

A New Design Method for TS Fuzzy Static Output Feedback Control of the Glucose/Insulin Model with Time-Delay

Mohammad Hassan Asemani*, Ramin Vatankhah, Sajad Taghvaei

Abstract— High blood glucose levels in the body named diabetes can increase damage in kidneys, eyes, heart and etc. In this investigation, a novel TS fuzzy static output feedback control structure is proposed to regulate the blood glucose level in the pre-defined desired values for type 1 diabetes using exogenous intra-venous insulin delivery rate. To this end, a nonlinear delay differential equation framework is considered to model the blood glucose/insulin endocrine metabolic regulatory system. The governing equations of the blood glucose/insulin model are approximated by a TS fuzzy model and then the proposed static output feedback controller is designed for this TS model.

Index Terms— Blood glucose, Glucose/insulin metabolism model, Delay differential equation, TS fuzzy systems, Output feedback controller.

I. INTRODUCTION

High levels of blood glucose known as a major chronic disease named "diabetes". This disease arises because of defects in insulin production, insulin action or both and so the body cannot adjust the amount of glucose in the blood [1, 2]. The main role of two hormones which are glucagon and insulin is to control the level of glucose in the blood. A healthy range of the blood glucose is identified as 70–120 mg/dL in healthy people [3, 4].

Failure and damage in different organs such as kidneys, eyes and heart and also abnormalities of lipoprotein metabolism, periodontal disease and hypertension occur in patients with high levels of blood glucose [5, 6]. Therefore, studying the dynamics behavior of the blood glucose/insulin and investigating the effects of insulin therapy in regulation of the amount of blood glucose are classified as significant subjects in the biomedical engineering literature. In this way, various methods have been proposed to model the blood glucose/insulin dynamics in literature.

Bergman et al. [7] proposed an original mathematical model for glucose disappearance to estimate insulin sensitivity. Caumo and Cobelli [8] modified the Bergman's model and

established a new two-compartment minimal model of glucose kinetics to describe the time-varying impulse response of the glucose system. Considering six-compartments representation of glucose homeostasis, Sorensen [9] investigated a novel mathematical model composed of almost 19 Ordinary Differential Equations (ODE) which illustrate physiologic compartments and spaces on the organ and tissue levels. Gaetano and Arino [10] prove that the delay of insulin secretion during the intravenous injection tolerance test can affect the dynamics behavior of the blood glucose, and consequently suggested a new model that can clarify the essential physiological mechanism with considering the delay of insulin secretion. In the above-mentioned models, constant insulin supply at the same average rate has been considered. Tolic et al. [11] developed a mathematical model of the insulin/glucose feedback regulation in man in which the effects of an oscillatory supply of insulin contain. Applying the mass conservation law, Li et al. [12] model the blood glucose/insulin endocrine metabolic regulatory system by Delay Differential Equations (DDE) with two time delay terms for insulin secretion.

One of the significant solutions for regulating the level of blood glucose in the desired healthy interval is designing a proper nonlinear control scheme to determine the insulin injection as the control input by a real-time algorithm. To this end, many investigators proposed and implemented various control strategies for different glucose/insulin mathematical models. In [13-15], Proportional-Integral-Derivative (PID) controllers have been proposed for model-less glucose/insulin systems in which the control rule is designed based on experimental data. Patra et al. [16] proposed a switching optimal robust controller for blood glucose regulation using clinically acceptable insulin delivery rates. Using a novel parametric programming algorithm, Dua et al. [17] suggested a model-based control technique for patients with type 1 diabetes. Palumbo et al. [18] considered the problem of tracking a desired plasma glucose evolution using intra-venous insulin administration in which the glucose/insulin system is modeled via a discrete-delay nonlinear differential equation. Using Mamdani-type fuzzy logic, Yasini et al. [19] proposed a knowledge-based controller for type 1 diabetes mellitus patients to control the level of glucose in the blood in the presence of uncertainty in model parameters and measurement noise. Considering the augmented minimal mode as the nonlinear model of type 1 diabetes, Goharimanesh et al. [20]

Manuscript received, November 3, 2016; accepted, February 3, 2017

M. H. Asemani is an assistant professor of Electrical Engineering with School of Electrical and Computer Engineering, Shiraz University, Zand St., Shiraz, Iran (email: asemani@shirazu.ac.ir). R. Vatankhah and S. Taghvaei are assistant professors of Mechanical engineering with School of Mechanical Engineering, Molasadra St., Shiraz, Iran (e-mail: rvatankhah@shirazu.ac.ir, sj.taghvaei@shirazu.ac.ir).

compared the performances of fuzzy type-1 and fuzzy type-2 controllers for blood glucose regulation with uncertainties in the model due to the daily meals and sudden stresses. Duangpim and Assawinchaichote [21] utilized Takagi-Sugeno-Kang (TSK) fuzzy scheme to model the nonlinear system of blood glucose and adjust the blood glucose in an acceptable range by means of linear matrix inequality (LMI) approach and H^∞ control structure.

