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

The Influence of Animal Ethics on Computational Modeling
(STS Paper)

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Lydia Erbaugh
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Technical Project Team Members:
Jasraj Raghuwanshi

On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

Signature Lydia Erbaugh Date 11/28/19
Lydia Erbaugh

Approved KEVIN JANES Date 11-25-19
Kevin Janes, Department of Biomedical Engineering

Approved Kent Date 12/3/19
Kent Wayland, Department of Engineering and Society

General Research Problem: The Effect of Controversy on Medical Research

How does controversial public opinion influence progress in the field of biomedical research?

Over the last century, medical research technology has progressed by leaps and bounds. Although many view the advancement of medicine as a purely scientific endeavor, the field's history is marked by the heavy influence of public opinion. For example, social controversies have greatly shaped experimentation with the human genome and, more recently, the manipulation of stem cells. In these cases, public debate has sometimes restricted biomedical innovation, but at other times it has facilitated the development of new technologies. While the specific effects of public dialogue on the aforementioned research areas are well-studied, the effects on other medical fields such as computational biology are not as clearly defined.

Computational biology, or the mathematical representation of biological systems, refers to the set of modeling methods that have recently developed in medical research. For example, scientists have used modeling techniques to represent biological processes such as the formation of blood vessels and cellular communication during cancer. *In silico* models such as these have emerged as invaluable tools for integrating an ever increasing amount of complex biomedical information (Wooley & Lin, 2005). A critical factor in the rise of these computational models is public debate, specifically the long-held controversy over the ethics of animal use in drug testing. By investigating the trends that underlie social influences on biomedical research while utilizing the resulting technologies, I hope to reveal how progress in the medical field is guided by public opinion in addition to technological needs. Conscious knowledge of these relationships may allow the public to exert a more purposeful influence on medical research. Alternatively, these findings will help medical personnel to more effectively respond to popular opinion and shape the direction of future medical advancements.

The Curation of a Computational Model for Cell-Signaling in Cancer

How do we assemble a mathematical representation of cell-signaling to improve our understanding of protein localization in cancer?

Cell-signaling networks are composed of a series of chemical reactions between proteins, which allows communication both internally and externally to the cell. Each signaling network enables the body to execute a biological process that is essential to life. One such signaling pathway, labeled the centromere-signaling network (CSN), serves to rectify errors in DNA separation during cell division by attracting a certain protein, chromosomal passenger complex (CPC), to locations where DNA is found in the cell. *In vitro* studies in cancer cells have suggested that imbalances in protein concentrations diminish the pathway's ability to eliminate errors in DNA separation (Trivedi & Stukenberg, 2016). When cells do not evenly divide their DNA during cell division, the resulting mutations may lead to certain types of aggressive cancers. However, the errors in CSN protein interactions that create these issues cannot be described by the limited techniques available for *in vitro* experimentation, so the predictions generated by the cellular experiments remain unverified.

To confirm the hypotheses derived from the aforementioned studies, a computational model of the system will be created to represent the specific chemical reactions of the CSN. The model, which will be composed of a set of partial differential equations describing the behaviors of proteins in the cell, will be created using the open source software, Virtual Cell. The relevant parameters needed to mathematically describe protein movement and interactions will be found in the existing literature on the CSN. Once the model is constructed, these parameters will be adjusted to represent cancerous conditions. The effects of these modifications on CPC localization will be quantified by the protein concentration outputs from the model, and the results will be used to answer the questions generated by previous studies. Because cellular mutations resulting from impaired protein localization are known characteristics of many cancer types, the increased knowledge of protein interactions derived from the model may serve as the foundation for future research in the prediction and subsequent prevention of the onset of cancer.

The Influence of Animal Ethics on Computational Biology

How is the advancement of computational modeling motivated by the controversy over drug testing on animals?

I propose to study the effect of the animal research controversy on the rise of computational modeling. The debate surrounding animal rights in medical research has been impacted by the development of computational technologies and has also served as an impetus for progress in the field. The discourse between animal rights groups and scientists as well as the resulting government regulations have pushed the medical research field to reduce, replace, and refine the need for animal testing by developing more sophisticated computational models (Smith, n.d.). Therefore, the interplay between the involved interest groups, which include research institutions and animal rights organizations, may have the potential to motivate and shape the progress of the biomedical field in creating better and more effective treatments. The results of this research will expose the influence of these organizations on the field of computational biology, which will provide a more thorough understanding of how citizens interact with advanced mathematical modeling. The results will enable citizens and scientists alike to more consciously navigate the interactions between medical research and society at large.

