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Chapter VI

The Clonal Selection Principle for In Silico and In Vitro Computing

Vincenzo Cutello, University of Catania, Italy

Giuseppe Nicosia, University of Catania, Italy

ABSTRACT

The chapter describes the theory of clonal selection and its usage in designing and implementing immunological algorithms for problem solving and learning. In detail, it presents various immune algorithms based on the clonal selection principle, analyzing computational time complexity, experimental results, similarities and differences. It introduces two paradigms to model immune algorithms: noisy channel, and Turing's reaction-diffusion systems to build artificial immune systems for effective information processing and computing. The authors show how Libchaber DNA algorithm can be interpreted as an "in vitro" implementation of the clonal selection principle by means of molecular biology technology. These similarities witness the ubiquity of such a kind of information processing in nature and give evidence of the universality of the concept of computation. The authors' intent is to provide a general framework that can be considered as a first core for in silico and in vitro computation based on the clonal selection theory.

INTRODUCTION

Living systems are dynamical and reside in water at 320 °*K*. The constituents are of small size. It is a stochastic world of large amplitude vibrations and very viscous friction; force is proportional to velocity. All relevant energies are between 1 to 20 *kT*,

and all processes are out of equilibrium. Such a world needs a strict organization to function as a precise dynamical system or *natural automata*. Von Neumann (1956) observed: "Natural automata are superior to artificial ones, they have power of self diagnosis and self repair... It is to be expected a close relation of self-reproduction to self repair." We can define the biological Immune System (IS) as the globally distributed self-repair system of host organisms.

The IS has to assure recognition of each potentially harmful molecule or substance, generically called *antigen*, that can infect the host organism. The IS first recognizes an antigen as harmful or extraneous and then mounts a response to eliminate it. To detect an antigen, the IS activates a recognition process. In vertebrate living organisms, a complex machinery of cellular interactions and molecular productions accomplishes this task. One can see the biological IS as a complex adaptive system of cells and molecules, distributed spatially, which provides the host organism with a basic defense against antigens.

Immunology is the scientific discipline that studies the protection of organisms from antigens and their response to antigens. The first line of defense against antigens is barrier tissues such as the skin, which prevent the antigens from entering the body. If, however, these barrier layers are penetrated, the body contains cells that respond rapidly to the presence of invaders. These cells include macrophages that engulf antigens and kill them without the need for antibodies. This form of immunity is the *innate* or *non-specific* IS that is continually ready to respond to invasions. Hence, immunity is the resistance to the onset of diseases after infection by harmful antigens. Immunology grew out of the simple observation that after recovering from a particular infectious disease, one would become immune to further cases of that disease, but not to other infectious diseases. A second line of defense is the *specific* or *adaptive* IS, which may take days to respond to a primary invasion (that is, infection by an antigen that has not hitherto been seen). In the specific IS we see the production of antibodies (soluble proteins that bind to foreign antigens) and cell-mediated responses in which specific cells recognize foreign pathogens and destroy them. In addition, the host organism develops immune responses against our own proteins (and other molecules) in *autoimmunity* and against its aberrant cells in *tumor immunity*.

The IS can learn about the outside environment and adapt to it. It remembers not only what it has interacted with, but also how it responded to the environmental challenges. Thus, immunity is *adaptive* and *specific*: two desirable features to have in an effective and robust computational system.

Computational immunology is the research field that attempts to reproduce *in silicon* the behavior of the biological IS (Brusic & Petrovsky, 2002; Nicosia, Castiglione, Motta & Mannella, 1999), using computational tools and methods. *Artificial immune systems* (AIS) represent a new field of *natural computing* that attempts to use theories, principles, and concepts of modern immunology to design IS-based applications in science and engineering (Dasgupta, 1999; De Castro & Timmis, 2002).

A new emerging discipline, called *immunocomputing* (Tarakanov, Skormin & Sokolova, 2003), explores the principles of information processing that proteins and immune networks utilize in order to solve specific complex problems while protecting from antigens. Immunocomputing develops proper concepts and mathematical definitions of IS's basic elements. Three main innovations are expected to emerge from