Carnegie Mellon University

Annual Progress Report: 2011 Formula Grant

Reporting Period

July 1, 2014 – June 30, 2015

Formula Grant Overview

The Carnegie Mellon University received $943,032 in formula funds for the grant award period January 1, 2012 through December 31, 2015. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Correlated Structure in Motor Cortical Populations – Motor control is one of the most important tasks the brain performs, and disorders of motor control affect millions of people. Although a wealth of psychophysical studies have led to good descriptions of the phenomenological processes underlying motor control and adaptation, the neural implementations of these processes are not well understood. One problem is that motor control is inherently a neural population phenomenon: movements are generated by groups of neurons that must work in a coordinated fashion to produce precisely timed muscle activation patterns. Using brain-computer interfaces, we will study how various features of the motor task act to shape the correlation structure of cortical population activity.

Anticipated Duration of Project

1/1/2012 – 12/31/2015

Project Overview

Volitional motor control is inherently a neural population phenomenon: to generate movements, neural activity from collections of neurons across multiple brain areas must be coordinated to result in precisely timed muscle activation patterns. This coordination is expressed by statistical dependencies in the tuning of groups of neurons, the so-called *signal correlation*, which arises from network constraints such as common inputs into groups of neurons. In motor control, these common inputs relate to the cognitive and behavioral factors underlying movement generation. By studying how signal correlations relate to various features of the task, like feedback or redundancy, we can probe how these parameters coordinate population activity in motor cortex and, ultimately, shape motor planning.

Note: This project is funded, in part, under a grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations or conclusions.

This project is a coupling of experimental and computational approaches to characterize the flexible correlation structure of motor neuronal populations. We will have monkeys implanted with chronic multielectrode recording arrays perform a combination of motor tasks including arm reaching and brain-computer interface (BCI) cursor control. Data from these tasks will be used to build a statistical model that fits the correlation structure as a function of both volitionally controllable driving inputs and task-dependent sensory feedback. Ultimately, the lessons we learn from the formulation of these models will improve our understanding of the cognitive and computational principles of motor control, and unite the neural encoding of movement with behavioral theories of motor control.

Specific Aim 1: Dissociate volitional from non-volitional dependencies in correlation patterns.
Specific Aim 2: Describe how correlation patterns change as a function of task redundancy.

Principal Investigator

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Other Participating Researchers

Andrew Schwartz, PhD – employed by the University of Pittsburgh

Expected Research Outcomes and Benefits

We anticipate several potential outcomes and benefits resulting from this study. (1) This research has direct implications for improving neural prosthetic devices, which have the potential to improve the quality of life for a substantial population of patients living with neurological movement disorders. Results from this study will be leveraged to current, ongoing clinical trials. (2) Robotic controllers generally lack the flexibility and robustness exhibited in physiological motor control. By furthering our understanding of the basic mechanisms of motor control, our findings could improve the design and performance of general autonomous control systems across a wide variety of applications. (3) Graduate students supported by this grant will be extensively cross-trained in both computational and experimental approaches to systems neuroscience, placing them at the forefront of a rapidly growing field. (4) Methodologies developed during this study will be directly incorporated into the classes taught by the Principal Investigator.

Summary of Research Completed

Milestones for reporting period:

Present Aim 1 preliminary results at conference. Finish Aim 2 experiments. Implant electrode array into hemisphere 2, start Aim 1 experiments using neurons from second hemisphere.

Research accomplished during this reporting period

In the prior reporting period we started recording from a non human primate engaged in experiments related to Aim 2. In this reporting period, recordings from the array are still very good (clearly distinguishable action potentials, see Fig. 1), so we have postponed surgery to implant another array in the second hemisphere. Experiments with Aim 2 are still on-going.

In the prior reporting period, we noted that neural tuning appeared to adapt independently across neurons when moving between tasks of different redundancy (Aim 2). In this reporting period we pursued this idea further, and found that the more a neuron was tuned to a dimension that becomes irrelevant in the redundant task, the more the tuning of that neuron changes (Fig. 2). This suggests that the phenomenon we are observing is dynamic range adaptation, something widely reported in sensory systems but not before seen in populations of motor neurons. We are currently working on a paper of these results.

The findings from Aim 2 reported in point 2, that neurons might be able to independently change their tuning, have led us to a new way of thinking about brain-computer interface design: neurons may be considered as providing control signals to a device as opposed to providing a static representation of motor intent. We formalized this thinking and presented it at the Statistical Analysis of Neural Data Workshop in May 2014:

> Zhang Y and Chase SM (2015) Recasting brain-machine interface design from a physical control system perspective. SAND7 Workshop.

