

Using sliding mode control in stability treatment of HIV disease

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Abstract

In this paper, a prey-predator system that called human immunodeficiency virus (HIV) models is considered, and sliding mode control (SMC) is used to stabilize this system. The basic model is a 3-dimensional nonlinear ODEs that describes the interaction of the HIV with target cell, $CD4^+$ T cell and macrophage. Lyapunove function is constructed to establish the global asymptotic stability of the uninfected and infected steady states by describing sliding surface (SS), after that by considering the derivation of SS as zero, someone can achieve the equivalent control that inbreed system stays on SS and tends to equilibrium point in infinite horizon.

Key word: HIV model, Sliding mode control, Sliding plane, Equivalent control, Lyapunove function.

1. Introduction

HIV is one of the more perilous malady in the world and the control of HIV growth requires special attention. The mathematical modeling of HIV has been approached by a few number of researchers, hence there are variety of models over the past decades ([1-4]).

Optimal treatment scheduling of HIV infection using a control theoretic approach is the subject of substantial research activity. In [5, 6, 7, 8, 9], open-loop type optimal controllers are designed using the Pontryagin's Maximum Principle (PMP). A major drawback of open-loop optimal controllers is their lack of robustness against disturbances/model uncertainties. In fact, HIV dynamics are poorly known, this leads to model inaccuracies and parameter uncertainties. Also, another source of disturbances may arise from immune system fluctuating or immune effect of a coinfection, in addition to the measurements errors and estimation errors when using an observer

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to estimate the unmeasured states. Therefore, the design of optimal treatment schedules based on open-loop optimal controller, may lead to undesired results. To overcome this problem, we have to design a feedback controller, which inherits a certain robustness to disturbances. Feedback control for HIV has been studied by [10, 11, 12].

In the last few years, model predictive control (MPC) method is developed for determining optimal treatment schedules for HIV patients [13, 14, 15]. The MPC method obtains the feedback control by solving a finite horizon optimal control problem at each time instant using the current state of the system as the initial state for the optimization and applying “the first part” of the optimal control. The study of stabilizing property of such schemes has been the subject of intensive research in recent years.

The concept of sliding mode control (SMC) introduced as a second order system by Emel’yanov [16] in the late 1960s based on the conceptions of variable structure control (VSC) in which the second order system trajectories has been driven towards a line in the state space termed as the sliding line and enforcing the trajectories to the origin.

SMC which is a particular type of control, known as variable structure control (VSC), is a powerful and robust control, and it has been extensively studied in the last three decades for many classes of linear and nonlinear systems, from theoretical concepts to industrial applications, including autonomous underwater robot [17], continuously stirred tank reactor [18], PUMA 560 robot [19], finger for a prosthetic hand [20], cable suspended loads [21] and four rotors helicopter [22].

On the other hand, many methods based on sliding mode and output feedback control schemes have been also proposed for robust stabilisation of uncertain systems [23, 24]. El-Khazali and DeCarlo [24] have designed sliding surfaces for linear time-invariant systems without disturbances using eigenvalue assignment and eigenvector techniques. Žak and Hui [23] have developed a geometric condition to guarantee the existence of a SS and the stability of the reduced order sliding motion. Most established results are based on the matched disturbances, i.e. the disturbances acts in the channels of the inputs. Even when there are uncertainties in the system with unknown structure, SMC is an appropriate control design method. When the system is in a sliding mode, the dimension of the system is reduced and it is the same the SS. This subsystem is termed the reduced-order system, and the stability of the original system depends on the stability of this subsystem.

In this paper, a novel method is proposed to design an appropriate SS and SMC for a mathematical model of HIV diseases, to enforce the system trajectories tend to the equilibrium point along the SS. This method guarantees a sliding mode motion and system stability so the HIV patient stay at a stable situation. Moreover, the proposed approach is straightforward without requiring any predication or conditions on the initials and using any iterative algorithm.

