g.*, Gabor filters) that are transformed differently for each neuron. For instance, two neurons may share the same receptive field structure, but prefer different orientations or locations in the visual field. In current state-of-the-art system identification models, these transformations are often entangled with nonlinear computations shared across neurons. For instance, scaled versions of the same receptive field currently have to be learned as distinct computations. In this work, we constructed a model that disentangles per-neuron transformations from the shared nonlinear computations. Our model achieves comparable performance to state-of-the-art CNN models in predicting the response of a population of neurons to arbitrary natural stimuli while only using a fraction of the number of parameters. The disentanglement allows our model to group neurons into clusters representing distinct nonlinear computations and learn neuron-specific transformations. Overall, our method proves to be a promising tool for identifying functional cell types that serve as the building blocks of complex computations in the visual cortex.

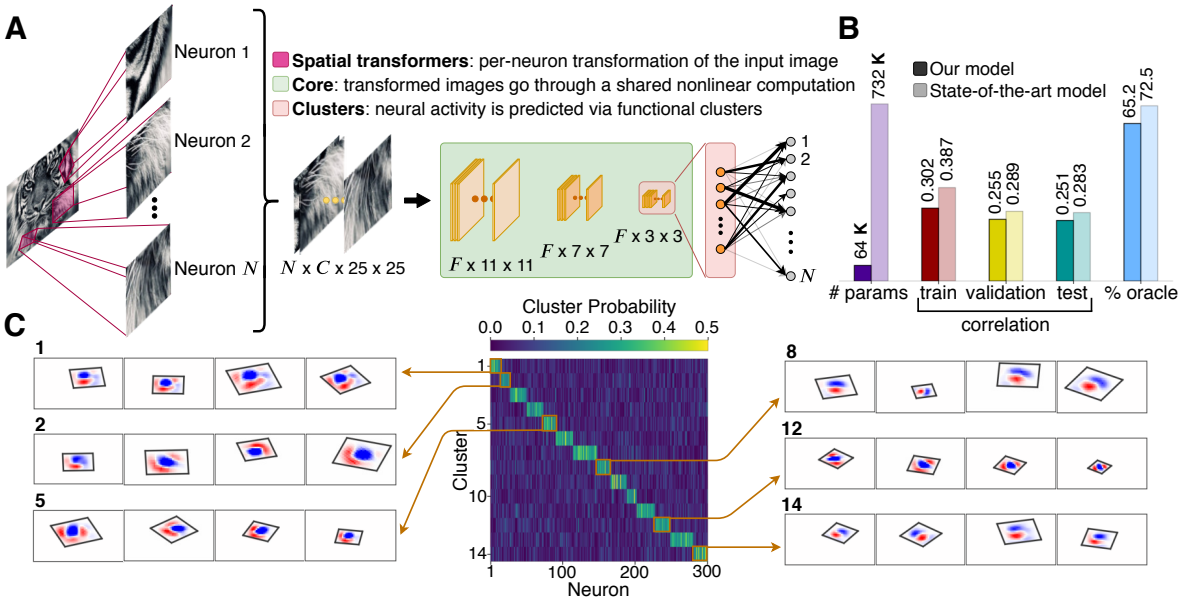


Figure 1. (A) Model architecture. C and F denote number of input channels and filters in each convolution layer, respectively. (B) Model comparison. Correlations are computed between the predicted and single trial neural responses. *Oracle* quantifies the performance of the model relative to best theoretically possible performance. (C) Probability assigned to each cluster for each neuron (middle) and linear receptive fields of four best predicted neurons in each selected cluster (left, right).

NEURO-INSPIRED DEEP LEARNING ARCHITECTURES

Spyridon Chavlis[*]*, Panayiota Poirazi*

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

Deep learning algorithms have enabled remarkable progress in numerous fields over the past decade. Inspired by biological neuronal networks, artificial neural networks are a key component of deep learning architectures. They typically consist of large numbers of nodes, each of which implements a weighted, linear summation of inputs followed by a nonlinear activation function.

A typical biological neuron, however, as revealed by both experimental and modeling studies, is far more complex than the aforementioned linear integrator. Specifically, synaptic inputs in biological neurons can actively modulate neighboring synaptic activity and lead to the generation of local events, the so-called dendritic spikes; Therefore, dendritic structures are highly nonlinear [1]. Such dendritic nonlinearities greatly enhance the processing [2] and storage capacity [3] of individual neurons, enhancing the overall learning capabilities of biological networks. Moreover, the way biological networks learn new information is different from the most popular learning rule in artificial networks, the so-called backpropagation. The latter retrogradely broadcasts a global error to all neurons within a network, in order to fine-tune their respective parameters. Biological networks use learning rules that are often local (*e.g.*, plasticity within a few dendritic branches) and do not have access to a global error signal.

In this study, inspired by the connectivity and learning rules of biological networks, we modeled nodes in deep learning architectures as two-layer units, consisting of non-linear dendritic compartments connected exclusively to their respective somata [4]. We also implemented biologically plausible learning rules and tested the performance of the new algorithm on a typical machine learning task, *i.e.*, the classification of images. We show that our algorithm can achieve excellent performance on the multiclass classification of digits and can outperform naive deep neural networks of similar complexity (same number of parameters). Finally, the use of a novel, brain-inspired learning rule that relies on detecting correlations among inputs results in faster network convergence compared to the backpropagation learning rule. These findings suggest that bio-inspired implementations of deep learning architectures that consider dendritic connectivity, dendritic non-linearities and unsupervised, local learning rules may furnish these networks with important performance advantages.

Acknowledgments

Supported by Stavros Niarchos Foundation.

References

1. Stuart, Spruston (2015) *Nat. Neurosci.* 18(12):1713–21, 10.1038/nn.4157
2. Poirazi, Brannon, Mel (2003) *Neuron* 37(6):989–99
3. Poirazi, Mel (2001) *Neuron* 29(3):779–96, 10.1016/s0896–6273(01)00252–5
4. Wu, Liu, Li, Wu (2018) *NIPS* 31: 8068–79

NEURAL PROCESSES FOR NEURAL PROCESSES (NP^2)

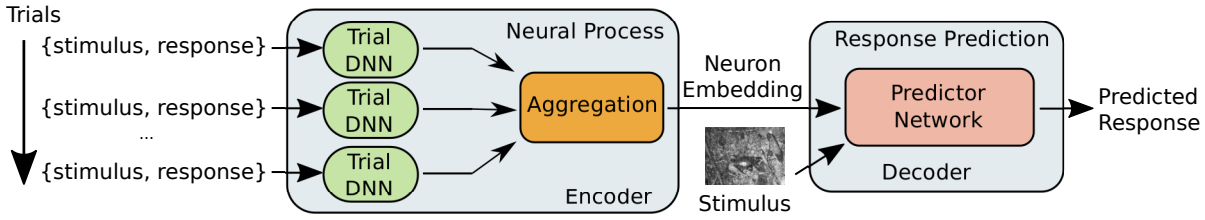
R. James Cotton[1–4,*], *Fabian Sinz*[3–6,†], *Andreas S. Tolias*[3,4,†]

[1] Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, USA
[2] Shirley Ryan AbilityLab, Chicago, USA
[3] Center for Neuroscience and Artificial Intelligence, Baylor College of Medicine, Houston, USA
[4] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[5] Institute for Biomedical Informatics, University of Tübingen, Tübingen, Germany
[6] Bernstein Center for Computational Neuroscience, Tübingen, Germany
[†] equal contribution
[*] rcotton@sralab.org

Deep neural networks can learn common feature spaces shared among many neurons. These models have recently demonstrated significant progress in their ability to predict the responses to arbitrary natural stimuli and are the state-of-the-art functional models of the visual cortex. They have also been used to develop a closed loop paradigm — inception loops — to search for stimuli *in silico* that maximize neural responses; predictions that have been validated *in vivo* [1]. However, parameters must be optimized for each new neuron recorded, making it challenging to apply these models for real-time prediction. Using a recently developed deep learning approach called Neural Processes [2], we replace this slow optimization step with rapid inference.

In our approach, an encoder network takes a set of images and responses from a neuron to produce an embedding representing the neuron response properties (*i.e.* tuning). A decoder network takes a novel image and this per-neuron embedding to predict responses. The entire system is trained end-to-end over many neural datasets. Crucially, this architecture allows a rapid forward pass to generate the neuron embedding and predict responses. This network can be interpreted as a distribution over visual tuning functions, with the embedding network selecting a sample function from this space.

A Neural Processes trained on simulated data successfully learned the visual tuning embedding and accurately predicted the responses to novel stimuli, which by design is computed very quickly. This embedding contained sufficient information to also reconstruct the linear receptive field of neurons and compute the most exciting images. We also trained this architecture on stimuli-response pairs recorded from from mouse primary visual cortex, and achieved comparable predictive performance to optimization-based approaches.



References

1. Walker, Sinz, Cobos, *et al.*, 2019, *Nat. Neurosci.* 22:2060–2065, 10.1038/s41593-019-0517-x
2. Garnelo, Schwarz, Rosenbaum, *et al.*, 2018, arXiv:1807.01622

DEEP CONVOLUTIONAL NEURAL NETWORKS TRAINED TO DECODE HAND MOVEMENTS FROM INTRACRANIAL EEG IN MOTOR CORTEX

Jiri Hammer[1,2,*], *Robin T. Schirrmeister*[2], *Petr Marusic*[1], *Tonio Ball*[2]

[1] Neuromedical AI Lab, Department of Neurosurgery, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany
[2] Department of Neurology, Second Faculty of Medicine and Motol University Hospital, Charles University, Czech Republic
[*] hammer@bcf.uni-freiburg.de

Deep learning based on artificial neural networks is a class of machine learning algorithms that has substantially increased the state-of-the art of hard machine learning problems [1]. Promising results were recently demonstrated also in the field of EEG data analysis and brain-machine interfaces (BMIs), where in particular deep convolutional neural networks (CNNs) yielded promising results [2]. The use of CNNs in BMI applications is an appealing strategy, because CNNs are capable of end-to-end learning, or learning from raw data, and thus automatize the steps of feature extraction, decoder selection and calibration. However, for safety-critical systems, such as the BMIs, it is necessary to understand how CNNs make their decisions and what the characteristics of the EEG features are that the networks have learned.

We applied the CNNs to decode continuous, hand movements in a car driving simulation task from intracranial EEG measured directly in the motor cortex of 12 epilepsy patients undergoing invasive monitoring for a clinical evaluation. We investigated the two main classes of informative iEEG features, namely spectral amplitude and phase, using an input-output perturbation correlation method [2] in the hidden layers of the deep CNNs.

The results show that: (i) the CNNs outperformed a more traditional multiple linear regression algorithm, (ii) were able to extract the spectral amplitude as well as signal phase information from motor cortex in physiologically plausible frequency ranges, consistent with previously published results on a similar dataset [3], and (iii) individual CNN convolution filters specialized in extraction of either the spectral amplitude or phase.

This study is thus an important step towards understanding the internal representation of CNNs trained on intracranial EEG data and underlines the potential of CNNs and deep learning for EEG-based BMIs and neurotechnological applications in general.

Acknowledgments

This work has been supported by GACR 20–21339S, and DFG EXC1086.

