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A different approach of optimal control on an HIV immunology model

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Abstract A system of ordinary differential equation, which describes the interaction of HIV and T cells in the immune system, is utilized, and optimal representing drug treatment strategies of this model are explored. Control model, in the sense of an optimal control problem shows the strategy of chemotherapy treatment setting through a dynamic treatment. In this model, the optimal control pair represents the percentage effect the chemotherapy on the $CD4^+$ T cells and virus production. An objective function characterized based on maximizing T cells and minimizing the systemic cost of the chemotherapy. The optimal control could characterize by using Pontryagin's Maximum Principle. Then by using an embedding method, we transfer the problem in to a modified problem in measure space. This transformation is an injection; one-one mapping, so the optimal pair and its image under the transformation could be identified. New problem could be solved by a linear programming problem.

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1. Introduction

AIDS-Acquired Immunity Deficiency Syndrome is the disease that has affected the whole world in the 20 years since it was first detected. It is caused by Human Immunodeficiency Virus (HIV). 34.3 million People live with HIV infection today that more than 24 million are in the developing world [1].

There is still much work to be completed in the search for an anti-HIV vaccine. Set of the chemotherapies are aimed at killing or halting the pathogen, but treatment which can boost the immune system can serve to help the body fight infection on its own [2]. The new treatments are aimed at reducing viral population and improving the immune response [1,3]. This brings new hope to the treatment of HIV infection, and we

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are exploring strategies for such treatments using optimal control techniques.

There are two kind drugs for treatment of HIV infection [1,4], the first kinds effect on the virus production and reduces the virus production, the second kinds effect on the $CD4^+T$ cells production and access $CD4^+T$ cells production [1,4]. In this paper, it is presented a control model for medical control of the chemotherapy treatment that uses the above two controls. Pathologists attempt to obtain drugs that have capability both works (access $CD4^+T$ cells production and reduce virus production). However some achievements obtained in this case, but still don't beget drugs that do this action [5].

Here our purpose was the representation control's model that control both cases and minimizing the cost of treatment.

2. The mathematical model

To begin the control procedure, it is necessary to have a model that describes the infected scenario. In [2] a simple model is given which simulates the interaction of immune system with HIV. This model is used here.

Let T; V represent the concentration of the uninfected CD_4^+T cells and free infectious virus particles respectively, and u_1, u_2 represent two different treatment strategies. As our control classes we choose measurable functions defined on a fixed interval (as treatments can't be continued for infinite time period due to hazardous side effects) satisfying $0 \leqslant a_i \leqslant u_i \leqslant b_i < 1\, i = 1{,}2$ For most of HIV chemotherapy drugs, the length of treatment is less then 500 days [6].

The state system is

$$\begin{aligned} \frac{dT}{dt} &= s_1 - \frac{s_2 V(t)}{B_1 + V(t)} - \mu T(t) - kV(t)T(t) + u_1(t)T(t) \\ \frac{dV}{dt} &= \frac{g(1-u_2(t))V(t)}{B_2 + V(t)} - cV(t)T(t) \end{aligned} \tag{1}$$

Satisfying $V(0) = V_0$, $T(0) = T$, where T represents the concentration of CD_4^+T cells, V the concentration of HIV particles. The term $s_1 - \frac{s_2 V(t)}{B_1+V(t)}$ is the source proliferation of unaffected T cells, $\mu T(t)$ is the natural loss of uninfected T cells, $kV(t)T(t)$ is loss by infection, $\frac{g(1-u_2(t))V(t)}{B_2+V(t)}$ is viral contribution to plasma and $cV(t)T(t)$ is the viral loss. Similarly, μ is death rate of T cells, k is infection rate of T cells, g is the input rate of an external virus source, c is the loss rate of virus and B_1, B_2 are half saturation constants. The controls u_1 and u_2 represent the immune boosting and viral suppressing drugs respectively. The definitions and numerical data for the parameters can be found in Table 1.

