**H∞ Fuzzy Controller Design for HIV/AIDS Infection System with Dual Drug Dosages via an LMI Approach**

Wudhichai Assawinchaichote and Sasiluk Junhom

**Abstract**—This paper presents a design of $H_\infty$ fuzzy controller for HIV/AIDS infection system with dual drug dosages. The Takagi-Sugeno (TS) fuzzy model is applied for fuzzy modeling of the HIV infection dynamic system. A sufficient condition of the controller for this system is given in term of Linear Matrix Inequalities (LMIs). The effectiveness of the proposed controller design methodology is finally demonstrated through simulation results. It has been shown that the anti-HIV vaccines are critically important in reducing the infected cells.

**Keywords**—$H_\infty$ Fuzzy control; Takagi-Sugeno (TS) fuzzy model; Linear Matrix Inequalities (LMIs); HIV/AIDS infection system

**I. INTRODUCTION**

The problems of HIV/AIDS are very importance in present world. Basically, AIDS is a kind of a disease that can be treated by using expedient drugs. From the present research, the complete cure mechanism has not yet been found. Presently, some antiretroviral therapies use reverse transcriptase inhibitors for fight against an enzyme from infected cells that called viral protease. All of anti-HIV drugs aim at preventing the virus, but they cannot kill virus particles or infected cells [1]. The dynamic HIV/AIDS studies have been shown by many researchers such as J. Guedj et al. [2], R.A. Filter et al. proposed [3], and R. Motta J. et al. [4]. HIV is a retrovirus that primarily infects vital organs of the human immune system such as CD4+T cells (a subset of T cells), macrophages and dendritic cells. It directly and indirectly destroys CD4+T cells. Once HIV has killed so many CD4+T cells such that there are fewer than 200 of these cells per micro liter ($\mu$L) of blood then cellular immunity is lost. In the absence of antiretroviral therapy, the average time of progression from HIV infection to AIDS is about nine to ten years, and the average survival time after developing AIDS is only 9.2 months [1]. However, the rate of treated disease progression is varied between individuals, from two weeks up to 20 years. Figure 1 shows the natural history of HIV infections dynamics as currently accepted [1], [2], [3], [4]. When a body has been received HIV virus in primary infection, a number of HIV virus will dramatically increase in first 30 days (resulting CD4+T cells reduction). After the primary infection period, a body builds HIV antibodies for agent virus so that, the infection still stabilizes an approximate steady state. In the last period, the antibody of healthy CD4+T cells will be drastically reduced. Finally, the patient develops to be an AIDS person.

Over the past few decades, the nonlinear $H_\infty$-control theory has been extensively studied by many researchers; see [9], [10], [11], [12]. The nonlinear $H_\infty$-control problem can be stated as follows: given a dynamic system with the exogenous input noise and the measured output, find a controller such that the $L_2$-gain of the mapping from the exogenous input noise to the regulated output is less than or equal to a prescribed value. Presently, there are two commonly used approaches for providing solutions to the nonlinear $H_\infty$-control problems. The first approach is based on the dissipativity theory and theory of differential games; see [9], [13], [15]. The second approach is based on the nonlinear version of classical Bounded Real Lemma; see [11], [12], [14]. Both approaches show that the solution of the nonlinear $H_\infty$-control problem is in fact related to the solvability of Hamilton-Jacobi inequalities (HJIs).

![Fig. 1. The natural history of HIV infections dynamics as currently accepted][1], [2], [3], [4].

Recently, many researchers consider the design of fuzzy $H_\infty$ for a class of nonlinear systems which can be represented by a Takagi-Sugeno (TS) fuzzy model; see [26], [27], [28], [30]. In this TS fuzzy model local dynamics in different state space regions are represented by local linear systems. The overall model of the system is obtained by ‘blending’ of these linear models through nonlinear membership functions.
In other words, a TS fuzzy model is essentially a multmodel approach in which simple sub-models are combined to represent the global behavior of the system.

