CENTER *for*
NEUROENGINEERING

ReEngineering the Human Nervous System

6th Annual Symposium

October 5, 2016
BioScience Research Collaborative

Organizers:

Behnaam Aazhang, Ph.D.
Rice University

Michael Beauchamp, Ph.D.
Baylor College of Medicine

Valentin Dragoi, Ph.D.
University of Texas Health Science Center at Houston

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Gulf Coast Consortia *for* Quantitative Biomedical Sciences

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Gulf Coast Cluster for NeuroEngineering
6th Annual Symposium
October 5, 2016

Agenda

Unless otherwise noted, proceedings will take place in the Auditorium.

8:30 AM	*Welcome and Introduction*
	Session Chair: Michael Beauchamp, Baylor College of Medicine
	Keynote I
8:40	***A Neural Model of Gravity and its Role in Spatial Orientation*** Dora Angelaki, Baylor College of Medicine
9:40	***Stimulation of Visual Cortex and Visual Cortical Prosthetics*** Bill Bosking, Baylor College of Medicine
10:05	***Toward a Fully Bidirectional and Autonomous Brain Machine Interface*** J.T. Francis, University of Houston
10:30	*Poster Judging*
	Session Chair: Badri Roysam, University of Houston
	Short Talks Session I
11:15	***Neural Mechanisms Underlying Dexterous Manipulation*** Pranav J. Parikh, University of Houston
11:40	***Closing the Loop: Interaction with Neural Circuits during Behavior*** Caleb Kemere, Rice University
12:05 PM	***Modeling Stroke in the Laboratory*** Louise D. McCullough, UTHealth
12:30	*Lunch (Event Space)*
	Session Chair: Ankit Patel, Baylor College of Medicine
	Short Talks, Session II
1:30	***Bayesian Models for the Analysis of fMRI Data*** Marina Vannucci, Rice University
1:55	***Hacking Proteins for Imaging Rapid Neural Electrical Activity*** Francois St-Pierre, Baylor College of Medicine
2:20 P	***Language Networks: Insights from Intracranial Recordings*** Nitin Tandon, UTHealth

Agenda

2:45	*Poster Viewing & Networking*
	Session Chair: Valentine Dragoi, UTHealth
	Trainee Talks
3:30	***Magnetoelectric Neural Modulation*** Amanda Wickens, Rice University
3:45	***Higher-order Coordination of Visual Cortical Activity Enhances Perceptual Accuracy*** Neda Shahidi, UTHealth
4:00	***Preference for Visual Mouth Movements Predicts Auditory Response in Human Superior Temporal Sulcus*** Lin Zhu, Baylor College of Medicine
	Session Chair: Jacob Robinson, Rice University
4:15	**Keynote Address II** ***Reading and Writing the Neural Code: Challenges in Neuroengineering*** Garrett Stanley, Georgia Tech
5:15	*Closing Remarks and Awards*
5:30	*Reception (Event Space)*

(In order of appearance)

Dora Angelaki, Professor, Neuroscience
Baylor College of Medicine

A Neural Model of Gravity and its Role in Spatial Orientation

About Dr. Angelaki:
Dr. Angelaki, Ph.D., is the Wilhelmina Robertson Professor of the Department of Neuroscience at Baylor College of Medicine, and Professor in the Department of Electrical and Computer Engineering at Rice University. She holds a PhD in Biomedical Engineering and a Masters of Biomedical Engineering from the University of Minnesota, and a BSc in Electrical Engineering from the National Technical University of Athens in Greece. Her key professional interests are navigation circuits, multisensory integration and computational neuroscience. The tools used involve both computational and experimental approaches, including behavioral analyses, single unit recording and microsimulation/inactivation of different brain regions of macaque monkeys and rodents. Her research focuses on understanding how multisensory information flows between subcortical and cortical brain areas, as well as spatial navigation, decision-making and episodic memory circuits, and how internal states modulate this information flow. Dr. Dora Angelaki is a member of the National Academy of Sciences, and a fellow of the American Academy of Arts and Sciences.

Abstract:
Whether running to catch a ball or turning to reach for a cup of coffee, the ability to navigate in the world and interact with the environment depends critically on knowing our current motion and allocentric orientation in the world. Motion sensors in the vestibular inner ear play a particularly important role in this process. However, moving in a gravitational environment complicates estimation of these signals. As pointed out by Einstein over a century ago, all acceleration sensors, including the otolith organs, sense accelerations associated with our motion through space but they also respond to the force of gravity. For example, when running to catch a ball our otoliths sense our forward motion (i.e., forward translation). However, tilting the head backward to look up at the falling ball stimulates these sensors in the exactly the same fashion, this time because the head reorients relative to gravity. Recent studies have shown that the brain is generally able to resolve this sensory ambiguity. Although illusions can occur when there are insufficient sensory cues available, under most circumstances the brain can accurately distinguish between tilting relative to gravity and translating through space, even in the absence of vision. We have identified a network of neurons in the macaque vestibulo-cerebellum that appears to perform the required computations by using multimodal sensory information from both sets of vestibular sensors to compute an “internal model of gravity”. In the absence of robust sensory information, perception of our movement through space becomes illusionary, as predicted by Bayesian priors that signal we are stationary in space.
Gravity signals have also been found in anterior thalamus neurons that encode 3D head orientation. This tuning is gravity-anchored, and occurs during passive motion in both dark and light conditions. These gravity signals are used to estimate visual orientation in the allocentric world, and bilateral labyrinthectomy causes deficits in both allocentric visual orientation perception and vertical arm movement planning and execution.

Notes

William Bosking, Assistant Professor, Neurosurgery
Baylor College of Medicine
Stimulation of Visual Cortex and Visual Cortical Prosthetics

About Dr. Bosking:
Dr. Bosking received a BS in Astronautical Engineering from the United States Air Force Academy in 1986. He then went to pilot training, and served as a pilot in the Air Force for six years. After that, he received a PhD in Neurobiology from Duke University Medical School in 2001. He worked as a post-doctoral fellow at Baylor College of Medicine, and the University of Texas at Austin. He then obtained a Research Scientist position at the Max Planck Florida Institute for Neuroscience before returning to Baylor College of Medicine as an Assistant Professor in Neurosurgery in 2015.

Dr. Bosking's interests include functional organization of the visual cortex, the neural basis of visually guided behaviors, the neural basis of perception, and the development of a visual cortical prosthetic device.

Abstract:
Objectives: Electrical stimulation of visual cortex causes the perception of small flashes of light known as phosphenes. Although the first attempts to use electrical stimulation as the basis for a visual cortical prosthetic device (VCP) were made over forty years ago, there are still many challenges that must be addressed before a functional device can be deployed. We use electrical stimulation in human subjects to investigate visual processing in the cerebral cortex, and to investigate electrical stimulation strategies that could be used with a VCP. We have previously investigated which visual areas can produce phosphenes when stimulated (Murphey et al, 2009), and identified another cortical area that appears to be critical for perception of phosphenes (Beauchamp et al, 2012). Currently, we are investigating the parameters that govern phosphene size and location, and we are attempting to understand how stimulation of multiple electrodes can be used to produce the perception of coherent shapes, or the perception of motion.
Methods: We conducted electrophysiological recording and electrical stimulation in epilepsy patients with subdural electrodes implanted for clinical monitoring purposes. We mapped the receptive fields of all electrodes, determined electrodes that could produce phosphenes, and mapped the size and location of the phosphenes at different current levels. We then stimulated sets of multiple electrodes, either all at once, or with different spatial temporal offsets, to produce the perception of specific forms or the perception of motion.
Results: We found that phosphene size varied with both the magnitude of current injected, and the location of the electrode within the map of visual space. As current was increased above threshold, phosphene size first increased rapidly, but then quickly saturated. Phosphenes produced by stimulation of sites near the representation of the fovea were small, while those produced by electrodes located in the cortical representation of the periphery were much larger. We created a simple model that could account for these observations.

Subjects could perceive up to five phosphenes at once when multiple electrodes were stimulated simultaneously, and could accurately discriminate between two stimulation patterns. However, when we used a static pattern of stimulation, subjects typically reported seeing a set of independent dots, and not coherent shapes. Results from experiments utilizing dynamic modulation of

the currents delivered to each electrode, and current steering in between electrodes, suggest that these techniques may improve the overall coherence of shape perception. In addition, we found that electrical stimulation of two nearby sites in visual cortex with small temporal offsets could be used to induce the perception of motion.

Conclusions: Electrical stimulation in human subjects is a powerful tool for exploring visual perception and for examining electrical stimulation paradigms that could be used in VCPs. Perception of simple forms, and perception of motion, can be generated with direct cortical stimulation. However it may be necessary to develop more sophisticated stimulation strategies, such as dynamic current steering, to improve the coherence of form perception, and to most effectively use the array of implanted electrodes.

Funding: NIH EY02333

J.T. Francis, Associate Professor, BME Cullen College of Engineering
University of Houston and Physiology and Pharmacology , SUNY Downstate Med School

Toward a Fully Bidirectional and Autonomous Brain Machine Interface

About Dr. Francis:
My research interest is centered on developing a fully integrated Brain Machine Interface (BMI) for the control of prosthetic limbs. I feel that our best chance of accomplishing such a goal will involve a unique strategy and point of view, one that can be gained by exploiting several experimental models. Much of my work involves rats, monkeys and humans making reaching movements while interacting with robotic systems. The robotic systems are used to produce novel dynamical situations allowing me to ask questions about motor learning and how different brain regions respond to such learning.

Abstract:
Recently several groups have been able to decode intentions directly from the brain in order to control computer cursors as well as robotic arms and hands. Such systems are called brain machine, or brain computer interfaces (BMI/BCI). It has become clear that somatosensory feedback from such neuroprosthetic limbs to the user should allow for more natural integration with the user and help make such systems become a part of one self, rather than being seen as a tool, or attachment. Over the past decade my lab has been working on both the movement intention decoding and sensory feedback problems. Recently we have discovered that there is reward modulation of mirror like neurons in the primary sensorimotor cortex, and we have coupled this information with a reinforcement learning (RL) architecture to produce an autonomous BMI, that senses when the system either needs to be corrected for future use, or is operating as the individual would like. On the sensory feedback side of the BMI we have utilized model predictive control and microstimulation of the sensory thalamus to produce natural like cortical responses in S1. We accomplished this by generating template S1 responses to natural touch and then minimized the difference between our prosthetically induce S1 responses and these templates. I will introduce and discuss both of these sides of our BMI development.

