Robust $H_\infty$ Controller for Bilinear System to Minimize HIV Concentration in Blood Plasma

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Abstract. Human Immunodeficiency Virus (HIV) is a type of virus which attacks CD$^4^+$ T cells. Insufficient numbers of CD$^4^+$ T cells will affect the performance of immunity systems so that someone become more risky to have AIDS or other diseases. HIV phenomenon is modelled as nonlinear system with disturbance, but there is no exact method to solve problems that related with analyzing nonlinear systems with control treatment. Thus, the nonlinear system is approximated into a bilinear system by using Carleman Bilinearization method. A robust $H_\infty$ controller is designed as a control input to accommodate the disturbances in the dynamic system. Generally, the treatment for HIV is merely to obstruct the replication process. Therefore, the robust control input is described as the chemotherapy of hypothetical drugs which aimed to clear off the HIV concentration in blood plasma. Robust $H_\infty$ control is built with the coefficient matrix of the bilinear system. The simulation result is analyzed by comparing the effect of the robust control toward bilinear and nonlinear system. From numerical simulations, an individual will experience heavy symptoms if the hypothetical drugs chemotherapy is not given. This finding is strengthening the urgency of robust control as a chemotherapy with a waiting time. Based on the numerical simulation with robust $H_\infty$ control input, bilinear system has trends that give similar interpretation with the trends of nonlinear system. Besides that, robust $H_\infty$ control on bilinear system has demolishing speed of HIV concentration and infected CD$^4^+$ T cells concentration which approximately equal to the demolishing speed from nonlinear system. Therefore, we can conclude that the performance of $H_\infty$ robust control on bilinear system is nearly same as the performance of nonlinear system.

1. Introduction
HIV is a virus that causes Acquired Immune Deficiency Syndrome (AIDS). HIV affects human's immune systems by infecting the CD$^4^+$ T cells in blood plasma [1]. CD$^4^+$ T cell is a type of lymphocyte which also called by helper T cells. CD$^4^+$ T cells are divided into memory T cells to remember antigen's genetic code and supressor T cells to respon cytotoxic T cells. Someone with a weak immune system is not only susceptible for AIDS, but also susceptible for other diseases e.g. pneumonia and meningitis [2]. The concentrations of CD$^4^+$ T cells in a healthy person are in the range of 500 to 1000 cells mm$^{-3}$. A person with HIV is considered whenever the concentrations of CD$^4^+$ T cells are between 200 to 500 cells mm$^{-3}$ [2, 3].
The HIV replication cycle is divided into six stages and illustrated in Figure 1 below [2, 4]. The stages are binding and entry, uncoating, reverse transcription, provirus integration, virus protein and assembly, and budding. In each stage of the HIV replication cycle, antiretroviral therapy is given as the efforts to decrease the concentration of HIV particles. Zidovudine (AZT) is the first registered drug which declared effective to fight HIV. The best condition that a person with HIV could have is having a treatment with the combinations of drugs. The combinations must be able to resist at least two out of six stages of the HIV replication.

Some mathematical works have been done in modelling this HIV replication in blood plasma. Tuckwell and Wan firstly constructed the dynamic system based on the phenomena [5]. Aguilar-Lopez developed the model by adding the control input and disturbance [1]. The constructed model is a nonlinear model which has weakness in the analysis method. Compared to linear or bilinear systems, nonlinear systems have no specific method to analyze the behavior of the system's state. The nonlinear system will be approximated by a bilinear system in order to be able to analyze the performance. The control input that used in the model is a $H_\infty$ robust controller. The $H_\infty$ robust controller is constructed by using the components of the bilinear systems. The same control will be applied both in the nonlinear and bilinear systems, then the effects toward both systems will be compared. Numerical experiments will be used to show the successful performance of the methodology in minimize HIV concentration in blood plasma.

