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Control of HIV/AIDS infection system with drug dosages design via robust $\mathcal{H}_\infty$ fuzzy controller [1]

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Abstract. The designing of $\mathcal{H}_\infty$ fuzzy controller for HIV/AIDS infected dynamic system has been considered in this paper. With TS fuzzy model and LMIs approach, the proposed controller is obtained for such a system. A set of sufficient conditions of the $\mathcal{H}_\infty$ controller is given to ensure the closed-loop system asymptotic stability and the prescribed $\mathcal{H}_\infty$ performance level. Finally, the effectiveness of the fuzzy controller design approach is finally presented through the simulation results.

Keywords: $\mathcal{H}_\infty$ control, TS fuzzy model, robust control, linear matrix inequalities (LMIs), HIV/AIDS infection system, robust control

1. Introduction

HIV/AIDS is one of most going issues in present day [1–7]. AIDS is certainly a kind of a disease that is possibly amended by the anti-HIV drugs. The recent researches are shown that the perfect remedied methodology has not yet been completely successful. Nowadays, the typical therapy has used the reverse transcriptase inhibitors for fighting against the virus. The objective of the anti-HIV drugs is to prevent the virus expansion; however, the virus particles have still been existed in the body when using the drug treatment [1]. Recently, a number of researchers have studied the HIV/AIDS dynamic system behavior; see [2–4]. HIV is a retrovirus that either directly or indirectly attacks the CD4+T cells. When HIV virus has destroyed the CD4+T cells such that the CD4+T cells in blood is less than 200 cells per microliter (μL), then the cellular immunity is nearly lost. If the patient absences from the antiretroviral therapy, the HIV infected development to AIDS is almost eight to ten years [1]. In addition, only 9.2 months are the survival time in average after being AIDS. However, the period of treatment is different between patients,

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from two weeks to twenty years. When the patient has been taken the HIV virus in early infection, the virus will significantly surge in next thirty days. As a result, the CD4+T cells in the human body are declined. After passing the initial stage of infection period, then the body will build the HIV antibodies to fight with the virus. The infection may be stable an approximate steady state for a while. Later, without some treatments, the CD4+T cells of the body will be significantly decreased again, so that the patient becomes an AIDS person in final time.

Recently, the researches of the fuzzy system to control problems have been considered in either theoretical areas or applications. Additionally, many fruitful results have been expressed in the literature. Although, there exist a number of successes in using fuzzy system, many basic issues still remain to be considered. Currently, a nonlinear system which is described by a Takagi-Sugeno fuzzy model has been extensively studied; see [8–11]. Actually, the TS fuzzy model is a family set of linear models which are easily combined via nonlinear fuzzy membership functions.

In recent period, a number of researchers have studied in the nonlinear $\mathcal{H}_\infty$-control theory; see [12,13]. So far, there have been two usually utilized methods for obtaining the solutions; i.e., the dissipativity theory and the Bounded Real Lemma; see [12–15]. The solutions on both approaches are actually involved with Hamilton-Jacobi inequalities.

Therefore, the contribution of this paper is to design a robust $\mathcal{H}_\infty$ TS fuzzy controller based on an LMI approach for HIV/AIDS infection system with dual drug. This paper is organized as follows. In Section 2, system descriptions and definition are stated. In Section 3, based on an LMI approach, the robust $\mathcal{H}_\infty$ fuzzy controller for HIV/AIDS infection system with dual drug is obtained . Then, the effectiveness of the proposed method is exposed through the simulation results shown in Section 4. Finally. the conclusion is provided in Section 5.

2. System descriptions and definition

2.1. HIV infected model

The HIV nonlinear dynamic model with treatment is shown as follows [5]:

$$\begin{aligned}
\dot{x}_1(t) &= s - dx_1(t) - (1-u_1(t))\beta x_1(t)x_3(t) + w_1(t) \\
\dot{x}_2(t) &= (1-u_1(t))\beta x_1(t)x_3(t) - \mu x_2(t) + w_2(t) \\
\dot{x}_3(t) &= (1-u_2(t))kx_2(t) - cx_3(t) + w_3(t)
\end{aligned} \tag{1}$$

