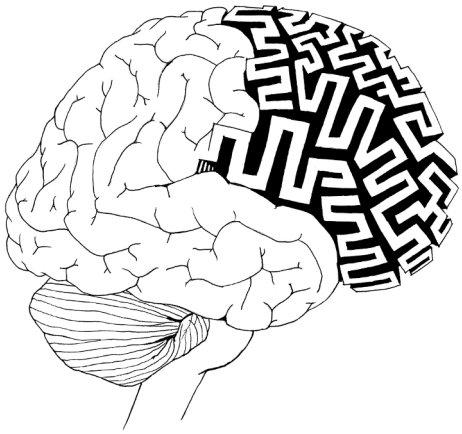
AREADNE 2016

Research in Encoding and Decoding of Neural Ensembles

Nomikos Conference Centre, Santorini, Greece

22-26 June 2016



AREADNE 2016
Research in Encoding and Decoding of Neural Ensembles
Nomikos Conference Centre, Santorini, Greece, 22-26 June 2016
John S. Pezaris and 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)

Celebrating 10 Years

AREADNE

Conferences

2006–2016

FOREWORD

Foreword

Welcome to AREADNE 2016, the ten-year anniversary of the first of these biennial conferences! We all are deeply indebted to Nicho Hatsopoulos and John Pezaris, the founders and prime movers of this conference. Nicho and John are proud members of the Greek diaspora, and they want all of you not merely to have great scientific interactions and an enjoyable time here: they fondly hope that you will come to love the country and culture of their ancestors. They have set up this conference to point you in that direction and urge you onward. The tone of AREADNE is always warm and welcoming, and they will exhort you to experiment with combining rigorous scientific debate with the local tempo and lifestyle.

Perhaps Nicho and John now have an efficient machine that they can crank up every two years, but the amount of initial planning must have been staggering. So many of the details that make this meeting unique were set in the first session: the famous location and dramatic setting; a conference schedule that encourages wine with lunch—neatly accommodating jet-lag by building in time for afternoon naps; poster sessions in a cobblestone echo-chamber fueled by John's ouzo proselytization; the requisite presence of two complementary and inexhaustible fonts of knowledge—Desmond Patterson's Kiwi drawling of the geophysics of volcanoes and Andronike "Nike" Makres's vivification of Bronze Age, Iron Age, and Classical Greece. At the heart of the meeting is the group of illustrious international speakers that Nicho and John have recruited over the previous two years, and you, dear reader, with your experiments, your analyses, your models.

The central topic of the meeting is the discovery and understanding of neuronal spike trains in brain circuits. Motor control in monkeys and humans seemed like the dominant theme at the outset, and brain-machine interfaces in humans have been a prominent subtopic. The first talk of the first meeting was by Apostopoulos Georgopoulos, on recordings of groups of spiking neurons in motor cortex of macaque monkeys and prospects for noninvasive neural prostheses. Quickly the topics were extended in the sensory direction and towards internal processing, and computation and general issues of coding and decoding gained platforms. Now all of the major themes of systems neuroscience are represented, and over the span of four days, one hears animated discussion of these subjects in every corner of the Nomikos Centre, and across the island.

In the course of the past decade of AREADNE conferences, Greece has been having a rough time, of course. The intellectual and physical pleasures of our conferences seem remote from the storms of economic and refugee crises, but they are so close. As you read this, think of all of those people living around you in Greece who are struggling to make ends meet; imagine refugees desperate to find a welcoming shore just to our east or trapped at Greece's northern border; picture the EgyptAir plane plummeting like Icarus from the sky not far away.

Nevertheless, each midwinter I find myself daydreaming of a swim out into the caldera from Amoudi Bay, with the pearly teeth of Oia hundreds of feet above me and the brown cliffs dipping beneath me to disappear in the blue-black depths—followed by a lunch of grilled fish and horta in one of the harbor tavernas, while debating the advances of computational models, the necessity of connectomics, the promise of some marvelous technological advance. Go out and create your own future daydreams!

Kenny Blum
Harvard University
2016

WELCOME

Welcome

Welcome to AREADNE 2016, the sixth AREADNE Conference on Research in Encoding and Decoding of Neural Ensembles, and a celebration of a decade of AREADNE meetings.

One of the fundamental problems in neuroscience today is to understand how the activation of large populations 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 over the past forty 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.

Recent technological advances have provided a glimpse into the global functioning of the brain. Such tools include functional magnetic resonance imaging, optical imaging methods, high-density electroencephalography and magnetoencephalography, 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 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. 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 2016 conference was organized by Nicholas Hatsopoulos and John Pezaris (Co-Chairs), along with Dora Angelaki, Yiota Poirazi, Thanos Siapas, and Andreas Tolias.

Local Organizers

Local organization effort has been provided by Nike Makres with assistance from Ariadne Pangalos and Elsie Zygouropoulou.

Sponsors and Support

Our conference is being sponsored with generous gifts from Dr. and Mrs. George Hatsopoulos, and Peter and Yayi Pezaris, to The AREADNE Foundation, a non-profit organization that runs the AREADNE Conferences. In addition, for 2016, the conference is being administered by the Massachusetts General Hospital, with financial or in-kind support from the National Science

Foundation (Grant number CBET-1637127), The Gatsby Charitable Foundation (Grant number GAT3291), The Wellcome Trust, Simons Foundation, and Foley & Lardner, LLC.

Carol Lucas, Ph.D.
Program Director, Biomedical Engineering
National Science Foundation
carlucas@nsf.gov

Sarah J. Caddick, Ph.D.
Neuroscience Advisor to Lord Sainsbury
Gatsby Charitable Foundation
sarah.caddick@gayfere.org.uk

John Isaac, Ph.D.
Science Porftolio Advisor
The Wellcome Trust
j.isaac@wellcome.ac.uk

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

Robert L. Martuza, M.D., F.A.C.S.
Chief, Neurosurgical Service
Massachusetts General Hospital
rmartuza@partners.org

The Myth of Ariadne

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

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

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

LOCAL INFORMATION

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

Restaurant Information

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

Restaurants in Fira and Firostefani

Archipelagos	+30-22860-23673	€ € €	caldera view, Santorinian cuisine
Assyrtiko	+30-22860-22463	€ € €	caldera view, wine restaurant
Kapari	+30-22860-27086	€ €	taverna, set back from main road
Koukoumavlos	+30-22860-22510	€ € € €	caldera view, nouvelle cuisine
Mama Thira	+30-22860-22189	€ €	caldera view, taverna
Poldo	+30-22860-24004	€	souvlaki stand, near the National Bank
Sphinx	+30-22860-23823	€ € € €	caldera view, Greek cuisine
The Greeks	+30-22860-22989	€ €	taverna, near the cable car
To Ouzeri	+30-22860-21566	€ €	Greek tapas, near main square

Restaurants in Oia

Iliovassilema	+30-22860-71614	€ €	fresh fish
Thalami	+30-22860-71009	€ €	ouzo bar
1800	+30-22860-71485	€ € € €	nouvelle cuisine

Restaurants in Perivolos-Vlychada

Vlychada	+30-22860-82819	€ €	Greek taverna by the beach
to Psaraki	+30-22869-82783	€ € €	fish tavern overlooking the marina
The Net	+30-22860-82818	€ € € €	fish tavern by the sea, local cuisine

Recommended Activities

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

Santozeum
open daily 10.00–18.00, tel +30 22860 21722, www.santorzeum.com, Fira

Archaeological Museum at Fira
open 08.30–15.00 (closed Mondays), tel +30-22860-22217, Ypapantis Street, Fira

Museum of Prehistoric Thera
open 08.30–15.00 (closed Mondays), tel +30-22860-23217, Mitropoleos Street, Fira

Folk Art Museum
open 10.00–14.00 and 18.00–20.00, tel +30-22860-22792, Kondohori, near Fira

Wine Museum
open daily 12.00–20.00, tel +30-22860-31322, located in Vothonas village

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

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

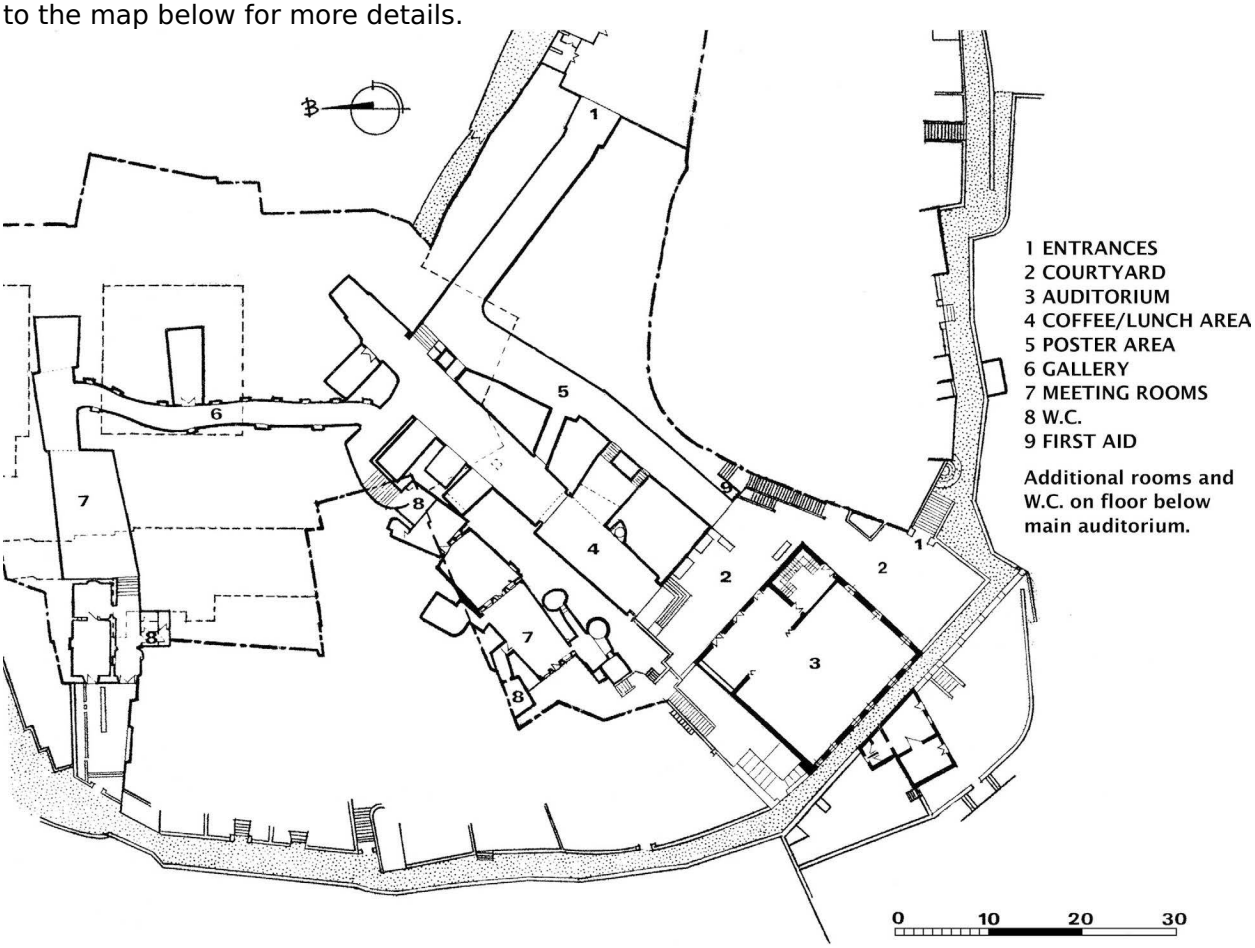
Monastery of Profitis Ilias
in Pyrgos, at the mountain peak; has a nice ecclesiastic museum; modest dress required

Main Beaches

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

Conference Centre Map

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



DAILY SCHEDULE AND PROGRAM

Overall Schedule

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

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

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

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

Saturday
09:00–12:00 optional excursions (no lunch provided)
17:00–21:30 lectures and coffee break, posters

Sunday
09:00–12:30 lectures and coffee break
12:30–14:00 lunch
17:00–19:45 lectures and coffee break
19:45–20:00 closing remarks
21:00–24:00 banquet dinner at Selene Restaurant in Pyrgos

WEDNESDAY, 22 JUNE 2016

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

THURSDAY, 23 JUNE 2016

08:00–08:30 registration

08:30–09:00 opening remarks

MORNING SESSION Kenny Blum, moderator

09:00–09:45 **Edvard Moser** (Norwegian University of Science and Technology)
Grid cells and entorhinal network dynamics, 35

09:45–10:30 **Lisa Giocomo** (Stanford University)
Calculating the algorithms of spatial maps, 29

10:30–11:00 coffee break

11:00–11:45 **Albert Lee** (HHMI Janelia Farm)
Intra- and extracellular studies of hippocampal memory formation, 32

11:45–12:30 **Neslon Spruston** (HHMI Janelia Farm)
Neuronal diversity and complexity in the hippocampus, 43

12:30–14:00 lunch

AFTERNOON SESSION Rowshanak Hashemiyoon, moderator

17:00–17:45 **Michael Roukes** (Caltech)
Toward very-large-scale interrogation of brain circuits, 40

17:45–18:20 coffee and light snacks

18:20–18:40 **James Jeanne** (Harvard Medical School)
Mapping higher-order connectivity using two-photon optogenetics, 51

18:40–19:00 **Karthikeyan Balasubramanian** (University of Chicago)
Neurodynamics observed in amputee non-human primates operating a closed-loop brain machine interface, 48

19:00–19:20 **Desmond Patterson** (University of Texas, Austin)
The great Minoan tsunami?, 38

19:20–19:40 **Andronike Makres** (Hellenic Education and Research Center)
The prehistoric (Minoan?) settlement of Akrotiri and the Ancient Greek city state of Ancient Thera: Two worlds apart, 33

20:00–21:30 posters, presenting author

Fritzie Arce-McShane (University of Chicago)
Spatiotemporal dynamics of coherence between primary motor and sensory cortical areas, 56

Mayte Bonilla Quintana (University of Nottingham)
A resonant integrate-and-fire network model for grid cell dynamics, 59

Thomas Demarse (University of Florida)
On the role of rich club topologies during information transmission among cell assemblies across hippocampal dentate and CA3 cocultured in vitro *networks*, 62

Tim Ebner (University of Minnesota)
Neural correlates of sensory prediction errors in purkinje cell simple spike discharge, 65

Emmanouil Froudarakis (Baylor College of Medicine)
A high throughput training method for investigating visual object recognition in mice, 68

Alexis Gkogkidis (University Medical Center, Freiburg)
Closed-loop interaction with the cerebral cortex: Exploring the parameter space of uECoG stimulation and read-outs, 71

Liberty Hamilton (University of California, San Francisco)
Feature extraction in the human primary to parabelt auditory cortex, 74

Hanna Kamyshanska (Frankfurt Institute for, Advanced Studies)
The influence of recurrent connectivity on angle discrimination for different visual map layouts, 77

Yiota Poirazi (IMBB-FORTH)
Dendritic contributions to synaptic and neuronal memory allocation, 80

Lynne Kiorpes (New York University)
Perceptual and neural deficits in processing naturalistic image structure in amblyopia, 83

Sreedhar Saseendran Kumar (University of Freiburg)
Autonomous control of network activity, 86

James Murray (Columbia University)
Temporal scaling and learning in basal ganglia, 89

FRIDAY, 24 JUNE 2016

MORNING SESSION Nicho Hatsopoulos, moderator

09:00–09:45 **Konrad Kording** (Northwestern University)
Linear nonlinear time warp models of neural activity, 30

09:45–10:30 **Alexander Ecker** (University of Tübingen)
What's the signal in the noise?, 28

10:30–11:00 coffee break

11:00–11:45 **Xaq Pitkow** (Baylor College of Medicine)
Nonlinear population codes, 39

11:45–12:30 **Matthias Bethge** (University of Tübingen)
Understanding complex neural network computations, 26

12:30–14:00 lunch

FRIDAY AFTERNOON SESSION Anthony Movshon, moderator

17:00–17:45 **Stephanie Palmer** (University of Chicago)
Understanding early vision through the lens of prediction, 37

17:45–18:15 coffee and light snacks

18:15–19:00 **Richard Born** (Harvard Medical School)
Bottom-up and top-down inputs drive the variability of cortical neurons, 27

19:00–19:20 **Diogo Peixoto** (Stanford University)
Real time decoding of a decision variable in a cognitive task, 52

19:20–19:40 **Theofanis Panagiotaropoulos** (Kings College London)
A non-monotonic spatial correlation structure in the macaque ventrolateral prefrontal cortex, 53

20:00–21:30 posters, presenting author

Stacey Bedwell (Nottingham Trent University)
Input and output connections of rat prefrontal cortex display a novel connectional gradient, in two distinct pathways, 57

Paul Fahey (Baylor College of Medicine)
Cell lineage directs the precise assembly of excitatory neocortical circuits, 60

George Denfield (Baylor College of Medicine)
Correlated variability in population activity: Noise or signature of internal computations, 63

SATURDAY, 25 JUNE 2016

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

AFTERNOON SESSION Georgia Gregoriou, moderator

17:00–17:45 **John Maunsell** (University of Chicago)
What is attention? Insights from the signals of individual neurons, 34

17:45–18:15 coffee and light snacks

18:15–19:00 **Stelios Smirnakis** (Harvard Medical School)
Dissecting neural activity patterns in supra-granular layers of mouse V1, 42

19:00–19:20 **Spyridon Chavlis** (Foundation for Research and Technology, Hellas)
Granule cell dendrites enhance pattern separation in dentate gyrus, 50

19:20–19:40 **Arkarup Banerjee** (Cold Spring Harbor Laboratory)
Linear readout of concentration invariant odor identity from the olfactory bulb output population, 49

20:00–21:30 posters, presenting author

Christina Bocklisch (Charité Universitätsmedizin, Berlin)
Functional anatomy of perirhinal projections to the somatosensory cortex, 58

Yuwei Cui (Numenta, Inc)
A theory of sequence memory in the neocortex, 61

George Dimitriadis (University College London)
T-SNE as a visualization step in the spike sorting pipeline, 64

Dominic Frank (Northwestern University)
Temperature processing in the drosophila brain, 67

Felix Gers (Beuth University Berlin)
Genetic growth of neuron morphologies with cellular automata, 70

Ralf Haefner (University of Rochester)
Endogenous attention in a probabilistic inference framework, 73

Katerina Kalemaki (IMBB-FORTH)
The contribution of developmental inhibitory changes in early postnatal circuits of the prefrontal cortex, 76

Bruno Cessac (INRIA)
Modeling the intrinsic mechanisms of immature starbust amacrine cellular network linked to the emergence of stage ii retinal waves during development, 79

SUNDAY, 26 JUNE 2016

MORNING SESSION Tania Pasternak, moderator

09:00–09:45 **Michael Stryker** (University of California, San Francisco)
A neural circuit that regulates cortical state and enhances plasticity, 44

09:45–10:30 **Irini Skaliora** (Biomedical Research Foundation Academy of Athens)
Cortical microcircuits in action: the maturation and neuromodulation of endogenous network dynamics, 41

10:30–11:00 coffee break

11:00–11:45 **Matthew Larkum** (Humboldt University of Berlin)
Probing the interactions of feed forward and feedback at both the cellular and network level, 31

11:45–12:30 **Gina Turrigiano** (Brandeis University)
Gating of firing rate homeostasis by sleep and wake states, 45

12:30–14:00 lunch

AFTERNOON SESSION Eilon Vaadia, moderator

17:00–17:45 **Sliman Bensmaia** (University of Chicago)
Biological and bionic hands: natural neural coding and artificial perception, 25

17:45–18:15 coffee and light snacks

18:15–19:00 **Michele Basso** (University of California, Los Angeles)
A role for the superior colluculus in decision-making and confidence, 24

19:00–19:45 **Leslie Osborne** (University of Chicago)
Adaptation and prediction in MT optimizes smooth pursuit, 36

19:45–20:00 closing remarks

21:00–24:00 banquet dinner at Selene Restaurant in Pyrgos

INVITED SPEAKER ABSTRACTS
(in alphabetical order by speaker)

A ROLE FOR THE SUPERIOR COLLICULUS IN DECISION-MAKING AND CONFIDENCE

Michele A. Basso [*], *Trinity B. Crapse, Piercesare Grimaldi*

University of California Los Angeles, Los Angeles, California, USA
[*] mbasso@mednet.ucla.edu

Evidence implicates the superior colliculus (SC) of the midbrain, a topographically organized map of visual space and saccadic eye movements, in the process of selection for action, attention and even perceptual decision-making. In a simple oddball choice task in which one differently-colored stimulus was chosen as a saccade goal (target) from among an array of same-colored stimuli (distractors), we previously found that when the discriminability between target and distractor neuronal activity was high, choices were likely to be accurate. When the discriminability between the target and distractor neuronal activity was low, choice performance was likely to be poor, consistent with the hypothesis that the SC encodes a decision variable. Here we extend these results to determine whether the SC also encodes the decision criterion and the decision confidence. Trained monkeys performed a simple, Yes-No perceptual decision task in two conditions, one in which the probability of the perceptual stimuli were equal across trials and a second in which the probability of one of the perceptual stimuli was higher than the others, as occurs in perceptual priming experiments. This manipulation resulted in consistent changes in behavioral response bias and decision criterion (α and c) but not sensitivity (β and d'). To assess the role of the SC, the data were sorted according to trial types; hits, misses, false alarms and correct rejections. After priming, consistent with a change in criterion, hit and false alarm rates increased whereas miss and correct rejection rates decreased. SC neuronal activity correlated directly with these increases and decreases. Furthermore, electrical stimulation of the SC mimicked the effect of perceptual priming by increasing the hit and false alarm rate and decreasing the miss and correct rejection rate. Importantly, the behavioral changes occurring with manipulation of SC activity did not depend on the location of the saccade goal and therefore, demonstrate that the SC encodes and is causally involved in setting decision criteria. To assess confidence, trained monkeys performed a random dot motion direction discrimination task in which we offered a safe bet option on 50% of the trials. The safe bet option always yielded a small reward, so if monkeys were less confident they would choose that instead of risking no reward for a wrong decision. The behavior of both monkeys showed that they were metacognitive, that is, they were more likely to choose the sure bet on difficult trials than on easy trials. Recordings from single and multiple neurons in the SC revealed two distinct populations of neurons: one that discharged more robustly for trials in which monkeys were confident and one that discharged more robustly when the monkeys were less confident. Together these finding show that the SC encodes information about decisions and decision confidence.

BIOLOGICAL AND BIONIC HANDS: NATURAL NEURAL CODING AND ARTIFICIAL PERCEPTION

Sliman Bensmaia[*], *Thierri Callier, Hannes Saal, Benoit Delhaye*

Department of Organismal Biology and Anatomy, University of Chicago, Chicago, Illinois, USA
[*] sliman@uchicago.edu

The first decade and a half of the twenty-first century brought about two major innovations in neuroprosthetics: the development of anthropomorphic robotic limbs that replicate much of the function of a native human arm and the refinement of algorithms that decode intended movements from brain activity. However, skilled manipulation of objects requires somatosensory feedback, for which vision is a poor substitute. For upper-limb neuroprostheses to be clinically viable, they must therefore provide for the restoration of touch and proprioception. In my lab, I am developing approaches to elicit meaningful tactile sensations through stimulation of neurons in somatosensory cortex. I adopt a biomimetic approach to sensory restoration, which leverages our current understanding about how information about grasped objects is encoded in the brain of intact individuals. I argue that not only can sensory neuroscience inform the development of sensory neuroprostheses, but also that the converse is true: stimulating the brain offers an exceptional opportunity to causally interrogate neural circuits and test hypotheses about natural neural coding.

UNDERSTANDING COMPLEX NEURAL NETWORK COMPUTATIONS

Matthias Bethge

University of Tübingen, Centre for Integrative Neuroscience, Tübingen, Germany
mbethge@tuebingen.mpg.de

The recent breakthrough in deep learning has led to a rapid explosion in the evolution of artificial neural networks that successfully perform complex computations such as object recognition or semantic image segmentation. Unlike in the past, the complexity of these networks seems essential for their success and cannot easily be replaced by much simpler architectures. In trying to understand how deep neural networks achieve robust perceptual interpretations of sensory stimuli, we face similar questions as we do in neuroscience even though their full connectome is known and it is easy to obtain the responses of all its neurons to arbitrary stimuli. How can we obtain precise descriptions of neural responses without relying on the specifics of implementation? Can we characterize the knowledge that such networks have acquired about the world and how it is represented? I will present recent results from my lab on assessing the meaning of neural representations in high-performing convolutional neural networks. More generally, I will argue that the rise of deep neural networks offers a particular chance for computational neuroscience to advance its concepts and tools for understanding complex computational neural systems, and I am hoping to spark stimulating discussions on how we could use this opportunity.

BOTTOM-UP AND TOP-DOWN INPUTS DRIVE THE VARIABILITY OF CORTICAL NEURONS

Camille Gómez-Laberge [1–3], *Alexandra Smolyanskaya* [1], *Jonathan J. Nassi* [1], *Gabriel Kreiman* [2,3], *Richard T. Born* [1,4,*]

[1] Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, USA
[2] Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, USA
[3] Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, USA
[4] Center for Brain Science, Harvard University, Cambridge, Massachusetts, USA
[*] rborn@hms.harvard.edu

Neurons in the cerebral cortex respond inconsistently to a repeated sensory stimulus, so how can they provide the basis for stable sensory experiences? Although the exact causes of neuronal response variability are unknown, the consistency with which it has been observed across a variety of cortical regions has encouraged the general view that each cell produces random spike patterns that noisily represent its response rate. In contrast to this view, we discovered that reversibly inactivating sources of either bottom-up (V2-to-MT) or top-down (V2-to-V1) input to cortical visual areas in the alert primate reduced both the spike train irregularity and the trial-to-trial variability of single neurons. A simple network model of integrate-and-fire neurons in which a fraction of the pre-synaptic inputs are silenced can reproduce this reduction in variability, provided that there exist temporal correlations primarily within, but not between, excitatory and inhibitory input pools. A large component of the variability of cortical neurons can therefore be ascribed to synchronous input produced by signals arriving from multiple sources. Taken together, our results impose strong constraints on theories of neuronal variability by causally linking the presence of bottom-up and top-down input to the spiking statistics of cortical neurons.

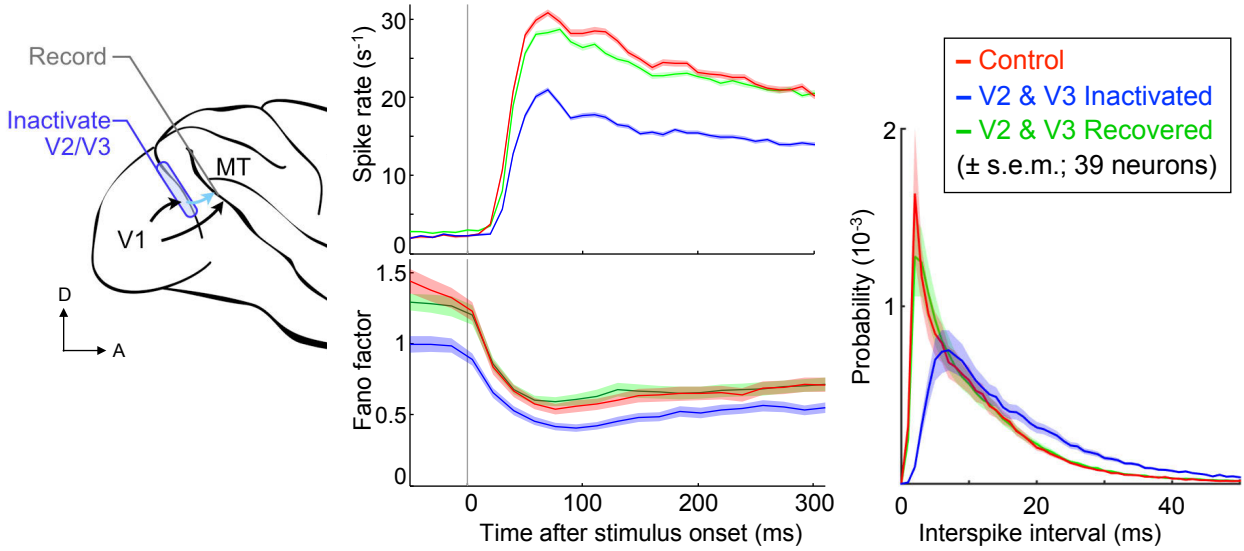


Figure 1. Reduction of spike train variability (Fano factor) and mean firing rate in MT when inactivating V2/V3 by localized cooling.

WHAT'S THE SIGNAL IN THE NOISE?

Alexander S. Ecker

Centre for Integrative Neuroscience, University of Tübingen, Germany
Bernstein Center for Computational Neuroscience, Tübingen, Germany
Baylor College of Medicine, Houston, Texas, USA
alexander.ecker@uni-tuebingen.de

Responses of cortical neurons are highly variable. Even repeated presentations of the same visual stimulus never elicit the same spike train. Identifying the origins of this variability remains a challenge. There is increasing evidence that it is not just noise arising from stochastic features of neuronal architecture, but at least partly represents meaningful top-down signals. One of the most prominent examples of such top-down modulation in the visual system is covert attention. I will present both theoretical and experimental results showing that trial-to-trial fluctuations of attentional state contribute significantly to response variability in primary visual cortex of awake, behaving monkeys. I will argue that much can be learned about information processing in the brain by using latent variable models of neuronal activity to help us identify and account for cognitive variables and make sense of single-trial neural population data.

CALCULATING THE ALGORITHMS OF SPATIAL MAPS

Lisa Giocomo

Neurobiology, Stanford School of Medicine, Stanford, California, USA
giocomo@stanford.edu

One of the largest gaps in neuroscience is in explaining cognitive processing in terms of cellular and circuit-level mechanisms. The medial entorhinal cortex is perhaps the best place to bridge this gap, as the basic response properties of its cells types are already known and it offers access to a tractable cognitive process, self-localization, or the ability to determine one's location in the environment. Neurons in the medial entorhinal cortex form the basic building blocks of an internal, neural navigation system by translating the external environment into a cognitive map of space. Despite the fascinating physiology of this system however, research has yet to determine the mechanisms underlying the response properties of spatially-selective entorhinal neurons. In this talk, I will discuss the contributions of single-cell and circuit dynamics to neural coding by entorhinal grid cells. The striking periodicity of the grid firing pattern has spurred multiple computational proposals for the emergence of grid cell firing properties, highlighting grid cells as an ideal system for investigating mechanisms of high-order cortical circuit computation.

LINEAR NONLINEAR TIME WARP MODELS OF NEURAL ACTIVITY

Patrick N. Lawlor[1–3], *Matthew Perich*[3], *Lee E. Miller*[3], *Konrad P. Kording*[1–3,*]

[1] Dept. of Physical Medicine and Rehabilitation, Northwestern University, Chicago, Illinois, USA
[2] Rehabilitation Institute of Chicago, Chicago, Illinois, USA
[3] Department of Physiology, Northwestern University, Chicago, Illinois, USA
[*] kk@northwestern.edu

Prominent models of spike trains assume only one source of variability — stochastic (Poisson) spiking — when stimuli and behavior are fixed. However, spike trains may also reflect variability due to internal processes such as planning. For example, we can plan a movement at one point in time and execute it at some arbitrary later time. Neurons involved in planning may thus share an underlying time-course that is not precisely locked to the actual movement. Here we combine the standard Linear-Nonlinear-Poisson (LNP) model with Dynamic Time Warping (DTW) to account for shared temporal variability. When applied to recordings from macaque premotor cortex, we find that time warping considerably improves predictions of neural activity. We suggest that such temporal variability is a widespread phenomenon in the brain which should be modeled.

PROBING THE INTERACTIONS OF FEED FORWARD AND FEEDBACK AT BOTH THE CELLULAR AND NETWORK LEVEL

Matthew Larkum

Humboldt University of Berlin, Berlin, Germany
matthew.larkum@gmail.com

Evidence suggests that the perceptual process involves feedback information to primary sensory regions. We have previously hypothesized that cortical pyramidal neurons are critical to this process because of their capability to integrate feed forward and feedback inputs using active mechanisms located in the apical dendrites. This hypothesis entails that features of dendritic integration at the single-cell level manifest at the network level. How can we test this hypothesis? It seems inevitable that we will need to study these phenomena in the intact brain during behavior and if possible, during psychophysical experiments in humans. So far, all experiments involving dendritic recordings have required technically demanding and invasive approaches only possible in animals. In this talk, I will discuss various possible approaches that may help us tackle this task including using EEG to measure dendritic activity and TMS to non-invasively manipulate dendritic activity. Our latest data suggest that EEG recordings might reflect dendritic activity to some extent and challenges the assumption that extracellular potentials predominantly reflect postsynaptic activity. These data suggest that studies of dendritic activity in humans are possible.