This paper is organized as follows: Section 2 briefly introduces HIV model. Section 3 addresses the proposed SMC approach. In Section 4, two examples are presented to illustrate the procedure and its validity of the proposed control design. Finally, conclusions are given in Section 5.

2. HIV basic model

In the literature, the basic model for mathematical modeling of HIV considers only three state variables (expressed as cell counts in blood per cubic millimeter) inside a whole body model. The model is mathematically described by [25]:

$$\dot{T} = s - dT + \beta TV \quad (2.1)$$

$$\dot{I} = \beta TV - \mu I \quad (2.2)$$

$$\dot{V} = kI - cV \quad (2.3)$$

where T denotes the healthy $CD4^+$ cells, I denotes the infected $CD4^+$ cells, V denotes the free virus particles. Free virus particles infect uninfected cells at a rate proportional to the product of their abundances, βTV . Infected cells produce free virus at a rate proportional to their abundance, kI . Infected cells die at a rate μI , and free virus particles are removed from the system at rate cV . The simplest assumption is that uninfected cells are produced at a constant rate, s , and die at a rate, dT .

By considering $\dot{T} = 0$, $\dot{I} = 0$, and $\dot{V} = 0$ someone can achieve the equilibrium point of the dynamical system (2.1)-(2.3) as $T = \frac{s}{d}$, $V = 0$, and $I = 0$. In the next section, we define an appropriate transformation such that change the equilibrium point from $(\frac{s}{d}, 0, 0)$ to the origin, then define sliding surface (SS) that cross from the origin and equivalent control which enforce motion stay on the SS.

3. Sliding surface design

Consider the following nonlinear time varying system

$$\dot{x}(t) = f(t, x) + B(t, x) u(t) + \rho(t, x), \quad (3.1)$$

where $x \in \mathbb{R}^n$ is the state, $u \in \mathbb{R}^m$ is the control input and $\rho(t, x) \in \mathbb{R}^n$ is the disturbance. It is assumed that $1 \leq m < n$.

Let $s : \mathbb{R}^n \rightarrow \mathbb{R}^m$ is a function where define the following hyper plane,

$$S = \{x \in \mathbb{R}^n : s(x) = 0\}. \quad (3.2)$$

Definition 3.1 Suppose there exists a finite time t_s such that the solution of (3.1) represented by $x(t)$, satisfies

$$s(x(t)) = 0 \quad \text{for all } t \geq t_s,$$

then an ideal sliding motion is said to be taking place for all $t \geq t_s$. Time t_s is termed the reaching time.

Assumed that at time t_s , the system trajectories (3.1) lie on the surface (3.2) and an ideal sliding motion takes place. This fact can be mathematically expressed as $s(t) = 0$ and $\dot{s}(t) = G\dot{x}(t) = 0$ for all $t \geq t_s$, where $G = \frac{\partial s}{\partial x}$. Substituting for $\dot{x}(t)$ from (3.1) gives

$$G\dot{x}(t) = G f(t, x) + G B(t) u(t) + G \rho(t, x) = 0 \quad \text{for all } t > t_s. \quad (3.3)$$

Suppose the matrix G is such that the square matrix $GB(t)$ is nonsingular.

Definition 3.2 The equivalent control associated with the nominal system (3.1) is defined to be the unique solution to the algebraic equation (3.3), namely

$$u_{eq} = -(GB(t))^{-1} G (f(t, x) + \rho(t, x)). \quad (3.4)$$

The ideal sliding motion is then given by substituting the expression (3.4) into equation (3.1) which results in a free motion, i.e. a motion independent of the control action and given by

$$\dot{x}(t) = (I_n - B(t)(GB(t))^{-1}G) f(t, x) + \rho(t, x) \quad \text{for all } t > t_s \text{ and } Gx(t_s) = 0. \quad (3.5)$$

