UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2013 Mary Gates Hall

Online Proceedings

Poster Session 1

Commons East, Easel 48

11:00 AM to 12:30 PM

Specialty Search Engine Design: an Empirical Study on the Optimization of Specialty Search Algorithms and Architecture

Marissa Ho, Sophomore, Pre-Sciences
Brennen Toru Smith, Senior, Informatics (Information Architecture)
Mentor: William Jones, The Information School

Specialty search engines cover the web, powering everything from product lookups to niche subject material. These small systems are tasked with indexing unique information and presenting small snippets of highly consolidated information, often on a certain domain or topic. As a result, the algorithms and techniques utilized are often different than a conventional search system, which aggregates vast amounts of diverse data. There are many different techniques employed by contemporary search systems to handle wide varieties of data. These systems are tailored to handle the widest range of data out of the box to provide a turnkey system. However, for these specialty search engines, these techniques are often too broad or do not encapsulate the scope properly. Our team's goal for the 2013 UW Research Symposium is to analyze the underlying mathematical models powering search appliances determine which algorithms have the greatest effect on the search engine's accuracy and precision while maintaining a sufficient recall rate. Our first phase is to analyze the mathematical models and algorithms which power search appliances to determine which have the greatest impact in narrowing scope and improving precision. The second phase is to implement our predictions on production servers scraping unique datasets. This data will be processed through a multivariate regression function to determine any trends and compared against our initial predicted data. Overall, our hypothesis is that current search engine platforms do not have optimal accuracy and precision and that through the analysis of the underlying data-processing techniques, these aforementioned values will be improved.

Session 1I

Developmental Neuroplasticity

Session Moderator: Sheri Mizumori, Psychology

251 MGH

1:15 PM to 2:45 PM

* Note: Titles in order of presentation.

Properties of Spontaneous Waves of Activity in Developing Cerebral Cortex Studied with a Microscopy-Compatible Microfluidic Electrode Array

Keiko Weir, Senior, Economics, Neurobiology
Howard Hughes Scholar, Mary Gates Scholar, Undergraduate Research Conference Travel Awardee
Mentor: William Moody, Biology

During early development, spontaneous waves of electrical activity propagate across many structures in the central nervous system. These waves are believed to regulate neuronal migration, physiological maturation, and synaptic connectivity. In the developing mouse cerebral cortex such waves manifest as increases in intracellular calcium and bursts of actions potentials that occur simultaneously in the majority of neurons in the cortex. We have developed a microfluidic multi-electrode array for use in the study of these waves of activity. This array records extracellular signals from twelve 50 micron microfluidic apertures that can also be used for focal electrical or chemical stimulation. The array is transparent and is compatible with simultaneous fluorescent imaging of intracellular calcium signals at single-cell resolution. We have used this array to study propagation patterns and mechanisms of cortical waves in postnatal (P) day 1 to day 5 brain slices. Waves initiate in the ventral (piriform) cortex and are detected by the array sequentially at each of the apertures placed along the ventral-dorsal axis of the slice, and by simultaneous calcium imaging as the spread of a fluorescence signal along the same propagation axis. The calcium signals outlast the electrical events by several seconds. We used a power spectral density analysis to identify the unique frequency components of different types of cortical waves. The signals from the dorsal regions show a prominent low-frequency oscillation late in the signal that is not present in ventral initiator regions. We have also used this device to study the contributions of the neurotransmitter GABA to net-

work development by investigating a transgenic mouse missing the primary enzyme that creates GABA. Use of this device will lead to a greater understanding of the development of neural networks in the mouse cortex.

POSTER SESSION 2

MGH 241, Easel 165

12:45 PM to 2:15 PM

DNase Mesosensitivity Predicts Differential Gene Regulation

Paul Martin (Paul) Ellenbogen, Senior, Computer Science, Mathematics
Mentor: Michael Hoffman, Department of Genome Sciences
Mentor: William Noble, Genome Sciences

