Feedback Linearization Control Strategy applied to a Mathematical HIV/AIDS Model

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Abstract: - This paper presents a novel feedback linearization control of nonlinear systems with uncertainties for the tracking and almost disturbance decoupling and develops an Acquired Immunity Deficiency Syndrome control strategy. The main contribution of this study is to construct a controller, under appropriate conditions, such that the resulting closed-loop system is valid for any initial condition and bounded tracking signal with the following characteristics: input-to-state stability with respect to disturbance inputs and almost disturbance decoupling. In order to demonstrate the applicability, this paper develops the feedback linearization design for the control of a mathematical HIV/AIDS model system to improve the viral load. The performances of drug treatment based on our proposed novel nonlinear geometric feedback control approach are better than some existing approaches, i.e., the healthy CD+ T cell population can be kept in original cells per cubic millimeter and the viral load is reduced only after more short days of drug treatment.

Key-Words: - Almost Disturbance Decoupling; Feedback Linearization Approach; Acquired Immunity Deficiency Syndrome; Human Immunodeficiency Virus

1 Introduction

Acquired Immunity Deficiency Syndrome (AIDS) is the disease that has controlled the human world about 30 years since it was first identified in 1981. Infection with the human immunodeficiency virus causes a continuously decay in the number of CD4-T – lymphocytes that eventually drives to the lethal AIDS. Once HIV invades the human body, the immune system is immediately turned on and tries to destroy it. The information of invasion is transferred to CD4+T cells. The CD4 plays a role of a protein protector in the surface of the T cell and the organ is responsible for maturing these cells after they move from the bone marrow where they are initially created. The protected surface of CD4+T owns a protein that can bind foreign substances such as HIV.

The HIV is in want of a host in order to reproduce and the above mentioned protein marker provides aegis. The HIV virus is a kind of retrovirus, the RNA of the HIV virus is transferred into DNA inside the CD4+T cell. Therein, when infected CD4+T cells multiply themselves to fight this pathogen, they produce more virus. Mathematical analysis of HIV infection is actively investigated since the middle the 90's. A great number of researches have attempted to develop mathematical models in order to the describe infection dynamics [31, 40]. These models are represented by a set of relatively complex nonlinear differential equations which model the immune system and the long term interaction with the virus. The new therapeutic strategies are aimed at the purpose of reducing viral load and improving the immune dynamic response. This creates new hope to the therapeutic strategies of HIV infection, and we are exploring strategies using nonlinear control techniques. One of them is based on the famous state feedback approach, but fortuneless it appears not very explored [6, 15]. As a matter of fact, feedback control of HIV-1 is difficult by the inherent nonlinear nature of the involved mechanisms [15].

Many approaches to design feedback controllers for nonlinear models have been proposed including feedback linearization, variable structure control (sliding mode control), backstepping, regulation control, nonlinear H^{∞} control, internal model principle and H^{∞} adaptive fuzzy control. [29] has proposed the use of variable structure control to deal with nonlinear system. However, chattering behavior that caused by discontinuous switching and imperfect implementation that can drive the system into unstable regions is inevitable for variable structure control schemes. Backstepping has proven to be a

powerful tool of synthesizing controllers for nonlinear systems. However, a disadvantage of this approach is an explosion in the complexity which a result of repeated differentiations of nonlinear functions [46, 50]. An alternative approach is to utilize the scheme of the output regulation control [24] in which the outputs are assumed to be excited by an exosystem. However, the nonlinear regulation approach requires the solution of difficult partial-differential algebraic equations. Another difficulty is that the exosystem states need to be switched to describe changes in the output and this creates transient tracking errors [41]. In general, nonlinear H^{∞} control requires the solution of Hamilton-Jacobi equation, which is a difficult nonlinear partial-differential equation [2, 25, 47]. Only for some particular nonlinear systems it is possible to derive a closed-form solution [23]. The control approach that is based on the internal model principle converts the tracking problem into a non-linear output regulation problem. This approach depends on solving a first-order partial-differential equation of the center manifold [24]. For some special nonlinear systems and desired trajectories, the asymptotic solutions of this equation have been developed using ordinary differential equations [16, 21]. Recently, H^{∞} adaptive fuzzy control has been proposed to systematically deal with nonlinear systems [9]. The drawback with H^{∞} adaptive fuzzy control is that the complex parameter update law makes this approach impractical in real-world situations. During the past decade significant progress has been made in researching control approaches for nonlinear systems based on the feedback linearization theory [22, 29, 38, 45]. Moreover, feedback linearization approach has been applied successfully to many real control systems. These include the control of an electromagnetic suspension system [26], pendulum system [10], spacecraft [44], electrohydraulic servosystem [1], car-pole system [3] and a bank-to-turn missile system [32].

Feedback linearization approach is one of the most significant nonlinear methods developed during the last few decades [22]. This approach may result in linearization which is valid for larger practical operating regions of the control system, as opposed to a local Jacobian linearization about an operating point [11]. Neural network feedback linearization (NNFBL) was first investigated in [7] and extensively addressed in [8]. NNFBL has been applied to many practical systems. [13] obtains the best published result in a cancer chemotherapy problem using NNFBL. [34] proposed a hybrid controller using NNFBL to control a levitated object a magnetic levitation system. In the field of aerospace engineering, neural networks have solved successfully the aircraft control problem. A cerebellar model articulation controller (CMAC) is addressed by [33] for command to life-of-sight missile guidance law design. The CMAC control is comprised of a CMAC and a compensation controller. The CMAC controller is used to imitate a feedback linearization law and the compensation controller is utilized to compensate the difference between these two controllers. NNFBL can be applied to complicated pharmacogenomics systems to find adequate drug dosage regimens [11] and extensively addressed in [12] and [14]. Continuous stirred tank reactor (CSTR) is widely utilized in chemical industry and can be simplified as an affine nonlinear system. [17] applied NNFBL to design a predictive functional control of CSTR and achieve good control performance.

It is difficult to obtain completely accurate mathematical models for many practical control systems. Thus, there are inevitable uncertainties in their models. Therefore, the design of a robust controller that deals with the uncertainties of a control system is of considerable interest. This study presents a systematic analysis and a simple design scheme that guarantees the globally asymptotical stability of a feedback-controlled uncertain system and that achieves output tracking and almost disturbance decoupling performances for a class of nonlinear control systems with uncertainties.

The almost disturbance decoupling problem, i.e., that is the design of a controller that attenuates the effect of the disturbance on the output terminal to an arbitrary degree of accuracy, was originally developed for linear and nonlinear control systems by [35] and [49] respectively. The problem has attracted considerable attention and many significant results have been developed for both linear and non-linear control systems [36, 42, 48]. The almost disturbance decoupling problem of non-linear single-input single-output (SISO) systems was investigated in [35] by using a state feedback approach and solved in terms of sufficient conditions for systems with nonlinearities that are not globally Lipschitz and disturbances bring linear but possibly actually bring multiples of nonlinearities. The resulting state feedback control is constructed following a singular perturbation approach.