where s is the inflow rate of uninfected CD+T cells, d is the natural death rate, β is the infected rate of CD+T cells with virus, μ is the death rate of infected cells, c is the clearance rate of virus, k is the rate of virions product per infection CD4+T cell, $x_1(t)$ is the level of healthy cells or T cells, $x_2(t)$ is the level of infected cells, $x_3(t)$ is the level of virions, $w_1(t)$, $w_2(t)$ and $w_3(t)$ are the disturbance factors due to the patient's conditions, the controller input $u_1(t)$ and $u_2(t)$ are a number of drugs in the treatment of the Highly Active Antiretroviral Therapy (HAART) represented by Reverse Transcriptase Inhibitors-RTI and Protease Inhibitors-PI, respectively, and t is as the time in days. The HIV model parameters are given in Table 1 [5].

Table 1
HIV MODEL PARAMETERS [5]

Parameter	Typical Value	Unit	Parameter	Typical Value	Unit
t	-	Days	s	100 mm^3	Per Day
d	0.02	Per Day	β	2.4 x 10^{-5} mm^3	Per Day
k	100	Count Cell^{-1}	c	2.4	Per Day
μ	0.24	Per Day			

2.2. Fuzzy dynamic model

According to the HIV nonlinear dynamic model, the antiretroviral treatment can be modelled by using a TS fuzzy system. In this paper, a TS fuzzy system with parametric uncertainties for such a system is examined as follows:

$$\begin{aligned}
\dot{x}(t) &= \textstyle\sum_{i=1}^{r} \mu_i(\nu(t)) \Big[[A_i + \Delta A_i]x(t) + [B_{1_i} + \Delta B_{1_i}]w(t) + [B_{2_i} + \Delta B_{2_i}]u(t) \Big] \\
z(t) &= \textstyle\sum_{i=1}^{r} \mu_i(\nu(t)) \Big[[C_{1_i} + \Delta C_{1_i}]x(t) + [D_{12_i} + \Delta D_{12_i}]u(t) \Big] \\
y(t) &= \textstyle\sum_{i=1}^{r} \mu_i(\nu(t)) \Big[[C_{2_i} + \Delta C_{2_i}]x(t) + [D_{21_i} + \Delta D_{21_i}]w(t) \Big]
\end{aligned} \tag{2}$$

where $\mu_i(\nu(t))$ is the fuzzy weighting function for each rule (i.e., $\mu_i(\nu(t)) \geq 0$ and $\sum_{i=1}^{r} \mu_i(\nu(t)) = 1$), $\nu(t) = [\nu_1(t) \ \cdots \ \nu_\vartheta(t)]$ is the premise variable, ϑ is the number of fuzzy sets, $x(t) \in \Re^n$ is the state vector, $w(t) \in \Re^p$ is the disturbance, $u(t) \in \Re^m$ is the control input, $y(t) \in \Re^\ell$ is the measured output, $z(t) \in \Re^s$ is the regulated output, the matrices $A_i, B_{1_i}, B_{2_i}, C_{1_i}, C_{2_i}, D_{12_i}$ and D_{21_i} are of appropriate matrix dimensions, and r is the number of IF-THEN rules. $\Delta A_i, \Delta B_{1_i}, \Delta B_{2_i}, \Delta C_{1_i}, \Delta C_{2_i}, \Delta D_{12_i}$ and ΔD_{21_i} are the uncertain matrices in the system and satisfy the following assumption.

Assumption 1 $\Delta A_i = F(x(t),t)H_{1_i}$, $\Delta B_{1_i} = F(x(t),t)H_{2_i}$, $\Delta B_{2_i} = F(x(t),t)H_{3_i}$,

$\Delta C_{1_i} = F(x(t),t)H_{4_i}$, $\Delta C_{2_i} = F(x(t),t)H_{5_i}$, $\Delta D_{12_i} = F(x(t),t)H_{6_i}$ *and* $\Delta D_{21_i} = F(x(t),t)H_{7_i}$

where H_{j_i}, $j = 1, 2, \cdots, 7$ *are the known structure of the uncertain matrix functions. Then, the following inequality holds:*

$$\|F(x(t),t)\| \leq \rho \tag{3}$$

for any known positive constant ρ.