References

1. LeCun, Bengio, Hinton, 2015, *Nature*, 521: 436–444, 10.1038/nature14539
2. Schirrmeister, *et al.*, 2017, *Hum Brain Mapp*, 38(11):5391–5420, 10.1002/hbm.23730
3. Hammer, Pistohl, Fischer, *et al.*, 2016, *Cereb. Cortex*, 26(6):2863–81, 10.1093/cercor/bhw033

OLFACTORY CODING

CELL-SPECIFIC LOCAL INHIBITION IMPROVES POPULATION CODING IN DOWNSTREAM NEURONS

Tal Dalal[*]*, Rafi Haddad*

The Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel
[*]taldalal123@gmail.com

Inhibitory interneurons are essential components of the neural circuits underlying various brain functions. Several mechanisms by which inhibitory interneurons improve stimulus representations have been suggested, including decorrelation, contrast enhancement, gain control, normalization, synchronization and sharpening of tuning curves. However, how reduction in firing rates in one brain region can improve downstream neuronal activity is much less understood. Here we recorded odor elicited responses in post-olfactory bulb (piriform cortex) neurons while optogenetically increasing the inhibition impinging on the olfactory bulb output neurons, the mitral and tufted (MT) cells. Strikingly, we found that optogenetically increasing granule cell (GC) activity, but not other GABAergic interneuron types, increased piriform neurons' odor responses and reliability. Furthermore, reducing MT cells' odor responses directly without increasing GC-mediated inhibition did not improve piriform cortex odor responses, suggesting that this effect is mediated mainly through the GC-MT dendro-dendritic synapses. In addition, we found that GC-mediated inhibition increases the SNR and reorganizes the spike-timing of MT odor responses. Finally, we show that increasing GC inhibition improves downstream neuron odor responses at the cost of increasing their odor detection threshold. Together, these results provide the first demonstration of how downstream neuron responses are improved by sharpening the activity of output neurons, via local inhibition. Moreover, they can explain how increasing interneuron activity improves animal performance, while pointing to the cost it may entail. Our findings recommend a shift of focus for future studies, from understanding how inhibition modulates the local spiking activity to how it enhances stimulus representation in downstream neurons.

ODOR NEURAL REPRESENTATION ACROSS SUBSEQUENT BRAIN REGIONS

Rafi Haddad

The Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel.
rafihaddad@gmail.com

Abstract Theoretical studies showed that expansion through random projections and sparsening of neural activity improves neural representations by increasing coding dimension, reducing stimuli overlap and distributing activity patterns more evenly. These mechanisms have been identified in several brain regions and sensory systems including the olfactory system. Here we recorded the activity of hundreds of neurons to nine odors in three successive olfactory processing levels: the olfactory bulb, anterior olfactory nucleus and piriform cortex. We found that in contrast to what is expected from theory, odor stimulus representations become less distinctive as they progress from the olfactory bulb to the cortex. This finding is valid in both awake and anesthetized states, was despite higher sparseness levels of the encoding cortical neurons and population and persisted even when recurrent interactions were abolished in the cortex. Simulation that uses actual odor responses as inputs shows that the observed degradation in odor neural representation in the cortex cannot be explained by differences in sparseness or synaptic connectivity levels but can be explained by assuming variation in the synaptic connectivity levels. This result emphasizes the importance of the synaptic connectivity distribution as opposed to the actual number of connections. These findings shed new light on how neural representation is transformed from the olfactory bulb to the olfactory cortex and question the roles of these olfactory cortices in odor processing. Furthermore, it challenges the contribution of sparse connectivity and non-linear mixing to neural representations.

SEQUENCES

HIERARCHICAL SEQUENCE PROCESSING IN THE MACAQUE PREFRONTAL CORTEX

Marie E. Bellet[*], *Marion Gay, Béchir Jarraya, Stanislas Dehaene, Timo van Kerkoerle, Theofanis Panagiotaropoulos*

CEA, NeuroSpin Center, Gif-sur-Yvette, France
[*]marie.bellet@cea.fr

The ventrolateral prefrontal cortex (VLPFC) has been identified as a potential processor of temporal sequences at multiple hierarchical levels, both in humans and nonhuman primates [1, 2]. However, it is unclear how sequence structures of different complexity are encoded by VLPFC neurons. Using chronic multielectrode recordings in the macaque VLPFC, we probed the responses of prefrontal neurons to visual sequences with different hierarchical levels. We found that VLPFC neurons commonly encode violations to local sequence regularity for both foveally and peripherally presented stimuli, in a stimulus-independent manner. In contrast, responses to global structure violations were sparse and did not generalize across days of recording. Our findings hint at the existence of an abstract prefrontal novelty detector that computes on different hierarchical levels.

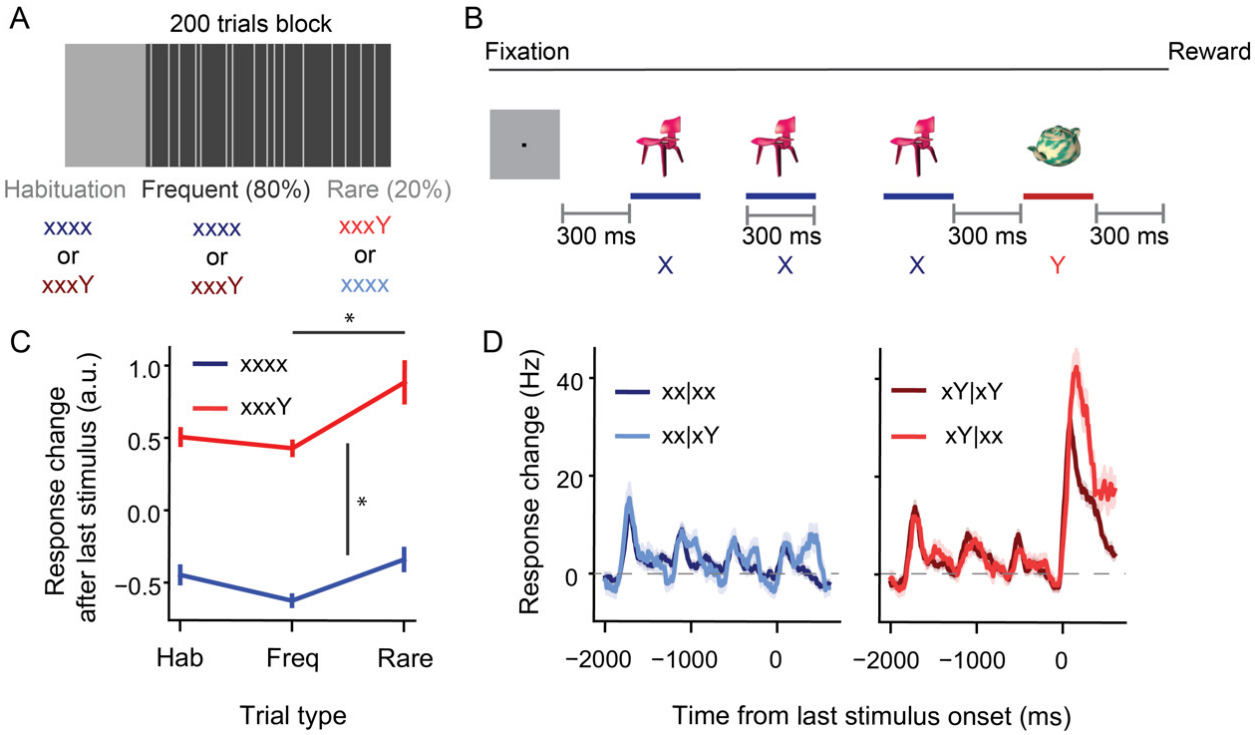


Figure 1. Hierarchical sequence paradigm. (A) Block structure. Habituation trials were followed by 80% frequent and 20% rare trials. (B) In each trial, a sequence of 4 stimuli was presented. (C) Example multi-unit activity with a main effect of local and global novelty. (D) PSTHs corresponding to C. Rare vs. frequent trials without local deviant (light vs. dark blue) and with local deviant (light vs. dark red).

References

1. Bekinschtein, Dehaene, Rohaut, *et al.*, 2009, *PNAS*, 106(5), 1672–1677
2. Uhrig, Dehaene, Jarraya, 2014, *J. Neurosci.*, 34(4), 1127–1132.

IDENTICAL ENCODING OF FLEXIBLE AND AUTOMATIC MOTOR SEQUENCES IN THE DORSAL LATERAL STRIATUM

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

To achieve specific goals, our motor system must quickly learn new movements, flexibly reorganize existing ones, and consolidate repeated motor sequences. Consider the feats of a concert pianist. After extensive training, the pianist can flexibly perform any number of sonatas or etudes when provided with sheet music. But to prepare for a concert, she extensively practices a single piece, making it automatic, effortless, and robust to mistakes. Although both the flexible and automatic performances can be kinematically similar, it is generally believed that they are controlled by different neural circuits [1].

In particular, flexible and automatic movements are thought to be differentiated in the dorsal lateral striatum (DLS), an essential node of the motor system and a major input to the basal ganglia. However, the specific mechanisms, as well as how these mechanisms generalize across flexible and automatic movements, remain poorly understood. One popular hypothesis is that the DLS dedicates specific circuitry to represent a well-trained sequence, forming what's called a motor chunk, and reducing cognitive load [2]. In an alternative hypothesis, the striatum encodes features relevant to the ongoing movement, independent of sequence learning [3]. To arbitrate between these hypotheses, we recorded from populations of single neurons in the DLS while rats performed the same movement sequence both in a flexible and automatic context.

In contrast to the generally accepted view that DLS differentiates flexible and automatic movements, we found that neural representation of similar movement kinematics was invariant to the context (*i.e.* automatic or flexible). Further characterization of the encoding scheme in the DLS suggested the units were also invariant to the specific sequence and ordinal position within the sequence, and instead primarily representing the basic motor element in an egocentric coordinate frame. These results are consistent with a low-level kinematic role of DLS independent of automaticity, cognitive load, or behavioral flexibility.

If the DLS tracks the ongoing movement, then where are flexible and automatic movements distinguished? We are currently testing this by recording from an upstream area, the motor cortex, looking for evidence of context, sequential, or ordinal information. Another hypothesis is that performing flexible sequences interleaved with automatic ones interferes with formiation of consolidated chunked representations in the DLS. We test this by recording from DLS of animals who have only performed sequences in the automatic context.

References

1. Ashby, Turner, Horvitz, 2010, *Trends Cogn Sci*, 14(5):208–215, 10.1016/j.tics.2010.02.001
2. Graybiel, 1998, *Neurobiol Learn Mem*, 70(1–2):119–136, 10.1006/nlme.1998.3843
3. Desmurget, Turner, 2010, *J Neurosci*, 30(22):7685–7690. 10.1523/JNEUROSCI.0163–10.2010

PRECISE SEQUENCES FROM IMPRECISE ENSEMBLES IN A BIRDSONG MODEL

Rich Pang[1,2,*], *Adrienne L Fairhall*[1,2]

[1] Department of Physiology and Biophysics, University of Washington, Seattle, WA, USA
[2] Computational Neuroscience Center, University of Washington, Seattle, WA, USA
[*] rpang@uw.edu

Complex learned behaviors like birdsong are thought to be controlled by precise neural activity. Zebra finch song, for instance, is accompanied by precisely timed spike sequences in premotor area HVC [1]. While several models have been proposed, how such temporal precision is generated by ensembles of neurons over timescales of song has not yet been established. As successful song requires HVC to also receive inputs from thalamic area Uva [2], we studied temporal precision in a network model inspired by these two areas. Specifically, we hypothesized that rather than generating precise spike times on its own, an HVC-like network could produce imprecise, error-prone spike times that could be corrected by feed-forward, fluctuating signals mimicking Uva input.

