Thesis Portfolio

A Reaction-Diffusion Model of the Centromere-Signaling Network
(Technical Report)

Mental Versus Medical: How Deep Brain Stimulation Could Tip the Balance
(STS Research Paper)

An Undergraduate Thesis
Presented to

The Faculty of the
School of Engineering and Applied Science
University of Virginia

In Partial Fulfillment
Of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

By Lydia Erbaugh

May 4, 2020

Technical Team Members:
Jasraj Raghuwanshi

TABLE OF CONTENTS

Biomedical engineering spans a broad range of disciplines, which includes the newly developed field of computational biology. The following body of work uses both technical and sociocultural approaches to explore how computational biology can be used to address healthcare. The technical component exemplified the use of computational medicine to validate a biological phenomenon at the beginning stages of a model's implementation. By creating a mathematical model to represent a biological system, the technical component developed an understanding of specific cellular events in cancer that has the potential to lead to further research and therapy development. In contrast, the sociocultural analysis explored the outcomes of computational medicine at the end stages of its application. This approach examined how the therapies developed from similar models can impact cultural beliefs to affect how patients are treated both medically and interpersonally. By examining the effects of computational biology at different stages in its development, this work will explore how computational approaches to medicine influence healthcare.

The centromere-signaling network (CSN) is a network of protein interactions that resolves errors in DNA separation during cell division. Although such errors are found in 40% of cancers, the specific role of this pathway in error resolution is unclear; therefore, a more thorough understanding of this pathway is required for further research in the prediction and subsequent prevention of cancer. To develop a better understanding of the relevant molecular interactions, a computational model of the CSN was created by specifying a set of partial differential equations in the software, Virtual Cell (VCell). The model was then used to determine which reactions are the most sensitive to perturbations in protein concentrations and reaction rates. The final model, which was able to create the experimentally observed distribution of protein concentrations, revealed that most of the molecular interactions involved are easily affected by changes in cellular conditions. The success of the model indicates that the CSN alone is sufficient for creating the conditions necessary for proper DNA segregation. Furthermore, the sensitivity of the pathway as a whole suggests that the CSN may be a source of errors in cell division and could thus be a target for new cancer therapies.

Psychiatric disorders affect approximately 20% of adults, but there remains a long-standing stigma around the controllability of these illnesses. The biological model, which asserts that the origin of psychiatric disorders is a physiological phenomenon in the brain, has the potential to change public opinion about a patient's ability to control their disorder, but more scientific support is required for this shift in perspective. This support may be obtained through deep brain stimulation (DBS), a recently developed psychotherapy that administers electrical stimulation to the brain. The following analysis of this issue is an exploration of the potential of DBS to diminish the stigma against psychiatric disorders through its connection with the biological model. It was found that DBS must move through a series of steps before it can influence cultural beliefs surrounding psychiatric disorders. The technology must first become a trusted therapy, appear in multiple forms of media, and finally integrate into societal vernacular where it can subconsciously

be integrated into the cultural belief system as support for the biological model. While DBS is well suited to move through this process of integration, the therapy lacks a sound scientific understanding, which creates a barrier for belief in the biological model. As a result, DBS is not currently able to shift the cultural understanding of psychiatric disorders, but the therapy is in a favorable position to do so in the near future.

Both sets of work offer valuable information to the healthcare field, and although the goals of each project shifted throughout their duration, the baseline objectives were ultimately met. Despite technical setbacks, we created a working model of the CSN with the potential to settle debates over the functionality of the protein network. Although it would have been beneficial to have more scientific validation incorporated into the model, its curation was a true accomplishment. Likewise, the analysis of DBS included a rigorous exploration of the cultural ramifications of psychiatric treatments, which resulted in a clear outline of treatment integration into societal beliefs. To continue this research, it would be necessary to determine exactly what information is still needed from DBS or other technology to promote the biological model. The next steps for the CSN model include adding more biological components of the pathway to provide a more comprehensive analysis. Furthermore, model parameters and results should be verified through cellular experiments. Through their progress and continued development, both projects prove that although technology takes many years of dedicated work to develop, it can make an immense difference in the healthcare available to patients.