Designing my SIP

Bobby Rohrkemper

June 10, 2003

1 Research Proposal

A Computational Approach to Pharmacological Modifications of Septo-Hippocampal Rhythms

Computational Neuroscience (CNS) is often used as a tool to integrate data from anatomical, physiological, pharmacological, and behavioral sources into mathematical models. My SIP (K Physics dept.) at KFKI Research Institute for Particle and Nuclear Physics, Hungarian Academy of Sciences will work toward further characterization of rhythm variations due to pharmacological modifications in the hippocampus by using computer models. This spring, I am working on a closely related research project involving the olfactory bulb (OB) of mice. For the OB project, Eric Zilli (K senior) and I will supervise a group of six other student researchers. Creating simulations of rhythms in the OB will give me a stronger background for the project this summer. The computational work will be done using two neural simulators entitled GENESIS and NEURON, both of which I have had some experience using. Using these software programs, I will be creating several types of models ranging from single cell models to network models.

Professor Érdi and his colleagues have developed complex computer-based models that can be used to simulate lesions, or the blocking of certain neurotransmitters, an effect similar to a patient taking a specific drug. To improve these models, we will computationally model the observed pharmacological modifications in humans and animals. From the models, I will study various parameters that change the rhythms. This goal of observing parameter dependence is very closely related to the OB project. First, I will determine characteristics of a single pyramidal or basket cell. This will involve creating a single cell model using the software GENESIS. This single cell will have two or more compartments between which ions may flow. The flow of ions will be modelled by the 'cable equations'. The specific parameters for these equations will be found from published anatomical data. More advanced models will contain a network of neurons (just basket cells or just pyramidal cells). Improving on networks with a single neuron type will be small networks containing both basket and pyramidal cells. Finally, our most advanced models will simulate the whole circuitry of the hippocampus including septal GABA cells, OLM interneurons, basket cells, and pyramidal cells.

From these models, several types of interactions can be observed. We will be able to modify the circuit by simulating pharmacological agents which influence noradrenergic-serotonergic metabolism. It is possible that this interaction will be GABAergic. This means that I will inhibit specific interactions within the network and observe the resulting changes in rhythms. From the network model of the entire circuitry of the hippocampus, I will be able to simulate what happens when breaks in the circuitry (lesions) occur. Furthermore, I will determine the number and strength of lesions necessary to suppress a specific rhythm. Anatomically this can be thought of as similar to a person taking a specific neurotransmitter blocking drug or even as a rat with a lesion in a section of the hippocampus.

The overall goal of the project is to generate artificial Electroencephalogram (EEG) data which can then be compared to biological data at a later time. The results may suggest more effective treatments for a category of diseases called 'dynamical diseases', which reside in an intact neural network. Two such diseases are Alzheimer's and Depression.

I have been doing background reading and learning software applications for about one year to prepare for my project this summer. A significant amount of thought has also gone into planning how I will be integrated with Dr. Érdi's research group. The planning will continue this spring with several of Dr. Érdi's graduate students who are now in the US: these students are Gergõ Orbán, Tamás Kiss, and László Zaláyni.

2 Personal Statement

My successful Intercultural Research Project (ICRP) on study abroad shows that I can effectively perform research overseas. While at Curtin University in Perth, Australia, I was able to complete a project in Solid State physics in a culture very different from my own. I worked with Dr. Robert Hart on the analysis of diffraction patters of kaolinite using synchrotron radiation. This was part of a larger project on the characterization and quantification of structural defects in clay minerals. I was also involved with work in the Materials Research Group including using laboratory x-ray analysis, transmission electron microscopy, and scanning electron microscopy.

Past research experience with Dr. Érdi suggests that this project will have a significant effect on my understanding of CNS. I took Dr. Érdi's CNS course last spring, and now I am a teaching assistant for the same course. I find CNS to be a rewarding experience because of the interdisciplinary nature of the work. I have found that his teaching methods allow for a very deep understanding of a specific topic, which allow me to apply my reasoning skills to new and exciting problems. Studying a topic in depth rather than having a brief overview of many topics is a characteristic of the Hungarian educational system. For this reason, I look forward to working in Budapest over the summer.

Thus far, my career has involved studying background material necessary for CNS as well as some research in the area. As I progress, I would like to pursue a terminal degree in CNS. I believe that my SIP will lead me toward acceptance into a competitive CNS graduate program. In fact, I think it will be more helpful than any project I have completed previously. Dr. Érdi will be an important mentor as I make this journey. I have been told that undergraduate research is something that sets the best graduate school applicants apart from the rest. Beyond graduate school, I see myself doing research that will make progress in curing diseases or developing new technological devices. The possibility of new treatments for several diseases is described briefly in my research proposal.

CNS consists of a relatively small group of people who are working on biologically related problems and have abilities in areas such as Physics, Computer Science, or Math. Despite being a discipline in which few people work, CNS has the ability to greatly impact medicine, and specifically the way we treat diseases such as Alzheimer's. It also has applications to next generation computing devices including navigational robots and even brain-like computers. CNS as a field of study is offered to very few undergraduates.