We tested our hypothesis using a chain-organized network model able to support a propagating spike pulse, and subjected it to a fluctuating Uva-like input. We modeled the former as a feed-forward chain of excitation, which was reciprocally connected to a global inhibitory population. We modeled Uva as a feed-forward and time-varying, but scalar-valued input to the inhibitory population, based on the strong spatial activity correlations observed in Uva during song [2]. Using our model we found that when a spike pulse was erroneously temporally advanced along the chain, fluctuating Uva input could robustly correct its timing and chain position, despite Uva having no information about the error. Notably, inhibition had to be nonuniformly spread over the chain so as to reflect the Uva time-course spatially, leading to effective spatiotemporal "correction zones" in which advanced spike pulses were caught and slowed during Uva activation but correct pulses were not. When Uva input to the inhibitory population was constant in time or inhibition was spread uniformly over the chain, advanced pulses remained advanced; thus, correction requires nonuniformities in both time and space.

Our work reveals a novel mechanism for precise timing by imprecise neural ensembles via a fluctuating input signal. This mechanism could explain other mysteries: it might coordinate left and right HVC during song, which do not connect directly, and/or allow slowing one HVC's activity to slow the other, as thought to occur in uniteral cooling studies [3], via thalamocortical feedback loops through Uva. For generic motor control, allowing greater imprecision in sequence-generating ensembles could make precisely timed outputs more robust to ongoing plasticity, as may occur, for instance, in HVC [4].

Acknowledgments

This work has been supported by NIH 1R01NS104925–01.

References

1. Hahnloser, Kozhevnikov, Fee, 2002, *Nature* 419.6902:65, 10.1038/nature00974
2. Danish, Aronov, Fee, 2017, *PLoS ONE* 12.6, 10.1371/journal.pone.0169568
3. Long, Fee, 2008, *Nature* 456.7219:189, 10.1038/nature07448
4. Liberti III, *et al.*, 2016, *Nat Neurosci* 19.12:1665, 10.1038/nn.4405

AFFECTIVE MEMORY REHEARSAL WITH TEMPORAL SEQUENCES IN AMYGDALA NEURONS

Tamar Reitich-Stolero[*]*, Rony Paz*

Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel
[*]tamar.stolero@gmail.com

Affective learning and memory are essential for daily behavior, with both adaptive and maladaptive learning depending on stimulus-evoked activity in the amygdala circuitry. Behavioral studies further suggest that post-association offline processing contributes to memory formation [1]. Here, we investigated spike sequences across simultaneously recorded neurons while monkeys learned to discriminate between aversive and pleasant tone-odor associations. We show that triplets of neurons exhibit consistent temporal sequences of spiking activity that differed from firing patterns of individual neurons and pairwise correlations. We further examine a sequence-like spatiotemporal maximum entropy (ME) model and show that the activity in the third order ME model is not explained by the second order, again suggesting sequence activity in triplets of neurons.

The sequences of spikes contained valence-related information after the stimuli terminated, so that some sequences were specific to the aversive post-trial epoch and others were specific to the pleasant one. By decoding valence from sequence activity along time, we show that this information was available throughout the long (up to 30 sec) post trial epoch. We further use decoding and mutual information measures to show that the information in sequences declined as learning progressed and that there is a negative correlation between this information and the conditioned response. This reduction of information is expected from a learning signal that is less needed once the association is formed.

In addition, post-trial sequences were selectively present in activity evoked by the recent pairing of a conditioned stimulus (CS) with an unconditioned stimulus (US). Thus, decoding stimulus valence from CS-US related sequences was feasible by training a maximum likelihood decoder on the post-trial activity. This suggests that post trial pleasant- and aversive- specific sequences are also valence specific during CS-US related activity. In addition, aversive specific post-trial sequences occurred more during the aversive CS-US association, and pleasant specific post-trial sequences occurred more during the pleasant CS-US association.

Our findings reveal that temporal sequences across neurons in the primate amygdala serve as a coding mechanism of aversive and pleasant association during post trial activity. In addition, these sequence might aid memory formation through the rehearsal of the recently experienced association [2].

References

1. Wagner, Rudy, Whitlow (1973) *J. Exp. Psychol.* 97:407–426
2. Reitich-Stolero, Paz (2019) *Nat. Neurosci.* 22:2050–2059

SPEECH

BRAIN-COMPUTER INTERFACE METHODS FOR IMAGINED SPEECH USING REIMANNIAN MANIFOLD FEATURE CLASSIFICATION

Panagiotis Artemiadis[1,*] *Chuong H Nguyen*[2], *George K Karavas*[2]

[1] Mechanical Engineering, University of Delaware, Newark, DE USA
[2] Mechanical Engineering, Arizona State University, Tempe, AZ USA
[*] partem@udel.edu

In recent years, several efforts of extracting human abstract thinking have been investigated. In contrast to visual imagery and motor imagery, speech imagery is quite consistent between users and easier to perform. Recently, Herff and T. Schultz [1] conducted a review of techniques deciphering neural signals for automatic speech recognition. Here, we propose a novel method for speech imagery using EEG signals features. The proposed method can perform multi-class recognition simultaneously, and significantly outperforms other methods found in the literature in terms of accuracy and sensitivity.

In this work, 15 healthy subjects performed three different types of imagined speech, namely imagined speech of *short words*, *long words* and *vowels*. The group of short words included the words *in*, *out* and *up*, while the group of long words consisted of *cooperate* and *independent*. These words were chosen in order to evaluate the effect of the meaning and the complexity of the words. In order to evaluate the effect of the sound, three phonemes were used, namely /a/, /i/ and /u/. The experimental setup is shown in Figure 1.

Figure 1. Experimental setup.

Our proposed method can be summarized in four main steps. First, we extract low level features from the preprocessed EEG signal. These features are extracted at each time instant and are considered as local features. Second, a covariance matrix descriptor is used to fuse them together in order to further boost their global discriminative power for the entire imagination period. Since the Covariance matrix lies in the Riemannian manifold, appropriate metrics need to be used to discriminate them. Hence, in the third step, we extract their tangent vectors as the final high level features vector, which are consequently fed to a Relevance Vector Machine (RVM) to classify their labels.

Results show that using our method, the decoding results are always significantly above change level. Moreover, long words decoding accuracy is greater than short words or vowels. Finally, results show that our proposed method provides in most cases statistically and significantly better performance than the mentioned approaches found in the literature, while our Reimannian feature extraction can be used with existing classification methods and improve their results too. In the future works, we would like to combine speech imagery with other modalities, such as motor and visual imagery to provide more degrees of freedom for BCI applications.

Acknowledgments

This work is supported by the U.S. Defense Advanced Research Projects Agency (DARPA) grant D14AP00068 and U.S. Air Force Force of Scientific Research (AFOSR) award FA9550-18-1-0221.

Reference

1. Herff, Schultz, 2016, *Front. Neurosci.* 10:429

SEMANTIC ENCODING DURING LANGUAGE COMPREHENSION IN HUMANS AT A SINGLE-CELL RESOLUTION

Mohsen Jamali[1,*], *Benjamin Grannan*[1], *Jing Cai*[1], *Evelina Fedorenko*[2], *Ziv Williams*[1]

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

Humans are able to convey remarkably rich and complex meanings via language over fine temporal scales and myriad contexts. Functional imaging studies suggest that this ability is subserved by a widely distributed frontotemporal and subcortical network of brain areas. To date, however, the degree to which semantic meaning is represented by single neurons remains unknown. Here we took a modeling-and-decoding approach on both single- and population-level neuronal data to (i) examine whether individual neurons in dominant, associative prefrontal areas, which are surgically accessible during intraoperative neuronal recordings, encode semantic content during language perception and (ii) model the semantic information encoded by populations of neurons to provide an estimate for the size of neuronal ensemble needed to decode the semantic meaning of a word during speech perception. Acute neuronal recordings were performed in 10 participants as they listened to naturalistic sentences. We then employed a word embedding approach (*i.e.*, word2vec) to determine how particular words grouped into semantic domains and identified 9 different domains. By tracking the action potential dynamics of neurons as they evolved during sentence comprehensions, we discovered that 22% of the cells in the population (48/220) were selective for at least one semantic domain ($p < 0.025$) over sub-second timescales. These neurons exhibited responses selective to specific semantic domain(s) when presented with words in complete, natural sentences, but not when presented with non-ordered random word lists or with homonym words with identical phonetics but different semantic meanings. This suggests that these neurons encoded the semantic meaning of words in sentences, rather than lower-level linguistic characteristics such as lexical or phonetic representations.

We further investigated the size of the prefrontal neuron ensemble needed to decode the semantic meaning of a word during sentence comprehension. Population decoding was performed with a multinomial logistic regression model (40% test data, 60% training data) across 1000 iterations. Using the population firing rate to predict the semantic domain of each word, the decoding accuracy reached about 45% (compared to 11% accuracy in after bootstrapped randomization of semantic labels). Interestingly, decoding performance dropped to chance when listening to the same words but in a randomly ordered word lists. Finally, Bayesian information criterion analysis indicated that about 20 neurons suffice to approach an optimal decoding. In conclusion, prefrontal neurons demonstrate firing rate activity that is selective for and representative of the semantic content within speech. These activities could further be used to predict the semantic domains over the natural time-course of speech. Together, these findings begin to illuminate the local cellular-level representation and processing of linguistic meaning during language comprehension in humans.

Acknowledgments

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

TECHNIQUE

NEURAL TOPIC MODELLING

Pamela E. Hathway[*]*, Dan F. M. Goodman*

Department of Electrical and Electronic Engineering, Imperial College London, London, UK
[*]p.hathway16@imperial.ac.uk

Recent advantages in brain recording techniques allow us to record from thousands of neurons simultaneously. The first findings from such large datasets have uncovered that neurons encode multiple internal and external variables at once *i.e.* superimpose task-related activity on top of the ongoing movement-related activity [1].

To disentangle these multiple layers of encoding, we introduce neural topic modelling — an unsupervised, scalable and interpretable neural data analysis tool. Neural topic modelling is based on latent Dirichlet allocation, a method used in text mining to group words according to topics. We convert spike trains into activity patterns (*e.g.*, neuron 1 has a higher firing rate than usual or neurons 2 and 3 spike at the same time) and then use neural topic modelling to group these activity pattern into ensembles.

Applied to an electrophysiological dataset of mouse visual cortex (VC), hippocampus (HC) and thalamus (TH) neurons during a visual task (sparse black and white squares on grey background), neural topic modelling identifies groups of activity patterns (ensembles) which exhibit common attributes such as overlapping receptive fields or proximity on the recording electrode (see Figure 1). Neural topic modelling recovers these relationships between activity patterns despite receiving no knowledge about the cortex topography or the spatial structure of the stimuli.

Since each neuron can give rise to multiple activity patterns (*e.g.*, firing rate-related activity and spike timing-related activity), neural topic modelling allows neurons to be part of multiple ensembles at the same time. It also takes into account that one neuron might use different encoding strategies in different contexts or for the processing of different stimuli.

Neural topic modelling investiagtes interactions between different encoding strategies and highlights interesting directions for further analysis of large-scale neural datasets.