The aim of [5] was to propose a strategy of control

of the HIV-1 infection via the original nonlinear geometric feedback control on a fundamental mathematical predator-prey model. Its result shows that the viral load is reduced after 720 days of drug treatment. An existing infectious model describing the interaction of HIV virus and the immune system of the human body is applied to determine the nonlinear optimal control for administering anti-viral medication therapies to fight HIV infection via a competitive Gauss–Seidel like implicit difference method [28]. The virus population in presence of treatment approaches to zero after 50 days of drug treatment. Another optimal control using an iterative method with a Runge–Kutta fourth order scheme that represents how to control drug treatment strategies of this model is examined [27]. However, the virus load in presence of treatment does not reach to zero and the healthy CD+ T cell population increase almost linearly up to 45 days and levels off after that time. On the contrary, based on our proposed approach in this study, the healthy CD+ T cell population can be kept in 1000 cells per cubic millimeter and the viral load is reduced only after 11 days of drug treatment.

We will propose a new method to guarantee that the closed-loop system is stable and the almost disturbance decoupling performance is achieved. In order to exploit the significant applicability, this paper also has successfully derived the tracking controller with almost disturbance decoupling for a biomedical HIV/AIDS model system. This paper is organized as follows. In section 2, we provide the nonlinear control design method. Section 3 is devoted to an application of HIV/AIDS model system. Some numerical results are also presented in section 3. After all, some concluding remarks are given in section 4.

2 Problem Formulation and Main Result

The following nonlinear uncertain control system with disturbances is considered.

$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\\ .\\ .\\ \dot{x}_n\end{bmatrix}=\begin{bmatrix}f_1(x_1,x_2,..,x_n)\\ f_2(x_1,x_2,..,x_n)\\ .\\ .\\ f_n(x_1,x_2,..,x_n)\end{bmatrix}+\begin{bmatrix}g_1(x_1,x_2,..,x_n)\\ g_2(x_1,x_2,..,x_n)\\ .\\ .\\ g_n(x_1,x_2,..,x_n)\end{bmatrix}u+\begin{bmatrix}\Delta f_1\\ \Delta f_2\\ .\\ .\\ \Delta f_n\end{bmatrix}+\sum_{i=1}^{p}q_i^*\theta_{id} \tag{2.1a}$$

$$y(t)=h(x_1,x_2,..,x_n) \tag{2.1b}$$

that is

$$\dot{X}(t)=f(X(t))+g(X(t))u+\Delta f+\sum_{i=1}^{p}q_i^*\theta_{id}$$

$$y(t)=h(X(t))$$

where $X(t):=\left[x_1(t)\ x_2(t)\cdots x_n(t)\right]^T\in\Re^n$ is the state vector, $u\in\Re^1$ is the input, $y\in\Re^1$ is the output, $\theta_d:=\left[\theta_{1d}(t)\ \theta_{2d}(t)\cdots\theta_{pd}(t)\right]^T$ is a bounded time-varying disturbance vector and $\Delta f:=\left[\Delta f_1\ \Delta f_2\cdots\Delta f_n\right]\in\Re^n$ is unknown nonlinear function representing uncertainty such as modelling error. Let Δf be described as

$$\Delta f=\sum_{i=1}^{p}q_i^*\theta_{iu}$$

where $\theta_u:=\left[\theta_{1u}(t)\ \theta_{2u}(t)\cdots\theta_{pu}(t)\right]^T$ is a bounded time-varying vector. $f, g, q_1^*,\cdots,q_p^*$ are smooth vector fields on $\Re^n$, and $h(X(t))\in\Re^1$ is a smooth function. The nominal system is then defined as follows:

$$\dot{X}(t)=f(X(t))+g(X(t))u \tag{2.2a}$$

$$y(t)=h(X(t)) \tag{2.2b}$$

The nominal system (2.2) consists of relative degree r [19], i.e., there exists a positive integer $1\le r<\infty$ such that

$$L_gL_f^kh(X(t))=0,\ k<r-1 \tag{2.3}$$

$$L_gL_f^{r-1}h(X(t))\neq 0 \tag{2.4}$$

for all $X\in\Re^n$ and $t\in[0,\infty)$, where the operator L is the Lie derivative [22]. The desired output trajectory $y_d(t)$ and its first r derivatives are all uniformly bounded and

$$\left\|\left[y_d(t),\ y_d^{(1)}(t),\cdots,y_d^{(r)}(t)\right]\right\|\le B_d \tag{2.5}$$

where B_d is some positive constant.

It has been shown [22] that the mapping

$$\phi:\Re^n\to\Re^n \tag{2.6}$$

defined as

$$\phi_i(X(t)):=\xi_i(t)=L_f^{i-1}h(X(t)),i=1,2,\cdots,r \tag{2.7}$$

$$\phi_k(X(t)) := \eta_k(t), k = r+1, r+2, \cdots, n \tag{2.8}$$

and satisfying

$$L_g \phi_k(X(t)) = 0, k = r+1, r+2, \cdots, n \tag{2.9}$$

is a diffeomorphism onto image. For the sake of convenience, define the trajectory error to be

$$e_i(t) := \xi_i(t) - y_d^{(i-1)}(t), i = 1, 2, \cdots, r \tag{2.10}$$

$$e(t) := \left[e_1(t)\ e_2(t) \cdots e_r(t)\right]^T \in \Re^r \tag{2.11}$$

the trajectory error multiplied with some adjustable positive constant ε

$$\overline{e_i}(t) := \varepsilon^{i-1} e_i(t), i = 1, 2, \cdots, r \tag{2.12}$$

$$\bar{e}(t) := \left[\overline{e_1}(t)\ \overline{e_2}(t) \cdots \overline{e_r}(t)\right]^T \in \Re^r \tag{2.13}$$

and

$$\xi(t) := \left[\xi_1(t)\xi_2(t) \cdots \xi_r(t)\right]^T \in \Re^r \tag{2.14a}$$

$$\eta(t) := \left[\eta_{r+1}(t)\eta_{r+2}(t) \cdots \eta_n(t)\right]^T \in \Re^{n-r} \tag{2.14b}$$

$$\begin{aligned} q(\xi(t), \eta(t)) &:= \left[L_f \varphi_{r+1}(t)\ L_f \varphi_{r+2}(t) \cdots L_f \varphi_n(t)\right]^T \\ &:= \left[q_{r+1} \quad q_{r+2} \quad \cdots \quad q_n\right]^T \end{aligned} \tag{2.14c}$$

Define a phase-variable canonical matrix A_c to be

$$A_c := \begin{bmatrix} 0 & 1 & 0 & \cdots & 0 \\ 0 & 0 & 1 & \cdots & 0 \\ & \vdots & & & \vdots \\ 0 & 0 & 0 & \cdots & 1 \\ -\alpha_1 & -\alpha_2 & -\alpha_3 & \cdots & -\alpha_r \end{bmatrix}_{r \times r} \tag{2.15}$$

where $\alpha_1, \alpha_2, \cdots, \alpha_r$ are any chosen parameters such that A_c is Hurwitz and the vector B to be

$$B := \left[0 \quad 0 \quad \cdots \quad 0 \quad 1\right]^T_{r \times 1} \tag{2.16}$$

Let P be the positive definite solution of the following Lyapunov equation

$$A_c^T P + P A_c = -I \tag{2.17}$$

$$\lambda_{\max} := \text{the maximum eigenvalue of } P \tag{2.18}$$

$$\lambda_{\min} := \text{ the minimum eigenvalue of } P \tag{2.19}$$

Assumption 1.