Although every cell in the human body has nearly the same DNA sequence, there are many different cell types performing different functions; for example, lymphoblast cells which differentiate into white blood cells or endothelial cells which provide a lining throughout the human vascular system. But cells do not always function as they should, for example, overproduction of white blood cells can be caused by lymphoblastic leukemia, a type of cancer. I intend to use data on the sensitivity of parts of the genome to deoxyribonuclease (DNase) digestion to explain the differences in cell behavior. Regions of the genome structure that are hypersensitive to DNase have already been shown to affect gene expression. I want to determine if portions of the genome which are mildly sensitive, or mesosensitive, to DNase play a role in cell differentiation. My hypothesis is that DNase can identify large scale regions, on the order of thousands of base pairs, that harbor cell type specific genes. I used Segway, software which uses a dynamic Bayesian network, to segment the genome based on DNase sensitivity data into regions of low sensitivity, mesosensitivity, and hypersensitivity on six different cell types. From my segmentations I removed the hypersensitive regions from considerations, and compared the low and mesosensitive regions to gene expression data. I found that regions Segway labels mesosensitive had higher levels of expression than low sensitivity regions. I expect to find that many of the regions responsible for cell type specific behavior are mesosensitive. If this is the case, I hope the results will be robust enough such that anyone with access to DNase data can determine what genes are active in a population of cells, enabling them to better predict the behavior of the cells. In furthering our understanding of gene regulation, we may better understand diseases such as leukemia.

POSTER SESSION 2

Commons East, Easel 51

12:45 PM to 2:15 PM

Characterizing Vessel Growth in Infarcted Mice Hearts to Improve Therapeutic Cell Graft Quality

Sin Yee (Cindy) Leung, Senior, Biology (Physiology)
Mentor: William Mahoney, Pathology
Mentor: Jill Weyers, Pathology, Center for Cardiovascular Biology

Cardiovascular disease is an epidemic, prevailing as the leading cause of death worldwide. One consequence of cardiovascular disease is a myocardial infarction (MI), or heart attack. An MI is caused by a blockage in the coronary arteries which cuts off the blood supply to a portion of the heart wall, forming nonfunctioning scar tissue. We are aiming to improve heart recovery post-MI by replacing scar tissue with functioning cardiac tissue through a cell engraftment therapy. Cardiac cell engraftment is difficult because cardiac cells die quickly due to lack of vascularization of the graft. We believe that by promoting vessel growth in grafts, we will improve therapeutic cardiac cell survival for better heart function during recovery. To study the coronary network's ability to vascularize cell grafts, we inject skeletal muscle cells, which survive better than cardiac cells, into the heart wall post-MI. We observed vessel development in mice 14 days after MI and engraftment, and compared it to vessel development at other time points to better understand how the coronaries can vascularize cell grafts. To characterize the graft vasculature, I used histology to mark vessels and quantify vessel growth in the graft. My results shows that the coronary vasculature is able to expand and vascularize newly implanted tissue grafts post-MI. I detected capillaries as well as smooth muscle coated vessels in the graft suggesting vascular remodeling has occurred by 14 days post MI. My work establishes a baseline comparison for future research that will identify factors to increase the vascularization of graft tissue. We hope that promoting vessel growth will improve cell therapy methods for heart recovery to become applicable to clinical practice in the future.

SESSION 2H

NEUROSCIENCE AND GENETICS: FROM DISORDERS TO TOOLS FOR DISCOVERY

Session Moderator: Gwenn Garden, Neurology

248 MGH

3:45 PM to 5:15 PM

* Note: Titles in order of presentation.

In Vitro Analysis of Reduced Inhibition within Dravet Syndrome Interneurons

Jordan Daniel Hardman, Senior, Biology (Molecular, Cellular & Developmental)
Howard Hughes Scholar, Mary Gates Scholar
Mentor: William Catterall
Mentor: John Oakley, Neurology
Mentor: Chao Tai, Pharmocology