Notes

Pranav J. Parikh, Assistant Professor, Health & Human Performance
University of Houston
Neural Mechanisms Underlying Dexterous Manipulation

About Dr. Parikh:
Pranav Parikh is an Assistant Professor in the Department of Health and Human Performance at the University of Houston and an Adjunct Professor in the School of Biological and Health Systems Engineering at Arizona State University since 2015. Pranav completed his Ph.D. studies at the University of Iowa in Human Motor Control/Neuroscience and his postdoctoral training in Systems and Behavioral Neuroscience with Prof. Marco Santello at Arizona State University. His long-term research goals are to understand the neural mechanisms underlying motor control and learning and develop therapeutic strategies to improve functional status in older adults, patients with Alzheimer's disease, and stroke survivors. Pranav uses a wide range of approaches including motion tracking, kinetics, electromyography, electroencephalography, transcranial magnetic stimulation, and transcranial direct current stimulation. He is currently a Guest Associate Editor for *Frontiers in Aging Neuroscience*.

Abstract:
Research over the last 30 years has used grasping tasks that constrain where the object is grasped, i.e., constrained grasping. However, recent behavioral work has shown that constraining digit placement enables subjects to use only one digit force control mechanism that relies on using the same forces used for previous manipulations. This is because, as digit placement cannot change across trials, subjects can retrieve and use the same digit forces they used for previous manipulations. In contrast, tasks that allow subjects to choose where to grasp the object, i.e., unconstrained grasping, are characterized by two important phenomena that are not found in constrained grasping tasks: (1) trial-to-trial variability of digit placement, and (2) concurrent modulation of digit forces to position. These two phenomena, that are unique to unconstrained grasping, point to the engagement of an additional force control mechanism which not only cannot rely on using the same forces used for previous manipulations, but that must also take into account digit placement on the current trial to modulate digit force accordingly. We reasoned that, although the manipulation task goal remains the same (grasping and lifting an object while minimizing object tilt), manipulation with an unconstrained versus a constrained grasp may involve different neural mechanisms. Therefore we addressed the question of whether the gain of corticospinal output may be modulated as a function of whether contacts are constrained or unconstrained. We quantified corticospinal excitability (CSE) over left motor cortex (M1) in participants (n=18) during a manipulation task using an unconstrained and constrained grasp of an object with an asymmetrical mass distribution. We assessed CSE during the reach and immediately after contact with the object. We also assessed grasp-dependent CSE modulation during planning. We found that CSE at point of object contact was greater when predictability about grasp locations were unconstrained compared to constrained, although digit positioning and force output were overall identical in both conditions. During planning and reach, there was no difference in CSE between these two conditions. The grasp condition-dependent CSE modulation after object contact underscores the functional significance of the contact event for processing sensory feedback necessary to modulate digit forces as a function of position. Thus, following contact, performance of an unconstrained versus a constrained grasp engages a different brain network and/or results in a higher gain of inputs from the same brain

network reaching M1 and/or differently modulates spinal structures. Alternatively, during unconstrained grasping, the initial object contact triggers somatosensory feedback that might be used to compute the relative position of the digits. In sum, differential processing of sensory feedback signals occurring after contact, but not during reach, might have resulted in grasp condition-dependent CSE modulation.

Caleb Kemere, Assistant Professor, Electrical & Computer Engineering
Rice University

Closing the Loop: Interaction with Neural Circuits during Behavior

About Dr. Kemere:

Caleb Kemere is an Assistant Professor in Electrical and Computer Engineering at Rice University, as well as an Adjunct Asst. Prof. in Bioengineering at Rice and in the Baylor College of Medicine Neuroscience Program. He received his PhD at Stanford University, working with advisors Teresa Meng and Krishna Shenoy to develop new classes of decoding algorithms for neural prosthetic interfaces.

Following, this, he was a postdoc in the Keck Center for Integrative Neuroscience at UCSF in the lab of Professor Loren Frank, studying the neural basis of memory using electrophysiology. As a postdoc, he was awarded the Sloan Swartz Fellowship in Theoretical Neurobiology and a Helen Hay Whitney fellowship. His lab at Rice develops novel technologies for neuroscience and neuro-therapeutics. His research is focused on using real-time signal processing in two areas: understanding learning and memory and understanding how Parkinson's disease disrupts neural circuits. Prof. Kemere has been awarded an NSF CAREER award and a HFSP Young Investigators award.

Abstract:

Engineers have driven advances in neural interfaces primarily based on novel inputs to the brain like artificial vision or novel outputs like prosthetic interfaces. In this talk, I will introduce areas of science and medicine in which bi-directional neural interfaces have the potential to revolutionize our understanding of the brain and our treatment of disease. Focusing in on the particular challenge of the manipulation of learning and memory, I will present data on our platform for closed loop neural interfaces and early results demonstrating the power of this approach to change our understanding of how the brain works.

Notes

Louise D. McCullough, Roy M. and Phyllis Gough Huffington Distinguished Chair
Professor and Chair, Neurology
UTHealth Science Center
Modeling Stroke in the Laboratory

About Dr. McCullough:
Dr. Louise McCullough is a physician-scientist who is examining the differences of sex and age in stroke and recovery. She received her PhD in Neuroscience from the University of Connecticut and her Medical Degree from the University of Connecticut School of Medicine. After graduating from medical school, Dr. McCullough continued her training at Johns Hopkins in Baltimore, Maryland for a Neurology Residency followed by a Fellowship in Cerebrovascular Disease.

After completing her training, she joined the faculty at Johns Hopkins Hospital and began her translational research career. Dr. McCullough relocated to Connecticut in 2004. She was a Professor in the Departments of Neurology and Neuroscience at The University of Connecticut Health Center and John Dempsey Hospital in Farmington, Connecticut, as well as the Director of Stroke Research and Education at Hartford Hospital, one of the largest stroke centers in New England. She recently relocated to the University of Texas Health Science Center at Houston and is currently Professor and Chair of the Department of Neurology and Chief of the Neurology Service at Memorial Hermann Hospital-TMC in Houston.

An energetic investigator, she is well recognized for her work in cerebral vascular disease and is known for her research identifying sex differences in cell death pathways during stroke, which are now recognized as major factors in the response to an ischemic insult. Her laboratory also studies aging and inflammation, and how these factors influence recovery after stroke. She has been funded by the National Institute of Health and The American Heart Association for her research and has published over 150 papers. She is certified by the American Board of Psychiatry and Neurology and has subspecialty board certification in vascular neurology as well as vascular ultrasound.

Dr. McCullough is a well-respected educator who is passionate about mentoring students and nurturing junior scientists. She is a member of eight professional societies, including the Society for Neuroscience and the American Academy of Neurology. Dr. McCullough is the recipient of many honors and awards, and has given numerous presentations both nationally and internationally. Dr. McCullough is also an active clinician, and she has been recognized as one of America's Top Doctors for the past eight years.

Abstract:
Stroke is the third leading cause of death for women (in comparison, stroke is the fifth leading cause of death for men) and the most frequent cause of adult disability. Each year 55,000 more women have a stroke than men. There is increasing evidence which suggests that sex differences exist in the etiology, presentation, treatment, and outcome from stroke. Stroke is a serious interruption or reduction of blood flow to the brain and women have unique risk factors. Because stroke occurs later in life for women, they are less likely to recover fully and return home to live independently. To meet the need for novel therapeutic approaches, experimental stroke research frequently employs rodent models of focal cerebral ischemia.

Basic molecular and animal studies in males and females have direct translational relevance, as treatments have revealed the efficacy in one sex has paradoxically shown a detrimental effect in the

other sex. This is now increasingly recognized in clinical stroke populations. Understanding the genetic and hormonal differences in inflammation across the life span is an important focus. The immune response to stroke differs in aged animals and elderly stroke patients. Studies are presently investigating the role of inflammation in stroke recovery. Current studies are manipulating age-related inflammation using bone marrow transplants, parabiosis and microbiome transfers. Factors such as depression and social isolation also dramatically impact recovery and mortality after experimental stroke as well as in stroke patients. Mechanisms currently being investigated are microRNA regulation of microglia and microbiome alterations with depression.

Marina Vannucci, Professor and Chair, Statistics
Rice University
Bayesian Models for the Analysis of fMRI Data

About Dr. Vannucci:
Marina Vannucci is Professor and Chair of Statistics at Rice University. She received a Laurea (B.S.) in Mathematics in 1992 and a Ph.D. in Statistics in 1996, both from the University of Florence, Italy. Prior to joining Rice in 2007, she was Research Fellow at the University of Kent at Canterbury, UK, during 1996-1998. In 1998 she joined the Department of Statistics at Texas A&M University, TX, as Assistant Professor, became Associate Professor in 2003 and Full Professor in 2005. Dr. Vannucci is currently an adjunct faculty member of the UT M.D. Anderson Cancer Center, TX, and the Rice Director of the Interinstitutional Graduate Program in Biostatistics. She also holds an Honorary appointment at the University of Liverpool, UK. Dr. Vannucci was the recipient of an NSF CAREER award in 2001 and won the Mitchell prize from the International Society for Bayesian Analysis in 2003. She is an elected Member of the International Statistical Institute (ISI), since 2007, and an elected Fellow of the American Statistical Association (ASA), since 2006, the Institute of Mathematical Statistics (IMS), since 2009, the American Association for the Advancement of Science (AAAS), since 2012, and the International Society for Bayesian Analysis (ISBA), since 2014.

Dr. Vannucci served as Editor-in-Chief for the journal Bayesian Analysis in 2013-2015. She has published over 110 research papers and has delivered more than 150 invited presentations. She has supervised 17 Ph.D. students and 8 postdoctoral fellows, since 1998.

Abstract:
Functional magnetic resonance imaging (fMRI) techniques, a common tool to measure neuronal activity by detecting blood flow changes, have experienced an explosive growth in the past years. Statistical methods play a crucial role in understanding and analyzing fMRI data. Bayesian approaches, in particular, have shown great promise in applications.
Fully Bayesian approaches allow flexible modeling of spatial and temporal correlations in the data, as well as the integration of multi-modal data. In this talk I will describe spatiotemporal models for activation detection as well as models for the estimation of brain connectivity.

Notes

François St-Pierre, Assistant Professor, Neuroscience
Baylor College of Medicine
Hacking Proteins for Imaging Rapid Neural Electrical Activity

About Dr. St-Pierre:
Dr. François St-Pierre hacks proteins to create tools for neuroscience. He is a McNair Scholar and faculty member in the Department of Neuroscience at Baylor College of Medicine and in the Electrical and Computer Engineering Department at Rice University. Prior to joining Baylor College of Medicine and Rice in 2015, St-Pierre earned his Bachelor of Arts and Master of Arts at the University of Cambridge (U.K.) in Natural Sciences. He completed his Ph.D. in Computational and Systems Biology at the Massachusetts Institute of Technology and his postdoctoral fellowship in bioengineering and neuroscience at Stanford University. At Baylor College of Medicine and Rice, his laboratory focuses on engineering, characterizing and deploying protein-based optical sensors of neural activity.

