Collaborative Research in Computational Neuroscience (CRCNS)

2017 Annual PI Meeting

Salomon Center for Teaching, Room 001 and Sayles Hall, Main Quad, Brown University

and

Workshop on Integrating Dynamics and Statistics in Neuroscience

Institute for Computational and Experimental Research in Mathematics (ICERM), 121 South Main St., 11th Floor

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WELCOME!

We are pleased to welcome you to Providence, Rhode Island, for the Collaborative Research in Computational Neuroscience (CRCNS) 2017 Principal Investigator's meeting, hosted by Brown University, the Brown Institute for Brain Science (BIBS) and the Institute for Computational and Experimental Research in Mathematics (ICERM).

The CRCNS program is managed by a consortium of research funders in the US (NSF and NIH), France (ANR), Germany (BMBF) and Israel (BSF). The annual meeting brings together principal investigators from grants funded under the program to discuss research progress and future directions of the field.

The first two days will be devoted to talks and posters from the CRSNS funded researchers, while the third day will be reserved for a workshop on Integrating Dynamics and Statistics in Neuroscience, hosted by ICERM. This year, we have added a panel discussion and posters on outreach, training, and broader impact efforts in the computational neuroscience community.

— *Matthew Harrison, Stephanie Jones, Hakon Heimer*
Organizers

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CRCNS 2017 PROGRAM

WEDNESDAY, June 14, 2017		
8:00-8:40	*BREAKFAST and REGISTRATION (Salomon Center)*	
8:40-9:00	Opening Remarks	**Matthew Harrison and Stephanie Jones,** *Brown University*
9:00-10:15	**SESSION 1**	**CHAIR: Michael Frank,** *Brown University*
9:00-9:50	Keynote Lecture: Deep reinforcement learning: Recent developments in AI and their implications for neuroscience	**Matthew Botvinick,** *DeepMind and University College London*
9:50-10:15	Toward socially aware computing and artificial intelligence	**Ming Hsu,** *University of California, Berkeley*
10:15-10:45	*BREAK*	
10:15-12:00	**SESSION 2**	**CHAIR: Carl Saab,** *Brown University*
10:45-11:10	Pain intensity coding in the anterior cingulate cortex	**Jing Wang,** *New York University Langone Medical Center*
11:10-11:35	Magnetic resonance elastography for brain studies with intrinsic actuation	**Keith Paulsen,** *Dartmouth University*
11:35-12:00	What wakes us up? Networked circadian clocks	**Erik Herzog,** *Washington University in St. Louis* **Hans-Peter Herzel,** *Institute for Theoretical Biology, Berlin*
12:00-1:00	*LUNCH (poster setup in Sayles Hall)*	
1:00-2:15	**SESSION 3**	**CHAIR: Wael Asaad,** *Brown University*
1:00-1:25	Striatal interneuron subtypes coordinate distinct aspects of network dynamics and motor plans	**Xue Han,** *Boston University*
1:25-1:50	Cell-specific pallidal intervention induces long-lasting motor recovery in dopamine depleted mice	**Aryn Hillary Gittis,** *Carnegie Mellon University*
1:50-2:15	Force encoding in muscle spindles: Towards a multiscale model for sensorimotor feedback control	**Lena Ting,** *Emory University and Georgia Institute of Technology*
2:15-2:45	Broader Impacts Panel	**Thomas Serre,** *Brown University*
2:15-2:45	Undergraduate training in computational neuroscience	**Rick Gerkin,** *Arizona State University* **Venkatesh Gopal,** *Elmhurst College* **John Hale,** *Cornell University* **Mitra Hartmann,** *Northwestern University* **Michael Spezio,** *Scripps College*
2:45-3:15	*BREAK*	
3:15-4:30	**SESSION 4**	**CHAIR: David Sheinberg,** *Brown University*
3:15-3:40	Optogenetic probing of glycinergic neuron function in brainstem respiratory circuits	**Yaroslav Molkov,** *Georgia State University*
3:40-4:05	Patient-specific models of local field potentials recorded from deep brain stimulation electrodes	**Cameron McIntyre,** *Case Western Reserve University*
4:05-4:30	OPTISTIM - Combining computational neuroscience and electrophysiology for optimal cortical electric stimulation	**Dana Brooks,** *University of Utah and Northeastern University*
4:30-5:00	*Leisure time*	
5:00-8:00	**POSTER PRESENTATIONS/RECEPTION** *(Sayles Hall)*	

THURSDAY, June 15, 2017

8:15-8:55	*BREAKFAST and REGISTRATION (Salomon Center)*	
8:40-9:00	Opening Remarks	**Matthew Harrison and Stephanie Jones,** *Brown University*
9:00-10:15	**SESSION 5**	**CHAIR: Takeo Watanabe,** *Brown University*
9:00-9:50	Keynote Lecture: Data-driven mimicking neural encoding/decoding systems	**Shin Ishii,** *Kyoto University, Kyoto, Japan*
9:50-10:15	A fast, foveated, fully convolutional network model for human peripheral vision	**Ruth Rosenholtz,** *Massachusetts Institute of Technology*
10:15-10:45	*BREAK*	
10:45-12:00	**SESSION 6**	**CHAIR: Amitai Shenhav,** *Brown University*
10:45-11:10	A two-stage model of sensory discrimination: An alternative to drift-diffusion	**Michael Landy,** *New York University*
11:10-11:35	Learning symbolic representations for planning in hierarchical reinforcement learning	**George Konidaris,** *Brown University*
11:35-12:00	Modelling theory of mind in the volunteer's dilemma using Partially Observable Markov Decision Processes (POMDPs)	**Rajesh Rao,** *University of Washington*
12:00-1:00	**LUNCH/POSTER PRESENTATIONS** *(Sayles Hall)*	
1:00-2:15	**SESSION 7**	**CHAIR: Wilson Truccolo,** *Brown University*
1:00-1:25	Finding essential nodes for integration in the brain using network optimization theory	**Hernan Makse,** *City College of New York*
1:25-1:50	Neural dynamics of the formation of spatial maps during fully-mobile human navigation	**Scott Makeig,** *University of California, San Diego*
1:50-2:15	Dynamic network analysis of human seizures for therapeutic intervention	**Eric Kolaczyk,** *Boston University*
2:15-2:45	Funding Q&A	**Program Officers**
2:45-3:15	*BREAK*	
3:15-4:55	**SESSION 8**	**CHAIR: Theresa Desrochers,** *Brown University*
3:15-3:40	Correlated variability in cerebral cortex at criticality during vision	**Ralf Wessel,** *Washington University in St Louis*
3:40-4:05	The generation and subtraction of predictions enhances neural coding and behavioral detection of external stimuli in an electric fish	**Nathaniel Sawtell,** *Columbia University*
4:05-4:30	Using high-order acoustic and neural response statistics to categorize sounds in that mammalian auditory midbrain	**Heather Read,** *University of Connecticut*
4:30-4:55	Maximum entropy models of population codes based on random projections	**Elad Schneidman,** *Weizmann Institute of Science*
4:55-6:30	*LEISURE TIME*	
6:30-9:00	**BANQUET and the Dorrance** *(60 Dorrance St.)*	

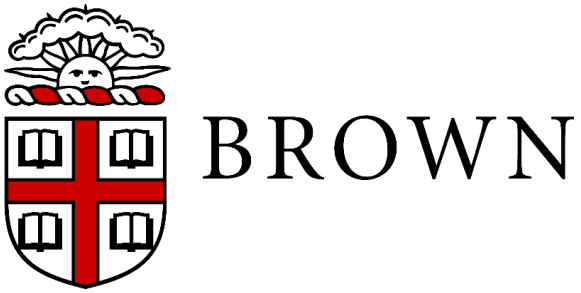
WORKSHOP: Integrating Dynamics and Statistics in Neuroscience

To be held at the Institute for Computational and Experimental Research in Mathematics (ICERM), adjacent to Brown's campus.

FRIDAY, June 16, 2017

8:15-9:00	BREAKFAST and REGISTRATION	
9:00-9:10	Opening Remarks	
9:10-9:45	The problem of dynamic network analysis	**Robert Kass,** *Carnegie Mellon University*
9:45-10:20	Integrating physical and statistical models in neuroscience: some examples	**Mark Kramer,** *Boston University*
10:20-10:50	BREAK	
10:50-11:25	Building functional nervous system networks from the bottom up	**Henry Abarbanel,** *University of California, San Diego*
11:25-12:00	Dynamics to coding through biophysics of single neurons	**Adrienne Fairhall,** *University of Washington*
12:00-1:00	LUNCH	
1:00-1:35	Neurobiology, brain imaging and information processing	**Dimitris Pinotsis,** *Massachusetts Institute of Technology*
1:35-2:10	Inferring the source of fluctuation in neuronal activity	**Shigeru Shinomoto,** *Kyoto University*
2:10-2:40	BREAK	
2:40-3:15	Data-driven geometry learning for parametrically-dependent dynamical systems with application to neuronal dynamics	**Ronald Coifman,** *Yale University*
3:15-3:30	Formal discussion in lecture hall	
3:30-5:00	Informal discussion at ICERM	

2017 HOSTS and SUPPORTERS



Thank you to Brown University's offices and departments for their generous contributions to the CRCNS meeting:

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Department of Cognitive, Linguistic, and Psychological Sciences
Department of Neuroscience
Department of Biostatistics
Graduate School

Botvinick, Matthew - Keynote

Deep reinforcement learning: Recent developments in AI and their implications for neuroscience

Matthew Botvinick
DeepMind and Gatsby Computational Neuroscience Unit, University College London, London, UK

The last few years have seen an explosion of progress in artificial intelligence. Neuroscientists have been rightly interested in what opportunities these developments might have for advancing brain research, but their focus to this point has been primarily on AI systems trained through supervised learning. The presentation will summarize recent AI models that cross deep learning with reinforcement learning, and consider the opportunities that such 'deep RL' models present for neuroscience, as well as ways in which brain research might in turn inform this side of AI.

Hsu, Ming

Toward socially aware computing and artificial intelligence

Ming Hsu, Petr Karashchuk, Adrianna Jenkins
University of California, Berkeley, Berkeley, CA, USA

There is increasing concern that the proliferation of AI-driven automation—particularly in areas dealing with labor markets, education, and criminal justice—may perpetuate and even amplify preexisting biases and social inequities facing certain groups of individuals. This is particularly challenging in cases where the typically large datasets used to train the AI systems may themselves be skewed.

However, despite the rich social scientific literature on these topics, relatively little attention has been paid to computational tools that can recognize, quantify, and correct social biases at the scale necessary to address these societal challenges. Here we connect (i) computational models developed from our group that maps stereotypes about specific groups to a small number of core dimensions, and relating them to behavior, and (ii) recent explosion in availability of text corpora in order to characterize and predict stereotypes about different social groups, as well as their real-world consequences. Our basic premise is that the language people use to describe and interpret the world reflects, and possibly even shapes, their thoughts and actions.

Specifically, we used *word embedding* models, which translate words and phrases into vectors of real numbers, trained on two large text corpora, Google News and Twitter, to investigate and compare the extent to which they reveal stereotypes about different social groups and their real-world consequences. We show that word embeddings of both text corpora can be used to make accurate predictions of stereotypes about social groups identified by occupation, geography, and race. Furthermore, such predictions generalize across social categories, such that models trained on e.g., geography and occupation can predict stereotypes about different races. Next, we show that word embeddings can successfully make predict disparate treatment of different groups in lab and field settings. Finally, we consider the possibility of "de-biasing" AI systems training on these data.

Keywords: stereotyping, discrimination, neuroeconomics, social psychology, computational linguistics

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Wang, Jing

Pain intensity coding in the anterior cingulate cortex

Jing Wang, Zhe Chen
New York University Langone Medical Center, New York, NY, USA

Pain is a complex sensory and affective experience, and it is not yet known how this experience is encoded in the brain. Previous imaging and EEG studies in humans have identified several regions of importance, but these studies are limited by their spatial and temporal resolutions and hence do not provide precise coding schemes. The anterior cingulate cortex (ACC) has been shown to play a critical role in the representation of the aversive component of pain. In our study, we combined experimental and computational approaches to test the hypothesis that the ACC can encode the intensity of pain. We examined neural firing in the ACC of rodents before, during and after the application of a range of noxious peripheral stimulations. We found a number of neurons that responded to noxious stimulations; a

subset of these neurons also responded to the intensity of stimulations by increasing their firing rates. When we used a machine learning approach to analyze the firing rate of individual neurons, we were able to accurately predict pain intensities based on neural spike data. To confirm the functional relevance of intensity coding in the ACC, we used optogenetics to modify neural function. Our results show that ACC neurons can bidirectionally control the aversive response to noxious stimulations. Finally, we found that chronic pain altered acute pain intensity representation in the ACC, leading to an enhanced aversive experience. Therefore, our study provides evidence for a crucial role of the ACC in pain intensity coding.

Keywords: pain, decoding, ACC, anterior cingulate cortex

Paulsen, Keith

Magnetic resonance elastography for brain studies with intrinsic actuation

Keith Paulsen[1,2], Ligin Solamen[1], Scott Gordon[1], Wei Zeng[1], Heather Wishart[3], Matthew McGarry[4], Elijiah Van Houten[5], Ingolf Sack[6], John Weaver[2]
[1]*Thayer School of Engineering, Dartmouth College, Hanover, NH, USA*
[2]*Department of Radiology, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA*
[3]*Department of Psychiatry, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA*
[4]*Department of Biomedical Engineering, Columbia University, New York, NY, USA*
[5]*Department of Mechanical Engineering, University of Sherbrooke, Sherbrooke, QC, Canada*
[6]*Department of Radiology, Charité University, Berlin, Germany*

Magnetic Resonance Elastography (MRE) is an MRI-based technique that estimates the spatial distribution of mechanical properties in tissues as a new form of contrast that offers information which may have clinical significance. Traditionally, MRE has required the anatomy of interest to be mechanically actuated (vibrated) by an external source that drives mechanical waves through tissue in the 50-100Hz range; the amplitude, phase and direction of which are sensed by the scanner through specialized pulse sequences with motion-encoding gradients. In the brain, external vibration has been successful and studies have reported on the viscoelastic mechanical properties of normal and diseased parenchyma. However, mechanical wave transmission is challenging because of the natural motion damping effects of the cranial system, and neuro-exam delivery is more difficult because it requires extra equipment (e.g., external actuators) that can be cumbersome and uncomfortable for patients. Measuring tissue motion based on the brain's natural cerebrovascular pulsations is possible, and is attractive for clinical brain MRE because no additional equipment is required, and standard flow sequences that are readily available on commercial scanners can be used to measure 3D displacement fields throughout the volume of interest. As a result, intrinsic MRE is really added as an additional sequence in ongoing neuro-imaging studies of healthy and diseased brain. In this presentation, we will discuss our experience with the development and use of intrinsic actuation brain MRE. Specifically, we will discuss results from phantom studies using a novel 1 Hz mechanical actuation system, new 3D versus 4D flow sequence acquisitions that reduce exam time substantially (e.g., from 30 minutes to 10 minutes or less), and initial clinical results in normal brain, and in patients with brain tumor, multiple sclerosis, and hydrocephalus. Studies to investigate intrinsic MRE in functional brain studies are also underway, and will be described.

Keywords: Magnetic Resonance Elastography, intrinsic actuation, brain tumor

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Herzog, Erik and Herzel, Hans-Peter

What wakes us up? Networked circadian clocks

Bharath Ananthasubramaniam[1], Cristina Mazuski[2], Christoph Schmal[1], **Erik D Herzog**[1], **Hans-Peter Herzel**[2]

[1]*Institute for Theoretical Biology, Berlin, Germany*
[2]*Washington University, St. Louis, MO, USA*

Daily rhythms in physiology and behavior arise from the coordinated activities of circadian cells in the brain and body. Using experimental and computational methods, this talk will explore the mechanisms by which circadian cells in the brain synchronize their intrinsic near-24 hour rhythms to each other and to environmental timing cues. We will show that key neurons in the master circadian clock depend on specific firing patterns to entrain daily rhythms in other cells and in behavior. By studying the synchronization dynamics, we find the network topologies and properties that couple circadian cells to each other.

Han, Xue

Striatal interneuron subtypes coordinate distinct aspects of network dynamics and motor plans

Xue Han
Boston University, Boston, MA, USA

Basal ganglion regulates movement, and disruption of basal ganglion network could lead to movement disorders, such as Parkinson's disease and Tourette's syndrome. Striatum, the input structure of the basal ganglion, consists mainly medium spiny projecting/output neurons (MSNs) that comprise ~95% of all striatal neurons, along with a sparse population of GABAergic and cholinergic interneurons. The sparse distribution of striatal interneurons has made it difficult to assess their contributions to striatal network dynamics and related motor functions. Building upon recent improvements in wide-field calcium imaging and genetic tagging techniques, we here monitored the activity of GABAergic parvalbumin+ interneurons (PV cells) and cholinergic interneurons (ChIs), in tandem with local MSN populations to better understand functional interactions of these interneuron types with striatal output MSNs. We discovered that PV interneurons tightly tracked motor output, MSN cell population activity, and interacted with nearby MSNs during vigorous motor output. ChIs, in contrast, poorly tracked movement but were selectively engaged during discrete time points in on-going motor plans. Furthermore, unlike PV interneurons, correlated ChI-MSN pairs were observed throughout the extent of the striatum, supporting a capacity for CHIs to augment MSN activity even over great distances. Together, these results demonstrate the unique capacity of striatal interneurons to organize networks of output/projecting MSNs in support of discrete aspects of motor control.

Keywords: Generalized linear model, network dynamics, optogenetics, large scale dataset

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Gittis, Aryn Hilary

Cell-specific pallidal intervention induces long-lasting motor recovery in dopamine depleted mice

Aryn Hilary Gittis[1], Kevin Mastro[2], Kevin Zitelli[1], Amanda Willard[1], Jonathan Rubin[2]
[1]*Carnegie Mellon University, Pittsburgh, PA, USA*
[2]*University of Pittsburgh, Pittsburgh, PA, USA*

The identification of distinct cell-types within the basal ganglia has played a critical role in our understanding of basal ganglia function and the treatment of neurological disorders. The external globus pallidus (GPe) is a key contributor to motor suppressing pathways in the basal ganglia, yet its neuronal heterogeneity has remained an untapped resource for therapeutic interventions. Here, we demonstrate that optogenetic interventions that dissociate the activity of two neuronal populations in the GPe – elevating the activity of PV-GPe neurons over that of Lhx6-GPe neurons – restores movement in dopamine depleted mice and attenuates pathological activity of basal ganglia output neurons for hours beyond stimulation. These results establish the utility of cell-specific interventions in the GPe to target functionally distinct pathways, with the potential to induce long-lasting recovery of movement despite the continued absence of dopamine.

Keywords: basal ganglia, optogenetics, Parkinson's

Ting, Lena

Force encoding in muscle spindles: towards a multiscale model for sensorimotor feedback control

Lena Ting[1], Kyle Blum[1], Timothy Cope[1,2], Kenneth Campbell[3], Paul Nardelli[2], Brian Horslen[1]
[1]*Biomedical Engineering, Emory University and Georgia Institute of Technology, Atlanta, GA, USA*
[2]*School of Biological Sciences, Georgia Institute of Technology, Atlanta, GA, USA*
[3]*Physiology, University of Kentucky, Lexington, KY, USA*

Proprioceptive information from muscle spindle sensory afferents plays a critical role in movement, yet we lack mechanistic models to tease apart how physiological and pathological at multiple scales changes alter sensorimotor control. Altered muscle spindle function is implicated in a wide range of sensorimotor impairments including dystonia, hypotonia, ataxia, and Parkinson's disease, as well as in spasticity, which affects those with stroke, cerebral palsy, spinal cord injury, and other neural injuries. But, despite decades of work, the basic mechanisms of muscle spindle sensory encoding are not well understood, and thus their role in sensorimotor disorders have not been clearly identified.

Our **objective is to develop a novel, mechanistic, multi-scale model of muscle spindle sensory encoding** to that will allow us to test hypotheses about the role of molecular, cellular, and circuit level mechanisms on sensorimotor control in healthy and impaired humans and animals. We will build a neuromechanical muscle spindle model incorporating muscle sarcomere cross-bridge dynamics, mechanical properties of the spindle-bearing musculotendon, and biophysical membrane properties of muscle spindle afferent neurons and motor neurons. The model will be a useful platform to integrate classical and new findings of muscle spindle function spanning molecular and behavioral levels.

We will identify sources of history-dependent characteristics of muscle spindle firing rates. Specifically, we will identify the mechanisms behind initial bursts, rate relaxation at constant length, and dynamic response modulation to ramps. We will dissociate the relationship of muscle spindle firing rates to kinetic (force) versus kinematic (length) variables using novel stretch perturbations applied to intact rat muscle *in vivo* (**Aim 1**), single muscle fibers from the same animals *in vitro* (**Aim 2**), and a multi-scale neuromechanical model incorporating cross-bridge dynamics, musculotendon viscoelastic properties, and spiking neuron models (**Aim 3**). We will also use the model to interpret our existing data from animals with sensory loss.

