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Chapter 7
Global Dynamics of an Immunosuppressive Infection Model Based on a Geometric Approach

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ABSTRACT

By clinical data, drug treatment sometimes is ineffective to eradicate the infection completely from the host in some human pathogens such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human T cell lymphotropic virus type I. Therefore, mathematical modeling can play a significant role to understand the interactions between viral replication and immune response. In this chapter, the author investigates the global dynamics of antiviral immune response in an immunosuppressive infection model which was studied by Dadi and Alizade (2016). In this model, the global asymptotic stability of an immune control equilibrium point is proved by using the Poincare–Bendixson property, Volterra–Lyapunov stable matrices, properties of monotone dynamical systems and geometric approach. The analysis and results which are presented in this chapter make building blocks towards a comprehensive study and deeper understanding of the dynamics of immunosuppressive infection model.

INTRODUCTION

In mathematical modeling of biological phenomena, one of complex systems is the immune system. The immune system is human body primary defense against pathogenic organisms and cells that have become malignantly transformed. Also, it involves multiple cell types and hundreds of soluble mediators and different receptor ligand interactions. The immune system can produce different types and intensity of responses, learn from experience and exhibit memory. Therefore, the modeling of immune system needs the knowledge about cells, molecules, and genes that make up that. This knowledge is based on the Human Genome Project progresses which uncover the genes and molecules that influence the behavior of single lymphocytes.

It is important to understand the behavior of the cells of immune system and how every cell of immune system interacts with other cells to generate an immune response. Furthermore, it should be noted that modeling in immunology is in contrast to the field of neurophysiology. In fact, the behavior of a single cell of immune system is not described in immunology. This means that the equivalents of the Hodgkin-Huxley (1952) equations do not exist in immunology. Hence, understanding interactions among the elementary components of a system in immunology is the major part in modeling. Quantitative results which are obtained by mathematical modeling can help researchers to modify and complete their understanding of immunological phenomena, (Barnes et al., 2002; Bekkering, Stalgis, McHutchison, Brouwer, & Perelson, 2001; Borghans, De Boer, Sercarz, & Kumar, 1998; Borghans, Noest, & De Boer, 1999; Borghans, Taams, Wauben, & De Boer, 1999; Butler & Waltman, 1986; Canabarro, Gléeria, & Lyra, 2004; Celada & Seiden, 1992; Celada & Seiden, 1996; Chun et al. 1997; Coppel,1965; Dadi & Alizade, 2016; De Boer & Perelson,1993; Detours & Perelson, 1999; Detours & Perelson, 2000; Diepolder et al. 1998; Fenton, Lello, & Bonsall, 2006; Hlavacek, Redondo, Metzger, Wofsy, & Goldstein, 2001; Kalams & Walker, 1998; Kepler & Perelson, 1993; Kesmir & De Boer, 1999; Komarova, Barnes, Klenerman, & Wodarz, 2003; Lang & Li, 2012; Lechner et al., 2000; Lechner et al., 2000b; Lewin et al. 2001; Li & Shu, 2010a, 2010b, 2011, 2012; Lifson et al., 2000, 2001; Liu & Wang, 2010; Lohr et al., 1998; Maini, & Bertoletti, 2000; McKeithan, 1995; McLean, Rosado, Agenes, Vasconcellos, & Freitas, 1997; Mukandavire, Garira, & Chiyaka, 2007; Nelson, Murray, & Perelson, 2000; Nelson & Perelson, 2002; Neumann et al., 1998; Ortiz et al. 2002; Percus, J.K., Percus, O.E. & Perelson, 1993; Perelson, 2002; Perelson, & Oster, 1979; Perelson & Weisbuch, 1997; Pugliese & Gandolfi, 2008; Rosenberg et al., 2000; Segel & BarOr, 1999; Shamsara, Mostolizadeh, & Afsharnezhad, 2016; Shu, Wang, &Watmough, 2014; Smith, Forrest, Ackley, & Perelson, 1999; Tam, 1999; Wang, Wang, Pang, & Liu, 2007; Whalley et al., 2001; Wodarz et al., 2000; Wodarz & Nowak, 1999; Zhu & Zou, 2008).

On the other hand, the interactions between the cells of immune system are very complicated. Therefore, the improvement of immunological models is a significant subject to study in recent decades.

The immune system has more than 10^7 different clones of cells that communicate via cell-cell contact and the secretion of molecules. It carries out pattern recognition tasks, learns, and preserves a memory of the antigens that it has fought. Like nervous system, cooperation among large numbers of the components of immune system for performing complex tasks such as learning and memory has attracted attention of many researchers who study on immunology, dynamical systems and statistical physics. Researchers believe that applying methods and concepts from statistical physics is especially suited to theoretical immunology, because there is not enough knowledge about the detail of mechanisms which are responsible for the observed behaviors in immune system. Moreover, dynamical systems help them to describe the time evolution of immune response. Researchers generally look for generic properties among the models of immune system, since these properties just depend on the general features of the model, and not on its details. According to Perelson and Weisbuch (1997), dynamical systems answer some of the questions about generic properties of the immune system such as: "Are the attractors limit points, limit cycles, or chaotic? What is their number? What are their basins of attraction? How do these properties relate to the parameters of the differential system? How can one force transitions among the different dynamical regimes? If our hypotheses about the universality of a model are true, the generic properties, qualitative classification of the attractors, and scaling laws should be evident in the phenomenology of the mammalian immune system." Indeed, theories and techniques of theoretical physics and mathematics play an important role to make towards increasing understanding of complex systems such as nervous system and immune system.

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