For all $t \geq 0$, $\eta \in \Re^{n-r}$ and $\xi \in \Re^r$, there exists a positive constant L such that the following inequality holds

$$\left\| q_{22}(\eta, \bar{e}) - q_{22}(\eta, 0) \right\| \leq L\left(\left\|\bar{e}\right\|\right) \tag{2.20}$$

where $q_{22}(\eta, \bar{e}) := q(\xi, \eta)$.

For the sake of convenience, define

$$d := L_g L_f^{r-1} h(X(t)) \tag{2.21a}$$

$$c := L_f^r h(X(t)) \tag{2.21b}$$

and

$$\bar{\bar{e}} = \alpha_1 \overline{e_1} + \alpha_2 \overline{e_2} + \cdots + \alpha_r \overline{e_r} \tag{2.22}$$

Definition 1. [29]

Consider the system $\dot{x} = f(t, x, \theta)$, where $f : [0, \infty) \times \Re^n \times \Re^n \to \Re^n$ is piecewise continuous in t and locally Lipschitz in x and θ. This system is said to be input-to-state stable if there exists a class KL function β, a class K function γ and positive constants k_1 and k_2 such that for any initial state $x(t_0)$ with $\left\|x(t_0)\right\| < k_1$ and any bounded input $\theta(t)$ with $\sup_{t \geq t_0} \left\|\theta(t)\right\| < k_2$, the state exists and satisfies

$$\left\|x(t)\right\| \leq \beta\left(\left\|x(t_0)\right\|, t - t_0\right) + \gamma\left(\sup_{t_0 \leq \tau \leq t} \left\|\theta(\tau)\right\|\right) \tag{2.23a}$$

for all . $t \geq t_0 \geq 0$. Now we formulate the tracking problem with almost disturbance decoupling as follows:

Definition 2. [36]

The tracking problem with almost disturbance decoupling is said to be globally solvable by the state feedback controller u for the transformed-error system by a global diffeomorphism (2.6), if the controller u enjoys the following properties.

<i>It is input-to-state stable with respect to disturbance inputs.

<ii>For any initial value $\bar{x}_{e0} := \left[\bar{e}(t_0)\ \eta(t_0)\right]^T$, for any $t \geq t_0$ and for any $t_0 \geq 0$.

$$\left|y(t) - y_d(t)\right| \leq \beta_{11}\left(\left\|x(t_0)\right\|, t - t_0\right) + \frac{1}{\sqrt{\beta_{22}}} \beta_{33}\left(\sup_{t_0 \leq \tau \leq t} \left\|\theta(\tau)\right\|\right)$$

(2.23b)

and

$$\int_{t_0}^{t}\left[y(\tau)-y_d(\tau)\right]^2 d\tau \le \frac{1}{\beta_{44}}\left[\beta_{55}\left(\left\|\bar{x}_{e0}\right\|\right)+\int_{t_0}^{t}\beta_{33}\left(\left\|\theta(\tau)\right\|^2\right)d\tau\right] \tag{2.23c}$$

where β_{22}, β_{44} are some positive constants, β_{33}, β_{55} are class K functions and β_{11} is a class KL function.

Theorem 1.

Suppose that there exists a continuously differentiable function $V_0:\Re^{n-r}\to\Re^{+}$ such that the following three inequalities hold for all $\eta\in\Re^{n-r}$.

$$\text{(a) } k_1\|\eta\|^2 \le V_0(\eta) \le k_2\|\eta\|^2,\ k_1,k_2>0 \tag{2.24a}$$

$$\text{(b) } (\nabla_\eta V_0)^T q_{22}(\eta,0) \le -k_3\|\eta\|^2,\ k_3>0 \tag{2.24b}$$

$$\text{(c) } \left\|\nabla_\eta V_0\right\| \le k_4\|\eta\|, k_4>0, \tag{2.24c}$$

then the tracking problem with almost disturbance decoupling is globally solvable by the controller defined by

$$\begin{aligned} u=&\left[L_g L_f^{r-1}h(X(t))\right]^{-1}\left\{-L_f^r h(X)+y_d^{(r)}\right.\\ &-\varepsilon^{-r}\alpha_1\left[L_f^0 h(X)-y_d\right]-\varepsilon^{1-r}\alpha_2\left[L_f^1 h(X)-y_d^{(1)}\right]\\ &\left.-\cdots-\varepsilon^{-1}\alpha_r\left[L_f^{r-1}h(X)-y_d^{(r-1)}\right]\right\}\end{aligned} \tag{2.25}$$

Moreover, the influence of disturbances on the L_2 norm of the tracking error can be arbitrarily attenuated by increasing the following adjustable parameter $N_2>1$.

$$N_2=\min\left\{k_{11},k_{22}\right\} \tag{2.26a}$$

$$k_{11}:=a_d-\left(2a_d\left\|\varphi_{\bar{\xi}}\right\|\|P\|\right)^2-0.25 \tag{2.26b}$$

$$k_{22}:=\mu k_3-\left(\mu L k_4\right)^2-\left(\mu L k_4\left\|\varphi_\eta\right\|\right)^2 \tag{2.26c}$$

$$\varphi_{\bar{\xi}}(\varepsilon):=\begin{bmatrix}\varepsilon\dfrac{\partial}{\partial X}hq_1^* & \cdots & \varepsilon\dfrac{\partial}{\partial X}hq_p^*\\ \vdots & & \vdots\\ \varepsilon^r\dfrac{\partial}{\partial X}L_f^{r-1}hq_1^* & \cdots & \varepsilon^r\dfrac{\partial}{\partial X}L_f^{r-1}hq_q^*\end{bmatrix} \tag{2.26d}$$

$$\varphi_\eta(\varepsilon):=\begin{bmatrix}\dfrac{\partial}{\partial X}\varphi_{r+1}q_1^* & \cdots & \dfrac{\partial}{\partial X}\varphi_{r+1}q_p^*\\ \vdots & & \vdots\\ \dfrac{\partial}{\partial X}\varphi_n q_1^* & \cdots & \dfrac{\partial}{\partial X}\varphi_n q_q^*\end{bmatrix} \tag{2.26e}$$

$$N_1:=\frac{1}{2}\sup_{t_0\le\tau\le t}\left\|\left(\theta_d+\theta_u\right)(\tau)\right\|^2 \tag{2.26f}$$

where a_d is strictly positive constants to be adjustable and $\mu(\varepsilon):\Re^{+}\to\Re^{+}$ is any continuous function satisfying

$$\lim_{\varepsilon\to 0}\mu(\varepsilon)=0 \text{ and } \lim_{\varepsilon\to 0}\frac{\varepsilon}{\mu(\varepsilon)}=0 \tag{2.26g}$$

where $\alpha\ge 2$ and μ are adjustable positive constants. Moreover, the output tracking error of system (2.1) is exponentially attracted into a sphere $B_{\underline{r}}$, $\underline{r}=\sqrt{N_1/N_2}$, with an exponential rate of convergence

$$\frac{-N_2}{\omega_2}+\frac{N_1}{\omega_2\underline{r}^2}\equiv-\alpha^* \tag{2.26h}$$

Where $\omega_2:=\min\left\{\varepsilon a_d\lambda_{\max},\mu k_2\right\}$ (2.26i)

Proof.