Surveying the literature, one can obtain that nonlinear discrete DDEs can better predict the dynamics behavior of glucose/insulin compared to the mathematical models derived based on nonlinear ODEs. This is because of the existence of delay in insulin secretion [22-24]. Consequently, it is expected that DDEs framework as a more accurate glucose/insulin model are chosen for controller design. A closed loop control system may be implemented based on the information provided from glucose sensors which presents the values of necessary states for calculation of the insulin infusion rate as the control signal.

In this paper, we propose a new method for designing a TS fuzzy static output feedback controller for the class of nonlinear systems with time-delay which are represented by the T-S model. In contrast with the other existing results in the literature for the static output feedback controller design of TS fuzzy systems such as [25-27], in our proposed method the equality constraint has not been directly used in the design of LMIs which improves the feasibility of the design conditions. Moreover, we approximate the glucose/insulin system dynamics by a TS fuzzy model and then apply the proposed static output feedback design method to this TS model. Finally, we illustrate the validity of the proposed controller in tracking pre-defined values of glucose and insulin.

II. PROBLEM FORMULATION AND PRELIMINARIES

In this section, we describe the glucose/insulin system and the TS fuzzy system with time-delay and then propose an approximate T-S fuzzy model of the glucose/insulin system will be obtained. Finally, some useful lemmas which will be used in the proof of the main results of the paper will be presented in this section.

The mathematical model of the glucose/insulin metabolism To describe the dynamics behavior of the glucose/insulin metabolism, we consider a time-delay differential equation framework as a more accurate glucose/insulin mathematical model. Due to proper balance between accuracy and simplicity, the single discrete-delay differential equation system reported in [24] is an appropriate glucose/insulin model. Considering apparent delay τ_g with which the pancreas varies secondary insulin release in response to varying plasma glucose concentrations and control input $u(t)$ as the exogenous intra-venous insulin delivery rate, the corresponding DDE of this model is written as [24]

$$\begin{aligned}\dot{G}(t) &= -K_{xgi} G(t)I(t) + \frac{T_{gh}}{V_G}, \\ \dot{I}(t) &= -K_{xi} I(t) + \frac{T_{iG \max}}{V_I} f(G(t - \tau_g)) + u(t),\end{aligned}\quad (1)$$

where the nonlinearity $f(\cdot)$ indicates the mathematical model of the pancreatic insulin delivery rate and is specified as [24]:

$$f(G) = \frac{\left(\frac{G}{G^*}\right)^\gamma}{1 + \left(\frac{G}{G^*}\right)^\gamma}.\quad (2)$$

In abovementioned equations, state variables $G(t)$ and $I(t)$ indicate plasma glycemia and insulinemia, respectively. Furthermore, K_{xgi} illustrates the rate of glucose uptake by tissues, T_{gh} is the net balance between hepatic glucose output and insulin-independent zero-order glucose tissue uptake, V_G shows the apparent distribution volume for glucose, K_{xi} indicates the apparent first-order disappearance rate constant for insulin, $T_{iG \max}$ is the maximal rate of second-phase insulin release, V_I states the apparent distribution volume for insulin, γ specifies the progressivity with which the pancreas reacts to circulating glucose concentrations and G^* is the glycemia at which the insulin release is half of its maximal rate [24].

A. TS Fuzzy Model with time-delay

A nonlinear system can be exactly represented by a TS fuzzy model using some IF-THEN rules, each of which define the linear input-output relation of the original nonlinear system. A TS fuzzy model is constructed by nonlinear combination of these linear models. The general form of a TS model with time-delay is described by the following equation:

$$\dot{x}(t) = \sum_{i=1}^r h_i(\mu(t)) \{A_i x(t) + A_i^\tau x(t - \tau) + B_{2i} u(t) + B_{1i} w(t)\},\quad (3)$$

