MATHEMATICAL MODELS IN IMMUNOLOGY

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Contents

Summary

Mathematical immunology is one of the youngest and extensively developed areas of contemporary mathematical biology and has only approximately a 30-year history. The subject of mathematical immunology is concerned with the study of the main regularities of immune system structure and function using mathematical methods. The subject of mathematical immunology owes its origin and development to the explosive

progress of immunology since the late 1950s, improved mathematical methods, and development of computing machinery.

One of the most widely used methods of application of mathematics in the study of the immune system is mathematical modeling. The whole complex of existing mathematical models describes a wide spectrum of immunological phenomena and is characterized by a wide diversity of the mathematical apparatus used. Mathematical models in immunology are applied to various problems, such as qualitative and quantitative description and prognosis of immune reactions dynamics as well as to control problems and analysis and planning of experimental studies. The structure of this research area is subject to continuous changes and additions. In view of this it neither seems possible nor advisable to present an exhaustive description of all the models developed so far. The primary goal of this article is to look through some basic models which characterize the most common properties of immune defense, as well as to consider some more complicated mathematical models which describe concrete mechanisms of immunity.

1. Introduction

Immune system is a collection of cells and molecules in an organism, whose primary function is the defense against nonself or modified self factors, the so-called *antigens*. Various factors such as pathogens (e.g. bacteria, viruses, and protozoa), malignantly transformed host cells, toxins, chemical substances, and other, may serve as antigens. So, one of the main properties of immune system is its ability to self-nonself discrimination. Recognition of antigen leads to immune reaction which results in the majority of cases in binding and elimination of antigen from the organism.

Human immune system represents an example of complex biological system, and consists of approximately 10^{12} cells (lymphocytes) and 10^{20} molecules (mainly immunoglobulins). For comparison, the number of cells in human nervous system is of the order 10^{10}. The immune system is a highly distributed system; its components are present in all tissues and organs of an organism. The major places of lymphocytes localization are the so-called *central* and *peripheral* lymphoid organs. Central lymphoid organs consist of the bone marrow, in which the stem cells (the predecessors of all blood cells) are reproduced, and of the thymus, in which maturation of T cells occurs. Peripheral lymphoid organs consist of the lymphatic nodes, the spleen, tonsils, Peyer patches, and some others. Two main transport systems of the organism connect the immune system components into the whole network. The majority of lymphocytes is situated in lymphoid organs, the fraction of lymphocytes in blood and other tissues is small, only about a few percent of the total.

A total number of various natural antigens is estimated to be approximately 10^6. Reaction of immune system with an antigen implies stereochemical interactions of lymphocyte surface receptors with antigen. The lymphocyte has only receptors of one specificity on its surface. A number of different specificities generated by the immune system is approximated by the value 10^7. Potential diversity of the immune system, i.e. a maximal number of specificities which may be generated using the existing mechanisms, reaches a value in the range 10^{10}–10^{11} for B cells and about 10^{16} for T cells. Therefore, the immune system may in principle interact with any, even artificially derived, antigen. Recognition of antigen by the immune system gives rise to specific immune reaction – immune response.

There exist two main types of immune response – T- and B-cellular (humoral). T-cellular immune response leads to the formation of the clone of specific cytotoxic (killer) T cells capable of damaging modified host cells (e.g. infected with viruses). B-cellular response leads to production of antibodies capable of binding extracellular antigens in blood and lymph. Other immune mechanisms of antigen neutralization exist, such as phagocytosis, as well as protective action of natural killer cells and complement, which may be called as nonspecific immune reactions. Pathophysiological processes, such as fever, oedema, and others, may also play a role.

The mechanisms of host immune defense are very complex and not completely understood. The discovery of the structure and function of immunoglobulins, the substantiation of the clonal selection theory and study of immune tolerance, determination of the role of major histocompatibility complex in the immune reactions, the study of idiotypic regulations, discovery of genetic grounds of antibody diversity, and others, have become important landmarks of the history of immunology. At the same time many problems remain unsolved, such as conventional schemes of cellular interactions in the immune response, the mechanisms of lymphocytes stimulation, suppression and apoptosis. We have no unified judgment about the role of idiotypic regulations in the immune defense. A major difficulty in the study of immunological phenomena and mechanisms is the lack of reliable data and nonuniqueness of their interpretation. In these circumstances the application of mathematical models has become useful for the theoretical study of immune reactions.

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Biographical Sketch

S.G. Rudnev studied at the Mechanical-mathematical department of Moscow State University (1987-1992). His Post-graduate study was at the Institute for numerical mathematics, RAS (1994-1997). He is presently a researcher.