Computational Modeling of the Movement of the *T. cruzi* Parasite in a Three Dimensional Environment

Cailin K. Andruss

Introduction

Chagas' Disease, caused by infection with the *Trypanosoma cruzi* parasite, is deadly and wide spread, with 16-18 million people infected and another 120 million at risk for infection [1]. Unfortunately, very little is known about the parasite that could be used in treatment and prevention. The goal of the Virtual Parasite Project (VPP) is to design an *in silico* laboratory that provides insight into the parasite-host dynamics of the *T. cruzi* parasite with its host by modeling the biophysical interactions [2].

To that end, this BBSI project seeks to expand upon the existing VPP model of *T. cruzi* parasites by adding modules for the parasites' movement through their environment and interactions with their surroundings. Once the basic framework for movement is in place the project will shift to pay special attention to the parasites' interaction with the host cell and the factors that influence whether or not each parasite infects the host cell.

Methods

The last summer's project dealt with writing a program in Scheme [3] that would produce output readable by the three dimensional graphical simulator SimRender [4]. The Scheme program includes functions for updating the position of each cell and a basic function that models the elastic collisions of the parasites with the walls of the world.

Over the next academic year, we will rewrite the program will in C++ as well as refine and expand it.

The first step will be to test the function for parasites interacting with walls and make sure that it is producing the correct results consistently. We also need to refine the calculation of the contact point of the parasite and the wall so that the interaction is calculated based on a point on the surface of the parasite instead of its center. Changing the shape of the parasite from a sphere to an ellipsoid will complicate these calculations, but will also result in a more accurate model.

Our next step will be to add the real physics into the program, including basic Newtonian mechanics (gravity, liquid drag, etc.), swimming force, van der Waals interactions with host cells, and charge-charge and mass-mass interactions with other parasites and the walls. Once the parasites start interacting only with objects in their immediate vicinity, we anticipate that the number of calculations the program will need to perform will go up exponentially. Thus we will need to find a method to optimize the calculations. We will also add a function that will randomize the order in which the cells are updated as well as functions that will produce random changes in the parasite's swimming direction at random intervals.

Possible results and their implications

We will test the accuracy of the simulation after each modification. This refinement of the model will set the stage for modeling of the host cell invasion and infection process. An accurate invasion model could lead to insights on how to stop the invasion process and prevent infection.

Budget

At this point in the project, it is not clear exactly what items will need to purchased. We anticipate the potential need for software, textbooks, and ancillary supplies to support the software and theoretical development of this project.

References

1. Special Programme for Research and Training in Tropical Diseases (TDR) (2002). *Strategic Direction for Research: Chagas Disease*, UNDP/World Bank/WHO, http://www.who.int/tdr/diseases/chagas/files/direction.pdf.

2. Witten, T. M., *et al.* (2005). *The Virtual Parasite Project – Towards a Biologically Sound Simulation Model of Parasite Dynamics: T-cruzi as a Prototype*, Internal operations document.

3. Programmed using DrScheme http://www.plt-scheme.org/software/drscheme/. For more information on the Scheme programming language visit http://www.schemers.org/.

4. SimRender (2004). In house CSBC software package for visualization of Virtual Parasite Program simulation data.