Applying the coordinate transformation (2.6) yields

$$\begin{aligned}\dot{\xi}_1(t)&=\frac{\partial\varphi_1}{\partial X}\frac{dX}{dt}=\frac{\partial h(X(t))}{\partial X}\left[f+g\cdot u+\Delta f+\sum_{i=1}^{p}q_i^*\theta_{id}\right]\\ &=L_f^1h(X(t))+L_gL_f^0h(X(t))u+\frac{\partial h(X)}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{iu}\\ &\quad+\frac{\partial h(X)}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{id}\\ &=L_f^1h(X(t))+\frac{\partial h(X)}{\partial X}\sum_{i=1}^{p}q_i^*\left(\theta_{id}+\theta_{iu}\right)\\ &=\xi_2(t)+\frac{\partial h(X)}{\partial X}\sum_{i=1}^{p}q_i^*\left(\theta_{id}+\theta_{iu}\right)\end{aligned} \tag{2.27}$$

⋮

$$\dot{\xi}_{r-1}(t)=\frac{\partial\varphi_{r-1}}{\partial X}\frac{dX}{dt}=\frac{\partial L_f^{r-2}h(X(t))}{\partial X}\left[f+g\cdot u+\Delta f+\sum_{i=1}^{p}q_i^*\theta_{id}\right]$$
$$=L_f^{r-1}h(X(t))+L_gL_f^{r-2}h(X(t))u+\frac{\partial L_f^{r-2}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{iu}$$
$$+\frac{\partial L_f^{r-2}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{id}$$
$$=L_f^{r-1}h(X(t))+\frac{\partial L_f^{r-2}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\left(\theta_{id}+\theta_{iu}\right)$$
$$=\xi_r(t)+\frac{\partial L_f^{r-2}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\left(\theta_{id}+\theta_{iu}\right) \quad (2.28)$$

$$\dot{\xi}_r(t)=\frac{\partial\varphi_r}{\partial X}\frac{dX}{dt}$$
$$=\frac{\partial L_f^{r-1}h(X(t))}{\partial X}\left[f+g\cdot u+\Delta f+\sum_{i=1}^{p}q_i^*\theta_{id}\right]$$
$$=L_f^{r}h(X(t))+L_gL_f^{r-1}h(X(t))u$$
$$+\frac{\partial L_f^{r-1}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{iu}+\frac{\partial L_f^{r-1}h(X(t))}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{id}$$
$$=L_f^{r}h(X)+L_gL_f^{r-1}h(X)u$$
$$+\sum_{i=1}^{p}\frac{\partial L_f^{r-1}h(X(t))}{\partial X}q_i^*\left(\theta_{id}+\theta_{iu}\right) \quad (2.29)$$

$$\dot{\eta}_k(t)=\frac{\partial\varphi_k(X)}{\partial X}\frac{dX}{dt}$$
$$=\frac{\partial\varphi_k(X)}{\partial X}\left[f+g\cdot u+\Delta f+\sum_{i=1}^{p}q_i^*\theta_{id}\right]$$
$$=\frac{\partial\varphi_k(X)}{\partial X}f+\frac{\partial\varphi_k(X)}{\partial X}gu$$
$$+\frac{\partial\varphi_k(X)}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{iu}+\frac{\partial\varphi_k(X)}{\partial X}\sum_{i=1}^{p}q_i^*\theta_{id} \quad (2.30)$$
$$=L_f\varphi_k(X)+\frac{\partial\varphi_k(X)}{\partial X}\sum_{i=1}^{p}q_i^*\left(\theta_{id}+\theta_{iu}\right)$$
$$=L_f\varphi_k+\sum_{i=1}^{p}\frac{\partial\varphi_k(X)}{\partial X}q_i^*\left(\theta_{id}+\theta_{iu}\right)$$
$$k=r+1,r+2,\cdots,n$$

Since

$$c(\xi(t),\eta(t)):=L_f^{r}h(X(t)) \quad (2.31)$$

$$d(\xi(t),\eta(t)):=L_gL_f^{r-1}h(X(t)) \quad (2.32)$$

$$q_k(\xi(t),\eta(t))=L_f\varphi_k(X),\quad k=r+1,r+2,\cdots,n \quad (2.33)$$

The dynamic equations of system (2.1) in the new co-ordinates are shown as follows.

$$\dot{\xi}_i(t)=\xi_{i+1}(t)+\sum_{i=1}^{p}\frac{\partial}{\partial X}L_f^{i-1}hq_i^*\left(\theta_{id}+\theta_{iu}\right)$$
$$i=1,2,\cdots,r-1 \quad (2.34)$$

$$\dot{\xi}_r(t)=c(\xi(t),\eta(t))+d(\xi(t),\eta(t))u$$
$$+\sum_{i=1}^{p}\frac{\partial}{\partial X}L_f^{r-1}hq_i^*\left(\theta_{id}+\theta_{iu}\right) \quad (2.35)$$

$$\dot{\eta}_k(t)=q_k(\xi(t),\eta(t))+\sum_{i=1}^{p}\frac{\partial}{\partial X}\varphi_k(X)q_i^*\left(\theta_{id}+\theta_{iu}\right)$$
$$k=r+1,\cdots,n \quad (2.36)$$

$$y(t)=\xi_1(t) \quad (2.37)$$

Define

$$v:=y_d^{(r)}-2\varepsilon^{-r}\alpha_1\left\lfloor L_f^0h(X)-y_d\right\rfloor-2\varepsilon^{1-r}\alpha_2$$
$$\left[L_f^1h(X)-y_d^{(1)}\right]-\cdots-2\varepsilon^{-1}\alpha_r\left[L_f^{r-1}h(X)-y_d^{(r-1)}\right]$$
$$-mB^g\bar{e} \quad (2.38)$$

According to equations (2.7)(2.10)(2.31) and (2.32), the tracking controller can be rewritten as

$$u=d^{-1}\left[-c+v\right] \quad (2.39)$$

Substituting equation (2.39) into (2.35), the dynamic equations of system (2.1) can be shown as follows.

$$\begin{bmatrix}\dot{\xi}_1(t)\\ \dot{\xi}_2(t)\\ \vdots\\ \dot{\xi}_{r-1}(t)\\ \dot{\xi}_r(t)\end{bmatrix}=\begin{bmatrix}0&1&0&\cdots&0\\ 0&0&1&0&\cdots&0\\ &\vdots&&&&\vdots\\ 0&0&0&\cdots&1\\ 0&0&0&\cdots&0\end{bmatrix}\begin{bmatrix}\xi_1(t)\\ \xi_2(t)\\ \vdots\\ \xi_{r-1}(t)\\ \xi_r(t)\end{bmatrix}+\begin{bmatrix}0\\0\\\vdots\\0\\1\end{bmatrix}v$$
$$+\begin{bmatrix}+\sum_{i=1}^{p}\frac{\partial}{\partial X}hq_i^*\left(\theta_{id}+\theta_{iu}\right)\\ +\sum_{i=1}^{p}\frac{\partial}{\partial X}L_f^1hq_i^*\left(\theta_{id}+\theta_{iu}\right)\\ \vdots\\ +\sum_{i=1}^{p}\frac{\partial}{\partial X}L_f^{r-1}hq_i^*\left(\theta_{id}+\theta_{iu}\right)\end{bmatrix} \quad (2.40)$$

