Control Theory for HIV Dynamics:
Sliding Mode Control in Antiviral Drug Therapy

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Abstract. We study the dynamics of human immunodeficiency virus (HIV) infection under HIV antiviral drug therapy. In sense of control theory, the drug efficiency is treated as a controller. In this paper, we reduce nonlinear terms and reconstruct problem as a mathematical model in control system. The sliding mode control (SMC) is applied to control contact rate between CD4+ T lymphocyte (CD4+ T-cell) and HIV. A switching controller is investigated to establish asymptotic stability of the sliding surface. Finally, we illustrate simulation results of CD4+ T-cells, infected T-cells, viral load and control action.

1. Introduction
HIV is the lentivirus, cause of acquired immune deficiency syndrome (AIDS). The mechanism of HIV infection starts with contraction between HIV and CD4+ T-cells of the host. By transcription from viral RNA to DNA of the target cell and back to viral RNA, these processes are completed by reverse transcriptase enzyme and integrase enzyme. The protease enzyme produces viral proteins. New virions are constructed and leave from target cell to infect other CD4+ T-cells. The challenge of reducing new virions lead to synthetic HIV enzyme inhibitors and antiviral drug.

Recently, control theory has applied to HIV therapy. The optimal treatment of single drug (RTI) was studied by Adam et al. [1]. At the same time, the model of multidrug therapy (RTI and PI) had developed and derived the optimal control for structured treatment interruption (STI) [2]. Another approach to control dynamics of HIV is based on feedback control [3] and SMC [4]. SMC is a nonlinear control method that drives the trajectory of the system along the surface \( S(x) = 0 \). SMC is composed of 2 controllers: equilibrium controller \( (u_{eq}) \) and reaching controller \( (u_r) \). The trajectory is switched by the reaching controller, if \( S \dot{S} \neq 0 \). When \( S \dot{S} = 0 \) for some finite time, the reaching controller is vanished. Then, the equilibrium controller drives trajectory along the surface \( S(x) = 0 \). Hence SMC drives a nonlinear system without linearization. Therefore, it suits drive the nonlinear system of antiviral drug therapy.

In this paper, we apply SMC to drive the system of antiviral drug therapy. The procedure is organized as follows: in section 2, we reduce nonlinear terms of the HIV model and rewrite in the simple form. Section 3 shows the methodology of using SMC on the model and its simulation results are shown in section 4. Conclusion and some recommendations are presented in the last section.
2. Model of HIV antiviral drug therapy

The dynamical system of HIV antiviral therapy is reduced from the original model [2] by combining both kinds of the population of uninfected CD4+ T-cells, infected CD4+ T-cells and virus, denoted by \( (T) \), \( (I) \) and \( (V) \) respectively. We obtain the following model:

\[
\begin{align*}
\dot{T} &= b_T - d_T T - (1 - U)c_T V \\
\dot{I} &= (1 - U)c_T V - d_I I \\
\dot{V} &= b_V d_I I - d_V V - (1 - U)r c T V,
\end{align*}
\]

where each parameter and its unit in table 1, defined from [3].

Table 1. Symbol, meaning and unit of parameters.

| parameter | meaning | unit |
|-----------|---------|------|
| \( b_T \) | birth rate of uninfected CD4+ T-cells | cells/(mm\(^3\) day) |
| \( d_T \) | death rate of uninfected CD4+ T-cells | 1/day |
| \( U \) | efficacy of antiviral drug | percent |
| \( c \) | attach rate between CD4+ T-cells and HIV | mm\(^3\)/viriions/day |
| \( d_I \) | death rate of infected CD4+ T-cells | 1/day |
| \( b_V \) | production rate of HIV from dead infected cells | virions/cells |
| \( d_V \) | death rate of HIV | 1/day |
| \( r \) | density of virions | virions/cells |

To reduce the nonlinear terms, we set \( x_1 = T \), \( x_2 = T + I \) and \( x_3 = V + rT \). Then (1) becomes

\[
\begin{align*}
\dot{x}_1 &= b_T - d_T x_1 - (1 - U)c x_1(x_3 - r x_1) \\
\dot{x}_2 &= b_T + (d_I - d_T)x_1 - d_I x_2 \\
\dot{x}_3 &= r b_T + (r d_V - r d_I - b_V d_I)x_1 + b_V d_I x_2 - d_V x_3.
\end{align*}
\]

We will use (2) to design sliding surface and control function for simulating the population of uninfected CD4+ T-cells, infected CD4+ T-cells and viral load including control action \((1 - U)\) which represents drug failure.