Keywords: sensory coding, muscle mechanics, proprioception, motor control

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Molkov, Yaroslav

Optogenetic probing of glycinergic neuron function in brainstem respiratory circuits

Yaroslav Molkov[1], Ana Abdala[2], William Barnett[1], Jeffrey Smith[3], Julian Paton[2]
[1]*Georgia State University, Atlanta, GA, USA*
[2]*University of Bristol, Bristol, United Kingdom*
[3]*National Institutes of Health, Bethesda, MD, USA*

Respiratory movements in mammals are produced by the brainstem respiratory central pattern generator (CPG). The normal breathing rhythm (eupnea) includes three phases of the cycle: inspiration, post-inspiration (post-I), and the second phase of expiration (E2). Synaptic inhibition in the CPG circuits has been proposed to be essential for generating this eupneic pattern. However, the importance of inhibitory interactions in the respiratory CPG as well as types of inhibitory neurotransmitters involved has been established based on pharmacological and modeling studies. As a first step in deciphering the CPG inhibitory circuits, we employed lentiviral vector-based gene transfer to express either channelrhodopsin (ChR2) or archaerhodopsin (Arch) photo-sensitive channels in glycinergic respiratory neurons in Wistar rats, and we used optical control for either ChR2-mediated excitation or Arch-mediated inhibition to stimulate/inhibit these neurons, respectively, while recording from multiple respiratory motor outputs and individual neurons. Optogenetic excitation of glycinergic neurons significantly increased respiratory frequency due to the disappearance of E2. Optogenetic inhibition also increased the frequency, but unlike optical excitation, activation of Arch suppressed the post-I phase. We used a well-established computational model of the respiratory CPG to mechanistically explain these increases in respiratory frequency and perturbations of the three-phase pattern. In the model, we found that similar perturbations could be induced by altering the activity of the inhibitory neuron populations of the respiratory CPG. Simulated excitation of these populations completely suppressed the activity of E2 neurons and, thus, augmented oscillation frequency. In contrast, inhibiting these populations completely abolished their activity, thus creating conditions for endogenous bursting of excitatory inspiratory neurons at a higher frequency. These interpretations were consistent with intracellular recordings from neurons of different phenotypes during stimulation. In summary, we demonstrated the functional importance of glycinergic interneurons for generation of eupnea and provided mechanistic insights for these responses using mathematical modeling.

Keywords: respiration, optogenetics, modeling, inhibition, brainstem

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McIntyre, Cameron

Patient-specific models of local field potentials recorded from deep brain stimulation electrodes

Cameron McIntyre[1], Nick Maling[1], Tom Stelwagen[1], Helen Mayberg[2]
[1]*Case Western Reserve University, Cleveland, OH, USA*
[2]*Emory University, Atlanta, GA, USA*

Emerging technological innovations in clinical deep brain stimulation (DBS) are enabling chronic recording of local field potentials (LFPs) from the implanted electrodes, with hopes that the signals could be useful as representative biomarkers of the patient-specific disease state. However, scientific details on the biophysical origin of these LFP signals remains elusive, and little is known about how the patient's unique brain anatomy and electrode placement impact the recording of such signals. To begin to address these questions, we developed a computational framework to theoretically analyze LFP recordings from clinical DBS electrodes that can be customized to individual patients. To demonstrate our model system, we analyzed 6 subjects, suffering from treatment-resistant depression (TRD),

who were implanted with the Medtronic Activa PC+S DBS system and had electrode contacts located in the subcallosal cingulate (SCC) region. For each subject, a patient-specific reconstruction of their head anatomy and DBS electrode implant location was generated using their clinical imaging data (MRI and CT). This patient-specific anatomical model was then used to define the parameters of a finite element volume conductor model, and to dictate the locations of thousands of multi-compartment cable model current sources relative to the implanted DBS electrode in an anatomically realistic way. We then used this model system to examine the impact of distributing subpopulations of highly synchronous neurons within the SCC region on the recorded LFP signal and compared those theoretical results to the experimentally measured LFPs. We found that incorporating patient-specific anatomical detail resulted in substantial changes to LFP signal compared to simplified models. Increasing the neuronal density near the electrode had a graded effect on LFP amplitude, while a more profound effect was generated by varying the synchrony of spatially discrete subpopulations of neurons.

Supported by NIH R01 MH106173

Keywords: stimulation, recording, model

Brooks, Dana

OPTISTIM – Combining computational neuroscience and electrophysiology for optimal cortical electric stimulation

Moritz Dannhauer[1,2], Kimia Shayestehfard[2,3], Seyhmus Guler[2,3], David Caldwell[7], Jeneva Cronin[7], Alexis Gkogkidis[4,5,6], Rob MacLeod[1,2], Tonio Ball[4,5,6], Jeff Ojemann[7], **Dana Brooks**[2,3]
[1]*Scientific Computing and Imaging Institute (SCI), University of Utah, Salt Lake City, UT, USA*
[2]*Center for Integrative Biomedical Computing (CIBC), University of Utah, Salt Lake City, UT, USA*
[3]*Electrical and Computer Engineering, Northeastern University, Boston, MA, USA*
[4]*Intracranial EEG and Brain Imaging Lab, Epilepsy Center, University Hospital Freiburg, Freiburg, Germany*
[5]*BrainLinks-BrainTools Cluster of Excellence, University of Freiburg, Freiburg, Germany*
[6]*Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany*
[7]*Seattle Children's Hospital, Department of Neurological Surgery, University of Washington, Seattle, WA, USA*

Electrodes arrays placed on the brain surface (electrocorticography, ECoG) or deeper in brain tissue (strips, needles, stereotactic) are deployed to study intrinsic brain activity with high spatio-temporal resolution (e.g., in epileptic patients) but are also used to inject current to modulate brain activity. Consenting subjects undergo additional, current stimulation on different scales (e.g., micro-electrocorticography, µECoG), current levels and patterns to elucidate or rehabilitate brain function. However, only little is known about either optimal design or optimal use of these systems. This project has clinical, computational, and experimental components to study these questions. In our clinical work, at University of Washington, we monitor current spreading with high spatial and temporal fidelity to better understand tissue properties, current delivery and its effect on brain functioning, as well as to validate our computational models. Validated computational models developed at University of Utah and Northeastern University (Fig. 1 A,B) allow us to to optimize current in target regions-of-interest while constraining it in non-ROI regions for safety as well as enhanced targeting (Fig. 1C). In the multi-national (US-German, Freiburg University) component of our collaboration we apply these models to validate and design cortical and subcortical indwelling µECoG arrays in phantoms (Fig. 2), animals (ovine) and humans using computed patterns of low-amplitude currents delivered to specific brain ROIs. In the future, we will use both i*n vivo* ECoG and µECoG measurements of stimulation-evoked brain responses to design and assess the functional effects of current patterns and thus improve both designs and deployment of cortical arrays.

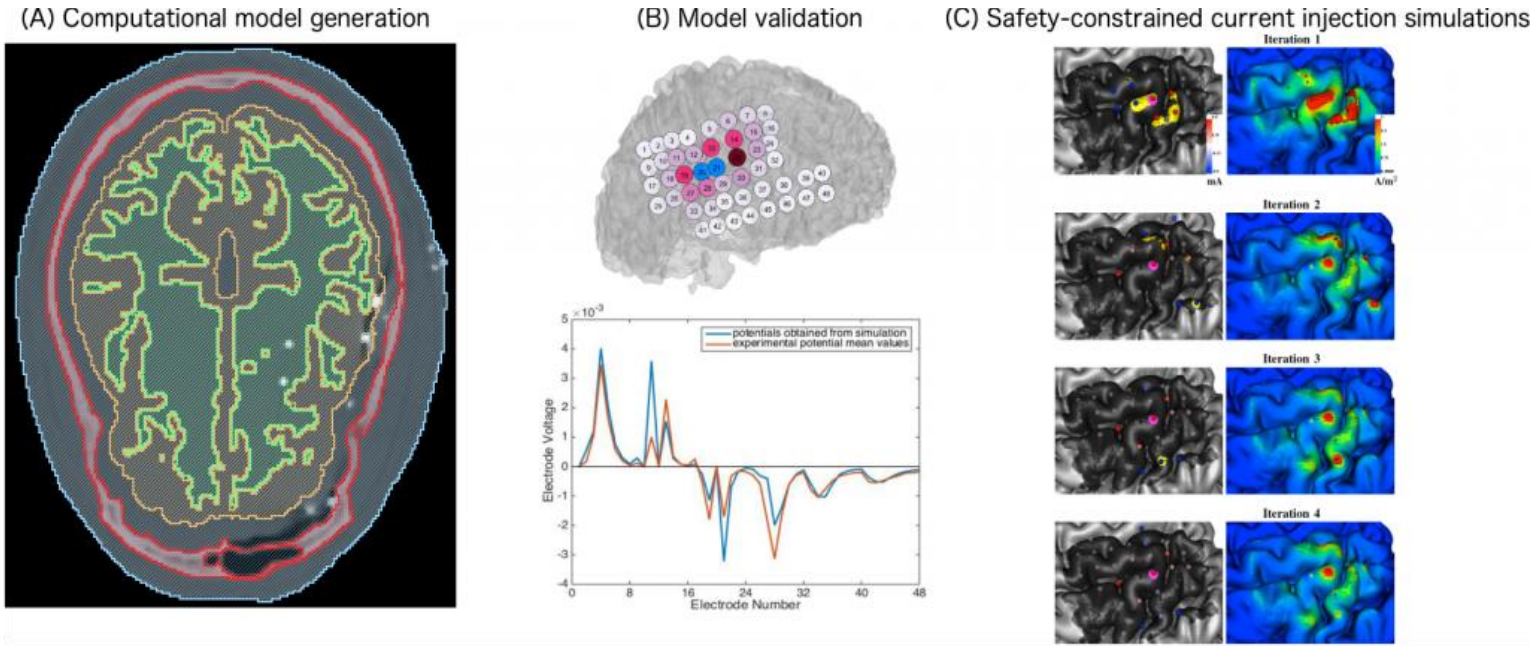

Fig. 1: (A) Human head model based on multimodal imaging; (B) Model validation of simulated and measured electrical potentials; (C) right column: Simulated current injection for cortical ROI (purple) using safety constraints to avoid 'hot-spots' (yellow) below ECoG grid (black; these colors in brackets refer to left column of subfigure).

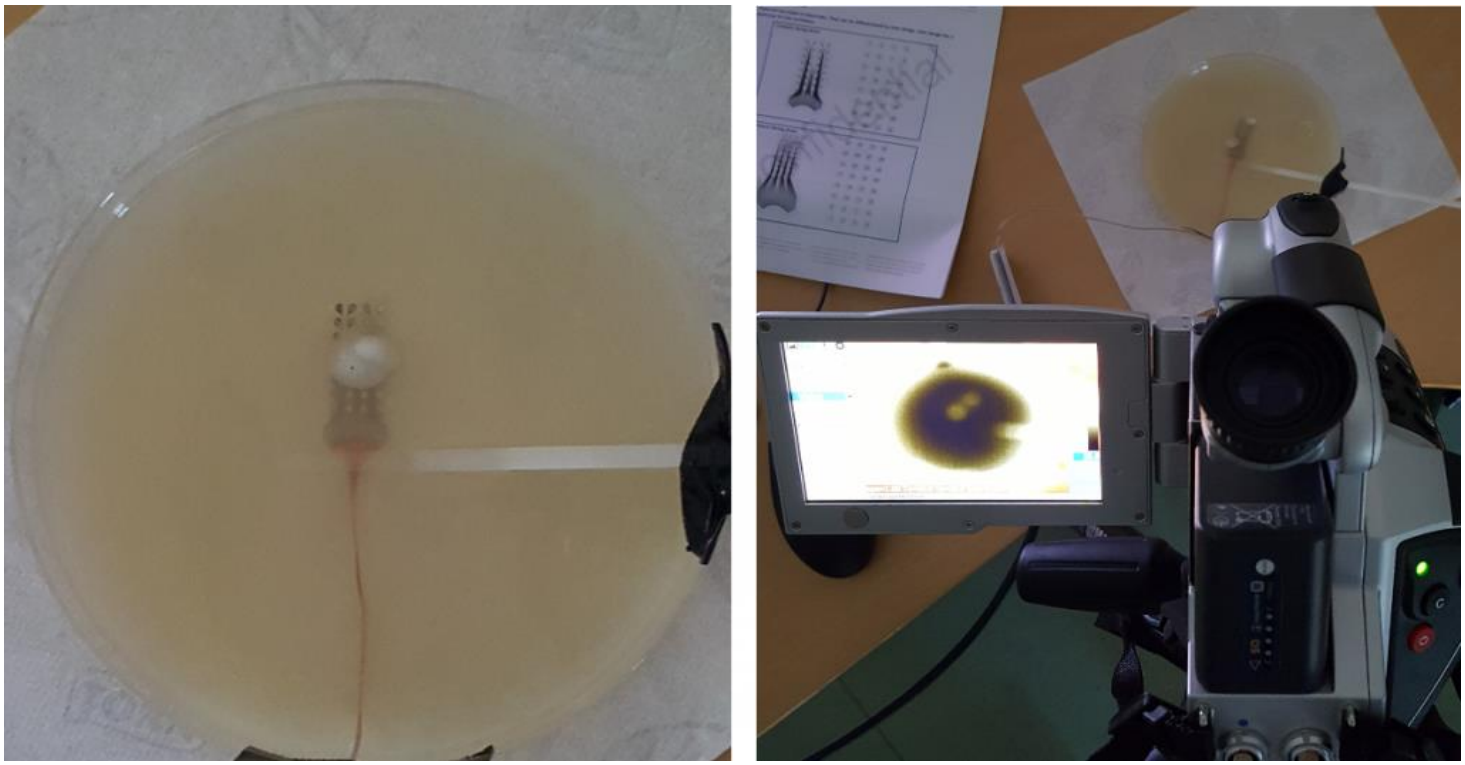

Fig. 2: Evaluating current density hot-spots using a thermal camera.

Keywords: Cortex, Brain, Stimulation, Electrocorticography, Electric

Ishii, Shin - Keynote

Data-driven mimicking neural encoding/decoding systems

Shin Ishii
Kyoto University, ATR Cognitive Mechanisms Laboratories, Kyoto, Japan

Recent progresses in various neuron/brain imaging technologies have allowed us to mimic neural encoding and decoding systems, which transform input to neuron/brain to its central activities and central activities to output from neuron/brain, respectively, in a data-driven fashion. In this presentation, I introduce several studies related to this topic, recently done in our group. The first topic is mimicking growth cone turning behaviors which are driven by Ca2+ signaling in the neurite growth cone. The growth cone shows complicated bidirectional turning behaviors, which were well mimicked by our simple local-activation and global-inhibition model. The second topic is mimicking the theromosensory system of C. elegans. Identifying the transformation from input temperature to Ca2+ activities of a worm's thermosensory neuron, we found the worm senses the temporal difference in the experienced temperature. The third topic is mimicking (or decoding) the spatial attention system of humans. Because our method can calibrate difference in electroencephalography (EEG) activities between individuals, by utilizing resting-state EEG activities, it can be used in a subject-transfer scenario; even if there is no task data of a certain subject to be decoded, his/her task can be decoded by employing other person's task EEG data. If there is some time, I will introduce another subject-transfer decoding, human fMRI-based spatial attention, which calibrates fMRI images by utilizing the structural connectivity information taken by diffusion weighted imaging (DWI).

Rosenholtz, Ruth

A fast, foveated, fully convolutional network model for human peripheral vision

Lex Fridman[1], Shaiyan Keshvari[1], Bryan Reimer[1], Christoph Zetzsche[2], **Ruth Rosenholtz**[1]
[1]*Massachusetts Institute of Technology, Cambridge, MA, USA*
[2]*University of Bremen, Bremen, Germany*

Visualizing the information available to a human observer in a single glance at an image provides a powerful tool for evaluating models of full-field human vision. The hard part is human-realistic visualization of the periphery. Degradation of information with distance from fixation (the *eccentricity*) is far more complex than a mere reduction of acuity that might be mimicked using spatially varying blur. Rather, successful models hypothesize that peripheral vision measures a large number of local texture statistics in pooling regions that overlap, grow with eccentricity, and tile the visual field. Synthesizing images in the equivalence class of this model – important for generating model predictions – is computationally costly, making testing on large image datasets or complex tasks prohibitive. We propose a "foveated" variant of a fully convolutional network for single-pass end-to-end foveation of an image. This network is trained on raw and foveated image pairs. The raw images are a subset of natural scenes from the Places dataset. The foveated images used for training derive from an existing, computationally intensive synthesis model. The proposed approach achieves a 21,000 fold reduction in average running time (from 4.2 hours to 0.7 seconds), and qualitatively and quantitatively similar results to the behaviorally validated model. Similar techniques applied to other models of peripheral vision allow expedited testing of a model on new tasks.

Keywords: peripheral vision, convolutional neural network, equivalence class, computational model

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Landy, Michael

A two-stage model of sensory discrimination: An alternative to drift-diffusion

Michael Landy, Peng Sun
New York University, Dept. of Psychology and Center for Neural Science, New York, NY, USA

Discrimination of the direction of motion of a noisy stimulus is an example of sensory discrimination under uncertainty. For stimuli that are extended in time, reaction time is quicker for larger signal values (e.g., discrimination of opposite directions of motion as compared to neighboring orientations) and larger signal strength (e.g., stimuli with higher contrast or motion coherence, that is, lower noise). The standard model of neural responses (e.g., in lateral intraparietal cortex) and reaction time for discrimination is drift-diffusion. This model makes two clear predictions. (1) The effects of signal strength and value on reaction time should interact multiplicatively because the diffusion process depends on signal-to-noise ratio. (2) If the diffusion process is interrupted, as in a cued-response task, the time-to-decision after the cue should be independent of the strength of accumulated sensory evidence. In two experiments with human

participants, we show that neither prediction holds. A simple alternative model is developed that is consistent with the results. In this estimate-then-decide model, evidence is accumulated until estimation precision reaches a threshold value. Then, a decision is made with duration that depends on the signal-to-noise ratio achieved by the first stage.

Keywords: reaction time, drift diffusion, sensory discrimination

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Konidaris, George

Learning symbolic representations for planning in hierarchical reinforcement learning

George Konidaris
Brown University, Providence, RI, USA

Hierarchical reinforcement learning provides a computational framework that formalizes learning and planning using high-level, temporally extended actions. However, while such methods abstract over actions, they currently do provide a mechanism for abstracting over states: the agent must still plan in the original, potentially high-dimensional, state space. This results in a major computational difficulty for agents - like humans and robots - whose native sensorimotor space is far too high-dimensional to serve as a feasible state space for many problems. Planning and learning using abstract actions is, in and of itself, insufficient to achieve flexible, goal-directed behavior in such agents.

Our recent work considers the question of whether state and action abstraction can be combined. More specifically, we have studied whether or not adding a collection of high-level actions to a reinforcement learning problem in a high-dimensional, continuous state space creates a state abstraction opportunity. We show how to compute an abstract, symbolic representation for such problems, and prove that our representation is necessary and sufficient for reasoning about any plan composed of the agent's high-level actions. We use this framework to autonomously learn - solely from interaction with the environment, and directly from sensorimotor data in the form of point clouds, joint angles, and map locations - an abstract representation of a physical robot manipulation task, and use that representation to perform task-level planning in milliseconds. Our framework exposes the intimate relationship between temporal and state abstraction, and has implications for the representations that humans might use when employing hierarchical abstraction to generate goal-directed behavior.

Keywords: Reinforcement learning, Hierarchical reinforcement learning

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Rao, Rajesh

Modelling theory of mind in the volunteer's dilemma using Partially Observable Markov Decision Processes (POMDPs)

Rajesh Rao[1,2], Koosha Khalvati[2], Jean-Claude Dreher[3]
[1]*Center for Sensorimotor Neural Engineering, University of Washington, Seattle, WA, USA*
[2]*Paul G. Allen School of Computer Science and Engineering, University of Washington, Seattle, WA, USA*
[3]*Institut des Sciences Cognitives Marc Jeannerod, CNRS, Lyon, France*

The "volunteer's dilemma" characterizes a group decision-making scenario in which a few group members can contribute to accomplish a task and bring common goods to the whole group. The dilemma arises from the fact that a lack of sufficient number of volunteers would lead to failure in the task and no common goods while having more than the required number of volunteers would waste resources. As a result, each member must have a very good sense of the intentions of others in the group before committing to an action.

We used a binary version of the Public Goods Game (PGG) with multiple rounds as a social task to study how humans tackle the volunteer's dilemma problem. The experiment involved 29 subjects playing five-person binary PGG multiple times. In some rounds, a minimum of four volunteers were needed to produce public goods while in other rounds, only two volunteers were required.

We employed the framework of Partially Observable Markov Decision Processes (POMDPs) to model each subject's belief about the intention of others and the optimal action based on this belief. The POMDP model is capable of modeling the uncertainty associated with a subject's "theory of mind" about others, and the desire by players to maximize utility. We show that the POMDP model provides a better prediction of subjects' behavior compared to previous models based on the history of actions in the game. The model also explains how players adjust their beliefs with the number of required volunteers in the task.

Keywords: Decision making, Bayesian models, social neuroscience

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Makse, Hernan

Finding essential nodes for integration in the brain using network optimization theory

Hernan Makse[1], Lucas Parra[1], Santiago Canals[2]
[1]*City College of New York, New York, NY, USA*
[2]*Institute de Neurociencia, CSIC and UMH, Alicante, Spain*

Global integration of information in the brain results from the complex interactions of segregated brain areas. Identifying the essential neuronal populations that efficiently bind the different processing units requires a theory of network integration. Here we apply network theory and pharmacogenetic interventions *in vivo* to predict and subsequently target the nodes responsible for global integration. Long-term potentiation of synapses in the dentate gyrus of the rodent hippocampus induces long-range correlations of activity with frontal and prefrontal neocortical regions and the nucleus accumbens (NAc), integrating these structures into a Network of Networks (NoN). Network optimization theory on top of this memory NoN identifies nodes in the NAc as essential for integration. We confirm this prediction by pharmacogenetic inactivation of the NAc shell, which prevents the formation of the integrated network. This result unveils an unexpected requirement of NAc activity for hippocampal-neocortical interactions. Network optimization theory can thus be used to predict essential nodes and design targeted interventions to manipulate the functional organization of the brain.