Definition 2.1 *Given a positive number* γ*, the system (2) is satisfied the prescribed* $\mathcal{H}_\infty$ *performance level* γ *if*

$$\int_0^{T_f} z^T(t)z(t)dt \leq \gamma^2 \left[\int_0^{T_f} w^T(t)w(t)dt \right], \ x(0) = 0 \tag{4}$$

for all $T_f \geq 0$ *and* $w(t) \in \mathcal{L}_2[0, T_f]$.

Note that $(*)$ as an ellipsis for terms are induced by the symmetric block matrices.

3. Main results

A robust $\mathcal{H}_\infty$ fuzzy controller for the HIV/AIDS infection system is given into the form

$$u(t) = \sum_{j=1}^{r} \mu_j K_j x(t) \tag{5}$$

where K_j is the fuzzy controller gain such that the inequality (4) holds. Thus, the HIV fuzzy system model (2) with the fuzzy controller (5) is given by

$$\dot{x}(t) = \sum_{i=1}^{r}\sum_{j=1}^{r} \mu_i\mu_j \Big[[(A_i + B_{2_i}K_j) + (\Delta A_i + \Delta B_{2_i}K_j)]x(t) + [B_{1_i} + \Delta B_{1_i}]w(t)\Big]. \tag{6}$$

Based on the Lyapunov approach, the following results show the sufficient conditions for the existence of a robust $\mathcal{H}_\infty$ fuzzy controller.

Theorem 1 *Given positive constants δ and γ, if there exist a matrix $P_\infty = P_\infty^T$ and matrices Y_j, $j = 1, 2, \cdots, r$, satisfying the following linear matrix inequalities:*

$$P_\infty > 0 \tag{7}$$

$$\Xi_{ii} < 0, \quad i = 1, 2, \cdots, r \tag{8}$$

$$\Xi_{ij} + \Xi_{ji} < 0, \quad i < j \le r \tag{9}$$

where

$$\Xi_{ij} = \begin{pmatrix} A_iP_\infty + P_\infty A_i^T + B_{2_i}Y_j + Y_j^T B_{2_i}^T & (*)^T & (*)^T \\ \tilde{B}_{1_i}^T & -\gamma I & (*)^T \\ \tilde{C}_{1_i}P_\infty + \tilde{D}_{12_i}Y_j & 0 & -\gamma I \end{pmatrix} \tag{10}$$

with

$$\tilde{B}_{1_i} = \begin{bmatrix} \delta I & I & \delta I & B_{1_i} \end{bmatrix}, \tilde{C}_{1_i} = \begin{bmatrix} \frac{\gamma\rho}{\delta} H_{1_i}^T & 0 & \sqrt{2}\lambda\rho H_{4_i}^T & \sqrt{2}\lambda C_{1_i}^T \end{bmatrix}^T, \tilde{D}_{12_i} = \begin{bmatrix} 0 & \frac{\gamma\rho}{\delta} H_{3_i}^T & \sqrt{2}\lambda\rho H_{6_i}^T & \sqrt{2}\lambda D_{12_i}^T \end{bmatrix}^T$$

$\lambda = \Big(1 + \rho^2 \sum_{i=1}^{r}\sum_{j=1}^{r} \Big[\|H_{2_i}^T H_{2_j}\|\Big]\Big)^{\frac{1}{2}}$ *then the inequality (4) holds for the system (2). Then, the suitable fuzzy controller is given by*

$$u(t) = \sum_{j=1}^{r} \mu_j K_j x(t) \tag{11}$$

where $K_j = Y_j P_\infty^{-1}$.

Proof: Using Assumption 1, the closed-loop fuzzy system (6) can be expressed as follows:

$$\dot{x}(t) = \sum_{i=1}^{r}\sum_{j=1}^{r} \mu_i\mu_j \Big([A_i + B_{2_i}K_j]x(t) + \tilde{B}_{1_i}\tilde{w}(t)\Big) \tag{12}$$

where $\tilde{B}_{1_i}$ is shown in (10), and the disturbance $\tilde{w}(t) = \begin{bmatrix} \frac{1}{\delta}F(x(t),t)H_{1_i}x(t) \\ F(x(t),t)H_{2_i}w(t) \\ \frac{1}{\delta}F(x(t),t)H_{3_i}K_jx(t) \\ w(t) \end{bmatrix}$.