2. Model Formulation

The model dynamically interprets the early infection phase of HIV particles and CD4$^+$ T cells. The model is originally developed by Tuckwell and Wan [5] which later improved by Aguilar-Lopez et al. [1] by adding the robust control and disturbance. It is shown through a compartment diagram in Figure 2 below.

![Figure 1. HIV Replication Process](image1)

![Figure 2. Compartment Diagram](image2)
The model has the nonlinear form as follow
\[ \dot{x}_1 = k_1 - k_2 x_1 - k_3 x_1 x_3, \]
\[ \dot{x}_2 = k_3 x_1 x_3 - k_4 x_2, \]
\[ \dot{x}_3 = k_5 x_2 - k_6 x_3 + u + d, \]
with \( x_1 \) is the amount of concentrations for uninfected CD4\(^+\) T cells, \( x_2 \) is the amount of concentrations for infected cells, and \( x_3 \) is the amount of concentrations for HIV particles in blood plasma. The model that developed by Aguilar-Lopez et al. use a sliding-mode controller as the control input for the system [1]. In this research, the control input will use the robust \( H_\infty \) controller that defined by van der Schaft [6]. The robust \( H_\infty \) control is defined as a hypothetical drug since the current chemotherapy is only for slowing down the damage that caused by the HIV. That chemotherapy is a Highly Active Anti-Retroviral Therapy (HAART) and it is used to determine the research parameters. The parameters are all assumed to be constant, positive, and defined in the Table 1 below.

### Table 1. Research Parameter (Laurino et al.)

| Parameters | Definition | Value | Units  |
|------------|------------|-------|--------|
| \( k_1 \)  | Constant rate of CD4\(^+\) T cells regeneration | 50    | \( mg L^{-1} d^{-1} \) |
| \( k_2 \)  | Diminishment rate of uninfected cells per capita | 0.05  | \( d^{-1} \) |
| \( k_3 \)  | Infection rate of CD4\(^+\) T cells by virus | 5 \( \cdot \) 10\(^{-4} \) | \( L mg^{-1} d^{-1} \) |
| \( k_4 \)  | Diminishment rate of infected cells per capita | 0.4   | \( d^{-1} \) |
| \( k_5 \)  | Growth rate of HIV particles | 40    | \( d^{-1} \) |
| \( k_6 \)  | Diminishment rate of HIV particles per capita | 9     | \( d^{-1} \) |

Nonlinear system at the equation 1 can be written in the form of state-space representation as follow
\[
\dot{x} = f(x) + g(x)u(t) + k(x)d(t),
\]
\[ y(t) = h(x) =Cx(t), \]
with \( x = [x_1, x_2, x_3]^T \in \mathbb{R}^3 \) is the state variable, \( u \in \mathbb{R} \) is the control input variable, \( y \in \mathbb{R} \) is the output variable, \( f(x) = [k_1 - k_2 x_1 - k_3 x_1 x_3, k_3 x_1 x_3 - k_4 x_2, k_5 x_2 - k_6 x_3]^T \), \( g(x) = [0 \ 0 \ 1]^T \), \( C = [0 \ 0 \ 1] \), and \( d \in \mathbb{R} \) is the disturbance.

In the equation 2 above, there are parameters \( k_i \), control input variable \( u \), and disturbance \( d \). Value and dimention of each parameter \( k_i \), for \( i = 1, \ldots, 6 \), is given at Table 1. Disturbance \( d \) is defined as a bounded and additive external disturbance. Aguilar-Lopez et al. used disturbance as \( d(t) = 5 \sin(10t) \) which assumed as a natural response toward HIV infection at CD4\(^+\) T cells [1]. The control input \( u(t) \) is a robust \( H_\infty \) controller which defined as hypothetical drugs. It is assumed that the hypothetical drugs will be able to totally diminish HIV particles (\( x_3(T) = 0 \)). Consequently, the mass of infected CD4\(^+\) T cells will also be totally diminished by the end of the observation time (\( x_2(T) = 0 \)).