What we intend to do in this paper is to design a fuzzy $H_{\infty}$ controller for HIV/AIDS infection system with dual drug dosages which can be represented by a Takagi-Sugeno (TS) fuzzy model. Based on an LMI approach, we develop a state-feedback controller for HIV/AIDS infection system with dual drug dosages such that the $L_2$-gain of the mapping from the exogenous input noise to the regulated output is less than a prescribed value. This paper is organized as follows. In Section II, system descriptions and definition are presented. In Section III, based on an LMI approach we develop a technique for designing a fuzzy $H_{\infty}$ controller for HIV/AIDS infection system with dual drug dosages that guarantees the $L_2$-gain of the mapping from the exogenous input noise to the regulated output is less than a prescribed value. The validity of this approach is finally demonstrated through simulation results in Section IV. Finally in Section V, the conclusion is given.

II. SYSTEM DESCRIPTIONS AND DEFINITION

A. HIV dynamic model

Figure 2 shows HIV model which describes the interaction of three variables; the healthy cells, the free virus, and the infected cells. In most cases, HIV virus affects the level of CD4+T cells which these cells are important in helping a body fighting to infection. Free virus means the HIV virus found in blood plasma. The healthy CD4+T cells are produced from a source, such as the thymus represented by constant rate $s$ and died at rate $d$. The coefficient $\beta$ is the infection rate. The infected cells result from the infection of healthy CD4+T cells and die at a rate $\mu$. A free-virus particle is known as virions, so called viral load, and cleared at a rate $c$ (death rate of virus). The variable $k$ is a rate of virions product per infection CD4+T cell.

The infection described previously can be summarized by differential equations [1].

\[
\begin{align*}
\dot{x}_1(t) &= s - dx_1(t) + \beta x_1(t)x_3(t) \\
\dot{x}_2(t) &= \beta x_1(t)x_3(t) - \mu x_2(t) \\
\dot{x}_3(t) &= kx_2(t) - cx_3(t)
\end{align*}
\]  

(1)

where $x_1(t)$ is concentration of healthy cells or T cells, $x_2(t)$ is concentration of infected cells, $x_3(t)$ is concentration of virions (free virus particles), $s$ is the constant rate to produce the healthy CD4+T cells, $d$ is the death rate of the healthy CD4+T cells, $\beta$ is the coefficient of the infection rate, $\mu$ is death rate of the infected cells, $k$ is a rate of virions product per infection CD4+T cell, and $c$ is death rate of virus.

Current treatment for HIV infection consists of highly active antiretroviral therapy, or HAART. The HAART treatment used drug in the group of protease inhibitor. The doctors will assess the viral load, CD4+T counts, rapidity of CD4+T decline, and patient readiness. While deciding, the doctors recommend initiating treatment to the patient [6]. The parameters and typical values are listed in Table 1 [5]. The information of HIV model parameters obtain from [5] which the initial conditions correspond to a healthy person infected with a virus given by Table I. In 2007, M. Barao and J.M. Lemos proposed the nonlinear dynamic model to describe HIV with treatment as follows [5]:

\[
\begin{align*}
\dot{x}_1(t) &= s - dx_1(t) + (1 - u_1(t))\beta x_1(t)x_3(t) \\
\dot{x}_2(t) &= (1 - u_1(t))\beta x_1(t)x_3(t) - \mu x_2(t) \\
\dot{x}_3(t) &= (1 - u_2(t))kx_2(t) - cx_3(t)
\end{align*}
\]