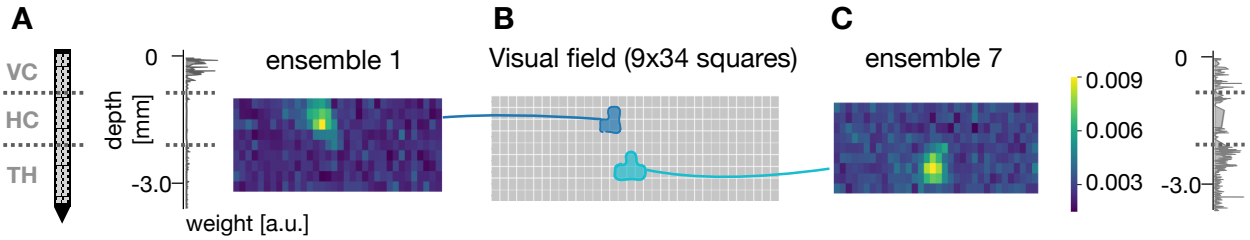


Figure 1. Receptive fields of two ensembles. (A) The activity patterns in Ensemble 1 originate in the VC (left) and appeared at a higher rate when a square was shown (B) at a very specific location in the visual field. (C) Activity patterns in Ensemble 7 also react to a specific stimulus location (different to the one of Ensemble 1), but are not limited to a particular brain region.

Reference

1. Stringer, Pachitariu, Steinmetz, *et al.*, 2019, *Science* 364(6437) 10.1126/science.aav7893

A REAL-TIME SPIKE SORTING SOFTWARE FOR A THOUSAND ELECTRODES

Baptiste Lefebvre[*]*, Olivier Marre, Pierre Yger*

Institut de la Vision, UMRS 968 – UMR 7210, Paris, France
[*]baptiste.lefebvre@inserm.fr

Recent technological advances have made it possible to record simultaneously from tens to thousands electrodes packed with high density. To analyze these extracellular data, scalable, accurate and semi-automated algorithms have been proposed to sort spikes from hundreds of recorded cells [1, 2]. However, these algorithms do not allow tracking the activity of individual neurons during the experiment, since the entire processing is run offline. This is a limitation for experiments where some decisions of the experimentalist could be guided by the recent activity of the recorded cells, and more generally for the design of closed loop experiments.

To address this issue we designed an online spike sorting software that accurately sorts spikes in real time for up to a thousand of electrodes. Our algorithm identifies the template waveforms and their spike times by combining a clustering algorithm and a greedy template matching algorithm. It handles well-known spike sorting issues such as misalignments in the spike detection or overlapping spike waveforms. The online clustering procedure allows dealing with slow changes of the templates over time, due to slow drifts of the electrodes. Depending on the number of electrodes to process, it can be run on a few desktop computers that communicate together through ethernet ports.

We validated that our software could sort spikes in real time for an increasing number of electrodes on simulated datasets. We assessed the accuracy of the results with both *in vitro* and *in vivo* ground truth datasets. Our software thus enables optimal experimental design and closed loop experiments, where the choice of the stimuli to present can be made as a function of the data acquired recently. It will also be a valuable tool for experimentalists to monitor their large-scale recordings during the experiment.

References

1. Pachitariu, Steinmetz, Kadir, *et al.*, 2016, *NIPS* 4448–4456
2. Yger, Spampinato, Esposito, *et al.*, 2018, *eLife* 7:e34518

IMPROVED CLASSIFICATION OF NEURONAL RESPONSIVENESS USING TIME-LOCKED SPIKING ANOMALIES

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

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

The validity of neurophysiological studies depends on a reliable quantification of whether and when a neuron responds to stimulation, be it sensory, optogenetically or otherwise. However, current statistical analysis methods to determine a neuron's responsiveness are often labour-intensive and/or only detect classically mean-rate modulated cells. This problem is becoming more acute with the recent advent of techniques that yield increasingly large numbers of cells, such as multi-plane calcium imaging and Neuropixels recordings. Moreover, using peristimulus time histograms (PSTHs) to determine a neuron's responsiveness still requires an a priori selection of an appropriate bin size, which can be heterogeneous over neurons. Here, we present a procedure, ZETA (Zenith of Event-based Time-locked Anomalies), that consistently and robustly outperforms common approaches for quantifying neuronal responsiveness, in the sense that it includes more cells at a similar false-positive rate (Figure 1). We show this effect to hold in both artificially generated benchmarking datasets with known ground truths, as well as in experimentally recorded electrophysiological data. Our procedure automatically includes otherwise undetectable non-trivially modulated neurons from a variety of brain regions and recording techniques, including Neuropixels recordings in mouse visual cortex and subcortical area SC (superior colliculus), as well as retinal ganglion cell spiking responses to light flashes recorded with multielectrode arrays, and calcium imaging in primary visual cortex with natural movies.

Finally, ZETA's timescale-, parameter- and binning-free nature allowed us to implement a ZETA-derived algorithm to calculate peak onset and offset latencies in neuronal spike trains with theoretically unlimited temporal resolution (Figure 1E). Open-source MATLAB code for ZETA and its derived latency-detection algorithm is available online github.com/JorritMontijn/TuningMetrics.

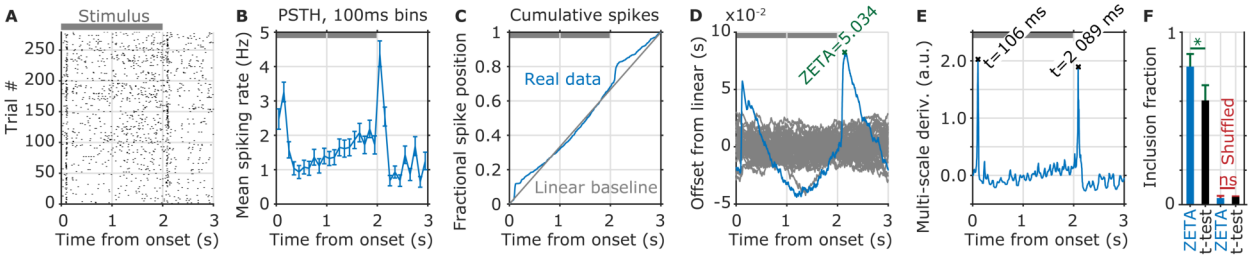


Figure 1. ZETA outperforms mean-rate t-tests in detecting visually responsive neurons. (A) Raster plot and (B) PSTH of an example neuron that shows both an onset and offset response to a visual stimulus (dark grey bar, 0–2 seconds). (C) ZETA avoids binning by using the spike times of the neurons to construct a fractional position for each spike (blue) and compares this with a null-distribution of a stationary spiking rate (grey). (D) The difference between these two curves gives a spike density offset from expectation (blue), where we define the peak in this curve as the Zenith of Event-based Time-locked Anomalies (ZETA, green), scaled by the standard deviation of jittered onsets (grey curves). A mean-rate t-test was not significant (p=0.477). (E) A ZETA-derived metric using multi-scale derivatives allows a reliable estimation of peak onset and peak offset. (F) Cell inclusion is higher using ZETA than a mean-rate t-test for all four types of data sets (green, blue vs black, p=0.040, n=4), while keeping the false positive rate around 5% (red, shuffled data sets, p=0.677, n=4).

DECODING RETINOTOPIC AND NATURALISTIC VISUAL INFORMATION FROM THE HUMAN BRAIN WITH HIGH DENSITY DIFFUSE OPTICAL TOMOGRAPHY

Kalyan Tripathy[1,], Zachary E. Markow[1], Andrew K. Fishell[1], Tracy M. Burns-Yocum[1], Alexandra M. Svoboda[1], Mariel L. Schroeder[1], Sean Rafferty[1], Adam T. Eggebrecht[1], Bradley L. Schlaggar[2], Joseph P. Culver[1]*

[1] Washington University School of Medicine, St. Louis, USA
[2] Kennedy Krieger Institute, Baltimore, USA
[*] tripathyk@wustl.edu

Encoding and decoding research in humans aims to build on findings from animal studies both to explore the biological basis of human behavior and to facilitate clinical applications, *e.g.*, brain-machine interfaces for augmented communication in patients with motor disorders. However, these applications are constrained by limitations of extant recording methods. Despite enabling promising laboratory studies, intracortical electrodes require invasive neurosurgery while MRI scanners are too cumbersome and expensive for uses like daily communication. Functional near infrared spectroscopy (fNIRS) is an alternative modality with logistical advantages, but its image quality is limited by sparse sampling. High-density diffuse optical tomography (HD-DOT) is an emerging method that collects thousands of measurements to improve image quality relative to traditional fNIRS as shown in previous encoding studies [1]. However, there are no prior studies investigating decoding of the hemodynamic correlates of ensemble activity measured with HD-DOT. Here, we evaluate visual decoding with HD-DOT.

Using HD-DOT systems developed at Washington University, we imaged adults as they viewed various visual stimuli. A template-matching strategy was used for decoding: (i) training data were block-averaged to construct templates of the oxyhemoglobin response for different stimulus conditions, (ii) Pearson correlation coefficients were calculated between each template and independent test data, and (iii) the template with the highest correlation indicated the stimulus state in the test data. First, we assessed stimulus position decoding with checkerboard wedges presented to either the left or right visual hemifield. This binary decoding was highly sensitive, specific, and reproducible; *e.g.*, ROC analysis of decoding across 10 sessions in a highly sampled participant yielded an area under the ROC curve of 0.98. We then explored decoding of stimulus location in greater detail using a checkerboard wedge that rotated through 36 positions. Across 3 highly sampled participants, stimulus phase was decoded within subjects with an error of 25.8±8.9°, and decoding between participants was also feasible based on permutation-based significance testing. Finally, participants watched 4 naturalistic movie clips twice each and we assessed decoding of clip identity using separate presentations for training and testing. Here, mean decoding accuracy across 10 sessions was 80%. This work shows that a range of visual information can be decoded from HD-DOT recordings of hemodynamic signals reflecting the activity of neural ensembles in human visual cortex. Our findings encourage future studies of other decoding (*e.g.*, language, movement) in clinical populations with HD-DOT.

Reference

1. Eggebrecht, Ferradal, *et al.*, 2014, *Nat Photonics* 8(6):448–454, 10.1038/nphoton.2014.107

TIMING AND SYNCHRONIZATION

NORADRENERGIC LOCUS COERULEUS ENSEMBLES FIRE AT DISTINCT TIMES TO EVOKE DIFFERENT CORTICAL STATES IN RAT PREFRONTAL CORTEX

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

[1] Neural Computation Laboratory, Istituto Italiano di Tecnologia, Rovereto, Italy
[2] Center for Mind/Brain Sciences, University of Trento, Rovereto, Italy
[3] Graduate Training Centre of Neuroscience, University of Tübingen, Germany
[4] Helsinki Institute of Life Science (HiLIFE), University of Helsinki, Helsinki, Finland
[5] Dept. of Physiol. of Cog. Processes, MPI Biological Cybernetics, Tübingen, Germany
[6] Division of Imaging Sci. and Biomed. Eng., University of Manchester, Manchester, UK
[†] Co-senior authors
[*] shahryar.noei@iit.it

The Locus Coeruleus (LC), a noradrenergic brain stem nucleus projecting throughout the forebrain, is thought to act as an undifferentiated state controller across all forebrain targets because LC neurons spike synchronously [1, 2]. However, recent work demonstrated ensembles in the LC and therefore made targeted neuromodulation a possibility [3]. This recent study used graph theory to reveal a static snapshot of LC ensembles. In order to now demonstrate that LC ensembles cause targeted neuromodulation, it is necessary to resolve LC ensemble dynamics over time in relation to ongoing cortical states.

Here, we used non-negative matrix factorization (NMF, [4]) on LC single unit recordings to investigate the spatial and temporal properties of ensemble activation patterns. We assessed the potential for targeted neuromodulation of the prefrontal cortex (PFC) using LC ensemble activity-triggered Local Field Potential (LFP) spectrograms. We analyzed 285 single units recorded from 15 urethane-anesthetized rats (range of 5 to 34 simultaneously recorded units). We found that ensembles are sparse and fire at different times. We observed four types of ensemble-triggered cortical state modulation, which shows diverse neuromodulatory effects across various LC ensembles. These results demonstrate that the LC is capable of differentiated modulation of its forebrain targets by dynamic firing patterns across subsets of LC neurons.