$$y(t) = \sum_{i=1}^r h_i(\mu(t)) C_i x(t),\quad (4)$$

where $\mu(t) = [\mu_1(t) \ \mu_2(t) \ \dots \ \mu_p(t)]$, $\mu_1(t) \sim \mu_p(t)$ are fuzzy premise variables which are functions of state variables, r is the number of rules, τ is the time-delay, $x(t) \in \mathfrak{R}^n$ is the state vector, $u(t) \in \mathfrak{R}^m$ is the control input vector, $y(t) \in \mathfrak{R}^q$ is the output vector, $w(t) \in \mathfrak{R}^d$ is the disturbance signal, and $A_i \in \mathfrak{R}^{n \times n}$, $A_i^\tau \in \mathfrak{R}^{n \times n}$, $B_{2i} \in \mathfrak{R}^{n \times m}$, $B_{1i} \in \mathfrak{R}^{n \times d}$, $C_i \in \mathfrak{R}^{q \times n}$ stand for linear sub-system matrices. Moreover, the functions $h_i(\mu(t))$ are defined as:

$$h_i(\mu(t)) = w_i(\mu(t)) / \sum_{i=1}^r w_i(\mu(t)),\quad (5)$$

with $w_i(\mu(t)) = \prod_{j=1}^p M_{ij}(\mu_j(t))$ and M_{ij} is the membership

function associated with the i -th rule and j -th premise variable. It is noted that in a TS model, the following equations hold:

$$0 \leq h_i(\mu(t)) \leq 1,$$

$$\sum_{i=1}^r h_i(\mu(t)) = 1. \quad (6)$$

Notation. The following notation will be used in this paper:

$$A_\mu = \sum_{i=1}^r h_i(\mu) A_i \quad (7)$$

B. TS fuzzy representation of the glucose/Insulin system

In the glucose model, one needs to set the value of the $G(t)$ and $I(t)$ into non-zero values and the controller design issue is in fact a tracking problem. Thus, we first define $\tilde{G}(t) = G(t) - G_{ref}(t)$ and $\tilde{I}(t) = I(t) - I_{ref}(t)$, then the dynamical equations (1)-(2) are transformed to the following error dynamics:

$$\begin{aligned} \dot{\tilde{G}}(t) = & -K_{xgi} \tilde{G}(t) \tilde{I}(t) - K_{xgi} \tilde{G}(t) I_{ref}(t) - K_{xgi} \tilde{I}(t) G_{ref}(t) \\ & - K_{xgi} G_{ref}(t) I_{ref}(t) + \frac{T_{gh}}{V_G} \dot{G}_{ref}(t), \end{aligned} \quad (8)$$

$$\begin{aligned} \dot{\tilde{I}}(t) = & -K_{xi} \tilde{I}(t) - K_{xi} I_{ref}(t) + \dot{I}_{ref}(t) \\ & + \frac{T_{iG \max}}{V_I} f(\tilde{G}(t - \tau_g) + G_{ref}(t - \tau_g)) + u(t). \end{aligned}$$

In this paper, we consider the signals $-K_{xgi} G_{ref}(t) I_{ref}(t) + \frac{T_{gh}}{V_G} \dot{G}_{ref}(t)$ and $-K_{xi} I_{ref}(t) + \dot{I}_{ref}(t)$ as disturbance signals $w_1(t)$ and $w_2(t)$, respectively. Thus, the dynamical error system is given by:

$$\begin{aligned} \dot{\tilde{G}}(t) = & -K_{xgi} \tilde{G}(t) \tilde{I}(t) - K_{xgi} \tilde{G}(t) I_{ref}(t) \\ & - K_{xgi} \tilde{I}(t) G_{ref}(t) + w_1(t), \\ \dot{\tilde{I}}(t) = & -K_{xi} \tilde{I}(t) + \frac{T_{iG \max}}{V_I} f(\tilde{G}(t - \tau_g) + G_{ref}(t - \tau_g)) \\ & + u(t) + w_2(t). \end{aligned} \quad (9)$$

In the sequel, we derive the TS model of the error system (9). Using the sector nonlinearity approach [28] and by assuming $G(t) \in [G_{\min}, G_{\max}]$ with positive pre-scribed values of G_{\min}, G_{\max} , it is not hard to show that the following time-delay TS fuzzy model is an approximation of the original nonlinear error dynamics (9):

$$\begin{aligned} \dot{x}(t) = & \sum_{i=1}^4 h_i(\mu) (A_i x(t) + A_i^\tau x(t - \tau) + B_{2i} u(t) + B_{1i} w(t)), \\ y(t) = & \sum_{i=1}^4 h_i(\mu) C_i x(t), \end{aligned} \quad (10)$$

where $\mu(t) = [\tilde{G}(t) \quad \tilde{G}(t - \tau_g)]$, $w(t) = [w_1(t) \quad w_2(t)]^T$, and:

$$\begin{aligned} A_1 = A_2 = & \begin{bmatrix} -K_{xgi} I_{ref} & -K_{xgi} G_{\max} \\ 0 & -K_{xi} \end{bmatrix}, \\ A_3 = A_4 = & \begin{bmatrix} -K_{xgi} I_{ref} & -K_{xgi} G_{\min} \\ 0 & -K_{xi} \end{bmatrix}, \\ A_1^\tau = A_3^\tau = & \begin{bmatrix} 0 & 0 \\ \tilde{f}_{\max} & 0 \end{bmatrix}, \\ A_2^\tau = A_4^\tau = & \begin{bmatrix} 0 & 0 \\ \tilde{f}_{\min} & 0 \end{bmatrix}, \\ B_{21} = B_{22} = B_{23} = B_{24} = & \begin{bmatrix} 0 \\ 1 \end{bmatrix}, \\ B_{11} = B_{12} = B_{13} = B_{14} = & I_2, \\ C_1 = C_2 = C_3 = C_4 = & [1 \quad 0], \end{aligned} \quad (11)$$

with:

$$\begin{aligned} \tilde{f}_{\max} = & \frac{T_{iG \max}}{V_I} \times \max_{\tilde{G}(t)} \frac{f(\tilde{G}(t))}{\tilde{G}(t)}, \\ \tilde{f}_{\min} = & \frac{T_{iG \max}}{V_I} \times \min_{\tilde{G}(t)} \frac{f(\tilde{G}(t))}{\tilde{G}(t)}. \end{aligned} \quad (12)$$

Moreover, the nonlinear aggregation functions $h_i(\mu(t))$ for $i = 1, \dots, 4$ are defined as:

$$\begin{aligned} h_1(\mu(t)) = & M_1(\tilde{G}(t)) N_1(\tilde{G}(t - \tau_g)), \\ h_2(\mu(t)) = & M_1(\tilde{G}(t)) N_2(\tilde{G}(t - \tau_g)), \\ h_3(\mu(t)) = & M_2(\tilde{G}(t)) N_1(\tilde{G}(t - \tau_g)), \\ h_4(\mu(t)) = & M_2(\tilde{G}(t)) N_2(\tilde{G}(t - \tau_g)), \end{aligned} \quad (13)$$

where:

$$\begin{aligned} M_1(\tilde{G}(t)) = & \frac{\tilde{G}(t) - \tilde{G}_{\min}}{\tilde{G}_{\max} - \tilde{G}_{\min}}, \\ M_2(\tilde{G}(t)) = & 1 - M_1(\tilde{G}(t)), \\ N_1(\tilde{G}(t - \tau_g)) = & \frac{\tilde{f}(\tilde{G}(t - \tau_g)) - \tilde{f}_{\min}}{\tilde{f}_{\max} - \tilde{f}_{\min}}, \\ N_2(\tilde{G}(t - \tau_g)) = & 1 - N_1(\tilde{G}(t - \tau_g)), \end{aligned} \quad (14)$$

with:

$$\tilde{f}(\tilde{G}(t - \tau_g)) = \frac{f(\tilde{G}(t - \tau_g))}{\tilde{G}(t - \tau_g)}. \quad (15)$$

C. Preliminaries

The following lemmas will be used in the proof of the main results of this section.

Lemma 1 [29]: For all matrices χ_{ij} , $i, j = 1, \dots, r$, if the following inequalities hold:

$$\chi_{ii} > 0, \quad i = 1, \dots, r, \quad (16)$$

$$\frac{2}{r-1} \chi_{ii} + \chi_{ij} + \chi_{ji} > 0, \quad i, j = 1, \dots, r, i \neq j, \quad (17)$$

then the following inequality holds:

$$\sum_{i=1}^r \sum_{j=1}^r h_i(\mu) h_j(\mu) \chi_{ij} > 0. \quad (18)$$

Lemma 2 [30]: Suppose that matrix $M \in \mathfrak{R}^{m \times n}$ with

$rank(M) = m$ is given. Assuming that $X \in \mathfrak{R}^{n \times n}$ is a symmetric matrix, then the equality $MX = \bar{X}M$ holds for a matrix $\bar{X} \in \mathfrak{R}^{m \times m}$ if and only if X is partitioned by:

$$X = V \begin{bmatrix} X_{11} & 0 \\ 0 & X_{22} \end{bmatrix} V^T, \quad (19)$$

where M is decomposed as $M = U[S \ 0]V^T$.