Abstract:
Electrical dynamics underlie critical functions in many cells, tissues and organs. In particular, spatiotemporal patterns of neuronal electrical activity are thought to underlie brain function, from sensory representations to decision making. For monitoring electrical dynamics, genetically encoded fluorescent reporters would be advantageous over electrodes by enabling cell type specificity and improved spatial resolution. We report here how we engineered fluorescent protein-based indicators that report voltage dynamics in neurons in vitro, in brain slices and in living flies. We further demonstrate how these sensors can track voltage across multiple subcellular locations in single neurons with millisecond-timescale resolution. We also show how voltage indicators can help us monitor and understand where and how critical computations arise in the Drosophila visual circuitry.

Notes

Nitin Tandon, Professor, The Vivian L. Smith Department of Neurosurgery, UTHealth Science Center

Language Networks: Insights from Intracranial Recordings

About Dr. Tandon:

I am a neurosurgeon and a cognitive neuroscientist, on faculty at the UT Health Medical School at Houston, where I have been based since 2004. I employ a multimodal approach to studying cognition, that combines intracranial electroencephalography (icEEG), cortical stimulation, fMRI and tractography. My lab has collected and analyzed large amounts of human intracranial EEG (icEEG) data during a variety of cognitive processes, but focused on language. Specifically, I am interested in how we are able to reliably, rapidly and precisely able to select and produce words and to decode written language.

Research on the neurophysiological basis of language processes is impeded by the difficulties of capturing the temporal dynamics of the cognitive processes within and between distributed the distributed sites of language processing. This limitation is due to the spatial and/or temporal resolution constraints of functional imaging and lesion mapping approaches. We integrate data from large cohorts of icEEG recordings to probe rapid interactions between distributed neural components. This is enabled by work in the lab over the past decade, that has focused on developing optimal tools that facilitate high-end analyses of icEEG data, and the development of optimized representational techniques. Over the next few months we will integrate high quality intracranial data during language processes in more than a 100 patients, to derive empirical evidence for defining models of brain behavior during relatively simple linguistic operations.

Abstract:

More than 150 years after first being implicated in speech, the mechanisms by which Broca's area and its surrounding network contribute to speech remain poorly understood. Using millisecond-resolution intra-cranial recordings during speech-production and an evaluation of functional connectivity in the high gamma band, we found specific spatio-temporal patterns of information flow between ventro-lateral prefrontal regions during word production. By varying retrieval, selection, and phonological loads, we identified specific functional coupling patterns coincident with the sub-processes of word production. We found correlational evidence that suggest that pars orbitalis may control lexical retrieval in pars triangularis via de-excitation and that lexical processes in Broca's area may be terminated by an inhibitory bottom up input from M1 at the onset of articulation. Taken together, intracranial recordings reveal that speech-production relies on distributed, transient task-specific inter-regional couplings that play out in rapid sequence in the language dominant hemisphere.

Notes

Amanda Wickens, Graduate Student, Applied Physics
Rice University
Magnetoelectric Neural Modulation

About Ms. Wickens:
Amanda Wickens graduated with a B.S. in Physics from Saginaw Valley State University in 2014. While there she completed her undergraduate honors thesis working with Dr. Marian Shih. During the summer of 2013 she conducted undergraduate research at the University of Florida in the Material Science Engineering Department with Dr. Jennifer Andrew working on multiferroic nanofiber synthesis. She is currently pursuing a Ph.D. in Applied Physics at Rice University working in Dr. Jacob Robinson's lab. Her research interests are in magnetoelectric neural stimulation.

Abstract:
A method to remotely stimulate neurons would allow for the study of deep brain regions in freely moving animals and lead to potential applications in new forms of treatment for disorders such as Parkinson's disease. For clinical applications, techniques that do not require genetic manipulations are most desirable. An ideal neuromodulation device would be enclosed in the tissue after implantation and externally activated to deliver a specific electrical signal to a deep brain region without the use of wires, which can cause tissue damage. Using the magnetoelectric coupling between a magnetostrictive and piezoelectric material we propose the use of magnetoelectric thin films as a novel neuromodulation device. This device will allow for specific less-invasive neural modulation by the application of a small external magnetic field that is transformed to a local electric field.

To create a biocompatible magnetoelectric film we bonded a piezoelectric material polyvinlydene fluoride and a magnetostrictive material Metglas. We then encapsulated the films to make them biocompatible. These films can generate voltages above four volts under resonant conditions using alternating magnetic fields with an amplitude of about 0.5 mT. We can also design the film geometry to resonate at different frequencies, which allows us to independently control multiple stimulation channels on a device. We have also shown these films to be biocompatible in vitro using cell viability assays over a period of seven days with no loss of device functionality.

In conclusion, these biocompatible magnetoelectric devices can convert magnetic fields that can penetrate the brain into electric fields that interact with surrounding cells to modulate their activity. Magnetoelectric materials could also be developed into a novel deep brain stimulation treatment for neural disorders like Parkinson's disease using devices that cause less neural damage compared to current electrodes.

Notes

Neda Shahidi, Graduate Student, Neurobiology and Anatomy
UTHealth Science Center Houston

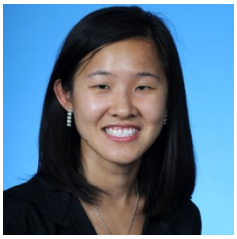
Higher-order Coordination of Visual Cortical Activity Enhances Perceptual Accuracy

About Ms. Shahidi:
Neda Shahidi is a PhD candidate at University of Texas, Medical school at Houston studying neural correlates of decision making in visual and prefrontal cortices. She has previous training as an Electrical Engineer (B.Sc. University of Tehran, M.Sc. The University of Texas at Austin) and research experience in artificial intelligence and robotics.

Abstract:
Visual perception is an active process of extracting relevant information for decision making. The degree to which spiking activities reflect perceptual choices widely vary across visual areas of cortex. We recorded from population of neurons in V1 and V4 areas of monkeys while they are engaged in an orientation discrimination task that evokes both areas. To our surprise, firing rates of single neurons as well as spike-time correlations of pairs of neurons were not correlated with behavioral choices.

However, in V4, coordination across three or more neurons was observed more often when the monkey correctly detected the orientation change in compare to when he failed. This is the first to show that a sizable population carries information that individual neurons or pairs of them do not. The method of detecting coordination was modified to detect functional connectivity between V1 and V4 and its correlation with behavioral choices, an effect that is too modest to be revealed by common pair-wise analyses. This finding suggests that effective feed-forward connectivity plays a crucial role for near threshold discrimination.

Notes



Lin Zhu, Medical Scientist Training Program
Baylor College of Medicine

Preference for Visual Mouth Movements Predicts Auditory Response in Human Superior Temporal Sulcus

About Ms. Zhu:
Lin was born in Shanghai, China and grew up in North Haven, CT. She attended Wellesley College and graduated cum laude with a BA in neuroscience and music. After college, she joined the lab of Dr. Gottfried Schlaug at Harvard Medical School, where she studied the effect of musical training on child development and stroke recovery. Lin joined the Medical Scientist Training Program at Baylor College of Medicine in 2010 and is currently working on her Ph.D. in the lab of Dr. Michael Beauchamp. For her thesis, she is studying how our brains use visual speech cues (such as mouth movements) to help us understand others during conversations.

Abstract:
It has long been known that cortex in and around the human posterior superior temporal sulcus (pSTS) is critical for speech perception. The pSTS has a complex organization, with some regions of the pSTS responding to visual stimuli (especially biological motion stimuli) and others to auditory stimuli (especially voices). However, the relationship between these axes of selectivity is unknown. Using high-resolution fMRI in twenty subjects, we show that auditory and visual selectivity are linked: subregions of the pSTS that prefer visual stimuli containing a moving mouth respond strongly to voices, with a significant preference for vocal compared to non-vocal stimuli. In contrast, subregions of the pSTS that prefer visual stimuli containing moving eyes do not respond to either vocal or non-vocal auditory stimuli. These findings can be explained by environmental statistics: in natural environments, we usually see visual mouth movements at the same time as we hear vocal speech, while there is no correspondence between visual eye movements and particular auditory cues. The strength of a voxel's preference for visual mouth movements was strongly correlated with the magnitude of its auditory speech response and its preference for vocal sounds, suggesting that these stimulus features are coded together in small populations of neurons.

Notes

Garrett Stanley, Professor, Biomedical Engineering
Georgia Tech & Emory University
Reading and Writing the Neural Code: Challenges in Neuroengineering

About Dr. Stanley:
Garrett B. Stanley received a bachelor's degree in mechanical engineering with highest honors from the Georgia Institute of Technology in 1992, and the M.S. and Ph.D. degrees in mechanical engineering (dynamics and controls) from the University of California at Berkeley in 1995 and 1997, respectively. From 1995 to 1997, he was an American Heart Association Predoctoral Fellow. From 1997 to 1999, he was a Postdoctoral Fellow in the Neuroscience Division of the Department of Molecular and Cell Biology at the University of California at Berkeley, and an NIH Postdoctoral Fellow. In 1999, he joined the faculty of the Division of Engineering and Applied Sciences at Harvard University, where until 2007 he was an Associate Professor of Bioengineering and an active member of the Harvard-MIT Division of Health Sciences and Technology (HST). In 2008, he joined the faculty in the Coulter Department of Biomedical Engineering at the Georgia Institute of Technology & Emory University, where he is the Carol Ann and David D. Flanagan Professor of Biomedical Engineering. His research interests include neural signal processing, experimental and theoretical approaches for understanding neural coding in sensory systems, neuronal point processes, parameter estimation, and the development of devices and strategies for recording from and stimulating the nervous system, with a long term in focus on neural prosthetics. His research program provides a unique combination of engineering-driven research in sensory function rooted in the basic science of neural circuitry and experimental neuroscience. In 2015, he became a Fellow of the American Institute for Medical and Biological Engineering.

Abstract:
The external world is represented in the brain as spatiotemporal patterns of electrical activity. Sensory signals, such as light, sound, and touch, are transduced at the periphery and subsequently transformed by various stages of neural circuitry, resulting in increasingly abstract representations through the sensory pathways of the brain. It is these representations that ultimately give rise to sensory perception. Deciphering the messages conveyed in the representations is often referred to as "reading the neural code". True understanding of the neural code requires knowledge of not only the representation of the external world at one particular stage of the neural pathway, but ultimately how sensory information is communicated from the periphery to successive downstream brain structures. Our laboratory has focused on various challenges posed by this problem, some of which I will discuss. In contrast, prosthetic devices designed to augment or replace sensory function rely on the principle of artificially activating neural circuits to induce a desired perception, which we might refer to as "writing the neural code". This requires not only significant challenges in biomaterials and interfaces, but also in knowing precisely what to tell the brain to do. Our laboratory has begun some preliminary work in this direction that I will discuss. Taken together, an understanding of these complexities and others is critical for understanding how information about the outside world is acquired and communicated to downstream brain structures, in relating spatiotemporal patterns of neural activity to sensory perception, and for the development of engineered devices for replacing or augmenting sensory function lost to trauma or disease.