Acknowledgments

Supported by Helsinki Institute of Life Science and the Department of Physiology of Cognitive Processes in the Max Planck Institute for Biological Cybernetics

References

1. Chandler, Jensen, *et al.*, 2019, *J Neurosci* 39(42):8239–49, 10.1523/jneurosci.1164-19.2019
2. Totah, Logothetis, Eschenko, 2019, *J Brain Res* 1709:50–56, 10.1016/j.brainres.2018.12.031
3. Totah, Neves, Panzeri, *et al.*, 2018, *Neuron* 99(5):1055–1068, 10.1016/j.neuron.2018.07.037
4. Lee, Seung, 1999, *Nature* 401(6755):788

A COMPUTATIONAL MECHANISM FOR PRECISE TIMING IN CEREBELLUM

Terence Sanger[1,*], *Mitsuo Kawato*[2]

[1] University of California, Irvine (UCI), USA
[2] Advanced Telecommunications Research Institutes (ATR), Keihanna Science City, Japan
[*] tsanger@uci.edu

We propose a new computational model to explain the production of precise time intervals in cerebellum. Intervals are identified from a replicable pattern of spike activity in a population of parallel fibers in the cerebellar cortex. The model depends on the presence of repeatable sequences of spikes in response to conditioned stimulus input. We emulate 2000 granule cells using a population of Izhikevich neuron approximations driven by random but repeatable mossy fiber input. We emulate long-term depression (LTD) and long-term potentiation (LTP) synaptic plasticity at the parallel fiber to Purkinje cell synapse:

$$\Delta w = g * ((1 - US(t)) * LTPrate - US(t) * LTDrate)$$

where w is the synaptic vector of weights w_i, g is a binary vector with $g_i = 1$ for every granule cell that fired, and $US(t)$ is the unconditioned stimulus at time t. We simulate a delay conditioning paradigm with a conditioned stimulus (CS) presented as 100 msec Poisson spike trains to 100 mossy fibers and an unconditioned stimulus (US) some time later issued on a climbing fiber to the Purkinje cell output. Purkinje cells rapidly adapt to decrease firing probability following onset of the CS only at the precise interval for which the US had occurred. Thus detection of replicable spike patterns provides an accurate and easily-learned timing structure that could be an important mechanism for behaviors that require identification and production of precise time intervals.

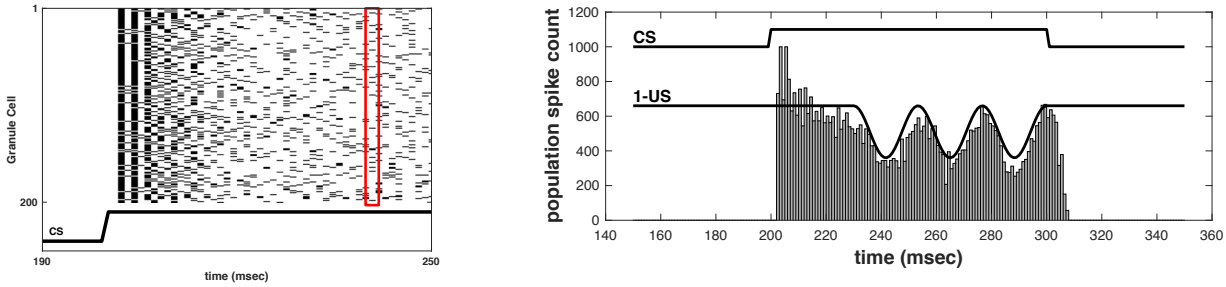


Figure 1. (left) The red box illustrates how a particular pattern of spikes on granule cells can uniquely identify a particular time interval following the start of the CS. (right) Combined output of 20 trained Purkinje cells for a smoothly varying training signal.

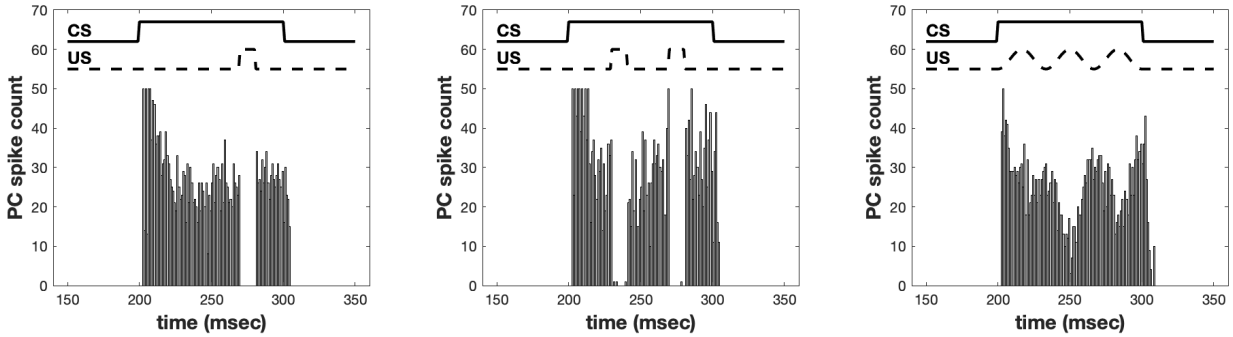


Figure 2. Single Purkinje cell output after training with different US patterns. (left) delay conditioning with US present from 270–280 msec. (middle) Double response with US present from 240–250 msec and 270–280 msec. (right) Smoothly varying US trained using the LMS algorithm.

LONG-RANGE SYNCHRONIZATION AS A MECHANISM FOR WORKING MEMORY RETENTION

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

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

Although the neural representation of working memory (WM) has been investigated for decades, recent developments in experimental and analysis approaches have questioned long-standing assumptions. For instance, recent electrophysiological and neuroimaging studies suggest that neurons in the prefrontal and parietal cortices do not always store task-relevant information. Instead, whether information is retained in these cortices can depend upon task demands. Moreover, the once widely accepted assumption that WM maintenance is supported by the elevated activity of single neurons during the delay period has come into question. Recent evidence have emphasized the idea that the retention of information in WM is accommodated by distributed patterns of activity and large scale interactions. Yet, our understanding of the particular contribution of prefrontal and parietal cortices, the kind of information that these cortices retain, as well as the type and role of parieto-frontal interactions during WM remains vastly incomplete.

To address these questions we performed simultaneous extracellular recordings in the frontal eye fields (FEF) and the lateral intraparietal area (LIP) of two macaque monkeys. We examined whether and how different aspects of visual information, specifically stimulus identity and location, are encoded in these areas using a visual search and a memory-guided saccade task respectively.

We found that for both spiking and LFP activity, FEF and LIP retained information about stimulus location but not about stimulus identity, in accordance with a role in resource allocation by means of prioritizing certain locations. Interestingly, although identity information was not retained locally within each area, selectivity about either stimulus identity or location was evident in low beta coherence (10–20 Hz) between the two areas. Analysis of directionality indicated that low beta activity was more prominent in the LIP to FEF direction. Moreover, an analysis of cross-frequency interactions indicated modulation of LIP gamma amplitude by FEF low beta phase. Taken together, these results suggest that low beta synchronization does not only play a prominent role in the coordination of parieto-frontal activity during WM but also provides a mechanism for WM maintenance.

Acknowledgments

Work supported by the Hellenic Foundation for Research and Innovation (HFRI) and the General Secretariat for Research and Technology (GSRT), under grant agreement No 1199 and by “Advanced Research Activities in Biomedical and Agro alimentary Technologies” (MIS 5002469), “Action for the Strategic Development on the Research and Technological Sector”, funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014–2020) and co-financed by Greece and the European Union (European Regional Development Fund).

THE EFFECT OF STDP ON THE ENCODING OF THE PHASE OF RHYTHMIC ACTVITY

Nimrod Sherf[1,2,*], *Maoz Shamir*[1–3]

[1] Department of Physics, Ben-Gurion University, Beer-Sheva, Israel
[2] Zlotowski Center for Neuroscience, Ben-Gurion University, Beer-Sheva, Israel
[3] Department of Physiology, Ben-Gurion University, Beer-Sheva, Israel
[*] sherfnim@post.bgu.ac.il

Rhythmic activity has been associated with a wide range of cognitive processes such as the encoding of sensory information, navigation, the transfer of emotional information and more. In many cases the phase of the rhythmic activity encodes information that is important to transmit downstream, such as on the angular position of a whisker during whisking. Recently, the role of spike timing dependent plasticity (STDP) in facilitating the transmission of rhythmic activity has been addressed [1]. However, the issue of the information content embedded in the phase of the rhythmic activity has been ignored. Moreover, it was shown that the phase relation between the up and downstream neurons is arbitrary and drifts in time due to synaptic weights dynamics. Thus, it is unclear how phase information can be relayed downstream in the face of a constant synaptic remodeling predicted by theory of STDP.

We addressed this issue in a modelling study. STDP dynamics is investigated in an architecture of a rhythmic population synapsing into a downstream population in a purely feedforward manner. Importantly, the phase distribution of the upstream population is not uniform, representing a certain feature of an external stimulus. We derive mean field Fokker Planck equations for the STDP dynamics in the limit of slow learning, and study the resultant rhythmic activity of the downstream neurons. We find that the downstream population develops the capacity for rhythmic activity. However, the phase difference between the up and downstream populations is indeed arbitrary and drifts in time. Nevertheless, drift velocity is not constant, but rather prefers certain phases over others. As a result, the phase preference is distributed non-uniformly in time. We show that an accurate estimate of the phase difference can be obtained by averaging over the downstream population. Thus, functionality is retained by distributing information over time.

Acknowledgments

This research was supported by the Israeli Science Foundation (ISF) grant number 300/16.

Reference

1. Luz, Shamir, 2016, *PLoS Comput. Bio.*, 12(4): e1004878, 10.1371

STDP INDUCED RHYTHMOGENESIS IN THE GAMMA BAND

Gabi Socolovsky[1,2,*], *Maoz Shamir*[1–3]

[1] Department of Physics, Ben Gurion University, Be'er Sheva, Israel
[2] Zlotowski Center for Neuroscience, Ben-Gurion University, Be'er Sheva, Israel
[3] Department of Physiology, Ben-Gurion University, Be'er Sheva, Israel
[*] gabisoco@post.bgu.ac.il

Rhythmic activity in the gamma band frequencies (30–100 Hz) has been observed in a wide range of animal species ranging from insects to humans. These oscillations have been reported in relation with: sensory stimulation, attention selection, working memory and more. Various experimental and theoretical studies investigated the rhythmic activity in the gamma band. Mainly, the theoretical efforts have been focused on the rhythmic activity of the neurons, assuming network connectivity satisfies certain fine-tuning conditions required to generate gamma oscillations. However, it remains unclear how this fine tuning is achieved [1]?

Here we investigate whether spike timing dependent plasticity (STDP) can provide the underlying mechanism for tuning synaptic connectivity in order to generate rhythmic activity in the gamma band, and if so, under what conditions?

We address this question in a modeling study. We investigate STDP dynamics in the framework of a network of excitatory and inhibitory neuronal populations that has been suggested to underlie the generation of gamma [2, 3]. We derive mean field Fokker Planck equations for the synaptic weights' dynamics in the limit of slow learning. This is facilitated by using an existing reduced rate model approximation to the network dynamics. Relying on this approximation we investigate what types of STDP rules will drive the system to exhibit gamma oscillations, and demonstrate how the parameters that characterize the plasticity rule govern the rhythmic activity.