INTRA- AND EXTRACELLULAR STUDIES OF HIPPOCAMPAL MEMORY FORMATION

Albert Lee

Janelia Research Campus, Howard Hughes Medical Institute, Ashburn, Virgina, USA
leea@janelia.hhmi.org

The hippocampus plays a crucial role in the conversion of novel experiences into long-term memories. What are the mechanisms underlying the initial formation of a memory representation and its subsequent storage? Previous measurements of rodent hippocampal and entorhinal neurons have shown differences in spiking activity between the first exposure to a novel spatial environment and later exposures when the environment has become familiar. These findings as well as more recent intra- and extracellular experiments have led to hypotheses about the specific role of inhibition, plasticity, excitability, and other processes in the learning process. Recently, we have performed whole-cell recordings of hippocampal CA1 neurons in head-fixed mice as they explored a series of familiar and novel virtual maze environments. These intracellular recordings allow measurements of inputs, intrinsic properties, and other features such as large, plasticity-related calcium events as a function of different levels of spatial experience. This data has allowed us to test several proposed mechanisms underlying hippocampal learning and has revealed new insights into spatial memory formation.

THE PREHISTORIC (MINOAN?) SETTLEMENT OF AKROTIRI AND THE ANCIENT GREEK CITY STATE OF ANCIENT THERA: TWO WORLDS APART

Andronike Makres

Greek Epigraphic Society Hellenic Education and Research Center (HERC), Athens, Greece
info@herc.org.gr

The small Cycladic island of Santorini has two very important archaeological sites: (1) The Bronze Age (possibly Minoan) site of Akrotiri that dates to the 2nd Millenium BCE and (2) Ancient Thera, a Greek city state (*polis*) that flourished in the 4th and 3rd centuries BCE.

In my presentation I shall discuss these two entirely different types of Ancient society and show in what way each one of them is of relevance to Modern Western Civilization. How exotic is the first one since we understand little about it and how familiar we are with the second since its political and social values constitute to a great extend fundamental values of Modern Western type democracies. Yet we are fascinated by the Bronze Age Civilizations (Minoan and Mycenean). Why is that so?

In the case of the Greek city states it is easy to understand the relevance: The Greek states used the alphabet for the first time, the citizens spoke and wrote Greek, they understood the potential of simple individuals to produce excellence and enjoyed to a greater or lesser extend political freedom. It is in this socio-political context, i.e. that of the Greek City states that, apart from philosophy, geometry, athletics, etc., also democratic and egalitarian practices and values emerged with the seminal example of the Ancient Athenian Democracy of the Classical Period (5th and 4th centuries BCE).

WHAT IS ATTENTION? INSIGHTS FROM THE SIGNALS OF INDIVIDUAL NEURONS

John Maunsell[*], *Thomas Zhihao Luo, Supriya Ghosh*

Department of Neurobiology, University of Chicago, Chicago, Illinois, USA
[*] maunsell@uchicago.edu

Attention is a critical factor for behavioral performance. The neurophysiological correlates of attention have been studied for decades, but we have no universally accepted definition of what attention is. The term is used to describe a range of phenomena, including arousal, selection and executive control, with different operational definitions used in each case. This approach has provided a wealth of information about the neuronal correlates of attention, but a detailed understanding of its nature remains elusive.

Our recent research has been directed toward reaching a more precise description of attention. We have focused on spatial visual attention. It has long been known that this type of attention can enhance the signals of individual neurons in visual cerebral cortex, and can greatly increase the quality of information provided by populations of neurons. To refine our understanding of attention, we have employed the well-developed framework of signal detection theory. Signal detection theory describes perceptual performance using two distinct parameters: behavioral sensitivity and behavioral criterion. Several studies have shown that when people attend to a visual field location their sensitivity increases at that location and their behavioral criterion for detecting targets is lowered there. Both these changes contribute to more targets being detected at the attended location. We found that rhesus monkeys performing visual spatial attention tasks also change both their behavioral sensitivity and criterion. This raised the question of whether behavioral improvements associated with changes in sensitivity and those associated with changes in criterion are supported by different neurobiological mechanisms.

By training monkeys to do a visual spatial attention task in which shifts in attention were associated exclusively with changes in behavioral sensitivity or exclusively with changes in behavioral criterion, we could test whether changes in neuronal responses in different brain structures were preferentially associated with one or the other. In area V4 in visual cortex, we found that attention-related changes in neuronal responses are associated only with changes in behavioral sensitivity. In contrast, changes in the activity of many neurons in prefrontal cortex are associated with attention-related changes in criterion.

These studies show that visual spatial attention is made up of separable neurobiological mechanisms, and suggest that careful examination of the changes in behaviors associated with attention and their relationship to neuronal signals can provide a more complete understanding of the processes we call attention.

GRID CELLS AND ENTORHINAL NETWORK DYNAMICS

Edvard Moser

Kavli Institute for Systems Neuroscience/Centre for Neural Computation, Norwegian University of Science and Technology
edvard.moser@ntnu.no

The medial entorhinal cortex (MEC) is part of the brain's circuit for dynamic representation of self-location. A key component of this representation is the grid cell, whose spatial firing fields tile environments in a periodic hexagonal pattern, but the circuit contains also other functional cell types, such as head direction cells and border cells. In this lecture, I will discuss the mechanisms by which grid patterns are updated in accordance with the animal's movement in the environment. I will show that running speed is represented in the firing rate of a ubiquitous but functionally dedicated population of MEC neurons. I will also show that speed is represented across a wider brain circuit that includes speed cells in the mesencephalic locomotor region, whose outputs may reach the MEC via speed cells in the diagonal band of Broca. Finally I will discuss how grid cells represent large and complex environments, and I will present data pointing to some of the mechanisms underlying the early development of the grid-cell system.

ADAPTATION AND PREDICTION IN MT OPTIMIZES SMOOTH PURSUIT

Leslie C. Osborne

Department of Neurobiology, University of Chicago, Chicago, Illinois, USA
osborne@uchicago.edu

In a rapidly changing world, the statistics of sensory stimuli can fluctuate across a wide range. Theoretically, in order to maximize the information sensory neurons can transmit, they should rescale their sensitivity to input fluctuations dynamically, allocating their limited response bandwidth to the current range of inputs. Such adaptive coding has been observed in a variety of systems, but the premise that adaptation optimizes behavior has not been tested. Here we show that adaptive rescaling maximizes information about visual motion in cortical MT neurons and, importantly, in pursuit eye movements guided by that cortical activity. We use time-varying motion signals that transition between different levels of direction variance and record isolated, extrastriate cortical area MT neurons and we record pursuit eye movements in monkeys. We find that adaptation drives a rapid (less than 100 ms) recovery of motion information after steps in variance because both neurons and behavior rescale sensitivity to compensate for differences in direction variance. We find that MT neurons adopt a response gain, a change in firing rate per degree of direction change that maximizes information about motion. We find that pursuit also adapts to a response gain that maximizes the mutual information between eye and target movements and that minimizes tracking errors. Thus efficient sensory coding is not simply an ideal standard but rather a compact description of real sensory computation that manifests in improved behavioral performance.

Adaptation to the temporal structure of sensory stimuli is particularly important for behaviors where delays in sensory processing give rise to a lag between a stimulus and the organism's reaction. This presents a particular challenge to tracking behaviors like smooth pursuit where a difference in eye and target motion creates image motion blur on the retina. We show that MT neurons can encode predictive information about stimulus motion that is reflected in short time scale (less than 200 ms) anticipatory eye movements. To explore the degree to which the brain can form an internal model in order to anticipate target motion over longer time scales, we measured eye movements while human subjects played a video game. The game is based on Atari Pong where the subject moves a paddle to keep a ball bounding within an arena. We controlled the level of predictability, keeping collisions elastic or adding stochasticity. Subjects also watched movies of the Pong game being played, or of a ball bouncing within an enclosed arena (no paddle). We then computed the mutual information between eye and target position at different time delays. We find substantial predictive information both tasks, but there is a striking difference during active game play versus passive movie watching. In active Pong, the mutual information in the eye position is very near the bound determined by the predictive information in the target itself, $I(T(t); T(t + \Delta t))$, extending over several seconds, thus nearly all that is predictable about the target is incorporated into behavior. Eye-target information peaks at zero delay, compensating for visual processing time. In contrast, watching a movie of the Pong game produces gaze that is more reactive than predictive, within the approximately 200 ms range of predictive coding in MT neurons. We propose that sensory adaptation can account for short time scale predictive eye movement behaviors, but that an alternate mechanism that is both efficient and voluntary underlies anticipatory gaze on longer time scales.

UNDERSTANDING EARLY VISION THROUGH THE LENS OF PREDICTION

Stephanie E. Palmer[1,2,*], *Olivier Marre*[3], *Stéphane Deny*[3], *Jared M. Salisbury*[1,2]

[1] Graduate Program in Computational Neuroscience, University of Chicago, Chicago, Illinois, USA
[2] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, Illinois, USA
[3] Vision Institute, Paris VI University, Paris, France
[*] sepalmer@uchicago.edu

Prediction is necessary for long-term planning and decision-making, as well as for overcoming the short-timescale sensory and motor delays present in all neural systems. In order to interact appropriately with a changing environment, the brain must respond not only to the current state of sensory inputs but to rapid predictions of these inputs' future state. To test whether the visual system performs optimal predictive compression and computation, we compute the past and future stimulus information in populations of retinal ganglion cells, the output cells of the retina, in salamanders and rats. For some simple stimuli with mixtures of predictive and random components to their motion, we can derive the optimal tradeoff between compressing information about the past stimulus while retaining as much information as possible about the future stimulus. We compare these results across the two species. By changing parameters in the input motion, we can explore qualitatively different motion prediction problems. This allows us to explore which prediction problems the retina has evolved to solve optimally. Taking the next step towards defining the predictive capacity of neural systems, we characterize the ensemble of spatiotemporal correlations present in the natural environment. To do so, we construct and analyze a database of natural motion videos. We have made high-speed, high-pixel-depth recordings of natural scenes and quantify the space-time power spectra and the local motion content of these scenes. Defining the predictable content of natural motion constrains which computational structures the optimal predictive brain might employ.

THE GREAT MINOAN TSUNAMI?

Desmond Patterson

University of Texas, Austin, Texas, USA
dpatterson@jsg.utexas.edu

A *tsunami* is a wave (or series of waves) generated by a vertical disruption of the water column. In the deep ocean tsunami typically have wavelengths about 300 km, very small amplitudes (less than 1 m) and speeds of as much as 800 km/h. As tsunami propagate into shallower water, the wave slows to less than ten m/s and amplitude grows until a crest that can be tens of meters high forms. At this point the wave has tremendous forward momentum and may reach or overtop (run-up) topographic features more than twice the height of the wave at the shoreline and penetrate many kilometers inland. Tsunami exhibit all the normal features of wave propagation such as dispersion, refraction, reflection, interference and resonance. The exact behavior of any given tsunami is extremely sensitive to bathymetric variations and the specific shape of the shoreline resulting in highly variable run-up and inundation from one coastal point to the next, even over remarkably short distances.

Volcanic activity may generate tsunami via a wide range of mechanisms including: collapse of an eruption column or the volcanic edifice, caldera formation, or phreatomagmatic explosions where water cataclysmically interacts with magma. As the *ca.* 1610 BC eruption of Thera (Santorini) was both extremely large (ranking in the six largest eruptions of the last 10,000 years) and exhibited all of these processes it is reasonable to predict the generation of tsunami at various times during the estimated four day duration of the eruption.

By analogy to the Krakatoa Tsunami of 1883, the Greek archeologist Spyridon Marinatos argued in 1939 that the Late-Bronze Age Minoan civilization of Crete was catastrophically destroyed by just such a tsunami generated by the *ca.* 1610 BC eruption of ancient Thera. Subsequent archeological research, however, has identified significant Minoan remains that clearly post-date the Theran eruption, effectively ruling out the truly apocalyptic vision of Marinatos. Nonetheless, the vision of the Minoan civilization so destroyed provides an enduring cultural meme both romantic and tragic that was magnified by the appalling devastation of recent tsunami in Japan (2011) and the Indian Ocean (2004).

Despite significant research efforts in the decades since 1939, the question of just how many, how big, and how damaging any Theran tsunami were to the Minoans remains unclear. Although evidence for near-field tsunami has been reported on the coast of Santorini near Pori and reworked deep-sea deposits of the eastern Mediterranean seafloor have been linked to a possible Theran tsunami, extensive surveys of the Cretan coastline found little evidence of a tsunami that could be linked to the Theran eruption. An exception is a unique deposit exposed in a beach cutting near the ruins of major Minoan settlement at Palaikastro at the far eastern end of Crete which appears to record a major tsunami. However, ongoing research at Palaikastro finds little evidence for a major tsunami affecting the main body of the town. While it is hoped than continued excavations may shed light on this apparent contradiction, it is likely the uncertainty and controversy surrounding the Theran tsunami may continue for some time.

NONLINEAR POPULATION CODES

Xaq Pitkow

Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
Department of Electrical and Computer Engineering, Rice University, Houston, Texas, USA
xaq@rice.edu

To understand the brain, we need to explain both how sensory signals drive neural responses (encoding), and how neural responses drive behavior (decoding). Models of encoding have grown in sophistication, while detailed models of decoding have lagged behind, mostly considering only linear readout of neural activity. Since these models guide our data analyses, we have been stuck with limited options to analyze experimental data. The standard data analysis method boils down to computing linear correlations between the choices of a behaving animal and its neural activity. This is a reasonable measure for simple tasks and the right brain areas, where the mean activities of neurons encode the relevant task variables. Indeed, recent theoretical work shows how to use this measure to infer a linear readout that explains the animal's behavior. However, for natural conditions and natural tasks, this is not possible: mean neural responses are confounded by task-irrelevant variables, so those means do not provide information about the task. We show how this induces a nonlinear code. Here we introduce a new way of thinking about decoding that is appropriate for these more challenging, nonlinear natural tasks. This comes with a practical experimental test of the quality of an animal's nonlinear decoding strategy. When we apply this test to neural responses recorded from primate visual cortex, we find intriguing evidence that animals are using efficient nonlinear decoders.

TOWARD VERY-LARGE-SCALE INTERROGATION OF BRAIN CIRCUITS

Michael Roukes

Division of Engineering and Applied Science, Caltech, Pasadena, California, USA
roukes@caltech.edu

Despite recent advances in microtechnology, it is fair to say that progress toward massively-multiplexed interrogation of brain activity by in vivo electrophysiology (Ephys) has proceeded, at best, very slowly. Since Lord Adrian's pioneering work almost 90 years ago, Ephys has been the preeminent methodology. Yet extrapolating its rate of evolution leads one to the conclusion that it will take another 85 years before we will be able to observe electrical activity over the entire mouse brain (about 75M neurons). Clearly, a paradigm shift is necessary — and milestones in nanotechnology now appear poised to enable this. In this presentation I will review recent progress towards massively-multiplexed neurotechnology (surveying the dominant methodologies), and discuss the advantages and shortcomings of contemporary paradigms that are now being applied with the hope of upscaling this rate of progress.

Functional optical imaging, employing free-space multiphoton optical techniques, provides the highest multiplexing achieved to date. However, its underlying physics precludes access to regions arbitrarily deep within the brain. Contemporary optical reporters also cannot yet temporally track brain activity faithfully. It appears that implantable probes will continue to be of importance for the foreseeable future. Yet, endoscopy is too damaging to be universally applicable, nor does it provide sufficient optical range to enable broad area coverage. Implantable, minimally-invasive probes for extracellular electrophysiology (e.g. tetrodes and ultranarrow silicon probes) are the standard for recording full-bandwidth brain activity — but will Ephys data, even if dense, prove sufficient? It is likely that multiphysical measurements will be essential for understanding brain circuits. Specifically, in addition to dense and temporally-faithful time records of the spiking of a multiplicity of cells, one expects that complementary knowledge of cell type, inter-neural connection strengths, and local spatiotemporal activity in the chemical domain (neuromodulation) will prove essential. Multiphysical reporter developments in the pipeline will make all of these accessible optically.

We have developed a new paradigm for implantable, minimally-invasive photonic nanoprobes that will enable massively-parallel optical interrogation at arbitrary depths in the brain. This new technology, which we term integrated neurophotonics, leverages recent advances in optical reporters and effectors (actuators) and chip-based integrated nanophotonic circuitry. With specifically-designed reporters, activity from a spectrum of measurement domains — including electrical (spiking), morphological (cell type), chemical (neuromodulation), and the force domain (synaptogenesis) — will become simultaneously accessible, each with cellular-scale spatial resolution. I will describe this new paradigm, extrapolate how far I think it can be pushed within the next decade, and report on our progress to date toward its development.

CORTICAL MICROCIRCUITS IN ACTION: THE MATURATION AND NEUROMODULATION OF ENDOGENOUS NETWORK DYNAMICS

Irini Skaliora[1,*], *Babis Sigalas*[1], *Dimitris Adamos*[2,3], *Pavlos Rigas*[1], *Nikos Laskaris*[2,4]

[1] Center for Basic Research, Biomedical Research Foundation of the Academy of Athens, Greece
[2] Neuroinformatics Group, Aristotle University of Thessaloniki, Greece
[3] School of Music Studies, Aristotle University of Thessaloniki, Greece
[4] Department of Informatics, Aristotle University of Thessaloniki, Greece
[*] iskaliora@bioacademy.gr

The mammalian cerebral cortex is a highly complex yet modular structure that exhibits distinct modes of activation, reflecting the state and processing capabilities of the brain. Spontaneous network activity during quiescent states is a ubiquitous characteristic of cortical networks and has an active role in information processing: through its effect on neuronal conductances and membrane potential it provides a mechanism for modification of neuronal excitability. In this way it is thought to provide the neuronal context within which external signals are processed and interpreted.

Among the many patterns of spontaneous cortical activity that have been reported, recurring epochs of self-maintained depolarizations (Up states) are unique in several respects: they are present throughout life, in all mammalian species and cortical areas examined; they are observed in vivo, during quiescent states, but also in vitro, in acute and even organotypic slices, indicating they are a robust phenomenon and that mechanisms are in place to actively maintain them. Importantly, spontaneous Up states are intrinsic to the cortex and occur naturally, as a result of the recurrent connectivity and the membrane and synaptic properties of its constituent elements, and as such they are thought to represent the default activity of cortical networks.

In our lab we have developed the technology to record this activity in mouse brain slices throughout the lifespan and under diverse experimental conditions. We find that spontaneous Up states are systematically modified by age, cortical region and sex, and can therefore serve as an index of the functional maturation and differentiation of the cerebral cortex. By combining recordings from wildtype and knockout animals with pharmacological manipulations, we also reveal a clear and previously disputed effect of nicotinic signaling in cortical synchronization. Ongoing experiments focus on the neuronal communication within local microcircuits using data from multi electrode arrays and graph theory analysis to investigate how functional connectivity patterns are altered during different states of endogenous cortical activity.

DISSECTING NEURAL ACTIVITY PATTERNS IN SUPRA-GRANULAR LAYERS OF MOUSE V1

Stelios M. Smirnakis[1–3,*], *Anna Palagina*[2, 3]

[1] Brigham and Women's Hospital, Boston, Massachusetts, USA
[2] Veteran's Administration Hospital, Boston, Massachusetts, USA
[3] Harvard Medical School, Boston, Massachusetts, USA
[*] smsmirnakis@partners.org

Ongoing spontaneous activity is a fundamental property of networks of neurons. In the neocortex this *resting state activity* is constantly present in the absence of sensory input and motor output, reflecting, in some sense, the internal state of the animal. In fact, activity elicited by sensory stimulation represents arguably represents a relatively small modulation on the background of ongoing activity [1].

It is highly likely that the structure of this activity is related both to the underlying network architecture and to the algorithmic principles of how sensory information is represented and processed by cortical networks. However the principles that underlie the organization of this activity remain largely unknown.

In this talk, I will discuss how spontaneous activity patterns evolve across neuronal ensembles in the supra-granular layer of the mouse primary visual cortex from early postnatal development to juvenile adulthood, exhibiting marked decorrelation in the process [2]. At each age, firing patterns obey scale invariant statistics, suggestive of a small-world network architecture. Preliminary results suggest that it is possible to group L2/3 pyramidal neurons into cliques on the basis of the relative timing of their firing and the firing of neighboring interneurons. These groups get refined over time so that by early adulthood a typical group consists of a set of pyramidal neurons linked to, on average, 1–2 neighboring interneurons. Interestingly, pyramidal neurons belonging to the same group appear to share functional properties suggesting that these groups may represent units of functional organization.

Reference

1. Fiser, Chiu, Weliky (2004) *Nature*, 431(7008):573–8
2. Golshani, Goncalves, Khoshkhoo, *et al.* (2009) *J. Neurosci*,

NEURONAL DIVERSITY AND COMPLEXITY IN THE HIPPOCAMPUS

Nelson Spruston

Janelia Research Campus, Howard Hughes Medical Institute, Ashburn, Virgina, USA
sprustonn@janelia.hhmi.org

The hippocampus plays a crucial role in learning and memory. In rodents, this function is manifested in both spatial and emotional memories, which are thought to be encoded in the dorsal and ventral aspects of the hippocampus, respectively. Although the cellular organization of the hippocampus has been extensively studied using traditional anatomical methods, the diversity of cell types that comprise the circuit can now be probed with modern molecular, genetic, anatomical, and physiological approaches. My lecture will outline our progress toward using these techniques to explore the cellular organization and function of the hippocampus. We have identified subclasses of the major cell types in the hippocampus and we are relating the key molecular, anatomical, and functional features of these cell types, with the long-term goal of understanding how the menagerie of cell types works together to produce sophisticated functions such as spatial maps and memories. About half of the talk will feature new, unpublished data.

A NEURAL CIRCUIT THAT REGULATES CORTICAL STATE AND ENHANCES PLASTICITY

Michael P. Stryker

Dept. of Physiology, University of California, San Francisco, San Francisco, California, USA
stryker@phy.ucsf.edu

The brain's response to sensory input is strikingly modulated by behavioral state. In the primary visual cortex (V1) of the mouse, responses are dramatically enhanced by locomotion [1], a tractable and accessible example of a time-locked change in cortical state. The high-gain state of V1 produced by locomotion allows better decoding of stimuli from the visual responses of recorded neurons, in an unpublished study from our laboratory. To find the neural circuits that convey behavioral state to sensory cortex to produce this modulation we activated the midbrain locomotor center optogenetically below the threshold for inducing locomotion and enhanced V1 visual responses, suggesting ascending connections to the basal forebrain [2]. In the cortex, locomotion activated vasoactive intestinal peptide (VIP)-positive neurons in mouse V1 in the dark, largely through nicotinic inputs from basal forebrain. Optogenetic activation of VIP neurons increased V1 visual responses in stationary awake mice, artificially mimicking the effect of locomotion, and photolytic damage of VIP neurons abolished the enhancement of V1 responses by locomotion [3]. These findings establish a cortical circuit for the enhancement of visual response by locomotion and provide a potential common circuit for the modulation of sensory processing by behavioral state.

In the mouse, as in human suffering from *amblyopia ex anopsia*, recovery of V1 responses from early sensory deprivation is slow and incomplete. Visual stimulation while the mouse cortex was in the high-gain state produced by locomotion dramatically enhanced recovery [4]. Neither visual stimulation nor locomotion alone worked. Responses to the particular visual stimuli viewed by the animal during locomotion recovered, while those to another normally effective stimulus did not, showing that the effects of locomotion are specific to the stimuli then viewed. Further experiments using tetanus toxin to block synaptic transmission from VIP and SST cells or optogenetic stimulation of VIP cells revealed that the recovery depended much more on the activation of the VIP-SST disinhibitory circuit than on some aerobic or metabolic consequence of locomotion [5]. Stimulus-specific short-term plasticity in adults was also dramatically enhanced by activation of this circuit. Taken together, these findings suggest that the global state of cortical activity is modulated by a specific neural circuit that also modulates plasticity. They may also suggest an avenue for improving recovery from amblyopia in humans.

References

1. Niell, Stryker (2010) *Neuron*
2. Lee, *et al*. (2014) *Neuron*
3. Fu, *et al*. (2014) *Cell*
4. Kaneko, Stryker (2014) *eLife*
5. Fu, *et al*. (2015) *eLife*

Acknowledgments

Supported by US NIH grant EY-02874 and the Simons Collaboration on the Global Brain. M.P. Stryker is a recipient of the Research to Prevent Blindness (RPB) Stein Innovation Award.

GATING OF FIRING RATE HOMEOSTASIS BY SLEEP AND WAKE STATES

Gina Turrigiano

Neuroscience Program, Brandeis University, Waltham, Massachusetts, USA
turrigiano@brandeis.edu

Homeostatic mechanisms stabilize neural circuit function by keeping firing rates (FRs) within a set-point range, but whether individual neocortical neurons regulate firing around a cell-autonomous set-point, and whether this process is restricted to certain behavioral states such as sleep or wake, is unknown. I will start by discussing the mechanisms of synaptic scaling, a form of cell-autonomous homeostatic plasticity, and the role of this plasticity in generating firing rate set-points in vivo. I will then discuss new work in which we follow the process of FR homeostasis in individual visual cortical neurons in freely behaving rodents as they cycled between sleep and wake states. When FRs are perturbed by visual deprivation, over time they returned precisely to a cell-autonomous set-point, and this restoration of firing occurred selectively during periods of active waking and was suppressed by sleep. Longer natural waking periods result in more FR homeostasis, as does artificially extending the length of waking. This exclusion of FR homeostasis from sleep raises the possibility that memory consolidation or some other sleep-dependent process is vulnerable to interference from homeostatic plasticity mechanisms.

ORAL ABSTRACTS
(in alphabetical order by first author)

NEURODYNAMICS OBSERVED IN AMPUTEE NON-HUMAN PRIMATES OPERATING A CLOSED-LOOP BRAIN MACHINE INTERFACE

Karthikeyan Balasubramanian[1,*], *Mukta Vaidya*[1], *Joshua Southerland*[2], *Islam Badlerdin*[3], *Ahmed Eleryan*[4], *Andrew Fagg*[2], *Karim Oweiss*[3], *Nicholas G. Hatsopoulos*[1]

[1] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[2] School of Computer Science, University of Oklahoma, Norman, OK, USA
[3] Dept. Electrical and Computer Engineering, University of Florida, Gainesville, FL, USA
[4] Dept. Electrical and Computer Engineering, Michigan State Univ., East Lansing, MI, USA
[*] karthikeyanb@uchicago.edu

Brain machine interfaces (BMIs) can be useful in restoring motor functions lost due to physical impairment or neural dysfunction. Simultaneously, they can also serve as frameworks to understand neural adaptation emergent with learning. Previous experiments with BMIs have shown changes in tuning curves and certain other adaptive metrics [1–4] of individual neurons in awake and behaving animals using *in vivo* neural interfaces. However, the ensemble-level adaptation with BMI learning has remained largely unexplored, especially in cases of chronically amputated primates. Here, we show the emergence of network connectivity among a population of M1 neurons under the paradigm of BMI learning. Two rhesus macaques were chronically implanted with multi-electrode arrays at the primary motor cortex, and were operantly conditioned to perform a reach-to-grasp behavior with a multi-DOF robot. We observed an increase in the network density, as general phenomena, in both the animals and was persistent with behavioral learning. As one of the monkeys operated the BMI with neuronal population on the ipsilateral side of the amputation, we observed a decay in the prevailing natural network before the emergence of a sustained network adaptation with neuroprosthetic learning. Though the ensemble neurons became more connected with longitudinal exposure to the BMI, they showed a paradoxical tendency of decorrelating themselves during specific behavior task epochs. Finally, we also show these statistically inferred networks to possess characteristics of excitation and inhibition in congruence with the behavior. These adaptation dynamics can have implications as how ensemble-level neural networks can affect the design and control of next-generation BMIs.

References

1. Ganguly, Dimitrov, Wallis, Carmena (2011) *Nature Neurosci* 14(5):662–667
2. Churchland, Cunningham, Kaufman, *et al.* (2012) *Nature* 487(7405):51–56
3. Orsborn, Carmena (2013) *Front Comput Neurosci* 7
4. Orsborn, Moorman, Overduin, *et al.* (2014) *Neuron* 82(6):1380–1393

LINEAR READOUT OF CONCENTRATION INVARIANT ODOR IDENTITY FROM THE OLFACTORY BULB OUTPUT POPULATION

Arkarup Banerjee[*], *Honggoo Chae, Dinu F. Albeanu*

Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, USA
[*] abandyop@cshl.edu

Perception is often invariant with respect to stimulus identity (*e.g.*, faces) even when other stimulus features (*e.g.*, light levels) vary widely. The neural mechanisms that enable concentration invariant behavioral output in the mammalian olfactory system remain largely unknown. Broadly tuned olfactory sensory neurons, while increasing encoding capacity to large number of odors, hinder concentration invariance because increasing concentration not only strengthens glomerular activation but also recruits additional glomeruli. We propose that a specific inhibitory circuit in the olfactory bulb (OB) reformats the OB output to facilitate efficient readout of concentration invariant odor identity by target cortical areas. We recorded activity of mitral and tufted cells, forming the OB output, to odors across varying concentrations (3 orders of magnitude) in anesthetized and awake mice using 2-photon microscopy. Although individual mitral cells exhibited diverse concentration response functions (CRFs), the mean population response increased only modestly across this large concentration range. We recently demonstrated a causal role of dopaminergic/GABAergic interneurons (DAT+ cells) in mediating this gain-control process. Building on the response properties and wiring diagram of the DAT+ cells, we constructed a simple network normalization model that explains not only the stability of the mean responses, but also the diversity of the mitral cell CRFs.

We turned to the ensemble encoding of odor identity and concentration by the OB output cells. Visualizing neural trajectories using PCA revealed that for a given odor, all sampled concentrations span low-dimensional manifolds (Figure 1a), similar to reports in the insect antennal lobe, suggesting an evolutionarily conserved computation. To probe whether the two OB output channels encoded odor identity and concentration differentially, we analyzed neural responses in awake mice to a large odor panel at two set concentrations. The dimensionality of responses for both cell types grew sub-linearly with increasing number of stimuli; mitral trajectories spanned a substantially higher state space than tufted. Finally, a linear neural network with sparse and non-negative weights was able to perform concentration invariant odor identification across all stimuli with high accuracy (over 80%), which significantly dropped when DAT+ cells were specifically ablated (Figure 1b). We conclude that a specific interneuron circuit (DAT+ cells) reformats the information carried by the OB output population in a manner suitable for linear readout of concentration invariant odor identity by cortical areas.

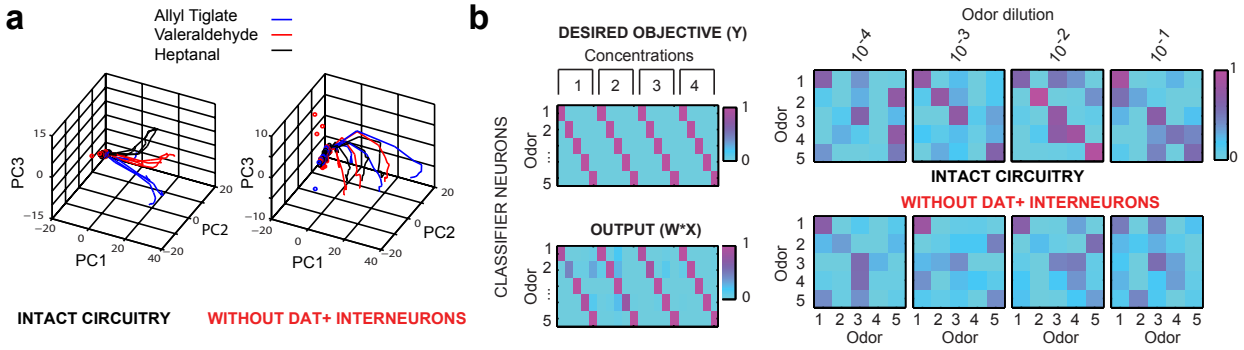


Figure 1. Olfactory bulb neural trajectories for three odors, and evidence for concentration-invariant odor encoding.

GRANULE CELL DENDRITES ENHANCE PATTERN SEPARATION IN DENTATE GYRUS

Spyridon Chavlis[1,2], *Panagiotis P. Petrantonakis*[1], *Panayiota Poirazi*[1,*]

[1] Institute of Molecular Biology and Biotechnology (IMBB), FORTH, Heraklion, Greece
[2] Department of Biology, University of Crete, Heraklion, Greece
[*] poirazi@imbb.forth.gr

The hippocampus plays an important role in memory formation, storage, and consolidation. Among its other functionalities, hippocampus has the ability to distinguish highly overlapping input stimuli and retrieve a specific stimulus given a partial or degraded one. Theorists refer to these computational tasks as pattern separation and pattern completion, respectively [1]. Dentate Gyrus (DG) principal cells, Granule cells, have been proposed to perform pattern separation by sparsifying and orthogonalizing their input. The ability to perform pattern separation is critical for ordinary brain function and its weakening is associated with many neurological diseases, such as Alzheimer's and temporal lobe epilepsy. Interestingly, these conditions are also characterized by morphological and/or biophysical alterations in granular dendrites. Thus, we investigate the role of granular dendrites in pattern separation using a simple computational, yet biophysical relevant, spiking neural network of the DG.