$$\begin{bmatrix}\dot{\eta}_{r+1}(t)\\ \dot{\eta}_{r+2}(t)\\ \vdots\\ \dot{\eta}_{n-1}(t)\\ \dot{\eta}_n(t)\end{bmatrix}=\begin{bmatrix}q_{r+1}(t)\\ q_{r+2}(t)\\ \vdots\\ q_{n-1}(t)\\ q_n(t)\end{bmatrix}+\begin{bmatrix}\sum_{i=1}^{p}\frac{\partial}{\partial X}\varphi_{r+1}q_i^*(\theta_{id}+\theta_{iu})\\ \sum_{i=1}^{p}\frac{\partial}{\partial X}\varphi_{r+2}q_i^*(\theta_{id}+\theta_{iu})\\ \vdots\\ \sum_{i=1}^{p}\frac{\partial}{\partial X}\varphi_{n-1}q_i^*(\theta_{id}+\theta_{iu})\\ \sum_{i=1}^{p}\frac{\partial}{\partial X}\varphi_n q_i^*(\theta_{id}+\theta_{iu})\end{bmatrix} \quad (2.41)$$

$$y=\begin{bmatrix}1 & 0 & \cdots & 0 & 0\end{bmatrix}_{r\times 1}\begin{bmatrix}\xi_1(t)\\ \xi_2(t)\\ \vdots\\ \xi_{r-1}(t)\\ \xi_r(t)\end{bmatrix}_{r\times 1}=\xi_1(t) \quad (2.42)$$

Combining equations (2.10) (2.12) (2.15) and (2.38), it can be easily verified that equations (2.40)-(2.42) can be transformed into the following form.

$$\begin{aligned}\dot{\eta}(t)&=q(\xi(t),\eta(t))+\varphi_\eta(\theta_d+\theta_u)\\ &:=q_{22}(\eta(t),\bar{e})+\varphi_\eta(\theta_d+\theta_u)\end{aligned} \quad (2.43a)$$

$$\varepsilon\dot{\bar{e}}(t)=A_c\bar{e}+\phi_\xi(\theta_d+\theta_u) \quad (2.43b)$$

$$y(t)=\xi_1(t) \quad (2.44)$$

We consider $V(\bar{e},\eta)$ defined by a weighted sum of $V_0(\eta)$ and $V_1(\bar{e})$,

$$V(\bar{e},\eta):=V_1(\bar{e})+\mu V_0(\eta), \quad (2.45)$$

as a composite Lyapunov function of the subsystems (2.43a) and (2.43b) [30, 34], where $V_1(\bar{e})$ satisfies

$$V_1(\bar{e}):=\varepsilon a_d\bar{e}^T P\bar{e}\,. \quad (2.46)$$

Where a_d and μ are strictly positive constants to be adjustable. In view of (2.20)-(2.22) (2.24) and (2.25), the derivative of $V(\bar{e},\eta)$ along the trajectories of (2.43a) and (2.43b) is given by

$$\dot{V}_1=a_d\left(\varepsilon\dot{\bar{e}}\right)^T P\bar{e}+a_d\bar{e}^T P\left(\varepsilon\dot{\bar{e}}\right)$$

$$=a_d\left\{A_c\bar{e}+\phi_\xi(\theta_d+\theta_u)\right\}^T P\bar{e}+a_d\bar{e}^T P\left\{A_c\bar{e}+\phi_\xi(\theta_d+\theta_u)\right\}$$

$$=a_d\left\{\bar{e}^T\left(A_c^T P+PA_c\right)\bar{e}\right\}+a_d\left\{2(\theta_d+\theta_u)^T\phi_\xi^T P\bar{e}\right\}$$

$$\le -a_d\|\bar{e}\|^2+2a_d\|(\theta_d+\theta_u)\|\,\|\phi_\xi\|\,\|P\|\,\|\bar{e}\|$$

$$\le -a_d\|\bar{e}\|^2+2a_d\|(\theta_d+\theta_u)\|\,\|\phi_\xi\|\,\|P\|\,\|\bar{e}\|$$

$$\le -a_d\|\bar{e}\|^2+\left(2a_d\|\phi_\xi\|\,\|P\|\right)^2\|\bar{e}\|^2+\frac{1}{4}\|(\theta_d+\theta_u)\|^2,$$

that is

$$\dot{V}_1\le -\|\bar{e}\|^2\left[a_d-\left(2a_d\|\phi_\xi\|\,\|P\|\right)^2\right]+\frac{1}{4}\|(\theta_d+\theta_u)\|^2$$

$$\mu\dot{V}_0=\mu\left(\frac{\partial V_0}{\partial\eta}\right)^T\dot{\eta}$$

$$=\mu\left(\frac{\partial V_0}{\partial\eta}\right)^T\left[q_{22}(\eta,\bar{e})+\varphi_\eta\theta-q_{22}(\eta,0)+q_{22}(\eta,0)\right]$$

$$\le\mu\left\|\frac{\partial V_0}{\partial\eta}\right\|\|q_{22}(\eta,\bar{e})-q_{22}(\eta,0)\|+\mu\left(\frac{\partial V_0}{\partial\eta}\right)^T q_{22}(\eta,0)$$

$$+\mu\left\|\frac{\partial V_0}{\partial\eta}\right\|\|\varphi_\eta\|\,\|(\theta_d+\theta_u)\|$$

$$\le\mu k_4L\|\eta\|\,\|\bar{e}\|-\mu k_3\|\eta\|^2+\mu k_4\|\phi_\eta\|\,\|\eta\|\,\|(\theta_d+\theta_u)\|$$

$$\le\left(\mu k_4L\right)^2\|\eta\|^2+\frac{1}{4}\|\bar{e}\|^2-\mu k_3\|\eta\|^2+\left(\mu k_4\|\varphi_\eta\|\right)^2\|\eta\|^2$$

$$+\frac{1}{4}\|(\theta_d+\theta_u)\|^2,$$

that is

$$\mu\dot{V}_0\le\|\eta\|^2\left[-\mu k_3+\left(\mu k_4L\right)^2+\left(\mu k_4\|\varphi_\eta\|\right)^2\right]+\frac{1}{4}\|\bar{e}\|^2$$

$$+\frac{1}{4}\|(\theta_d+\theta_u)\|^2.$$

Therefore

$$\dot{V}=\dot{V}_1+\mu\dot{V}_0\le-\|\bar{e}\|^2\left[a_d-\left(2a_d\|\varphi_\xi\|\,\|P\|\right)^2-\frac{1}{4}\right]-\cdots$$

$$\|\eta\|^2\left[\mu k_3-\left(\mu k_4L\right)^2-\left(\mu k_4\|\varphi_\eta\|\right)^2\right]+\frac{1}{2}\|(\theta_d+\theta_u)\|^2$$

$$\le-k_{11}\|\bar{e}\|^2-k_{22}\|\eta\|^2+\frac{1}{2}\|(\theta_d+\theta_u)\|^2$$

$$\le-N_2\left(\|\bar{e}\|^2+\|\eta\|^2\right)+\frac{1}{2}\|(\theta_d+\theta_u)\|^2$$

$$:=-N_2\|y_{total}\|^2+\frac{1}{2}\|(\theta_d+\theta_u)\|^2 \quad (2.47)$$

where

$$\|y_{total}\|^2 := \|\bar{e}\|^2 + \|\eta\|^2. \tag{2.48}$$

By virtue of Theorem 5.2 of [29], equation (2.47) implies the input-to-state stability for the closed-loop system. Furthermore, it is easy to see that

$$\omega_1\left(\|\bar{e}\|^2 + \|\eta\|\right) \le V \le \omega_2\left(\|\bar{e}\|^2 + \|\eta\|^2\right)$$

that is

$$\omega_1\|y_{total}\|^2 \le V \le \omega_2\|y_{total}\|^2 \tag{2.49}$$

where $\omega_1 := \min\{\varepsilon a_d \lambda_{\min}, k_1\}$ and $\omega_2 := \min\{\varepsilon a_d \lambda_{\max}, \mu k_2\}$. Equations (2.47) and (2.49) yield that

$$\begin{aligned}\dot{V} &\le -\frac{N_2}{\omega_2}V + \frac{1}{2}\|(\theta_d + \theta_u)\|^2 \\ &\le -\frac{N_2}{\omega_2}V + \frac{1}{2}\left(\sup_{t_0\le\tau\le t}\|(\theta_d + \theta_u)(\tau)\|\right)^2\end{aligned} \tag{2.50}$$

