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Optimal sigmoid nonlinear stochastic control of HIV-1 infection based on bacteria foraging optimization method

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ABSTRACT

Using nonlinear stochastic state-space model of HIV-1 infection, having as state variables the concentration of healthy and infected cells and the concentration of virions (free virus particles), utilized for design a control method. In this paper, a new optimal nonlinear stochastic controller is presented based on a bacterial foraging optimization (BFO) method to decrease the number of infected cells in presence of stochastic parameters of HIV dynamic. Bacterial foraging optimization sigmoid nonlinear control (BFO-SNC) is a novel nonlinear robust optimal method that can control the biological characteristics of nonlinear stochastic HIV dynamic by drug dosage management. The BFOA should optimize this kind of controller included three parameters. The proposed control method searches the best controller parameters domain subject to minimize a stochastic expected value of cost function. Simulation results show that the proposed BFO-SNC scheme does improve the treatment performance in compare to other control methods. For comparison with BFO-SNC method, a modified PID controller is chosen as controller structure.

1. Introduction

Therapy of human immunodeficiency virus (HIV) has remained a great challenge. About thirty-half years ago, HIV began to occurrence around the world at a threatening rate. The problems of HIV/AIDS are very important in present world. Acquired Immunodeficiency Syndrome (AIDS) is a kind of disease that can be treated by using expedient drugs. AIDS occurs when infection with the HIV destroys the body's natural protection from illness. The immune system weakens to the point where opportunistic infections and certain cancers can attack us [1]. These infections would not cause problems for healthy people, but for people with AIDS, they may cause serious or even life-threatening problems.

Blood is a significant part of the body's immune system. White bloods cells help to protect people from disease. Important parts of white bloods cells called T-cells perform a critical role. Some of the special T-cells are called "helper" cells that the HIV viruses attack and destroy them. When enough cells are destroyed, the immune system no longer works and the patient has AIDS. The good news is that HIV and its complications often can be treated. The proper treatment can lead HIV carrier patients to relatively normal lives for many years. Treatment options include antiviral therapy known as antiretroviral drugs:

1. Treatments for infections
2. Treatments for cancers
3. Treatments for symptoms antiretroviral drugs slow the progress of HIV because fewer HIV cells have formed [1].

Mathematical modeling has developed a substantial impact on clinical result consideration of HIV-1 infection. A massive amount of deterministic models has been developed to describe the immune system and its interaction with HIV-1 as well as the results of drug therapy [2]. Detailed studies that combine modeling analysis with clinical results show that the initial infection phase may be represented using simple nonlinear state models [3]. This fact has illustrated the generation of an increasing number of papers where therapy strategies derived from control principles. In most proposed methods, their mathematical model has based in relatively complex systems of nonlinear dynamic equations.

The majority of existing studies consider the HIV dynamics as a system with two independent control inputs; each input is related to one of the two drug types, i.e. RTIs and PIs. Many researchers have shown the dynamic HIV/AIDS studies [4]. Several of the papers illustrated analytical base of therapeutic aspects, such as switching protocols drugs on or off during the period of infection. Systems and control strategies have been applied to the specification of therapeutic methods in [4,5,3,6], using of open-loop optimization or stabilization based on close-loop control. All of these methods and design studies are according to ordinary differential equations.

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The problem of designing a heavy-duty control that provides global stability for an uncertain nonlinear system has been the subject of considerable research over the last decade. Classical methods of control design assume full knowledge of the system arrangement and its constant parameters. If this condition is not fulfilled, heavy-duty control is recommendable for design with uncertain parameters varying in the given interval [11]. For nonlinear systems with unknown static nonlinearities satisfying known functional bounds, the current literature focuses on deterministic worst-case robust analysis and synthesis. For parametric uncertainty, guaranteed stability-bound estimates frequently are unduly conservative, and the resulting controller usually needs very high control attempt. The convex programming problems arise often in mathematics, engineering and finance problems. Many publications deal with this problem by numerical algorithms. Since the computing time greatly depends on the dimension and the structure of the problems, numerical algorithm is usually less effective in large-scale or real-time optimization problems. The bacteria foraging algorithm (BFA), on the other hand, have massively paralleled distributed computation and fast convergence. It can be considered as an efficient method to solve large-scale or real-time optimization problems.

The essence of bacteria foraging optimization is to establish an energy function (nonnegative). The dynamic system is normally in the form of first order ordinary differential equations. It is expected that for an initial point, the dynamic system will approach its static state (or equilibrium point) which corresponds the solution of the underlying optimization problem. An important requirement is that the energy function decreases monotonically as the dynamic system approaches an equilibrium point.

Motivated by the above discussions, this paper proposes a strategy that combines sigmoid function as convex controller and BFOA in existence of stochastic uncertain parameters that convince best drug dosage management. Due to the wide variability of the dynamics associated to different patients, the capacity of a controller to stabilize models that are different from the nominal one is quite important.