The network consists of the four major neuronal types found in DG, the granule, mossy, basket, and hipp cells. Each neuronal type is simulated as a point neuron using the adaptive exponential integrate-and-fire neuronal model [2]. However, the granule cell is simulated as an extended point neuron, consisted of a leaky integrate-and-fire somatic compartment connected with variable number of dendrites. To investigate the role of dendritic number in pattern separation, we implement three DG network models, whereby granule cells have 12, 6, or 3 dendrites. Interestingly, we predict a positive correlation between the dendritic number and the pattern separation efficiency; while dendritic number is reduced, the network performs less efficiently pattern separation. To study the effect of biophysical alterations on pattern separation, we also implement granule cell models with partial (50%) and complete (90%) blockade of NMDAR currents, respectively. Our results indicate that the DG model performs worst only if the NMDAR reduction is accompanied with dendritic atrophy (*i.e.*, if GCs have 3-dendrite). Finally, we test our DG model network under conditions of spine loss by reducing the number of afferents on granule cell dendrites and decreasing their membrane capacitance. Yet again, the model performs worst when both spine loss and dendritic atrophy conditions are present.

Our results predict that dendrites serve as a means of enhancing pattern separation in the DG and increase its robustness to spine loss and NMDAR deficits. The next goal is to extend the DG network to include the CA3 hippocampal subregion in order to further investigate the neuronal mechanisms that govern pattern separation in the hippocampus.

References

1. Yassa, Stark (2011) *Trends Neurosci* 34(10):515–525, 10.1016/j.tins/2011.06.006
2. Brette, Gerstner (2005) *J Neurophysiol* 94(5):3637–3642, 10.1152/jn.00686.2005

MAPPING HIGHER-ORDER CONNECTIVITY USING TWO-PHOTON OPTOGENETICS

James M. Jeanne [†,*], *Mehmet Fişek* [†], *Rachel I. Wilson*

Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, USA
[†] equal contributions
[*] james_jeanne@hms.harvard.edu

The brain encodes sensory information with large populations of neurons, yet to understand such a code we must first understand how downstream neurons interpret this population activity. This goal has historically been challenging because of the difficulty in identifying shared postsynaptic targets of defined neural populations. We overcome this difficulty using two-photon optogenetics to map the connectivity between two layers of olfactory processing in the fruit fly, *Drosophila melanogaster*, with single neuron resolution. This map reveals an anatomical substrate for how the brain interprets a sensory population code.

In the olfactory system, odors are encoded by the combined activity of multiple glomeruli, but how downstream circuitry integrates the glomerular population code is incompletely understood. In the fruit fly, glomerular projections target the mushroom body and lateral horn, two regions of higher-order olfactory processing. The lateral horn has been implicated in mediating innate odor-driven behavior and, consistently, glomerular projections to the lateral horn are stereotyped across animals. However, the connectivity patterns between glomeruli and lateral horn neurons (LHNs) have only been studied for a few specific LHNs. A comprehensive understanding of connectivity rules in this system is therefore lacking.

To uncover connectivity with single glomerulus and single LHN resolution, we combined two-photon optogenetics with whole-cell patch-clamp electrophysiology. We expressed a red-shifted channelrhodopsin in projection neurons innervating each glomerulus and focally stimulated each glomerulus with infrared light using a two-photon microscope. Simultaneously, we monitored postsynaptic activity in individual LHNs with patch-clamp recordings. Functional connections could be assessed by the presence or absence of depolarizations in response to stimulation of each glomerulus.

This methodology allows us to systematically map the glomerular inputs to individual LHNs in individual experiments. Assembling data from many LHNs results in a connectivity map that reveals how the brain integrates the glomerular population code. These results constitute an important step towards understanding the computations that underlie innate behavioral responses to olfactory signals.

REAL TIME DECODING OF A DECISION VARIABLE IN A COGNITIVE TASK

Diogo Peixoto[1,2,*], *Roozbeh Kiani*[3], *Jonathan C. Kao*[4], *Paul Nuyujukian*[5], *Chandramouli Chandrasekaran*[4], *Krishna Shenoy*[1,4,5], *William T. Newsome*[1]

[1] Neurobiology Department, Stanford University, Stanford, California, USA
[2] Champalimaud Neuroscience Programme, Lisbon, Portugal
[3] Center for Neural Science, New York University, New York, New York, USA
[4] Electrical Engineering Department, Stanford University, Stanford, California, USA
[5] Bioengineering Department, Stanford University, Stanford, California, USA
[*] dpeixoto@stanford.edu

In dynamic environments, subjects often integrate multiple samples of a signal and combine them to reach a categorical judgment. This evidence integration process can be described by a time-varying decision variable (DV) reflecting the current judgment of the subject. Sometimes, these categorical judgments can change as additional evidence becomes available, a phenomenon that has been termed *changes of mind* (CoM). Identifying CoMs and their neural correlates, and understanding why and how they occur, requires two key elements: (i) an instantaneous single-trial readout of population neural activity and (ii) validating the relationship between the time-varying DV and decision commitment. Using electrode array recordings and classification techniques, we have previously shown [1] that during a visual motion discrimination task, population neural activity in the dorsal premotor cortex (PMd) and motor cortex (M1) carry choice-predictive signals with DV-like features. Using a logistic classifier to estimate the DV, we find that the choice-prediction accuracy: (i) departs from chance levels shortly after stimulus presentation (180/250 ms for PMd/M1), (ii) increases in magnitude throughout the trial, and (iii) varies systematically with stimulus difficulty, increasing faster for easier stimuli. Thus, neural activity in PMd and M1 covaries with the decision formation process with very short latency and high accuracy, making these areas excellent candidates for studying the neural correlates of CoM. Building on these observations, we assembled a real-time setup that estimates instantaneous DV every 10 ms using 50 ms of spiking data of up to 192 independent channels from two microelectrode arrays. We demonstrate excellent online choice prediction accuracy across the trial: 95%/93% during the second half (600–1200 ms) of stimulus presentation for Monkey H/F. The linear decoder was stable for long periods of time with performance demonstrating only modest fluctuation over several weeks: 2.5% maximum accuracy difference over a 4-week span. We leveraged this real-time readout to perform two closed loop experiments in which the termination of the stimulus is contingent to a specific neural state. In the first experiment, we established threshold values for DV that, if reached, triggered the termination of the stimulus and cued the monkey to report its decision. Strikingly, using only 50 ms of data to estimate the DV that triggered termination, the difference between the observed likelihood of a given choice and that predicted by the logistic function was only, on average, 1.5%/1.8% for Monkey H/F. In the second experiment we triggered the stimulus termination on robust changes in DV sign (interpreted as potential CoM) that meet specific parameters within experimental control. The DV following putative CoM predicted choice nearly as accurately as on trials with no CoM. In addition, the statistical regularities of these covert neural events follow those detected behaviorally in humans performing an identical task [2]. These initial results validate our real-time readout DV and its relation to commitment state and demonstrate how a closed loop setup can be used to understand covert cognitive processes.

References

1. Peixoto, Kiani, Chandrasekaran, *et al.* (2014) Soc Neurosci Annu Meeting 435.12
2. Resulaj, Kiani, Wolpert, *et al.* (2009) *Nature* 461(3):263–6, 10.1038/nature08275

A NON-MONOTONIC SPATIAL CORRELATION STRUCTURE IN THE MACAQUE VENTROLATERAL PREFRONTAL CORTEX

Shervin Safavi[1,2], *Abhilash Dwarakanath*[1], *Michel Besserve*[1,3], *Vishal Kapoor*[1,2], *Nikos K. Logothetis*[1,4], *Theofanis I. Panagiotaropoulos*[1,5,6,*]

[1] MPI for Biological Cybernetics, Tübingen, Germany
[2] IMPRS for Cognitive and Systems Neuroscience, University of Tübingen, Tübingen, Germany
[3] MPI for Intelligent Systems, Tübingen, Germany
[4] Div. of Imaging Science and Biomedical Engineering, University of Manchester, Leicester, UK
[5] Centre for Systems Neuroscience, University of Leicester, Leicester, UK
[6] Inst. of Psychiatry, Psychology and Neuroscience, Kings College London, London, UK
[*] theofanis.panagiotaropoulos@tuebingen.mpg.de

Anatomical investigations of the primate prefrontal cortex revealed fundamental structural differences compared to early sensory areas, ranging from cell morphology to patterns of intra-areal connectivity. In order to make a bridge between anatomy and function in this area it is necessary to use measures that are functionally interpretable like noise correlation. In the present study, we characterized the spatial structure of pairwise noise correlations in the ventrolateral Prefrontal Cortex (vlPFC) to investigate potential differences in vlPFC functional connectivity compared to early sensory areas.

We recorded the spiking activity of spatially distributed neural populations with a Utah array in the vlPFC of two anaesthetized monkeys during visual stimulation with short duration (10 seconds) movie clips. Our findings suggest that many of the correlation properties in the vlPFC are similar to those observed in early sensory areas (*e.g.*, relationship between noise and signal correlations). However, in contrast to early sensory areas, we found that the vlPFC connectivity kernel is neither homogeneous nor monotonic. Specifically, we observed that following an initial monotonic decrease of correlations for intermediate distances (below 2 mm) correlations for remote neurons (inter-electrode distance above 2 mm) increase significantly, and are of equal strength to the magnitude of correlations for nearby neuronal pairs.

To further examine the connectivity pattern, we built a functional connectivity graph of the array (based on pairwise noise correlations), and analyzed its topology using eigenvector centrality. This analysis revealed spatially segregated subnetworks with densely connected patches of neurons. The correlation structure within the patches contributes significantly to the overall structure of correlations.

Our analysis suggests that the vlPFC circuits are organized in non-homogeneous subnetworks, compatible with anatomical studies of this region [1–3]. Such a connectivity pattern could constrain theoretical models of prefrontal function, as it might be instrumental to large-scale coordination of distributed information processing in prefrontal cortex.

References

1. Elston (2003) *Cerebral Cortex*, 13(11), 1124-1138
2. Pucak, Levitt, Lund, *et al.* (1996) *J Comp Neurol*, 376(4), 614-30
3. Levitt, Lewis, Yoshioka, *et al.* (1993) *J Comp Neurol*, 338(3), 360-76

POSTER ABSTRACTS

(in alphabetical order by first author)

SPATIOTEMPORAL DYNAMICS OF COHERENCE BETWEEN PRIMARY MOTOR AND SENSORY CORTICAL AREAS

Fritzie I. Arce-McShane[1,*], *Callum F. Ross*[1], *Kazutaka Takahashi*[1], *Barry J. Sessle*[2], *Nicholas G. Hatsopoulos*[1,3]

[1] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[2] Faculty of Dentistry, University of Toronto, Toronto, Ontario, Canada
[3] Committees on Comp. Neuroscience and Neurobio., University of Chicago, Chicago, IL, USA
[*] fritziea@uchicago.edu

Coherence between cortical areas has been implicated in neuronal communication and plasticity. Sensorimotor integration and formation of motor memories during learning are examples wherein effective communication between sensory and motor areas of the cerebral cortex is critical. However, very few studies have investigated coherence between the somatosensory and motor pathways in primates. These past studies have been confined to upper limb tasks and none of them looked at changes in coherence during learning. Here, we measure intercortical coherence between the spiking of neurons in the orofacial motor (MIo) or somatosensory (SIo) areas of cortex with the local field potentials (LFPs) in SIo or MIo, respectively, as monkeys learn to generate tongue-protrusive force. We report that neuroplastic changes in coherence gradually emerge over a few days and that spike-field coherence occurs in both directions, *i.e.* MIo spike-SIo LFPs (MSf) and SIo spike-MIo LFPs (SMf), and in multiple frequency bands, *i.e.* theta (2–6 Hz) alpha (6–13 Hz), beta (15–30 Hz), and gamma (30–50 Hz). These functional networks of coherent spiking and LFPs exhibit frequency-specific spatiotemporal properties. First, theta coherence was stronger in MSf than SMf while gamma coherence was stronger in SMf than MSf. Differences in firing rates of neurons cannot account for these results as no linear relations were found between firing rates of MIo or SIo neurons and the MSf/SMf coherence in either theta or gamma bands. Second, the distribution of time of peak theta coherence was unimodal and centered at force onset, whereas the distributions of time of peak coherence in alpha, beta, and gamma bands were bimodal with peaks at ± 0.3 s around force onset. Third, unlike coherence in the higher frequency bands, the distribution of the phase at peak theta coherence was bimodal with peaks near 0° and $\pm 180^\circ$, suggesting two subnetworks of coherent signals, *i.e.* in-phase and anti-phase. Lastly, time of peak theta coherence exhibited a spatial gradient consistent with the temporal relation of MIo neurons' spiking to tongue force and on the spatial features of MIo and SIo neurons' receptive fields. Overall, the results suggest that communication between somatosensory and motor areas is coordinated spatiotemporally. Time-sensitive sensorimotor integration and plasticity may rely on coherence of local and large-scale functional networks for cortical processes to operate at multiple temporal and spatial scales.

Acknowledgement

This work was supported by CIHR Grant MOP-4918 and NIH R01DE023816.

INPUT AND OUTPUT CONNECTIONS OF RAT PREFRONTAL CORTEX DISPLAY A NOVEL CONNECTIONAL GRADIENT, IN TWO DISTINCT PATHWAYS

Stacey A. Bedwell[1,*], *Chris J. Tinsley*[2]

[1] Division of Psychology, Nottingham Trent University, Nottingham, UK
[2] Biosciences, Nottingham Trent University, Nottingham, UK
[*] stacey.bedwell@ntu.ac.uk

The organization of connections is typically ordered throughout the cerebral cortex. Studies indicate that this is the case in Prefrontal Cortex (PFC). We injected the neuroanatomical tracers Fluoro-Gold and Fluoro-Ruby into sub-regions of PFC. Tracer injections were made into 3 coronal levels within the PFC (anterior, central and posterior), separated by 1 mm. We found that both tracers produced prominent labelling in temporal and sensory-motor cortex. Fluoro-Gold produced retrograde labelling and Fluoro-Ruby produced largely anterograde labelling. Statistical analysis of the 3-dimensional location of these connections within temporal and sensory-motor cortex revealed consistent ordering ($p < 0.001$). At the anterior and central coronal levels, injections (*i.e.*, equivalently located injections employing the same tracer) produced a similar pattern of ordering, this was particularly prominent within temporal cortex. However, at the posterior coronal level this pattern of ordering was reversed in temporal cortex and was also changed in sensory-motor cortex. This provides evidence for differential ordering of connections in the anterior-posterior axis of PFC.

FUNCTIONAL ANATOMY OF PERIRHINAL PROJECTIONS TO THE SOMATOSENSORY CORTEX

Christina Bocklisch[1], *Matthew E. Larkum*[1,2,*]

[1] Neurocure Cluster of Excellence, Charité Universitätsmedizin Berlin, Germany
[2] Biology Department, Humboldt University, Berlin, Germany
[*] matthew.larkum@gmail.com

The perirhinal cortex (PRh) as part of the parahippocampal structures has been implicated in the transfer of a wide range of mnemonic signals to various parts of the neocortex. Anatomical studies have shown that there is considerable connectivity between the PRh and the somatosensory cortex (S1) [1]. However, the functional connectivity between the two areas has so far not been investigated.

Using optogenetic tools and *in vitro* recordings of mouse S1 barrel cortex slices, we found that PRh fibers target predominantly the upper layers of S1 barrel cortex, in particular in layer 1 (L1), in line with projection patterns from other feedback projections [2]. While light-activating PRh fibers, we recorded from layer 5 pyramidal cells (L5 PCs), which generate the main output of the neocortex, as well as from local inhibitory interneurons (L1 INs). We found that both populations receive functional depolarizing synaptic inputs (L5 PCs: 4.01$\pm$0.95 mV, L1 INs: 9.56$\pm$1.35 mV). We checked whether there is cholinergic modulation of these PRh synapses, as it is known that cholinergic signaling is crucial for memory encoding [3] and that cholinergic fibers from the Nucleus Basalis project to the upper layers of the neocortex. Indeed, perfusing the slices with 20 µM Carbachole decreased the PRh inputs significantly to 60.2$\pm$15% of their initial amplitude.

Our results suggest that PRh projections increase membrane excitability of its targets in layer 1 and that cholinergic modulation dampens this input. Further *in vivo* studies will be necessary to assess the PRh influence on the network activity in S1.

References

1. Agster, Burwell (2009) *Hippocampus*, 19:1159–1186, 10.1002/hipo.20578
2. Insausti, Herrero, Witter (1997) *Hippocampus*, 7:146–183
3. Letzkus, Wolff, Meyer, *et al.* (2011) *Nature*, 480:331–335, 10.1038/nature10674

A RESONANT INTEGRATE-AND-FIRE NETWORK MODEL FOR GRID CELL DYNAMICS

Mayte Bonilla Quintana[*], *Stephen Coombes, Reuben O'Dea*

School of Mathematical Sciences, The University of Nottingham, Nottingham, UK
[*] pmxmb8@nottingham.ac.uk

In 2005, Hafting and colleagues in the Moser Lab, discovered grid cells in the Medial Entorhinal Cortex (MEC). These cells fire at multiple locations while an animal is wondering through an environment defining a periodic triangular array that covers the entire surface, hence the name. Furthermore, grid cells fire at the same position regardless of changes in the animal's speed and direction, and firing persists in the absence of visual input. It is therefore believed to correspond to the animal's own sense of location. For the discovery of these type of cells May-Britt and Edvard Moser won the 2014 Nobel Prize in Physiology or Medicine.

Since the discovery of grid cells many models have been developed in order to address the mechanism of grid cell firing. However only few models, like the one in [1], link the firing of grid cells to data on intracellular resonance and rebound spiking in layer II stellate cells of the MEC, that represent the 70% of the total MEC II neural population and therefore a large fraction of the grid cell population.

We propose a neural field integrate and fire model with a hyperpolarisation-activated cation current (h-current). This type of current has been studied even before the discovery of grid cells because it underlies resonance at theta frequency and causes a depolarising rebound spike following a hyperpolarising current injection. We based our description of the h-current on a Hodgkin-Huxley type model obtained from experimental data [2]. Furthermore, inspired by relevant MEC data we consider only inhibitory neural connectivity. Simulations of our model show sustained rebound spiking that is propagated across the network after injecting a initial hyperpolarising current to a small fraction of the neurons.

Our aim is to show that a difference in neural resonance frequency seen experimentally along the dorsal to ventral axis of the MEC can produce a difference in the size and spacing between the grid cell firing fields. In order to achieve this, we first perform a piece-wise linear reduction of our model that preserves its dynamics. Such a reduction allows us to obtain a self-consistent solution for a periodic travelling wave. We study this wave under parameter variation to observe a strong dependence of the period on the resonant frequency arising from the h-current.

References

1. Hasselmo (2014) *Phil. Trans. R. Soc* 369(1635):20120523, 10.1098/rstb.2012.0523
2. Kopell, LeMasson (1994) *PNAS* 91(22):10586–10590

CELL LINEAGE DIRECTS THE PRECISE ASSEMBLY OF EXCITATORY NEOCORTICAL CIRCUITS

Cathryn R. Cadwell[1,*], *Xiaolong Jiang*[1], *Fabian H. Sinz*[1], *Philipp Berens*[1–5], *Paul G. Fahey*[1], *Dimitri Yatsenko*[1], *Emmanouil Froudarakis*[1], *Alexander S. Ecker*[1,2,4,6], *Ronald J. Cotton*[1], *Andreas S. Tolias*[1,2]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[2] Bernstein Center for Computational Neuroscience, Tübingen, Germany
[3] Institute for Ophthalmic Research, University of Tübingen, Tübingen, Germany
[4] Reichardt Center for Integrative Neuroscience, University of Tübingen, Tübingen, Germany
[5] Institute of Theoretical Physics, University of Tübingen, Tübingen, Germany
[6] MPI for Biological Cybernetics, Tübingen, Germany
[*] crhughes@bcm.edu

The neocortex carries out complex mental processes such as perception and cognition through the interactions of billions of neurons connected by trillions of synapses. Recent studies suggest that excitatory cortical neurons with a shared developmental lineage are more likely to be synaptically connected to each other than to nearby, unrelated neurons [1, 2]. However, the precise wiring diagram between clonally related neurons is unknown, and the impact of cell lineage on neural computation remains controversial. Here we show that vertical connections linking neurons across cortical layers are specifically enhanced between clonally related neurons (Fig. 1). In contrast, lateral connections within a cortical layer preferentially occur between unrelated neurons (Fig. 1). Importantly, we observed these connection biases for distantly related *cousin cells*, suggesting that cell lineage influences a larger fraction of connections than previously thought. A simple quantitative model of cortical connectivity based on our empirically measured connection probabilities reveals that both increased vertical connectivity and decreased lateral connectivity between cousins promote the convergence of shared input onto clonally related neurons, providing a novel circuit-level mechanism by which clonal units form functional cell assemblies with similar tuning properties [3, 4]. Taken together, our data suggest that the integration of feedforward, intra-columnar input with lateral, inter-columnar information may represent a fundamental principle of cortical computation that is established, at least initially, by developmental programs.

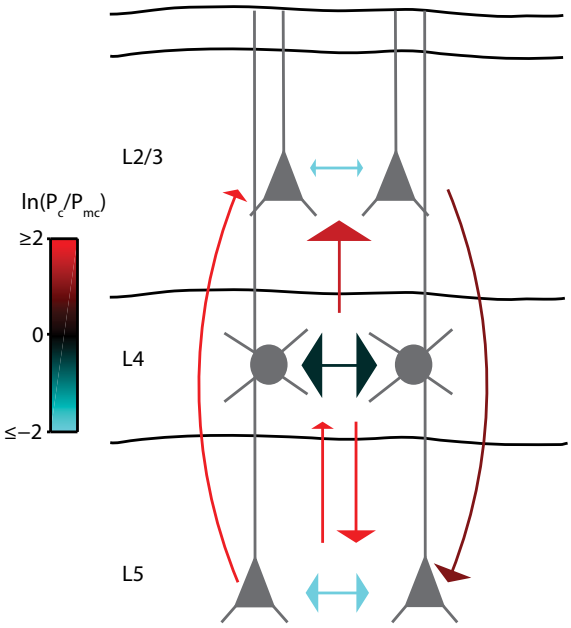


Figure 1. Summary of the influence of cell lineage on the layer-specific connectivity diagram between excitatory cortical neurons. Line width reflects the overall connection probability and color reflects the natural log of the raio between cousin (P_C) and matched (P_{mc}).

References

1. Yu, Bultje, Wang, *et al.* (2009) *Nature*, 458(7237):501–504, 10.1038/nature07722
2. Yu, He, Chen, *et al.* (2012) *Nature*, 486(7401):113–117, 10.1038/nature10958
3. Li, Lu, Cheng, *et al.* (2012) *Nature*, 486(7401):118–121, 10.1038/nature11110
4. Ohtsuki, Nishiyama, Yoshida, *et al.* (2012) *Neuron*, 75(1):65–72, 10.1016/j.neuron.2012.05.023

A THEORY OF SEQUENCE MEMORY IN THE NEOCORTEX

Yuwei Cui[*], *Subutai Ahmad, Jeff Hawkins*

Numenta, Inc, Redwood City, California, USA
[*]ycui@numenta.com

The ability to recognize and predict temporal sequences of sensory inputs is vital for survival in natural environments. Extensive experimental evidence demonstrates that sequence learning occurs in multiple cortical regions, yet the underlying neural mechanism remains obscure. It has been proposed that non-linear properties of dendrites enable neurons to recognize multiple patterns. Here we extend this idea by showing that a neuron with several thousand synapses arranged along active dendrites can learn to accurately recognize hundreds of unique patterns of cellular activity. We propose a neuron model with distinct synaptic integration zones: patterns recognized by proximal dendrites lead to action potentials and define the classical receptive field, whereas patterns recognized by distal dendritic segments act as predictions by slightly depolarizing the neuron without immediately generating an action potential. We then show that a network model using neurons with these properties learns a robust model of time-based sequences. We evaluate the model on both artificial and real-world sequence prediction problems. Our model not only achieves comparable or better accuracy than state-of-the-art sequence prediction algorithms, including ARIMA, echo state networks and LSTM networks, but also exhibits other properties critical for sequence learning. These properties include online learning, the ability to handle multiple simultaneous predictions and branching sequences, robustness to sensor noise, and high fault tolerance. Our work represents a theory of sequence learning that not only integrates many fundamental cellular and physiological properties of cortical neurons, but also makes a number of testable predictions for future experiments, and thus has profound implications for the neural mechanism of sequence learning in the cortex.

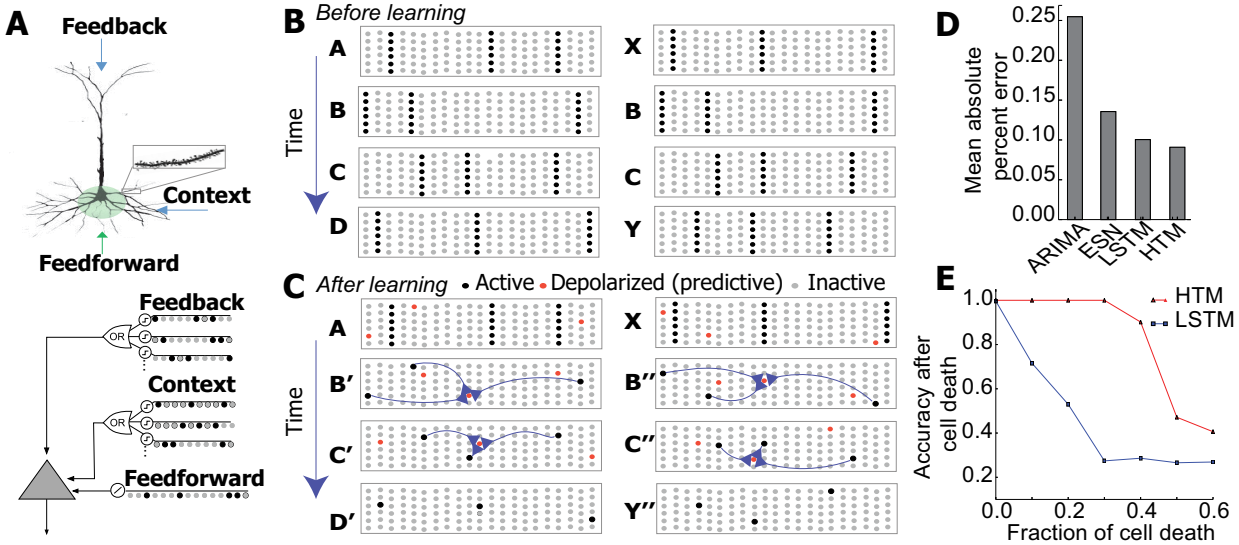


Figure 1. **A**, An HTM neuron (bottom) has three distinct integration zones, corresponding to different parts of the dendritic tree of pyramidal neurons (top). **B–C**, Learning high Markov-order sequences. Each input invokes a sparse set of mini-columns due to inter-column inhibition. **B**. Before learning, all the cells in a mini-column become active. **C**. After learning, cells that are depolarized through lateral connections become active faster and prevent other cells in the same column from firing through intra-column inhibition. **D**. Performance on a real-world problem of predicting taxi demand. **E**. Robustness to loss of cells.

ON THE ROLE OF RICH CLUB TOPOLOGIES DURING INFORMATION TRANSMISSION AMONG CELL ASSEMBLIES ACROSS HIPPOCAMPAL DENTATE AND CA3 COCULTURED IN VITRO NETWORKS

Thomas DeMarse[1,2,*], *Greg Brewer*[3], *Bruce Wheeler*[1,4]

[1] Department of Biomedical Engineering, University of Florida, Gainesville, Florida, USA
[2] Department of Pediatric Neurology, University of Florida, Gainesville, Florida, USA
[3] Department of Biomedical Engineering, University of California, Irvine, California, USA
[4] Department of Biomedical Engineering, University of California, San Diego, California, USA
[*] tdemarse@bme.ufl.edu

In this study P4 rat Hippocampal neurons (Fig. 1A) dissociated from DG and CA3 (Group DG-CA3), or DG alone (DG-DG), or CA3 alone (CA3-CA3) controls were co-cultured within a two-chamber device permitting cross-population axonal connectivity via micro-tunnels over an 8×8 grid of extracellular electrodes (Fig. 1B, C) and electrophysiology (Fig. 1D, for two channels). Functional connectivity (Fig. 1E), assessed via scaled correlation from single unit spike trains, revealed distinct structural characteristics associated with anatomically correct DG-CA3 vs. DG-DG, or CA3-CA3 controls including clustering coefficients, centrality, and long-tailed node-degree distributions associated with unique firing dynamics. These differences in the network structures between groups coincided with changes in the number of detected cell assemblies activated during the emergence and spontaneous propagation of population wide bursts of neural activity between chambers as well as the fidelity of neural transmission between hippocampal populations.

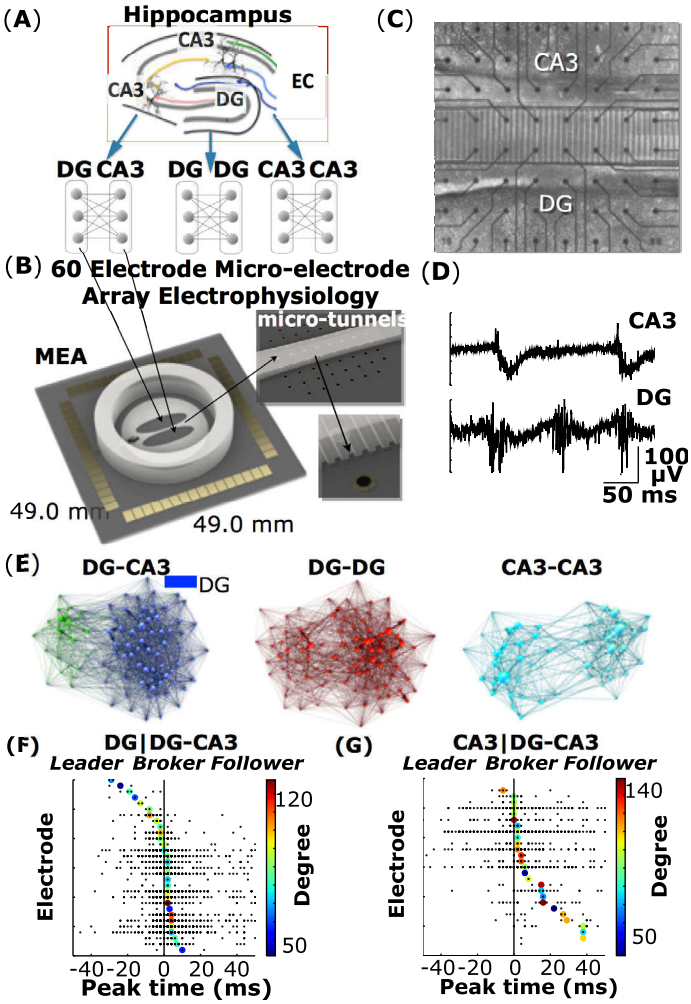


Figure 1. Broker dynamics of hub neurons during transmission of activity between two chamber living hippocampal networks.

During development dissociated neural networks such as these are known to naturally form small-world *rich-club* topologies and power law-like avalanche statistics among bursts of activity suggestive of networks at or near criticality. However, the role these rich-club networks or hub neurons may play during neural transmission or interaction with cell assemblies is unknown. Here we report a reliable broker-like role of high-degree putative hub neurons during bursts (Fig. 1F) in DG cultures, in which cell types are primarily GABAergic, but more variable membership in CA3 when driven by DG (Fig. 1G) or cultured alone (CA3-CA3).

CORRELATED VARIABILITY IN POPULATION ACTIVITY: NOISE OR SIGNATURE OF INTERNAL COMPUTATIONS

George H. Denfield[1,*], *Alexander S. Ecker*[1–3], *Matthias Bethge*[2,3], *Andreas S. Tolias*[1]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[2] CIN-ITP, University of Tübingen, Tübingen, Germany
[3] Max Planck Institute for Biological Cybernetics, Tübingen, Germany
[*] ghdenfie@bcm.edu

Neuronal responses to repeated presentations of identical visual stimuli are variable. The source of this variability is unknown, but it is commonly treated as noise and seen as an obstacle to understanding neuronal activity. We argue that this variability is not noise but reflects, and is due to, computations internal to the brain. Internal signals such as cortical state or attention interact with sensory information processing in early sensory areas. However, little research has examined the effect of fluctuations in these signals on neuronal responses, leaving a number of uncontrolled parameters that may contribute to neuronal variability. One such variable is attention, which increases neuronal response gain in a spatial and feature selective manner. Both the strength of this modulation and the focus of attention are likely to vary from trial to trial, and we hypothesize that these fluctuations are a major source of neuronal response variability and covariability.

We first examine a simple model of a gain-modulating signal acting on a population of neurons and show that fluctuations in attention can increase individual and shared variability and generate a variety of correlation structures relevant to population coding, including limited range and differential correlations. To test our model's predictions experimentally, we devised a cued-spatial attention, change-detection task to induce varying degrees of fluctuation in the subject's attentional signal by changing whether the subject must attend to one stimulus location while ignoring another, or attempt to attend to multiple locations simultaneously. We use multi-electrode recordings with laminar probes in primary visual cortex of macaques performing this task.

We demonstrate that attention gain-modulates responses of V1 neurons in a manner consistent with results from higher-order areas. Consistent with our model's predictions, our preliminary results indicate neuronal covariability is elevated in conditions in which attention fluctuates and that neurons are nearly independent when attention is focused. Overall, our results suggest that attentional fluctuations are an important contributor to neuronal variability and open the door to the use of statistical methods for inferring the state of these signals on behaviorally relevant timescales.