Acknowledgments

This work has been supported by the ISF grant number 300/16.

References

1. Shamir, 2019, *Curr Opin* 58:70–77, 10.1016/j.conb.2019.07.005
2. Battaglia, Hansel, 2011, *PLoS Comput Biol*, 7(10):e1002176
3. Roxin, Brunel, Hansel, 2006, *Prog Theor Phys Supp*, 161:68–85.

VISION

RETINAL GANGLION CELLS CAN RAPIDLY CHANGE POLARITY IN NATURAL CONTEXT

Ulisse Ferrari[1,†,*], *Baptiste Lefebvre*[1,†], *Pierre Yger*[1], *Thierry Mora*[2], *Olivier Marre*[1]

[1] Institut de la Vision, Sorbonne Université, CNRS, INSERM, Paris, France
[2] Ecole Normale Supérieure, Paris, France
[†] Equal contribution
[*] ulisse.ferrari@gmail.com

Sensory neurons, and in particular retinal ganglion cells, are classically thought of as extracting a feature from the visual scene. However, it is also known that the processing they performed on this scene is strongly dependent on the visual context. It is thus not clear if they always extract the same feature, and therefore a stable representation of the visual world, across different contexts. Previous works have shown that changes in the ambient luminance of the visual scene can change the polarity of ganglion cells: some cells turned from ON to OFF, or vice versa, when changing the background light level [1]. This suggest that ganglion cells extract a different feature depending on the ambient luminance. However, for a fixed background luminance, and for natural stimuli, it is unclear if feature extraction is kept stable, or is more context-dependent. To address this issue, we used a perturbative approach. We recorded many ganglion cells in the salamander retina while stimulating them with flashed natural images slightly perturbed by patterns of checkerboard. Thanks to this protocol we were able to measure a receptive field from the responses to many checkerboard patterns superimposed on the same natural image, *i.e.* an image-dependent receptive field. We found that this receptive field strongly depended on the natural image. When changing the image, it could entirely switch its polarity from ON to OFF. Our results suggest that the processing performed by ganglion cells in response to natural images is strongly context-dependent. We hypothesize that multiple parallel pathways, each encoding different features, are dynamically and rapidly selected to generate the retinal ganglion cell responses in a natural context. We are currently testing if a phenomenological, multi-layer model could reproduce these polarity reversals, and will discuss if this context dependency is helpful or detrimental to extract stable representations downstream in the visual pathway.

Reference

1. Tikidji-Hamburyan A, Reinhard K, Seitter H, *et al.*, 2015, *Nat. Neurosci.* 1:66–74.

SPATIALLY-VARIANT ORIENTATION SELECTIVITY IN MOUSE PRIMARY VISUAL CORTEX

Jiakun Fu[1,2,*], *Taliah Muhammad*[1,2], *Andreas S. Tolias*[1–3]

[1] Dept. Neuroscience, Baylor College of Medicine, Texas, USA
[2] Ctr. Neuroscience and Artificial Intelligence, Baylor College of Medicine, Texas, USA
[3] Dept. Electrical and Computer Engineering, Rice University, Houston, Texas, USA
[*] jiakun.fu@bcm.edu

Since Hubel and Wiesel's discovery of orientation tuned neurons, orientation selectivity has been a defining character of V1 neurons [1]. In primates and cats, V1 cells form cluster based on their orientation selectivity, and connect preferentially to similarly tuned neighbors. However, in mouse V1, Walker and colleagues have recently reported complex receptive fields revealed by convolutional neural network (CNN) models of V1 [2]. To understand whether mouse V1 encodes orientation, we measured changes in orientation tuning at different locations *in vivo* and *in silico*, using Walker *et al.*'s predictive model. Visual stimuli are Gabor patches of 7° in size, shown in 16 overlapping locations tiling the center of the screen (Figure 1B). We find that the majority of V1 neurons change preferred orientation with stimulus location (Figure 1A, 1C), violating the assumption that a neuron's orientation selectivity in V1 is uniform across visual space. The predictive model captures the complex structure of V1 receptive fields and predicts local orientation preference. We discover mouse V1 neurons' orientation selectivity may arise from more complex tuning functions beyond what is known in the primates and cats. We will further investigate the tuning properties of V1 cells and how they relate to contextual modulation using the CNN predictive model.

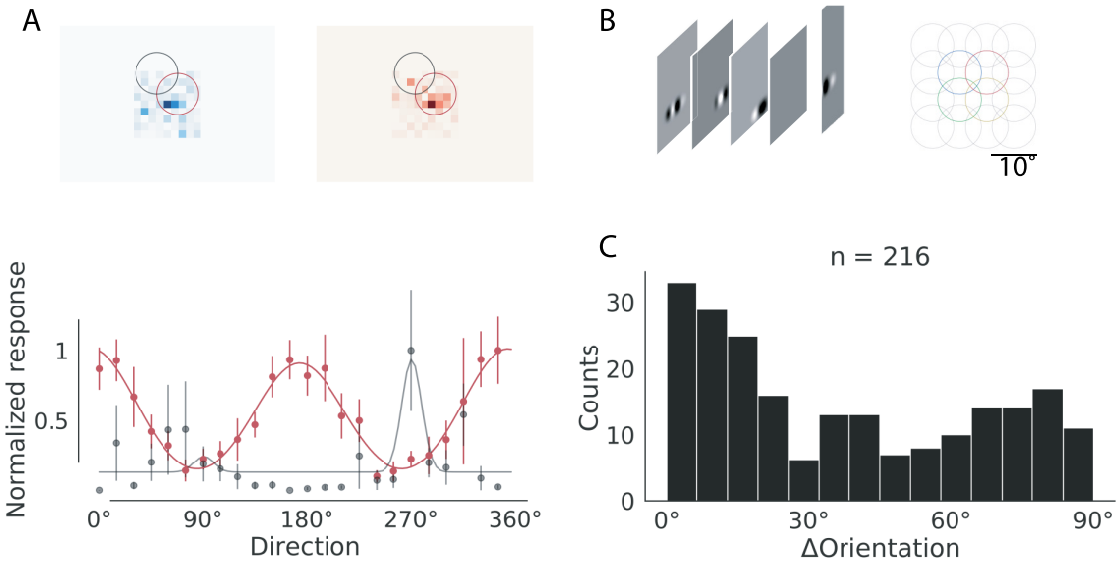


Figure 1. (A) Example neuron receptive field and orientation tuning at two locations; top: off (blue) and on (red) receptive field; bottom: trial average response; solid lines represent fitted double von Mises tuning curve; colors correspond to stimulus locations shown in top panel. (B) Visual stimulus at 16 locations. (C) Difference in orientation tuning between two locations for all recorded V1 neurons. Number of animals=4, number of cells=216.

References

1. Hubel, Wiesel, 1962, J. Physiology 160(1):106–154
2. Walker, Sinz, Cobos, *et al.*, 2019, *Nat. Neurosci.* 22(12): 2060–2065

INVESTIGATING HOW SPECIFIC CLASSES OF RETINAL CELLS CONTRIBUTE TO VISION WITH A MULTI-LAYERED SIMULATOR

Evgenia Kartsaki[1,2,*], *Gerrit Hilgen*[2], *Evelyne Sernagor*[2], *Bruno Cessac*[1]

[1] Université Côte d'Azur, Inria, Sophia Antipolis, France
[2] Biosciences Institute, Newcastle University, Newcastle, UK
[*] evgenia.kartsaki@inria.fr

Thanks to the astonishing functional and anatomical diversity within retinal neuronal classes, our brain can recreate images from interpreting parallel streams of information emitted by the retina. However, how these neuronal classes interact to perform these functions remains largely a mystery.

To track down the signature of a specific cell class, we employ a novel experimental approach that is based on the ability to pharmacologically control the level of neural activity in specific subgroups of retinal ganglion cells (RGCs), specialized cells which connect the retina to the brain via the optic nerve and amacrine cells (ACs), interneurons that modulate RGCs activity over a wide area via lateral connectivity. We modified the activity of Scnn1a- and Grik4-expressing RGCs and ACs through excitatory DREADD (Designer Receptors Exclusively Activated by Designer Drugs) activation using clozapine-n-oxide (CNO). We hypothesize that modifying the activity of RGCs and/or ACs may not only affect the individual response of these cells, but also their concerted activity to different stimuli, impacting the information sent to the brain, thereby shedding light on their role in population encoding of complex visual scenes. However, it is difficult to distinguish the pharmacological effect on purely experimental grounds when both cell types express DREADDs and respond to CNO, as these cells antagonize each other. Contrarily, modeling and numerical simulation can afford it.

To this end, we have developed a novel simulation platform that can reflect normal and impaired retinal function (from single-cell to large-scale population). It is able to handle different visual processing circuits and allows us to visualize responses to visual scenes (movies). In addition, it simulates retinal responses in normal and pharmacologically induced conditions; namely, in the presence of DREADD-expressing cells sensitive to CNO-induced activity modulation.

Firstly, we deploy a circuit that models different RGCs classes and their interactions via ACs and emulates both their individual and concerted responses to simple and complex stimuli. Next, we study the direct (single-cell) or indirect (network) pharmacological effect when the activity of RGCs and/or ACs is modified in order to disentangle their role in experimental observations. To fit and constrain the numerical models and check their validity and predictions, we use empirical data. Ultimately, we expect this synergistic effort (1) to contribute new knowledge on the role specific subclasses of RGCs play in conveying meaningful signals to the brain, leading to visual perception and (2) propose new experimental paradigms to understand how the activation of ensembles of neurons in the retina can encode visual information.

Acknowledgments

This project is funded by the Leverhulme Trust (RPG-2016–315 to ES and BC).

TEMPORAL STRUCTURE OF SPONTANEOUS CORTICAL NETWORKS IN LAYER 2/3 OF THE PRIMARY VISUAL CORTEX OF THE MOUSE

Vassilis Kehayas[2], Epistimi-Anna Makedona[2], Ganna Palagina[3], Orestis Mousouros[1,2], Ioannis Smyrnakis[2], Stelios M. Smirnakis[3], Maria Papadopouli[1,2,]*

[1] Department of Computer Science, University of Crete, Heraklion, Greece
[2] Institute of Computer Science, FORTH, Heraklion, Greece
[3] Dept. Neurol., Brigham and Women's Hosp. / JP Veteran's Admin., Harvard Medical School, Boston, MA, USA
[*] mgp@ics.forth.gr

The brain's neocortex is a six-layered structure that consists of billions of densely interconnected neurons. Over time much has been learned about the computational properties of single neurons of the neocortex. However, there is uncertainty in the responses of single neurons to the same stimulus. Downstream neurons must integrate activity from large neuronal populations that exhibit coordinated activity. Nevertheless, on average, neurons display close to zero correlation [1]. We remain far from understanding how networks of cortical cells interact with each other to process information. Here we study the functional architecture of cortical networks during spontaneous activity, recorded from layer 2/3 neurons of the primary visual cortex of the mouse with mesoscopic two-photon imaging, which allows the near-simultaneous recording of fields of views on the order of millimeters that contain up to some 5000 cells.