III. NOVEL TS FUZZY H_∞ DELAYED STATIC OUTPUT FEEDBACK CONTROLLER DESIGN

In this section, we propose a new method for TS fuzzy H_∞ static output feedback controller design of TS fuzzy systems with time-delay in the form of

(3)-(4). The design goal is to find a controller such that the following H_∞ -performance criterion is satisfied:

$$\sup_{\substack{w(t) \in L_2 \\ w(t) \neq 0}} \frac{\|z(t)\|_{L_2}}{\|w(t)\|_{L_2}} \leq \gamma, \quad (20)$$

where $z(t) = C_1 x(t)$ is the controlled output and γ is the disturbance attenuation level.

To design the static output feedback controller, we assume that the TS fuzzy system output matrices are the same; i.e. $C_{2i} = C$ ($i = 1, \dots, r$).

A. Static output feedback controller

The static output feedback control signal is defined as:

$$u(t) = \sum_{i=1}^r h_i(\mu(t)) K_i y(t), \quad (21)$$

where K_i 's are controller gains to be designed.

B. Closed-loop dynamics

By substituting the controller (21) in

(3)-(4), the following closed-loop dynamics will be derived:

$$\begin{aligned} \dot{x}(t) = & \sum_{i=1}^r \sum_{j=1}^r h_i(\mu(t)) h_j(\mu(t)) \\ & \times \{(A_i + B_{2i} K_j C)x(t) + A_i^\tau x(t - \tau) + B_{1i} w(t)\}, \end{aligned} \quad (22)$$

or equivalently:

$$\dot{x}(t) = A_{cl}^{\mu\mu} x(t) + A_{cl}^\tau x(t - \tau) + B_{1\mu} w(t), \quad (23)$$

Where $A_{cl}^{\mu\mu} = \sum_{i=1}^r \sum_{j=1}^r h_i(\mu(t)) h_j(\mu(t)) \{(A_i + B_{2i} K_j C)$ and

notation (7) is used.

It should be noted that the approximate TS model of the glucose/insulin system in

(10) is in the form of the T-S fuzzy system with time-delay (3)-(4) and the proposed results of the next section will be applicable to this system.

C. Novel TS fuzzy controller design

In the following Theorem, we propose some LMIs to design the controller (21) such that the performance criterion (21) is

satisfied for the closed-loop system (23).

Theorem 1. Suppose that the TS fuzzy system output matrix C is represented by its SVD form as $C = U[S \ 0]V^T$. Then, the closed-loop TS system with time-delay (23) is asymptotically stable when $w(t) = 0$ and satisfies the performance index (21) with $w(t) \neq 0$ if there exist symmetric positive definite matrices $X_{11}, X_{22}, \bar{P}_1$ and matrices M_i ($i = 1, \dots, r$) such that the following LMIs hold:

$$\Omega_{ii} < 0, \quad i = 1, \dots, r, \quad (24)$$

$$\frac{2}{r-1} \Omega_{ij} + \Omega_{ij} + \Omega_{ji} < 0, \quad i, j = 1, \dots, r, i \neq j, \quad (25)$$

where:

$$\Omega_{ij} = \begin{pmatrix} \Omega_{ij}^{11} & A_i^\tau X & B_{ii} & X C_1^T \\ X (A_i^\tau)^T & -\bar{P}_1 & 0 & 0 \\ B_{ii}^T & 0 & -\bar{\gamma} I & 0 \\ C_1 X & 0 & 0 & -I \end{pmatrix}, \quad (26)$$

with $\Omega_{ij}^{11} = A_i X + B_{2i} M_j C + (A_i X + B_{2i} M_j C)^T + \bar{P}_1$, $\bar{\gamma} = \gamma^2$ and:

$$X = V \begin{bmatrix} X_{11} & 0 \\ 0 & X_{22} \end{bmatrix} V^T. \quad (27)$$

Moreover, the static output feedback controller gains K_i are derived by:

$$K_j = M_j \bar{X}_2^{-1}, \quad (28)$$

for $j = 1, \dots, r$, where $\bar{X}_2 = U S X_{11} S^{-1} U^{-1}$.