T-SNE AS A VISUALIZATION STEP IN THE SPIKE SORTING PIPELINE

George Dimitriadis [*], *Joana Neto, Adam Kampff*

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

Systems neuroscience is entering the Big Data era where recordings from multiple brain regions are made with probes containing hundreds to thousands of individual electrodes. One of the methodological problems introduced by these technologies is the transformation of the collected data into physiologically meaningful signals. Deriving the spiking information of individual neurons from such spatiotemporally dense sets is a problem that has attracted some attention [1, 2] but is still far from resolved. Methodologies solely based on human input are becoming less appealing as the data sets increase in size and complexity. In tandem, as the feature space of the available automated algorithms explodes, the previewing and manual correction of their results becomes impossible to achieve.

Here we introduce the *t-student stochastic neighbor embedding* (t-sne) dimensionality reduction method [3] as an extra step in the spike sorting pipeline. We position this step after the reduction of the raw signal with PCA of the detected spikes and before any further clustering. T-sne allows the embedding the n-dimensional spike ($n = N_{\text{channels}} \cdot M_{\text{pcs}}$) into a low (usually two) dimensional space. We show that this embedding creates obvious clusters of spikes that can be easily previewed and manually delineated with very little effort and a high degree of confidence. We propose that these clusters represent single units and test the quality of this assertion by running our algorithm on labeled data sets both from hybrid [2] and paired juxtacellular/extracellular recordings [4]. Finally, we develop a GPU based extension to the algorithm that allows for fast embedding of millions of spikes.

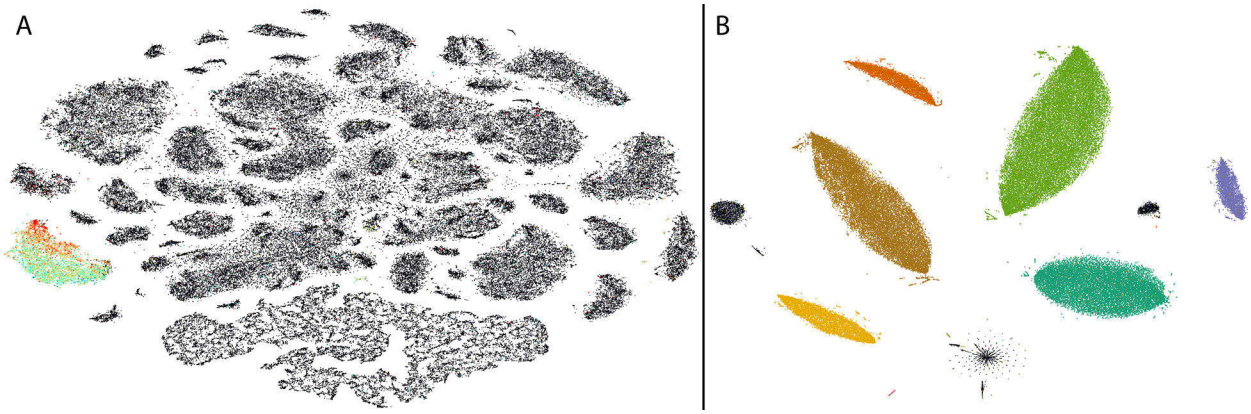


Figure 1. Spikes embedded in t-sne space. **A**, Paired recordings with one cell labeled by a parallel juxtacellular recording (color indicates size of juxtacellularly recorded spikes). **B**, Hybrid data with 7 units labelled (color indicates the units, black is unlabeled spikes).

References

1. Rey, Pedreira, Quian Quiroga. Past (2015) *Brain Res Bull*, 119:106–117
2. Rossant, *et al.* (2015) *bioRxiv* 10.1101/015198
3. Van der Maaten, Hinton (2008) *J Mach Learn Res*, 9:85
4. Neto, *et al.* (2016) *bioRxiv* 10.1101/037937

NEURAL CORRELATES OF SENSORY PREDICTION ERRORS IN PURKINJE CELL SIMPLE SPIKE DISCHARGE

Timothy J. Ebner[*], *Martha L. Streng, Laurentiu S. Popa*

Department of Neuroscience, University of Minnesota, Minneapolis, Minnesota, USA
[*] ebner001@umn.edu

It is widely accepted that the CNS implements forward internal models that predict the sensory consequences of motor commands. Predictions are compared to actual sensory consequences, generating sensory prediction errors (SPEs) used to improve subsequent predictions and guide motor learning. Although the cerebellum appears to play a major role, the neural representations of SPEs are unknown. Of particular interest are the signals encoded by Purkinje cells (PCs), the primary output neurons of the cerebellar cortex. Although a long-standing hypothesis is that low frequency complex spike (CS) discharge of PCs encodes errors, recent results demonstrate that simple spike (SS) discharge encodes predictive and feedback information, suggesting that SS signals are the neural components of SPEs.

To explicitly test this hypothesis, we are investigating how disrupting sensory information alters SS predictive and feedback activity as Rhesus macaques manually track a pseudorandomly moving target. Visual feedback is altered by not displaying the cursor while it is inside the target (Hidden Cursor Condition) or by introducing a lag between manipulandum and cursor movement (Delay Condition). In the Hidden Condition, the linear encoding of errors is reduced with SS modulation concentrated on the target edge, where visual feedback was available (Fig. 1). Conversely, predictive encoding of errors was unaffected. In the Delay Condition, the timing of predictive encoding is negatively shifted equal to the duration of the delay, consistent with a forward internal model that has not adapted to the delay and makes predictions with respect to the movement of the manipulandum rather than the delayed cursor. Predictive and feedback encoding of arm kinematics is unaffected by either manipulation of visual feedback. Intriguingly, CS discharge is only weakly modulated by performance errors when the visual feedback is intact. However, CS error sensitivity increases during the visual feedback manipulations, suggesting CS discharge plays a role in tuning sensitivity to errors.

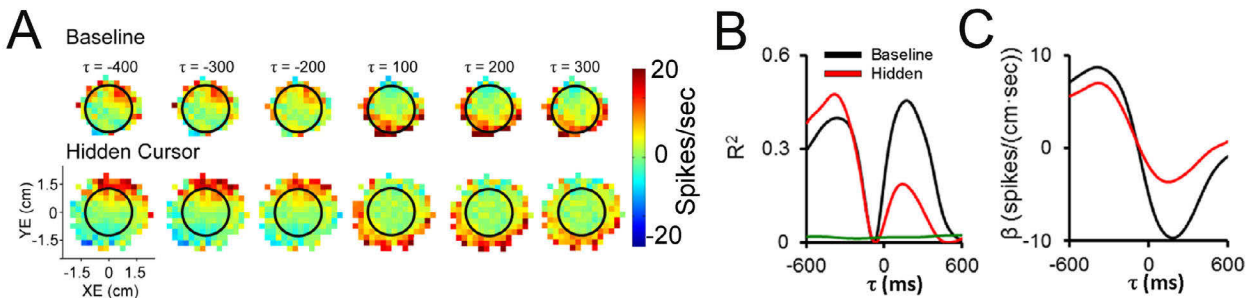


Figure 1. **A**, SS firing plots from PC illustrating decreased feedback signaling of position error (XE and YE) inside the target space and increased firing along the target edge. Black circles indicate target outlines. **B–C**, Example regression analysis of XE encoding by SS discharge. In the Hidden Cursor Condition (red traces), magnitudes of both the R2 and beta feedback peaks are markedly reduced compared to Baseline (black traces), whereas feedforward peaks are less affected. Green traces denote control regressions on trial shuffled data.

The results support the hypothesis that dual encoding of signals by SS discharge represents the predictive and feedback signals necessary for the generation of SPEs.

Acknowledgements

Supported in part by: NIH R01 18338, T32 GM008471; NSF IGERT DGE-1069104, F31 NSO95408.

FIRING RATE OF INTEGRATE AND FIRE NEURONS WITH TEMPORALLY CORRELATED SYNAPTIC INPUT

Farzad Farkhooi[1,2,*], *Carl van Vreeswijk*[3,4]

[1] Institut für Mathematik, Technische Universität Berlin, Berlin, Germany
[2] Bernstein Center for Computational Neuroscience, Berlin, Germany
[3] Centre de Neurophysique Physiologie et Pathologie, Descartes University, Paris, France
[4] CNRS UMR 8119, Paris, France
[*] farzad@bccn-berlin.de

We derive an analytical expression for the firing rate of a linear integrate and fire neuron that receives a constant input as well as synaptic low-pass filtered Gaussian noise with arbitrary time-scale. This is known to be difficult problem as the formal way to analyze this system is to transfer the stochastic differential equations of the neuron model into a deterministic two dimensional partial differential equation known as Fokker-Planck equation with non-trivial boundary conditions. We develop a framework in which this analysis can be posed within the renewal theory and therefore firing statistics can be determined [1].

Using this approach we were able to calculate an exact expression for output firing rate of the neuron with any correlation time in the synaptic filtering. As our approach could determine probability flux observing spike given its noise level at threshold and this readily determined the firing rate of the system. Moreover, we recovered formerly derived expressions for a very short [2] and an extremely long synaptic time-scale [3]. We further discuss how our result could be exploited to study multi-time scales fluctuations that are commonly observed across cortices [4].

References

1. Farkhooi, van Vreeswijk (2015) *Physical Review Letters* 115(3)
2. Brunel, Sergi (1998) *J Theoretical Biol*, 195(1):87–95
3. Moreno-Bote, Parga (2010) *Neural Comp* 22(6):1528–1572
4. Murray, Bernacchia, Freedman, *et al.* (2014) *Nat Neurosci* 17(12):1661–1663

TEMPERATURE PROCESSING IN THE DROSOPHILA BRAIN

Dominic D. Frank[*], *Marco Gallio*

Neurobiology Department, Northwestern University, Evanston, Illinois, USA
[*] dfrank@u.northwestern.edu

Animals are able to respond to a wealth of diverse sensory stimuli, with consequences often crucial to their survival. Sensory maps are a common theme in early sensory processing, where information about the outside world is represented as topographic patterns of activity in the brain. Much remains to be understood on how downstream sensorimotor circuits utilize this sophisticated representation to coordinate directed behaviors.

Previously, we have shown that rapid temperature changes are detected at the periphery by dedicated receptors forming a simple sensory map for hot and cold in the drosophila brain. Temperature drives a host of complex innate and learned responses in the fly, indicating that they are able to extract a range of information from this simple input. Our lab is now using a comprehensive neurogenetic and behavioral approach to investigate the full transformation of thermosensory information, from input to behavior.

Using photo-conversion of PA-GFP (photo activatable green fluorescent protein) and trans-synaptic GFP reconstitution, amongst other approaches, we identified the second- and third-order neurons of the thermosensory system, *i.e.* the circuit components that receive input from the sensory receptors. Patch-clamp electrophysiology and calcium imaging with two-photon microscopy is now revealing that substantial processing of temperature information takes place at subsequent synapses of the thermosensory circuit, illustrating how stimulus quality (hot versus cold), temporal structure, and intensity can be extracted from a simple sensory map and eventually channeled into unique, behaviorally relevant neuronal conduits.

Our current goal is to understand the logic of signal transformation at each station of the thermosensory circuit which underlies innate temperature avoidance and, through this, possibly identify universally conserved principles of sensory processing.

A HIGH THROUGHPUT TRAINING METHOD FOR INVESTIGATING VISUAL OBJECT RECOGNITION IN MICE

Emmanouil Froudarakis[1,*], *Edgar Y. Walker*[1], *Saumil Patel*[1], *Andreas S. Tolias*[1,2]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[2] Department of Computational and Applied Mathematics, Rice University, Houston, Texas, USA
[*] froudara@bcm.edu

Most current methods of training mice to perform perceptual decision tasks while recording neural activity require that animals remain head-restrained for long periods of time. Training of head-fixed animals has a number of drawbacks. It requires significant experimental and personnel resources (since the animal must be removed from its cage and trained for long periods each day), it may continue to be stressful even after multiple training sessions, and it uncouples stimulus presentation from natural exploratory behaviors. These factors limit the complexity of tasks and stimuli that can be learned within a limited time window.

To this end we have designed a novel training method that allows large numbers of mice to be trained on an object memory task while remaining unrestrained in their home cages. In this approach, water is provided to water-deprived mice through a custom lick port, with delivery coupled to the presence of stimuli presented on a monitor outside their cages. Our preliminary data indicates that with this training method, mice can be taught to lick during the presentations of the remembered target object and its non-deforming transformations and to refrain from licking during the presentations of the distractor object.

A COMPUTATIONAL STUDY OF THE SINGLE CELL AND NETWORK PROPERTIES DIFFERENTIATING THE RESPONSE OF MITRAL AND TUFTED CELLS OF THE OLFACTORY BULB

Eleni Genitsaridi[1], *Athanasia Papoutsi*[2], *Constantinos Melachrinos*[2], *Panayiota Poirazi*[2,*]

[1] School of Medicine, University of Crete, Heraklion, Greece
[2] IMBB Foundation for Research & Technology (FORTH), Heraklion, Greece
[*] poirazi@imbb.forth.gr

The mammalian olfactory bulb is the first relay of the odor-processing pathways. The active role of the olfactory bulb circuits in the processing of odor information is evident by the diversity of the local interneurons and projection neurons and by the complexity of their connections. Projection neurons of the olfactory bulb comprise a highly diverse population but can be categorized into two main subpopulations with distinct morphological, biophysical and synaptic properties: the mitral and the tufted cells. The functional role of each subpopulation in odor information coding is not fully elucidated.

In this study we aim to investigate the role of single-cell and network properties in differentiating the response of Mitral and Tufted cells. Towards this goal, we expanded a single cell model of a mitral cell [1] (ModelDB Accession Number: 149739) to develop a mitral and a tufted single-cell model, simulated in the NEURON simulation environment. Single cell models were extensively validated against recently published experimental data regarding the distinct intrinsic biohysical properties of mitral and tufted cells [2]. Next, we incorporated these cells into two distinct, non-overlapping networks (Mitral network and Tufted network) of the olfacory bulb, each consisting of 25 projection neurons, 25 periglomerular cells and 100 granule cells [1]. We used these two networks of projection neurons to investigate the mechanisms responsible for their distinct response properties after odor-simulating inputs. Single-cell and network parameters were systematically modified and the effect of each modifications in the network output was examined. Using this approach we were able to pinpoint to optimum parameters for the two networks that corresponded to the main differences reported in literature [3,4] in response to odor stimuli. In particular, compared to mitral cells, tufted cells responded to the simulated odor input with increased firing rates and with shorter response onset latency. Ongoing simualtions investigate the ability of this dual network to code for the concentration of the odor input and to differentiate similar input patterns. Overall, our results are in aggreement with the opinion that the two networks use different coding mechanisms to encode the different aspects of odor information.

References

1. Li, Cleland (2013) *J Neurosci*, 33(7):3037–3058, 10.1523/JNEUROSCI.2831–12.2013
2. Burton, Urban (2014) *J Physiol*, 592(10):2097–2118, 10.1113/jphysiol.2013.269886
3. Nagayama, Takahashi, Yoshihara, *et. al.* (2004) *J Neurophysiol*, 91(6):2532–2540
4. Fukunaga, Berning, Kollo, *et al.* (2012) *Neuron*, 75(2):320–329

GENETIC GROWTH OF NEURON MORPHOLOGIES WITH CELLULAR AUTOMATA

Felix A. Gers

Beuth University of Applied Science, Berlin, Germany
gers@beuth-hochschule.de

With the CoDi Cellular Automaton (CA) large neural structures can be grown, simulated and analyzed in a discrete cellular space [1]. Evolutionary techniques can be applied to optimize the structure and connectivity with respect to a desired functionality [2,3]. We propose a new genetic growth model for CoDi which produces morphologies similar to biological neurons. The results are compared to real neurons from a database. In an approach by Cuntz [4], branch points are randomly distributed around a neuron body as a center and are gradually connected to its axon- or dendrite-tree.

The CoDi CA operates in two phases: growth phase and signaling phase. The type of a cell can only change during the growth phase, *e.g.*, a blank cell can change to an axon or a dendrite cell. Neurons start growing from neuron body cells as a seed points. Traditionally growth is deterministic, based on a gene extending over the whole cellular space. Each cell contains a portion of the genetic information of the form *grow-straight*, *split-right*, etc. In the signaling phase cells propagate action- and membrane-potentials.

For bio-plausible growth, a cell on a growing axon or dendritic branch must have knowledge of its position and nesting level within the tree structure. In this context the genome is interpreted. We propose a new probabilistic growth model based on a gene with 7 parameters: forward vector, probabilities to branch or to stop growth, offset of the first branch, minimum distance between branches, minimum length of the main branch and of a side-branch.

For the neuron on the right side of Figure 1, the probability to branch on the dendrite is higher and the minimum branch length is longer, which leads to a denser structure. For the axon of the left neuron the offset of the first branch and the minimum distance between branches is smaller, hence the ramifications begin earlier and branching is more frequent.

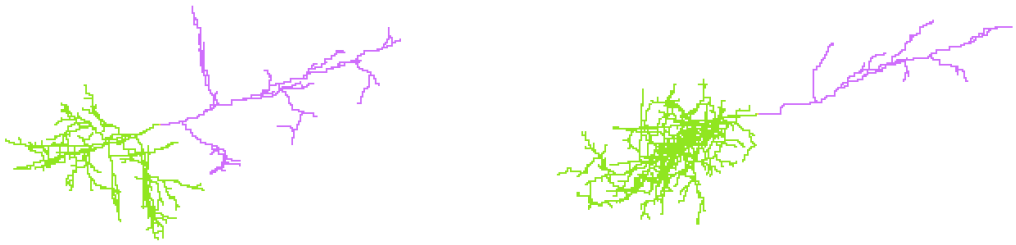


Figure 1. Two neurons with different genomes grown with a 3D CoDi cellular automaton, the dendrite is green (without distinction between basal and apical) and the axon is magenta.

The new gene-controlled, probabilistic growth process produces realistic neural structures. Genes can be adapted to generate morphologies for different types of neurons.

References

1. Gers, De Garis (1998) *Artif Evolution* 315–333, 10.1007/BFb0026610
2. Hough, *et al.* (1999) *Int Conf Robotics and Artificial Life*
3. Schwarzer (2004) Logos, Verlag Berlin, ISBN 978-3-8325-0628-5
4. Cuntz, *et al.* (2010) *PLoS Comput Bio*, 10.1371/journal.pcbi.1000877

CLOSED-LOOP INTERACTION WITH THE CEREBRAL CORTEX: EXPLORING THE PARAMETER SPACE OF µECOG STIMULATION AND READ-OUTS

Alexis Gkogkidis[1,2,*], *Xi Wang*[1,2], *Mortimer Gierthmühlen*[3], *Martin Schüttler*[4], *Thomas Stieglitz*[2], *Tonio Ball*[1]

[1] Intracranial EEG Lab, University Medical Center, Freiburg, Germany
[2] Department of Microsystems Engineering, Albert-Ludwig-University, Freiburg, Germany
[3] Department of Neurosurgery, University Medical Center, Freiburg, Germany
[4] CorTec GmbH, Freiburg, Germany
[*] alexis.gkogkidis@uniklinik-freiburg.de

Closed-loop electrical stimulation for interaction with the cerebral cortex promises new treatment options for neuropsychiatric disorders. Currently, great efforts are being made to develop implantable devices with closed-loop stimulation functionality to identify suitable stimulation patterns and to evaluate feasibility of efficient long-term application. In an illustrative case study performed in sheep, we aimed at closed-loop electrical stimulation to elicit stimulation-dependent changes in brain activity using a wireless implantable device.

A wireless closed-loop micro-electrocorticography (µECoG) based device was chronically implanted on the somatosensory cortex of one sheep. The electrode array comprised 16 recording channels and 8 stimulation channels. Single pulse stimulation was applied in the anesthetized sheep to elicit cortico-cortical evoked potentials (CCEPs) which determined the contacts subsequently used for closed-loop stimulation. Brain activity was continuously analyzed and stimulation pulse trains of either beta or gamma frequencies within one stimulation session were applied in an activity-dependent fashion. The thereby obtained data underwent stimulation artifact removal and was analyzed post hoc regarding spectral changes in the respective read-out bands.

Single pulse stimulation elicited CCEPs while closed-loop stimulation elicited specific cortico-cortical spectral responses (CCSRs). The most widespread CCSRs were observed for the combination of beta read-out band and beta stimulation frequency followed by beta read-out/gamma stimulation, gamma read-out/beta stimulation and gamma read-out/gamma stimulation, which showed the least spatial spread of CCSRs. In general, CCSRs where more focalized when using gamma-band read-out compared to beta-band read-out as well as the cortical area where CCEPs could be observed, independent of stimulation frequency.

We elicited CCEPs and closed-loop stimulation frequency-specific CCSRs by the use of µECoG technology combined with a wireless implant. For closed-loop interaction, we suggest that a gamma-band read-out may be an optimal choice, rather than beta-band or CCEPs, particularly if spatially precise interaction is desired and that CCSRs may provide a new useful measure of functional connectivity and guide closed-loop modulation of connectivity. The approach presented here will be useful for the exploration of the parameter space of µECoG stimulation patterns and read-outs and hence in addressing basic and technical questions that remain to be solved on the way to clinical application of closed-loop brain implants.

Acknowledgments

This work was supported by the Deutsche Forschungsgemeinschaft, DFG, [EXC1086 BrainLinks-BrainTools] and by the German Federal Ministry of Education and Research, BMBF, [0316064C BrainCon and 13GW0053D MotorBic].

POPULATION DYNAMICS IN THE MEDIAL PREFRONTAL CORTEX OF THE MOUSE DURING WORKING MEMORY

Caroline T. Golden[1,*], *João Afonso*[2], *Matthew T. C. Brown*[1], *Sebastien Royer*[3], *Alfonso Renart*[2], *Paul Chadderton*[1]

[1] Department of Bioengineering, Imperial College London, UK
[2] Champalimaud Centre for the Unknown, Lisbon, Portugal
[3] Korea Institute for Science and Technology, Seoul, Republic of Korea
[*] cg811@ic.ac.uk

In working memory, sequential and sustained activity within the prefrontal cortex (PFC) is proposed to guide behavior in the absence of overt sensory feedback. Dynamics of working memory in the PFC have been examined in the monkey [1] and rodent [2], but we know comparatively little about how PFC populations guide decision-making. To address this problem, we have developed a simple delayed-response (DR) task to probe mechanisms of working memory in the PFC of head-fixed freely running mice. Animals were presented with one of two brief tones (T1 or T2) at the start location on a linear cue-enriched treadmill. In T1 trials, animals completed a *hit* trial and received a water reward by running to the reward zone and pausing for 500 ms. In T2 trials, correct rejections were achieved by running through without stopping. Animals performed many trials per session (mean 265 trials), with high accuracy (mean $d' = 1.6$, p(hit) = 0.81, p(false-alarm) = 0.23). To assay neural dynamics during this goal-directed behavior, recordings were made from the anterior cingulate cortex using high-density multi-site microelectrodes (mean 29 neurons, $n = 6$ mice).

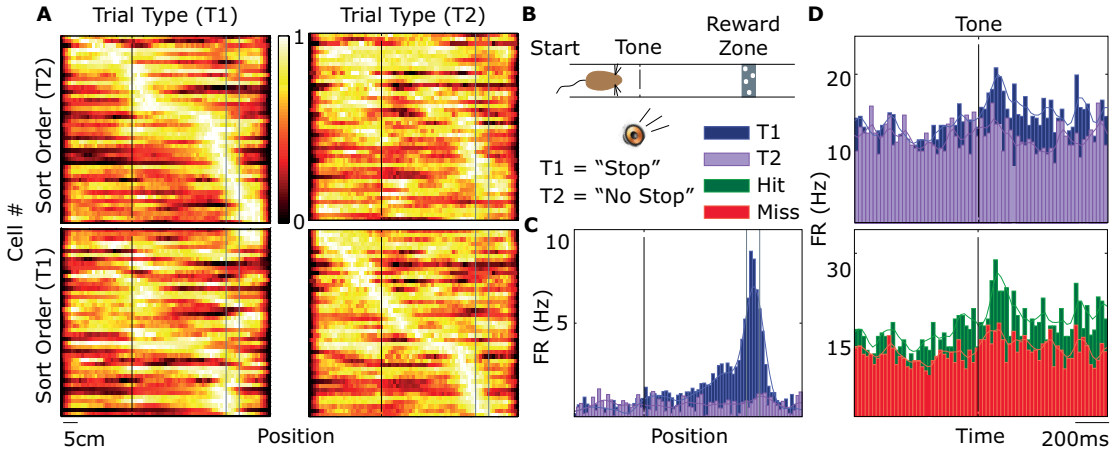


Figure 1. **A**, Normalized firing rates (FRs) ranked by peak activation on treadmill. **B**, DR task. **C**, An example FR histogram for T1 versus T2 trials. **D**, Single cell PSTH for all T1-T2 trials (upper), and Hit-Miss T1 trials (lower).

Our results show robust encoding of task specific information through altered firing dynamics in T1 and T2 trials. We observed discrete temporal sequences of activation that encompassed the full duration of the task (Fig. 1A–C). Many cells showed differences in response to the same cue stimulus in a manner that predicted later behavioral outcomes, such as *hit* versus *miss* trials (Fig. 1D). Our results confirm that neurons in PFC are privy to future outcomes in spatial working memory. By using brief optogenetic interventions to disrupt PFC activity, we are exploring the extent to which these population dynamics are causally determining behavior. This work is supported by the Human Frontier Science Program.

References

1. Goldman-Rakic (1995) *Neuron* 14(3):477–85
2. Fujisawa, AmarasingHam, Harrison, *et al.* (2008) *Nat. Neurosci.* 11(7):823–33

ENDOGENOUS ATTENTION IN A PROBABILISTIC INFERENCE FRAMEWORK

Ralf M. Haefner[1,*], *Pietro Berkes*[2], *József Fiser*[3]

[1] Brain and Cognitive Sciences, University of Rochester, Rochester, New York, USA
[2] Sloan-Swartz-Center for Theoretical Neurobiology, Brandeis University, Waltham, Mass., USA
[3] Department of Cognitive Science, Central European University, Budapest, Hungary
[*] ralf.haefner@gmail.com

During perception, the brain combines information received from its senses with an internal model representing prior information about the outside world. Assuming that the responses of sensory neurons encode posterior beliefs about the variables encoded the neurons, the function of the anatomically ubiquitous feedback connections to lower sensory areas is to communicate such prior information. We have recently derived predictions from this framework in the context of common perceptual decision-making tasks and shown that they agree with a range of empirical observations that have been hard to explain by previous models [1].

Based on this work, we here propose a new theory for the role of endogenous (top-down, or covert) attention during perceptual decision-making. Assuming that the ultimate goal of the brain is *not* veridical perception but *is* optimal decision-making, we suggest two mechanisms by which the brain achieves this goal, addressing the two principal ways in which perceptual inference can be sub-optimal. Mechanism A minimizes the mismatch between the generative model learnt by the brain and the one used by the experimenter for the task. Mechanism B tailors the brain's approximation to the correct posterior to the task-defined loss/reward-function. We have derived empirical predictions from both mechanisms in the context of a perceptual 2AFC task by extending both the large scale model in [1] and by analytically investigating a simplified toy model. As an example for Mechanism A we suggest that attention suppresses the temporal correlations assumed by the internal model adapted to natural inputs (which have strong temporal correlations), in order to better approximate the generative model underlying 2AFC tasks in which consecutive trials are uncorrelated. We show that this leads to the lower observed response gains, and choice probabilities in high reward trials as compared to low-reward trials [2], and to a decrease in noise correlations [3]. While this proposal is independent of the nature of the neural encoding of probabilities, Mechanism B proposed by us relies on our assumption of a neural-sampling based representation. Since only a limited number of samples can be collected under time pressure, the brain improves decision-making by biasing samples away from the correct posterior towards parts of the state space in which the amplitude of the loss-function is largest. In other words, we propose that the brain employs a loss-calibrated approximation to the posterior, and that the limited resource postulated in psychological models of attention is the number of samples that it can base a decision on. We show that such a mechanism can explain neurophysiological findings like increased response gain and decreased neural variability during spatial and feature-based attention tasks.

References

1. Haefner, Berkes, Fiser (2016) *Neuron*, http://arxiv.org/abs/1409.0257
2. Nienborg, Cumming (2009) *Nature* 459(7243):89–92, 10.1038/nature07821
3. Ruff, Cohen (2014) *Nat Neurosci* 17(11):1591–7, 10.1038/nn.3835

FEATURE EXTRACTION IN THE HUMAN PRIMARY TO PARABELT AUDITORY CORTEX

Liberty S. Hamilton [1,2,*], *Edward F. Chang* [1,2]

[1] Center for Integrative Neuroscience, University of California, San Francisco, California, USA
[2] Department of Neurological Surgery, University of California, San Francisco, California, USA
[*] liberty.hamilton@ucsf.edu

To process speech, the brain transforms highly variable acoustic features to a more invariant representation of higher-order linguistic features (phonemes, syllables, and words). How and where this transformation occurs in the auditory hierarchy remains unclear. Here, we investigated feature representation in the human primary auditory cortex and parabelt areas using invasive intracranial recordings from human patients undergoing clinical monitoring for intractable epilepsy. We obtained simultaneous high-density recordings from 5 patients with 32-channel intrasylvian grids (4 mm center-to-center spacing) placed over the surface of the temporal plane (Heschl's gyrus, planum temporale, and planum polare) and 256-channel grids (also 4 mm spacing) placed over the lateral surface of the left hemisphere, with coverage of the superior temporal and middle temporal gyri (STG and MTG). We recorded the local field potential from each electrode and bandpassed in the high gamma range (70–150 Hz) to extract stimulus-related activity. During recordings, participants listened to English sentences from the TIMIT acoustic-phonetic database. A subset of participants also listened to pure tones played in the same frequency range as the speech stimuli (75 Hz to 8 kHz). To model acoustic and phonetic transformations in primary and non-primary areas, we used linear encoding models to describe the high gamma activity recorded at each electrode as a weighted sum of stimulus features over time. The models were of the form:

$$\hat{x}(t) = \sum_{f} \sum_{\tau} \beta(\tau, f)\, S(f, t-\tau)$$

Where x is the neural activity recorded at a single electrode, $\beta(\tau, f)$ contains the regression weights for each feature f at time lag τ, and S is the stimulus representation. We used several stimulus representations, including the mel-band spectrogram and a binary phoneme feature matrix, to test whether the primary and parabelt areas show differences in how well they are modeled by lower-level acoustic versus higher-level phonetic features. We found that electrodes in primary auditory areas were better modeled by an acoustic representation rather than a phoneme feature representation, whereas phoneme feature invariance appeared to arise at the level of the STG. In addition, the STG was found to integrate auditory information over longer periods of time compared to Heschl's gyrus. We next compared the modulation transfer function of the acoustic spectrotemporal receptive fields in electrodes in primary and parabelt areas and found that the primary auditory cortex is selective for faster temporal modulations, whereas the STG responds to high spectral modulations present in speech. Finally, we compared the responses to pure tones and found narrowly tuned, tonotopic representations across the Heschl's gyrus that were absent in the STG. Instead, we observed some limited responses to tones in the STG, where responses were primarily in posterior STG and showed wide bandwidth, high threshold responses. This work has important implications for understanding how linguistic features important for speech perception arise in the auditory hierarchy.

Acknowledgments

The authors would like to thank Matthew Leonard, Leah Muller, Matthias Sjerps, and Kunal Raygor for assistance with recordings and data collection.

INFORMATION PROFILE IN LARGE NEURONAL POPULATION SIGNALS MAY SYSTEMATICALLY DIFFER FROM THE SINGLE NEURON LEVEL

Jiri Hammer[1,2,*], *Tonio Ball*[1,3]

[1] Epilepsy Center, University Medical Center Freiburg, Freiburg, Germany
[2] Department of Neurology, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic
[3] Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany
[*] hammer@bcf.uni-freiburg.de

There is a gap in the understanding of functional properties of human brain measured on a single neuron level and on a large-scale neuronal population level. The invasive nature of measurements of single unit activity (SUA) or local field potentials (LFP) makes such data to be rather scarce from human brain, and simultaneous measurements of SUA and a more common electroencephalography (EEG) are largely missing. We attempted to bridge this gap by investigating directional and speed tuning in human motor cortex, both by numerical simulations of neuronal populations and experimental observations from subdural electrocorticography (ECoG) — an intermediate signal between SUA and EEG.

In single neuron activity of the motor cortex, directional tuning dominates over speed tuning during hand-arm movement tasks [1]. We hypothesize that the reverse should be found in motor cortical population signals that reflect the firing rate changes of thousands of neurons. Assuming linearly speed tuned and cosine directionally tuned neurons with random preferred directions, we simulated neuronal populations of different sizes as a sum of the instantaneous firing rates of the underlying neurons. We show that the mean firing rate of the neuronal population increases with movement speed and that the signal-to-noise ratio (SNR) of speed tuning grows with population size, while the SNR of the directional tuning remains constant.

As the high-gamma component of the ECoG has been shown to reflect changes in the average population firing rate [2], we analyzed the high-gamma ECoG recorded from human motor cortex during a continuous hand movement task to compare representation of speed and velocity. We show that the high-gamma ECoG increased with movement speed and that speed tuning indeed clearly and reproducibly dominated over directional tuning, confirming our predictions. The predominance of speed even extended to the 300–1000 Hz ECoG components, a frequency range that is thought to closely correlate to the mean firing rate of the underlying population.