Background

With the rise of computational modeling in biomedical experimentation, animal rights activists have advocated for the total eclipse of animal testing in favor of *in silico* methods. While researchers prioritize efficiency and accuracy, proponents of animal rights put the humane treatment of animals above all else. In an attempt to placate these activists, strict regulations have been placed on animal testing to ensure that it remains reasonably cruelty-free (National Research Council, 2004). Such regulations hinder the progress of certain types of biomedical research, which affects consumers who may be in dire need for the development of new treatments that are both effective and safe to use (Gelzer, 1979). However, the discourse surrounding animal testing simultaneously fuels the advancement of research technologies by motivating treatment developers to develop computational alternatives to animal techniques. The resulting field of computational modeling consists of a plethora of techniques for mathematically representing biological processes, which has the potential to facilitate the development of more accurate and efficient medical therapies. By analyzing the mutual influences of mathematical modeling and the invested groups, I hope to help the reader understand the interchange between computational biology and public debate as well as the resulting costs of both computational and animal-derived treatment development.

Data Analysis

To study the mutual influence of computational modeling and the controversy over animal testing, I will explore the claims and responses of both humane and scientific organizations as well as the government regulations that mediate their interactions. For example, the similar arguments made by various animal rights groups such as the US Humane Society and PETA can be found on their web pages. These sites include their suggestions for alternatives to animal testing such as *in vitro* and human experimentation (PETA, 2010). This data will be used to study the methods they proposed for eliminating animal research both before and after the advent of computational modeling and to discover any other resulting shifts in their arguments.

Scientific organizations like the Foundation of Biomedical Research publish their claims and responses to animal rights societies on websites of their own (The Foundation for Biomedical Research, n.d.). While researchers and scientists acknowledge the concerns of humane societies, they tend to prioritize scientific progress, recognizing animal testing as a necessary institution in medical advancement. However, specific research institutes have formed groups that research and develop alternatives for animal experimentation, which can be used as evidence that researchers place importance on animal protection despite differences in viewpoints and priorities. For example, the Center of Alternatives to Animal Testing at Johns Hopkins University uses its website to describe the technologies they have developed as well as responses to those who are concerned with the humane treatment of animals (Smith, n.d.). Scientific literature from other fields such as toxicology will also prove useful as examples of areas in which research has already shifted from animal to computational techniques (Langley et al., 2015).

Analysis of policy history will also be used to uncover the causal relationships between developments in the debate and medical research. The interactions between animal rights societies and research institutions are often arbitrated by government organizations, which are obligated to attend to the needs of both groups and mediate controversy through regulations. In particular, the United States Department of Agriculture (USDA) National Agriculture Library contains a wealth of information on regulatory developments and their motivation ("National Agricultural Library," n.d.). The resources available on their website include the hearings, regulations, and amendments that occurred during the preparation or as a result of the Animal Welfare Act of 1966 (AWA). Supplemental information concerning the AWA can be found in the Federal Register, the USDA Animal and Plant Health Inspection Service (APHIS), and the National Academies of Science.

Once the data has been collected, I will use content analysis to characterize the interactions and influences of the invested groups. This technique involves the systematic examination of different resources with the purpose of detecting themes and relationships. For example, the statements published by animal rights groups contain similar claims as do those written by scientific organizations. By comparing the materials obtained from various sources, the collective opinion of each group will emerge.

In the controversy over the humane treatment of animals in medical research, the stances of the involved groups have been clearly established through publications that outline their respective claims. Interactions between this debate and progress in the medical field have formed through the development of computational alternatives to animal testing, but these connections have not been defined. The proposed research is intended to illuminate the trends in these relationships, which will provide a greater understanding of the potential of public opinion to shape both research directions and medical technology, particularly in the field of computational biology. Both researchers and animal rights proponents may be able to use the resulting information to communicate more effectively and resolve their concerns.

Conclusion

By studying the mutual shaping of the animal rights debate and computational modeling in medical research, I aim to show whether this controversy has led to the development of more sophisticated modeling techniques such as the reaction-diffusion method I will be employing in my technical project. The integration of both projects will reveal how developments in the medical field are equally motivated by technological need and public debate. The analysis framework set forth by the results of this research may prove useful to other researchers who are interested in the ability of the greater population to influence medical research technology and policy through similar controversies. Altogether, these studies would have the potential to indicate the future direction of medical research in response to current disputes. This expanded knowledge may aid medical personnel in making informed decisions surrounding the interactions of the medical field with the general population. For example, leading scientists and medical administrators will be able to utilize this information to make critical decisions concerning the future progress of medical research in response to public demand. In turn, the proposed research can be utilized by the public to more purposefully influence advancements in healthcare. Overall, any group affected by the medical research system can benefit from this knowledge by gaining a more conscious understanding of their position in the system, which they can wield to advance their own interests.

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