Proof: The Lyapunov-Krasovskiy functional candidate is defined as:

$$V(x(t)) = x^T(t) P x(t) + \int_0^\tau x^T(t-s) P_1 x(t-s) ds, \quad (29)$$

where $P = P^T > 0$ and $P_1 = P_1^T > 0$. The derivative of (29) along the closed-loop trajectories (23) is obtained as:

$$\begin{aligned} \dot{V}(x(t)) &= \dot{x}^T(t) P x(t) + x^T(t) P \dot{x}(t) + x^T(t) P_1 x(t) \\ &\quad - x^T(t - \tau) P_1 x(t - \tau) + x^T(t) P w + w^T P x(t) \\ &= x^T(t) (P A_{cl}^{\mu\mu} + (A_{cl}^{\mu\mu})^T P + P_1) x(t) \\ &\quad + x^T(t) P A_{cl}^\tau x(t - \tau) + x^T(t - \tau) (A_{cl}^\tau)^T P x(t) \\ &\quad - x^T(t - \tau) P_1 x(t - \tau) + x^T(t) P B_{1\mu} w + w^T B_{1\mu}^T P x(t). \end{aligned} \quad (30)$$

It is well-known that the following inequality is a sufficient condition for (21):

$$\dot{V}(x(t)) + z^T(t) z(t) - \gamma^2 w^T(t) w(t) < 0. \quad (31)$$

Replacing $\dot{V}(x(t))$ in (30) into (31)

$$\begin{pmatrix} x(t) \\ x(t - \tau) \\ w(t) \end{pmatrix}^T \tilde{\Omega} \begin{pmatrix} x(t) \\ x(t - \tau) \\ w(t) \end{pmatrix} < 0, \quad (32)$$

with:

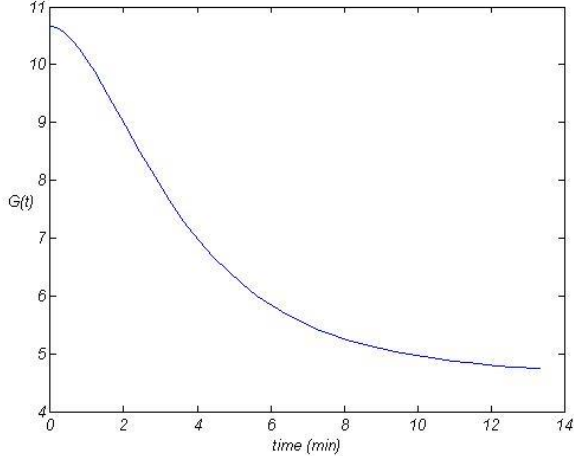


Fig. 1. Variations of plasma glycemia, G [mM] in terms of time [min].

$$\tilde{\Omega} = \begin{pmatrix} PA_{cl}^{\mu\mu} + (A_{cl}^{\mu\mu})^T P + P_1 + C_1^T C_1 & PA_{\mu}^{\tau} & PB_{1\mu} \\ (A_{\mu}^{\tau})^T P & -P_1 & 0 \\ B_{1\mu}^T P & 0 & -\gamma^2 I \end{pmatrix}$$

or equally:

$$\begin{pmatrix} PA_{cl}^{\mu\mu} + (A_{cl}^{\mu\mu})^T P + P_1 + C_1^T C_1 & PA_{\mu}^{\tau} & PB_{1\mu} \\ (A_{\mu}^{\tau})^T P & -P_1 & 0 \\ B_{1\mu}^T P & 0 & -\gamma^2 I \end{pmatrix} < 0. \quad (33)$$

Pre- and post-multiplying (33) **Error! Reference source not found.** by $\text{diag}(X, X, I)$ with $X = P^{-1}$ results in:

$$\begin{pmatrix} \tilde{\Theta} & A_{\mu}^{\tau} X & B_{1\mu} \\ X (A_{\mu}^{\tau})^T & -\bar{P}_1 & 0 \\ B_{1\mu}^T & 0 & -\gamma^2 I \end{pmatrix} < 0, \text{ where} \quad (34)$$

$\tilde{\Theta} = A_{cl}^{\mu\mu} X + X (A_{cl}^{\mu\mu})^T + \bar{P}_1 + X C_1^T C_1 X$ and $\bar{P}_1 = X P_1 X > 0$ is an LMI variable. The term $A_{cl}^{\mu\mu} X + X (A_{cl}^{\mu\mu})^T$ is expressed as:

$$\begin{aligned} A_{cl}^{\mu\mu} X + X (A_{cl}^{\mu\mu})^T \\ = A_{\mu} X + B_{2\mu} K_{\mu} C X + (A_{\mu} X + B_{2\mu} K_{\mu} C X)^T. \end{aligned} \quad (35)$$

