Project Summary

Intellectual Merit

The immune system in humans relies on the ability of individual cells to organize spatially in a timely manner in response to pathogens. When immune cells detect foreign molecules, they secrete soluble factors that attract other immune cells to the site of the infection. According to a mathematical model by Thomas B. Kepler in the Duke University Center for Computational Immunology, these soluble factors are governed by a system of reaction-diffusion equations where the source terms are centered on the cells. The motion of the model cells is a Langevin process that is biased toward the gradient of the soluble factors. This reaction-diffusion-stochastic system can be solved numerically using operator splitting. In current simulations the majority of the computational time is spent solving the diffusion using a backward Euler scheme and multigrid. The goal of this project is to develop new techniques that will significantly improve the performance of the simulation.

A more biologically accurate model of the secretion of soluble factors by immune cells is a flux through the surface of the cell. In this model the cells themselves are boundaries where the normal derivative at each cell surface is given by the secretion rate. This initial-boundary value problem can be solved using layer potentials. The solution to the diffusion equation can be written as the integral of the convolution of the heat kernel with an unknown function on the boundary called a layer potential. Given an appropriate boundary condition, this leads to a Volterra integral equation of the second kind on the boundary. In this case solving the diffusion requires both solving the integral equation and evaluating the layer potential. Both of these steps are essentially two dimensional problems. A new algorithm based on these ideas will be considerably faster than the current multigrid based methods in three dimensions. The difficulty of this project lies in the fact that the immune cells are moving toward each other until they touch. Solving the diffusion in this context will require new ideas due to the fact that the classical layer potential theory breaks down.

Broader Impacts

Although the motivation for this project is an immunological model, but the methods described above will be useful for a wide variety of problems that involve diffusion. Accurately solving a diffusion problem in three dimensions with simple boundary conditions requires a large amount of memory and computational power. Reducing the problem to two dimensions using layer potentials decreases the memory requirements and increases the efficiency of the numerical simulation. This allows for the consideration larger scale problems with more complex boundary conditions.

The impact of this project also goes beyond the mathematical community. The numerical simulations described above will aid in understanding the motion and coordination of immune cells in response to harmful bacteria.The software developed for this project will be released to the immunological community to aid in the study of the behavior of the immune system. At Duke University, this information will be used to design more effective adjuvants in vaccines. Considering the growing concern of bio-terrorism, inoculation against deadly bacteria will help protect Americans at home and abroad.