3. Controllers design

In this section, we will investigate the sliding mode controller. We begin to define the sliding surface then, define the control function \( U \). Let \( \lambda \) be a positive real number and \( t^* \in [0, \infty) \). The sliding surface \( S(x) \) is given by

\[
S(x) = x_1 - \lambda(1 + x_2 + x_3),
\]

such that \( S(x) = 0 \) for all \( t \geq t^* \). To define the control function \( u \) which preserves stability of (2). For convenient, we rewrite (2) as \( \dot{x}_1 = f(x_1) - (1 - u)c x_1(x_3 - r x_1) \), \( \dot{x}_2 = g(x_1, x_2) \) and \( \dot{x}_3 = h(x_1, x_2, x_3) \). Hence \( \dot{S} = \dot{x}_1 + \lambda \dot{x}_2 + \dot{x}_3 = 0 \), if

\[
u = 1 - \left( \frac{f + \lambda(g + h)}{c x_1(x_3 - r x_1)} \right).
\]
We will show that (2) with the controller $u$ in (4) is asymptotically stable according to Lyapunov stability theory [5]. Define Lyapunov function $V : \mathbb{R}^2 \to \mathbb{R}$ by

$$V(x_2, x_3) = \frac{1}{2} \left(x_2^2 + x_3^2\right).$$

We see that

$$\dot{V} = x_2 \dot{x}_2 + x_3 \dot{x}_3$$
$$= b_I x_2 + rb_T x_3 - \lambda(1 + x_2 + x_3)(d_I x_2 + rd_v x_3) + b_v d_l x_2 x_3$$
$$-(d_T x_1 x_2 + d_l x_2^2 + rd_T x_1 x_3 + b_v d_l x_1 x_3 + d_v x_3^2).$$

Choosing the sufficient small $\lambda$, it yields $\dot{V} < 0$. This implies that the system is controlled to reach the sliding surface (3) in finite time. On the other hand, if $t \leq t^*$, we take the reaching controller with positive scale $\gamma$, $u_r = -\gamma \text{sgn}(S)$ where $\text{sgn}$ is the signum function. Claim that $\dot{S} > 0$ when $S(x) < 0$ then, we obtain $\gamma < u$. Similarly for $S(x) > 0$, $-u < \gamma$. Hence $\gamma < |u|$ is a condition that give reaching controller $u_r$. Therefore, the system is going to slide along the surface because of $S \dot{S} < 0$. Consequently, (2) converges to the sliding surface (3) in finite time $t^*$ with the following sliding mode controller

$$U = 1 - \left(\frac{f + \lambda(g + h)}{c x_1 (x_3 - r x_1)}\right) - \gamma \text{sgn}(S).$$

4. Simulation results

We use the following parameters to simulate: $b_T = 8$, $d_T = 0.008$, $c = 6 \times 10^{-4}$, $r = 1$, $d_l = 0.9$, $d_v = 15$ and $b_v = 90$ with initial condition $(T_0, I_0, V_0) = (1000, 10, 50)$. By selecting $\gamma = 0.0001$ and $\lambda = 0.00001$. In the figure 1, the population of uninfected CD4+ T-cells is decreasing from 1000 and converges on the interval (999.9968,999.9966). Both population of infected CD+4 T-cells and HIV are approaching to zero, see the figure 2 and the figure 3. The antiviral drug failure is shown in the figure 4.

![Figure 1](image-url)  

**Figure 1.** The population of uninfected CD4+ T-cells
Figure 2. The population of infected CD4+ T-cells

Figure 3. The population of HIV.

Figure 4. Control action.
5. Conclusion
The dynamical model of HIV antiviral drug therapy can be reduced nonlinear terms from three to one. The drug efficiency represents a controller. This nonlinear control problem was applied by SMC. The sliding surface with the sufficient small constant which preserves Lyapunov stability theory coupled with the sufficient small constant which give the sliding mode controller, can be controlled the system to be asymptotically stable. The demonstration in this paper found that CD4+ T-cells is decreasing very small because those parameters are the parameters of the healthy patient. However, the results will be more valid if disturbances in treatment are added to the model.

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