Now, suppose that the constraint $CX = \bar{X}C$ holds, where \bar{X} is a matrix variable. Then, equation (35) can be written by:

$$\begin{aligned} A_{cl}^{\mu\mu} X + X (A_{cl}^{\mu\mu})^T \\ = A_{\mu} X + B_{2\mu} M_{\mu} C + (A_{\mu} X + B_{2\mu} M_{\mu} C)^T, \end{aligned} \quad (36)$$

with $M_{\mu} = K_{\mu} \bar{X}$. By replacing (34) in (34) and then applying Schur complement on the resulting inequality, the following inequality is obtained:

$$\begin{pmatrix} \Theta & A_{\mu}^{\tau} X & B_{1\mu} & X C_1^T \\ X (A_{\mu}^{\tau})^T & -\bar{P}_1 & 0 & 0 \\ B_{1\mu}^T & 0 & -\gamma^2 I & 0 \\ C_1 X & 0 & 0 & -I \end{pmatrix} < 0. \quad (37)$$

with $\Theta = A_{\mu} X + B_{2\mu} M_{\mu} C + (A_{\mu} X + B_{2\mu} M_{\mu} C)^T + \bar{P}_1$.

Finally, by employing Lemma 1, it is clear that (24)-(25) is a sufficient condition for satisfying (37).

In the sequel, we use Lemma 2 to find equivalent conditions to satisfy $CX = \bar{X}C$. Using Lemma 1 and the SVD form of the matrix C , the condition $CX = \bar{X}C$ holds if X is partitioned as in (19). Therefore, to recover the controller gains from the solutions of the LMIs (24)-(25), one has:

$$K_j = M_j \bar{X}^{-1}. \quad (38)$$

Moreover, since \bar{X} is not directly appeared in the LMIs, we should offer a method to find it. One can use the conditions $CX = \bar{X}C$ associated by the special form of X in (27) to find the matrix \bar{X} :

$$U[S \ 0]V^T \begin{bmatrix} X_{11} & 0 \\ 0 & X_{22} \end{bmatrix} V^T = \bar{X}U[S \ 0]V^T. \quad (39)$$

It is known that $V^T V = I$ by using the properties of the SVD. Then, (39) can be written as:

$$\bar{X} = USX_{11}(US)^{-1} = USX_{11}S^{-1}U^{-1}. \quad (40)$$

Finally, the matrix \bar{X} is obtained by:

$$\bar{X} = USX_{11}(US)^{-1} = USX_{11}S^{-1}U^{-1}. \quad (41)$$

This completes the proof.

Remark 1. The main superiority of the proposed method in Theorem 1 in contrast with the other existing results in the literature for the static output feedback controller design of TS fuzzy systems with time-delay [27-29] is that the equality constraint $CX = \bar{X}C$ has not been directly used in the design LMIs which improves the feasibility of the design conditions. It is well-known that equality constraint is hard to be satisfied and complicates the solving procedure of the LMIs. This disadvantage of the equality constraint is not seen in our method since by using Lemma 2 we avoided appearance of this constraint in the design LMIs.

Remark 2. In the case that the reference signal of the glucose state variable in the glucose/insulin model (9) is constant; i.e. $G_{ref}(t) = G_{ref}$, an alternative method for designing the static output feedback controller without considering the H_{∞} -performance criterion could be considered. In fact, in this case the disturbance signal $w_1(t)$ equals to zero since $\dot{G}_{ref}(t) = 0$ and the special values of the parameters

$$K_{xgi}, G_{ref}, I_{ref}, T_{iG \max} \text{ and } V_G \text{ cause that } K_{xgi} G_{ref} I_{ref} = \frac{T}{V_G} [24].$$

Moreover, one can re-define the control signal $u(t)$ as $\bar{u}(t) + K_{xi} I_{ref}(t) - \dot{I}_{ref}(t)$, where $\bar{u}(t)$ is the new control signal to be designed. Thus, by this choice the term $w_2(t) = -K_{xi} I_{ref}(t) + \dot{I}_{ref}(t)$ is vanished. As a result, both disturbance signals $w_1(t)$ and $w_2(t)$ equal to zero. In this special case, one can use the following corollary to design the static output feedback controller.

Corollary 1. Suppose that the TS fuzzy system output matrix C is represented by its SVD form as $C = U[S \ 0]V^T$. Then, the closed-loop TS system with time-delay (23) with $w_1(t) = 0$, $w_2(t) = 0$ is asymptotically stable if there exist

symmetric positive definite matrices $X_{11}, X_{22}, \bar{P}_1$ and matrices $M_i (i = 1, \dots, r)$ such that the following LMIs hold:

$$\bar{\Omega}_{ii} < 0, \quad i = 1, \dots, r, \quad (42)$$

$$\frac{2}{r-1} \bar{\Omega}_{ii} + \bar{\Omega}_{ij} + \bar{\Omega}_{ji} < 0, \quad i, j = 1, \dots, r, i \neq j, \quad (43)$$

where:

$$\bar{\Omega}_{ij} = \begin{pmatrix} \bar{\Omega}_{ij}^{11} & A_i^T X \\ X (A_i^T)^T & -\bar{P}_1 \end{pmatrix}, \quad (44)$$

with $\bar{\Omega}_{ij}^{11} = A_i X + B_{2i} M_j C + (A_i X + B_{2i} M_j C)^T + \bar{P}$, $\bar{\gamma} = \gamma^2$ and X is defined as (27) and the static output feedback controller gains K_i are derived by (28).