In the sequel, the control system of HIV is considered as follow:

$$\dot{T} = s - d T + \beta T V (1 - U) \quad (3.6)$$

$$\dot{I} = \beta T V - \mu I - \beta T V U \quad (3.7)$$

$$\dot{V} = k I - c V, \quad (3.8)$$

where $0 \leq U(t) \leq 1$. The most drug efficiency is in the case $U = 1$ which means $CD4^+$ T cells are not infected by viral load anymore. At the other side, $U = 0$ is the case which the drug does not change the disease progression. Then, the regular form of HIV control system is as:

$$\dot{T} = s - d T + \beta T V (1 - U) \quad (3.9)$$

$$\dot{T} + \dot{I} = s - d T - \mu I \quad (3.10)$$

$$\dot{V} = k I - c V. \quad (3.11)$$

Now, by assuming $x_1 = \frac{s}{d} - T$, $x_2 = I + T - \frac{s}{d}$ and $x_3 = V$, (3.9)-(3.11) changes to:

$$\dot{x}_1 = -d x_1 + \beta \left(\frac{s}{d} - x_1\right) x_3 (1 - U) \quad (3.12)$$

$$\dot{x}_2 = d x_1 - \mu (x_2 + x_1) \quad (3.13)$$

$$\dot{x}_3 = k (x_2 + x_1) - c x_3. \quad (3.14)$$

For the dynamical system (3.12)-(3.14) define the SS as follow:

$$S(x) = x_1 + \alpha((d - \mu)x_2 + kx_3) = 0, \quad (3.15)$$

or

$$x_1 = -\alpha((d - \mu)x_2 + kx_3), \quad (3.16)$$

where α is an adequate positive number, and by considering $\dot{S}(x) = 0$, the equivalent control achieves as

$$U_{eq} = \frac{1}{\beta \left(\frac{s}{d} - x_1\right) x_3} \left(-d x_1 + \beta \left(\frac{s}{d} - x_1\right) x_3 + \alpha \left((d - \mu)(d x_1 - \mu (x_2 + x_1)) + k (x_2 + x_1) - c x_3 \right) \right). \quad (3.17)$$

Thus the control action of system is described as

$$U = \begin{cases} U_r = -L \text{sign}(S(t)) & 0 \leq t < t_s \\ U_{eq} & t \geq t_s, \end{cases} \quad (3.18)$$

where L is an adequate positive number and U_r is denoted for reaching control (the control imposed to system before reaching SS). We have the following stability theorem:

Theorem 1. The dynamical system (3.12)-(3.14) is asymptotically stable (by Lyapunove sense) if the SS define as (3.16), control function define as (3.18) and $\alpha, L \in \mathbb{R}^+$ be chosen as an adequate positive number.

Proof. Define the Lyapunov function $V(x_2, x_3)$ from R^2 to R by:

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

Now,

$$\dot{V}(x_2, x_3) = x_2 \dot{x}_2 + x_3 \dot{x}_3 = x_2 (d x_1 - \mu (x_2 + x_1)) + x_3 (k (x_2 + x_1) - c x_3) = -\mu x_2^2 - c x_3^2 + x_1((d - \mu)x_2 + kx_3) + kx_2x_3,$$

by SS equation (3.16) and since the trajectories function x_1, x_2 , and x_3 are bounded, one can choose α such that

$$\dot{V}(x_2, x_3) = -\mu x_2^2 - c x_3^2 - \frac{1}{\alpha} x_1^2 + k x_2 x_3 < 0.$$

Choosing U as (3.18), when $t \leq t_s$, by imposing reaching control U_r , we have $S(x) \dot{S}(x) < 0$, so trajectories tend to the SS. Now, on the SS (3.16) ($t \geq t_s$), using the U_{eq} as (3.17), tends to $V(x) \dot{V}(x) < 0$, and this fact guarantee the asymptotically stable (by the sense of Lyapunove) of the system (3.12)-(3.14) on the SS (3.16). ■

In the next section, we illustrate two numerical examples to demonstrate the applicability of our method.