(2)

where the controller input $u_1(t)$ and $u_2(t)$ are a number of expedient drugs in the treatment of HAART represented by Reverse Transcriptase Inhibitors-RTI (to reduce the virus performance) and Protease Inhibitors-PI (to reduce the productivity of free virions), respectively [5]. The healthy CD4+T cells are produced from a source, such as the thymus represented by constant rate $s$ and died at rate $d$. The coefficient $\beta$ is the infection rate. The death rate of virus is described by $c$.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Typical Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t$</td>
<td>-</td>
<td>Days</td>
</tr>
<tr>
<td>$d$</td>
<td>0.02</td>
<td>Day</td>
</tr>
<tr>
<td>$k$</td>
<td>100</td>
<td>Count Cell$^{-1}$</td>
</tr>
<tr>
<td>$s$</td>
<td>100 mm$^3$</td>
<td>Day</td>
</tr>
<tr>
<td>$\beta$</td>
<td>$2.4 \times 10^{-5}$ mm$^3$</td>
<td>Day</td>
</tr>
<tr>
<td>$c$</td>
<td>2.4</td>
<td>Day</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.24</td>
<td>Day</td>
</tr>
</tbody>
</table>

The model includes antiretroviral treatment and factors such as adhesion and medication potency. The concepts of our proposes are joined with fuzzy set theory and exogenous input noise with biological variable values such as person factor, mental state etc.

Mostly, HIV virus dynamics are modeled using a nonlinear represented by cell. Each cell represents an uninfected cell, an infected cell of the type T lymphocyte of CD4+, a free virus particle, or specific antibodies such as CTL (Cytotoxic T Lymphocyte). Due to the inherent uncertainties of HIV, the antiretroviral treatment is modeled using a fuzzy rule-based system whose output depends on the medication potency and the rate of adhesion to the treatment. The fuzzy rule-based system consists of input processor, fuzzy rule-based (a collection of fuzzy rules), fuzzy inference machine, and
output processor. Inputs processors are encoded into fuzzy sets
on the respective universes of the input variables. While the
rule-based is a component of fuzzy rule-based systems, which
is a collection of fuzzy conditional propositions in the form
of if-then rules. Fuzzy rules are an effective mean to encode
expert knowledge expressed through linguistic statements.
In general, if-then rules describe relationships between linguistic
variables. Fuzzy machine performs an approximate reasoning
use the compositional rule of inference. Finally, in fuzzy
rule-based systems, the inferred output is a fuzzy set. Often,
especially in biological systems model, we require a real-
valued output.

B. Nonlinear fuzzy model

The class of nonlinear systems under consideration is described
by the following fuzzy system model:

Plant Rule i:

IF \( x_1(t) \) is \( M_{i1} \) and ... and \( x_v(t) \) is \( M_{iv} \)
THEN

\[
\begin{align*}
\dot{x}(t) &= A_i x(t) + B_w w(t) + B_i u(t), \\
z(t) &= C x(t) + D u(t)
\end{align*}
\]

where \( i = 1, 2, \ldots, r \), \( M_{ik} \) are fuzzy sets, \( x_i(t) \)
are premise variables, \( x(t) \in \mathbb{R}^n \) is the state vector,
and \( w(t) \in \mathbb{R}^p \) is the disturbance. \( z(t) \in \mathbb{R}^s \)
is the controlled output, \( A_i, B_i, B_w, C \) and \( D \)
are of appropriate dimension and \( r \) is the number of IF-THEN
rules.

For given any state vector \( x(t) \) and the control input \( u(t) \),
the TS fuzzy model is inferred as follows:

\[
\begin{align*}
\dot{x}(t) &= \sum_{i=1}^{r} h_i(x) A_i x(t) + \sum_{i=1}^{r} h_i(x) B_i u(t) + B_w w(t), \\
z(t) &= C x(t) + D u(t)
\end{align*}
\]

where \( h_i(x(t)) = \prod_{k=1}^{v} M_{ik}(x_k(t)), \quad h_i(x(t)) = \sum_{i=1}^{r} \bar{w}_i(x(t)) \).