Table 1 The definitions and numerical data for the parameters [3].

Parameters and constant	Values
s_1	$2\ d^{-1}\ \mathrm{mm}^3$
s_2	$1.5\ d^{-1}\ \mathrm{mm}^3$
μ	$0.002\ d^{-1}$
k	$2.5\times10^{-2}\ d^{-1}\ \mathrm{mm}^3$
g	$30\ d^{-1}\ \mathrm{mm}^{-3}$
c	$0.007\ cd^{-1}\ \mathrm{mm}^{-3}$
b_1	14
b_2	1

The objective functional to be maximized is

$$J(u_1,u_2) = \int_0^{t_f} \left[T - \left(A_1u_1^2(t) + A_2u_2^2(t)\right)\right]dt \tag{2}$$

The first term represent the benefit of T cells and the other terms are systemic costs of the drug treatments. The positive constants A_1 and A_2 balance the size of the terms, and u_1^2, u_2^2 reflect the severity of the side effects of the drugs. When drugs such as interleukin are administered in high dose, they are toxic to the human body, which justifies the quadratic terms in the functional. Our goal is maximizing the number of T cells and minimizing the systemic cost to the body. We seek an optimal control pair u_1^*, u_2^* such that $J(u_1^*,u_2^*) = \max\{J(u_1,u_2)|\ (u_1,u_2) \in U\}$ where $U = \{(u_1,\ u_2)|\ u_i\ \textit{measurable}\ \ i = 1,\ 2\ \ t \in [0,\ t_f],\ a_i \leqslant u_i \leqslant b_i\}$ is the control set.

Is recommend that the reader see [2–4] for a more complete background and analysis of the model.

3. Application of measure theory in optimal control problem

3.1. Further analysis of the classical control problem

In the section it is followed from Rubio [7].

Consider:

(i) A real closed interval $J = [t_a, t_b]$, with $t_a < t_b$. the interior of this interval in the real line will be denoted by $J^0 = (t_a, t_b)$.
(ii) A bounded, closed, path wise–connected set A in R^n.
(iii) Two elements of A, x_a and x_b, which are to be the initial and final states of the trajectory of the controlled system.
(iv) A bounded, closed subset U of R^m.
(v) Let $\Omega = J \times A \times U$, and f_0: $\Omega \to R$, g_i: $\Omega \to R$; $i = 1, 2, \ldots, n$. a continuous function.

Consider the differential equation $\dot{x}(t) = g(t, x(t), u(t)),\quad t \in J^0$,

Where the trajectory function $x(t) \in A$, $t \in J$ is a absolutely continuous and the control function $u(t) \in U$, $t \in J$ is Lebesgue-measurable.

Let $p = [x(.), u(.)]$ Be an admissible pair, and B an open ball in R^{n+1} containing $J \times A$; we denote by $C'(B)$ the space of real-valued continuously differentiable functions on B.

Let $\phi \in C'(B)$, and define

$$\begin{aligned} &\phi^g(t,x,u) = \phi_x(t,x)^t g(t,x,u) + \phi_t(t,x). \\ &\phi_x(t,x) = \left(\frac{\partial\phi}{\partial x_1}, \frac{\partial\phi}{\partial x_2}, \ldots, \frac{\partial\phi}{\partial x_n}\right), \quad (t,x,u) \in \Omega \end{aligned} \tag{3}$$

Since $p = [x(.), u(.)]$ is an admissible pair,

$$\begin{aligned} \int_J \phi^g[t,x(t),u(t)]dt &= \int_J \{\phi_x[t,x(t)]x'(t) + \phi_t[t,x(t)]\}dt \\ &= \int_J \dot{\phi}[t,x(t)]dt \\ &= \phi(t_b,x_b) - \phi(t_a,x_a) \equiv \Delta\phi, \end{aligned} \tag{4}$$

For all $\phi \in C'(B)$.

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