The next part that will be discussed is the equilibrium point of the HIV replication model at the equation 1. By solving \( f(x) = 0 \), then there will be two equilibrium points (\( x_1^*, x_2^*, x_3^* \)) i.e.
\[
E_0 = \left( \frac{k_1}{k_2}, 0, 0 \right),
\]
\[
E_1 = \left( k_5 k_6, k_4 k_5 k_6 - k_2 k_4 k_6, k_3 k_5 k_6 - k_2 k_4 k_6 \right),
\]
with \( E_0 \) is an HIV-free equilibrium point and \( E_1 \) is the equilibrium point which the HIV particles are still inside our body. The Jacobian matrix, which derived from system 1, is
\[
J = \begin{pmatrix}
-k_2 x_2 - k_3 x_3 & 0 & -k_3 x_1 \\
k_3 x_3 & -k_4 & k_3 x_1 \\
0 & k_5 & -k_6
\end{pmatrix}
\]
The Jacobian matrix for each equilibrium point is formulated by substituting \( E_0 \) and \( E_1 \) into matrix \( J \), i.e.
\[ J(E_0) = \begin{pmatrix} -k_2 & 0 & -(k_3 k_5)/k_2 \\ 0 & -k_4 & (k_3 k_4)/k_2 \\ 0 & k_5 & -k_6 \end{pmatrix}, \]
\[ J(E_1) = \begin{pmatrix} -\alpha - k_2 & 0 & -(k_4 k_6)/k_5 \\ \alpha & -k_4 & (k_4 k_6)/k_5 \\ 0 & k_5 & -k_6 \end{pmatrix}, \]

with \( \alpha = (k_1 k_3 k_5 - k_2 k_4 k_6)/k_4 k_6 \). Routh-Hurwitz criteria is used to determine the stability condition from equilibrium points \( E_0 \) and \( E_1 \). The characteristic polynomials that derived from the \( J(E_0) \) and \( J(E_1) \) are

\[ P_{E_0} = \lambda^3 + (k_2 + k_4 + k_6)\lambda^2 + \frac{k_1 k_3 k_5 - k_2^2 k_4 - k_2^2 k_6 - k_2 k_4 k_6}{k_2} \lambda + (k_2 k_4 k_6 - k_1 k_3 k_5) \]
\[ P_{E_1} = \lambda^3 + \frac{k_1 k_3 k_5 + k_2^2 k_6 + k_4 k_6^2}{k_4 k_6} \lambda^2 + \frac{k_1 k_3 k_5(k_4 + k_6)}{k_4 k_6} \lambda + (k_1 k_3 k_5 - k_2 k_4 k_6) \]

Based on the Routh-Hurwitz's stability criterion and the values of parameters at Table 1, equilibrium point \( E_0 \) is unstable and equilibrium point \( E_1 \) is stable. Because of that, robust \( H_\infty \) control is used as the control input to make equilibrium point \( E_0 \) stable and eliminate the concentrations of HIV particles in blood plasma.

3. Bilinearization

Bilinearization is used since there is no specific method to solve all kinds of nonlinear systems. Carleman Bilinearization method is used to be able to have a bilinear system to approximate the nonlinear model [7, 8]. Carleman Bilinearization method is modifying the Carleman Linearization method. This method uses a specific mapping to produce the output's behavior similar to the behavior of bilinear systems [8]. The product of this method is the approximation for nonlinear system in the bilinear form. As an approximation, the bilinear system supposedly gives performance that would be similar to the performance of the nonlinear system.