Keywords: network theory, functional connectivity, LTP, memory and learning

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Scott Makeig

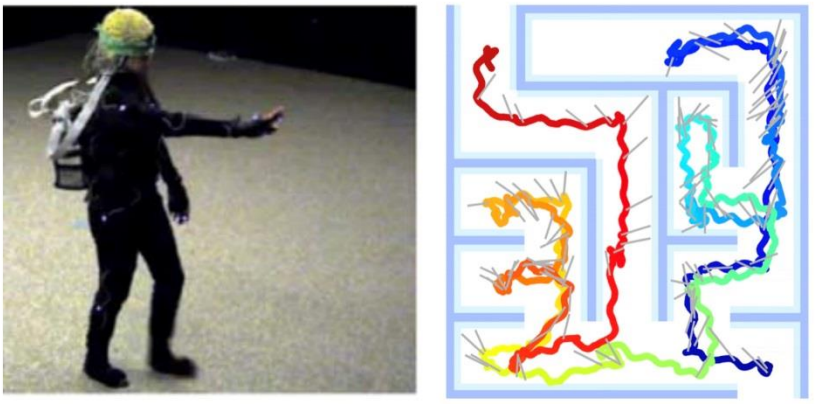
Neural dynamics of the formation of spatial maps during fully-mobile human navigation

John Iversen[1], Makoto Miyakoshi[1], Klaus Gramann[2], **Scott Makeig**[1]
[1]*Swartz Center for Computational Neuroscience, University of California, San Diego, La Jolla, CA, USA*
[2]*Berlin Technical University, Berlin, Germany*

How do we learn our way around a new city or building environment that is new to us? Spatial learning occurs as we integrate sensory impressions we gather as we move through an environment. Our US-German CRCNS project investigates the brain dynamics of humans freely navigating laboratory virtual mazes (free-field 'audiomaze' in San Diego, V-R 'visiomaze' in Berlin). Virtual 'wall probe' hand thrusts by an ambulatory participant in the room-sized motion-capture space elicit directional white-noise (or light-cloud) 'wall touch' feedback giving discrete 'atoms' of auditory (or visual) spatial information about the local 3-D environment that allow participants to explore and eventually learn the layout of a virtual maze (which can then easily be transformed digitally into a new maze).

Our goal is to observe and model the distributed brain dynamics that support spatial learning during active human navigation, particularly as participants create an allocentric 'map' model of the maze environment. To do this, we will use an original, non-invasive 'mobile brain/body imaging' (MoBI) data recording approach that combines simultaneous full-body motion capture as participants navigate a large environment with high-density scalp electrical (EEG) recording.

We will present results of an initial study that demonstrates robust maze-learning and localizable cortical responses to the atoms of navigational knowledge that are collected with each virtual wall touch (or miss). Maze learning is indicated behaviorally by a reduction in the number of wall touches needed to successfully navigate and by an increasingly accurate drawing of the maze geometry after each maze traverse. Source-resolved cortical dynamics associated with wall touches index early sensory and attentional processing followed by a later response in retrosplenial cortex, a region we have previously shown to be associated with retrieval of route information from an allocentric (map-like) reference frame (Gramann et al., 2011; Chiu et al., 2012).



(left) A participant freely exploring a virtual 'audiomaze' while 32-channel body marker positions and 128-channel EEG data are recorded. (right) Participant body movement trajectory and wall-touch feedback points as they fully explore a virtual maze. The body motion track is color-coded by time-on-task (from blue at Start to red at the Goal). Wall touches, as signaled to the subject by audible wall feedback events, are plotted as short gray lines indicating the distance and angle of the probing hand from the body.

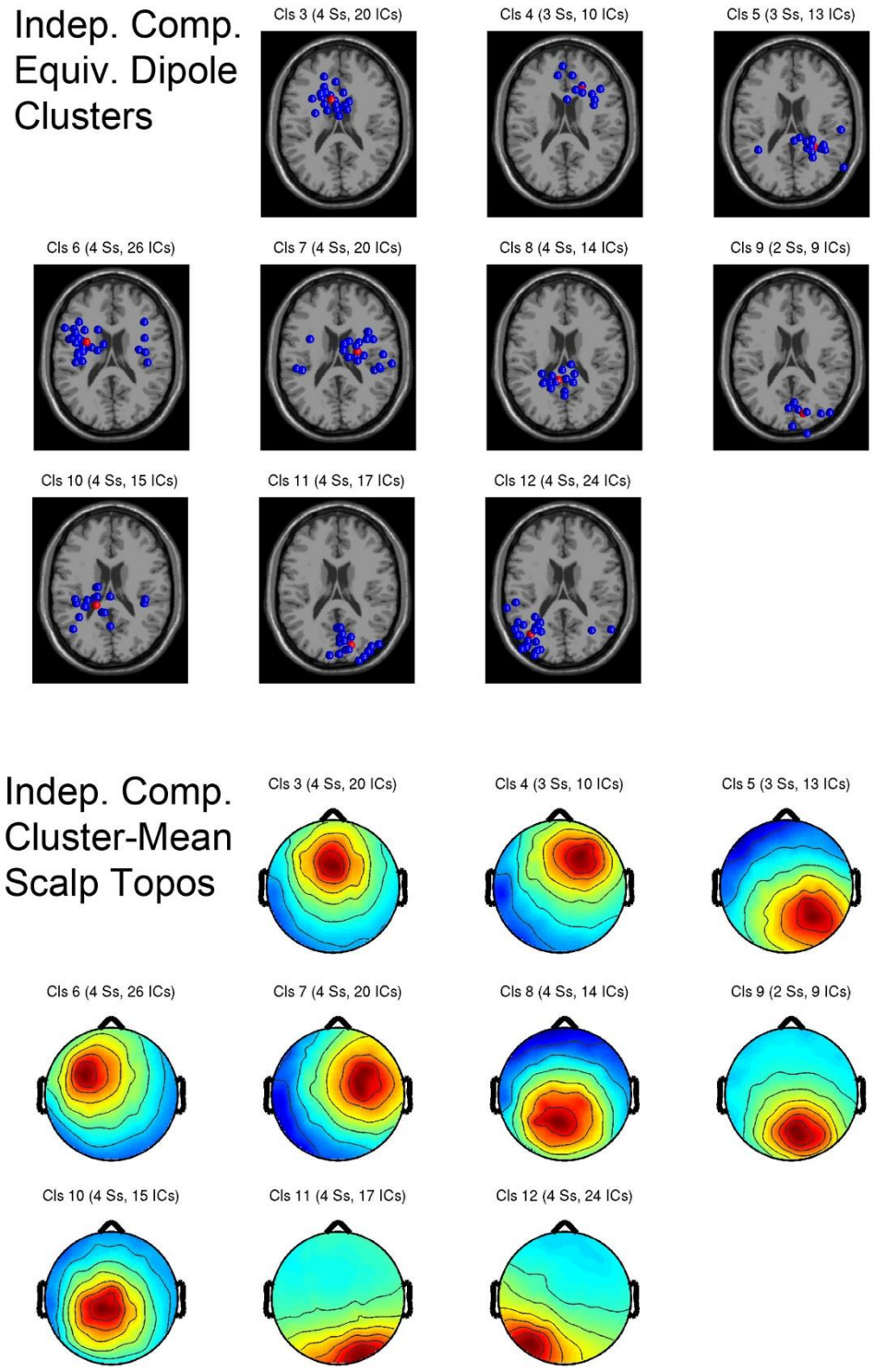


Figure 2. Top, results from clustering analysis on equivalent current dipoles of independent components (ICs) from four participants exploring mazes. Total of 170 ICs representing effective sources of brain EEG were separated into ten clusters using their locations. Blue dots, ICs; Red dots, cluster centroid. Bottom, the cluster mean of scalp projections.

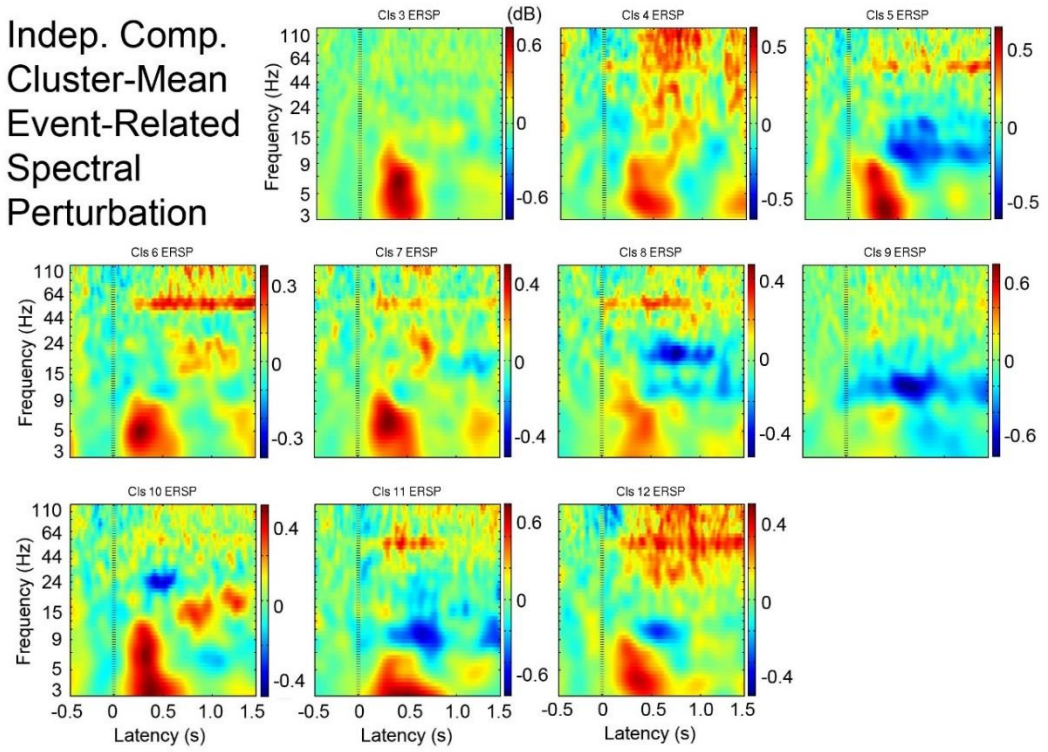


Figure 3. Cluster mean of event-related spectral perturbation (ERSP) across all ICs. Latency zero represents the onset of wall touch. There were mean of 504 wall touches (range: 403-598) during 45 total minutes of maze exploration. Note that occipital clusters (Cls 5, 9, 11 ,12) showed transient alpha power suppression which indicates early attentional processes. Note also that Cls 8 has dipole distribution centered at Retrosplenial Cortex, and this cluster showed showed power decrease in alpha and beta bands following the initial theta power increase.

Keywords: navigation, EEG, VR, ERSP, ICA

Kolaczyk, Eric

Dynamic network analysis of human seizures for therapeutic intervention

Eric Kolaczyk[1], Mark Kramer[1], Sydney Cash[2,3], Catherine Chu[2]
[1]*Boston University, Boston, MA, USA*
[2]*Massachusetts General Hospital, Boston, MA, USA*
[3]*Harvard Medical School, Boston, MA, USA*

Epilepsy is one of the most common neurological syndromes, affecting an estimated 50 million people worldwide. In one-third of these patients, seizures cannot be controlled despite maximal medication management. It is increasingly recognized that epileptic seizures represent an interplay of neural network dynamics. The complexity of the network interactions which define the epileptogenic cortex and drive seizure initiation and spread makes understanding and treating epilepsy a unique challenge. Utilizing invasive brain voltage recordings from patients with intractable epilepsy, we infer dynamic functional networks during spontaneous seizures and use these networks to inform several interacting streams of research on this project. In particular, our work includes development of fundamental methods for (i) identification and tracking well-connected subsets of nodes (a.k.a. communities) across time, and characterization of these evolving subsets; (ii) statistical hypothesis testing of alternative network percolation regimes as competing characterizations of network dynamics at seizure onset; and (iii) novel coupling statistics. At the same time, complementary efforts in our group are

producing (a) a growing database of invasive recordings which include both surface electrode arrays grids and intraparenchymal electrodes (sEEG), now including well over 1000 seizures from over 100 patients, and (b) software for our procedures in an online version control system, the repository for which will be publicly available, for reuse and further development by the community. Using prospective and retrospective studies, we plan to apply these methods to these data via this software to identify principled surgical targets, and predict which patients will - and will not - benefit from surgery and to suggest alternative surgical and control strategies. Ultimately, such dynamic network analysis and statistical modeling of human seizure data could provide new approaches to improve patient care of medically refractory epilepsy.

Keywords: dynamics, epilepsy, networks, seizures

Wessel, Ralf

Correlated variability in cerebral cortex at criticality during vision

Ralf Wessel[1], Nathaniel Wright[1], Mahmood Hoseini[1], Woodrow Shew[2]
[1]*Washington University in Saint Louis, Saint Louis, MO, USA*
[2]*University of Arkansas, Fayetteville, AR, USA*

The confusing thicket of malleable connections between billions of neurons renders the brain a complex adaptive system. The subjective experience of vision is thought to emerge from the impact of incoming spatiotemporal stimuli onto this pliable tangle of neuronal interactions. Yet, to date, a convincing computational framework for the processing of visual stimuli in neural circuits remains elusive. The construction of a solid understanding of cortical circuit dynamics is likely to provide a useful launch pad for ongoing and future investigations of cortical computation and sensory processing.

In this talk, I will provide insight into cortical circuit dynamics from two complementary perspectives. First, based on recorded cortical population activity, I will present evidence for the notion that cortical circuits self-organize to operate at a point of optimized signal processing, including during intense visual stimulation. Second, I will switch the viewpoint to cortical pyramidal neuron membrane potential fluctuations, which represent the integrated activity of the presynaptic pool of cortical neurons. I will show that membrane potential fluctuations are highly variable across repeated stimulus presentations and that this variability can be correlated across neurons. Specifically, based on dual membrane potential recordings, I will present evidence that during continued visual stimulation correlated membrane potential variability adapts towards an intermediate level. Further, our data indicate that this correlation dynamic is likely mediated by intracortical mechanisms. Finally, I will close with showing how a model network with external inputs, synaptic depression, and structure reproduces the observed dynamics of correlated variability. Together, these results suggest that intracortical adaptation self-organizes cortical circuits towards a balanced critical regime at which correlated variability is maintained at an intermediate level.

Keywords: vision, cortex, criticality, correlation, membrane potential

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Sawtell, Nathaniel

The generation and subtraction of predictions enhances neural coding and behavioral detection of external stimuli in an electric fish

Nathaniel Sawtell, Larry Abbott, Armen Enikolopov
Columbia University, New York, NY, USA

Understanding how synaptic plasticity operating within a well-defined circuit shapes adaptive neural processing and behavior is a central, but rarely met, goal of neuroscience. Past studies of the electrosensory lobe (ELL) of mormyrid fish have led to a relatively detailed model of how synaptic plasticity sculpts corollary discharge responses into a prediction, or negative image, of self-generated sensory inputs, but did not link these circuit effects to behavior. Here we directly quantify improvements in neural coding and behavioral detection of prey-like stimuli due to the generation and subtraction of negative images. In addition, we find that manipulating synaptic plasticity leads to specific changes in circuit output which disrupt neural coding and behavioral detection of prey-like stimuli, providing behavioral support for past circuit-level models. These results link synaptic plasticity, neural coding and behavior and also provide a circuit-level illustration of how combining external sensory input with internally-generated predictions may enhance perception. We will also report on initial efforts to develop a more realistic, network-level model of negative image formation in ELL. Experiments and modeling suggest that negative image formation involves plasticity occurring at two separate stages within ELL at synapses conveying corollary discharge signals to both inhibitory interneurons and output cells. Plasticity at synapses onto interneurons appears to be regulated by feedback from a higher processing stage that receives input from ELL.

Keywords: synaptic plasticity, corollary discharge, electric fish, cerebellum

Read, Heather

Using high-order acoustic and neural response statistics to categorize sounds in that mammalian auditory midbrain

Monty Escabi, Fatemeh Khatami, Mina Sadeghi, Ian Stevenson, **Heather Read**
University of Connecticut, Storrs, CT, USA

Barlow and others have suggested that organisms and the neural networks that underlie sensory perception are optimized to capture statistical regularities in sensory scenes. Accordingly, high-order statistical regularities in natural sounds are critical for perceptually discriminating and categorizing sounds (McDermott and Simoncelli, 2011; Geffen et al., 2011). Though neural responses in the central auditory system vary with modulation and correlation sound statistics (Escabi and Schreiner, 2002, Rodriguez et al., 2012) it remains unclear whether sensitivity to high-order statistics could be used to discriminate sound category and how this might be instantiated. Here we characterize single neuron activity of central auditory neurons in the inferior colliculus of awake rabbits in response to an ensemble of sound textures including water, fire, birdsong chorus, snake sounds, and speech babble. We synthetically manipulate each sound by selectively adding or removing high-order statistics using the synthesis algorithm developed by McDermott and Simoncelli (2011). First, we find neural response statistics including spike timing precision and firing reliability change systematically with the sound statistics. Second, we find correlated spiking across pairs of neurons varies with sound category and its synthetically manipulated statistics. Using neurometric and ideal observer analyses we demonstrate that neural response statistics can be used to discriminate sounds. Systematic removal of the high-order sound statistics decreases the neural-based sound classification performance. Conversely, systematic increase in the number of neurons used increases neural-based sound classification performance. This study indicates that neural response statistics in the inferior colliculus have the capacity to capture statistical regularities in sounds that are critical for sound categorization. These findings are significant as they support the concept that statistical regularities are major drivers of sensory systems in general. Moreover, our findings support the concept that mammalian systems have the capacity to optimize sensory categorization through correlated activity in neuron populations.

Keywords: sound identification, auditory, statistics, population coding, correlation

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Schneidman, Elad

Maximum entropy models of population codes based on random projections

Elad Schneidman[1], Roozbeh Kiani[2]
[1]*Weizmann Institute of Science, Rehovot, Israel*
[2]*Center for Neural Science, New York University, New York, NY, USA*

Neural codes are often modeled as probabilistic maps between population activity patterns and sensory stimuli or motor outputs. High-dimensionality of the stimulus space, combinatorial nature of population activity patterns, and neural noise make inference of neural codes intractable unless we can find simplifying principles. Pairwise maximum entropy models have suggested such a principle, where strongly correlated population activity patterns in tens of neurons were accurately described by minimal models that rely only on pairwise interactions between the cells. However, pairwise models are insufficient in describing larger neural populations, and it is difficult to identify which interaction terms they should be augmented with.

We present a new family of probabilistic models of neural populations: Maximum Entropy distributions based on Randomly chosen Projections of the network activity (MERP). Applied to large populations of cortical neurons in behaving primates, we show that MERP models match or surpass the accuracy of the best existing models when employing a similar number of constraints. These models are easily extendable by adding more constraints, but we show that they can perform as well with a significantly smaller number of projections by adaptively replacing non-contributing constraints with newly drawn random constraints. Moreover, we show that MERP is superior to other models in particular when the population activity is severely under-sampled.

We demonstrate the equivalence of randomly connected feed-forward neural circuits and MERP models, suggesting a biologically plausible way for neural circuits to estimate the saliency or log-likelihood of their inputs by reweighting the contributions of a large set of random projections. These shallow network models, in which multiple models can share a common set of random projections, present an efficient, scalable and highly accurate probabilistic representation of their joint inputs - suggesting them as a possible design principle for neuronal architectures.

Keywords: probabilistic models, population code, maximum entropy, neural networks, saliency

POSTERS LISTED ALPHABETICALLY BY PRESENTER *(Name – Poster Board #)*

POSTERS LISTED BY POSTER BOARD NUMBER

Spezio, Michael - 1

Computational neuroscience in the context of the liberal arts

Michael Spezio[1,2], Yuqing Lei[1,4], Vanessa Hayes[1], Shannon Klotz[1,4], Shota Yasunaga[3,5], Tessa Rusch[2], Saurabh Kumar[2], Jan Glaescher[2]
[1]*Psychology & Neuroscience, Scripps College, Claremont, CA, USA*
[2]*Institute for Systems Neuroscience, University Medical Center - Eppendorf, Hamburg, Germany*
[3]*Computer Science, Harvey Mudd College, Claremont, CA, USA*
[4]*Computer Science, Pomona College, Claremont, CA, USA*
[5]*Neuroscience, Pitzer College, Claremont, CA, USA*

Most serious challenges facing societies and cultures are so complex that proposed responses to them require multiple disciplines, even inter- and transdisciplinary thinking. A liberal arts education seeks to foster such critical thinking across a breadth of areas of inquiry, usually within a strongly interdisciplinary approach, crossing boundaries between mathematics, natural sciences, social sciences, humanities, and the arts. The extreme breadth of a liberal arts education, though, presents special challenges for pedagogy in quantitatively and technically demanding areas, such as computational neuroscience. Robust progress in training undergraduates in computational neuroscience requires a program of tiered theoretical and applied coursework, together with directed research mentoring by faculty. Mentoring must gradually increase conceptual difficulty while maintaining a supportive environment that prioritizes the excitement of discovery. Yet most majors and programs in the liberal arts are flat and work under the assumption that knowledge is not cumulative. Additionally, most students, faculty, and administrators in the liberal arts have little if any experience with tiered programs that foster cumulative learning, especially in computation. Even when tiered learning is implemented in neuroscience programs in the liberal arts, quantitative and computational emphases vary. Undergraduate programs of neuroscience in liberal arts colleges that try to balance the need for great breadth of study with the need for tiered learning often align more closely with the priorities of pre-health and wet lab students than those of students in computational neuroscience. This presentation covers ideas for and experiences of successful redirection of faculty and student efforts to foster functional expertise in computational neuroscience. The suggestions come directly from work with students and draw on students' own statements about their motivations, experiences, successes, and ongoing challenges.

Keywords: pedagogy, interdisciplinary, cumulative learning, algorithms

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Hartmann, Mitra/Gopal, Venkatesh - 2

Responses of the rodent vibrissal-trigeminal system to air currents

Mitra Hartmann[2], **Venkatesh Gopal**[1], Neelesh Patankar[2]
[1]*Elmhurst College, Elmhurst, IL, USA*
[2]*Northwestern University, Evanston, IL, USA*

Mechanisms for flow sensing and anemotaxis are well studied in arthropods, but remarkably few studies have investigated the sensory cues used by terrestrial mammals for anemotaxis. Our collaborative work has combined mechanical, behavioral, neural, and robotic approaches to investigate the cues that allow terrestrial mammals to detect and localize airflow, with a particular focus on the role of vibrissae (whiskers).