4. Numerical example

Example 1. Consider the following data for an illness [26]:

$$c = 2, d = 0.007, k = 40.67, s = 7, \mu = 0.0999, \beta = 0.00000042163.$$

Thus, the SS defines as follow:

$$x_1 = -\alpha((0.007 - 0.0999)x_2 + 40.67x_3),$$

and, U_{eq} is

$$U_{eq} = \frac{1}{0.00000042163(1000-x_1)x_3} \left(-0.007 x_1 + 0.00000042163 (1000 - x_1)x_3 + \alpha \left((0.007 - 0.0999)(0.007 x_1 - 0.0999 (x_2 + x_1)) + 40.67 (x_2 + x_1) - 2x_3 \right) \right) - L \operatorname{sign}(S).$$

We solve this problem with $\alpha = 0.001$, where the initial point on SS is taken as (1004, 50, 10). Figure 1 shows the action of the equivalent control, and the behavior of the states using this SMC.

One can compare these trajectories with results that achieve by using discretization method in [27] and can see that our results are more accurate than them.

Example 2. The same dynamical system as Example 1, with the following data from [28]:

$$c = 2, d = 0.00136, k = 50, s = 0.272, \mu = 0.33, \beta = 0.00027.$$

Thus, the SS defines as follow:

$$x_1 = -\alpha((0.00136 - 0.33)x_2 + 50x_3),$$

and, u_{eq} is

$$U_{eq} = \frac{1}{0.00027(200 - x_1)x_3} (-0.00136x_1 + 0.00027(200 - x_1)x_3 + \alpha((0.00136 - 0.33)(0.00136x_1 - 0.33(x_2 + x_1)) + 50(x_2 + x_1) - 2x_3)) - L \text{sign}(S).$$

We solve this problem with $\alpha = 0.0005$, where the initial point on SS is taken as $(201.2484, 10, 50)$. Figure 2 shows the action of the equivalent control, and the behavior of the states using this SMC.

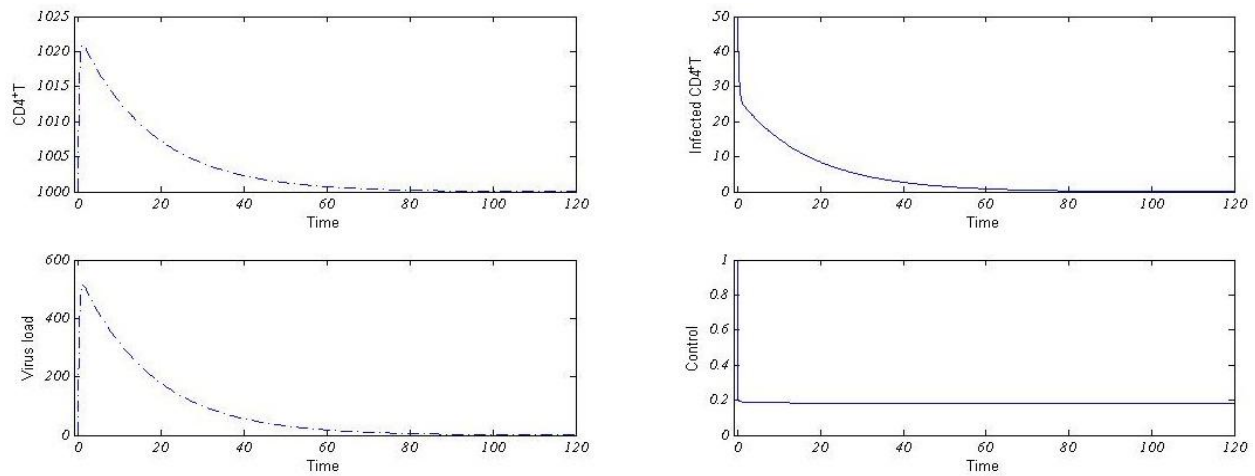


Figure 1. Trajectories and control function of Example 1.