We have also written these results as a review article, which was accepted this reporting period:

> Zhang Y and Chase SM (*in press*) Recasting brain-machine interface design from a physical control system perspective. Review. J Comp Neurosci.

Our findings described in above have also caused us to extend our investigation on-line into how neural tuning changes might develop during motor skill learning. This is a natural extension of the work because the tuning changes observed during redundant tasks might be thought of as the intrinsic capabilities of the system, while skill training might be expected to change those intrinsic capabilities. Both of these may change the natural correlation structure of the population.

Finally, to further our understanding of the correlation structure of neural populations during movement, in off-line studies we compared the correlations of neural activity recorded as threshold crossings to the correlations of neural activity recorded as local field potentials. We have found distinct differences between the two recording modalities in terms of how correlation strength decays over space. These results have recently been accepted for publication:

Perel S, Sadtler PT, Oby ER, Ryu SI, Tyler-Kabara EC, Batista AP, and Chase SM (*in press)*. Single-unit activity, threshold crossings and local field potentials in motor cortex differentially encode reach kinematics. J Neurophysiol.

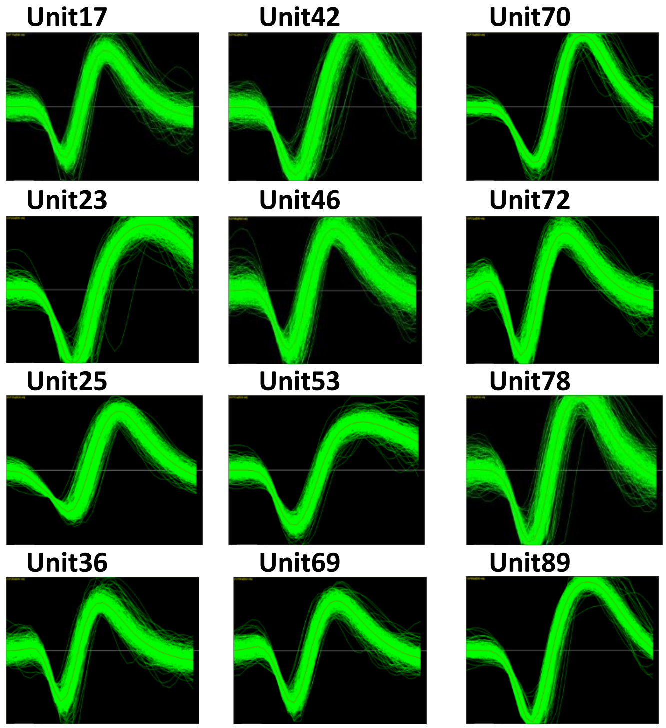

Figure 1: Samples of recordings from the multielectrode recording array chronically implanted in the primary motor cortex of the monkey on this project. Recordings are shown roughly 14 months post-surgery. There are clear indications of many isolatable units still on the array.

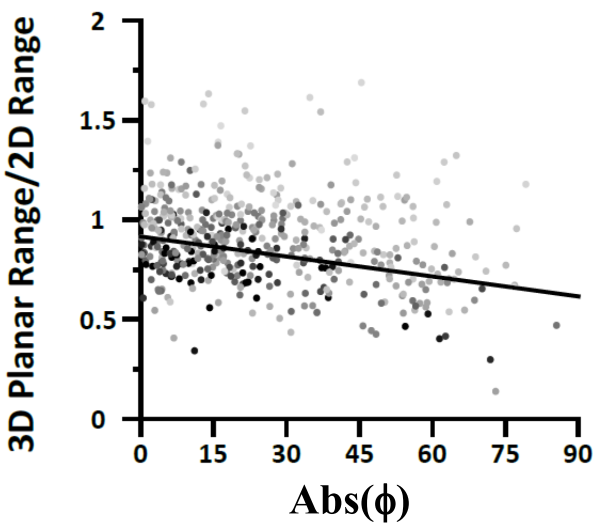

Figure 2: Tuning changes depend on degree of irrelevance. The x-axis shows the strength of tuning to the irrelevant dimension (where 0° is no tuning to the irrelevant dimension and 90° is full tuning). The y-axis shows the tuning change of the neuron between the two contexts: depth of tuning to targets in the 3D task are divided by depth of tuning to the same targets when presented in the 2D (redundant) context. The more a neuron is tuned to the irrelevant dimension, the more its tuning changes between the two contexts.