Gulf Coast Cluster for NeuroEngineering
6th Annual Symposium
October 5, 2016

Poster Presenters

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2	Ariana	Andrei	UTHealth	*How Populations of Neurons in V1 Encode Information for Perceptual Detection*
3	Krishna	Badhiwala	Rice University	*Microdevices for Scalable Neuroscience in Hydra*
4	Zhiting	Cai	Rice University	*Using Directed Information to Infer Functional Connectivity in Neuronal Networks*
5	Ziying	Chen	Rice University	*Comparison Between Optical Signature from Fiber Photometry and LFP from Electrical Recording of Hippocampus in Freely Moving Rat*
6	Joshua	Chu	Rice University	*Investigating Hippocampal Replay and Working Memory During Spatial Learning*
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11	Eric	Lewis	Rice University	*Wireless Programmable Rodent Deep Brain Stimulation System*
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14	Luca	Pollonini	UH	*PHOEBE: A Software Tool For Optimized Guided Placement of fNIRS Optodes*
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18	Andrey	Tsvetkov	UTHealth	*Repairing Chemotherapy-Induced Neuronal Damage with An Automated Microscopy System, Single Neuron Analysis, and High-Throughput Drug Screening*
19	Sudha	Yellapantula	Rice University	*Reverse Aphasia in Permanently Impaired Adults*
20	Joe	Young	Rice University	*Probabilistic Analysis of Changing Relationships Between Local Field Potentials & Spike Times in Visual Cortical Networks During Perceptual Learning*
21	Renan	Costa	UTHealth	*L-DOPA Differentially Modulates Specific Neuron Ensembles In A Concentration-Dependent Manner*

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Poster #	First Name	Last Name	Institution	Abstract Title
22	John	Magnotti	Baylor College of Medicine	*Causal Inference During Multisensory Speech Perception*
23	Curtis	Neveu	UTHealth	*Combining Voltage-Sensitive Dye (VSD) Imaging with Extracellular Nerve Recordings Aid in the Identification of Neurons*
24	Quanli	Yang	Rice University	*Measuring Effective Nonlinearities in Neural Decoding*
25	Müge	Özker	Baylor College of Medicine	*Evidence from Electrocorticography for an Anterior-to-Posterior Boundary in the Superior Temporal Gyrus for Audiovisual Speech Processing*
26	Suganya	Karunakaran	UTHealth	*Characterization of Epileptogenic Network Using Interictal Spikes*
27	Kiefer	Forseth	UTHealth	*Heteromodal Semantic Convergence Occurs in Anterior Fusiform Cortex*

Hidden Markov Models of the Rodent Hippocampus

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The activity of ensembles of neurons within the hippocampus is thought to enable memory formation, storage, and recall, and even potentially decision making. Temporally ordered, sequential activity of these neurons is thought to enable associations across time and episodic memories that span longer periods. As hippocampal neural activity is communicated to nearly the entire neocortex, variability in these sequences may potentially have a significant impact. Despite numerous phenomenological expositions, our understanding of the variability of hippocampal sequences is lacking, due in large part to a lack of quantitative metrics of sequential variability. Two forms of variability exist, namely variability in the co-firing of subsets of cells (which we refer to as contextual variability) as well as variability in the sequential ordering of neural activity. Here we use hidden Markov models (HMMs) to characterize sequences of neural activity, and we use the HMM framework to derive a two component sequence score that allows us to determine to what extent a candidate sequence is sequentially consistent. In particular, this score quantifies both contextual as well as sequential (trajectory) information of putative sequences

In rodents, hippocampal “place cells” are known to encode an animal’s location in its environment as it explores. Hence, populations of these neurons fire in sequences corresponding to the spatiotemporal trajectories the animals traverse. HMMs are well suited to model this sort of sequential activity—even more so for behavioral correlates of memory that are non-spatial (e.g., odors). Of particular interest are hippocampal replay events in which neurons recapitulate their spatially ordered sequences during periods of quiescence or sleep. In studies of replay, the “quality” of a candidate sequence has been evaluated by comparison to a firing rate model constructed using average neural responses over multiple behaviorally-correlated ensemble firing instances. Such an approach critically relies on the availability of non-neural behavioral data to properly generate models. What if we don’t have access to this data? Here we describe how we can use the HMM framework to use only ensemble activity to effectively learn consistent underlying hidden states which we demonstrate correspond with behavioral correlates when they are available. We also demonstrate how our novel sequence score can be used to determine to what extent the neural activity is consistent with trajectories through the latent ensemble states or virtual place fields in an associated environment.

Funding sources: This work was funded by an NSF CAREER award (CBET-1351692), an NSF BRAIN EAGER award (1550994), an HFSP Young Investigator's award (RGY0088), and with seed funding from the Ken Kennedy Institute for Information Technology.

How Populations of Neurons in V1 Encode Information for Perceptual Detection

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It is currently unknown how information across large populations of neurons is integrated during the formation of sensory percepts. In this study, we used optogenetic methods to investigate how the population activity of glutamatergic neurons in primary visual cortex (V1) impacts an animal's ability to detect near-threshold visual stimuli. Studying the system at the limits of sensory detection allows for us to observe how additional, artificially-induced, spiking information is incorporated with the endogenously visually-evoked activity to alter visual detection performance. We delivered the channelrhodopsin (ChR2) gene to multiple sites in V1 using a lentivirus vector with a CaMKII promoter in two monkeys (macaca mulatta). Starting 4 weeks after the injection, single and multi-unit activity were recorded using laminar electrodes and a laser-connected fiber optic cable positioned 0.6mm from the nearest recording site. Monkeys performed a visual detection task – while maintaining fixation, oriented gratings with differing luminance contrast levels were presented parafoveally over the receptive fields of the neurons of interest. Monkeys signaled the presence or absence of a stimulus by releasing or holding a response bar. Half of the trials were paired with simultaneous optical stimulation (20-50Hz, for ~300ms). We recorded a total of 48 sessions, and analyzed a total of 473 light-responsive single and multi-units. 22/48 sessions activated neuronal populations optimally tuned to the stimulus orientation, while 14/48 sessions activated non-optimally-tuned populations and 12 session included both types orientations. We found that optical stimulation of populations of excitatory neurons tuned to the visual stimulus resulted in an 8.0% ± 2.2 SEM improvement in behavioral detection of near-threshold stimuli (P=0.0022, Wilcoxon signed rank test). In contrast, optical stimulation of neurons unresponsive to the visual stimuli resulted in no change in task performance. Since orientation, but not luminance contrast is represented in V1 in a topographical manner, the orientation dependency of the performance increase with the optical stimulation suggests that spiking activity used for detection is integrated in local, spatially defined pools. At the neuronal level, while all sessions showed robust firing rate augmentation and increases in signal to noise ratio, pairs of neurons from optimally-tuned sessions also showed a significant decrease in noise correlations (P=0.0001, Wilcoxon signed rank test, n=2436 pairs) following optical stimulation in conditions where detection was augmented.

Funding sources: NIH Eureka Program, BRAIN Initiative Grant

Microdevices for Scalable Neuroscience in Hydra

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The ability to observe the activity of every neuron as an organism interacts with its environment would reveal more about how the nervous system drives animal behavior – a fundamental goal of neuroscience. To reach this goal, we are developing a scalable microfluidic platform that will allow us to immobilize and interrogate the transparent cnidarian *Hydra*, which has a spiking network of few hundred to thousand of distributed neurons that can be individually imaged using optical microscopy. A major advantage of Hydra as a model system for neuroscience is the fact that these millimeter scale invertebrates can be confined to quasi-two-dimensional recording chambers that can be arrayed on a chip. This quasi-2D geometry allows us to perform high-speed volumetric optical imaging and implement a range of microfabricated technologies to control the local environment and record cellular-scale electrical activity. In particular, we show that our platform can combine the high-spatial resolution optical imaging with the high-temporal resolution electrophysiology to track contraction bursts (CB) and tentacles pulses (TP) as they correlate with behavior. Moreover, arrays of nanofabricated electrodes allow us to measure action potential propagation or deliver local electrical stimuli to provoke behavioral responses. Together, the spiking neural network of the *Hydra* combined with the microfabricated interrogation chambers provides a scalable “neuroscience on a chip” for studying the relationship between behavior and whole-brain activity at a single cell level.

This work is supported by a training fellowship from the Gulf Coast Consortia, on the IGERT: Neuroengineering from Cells to Systems, National Science Foundation (NSF) 1250104, DARPA Young Faculty Award and Hamill Foundation.

Using Directed Information to Infer Functional Connectivity in Neuronal Networks

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The ways in which organization of individual neurons into circuits enables learning, memory and other brain functions is poorly understood. With the advancement in large-scale simultaneous neuronal recording techniques, it is becoming possible to delineate the circuits underlying these recordings, which will also enable us to examine reorganization of these circuits during learning processes. In our experiments, multichannel analog data was obtained from the buccal ganglion of Aplysia using voltage sensitive dye (VSD) recording and converted into binary spike trains. Directed information (DI) was used to measure unidirectional influence between neuron pairs, with context tree maximizing (CTM) algorithm serving as the estimator for their stochastic properties. CTM is a data-driven, consistent estimator that automatically finds the best model based on a cost criterion. The analyses also included other biophysical properties such as whether the connections are excitatory or inhibitory and whether their actions were fast or slow. A connectivity diagram with neurons as nodes and connections as edges was then generated and parameters such as the in-/out-degree and the net-flow of a node were calculated. The method was validated using several realistic Hodgkin-Huxley network models where it not only correctly identified the direct connections but also was robust against synapses with nonlinear dynamic properties such as depression and facilitation. The algorithm was applied to VSD recordings. It detected several putative connections, sources, and sinks. This method of augmenting large-scale recording techniques with signal processing tools to construct functional connectomes offers an automated tool to map neural circuits and the ability to capture changes in synaptic strength as well as the saliency of neurons across different epochs, which will help identify network modifications due to learning and decision-making.

This work was supported by a seed grant from the University of Texas System Neuroscience and Neurotechnology Research Institute.