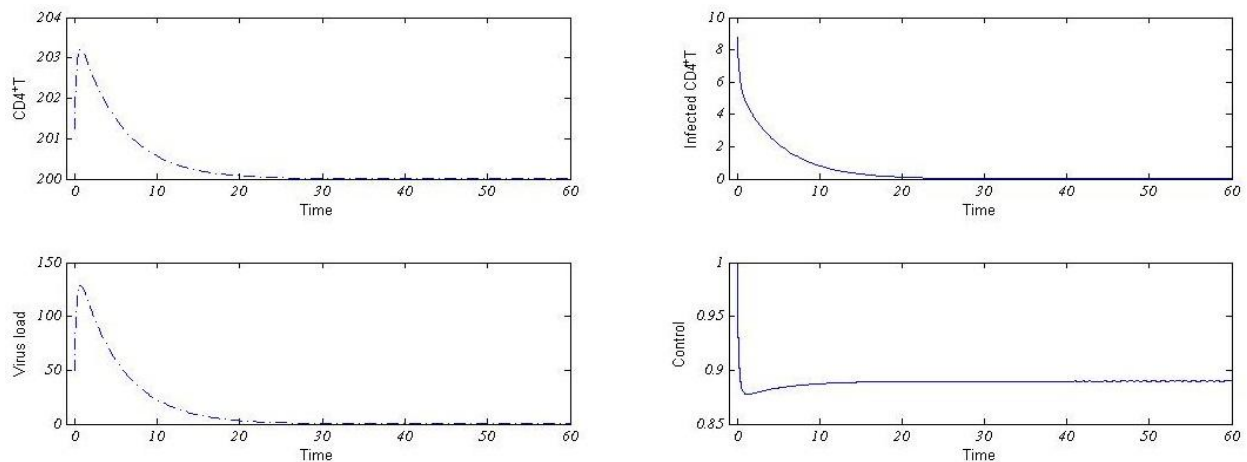


Figure 2. Trajectories and control function of Example 2.

5. Conclusion

A novel strategy for treating HIV is proposed by designing of sliding plane, and equivalent control for asymptotically stabilizing (by the Lyapunove sense). By choosing an appropriate control (called equivalent control), it is shown that the Lyapunove stability condition $\dot{V} < 0$ is satisfied on sliding surface $S(x, t) = 0$. The easy and straight forward method implemented in this paper, provides a frame for further research instabilizing treatment of diseases.

6. References

- [1] Noy-Meir, I., (1975). Stability of grazing systems: an application of predator-prey graphs. *J. Ecol.*, 63 (2), 459-481.
- [2] Perelson, A. S., Nelson, P. W., (1999). Mathematical analysis of HIV-1 dynamics in vivo. *SIAM Review*, 41, 3-44.
- [3] Nowak, M. A., May, R. M., (2000). *Virus dynamics: Mathematical principles of immunology and virology*. New York: Oxford University Press.
- [4] Covert, D., Kirschner, D., (2000). Revisiting early models of the host-pathogen interactions in HIV infection. *Comments Theoretical Biology*, 5, 383-411.
- [5] Kwon, H. D., (2007). Optimal treatment strategies derived from a HIV model with drug-resistant mutants, *Appl. Math. Comput.*, 188, 1193-1204.
- [6] Ledzewicz, U., Schattler, H., (2003). On optimal controls for a general mathematical model for chemotherapy of HIV, in: *Proceedings of American Control Conference*, Denver, 3454-3459.
- [7] Adams, B.M., Banks, H.T., Kwon, H.D., Tran, H.T., (2004). Dynamic multidrug therapies for HIV: optimal and STI control approaches, *Math. Biosci. Eng.*, 1, 223-241.
- [8] Adams, B.M., Banks, H.T., Davidian, M., Kwon, H.D., Tran, H.T., Wynne, S.N., Rosenberg, E.S., (2005). HIV dynamics: Modeling, data analysis, and optimal treatment protocols, *J. Comput. Appl. Math.*, 184, 10-49.
- [9] Culshaw, R.V., Ruan, S., Spiteri, R.J., (2004). Optimal HIV treatment by maximizing immune response, *J. Math. Biol.*, 48 (5), 545-562.
- [10] Alvarez-Ramirez, J., Meraz, M., Velasco-Hernandez, J.X., (2000). Feedback control of the chemotherapy of HIV, *Int. J. Bifur. Chaos*, 10 (9), 2207-2219.
- [11] Banks, H.T., Kwon, H.D., Toivanen, J.A., Tran, H.T., (2006). A state-dependent Riccati equation-based estimator approach for HIV feedback control, *Optimal Control Appl. Methods*, 27, 93-121.
- [12] Brandt, M.E., Chen, G., (2001). Feedback control of a biodynamical model of HIV-1, *IEEE Trans. Biom. Engrg.*, 48, 754-759.