The state variable of bilinear system is formulated as the following form

\[ \dot{\tilde{x}} = (x^{(1)} \ x^{(2)} \ ... \ x^{(N)})^T \in \mathbb{R}^{\sum_{i=1}^{n} i}, \]  

with \( x^{(i)} \) is the result of \( i - 1 \) times of Kronecker product i.e. \( x^{(i)} = x \otimes x \otimes ... \otimes x \). Therefore, the bilinear system can be written in the bilinear form as follow

\[ \dot{\tilde{x}}(t) = A\tilde{x}(t) + Bu(t) + \sum_{k=1}^{m} N_k \tilde{x}(t) u(t), \]
\[ y(t) = C\tilde{x}(t) + y_0(t), \]

with \( C = [C \ 0 \ ... \ 0], \)

\[ \begin{bmatrix} F_{1,1} & F_{1,2} & ... & F_{1,N} \\ F_{2,0} & F_{2,1} & ... & F_{2,N-1} \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & ... & F_{N,1} \end{bmatrix}, N_k = \begin{bmatrix} G_{1,1}^k & G_{1,2}^k & ... & G_{1,N-1}^k \\ G_{2,0}^k & G_{2,1}^k & ... & G_{2,N-2}^k \\ \vdots & \vdots & \ddots & \vdots \\ 0 & G_{3,0}^k & ... & G_{3,N-3}^k \end{bmatrix} \]
\[ B = \begin{bmatrix} G_{1,1}^{[1]} & G_{1,0}^{[2]} & ... & G_{1,0}^{[m]} \\ 0 & 0 & ... & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & ... & G_{N,0}^{[k]} \end{bmatrix}. \]

\( F_{i,j} \), for \( i = 1 \), is defined by \( F_{i,j} = F_j \), and, for \( i > 1 \), is defined by

\[ F_{i,j} = F_j \otimes I_n \otimes \ldots \otimes I_n + I_n \otimes F_j \otimes \ldots \otimes I_n + \ldots + I_n \otimes I_n \otimes \ldots \otimes F_j, \]

with \( j = 1, 2, ..., N \). Same ways are used to defined \( G_{i,j} \). For \( i = 1 \), is defined by \( G_{i,j} = G_j \), and, for \( i > 1 \), is defined by

\[ G_{i,j} = G_j \otimes I_n \otimes \ldots \otimes I_n + I_n \otimes G_j \otimes \ldots \otimes I_n + \ldots + I_n \otimes I_n \otimes \ldots \otimes G_j, \]

with \( j = 1, 2, ..., N - 1 \).

By choosing \( N = 6 \) at the equation 5, state variable for bilinear system is rearranged into the following form
\[
\ddot{x} = \begin{pmatrix}
F_{1,1} & F_{1,2} & F_{1,3} & F_{1,4} & F_{1,5} & F_{1,6} \\
F_{2,1} & F_{2,2} & F_{2,3} & F_{2,4} & F_{2,5} & F_{2,6} \\
F_{3,1} & F_{3,2} & F_{3,3} & F_{3,4} & F_{3,5} & F_{3,6} \\
F_{4,1} & F_{4,2} & F_{4,3} & F_{4,4} & F_{4,5} & F_{4,6} \\
F_{5,1} & F_{5,2} & F_{5,3} & F_{5,4} & F_{5,5} & F_{5,6} \\
F_{6,1} & F_{6,2} & F_{6,3} & F_{6,4} & F_{6,5} & F_{6,6}
\end{pmatrix}
\quad G = \begin{pmatrix}
G_{1,1} & G_{1,2} & G_{1,3} & G_{1,4} & G_{1,5} & 0 \\
G_{2,1} & G_{2,2} & G_{2,3} & G_{2,4} & 0 & 0 \\
G_{3,1} & G_{3,2} & G_{3,3} & 0 & 0 & 0 \\
G_{4,1} & G_{4,2} & 0 & 0 & 0 & 0 \\
G_{5,1} & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix}
\]
\]

It is shown from equation 7 that the bilinear system has state variables \( \ddot{x} \in \mathbb{R}^{1092} \). The state-space representation can be written as follow:

\[
\dot{\bar{x}}(t) = A\bar{x}(t) + \bar{B}u(t) + \bar{N}\bar{x}(t)u(t),
\]

\[
\bar{y}(t) = \bar{C}\bar{x}(t).
\]

\( \bar{A}, \bar{B}, \bar{N}, \) and \( \bar{C} \) are coefficient matrices with specific dimensions. The components \( F_{i,j} \) and \( G_{i,j} \) on each of the coefficient matrices are the components that derived from the Carleman Bilinearization method.