Our results confirm the predominance of speed over direction in a neuronal population signal, thus demonstrating that the information profile in large population signals may substantially differ from the single neuron level, as a result of the summation of the different tuning characteristics of various kinematic parameters on the single neuron level. This principle is likely fundamental for understanding the relation between the single neuron level and neuronal population signals, including EEG and fMRI, in general.

References

1. Moran, Schwartz (1999) *J Neurophysiol*, 82:2676–2692
2. Ray, Maunsell. (2011) *PLoS Biol*, 9:e1000610

THE CONTRIBUTION OF DEVELOPMENTAL INHIBITORY CHANGES IN EARLY POSTNATAL CIRCUITS OF THE PREFRONTAL CORTEX

Katerina Kalemaki[1,2,*], *Kyriaki Sidiropoulou*[3], *Domna Karagogeos*[1,2]

[1] Department of Basic Science, Faculty of Medicine, University of Crete, Heraklion, Greece
[2] Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[3] Department of Biology, University of Crete, Heraklion, Greece
[*] kalemaki@imbb.forth.gr

The cerebral cortex starts developing during the embryonic period, but fully matures following protracted postnatal development through a process that also requires environmental experiences. GABAergic interneurons, comprising 20% of all cortical neurons, are involved in fundamental aspects of physiological mature brain function through their synaptic contacts. Impaired interneuron function, during early development, results in severe neurodevelopmental disorders such as schizophrenia, epilepsy and autism spectrum disorders. It is known that the prefrontal cortex (PFC) develops later, compared to the primary cortical areas, such as the somatosensory barrel cortex (BC).

Our aim is to investigate the early postnatal development of interneurons in the PFC in comparison with BC, and how their maturation affects the functionality of developing cortical circuits and the network activity generated. Using a mouse model, we measured basal synaptic responses during the early postnatal period, postnatal day (PD10 and PD20). We observed a decrease in basal synaptic transmission, from PD10 to PD20, within the upper layers of PFC and BC and the deep layers of BC, but not in the deep layers of PFC. These results are correlated with differential distribution of interneuron subtypes in these two regions; in particular, parvalbumin-positive (PVA+) interneurons are detected in BC deep layers at PD10, but not in the PFC at the same age.

We next investigated how these developmental changes in basal synaptic transmission are altered in conditions of decreased inhibitory function. For this reason, we have generated and analyzed mice that exhibit a severe reduction of GABAergic interneurons in the embryonic and postnatal neocortex ($Rac1^{fl/fl}$; $Rac3^{-/-}$; $Nkx2.1^{+/Cre}$; $R26R\text{-}YFP^{+/-}$). These mice exhibit an 80% decrease in MGE-derived interneurons (PVA+ and SST+), in their postnatal cortices and die by PD15. Their embryonic development is perturbed and they show gross cytoskeletal defects *in vitro*, with the length of their leading processes significantly reduced and a clear multipolar morphology. In the absence of *Rac1*/*Rac3*, cortical interneurons fail to tangentially migrate towards the pallium due to defects in actin and microtubule cytoskeletal dynamics [1]. Using this tool we are performing cellular and electrophysiological studies in order to determine how the local networks within PFC and BC mature in the absence of the majority of interneurons .

References

1. Tivodar, Kalemaki, *et al.* (2015) Cerebral Cortex 25(9):2370–2382, 10.1093/cercor/bhu037

THE INFLUENCE OF RECURRENT CONNECTIVITY ON ANGLE DISCRIMINATION FOR DIFFERENT VISUAL MAP LAYOUTS

Hanna Kamyshanska [*], *Dmitry Bibichkov, Matthias Kaschube*

Frankfurt Institute for Advanced Studies, Frankfurt am Main, Germany
[*] kamyshanska@fias.uni-frankfurt.de

The layout of orientation preference in primary visual cortex varies considerably across mammalian species [1]. In this work we model the influence of these differences on processing abilities of underlying neural networks. We study which biologically plausible network structure would be optimal for solving an angle discrimination task for moving and static oriented patterns.

We consider a rate model of a single-layer recurrent neural network, which receives a feed forward input, consisting of visual patterns passed through properly oriented Gabor filters. We test two different layouts of feed forward selectivity: a smooth orientation preference map (observed in primates and carnivores) and a map with salt-and-pepper organization (observed in rodents). Recurrent connectivity is considered as either purely distant-dependent or also orientation dependent, with excitation between units with similar preferred orientations and inhibition between units with orthogonal ones [2].

We measure the discrimination performance of our networks using a logistic regression classifier of population activity and study its dependence on the relative strength of recurrent connectivity and feed-forward selectivity.

We find that feed-forward networks with salt-and-pepper organization are slightly better in orientation discrimination. Recurrent connections generally improve the classification performance for both layouts. This effect is stronger for smooth orientation maps, such that recurrent networks with smooth map organization are most effective in performing orientation discrimination tasks.

Their improved performance can be attributed in part to a strengthening of tuning curves of single neurons due to recurrent interactions, and to an improvement of network denoising properties manifested in higher signal to noise ratios.

References

1. Kaschube (2014) *Cur Opinion Neurobiol*, 24:95–102
2. Blumenfeld, Bibitchkov, Tsodyks (2006) *J Comp Neurosci*, 20.2:219–241

Acknowledgement

This work was supported by the BMBF projects BFNT Frankfurt FKZ 01GQ0840, FKZ 01GQ1413 and FKZ 01GQ1507. The Tesla K40 used for this research was donated by the NVIDIA Corporation.

SEQUENTIAL NEURONAL ACTIVITY IN THE LATERAL PREFRONTAL CORTEX DURING THE TASK OF BINOCULAR FLASH SUPPRESSION

Vishal Kapoor[1,2,*], *Michel Besserve*[1,3], *Nikos K. Logothetis*[1,4], *Theofanis I. Panagiotaropoulos*[1,5,6]

[1] MPI for Biological Cybernetics, Tübingen, Germany
[2] Graduate School of Neural and Behavioral Sciences, IMPRS, Univ. of Tübingen, Germany
[3] MPI for Intelligent Systems, Tübingen, Germany
[4] Imaging Science and Biomedical Engineering, University of Manchester, Manchester, UK
[5] Centre for Systems Neuroscience, University of Leicester, Leicester, Great Britain
[6] Institute of Psychiatry, Psychology and Neuroscience, King's College, London, Great Britain
[*] vishal.kapoor@tuebingen.mpg.de

Neurons in the lateral prefrontal cortex exhibit a huge diversity in their activity patterns mediating various cognitive functions ranging from working memory to monitoring of serial order and even visual awareness. In a previous study, we examined the neuronal activity in this region utilizing an ambiguous visual stimulation paradigm called the binocular flash suppression and found that a majority of the feature selective single unit responses were also perceptually modulated. The proportion of units displaying feature selective responses among all the neurons recorded, were but a minority. The present study aimed at characterizing any other task related patterns if any among the remaining single units. In order to do this, we decomposed the matrix of peristimulus time histograms of the remaining neurons utilizing the non-negative matrix factorization procedure, enabling us to characterize five dominant response patterns. Interestingly, the peak amplitudes of the different patterns were distributed across different phases of a trial. Further, a majority of neurons with firing profiles similar to a given response pattern did not display significant differences in their modulation during the monocular and binocular conditions of the task, thus indicating that sequential firing in the PFC is unaffected by sensory visual competition.

Next, we aimed at assessing the functional connectivity as measured with noise correlations between pairs of neurons with modulation patterns similar to the five different response patterns obtained. Pairs of single units with firing profiles similar to identical response patterns displayed higher correlations, thus indicating a stronger functional coupling among units that were temporally coincident. However, when neurons were chosen from temporally separated populations, we observed a reduction in correlations. When positive and negative correlations were evaluated separately, such a correlation structure was observed specifically for positive correlations. Surprisingly, the negative correlations were uniformly distributed across the different populations. This possibly suggests a computational network principle mediating a representation of sequential patterns of activity in the lateral prefrontal cortex.

MODELING THE INTRINSIC MECHANISMS OF IMMATURE STARBUST AMACRINE CELLULAR NETWORK LINKED TO THE EMERGENCE OF STAGE II RETINAL WAVES DURING DEVELOPMENT

Dora Karvouniari [1,*], *Lionel Gil* [2], *Olivier Marre* [3], *Serge Picaud* [3], *Bruno Cessac* [1,*]

[1] INRIA BioVision Team, Sophia-Antipolis, France
[2] INLN Sophia-Antipolis, France
[3] Institut de la Vision, Paris, France
[*] theodora.karvouniari@inria.fr, bruno.cessac@inria.fr

Retinal waves are spontaneous bursts of activity propagating in the developping retina and found to play a central role in shaping the visual system and retinal circuitry. They first occur at early embryonic stages of development and gradually disappear upon maturation. Understanding their generating mechanisms may help to control and use them in order to re-train the retina for rewiring and possibly improve vision restoration, after treatment, in some degenerative retinal diseases. Retinal waves emergence is shown experimentally to depend on autonomous local cellular mechanisms combined with neurons coupling [1]. In order to describe, reproduce and explain experimental results, there is a need for careful biophysical modelling of the underlying cellular mechanisms, specific to the population of neurons involved. Our goal is also to link biophysical mechanisms to dynamical systems and bifurcations theory.

We have developed a biophysical model of developmental stage II retinal waves, reproducing the spontaneous intrinsic cell-autonomous rhythmic bursting in Starbust Amacrine Cells (SACs) and the slow After Hyperpolarisation Current (sAHP), which modulates the refractory process inbetween two consecutive bursts, observed experimentally by Zheng and colleagues [1]. We describe the dynamical influence of cholinergic synapses, ensuring the level of SAC synchrony necessary for the emergence of waves, as shown by Abel and colleagues [2]. To summarize we obtain: (i) a plausible generic mechanism generating spontaneous retinal waves in development (see Figure 1), without any need for external stimulation as opposed to existing models [3, 4] and (ii) a mathematical characterization of retinal waves. Especially, a biophysical parameter controls the wave arousal and the corresponding shape, for example spirals (not shown). In this conference, we shall present the biophysical grounds of this model, the mathematical analysis of its behaviour, and experimental results confirming its validity.

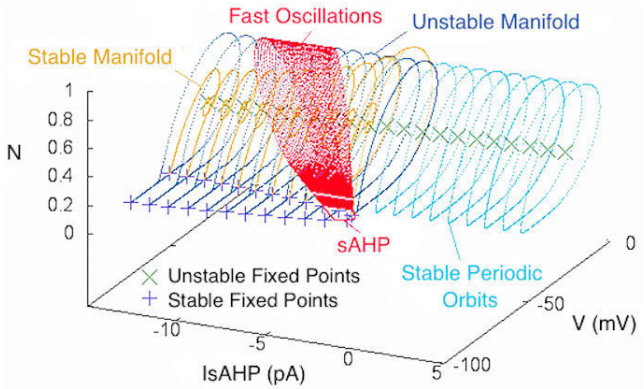


Figure 1. 3D projection of the local bursting mechanism involving three typical variables: V (membrane potential), N (fast Potassium current), I_{sAHP} (Calcium-gated slow after hyperpolarization Potassium current). When $I_{sAHP} = 0$, there exists a limit cycle corresponding to local bursting. During bursting, Calcium loads and I_{sAHP} becomes more negative inducing a bifurcation leading to the rest state. In the rest state, Calcium unloads and I_{sAHP} increases to 0 giving rise to bursting again. Upon cholinergic coupling this mechanism leads to the emergence of retinal waves.

References

1. Zheng, Lee, Zhou (2006) *Nat Neurosci* 9:363–371
2. Abel, Lee, Callaway, *et al.* (2004) *J Neurophysiol* 91:324–335
3. Hennig, Adams, Willshaw, *et al.* (2009), *J Neurosci* 29(4):1077–1086
4. Lansdell, Ford, Kutz (2014) *PLoS Comput Biol* 10(12):e1003953

DENDRITIC CONTRIBUTIONS TO SYNAPTIC AND NEURONAL MEMORY ALLOCATION

Georgios Kastellakis[1,2], *Panayiota Poirazi*[1,*]

[1] Institute of Molecular Biology and Biotechnology, FORTH, Heraklion, Greece
[2] Department of Biology, University of Crete, Heraklion, Greece
[*] poirazi@imbb.forth.gr

Associative memories are believed to be stored in distributed neuronal assemblies through synaptic and intrinsic plasticity. The long-term plasticity of synapses involves the long-term potentiation/depression of synaptic responses, spine growth/elimination, protein synthesis and capture, homeostatic plasticity etc. Synaptic plasticity in excitatory neurons in the cortex, however, takes place primarily in their dendritic regions. The evidence suggests that dendrites can function as autonomous computational [1, 2] and plasticity units [2, 3]. In addition, dendritic phenomena such as synaptic clustering [1], synaptic tagging and capture [4] and local protein synthesis [3] contribute to different aspects of memory storage.

Based on experimental evidence, we developed a simplified computational model of plasticity that examines the role of dendrites during neuronal and synaptic memory allocation [4]. We use multiscale modeling to model synaptic processes which span different temporal and spatial scales, such as calcium influx, protein synthesis and delivery, synaptic tagging and homeostasis in order to assess how distinct memories are encoded in a cortical population of neurons. Using the model, we show that memory storage increases the sparsity of population firing, and that this depends on whether the plasticity-related protein synthesis takes place in the soma or at the dendrites. We show that local protein synthesis promotes dendritic synaptic clustering.

We use the model to simulate the behavioral tagging experimental paradigm, in which a strong memory is paired with a weak one. We show that the rescue of the weak memory is dependent on the co-allocation of the two memories in highly overlapping populations of neurons and dendrites, creating clusters of synapses. We additionally show that intrinsic excitability can enhance this co-allocation when the strong memory precedes the weak. Generalizing, we show that increased excitability and synaptic capture both contribute to the co-allocation of related memories, in different ways. Our model suggests that the temporal proximity of memories translates to co-allocation in overlapping neuronal and dendritic populations, indicating the possible roles of synaptic tagging and intrinsic excitability in linking together memories. Finally, we propose that the same mechanisms can bind together sequential memories, creating memory episodes.

References

1. Poirazi, Mel (2001) *Neuron* 29(3):779–96
2. Branco, Häusser (2010) *Current Opinion in Neurobiology* 20(4):94–502
3. Sutton, Schuman (2006) *Cell* 127(1):49–58
4. Rogerson, *et al.* (2014) *Nature Rev Neurosci* 15:157–169

DYNAMICS OF DIRECTIONAL SELECTIVITY ACROSS MACAQUE MOTOR CORTICAL LAYERS DURING EXECUTION OF PLANNED REACHING MOVEMENTS

Bjørg E. Kilavik

Institut de Neurosciences de la Timone, CNRS & Aix-Marseille Université, Marseille, France
bjorg.kilavik@univ-amu.fr

Motor cortical areas hold established roles in movement planning and execution processes. Neurons in these areas are selective to different movement parameters, such as the direction of arm reaching movements. This directional selectivity has been extensively studied, yet we still know very little about how it is distributed and dynamically modulated across different cortical depths. While superficial motor cortical layers are predominantly involved in cortico-cortical processing, and receive a majority of the sensory feedback, neurons in deep layers mainly project to sub-cortical structures and to the periphery. We might therefore not only expect different degrees of (directional) selectivity in different cortical depths, but also differences in the temporal dynamics of such selectivity.

Directional selectivity was explored in a macaque monkey performing a pre-cued center-out reaching task. In this task the movement direction was cued visually for 300 ms, 1000–3000 ms before the onset of a directionally non-informative GO signal (onset of all four possible peripheral targets). During the delay, the monkey had to memorize the direction and prepare the movement, with a limited reaction and movement time allowance (500 ms each). The monkey had to hold his hand in the correct peripheral target for 300 ms, before waiting an additional 500 ms before reward delivery. Recordings were made simultaneously from superficial and deep cortical layers with multi-contact linear array (laminar) electrodes, in arm regions of dorsal premotor cortex (PMd) and the transition zone between PMd and primary motor cortex (M1).

Before the onset of the planned reaching movement and during its dynamic phase, significantly more neurons were directionally selective in superficial than in deep layers (68% vs. 49% before onset; 76% vs. 62% during movement). The neurons in deep layers became more selective towards the end of the reaching movement, as the monkey's hand arrived and stopped in the peripheral target. In this epoch, equal proportions of superficial and deep neurons were directionally selective (73% and 74%). Furthermore, the selectivity strength of the directionally selective neurons was significantly larger for superficial compared to deep neurons in the pre-onset epoch, and similar across depth at the end of the movement.

One might speculate how these different dynamics of directional selectivity across cortical layers is related to both the nature of the task and the different predominance of cortico-cortical processing vs. cortico-spinal projections of superficial vs. deep motor cortical layers, respectively. While the movement could be planned well in advance, eye movement monitoring demonstrated that the monkey always made use of visual feedback (target location and displacement of arm cursor) before and during the dynamic phase of the movement. This sensory-input reliance might be reflected in increased selectivity of neurons in superficial layers in these movement epochs. Furthermore, the increased selectivity of neurons in deep layers towards the movement end might be related to final motor command adjustments to successfully arrive and maintain the hand within the peripheral target for the required hold period.

Acknowledgments

Financial support: CNRS-PEPS; ANR-GRASP; EU grant 269921 (BrainScaleS)

DECODING NATURAL VISUAL INPUT IN THE PRIMATE LATERAL GENICULATE NUCLEUS

Nathan J. Killian[1,2], *Margee J. Kyada*[1,3], *John S. Pezaris*[1,2,*]

[1] Department of Neurosurgery, Massachusetts General Hospital, Boston, Massachusetts, USA
[2] Department of Neurosurgery, Harvard Medical School, Boston, Massachusetts, USA
[3] Northeastern University, Boston, Massachusetts, USA
[*] john@pezaris.com

Can we reconstruct a visual stimulus presented to a rhesus macaque based on the receptive field properties of cells in the lateral geniculate nucleus of the thalamus (LGN)? Is a classical linear model sufficient in the primate, or does an extra-classical model provide substantial additional information when there are multiple, potentially redundant channels? We are motivated to ask these questions based on similar work performed in the cat [1], and recent advances in understanding encoding of nonlinear stimulus features and eye movements in the early visual system [2,3].

We implanted custom-built 64-microwire bundle electrodes in LGN bilaterally in one animal and made wideband field potential (WFP) and single-unit recordings while the animal was presented with a selection of visual stimuli. One set of stimuli were Gaussian noise movies spanning both luminance and chrominance spaces (GN). The GN stimuli had power spectra proportional to one over frequency, yielding naturalistic correlations in space and time. The random spatiotemporal correlations of the GN stimuli made them suitable for probing a variety of potential extra-classical response field properties, such as responses to motion or fields with spatial asymmetry. The second set of stimuli were clips taken from a recent cinematic release that featured natural scenes of monkeys in the wild (NS) [4]. A trial-based task was used to present segments from each stimulus set in a balanced random fashion. To begin each trial, animals were required to fixate a centrally presented point on a computer screen and engage the video clip. For GN clips, animals were required to maintain fixation for the duration of the animated stimulus. For NS clips, animals were allowed to free-view once the animated stimulus began.

Multiple linear receptive fields (LRFs) were computed from recordings made during the presentation of noise stimuli using reverse-correlation techniques to create full-color spatio-temporal response fields. We then performed a decoding procedure to reconstruct portions of NS segments by convolving neural signals with LRFs, translated by the gaze location recorded during free viewing.

References

1. Stanley, Li, Dan (1999) *J. Neurosci.* 19(18)8036–8042
2. Mante, Bonin, Carandini (2008) *Neuron*, 58(4)625–638
3. McFarland, Bondy, Cumming, Butts (2015) Cosyne 2015 Abstracts
4. Linfield, Fothergill (2015) “Monkey Kingdom”, DVD/Blu-Ray release, Walt Disney Studios

Acknowledgments

NIH R01EY019678, NIH F32EY025542, NIMA Foundation, Rappaport Foundation, Philipe Laffont, Peter Pezaris, William and Lori Goldenthal, John and Genevieve Wolfe, Teddy and Soo-Mi Cho.

PERCEPTUAL AND NEURAL DEFICITS IN PROCESSING NATURALISTIC IMAGE STRUCTURE IN AMBLYOPIA

Lynne Kiorpes[*], *J. Anthony Movshon*

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

Amblyopia is a developmental visual disorder that affects visual acuity and contrast sensitivity. Many amblyopes also suffer losses on higher-order visual tasks, such as contour integration and form discrimination, the neural bases of which remain unexplained. While neural abnormalities have been found at the level of V1 in amblyopia, it is likely that there are significant processing defects in higher-order visual areas. We recently reported that sensitivity to the higher-order statistics of naturalistic texture images is a signature of processing in area V2 [1]. We therefore asked whether amblyopes are poorer at detecting these statistics and whether there is a corresponding neural deficit in V2.

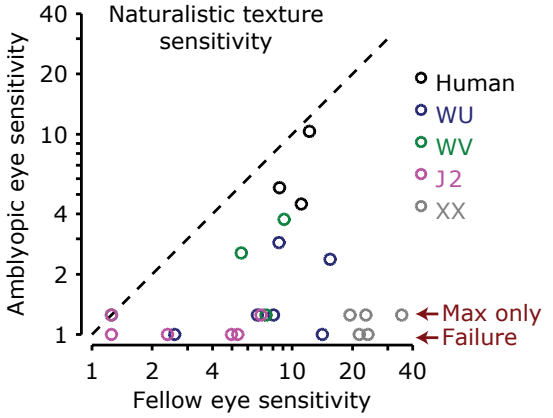


Figure 1. Amblyopic eye sensitivity to naturalistic texture statistics is severely compromised.

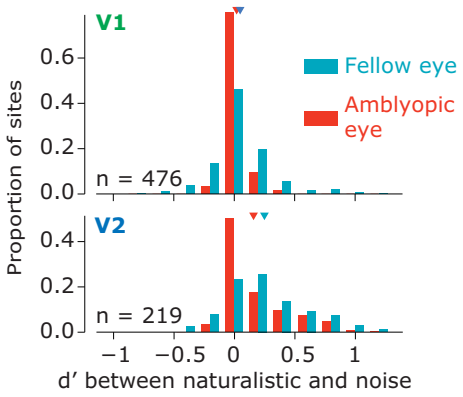


Figure 2. Amblyopic eye neurons in V2 discriminate naturalistic texture less reliably than fellow eye neurons; triangles show means.

We tested 5 amblyopes (4 macaques, 1 human) using a spatial 2AFC task. They discriminated texture patterns that retain variable amounts of the higher-order statistical structure of original natural images from noise images that retain only the orientation and spatial frequency content. The synthetic patterns were derived from a texture synthesis model [2]. All amblyopes were impaired on the discrimination when viewing with their amblyopic eyes (Fig. 1). To investigate whether there was a related neural deficit, we measured neuronal sensitivity to naturalistic structure in 5 amblyopic macaques under anesthesia. We used 96-electrode Utah arrays to record multiunit activity and found that V2 sites driven by the amblyopic eye showed a reduced ability to distinguish naturalistic images from their noise counterparts relative to the fellow eye; V1 neural activity was similar for amblyopic and fellow eyes (Fig. 2). We conclude that amblyopia modifies the processing of naturalistic visual structure.

References

1. Freeman, Ziemba, Heeger, Simoncelli, Movshon (2013) *Nat Neurosci* 16:974–981
2. Portilla, Simoncelli (2000) *Int J Computer Vis* 40:49–70.

Acknowledgments

This work was supported by NIH grants EY05864, EY22428, EY21894

GEOMETRY AND STATE-DEPENDENCE OF SOUND REPRESENTATIONS IN RAT AUDITORY CORTEX

Dmitry Kobak [*], *Jose Pardo-Vazquez, Mafalda Valente, Christian Machens, Alfonso Renart*

Champalimaud Center for the Unknown, Lisbon, Portugal
[*] dmitry.kobak@neuro.fchampalimaud.org

There is a large body of theoretical work on how the structure of neural variability in sensory neurons shapes the accuracy of representations. The standard view is that noise correlations can severely limit the amount of stimulus information that the neural population is able to encode. However, not all noise correlations are information-limiting and experimental evidence of the impact of variability on population encoding is scarce. Here we perform a systematic empirical investigation of this problem by analyzing the structure of variability in large, simultaneously recorded cortical populations across different brain states. Brain state changes are useful to examine the impact of correlations on coding because they have been shown to fundamentally change the structure of noise correlations in cortical circuits [1].

We used silicon probes to record population spiking activity (10 sessions, about 100 simultaneously recorded neurons each) in the primary auditory cortex of urethane-anesthetized rats. Animals were repeatedly presented with 150 ms stationary noise stimuli delivered bilaterally through custom-made headphones. Stimuli differed in overall intensity (absolute binaural level, ABL: 20 to 60 dB) and in perceived lateralization (inter-aural level difference, ILD: −20 to +20 dB). As typical under urethane, different recording sessions span different levels of cortical activation, ranging from very active (population firing nearly constant) to very inactive (population firing markedly switching between 1-second long *up* and *down* states).

Analysis of the N-dimensional structure of population responses suggests that the geometry of stimulus representation strongly depends on the brain state. Not only the noise correlations differ, but the signal subspace is changing as well. During the active states, the signal and noise subspaces are largely orthogonal, leading to high signal-to-noise ratio and good stimulus encoding. In contrast, during inactive states the noise is primarily lying parallel to the uniform axis (the axis of all ones), corresponding to *up-down* fluctuations of the network; however, the signal space turns itself to become largely aligned with the uniform axis as well, thus reducing signal-to-noise ratio and making noise correlations information-limiting.

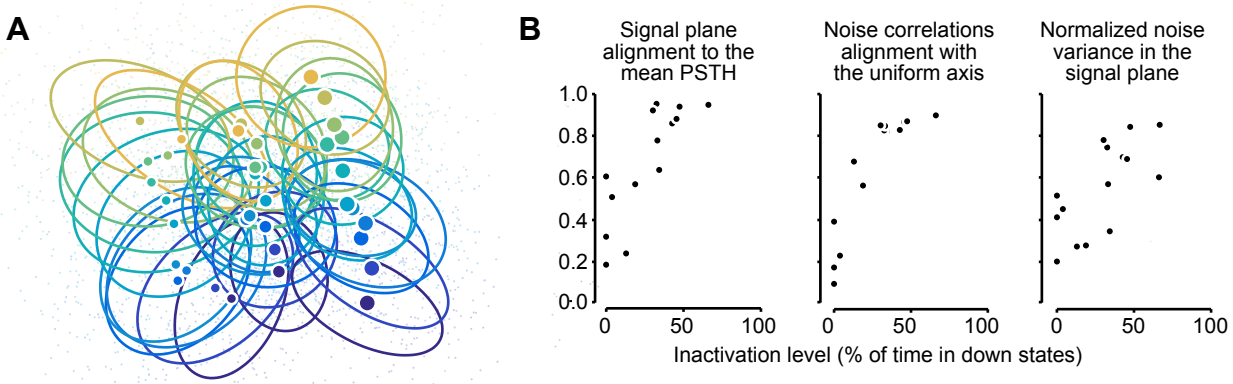


Figure 1. **A**, Signal plane obtained by doing PCA on the PSTHs (mean activity during 200 ms after stimulus onset). Dots represent stimulus PSTHs (size codes ABL, color codes ILD), ellipses represent single trial distributions. **B**, Various measures of the alignment between signal, noise, and the uniform axis.

Reference

1. Renart, *et al.*, *Science*, 2010

DOPAMINERGIC NETWORK DYNAMICS DURING BEHAVIORAL EXPLORATION

Aaron C. Koralek [*], *Rui M. Costa*

Champalimaud Neuroscience Programme, Lisbon, Portugal
[*] aaron.koralek@neuro.fchamplimaud.org

We are constantly faced with the trade-off between exploiting past actions with known outcomes and exploring novel actions whose outcomes may be better. When environmental rewards are stable, it is preferable to perform actions that are known to be most rewarding. However, when environmental rewards are changeable, it is adaptive to explore alternative actions and revisit previous actions whose value may have changed. This balance between exploitation and exploration is thought to be coded by cortico-basal ganglia circuits, and particularly by midbrain dopaminergic neurons of the substantia nigra pars compacta (SNc). However, little is known about the precise ways in which environmental changes impact variability in action selection, and even less is known about dynamics in midbrain dopaminergic networks during behavioral exploration.

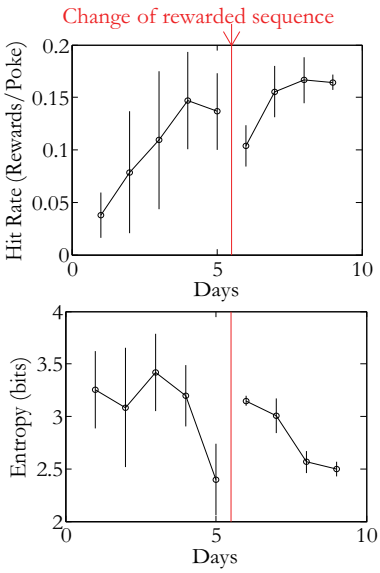


Figure 1. **Top**, Performance suffers following changes in reward (arrow), but quickly recovers. **Bottom**, Entropy increases following changes in reward, but decreases again with new learning.

We developed a novel behavioral paradigm in mice to investigate how SNc ensembles code for behavioral variability. Mice were placed in an environment with three equidistant nose poke ports and had to explore the environment to discover which sequence of three nose pokes was rewarded. Importantly, mice received no cues to guide learning, but rather had to actively explore the environment to determine the reward structure. There were a total of 27 three-poke sequences, providing a distribution for action selection, and the entropy of this distribution was used to quantify behavioral exploration. Entropy increased following changes of the rewarded sequence and decreased as animals learned the newly rewarded sequence (Fig. 1), and entropy was higher in sessions in which reward was delivered probabilistically rather than deterministically.

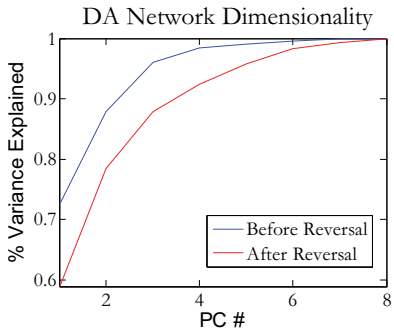


Figure 2. More network variance is explained with fewer principal components before relative to after changes in reward.

We then performed chronic calcium imaging in freely behaving mice to characterize SNc network responses during task performance. Mice expressed GCaMP6f in SNc dopamine (DA) neurons, allowing us to simultaneously record activity in large populations of genetically-identified neurons and track the same populations of neurons throughout training. We saw an evolution of single-cell responses associated with reward expectation, reward delivery, and action initiation over the course of learning. In addition, we found alterations in large-scale network dynamics following changes in the reward structure of the environment, with SNc network activity being higher-dimensional and more complex during periods of exploration relative to periods of exploitation (Fig. 2).

The current experiments support a role for dopaminergic networks in behavioral exploration.

AUTONOMOUS CONTROL OF NETWORK ACTIVITY

Sreedhar S. Kumar[1,2,*], *Jan M. Wülfing*[3], *Samora Okujeni*[1,2], *Joschka Boedecker*[3], *Martin Riedmiller*[3], *Ulrich Egert*[1,2]

[1] Biomicrotechnology, IMTEK, University of Freiburg, Freiburg, Germany
[2] Bernstein Center Freiburg, Freiburg, Germany
[3] Machine Learning Lab, University of Freiburg, Freiburg, Germany
[*] sreedhar.kumar@imtek.uni-freiburg.de

Electrical stimulation of the brain is increasingly used as a strategy to alleviate the symptoms of a range of neurological disorders, and as a possible means to artificially inject information into neural circuits, *e.g.*, towards bidirectional neural prostheses [1]. Conventionally, stimulation of neuronal networks explicitly or implicitly assumes that the response to repeated constant stimuli is predictable. The measured response, however, typically interacts with additional neuronal activity not controlled by the stimulus [2]. Constant stimuli are therefore not optimal to reliably induce specific responses. Yet, without suitable models of the interaction between stimulus and ongoing activity it is not possible to adjust individual stimuli such that a defined response feature is achieved optimally.

To address these challenges, we propose an autonomous closed-loop paradigm using techniques of Reinforcement Learning (RL). In a proof-of-principle study we demonstrate how an RL controller may be used to autonomously adjust stimulus settings by interacting with a generic network of neurons. The approach poses the following questions: How to (i) capture the interaction of network activity, stimulus and response in a quantifiable state so to forumlate a well posed problem, (ii) find the optimal state for stimulation, and (iii) evaluate solutions found.

We employed generic neuronal networks *in vitro* as a model system. Previous studies offer a partial understanding of the dynamics in such networks and of the rules governing their interaction with electrical stimuli [3] that help us test the quality of the solutions found by an RL controller. Neuronal networks in cell culture exhibit characteristic network-wide spontaneous bursts (SB) separated by periods of reduced activity. Electrical stimulation of the network also evokes bursts of action potentials. Their strength depends on the stimulus latency relative to the previous SB [3]. We posed the following optimization problem: find the stimulus latency that maximizes the number of spikes evoked per SB.