Research Project 2: Project Title and Purpose

Non-invasive Optical Imaging of Perceptual Learning and Development – The reliability and consistency of ordinary sight and hearing makes it natural to presume that perceptual systems are hard-wired and stable. Instead, however, they are highly dynamic and adapt flexibly to allow perceivers to discover regularities in the environment. In fact, over time perceptual expertise develops such that the brain's response to some classes of highly significant stimuli (faces, written words, speech) is markedly distinct. Our ultimate objective is to understand the learning mechanisms that serve the development of perceptual expertise to better understand developmental disorders (autism, dyslexia) and brain injuries that affect perception and to engineer devices to improve perception among those with impairments.

Anticipated Duration of Project

1/1/2012 – 12/31/2015

Project Overview

Our ultimate goal is to understand how perceptual systems are shaped by experience to develop perceptual expertise for some classes of stimuli. Humans exhibit such expertise for faces and native-language speech sounds and, later with developing literacy, for printed words. Human perceptual expertise for recognizing and categorizing these stimuli well exceeds the capacity of even the most sophisticated software for face and speech recognition. Understanding the learning mechanisms involved with extracting perceptual regularity from an inherently noisy and variable environment will provide insight about how to improve automatic machine recognition systems. It will also inform how to remediate perceptual problems arising from brain injury and developmental disorders and how to build effective rehabilitation programs for individuals with perceptual impairments.

The specific long-term aim is to address the development of perceptual expertise among pre-school aged children, a developmental window during which perceptual systems are thought to be highly malleable and during which time developmental disorders that impact perceptual expertise (autism, specific language impairment) tend to be discovered. The present research is unique and innovative because it allows for simultaneous measurement of brain and behavioral responses in young children who are unable to participate in many other forms of neuroimaging research, thus allowing us to probe the development of perceptual expertise. In the present project, we test the hypothesis that adaptation of an optical neuroimaging signal will serve as a more sensitive measure of children's phonetic representations than their behavioral responses and 2) that acoustic context will further shape these representations. At a broad level, achieving our aims will set the stage for Carnegie Mellon University's faculty to focus its research expertise toward innovative new approaches to studying the development of perceptual expertise and its health implications.

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Other Participating Researchers

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Theodore Huppert, PhD – employed by the University of Pittsburgh

Expected Research Outcomes and Benefits

Perceptual learning is a robust phenomenon, measurable throughout the lifespan in humans and other species that is thought to support a variety of basic cognitive, perceptual and language functions. It is important because changes in the way that perceptual input is processed and represented impact all subsequent processing at higher levels. Understanding brain function as it relates to developing perceptual expertise for particular classes of stimuli will allow us to generate models of how perceptual learning can be harnessed to improve perceptual processing (such as training physicians to better detect tumors in visually-noisy scans) and remediate everyday perception when perceptual systems go awry. Deficits in perceptual learning are observed across a variety of brain disorders including schizophrenia for auditory processing, autism for faces and speech, specific language impairment and dyslexia for spoken language and words, and in response to traumatic brain injury, stroke, and seizure. Determining how to engineer systems to remediate brain disorders affecting perceptual processing requires an understanding of the relationship of brain function to perceptual learning and how perceptual expertise for specific classes of stimuli develops. Neuroimaging tools that can be used effectively to study the developing brain are necessary in this endeavor. The present project exploits functional near-infrared spectroscopy (fNIRS) as a neuroimaging technique suitable for use with children and therefore significant for measuring brain development. By understanding how the brain changes with development of perceptual expertise, we believe we can better understand the causes of perceptual symptoms for brain disorders.

Summary of Research Completed

This research grant has enabled Carnegie Mellon to initiate and quickly grow a new and exciting line of research in near infrared spectroscopy (NIRS). It has provided funding for the essential instrumentation and personnel, thus helping coalesce and nucleate new collaborations, many of which have already developed grant proposals for follow-on funding that build upon the CURE grant investment. Below we describe progress toward our scientific aims as well as how this grant has enhanced our overall research program.

In the prior reporting period, we reported that researchers from PI Fisher's laboratory designed an investigation of the neural underpinnings of developmental changes in top-down regulation of sustained attention. In the current reporting period, they designed a second investigation: the neural underpinnings of developmental changes in rule-based reasoning. We have secured IRB approval for including adults and children between the ages of 2 and 17 in both studies. This is an exciting new development that allows us to begin to expand NIRS research at CMU to child participants. Especially promising, the NIRS system is situated in the Carnegie Mellon University Children's School, which is a laboratory school. This allows researchers to test child participants ages 3-5 years old readily and allow for longitudinal studies.

