Immune Network: An Example of Complex Adaptive Systems

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Abstract. The phenomenon of immunological memory has been known for a long time. But, the underlying mechanism is poorly understood. According to the theory of clonal selection the response to a specific invading antigen (e.g., bacteria) is offered by a specific clone of the cells. Some of the lymphocytes activated during the primary response remain dormant and keep circulating in the immune system for a long time carrying the memory of the encounter and, therefore, these long-lived cells are called memory cells. Proponents of the alternative network theory maintain that the immune response is offered by a “network” of clones in a connected manner. In recent years several possible scenarios of the “structure” and function of the immune network have been considered. We have developed mathematical models for describing the population dynamics of the immunocompetent cells in a unified manner. We have incorporated intra-clonal as well as inter-clonal interactions in a discrete formulation and also studied a continuum version of this model.

1 Introduction

The Latin word “immunitas” is related to the concept of exemption from a service or duty or from civil laws (e.g., “diplomatic immunity” of an ambassador of one country in another). It has been known for more than two thousand years [1] that individuals who recover from a disease become “immune” to it; this is the phenomenon of “acquired immunity”. The scientific investigation of immunology, however, began much later when Jenner utilized this phenomenon of “acquired immunity” to develop a vaccine against smallpox. The first breakthrough in understanding the mechanism of this remarkable phenomenon was made by Louis Pasteur in 1880. Over the last hundred years we have collected an enormous amount of information on the “hardware” of the immune system (e.g., the molecules and cells involved) [2–4] but we understand very little about the “software” that runs it, i.e., the principles governing various immunological processes.

Theoretical immunology [5,6] deals with the mathematical modelling of immunological processes at various levels, e.g., molecular level, cellular level and the level of cell populations. One of the major aims of theoretical immunology [7,8] is to predict “macroscopic” properties of the immune system.
from the properties and interactions among its elementary "microscopic" consti-
stituents; this problem is similar to those usually studied by physicists using 
the techniques of statistical mechanics. Theoretical immunologists develop 
mathematical models to understand how the immune system evolves over 
long time scales, how its size and inter-cellular interactions vary with time, 
how these interactions govern the dynamics of the populations of various 
types of cells during an immune response to a specific antigen and how it 
"learns" adaptively about new antigens (i.e., acquires new knowledge) and 
how it retains the newly acquired knowledge in its "memory" and, finally, 
how it retrieves information from its memory. Several mathematical models 
have been developed so far to capture the known immunological phenomena 
as well as to predict new ones. In this chapter we summarize some of the 
modern approaches to the mathematical modelling of the immune system 
and illustrate these with specific examples. We hope that some of the mod-
elling strategy developed for the immune system may find applications in 
designing artificial immune systems.

2 A Brief Summary of Experimental Phenomena 
to be Modelled Theoretically

 Millions of different varieties of lymphocytes are known to be produced by 
the immune system. However, according to the clonal selection theory, only 
a specific type can respond to a specific antigen. This is in sharp contrast to 
the non-antigen-specific response offered by the macrophages to the antigens. 
The body seemingly anticipates all the types of antigens it may encounter 
in the future and prepares accordingly by producing a large variety of lym-
phocytes. For an antigen-specific response the antigen must be, first of all, 
properly recognized by the specific lymphocytes. Different types of lympho-
cytes identify the antigens in different manners. Following the recognition of 
the antigen, a specific type of lymphocyte, which fit best with the antigen, 
proliferates rapidly through cell division into a clone (a population of ge-
etically identical cells). The corresponding process is called clonal selection 
because the antigen selects which lymphocytes must develop into a clone [9].

 There are several alternative and complimentary routes of immune re-
response. In a humoral immune response a specific type of B-cell proliferates 
and the terminal differentiation of a fraction of this B-cell population leads 
to plasma cells. These produce antibodies, which react with the antigen and 
eventually lead to the elimination of the antigen from the host system. The 
remaining fraction of the proliferating B-cells become dormant and keep cir-
culating in the bloodstream carrying a memory of the encounter with the 
antigen; the latter variety of the long-lived B-cells are called memory B-cells. 
In the cell-mediated immune response a specific type of T-cell becomes cyto-
toxic and kills the antigen directly. Memory of the encounter with the specific 
antigen is thereafter carried by the corresponding long-lived memory T-cells.