Comparison between Optical Signature from Fiber Photometry and LFP from Electrical Recording of Hippocampus in Freely Moving Rat

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Fiber photometry is a novel optical recording tool that can report collective activity of a specific population of neurons as single scalar value in real time, similar to local field potential (LFP) that is usually acquired through non-trivial computation of electrical recording and from non-specific population of neurons. However, the distinction between the optical and electrical signatures of hippocampal activity remains lacking. A fiber photometry system was developed for recording optical signal from genetically encoded fluorescent calcium sensors in hippocampus of a free moving rat. In order to achieve synchronization of two signals in brain, photometry system was integrated with current electrophysiological recording system. Finally, the method was implemented on a rat during spatial task in a linear track for recording from its hippocampus of both hemispheres and the LFP in hippocampal area is expected to correlate with optical signature from photometry recording.

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Investigating Hippocampal Replay and Working Memory during Spatial Learning

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The hippocampus is known to play a critical role in learning and memory. Through the neural activity of spatially-tuned place cells, rodent hippocampus participates in the encoding of present location and replay of past experiences. The occurrence of 150-250 Hz network oscillations known as sharp wave ripples (SWR) is associated with these replay events, time-compressed sequences of place cell firing on a millisecond timescale. Although disruption of SWRs results in learning and memory deficits, the role that hippocampal replay takes in these functions is not well-understood. Here we present a study that will enable us to investigate the contribution of replay events to working memory. We anticipate that a radial maze where specific arms contain liquid rewards will help give us insight into the interaction between replay, working memory, and decision making as a rat learns to prefer the reward arms. In conjunction with clusterless decoding techniques presented in [1], this study will lay the framework for the next generation of experiments investigating replay content-based SWR disruption in real time during learning.

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Activation Mechanism of the Recently Reported Magnetogenetic Protein MagV4

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The development of magnetogenetic tools permits the wireless stimulation of specific neurons located deep inside the brain. This new capability has the potential to improve the exploration of neural networks, the mapping of regions of the brain that cannot be reached with optogenetic tools, and the stimulation of neurons in freely moving animals. The most recent advance in developing magnetically gated channels has been the development of a TRPV4-ferritin chimera, which responds to steady magnetic field and is able to trigger action potentials in neurons. The iron-sequestering eukaryotic protein ferritin serves as the magnetically-sensitive element inside the cell. The protein TRPV4 forms a cation selective channel which responds to mechanical stress and temperature. Although it has been initially proposed that ferritin provokes TRPV4 gating through mechanical stimulation, calculations point to a discrepancy between the assumed mechanism and the force that can be produced by ferritin under a magnetic field.
Here, we propose a more plausible functional mechanism by which a paramagnetic nanoparticle such as ferritin can stimulate a temperature sensitive channel under stimulation by a static magnetic field. Using the laws of thermodynamics, we have determined that the activation of TRP channels by magnetic nanoparticles is based on the magnetocaloric effect that converts changes in magnetic entropy into heat. We support this hypothesis by calculations and data obtained from measurements in cultured HEK cells. In addition to reconciling the biological observations with the physical properties of artificial and genetically coded magnetic nanoparticles, our explanations permit the engineering of new magnetically-sensitive channel that can respond to various magnetic stimuli and operate at different temperatures.

Low Latency, Open Source, Real-Time Sharp-Wave Ripple Detection System

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Sharp-wave ripples (SWRs) are oscillatory patterns (~150-250 Hz) of neural activity observed in the local field potential of the CA1 region of the mammalian hippocampus. These patterns, coinciding with ensemble spiking activity within the region, have been shown to have associations with various aspects of learning and memory (e.g. memory consolidation, replay, memory-based decision making). Studies throughout this decade have shown that silencing the hippocampus immediately after online detection of SWRs impairs memory consolidation and affects the learning process. In order to understand the extent to which SWRs contribute to learning and memory, further investigations of online detection and manipulations of these events must be conducted. However, challenges of real-time signal processing and hardware limitations have made such investigations difficult for many researchers. We present an online SWR detection module implemented on an open-source software suite (Trodes) and paired with open-source hardware (OpenEphys or SpikeGadgets). Our system achieves low latency SWR detections across multiple channels in real-time. With a “gold-standard” data set, we demonstrate our system achieves accurate detections with low latency (~10-15ms from offline detections, ~40-60 ms latency from onset of ripple). Lastly, we describe how our module can incorporate position tracking and multiunit activity to the SWR detection process. Overall, we believe that our modular system will enable closed loop experimental techniques to establish causal relationships within the brain.

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Visual Population Receptive Field Mapping of Human Superior Colliculus

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Superior colliculus (SC) is a small midbrain structure that is critical for head and eye movement and for visual attention. Visually responsive neurons form a retinotopic map in its superficial layers. SC has been studied extensively in animal models, but in vivo functional magnetic resonance imaging (fMRI) of SC in humans is hindered by its small size, deep location in the head, and nearby vasculature. Here we present a combination of high-resolution imaging and population receptive field (pRF) mapping methods that allows for resolution of retinotopy in human SC.

Methods: 5 subjects (10 SC) fixated on a point at the edge of the screen and performed a speed discrimination task on radially moving (4°/s) black and white dots within a 50° polar angle segment of visual space that was presented at six eccentricities (5–30°). 8 quasi-axial slices that covered both SC were acquired using interleaved 3-shot spiral acquisition (TR = 1000 ms; 1.2 mm voxel). Functional data were transformed into a high-resolution (0.7 mm) anatomy and depth-averaged onto the surface of SC (0–1.6 mm). Since the stimulus is cyclical, we averaged the BOLD response across cycles to boost our signal. PRF parameters for each voxel were selected based on the smallest residual sum of the squares between each model response and the timeseries. We analyzed these parameter maps on 3D surfaces created from each subject's segmented anatomy. To quantify how pRF parameters vary with collicular distance, we calculated the manifold distance from each surface node to a foveal coordinate.

Results: Good pRF model fits were found across the majority of each SC. In 7 out of 10 SC, pRF eccentricity versus collicular distance is described by a linear function with $R^2 > 0.5$. In 6 out of 10 SC, pRF size versus collicular distance is described by a linear function with $R^2 > 0.5$. There is a clear linear relationship between pRF size and eccentricity. We later modified the stimulus to include blank periods, which improved modulation of the BOLD response, and have so far performed this experiment on 2 subjects (3 SC). Results show reliable linear progression of pRF size and eccentricity across the entire extent of SC.

Conclusions: The visual response of the superficial layers of human SC can be reliably mapped from 0–30° away from fixation using a combination of high-resolution fMRI and standard pRF analysis. We also quantify the slope of collicular magnification along the curvature of SC, as has been done in visual cortex. There is some indication that there is an appreciable difference between pRF size in upper and lower visual field, which would corroborate recent studies in non-human primates. Our modified stimulus will help us to better resolve pRF size and thereby determine if this size difference is significant. These methods allow us to acquire and analyze data from small brain structures that are notoriously difficult to image.

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Minimally Invasive High Resolution Imaging of Auditory Neurons inside a Living Cochlea

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In United States, 30 million people aged 12 years or older have hearing loss in both ears. Between different types of hearing loss, sensorineural hearing loss is the most common, which involves damage to the neural structures in the inner ear. Most people with sensorineural hearing loss do not know the underlying cause, as it is highly challenging to biopsy the inner ear due to the limited access to the area. The difficulty lies in the surrounding dense temporal bone and delicate inner environments of cochlea, which can only tolerate minimal disturbances. One of the common treatment methods for this hearing loss is cochlear implant, which involves direct stimulation of auditory nerve based on the sound picked up. Current cochlear implants, however, cannot perfectly mimic the natural sound, one of the reasons for which being the lack of frequency resolution. This is currently due to the design of the implant, which involves between 4 and 22 electrodes that stimulate the auditory nerve, which is normally done by several thousands of hair cells in a natural ear. Besides such engineering challenge in the implant design, there is also a lack of knowledge in details of the auditory nerve activation for different amplitudes and frequencies of sound. For instance, there is not much in vivo data on how many auditory fibers get activated for different types of sounds, details of which should be understood in order to develop a cochlear implant that can more closely mimic the workings of natural ear. In my research, I propose to develop an optical imaging device that can investigate the details of auditory nerve activation for different amplitudes and frequencies of sounds. Ultimately, the data collected can be used by the cochlear implant manufacturers to further improve their designs so that they can better mimic natural sounds and aid in restoring hearing functions to those with hearing loss.

The device will consist of a custom-made miniature objective of 1.4 mm diameter, thin fiber bundle (diameter < 1mm), light source, relay lenses, custom-made image mapper, collecting lens, prism-lenslet array, and an image sensor. Before imaging with this device, the temporal bone surrounding the cochlea will be first drilled using a femtosecond laser. The femtosecond laser ablation will enable us to minimally invasively access the inside of cochlea. The miniature objective will then be placed through the hole drilled by the laser. The target of interest, auditory nerves, will be pre-loaded with voltage sensitive dyes, which will emit fluorescent signal when sound is played. The miniature objective will collect this signal and relay it through the fiber bundle and relay lenses. Image of the target will then be projected onto the image mapper. The image mapper will map different rows of the image to different parts of the image so that blank regions are created between adjacent image rows. The collecting lens will then capture the newly mapped image and project it onto a row of prisms, which will disperse the rows of the image into their adjacent blank regions. The array of lenses will then form dispersed images onto an image sensor, a sCMOS camera. In the end, each pixel on the detector will contain the object's unique spatial and spectral information, which will enable simultaneous imaging of multiple dyes of different emission wavelengths. This capability will be helpful toward investigation of afferent neurons amidst different hair cell structures and other activities such as calcium signaling. The specifications of the device will include a field of view of 200 to 500 μm, spatial sampling of 1 to 4 μm, spectral range of 500-670 nm, and sampling rate of 100 to 400 frames/second.

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Wireless Programmable Rodent Deep Brain Stimulation System

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Typical experiments in rodent models of Parkinson's disease rely on a tether to deliver deep brain stimulation (DBS) to the implanted electrode. Tethered studies make long-term stimulation and complex behavior study difficult or impossible. While tether-free rodent-scale pulse generators were developed to address this need, they lack the flexibility required to easily test different patterns of stimulation. We developed a wirelessly programmable stimulator and a customizable 3-D printed housing that allow for chronic delivery of normal or novel patterns of DBS in rats. The housing weighs 16.5 g and is: 35 x 26 x 34 mm (l, w, h). The stimulator utilizes an embedded microcontroller to generate biphasic current pulses to a concentric electrode in the subthalamic nucleus. The amplitude of stimulation ranges from 30 to 110 μA, at a frequency of 50 to 200 Hz with a pulse width from 30 to 90 μs. As an additional feature, we are adding the ability to optionally introduce a random offset to the inter-pulse interval. We have previously shown that such jitter, which can vary from 1 to 4 μs, may have therapeutic benefit. These programming settings can be changed wirelessly through near field communication (NFC) with an Android mobile application. We tested our device in vivo in hemiparkinsonian rats (unilaterally-lesioned using injections of 6-OHDA), assessing rotational behavior following amphetamine administration. We found similar behavioral responses to stimulation using a traditional tethered stimulator and our untethered unit. The results of this approach provide a cost effective method for future high throughput studies in rodent DBS. Thus, we anticipate that our open source platform will provide tremendous value to our experiments and to future studies involving chronic stimulation in rodent disease models.

