

Walter Reed Army Institute of Research (2001-2002). In high school I worked with Dr. Richard Bauman to evaluate the neuroprotective efficacy of cyclosporine, a T cell immunosuppressant. We simulated injury in rats by simultaneous blunt head trauma and hypoxia. Cyclosporine was administered immediately post-injury and evaluated by comparing neurological and physiological function pre- and post-injury. Specifically, I designed three vestibulomotor assessment tasks and then evaluated treated and control rat performance on each of these tasks pre- and post-injury. Currently Dr. Bauman is collaborating with industry to develop a formulation appropriate for first-response treatment. My internship at Walter Reed was invaluable. It provided me my first research experience and instilled in me a commitment to translational medicine.

Biotechnology Division, National Institute of Standards and Technology (2003). To gain experience in rigorous, quantitative biology, I next worked with Dr. Adolfas Gaigalas, a physicist, who was trying to improve fluorescence quantification technology to facilitate comparison of biological assays across different instruments. I worked with Dr. Gaigalas to reduce fluorophore photodegradation by temporally modulating the intensity of the excitation laser. I incorporated excitation intensity modulation hardware and software into an existing flow cytometry system and showed that this reduced the photodegradation of fluorescein. Working with Dr. Gaigalas was a great experience. He taught me how to think quantitatively about biological systems, design rigorous experiments, and, most importantly, how to be a patient, persevering scientist.

McGovern Institute for Brain Research, MIT (2004-2006). Combining my interests in neuroscience and quantitative biology from working at Walter Reed and NIST, I chose to spend the later half of college working with Professor Michale Fee to improve the accuracy of electrode implantation in songbirds to facilitate the study of specific brain areas that generate complex behaviors. First, I worked with Professor Fee to develop a device that predicts the location of brain structures by 1) constructing a 2-dimensional model of the cranial midline using a laser, cylindrical lens, CCD camera and image processing software, and 2) comparing the midline model to a library of models to which we planned to associate the locations of various brain structures by burn lesioning and sectioning. Initial data, however, suggested there was little correlation between midline topology and brain architecture, leading us to switch to an x-ray based approach. Second, I developed software to trigger and acquire data from an x-ray camera and worked with two other students to build hardware controls for the x-ray source and develop cranial bone segmentation software. In contrast to my experience as NIST, working with Professor Fee taught me to be an impatient scientist – to quickly take charge, make decisions, and solve problems.

Graduate Program in Translational Medicine, Stanford University (2006-2007). To better prepare myself to address medically relevant problems, I decided to enroll in the translational medicine masters program at Stanford and complete the pre-clinical medical curriculum. The goal of my first two projects under this program was to learn how to think quantitatively about problems in translational medicine while addressing two specific medical problems: 1) infection diagnosis, and 2) antibiotic resistance. I initiated both projects to fulfill course requirements and consequently conducted both projects independently with only published literature and publicly available data. The goal of my first project was to develop a broadly applicable scheme for rapid infection diagnosis. To achieve this I developed software that BLASTs expressed sequence tags (ESTs), which in the future could be sequenced from biopsies of infections, against a database of sequences of viral, bacterial, and parasitic pathogens. In lieu of testing the software with real data, I constructed and used simulated infection EST data to characterize the software's performance

and tolerance for contamination by commensal organisms and human tissue. I concluded that at reasonable contamination levels (eg. 75%) the software identifies the correct pathogen in 80% of cases. When EST infection sequencing becomes feasible, I hope to further develop this technology.

My second project in graduate school was inspired by an article by Drs. Nathan Alder and Steven Theg that enumerated several factors that affect the energetic cost of molecular transport across membranes, and a review by Dr. Christopher Higgins, which discussed the energetic requirements of multi-drug transporters. Combining these ideas, I reasoned that one solution to the problem of antibiotic resistance due to multi-drug transporters is to derivatize existing antibacterials to increase their energetic cost of efflux by bacterial multi-drug transporters, thereby decreasing their rate of efflux. For my project I wrote a review summarizing this idea. Working on these projects with limited resources was a very instructive exercise. It forced me to explore the breadth of publicly available data and become a more resourceful scientist.

Department of Chemical & Systems Biology, Stanford University (2007). To gain experience in model-driven experimental biology more strongly grounded in first physics and chemistry principles, I chose to work on a systems biology project with Professor Jim Ferrell for my first formal graduate research project. Specifically, I worked to test the predictions of two opposing models of mitosis regulation: 1) a single master regulator model where a single protein initiates each mitotic event that predicts that the time intervals between mitotic events are correlated, and 2) a regulatory chain model, which predicts that these time intervals are uncorrelated because their initiations are controlled by a series of proteins. With another graduate student, I discriminated between these models by measuring the timing intervals between the G2/M transition, centrosome separation, nuclear accumulation of cyclin B1, and nuclear envelope breakdown by double thymidine block and microscopy of HeLa cells transfected with fluorescently labeled cyclin B1 and a nuclear marker, MBS. After learning how to culture cells, transfect DNA, and optimize experimental conditions, we concluded that the time intervals between mitotic events are uncorrelated, supporting the regulatory chain model. Perhaps most importantly, I learned the value of model-driven biology – using a quantitative model to plan new experiments and using those experiments to refine the model.

Department of Bioengineering, Stanford University (2007-present). Currently I am working with Professor Markus Covert to gain additional experience in systems biology. I am developing mathematical tools for analyzing systems-level flow cytometry cancer data collected by our collaborators in the Department of Medicine to infer how B cell signaling networks in follicular lymphoma patients differ from those of healthy individuals. To accomplish this I am developing web-based software that enables scientists and clinicians to perform supervised Bayesian structural inference of signaling networks, build consensus models of signaling networks across patients by network alignment, and visualize systems level data as animated network diagrams. I recently reported this work at two conferences on computational biology and interdisciplinary cancer biology [1,2]. With the support of an NSF fellowship, in the future I hope to leverage my neuroscience and systems biology expertise to elucidate the basic mechanisms of synaptic plasticity, which in the future I will hopefully use to inform the pathophysiology and treatment of memory disorders.

Posters & Presentations

[1]. National Cancer Institute Integrated Cancer Biology Program Meeting. 2007.

[2]. Biological Computation at Stanford Symposium. 2007.

[3]. United States Army/George Washington University Joint Symposium. 2001, 2002.

[4]. Walter Reed Research Center/Naval Medical Research Center Joint Symposium. 2001, 2002.