### 4. Robust \( H_\infty \) Control Design

With the analogy of robust \( H_\infty \) control at linear system, van der Schaft defined robust \( H_\infty \) control for nonlinear system with state-feedback input. The following theorem is used to satisfy the stability condition with robust \( H_\infty \) control as a globally asymptotic stable condition.

**Theorem 1 [6]** Consider the state-space representation as in equation 2 for a nonlinear system with disturbance. For any \( \gamma > 0 \), there exist a function \( V(x) \geq 0 \) satisfy the following Hamilton-Jacobi equation

\[
\frac{\partial V(x)}{\partial x} f(x) + \frac{1}{2} \frac{\partial^2 V(x)}{\partial x^2} M(x) \frac{\partial^2 V(x)}{\partial x} + \frac{1}{2} h^T(x)h(x) = 0,
\]

or satisfy the following Hamilton-Jacobi inequality

\[
\frac{\partial V(x)}{\partial x} f(x) + \frac{1}{2} \frac{\partial^2 V(x)}{\partial x^2} M(x) \frac{\partial^2 V(x)}{\partial x} + \frac{1}{2} h^T(x)h(x) \leq 0,
\]

with \( M(x) = \frac{1}{\gamma^2} k(x)k^T(x) - g(x)g^T(x) \). A closed-loop system has \( L_2 \)-gain from \( d \) into \( \mathcal{Y} \) less than or equal to \( \gamma \) for a state-feedback input

\[
u = -g^T(x) \frac{\partial^2 V(x)}{\partial x},
\]

Robust \( H_\infty \) control input is constructed by using the matrices component of the bilinear system. By using Theorem 1, a \( \gamma > 0 \) and \( \dot{V}(x) \geq 0 \) must be chosen to satisfy equation 9 or inequality 10. Therefore, for a state-feedback input as in equation 11, system has \( L_2 \)-gain from \( d \) into \( \mathcal{Y} \) less than or equal to \( \gamma \). \( P(\bar{x}) \) is defined as

\[
P(\bar{x}) = \frac{\partial V(\bar{x})}{\partial x} f(\bar{x}),
\]

where \( \gamma = 0.5 \), is chosen as follow

\[
V(\bar{x}) = g_0(\bar{x}_1 + \bar{x}_2) + g_1 \sqrt{1 + \bar{x}_3^2}
\]

Since \( \bar{x}_1 \geq 0 \), then the condition \( \dot{V}(x) \geq 0 \) is satisfied by choosing \( g_0, g_1 \in \mathbb{R}^+ \) appropriately. The first derivative of \( V(\bar{x}) \) is written on equation 13 below.
\[ V(\bar{x}) = \begin{bmatrix} g_0 & g_0 \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}} & 0 & \cdots & 0 \end{bmatrix}. \]  

(13)

\[ W(\bar{x}) \] is defined on the following equation  

\[ W(\bar{x}) = P(\bar{x}) + \frac{1}{2} M(\bar{x}) + \frac{1}{2} h^T(\bar{x}) h(\bar{x}), \]  

(14)

then it needs to be shown that \( W(\bar{x}) \leq 0 \). \( P(\bar{x}), M(\bar{x}), \) and \( W(\bar{x}) \) can be written by following  

\[ P(\bar{x}) = g_0(k_1 - k_2 \bar{x}_1 - k_4 \bar{x}_2) + \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}}(k_5 \bar{x}_2 - k_6 \bar{x}_3), \]

\[ M(\bar{x}) = \left( \frac{1}{\gamma^2} - 1 \right) \left( \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}} \right)^2 \]

\[ W(\bar{x}) = g_0(k_1 - k_2 \bar{x}_1 - k_4 \bar{x}_2) + \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}}(k_5 \bar{x}_2 - k_6 \bar{x}_3) + \frac{1}{2} \left( \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}} \right)^2 \]