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Young Investigators award (RGY0088) and a training fellowship from the Gulf Coast Consortia, on the IGERT: Neuroengineering from Cells to Systems, National Science Foundation (NSF) 1250104.

Identifying Seizure Mechanisms from ECoG Data Using Directed Information

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Epilepsy is a common neurological disease characterized by repeated, unprovoked seizures. Epilepsy affects about 65 million people worldwide. Resective surgery and neuromodulation treatments like vagus nerve stimulation used in treating epilepsy currently don't have great efficacy. Selective spatial modulation of epileptic networks in the brain represents a possible option for better treatments. A crucial first step in this endeavor is understanding seizure generating mechanisms. We studied the seizure mechanisms via causal connectivity graphs inferred from electrocorticographic (ECoG) data during preictal, ictal and postictal periods from twelve seizures in five patients with epilepsy. Causal connectivity is quantified by directed information (DI) and inferred using two different estimators of DI. Causal connectivity inferred from the first DI estimator assumes ECoG data is derived from multivariate autoregressive process (model-based) and captures linear causal interactions between ECoG channels. Causal connectivity graph obtained from the second DI estimator doesn't impose any parametric model assumptions on ECoG data (model-free) and captures both linear and nonlinear causal interactions. We observed that model-free approach captured more causal information than model-based approach. We also intuitively expect seizure onset zone (SOZ) electrodes to act as strong sources at the beginning of a seizure and drive rest of the brain into seizure. The inference from model-free approach agreed with this intuition, while that from model-based approach did not. In fact, SOZ electrodes are weakly connected when model-based approach is used. These observations imply model-free approach is superior to model-based approach particularly while modeling seizure mechanisms. Our preliminary analysis using model-free approach also indicated that SOZ continuously tries to drive the rest of the brain into a seizure and becomes deactivated immediately after the seizure ends. We are extending this analysis to larger patient cohorts and this analysis potentially holds the key to develop better treatments for epilepsy.

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A Probabilistic Framework for Deep Learning

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We develop a probabilistic framework for deep learning based on the Deep Rendering Model (DRM), a generative probabilistic model that explicitly captures variations in the data due to latent nuisance variables. We demonstrate that Max-Sum message passing in the DRM corresponds directly to the operations in deep convolutional neural networks (DCNs). Our framework provides new insights into the success and shortcomings of DCNs as well as a principled route to their improvement. DRM training via the Expectation-Maximization (EM) algorithm is a powerful alternative to DCN back-propagation, and initial training results are promising. DRM-based classification outperforms DCNs in supervised digit classification, training 2-3 faster and achieving better accuracy (1.21% vs. 1.30%), and they show comparable results to prior art in semi-supervised and unsupervised learning tasks (with no hyper-parameter tuning nor any regularization). In sum, our theoretical and training results demystify the structure of DCNs and support a unified approach to supervised, unsupervised, and semi-supervised learning.

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PHOEBE: A Software Tool for Optimized Guided Placement of fNIRS Optodes

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Objectives: Functional near-infrared spectroscopy (fNIRS) is an optical imaging technique for mapping neural activity by measuring hemodynamic changes in the cerebral cortex associated with resting or evoked brain activity. With recent fNIRS instrumentation encompassing large numbers of optodes, it is possible to reconstruct a hemodynamic image of the entire cerebral cortex with a lateral resolution on the order of a few centimeters, which can be improved to a few millimeters when a regional cortical activity is investigated using a smaller but denser optode layout. Despite these advantages, several unresolved issues currently limit use of fNIRS with adult human subjects. One of the main challenges encountered by fNIRS researchers is collecting optical signals from all channels with a signal-to-noise ratio (SNR) that is sufficient to carry out a reliable estimation of cortical hemodynamics. Another issue that limits the use of fNIRS with humans is the considerable amount of time that placing individual optodes may take, particularly with individuals for whom achieving good optical coupling to the scalp is difficult due to thick or dark hair.

Methods: To address these issues, we developed a numerical method named PHOEBE (Placing Headgear Optodes Efficiently Before Experimentation) that: 1) computes an objective measure of the signal-to-noise ratio (SNR) for a given fNIRS channel in real time during optode placement, akin to electrode conductivity used in electroencephalography (EEG), and 2) determines and displays the coupling status of all individual optodes on a model of a human head to indicate which optodes require adjustment for optimum fNIRS data acquisition.

Results: PHOEBE determines the coupling status of each individual optode by representing the topology of the optical layout as a connected graph in which nodes represent the individual optodes and edges represent the optode pairings weighed by their SNR (Figure 1a,b). A system of Boolean equations is then solved to determine which uncoupled nodes are contributing to low SNR values at the connected edges. Based on this information, optodes that are initially displayed as uncoupled or undetermined can be easily identified and adjusted to achieve optimum placement of the entire fNIRS probe (Figure 1c).

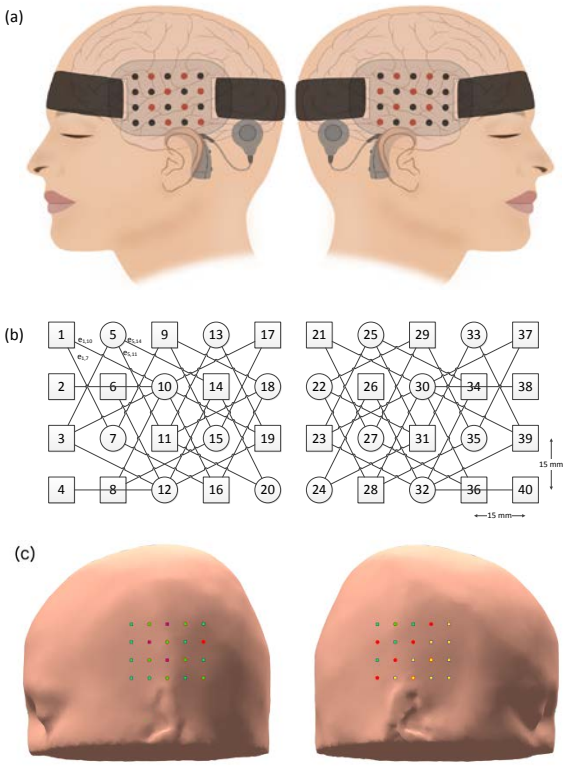

Figure 1: (a) Optical layout with 8 sources (red dots) and 12 detectors (black dots), (b) connected graph of the optical layout, and (c) screenshot of PHOEBE displaying scalp coupling of optodes in different colors: green (coupled), red (uncoupled) and yellow.

Cortical Activation Patterns Correlate with Speech Understanding after Cochlear Implantation

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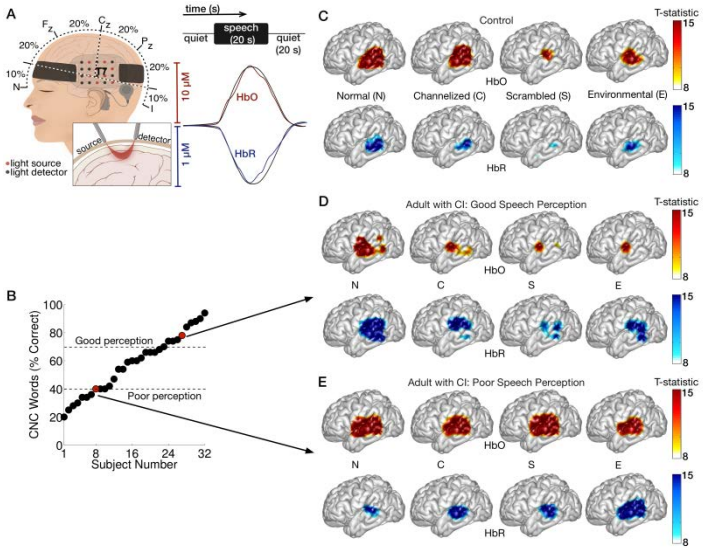
Objectives: Cochlear implants are a standard therapy for deafness, yet the ability of implanted patients to understand speech varies widely. This holds for both prelingually and postlingually deafened cochlear implant users. To better understand this variability in outcomes, we used functional near-infrared spectroscopy (fNIRS) to image cortical activity in postlingually deafened adults hearing through their cochlear implants. We then compared their fNIRS results to standard behavioral measures of their speech perception abilities.

Methods: Thirty-two deaf adults hearing through cochlear implants were tested, along with 35 normal-hearing controls. Regions of interest measured using fNIRS were the left and right lateral temporal lobes. The speech stimuli included four conditions varying in intelligibility. These included normal speech, channelized speech (vocoded into 20 frequency bands), scrambled speech (the 20 frequency bands were shuffled in random order), and environmental sounds (a non-speech control stimulus). Behavioral measures of speech perception consisted of an individual's speech reception threshold, as well as sensitivity to consonant-nucleus-consonant words and AzBio sentence tests measured in quiet.

Results: Both control and implanted participants with good speech perception (as measured behaviorally) exhibited greater amounts of cortical activation to natural speech than to unintelligible speech. In contrast, implanted participants with poor speech perception (also as measured behaviorally) had robust, indistinguishable cortical activation in response to all four classes of stimuli. The ratio of cortical activation to normal speech to that of scrambled speech directly correlated with patients' scores on the consonant-nucleus-consonant words and the AzBio sentences. Critically, this pattern of cortical activation was not correlated with auditory threshold, age, side of implantation, or time after implantation. Moreover, turning off the implant reduced cortical activation across implanted participants, regardless of speech perception ability as determined behaviorally.

Conclusions: Together, these data indicate that the responses we measured within the implant patients' lateral temporal regions, including middle and superior temporal gyri, correlate with their behavioral measures of speech perception and in a counterintuitive direction, thus demonstrating a cognitive mechanism that we are able to substantiate with neural data for the variability in speech understanding outcome following cochlear implantation.



A Power Harvesting System for Scalable Wireless Neural Recording Devices with an On-chip Antenna

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In this work, we demonstrate the first fully on-chip power harvesting system. The system receives RF waves at 3GHz through a wireless link that attenuates the transmitted power from the external source by 27 dBm. The received sinusoidal waves are rectified and energy is stored over a 1.2 nF on-chip capacitor. A power management unit divides the operation of the system into two phases with an average current consumption of 10nA. The system is capable of delivering up to 1mW to an external load when the power management unit enables the voltage regulator of the system. An array of four low noise amplifiers is also implemented on the same silicon chip that can amplifies EEG signals by 40 dB. The system is fabricated in 180nm SOI CMOS technology occupying 1.6x1.6mm2 including an on-chip loop antenna.