Collection of pilot data has commenced on both of these investigations, and have so far tested four 3- to 7-year-old children (see Figure 1). Both investigations target similar neural substrates (areas within the prefrontal cortex) and have potential to answer questions about developmental changes in recruitment of prefrontal cortex for critically important cognitive skills (i.e., attention regulation and higher-order reasoning). The attention investigation is in collaboration with Dr. Erik Thiessen and graduate student Sandrine Girard; the reasoning investigation is in collaboration with Layla Unger (a graduate student) and Francois Ban (an undergraduate researcher). All of these students have been trained on using NIRS data acquisition; training in NIRS data analysis is in progress. Additionally, these students have been regular participants and contributors to several relevant reading groups. Therefore, this award has not only advanced our understanding of critical questions about cognitive development, it has contributed to the state-of-the-art training opportunities of a new generation of researchers.

Researchers from PI Erik Thiessen's lab began investigating the neurological underpinnings of statistical learning of syllabic and tonal sequences in adults. IRB approval for this investigation was secured and data collection was finished in this period. Currently, we are analyzing the results. Preliminary analyses suggest that the left temporal cortex responds differently to syllabic input with a predictable statistical structure than to syllabic input with a random, unpredictable structure. In the left hemisphere, this neurological response to structure appears to be stronger for syllabic input than it is for tonal input. This investigation was carried out in collaboration with Sandrine Girard (graduate student) and Christina Cabrera-Mino (as an undergraduate student thesis). Both of these students have been trained on NIRS data acquisition and NIRS data analysis. As such, this investigation not only helps to advance our understanding of statistical learning, but also contributes to the state-of-the-art training opportunities of apprentice researchers. Currently, we are preparing to submit the investigation as a poster presentation at a conference on neuroscience.

In the prior reporting period, we reported that researchers from PI Holt's laboratory developed and preliminarily tested the effectiveness of a simple incidental training paradigm, the Systematic Multimodal Associations Reaction Time (SMART) task, in training listeners to categorize sounds. In the current reporting period, this paradigm was further validated behaviorally in the domain of second language learning. Native English adults were able to acquire perceptual categories that supported acquisition of Mandarin Chinese speech. This work was a part of Ran Liu's Ph.D. dissertation.

Dr. Ted Huppert organized a 4-week intensive workshop on brain imaging techniques (including NIRS) data acquisition and analysis; this workshop was open to the NIRS-network investigators at CMU and provided an excellent training opportunity for several graduate students (Layla Unger, Sandrine Girard, and Bo Powers) and undergraduate researchers (Francois Ban, Christina Cabrera-Mino).

The investigators involved in this project played a role in the faculty recruitment of Dr. Jana Kainerstorfer to join the Carnegie Mellon University Department of Biomedical Engineering. Dr. Kainerstorfer, a rising star and expert on optical imaging, received her PhD in 2010 from the University of Vienna. The presence of an energetic cohort of NIRS investigators on campus, supported through this award, was a key factor leading to successful recruitment. Her expertise will be an important contributor to the continued growth and success of the NIRS research seeded by this grant.

Jaeah Kim was hired as a laboratory technician to facilitate NIRS research among the NIRS-network investigators. Ms. Kim was trained by Dr. Ted Huppert (a leading scientist in NIRS research and instrument development at University of Pittsburgh) in data acquisition and analysis. Ms. Kim’s main responsibilities include: (1) assisting researchers in programming experiments to enable collection of NIRS data; (2) collecting NIRS data from children and adults; (3) analyzing NIRS data; (4) training new researchers in collecting and analyzing NIRS data. To-date Ms. Kim’s accomplishments include: programming NIRS experiments for three different studies (a. selective sustained attention in the visual domain; b. statistical learning in the auditory domain; and c. inductive reasoning about biological kinds); collecting and analyzing pilot data from adults on two of these studies (a & b); collecting pilot data from children on two studies (a & c); and training two graduate students and two undergraduate students in NIRS data collection.

Figure 1: A child participant is being tested in a NIRS study of inductive reasoning about biological kinds. NIRS developmental data acquisition protocol was developed in collaboration with Dr. Ted Huppert and Ms. Jaeah Kim. This protocol involves securing the optical array with a colorful neoprene cap; a wide array of cap design choices helps motivate children to participate in the studies while providing an excellent solution to the problem of securing the optical array in a way that is safe and comfortable for young children.