Dravet syndrome (DS), also known as severe myoclonic epilepsy of infancy (SMEI), is a rare genetic form of epilepsy, caused by a mutation in the neuronal voltage-gated sodium channel, NaV1.1, encoded by the SCN1A gene. This form of epilepsy is characterized by febrile seizures at infancy that often change with age into afebrile seizures, which include generalized tonic-clonic and myoclonic seizures. In most cases, DS is a debilitating disorder that renders patients with decreased cognitive function and impaired development. To study this disorder, a mouse model of DS, with heterozygous deletion of the SCN1A gene (Scn1a +/-), was developed, demonstrating a phenocopy of the DS condition, with similar seizure patterns and atypical behaviors. In vitro work in the model demonstrates selective loss of sodium current and excitability in hippocampal GABAergic interneurons. However, it remains unknown if similar changes in neocortical GABAergic interneuron excitability occur. We hypothesize that fast spiking neocortical interneurons are responsible for control of cortical excitability via GABAergic inhibition and that reduced excitability of fast spiking interneurons associated with heterozygous loss of NaV1.1 contributes to hyperexcitability and seizures. To explore this hypothesis, we will compare neocortical interneuron excitability measured from single action potential parameters and repetitive action potential firing patterns in unaffected wild type mice and the DS mouse model, using pre-existing single-cell recordings. Excitability will be determined from the peak amplitude, width at half height, threshold for single action potentials, and from total number of action potentials in induced neuronal spike trains. If this hypothesis is correct, we expect that there will be atypical action potentials and firing patterns showing reduced excitability. This experiment will provide more insight into DS epilepsy and better therapeutic targets for the disorder.

POSTER SESSION 3

Commons East, Easel 49

2:30 PM to 4:00 PM

The Human NLRC4 Inflammasome and Immune Defense against *Pseudomonas aeruginosa*

Kelsey Christine (Kelsey) Nebeck, Non-Matriculated,
Mentor: William Berrington, Medicine
Mentor: Thomas Hawn, Medicine
Mentor: Glenna Peterson

Pseudomonas aeruginosa (*P. aeruginosa*) is a ubiquitous species of pathogenic bacteria and a major cause of hospital-acquired pneumonia. Immune responses to *P. aeruginosa* infection in mice are mediated by a cytosolic multiprotein complex called the NLRC4 inflammasome. The NLRC4 inflammasome assembles upon ligand recognition leading to the release of the pro-inflammatory cytokine interleukin (IL)-1β and culminating in cell death. *P. aeruginosa* elicits a flagellin-dependent release of IL-1β and cell death in mouse macrophages, but research has not found human macrophages to recognize flagellin. This immune response is evoked in human macrophages by needle protein, an element of the type three secretion system (T3SS) infection apparatus used by *P. aeruginosa*. The mechanisms human macrophages use to regulate immune response to *P. aeruginosa* have not been fully established. We hypothesize that NLRC4 regulates immune response to *P. aeruginosa* in humans and therefore, NLRC4 deficient macrophages infected with *P. aeruginosa* will have impaired cell death and IL-1β production compared to normal NLRC4 expressing cells. Small interfering RNA (siRNA) will be used to knock down mRNA and protein expression of NLRC4. Macrophages treated with non-specific siRNA and NLRC4 targeted siRNA will be infected with live *P. aeruginosa*. We will then assay for IL-1β with ELISA and cell death using a lactate dehydrogenase (LDH) release assay. We expect NLRC4 knockdown cells to release less IL-1β and LDH compared to cells treated with non-specific siRNA thus indicating that in humans, the NLRC4 inflammasome is associated with defense against *P. aeruginosa* infection. Upon establishing the function of human NLRC4 during *P. aeruginosa* infection, we will proceed to investigate the roles of NLRC4 inflammasome subunits in ligand recognition and initiation of an immune response. Defining these roles could further our understanding of mechanisms behind immunity or susceptibility to *P. aeruginosa* and potentially lead to novel treatments for infection.

POSTER SESSION 3

MGH 241, Easel 149

2:30 PM to 4:00 PM

The Role of Calcium Signaling in the Development of Cortical Interneurons

Charles William (Charlie) Dickey, Senior, Digital Arts & Experimental Media, Neurobiology
Mary Gates Scholar
Mentor: William Moody, Biology
Mentor: Curtis Easton, Biology

Waves of synchronous spontaneous activity (SSA) propagate throughout the nervous system during early stages of development. These waves consist of simultaneous action potential firing across large cell populations, with correlated increases in cellular calcium levels. Specific types of cal-

cium signals mediate different developmental processes in the brain. While calcium signaling is known to regulate activity-dependent developmental programs that help to finalize the maturation and connectivity of neurons, the particular function of calcium waves in neuronal migration is unknown. The aim of this project is to determine the contribution of calcium waves to the development of cortical inhibitory interneurons. To label inhibitory interneurons in the developing cortex we are using red fluorescent protein (RFP) under control of the dlx5/6 promoter region to drive RFP expression in these cells. We used a fluo4 calcium indicator to measure single cell activity of these interneurons. We have found both cortical interneurons that participate in asynchronous activity mediated by L-type calcium channels, and also cells that participate in synchronous activity mediated by synaptic mechanisms. We seek to determine whether the asynchronous interneuron population becomes synchronous at the time of migration termination and whether this shift in the synchronicity of calcium activity is a mechanism for migration termination.