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Spatially Controlled Photo-Patterning of Multi-Material Sensory Organ Mimics

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Motivation

Mammalian sensory organs rely on intricate layering and compartmentalization of heterogeneous cell populations, but there does not currently exist a fabrication platform that is capable of recapitulating this heterogeneous composition in vitro. Our lab has recently developed an open-source, projection stereolithography platform capable of fabricating 3D multi-material hydrogels for heterogeneous tissue construction. Drawing on the highly tunable properties of photocurable hydrogels, we are able to produce monolithic constructs with heterogeneity in the X, Y, and Z directions. Furthermore, the layer-by-layer fabrication process enables us to endow these gels with networks of fluidic conduits, thus providing means of enhanced mass transport. The central objective of this study is to use projection stereolithography (PSL) to pattern multi-material, cell-laden hydrogel constructs that mimic the heterogeneous organization of sensory tissue systems such as the retina and cochlear stria vascularis.

Methods

Through the use of PSL we are able to produce cellularized hydrogel constructs with heterogeneity in the X, Y, and Z directions. In PSL, binary patterns of light are projected onto a photosensitive polymer solution in order to selectively crosslink thin film gels of 100 um thickness. The process can then be repeated in a layer-by-layer fashion to build rigid 3D constructs. Our modified PSL apparatus is capable of patterning multiple types of hydrogels during the same print and integrating them in a co-planar or non-coplanar fashion, thus yielding monolithic gels with multi-dimensional heterogeneity. In order to visualize the presence of unique hydrogel regions, fluorescent beads of varied spectral profiles were incorporated into the different polymer solutions prior to photo-patterning. Populations of hMSCs and C2C12 myoblasts were also encapsulated within these gels, and LIVE/DEAD staining provided a means to assess the persistence of viability throughout the printing process.

Results

Encapsulation of fluorescent beads revealed successful patterning of multi-material hydrogel constructs, and minimum feature diameters of 300 μm were achievable despite this monolithic heterogeneity. In cell-laden gels, LIVE/DEAD staining showed that hMSCs maintain >90% viability 1 day after patterning. Additionally, it was found that C2C12 myoblasts are not only able to maintain viability during patterning, but they are also able to spread, proliferate, and remodel the hydrogel matrix when encapsulated in an enzymatically-degradable gel.

Conclusions and Future Work

We have developed a novel PSL system capable of fabricating multi-material hydrogel constructs with high geometric fidelity and biocompatibility. Future work will aim to endow these heterogeneous constructs with hollow fluidic networks that mimic native vasculature, which plays in important role in pathological development. We will then identify cell lines for encapsulation that are physiologically relevant to the cochlea and retina, and printing parameters such as hydrogel composition and irradiation dosage will be optimized to support phenotypic retention during the fabrication process.

This work supported by a training fellowship from the Gulf Coast Consortia, on the IGERT: Neuroengineering from Cells to Systems, National Science Foundation (NSF) 1250104.

Repairing Chemotherapy-Induced Neuronal Damage with an Automated Microscopy System, Single Neuron Analysis, and High-Throughput Drug Screening

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Neurotoxicity may occur in cancer patients and survivors during or after chemotherapy. Establishing cause-and-effect relationships in the fixed animal brain samples can be misleading due to the complexity of processes occurring in the brain during chemotherapy. To overcome these limitations, we use a model of chemotherapy-induced changes in neurons based on cultured rat cortical neurons. Neurons are cultured in a dish for 10-14 days to allow them to mature synaptically prior to treatment with a chemotherapy drug (e.g., doxorubicin) or with a combination of drugs (e.g., doxorubicin + potential neuroprotectors). Neurons are then fixed, stained with antibodies to visualize various neuronal structures. Neurons are analyzed with the powerful state-of-the-art CellInsight CX5 High-Content Screening Platform. The system is equipped with a 5-channel fluorescent imaging engine and the Neuronal Profiling V4 Bioapplication software. Importantly, the software allows simultaneous rapid multiparametric analysis of neuronal cells, which includes the analysis of neurites, neurite arborization, synapses, DNA damage, et cetera. This represents an unparalleled fluorescence microscopy–statistical modeling system for rapid, robust and sensitive assessment of the effects of chemotherapeutics and neuroprotectors on neuronal health. Our studies could form the basis for neuroprotector-based cancer co-therapy, with applications to many cancers and chemotherapies.

Reverse Aphasia in Permanently Impaired Adults

Aphasia is an acquired language disorder that involves speech, comprehension, reading or writing dysfunction, while other cognitive abilities remain intact. More than 2 million people in the United States suffer from aphasia after stoke or other brain injury. According to the National Stroke Association, 60% of stroke survivors live with serious permanent impairments, while the rest of the survivors recover with minor impairments. The ultimate goal would be to restore lost functionality, to patients who are deemed to be permanently impaired. While this could possibly be accomplished by a physical implant in the brain, or through electrical stimulation to aid in rewiring healthy areas of the brain to restore lost functionality, it is undeniable that understanding the underlying structure of language is a pre requisite step. The language models need to be understood from the perspective of lost functionality due to various lesions, and why some lesions cause permanent damage and others recover. The goal would be to restore functionality even when lesions seem to cause permanent damage.

We hypothesize that areas of the brain are wired for a certain functionality based on the inputs it receives. Sur et al demonstrated in a Nature paper in 2000 that when developing ferrets' brains were rewired such that an optic nerve was redirected to the area of the cortex where the auditory cortex would normally develop, this caused visually responsive cells like in V1 to develop in the auditory cortex, causing the ferrets to have functional vision from the auditory cortex of the brain. We also know that brain scans show activity in the "visual" areas of blind people when using Braille to read, and "auditory" areas of deaf people are activated when using sign language. Another piece of evidence of the brain's capability to rewire to a different input is evident from the way a cochlear implant works. The auditory nerve remains intact but now receives signals from an electrode array connected to microphones, instead of receiving signals from the hair cells in the cochlea. At first people hear sound that is not natural at all, while with time, the auditory region of the brain starts to process this different input and the patients start to understand speech. These are just some of the many examples that demonstrate the plasticity of the brain, and how it develops based on the inputs it receives. It is evident that regions of the brain receiving input from the external world develops in response to the input it receives. Why should the rest of the brain be any different? If we can assume that it is true that every region of the brain develops in response to the inputs it receives from the other brain regions, we can hypothesize why some lesions cause permanent damage, and others don't. At a macro scale, we can imagine the language areas of the brain to be interconnected systems. A lesion causes a brain area to stop working, and we can imagine that the outputs from the dead system which would be inputs to downstream areas are now defunct. Outputs from the brain lesion would not be one connection, but a large network of neuronal connections. If some connections survive, in other words, if the areas downstream of the lesion receive some input, albeit a diminished strength after the lesion, it is possible that downstream areas of the brain are able to rewire themselves to perform the tasks originally performed by the lesioned part of the brain. If however, many important processes are killed by the lesion, and no outputs reach the downstream areas, some functionality is permanently lost.

With this idea of how the brain works based on the input it receives, it would seem that any functionality lost after a lesion, can be restored if the outputs from areas that were inputs to the lesioned area could be redirected to bypass the lesion, and directed to the areas downstream of the lesion. The downstream brain regions would adapt to this new input and recreate the functionality that was present in lesioned part of the brain. As the language system in adults is well developed, it should be possible that given the brains plasticity, the further away a system is from the lesioned area, the less restructuring it would have to undergo, to make up for the lost functionality. Whether this redirection of signals is accomplished by stimulation, prosthetic implants, or hitherto unknown mechanism, it remains that having the knowledge of inputs and outputs of the lesioned region is pre-requisite to the redirection step, if we aim to restore lost functionality.

Probabilistic Analysis of Changing Relationships between Local Field Potentials & Spike Times in Visual Cortical Networks during Perceptual Learning

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Perceptual learning is a well observed phenomenon but is poorly understood in terms of neurophysiology. Specifically, neuronal network changes occurring during *visual task learning*, a form of perceptual learning, remain elusive. Following a recent publication reporting *local neuronal synchronization* in region V4 of the *visual cortex*, we will develop a novel probabilistic metric capturing such phenomena with robustness to multi-phase frequency synchronization.

As a preliminary step in developing our new metric, we have used an information theoretic tool called *mutual information* in the time domain to measure pairwise dependency between local field potentials (LFPs) and spike times. LFPs represent populations of neurons, and spike times represent individual neurons. Thus, mutual information can measure the relationship between populations and individual neurons.

Current results reveal notable changes in the estimated mutual information (time domain) between LFPs and spike times when comparing trials during learning and after learning. During learning, the mutual information estimate exhibits a peak around a time shift of zero milliseconds, implying that there is a time relationship between LFPs and spike times. Analysis of this estimate after learning reveals the disappearance of the peak, implying that a time relationship no longer exists between the LFPs and spike times.

Marked changes in the mutual information estimates for learning and no learning therefore reveal changes occurring in the relationship between populations of neurons and individual neurons. These changes imply that a *temporal relationship* existing between populations and individual neurons during learning in fact *disappears after learnin*g. Future work will focus on developing a new metric in the *frequency domain* which will better capture and quantify such dependency between populations and individual neurons.

Funding sources: N/A

L-DOPA Differentially Modulates Specific Neuron Ensembles in A Concentration-Dependent Manner

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Dopamine is known to play an important role in motor control. L-DOPA, the precursor of dopamine biosynthesis, has been shown to increase rhythmic activity in the motor-pattern-generating buccal ganglia of Aplysia (Kabotyanski et al., 2000). Dopamine has also been implicated in associative learning in that model system (Nargeot et al., 1999). However, the circuit-wide changes induced by L-DOPA remain poorly understood. The buccal ganglia contain a Central Pattern Generator (CPG) that continues to produce at least four distinct fictive behaviors when isolated from the animal—rejections, bites, swallows, and intermediate patterns. Here we use a combination of Voltage-Sensitive Dye (VSD) Imaging and extracellular nerve recordings to probe network-wide changes underlying the modulation of fictive feeding by L-DOPA.

We find that different concentrations of L-DOPA increase the overall number of patterns, but simultaneously bias the activity towards intermediate patterns (low concentration, 40 μM) or bites (high concentration, 250 μM). VSD recordings revealed a concentration-dependent increase in coordinated firing, shown by a narrowing of the distribution of spikes occurring in all cells during patterns. In order to clarify the modulatory effects of L-DOPA on specific cell ensembles, we then used a simple but effective burst detection and cell classification algorithm to separate neurons based on their preferred phase of activity. While low and high concentrations of L-DOPA had similar effects on neurons active during the retraction phase, neurons active during protraction fired for a shorter time window following treatment with 250 μM of L-DOPA, when compared to 40 μM. Restricting coordinated firing to a smaller window in both ensembles likely allows for an increased overall number of patterns. Modulation of neurons active during protraction may be responsible for biasing the patterns towards a specific type.