Mechanical results indicate that a whisker bends in response to airflow and then vibrates around its new deflected position. The primary direction of bending indicates airflow direction; bending amplitude is correlated with airspeed; vibration frequencies are close to the natural resonances of the vibrissa. Computational fluid dynamics simulations were used to investigate three possible mechanisms for these vibrations: unsteady vortex shedding from the vibrissa, aeroelastic vibrations, or fluctuations in incident airflow. Our results indicate that aeroelastic vibration is the dominant mechanism.

Behavioral work in rats showed that the vibrissae play an important role in anemotaxis: five animals trained on a five-alternative forced-choice airflow localization task exhibited significant performance decrements after vibrissal removal, while in contrast, vibrissal removal did not disrupt performance of control animals trained to localize a light source. Correspondingly, recordings from primary sensory neurons in the trigeminal ganglion indicate higher firing rates in response to higher airspeeds, with a secondary effect of orientation.

Undergraduates at Elmhurst College developed a robot with artificial whiskers that can track air currents to their source. Robotic experiments showed that ambient air currents carried a flow signature that allowed four different flow environments to be distinguished - grass, bushes, concrete, and a “mixed” environment containing elements of all three environments.

Together, our results demonstrate that the rodent vibrissal system, which has a well-established tactile role, also contributes significantly to anemotaxis. This discovery provides a link between the vibrisso-trigeminal system and olfactory search.

In addition, we also discuss our experiences working with "first-generation students," those who are the first in their families to go to college, and describe the highly positive impact that participating in undergraduate research has had on their academic trajectories.

Keywords: whisker, trigeminal, touch, sniffing, fluid mechanics

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Thoroughman, Kurt - 3

Science of Learning Program at NSF

Kurt Thoroughman
National Science Foundation, Arlington, VA, USA

NSF has a central structure: Directorates support scientific disciplines; Divisions foster multiple fields; Programs manage individual portfolios, usually around a specified field or level of study. These structural elements collaborate to build larger enterprises, such as CRCNS. Another set of examples was Science of Learning. NSF supported six large Centers, then organized two rounds of solicitations for Collaborative Networks.

In 2017, Science of Learning is now a home Program (bit.ly/SL_NSF). Our defining goal, for a Program, is unusually broad: "to develop basic theoretical insights and fundamental knowledge about learning principles, processes and constraints." Investigators can meet this goal through single or multiple approaches; at any time or length scale; using science from the biological through behavioral, cultural, and social; and integrating models and technology. As a home program, we have regular semiannual due dates, and the full catalog of NSF grant mechanisms.

In this poster, I will describe the program and connect with investigators seeking to take advantage of this new opportunity.

Gerkin, Richard C - 4

MyBinder for configuration-free teaching of cutting edge computational neuroscience

Richard C Gerkin
Arizona State University, Tempe, AZ, USA

Teaching computational neuroscience material presents several challenges. Among these are the distribution of datasets, code, and most importantly complete software development environments to students in a classroom setting. This last challenge is especially important because using cutting-edge scientific computation software usually involves complicated installation steps and even the manual compilation of various dependencies. This often precludes classroom use of interactive applications based on such software.

Here I report on my success using MyBinder (http://mybinder.org, courtesy Jeremy Freeman lab), a web application for launching complete development environments based on the lightweight virtualization environment Docker and interactive Jupyter notebooks. Using this application, I was able to deploy interactive scientific computation problems (and solutions) to a room of students. Each student required only a web browser and had independent control of each example, allowing them to execute pre-set code blocks and visualize graphical results, or to edit the code and examine the resulting changes. Set-up from the instructor's end required only the authoring of the problems and the specification of a simple requirements file containing the installation dependencies handled by the application ahead of time. All examples I deployed were based on Python, but a few other open source languages are supported in principle, including R and Julia.

This container-based approach to packaging teaching materials can substantially reduce the burden on instructors and students for coursework at all levels. It could also be deployed for workshops or interactive seminars.

Keywords: teaching, workshop, scalable

Gerkin, Richard C - 5

Optimization of reduced models against diverse experimental neuron physiology datasets with NeuronUnit

Russell J Jarvis, Sharon M Crook, **Richard C Gerkin**
Arizona State University, Phoenix, AZ, USA

Understanding neural circuits requires the construction of abstract models that can reproduce experimental findings. *NeuroML*, a model description language for neuroscience, facilitates reproducibility and exchange of such models by providing an implementation-agnostic model description in a modular format. *NeuronUnit* evaluates model accuracy by subjecting models to experimental data-driven validation tests, a formalization of the scientific method. In order to scale such tests to a wide variety of biological neuron types, a range of model classes, and good coverage of experimental data (available through *Neuroelectro.org*, the *Allen Institute Cell Types* database, *The Blue Brain Project*, and from individual labs), computationally efficient techniques for test-driven model optimization against a wide range of experimentally observed features are needed. Here we use parallel genetic algorithms to efficiently sample a large model parameter space in the context of *NeuronUnit* testing using the above data sources. For each model class (e.g. an Izhikevich model) and for each biological neuron type (e.g. a CA1 pyramidal cell) we obtained (using either summary data from collections of cells or data from individual cells) an error surface via a parallel Non-Dominated Sort Genetic Algorithm (NSGA), which is deliberately agnostic about the relative importance of each feature of the experimental data. This surface corresponds to plausible subsets of candidate parameter values that, importantly, respect both intrinsic biological diversity and degeneracy of the solution space. Using the super-computing resources of the *Neuroscience Gateway*, we are delivering hundreds of optimized, reduced models tailored to the requirements of specific research questions. Ultimately this work will result in data-driven model optimization as a web service, where experimentally-robust neural models can be interrogated and explored online.

Keywords: modeling, simulation, validation, optimization, neuroinformatics

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Halchenko, Yaroslav - 6

Continuous data discovery, consumption and sharing of data and meta-data using DataLad

Yaroslav Halchenko[1], Michael Hanke[2]
[1]*Dartmouth College, Hanover, NH, USA*
[2]*Otto-von-Guericke University, Magdeburg, Germany*

Distributed version control systems, such as Git, and support portals, such as github.com, served as a catalyst for open science, collaboration, and sharing. Consistent and efficient management of scientific data should become a common practice in empirical fields of study, such as neuroscience. DataLad project (http://datalad.org) aims to provide solution for all steps of scientific data management, from discovery to publishing of new or derived data. Based on git-annex (http://git-annex.branchable.com), which provides git-based framework for data logistics and versioning, DataLad makes a rich collection of disjoint neuroscience datasets available through a simple unified interface of a "data distribution" and facilitates large and small-scale collaborations while allowing for efficient and version controlled management of the data. In this talk we will present how data could be discovered, obtained for local processing, and "published" online to facilitate open and efficient collaboration and efficient data reuse.

Keywords: neuroinformatics, data sharing, data management, open source

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Kiani, Roozbeh - 7

The structure of response correlation matrix is stable in the primate visual cortex and reveals the anatomical boundary of V1 and V2

Roozbeh Kiani, Mohamad Saleh Esteki
Center for Neural Science, New York University, New York, NY, USA

Correlations between neural responses have profound effects on the ability of neural populations to compute and encode information. However, the organization of these correlations and the mechanisms that give rise to them are not well understood. Here we investigated the pattern of correlations in the primary and secondary visual cortices (V1 and V2). We used 96-channel microelectrode arrays to simultaneously record visually-evoked and spontaneous activity of tens of neurons in the vicinity of V1-V2 border in two anesthetized macaque monkeys. Histology following the experiments revealed that nearly half of the electrodes were located in each area and

recordings were largely limited to layer IV and bottom of layer III. We calculated spike count correlations of all pairs of recorded units, forming a correlation matrix. We found that, although the magnitude of the correlations may depend on the stimulus, the overall structure of the correlation matrix is largely stable. Furthermore, the correlation matrix structure reflects the V1-V2 border. Unsupervised clustering algorithms could retrieve the location of the anatomical boundary even in the absence of a priori information about the electrode locations in cortex. We show that this cortical parcellation is not shaped solely by the distance separating units, their cortical layer, overlap of RFs, orientation preference, or ocular dominance. Rather, the correlation matrix structure is shaped mainly by "common noise": spontaneous activity or the residual fluctuations around the stimulus-evoked response. We suggest that the population response dynamics which give rise to the stability of the correlation structure are furnished by intrinsic connectivity within an area, V1 or V2. The stability of the structure of correlation matrix in visual cortices is reminiscent of previous reports on the primate prefrontal cortex (Kiani et al, Neuron 2015), indicating an organizational principle preserved across sensory and association cortices.

Keywords: Visual cortex, response covariance, unsupervised clustering, functional connectivity, intrinsic connectivity

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Park, Cheolwoo - 8

Regularized aggregation of statistical parameter maps

Cheolwoo Park[1], Li-Yu Wang[1], Hosik Choi[2], Amanda Rodrigue[1], Jordan Pierce[1], Brett Clementz[1], Jennifer McDowell[1]
[1]*University Of Georgia, Athens, GA, USA*
[2]*Kyonggi University, Suwon, Korea*

Combining statistical parameter maps (SPM) from individual subjects is the goal in some types of group-level analyses of functional magnetic resonance imaging (fMRI) data. Brain maps are usually combined using a simple average across subjects, making them susceptible to subjects with outlying values. Furthermore, t tests are prone to false positives and false negatives when outlying values are observed. We propose a regularized unsupervised aggregation method for SPMs to find an optimal weight for aggregation, which aids in detecting and mitigating the effect of outlying subjects. We also present a bootstrap-based weighted t test using the optimal weights to construct an activation map robust to outlying subjects. We validate the performance of the proposed aggregation method and test using simulated and real data examples. Results show that the regularized aggregation approach can effectively detect outlying subjects, lower their weights, and produce robust SPMs.

Keywords: Functional magnetic resonance imaging data, Penalized unsupervised learning, Robustness, Statistical parameter map

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Herzel, Hans-Peter - 9

Measuring coupling strength in the suprachaismatic nucleus

Hans-Peter Herzel[1], Christoph Schmal[1]
[1]*Institute for Theoretical Biology, Berlin, Germany*

In mammals, the suprachiasmatic nucleus (SCN) orchestrates daily sleep-wake rhythms. About 20000 densely packed neurons constitute the SCN in rodents. Gene-regulatory feedback loops induce in most neurons autonomous modulations of the firing rate. As shown by Welsh, Honma and Herzog single cell rhythms are rather irregular (period standard deviation of about 2 hours) whereas SCN slices generate quite precise rhythms. These robust rhythms are achieved by coupling involving VIP, AVP and GABA.

Together with experimental groups (Erik Herzog, Washington University; Sato Honma, Hokkaido; Jihwan Myung, Okinawa) we explore the role of coupling between SCN neurons. Our theoretical approach is based on simulations of coupled oscillators. Parameters of single cells are extracted by fitting reporter signals from dispersed neurons. It turns out that the phase of coupling is particularly relevant. This finding is based on the interference of paracrine signals with intracellular feedback loops since both converge at the activation of Period genes.

Modeling requires the quantification of coupling strength between neurons. Currently, these parameters cannot be extracted directly. Thus we present statistical methods to quantify coupling strength from slice data. We study spatial coherency using Moran's I and empirical orthogonal functions. Moreover, we analyze period, phase and amplitude distributions of individual oscillators. Using simulated networks and slice data we show that these emergent network properties provide information on coupling strength. We apply our concept to SCN slices with Cryptochrome mutants, slices from in early development, and during application of inhibotors such as TTX.

Keywords: suprachiasmatic nucleus, oscillator, circadian clock, coupling, synchronization

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Herzog, Erik - 10

A neural code for circadian entrainment

Erik Herzog[1], Cristina Mazuski[1]
[1]*Washington University, St. Louis, MO, USA*

The mammalian suprachiasmatic nucleus (SCN) functions as the master pacemaker, integrating environmental input into coherent daily rhythms. Approximately 10% of SCN neurons express the neuropeptide vasoactive intestinal polypeptide (VIP). VIP signaling is necessary to maintain synchrony among SCN neurons and for behavioral rhythms. However, it is not known how and if firing activity of VIP SCN neurons can influence circadian rhythms in gene expression and behavior. Using optical tagging to identify individual VIP neurons while recording from approximately 100 SCN neurons, we characterized spontaneous electrical activity patterns with microsecond resolution over three days. We found most SCN VIP neurons had circadian firing activity over days with daily peak rates above 2 Hz. Surprisingly, these 1500 neurons were reliably clustered according to their short-term firing patterns as either tonic or irregular neurons. We next tested whether optogenetically stimulating SCN VIP neurons with these physiologically-relevant firing patterns sufficed to phase shift and entrain circadian rhythms in gene expression and locomotor behavior. We found that stimulation with high, but not low, instantaneous rates shifted daily rhythms in gene expression in SCN explants. This stimulation also evoked cFOS expression throughout the SCN *in vivo* indicating the VIP neurons influence excitability across the SCN network. Daily high frequency stimulation of SCN VIP neurons *in vivo* rapidly entrained circadian locomotor activity. In contrast, low frequency stimulation entrained daily rhythms in behavior more gradually. We conclude that VIP neurons use tonic or irregular firing at frequencies at or above 2 Hz to synchronize molecular and behavioral circadian rhythms between cells and to the local light cycle.

Keywords: suprachiasmatic nucleus (SCN), multielectrode array, channel rhodopsin, vasoactive intestinal polypeptide (VIP), tonic firing pattern

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Bouix, Sylvain - 11

Subject-specific abnormal region detection in traumatic brain injury using sparse model selection on high dimensional diffusion data

Sylvain Bouix[1], Matineh Shaker[2], Deniz Erdogmus[2], Jennifer Dy[2], Demian Wassermann[3]
[1]*Brigham & Women's Hospital, Boston, MA, USA*
[2]*Northeastern University, Boston, MA, USA*
[3]*INRIA Sophia Antipolis, Sophia Antipolis, France*

We present a method to estimate a multivariate Gaussian distribution of diffusion tensor features in a set of brain regions based on a small sample of healthy individuals, and use this distribution to identify imaging abnormalities in subjects with mild traumatic brain injury. The multivariate model receives *apriori* knowledge in the form of a neighborhood graph imposed on the precision matrix, which models brain region interactions, and an additional L_1 sparsity constraint. The model is then estimated using the graphical LASSO algorithm and the Mahalanobis distance of healthy and TBI subjects to the distribution mean is used to evaluate the discriminatory power of the model. Our experiments show that the addition of the *apriori* neighborhood graph results in significant improvements in classification performance compared to a model which does not take into account the brain region interactions or one which uses a fully connected prior graph. In addition, we describe a method, using our model, to detect the regions that contribute the most to the overall abnormality of the DTI profile of a subject's brain.

Keywords: Sparse learning, Graphical lasso, TBI, DTI

Coifman, Ronald - 12

Data-driven geometry learning for parametrically-dependent dynamical systems

Ronen Talmon[1], Hadas Benisty[1], Gal Mishne[2], Ron Meir[1], Jackie Schiller[1], **Ronald Coifman**[2]
[1]*Technion - Israel Institute of Technology, Haifa, Israel*
[2]*Yale University, New Haven, CT, USA*

The extraction of models from data is a fundamental cognitive and scientific challenge. Neuronal activity recordings are an example of highly intricate data, which do not have existing definitive models. The complexity and richness of neuronal activity pose many challenging questions, such as the organization of neurons into subgroups of mutual functionality, correspondence to behavior, and existence of time-evolving connectivity patterns. Motivated by these challenges, we aim to organize neuronal activity using geometry learning from a novel standpoint of nonlinear dynamical systems. In particular, we demonstrate a geometric/analytic unsupervised

learning algorithm capable of creating minimal descriptions of parametrically-dependent unknown nonlinear dynamical systems. We present an approach that enables us to discover in a data-driven manner useful intrinsic state variables and parameters, in terms of which one can empirically model the underlying dynamics. This is accomplished by "tiling" the joint space of recovered parameters and state variables; the tiling procedure is able to capture co-dependencies between different dynamical regimes and to build empirical bifurcation maps. This procedure can be viewed as analogous to the Wavelet analysis with two important distinctions. First, Wavelet analysis is applied to the time-frequency domain, whereas our tool tiles the *inferred* space of the latent parameters and variables. Second, while the wavelets are usually predefined, our "tiles" define the support of a set of *data-driven* filters. We demonstrate our toolbox on simulation data arising from two systems: a cellular chemotaxis and spike trains governed by latent Lorenz variables. In both cases, we show that our method reveals the true, intrinsic parameters and state variables, without prior knowledge, and enables to successfully detect chaotic regimes, as well as phase transitions, manifested by the change in the dimensionality of the latent intrinsic variables. In addition, we show results on real recordings, including neuronal spiking data and implanted EEG electrodes.

Keywords: geometry learning, manifold learning, nonlinear dynamical systems, data analysis

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Aminzare, Zahra - 13

A bursting neuron CPG model: phase reduction, dynamical mechanisms, and gait transitions

Zahra Aminzare[1], Vaibhav Srivastava[2], Philip Holmes[1]
[1]*Princeton University, Princeton, NJ, USA*
[2]*Michigan State University, East Lansing, MI, USA*

Insects are capable of complex walking gaits in which various combinations of legs can be simultaneously in stance and swing. It has been observed that fast running insects employ a tripod gait with three legs lifted off the ground simultaneously in swing, while slow walking insects use a tetrapod gait with two legs lifted off the ground simultaneously. Fruit flies use both gaits and exhibit a transition from tetrapod to tripod at intermediate speeds. Our goal is to understand the effect of stepping frequency on transitions between these gaits in an ion-channel bursting neuron model in which each cell represents a hemi-segmental thoracic circuit of the central pattern generator. Employing phase reduction and bifurcation theory, we study the existence and stability properties of tetrapod, tripod and transition gaits, analytically. We support our theory by showing two sets of data fitted to freely walking fruit flies.

Keywords: insect gaits, bifurcation, coupling functions, phase response curves, stability

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Drew, Patrick - 14

Modeling the effects of nitic oxide diffusion and degradation on neurovascular coupling

Patrick Drew, William Haselden
Pennsylvania State University, University Park, PA, USA

Nitric oxide (NO) is a gaseous vasodilator, and is thought to play an important role in neurovascular coupling. NO is produced by neurons, but the degradation rate of NO varies greatly by tissue type. Within the lumen of a vessel, the rate constant for NO degradation will be >1000 higher than in nervous tissue where NO is produced. Because the site of vasodilatory action of NO is in smooth muscle, which is adjacent to the vessel lumen, this difference in degradation rate will produce a steep concentration gradient that may impact neurovascular coupling dynamics. Because direct measurements of NO levels are technically challenging, we used computer simulations to understand how the spatial distribution of NO production and degradation will affect the concentration of NO in the tissue. We simulated a single penetrating arteriole and surrounding parenchymal tissue and varied the spatial pattern of NO production to determine how various manipulations would affect the NO concentration in the smooth muscle. Through our simulations, we demonstrate that localized release of NO near the vessel is required to provide an effective dilatory concentration of NO to the smooth muscle. We also observed that the concentration of NO in the smooth muscle depended on the vessel diameter, suggesting the vasodilatory effects of NO depend on the vessel size. Modeling the release and absorption dynamics of NO allows us to better understand how the spatial dynamics of NO production affect neurovascular coupling.

Keywords: Neurovascular coupling, diffusion, nitric oxide

Lee, Adrian KC - 15

Inferring functional connectivity with sparse plus low-rank graphical models of time series: an auditory attention task example

Nicholas J Foti, **Adrian KC Lee**, Emily B Fox
University of Washington, Seattle, WA, USA

Connectivity of the dynamical brain at a systems neuroscience level is a relatively underexplored area, owing perhaps to the unsolved challenge of modeling structured relationships between time series in a big data setting. We have recently developed a method based on graphical models of time series to infer functional connectivity between brain regions from magnetoencephalography (MEG) data collected while subjects perform an auditory attention task. We represent the functional connectivity network through conditional independence statements between the cortex localized signals, encoded via a graphical model of time series. Unlike typical graphical modeling approaches, we treat the MEG signals as time series rather than i.i.d. observations thus accounting for the underlying dynamics. Importantly, we incorporate a low-rank component that accounts for latent signals that would otherwise lead to inferring spurious connections. We develop an efficient algorithm to learn the model parameters from large MEG data sets, and evaluate the model on synthetic data. We also used collected MEG data to reveal the connectivity of the auditory attentional network when subjects were asked to either maintain or switch attention between two competing sound streams.

This computational development paves the way to study the neurobiological basis of a still-controversial clinical construct known as central auditory processing disorder. Specifically, this approach provides a way for us to answer this open question: whether the connectivity structure of the auditory attentional network helps to elucidate the neural underpinnings of certain aspects of auditory dysfunction, e.g., the inability to maintain or switch attention between speakers.

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Keywords: neuroimaging, connectivity, graphical models, attention, auditory

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Shouval, Harel Shouval - 16

Maintenance of synaptic plasticity: computational principles and the role of PKMζ

Harel Shouval Shouval[1], Marco Huertas[1], Todd Sacktor[2]
[1]*McGovern Medical School, The University of Texas, Houston, TX, USA*
[2]*SUNY Downstate Medical Center, New York, NY, USA*

Memories that last a lifetime are stored as persistent changes of specific synaptic efficacies, and the ability to preserve these over long time scales constitutes the maintenance phase of synaptic plasticity. The synaptic mechanism underlying these persistent changes, late long-term potentiation (L-LTP), depends on the state and number of specific synaptic proteins. These proteins, however, have limited synaptic dwell times due to molecular turnover and diffusion, raising a fundamental question: how can this transient molecular machinery store memories lasting a lifetime?