We follow the hypothesis that cortical networks are organized into functional sub-networks that can be identified during spontaneous activity [2]. To construct graphs of temporal correlations, we extended the spike time tiling coefficient [3], a correlation metric robust to activity fluctuations, to estimate the directional temporal correlation between neurons. The identification of edges is robust for recording duration longer than about 9 min. The observed graphs exhibit temporal structure across multiple correlation thresholds, beyond that expected from graphs constructed by circularly-shifting the observed activity patterns, which destroys correlations between neurons but leaves inter-event interval distributions intact. Observed graphs have a higher proportion of high-degree nodes, longer average shortest paths, and higher average clustering coefficients compared to equivalent Erdös-Rényi networks, a model of irregular connectivity architecture constructed by shuffling the edges between nodes. The observed graphs manifest a small-world architecture, which is associated with efficient information transfer [4], across multiple scales of correlation strength. Our results show substantial temporal structure in spontaneous cortical activity despite low, on average, pairwise correlation coefficients.

Acknowledgments

Funded by the Archers SNF-FORTH, HFRI and GSRT, and NINDS R21

References

1. Renart *et al.*, 2010, Science, 327(5965):587–590, 10.1126/science.1179850
2. Luczak, Barthó, Harris, 2009, *Neuron*, 62(3):413–425, 10.1016/j.neuron.2009.03.014
3. Cutts, Eglen, 2014, *J. Neurosci.*, 34(43):14288–14303, 10.1523/jneurosci.2767-14.2014
4. Watts, Strogatz, 1998, *Nature*, 393(6684):440–442, 10.1038/30918

A FUNDAMENTAL DIFFERENCE BETWEEN MOUSE AND PRIMATE OBJECT VISION

Francisco J. Luongo[1,*], *Lu Liu*[1], *Janis Hesse*[1,3], *Doris Y. Tsao*[1–3]

[1] Division of Biology and Biological Engineering, Caltech, Pasadena, California, USA
[2] Howard Hughes Medical Institute
[3] Computation and Neural Systems, Caltech, Pasadena, California, USA
[*] fluongo@gmail.com

The rodent visual system has attracted great interest in recent years, owing to its experimental tractability but the fundamental mechanisms used by the mouse to represent the visual world remain unclear. In the primate, researchers have argued from both behavioral and neural evidence that a key step in visual representation is *figure-ground segmentation*, the delineation of figures as distinct from backgrounds [1–3]. To determine if mice also show behavioral and neural signatures of figure-ground segmentation, we trained mice on a figure-ground segmentation task where figures were defined by gratings and naturalistic textures moving counterphase to the background. Unlike primates, mice were severely limited in their ability to segment figure from ground using the opponent motion cue, with segmentation behavior strongly dependent on the specific carrier pattern. Remarkably, when mice were forced to localize naturalistic patterns, they adopted a strategy of brute force memorization of texture patterns. Primates, in contrast, could readily segment figures independent of carrier pattern using the opponent motion cue. Neural responses to the same stimuli, recorded in mouse visual areas V1, RL, and LM using 2-photon imaging and electrophysiology, were consistent with mouse behavior. Modeling revealed that the texture dependence of both the mouse's behavior and neural responses could be explained by a feedforward neural network model lacking explicit segmentation capabilities. These findings reveal a fundamental limitation in the ability of mice to segment visual objects compared to primates.

Acknowledgments

We thank the Arnold & Mabel Beckman Foundation, Burroughs Wellcome Fund, NIH and HHMI for financial support.

References

1. Lamme, 1995, *J. Neurosience* 15(2):1605–15
2. Poort, Florian, Aurel, *et al.*, 2012, *Neuron*, 75(1): 143–56, 10.1016/j.neuron.2012.04.032
3. Qiu, von der Heydt, 2005, *Neuron*, 47(1): 155–66, 10.1016/j.neuron.2005.05.028

GENERALIZATION OF DATA-DRIVEN REPRESENTATIONS IN MOUSE VISUAL CORTEX

Konstantin-Klemens Lurz[1], *Edgar Y. Walker*[1,2], *Santiago A. Cadena*[3], *Taliah Muhammad*[2], *Erick Cobos*[2], *Andreas S. Tolias*[2], *Alexander S. Ecker*[2,4], *Fabian H. Sinz*[1–3,*]

[1] Institute for Biomedical Informatics, University of Tübingen, Tübingen, Germany
[2] Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA
[3] Bernstein Center for Computational Neuroscience, Tübingen, Germany
[4] Department of Computer Science, University of Göttingen, Göttingen, Germany
[*] fabian.sinz@uni-tuebingen.de

Deep neural networks (DNN) have set new standards at predicting responses of neural populations to visual input. In order to train these DNNs, two major approaches are common: *Data-driven* DNNs are trained end-to-end on neural data. *Task-driven* models use a fixed core network pre-trained on a task like object recognition and only train a final readout layer on neural data. While the latter approach was shown to produce the state-of-the-art model in monkeys, it is unclear whether the same holds true for mice. In this study we pose three questions: (Q1) Does a data-driven core outperform a task-driven core in mice? (Q2) What are determining factors to obtain a good data-driven core? (Q3) How well does a data-driven core capture characteristic properties of the visual cortex, that generalize across neurons *and* mice? Regarding Q1, we find that a data-driven core generalizes substantially better to new neurons in the same animal than a task-driven model (VGG16) which itself does not perform much better than comparable networks with random weights (Figure 1a). Regarding Q2 we find that the generalization (transfer) performance across neurons of a data-driven core scales with the number of images and neurons like the product of a power and log law (Figure 1a). Furthermore Q3, a core trained on our biggest dataset with 17k image presentations, can predict population responses in a new mouse *as well* as a core directly trained on the respective neurons (Figure 1b). This indicates that it captured general nonlinear features characteristic for mouse primary visual cortex.

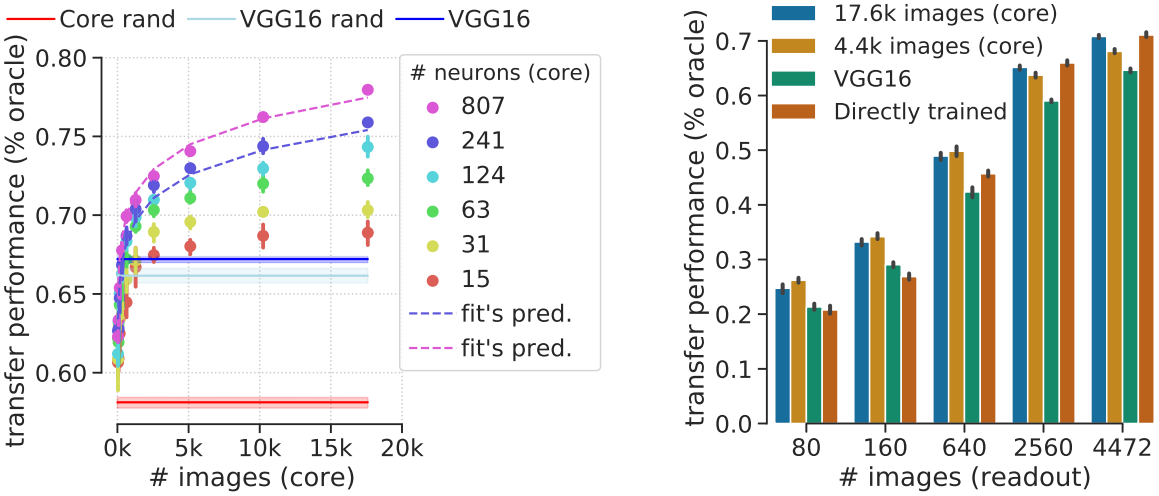


Figure 1. (A) Within animal, across neuron generalization performance. The cores were trained on varying numbers of images and neurons. A function $\rho \sim \iota^{\alpha_1} \cdot \log(\alpha_2 \cdot \nu) \cdot \alpha_3 + \alpha_4$ was fitted to parts of the data and used to predict (dashed line) the left out data-points (ρ = transfer performance, ι = # images, ν = # neurons). (B) Generalization across animals. Test performance as a function of the number of images used to train the readout while the core was transferred from: a task-trained VGG16, two cores trained on data from two different mice to ∼4,400 and ∼17,600 images, respectively, and the core trained on the neural data from the animal itself, for comparison. Errorbars and shaded areas denote 95% confidence intervals over five different selections of neurons.

SPIKES REPRESENTING MOTION DIRECTION ARE PHASE-LOCKED TO THE LFP WITHIN AND BETWEEN VISUAL AREAS MT AND V1

Brian H. Oakley[1,*], *Elizabeth Zavitz*[1], *Maureen A. Hagan*[1], *Yan T. Wong*[1,2], *Nicholas S.C. Price*[1]

[1] Department of Physiology, Monash University, Clayton, Australia
[2] Department of Elec. and Comp. Sys. Eng., Monash University, Clayton, Australia
[*] brian.oakley@monash.edu

In the cortex, many specialised visual areas must communicate effectively to produce our visual perception. It is generally accepted that action potentials (or *spikes*) are important for successful communication between neuronal populations, but there is evidence that the local field potential (LFP) may play a role in coordinating this spiking [1]. We know that within an area, spikes are phase-locked to the LFP and orientation selectivity is modulated by the phase of the gamma-band oscillations [2]. This is consistent with the theory that communicating areas may rely on transient increases in coherence, to ensure that signal propagate from one area to another. In awake macaques, attention has been shown to determine which of two visually stimulated V1 populations entrains a downstream area [3], but it is not known whether this entrainment occurs in the absence of attentional modulation.

We test this by performing simultaneous electrophysiological recordings from connected visual areas V1 and MT, in sufentanil-anaesthetised marmosets. As previously seen in V1, we found that both V1 and MT spiking is phase-locked to the LFP, and the strength of information about the direction of motion varies with LFP phase. We also found that spikes were phase locked to the LFP in the second area, for feed-forward and feed-back signalling. Finally, direction selectivity evident in the spiking of one area is modulated by the phase of the LFP in the other area.

These results suggest phase-locked stimulus information is present even in the absence of attentional modulation, and therefore represents a fundamental characteristic of inter-area cortical communication.

Acknowledgments

This work was supported by NHMRC (APP1066588, and APP1120667); ARC (CE140100007); DECRA (DE180100344); and by an Australian Government Research Training Program (RTP) Scholarship.

References

1. Hagan, Dean, Pesaran. (2012) *J Neurophysiol* 107(5):1275–1290
2. Womelsdorf, Lima, Vinck, *et al.* (2012) *PNAS* 109(11):4302–4307
3. Bosman, Schoffelen, Brunet, *et al.* (2012) *Neuron* 75(5):875–888

TASK REPRESENTATION IN EVOKED AND SPONTANEOUS ACTIVITY IN V1

Gergo Orbán[1,] Márton A. Hajnal[1] Duy T. Tran[2], Michael C. Einstein[2] Pierre-Olivier Polack[3] Peyman Golshani[2]*

[1] Comput. Syst. Neurosci. Lab, MTA Wigner Research Centre for Physics, Budapest, Hungary
[2] Dept. of Neurol. and Psych., David Geffen School of Medicine, UCLA, Los Angeles, CA, USA
[3] Ctr. for Molecular and Behav. Neurosci., Rutgers, State Univ. New Jersey, Newark, NJ, USA
[*] orban.gergo@wigner.mta.hu

Sensory areas of the cortex display rich activity even without stimulus presentation, which has been linked to the representation of expectations [1]. Recent work, however, demonstrated that a large portion of the activity recorded in a passive animal when stimulus is absent is related to behavioural activity [2, 3]. Here we argue that in task engaged animals a task-relevant variable is reliably represented in the intertrial interval, when stimulus is not presented.