Across networks we observed that in 89% of the sessions ($n = 56$, 8 networks), the total number of response spikes/SB was enhanced post learning. Concurrently, in 93% of the sessions, the percentage of interrupted events per session diminished, supporting the effectiveness of the learning algorithm. The learned latencies also agreed with those predicted from open-loop studies ($r = 0.94$, $p < 10^{-8}$, $n = 17$ networks), indicating optimality of the interaction. Our results demonstrate that RL-based techniques can autonomously exploit quantitative relationships underlying a complex neuronal network by interacting with it and adapt to ongoing activity to choose optimal actions.

References

1. Raspopovic, *et al.* (2014) *Sci Transl Med* 6, 222ra19
2. Arieli, *et al.* (1996) *Science* 273:1868–1871
3. Weihberger, *et al.* (2013) *J Neurophysiol* 109:1764–1774

Acknowledgments

This project was supported by BrainLinks-BrainTools Cluster of Excellence (DFG-EXC 1086) and the Bernstein Focus Neurotechnology Freiburg*Tübingen(BMBF FKZ 01GQ0830).

LEARNING NEURAL POPULATION CODES WITH MAXIMUM ENTROPY MODELS BASED ON SPARSE NON-LINEAR CONSTRAINTS

Ori Maoz[1,*], *Gasper Tkacik*[2], *Roozbeh Kiani*[3], *Elad Schneidman*[1]

[1] Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel
[2] Institute of Science and Technology Austria, Klosterneuburg, Austria
[3] Center for Neural Science, New York University, New York, New York, USA
[*] ori.maoz@weizmann.ac.il

The code of neural systems can be described in terms of a dictionary between population activity patterns and sensory stimuli or motor output. Learning such dictionaries for large populations is hard because of the sparseness of neural activity, neuronal noise, and the exponentially large space of possible population activity patterns. Overcoming these problems requires accurate probabilistic models of the population activity.

In different neural systems, the vocabulary of groups of tens of neurons has been accurately characterized with maximum entropy models that rely on the firing rates and pairwise correlations between cells. These models are the minimal models that satisfy the firing rates and pairwise correlations, but do not make additional assumptions about the nature of the code. For groups of many tens to a hundred cells, pairwise models are often insufficient to capture the distribution of population spiking statistics at the level of individual patterns, and must be augmented with higher order correlation terms. However, it is often unclear which high order terms should be added, and how these models can be learned efficiently or scale up to hundreds and thousands of cells.

We present a new class of maximum entropy models that instead of adding constraints based on their order, uses a randomly selected set of sparse nonlinear projections of the population activity as the constraints for the model. We use these models to learn the vocabulary of joint activity patterns of tens of neurons recorded from the primate visual cortex, and explore the accuracy of these models for different numbers of such constraints.

We show that these models are more accurate than pairwise maximum entropy models, and are on par with maximum entropy models that rely on pairs and the synchrony among cells — using a similar number of constraints. Moreover we show that this class of models is particularly superior to the other models when population activity is under-sampled, where the pairwise and higher-order maximum entropy models break down. The ability to add constraints according to the model's performance suggests this as a scalable approach to building accurate probabilistic models of neural responses based on limited data from large neuronal populations.

UNDERSTANDING THE IMPACT OF LATERAL INTERACTIONS ON POPULATION TUNING

Kartheek Medathati[1,2,*], *Andrew I. Meso*[3], *Guillaume S. Masson*[3], *Pierre Kornprobst*[1], *James Rankin*[4]

[1] Inria, Sophia Antipolis, France
[2] University of Côte d'Azur, Sophia Antipolis, France
[3] Aix Marseille University, Marseille, France
[4] Center for Neural Science, New York University, New York, New York, USA
[*] kartheek.medathati@inria.fr

A central question in neuroscience is how to infer the functional connectivity between neurons or groups of neurons by observing their response to controlled stimulation in terms of their tuning properties or resultant behavior. Traditionally, this has been a difficult problem as the number of samples we could obtain to various input stimulation conditions is low and sparse, and experimentation *in vivo* conditions continues to be difficult and slow. In this context, computational simulation studies play a crucial role as they allow us to rapidly verify the hypothesis about the underlying functional connectivity by simulating the resulting population dynamics [1, 2]. In this work, we study how the population tuning dynamics of a ring network of neurons depends on the lateral competition using different forms of centre-surround connectivity in terms of extent and strength of local excitations and surrounding inhibition when the network is stimulated with a structured driving input.

We define the input by a linear combination of two Gaussian functions with varying peak widths and separations, with the weighted difference of Gaussian functions as a generalized form of connectivity. We use bifurcation analysis to explore the parameter regions where different qualitative behaviors coexist. For combinations of connectivity kernel and input, we examined the response of the network and its ability to represent either one of the components of input, their average or to preserve both of them. Probabilities of convergence to various stable solutions depending on random initial conditions measured using 100 trials could be seen in Figure 1. Our results indicate a variety of co-existing stable solutions depending on the inhibition kernel and driving input. These results could help us to model observations in psychophysics and physiology [3] to infer the functional connectivity.

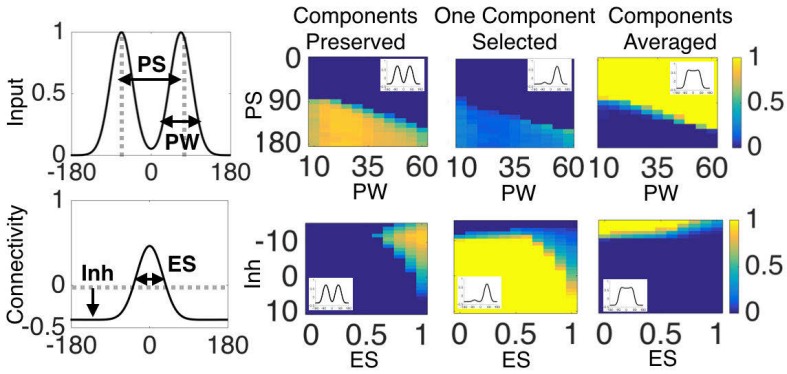


Figure 1. Probabilties of stable solutions with respect to varying input and connectivity conditions.

References

1. Ellias, Grossberg (1975) *Biological Cybernetics* 20(2):69–98
2. Marti, Rinzel. (2012) *Neural Computation* 25(1):1–45
3. Xiao, Huang (2015) *J Neurosci* 35(49):16180–98

TEMPORAL SCALING AND LEARNING IN BASAL GANGLIA

James M. Murray [*], *Sean Escola*

Center for Theoretical Neuroscience, Columbia University, New York, New York, USA
[*] jm4347@columbia.edu

Behavioral experiments using multicell recordings in rodents have shown that the striatum plays a crucial role in timing-related behavior, with neurons exhibiting a stereotypical pattern of sequential firing over tens of seconds. While maintaining the same firing pattern, the sequence of neural activity speeds up or slows down in proportion to the duration of the time interval in lever press delay tasks [1]. We address these observations by modeling the striatum as a recurrent inhibitory network with depressive adaptation and show that robust and repeatable sequential firing can be obtained. Further, the overall strength of external input can be used to control the speed of the sequential firing by up to an order of magnitude while the same pattern is maintained, without requiring any synaptic weights to be relearned each time the delay is changed.

By introducing a learning rule at inhibitory synapses, all of these features can be realized even in an initially unstructured network receiving repeated time-dependent input, with the external input acting as a tutor for the inhibitory network. Once the pattern has been learned, it can be reproduced and rescaled even if the time-varying input is taken away and replaced by a tonic input. This provides an explanation for recent experiments showing that cortical input to basal ganglia is necessary for learning new behaviors, but that already-learned behaviors can still be performed even if this input is removed by lesioning motor cortex [2].

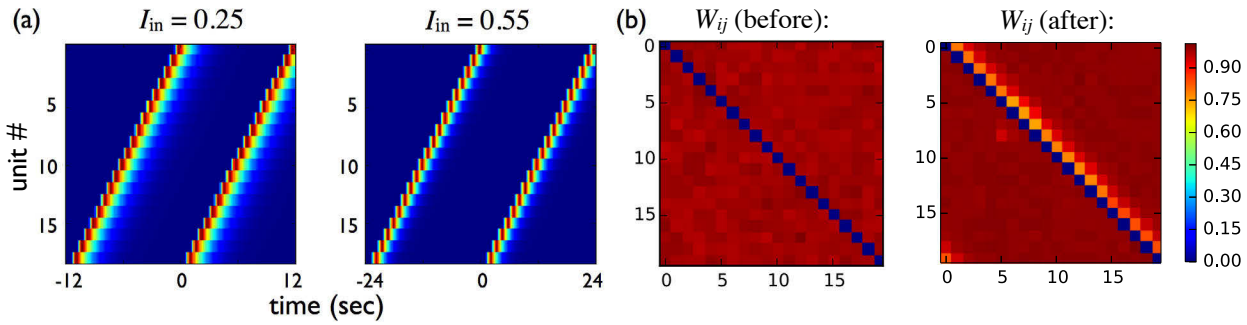


Figure 1. **A**, Sequential firing in a model of recurrently connected inhibitory neurons with fixed synaptic weights. The two panels show that the strength of external input can be used to control the speed of the firing sequence. **B**, By including an anti-Hebbian learning rule at inhibitory synapses, the recurrent weights W_{ij} in an initially unstructured network with time-dependent input can evolve a structure in which certain synapses are weakened, leading to sequential firing sequences such as those shown in A.

References

1. Mello, Soares, Paton (2015) *Curr Bio*, 25:1113–1122, 10.1016/j.cub.2015.02.036
2. Kawai, Markman, Poddar *et al.* (2015) *Neuron* 86:800–812, 10.1016/j.neuron.2015.03.024

MULTI-SCALE ELECTROPHYSIOLOGY IN MACAQUE MOTOR CORTEX DURING REACHING

Amy L. Orsborn[1,*], *Charles Wang*[2], *Ken Chiang*[2], *Nia Channel Boles*[1], *Jonathan Viventi*[2], *Bijan Pesaran*[1]

[1] Center for Neural Science, New York University, New York, New York, USA
[2] Department of Biomedical Engineering, Duke University, Durham, North Carolina, USA
[*] amyo@nyu.edu

Neural computations governing our behavior span many spatial scales, from individual neurons to networks of neurons within and across brain areas. Similarly, electrophysiology can monitor neural activity from from microns, to millimeters, and up. The relationships between these neural measures, and how each relates to behavior is poorly understood. Connecting neural computations across spatial scales will require simultaneous multi-scale measurements during behavior. We therefore developed a flexible platform to combine multiple measurement scales and used it to study motor cortex during reaching.

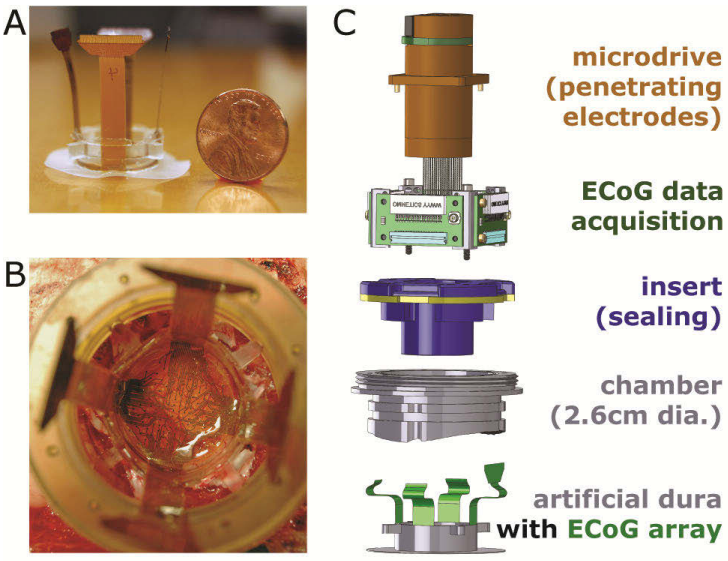


Figure 1. µECoG arrays are embedded in an artificial dura (**A**) and implanted subdurraly (**B**). The chamber aligns µECoG arrays with microdrive electrodes, which pass through holes in the array into tissue below (**C**).

Our platform can integrate subdural micro-electrocorticography (µECoG) and a microdrive of independently movable electrodes to measure action potentials, local field potentials (LFP), and surface potentials (ECoG) within the same volume of tissue (Fig. 1). We implanted this multi-scale system in the primary motor cortex of a macaque. A 124-contact µECoG array (polyimide with 5 µm thick Cu, 3 µm Ni, and 150 µm Au traces; 200 µm contact diameter, 0.75–1.5 mm spacing) was implanted, followed by a 32-electrode microdrive (Gray Matter Research; glass-coated tungsten electrodes, 125 µm diameter; 1.5 mm spacing). Spiking, LFP, and µECoG activity were recorded during rest, full-field light-flash visual stimulation, and a reach-to-grasp task. Visual stimulation-triggered responses were used to assess day-to-day variability in signal recordings. Reaching behavior was monitored with motion tracking (Motion Analysis Inc.) of the shoulder, elbow, wrist, and hand locations in 3-dimensions. The subject performed a naturalistic reach and grasp task in which he grasped a small square with a power grip presented in random locations in the workspace. We will present analysis of spike, LFP, and ECoG signals' relationships to behavior (decoding analyses) and relationships between each measurement scale.

A key feature of our platform is the flexibility afforded by the artificial dura approach, which allows the surface to be instrumented for electrophysiology while still maintaining access to the brain. Future work will extend the technique to include new approaches such as high-density active electronics and transparent µECoG arrays that allow optical access.

VISUAL FEATURE-SELECTIVE SUBNETWORKS OF CORTICAL NEURONS SHAPE SPONTANEOUS MULTINEURONAL EVENTS IN MOUSE V1

Ganna Palagina [1,2,*], *Stelios M. Smirnakis* [1,2]

[1] Department of Neurology, Baylor College of Medicine, Houston, Texas, USA
[2] Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[*] palagina@bcm.edu

We investigated the population activity of pyramidal cells and interneurons in layer 2/3 of the mouse V1 over the course of visual cortical maturation (postnatal days 7–45). Spontaneous and visually evoked neuronal responses were recorded over several hours using calcium-sensitive indicators and 2-photon imaging. The beginning of the population event was defined by occurrence of the time frame with at least one cell's response, and the end by the next encounter of the empty frame. Population events were thus characterized by their size (the number of participating cells) and duration. We next checked the relationship between event sizes and durations versus the probability to observe the event of certain size and duration. We found that, at every inspected age (P7–P10, *before eye opening*; P12–P15, *during eye opening*; and P20+, *adult*) the sizes of events formed heavy-tailed distributions that conform to power law dynamics and are scale-free. This suggests that the network underlying those spontaneous population events has a small-world architecture, characterized by the groups of high local connectivity (*small worlds*), that are connected to each other via the restricted number of links between specific hub nodes. To see if the equivalent of small world groups could be observed during spontaneous population events, we used the algorithm [1] that allowed us to link neurons into groups based on: (i) statistical similarity between temporal response patterns in the pyramidal neurons, and, (ii) whether or not their responses were temporally followed by the responses of the specific interneuron. We identified the clusters or interneuron-linked pyramidal cells at every inspected age. During postnatal development the size of clusters decreased. In animals before eye opening the mean cluster size was 31 cells; during eye opening it reduced to 22 neurons. In adult mice the average cluster size was 12 cells. Similar changes affected the overlap between the clusters: in animals before eye opening the clusters shared on average 54% of their member pyramidal neurons; during eye opening 35% of the neurons were shared, and in adult group only 20% of neurons were shared. Most pyramidal neurons were associated with multiple interneurons before eye opening. After eye opening, the preference of pyramidal cells for interneurons increased, so that by early adulthood most pyramidal cells were associated with only 1 or 2 interneurons. Interestingly, interneurons and their partner pyramidal cells shared functional properties in adult animals. For example, the population tuning curves for the pyramidal members of the cluster and the linked interneuron had a high degree of similarity. Individually, 30% of the pyramidal members of the cluster shared orientation or direction preference with their partner tuned interneuron, while 65% had their preferred direction/orientation within $\pm 30^{\circ}$ of interneuron preferred orientation or direction. Our findings suggest that population events in the visual cortex rely on subnetworks of pyramidal neurons that share functional properties and work in concert with one or more local interneurons for the control of network event propagation. In neonatal and adolescent pups such clusters of pyramidal cells partner up with several interneurons, while later in the development the number of partner interneurons falls down to 1–2 per group.

Reference

1. Feldt, Waddell, Hetrick, *et al.* (2009) *Phys Rev E Stat Nonlin Soft Matter Phys* 79(5pt2):056104

MIRROR NEURONS ENCODE THE KINEMATICS OF THE OBSERVED ACTION

Vassilis Papadourakis[1,2,*], *Vassilis Raos*[1,2]

[1] Department of Basic Sciences, Faculty of Medicine, University of Crete, Heraklion, Greece
[2] Institute of Applied and Computational Mathematics, FORTH, Heraklion, Greece
[*] vpapadourakis@edu.med.uoc.gr

A crucial factor for orchestrating our own behavior to achieve efficient social communication, is to grasp the meanings conveyed by the actions of others. The discovery of mirror neurons (MirNs) revived the interest of several researchers across many disciplines to investigate the mechanisms and processes underlying social cognition. MirNs are sensorimotor neurons that fire both when an animal performs a goal-directed action and also when the same animal observes another agent performing the same or a similar transitive action. Supposedly, the activation evoked in the observer's brain by the seen action matches that in the actor's brain and thus the action is understood. However, the existing hard evidence on the properties of MirNs is very limited and often the theories attempting to take advantage of MirNs to explain aspects of social behavior are not grounded on empirical facts.

We recorded the activity of MirNs in the ventral premotor area F5 while two monkeys executed transitive and observed transitive and intransitive actions. Here we show that MirNs are activated by the observation of both transitive and intransitive actions in contrast to the prevalent claim that MirNs respond exclusively to object-directed actions. Furthermore, the finding that the discharge of MirNs is correlated with the kinematics of the observed actions undermines the, inductively reasoned, action-goal encoding. Moreover, MirNs and non-MirNs of area F5 have different action coding in contrast to the notion that these two neural subpopulations employ similar codes during action execution. Our results challenge main properties that MirNs were hypothetically endowed with and which composed the foundations of their proposed function. We propose that MirNs may be involved in understanding high-level cognitive aspects of an observed action by detecting its low-level kinematics.

Acknowledgments

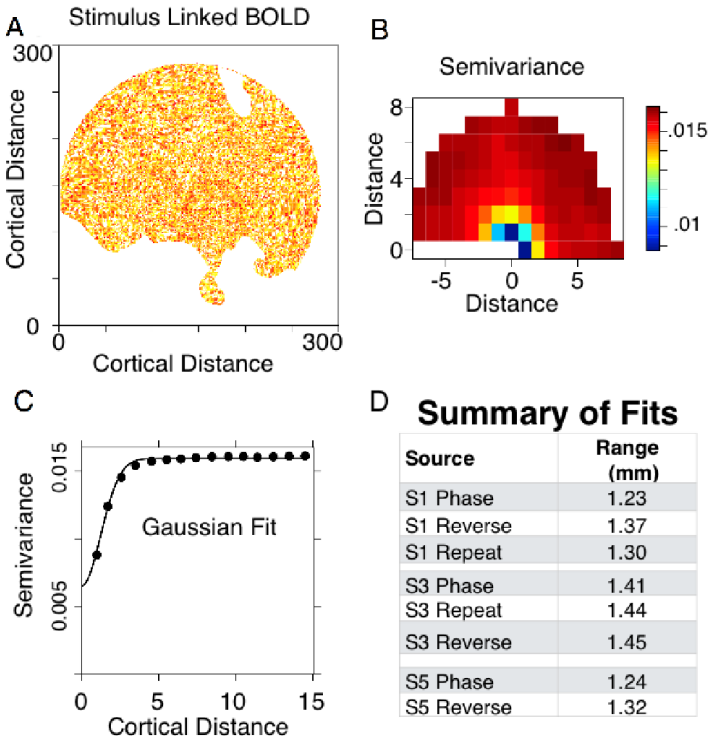
GSRT 14TUR OBSERVENEMO, BIOSYS (KRIPIS), METR (ARISTEIA II), Latsis Foundation

SPATIAL CORRELATIONS IN VISUAL-AREA-SPECIFIC BOLD INFLUENCE THE SEARCH FOR COLUMNAR STRUCTURE AT 7T FIELD STRENGTH IN HUMANS

Andrew J. Parker[1,*], *Holly Bridge*[2]

[1] Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK
[2] FMRIB Centre, Clinical Neuroscience, University of Oxford, Oxford, UK
[*] andrew.parker@dpag.ox.ac.uk

Functional magnetic resonance imaging (fMRI) of the cerebral cortex in living human participants is increasingly used to study the internal organization of identified cortical areas. Measurements of blood-oxygen level dependent (BOLD) signals at 7T field strengths provide the signal strength (and thereby the spatial resolution) to characterize the neural architecture of single cortical areas, potentially down to the level of identifying cortical columns in individual participants. Our goal has been to measure columnar structure for binocular disparity, using a stimulus that has a time-varying change in disparity.



Source	Range (mm)
S1 Phase	1.23
S1 Reverse	1.37
S1 Repeat	1.30
S3 Phase	1.41
S3 Repeat	1.44
S3 Reverse	1.45
S5 Phase	1.24
S5 Reverse	1.32

Figure 1. The steps in processing the variogram from MRI data. **A**, flattened map of BOLD activity covaries with the disparity waveform of stimulus. **B**, semivariance calculated in different directions relative to sample point (0, 0); the data are isotropic. **C**, radially symmetric variogram with Gaussian curve fitted. **D**, summary table of range parameter for subjects S1, S3, and S5. *Reverse* and *Repeat* variants of the stimulus waveform. All distances are in units of 0.7 mm average voxel size, except table at D

Here we show that spatial correlations of the BOLD signal across the cortical surface have the capacity to disrupt physiological characterization of columnar architecture using BOLD imaging. Not only do these correlations limit the resolution of BOLD images, but they intrude upon quantification of structures with repeat patterning across the cortical surface. We present a way of quantifying these spatial correlations, which is widely used in field biology and geology, but little used in the fMRI research field. This method uses a distance-dependent measure of semivariance: $\gamma(dx, dy) = \frac{1}{2}\mathrm{E}[\langle Z(x+dx, y+dy) - Z(x,y)\rangle^2]$, also called the variogram. The variogram in Fig. 1C shows that the variance between nearby points is lower than the variance between distant points across the imaging field. This change of variance captures the spatial correlations in the imaging data and can be quantified with a model of spatial statistics, Gaussian in this case. This spread of this Gaussian in Fig. 1D measures the practical resolving limit of the BOLD imaging at 7T in our measures.

Measurement of the variogram also takes us toward the goal of identifying column structure, since we can now model the effect of spatial noise correlations prior to searching for columnar structure in individual identified visual cortical areas.

VOLITIONALLY ENHANCED BETA-BAND OSCILLATIONS BY OPERANT CONDITIONING AFFECTS BEHAVIOR IN PRIMATES

Oren Peles[1,2,*], *Uri Werner-Reiss*[1,2], *Hagai Bergman*[1,2], *Zvi Israel*[3], *Eilon Vaadia*[1,2]

[1] Department of Medical Neurobiology, The Hebrew University, Jerusalem, Israel
[2] Edmond and Lily Safra Center for Brain Sciences, The Hebrew University, Jerusalem, Israel
[3] Department of Neurosurgery, Hadassah University Hospital, Jerusalem, Israel
[*] oren.peles@mail.huji.ac.il

Beta frequency band oscillatory activity is prevalent in the motor cortex. Previous studies demonstrated that it increases during hold periods, attenuates during voluntary movement and re-emerges thereafter. However the exact role of beta oscillations in the planning and execution of motor action is still not understood.

In this work, we implanted an array of 96 microelectrodes in the motor cortex of a macaque monkey. The monkey was trained to volitionally enhance the neuronal oscillatory activity in the beta band (20–30 Hz) at local selected sites by neural operant conditioning, using a real time brain machine interface (BMI) platform. At the same time, the monkey had to perform a sensorimotor task involving color discrimination.

We show that the monkey learned to robustly increase beta band cortical oscillations and that many neurons were phase locked to the oscillations. Furthermore, we found that the LFP beta-power before the execution of the motor action was positively correlated with the reaction times, and negatively correlated with behavioral performance (success rate).

Our results suggest that during high beta epochs new motor actions take longer to initiate and the perception of sensory inputs is impaired. These findings may support the widely accepted hypothesis that beta oscillations are tied to preservation of current motor state and help in unraveling the functional role of cortical oscillations and their effect on neural synchrony.

Acknowledgments

The study was partly supported by MAFAT, the Rosetrees Trust, the Gatsby charitable foundation, the Ida Baruch fund and the Jack H. Skirball fund. O.P. is supported by Khazzam-Goren scholarship.

INTERPRETATION OF CORRELATED VARIABILITY FROM MODELS OF SPIKING NEURAL NETWORKS

Volker Pernice[*], *Rava Azeredo da Silveira*

Department of Physics, Ecole Normale Supérieure, Paris, France
[*] volker.pernice@lps.ens.fr

The variability of the responses of a neural population to the repeated presentation of sensory stimuli is a universally observed phenomenon. Given a set of measured responses, different questions can be asked. First, there is the mechanistic problem of what can be inferred about the underlying network from observed statistics like average responses and correlations. Second, there is the function of the circuit: how does the variability of responses affect the ability of the population to encode different stimuli? In order to interpret correlated variability in an experimental data set we want to consider both sides of the problem. We aim to identify a model system that sheds some light on how observed activity statistics are generated as well as assess the consequences of noise and correlations arising in such a system on information about input stimuli in the response distribution.

Potential mechanisms contributing to correlated variability in neural networks include unreliable spike generation in the neurons, external influences and shared input from recurrent or feed-forward connections. We consider different scenarios in a point process framework [1], in particular correlations arising in a recurrent network, in comparison to scenarios in which correlations are induced by divergent input in a feed-forward architecture, or by a common signal shared across the population. These models differ in their predictions about the variation of covariances and average responses across stimuli. We analyze recordings of neural populations in mouse auditory cortex responding to a set of sound stimuli [2] and find statistics consistent with those that emerge in a model of a recurrent network with random effective connections and weak input signal correlations.

The relevance of observed correlations for coding can be estimated from the effect of their removal (by shuffling responses across trials) on how well one can discriminate between pairs of stimuli based on the population responses. The model explains how correlations with positive as well as negative effects, depending on the stimulus pair, are generated. Differences across neural populations can be related to properties of the network—in our case the distribution of effective connections within the populations. Furthermore, model parameters give an idea of the amount of network generated noise, which determines the loss of information inflicted by the transformation of input to output. Parameters inferred from the experimental data suggest that external noise as well as noise resulting from spike generation is correlated and amplified by the recurrent connections of the network. From this point of view, incoming signals would be amplified at the cost of increased noise.

References

1. Hawkes (1971) *J R Stat Soc Ser B*, 33(3):438–443.
2. Bathellier, Ushakova, Rumpel (2012) *Neuron*, 76(2):435–49, 10.1016/j.neuron.2012.07.008

DECODING V4 LAMINAR POPULATION RESPONSE DURING COVERT AND OVERT ATTENTION

Warren W. Pettine[1,2,*], *Nicholas Steinmetz*[1–4], *Tirin Moore*[1,2]

[1] Howard Hughes Medical Institute
[2] Department of Neurobiology, Stanford University School of Medicine, Stanford, Calif., USA
[3] Institute of Neurology, Univertisy College London, London, UK
[4] Dept. of Neuroscience Physiology and Pharmacology, University College London, London, UK
[*] wpettine@stanford.edu

The cerebral cortex's functional architecture is characterized by distinct lamination patterns, defined in part by cell type, connectivity and response properties. Previous studies of attentional modulation of V4 neural activity have found laminar differences in local field potentials, but not in spiking activity.

We recorded spiking activity across the cortical layers of single cortical columns of area V4 in two rhesus macaques using a linear array microelectrodes during a selective attention task. For this task, the monkey fixated on a central point, while four gabor patches appeared, one in each quadrant. A cue then was presented indicating the gabor patch that was most likely to change orientation. If the orientation changed after a delay, the monkey was rewarded for saccading to the opposite gabor patch. The two Gabor patches orthogonal to attended locations were considered controls. This task dissociated overt attention (the preparation and execution of orienting eye movements), from covert attention (selective processing without overt orienting).

We then used machine learning classification to distinguish between behavioral conditions (covert, overt and control) on a trial-by-trial basis from population activity. Feature vectors consisted of neuronal ensemble firing rates and inter-spike interval distributions. Alternative pseudo-populations were also created through multi-ensemble feature grafting, which permitted independent testing of waveform classes, as well as the location of neurons within superficial or deep layers. Classification was applied to data during the epoch following the presentation of a cue that indicated which of four stimuli was the target of covert (or overt) attention.

We found that neuronal ensembles and pseudo-populations of V4 neurons were able to distinguish between conditions in which overt, covert or no attention was directed toward the receptive field stimulus. The effect was significant for both narrow-spiking (putative interneurons) and broad-spiking (putative pyramidal) neurons, as well as for both superficial and deep layer neurons. These results suggest that the source of attentional modulation in V4 operates equally across cortical layers. Furthermore, our methods also provide a novel way to preserve raw population spike dynamics on a trial-by-trial basis when analyzing neural ensembles.

BIOPHYSICAL GROUND TRUTH DATA FOR IN VIVO SYNAPTIC CONNECTIVITY STUDIES

Jonathan Platkiewicz[1], *Asohan Amarasingham*[1–3,*]

[1] Department of Mathematics, The City University of New York, New York, New York, USA
[2] Department of Biology, The City University of New York, New York, New York, USA
[3] Department of Psychology, The City University of New York, New York, New York, USA
[*] aamarasingham@ccny.cuny.edu

There has been recently a great deal of interest in mapping the brain, namely in establishing the precise structural organization of neural microcircuits. High-density extracellular recordings offer the unique opportunity to observe simultaneously the activity of hundreds of neurons with millisecond precision in the behaving mammal. Neural connectivity is typically inferred from this recording type by extracting the spikes from the extracellular potentials and seeking the cell pairs that exhibit finely-timed spike correlation. Alternative statistical methods, such as the generalized linear model or the maximum entropy model, have also been applied, but these methods still rely on the assumption that a correlation, of some type, between two spike trains reflects a direct synaptic coupling. There is, however, no widely-accepted biophysical justification for this assumption, nor is there much ground truth data that might provide validation.

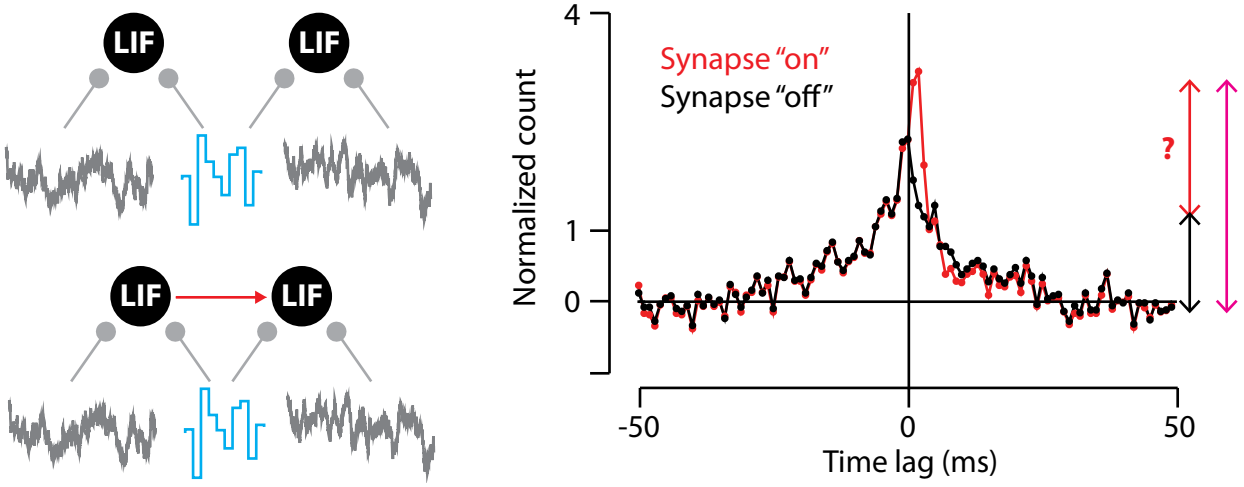


Figure 1. How can one detect the presence of a monosynapse *in vivo* from extracellular spike recordings? **Left**, Biophysical models of *in vivo* monosynaptic spike transmission based on standard leaky integrate-and-fire models (LIF). Independent noisy currents (gray) and common fluctuating current (cyan) are injected in the cell pairs (same exact input in both cases: synaptically connected or not). **Right**, Resulting cross-correlation histogram.

Numerical simulations of biophysical models of monosynaptic spike transfer, which are biologically faithful to some degree, are natural candidates with which to approach this issue, given current experimental limitations. First, we show that a millisecond spike correlation can be observed between monosynaptically connected neurons, regardless of the timescale of the postsynaptic potential response. The demonstration is based on the theory of stochastic processes—in particular on an escape noise model—and numerical simulations of biophysical models of monosynaptic spike transfer. Second, using the developed biophysical models, we highlighted the relevance of nonparametric statistical methods based on conditional inference, in connectivity analysis from spike trains, even in settings of extreme firing rate nonstationarities.