Here we report both on the computational principles underlying maintenance at the molecular level and about a specific experimentally tested molecular pathway that instantiates this mechanism. At the theoretical level, we show that a positive feedback at the level of the translation of new proteins is able to maintain synaptic plasticity even though the synaptic proteins have fast turnover rates. This theory can account for many experimental results including the dependence of L-LTP on protein synthesis and for the different effects of protein synthesis and protein kinase inhibitors.

Robust experimental evidence indicates that a specific atypical protein kinase C, *PKMζ,* plays a central role in the maintenance of synaptic plasticity. Recent work has shown that specific inhibition of the synthesis of *PKMζ* can prevent long-term memory formation, and even reverse it. These results establish a mapping between our theory and *PKMζ* because, as in our theory, ongoing synthesis of *PKMζ* is essential for maintenance. Our experiments also provide an explanation to results in which *PKMζ* knock-out animals exhibit normal memory by showing this occurs through the upregulation of another atypical protein kinase C (*PKCι/λ*).

Using a computational reaction-diffusion implementation of this theory we investigated the theoretical conditions and limits of synapse specificity. We conclude that local protein synthesis of *PKMζ* must occur within synaptic spines; an experimentally testable prediction.

Keywords: Synaptic Plasticity, Long-Term memory, LTP, reaction-diffusion

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Blackwell, Kim - 17

Multiple signaling molecules flexibly contribute to hippocampal synaptic plasticity

Kim Blackwell[1], Joanna Jedrzejewska-Szmek[1], Ted Abel[2]
[1]*George Mason University, Krasnow Institute for Advanced Study, Fairfax, VA, USA*
[2]*Iowa Neuroscience Institute, University of Iowa, Iowa City, IA, USA*

Long-term potentiation of the strength of synaptic connections is a mechanism of learning and memory storage. One of the most confusing aspects of hippocampal synaptic potentiation is that numerous experiments have revealed the requirement for a plethora of signaling molecules. Further complexity stems from spatial aspects of signaling networks, such that some molecules function in the dendrite and some are critical in the spine. We investigated whether the diverse experimental evidence can be unified by creating a spatial, mechanistic model of multiple signaling pathways in hippocampal CA1 neurons. We use our novel, computational efficient simulator, NeuroRD, to simulate stochastic interactions both within spines and between spines arranged along a dendrite. Our results show that the combination of activity of several key kinases can predict the occurrence of long-lasting forms of LTP for multiple experimental protocols. We also show that activation of beta-adrenergic receptors by the stress response appears to be involved in most forms of synaptic potentiation, though in some cases non-canonical (Gi-coupled) pathways are utilized. Results of simulations of a dendrite with multiple spines are consistent with the spatial specificity of homo- and hetero-synaptic plasticity suggested by imaging of spine morphological plasticity. Specifically, stimulation of two spines on the same branch produces a spatially diffuse elevation in signaling molecules in the dendrite, while maintaining a spatially specific elevation in signaling molecules in the spine. Simulations make the experimentally testable predictions that a complete antagonist of the beta- adrenergic receptor will block long-lasting LTP in response to strong stimulation. Several predictions of the model will be tested using biosensor imaging and electrophysiological recording. Collectively these results suggest that converging molecular mechanisms allow CA1 neurons to flexibly utilize signaling mechanisms best tuned to temporal pattern of synaptic input to achieve long-lasting LTP and memory storage.

Keywords: LTP, beta adrenergic receptor, protein kinase A

Khatami, Fatemeh - 18

Neural discrimination of sound category utilizes high-order sound statistics in the central auditory nervous system

Fatemeh Khatami, Mina Sadeghi, Heather Read, Ian Stevenson, Monty Escabi
University of Connecticut, Storrs, CT, USA

Barlow and others have suggested that organisms and the neural networks that underlie sensory perception are optimized to capture statistical regularities in sensory scenes. Accordingly, high-order statistical regularities in natural sounds such as water and fire are critical for perceptually discriminating and categorizing sounds (McDermott and Simoncelli, 2011; Geffen et al., 2011).

Though neural responses in the central auditory system vary with modulation and correlation sound statistics (Escabi and Schreiner, 2002, Rodriguez et al., 2012) it remains unclear whether sensitivity to high-order statistics could be used to discriminate sound category and how this might be instantiated. Here we characterize single neuron activity of central auditory neurons in the inferior colliculus of awake rabbits in response to an ensemble of sound textures including water, fire and speech babble. We synthetically manipulate each sound by selectively adding or removing high-order statistics using the synthesis algorithm developed by McDermott and Simoncelli (2011). First, we find neural response statistics including spike timing precision and firing reliability change systematically with the sound statistics. Second, we find correlated spiking across pairs of neurons varies with sound category and its synthetically manipulated statistics. Using neurometric and ideal observer analyses we demonstrate that neural response statistics can be used to discriminate sounds. Systematic removal of the high-order sound statistics decreases the neural-based sound classification performance. Conversely, systematic increase in the number of neurons used increases neural-based sound classification performance.

This study indicates that neural response statistics in the inferior colliculus have the capacity to capture statistical regularities in sounds that are critical for sound categorization. These findings are significant as they support the concept that statistical regularities are major drivers of sensory systems in general. Moreover, our findings support the concept that mammalian systems have the capacity to optimize sensory categorization through correlated activity in neuron populations.

Keywords: sound statistics, Neural discrimination, neuron population, central auditory nervous system

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Cox, Daniel - 19

Formin3 regulates dendritic architecture via microtubule stabilization and is required for somatosensory nociceptive behavior

Ravi Das[1], Jenna Harris[1], Istvan Foldi[2], Sumit Nanda[3], Shatabdi Bhattacharjee[1], Surajit Bhattacharya[1], Jozsef Mihlay[2], Giorgio Ascoil[3], **Daniel Cox**[1]
[1]*Georgia State University, Atlanta, GA, USA*
[2]*Biological Research Centre, Hungarian Academy of Sciences, Institute of Genetics, Szeged, Hungary*
[3]*George Mason University, Fairfax, VA, USA*

Transcription factors (TFs) are critical in modulating dendritic architecture, however the molecular mechanisms by which TF activity converges on the cytoskeleton to control neuronal arborization are incompletely understood, as are functional relationships between aberrant dendritic development and impaired peripheral sensitivity. Studies in *Drosophila* have demonstrated that the conserved TFs Cut and Knot exert combinatorial control over aspects of dendritic cytoskeleton development. To investigate transcriptional targets of Cut and/or Knot regulation, we conducted neurogenomic studies, coupled with *in vivo* genetic screens utilizing multi-fluor cytoskeletal and membrane reporters. Moreover, we introduced novel multichannel reconstructions facilitating co-registration of subcellular cytoskeletal components thereby enabling statistical analyses of structural changes that emerge from disruptions in molecular processes. These analyses provide deeper biological insight into the mechanisms by which genetic alterations exert control over dendritic arborization. We uncovered more than fifty previously uncharacterized genes involved in cytoskeletal regulation, ribosomal regulatory function, autophagy, and chaperonin activity. Among these, we identified Formin3 (Form3) as a convergent nodal point of combinatorial Cut/Knot regulation. Time-lapse analyses reveal Form3 is cell autonomously required for maintenance of complex dendritic arbors. Cytoskeletal imaging demonstrates *form3* mutants exhibit a specific destabilization of the dendritic microtubule (MT) cytoskeleton, which leads to defective dendritic trafficking of mitochondria and satellite Golgi. Biochemical studies reveal Form3 directly interacts with MTs via FH1-FH2 domains and promotes MT stabilization via acetylation. Neurologically, mutations in human Inverted Formin 2 (INF2; ortholog of *form3*) have been causally linked to Charcot-Marie-Tooth (CMT) disease. CMT sensory neuropathies lead to impaired peripheral sensitivity. Defects in *form3* function in nociceptive neurons results in a severe impairment in noxious heat evoked behaviors. Expression of INF2 FH1-FH2 domains rescues *form3* defects in MT stabilization and nocifensive behavior revealing conserved functions in regulating the cytoskeleton and sensory behavior thereby providing novel mechanistic insights into etiological bases of CMT neuropathies.

Keywords: dendrite, cytoskeleton, behavior, neurological disease, digital reconstructions

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Queisser, Gillian - 20

Deciphering the dynamical microscale structure-function relation of dendritic spines

Markus Breit[2], Dinu Patirniche[3], Pablo Monteagudo[3], Tino Weinkauf[5], Martin Stemmler[3], Mark Ellisman[4], Andreas Herz[1,3], **Gillian Queisser**[1]
[1]*Temple University, Philadelphia, PA, USA*
[2]*Goethe University, Frankfurt, Germany*
[3]*Ludwig Maximilian University, Munich, Germany*
[4]*UCSD, San Diego, CA, USA*
[5]*KTH Royal Institute of Technology, Stockholm, Sweden*

Dendritic spines are highly plastic and are likely to partake in learning and memory. To gain a quantitative understanding of the influence of a spine's micro-scale architecture on the electro-chemical signals transferred to dendrites, we are developing a numerical framework to solve an electro-diffusion model described by the Poisson-Nernst-Planck (PNP) equations. Computational complexity is addressed by introducing a novel hybrid-dimensional discretization approach and by developing specialized numerical methods based on Finite Volume discretization and geometric multi-grid solvers. Ultra-structural spine reconstructions are integrated as computational domains into this simulation framework. Electron microscopy tomography (EMT) is so far the only imaging method that provides the required spatial resolution. Applying an advanced topological segmentation-algorithm onto EMT image stacks, we were able to extract the entire actin cytoskeleton of spines from mouse cerebellar and hippocampal spines. We focused on the cytoskeletal spatial organization as morphological alterations of dendritic spines are driven by changes of the underlying macromolecular structure that provides their mechanical stability. These findings are complemented by results from micro-scale simulations that can be used to further develop macro-scale descriptions of synaptic transmission and plasticity.

Keywords: dendritic spines, electron microscopy tomography, numerical simulation, Poisson-Nernst-Planck, multi-scale dynamics

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Howard, Marc - 21

Scale-invariant neural memory in the rodent hippocampus

William Mau, Zoran Tiganj, Jingjin Wei, Gene Stanley, **Marc Howard**, Howard Eichenbaum
Boston University, Boston, MA, USA

Theories of human memory have long hypothesized that memory relies on a representation of time. Recently it has been hypothesized that the representation of time should obey the Weber-Fechner law, with logarithmic spacing of receptive fields in time. This representation is scale-invariant, with similar temporal properties over all possible time scales. We test these predictions using optical imaging that allows monitoring of the activity patterns of hundreds of neurons in mouse hippocampus simultaneously. Consistent with prior findings from tetrode recordings we observed sequentially-activated time cells during a period of time on each trial while the animal was running in place on a treadmill. Because each time cell fires during a circumscribed period of time on a given trial, one can observe which cells are firing and infer how much time has passed since the beginning of the treadmill run. The large number of simultaneously-recorded cells enabled us to quantitatively assess the properties of the temporal representation. We found that the distribution of time fields obeyed a power law with exponent near -1, consistent with the Weber-Fechner law. To test if the representation was scale-invariant, we binned the time series at different scales ranging from seconds up to days. We found reliable changes in the response of the hippocampal ensemble at all time scales considered. We discuss the implications for computational theories of hippocampal function and cognitive theories of memory.

Keywords: hippocampus, time, memory, scale-invariance

Weitzenfeld, Alfredo - 22

An integrated hippocampus-prefrontal cortex model for spatial sequence learning by concatenating replayed place-cell snippets

Alfredo Weitzenfeld[1], Pablo Scleidorovich[1], Martin Llofriu[1], Jean-Marc Fellous[2], Nicolas Cazin[3], Peter Dominey[3], Bruce Harland[2]
[1]*University of South Florida, Tampa, FL, USA*
[2]*University of Arizona, Tucson, AZ, USA*
[3]*INSERM, Lyon, France*

Experimental studies have shown that rats are able to efficiently navigate between multiple rewarded sites in an open field. From trial to trial, rats explore both inefficient path segments as well as segments that contribute to the final path. During inter-trial pauses, recently traversed place fields reactivate in short sequences ("snippets") in the hippocampus. We hypothesize that this hippocampal replay exposes prefrontal cortical (PFC) circuits to subsequences of the final sequence that should be generated. We test the hypothesis that by selecting efficient segments that include a reward, the model can learn to reconstruct the efficient final trajectory. Furthermore, when exposed to snippets from different overlapping sequences the model is able to produce a more efficient sequence by combining the shortest segments from each of them. In previous work we have implemented a PFC reservoir model with feedback, capable of concatenating snippets that have place fields with sufficient overlap. In our latest work, we embed our Hippocampus-PFC model in a simulated rat to (1) test the extent to which the output of the model can guide navigation, and (2) measure how much training sequences differ from each other and from the final sequence and how the model is able to produce a near optimal trajectory. In particular, we assess the effect of different initial movement strategies that generate training sequences, by changing the probability of moving to the closest rewarded site, and the probability of moving to a non-previously visited reward location. Finally, we also present the implemented architecture that combines hippocampus snippet formation with the PFC reservoir module.

Keywords: Hippocampus, Prefrontal Cortex, Spatial Sequence Learning, Replay, Place Cells

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Krusienski, Dean - 23

REvealing SPONtaneous Speech processes in Electrocorticography (RESPONSE)

Dean Krusienski[1], Christian Herff[2], Garett Johnson[1], Srdjan Lesaja[1], Hassan Baker[1], Jerry Shih[3], Tanja Schultz[2]
[1]*Old Dominion University, Norfolk, VA, USA*
[2]*University of Bremen, Bremen, Germany*
[3]*University of California San Diego Epilepsy Center, San Diego, CA, USA*

The complex dynamics of brain activity and the fundamental processing units of continuous speech production and perception are largely unknown, and such dynamics make it challenging to investigate these speech processes with traditional neuroimaging techniques. Electrocorticography (ECoG) measures electrical activity directly from the brain surface and covers an area large enough

to provide insights about widespread networks for speech production and understanding, while simultaneously providing localized information for decoding nuanced aspects of the underlying speech processes. Thus, ECoG is instrumental and unparalleled for investigating the detailed spatiotemporal dynamics of speech. Prior work using ECoG has largely focused on studying prompted and isolated aspects of speech. In pursuit of the ultimate objective of developing a natural speech neuroprosthetic for the severely disabled, the present work investigates the neural processes of continuously-spoken modal and imagined speech production. ECoG data have been collected from subjects undergoing clinical monitoring for epilepsy at Mayo Clinic Florida and the University of California San Diego Epilepsy Center. The subjects performed a battery of speech tasks including modal and imagined continuous speech based on phonetically-balanced sentence prompts, as well as spontaneous modal and imagined speech via standard picture description and directed conversation tasks. The high gamma-band power (70-170 Hz) of EGoG, which has been shown to be highly correlated with a variety of cognitive processes, was extracted and analyzed in conjunction with the recorded speech signals. Traditional automatic speech recognition (ASR) techniques with a customized ECoG frontend were applied to time-align speech with the corresponding phones, thus facilitating the analysis of phone alignments and the spectral reconstruction in preparation of parametric speech synthesis. Preliminary results related to spectrogram reconstruction and speech synthesis will be presented; in addition, an investigation of the neural correlates of mouth movements of spontaneous speech from video recordings will be described.

Keywords: ECoG, speech, ASR, neuroprosthetic

Jagota, Anand - 24

Coarse-grained model of SNARE proteins addresses mechanistic bases for synaptic transmission

Nicole Fortoul[1], Maria Bykhovskaia[2], **Anand Jagota**[3]
[1]*Lehigh University, Bethlehem, PA, USA*
[2]*Wayne State University, Detroit, MI, USA*
[3]*Lehigh University, Bethlehem, PA, USA*

SNARE proteins drive the fusion of synaptic vesicles that underlies synaptic transmission. The SNARE complex includes the vesicle protein synaptobrevin and the membrane protein synaxtin. The cytosolic protein SNAP25 binds to syntaxin forming t-SNARE, and together the SNARE proteins form a coiled coil four-stranded bundle which meditates the attachment of a synaptic vesicle to the plasma membrane. We aim to develop a mechanistic understanding of the molecular processes of the SNARE assembly and unraveling using computational models. We present a new coarse-grained model for the canonical four-helix SNARE protein bundle. The model places beads at the sites of each alpha-carbon, representing the entire residue. This is the greatest level of simplification that still retains sequence specificity. Intra-helical interactions are represented by a spring-network; inter-helical interactions, which provide the adhesion energy to drive docking and fusion, are based on the Miyazawa-Jernigan model. The model is solved using Brownian Dynamics, so the fluid resistance to motion and random forces due to the solvent are represented implicitly. We will present two applications of this model that address basic questions regarding mechanisms of synaptic transmission. First, we combine the coarse-grained model with a model for long-range vesicle-membrane repulsion and deformation to answer the question: How many copies of SNARE are needed for docking? We show that 4-8 SNAREs are optimal if the criterion is minimization of distance between the vesicle and plasma membrane. The second question we address asks: What is the time-scale for SNARE assembly and how close does synaptobrevin need to be to the t-SNARE for assembly to occur rapidly? We show that assembly time grows exponentially with distance between the proximal ends of synaptobrevin and syntaxin, suggesting that an additional agent is required to initiate assembly but that, once brought close, zippering can occur at the micro-second time scale.

Keywords: SNARE, Synaptic Transmission, Coarse-Grained Model, Brownian Dynamics

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Guntupalli, J. Swaroop - 25

Connectivity hyperalignment reveals finer parcellation of cortex

J. Swaroop Guntupalli[1,2], James Haxby[1,2]
[1]*Center for Cognitive Neuroscience, Dartmouth College, Hanover, NH, USA*
[2]*Department of Psychological and Brain Sciences, Dartmouth College, Hanover, NH, USA*

Functional connectivity measured during the resting state fMRI (rsfMRI) has been used to divide the cortex into parcels. Nodes in each parcel have similar patterns of connectivity with rest of the brain and are thought to be a major component of cortical functional architecture. Network and connectivity analyses to explore cortical architecture, to relate connectivity structure to behavior, and for diagnosis of clinical conditions are done using these parcels assuming a common connectivity within each parcel. Parcellation is typically derived at the group level by aggregating connectivity profiles across individuals based on anatomy. This could potentially smooth the fine-scale variation that does not covary with anatomy resulting in 1) smaller differences in connectivity profiles across parcel borders

as they don't always follow anatomy, and 2) coarser parcels that survive the averaging. We developed an algorithm called Connectivity Hyperalignment (CHA) that aligns cortical nodes in a high dimensional space based on their connectivity profiles. CHA applied to rsfMRI preserved the shared fine-scale connectivity structure across individuals. Applying cortical parcellation to rsfMRI after CHA resulted in 1) larger differences in connectivity profiles across parcel boundaries and 2) more parcels for a given threshold compared to anatomy based alignment. Our results show that using CHA reveals shared fine-scale substructure within large parcels that captures finer variation in connectomes. This fine-scale variation could potentially reveal a stronger link to behavior and individual variability related to diagnoses.

Keywords: Hyperalignment, Parcellation, Functional connectivity, fMRI

Mazer, James - 26

Saccades trigger predictive updating of attentional topography in area V4

Alexandria Marino[2], **James Mazer**[1,2]
[1]*Montana State University, Cell Biology and Neuroscience, Bozeman, MT, USA*
[2]*Yale University School of Medicine, Neuroscience, New Haven, CT, USA*

Saccades and attention both facilitate efficient allocation of limited neural resources. Attention is mediated by retinotopic brain areas, thus the specific neurons representing an attended feature change with each saccade. How attentional topography in the brain is updated to compensate for eye movements is currently not well understood. We asked whether saccade plans could trigger predictive attentional shifts in extrastriate area V4, a cortical region critical for attentional targeting, by recording from neurons in monkeys performing a novel spatiotopic target detection task where performance depended on robust saccade compensation. Using reverse correlation-based analysis of neural responses to task-irrelevant probe stimuli appearing throughout each trial we characterized attentional modulation before, during and after saccades. The results reveal found evidence of a predictive attentional "hand-off" starting before saccade onset. This hand-off reflects a transfer of attentional state from neurons with RFs inside the attentional focus before the saccade to those with RFs that would fall inside the focus after the saccade, suggesting spatiotopic attention is maintained by predictive attentional updating in V4.

Keywords: V4, attention, saccades, predictive, remappingSaccades trigger predictive updating of attentional topography in area V4

Dougherty, Kimberly - 27

Relative contributions of intrinsic properties and connectivity to rhythmogenesis in spinal interneurons

Ngoc Ha[1], Lihua Yao, Natalia Shevtsova, **Kimberly Dougherty**
Drexel University College of Medicine, Philadelphia, PA, USA

The hindlimb locomotor central pattern generator (CPG) is located in the thoracolumbar spinal cord and can generate the basic locomotor rhythm and pattern without supraspinal input or sensory feedback. It was suggested that the CPG has two functional levels: the rhythm generating level which sets the rhythmic output of the system and the pattern formation level which coordinates motor neuron activation. The rhythm generating level on each side includes flexor and extensor rhythm generator (RG) interneurons (INs), reciprocally inhibiting each other via inhibitory INs. Previous studies proposed an asymmetric flexor/extensor organization where flexor RG INs are intrinsically rhythmic while extensor RG INs fire tonically at a higher excitability state and are driven into rhythmicity by phasic inhibition from bursting flexor RG INs via inhibitory INs. The goal of the present study is to determine potential factors contributing to RG flexor/extensor asymmetry, focusing on connectivity and intrinsic properties related to excitability and rhythmogenesis. INs expressing the transcription factor Shox2 were shown to be a cellular component of the rhythm generator. Therefore, we performed whole cell patch clamp recordings from identified Shox2 INs in reduced isolated spinal cord preparations from neonatal Shox2:Cre; tdTomato mice. Flexor and extensor RG INs were identified by fluorescence and their preferred firing phase during drug-evoked locomotion *in vitro*. Intrinsic passive and active properties were measured, including ionic currents linked to cellular rhythmicity. Our data suggest that there are minimal differences in intrinsic excitability between flexor- and extensor-related Shox2 INs. Potential rhythmogenic currents including I_h, persistent inward current, and T-type Ca^{2+} current are present in some of these INs. Dual Shox2 IN recordings show that interconnectivity can be either unidirectional or bidirectional and may be preferential within flexor and extensor RG populations. Therefore, connectivity and expression of particular ionic currents in RG INs may contribute to flexor-extensor asymmetry.