Hence,

$$V(t) \le V(t_0)e^{-\frac{N_2}{\omega_2}(t-t_0)} + \frac{\omega_2}{2N_2}\left(\sup_{t_0\le\tau\le t}\|(\theta_d + \theta_u)(\tau)\|\right)^2 \tag{2.51}$$

which implies

$$\begin{aligned}|e_1(t)| \le{}& \sqrt{\frac{V(t_0)}{\varepsilon a_d \lambda_{\min}}}e^{-\frac{N_2}{2\omega_2}(t-t_0)} \\ &+ \sqrt{\frac{\omega_2}{2N_2\varepsilon a_d \lambda_{\min}}}\left(\sup_{t_0\le\tau\le t}\|(\theta_d + \theta_u)(\tau)\|\right)\end{aligned} \tag{2.52}$$

So that equation (2.23b) is proved. From equation (2.47), we get

$$\dot{V} \le -N_2\left(\|\bar{e}\|^2 + \|\eta\|^2\right) + \frac{1}{2}\|(\theta_d + \theta_u)\|^2 \tag{2.53}$$

which easily implies

$$\int_{t_0}^{t}(y(\tau) - y_d(\tau))^2 d\tau \le \frac{V(t_0)}{N_2} + \frac{1}{2N_2}\int_{t_0}^{t}\|(\theta_d + \theta_u)(\tau)\|^2 d\tau$$

(2.54)

so that equation (2.23c) is satisfied and then the tracking problem with almost disturbance decoupling is globally solved. Finally, we will prove that the sphere $B_{\underline{r}}$ is a global attractor for the output tracking error of system (2.1). From equations (2.26f) and (2.53), we get

$$\dot{L} \le -N_2\left(\|y_{total}\|^2\right) + N_1 \tag{2.55}$$

For $\|y_{total}\| > \underline{r}$, we have $\dot{L} < 0$. Hence any sphere defined by

$$B_{\underline{r}} \equiv \left\{\begin{bmatrix}\bar{e}\\ \eta\end{bmatrix} : \|\bar{e}\|^2 + \|\eta\|^2 \le \underline{r}\right\} \tag{2.56}$$

is a global final attractor for the tracking error system of the nonlinear control systems (2.1). Furthermore, for $y \notin B_{\underline{r}}$, we have

$$\begin{aligned}\frac{\dot{L}}{L} &\le \frac{-N_2\|y_{total}\|^2 + N_1}{L} \le \frac{-N_2\|y_{total}\|^2 + N_1}{\omega_2\|y_{total}\|^2} \\ &\le \frac{-N_2}{\omega_2} + \frac{N_1}{\omega_2\|y_{total}\|^2} \le \frac{-N_2}{\omega_2} + \frac{N_1}{\omega_2\underline{r}^2} \equiv -\alpha^*\end{aligned} \tag{2.57}$$

that is, $\dot{L} \le -\alpha^* L$.

According to the comparison theorem [37], we get

$$L(y_{total}(t)) \le L(y_{total}(t_0))\exp\left[-\alpha^*(t-t_0)\right]$$

Therefore,

$$\begin{aligned}\omega_1\|y_{total}\|^2 &\le L(y_{total}(t)) \\ &\le L(y_{total}(t_0))\exp\left[-\alpha^*(t-t_0)\right] \\ &\le \omega_2\|y_{total}(t_0)\|^2\exp\left[-\alpha^*(t-t_0)\right]\end{aligned} \tag{2.58}$$

Consequently, we get

$$\|y_{total}\| \le \sqrt{\frac{\omega_2}{\omega_1}}\|y_{total}(t_0)\|\exp\left[-\frac{1}{2}\alpha^*(t-t_0)\right]$$

that is, the convergence rate toward the sphere $B_{\underline{r}}$ is equal to $\alpha^*/2$. This completes our proof.

According to the previous theorem and discussion, an efficient and programmable algorithm for deriving the feedback linearization control is proposed as follows.

1) Step 1: Calculate the vector relative degree r of the given control system.
2) Step 2: Choose the diffeomorphism φ such that the assumption 1 is satisfied.
3) Step 3: Adjust some parameters α such that the matrices A_c are Hurwitz and calculate the positive definite matrices P of the Lyapunov equations (2.17) by some software package, such as MATLAB.
4) Step 4: Based on the famous Lyapunov approach, design a Lyapunov function to solve the conditions (2.24a) to (2.24c). If the relative degree is equal to the system dimension n, then this step should be omitted and immediately go to the next step.
5) Step 5: Appropriately tune the parameters μ, ε such that $N_2 > 1$ and go to the next step. Otherwise, we go to the step 3 and repeat the overall designing procedures.
6) Step 6: According to the equation (2.25), the desired feedback linearization controller can be constructed such that the uniform ultimate bounded stability is guaranteed. That is, the system dynamics enter a neighborhood of zero state and remain within it thereafter.

3 Feedback Linearization Control Strategy for a Mathematical HIV/AIDS System

The researching data appeared to show that the virus concentration fell exponentially for a short period after a patient was treated on a potent antiretroviral drug [40]. Thus, the following dynamic model was proposed

$$\frac{dV}{dt} = P - eV \tag{3.1}$$

where P is an unknown function denoting the rate of virus production, e is the clearance rate constant, and V is the free virus load. Virus is created by productively infected cells. Here we have made an assumption that on average each productively infected cell creates N virions during its lifetime. Since the average lifetime of a productively infected cell is $1/\delta$, the average rate of virion production is

TABLE. 1 HIV/AIDS MODEL PARAMETERS

Symbol	Description	Typical values and units
b	Infectivity rate of free virus particles	4.1×10^{-6} mm^{-3} per day
d	Death rate of healthy T cells	0.009 per day
e	Death rate of virus	0.6 per day
k	Rate of virions produced per infected T cell	75 counts cell^{-1}
s	The constant rate of production of healthy T cells	9 mm^{-3} per day
t	Time	days
w	Death rate of infected T cells	0.3 per day
p	Maximum proliferation rate	0.03 per day
T_{max}	Maximum T cell population density	1500 mm^{-3} per day

$N\delta$ and the dynamic equation (3.1) can be written as

$$\frac{dV}{dt} = N\delta T_{pi} - eV \equiv kT_{pi} - eV \tag{3.2}$$

where T_{pi} denotes the productively infected CD4+ cells and $k \equiv N\delta$.

