Optimal Control of a Fractional-Order HIV-Immune System With Memory

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***Abstract*—The fact that fractional-order models possess memory leads to modeling a fractional-order HIV-immune system. We discuss the necessary conditions for the optimality of a general fractional optimal control problem whose fractional derivative is described in the Caputo sense. Using an objective function that minimizes the infectious viral load and count of infected $\mathrm{CD4}^+$ T cells, the optimal control problem is solved for the fractional-order optimality system with minimal dosage of anti-HIV drugs and the effects of mathematically optimal therapy are demonstrated. Simulation results show that the fractional-order optimal control scheme can achieve improved quality of the treatment.**

***Index Terms*—Fractional-order model, human immunodeficiency virus (HIV) dynamics, numerical simulation, optimal control, ordinary differential equation (ODE).**

I. Introduction

SINCE the first case of acquired immure deficiency syndrome (AIDS) was reported during the early 1980s, large amounts of work have been done on modeling the dynamics of human immunodeficiency virus (HIV)-immune system, and the disease has become the subject of intense modeling efforts [1], [2]. Perelson *et al.* proposed an ordinary differential equations (ODE) model of cell-free viral spread of HIV in a well-mixed compartment such as the bloodstream [3]. This model consists of four components: uninfected healthy $\mathrm{CD4}^+$ T cells, latently infected $\mathrm{CD4}^+$ T cells, actively infected $\mathrm{CD4}^+$ T cells, and free virus. It has played an important role in the field of mathematical modeling of HIV-infected immune system, which results in the proposals of several other models [1], [4]–[7]. For example, Culshaw and Ruan simplified this model into the one consisting of only three components and introduced a discrete time-delay to this model [4]. Zhou *et al.* studied a differential equation model of HIV infection of $\mathrm{CD4}^+$ T cells with cure rate [6]. In [7], the identifiability properties of a four dimensional model of HIV/AIDS were studied.

On the other hand, different control problems have been addressed in the literature and various existing control theories have been applied to HIV-immune systems, such as feedback control [8]–[10], optimal control [11]–[15], and fuzzy discrete event system approach [16], [17]. It is worth pointing out that all of the aforementioned models have been restricted to integer-order ordinary (or delay) differential equations. Recently, the problem of modeling real processes using *fractional differential equations* (FDEs) has started to draw some initial research attention leading to inspiring results, see, e.g., [18]–[20]. For example, Ding and Ye [21] introduced the fractional order into a model of HIV infection of $\mathrm{CD4}^+$ T cells and carried out a detailed analysis on the stability of equilibrium. The global stability of an infection-free equilibrium was established and the optimal efficacy level of anti-retroviral therapy was obtained [22].

Considering the memory which is one of the main features of immune response [23], based on the model in [1], the fractional-order HIV-immune system with memory is proposed in this brief. A particular focus is on the fact that fractional-order models possess memory [20]. Then, the necessary conditions for the optimality of a general fractional optimal control problem are discussed. As such, the optimal control problem is solved for a fractional-order HIV-immune system with minimal dosage of anti-HIV drugs. The main contributions of this brief are summarized as follows. First, we proposed a fractional optimal control problem for a HIV-immune system as a generalization of an integer-order OCP. Then, a general formulation is developed for a class of fractional optimal control problems whose fractional derivative is described in the Caputo sense. Furthermore, the addressed optimal control problem is completely solved for the fractional-order HIV-immune system, which represents one of the first few attempts to apply the fractional optimal control theory in this area.

The rest of this brief is organized as follows. Section II gives a general formulation for fractional optimal control problem and discusses the necessary conditions for its optimality. The fractional-order HIV-immune system is described and the analysis of fractional-order optimization problems is conducted in Section III. In Section IV, the numerical simulation results are given and the conclusions are summarized in Section V.

II. General Formulation for Fractional Optimal Control Problem (FOCP) and the Necessary Conditions for its Optimality

A fractional dynamic system (FDS) is a system whose dynamics is described by FDEs and, accordingly, a FOCP is an optimal control problem for a FDS. In 2004, a general formulation was presented by Agrawal and a controller design procedure was given for a class of FOCPs whose fractional deriva-

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