Keywords: spinal cord, locomotion, central pattern generator

Gläscher, Jan - 28

Investigating Theory of Mind during cooperative decision-making

Tessa Rusch[1], Yuqing Lei[2], Vanessa Hayes[2], Michael Spezio[2], **Jan Gläscher**[1]
[1]*Hamburg University Medical Center, Hamburg, Germany*
[2]*Scripps College, Claremont, CA, USA*

Assessment of Theory of Mind typically involves variations of a "False Belief Task", in which a participant must reason about another person's belief states, separate from her own, for successful performance. We investigated mentalizing by requiring it for successful performance in a novel cooperation task involving real stakes for the participants.

Two participants engage in a probabilistic choice task that depends on understanding each partner's beliefs and preferences. High rewards result from "cooperative" choices (both players obtaining their respective "good" or "poor" option). Outcome distributions reverse after several trials of cooperation, though only the one participant (the Teacher) knows this. The other participant (the Learner) thus has a false belief about the state of the world. To facilitate cooperative success, the Teacher must track how the Learner's false belief evolves and communicate the contingency reversal to the Learner. The Lerner needs to recognize the Teacher's intention and react accordingly. On each trial both players make predictions about their partner's choices before making their own. EEG hyperscanning data from both participants allows analyses of neural systems underlying accurate theory of mind.

Analyses of behavioral choices and RT data suggest that both participants closely monitor partners' choices and engage in costly mentalizing processes about partners' intentions. Although the Teacher knows that contingencies have reversed for the Learner, she still predicts the Learner's formerly good choice, because the Teacher knows that the Learner cannot know about the reversal yet. Following the reversal, the Learner gradually switches to her new best choice, which closely matches the Teacher's predictions.In conclusion, our novel cooperation task elicits strong mentalizing processes, which we model using both game theoretic and interactive POMDP approaches. Computing belief updates in both players and their level of recursive thinking when constructing a model of their partner results in model-based signals that inform the analysis of the neural data.

Keywords: Theory of Mind, mental models, cooperative decision-making, I-POMDP, EEG hyperscanning

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Lefebvre, Germain - 29

Neurocomputational substrates of the monetary exchange: an interdisciplinary investigation

Sacha Bourgeois-Gironde[1,3], Ming Hsu[5], Stefano Palminteri[2,4], **Germain Lefebvre**[1,2]
[1]*Laboratoire d'Économie Mathématique et de Microéconomie Appliquée (LEMMA), Université Panthéon-Assas, Paris, France*
[2]*Laboratoire de Neurosciences Cognitives, Institut National de la Santé et de la Recherche Médicale, Paris, France*
[3]*Institut Jean-Nicod (IJN), CNRS UMR 8129, Ecole Normale Supérieure, Paris, France*
[4]*Institut d'Étude de la Cognition, Departement d'Études Cognitives, École Normale Supérieure, Paris, France*
[5]*Haas School of Business, University of California, Berkeley, Berkeley, CA, USA*

Money raises a fundamental question: why and how intrinsically useless objects can acquire a positive exchange value? In our research, we more particularly seek to elucidate the set of cognitive processes that have made money-emergence possible, as well as to investigate their neural underpinnings. To this aim we deploy computational modeling of human behavior on a money emergence task. The latter is based on a game theoretic model first proposed by Kiyotaki and Wright, which remains one of the most influential theoretical models of money emergence. In this paradigm, a Type $i = 1, 2, 3$ agent desires to consume the good corresponding to his type (Good i) but produces Good $i + 1$, so that there is no double coincidence of wants. This absence of a double coincidence of needs is the staple hypothesis of why money has emerged. From here, the individual is facing a dilemma concerning the storage of commodities that are not of immediate use but could be traded against desirable goods in the future. In this research, we in fact use a task that allows us to characterize the process itself that leads to the identification of a behavioral strategy that implies the utilization of a priori non-valuable items as mean of exchange (i.e. money) to obtain a reward. From a computational perspective, this strategic learning process is analyzed through a spectrum of temporal difference reinforcement learning models, beliefs learning and hybrid models. Once established the computational processes of money emergence, we will look for the neural implementation of these computations, first, with functional magnetic resonance imaging (fMRI), secondarily with classical neuro-psych-o-logical lesion-function mapping. Our research is then focused on the brain mechanisms which underpin emergence of media for exchange in stylized decision environments such as those offered by the basic search-theoretical structures that we use.

Keywords: Money emergence, Reinforcement Learning, Belief Learning, fMRI

Llano, Daniel - 30

Dynamic network analysis of thalamocortical interactions in a brain slice preparation

Daniel Llano[1], Tanya Berger-Wolf[2], Robert Kenyon[2], Umberto DiFabrizio[2], Aynaz Taheri[2], Chihua Ma[2], Kevin Stebbings[1], Baher Ibrahim[1]
[1]*University of Illinois, Urbana, IL, USA*
[2]*University of Illinois, Chicago, IL, USA*

Recent evidence suggests that the representation of sensory information undergoes a significant transformation between the thalamus and the cerebral cortex. For example, several investigators have found that cortical responses to thalamic stimulation comprise population patterns of activity that are non-linear, i.e., not strongly related to the temporal details of thalamic activity. To examine the mechanisms underlying this transformation, we used the auditory colliculo-thalamocortical mouse brain slice preparation, developed by our laboratory, which retains synaptic connectivity between inferior colliculus (IC), medial geniculate body (MGB), and auditory cortex. Using flavoprotein autofluorescence (FA) to measure the activity in each of the circuit components, we observed all-or-none cortical FA responses without any change in IC and MGB responses following IC stimulation. To examine the mechanisms underlying this phenomenon, we applied a novel dynamic network analysis method, called CommDy (community dynamic) analysis, to activations seen in the auditory cortex. CommDy is inspired by social network theory and is based on combinatorial optimization algorithms to monitor the changing membership of different communities of individuals in a network. We recently adapted this technique to study the impact of aging on network behavior in the aging auditory cortex and found that CommDy identified strong differences between these population groups based on network cohesion. We also applied a series of physiological manipulations to the slice preparation and found that blockade of $GABA_A$ receptors linearized the relationship between thalamus and cortex. These data suggest that the thalamus may recruit cortical ensembles rather than linearly encoding ascending stimuli, and that GABAergic inhibition may play a role in selecting cortical ensembles for activation.

Keywords: thalamus, cortex, dynamic, imaging, flavoprotein

Rotstein, Horacio - 31

Inhibition-based theta resonance in a hippocampal network

Horacio Rotstein[1], Eran Stark[2]
[1]*New Jersey Institute of Technology, Newark, NJ, USA*
[2]*Tel Aviv University, Tel Aviv, Israel*

A crucial issue in the understanding of neuronal oscillations is to elucidate the microcircuits that are the substrate to these rhythms. This raises the question of whether and how the individual neurons' preferred frequency responses to oscillatory inputs are communicated to spiking and network regimes.

We address these issues theoretically in the context of the unexpected in vivo experimental results reported in Stark et al (Neuron, 2013). Briefly, pyramidal cells (PYR) and PV+ interneurons (INT) were optogenetically activated using wide-band (WB) oscillatory signals. While PYR have been shown to exhibit theta subthreshold resonance in vitro, in vivo responses of individual directly activated PYR were not predominantly at theta, but rather WB. In contrast, PYR exhibited theta band-limited spiking induced through direct activation of INT in the absence of PYR activation. INT exhibited a WB response in both cases.

We present a minimal biophysical model of a CA1 hippocampal network that captures these experimental results. The basic model includes PYR and INT. The extended models include also OLM cells and synaptic depression. PYR and OLM included h-currents. The presence of subthreshold resonance in isolated PYR is not communicated to the spiking regime mainly due to the strong effect of the oscillatory input amplitude. PYR theta-band response results instead from a combination of rebound spiking and a timing mechanism. Rebound spiking is responsible for the generation of spikes at input frequencies that are low enough for the voltage response to be above threshold. The timing mechanisms are responsible for “erasing” spikes generated by input frequencies lower that theta. We implemented three such mechanisms: (i) network-mediated inhibition from OLM, (ii) synaptic depression of INT synapses, (iii) INT gamma resonance. They are examples of the generic classes of "deleting" and "preventing" mechanisms. Overall, these results provide a mechanistic understanding of network resonance at theta frequencies.

Keywords: frequency preference, oscillations, rhythms

Smolinski, Tomasz - 32

Analyzing adaptive modulation in spinal motor neurons using Multi-Objective Evolutionary Algorithms and GPU computing

Karla Miletti[1], Kofi Forson[1], Kyrhee Powell[1], Curtis Hite[1], Joseph Lombardo[2], Melissa Harrington[2], **Tomasz Smolinski**[1]
[1]*Department of Computer and Information Sciences, Delaware State University, Dover, DE, USA*
[2]*Department of Biological Sciences, Delaware State University, Dover, DE, USA*

Plasticity is a defining feature of the nervous system that allows it to undergo changes in response to stimuli. It is therefore important to study how nerve cells' behavior can be modified for the advancement of basic science, prosthetics, and therapy. We hypothesize that the alteration in the function of the Kv7.2 channel (which carries the M current) and changes in the axonal initial segment (AIS) properties are the primary mechanisms of adaptation of spinal motoneurons to prolonged network activation. This hypothesis is supported by literature and our own experimental data. To further test our hypothesis, we developed a realistic computational model of a spinal motoneuron, accounting for its attributes before and after persistent network activation. This computational approach allowed us to employ an evolutionary algorithm, which uses mechanisms inspired by biological evolution, such as reproduction, mutation, recombination, and natural selection, to generate biologically feasible models. We adjusted the range of model parameter values to reflect the experimental data to anchor our methods in biology, and to take advantage of the algorithm's ability to create many different models fitting that biological description. Our algorithm matched multiple selection criteria simultaneously (*e.g.*, input resistance, current threshold) and generated entire collections of neuronal models that could be mined for rules elucidating the behavior captured experimentally, including those describing relationships between neuronal activity and model parameters. Furthermore, we parallelized the evolutionary algorithm by utilizing the OpenACC programming paradigm, which enabled us to employ the speed of Graphics Processing Units (GPUs) for scientific computing.

Keywords: Adaptation, plasticity, spinal motoneurons, computational models, multi-objective evolutionary algorithms

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Cheng, Sen - 33

Intrinsic sequences in the hippocampus for spatial navigation and memory storage

Sen Cheng
Ruhr University Bochum, Bochum, Germany

The hippocampus in the mammalian brain is known for two seemingly disparate functions: episodic memory and spatial representations. However, how does the hippocampus implement these two functions and what do they have in common? I will discuss our modeling results that show that neuronal sequence generation in the CA3 subregion might be key to understanding the role of the hippocampus separately in spatial navigation and in episodic memory. With respect to episodic memory, I recently proposed that CA3 intrinsically produces neuronal sequences, which are hetero-associated during memory encoding with sequences in other subregions that are driven by sensory inputs. During retrieval, sequences in CA3 reactivate the original sequences in downstream regions. Memory performance is determined by the network's ability to perform sequence completion, i.e., the output should be more similar to the original sequence than the retrieval cue. We found that the robustness of sequence retrieval depends on the neural dynamics of CA3 and the input statistics, but can be surprisingly high for biologically plausible cases. Sequential activity also plays an important role in spatial behaviors. During immobility or sleep, place cells are reactivated in a sequential order that reflects the sequence of the animal's prior locations or the upcoming trajectory. During running, the activity of place cells occurs in a sequential order within a single cycle of the theta oscillation in the LFP. While a recent study suggested that replay and theta sequences are dissociated, we can account for both types of sequential activity and their differences within a single model. Differences arise simply due to the different inputs in the two behavioral states. I thus conclude that the key function of CA3 is to generate intrinsic sequences that are used for episodic memory and spatial navigation.

Keywords: sequences, hippocampus, episodic memory, spatial navigation, spatial representation

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Kuokkanen, Paula - 34

Differential tuning of the low- and high-frequency components of the neurophonic spectrum reveals the spike contribution of barn owl's nucleus laminaris neurons

Paula T Kuokkanen[1,2,3], Anna Kraemer[3], Thomas McColgan[1,2], Catherine E Carr[3], Richard Kempter[1,2]
[1]*Institute for Theoretical Biology, Humboldt-University Berlin, Berlin, Germany*
[2]*Bernstein Center for Computational Neuroscience Berlin, Berlin, Germany*
[3]*Department of Biology, University of Maryland, College Park, MD, USA*

Extracellular field potentials (EFPs) are challenging to interpret. Our aim is to reveal the neural sources of the "neurophonic", a robust frequency-following EFP recorded in the nucleus laminaris (NL) in the brainstem of the barn owl. Putative generators of the neurophonic are the activity of afferent axons, synapses onto NL neurons, and NL neurons' spikes.

We recorded the neurophonic in response to binaural high-frequency tones (3–7 kHz), varying the interaural time difference (ITD). The mean activity of the monaural inputs to NL does not change with ITD. However, their relative phase does, causing cancellation or summation of input signals. The firing rate of NL neurons strongly depends on ITD. To disentangle these two components, we analyzed the broadband power spectrum (PSD) of the response.

The PSD's low-frequency component (LFc, 200–700 Hz) depended on ITD and closely resembled the spectrum of extracellularly recorded NL neurons' spikes. Thus, the LFc reflects the contribution of NL neurons' spikes. The PSD at the stimulus frequency (SFc, 3–7 kHz) was much stronger than the LFc. The SFc also depended on ITD, reflecting the inputs' activities and their relative phase change with ITD. PSD at other frequencies did not depend on ITD.

Finally, we compared the ITD and frequency tuning of the LFc and the SFc at each recording site. Interestingly, their best ITDs were independent. Also, their tuning to stimulus frequency was different. Both findings indicate that the LFc might originate from NL neurons' axons near the electrode. Related NL somata can be located hundreds of micrometers away. Together, these findings are consistent with the anatomy of NL and reveal the small contribution of NL neurons to the neurophonic.

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Keywords: Auditory system, extracellular field potential, neurophonic, auditory coincidence detector, action potential

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Riecke, Hermann - 35

The effect of structural plasticity and network reorganization on olfactory output

Hermann Riecke[2], John Hongyu Meng[1], Kurt Sailor[2], Soham Saha[2], Pierre-Marie Lledo[2]
[1]*Northwestern University, Evanston, IL, USA*
[2]*Institut Pasteur, Paris, France*

Persistent plasticity in the mammalian olfactory bulb is a striking feature of early olfactory processing and structural plasticity is a central component of it. An extreme component of this plasticity arises through adult neurogenesis of the olfactory bulb's dominant interneuron population (granule cells), which undergo persistent addition and loss throughout the life of the animal. Additionally, the mature granule cells exhibit highly dynamic, persistent turnover of their apical dendritic spines, with matching dynamics in the GABAergic synapses of their connected partners, mitral/tufted cells, the bulb's principal output neurons. Previously, using computational modeling of structural plasticity in the olfactory bulb circuit, we identified potential advantages of structural changes in connectivity in such a sparsely connected network. Yet, the impact of this structural plasticity on the activity of granule cells or connected mitral/tufted cells is not clear.

Using in-vivo Ca-imaging in awake, head-fixed mice we investigate how activity affects the structural plasticity of granule cells. Animals were labeled with the genetically encoded calcium indicator GCaMP6f and TdTomato to track activity and structural changes, respectively. We investigate how activity modifies the responses of these neurons with the ensuing effect on olfactory bulb output. These data provide input for our computational modeling. We build on models for the network restructuring through adult neurogenesis and spine fluctuations that we have developed previously. The modeling predicts that exposure to an odor predominantly reduces the response of the mitral cells to that odor (i.e. adaptation), while the response of the same mitral cells to a novel odor is typically much less adapted. Comparing the impact of the learning of an easy discrimination task with that of a difficult task the model predicts that differences in the odor representations corresponding to the difficult task are enhanced while differences for the easy task are reduced.

Keywords: structural plasticity, neurogenesis, spine dynamics, stimulus discrimination, olfaction

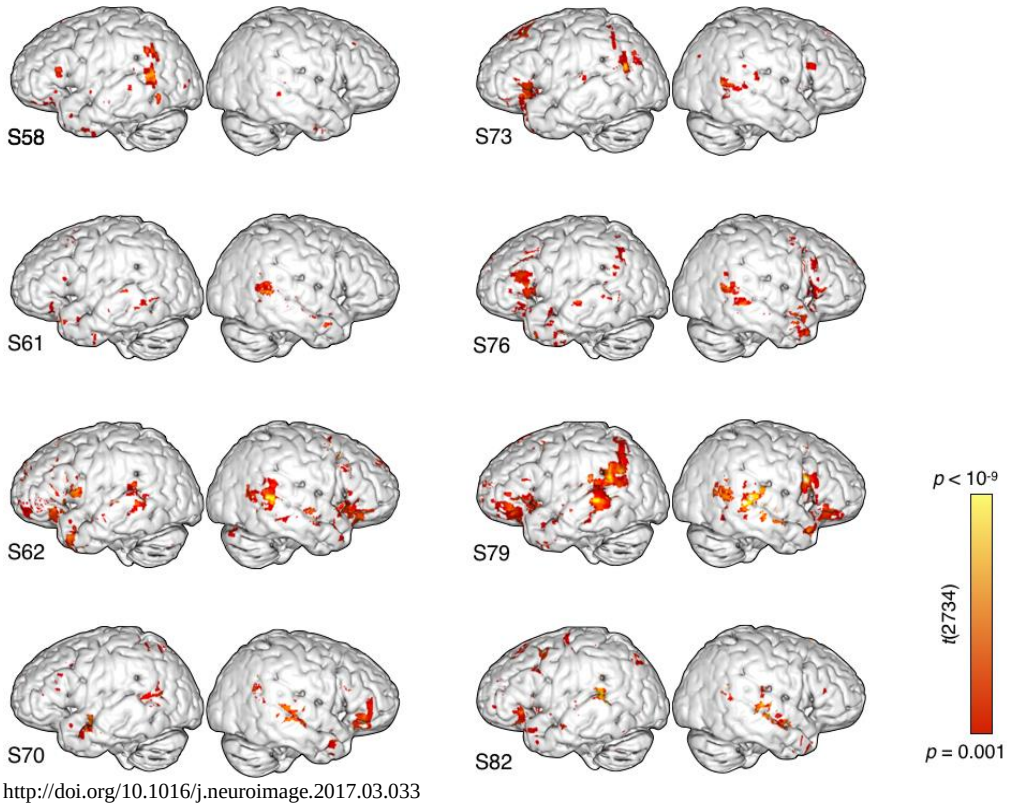
Neuroimaging the language network with a parsing algorithm

John Hale[1], Jonathan Brennan[2], Shohini Bhattasali[1], Wen-Ming Luh[1], Christophe Pallier[3]
[1]*Cornell University, Ithaca, NY, USA*
[2]*University of Michigan, Ann Arbor, MI, USA*
[3]*Université Paris-Saclay, Paris, France*

Language comprehension is sub-served by a left-lateralized perisylvian network of brain areas. In passive listening scenarios, previous work has highlighted the role of the temporal lobe specifically in the comprehension of linguistic structure, or syntax (e.g. Brennan et al. 2012). We scale up from previous work at the group level to identify functionally precise networks of syntax processing in individual participants. We analyzed multi-echo fMRI timecourses (Kundu et al, In Press) that were recorded during a passive story-listening task using predictors derived from a linguistically-plausible parsing algorithm. The results implicate temporal and frontal areas whose contribution to this specific cognitive function varies across individuals. This finding accords well with proposals that emphasize Broca's area in addition to temporal regions (e.g. Friederici and Gierhan 2013), and sets the stage for ongoing efforts to model the functional contribution of individual elements within this network.

Participants (N=26, 16 female) listened to a spoken recitation of THE LITTLE PRINCE for 1.5 h. Their comprehension was confirmed through multiple-choice questions. Using automatically-assigned phrase structure trees for the 15,468 words of this stimulus, the number of "reduce" steps that an incremental, bottom-up parser would execute in between each word (see chapter 3 of Hale 2014) was entered as a regressor in a GLM that also included nuisance variables such as word frequency and acoustic silence. Individual participants showed stable effects for parsing in perisylvian regions including the left inferior frontal gyrus, the posterior superior temporal lobe, and the anterior temporal lobe. The relative contributions of these regions appear to vary across individuals. Developing fine-grained computational models of this variation is a target of our ongoing efforts. More broadly, temporal and frontal regions seem to do a computation that is well-modeled by a word-by-word parsing algorithm.