The final fuzzy controller can be inferred as

\[
\begin{align*}
\dot{x}(t) &= \sum_{i=1}^{r} \sum_{j=1}^{r} h_i(x) h_j(x) [A_i + B_i K_j] x(t) + B_w w(t), \\
z(t) &= \sum_{j=1}^{r} h_j(x) [C + DK_j] x(t).
\end{align*}
\]

The following result deals with the system above.

Theorem 1: Given the system (11)-(12), the inequality (9)
holds if there exists a positive definite symmetric matrix \( P \)
satisfying the following conditions

\[
\begin{bmatrix}
A_i P + P A_i^T \\
+ B_i Y_j + Y_j^T B_i^T \\
B_w^T \gamma I \\
CP + DY_j
\end{bmatrix}
\begin{bmatrix}
(*)^T \\
(*)^T \\
-\gamma^2 I \\
-\gamma^2 I
\end{bmatrix}
< 0,
\]

\[
\forall i, j = 1, 2, \ldots, r.
\]

Furthermore, a suitable choice of the fuzzy controller is

\[
u(t) = \sum_{j=1}^{r} h_j(x) K_j x(t)
\]

where

\[
K_j = Y_j P^{-1}.
\]

Proof: Let choose a Lyapunov function

\[
V(x(t)) = x^T(t) Q x(t).
\]

Let us recall the following definition.

Definition 2.1: Suppose \( \gamma \) is a given positive real number.
A system of the form (7)-(8) is said to have \( L_2 \) gain less than
or equal to \( \gamma \) if

\[
\int_0^{T_f} z^T(t) z(t) dt \leq \gamma^2 \int_0^{T_f} w^T(t) w(t) dt,
\]

(9)

for all \( T_f \geq 0 \) and \( w(t) \in L_2[0, T_f] \).

Note that for the symmetric block matrices, we use (*) as an
elliptis for terms that are induced by symmetry.
Differentiate $V(x(t))$ along the system (11) with the controller (14) yields

$$
\dot{V}(x(t)) = z^T(t)Qz(t) + x^T(t)Q\dot{x}(t)
$$

or in a more compact form as:

$$
\begin{pmatrix}
(A_i + B_iK_j)^T Q \\
+Q(A_i + B_iK_j) \\
+(C + DK_j)^T(C + DK_j)
\end{pmatrix}
\begin{pmatrix}
(*)^T \\
(*)^T \\
(*)^T
\end{pmatrix} < 0. \quad (23)
$$

Since (23) is less than zero and the fact that $h_i(x) \geq 0$ and $\sum_{i=1}^r h_i(x) = 1$, (18) becomes

$$
\dot{V}(x(t)) \leq -z^T(t)z(t) + \gamma^2 w^T(t)w(t). \quad (24)
$$

Integrate both sides of (24) yields

$$
\int_0^{T_f} \dot{V}(x(t))dt \leq \int_0^{T_f} [-z^T(t)z(t) + \gamma^2 w^T(t)w(t)] dt
$$

$$
V(x(t)) + V(x(0)) \leq \int_0^{T_f} [-z^T(t)z(t) + \gamma^2 w^T(t)w(t)] dt.
$$

Assuming that initial condition $x(0) = 0$, we have

$$
V(x(t)) \leq \int_0^{T_f} [-z^T(t)z(t) + \gamma^2 w^T(t)w(t)] dt.
$$

Since $V(x(t)) > 0$, this implies

$$
0 \leq \int_0^{T_f} [-z^T(t)z(t) + \gamma^2 w^T(t)w(t)] dt
$$

or

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

Hence, the inequality (9) holds.