- [13] Elaiw, A.M., Kiss, K., Caetano, M.A.L., (2005). Stabilization of HIV/AIDS model by receding horizon control, *J. Appl. Math. Comput.*, 18 (1–2), 95–112.
- [14] Jeffery, A.M., (2006). A control theoretic approach to HIV/AIDS drug dosage design and timing the initiation of therapy, PhD thesis, department of electrical, electronic and computer engineering, University of Pretoria.
- [15] Zurakowski, R., Teel, A.R., (2006). A model predictive control based scheduling method for HIV therapy, *J. Theoret. Biol.*, 238, 368–382.
- [16] Emel'yanov, S.V., (1967). *Variable Structure Control Systems*, Nauka, Moscow (in Russian).
- [17] Chatchanayuenyong, T., Parnichkun, M., (2006). Neural network based-time optimal sliding mode control for an autonomous underwater robot, *Mechatronics*, 16, 471-478.
- [18] Koshkouei, A.J., (2007). Sliding-mode control with passivity for a continuously stirred tank reactor, *Proc. IMechE*, 221, 749-755.
- [19] Mozaryn, J., Kurek, J.E., (2002). Design of decoupled sliding mode control for the PUMA 560 robot manipulator, *Proc. the Third International Workshop on Robot Motion and Control*, Warsaw, Poland, 45–50.
- [20] Yagiz, N., Arslan, Y. Z., Hacıoglu, Y., (2007). Sliding mode control of a finger for a prosthetic hand, *Vibration and control*, 13(6), 733-749.
- [21] Nowacka-Leverton, A., Bartoszewicz, A., (2008). IAU optimal sliding mode control of cable suspended loads, *CEAI*, 10, 3-10
- [22] Bouadi, H., Tadjine, M., (2007). Nonlinear observer design and sliding mode control of four rotors helicopter, *PWASET*, 25, 225-229.
- [23] Žak, S. H., Hui, S., (1993). On variable structure output feedback controllers for uncertain dynamic systems, *IEEE Trans. Automatic Control*, 38, pp. 1509-1512.
- [24] El-Khazali, R., DeCarlo, R., (1995). Output feedback variable structure control design, *Automatica*, 31, 805–816.
- [25] Landi, A., Mazzoldi, A., Andreoni, Ch., Bianchi, M., Cavallini, A., Laurino, M., Riccoti, L., Iuliano, R., Matteoli, B., Ceccherini-Nelli, L., (2008). Virus Modelling and control of HIV dynamics, *Computer Method and Programs in Biomedicine*, 89, 162-168.
- [26] Xiaohua Xia (2003). Brief Paper Estimation of HIV/AIDS parameters, *Automatica*, 39, 1983-1988.
- [27] SHiraziyan, M., Farahi, M. H., (2010). Optimal Control Strategy for a Fully Determined HIV Model, *Intelligent Control and Automation*, 1, 15-19.
- [28] Tuckwell, H. C., Wan, F. Y. M., (2004). On the behavior of solutions in viral dynamical models, *BioSystems*, 73, 157–161.