Let consider a Lyapunov function

$$V(x(t)) = \gamma x^T(t) Q x(t)$$

where $Q = P_\infty^{-1}$. Differentiate $V(x(t))$ along the closed-loop system (12) yields

$$\dot{V}(x(t)) = \gamma \dot{x}^T(t) Q x(t) + \gamma x^T(t) Q \dot{x}(t) \tag{13}$$

Adding and subtracting $-\tilde{z}^T(t)\tilde{z}(t) + \gamma^2 \sum_{i=1}^r \sum_{j=1}^r \sum_{m=1}^r \sum_{n=1}^r \mu_i\mu_j\mu_m\mu_n[\tilde{w}^T(t)\tilde{w}(t)]$ to and from (13), and using the fact that $\mu_i \geq 0$ and $\sum_{i=1}^r \mu_i = 1$, then (13) becomes

$$\dot{V}(x(t)) \leq -\tilde{z}^T(t)\tilde{z}(t) + \gamma^2 \sum_{i=1}^{r}\sum_{j=1}^{r}\sum_{m=1}^{r}\sum_{n=1}^{r} \mu_i\mu_j\mu_m\mu_n[\tilde{w}^T(t)\tilde{w}(t)] \tag{14}$$

where $\tilde{z}(t) = \sum_{i=1}^r \sum_{j=1}^r \mu_i\mu_j[\tilde{C}_{1_i} + \tilde{D}_{12_i}K_j]x(t)$ together with $\tilde{C}_{1_i}$ and $\tilde{D}_{12_i}$ as shown in (10). By integrating both sides of (14) and using the fact that $x(0) = 0$ and $V(x(T_f)) \geq 0$ for all $T_f \neq 0$, we get

$$\int_0^{T_f} \tilde{z}^T(t)\tilde{z}(t)dt \leq \gamma^2 \left[\int_0^{T_f} \sum_{i=1}^{r}\sum_{j=1}^{r}\sum_{m=1}^{r}\sum_{n=1}^{r} \mu_i\mu_j\mu_m\mu_n[\tilde{w}^T(t)\tilde{w}(t)]dt \right]. \tag{15}$$

Using Assumption 1 and placing $\tilde{z}(t)$ and $\tilde{w}(t)$ into (15), finally we obtain

$$\int_0^{T_f} z^T(t)z(t) \leq \gamma^2 \int_0^{T_f} w^T(t)w(t)\, dt. \tag{16}$$

Therefore, the inequality (4) holds. This completes the proof.

4. Simulation results

The steps of designing a robust TS fuzzy controller for HIV infected system are illustrated as follows. First, let us recall (1). The values of each parameter are listed in Table 1. The regulated output is given by

$$z(t) = [x_1(t) \;\; u_1(t) \;\; u_2(t)]^T. \tag{17}$$

With the three membership functions; i.e., the healthy cell of CD4+T, the infected cells and the free cells as shown in Figure 1, the HIV nonlinear dynamic model is written as the the TS fuzzy plant model by the following TS fuzzy rules.

Plant Rule i:

IF $x_1(t)$ is H_i and $x_2(t)$ is I_j and $x_3(t)$ is V_k THEN

$$\dot{x}(t) = [A_i + \Delta A_i]x(t) + B_i u(t) + B_w w(t), \;\; z(t) = Cx(t) + Du(t)$$

where $i, j, k = 1, \cdots, 3$

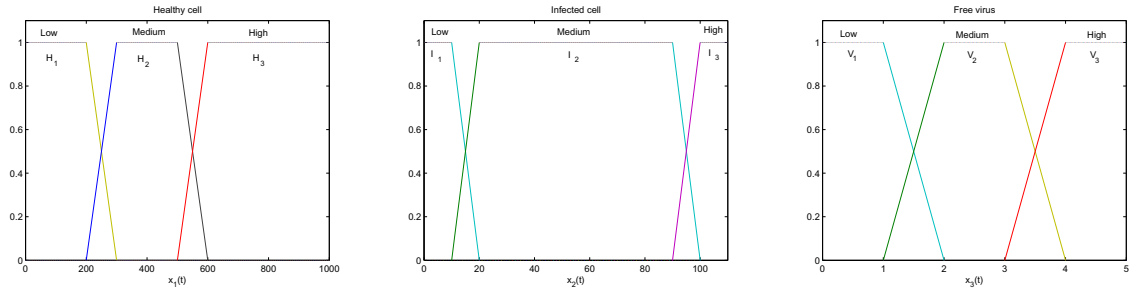

Fig. 1. Membership function of three variables.