We trained fourteen mice to perform a pair of tasks where the same set of multi-modal stimuli were used in different contexts: in one task context the animals were expected to make decisions based on visual stimulus content and ignore the auditory stimulus and in the other roles were reversed. Importantly, no cue was provided that could indicate whether to attend or ignore the visual stimuli, thus decoupling task context, stimulus identity, and behavioural outcome. Unit recordings were obtained from all layers of V1 using 128-channels silicon probes.

We found that task context was represented not only during stimulus presentation but a task representation consistent with on-stimulus activity was present during pre-stimulus activity as well. Representation of task context was achieved through recruiting a population overlapping with the one representing the visual stimulus but establishing an orthogonal representational space. This task-related activity was a major component of the activity recorded without stimulus and spanned only a low dimensional subspace. Context was invariantly represented in the same subspace throughout the session while transitioning to the other context. Further, representation of task context was indicative of behavioral performance: animals with a more reliable task representation performed better in the task. We found a representation of choice that emerged early in the trial, prior to actual behaviour and this choice representation resided again in a linearly independent subspace of the population activity space. We found more reliable decoding of visual stimulus content from population responses in the attend-visual condition but this improvement could be traced back to correlated choice and stimulus related activity components. Taken together, our results demonstrate that a structured activity pattern is present both in the pre-stimulus and on-stimulus activities in V1, which reflects cognitive variables relevant to task execution.

Acknowledgments

This work has been supported by Human Frontier Science Program grant (GO, PG) and the Hungarian Brain Research Program (2017–1.2.1-NKP-2017–00002, GO)

References

1. Berkes, Orbán, Lengyel, Fiser, 2011, *Science*, 331:83–87
2. Stringer, Pachitariu, Steinmetz, *et al.*, 2019, *Science*, 364:eaav7893
3, Musall, Kaufman, Juavinett, *et al.*, 2019, *Nat. Neurosci.*, 22:1677–1686

ROD BIPOLAR CELL CONTRIBUTION TO GANGLION CELL SURROUND

Berat S. Sermet[*]*, Giulia B. Spampinato, Francesco Trapani, Elric Esposito, Emiliano Ronzitti, Eirini Papagiakoumou, Pierre Yger, Deniz Dalkara, Serge Picaud, Jens Duebel, Valentina Emiliani, Olivier Marre*

Institut de la Vision, Sorbonne Université, Paris, France
[*]berat.sermet@inserm.fr

The retina sends information about the visual scene in the form of action potentials to the brain. Photoreceptors transduce light into electrical currents; bipolar cells process this signal and transmit it to ganglion cells, the retinal output. A key component of retinal processing is the information transfer from the intermediate bipolar cell layer to the ganglion cell layer. Our understanding of this transfer is limited: while multi-electrode arrays allow recording of many ganglion cells, bipolar cells cannot be easily recorded or stimulated in the intact retinal circuit.

Here we designed a combination of tools to selectively stimulate rod bipolar cells while recording the spiking activity of large ensembles of ganglion cells using a high-resolution stimulation technique with a multi-electrode array. We used an AAV with a specific promoter to express light-gated cation channels, selectively in rod bipolar cells. We then used 2-photon digital holography, a technique to pattern light to stimulate individual neurons in specific locations, while simultaneously recording ganglion cells with a multi-electrode array (Figure 1). Using this opto/electrophysiological tool set we manipulated the activity of rod bipolar cells while recording ganglion cells. Our method also allowed us to stimulate several bipolar cells simultaneously to measure the impact of complex stimulation patterns on the ganglion cell layer.

With the help of this new tool we present some evidence suggesting that rod bipolar cells could be a significant contributor to the surround of ganglion cells. Our results begin to provide a more complete understanding of the functional connectomics of the retina.

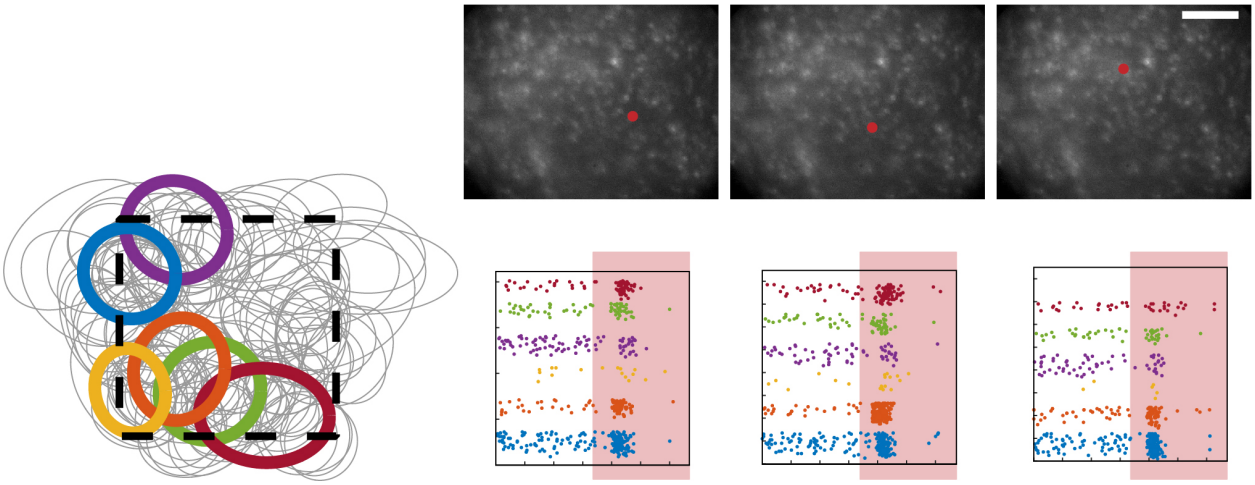


Figure 1. Rod bipolar cell (RBC) stimulation with 2-photon digital holography activates ganglion cells. Fluorescence image of RBCs expressing CoChR-GFP (top). Columns correspond to a different RBC stimulation (red spots drawn on top of the fluorescence image of the RBC layer). Each cell in the cluster is identified with a different color, which is the same for receptive field centers and rasters. Rasters represent responses to the spot in the column of all the cells in the cluster. Pink shading indicates the duration of the holographic stimulation. Scale bar, 100 µm.

DISSECTING THE CONTRIBUTION OF ROD BIPOLAR CELLS TO RETINAL GANGLION CELLS IN MOUSE RETINA

Francesco Trapani[*]*, Semihcan B. Sermet, Giulia L. B. Spampinato, Elric Esposito, Emiliano Ronzitti, Eirini Papagiakoumou, Deniz Dalkara, Jens Duebel, Valentina Emiliani, Pierre Yger, Olivier Marre*

Institut de la Vision, Sorbonne Université, INSERM, CNRS, Paris, France
[*]francesco.trapani@inserm.fr

Rod bipolar cells (RBCs) have received particular attention because they play a key role in relaying the rod signal during scotopic vision. More recently, it has been shown that they are also active during mesopic and possibly photopic light levels. A striking feature of RBCs is that they are not directly wired to the Retinal Ganglion Cells (RGCs): their signal is instead pooled by amacrine cells, including AII amacrine cells, which connect to both ON and OFF cone bipolar cells. The signal from RBC has therefore to cross at least 3 synapses to reach RGCs. Previous works [1] have shown how the information transfer from RBC to cone bipolar cell can be modulated by the level of network activation. Yet it is unclear how ganglion cells integrate the signal of multiple RBCs across space.

Here we use a combination of techniques to stimulate small groups of RBCs using optogenetics and digital holography, while recording population of ganglion cells with a multi-electrode array. We use these data to model how ganglion cells integrate the signal coming from RBCs. Preliminary results show that for ON RGC types the integration of RBCs signals can be modeled with a simple Linear-NonLinear model, where the inputs from different rod bipolar cells are summed linearly, followed by a static non-linearity capturing the spike emission process. Our results suggest that linearity is preserved along the polysynaptic way from RBC to ON RGCs. We are currently testing if more complex models are required for OFF RGCs where non-linear summation of RBCs contributions might be required.

These findings corroborate and complement previous studies of the RBC microcircuit, and suggest that a complex synaptic circuit can be modeled by a simple linear model. They also pave the way towards a full modeling of the retinal circuit by putting together multiple models of specific circuits of the retinal network.

Reference

1. Graydon, *et al.*, 2018, *Cur Biol*, 28(17):2739–2751

ENSEMBLE PROCESSING OF CINEMATIC MATERIAL IN POSTERIOR PARIETAL CORTEX OF MACAQUES

Lei Wang[1], Shuzhen Zuo[1], Michael Ortiz-Rios[2], Vincent Hakim[3], Makoto Kusunoki[4,5], Yong-di Zhou[6], Sze Chai Kwok[1,]*

[1] Shanghai Key Laboratory of Brain Functional Genomics, School of Psychology and Cognitive Science, East China Normal University, China
[2] Bioscience Institute, Faculty of Medical Sciences, Newcastle University, UK
[3] Laboratoire de Physique Statistique, École normale supérieure, CNRS, PSL University, Sorbonne Université, Paris, France
[4] MRC Cognition and Brain Sciences Unit, Cambridge, UK
[5] Department of Experimental Psychology, University of Oxford, UK
[6] School of Psychology, Shenzhen University, Shenzhen, China
[*] sze-chai.kwok@st-hughs.oxon.org

A recent fMRI study has delineated a social processing network including the posterior parietal cortex (PPC) in monkeys [1], suggesting the region is implicated in higher cognitive processes for complex dynamic information. Using complex natural movies we first conducted whole-brain functional magnetic resonance imaging (fMRI) in two macaque monkeys and found a large-scale activity pattern that included higher-level regions in the inferotemporal, frontal, parietal cortex. To further investigate whether and how such processing operate at single neural or ensemble level in the monkey PPC, we recorded multi-unit neuronal activities from the medio-posterior parietal cortex using 32-channel independently movable micro-electrodes on another two macaque monkeys while they underwent a natural video-viewing experiment. In each recording session, we had the macaques view three different 30-s videos, each for 30 repetitions. We used 27 unique videos and acquired neuronal data from 60 repetitions for each video across two consecutive days (in total 1620 video-viewing trials per monkey). The videos contained either depiction of primate animals, or depiction of non-primate animals, or of plain scenery (Category: primates/non-primates/scenery). We also manipulated contextual changes among the videos (Context: no boundary/one-boundary/two-boundary). By comparing the firing frequency across conditions, we show that distinct populations of neurons are selectively responsive to the content of the different videos. Moreover, using a leave-one-out cross-validation SVM classification method (*i.e.*, training SVM using 29 repetitions and testing it on the 30th repetition), we found that PPC neural activities can predict individual videos at a far higher than chance accuracy. This decoding approach was successful at both single-neuron (51.8% against 33.3% [Primate: 64.3%, Non-primate: 46.1%, Scenery: 45.1%]) and population levels (8.6% against 3.33% [Primate: 14.1%, Non-primate: 5.7%, Scenery: 5.9%]). We also looked into the firing patterns using 1-s time bins across the whole 30 seconds with the same decoding method. The results show that at both single-neuron or population levels, we can reliably decode the second-by-second segment of the videos. These results help elucidate the neurophysiological basis of dynamic cinematic information processing in the primate medio-posterior parietal cortex.

Reference

1. Sliwa, Freiwald, 2017, *Science* 356(6339):745–749

AUTHOR, SPONSOR AND STAFF INDEX

Entries for authors, sponsors and staff are listed by last name. Page numbers in bold (**00**) indicate first authorship on an accepted abstract, in normal typeface (00) indicate non-first authorship or other reference in the program text, in italics (*00*) indicate sponsorship, and underlined (00) indicate membership in the organizing committee.