# The Immune System as a Complex Adaptive System: A RePast Simulation of the Anti-Viral Immune Response.

Virginia A. Folcik and Charles G. Orosz, Department of Surgery/Transplant, The Ohio State University College of Medicine and Public Health

The immune system is a prime example of a complex adaptive system, with Individual cells that follow rules for behavior based upon detection of signals and contacts with other cells in the environment. We have created a simulation of a human anti-viral immune response using the RePast software framework. The agent-based simulation includes three windows that represent a generic tissue site with parenchyma that becomes infected with virus, a lymph node site with cells that can become activated to fight the viral infection, and the peripheral blood that carries the responding immune cells and antibodies back to the site of infection. The simulation uses seven agent types and twenty signals to represent Parenchymal Cells, B-Cells, T-Cells, Macrophages, Dendritic Cells, Natural Killer Cells and the virus, and pro- and anti-inflammatory cytokines, chemokines and antibodies that such cells use to communicate with each other. The numbers of agents present as well as the quantity and types of signals present depend upon rules for proliferation and the release of cytokines that the agent types follow. Individual agents have various states, migrate from one window to another and live or die as the rules for their behavior dictate.

A typical run of the simulation involves the entry of initial conditions (ratios of immune cell types), then the execution of the simulation during which the numbers of agents and quantities of signals are recorded. Given sufficient time, the outcome of a run may be either that the virus infects all of the parenchymal cells resulting in the death of the tissue (a viral "win") or the elimination of the virus and all virally infected cells with regeneration of healthy cells and restoration of the tissue to equilibrium conditions (an immune system "win"). Consistent with the theoretical properties of a complex system, our experiments have found initial conditions that always produce the same win/loss results, but the profiles of cell proliferation and signal production that occur are unique for every run of the simulation. Other initial conditions have been found that produce varying win/loss ratios.

We plan to be able to use our simulation to explore formative patterns of agent behavior that develop within a complex adaptive system, to evaluate how information is used for decision making as responses evolve, and to develop methods of generating and evaluating simulator data that can be used to identify the strengths and weaknesses of clinical and experimental tools that are currently in use.