IV. Simulation results

A simulation result is given in this section to illustrate the procedure of designing a fuzzy controller. Let us recall (2) included with noise term. The parameters and typical values are listed in Table 1.

$$
\begin{align*}
\dot{x}_1(t) &= s - dx_1(t) - (1 - u_1(t))b_x1(t)x_2(t) + w_1(t) \\
\dot{x}_2(t) &= (1 - u_1(t))b_x2(t)x_1(t) - mx_2(t) + w_2(t) \\
\dot{x}_3(t) &= (1 - u_2(t))kx_2(t) - c_3x_3(t) + w_3(t)
\end{align*}
$$

where $w_1(t), w_2(t)$ and $w_3(t)$ are the disturbance factor from the patients and the controlled output is

$$
z(t) = [x_1(t) \quad u_1(t) \quad u_2(t)]^T. \quad (26)
$$

The nonlinear system plant can be approximated by TS fuzzy rules. Let us choose the membership functions of the fuzzy sets as follows.

$$
M_1(x_1(t)) = \begin{cases} 
1 & : x_1(t) \leq 200 \\
3 - 0.01x_1(t) & : 200 < x_1(t) \leq 300 \\
0 & : x_1(t) > 300
\end{cases}
$$

$$
M_2(x_1(t)) = \begin{cases} 
0.01x_1(t) - 2 & : 200 < x_1(t) \leq 300 \\
1 & : 300 < x_1(t) \leq 500 \\
6 - 0.01x_1(t) & : 500 < x_1(t) \leq 600
\end{cases}
$$

$$
M_3(x_1(t)) = \begin{cases} 
0 & : x_1(t) \leq 500 \\
0.01x_1(t) - 5 & : 500 < x_1(t) \leq 600 \\
1 & : x_1(t) > 600
\end{cases}
$$
The membership functions of three variables which are the healthy cell of CD4+T, the infected cells and the free cells are shown in Figure 3. The TS fuzzy plant model can be obtained as:

**Plant Rule i:**

IF $x_1(t)$ is $M_i$ and $x_2(t)$ is $N_j$ and $x_3(t)$ is $q_k$

THEN

$$
\dot{x}(t) = A_i x(t) + B_i u(t) + B_w w(t),
$$

$$
z(t) = C x(t) + D u(t)
$$

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

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

$$
B_i = \begin{bmatrix} \beta x_1(t) x_2(t) & 0 & 0 \\ -\beta x_1(t) x_3(t) & 0 & 0 \\ 0 & k x_2(t) & 0 \end{bmatrix},
C = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},
$$

$$
D = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}.
$$

Using the LMI optimization algorithm and following Theorem 1 with set as $\gamma = 0.1$, we obtain the results given in Figure 4 - 6.

**Remark 1:** When a body has been received HIV virus in primary infection (about 4-8 weeks), the doctors will assess the viral load, CD4+T counts, rapidity of CD4+T decline, and patient readiness before beginning treatment. The simulation results given in Figure 4 show the level of CD4+T counts,
reverse transcriptase inhibitors-RTI to reduce the virus performance, and protease inhibitors-PI to reduce the productivity of free virions. Figure 4 shows the plot of healthy calls, i.e., if CD4+T are more than 500 cells/µL the patient will develop the disease of HIV at low risk. Figure 5 shows the plot of Reverse Transcriptase Inhibitors-RTI, which are a class of antiretroviral drug used to treat HIV infection, tumors, and cancer. RTIs inhibit activity of reverse transcriptase, a viral DNA polymerase enzyme that retroviruses need to reduce the virus performance, and Figure 6 shows the plot of Protease Inhibitors-PI, which are molecules that inhibit the function of proteases.

![Graph 1: Healthy cell count over time](image1.png)

**Fig. 4.** The simulation result of dual drug dosages for healthy cell, $x_1(t)$.

![Graph 2: Drug concentration over time](image2.png)

**Fig. 5.** The simulation result of dual drug dosages for RTI, $u_1(t)$.

V. CONCLUSION

This paper has presented a $H_\infty$ fuzzy control design for nonlinear positive HIV infection dynamic model. This paper has developed a fuzzy controller for applying in HIV nonlinear dynamic model to solve with antiretroviral therapy by used a fuzzy rule-based system with two inputs, the medication potency and the treatment adhesion rate. The effective of controller can prevent infection. The progression is the key to success of fighting against AIDS.

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