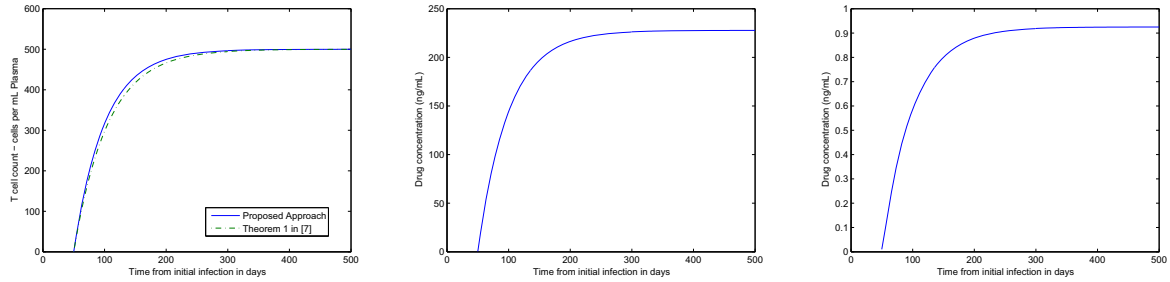

Fig. 2. Healthy cell, $x_1(t)$, Drug dosage for RTI, $u_1(t)$ and Drug dosage for PI, $u_2(t)$.

$$A_i = \begin{bmatrix} -d & 0 & -\beta x_1(t) \\ 0 & -\mu & \beta x_1(t) \\ 0 & k & -c \end{bmatrix},\ B_w = \begin{bmatrix} 1\,0\,0 \\ 0\,1\,0 \\ 0\,0\,1 \end{bmatrix},\ B_i = \begin{bmatrix} \beta x_1(t)x_3(t) & 0 \\ -\beta x_1(t)x_3(t) & 0 \\ 0 & kx_2(t) \end{bmatrix}, C = \begin{bmatrix} 1\,0\,0 \\ 0\,0\,0 \\ 0\,0\,0 \end{bmatrix},\ D = \begin{bmatrix} 0\,0 \\ 1\,0 \\ 0\,1 \end{bmatrix},$$

$$x(t) = [x_1^T(t)\ x_2^T(t)\ x_3^T(t)]^T, \qquad w(t) = [w_1^T(t)\ w_2^T(t)\ w_3^T(t)]^T, \Delta A_i = F(x(t),t)H_{1_i}.$$

Assume that in (2), $\|F(x(t),t)\| \leq \rho = 1$ and μ, d, and c are the parameters which are uncertain but bounded within 10% of their nominal value in (1), we get

$$H_{1_i} = \begin{bmatrix} -0.1d & 0 & 0 \\ 0 & -0.1\mu & 0 \\ 0 & 0 & -0.1c \end{bmatrix}.$$

Applying Theorem 1 with setting $\gamma = 0.1$, the results are obtained as shown in Figure 2.

Remark 1 When the patient has received the HIV virus at the early stage of the infection in approximately 4-8 weeks, the physicians will start assessing the condition of patient by counting the CD4+T cells. If the rapidity of CD4+T declines, then the patient must be begun with the remedied treatment. Figure 2 show the concentration of CD4+T, RTI and PI. Note that if CD4+T are less than 500 cells/μL, the patient may become an AIDS person.

Remark 2 Figure 2 shows the comparisons between the proposed approach and the Theorem 1 in [7] by which the CD4+T counts of the proposed approach reaches an approximate steady-state faster than the Theorem 1 in [7]. In addition, if the value of μ, d, and c are the parameters which are uncertain but bounded within 30% of their nominal value in (1), i.e., 0.3, the Theorem 1 in [7] is not valid anymore; however, the proposed methodology is still possible to obtain the solution.

5. Conclusion

This paper examines the robust $\mathcal{H}_\infty$ TS fuzzy controller design for HIV infection nonlinear dynamic model with drug dosages. Based on an LMI approach, the development of a fuzzy controller for such a system has been examined in order to satisfy the $\mathcal{H}_\infty$ performance index. Finally, the simulation results have been shown that the proposed controller can well perform the remedied treatment of HIV-infection for the infected patient.

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