The BFOA proposed by Passino, is a family of nature-inspired optimization algorithms. For over the last five decades, optimization algorithms like genetic algorithms (GAs), Evolutionary Programming (EP) and Evolutionary Strategies (ES) have been developed by researchers. Recently natural swarm inspired algorithms like Particle Swarm Optimization (PSO) and Ant Colony Optimization (ACO) have found their way into this domain and proved their effectiveness. Following the same study of swarm-based algorithms, Passino proposed the BFOA in application of group foraging strategy of a swarm of *E. coli* bacteria in multi-optimal function optimization that is the key idea of the new algorithm. Bacteria look for nutrients in a manner to maximize energy obtained per unit time. Sending signals, Specific bacterium also communicates with others. A bacterium takes foraging decisions after considering two previous factors. The process, where a bacterium moves by taking small steps while searching for nutrients, is called chemo taxis; and the key idea of BFOA is based on chemo tactic that movement of virtual bacteria in the problem searches space [15].

This paper presents BFO-sigmoid nonlinear control systems (BFO-SNC) and introduces some basic properties like controllability, stability and optimality for this class of systems. The previous studies developed several approaches in the control of the HIV infection [3,6–8]. Entrance the control strategies in biological system control generated the production of an increasing number of papers where therapy strategies are developed from control theory. Examples include nonlinear control based on Lyapunov methods; state drive using bang–bang control [6], adaptive control [7], optimal control, predictive control and model based feedback [8]. Various methods based on time-delay feedback control are shown in [9]. HIV-1 infection control strategy is developed based on nonlinear geometric control (feedback linearization) [10].

The influence of this paper illustrated in two parts. First, a theoretical setting is introduced for stochastic nonlinear HIV-1 infection dynamic modeling where it has applied virus concentration as a stochastic variable with Gaussian distribution. Second, BFO-sigmoid controller is designed as an automatic drug dosage management method and applied to HIV dynamics in a more biological feasible approach.

Table 1
Model parameters.

Parameter	Value	Units	Meaning
X_1	10	$mm^{-3}\,S^1$	Production rate of healthy cell
d	2×10^{-2}	S^1	Natural death of the cells
K	100	S^1	Growth rate of CTL effectors
X_1	24×10^{-2}	S^1	Natural death rate of infected cell
β	2.4×10^{-5}	$mm^3\,S^1$	Infection rate coefficient
C	2.4	S^1	Natural death rate of Virions

2. Dynamical model of the HIV-1 infection

The nonlinear state space model for illustrating the HIV-1 biological behaviors has based on the following three state variables:

X_1 *Number of healthy cells.*
X_2 *Number of infected cells.*
X_3 *Number of virions (free virus particles).*

In most cases, HIV virus affects the level of CD4+ T cells, these cells are important in helping a body against to infection. Free virus means the HIV virus is found in blood plasma. The healthy CD4+ T cells are produced from a source, such as the thymus that is represented by constant rate S and died at rate d. The coefficient β is the infection rate. The infected cells result from the infection of healthy CD4+ T cells and die at a rate μ. A free-virus particle is known as virions, so called viral load, and clear at a rate C (death rate of virus). The variable K is a rate of free virus particles product per infection CD4+ T cell. The nonlinear dynamic model to describe HIV with treatment is as follows [13]:

$$\begin{cases} \dot{X}_1 = s - dX_1(t) - (1-U_1(t))\beta X_1(t)X_3(t) \\ \dot{X}_2 = (1-U_1(t))\beta X_1(t)X_3(t) - \mu X_2(t) \\ \dot{X}_3 = (1-U_2(t))KX_2(t) - CX_3(t) \end{cases} \quad (1)$$

where the controller input $U_1(t)$ and $U_2(t)$ are numbers of expedient drugs. $U_1 = 0$ corresponds to the absence of drug and $U_1 = 1$ to a drug efficiency in preventing infection of 100%. Actually, with the available drugs, the efficiency is below 100%, and U_1 is constrained to the interval $[0, U_{\mathrm{Max}}]$ with $U_{\mathrm{Max}} < 1$.

Fig. 1 shows the transient time reply to an HIV-1 infection. The parameters used [12] are the ones of Table 1. The initial conditions correspond to a healthy person infected with a virus concentration of one copy per mm^3.

By looking at the third state dynamic in X_3, it is seen the defines a stable linear system with input X_2 and the system can reduce in model. The reduced model of HIV-1 is as follows:

$$\begin{cases} \dot{X}_1 = s - dX_1 - (1-u)\dfrac{\beta K}{C}X_1X_2 \\ \dot{X}_2 = (1-u)\dfrac{\beta K}{C}X_1X_2 - \mu X_2 \end{cases} \quad (2)$$

Since the equation for X_3 is stable and unites fast to the equilibrium, the controller does not need to control this state explicitly