Carnegie Mellon University

Annual Progress Report: 2010 Formula Grant

Reporting Period

July 1, 2014 – December 31, 2014

Formula Grant Overview

The Carnegie Mellon University received $860,191 in formula funds for the grant award period January 1, 2011 through December 31, 2014. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Research Program in Sensory Computation - Sensory systems allow humans and other species to collect information about the world. Our brains then integrate information from a variety of sensory modalities with stored information to generate our beliefs about what is happening around us. For many kinds of stimuli – e.g., written words, voices, faces, smells – humans are much better at interpreting stimuli than any machine ever created. Our goal is to understand the kinds of computations that underlie our remarkable abilities to interpret complex stimuli. Improving our understanding of such sensory computations will allow us to better understand brain disorders that involve abnormal perception (such as hallucinations observed in epilepsy or schizophrenia or the heightened sensitivity to certain stimuli seen in autism) and also possibly to engineer devices to improve perceptual abilities in individuals who have impaired vision, audition or other sensory systems.

Duration of Project

1/1/2011 – 12/31/2014

Project Overview

Our long term goal is to understand how human sensory systems are able to collect, process and integrate information about the world. This process happens in the face of a highly variable and noisy sensory world, as well as in the face of growth, degradation and damage of peripheral sensory structures. Even the most sophisticated artificial sensory systems, such as airport scanners and face and speech recognition software fail or require human intervention when stimuli are embedded in noise or distorted. Human and animal sensory systems cope with or even exploit the variation seen in real world objects and conditions to improve their performance in a way that is unmatched by artificial systems.

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.

The specific hypothesis that we plan to investigate is that the diversity in the individual neurons and in local neuronal circuits improves the brain's ability to effectively extract information from sensory stimuli. This hypothesis highlights the differences between machines, in which variations in hardware degrade performance, and brains, where we have evidence that variation in neuronal properties reduces performance. We will address this hypothesis by experiments and analysis designed to achieve the following specific aims:

Aim 1: To understand how differences in the properties of cortical neurons contribute to accurate stimulus encoding in a variety of sensory systems.
Aim 2: To understand how trial-to-trial differences in neuronal responses influence performance in sensory systems.

In both these aims, in addition to collecting the data, we will develop approaches for using machine learning and information theoretic analyses to determine how the variability in neuronal responses contributes to or limits processing of sensory information.

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Expected Research Outcomes and Benefits

Understanding and treating the root causes of brain disorders requires an understanding of brain function and the relationship between brain function and perceptual and cognitive abilities. Many brain disorders include perceptual deficits as primary or secondary symptoms. Auditory hallucinations are a key symptom in schizophrenia, visual disturbances and auras are common in migraines, and olfactory and somatosensory abnormalities are commonly associated with seizures. Autism and dyslexia involve highly specific deficits in face and word recognition, respectively, along with abnormal sensitivities to certain kinds of stimuli. Many stroke and traumatic brain injury patients experience abnormalities in sensory perception. In some cases, these perceptual symptoms are among the most prominent and debilitating (such as the voices heard in schizophrenia), whereas in other cases they are not (such as in seizures). Nonetheless, in all cases perceptual symptoms can readily be studied both in patients and also in animal models of disease and thus can provide important insights into cellular and circuit level abnormalities that may be common across many brain areas. The proposed work will allow us to

generate models of how diverse types of neurons and circuits are harnessed to improve perceptual abilities, especially in the context of discrimination and recognition of complex stimuli. We believe that understanding these models of perception will provide insights into the causes of and treatments for perceptual symptoms of many brain disorders.

Summary of Research Completed

Work in the past time period focused on Aim 2 and included analysis of magnetoencephalography (MEG) data acquired to measure the properties of trial-to-trial reliability in human subjects performing sensory discrimination tasks. The goals of these analyses have been to develop models that explain the connection between cellular and trial-to-trial variability to improve sensory discrimination. Stimulus strength, duration and familiarity were varied to determine their influence on the reliability of these responses.

We used a three-parameter Generalized Linear Model (GLM) to model acquired MEG data. Data were pre-processed using down-sampling, DC component removal and normalizing to the amplitude of the stimulus noise, and then fitting a Linear-nonlinear-Poisson (LNP) model. GLMs were trained using the first 90% of the stimulus presentation and validated using the remaining 10%. We validated fit by comparing real and simulated peri-stimulus time histograms (PSTHs) using Pearson's correlation coefficient as a measure of similarity. To assess whether the GLM fitting procedure could also fit neuron responses to multiple stimulus types, we performed an additional set of experiments on mitral cells in which each neuron was presented with both a high- and low-frequency stimulus. We found that the GLM modeling procedure could sufficiently fit neuron responses to each of those stimuli, indicating that the fitting procedure is not biased to the particular stimulus type used to evoked responses in this study.

We computed average firing rates and trial-to-trial reliability from the fitted GLMs by simulating approximately 2 minutes of continuous stimulation and computing the statistics of responses. Neuron reliability was computed by stimulating each model neuron with multiple repeat stimuli and calculating the average zero-lag correlation across the trials. To calculate the extent to which neurons were driven by intrinsic (history plus bias) versus stimulus components, we used the GLM to simulate spike trains while storing the stimulus and intrinsic "currents," which generated the spike trains. Here the stimulus-driven component consists of the convolution of neuron's stimulus filter with the input stimulus; whereas, the intrinsic component is defined as the bias term plus convolution of neuron's spike train with its post-spike filter.

We decoded the population spiking responses using the maximum a posteriori (MAP) estimator, which finds the most probable stimulus given a particular population spike response. Stimuli were decoded using a new Gaussian approximation method and numerical optimization techniques. This method also provides an estimate of the uncertainty of the stimulus representation.