HIV attacks cells that carry the CD4+ cell surface protein as well as coreceptors. The major target of HIV infection is the CD4+ T cell. After becoming attacked, such cells can create new HIV virus virions. Thus, to model HIV infection we address a population of healthy target cells, T, and productively infected cells, T_{pi}. The population dynamics of CD4+ T cells in humans is not well understood. Nevertheless, a reasonable and acceptable model for this population of cells is

$$\frac{dT}{dt} = s + pT\left(1 - \frac{T}{T_{\max}}\right) - dT \tag{3.3}$$

where T denotes the healthy CD4+ cells, d is the death rate per T cell and s represents the rate at which new T cells are created from sources within the body. T cells can also be produced by proliferation of existing T cells. We describe the proliferation by a logistic function in which p is the maximum proliferation rate and $T_{\max}$ is the T cell population density at which proliferation stops. While there is no direct research that T cell proliferation is

described by the logistic equation, there are recommendations that the proliferat on rate is density-dependent with the rate of proliferation slowing as the T cell count gets high [20, 43].

The simplest and most common approach of modeling infection is to augment (3.3) with a "mass-action" term in which the rate of infection is given by bTV, with b being the infection rate constant. This mass-action term is reasonable, since virus must meet T cells in order to attack them. When V and T behaviors can be regarded as independent, we can make an assumption that the probability of virus encountering a T cell at low concentrations is proportional to the product of their concentrations. Thus, we can assume that infection occurs by virus, causing the loss of healthy T cells at rate $-bTV$ and the generation of infected T cells at rate bTV. The models that we focus on are one-compartment models in which V and T are identified with the virus concentration and T cell counts measured in blood. In fact, infection is not restricted to blood and the majority of CD4+ T cells are in lymphoid tissue. However, the available research recommends that the concentration of virus and CD4+ T cells measured in blood is a acceptable consideration of their concentrations throughout the body [18, 39], as one would expect for a system in equilibrium state. With the mass-action infection term, the rates of change of healthy cells and productively infected cells are

$$\frac{dT}{dt} = s + pT\left(1-\frac{T}{T_{\max}}\right) - dT - bTV \tag{3.4}$$

$$\frac{dT_{pi}}{dt} = bTV - wT_{pi} \tag{3.5}$$

Finally, we can summary the HIV/AIDS mathematical model [15] to be described as

$$\frac{dT}{dt} = s + pT\left(1-\frac{T}{T_{\max}}\right) - dT - bTV \tag{3.6}$$

$$\frac{dT_{pi}}{dt} = bTV - wT_{pi} + u(t) \tag{3.7}$$

$$\frac{dV}{dt} = kT_{pi} - eV \tag{3.8}$$

where the control $u(t)$ represents the pharmacological action (dose) of antiretroviral drug applied to the system. The system parameters used in the HIV/AIDS model are listed in Table 3.1. These same parameters have been used in [5].

The goal of the control strategy $u(t)$ is to keep the system around the equilibrium point where the viral load has a value near to zero. The HIV/AIDS model can be written in the general form

$$\dot{x}(t) = f(x) + g(x)u(t), \tag{3.9a}$$

$$y(t) = h(x) = x_2(t). \tag{3.9b}$$

Where

$$x = \begin{bmatrix} T \\ T_{pi} \\ V \end{bmatrix} = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix},$$

$$f(x) = \begin{bmatrix} s - dx_1 - bx_1x_3 + px_1\left(1-\frac{x_1}{T_{\max}}\right) \\ bx_1x_3 - wx_2 \\ kx_2 - ex_3 \end{bmatrix}, \quad g(x) = \begin{bmatrix} 0 \\ 1 \\ 0 \end{bmatrix}.$$

Now we will show how to explicitly design the control strategy $u(t)$ of antiretroviral drugs. Let's arbitrarily choose $\alpha_1 = 0.005$, $A_c = -0.005$, $P = 100$ and $\lambda^*_{\min} = \lambda^*_{\max} = 100$. From equation (2.25), we obtain the desired tracking controllers

$$u = d^{-1}\left[-c + v\right] = -\left(bx_1x_3 - wx_2\right) + \left\lfloor -\varepsilon^{-1} \times \alpha_1 \times \left(x_2\right) \right\rfloor. \tag{3.10}$$

It can be verified that the relative conditions of Theorem 1 are satisfied with $\varepsilon = 0.0025$, $B_d = 0$, $k_1 = k_2 = 1$, $k_4 = 2$, $k_3 = 1$, $L = \sqrt{2}$ and $\mu = \sqrt{\varepsilon}$. Hence the tracking controllers will steer the output tracking errors of the closed-loop system, starting from any initial value, to be asymptotically attenuated to zero by virtue of Theorem 1.

Firstly, we will observe the evolution of the infection in an individual without the treatment strategy of antiretroviral drugs (i.e. $u(t) = 0$). The software simulations are evaluated by the commercial software MATLAB/SIMULINK 2016b® and the initial conditions and the parameters of the HIV/AIDS model are chosen as follows: $s = 9$, $d = 0.009$, $b = 0.0000041$, $w = 0.3$, $e = 0.6$, $k = 7$, $T(0) = 1000\,\text{cells/mm}^3$, $T_{pi}(0) = 0$, $V(0) = 0.3$ (i.e. 300 copies/ml).

The simulation results are shown in Fig.s 3.1-3.2. When the HIV virus invades the human body, it kills the healthy CD4+ T cells and consequently the amount of healthy CD4+ T cells decreases rapidly in the absence of treatment (Fig. 3.1). At the acute

infection stage, the healthy CD4+T cell drops from the usual 1000 cells per cubic millimeter to less than 400 cells after about 120days. The free virus and the infected CD+ T cells do not stop to proliferate and so the abundances increase (Fig. 3.1). Subsequently, if we introduce the treatment, the situation will change. The simulation results are shown in Fig.s 3.2. The amount of healthy CD4+ T cells decreases, but it will be kept in acceptable level when control chemotherapy is used. The action of chemotherapy begins to appear and makes the growth of healthy CD4+ T cells and the diminishing of the free virus and the infected CD+ T cells. The feedback linearization control input (Dose) $u(t)$ for drug administration is represented through Fig. 3.3 by the control (3.3).

It is obvious to see that the amount of infected CD+ T cells is kept to be zero cells per cubic millimeter all the time when our proposed control treatment is used. But, the result of [5] show that the amount of infected CD+ T cells decreases to zero after about 120 days. Moreover, the viral load approaches to zero after about 11 days with the action of our control treatment. However, the results of [5] and [28] show that the amount of the viral load decreases to zero after 720 and 50 days of drug treatment, respectively. Another optimal control using an iterative method with a Runge–Kutta fourth order scheme that represents how to control drug treatment strategies of this model is examined [27]. However, the virus load in presence of treatment does not reach to zero and the healthy CD+ T cell population increase almost linearly up to 45 days and levels off after that time.

