Computational Modeling of *T. cruzi* Parasite motion in a Three Dimensional fluid cell culture

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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. Now that the basic framework for movement is in place, the focus has shifted to pay special attention to the parasites' interaction with the host cells and the factors that influence whether or not each parasite infects the host cell.

Methods

The first 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 included 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 past academic year several aspects of physics were added to the basic movement functions, including gravity and buoyancy. The program was also rewritten to increase efficiency and eliminate errors.

The next step will be to finish adding the real physics into the program: primarily liquid drag and swimming force. 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. Most importantly, however, are the functions that will model the invasion of host cells by the parasites. This will require functions controlling van der Waals interactions, and functions that determine whether the parasite invades based on the cell cycle state of the host cell. When this is done, charge-charge and mass-mass interactions with other parasites and the walls will also need to be programmed.

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

This summer the funds will be used to purchase an Apple MacBook laptop and Office 2004 for Mac, as well as any additional supplies needed. This purchase will allow us to port the simulation to a Mac OS based environment and facilitate future development with the CSBC Apple cluster.

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.