EXPLORING THE ROLES OF BYPASS PATHWAYS IN VISUAL OBJECT RECOGNITION

Carlos R. Ponce[1,*], *Stephen G. Lomber*[2], *Margaret S. Livingstone*[1]

[1] Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, USA
[2] Department of Psychology, University of Western Ontario, London, Ontario, Canada
[*] crponce@gmail.com

Visual object recognition is a parallel problem in experimental neuroscience and machine learning. The machine learning community has made impressive progress, having just designed models that can outperform humans in some tasks. These models are called convolutional neural networks or *convnets*. We are interested in comparing the performance of different types of convnets with more biologically grounded models of the visual recognition system. One such biologically grounded model includes a bypass pathway architecture. What is a bypass pathway? Standard convnets have a linear architecture: layer 1 outputs to layer 2, which outputs to layer 3, and so for several layers. If we think of layers as cortical areas, this is analogous to the cortical stream V1 $\rightarrow$ V2 $\rightarrow$ V4 $\rightarrow$ inferotemporal cortex (IT). We can understand a lot about visual recognition using this network path, but it is not the only one present in the brain. The primate brain also has shorter paths from V1 to IT, such as V1 $\rightarrow$ V2 $\rightarrow$ IT and V1 $\rightarrow$ V4 $\rightarrow$ IT. This is equivalent to having the outputs of one convnet layer skipping one processing stage. These bypass pathways do not have a defined role in convnets or biology.

We are defining the functional advantages of the bypass pathways in the macaque brain. We implanted microelectrode arrays in posterior IT (pIT) cortex to define the image preferences of a sample of pIT multiunits. At the same time, we implanted deactivation devices in different cortical areas inputting to pIT, including V2, V3 and V4 (these devices were cortical cooling loops, or *cryoloops*). Our goal was to eliminate different input pathways to pIT, while measuring consequent changes in pIT response properties, like image preferences. We trained two macaques to perform a fixation task while we cooled areas V2 and V3 concurrently, or area V4 separately, constantly recording from pIT.

To quantify how much information was lost within each condition, we trained support vector machines (SVMs) using population response vectors. Each SVM was trained to classify each individual image in an all-vs.-all design. This analysis showed an overall decrease in classification accuracy during both cooling conditions, with the V4 deactivation leading to a statistically larger drop in classification accuracy than the V2(3) deactivation. In contrast, overall firing rate decrease did not reliably distinguish between both deactivation conditions. Using a multidimensional neural space trajectory analysis, we found that V4 inactivation is more likely to scramble the activity space representation of individual images, independently of the common reduction in firing rate across the population. We looked for image-dependent features that explained the larger effect of V4 cooling, but did not find any overt differences. We then used a published convolutional network that included bypass pathways (T. Poggio laboratory), and we expanded it to include both V1 $\rightarrow$ V4 and a V2 $\rightarrow$ pIT bypass pathway. We found that the accuracy performance of the V1 $\rightarrow$ V4 pathway was greater than the performance of the V2 $\rightarrow$ pIT pathway. We further examined this model and found that the key contrast in function was not between the two bypass pathways, but between the bypass pathways and the main pathway. Bypass pathways diversified model pIT sensitivity by introducing preferences for less complex shapes, which proved helpful for classification tasks that depended on simpler geometric features. We conclude that bypass pathways help to balance the parallel needs of developing selectivity to high-level images (like faces) and preserving selectivities for low-level visual features (like corners and angles).

DATAJOINT: MANAGING BIG SCIENTIFIC DATA USING MATLAB OR PYTHON

Jacob Reimer[1,*], *Dimitri Yatsenko*[1], *Alexander S. Ecker*[1,2,3], *Edgar Y. Walker*[1], *Fabian Sinz*[1], *Philipp Berens*[1,2,4], *Andreas Hoenselaar*[5], *R. James Cotton*[1], *Athanassios G. Siapas*[5], *Andreas S. Tolias*[1,6]

[1] Baylor College of Medicine, Houston, USA
[2] Bernstein Center for Computational Neuroscience, Center for Integrative Neuroscience and Institute for Theoretical Physics, University of Tübingen, Germany
[3] Max Planck Institute for Biological Cybernetics, Tübingen, Germany
[4] Institute of Ophthalmic Research, University of Tübingen, Germany
[5] California Institute of Technology, Pasadena, USA
[6] Department of Applied Mathematics, Rice University, Houston, USA
[*] reimer@bcm.edu

The rise of big data in modern research poses serious challenges for data management: Large and intricate datasets from diverse instrumentation must be precisely aligned, annotated, and organized in a flexible way that allows swift exploration and analysis. Data management should guarantee consistency of intermediate results in subsequent multi-step processing pipelines such that changes in one part automatically propagate to all downstream results. Finally, data organization should be self-documenting to ensure that lab members and collaborators can access the data with minimal effort, even years after it was collected. While high levels of data integrity are expected, research teams have diverse backgrounds, are geographically dispersed, and rarely possess a primary interest in data science.

While the challenges associated with large, complex data sets may be new to biologists, they have been addressed quite successfully in other contexts by relational databases, which provide a principled approach for effective data management. DataJoint is an open-source framework that provides a clean implementation of core concepts of the relational data model to facilitate multi-user access, efficient queries, distributed computing, and cascading dependencies across multiple data modalities. Critically, while DataJoint relies on an established relational database management system (MySQL) as its backend, data access and manipulation are performed transparently in the commonly-used languages MATLAB or Python, and DataJoint can be integrated into new and existing analyses written in these languages with minimal effort or additional training. DataJoint is not limited to particular file formats, acquisition systems, or data modalities and can be quickly adapted to new experimental designs. DataJoint and related resources are available at http://datajoint.github.com.

EXPECTATION MODULATES ACTIVITY IN VISUAL CORTEX

Ilias Rentzeperis[*], *Steeve Laquitaine, Justin L. Gardner*

Stanford University, Stanford, California, USA
RIKEN Brain Science Institute, Wako, Japan
[*] rentzi@stanford.edu

Humans can exploit the prior probability of whether an event will occur to improve their interpretation of the world. Signal detection theory provides a prediction for how to optimally set decision criterion according to prior expectations. We ask the following: Does activity in visual cortex change in accordance to our prior expectations? If so, how do prior expectations modulate activity in visual cortex? We designed a signal detection task in which we manipulated prior expectation and measured cortical responses in visual cortex with functional MRI. Subjects were asked to detect the presence or absence of a threshold contrast sinusoidal grating. Expectation was manipulated by indicating the prior stimulus presence probability with a cue before the stimulus interval (pre-cue indicating either 70% or 30% probability).

Subjects were able to adjust expectation (bias) using the pre-cues that were provided. When the pre-cue specified that targets were 70% likely to be present, subjects were biased to answer that the stimulus was present compared to when the pre-cue specified that targets were only 30% likely to be present (Fig. 1, blue trace). Changing expectation had a smaller effect on sensitivity (d') to stimulus presence (Fig. 1, red trace).

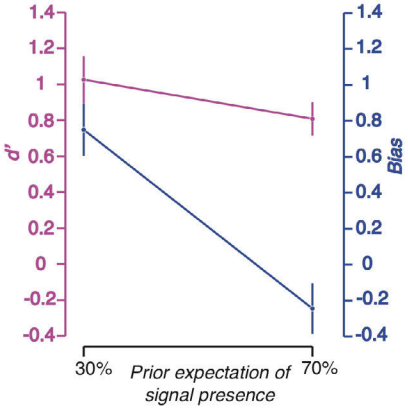


Figure 1. Behavioral results.

We found that cortical responses in V1 were modulated by expectation according to predictive coding theories. That is, there was a smaller response when subject perception matched their expectation compared to when their perception did not match. The hemodynamic response (averaged across voxels in V1 that responded to the stimulus location) evoked when subjects perceived that the stimulus was present was greater when they were not expecting the stimulus to be present (30% condition) compared to when they were expecting it (70% condition, Hits and False Alarms). The reverse was true when the subjects perceived that the stimulus was absent (Fig. 2, Misses and Correct Rejects subpanels). These responses are not expected by a strict signal detection theory account, but suggest signals consistent with a predictive coding framework.

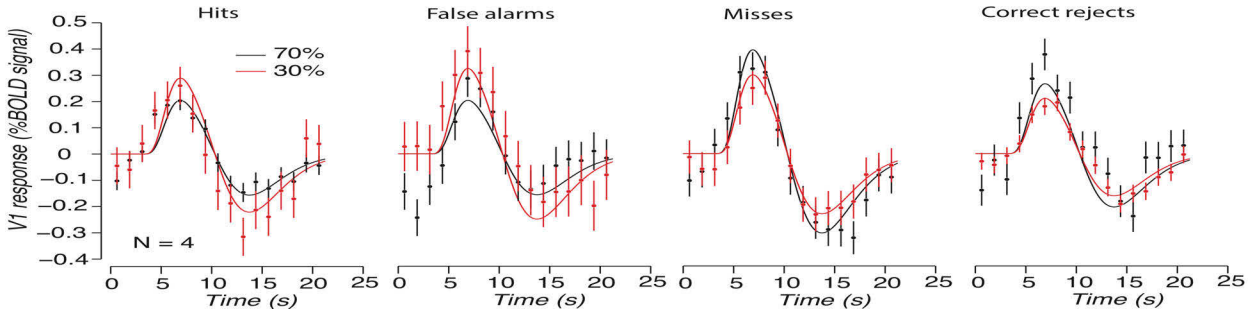


Figure 2. Expectation modulates the responses evoked by perception.

DECODING SUBJECTIVE DECISIONS FROM THE ORBITOFRONTAL CORTEX

Erin L. Rich [*], *Jonathan D. Wallis*

Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, California, USA
[*] erin.rich@berkeley.edu

When making a subjective decision, the brain must compute a value for each available option then compare those values to make a choice [1,2]. Neuropsychology studies demonstrate a clear role for the orbitofrontal cortex (OFC) in such value-based decisions [3,4], but the neural mechanisms of its contribution are debated. One limitation has been that internal factors, such as deliberation, can alter the dynamics of the decision process from trial to trial, but are difficult to measure or control. Here, we used a novel approach to decode dynamic neural states from multidimensional OFC data during individual choices, shedding light on the mechanisms of OFC's contribution to subjective decision-making.

We recorded multiple OFC neurons and local field potentials while two non-human primate subjects performed a reward preference task. Eight familiar pictures predicted four reward amounts. On interleaved trials, pictures were presented either singly or in pairs, the later of which required the subject to make a choice. We used single picture trials to train a classifier to recognize patterns of OFC activity associated with each picture value, then used the classifier to decode values as each choice was being made.

During individual choices, OFC alternated between states associated with the value of two available pictures (Fig. 1). Neuron-dropping analyses confirmed that these states were not strongly dependent on the activity of any single neuron. The decoded patterns predicted trial-by-trial variability in the subjects' behavior. Stronger representations of the picture that was ultimately chosen predicted faster choices, while stronger representations of the picture that was not chosen predicted slower choices. Deliberation was quantified by the amount the subject viewed each option before making a decision, and we compared trials with and without deliberation that were otherwise objectively identical. When the subject did not deliberate, the chosen representation was stronger than that of the unchosen option, but when he did, the two representations were similar. Finally, aligning single neuron firing rates to the onset of decoded states revealed that individual neurons dynamically encoded the value of either picture, shifting activity patterns as the network evaluated each option. Thus, the mechanism of subjective decision-making includes the dynamic activation of OFC states associated with each choice alternative.

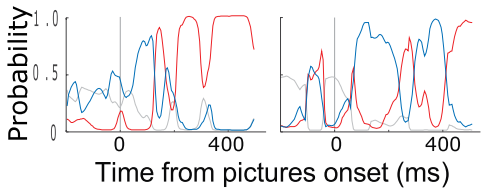


Figure 1. Posterior probabilities of the picture value chosen by the subject (red), not chosen (blue), or not available (gray), decoded in 20 ms windows stepped forward by 5 ms, on two representative choice trials.

References

1. Padoa-Schioppa (2011) *Annu Rev Neurosci* 34:333–59, 10.1146/annurev-neuro061010-113648
2. Rangel, Camerer, Montague (2008) *Nature Rev Neurosci* 9(7):545–56, 10.1038/nrn2357
3. Rudebeck, Murray (2014) *Neuron* 84(6):1143-56, 10.1016/j.neuron.2014.10.049
4. Fellows (2011) *Ann N Y Acad Sci*. 1239:51-8, 10.1111/j.17496632.2011.06229.x

GRIP- AND FORCE-SELECTIVE NEURAL TRAJECTORIES IN LARGE POPULATIONS OF NEURONS OBTAINED DURING A DELAYED REACH-TO-GRASP TASK

Alexa Riehle[1–3,*], *Thomas Brochier*[1]

[1] Inst de Neurosciences de la Timone (INT), Aix Marseille Univ, CNRS, Marseille, France
[2] RIKEN Brain Science Institute, Wako-Shi, Japan
[3] Inst of Neuroscience & Medicine (INM-6), Research Center Jülich & JARA, Jülich, Germany
[*] alexa.riehle@univ-amu.fr

Grasping an object involves shaping the hand and fingers in relation to the object's physical properties. Following object contact, it also requires a fine adjustment of grasp forces for secure manipulation. Earlier studies suggest that the control of hand shaping and grasp force involve partially segregated motor cortical networks. However, it is still unclear how information originating from these networks is processed and integrated. We analyzed massively parallel single neuron spiking activities recorded during a delayed reach-to-grasp task. We used a 100-electrodes Utah array implanted in motor cortex. Two monkeys were trained to reach, grasp, pull and hold an object as response to a GO signal. We manipulated independently two parameters: the grip type for grasping the object (precision grip or side grip) and the object weight requiring a high or low force [1]. One second before GO, a cue provided prior information about either grip (Grip-first condition) or force (Force-first condition), while the subsequent GO signal provided the complementary information about force and grip, respectively. This experimental protocol allows one to study both parameters separately during the instructed delay and their combination during movement execution.

The goal of this study was to explore how neural trajectories reflect the dynamic encoding of the two task parameters and their integration over time. We analyzed our data (up to 160 neurons) to extract neural trajectories by performing different dimensionality reduction techniques to project full neural trajectories in a lower dimensional space. We used the DataHigh analysis toolbox [2] for dimensionality reduction using the principal component analysis (PCA), the factor analysis (FA), and especially the Gaussian-process factor analysis (GPFA) [3]. We then related the obtained neural trajectories to the behavioral output in terms of reaction, reach movement and pulling times, force traces and object displacement.

Our results show a clear separation of neural trajectories for each parameter as a function of prior information in each task condition. In the Grip-first condition, adding information about the force at GO does not influence the ongoing grip processing during movement execution, whereas in the Force-first condition adding information about the grip diminishes temporarily force coding. This is in agreement with a study in which we performed single-trial decoding of force and grip information from LFP signals recorded in the same task [4]. These results confirm our working hypothesis that the two parameters grip and force are differentially encoded in motor cortex as soon as information about them is provided.

Acknowledgments

SMHB, BrainScaleS (EU Grant 269912), ANR-GRASP, Riken-CNRS Research Agreement.

References

1. Riehle, Wirtssohn, Grün, Brochier (2013) *Front Neural Circuits* 7:48
2. Cowley, Kaufman, Butler *et al.* (2013) *J Neural Eng* 10:066012
3. Yu, Cunningham, Santhanam, *et al.* (2009) *J Neurophysiol* 102:614–635
4. Milekovic, Trucculo, Grün, *et al.* (2015) *NeuroImage* 114:338–355

EARLY LIFE SEIZURES HAVE DISTINCT AND REGION-SPECIFIC EFFECTS ON CORTICAL DYNAMICS AND PROPENSITY TO EPILEPTOGENESIS

Pavlos Rigas, Ani Kaplanian, Christos Zlatanos, Leonidas Leontiadis, Konstantinos Armaos, Irini Skaliora *

Biomedical Research Foundation of the Academy of Athens, Athens, Greece
* iskaliora@bioacademy.gr

We have employed a multidisciplinary experimental approach in order to investigate the long-term effects of early life seizures (ELSs) on behaviour, cortical physiology and propensity to epileptiform activity in mice.

Single or multiple seizures were induced at different developmental stages [P10–15 or P20–25] in order to examine the factors of seizure severity and brain maturational status on vulnerability to ELS. Mouse behaviour and cognition was assessed with a battery of tests, including spatial learning tasks, recognition memory, and species-specific behaviours (nest building, hoarding, marble burying). No significant effects were detected in any of these tasks, except for a consistent decrease in locomotion and exploratory activity in all animals that had received ELSs.

Cortical physiology was assessed by comparing: (i) spontaneous network activity (Up/Down states) in brain slices of adult (over 4 mo) mice, and (ii) the induction and expression of cortical epileptiform activity *in vitro*, in the 0 [Mg^{++}] model. In these experiments we examined two distinct cortical regions, primary motor (M1) and somatosensory (S1) cortex in order to investigate regional differences in vulnerability to ELSs.

While single ELSs at P20–25 had no effect on Up state activity, multiple seizures induced during the same period resulted in a significant decrease in Up state duration. This effect was only present in S1 cortex. In contrast, a single ELS during the early developmental period (P12) resulted in a significant increase in Up state occurrence in M1 but not in S1 cortex. These results reveal that even moderate experience of ELS can have long lasting effects in cortical dynamics that are expressed in distinct form (reduced vs increased excitability) in different cortical regions.

Acknowledgments

General Secretariat for Research and Technology, Greece

ANTICIPATION OF SOCIAL INTERACTION BASED ON EYE CONTACT DURATION, A BEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDY

Alexandros Rouchitsas[1,2,*], *Irini Skaliora*[1,2]

[1] Graduate Program in Cognitive Science, University of Athens, Greece
[2] Biomedical Research Foundation of the Academy of Athens, Greece
[*] alexandros.rouchitsas@gmail.com

Direct gaze is considered a critical social stimulus as it conveys valuable information about the intentions of conspecifics regarding communication and social interaction. Consequently, perceived eye contact modulates arousal, attention, cognition, and action. Furthermore, a study showed that likeability ratings were higher for direct than for averted gaze and increased linearly with increasing direct gaze duration. However, another study showed that expressionless eye contact of more than 3.2 sec may be considered inappropriate or hostile, and cause distraction or discomfort. How do gaze direction and duration interact to affect an inference about the communicative intent of a conspecific? Direct gaze supposedly signals communicative intent. But, will we infer intention to engage socially even if our eyes meet for a fraction of a second? Or is prolonged eye contact required so as to start anticipating that some type of social interaction scenario will soon unfold?

In our study a facial movement detection task will be employed where participants will be asked to fixate on the eyes of a face stimulus and respond as quickly as possible to a facial movement. Two different facial movements will be used: a socially relevant facial movement (mild smile with a closed mouth); and an arbitrary and socially irrelevant facial movement (puffed cheeks). The stimulus will be presented with a direct or averted gaze for a duration of 1.0, 2.0, 3.0, or 4.0 sec. Towards the end of each trial (0.5 sec prior to the end, irrespective of gaze duration) there will be either a smile or puffed cheeks. If participants indeed start anticipating that some type of social interaction scenario will soon unfold as eye contact duration increases, they will be faster at detecting socially relevant facial movements for the 2.0 sec and 3.0 sec eye contact durations compared to an arbitrary and socially irrelevant facial movement. For the 1.0 sec and 4.0 sec conditions, both types of facial movement will be detected equally fast, since anticipation presumably won't have arisen by 0.5 sec, and the expressionless eye contact for 3.5 sec will have created a distracting effect on task performance. In the averted gaze condition, it is hypothesized that both types of facial movement will be detected with equal speed irrespective of gaze duration since no anticipation of upcoming social interaction will ever arise to prime the detection of socially relevant stimuli. In addition to response times, event-related potentials will be recorded in order to assess the time-window in which expectancy of social interaction arises. If our hypothesis is correct, an ERP effect should appear for the longer gaze durations (*i.e.*, over 1.0 sec). Furthermore, this ERP effect presumably will fail to show up in the averted gaze condition, irrespective of gaze duration since no anticipation of social interaction will have arisen.

INTEGRATION OF SEPARATE SENSORY CHANNELS IN SOMATOSENSORY CORTEX

Hannes P. Saal[1,*], *Michael A. Harvey*[2], *Sliman J. Bensmaia*[1]

[1] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL, USA
[2] Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, TN, USA
[*] hsaal@uchicago.edu

Traditionally, different classes of cutaneous mechanoreceptive afferents are ascribed different and largely non-overlapping functional roles (for example texture or motion) stemming from their different response properties. This functional segregation is thought to be reflected in cortex, where each neuron receives input from a single submodality. Here, we present work that challenges this notion.

Our goal is to characterize the transformation and (potential) integration of tactile information from the somatosensory periphery to cortex. To this end, we implement a simple computational model that describes how the responses of neurons in somatosensory cortex of awake, behaving monkeys are shaped by the peripheral input, reconstructed using simulations of neuronal populations that reproduce natural spiking responses in the nerve with millisecond precision. Specifically, we recorded the single-unit responses of neurons in primary somatosensory cortex (S1) to simple and complex skin vibrations, and simulated the peripheral responses of rapidly adapting (RA) and Pacinian (PC) afferents to these same stimuli. This allowed us to fit temporal receptive fields to individual cortical neurons describing how these integrate the RA and PC input.

We find that most cortical neurons receive input from both afferent populations. Importantly, the two inputs affect the cortical responses in different ways: the strength of cortical responses is driven by one population of nerve fibers (RA) whereas the precise spike timing of cortical responses is shaped by another (PC).

Next, we ask why the two channels drive cortical neurons in different ways. We reasoned that the integration process should reflect differences in the response properties of the input channels. To this end, we optimized the temporal receptive fields such that they were maximally informative about the stimulus on a fine timescale. Filters were optimized on recordings of skin vibrations obtained when scanning natural textures across the skin. We found that the filters optimized to convey information about texture closely matched the filters derived from measured S1 responses. We conclude that RA and PC integration in S1 is optimized to encode stimuli that are commonly encountered during interactions with objects.

Separate sensory channels that convey complementary but overlapping information are commonplace in sensory systems and not limited to the sense of touch. Distributing sensory information across channels has distinct advantages such as parsing the behaviorally relevant range, keeping energy expenditure low, and optimizing information transmission in the presence of noise. To the extent that these parallel input channels represent information in disparate ways (differing in response latency, adaptation properties, or spiking precision, among others), their integration should reflect and exploit such differences, a process that can be described using the type of model introduced here.

CORTICAL REPRESENTATION OF DYNAMICS

Terence D. Sanger

Department of Biomedical Engineering, University of Southern California, Los Angeles, CA, USA
terry@sangerlab.net

In a dynamic environment, predictions of future state are essential for rapid responses to threats, identification of unexpected but salient sensory phenomena, and optimization of short and long-term motor behavior. Animals higher on the phylogenetic spectrum have greater abilities for prediction, and humans make increasingly longer-term predictions during development, suggesting that cortical size and maturation are important substrates. In the field of motor control, predictions of dynamics are taken as evidence of internal models yet neurophysiological mechanisms are not understood. I propose that dynamics for certain classes of sensory-motor processing are represented as time-varying patterns of activity within cortex.

I model two classes of experimentally-observed dynamic phenomena in cortex: Class A, time-varying patterns of propagating activity in response to a step or pulse sensory input, and Class B, changes in sensory threshold in response to spontaneous changes in cortical activity. The models are performed at the time-scale of single spikes, but it is interesting to note that Class B has also been observed at a much slower time-scale in resting-state fMRI experiments.

Assuming primarily local connectivity, the cortical dynamics can be modeled as a standard 2D flow field over the time-varying probability of a local spike $p(x,t)$:

$$\left.\frac{\partial p}{\partial t}\right|_x = -\alpha^T(x)\frac{\partial p}{\partial x} + s(x,t) \tag{1}$$

where x is the 2D location on the cortical sheet, $\alpha(x)$ is a 2D local flow vector, $\partial p/\partial x = \nabla p$ is the local gradient, and $s(x,t)$ is sensory input. For non-local connectivity, this can be generalized using a linear operator L on the space of fields p so that $\dot{p} = Lp + s$. In this case, local connectivity corresponds to an almost diagonal L. Non-local influences (perhaps from cerebellum or basal ganglia) are represented by off-diagonal elements and are generally sparse.

Appropriate choice of $\alpha(x)$ (or L) allows the cortex to model different dynamic phenomena. For example, if $\alpha(x)$ is learned from prior observations of the response $\partial p/\partial t$ to $\partial p/\partial x$, then it can be used to predict future responses. If a particular dynamic response is desired, perhaps for motor output, then $\alpha(x)$ can be selected appropriately. Note that the response to a non-time-varying $\alpha(x)$ is a time-varying $p(x,t)$, thus modeling our desired phenomenon (1). Also note that the response to time-varying sensory input $s(x,t)$ will be increased if $\alpha(x)$ already describes the dynamics of the sensory input, thus modeling our desired phenomenon (2). Furthermore, note that $\alpha(x,t)$ can itself be time-varying, thus allowing flexible motor dynamics and context-dependent responses to sensory input.

Equation (1) is simulated using 1.5 million integrate-and-fire neurons with local connectivity in a 640×480 sheet on an nVidia GPU with real-time processing of visual images and closed-loop control of a desktop robot. The robot learns visually-guided reaching along a desired path with movements that are stable to perturbation. The mapping between the time-varying cortical activity and the external robot dynamics can be directly visualized. This model therefore provides a mathematical framework for understanding autonomous time-varying behavior in cortex and a potential mechanism to explain how internal models make predictions of external dynamic behavior.

THE ROLE OF PARIETAL AND PREFRONTAL CORTICES IN VISUAL SEARCH

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

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

When we scan a cluttered visual scene to locate an object, we rely on its features (*e.g.*, shape, colour) to guide the search. Feature-based attention serves as a selection mechanism that enhances processing of stimuli, which share features with the sought for object. The frontal eye fields (FEF), in the anterior bank of the arcuate sulcus, and the lateral intraparietal area (LIP), in the lateral bank of the intraparietal sulcus, are considered to control spatial attention through the generation of saliency maps in which stimuli are represented according to their behavioural relevance. However, the exact role of each area in feature attention and the dynamics of their interaction are largely unknown.

We investigated the role of FEF and LIP in visual search while two macaque monkeys were engaged in a free-viewing visual search paradigm. In each session, up to four electrodes were lowered in each area to record spiking activity and LFPs. Animals were instructed to find a target among stimuli that either shared the target's colour/shape or had nothing in common with the target.

In both areas, neuronal responses to the target were higher compared to those to an irrelevant distractor, while responses to stimuli that shared the target's features were in-between, in agreement with the predictions of a saliency map. This feature effect was present when monkeys made a saccade outside the neurons' receptive field and was thus dissociated from spatial attention. Effects were more pronounced and emerged earlier in the FEF, indicating that FEF (rather than LIP) neurons signal first the behavioural relevance of stimuli. Furthermore, we found enhanced synchronisation between the two areas mainly in in the beta frequency range. This finding provides further evidence for a role of beta-frequency synchronisation in long-range communication.

Acknowledgments

Work supported by actions "ARISTEIA II" and "Supporting Postdoctoral Researchers" of the Operational Program "Education and Lifelong Learning", (Action's Beneficiary: General Secretariat for Research and Technology), co-financed by the ESF and the Greek State and by a Fondation Santé Grant.

STRUCTURED COACTIVATION OF CA1 NEURONS SUPPORTS PRECISE SPATIAL CODING IN THE HIPPOCAMPUS

Cristina Savin [*], *Jozsef Csicsvari, Gašper Tkačik*

IST Austria, Klosterneuburg, Austria
[*] csavin@ist.ac.at

While the idea of collective network dynamics underlying circuit computation has a long history in the hippocampus, analyses of neural activity in this region almost always ignore dependencies across neurons. This paradox is explained by the fact quantifying collective effects in hippocampal activity has proven particularly difficult. Part of the reason is that although hippocampal responses are strongly correlated, a large part of these dependencies are stimulus driven (due to cells with overlapping place fields being co-activated as the animal moves through the environment) or owed to global network oscillations (*e.g.*, theta). Furthermore, neither of these sources of shared variability are under the experimenter's control, which excludes traditional noise correlations type analyses. Thus, to make inferences about statistical dependencies across cells, one needs to first factor out the effects of the animal's movements within the environment and those of global oscillations. To this aim, we developed a novel maximum entropy model that takes these sources of correlations into account but is otherwise maximally unstructured and compared it against neural data. This allowed us to detect excess correlations for any simultaneously recorded cell pair.

In more detail, we obtained Bayesian estimates of the place field selectivity of cells (Gaussian Process prior with Poisson observation noise), that enabled us to propagate any uncertainty about the stimulus selectivity of the cells throughout subsequent analyses. As a proxy for the global population state, we additionally constrained the total number of spikes emitted by the population within each time bin (25 ms) to match the data. We used rejection sampling to generate surrogate data from this null model and used rigorous statistical testing to detect deviations of the data from the model predictions (Bonferroni-corrected to account for multiple comparisons). After validating the method on simulated data with known statistics, we applied it to tetrode recordings from the CA1 of rats during open field exploration (50–100 simultaneous neurons per animal). We found a subset of CA1 neurons to be functionally coupled, about 6% of the E-E pairs recorded on different tetrodes (to avoid shared measurement noise). Moreover, this connectivity reflects stimulus preferences: positive excess correlations tend to be detected between cells with similar place fields, on top of a less specific set of excess negative correlations. Importantly, this structure has been obscured in previous analyses that do not explicitly take into account global oscillations.

To investigate the importance of couplings, we constructed a network model in which we could systematically vary the strength and topology of these noise correlations and used decoding to asses the quality of the emerging neural representations. We found that that data-like connectivity improves the precision of the spatial representation, suggesting that collective behaviour in CA1 optimises the encoding of the animal's position. Furthermore, the model makes a series of predictions concerning the effects of learning on the encoding of space in CA1, which we have begun to confirm experimentally by comparing neural responses to novel versus familiar environments. More generally, the work highlights the utility of maximum entropy models for making sense of neural population responses, by creating a hierarchy of precise control ensembles against which rigorous statistical tests are possible.

RANDOM CONNECTIONS FROM THE OLFACTORY CORTEX SUPPORT GENERALIZATION ACROSS ODORS AND ANIMALS

Evan S. Schaffer[*], *Dan D. Stettler, Daniel Kato, Larry Abbott, Richard Axel*

Department of Neuroscience, Columbia University, New York, New York, USA
[*] ess2129@cumc.columbia.edu

Learning to associate sensory stimuli with appropriate behavioral responses requires a compromise between specificity and generalization. Stimulus representations that vary discontinuously between similar stimuli allow those stimuli to be discriminated and associated with different behaviors. Conversely, representations that vary smoothly between similar stimuli permit generalization of the same behavior across stimuli. In the olfactory system, projections from the olfactory bulb to the piriform cortex are unstructured. Their apparent randomness might suggest that the olfactory system has opted for specificity over generalization because random connections tend to decorrelate responses.

To determine how well piriform odor representations support generalization, we compared calcium-imaging data from piriform cortex to a bulb-piriform model with random feedforward connectivity. In our imaging data, although representations of most odorant pairs are uncorrelated, odorants of similar structure have correlated representations, manifesting in higher than chance overlap between these representations. The model can generate correlated output matching our imaging data purely from correlated input because random connectivity does not completely decorrelate. Moreover, many model piriform neurons respond similarly across a class of related odorants despite the randomness of their input. Thus, random connectivity can support generalization, and smooth response tuning does not imply structured connectivity. To test for generalization in learning, we trained a perceptron-like readout receiving piriform input to respond to a single odorant. With no further training, this readout responds to similar odorants and to mixes containing the trained odorant but not to odorants unrelated to the trained odorant.

We observe that expansive random projections of the type connecting olfactory bulb to piriform has the counterintuitive property of making hard discrimination tasks easier while making easy discrimination tasks harder (Fig. 1A). Finally, we studied generalization across animals by generating multiple random models with the same statistics. These models exhibit similar generalization after learning (Fig. 1B), so the agreement between responses across mice will be high. Thus, behavioral consistency across animals does not require similarity in the wiring of their olfactory systems. This leads to the counterintuitive prediction that mice with different random odorant representations will tend to make the same mistakes in an olfactory task.

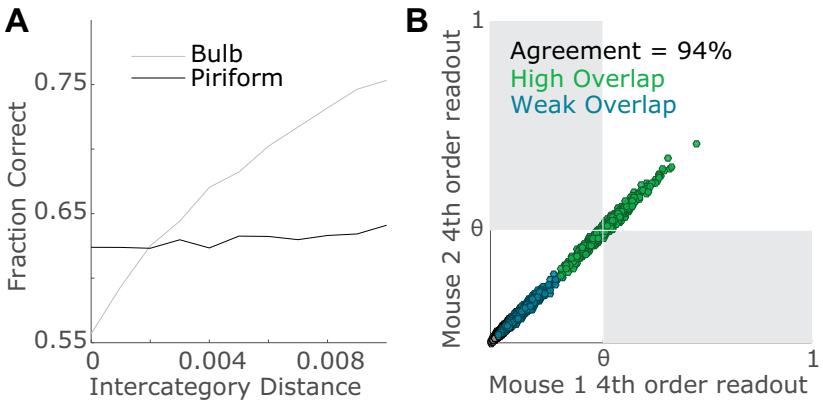


Figure 1. **A**, Performance of a readout unit trained to discriminate two random classes of odors, from the output of either the olfactory bulb or the piriform. **B**, Comparison of model readouts for two simulated mice, responding to very similar or moderaterly similar odors (green and blue, respectively).