(15)

The form \( W(\bar{x}) \) on equation 15 can be rewritten into \( W(\bar{x}) = W_1(\bar{x}) + W_2(\bar{x}) \) with  

\[ W_1(\bar{x}) = g_0(k_1 - k_2 \bar{x}_1 - k_4 \bar{x}_2), \]

\[ W_2(\bar{x}) = \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}}(k_5 \bar{x}_2 - k_6 \bar{x}_3) + \frac{1}{2} \left( \frac{g_1 \bar{x}_3}{\sqrt{1 + \bar{x}_3^2}} \right)^2 + \frac{1}{2} \bar{x}_3^2 \]

Parameters \( k_i \) are described on Tabel 1. Aguilar-Lopez defined the coefficient for control as \( g_1 = 1100d^{-1} \) [1], while \( g_0 = 60000d^{-1} \) is determined from the simulation result. Since \( \bar{x}_i \geq 0 \) for \( i = 1, 2, 3 \), then the condition \( W_1(\bar{x}) < 0 \) and \( W_2(\bar{x}) > 0 \) can be satisfied. In other words, condition \( W_1(\bar{x}) \leq -W_2(\bar{x}) \) always be satisfied for \( t \in [0, T] \). Since \( W_1(\bar{x}) \leq -W_2(\bar{x}) \), then inequality \( W(\bar{x}) \leq 0 \) is satisfied.

Therefore, bilinear system has \( L_2 \)-gain from \( d \) into \( \left[ \begin{array}{c} y_f \\ u_t \end{array} \right] \) less than or equal to \( \gamma \). In other words, the constructed robust \( H_\infty \) control can guarantee a robustly stable condition and the stability is also a globally asimptotic stable. Robust \( H_\infty \) control that used in this research is  

\[ u = -1100 \frac{\bar{x}_3}{\sqrt{1 + \bar{x}_3^2}} \]

(16)

Control input at equation 16 is categorized as a control input for bilinear system with \( V(\bar{x}) \) at equation 12. The bilinear system is an approximation for nonlinear system with the state variables are extended into 1092 dimention. However, the effects of control input will only be compared between the performances of state variables \( \bar{x}_1, \bar{x}_2, \) and \( \bar{x}_3 \) of bilinear system and \( x_1, x_2, \) and \( x_3 \) of nonlinear system. Since the bilinear system is the approximation of its nonlinear form, then it will be determined whether the performance of bilinear systems will be similar or not with the performance of nonlinear system.

5. Results and Discussion

Previously, the equilibrium points of the systems are obtained as shown at equation 3 and 4. Based on the analysis of equilibrium points, \( E_1 \) is the only stable equilibrium point. It means that the initial value that being used must represent the existence condition of HIV particles in blood plasma \( (x_3 \neq 0) \). Without loss of generality, the initial value for the numerical simulations are given as follow  

\[ \begin{array}{c}
 x_1(0) \\
 x_2(0) \\
 x_3(0)
\end{array} = \begin{array}{c}
 \bar{x}_1(0) \\
 \bar{x}_2(0) \\
 \bar{x}_3(0)
\end{array} = \begin{array}{c}
 400 \text{mgL}^{-1} \\
 200 \text{mgL}^{-1} \\
 75 \text{mgL}^{-1}
\end{array} \]

(17)