POSTER SESSION 3

MGH 241, Easel 148

2:30 PM to 4:00 PM

Role of Individual Cell Properties in Creating Regional Activity Differences in the Neonatal Mouse Cortex

Cara C, Senior, Bioengineering, Neurobiology
Mary Gates Scholar
Mentor: William Moody, Biology

During the first week following birth in mice, waves of synchronous spontaneous activity (SSA) initiate in the ventral piriform cortex, and some propagate past the rhinal fissure into the dorsal cortex. These large-scale waves of electrical activity, involving a vast number of neurons firing action potentials simultaneously, are critical for the early postnatal stages of cortical development. By examining what combination of cellular and emergent network properties cause these regional activity differences (the initiation of waves in the ventral cortex and the participation of waves in the dorsal cortex), we have gained insight into the generation of SSA. Cellular activity can be observed by imaging calcium transients, which serve as an indicator of electrical activity. In the present experiments we demonstrate that ventral neurons are more asynchronously active between waves of SSA than are dorsal neurons. In order to determine what portion of the activity is an autonomous property of the neurons (i.e. independent of synaptic communication), we applied synaptic receptor antagonists during calcium imaging to eliminate synaptic transmission between cells. In the presence of synaptic blockers, we observed a greater reduction in activity in the dorsal cortex, whereas many ventral cells remained highly active. Our findings suggest that ventral neurons have a higher probability of being active in the absence of synaptic input, which supports the hypothesis that they may be more likely to initiate SSA if a sufficient number become synchronously active by chance. Since cortical interneurons are believed to play a key role in generating cortical waves of SSA, we are currently performing a similar analysis using a transgenic mouse, in which the interneurons express a red fluorescent protein, Td-Tomato. By determining if interneurons are more intrinsically active than other neurons in the ventral cortex and if they tend to initiate waves based on their temporal firing patterns, we can gain a greater understanding of the interneurons role in SSA.

POSTER SESSION 3

MGH 241, Easel 131

2:30 PM to 4:00 PM

Quantification of Quantum Dots in Solution using Surface Plasmon Resonance and Analytical Ultracentrifugation

Chinonso C (Chinonso) Opara, Junior, Biochemistry
Amgen Scholar, McNair Scholar
Mentor: William Atkins, Medicinal Chemistry
Mentor: John Sumida, Medicinal Chemistry

Quantum dots are nanoparticles with several applications including cellular imaging and drug delivery. Because of quantum confinement, their ability to fluoresce under ultraviolet light is size dependent. However, quantum confinement not only plays a role in emissive properties, but is also a factor in the absorbance spectrum of quantum dots. As a result, there is not a simple relationship between the concentration of quantum dots and optical density. It is the goal of this project to craft a new approach in accurately measuring the concentration of quantum dots in solution. We have determined a correction factor relating response units as measured by surface plasmon resonance (SPR) to values of refractive index. With this, we further use SPR in conjunction with analytical ultracentrifugation (AUC) to determine the concentration dependence of the refractive index, dn/dc, for TOPO-PMAT quantum dots. The measurement of dn/dc for the quantum dots allows us to use an interferometric determination of their total fringe increment observed by AUC synthetic boundary to measure the concentration of quantum dots in solution. We have estimated a dn/dc for 565 TOPO-PMAT CdSe quantum dots. In addition, we have used AUC to show that total fringe increments scale with concentration. Furthermore, we have estimated mass extinction coefficients for all wavelengths at which absorbance is observed for these quantum dost. This allows for UV-vis determination of concentration. Our results indicate that our strategy holds promise for providing a new method for measuring the concentration of quantum dots in solution.