In silico modeling of the motility of the *T. cruzi* parasite

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Introduction

Despite the advances that modern medicine has made to protect against disease, parasitic diseases are still a worldwide epidemic. Three prevalent diseases caused by parasites are malaria, schistosomiasis, and Chagas' disease. It is estimated that 16 to 18 million people are infected with Chagas' disease, and 50,000 people of those infected will die each year (CDC, 2004).

Trypanosoma cruzi (*T. cruzi*) is the parasite that causes Chagas' disease. It is a uniflagellate protozoan parasite that belongs to the order Kinetoplastida (Bastin, 2000). During its life cycle the parasite lives in both an insect host and a mammalian host, and has 3 developmental stages that are seen in both the invertebrate and vertebrate host (De Souza, 2002). Due to the complexity of the organism's life cycle dynamics, it is an intriguing model to study host-parasite interactions.

In particular, the flagellum of the *T. cruzi* parasite is a very interesting structure to study. The flagella of the *T. cruzi* is hypothesized to be involved with its ability to reach and invade host cells as well as be involved with the attachment to the host cell (Bastin, 2000), thereby making it an important component of the parasite's behavior. Thus, the more we understand about the flagellum of the *T. cruzi* and how the *T. cruzi* interacts with its environment, the greater ability one will have to fight diseases caused by parasites.

Methods

In order to analyze the flagella and the motion of the *T. cruzi* an "*in silico*" approach will be used. Using a combination of computer modeling, mathematical modeling, and biological

data, a model of how a single *T. cruzi* parasite swims will be developed. The overall project's intent is to create an "*in silico*" representation of *T. cruzi* parasites swimming and interacting with each other and with host cells. This current project will be involved with modeling the dynamics of a single parasite in the mammalian host. The model will then be incorporated and used in the overall project. The "*in silico*" modeling will be supported by research and laboratory experimentation performed in cooperation with a local medical school biological team currently studying the dynamics of *T. cruzi*.

The *T. cruzi* flagellum is composed of two major components; the axoneme, and the paraflagellar rod. The axoneme is conserved throughout all eukaryotic organisms and the *T. cruzi* flagellum has the same organization as all other eukaryotes (Gibbons, 1981). In addition to the conventional axoneme, *T. cruzi* have a paraflagellar rod (PFR) that has only been observed in the three groups of protists; kinetoplastids, euglenoids, and dinoflagellates. The function of the paraflagellar rod is still under investigation, but it has been shown that PFR mutants have reduced motility (Bastin, 1998). Also, while most eukaryotic flagellated cells propagate through the medium by being propelled by the flagella, the *T. cruzi* is actually pulled through the water by the flagella. The trypanosome flagella are attached along the length of the cell body, as opposed to the conventional free flagella. Current research has also determined that flagella are capable of creating waveforms that are characterized by stable or unstable translating conic functions. (Hutchings, 2004)

All of these factors make the flagella an intriguing organelle to study. The purpose of this specific project is to accurately model the *T. cruzi* flagella "in silico." This will provide the overall project with a more information on how the *T. cruzi* reaches and infects the host-cells. Obviously, this is a very important part of parasite dynamics, which needs to be studied in

further detail.

Results/Implications

The overall project of modeling the *T. cruzi* behavior "*in silico*" and then possibly other parasites has great implications. This project will create an "*in silico*" laboratory, which will allow scientists to conduct experiments in the computer. The ability for experiments to be run computationally will drastically reduce the dangers of working with infectious parasites, and the time it takes to complete current experiments. A biomathematically complete model of the *T. cruzi* flagella should allow better conclusions to be made concerning how the parasite swims and reaches its host. While this has many great benefits, it could take years to complete. The dynamics and behaviors of these organisms are very complex, and much understanding is needed to create an "*in silico*" world where experiments can take place.

Resources

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