The initial value at equation 17 has a meaning that an individual is still in the normal condition though the HIV particles are inside the body and already infecting the CD4+ T cells. The first simulation is the simulation without using control input \( (u(t) = 0) \). The simulation result for nonlinear system and bilinear system is illustrated in Figure 3.
The observation time for the first simulation is 75 days ($T = 75$). The first simulation for the nonlinear system gives the result that the trajectories of state variables are convergent to the equilibrium point $E_1$. For bilinear system, the first simulation shows that the final mass concentration of the CD$^4$+ T cells ($\tilde{x}_1$ and $\tilde{x}_2$) is $251.5 \text{ mgL}^{-1}$. For nonlinear system, the first simulation shows that the final mass concentration of the CD$^4$+ T cells ($x_1$ and $x_2$) is $282.5 \text{ mgL}^{-1}$. The result indicates that an individual is experiencing heavy symptoms and susceptible towards illness that attacks weak immune system. Therefore, the control input as a hypothetical drugs chemotherapy is applied to minimize the HIV concentrations as well as keeping the CD$^4$+ T cells' condition in the normal shape.

The next numerical simulations are the application of robust $H_\infty$ control as the control input for the dynamic systems. The purpose of this simulation is to determine the performance of each state variable after the control input is used. For the bilinear system, the robust $H_\infty$ control input is described in the equation 16. Since we want to compare the effect of robust $H_\infty$ control input on bilinear and nonlinear system, then the control input for nonlinear system takes the form as in the equation 16 too. The difference only by changing the state variables $\tilde{x}$ (on the bilinear system) with the state variables $x$ (on the nonlinear system).

Second simulation is the simulation for nonlinear system with robust $H_\infty$ controller. The simulation result is illustrated in the Figure 4a. It shows that $x_3$, which defined the mass concentration of HIV particles, is convergent to the original point since day 13 after the robust $H_\infty$ control input is given. In
other words, it takes 88 days to totally diminish the HIV particles from the body. The diminishment happens because of the effect of hypothetical drugs chemotherapy that started at the 75th day. The diminishment process significantly affects the mass concentration of the infected CD4$^+$ T cells. It shows that $x_2$, which defined the mass concentration of infected CD4$^+$ T cells, is convergent to the origin point since day 23 after the robust $H_\infty$ control input is given. In other words, it takes 98 days for the body to not contain any infected CD4$^+$ T cells. Figure 4b illustrates the convergency of both infected cell's trajectory ($x_2$) and HIV particle's trajectory ($x_3$).

Third simulation is the simulation for bilinear system with robust $H_\infty$ controller. The simulation result is illustrated in the Figure 5a. $\tilde{x}_3$, which defined the mass concentration of HIV particles, is convergent to the origin point since day 12 after the control treatment is given. In other words, it takes 87 days to totally diminish the HIV particles from the body. The diminishment happens because of the effect of hypothetical drugs chemotherapy that started at the 75th day. As also happened in the nonlinear system, the diminishment of HIV particles also affects the mass concentration of infected CD4$^+$ T cells. $\tilde{x}_2$, which defined the mass concentration of infected CD4$^+$ T cells, is convergent to the origin point since day 21 after the control treatment is given. In other words, it takes 96 days for the body to not contain any infected CD4$^+$ T cells. Figure 5b illustrates the convergency of both infected cell's trajectory ($\tilde{x}_2$) and HIV particle's trajectory $\tilde{x}_3$).

Overall, the numerical simulations is divided into two types of observation i.e. observation of system with no control input and observation of system with robust $H_\infty$ control input. All simulations are interpreted towards the phenomena about HIV replication in the blood plasma. The first simulation shows that the mass concentrations of CD4$^+$ T cells (both infected and uninfected cells) are decreasing at both bilinear and nonlinear system. Table 2 below shows the decreasing mass concentrations of CD4$^+$ T cells up to 53% for nonlinear system and 58% for bilinear system. From the result on Table 2, it can be seen that the bilinear system's result gives a good approximation towards the nonlinear system's results.