It is worthy to note that our proposed nonlinear feedback linearization control needs the quantification of all the state variables for HIV/AIDS system. All the state variables including the healthy CD4+ cells, the infected CD4+ cells and the free virus load will be measured in the clinic. We will begin clinical study of the feedback linearization controller (3.3) of antiretroviral drugs based on the utilization of electronic taste chip system, Harvard PHD 2000 programmable research pump and computer with Java program shown in Fig. 3.4-3.6. Electrically automatic apparatus for providing antiretroviral drugs could be constructed based on the quantification of the immune variables. The desired feedback linearization control algorithm will be programmed in Java language chosen for its multiplatform portability and proto-typing. The Java program will be divided into five blocks, which include states-loader, states-logger, controller, pump-logger, and pump-loader. States-loader and states-logger handle the communication between electronic taste chip system and computer, while pump-logger and pump-loader control the micro-pump device. The dose input (3.3) is calculated by the controller block and communicated to the infusion micro-pump using a 9600 baud rate, eight data bits, two stop bits, and zero parity with the utilization of a universal serial bus port connector. Finally, the pump-loader opens the communication port to the micro-pump and constructs the communication protocol, while pump-logger transfers the dose input *u(t)* to the micro-pump.

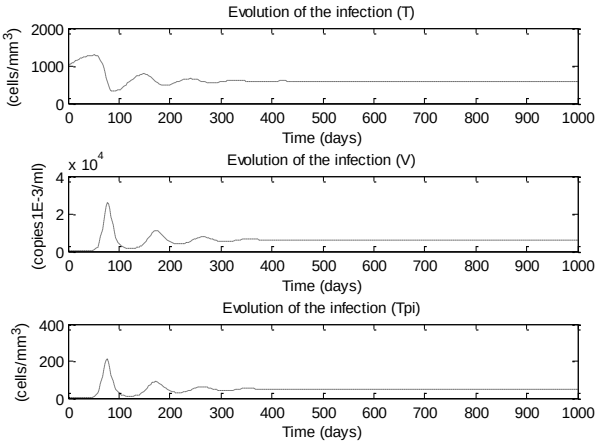

Fig. 3.1 Evolutions of healthy CD4+ T cells, the free virus and infected CD+ T cells without control.

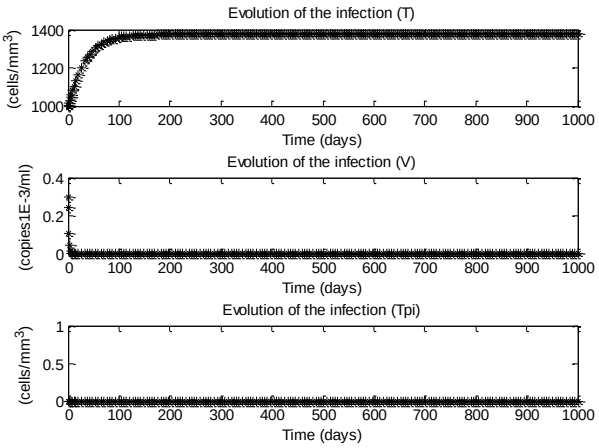

Fig. 3.2. Evolutions of healthy CD4+ T cells, the free virus and infected CD+ T cells with control.

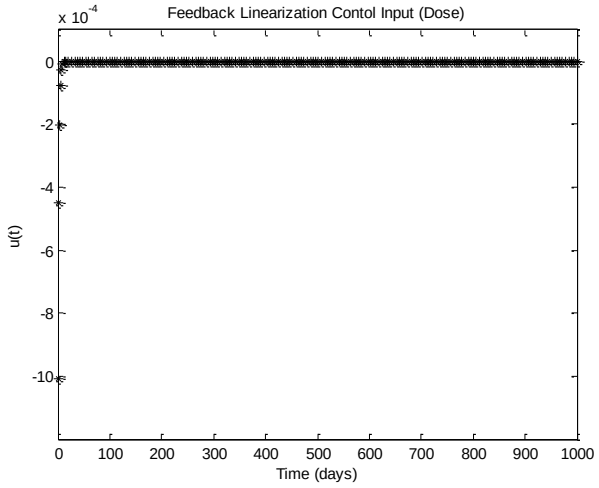

Fig. 3.3 Feedback linearization control input. (Dose)

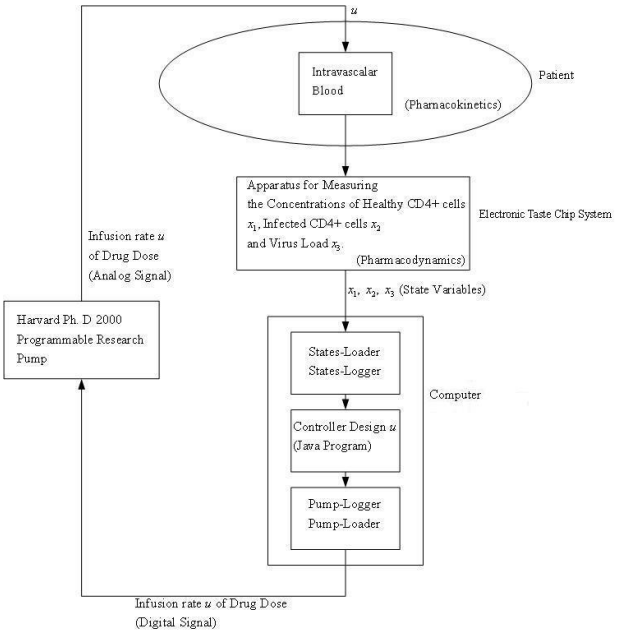

Fig. 3.4 Block diagram for the clinical study of the feedback linearization controller (3.3) of antiretroviral drugs.

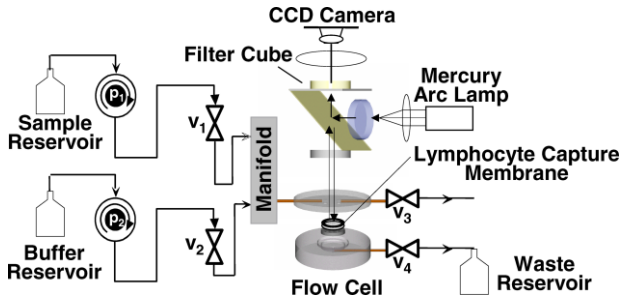

Fig. 3.5 Electronic Taste Chip System. (Bentwich, 2005).

Fig. 3.6 Harvard PHD 22/2000 Programmable research Pump.

4 Conclusion Remarks

A novel feedback linearization control to globally solve the tracking problem with almost disturbance decoupling for nonlinear system with uncertainties and develop an Acquired Immunity Deficiency Syndrome control strategy has been proposed. A discussion and a practical application of feedback linearization of nonlinear control systems using a parameterized coordinate transformation have been presented. A practical treatment of HIV/AIDS model system has been used to demonstrate the applicability of the proposed feedback linearization approach and composite Lyapunov approach. Simulation results have been presented to show that the proposed methodology can be successfully applied to feedback linearization problem and is able to achieve the desired tracking and almost disturbance decoupling performances of the controlled system. The technique of controlling the HIV/AIDS based on the feedback linearization control has demonstrated to be effective in the simulations.

In comparison with some existing approaches, the performances of drug treatment based on our proposed novel nonlinear geometric feedback control approach are better, i.e., the healthy CD+ T cell population can be kept in original cells per cubic millimeter and the viral load is reduced only after more short days of drug treatment. All the state variables of HIV/AIDS model system can be measured using the electronic taste chip system, programmable research micro-pump and computer with Java program in the clinical study. Finally, we believe that the novel methodology can be used for solving many control problems in biomedical areas in future.

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