Brain activity from 8 representative participants showing relationship between incremental sentence parsing and a network of frontal and temporal regions



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Multi-Echo fMRI: A Review of Applications in fMRI Denoising and Analysis of BOLD Signals
Prantik Kundu, Valerie Voon, Priti Balchandani, Michael V. Lombardo, Benedikt A. Poser, Peter Bandettini
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Keywords: language, parsing, syntax, Broca, temporal

Hein, Bettina - 37

Long-range order from local interactions: organization and development of distributed cortical networks

Bettina Hein[1], Gordon B Smith[2], David E Whitney[2], David Fitzpatrick[2], Matthias Kaschube[1]
[1]*Frankfurt Institute for Advanced Studies, Frankfurt, Germany*
[2]*Max Planck Florida Institute for Neuroscience, Jupiter, FL, USA*

The cortical networks that underlie behavior exhibit an orderly functional organization at local and global scales, an organization that is especially evident in the visual cortex of carnivores and primates. Here, neighboring columns of neurons occupying a millimeter of cortical surface area represent the full range of stimulus orientations and are anatomically linked into distributed networks spanning several millimeters that share similar functional properties and are arranged in a modular fashion. In this study, we use spontaneous (endogenous) cortical activity patterns to explore the fine-scale functional structure of this distributed network and how the coordinated local and large-scale structure of this network arises during development. Using in vivo imaging of calcium signals in mature ferret visual cortex, we find that spontaneous activity exhibits remarkably widespread and specific modular correlation patterns such that the local structure of orientation columns is accurately predicted by the spontaneous activity of neurons that lie several millimeters away. We observe 'fractures' reflecting the global spontaneous correlation structure and find that these are in tight register with pinwheel center discontinuities in the orientation map. Chronic in vivo imaging experiments demonstrate that these large-scale modular correlation patterns and fractures are present and predictive of the mature network structure at early stages of cortical development, prior to the elaboration of long-range horizontal network connections. Moreover, we observe that spontaneous activity is relatively low dimensional. A minimal statistical model suggests that constraining the spatial activity patterns to a low dimensional set is sufficient to generate long-range correlations and fractures. A circuit model designed to achieve low-dimensionality shows that local connections are sufficient to explain the emergence of long-range correlations and fractures. These results suggest that local connections in early cortical circuits generate structured long-range network correlations that underlie the formation of distributed functional networks.

Keywords: visual cortex, ferret, development, distributed networks, spontaneous activity

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Quinn, Roger - 38

Developing a neuromechanical model of mammalian locomotion that captures stability mechanisms

Roger Quinn[1], Hillel Chiel[1], Alexander Hunt[3], Martin Fischer[2], Emanuel Andrada[2], Dirk Arnold[2]
[1]*Case Western Reserve University, Cleveland, OH, USA*
[2]*Friedrich-Schiller-University, Jena, Germany*
[3]*Portland State University, Portland, OR, USA*

We are conducting animal and computational experiments to gain a better understanding of the neural mechanisms that allow animals to maintain stability as they walk and run despite perturbations. Our goal is to develop a biologically plausible model of the spinal and peripheral circuits responsible for locomotion and stability in the hind legs of tetrapods. We will present data on three-dimensional kinematics, kinetics, and muscle activity of dog locomotion in a split belt preparation, collected through bi-planar X-ray videography, force plates, and EMG recordings. In our future work, we plan to collect similar data on rats running on a treadmill and experiencing unexpected perturbations including trapdoors, holes and lateral accelerations. Biomechanical models are used to calculate and infer important parameters that cannot be directly or completely measured. For example, an inverse dynamics model uses kinematics and force plate data to calculate joint torques in the legs. Then, using that data and EMG recordings from a subset of muscles, a higher fidelity biomechanical model is used to infer the likely muscle activity in the many other muscles in the legs during the behaviors of interest. Motoneuron activation is then estimated from muscle activity, which is the desired output of the computational neural network that we are developing. We will also present our current neural model for controlling the hind legs of a rat biomechanical model in the sagittal plane. The neural model includes a pattern formation network with oscillators at each joint and lower level afferent feedback networks. Its architecture and synaptic connections are based on the literature and our observations. In the future, we will integrate a higher-level rhythm generator CPG.

Keywords: high-speed x-ray videography, central pattern generators, sensory afferent feedback, neural network control

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Smith, Elliot - 39

Spectral features of high-frequency local field potentials during epileptiform discharges on ECoG and microelectrodes

Elliot Smith[1], Jyunyou Liou[1], Edward Merricks[1], Columbia University Comprehensive Epilepsy Center[1], Catherine Schevon[1]
[1]*Columbia University Medical Center, New York, NY, USA*

High-frequency oscillations (> 40 Hz; HFOs) recorded from intracranially implanted surface or depth electrodes have been extensively investigated as a biomarker of epileptic brain regions. Here we characterize seizures with a rhythmic slow wave (< 8 Hz) onset pattern, which often exhibit large, high amplitude HFOs at their onset. Using electrocorticography and microelectrode array recordings from human epilepsy patients, we examine spectral characteristics of epileptic discharges during three seizure epochs: *pre-recruitment*, *post recruitment*, and *pre-termination*. These epochs were operationally defined and characterized in a previous paper from our lab (Smith et al., 2016).

As assessed from ECoG, *pre-recruitment* discharges were associated with high-amplitude, gamma-range (30 - 50 Hz) oscillations. These high-amplitude HFOs occurred across large brain regions and were not limited to the location of tissue that was recruited into the seizure (i.e. the ictal core (Schevon et al., 2012)).

Post-recruitment discharges also exhibited high-amplitude phase-locked HFOs, however these discharges were significantly larger, higher-frequency, and broader-band than earlier discharges. Furthermore, these discharges correlated with the location of the ictal core. Discharges in the *post-recruitment* and *pre-termination* epoch exhibited similar amplitudes, both exhibited significantly more spectral complexity than *pre-recruitment* discharges, as measured by spectral entropy.

Upon examining microelectrode recordings of the same seizures, we found the similar LFP features on microelectrodes as described above for ECoG. Multi-unit activity was significantly greater for pre-recruitment than both post-recruitment and pre-termination periods.

We conclude that the spectral features of these discharges and their associated neuronal activity suggest that discharges which occur outside of the ictal core arise from tissue in which feed-forward inhibition remains intact, implying that HFOs arise from the interplay between fast-spiking interneurons and pyramidal cell activity. Discharges arising from the ictal core are the result of paroxysmal excitatory activity, and their associated HFOs are not true oscillations, but result from jittered asynchronous excitatory population firing.

Keywords: high frequency oscillations, human, seizures, inhibition, neurons

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Kay, Leslie M. - 41

Gamma to beta oscillation transitions in odor sampling: mechanisms of cognitive state changes?

Leslie M. Kay[1,3], Bolesław L. Osinski[2,3], Thomas A. Cleland[4]
[1]*Department of Psychology, University of Chicago, Chicago, IL, USA*
[2]*Graduate Program in Biophysical Sciences, University of Chicago, Chicago, IL, USA*
[3]*Institute for Mind and Biology, University of Chicago, Chicago, IL, USA*
[4]*Department of Psychology, Cornell University, Ithaca, NY, USA*

Mammalian olfactory systems exhibit local field potential (LFP) oscillations and only gamma (40-110 Hz) is partially understood from mechanistic to functional levels. Beta oscillations (15-30 Hz) arise in response to odor discrimination and sensitization following endogenous olfactory bulb (OB) gamma and are coherent with beta in pyriform cortex (PC). Beta oscillations occur late in odor sampling in discrimination tasks, with a fast (<100 msec) transition from gamma-dominated activity after 2-4 sniffs. Our previously published model suggests that when axonless GABAergic granule cells (GCs) are rendered highly excitable, longer decay times of voltage dependent calcium channels (VDCCs) and NMDA receptors favor a transition to beta (with VDCCs dominating), even if only a subset of GCs are potentiated. GCs may become excitable through neuromodulatory effects or top-down perisomatic inputs, among other factors. When GCs are more excitable, they should produce more somatic spikes. We test three model predictions: (1) decreased GC excitability will decrease beta oscillations, (2) GC NMDARs are not essential for beta, and (3) a subset of GCs should increase firing during beta oscillations. We provide evidence supporting these predictions. Acetylcholine enhances GC excitability via muscarinic receptors. When we infused scopolamine (muscarinic antagonist) into the OB, beta oscillations decreased. Infusion of APV (NMDAR antagonist) reduced gamma but left beta power intact. We also report spiking neurons recorded from the GC layer for the first time in freely moving awake rats and show that there are many different types of spiking relationships of cells to the LFP in this layer during odor sampling, a subset of which increase firing during and lock strongly to beta oscillations. These results present a plausible mechanism for fast transitions from early odor sampling and local processing (gamma) to later beta band activity coordinated across

brain areas that may support decision or action preparation.

Keywords: olfactory bulb, gamma oscillations, beta oscillations, granule cells, scopolamine

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Schevon, Catherine - 42

Modeling the spatiotemporal dynamics of human focal seizures

Jyun-you Liou, Larry Abbott, **Catherine Schevon**
Columbia University, New York, NY, USA

Neocortical focal seizures, despite their huge heterogeneity in etiology, share common clinical manifestations – gradual recruitment of new territory (e.g. the Jacksonian march), tonic-clonic transitions, and terminal slowing – that tend to occur consecutively. Recently, we have published direct observations of neuronal activities during human focal seizures (Smith et al 2016). These observations raise new questions about mechanisms supporting seizure onset, propagation and termination.

We have constructed a model that matches the spatiotemporal activity patterns seen in the seizure data. In the model, seizure activity starts with a localized group of neurons firing asynchronously at very high rates (the activity bump). Surround inhibition (modeled by Mexican-hat connectivity) initially limits the spatial spreading of this activity, but in the area immediately outside the bump, chloride starts to accumulate intracellularly due to a strong feedforward inhibitory effects. Dissipation of transmembrane chloride gradient compromises surround inhibition and leads to slow expansion of seizure territory. Meanwhile, at the bump center, intense neuronal firing activates slow adaptation currents. Within seconds, the bump center collapses and transitions to the "clonic phase" characterized by recurring periodic neuronal bursts. Traveling waves emerge and propagate inwardly along the gradient of adaptation current strength, a new phenomenon not previously modeled. Further strengthening of adaptation currents increases interburst intervals and decreases traveling wave speed, both of which we observed during seizure termination in the human recordings. After a critical transition, the traveling wave solution is no longer supported and the resting state is restored. If we include spike-timing dependent plasticity in the model, the spatiotemporal evolution of the seizure creates centripetal connectivity that results in a decreased threshold for the next seizure. Overall, our model explains the complex spatiotemporal dynamics of focal seizures with minimal assumptions, and it may provide a guide for future developments of close-loop devices designed to control epilepsy.

Keywords: epilepsy, seizure, computational modeling, surround inhibition, human microelectrode recordings

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Kath, William - 43

Finding thresholds in active dendrites

William Kath
Applied Mathematics and Neurobiology, Northwestern University, Evanston, IL, USA

The integration of synaptic inputs in a neuron can be nonlinear not just at the axon, but also locally in the dendrites if they contain active voltage-gated ion channels. For example, CA1 pyramidal neurons have high densities of sodium and potassium and currents in their dendrites, and the densities can vary substantially with location in the arbor. When combined with diameter changes at branch points in the dendritic tree, such nonlinearities can lead to compartmentalized responses to inputs: each branch can act as an individual nonlinear unit in which action-potential-like events known as dendritic spikes occur.

To fully comprehend how pyramidal neurons integrate their inputs, it is therefore necessary to understand the conditions under which combined synaptic inputs initiate dendritic spikes, and how and when these spikes interact with other inputs to generate a somatic action potential.

In contrast to single cell neuron models, however, the dividing line between an active and non-active event in a full compartmental model is a steady-state, unstable, spatially-varying solution. These properties (in particular, instability and spatially variation) make finding such dividing lines and the critical synaptic conductance(s) leading to them troublesome.

The steady-state solution often has only a single unstable eigenvalue, however, leading to several methods to find the dividing line between super- and sub-threshold events. First of all, a projective shooting method that focuses on dynamics in the unstable direction can be used. Second, one can employ a Recursive Projection Method, a functional iteration devised to find steady-states with a finite number of unstable eigenmodes. Finally, Newton's method can be used. The pros and cons for each of these methods will be discussed. In addition, examples will be given showing how the method determines changes in the threshold for dendritic spikes due to variations in branch geometry or ion channel densities.

Keywords: synapses, dendrites, integration, spikes, modeling

Fitzpatrick, David - 44

High cellular and columnar variability underlies the absence of early orientation selectivity

David Fitzpatrick[1], David Whitney[1], Gordon Smith[1], Bettina Hein[2], Matthias Kaschube[2]
[1]*Max Planck Florida Institute for Neuroscience, Jupiter, FL, USA*
[2]*Frankfurt Institute for Advanced Studies, Frankfurt am Main, Germany*

Selectivity for stimulus orientation is a fundamental property of primary visual cortex in primates and carnivores, where it is organized into a smoothly varying columnar map that emerges in an activity-dependent manner during early postnatal life. Despite extensive experimental and theoretical work, it remains unclear what factors limit the emergence of orientation selectivity, such as weak responsiveness to visual stimuli, high trial-to-trial variability, and/or an intermixed 'salt-and-pepper' organization of orientation preferences at the cellular level. To distinguish between these potential factors, we visualized population activity in the visual cortex of developing ferrets with longitudinal imaging of GCAMP6s at both cellular resolution with two-photon calcium imaging and columnar resolution with wide-field epifluorescence imaging. Prior to eye opening, we show that cellular and population responses evoked by single presentations of a grating stimulus surprisingly exhibit robust, modular patterns of network activity resembling activity patterns evoked by gratings in mature animals. However, the spatial location and pattern of domains activated by presentation of the identical stimulus orientation varies substantially across trials, a variability that accounts for the low orientation selectivity of individual neurons and the inability to visualize coherent maps of orientation preference. Yet variability in network activity patterns is not a general feature of the developing cortex, as the modular patterns of network activity evoked by uniform luminance steps are already selective at these ages. Furthermore, we show that trial-averaged activity patterns evoked by gratings show similarity to the mature orientation map as early as 1-2 days prior to eye opening. We conclude that the early disassociation between stimulus orientation and consistent patterns of modular network activity is a major factor underlying the absence of orientation selectivity in a developing cortical network already exhibiting highly modular functional organization.

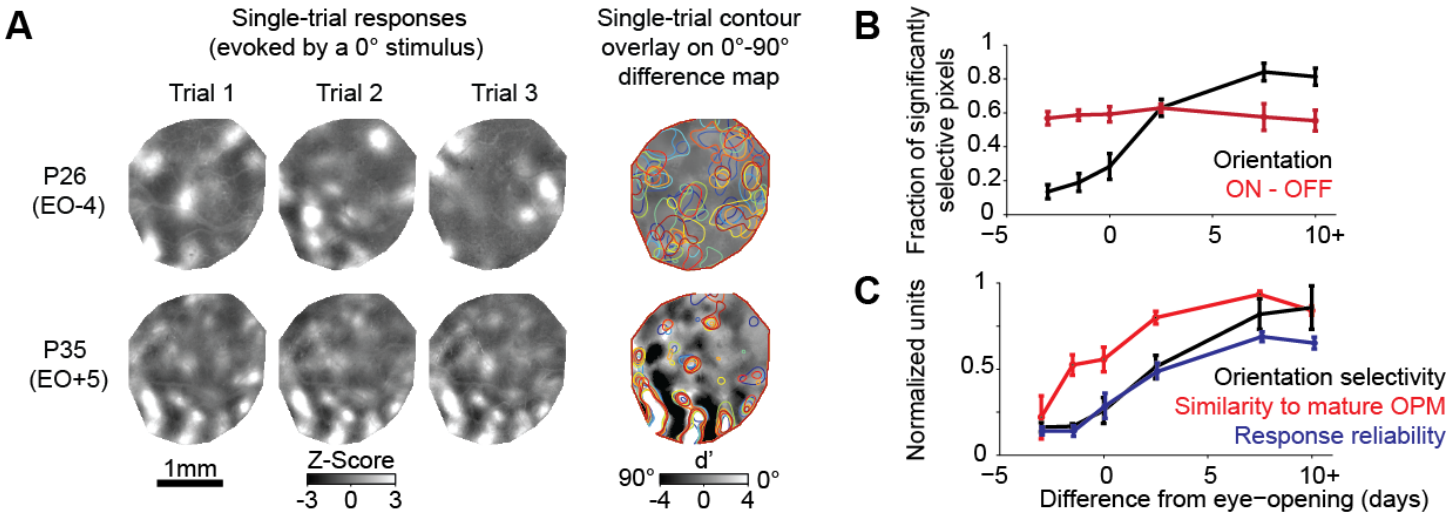

Figure: Response variability underlies the early absence of orientation maps.
(A) Prior to eye-opening, single trial cortical responses to gratings are robust and modular, but highly variable, resulting in absent orientation maps.
(B) While orientation preference maps are absent prior to eye-opening, uniform increases and decreases in luminance (ON and OFF respectively) are already mapped.
(C) Rises in orientation-selectivity closely match increases in response reliability, but lag the earlier establishment of orientation map structure.

Keywords: Response variability, development, functional imaging, orientation selectivity, visual cortex

Ramadge, Peter - 45

Learning factor models using multi-dataset multi-subject fMRI data

Hejia Zhang, Po-Hsuan Chen, **Peter Ramadge**
Princeton University, Princeton, NJ, USA

fMRI brain patterns are high dimensional, and the number of time samples gathered during a single session is relatively small. Hence, there is interest in fMRI analysis across datasets and subjects. The challenge of such analysis comes from inherent anatomical and functional variability across subjects and the inconsistency between the stimuli associated with different datasets. However, we observe that many datasets share one or more subjects with another dataset. We propose a model that covers this situation, show that it is computationally tractable, and yields improved fMRI analysis performance. Our model assumes there are *D* fMRI datasets and a pool of *M* subjects, but not every subject needs to be in each dataset. Instead, we assume the datasets are connected in the sense that between any two datasets, there is a path from the first to the second formed by shared subjects. Each subject *m* has a subject-specific basis matrix *W(m)* and each dataset *d* has a dataset-specific time-course matrix *S(d)*. The goal of the model is to jointly optimize all *W* and *S* so that the data matrices *X(m,d)* are well approximated by the factor model *W(m)S(d)*. Validation using classification tasks demonstrates that our learned model can effectively aggregate information across datasets and subjects and out-performs post-hoc models that align multiple subjects in the same dataset first and then align datasets. Our model can be used to merge small datasets, or to attach a small dataset with few samples to a larger dataset and hence improve performance.

Keywords: fMRI analysis, multi-dataset, multi-subject

Meriney, Stephen - 46

MCell simulations of the mouse neuromuscular junction transmitter release site

Stephen Meriney[1], Rozita Laghaei[2], Scott Ginebaugh[1,2], Kristine Ojala[1], Markus Dittrich[1]
[1]*Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA, USA*
[2]*Pittsburgh SupercComputing Center, Carnegie Mellon University, Pittsburgh, PA, USA*

The neuromuscular junction is a reliable synapse in which reliability derives from the summed activity of numerous unreliable elements, each consisting of a synaptic vesicle and associated voltage gated calcium channels (VGCCs). Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disease that reduces reliability, leading to muscle weakness. This weakness is due to an autoantibody-mediated removal of some of the VGCCs that are critical for transmitter release, an upregulation of other VGCC types, and a disruption in organization of these VGCCs. We have used a combination of electrophysiological recording from ex vivo neuromuscular preparations and MCell computer simulations to examine structure-function relationships, the disease LEMS, and novel LEMS treatment strategies. We find that the organization of the transmitter release site (especially the number and distribution of VGCCs) is a critical determinant of physiological function. Further, we find that LEMS effects on physiology cannot simply be explained by a loss of VGCCs. We have used an iterative approach with MCell simulations and synaptic physiology to refine our mammalian model of the neuromuscular active zone. With this validated MCell model in hand, we have explored the changes in this active zone structure and organization that correspond to pharmacological and disease states (LEMS). This newly refined model is being used to explore LEMS symptomatic treatment strategies that target calcium channel activation during an action potential (the potassium channel blocker DAP) and calcium channel gating (the novel calcium channel agonist GV-58). These computer simulations expand our understanding of presynaptic function, neuromuscular disease, and the effects of disease treatment strategies.

Keywords: neuromuscular junction, calcium channel, presynaptic, nerve terminal, synapse

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Gluckman, Bruce - 47

Connnecting models of sleep regulation to brainstem unit recordings with data assimilation

Bruce Gluckman
Center for Neural Engineering, Penn State University, University Park, PA, USA

Sleep-Wake transition dynamics are thought to be regulated by a relatively confined network of cell groups spread across the brainstem. Observation of wake-active, NREM-active, and REM-active groups, and associated pharmacological and lesion-based perturbations have led to models of these cell group's role and interaction, and such models have been embodied into mathematical dynamical models. In earlier work, we demonstrated that data assimilation (DA) can be used to reconstruct the states of these mathematical models from incomplete state observations. We've now extended this computational work to do multi-parameter fitting. Experimentally, we have now developed recording techniques to simultaneously measure unit activity from multiple of these widespread

cell groups simultaneously for extended periods in freely behaving rats. We are now working to assimilate this data stream with these computational models.

Keywords: Sleep, data assimilation, unit recordings

Merricks, Edward - 48

Long-term and ictal spike shape changes in human microelectrode recordings

Edward Merricks[1], Andrew Trevelyan[2], Elliot Smith[3], Sameer Sheth[3], Guy McKhann[3], Columbia Comprehensive Epilepsy Center[1], Catherine Schevon[1]
[1]*Dept of Neurology, Columbia University Medical Center, New York, NY, USA*
[2]*Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, United Kingdom*
[3]*Dept of Neurological Surgery, Columbia University Medical Center, New York, NY, USA*

Spike sorting of extracellular data relies on consistency of recorded action potential waveforms. These are known to drift over time, due to slow or fast changes in microelectrode position. A hallmark of seizures in animal models is the paroxysmal depolarizing shift (PDS), resulting in substantial alteration of waveforms, though this has not been demonstrated in humans.

Twenty patients undergoing epilepsy surgery evaluation were recorded with Behnke-Fried electrodes (63 total bundles). Of these, at least one bundle recorded units from the ictal core in 6 seizures from 5 patients, while simultaneously another bundle recorded penumbra. We also analyzed long-term single-unit recordings over 48 hours from all patients, using drift in principal component space and cell-intrinsic firing patterns such as the inter-spike interval (ISI) as metrics for stability in each unit.

Ictal activity typically caused spike sorting to fail, however, in one recording, action potentials from a single neuron were trackable throughout the seizure due to its proximity to the electrode. This permitted direct observation of waveform alterations as the ictal wavefront progressed, including post-ictal return of spike shape. Similar alteration was recorded at a second electrode shortly after, consistent with a slowly travelling wavefront, and unlikely to be explained by artifact.