**Table 2. The Comparison of CD4$^+$+T Cells' Decreasing**

| Dynamical System | Initial Condition ($T = 0$) | Final Condition ($T = 75$) | Decreasing Percentage |
|------------------|----------------------------|----------------------------|-----------------------|
| Nonlinear System | 600 $mgL^{-1}$             | 282 $mgL^{-1}$             | 53%                   |
| Bilinear System  | 600 $mgL^{-1}$             | 251.5 $mgL^{-1}$           | 58%                   |
The next part that will be analyzed is the trajectory's trend of each system. Without no control input, the uninfected and infected CD$^+$ T cells are decreasing and the HIV particles are increasing. This phenomena can be seen in both systems. An individual, whom in a good condition at the start of the observation, will experience heavy symptomps and have a weak immunity system at the end of the observation. Bilinear system is able to representatively approximate the performance of nonlinear system in observation with no control input.

The control input for this research is robust $H_\infty$ controller which defined as a hypothetical drugs chemotherapy. This hypothetical drugs chemotherapy is assumed to be able to fully diminish the HIV particles. The interpretation from Figure 5a and Figure 5b shows that all the trajectories are convergent to the equilibrium point $E_0$. Besides that, it is clearly seen that the trend of all trajectories of bilinear system have the same trend as the trajectories of nonlinear system.

The convergency of all state variables after the implementation of robust $H_\infty$ controller proves the effectivity of the controller. It is known that the state variables converges to the HIV-free equilibrium point at the end of observation time. The convergency of $x_2$ and $x_3$ to the origin point means that the mass concentration of infected cells and HIV particles are fully diminished. Then, the convergency of $x_1$ to the condition $x_1 = 1000$ means that all CD$^+$ T cells are the uninfected cells. Therefore, robust $H_\infty$ controller is successfully able to make the system is robustly stable.

Tabel 3. Comparison of Rate of Diminishment at Both Systems

| Bilinear System                      | Nonlinear System                      |
|-------------------------------------|---------------------------------------|
| HIV particles are diminished with the rate 34.17 $mgL^{-1}$ per day | HIV particles are diminished with the rate 35.04 $mgL^{-1}$ per day |
| Infected cells are diminished with the rate 4.35 $mgL^{-1}$ per day | Infected cells are diminished with the rate 4.46 $mgL^{-1}$ per day |

The last part to be discussed is the rate of diminishment of the infected cells and HIV particles of both bilinear and nonlinear system. The comparison result is shown at the Table 3. It can be seen that the state variables of bilinear system has rate of diminishment that approximate the rate of diminishment of the state variables of nonlinear systems. Since the bilinear system is generated as an approximation of nonlinear system, then this result clearly state the benefits of implementing robust $H_\infty$ system at the bilinear system.

It is known that a complex computational method is needed to analyze the nonlinear system. This complexity of the method leads to the needs of extra efforts to solve problems related with nonlinear systems. Besides that, there is no specific method to be able to accommodate all types of nonlinear systems. Therefore, the result about decreasing's percentage, trends of the trajectories, and rate of diminishment are sufficient enough to show the effectiveness of implementing bilinear system as the approximation of nonlinear system.

6. Conclusions

In this research, phenomena about HIV replication in blood plasma is modelled into a nonlinear system. Due to the barriers to analyze nonlinear system, alternative way to approximate the nonlinear system by a bilinear system is used. The purpose of this research is to find a control input to solve the modelling problems. The robust $H_\infty$ controller is used as the control input because the model contains disturbance. The robust $H_\infty$ controller is constructed by the method developed by van der Schaft with the components of bilinear system. The result shows the effectiveness of robust $H_\infty$ controller to minimize the HIV particles in blood plasma. Several findings from the comparison between bilinear and nonlinear system also strengthen the result that the bilinear system would representatively approximate the nonlinear system. By the end of the observation, blood plasma only contains the uninfected CD$^+$ T cells.
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