INFORMATION PROCESSING BY SYNCHRONIZED NEURONAL ENSEMBLES IN THE PRIMARY AUDITORY CORTEX

Jermyn Z. See[*], *Craig A. Atencio, Vikaas S. Sohal, Christoph E. Schreiner*

University of California San Francisco, San Francisco, California, USA
[*]jermyn.see@ucsf.edu

The primary auditory cortex (A1) contains interconnected populations of neurons that are responsible for auditory information processing. Most studies of information processing in A1 involve either single unit spectrotemporal receptive field (STRF) estimation or paired neuronal correlation analyses, and thus assume that A1 neurons filter auditory information either as individual entities or as pairs. However, mounting evidence suggests that sensory stimuli are processed by interconnected, co-activated populations of neurons. Therefore, determining how A1 encodes information will require an integrated approach that combines receptive field and multi-neuronal ensemble analyses.

To assess multi-neuronal information processing in A1, we performed multi-electrode extracellular recordings in rat A1 while presenting dynamic, broadband stimuli, which allowed us to construct STRFs. We then used dimensionality reduction techniques to identify distinct groups of A1 neurons (neuronal ensembles, or NEs) that reliably fired synchronously in A1. For each NE, we identified synchronous spiking events, and then used the events to assess spectrotemporal information processing. For neurons that were members of an NE, the spikes associated with the NE conveyed greater information than the spikes that were not associated with the NE. We also identified single neurons that participated in multiple NEs and found that the spikes associated with each NE represented receptive field properties that were significantly different from receptive field properties associated with other NEs, even though the spikes originated from the same neuron.

These findings challenge the classical idea that A1 neurons produce a homogeneous set of spikes that may be equally weighted to estimate a single STRF. Instead, A1 neurons can have multiple receptive fields based on contributions from different NEs, with each NE representing the convergence of thalamocortical, intracortical and top-down inputs into A1. For each A1 neuron, equally weighting all neuronal spikes to form a single STRF ignores this enhanced coding capacity. Therefore, by taking into account the stimulus preferences associated with each NE, we may gain a more complete evaluation of information processing in A1.

SLEEPING DRAGONS AND THE EVOLUTION OF TWO-STATE SLEEP

Mark Shein-Idelson, Janie M. Ondracek, Hua-Peng Liaw, Sam Reiter, Gilles Laurent *

MPI Brain Research, Frankfurt am Main, Germany
* gilles.laurent@brain.mpg.de

Sleep is a fundamental behavior in the animal kingdom. Yet, neural manifestations specific to sleep, such as rapid eye movement (REM) and slow wave (SW) activity, have been described only in mammals and songbirds. It has therefore been suggested that electrical sleep is a result of convergent evolution brought about by similar pressures related to homeothermia. An alternative explanation, however, is that all electrical sleep evolved early in, or prior to amniote evolution, in which case it should be seen also in reptiles. Thus far, neurophysiological data from reptiles have been negative.

We addressed this question by recording the electrical activity from the brain of Australian Dragons (*Pogona vitticeps*) during sleep and wakefulness. We found that during sleep, brain activity alternates periodically between two states with a period of about 80 seconds. The first state is reminiscent of SW sleep, with relatively higher power in the delta range (below 4 Hz); the second is characterized by a flatter spectrum, closer to awake spectral profiles. Analysis of eye movement filmed during sleep show that rapid eye-movements occur periodically, and do so during non-SW sleep periods, suggesting a close similarity to REM sleep as described in mammals and birds.

We show that SW sleep consists of repeated LFP spikes, bearing strong similarity with sharp waves (SPW) observed in rodent hippocampal CA1. Superimposed on the descending phase of these SPWs, we find fast oscillations (above 70 Hz), that resemble ripple events described in hippocampal CA1. Single-neuron firing is very sparse during ripples and close to zero on average during SW sleep, contrasting with elevated firing rates during REM and awake states.

Taken together, our results indicate that two-state sleep exists in reptiles, suggesting that such sleep patterns existed in the common ancestor of all amniotes, pushing back the emergence of two-state sleep to at least 300 MYA. Because of their resistance to anoxia, reptiles may constitute a unique *in vitro* model for mechanistic sleep studies. Thus, for example, they may prove beneficial for exploring memory consolidation and fast replay during SPW. Finally, we propose that examining the neurophysiological substrate of sleep across the animal kingdom may not only provide a deeper understanding of the evolution of sleep, but may help identify generic principles governing brain dynamics during sleep and examine their function.

CELL TYPE-SPECIFIC FEEDBACK FROM LM TO V1 ENFORCES A NARROW TEMPORAL WINDOW FOR SUPRA-LINEAR ENHANCEMENT OF FEED-FORWARD INPUTS

Shan Shen[*], *Xiaolong Jiang, Jacob Reimer, Fabian Sinz, Andreas S. Tolias*

Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[*] shans@bcm.edu

Cortical sensory hierarchies are linked by extensive top-down feedback connections whose function remains elusive. We combined multiple whole-cell recordings with optogenetics to examine the connectivity of feedback from secondary visual area LM (lateromedial area) to primary visual cortex (V1) in mice. We found that LM provided strong monosynaptic excitation to Layer 2/3 parvalbumin and somatostatin expressing interneurons and weaker input to all other cell types. This connectivity pattern happens to be very unique, which is different from other feedback pathways, both the feedback primary motor cortex to barrel cortex, or from another higher visual area PM (posterior medial area) to V1.

Activation of feedback from LM elicited biphasic membrane potential responses in V1 excitatory neurons, with an initial brief depolarization followed by a longer-lasting hyperpolarization. Feedback activation alone rarely elicited spikes on V1 principle cells, but when paired with visual stimuli, firing rates were increased three-fold within a narrow temporal window. Our results suggest that feedback from LM to V1 enforces a narrow window of opportunity for supra-linearly enhancing feed-forward information, consistent with models of vision where top-down priors and bottom-up evidence are combined for optimal inference.

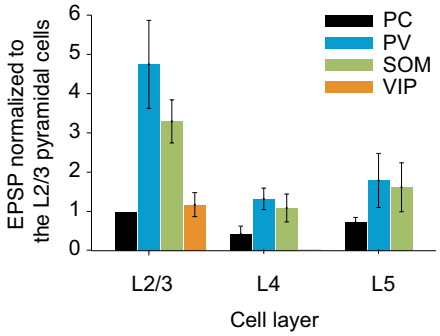


Figure 1. LM to V1 feedback driven EPSPs normalized to L2/3 cells in the same slices, recording at resting memberane potential (about −70 mV). Among all the cell types we recorded from, L2/3 PV+ and SOM+ neurons received the strongest excitatory inputs.

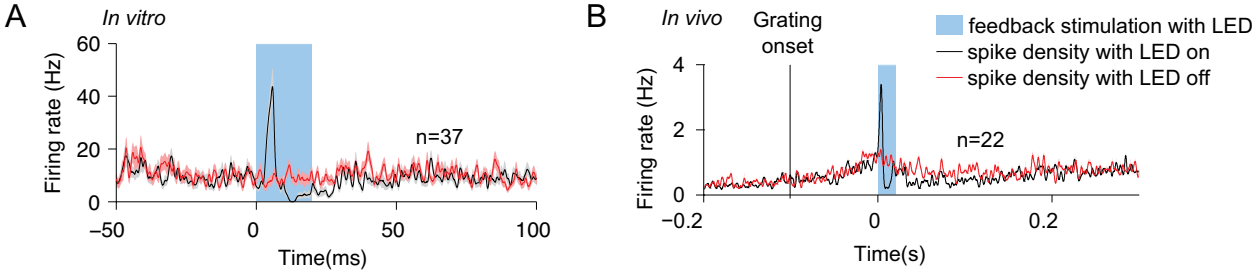


Figure 2. Activation of LM to V1 feedback elicits transient excitation followed by prolonged inhibition on V1 principal cells both *in vitro* and *in vivo*. **A**, In slices, cells were driven to fire with current injection, and feedback was stimulated with blue LED. Compared to the control (red), feedback excitation creates a narrow time window to enhance cell firing. **B**, Same as A, but cells were recorded *in vivo* and driven with grating stimuli.

SEX DIFFERENCES IN SPONTANEOUS CORTICAL NETWORK ACTIVITY IN VITRO

Charalambos Sigalas[1,*], *Eleni Konsolaki*[2], *Irini Skaliora*[1]

[1] Biomedical Research Foundation Academy of Athens, Athens, Greece
[2] DEREE, The American College of Greece, Athens, Greece
[*] csigalas@bioacademy.gr

During quiescent behavioural brain states, such as non-REM sleep, a spontaneous slow-rhythm synchronized activity develops in the cerebral cortex. This activity is maintained in slice preparations of isolated cortex in the form of Up/Down states, despite the absence of sensory inputs or active neuromodulation, indicating that it is chiefly the outcome of intrinsic properties of the local neuronal networks. Hence, this type of synchronized activity has been suggested to reflect the default activity of the cortex, but the mechanisms that facilitate its manifestation and its functions are poorly understood. Although many studies have utilized Up/Down state activity to investigate cortical network function, the sexual dimorphism of the brain has been greatly neglected. Accumulated evidence suggests that brain network function is modulated by sex, both in health and disease. Moreover, these effects seem to be age-dependent. In this study we have investigated the sex differences in endogenous cortical network function by monitoring Up/Down state activity in brain slices of male and female C57BL/6 mice in three age groups: pre-puberty (17–19 days old), adult (3–9 months) and old (19–24 months). Local field potential recordings revealed that female mice exhibited longer Up state event duration and higher occurrence compared to male mice at all ages tested. We also found sex differences in the relative proportion of delta and theta bands of the power spectrum (normalized to the total power of Up state events), with female mice exhibiting lower delta and higher theta power compared to male mice at all ages. Moreover, we found that Up states in adult female mice exhibited higher latency to peak amplitude of the Up state events compared to adult male mice, whereas no sex differences were observed in either pre-puberty or old mice. Taken together our results reveal significant sex differences in cortical dynamics, some of which are already present in juvenile mice and persist throughout life, while others only occur during adulthood. These results underscore the necessity to take sex differences into consideration when designing and interpreting studies of basic network function and could provide a framework for future investigations about the way sex affects cortical dynamics and information processing.

SIGNAL REPRESENTATION IN INHIBITORY NETWORKS WITH DISTANCE-DEPENDENT CONNECTIVITY

Sebastian Spreizer[1,2,*], *Martin Angelhuber*[1,2], *Ad Aertsen*[1,2], *Arvind Kumar*[2,3,*]

[1] Faculty of Biology, University of Freiburg, Freiburg, Germany
[2] Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany
[3] Dept. Comp. Science and Technology, KTH Royal Institute of Technology, Stockholm, Sweden
[*] sebastian.spreizer@bcf.uni-freiburg.de, arvkumar@kth.se

Unlike in the neocortex, neuronal networks in the basal ganglia, amygdala and cerebellum are composed of only inhibitory neurons. To understand the functional properties of these networks it is important to characterize how incoming feedforward excitatory inputs interact with the ongoing activity dynamics. While randomly connected inhibitory networks have been extensively studied, the dynamics of inhibitory networks with distance-dependent connectivity is poorly understood. Therefore, we investigated the effect of spatial connectivity structure on the emergence and maintenance of spatially clustered activity in large-scale inhibitory networks (10K leaky-integrate-fire neurons). We considered spatial connectivity structures in which connection probability changed as a function of distance according to either a Gamma [1] or a Gaussian function.

We found that the activity dynamics in networks with a Gamma-connectivity profile were largely determined by the mean and variance of the external input: weak external input or high input variance induced unstructured asynchronous-irregular activity (AI), whereas stronger external inputs or low input variance induced stable winner-takes-all (WTA) dynamics and formed hexagonal formations in a spatial map. In an input regime close to the noise threshold the activity organized into unstable spatial bumps, rensembling the experimentally observed neuronal assemblies and winner-less-competition [2]. By contrast, a distance-dependent connectivity according to a Gaussian function supported spatially structured activity in the network. The dynamic state of bump activity also determined the impact of external stimuli on the network model: the response was easily separated in the AI state, whereas in WTA state only strong stimuli could generate separable responses.

The stable bump state observed in our networks closely resembles the grid patterns often observed in the medial entorhinal cortex of rodents. In fact, in the computational models of grid-cell formation the distance dependent connectivity was modelled as a non-monotonic function of distance [3,4]. In summary, we conclude that a Gamma-shaped spatial connectivity provides the inhibitory network with a rich dynamical repertoire, enabling the the ongoing activity to switch dynamically between different network activity states.

Acknowledgements

This work was funded in parts by the German-Israeli Foundation, the EU Erasmus PhD program NeuroTime, and the Carl-Zeiss Foundatation. All simulations were carried out with NEST (http://www.nest-initiative.org).

References

1. Rinzel (1998) *Science* 279(5355):1351–1355, 10.1126/science.279.5355.1351
2. Rabinovich, *et al.* (2006) *RevModPhys* 78(4):1213–1265, 10.1103/RevModPhys.78.1213
3. Couey, Witeolar, Zhang, *et al.* (2012) *Nat Neuro* 16(3):318–324, 10.1038/nn.3310
4. Roudi, Moser (2014) *Nat Neuro* 17(5):639–641, 10.1038/nn.3704

DENDRITIC DYNAMICS IN SENSORY PERCEPTION

Naoya Takahashi[1,*], *Matthew Larkum*[1,2]

[1] Neurocure Cluster of Excellence, Charité Universitätsmedizin Berlin, Berlin, Germany
[2] Department of Biology, Humboldt-Universität zu Berlin, Berlin, Germany
[*] n.takahashi0906@gmail.com

Perception is a process that requires the matching of an internal representation of previous experience with real-world sensory data, for which the cellular mechanisms are poorly understood. There is abundant evidence that feedback information to primary sensory regions is integral to the perceptual process [1,2]. Recent data suggest that feedback information activates dendritic processes in pyramidal neurons that are linked to cognitive function [3,4]. Here, we show that calcium activity in the apical dendrites of a subset of layer 5 (L5) pyramidal neurons in primary sensory cortex correlates with the perceptual detection of whisker-based tactile stimulation in rodents. Another population of apical dendrites of L5 neurons was negatively correlated. The same positive and negative correlations were found for bursts of somatic spikes in L5 neurons that preceded the behavioral actions of the animals. The perception-relevant dendrites were sparse and distributed randomly in space. Using pharmacological and optogenetic approaches, we show that the dendritic activity is causally linked to the animal's behavior, demonstrating that the perceptual process depends critically on activation of the apical dendrites of L5 pyramidal neurons in primary sensory cortex.

References

1. Supèr, Spekreijse, Lamme (2001) *Nat Neurosci* 4(3):304–310, 10.1038/85170
2. Gilbert, Sigman (2007) *Neuron* 54(5):677–696, 10.1016/j.neuron.2007.05.019
3. Xu, Harnett, Williams, *et al.* (2012) *Nature* 492(7428):247–251, 10.1038/nature11601
4. Manita, Suzuki, Homma, *et al.* (2015) *Neuron* 86(5):1304–1316, 10.1016/j.neuron.2015.05.006

A DYNAMIC MODEL FOR DECODING DIRECTION AND ORIENTATION IN MACAQUE PRIMARY VISUAL CORTEX

Wahiba Taouali[1,2], *Giacomo Benvenuti*[1,2], *Frédéric Y. Chavane*[1,2], *Laurent U. Perrinet*[1,2,*]

[1] Institut de Neurosciences de la Timone – UMR7289, CNRS, France
[2] Aix-Marseille Université, France
[*] laurent.perrinet@univ-amu.fr

Natural scenes generally contain objects in motion. The local orientation of their contours and the direction of motion are two essential components of visual information which are processed in parallel in the early visual areas. Focusing on the primary visual cortex of the macaque monkey (V1), we challenged different models for the joint representation of orientation and direction within the neural activity. Precisely, we considered the response of V1 neurons to an oriented moving bar to investigate whether, and how, the information about the bar's orientation and direction could be encoded dynamically at the population activity level.

For that purpose, we used a decoding approach based on a space-time receptive field model that encodes jointly orientation and direction. We based our decoding approach on the statistics of natural scenes by first determining optimal space-time receptive fields (RFs) that encode orientation and direction. For this, we first derived a set of dynamic filters from a database of natural images [1] and following an unsupervised learning rule [2]. More generally, this allows us to propose a dynamic generative model for the joint coding of orientation and direction. Then, using this model and a maximum likelihood paradigm, we infer the most likely representation for a given network activity [3, 4]. We tested this model on surrogate data and on extracellular recordings in area V1 (67 cells) of awake macaque monkeys in response to oriented bars moving in 12 different directions. Using a cross-validation method we could robustly decode both the orientation and the direction of the bar within the classical receptive field (cRF).

Furthermore, this decoding approach shows different properties: First, information about the orientation of the bar is emerging *before* entering the cRF if the trajectory of the bar is long enough. Second, when testing different orientations with the same direction, our approach unravels that we can decode the direction and the orientation independently. Moreover, we found that, similarly to orientation decoding, the decoding of direction is dynamic but weaker. Finally, our results demonstrate that the orientation and the direction of motion of an ambiguous moving bar can be progressively decoded in V1. This is a signature of a dynamic solution to the aperture problem in area V1, similarly to what was already found in area MT [5].

References

1. Burge, Geisler (2015) *Nature* Communications, 6:7900, 10.1038/ncomms8900
2. Perrinet (2010) *Neural Computation*, 22(7):1812–36
3. Jazayeri, Movshon (2006) *Nat Neurosci*, 9(5):690–696
4. Taouali, Benvenuti, Wallisch, *et al.* (2015) *J Neurophysiol*
5. Pack, Born (2001) *Nature*, 409(6823):1040–1042

Acknowledgements

This work was supported by BrainScaleS (EC FP7–269921) and FACETS-ITN (FP7–237955).

BEHAVIOR-RELATED SPIKE SYNCHRONIZATION IN MONKEY MOTOR CORTEX DURING AN INSTRUCTED DELAY REACH-TO-GRASP TASK

Emiliano Torre[1,*], *Pietro Quaglio*[1], *Michael Denker*[1], *Thomas Brochier*[2], *Alexa Riehle*[2,1,3], *Sonja Grün*[1,4,3]

[1] INM-6/IAS-6 & JARA BRAIN Institute I, Jülich Research Centre, 52425 Jülich, Germany
[2] Institut de Neurosciences de la Timone, UMR 7289, CNRS-AMU, Marseille, France
[3] RIKEN Brain Science Institute, Wako Shi, Japan
[4] Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany
[*] e.torre@fz-juelich.de

A hotly debated question among neuroscientists is whether spike synchronization at millisecond precision among groups of neurons in the cerebral cortex plays a role in information coding. A network model known as synfire chain [1] was proposed. It performs computations and transmits information by the propagation of spike synchronization across successive groups of neurons. Studies performed on data with simultaneous recordings of only a few neurons provided experimental evidence that low-order (mainly pairwise) synchronization occurs in relation to behavior (*e.g.*, [2]).

Modern electrophysiology provides today the possibility to simultaneously sample the spiking activity of largely more than 100 neurons *in vivo*. This opens the possibility to investigate the presence of correlations in larger populations of cells, and their relation to behavior. To this end, we recently published a method, named SPADE (spike pattern detection and evaluation [3]), which searches massively parallel spike train data for subgroups of neurons synchronizing their activity significantly more often than expected on the basis of the neuronal firing rates only. The method exploits a combination of data mining and statistical techniques to solve the computational and multiple testing problems raised by the high dimensionality of this type of data.

Here we apply our method to simultaneous recordings using 100-electrode Utah arrays implanted in motor cortex of two monkeys engaged in an instructed delay reach-to-grasp task [4], to determine the emergence of spike synchronization in relation to behavior. We show that a multitude of patterns of synchronous (millisecond precision) spikes arise during task execution. Patterns are preferentially aligned along a medio-lateral orientation on the brain surface. Their occurrence is highly specific to behavior, indicating that different behaviors are associated to the synchronization of different groups of neurons. However, groups of pooled patterns that overlap in neuronal composition do not exhibit high specificity, suggesting that exclusive cell assemblies become active during different behaviors, but can recruit partly identical neurons. These findings are consistent across multiple recording sessions analyzed in the two monkeys.

Acknowledgments

SMHB, EU BrainScaleS, HBP (EU 604102), ANR-GRASP, Riken-CNRS Research Agreement

References

1. Abeles (1991) Corticonics: Neural circuits of the cerebral cortex. Cambridge Univ Press
2. Riehle, Grün, Diesmann, Aertsen (1997) *Science* 278:1950–1953
3. Torre, Picado-Muino, Denker, *et al.* (2013) *Front Comput Neurosci* 7:132
4. Riehle, Wirtssohn, Grün, Brochier (2013) *Front Neural Circuits* 7:48

EMERGENT COORDINATION UNDERLYING LEARNING REACH TO GRASP WITH A BRAIN MACHINE INTERFACE

Mukta Vaidya[1,*], *Karthikeyan Balasubramanian*[1], *Leslie Osborne*[1], *Joshua Southerland*[2], *Islam Badreldin*[3], *Ahmed Eleryan*[4], *Kelsey Shattuck*[5], *Suchin Gururangan*[1], *Karim Oweiss*[3], *Andrew Fagg*[2], *Nicholas G. Hatsopoulos*[1]

[1] University of Chicago, Chicago, Illinois, USA
[2] University of Oklahoma, Norman, Oklahoma, USA
[3] University of Florida, Gainesville, Florida, USA
[4] Michigan State University, East Lansing, Michigan, USA
[5] University of Massachusetts, Amherst, Massachusetts, USA
[*] mukta.p.vaidya@gmail.com

The development of coordinated reach to grasp has been well-studied in infants and children; as children age, their inter-joint coordination becomes more stereotyped [1, 2]. Less is known about the role of motor cortex in developing coordinated reach-to-grasp. Similarly, studies have shown that after amputation, the cortical area previously involved in the control of the lost limb undergoes reorganization [3, 4], but it has not been previously shown that cortical neurons can be used to control a brain machine interface in chronically amputated primates. Here we studied the emergence of coordinated reach-to-grasp behavior in rhesus macaques that had been the recipients of therapeutic amputations, and were being taught to cortically control a robotic arm through operant conditioning using neurons that weren't explicitly reach- or grasp-related. Over the course of training, stereotypical patterns emerged and stabilized in the cross-covariance between the reaching and grasping velocity profiles, between pairs of neurons involved in decoding reach and grasp, and, to a lesser extent, between other stable neurons in the network. In addition, we found that the degree to which a pair of neurons covaries, either positively or negatively, has a direct effect on the extent to which the behavior is coordinated. This paradigm gives us a unique model for studying the development of coordination of a novel motor behavior at the behavioral and cortical level. In addition, the possibility of training subjects to perform a naturalistic motor task by modulating cortical neurons using an artificial mapping and influencing large-scale network activity in a lasting manner could have clinical implications for patients with amputations or strokes.

References

1. Von Hofsten, Fazel-Zandy (1984) *J Exp Child Psych*, 38(2):208–19
2. Kuhtz-Buschbeck, Stolze, Jöhnk, *et al.* (1998) *Exp Brain Res*, 122(4):424–32
3. Qi, Stepniewska, Kaas (2000) *J Neurophysiol*, 84(4):2133–47
4. Wu, Kaas (1999) *J Neurosci*, 19(17):7679–97

USING RELATIONAL MAPS TO IDENTIFY FUNCTIONAL NEURONAL ENSEMBLES

Carlos E. Vargas-Irwin[1,*], *Jonas B. Zimmermann*[1], *David M. Brandman*[1], *Michael J. Black*[2], *John P. Donoghue*[1]

[1] Neuroscience Department, Brown University, Providence, Rhode Island, USA
[2] MPI for Intelligent Systems, Tubingen, Germany
[*] carlos_vargas_irwin@brown.edu

Neurons often display complex response properties reflecting multiple behavioral and cognitive parameters at various time scales. The analysis of cortical activity frequently focuses on tabulating groups of neurons with specific properties, but a rigorous mathematical framework to evaluate the separation between these putative neuronal subtypes is lacking. Here, we present a novel method to quantify and display the similarity between the firing patterns of individual neurons, identifying functional sub-ensembles based on spike train similarity.

We wish to identify neurons with equivalent informational content, meaning those that have similar sets of parameters governing their activity. Relational mapping using the SSIMS algorithm [1] allows us to evaluate the similarity between the firing patterns emitted by a single neuron at various time points (corresponding to multiple experimental conditions). This is accomplished by embedding the neural data into a high-dimensional pairwise similarity space based on spike train metrics [2] and then projecting the data into a more compact (low-dimensional) representation using t-SNE [3]. Intuitively, neurons with equivalent informational content should produce similar relational maps. In other words, if two conditions generate similar spiking patterns in neuron A, they should also generate similar spiking patterns in neuron B (and conversely, conditions that generate different spiking patterns should also do so for both neurons). Note that the spiking patterns for each neuron could be completely different, what matters is the relative similarity across conditions. This can be quantified by examining the correlation between the matrices of pair-wise distances representing the relational map for each neuron.

Relational encoding using SSIMS expands the scope of analysis beyond rate-based methods, making it possible to: (a) Take into account single trial data instead of averages, (b) Evaluate information inherent in precise spike timing, even when examining relatively large time windows, (c) Generalize across encoding schemes, finding equivalence between rate and precise temporal timing codes, and (d) Detect non-synchronous equivalence between activity patterns over a specified time window. Furthermore, this approach is applicable to single neurons as well as larger neuronal ensembles. We validate our method using synthetic data as well as cortical recordings from rhesus macaques performing a reaching and grasping task [4]. Our results show a continuous spectrum of neuronal diversity reflecting graded combinations of sensory-motor parameters.

References

1. Vargas-Irwin, *et al.* (2015) *Neural Comput* 27:1–31
2. Victor, Purpura (1997) *Network: Computation in Neural Systems* 8(2):127–164
3. van der Maaten, Hinton (2008) *J Machine Learn Res* 9:2579–2605
4. Vargas-Irwin, *et al.* (2015) *J Neurosci* 35(30):10888–97

DYNAMICS OF NEURONAL ENSEMBLES IN THE MAIN OLFACTORY BULB

Spencer Waddle [1], *Edward Lyman* [1,2], *Krishnan Padmanabhan* [3,*]

[1] Department of Physics, University of Delaware, Newark, Delaware, USA
[2] Department of Chemistry, University of Delaware, Newark, Delaware, USA
[3] Department of Neuroscience, University of Rochester School of Medicine, Rochester, NY, USA
[*] krishnan_padmanabhan@urmc.rochester.edu

Spontaneous activity across ensembles of neurons can reveal important features of network architecture, the responses of networks to inputs, and ultimately the encoding and decoding of sensory stimuli. In the olfactory system of the mammal, the main olfactory bulb is one of the first processing centers for sensory information. Complex interactions between the principle excitatory cells, the mitral and tufted cells, and local inhibitory neurons, govern the dynamics of activity, shaping how information is transmitted to higher processing centers. Understanding the dynamics of activity among these neurons, and the effect of those dynamics on olfactory coding remains an open question.

Using high-density recordings in the main olfactory bulb, we characterized the dynamics of neuronal ensembles of mitral/tufted cells during epochs of sensory independent spontaneous activity. Complex interactions among populations of neurons were uncovered using maximum entropy models, providing important insight into structure of activity within the bulb. In addition to examining the features of activity across ensembles of neurons, we also developed a new approach to examine the effect that previous patterns of activity had on shaping future patterns of activity. Together, our work provides an important clue into how activity patterns in the bulb are evolved from the interactions between neurons, and how this activity is affected by the history of activity that preceded it.

NEURONAL POPULATIONS IN MACAQUE PRIMARY VISUAL CORTEX ENCODE UNCERTAINTY DURING PERCEPTUAL DECISIONS

Edgar Y. Walker[1,*], *R. James Cotton*[1], *Wei Ji Ma*[2], *Andreas S. Tolias*[1]

[1] Department of Neuroscience, Baylor College of Medicine, Houston, Texas, USA
[2] Center for Neural Science, New York University, New York, New York, USA
[*] eywalker@bcm.edu

Organisms typically base their perceptual decisions on noisy and ambiguous sensory observations. There can be top-down sensory uncertainty due to ambiguity and bottom-up sensory uncertainty due to noise in the perception system. In many tasks, optimal performance requires the brain to represent and utilize, on every trial, knowledge about the level of both bottom-up and top-down uncertainty. In earlier work, we introduced a simple orientation classification task with controlled top-down and bottom-up sensory uncertainty for which optimal performance requires the observer to utilize sensory uncertainty on a trial-by-trial basis, and demonstrated that both humans and monkeys do so.

Here, our goal is to identify the neural substrates of this computation. The theoretical framework of probabilistic population coding (PPC) postulates that the brain decodes sensory uncertainty from a noisy pattern of population activity through a likelihood function over the stimulus. This function represents the probability of the observed pattern given each hypothesized stimulus value, and the width of this function is a proxy of sensory uncertainty. We hypothesized that the width of the likelihood function that can be decoded from trial-to-trial population activity in primary visual cortex (V1) is informative about the animal's decision. To test this hypothesis, we trained macaque monkey on our classification task. We implanted a chronic multi-electrode array in V1 to record the population activity while the monkey performed the classification task. On each trial, we decoded from single-trial V1 population activity the width of the likelihood function under a Poisson-like population coding model.

The monkey's trial-by-trial classification decisions were better predicted by a Bayesian model utilizing the width of the likelihood function than by a non-Bayesian model only utilizing a point estimate of the stimulus orientation. We also tested the models on a shuffled data where the widths of the likelihood functions were shuffled among trials with identical stimulus condition, effectively removing trial-by-trial correlation between the likelihood width and the monkey's decision, while keeping the average correlation between likelihood widths and stimulus orientations intact. We observed that Bayesian model's performance dropped significantly on the shuffled data when compared to the fits on the original data, supporting our hypothesis that trial-by-trial variation in the likelihood width is informative about the decision. This result provides population-level physiological evidence in support of the PPC framework.

REMEMBERING VISUAL MOTION OR LOCATION: BEHAVIORAL MEASURES AND PREFRONTAL ACTIVITY DURING MEMORY-GUIDED PERCEPTUAL DECISIONS

Klaus Wimmer[1,2,*], *Philip Spinelli*[2], *Aaron Ketting-Olivier*[2], *Albert Compte*[1], *Tatiana Pasternak*[2]

[1] Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain
[2] Department of Neuroscience, University of Rochester, Rochester, New York, USA
[*] wimmer.klaus@gmail.com

The lateral prefrontal cortex (LPFC) is implicated in working memory and in selective attention. However, the nature of its role in these processes is still debated, with a storage function being more consistently supported for locations than for other stimulus features maintained in working memory. Working memory for locations has been probed with oculomotor delayed response tasks, revealing persistent activity of LPFC neurons that is selective to cue location. On the other hand, delay activity for features has been recorded under different behavioral paradigms that require comparisons between current and remembered stimuli. During such tasks, stimulus-selective activity during the delay is usually transient, appearing in different neurons at different times. It is unknown whether these distinct patterns of population activity reflect a difference in the LPFC storage mechanisms of stimulus features and their locations, or the difference in the role of LPFC in these behavioral tasks.

We used matched behavioral tasks to examine how the information about motion direction or location is retained, integrated and utilized while monkeys perform comparisons between the current and remembered random-dot stimuli. In the memory for direction task, subjects reported whether two stimuli, separated by a delay, moved in the same or in different directions. In the memory for location task, stimuli were identical, but subjects reported whether they appeared at the same or at different locations. In psychophysical experiments, the precision with which motion direction and location are retained was measured over a range of delays, revealing striking differences in the retention of the two types of information. While memory for location persisted with increasing delay (up to 3 seconds), the retention of direction rapidly deteriorated, suggesting that location and direction may be supported by different neuronal mechanisms.

We then examined neuronal activity in the LPFC while monkeys performed the two tasks. We reasoned that if LPFC is equally engaged in storage during these two tasks, different mechanisms should be revealed by contrasting delay period activity. We found that many LPFC neurons show selectivity for direction in response to motion during the direction task and location-selectivity during the location task. The parallels in the behavior of LPFC neurons during the two tasks were also apparent during the delay, with similar patterns of delay activity in single neurons. In both cases, this activity reflected the direction or location of the preceding stimulus but this selectivity was mostly transient, occurring in different neurons at different times and only a few neurons presented selectivity sustained for most of the delay, suggesting a distributed network code. By using linear decoders we found that both direction and location could be reliably decoded during the delay from the LPFC population activity, with comparable stability of decoding performance over time.

The similarity in the nature of delay activity recorded during the memory-guided location and direction comparison tasks is in contrast to the difference in the subject's ability to retain information about the two stimulus dimensions. This raises the question about the nature of prefrontal contribution to the retention of information during memory-guided perceptual decisions.

ATTENDEE INFO AND AUTHOR INDEX

Entries for speakers, oral authors, poster authors, session moderators, and attendees are listed with last name, first name, affiliation, and email. Page numbers in bold (**00**) indicate presenting authorship, in italics (*00*) indicate session moderation, in normal typeface (00) indicate non-presenting authorship or other reference in the program text.