Our long-term analyses found alterations to waveform are common, but usually occur gradually, allowing for tracking through time. Despite waveshape alterations, ISIs remain stable, allowing for assessment of unit identities. The pattern of alteration noted during the seizure was not seen interictally.

We have demonstrated that Behnke-Fried electrodes can identify single-unit firing patterns during recruitment to seizures, though this is rare, occurring in a single instance in this dataset. This provides the first direct evidence of PDS in humans, during a spontaneous seizure. Movement of neurons can cause waveform alterations, and cell-intrinsic features should be used to monitor unit identities.

Keywords: epilepsy, single unit, seizures, spike sorting, microelectrode

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Law, Robert - 49

Slow inhibition links somatosensory beta rhythms and tactile perception

Robert Law[1,2], Hyeyoung Shin[1], Shane Lee[1], Christopher Moore[1], Stephanie Jones[1,2]
[1]*Brown University, Providence, RI, USA*
[2]*Providence VA Medical Center, Providence, RI, USA*

We provide the first theoretical account for the preemptive suppression of tactile perception by beta rhythms (15-29Hz). Recent work has shown that high-power transient beta rhythms ("beta events") can emerge from simultaneous layer-specific inputs to cortex (Sherman, et al 2016). The prestimulus rate of these events correlates with (non-)perception, with events being particularly predictive of "miss" trials when they occur less than ~300ms before stimulus onset (Shin, et al, 2017). Building from these findings, we use a detailed biophysical model of primary somatosensory cortex (SI) to study the impact of beta events on tactile evoked responses, identifying features that correspond to tactile detection.

We examine two scenarios. In the first, subthreshold beta spills over into the poststimulus period, directly modulating SI's response to tactile input. In the second, superthreshold beta acts before stimulus arrival by initiating spikes, causing a cascade of activity that interferes with tactile input. We find that both cases can act through an opening of GABAB channels, which silences transcortical messaging from pyramidal cells in SI at the observed ~300ms timescale. We claim that this silencing through GABAB is the final common pathway for beta's suppression of somatosensory detection.

The two scenarios yield different patterns of model evoked activity despite their common end-mechanism, which allows us to test the theory using source-localized MEG from a detection task (Jones, et al 2007). We confirm the existence of several predicted differences using a modern nonparametric test that constrains familywise error in time series. The predicted role of GABAB suggests that specific interneuron types, e.g. the neurogliaform and Martinotti cells, may be critical to beta's influence on perception. Pharmacological and/or brain stimulation methods aimed at specifically modulating these GABAergic processes may lead to novel techniques to improve healthy perception or to suppress pain.

Keywords: Beta rhythms, GABA, tactile detection, MEG, nonparametric statistics

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Paninski, Liam - 50

Nonlinear amortized Bayesian decoding of natural scenes from retinal responses

Nikhil Parthasarathy[2], Ella Batty[1], Will Falcon[1], Tom Rutten[1], Mohit Rajpal[1], EJ Chichilnisky[2], **Liam Paninski**[1]
[1]*Columbia University, NYC, NY, USA*
[2]*Stanford, Palo Alto, CA, USA*

Most computational work on sensory coding focuses on the development of encoding models that capture the transformation from stimuli to neural spiking responses. The problem of decoding stimuli from neural responses provides a complementary approach to assess the information contained in neural responses about the sensory world. Here we develop new methods for decoding natural images from the spiking activity of large populations of retinal ganglion cells (RGCs).

The most common and well understood decoding approach involves simple linear regression decoding. This method has been applied to many decoding problems (e.g., reconstructing white noise temporal signals from RGC activity). Bayesian inference offers a potentially more powerful method for constructing optimal decoders that properly incorporate prior information about natural signal structure. However, computation of e.g. the posterior mean is challenging when the signal prior is neither Gaussian, Markovian, nor log-concave - as in the case of natural images. Indeed, despite decades of effort, even writing down a proper prior distribution on natural images has proven highly challenging - let alone computing the posterior on images given neural responses.

Our approach sidesteps this difficulty, by exploiting "amortized inference" tools from the burgeoning recent literature on artificial neural networks for computer vision tasks such as super-resolution, denoising, and inpainting. We begin by fitting an accurate encoder model (taking sensory stimuli into predictions of spike trains; Batty et al, ICLR 2017), then train our decoder by sampling as many pairs of natural stimuli and simulated responses as necessary to learn an accurate and easily-computed map from neural responses back to the corresponding natural stimulus. This approach generalizes well given limited data (since training the encoder requires relatively little data) and bakes natural signal priors implicitly into the obtained decoder, which significantly outperforms the basic linear decoder.

Keywords: retina, decoding, neural networks, spiking

Siu, Ricardo - 51

A neuromorphic system for adaptive closed-loop control of ventilation after spinal cord injury

Ricardo Siu[1], James Abbas[2], Brian Hillen[1], Sylvie Renaud[3], Ranu Jung[1]
[1]*Florida International University, Miami, FL, USA*
[2]*Arizona State University, Tempe, AZ, USA*
[3]*Université de Bordeaux, Talence, France*

After incomplete spinal cord injury at the cervical level, ventilatory control can be significantly impaired because of interrupted neural commands to the diaphragm or thoracic inspiratory muscles. Mechanical ventilation is often required when ventilatory function is impaired. Electrical stimulation of the phrenic nerve or direct electrical stimulation of the diaphragmatic muscle offers an alternate approach to achieve sufficient ventilation. Current respiratory pacing systems are open-loop, require tuning of stimulation parameters, and do not have the ability to respond to muscle fatigue or changes in metabolic demand. In this project, an adaptive closed-loop ventilatory controller has been developed to address these limitations.

The neuromorphic controller consists of a pattern generator to produce the respiratory rhythm and a pattern shaper to determine stimulation parameters that affect breath volume. The pattern generator (PG) is based off a physiological model for ventilatory control which consists of mutually inhibitory and excitatory neuronal populations to recreate the oscillations observed in spontaneous breathing. The pattern shaper (PS) consists of a network of neurons with time-shifted activation profiles; the weighted summation of their outputs determines the stimulation values. An adaptive algorithm adjusts the output weights to achieve a desired volume profile. The PS was

implemented and validated computationally and in experiments in intact and cervical hemisected anesthetized rats. With consistent PG drive, the PS controller could increase and maintain breath volume by an average 51% to match the breath volumes to pre-injury levels in all hemisected subjects. End-tidal CO_2, which had increased due to reduced breath after hemisection, was reduced from an average 6.8% to 5.9%. The effects of varying the periodicity of PG drive on PS adaptation was explored computationally. These studies demonstrated that the PS was able to adapt the stimulation patterns to achieve desired breath volume profiles in response to changes in PG drive.

Supported by R01-NS086088
Keywords: Ventilation, spinal cord injury, neural network, adaptive control

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Bazhenov, Maxim - 52

Effect of learning cues on sleep-related memory consolidation

Maxim Bazhenov, Yina Wei, Giri Krishnan
University of California, San Diego, La Jolla, CA, USA

During awake, new information is initially encoded in both hippocampus and neocortex, while during the following sleep, such as slow-wave sleep (SWS), the newly acquired memory traces are spontaneously reactivated, leading to consolidation of synaptic changes. Recent empirical studies revealed that auditory cues or stimuli preferentially enhance memory consolidation when presented at specific phase of slow oscillation during SWS. In this new study, we aimed to understand the mechanisms behind effect of external stimulation (representing learning-related cues) on memory consolidation using a computational model including effects of neuromodulators, allowing transitions between awake and SWS sleep, and synaptic plasticity. Memory performance to recall a sequence of cortical cell spiking was compared before and after a period of sleep following awake training.

We previously reported an increase in the memory performance in the model that experienced SWS compare to the model remained in awake state. Newly learned sequences were reactivated spontaneously during Up states of sleep slow oscillation leading to recall improvement after the sleep. In this new study, we found that in closed loop stimulation protocol, when local external stimuli were presented during the later phase of the Down states of slow oscillation, the Up states were more likely to initiate around the stimulation site; this shaped the spatio-temporal pattern of the slow waves and facilitated sequence replay. This was also the optimal phase of stimulation to maximize synaptic changes and memory improvements after the sleep. Our study proposes a mechanism to explain closed loop sensory stimulation and provides insight into how the memory consolidation may be affected by sensory cues during sleep.

Keywords: sleep, memory consolidation, plasticity, replay, learning

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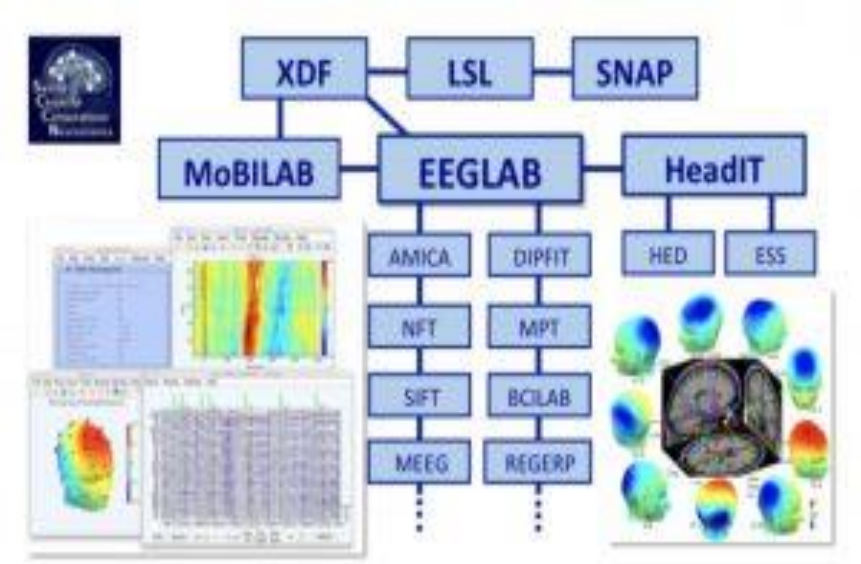
Makeig, Scott - 53

Tools for EEG data analysis: EEGLAB

Scott Makeig
Swartz Center for Computational Neuroscience, University of California, San Diego, La Jolla, CA, USA

Our paradigm leverages ongoing development of a software library that enables to perform the experiment and analyze the multi-modality data. We distribute the product of these efforts as a part of extensible open source, freely downloadable software environment, EEGLAB (Delorme, et al., 2004), that, like many other open source neuroimaging packages, runs on MATLAB (The Mathworks, Inc.). EEGLAB now has over 75 modular extensions developed and contributed by us and by many other users, and is the most widely used EEG analysis environment in cognitive neuroscience research with over 6,000 registered users (Hanke and Halchenko, 2011). Major extensions include a source information flow toolbox (SIFT), tools for creating anatomically detailed electrical head models (NFT), for synchronizing and analyzing multimodal data (LSL and MoBILAB), and developing brain computer interfaces (BCILAB). We run an extensive series of EEGLAB workshops around the world, by invitation, or coupled with meetings such as the Society for Neuroscience, as well as provide extensive online training materials and virtual workshops. (http://sccn.ucsd.edu/eeglab).



Keywords: EEG, EEGLAB, ICA, analysis, connectivity

Koulakov, Alexei - 54

Network cloning using DNA barcodes

Alexei Koulakov, Sergey Shuvaev, Batuhan Baserdem, Tony Zador
Cold Spring Harbor Laboratory, cold Spring Harbor, NY, US

The connections between neurons determine the computations performed by both artificial and biological neural networks. Recently, we have proposed SYNseq, a method for converting the connectivity of a biological network into a form that can exploit the tremendous efficiencies of high-throughput DNA sequencing. In SYNseq, each neuron is tagged with a random sequence of DNA—a "barcode"—and synapses are represented as barcode pairs. SYNseq addresses the analysis problem, reducing a network into a suspension of barcode pairs. Here we formulate a novel and complementary synthesis problem: How can the suspension of barcode pairs be used to "clone" or copy the network back into an uninitialized tabula rasa network? Although this synthesis problem might be expected to be computationally intractable, we find that, surprisingly, this problem can be solved efficiently, using only neuron-local information. We present the "one barcode one cell" (OBOC) algorithm, which forces all barcodes of a given sequence to coalesce into the same neuron, and show that it converges in a number of steps that is a power law of the network size. Rapid and reliable network cloning with single synapse precision is thus theoretically possible.

Sundaram, Padmayathi - 55

Revealing human thalamocortical dynamics with non-invasive MEG/EEG, computational neural modeling, and invasive patient recordings during median nerve stimulation and sensorimotor adaptation tasks

Padmavathi Sundaram[1], Julie Guerin[2,3], Shane Lee[2,3], Mainak Jas[4], Wael Assad[2,3], Alexandre Gramfort[4*], Matti Hämäläinen[1*], Stephanie R. Jones[2*]
** Co-PI Team: US-French Collaboration*
[1]*Athinoula A. Martinos Center, Massachusetts General Hospital, Charlestown, MA*
[2]*Department of Neuroscience, Brown University, Providence, RI, USA*
[3]*Rhode Island Hospital, Providence, RI, USA*
[4]*Telecom ParisTech, Paris, France*

Magneto- and Electro-enchephalography (MEG/EEG) provide direct neural correlates of human information processing with millisecond resolution. Many challenges remain in elucidating the location and neural mechanisms underlying the signals, particularly the involvement of deep sources such as the thalamus. We are integrating MEG/EEG, computational neural modeling, and invasive thalamocortical recordings in human Essential Tremor (ET) patients to advance methods of imaging and interpreting human thalamocortical dynamics. Essential Tremor is a common movement disorder in which patients have an involuntary tremor during

intentional movements. For medication-refractory cases, deep brain stimulation (DBS) of the cerebellar motor thalamus can be an effective treatment. DBS surgery provides a unique opportunity to record from thalamic and cortical signals in humans. We are collecting thalamic local field potential and microelectrode recording simultaneous with ECoG signals in ET patients during median nerve stimulation and performance of a sensorimotor adaptation task. Patients undergo the same paradigms during MEG/EEG and are compared to age-matched healthy controls. We present initial results towards several goals. First, we have developed new analysis approaches to be able to analyze the MEG-EEG data and localize both the cortical and the subcortical response during the median nerve stimulation. Results will be compared to invasive recordings and integrated into computational models of thalamic and cortical signals. Second, we are analyzing the MEG-EEG and intraoperative invasive recordings during the sensorimotor adaptation tasks to understand the dynamics of activity in different frequency bands (alpha, beta, gamma) in the cerebellar-thalamo-cortical network (please see corresponding poster on beta rhythms: Law et al.). Third, we are applying our model of thalamic signals to better understand the mechanisms of DBS, toward a goal of improving treatment. Taken together, our study is providing unprecedented insight into healthy and disrupted thalamocortical dynamics in humans.

WORKSHOP:
Integrating Dynamics and Statistics in Neuroscience

To be held at the Institute for Computational and Experimental Research in Mathematics (ICERM), adjacent to Brown's campus.

FRIDAY, June 16, 2017

8:15-9:00	BREAKFAST and REGISTRATION	
9:00-9:10	Opening Remarks	
9:10-9:45	The problem of dynamic network analysis	**Robert Kass** *Carnegie Mellon University*
9:45-10:20	Integrating physical and statistical models in neuroscience: some examples	**Mark Kramer** *Boston University*
10:20-10:50	BREAK	
10:50-11:25	Building functional nervous system networks from the bottom up	**Henry Abarbanel** *University of California, San Diego*
11:25-12:00	Dynamics to coding through biophysics of single neurons	**Adrienne Fairhall** *University of Washington*
12:00-1:00	LUNCH	
1:00-1:35	Neurobiology, brain imaging and information processing	**Dimitris Pinotsis** *Massachusetts Institute of Technology*
1:35-2:10	Inferring the source of fluctuation in neuronal activity	**Shigeru Shinomoto** *Kyoto University*
2:10-2:40	BREAK	
2:40-3:15	Data-driven geometry learning for parametrically-dependent dynamical systems with application to neuronal dynamics	**Ronald Coifman** *Yale University*
3:15-3:30	Formal discussion in lecture hall	
3:30-5:00	Informal discussion at ICERM	

Kass, Robert

The problem of dynamic network analysis

Robert E. Kass
Department of Statistics and Machine Learning Department, Center for the Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh, PA, USA

I will describe what I mean by "the problem of dynamic network analysis," which I consider one of the biggest statistical challenges in computational neuroscience. I will then give some examples of small steps my colleagues and I have taken that may at least suggest strategies for solving the problem. Finally, I will give my opinion about the potential for fruitful interaction between mechanistic modeling and statistical analysis of neural data.

Kramer, Mark

Integrating physical and statistical models in neuroscience: some examples

Mark Kramer
Boston University, Boston, MA, USA

To understand neural activity, two broad categories of models exist: statistical and physical. While statistical models possess rigorous methods for parameter estimation and goodness-of-fit assessment, physical models provide mechanistic insight. In general, these two categories of models are separately applied; understanding the relationships between these modeling approaches remains an area of active research. In this talk, we will outline these two modeling approaches, and provide examples of their integration to address problems in neuroscience.

Abarbanel, Henry

Building functional nervous system networks from the bottom up

Henry D. I. Abarbanel
University of California, San Diego/Scripps Institution of Oceanography

Using statistical data assimilation, we will describe how one may use laboratory current clamp data to estimate the biophysical parameters in neuron models. We will say a few words about challenges in network estimation.
We will describe how the methods have now been shown to make VLSI implementations of neuron networks reliable.

Fairhall, Adrienne

Dynamics to coding through biophysics of single neurons

Adrienne Fairhall
University of Washington, Seattle, WA, USA

Pinotsis, Dimitris

Neurobiology, brain imaging and information processing

Dimitris Pinotsis
Massachusetts Institute of Technology, Cambridge, MA, USA

Cognition arises from coordinated activity of different neuronal populations that form cortical networks. The activity in each of these populations is the result of input from all other populations connected to it. Therefore, connectivity is a central notion in describing the function of cortical networks and understanding cognition. In this talk, I will describe an approach for the analysis of brain connectivity using neuroimaging data, called Dynamic Causal Modeling (DCM). DCM is a systems identification approach for biological circuits. It unifies results from animal and human studies, different neuroimaging modalities and experimental tasks. It also sheds light on the information processing performed by neuronal populations and their neurobiological properties. In this talk, I will show how DCM can be extended to analyze high resolution invasive brain imaging data from different cortical layers. I will then apply this new method to a

visual perception task involving optogenetics. The analysis that results from the new method reveals the effects of neuromodulation on visual perception. It also links neuromodulatory effects to learning and Predictive Coding and elucidates the various computations performed in different cortical layers.

Shinomoto, Shigeru

Inferring the source of fluctuation in neuronal activity

Shigeru Shinomoto
Department of Physics, Kyoto University, Kyoto, Japan

Neuronal activity in vivo may fluctuate largely when animals are behaving or stimulated extrinsically. But the activity may also fluctuate even in the absence of stimulus [1,2]. We have revealed recently that the Hawkes process that describes general feedback or self-exciting mechanisms in point processes may exhibit nonstationary occurrence of spikes even if the system is not receiving any external stimulation [3,4]. Given a spike train or a time series of point events, we wish to know whether the nonstationary fluctuation is internally generated by the system itself or stimulated extrinsically. Here we develop a statistical model to make the inference for the cause of nonstationarity: We developed an Empirical Bayesian framework equipped with the self-exciting interaction term and applied it to spike trains generated by the nonlinear Hawkes model of the GLM type to test if the model may infer the presence of intrinsic excitation in addition to external stimulation. I shall demonstrate the result in my talk and also present related issues.

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Coifman, Ronald

Data-driven geometry learning for parametrically-dependent dynamical systems with application to neuronal dynamics

Gal Mishne[1], **Ronald Coifman**[1], Hadas Benisty[2], Ronen Talmon[2], Ron Meir[2], Jackie Schiller[2]
Yale University, New Haven, CT, USA
Technion University, Haifa, Israel

The extraction of models from data is a fundamental cognitive as well as scientific challenge. Neuronal activity recordings are an example of highly intricate data, which do not have existing definitive models. The complexity and richness of neuronal activity pose many truly challenging questions, such as the organization of neurons into subgroups of mutual functionality, correspondence to behavior, and existence of time-evolving connectivity patterns, just to name a few.

Motivated by these challenges, we aim to organize the dynamics of neuronal activity using geometry learning from a novel standpoint of nonlinear dynamical systems. In particular, we demonstrate a geometric/analytic unsupervised learning algorithm capable of creating minimal descriptions of parametrically-dependent unknown nonlinear dynamical systems. We present an approach based on informed observation geometry that enables us to discover in a data-driven manner useful intrinsic state variables and parameters, in terms of which one can empirically model the underlying dynamics. This is accomplished by "tiling" the joint space of recovered parameters and state variables; the tiling procedure is able to capture co-dependencies between different dynamical regimes and to build empirical bifurcation maps. This procedure can be viewed as analogous to the traditional Wavelet analysis with two important distinctions. First, Wavelet analysis is applied to the time-frequency domain, whereas our tool tiles the inferred space of the latent parameters and variables driving the system, solely from observations. Second, while the "Wavelet filters" are usually predefined, our "tiles" define the support of a set of data-driven filters.

We validate our toolbox on simulation data arising from two complex dynamical systems: a velocity jump process modeling the microscopic dynamics of a cellular chemotaxis environment and a stochastic dynamical system emitting spike trains governed by latent Lorenz variables. In both cases, we show that our data-driven method reveals the true, intrinsic parameters and state variables, without prior knowledge. In addition, we are able to successfully tile the recovered joint parameters-variables space into the different dynamical regimes. More specifically, we are able to detect chaotic regimes, as well as phase transitions, manifested by the change in the dimensionality of the latent intrinsic variables and parameters of the examined dynamical systems.

A by-product of the dynamic organization is an *automated* detailed in-depth morphology of the imaged brain.