Here we show that two different ensembles of bursting cells active during either protraction or retraction were differentially modulated by L-DOPA in low or high concentration. Additionally, the two treatments had distinct effects on fictive behaviors. While both increased their number, high L-DOPA did so to a greater extent. Furthermore, the low concentration biased the patterns towards intermediate and high concentration biased them towards bites. Though the modulation of specific ensembles may be the mechanism underlying these changes, it remains unclear whether the change in number of patterns and the pattern type bias are induced by the same or different mechanisms. In the future we will explore that question, and investigate the effects of L-DOPA on additional identified ensembles.

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Causal Inference during Multisensory Speech Perception

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Audiovisual speech integration combines information from auditory speech (talker's voice) and visual speech (talker's mouth movements) to improve perceptual accuracy. However, if the auditory and visual speech emanate from different talkers, integration decreases accuracy. Therefore, a key step in audiovisual speech perception is deciding whether auditory and visual speech have the same cause, a process known as causal inference. A primary cue for this decision is the disparity between the auditory and visual speech content, with lower disparity indicating a single cause. A well-known audiovisual illusion, the McGurk Effect, consists of incongruent audiovisual syllables, such as auditory "ba" + visual "ga" (AbaVga), that are integrated to produce a fused percept ("da"). This illusion raises at least two questions: first, given the disparity between auditory and visual syllables, why are they integrated; and second, why does the McGurk Effect occur for some syllables (e.g., AbaVga) but not other, ostensibly similar, syllables (e.g., AgaVba). We describe a Bayesian model of causal inference in multisensory speech perception (CIMS2) that calculates the percept resulting from assuming common vs. separate causes; computes the likelihood of common vs. separate causes using content disparity; combines the common and separate cause percepts weighted by their likelihood; and finally applies a decision rule to categorize the combined percept.

We apply the CIMS2 model to behavioral data collected from 265 subjects perceiving two incongruent speech stimuli, AbaVga and AgaVba. The CIMS2 model successfully predicted both the integration (McGurk Effect) observed when human subjects were presented with AbaVga and the lack of integration (no McGurk Effect) for AgaVba. An identical model without causal inference predicted integration for both stimuli. Our results demonstrate a fundamental role for causal inference in audiovisual speech perception, and provide a computational framework for studying speech perception in conditions of varying audiovisual disparity.

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Combining Voltage-Sensitive Dye (VSD) Imaging with Extracellular Nerve Recordings Aid in the Identification of Neurons

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VSD imaging can be used to simultaneously record spike activity in 10s-100s of neurons, which provides important advances in our understanding of circuit dynamics. To better understand the physiological role of the neuronal activity it is important to identify the recorded neurons which requires information of not only the size, position, and phasic activity but also the axonal projections of each neuron. Previous research has combined extracellular nerve recording and VSD to characterize neuronal projections of neurons in the feeding network of Aplysia (Morton et al. 1991), but did not attempt to identify the recorded neurons. Here we combined VSD recordings and extracellular nerve recordings to identify neurons in order to ascertain their role in feeding motor patterns. A first step in the process was a meta-analysis of previous extensive research characterizing the neurons of the buccal ganglia. Of the 51 neurons that have been studied to date about 14% were local interneurons, 45% send a single ipsilateral projection, and 18% send projections through multiple nerves. The phasic activity of all neurons was also categorized. 63% were active during either protraction or retraction or both, while only 10% were active during post-retraction. We next characterized the projections and phasic activity of neurons and compared our results with our catalogue in order to identify neurons. Suction electrodes were applied to 7 nerves that connect the buccal ganglia to the periphery (ipsi and contra Bn1,2,3 and ipsi-Rn). Ganglia were stained with RH-155 and the activity of the nerves and VSD were recorded simultaneously for two (2 min) recordings separated by 15 min. A projection was considered to occur if a spike in the nerve followed a spike in the cell with a consistent delay. Using this information from the meta-analysis we identified up to 9 neurons during a single recording. With future experiments we hope to refine our methods to increase our ability to identify neurons and to identify new neurons which have yet to be characterized. We hope to use this technique in the future to track changes in each neuron before and after learning and compare the changes of each neuron between animals.

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Measuring Effective Nonlinearities in Neural Decoding

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To extract task-relevant information from sensory variables, the brain must eliminate nuisance variables that affect sensory inputs. This requires nonlinear computation. We contribute new statistical methods to understand and measure nonlinear computation downstream of recorded neurons. Recent recent studies showed that linear decoding weights can be inferred from linear correlations between neurons and behavior. However, these weights are not useful for understanding the neural code when it is not the means but the covariances and higher-order statistics of neural responses that are tuned to the task, such that task-relevant stimulus information can be extracted only by nonlinear operations. As one example, detecting an object boundary in an image requires contrast-invariant edge responses: the foreground may be darker or lighter than the background, so no linear weighting can correctly give the same response in both circumstances. Here we generalize past weight-inference methods to determine the brain's effective nonlinear neural computations from joint higher-order statistics of neural activity and behavioral outcomes on perceptual tasks. This method is based on a feedforward model of neural processing and a new statistical measure we call nonlinear choice correlation, defined as the correlation between behavioral choices and a nonlinear function of measured neural responses. The exact neural transformations may not be uniquely identifiable, as many neural nonlinearities can generate the same behavioral output. This will likely be the case when the cortical representation has many more neurons than the sensory periphery, which creates a high degree of redundancy. Nonetheless, we demonstrate that our approach successfully retrieves key properties of the brain's nonlinear transformation, which can then be decomposed and analyzed in terms of nonlinear type and functional importance.

Evidence from Electrocorticography for an Anterior-to-Posterior Boundary in the Superior Temporal Gyrus for Audiovisual Speech Processing

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During speech perception, visual information from the face of the talker can compensate for noisy auditory speech. We obtained neural recordings from electrodes implanted in the brains of epileptic patients (electrocorticography or ECoG) to examine the neural mechanisms of multisensory speech perception. Subjects viewed audiovisual words with either clear auditory speech (AV) or noisy auditory speech (AnV), identifying the presented words with a button press. In ECoG, electrodes in superior temporal gyrus (STG) responded to words with a burst of high-gamma (70-100 Hz) activity. Electrodes in the anterior STG (n=16) showed more activity for AV speech while electrodes in the posterior STG (n=11) showed more high-gamma activity for AnV speech (Anterior: AV=175±40%, AnV=75±10%; Posterior: AV=80±20%, AnV=120±20%, mean±SEM, RM-ANOVA p=10-5). Adding noise to the auditory component of speech resulted in weaker responses in the anterior STG but not in the posterior STG, possibly because the posterior STG receives more visual inputs that compensate for the degraded auditory signals.

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Title: *Characterization of Epileptogenic Network Using Interictal Spikes*

Authors: Karunakaran, Suganya, Kadipasaoglu, Cihan M, Kalamangalam, Giridhar P., Aazhang, Behnaam, Tandon, Nitin

Rationale: The epileptogenic region in mesial temporal lobe epilepsy (MTLE) extends beyond the hippocampus to a network of cortical and subcortical structures. The extent of epileptogenic network and clinical manifestation of seizures vary substantially across patients. Identification of patient-specific epileptogenic networks is essential for therapeutic modulation strategies and for characterizing commonly involved structures in a cohort of MTLE patients. To address this, multiple non-invasive methods including fMRI, scalp EEG, PET have been used to characterize epileptogenic networks. However, these methods either lack the spatio-temporal resolution or consistent activation to allow precise localization of epileptiform activity for characterizing epileptogenic networks. Here, we used intracranial recordings, which provides drastically high spatio-temporal resolution, and thus would be an optimal method for delineating these networks. We particularly target interictal spikes, rather than seizures, as the biomarker of epilepsy. This allows us to estimate the flow of information between different brain regions because interictal spikes are frequent and occur over similar components of the MTLE network as seizures.

Methods: Intracranial recordings of one-hour duration with frequent interictal discharges were selected from pre-surgical intracranial recordings of 10 medically refractory epilepsy patients. Conditional probability and latency of propagation of interictal spikes were computed using pairwise estimates of activity from all channels to generate a graph theoretical model between all nodes (channels). To estimate the influence of each node in this graph, directed node degree was defined as the total number of outward links from a node. A logistic regression model was then used to predict surgically resected channels using directed node degree, number of spikes in each channel and their interaction as predictors. The best predictor from this regression was normalized, thresholded and combined across patients to visualize a grouped MTLE network.

Results: Directed node degree was the best predictor to classify the surgically resected epileptogenic zone, determined by conventional clinical methods based on ictal onsets. The grouped network map in these MTLE patients revealed strong connections between hippocampus, amygdala and regions in frontal lobe, limbic system and temporal lobes.

Conclusions: When compared to imprecise non-invasive techniques and interventional, time-consuming stimulation methods, our method utilizes the routinely collected interictal data to generate a map of the MTLE network. These maps allow us to a) identify targets of a broader network for neuromodulation b) identify patients having deviations from the “typical” epilepsy network who may not benefit from a resective procedure targeting medial structures and c) compare interictal maps with a similar network obtained during seizure onset.

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Heteromodal Semantic Convergence Occurs in Anterior Fusiform Cortex

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Whether we see an apple or hear one described, we are able to articulate an inveterate object name. Language relies upon this effortless capability to access and relate concepts – a set of cognitive processes referred to as semantics. Two opposing hypotheses explain semantic cognition. In the first, a widely distributed network spanning the lateral cortex associates features between specialized cortical substrates to generate concepts. The second holds that this distributed network processes sensory information, but feeds features to a discrete neuroanatomical substrate in which semantic relations are encoded. We study electrocorticography (ECoG) and cortical stimulation mapping (CSM) in a large cohort (N = 25) with two semantic contrasts: auditory verbal and visual nonverbal object naming. Using a direct spectral measure of cortical activity, we identified 3 network states that were common to both sensory modalities: primary sensory processing, semantic cognition, and articulatory planning. The second state – semantic cognition – yielded coactive regions in the anterior fusiform (AF) and inferior frontal gyrus (IFG). CSM confirmed that the AF region was co-localized with the basal temporal language area (BTLA). IFG is well-known to exert top-down regulation over the semantic network. Therefore, we present strong evidence to reject the distributed-only hypothesis of semantic cognition in favor of a model that includes a distinct neuroanatomical substrate for semantic information located in the AF.

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