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Title: Simulating the Complexity of Immune Responses

Presentation Materials: PDF

Streaming Video: Real Media

Despite the vast amount of information about the immune system has accumulated, we still understand very little about how the immune system functions to provide protection or to promote pathologies. While we are adept at teasing out and characterizing the various pieces of complex immune responses, we are relatively inept at reassembling these pieces into a coherent perception of immune system function. At its most basic level, the immune system is a large collection of many simple, autonomous members, each of which reacts individually to the state of the local environment according to a set of internal rules. As such, it qualifies as a complex, adaptive system, and it displays the inherent characteristics of such systems, i.e., the ability to adjust to stimuli, to maintain coherence in the face of change, and to learn. These are important competitive advantages that complexity bestows on the immune system, making it remarkably effective under a variety of conditions.

Clearly, the immune system is a rich network of interactive agents. While this is commonly acknowledged, it is routinely ignored. Immune responses are usually treated as small, isolated, linear arrays of cause-and-effect activities. The problem is that most biologists do not know how to deal with complex, networked processes. They find them too complicated and too unpredictable. The fact that causality and outcome are often obscured by the many different functional options within a network poses a major problem for investigators. Nevertheless, a true understanding of immune function requires an appreciation for how complex, adaptive networks operate.

Unfortunately, the human brain has difficulty dealing with networked activities. However, it has conceived a tool for which networked activities provide no problems at all: the computer. Unlike the human brain, a computer can patiently and efficiently track an unlimited number of interacting agents, and follow them to an outcome. This leads to the question: Can we use a computer to study the function of complex adaptive systems, in general, and the function of the immune system, in particular? This is a central question of our current studies in theoretical immunology.

To employ the computer for this purpose, we used the Repast software library to develop a prototypic computer simulation of the immune response to a generalized viral infection. We needed to simulate a phenomenon that involved large numbers of different elements operating in a defined space, and these elements needed to interact with each other in defined ways via direct contact or via secreted signals that diffused through the environment. The Repast software was exceptionally useful for the creation of a computer simulation of this response. It is important to note that we did not attempt to model all of the elements of an immune response. Rather, we chose to simulate its design principles. Regardless of the accuracy of he simulator with regard to the operative features of the immune response, the simulation represents a complex adaptive system that functions in silico, and can be studied as such. Our current studies involve the refinement of this simulator to more accurately reflect the design principles of the immune system. We plan to use the simulator to explore key, formative patterns of agent behavior that develop within complex adaptive systems, to evaluate how information flows through complex adaptive systems and how it is used for decision making as immune responses evolve, and to evaluate the strengths and weaknesses of clinical and experimental tools (such as biopsy and gene chip analysis) that are currently in use.