IV. SIMULATION RESULTS

To show the validity of the proposed controller, the system is simulated on the basis of the dynamic model of equations (1-2) and the controller described in Theorem 1. In order to solve LMIs, we use SeDuMi [31] in MATLAB®. The model parameters used in the simulation are the ones reported in [24][24] in which $V_G, \tau_g, K_{xgi}, K_{xi}, T_{gh}$ and γ are estimated so as to avoid nonnegative values. The mentioned case is a virtual patient subjected to Type 2 Diabetes Mellitus with reduced pancreatic glucose sensitivity $T_{igmax} = 0.236$ which effectively result in the values for $G_b = 10.66$ and $I_b = 49.29$ [24]. The other parameters are listed below:

$$\begin{aligned} V_G &= 0.187, \quad K_{xi} = 1.211 \times 10^{-2}, \quad \tau_g = 24, \quad T_{gh} = 0.003, \\ \gamma &= 3.205, \quad V_f = 0.25, \quad K_{xgi} = 3.11 \times 10^{-5}, \quad G^* = 9. \end{aligned} \quad (27)$$

By assuming the above mentioned parameters, the solution of the LMIs in Corollary 1 yield the following controller gains are obtained:

$$K_1 = 0.0156 \quad K_2 = 0.0155 \quad K_3 = K_4 = 3.11 \cdot 10^{-5} \quad (28)$$

Figure 1, 2, 3 shows the results of the closed-loop dynamics of the system and the control signal. The initial conditions for the simulation are: $G(0) = G_b, I(0) = I_b$.

It should be noted that for the simulation, the original nonlinear model (1) is used instead of its T-S model representation in (10).

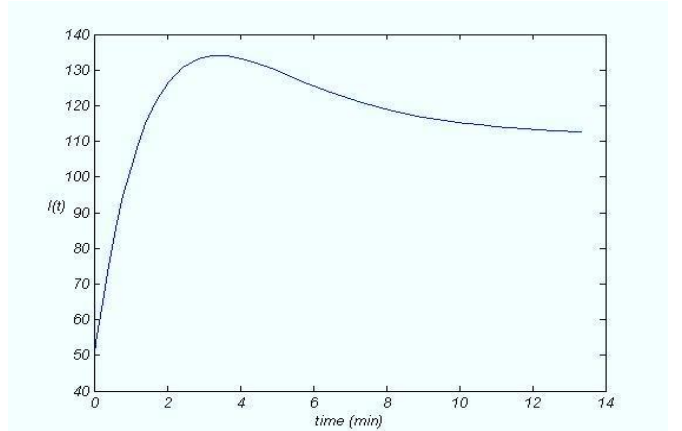


Fig. 2. Variations of insulinemia, I , [pM] in terms of time [min].

It is clear that the proposed controller asymptotically stabilizes the closed-loop error systems and thus the state

variables of system asymptotically converge to the desired values $G_{ref} = 5.0, I_{ref} = 112.69$, which shows the effectiveness of the proposed T-S fuzzy output feedback controller for regulating the amount of blood glucose.

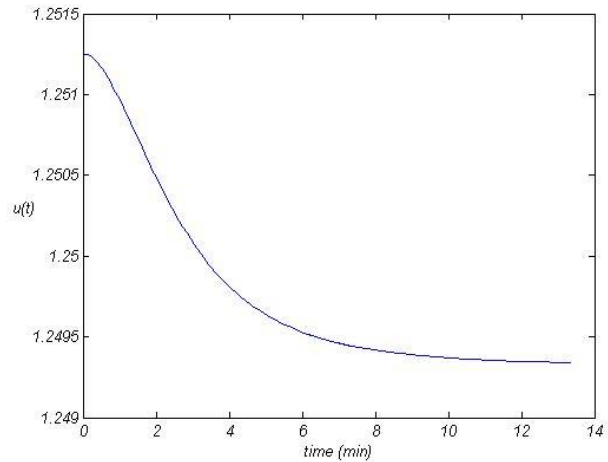


Fig. 3. Variations of exogenous intra-venous insulin delivery rate, u , [pM/min] in terms of time [min].

V. CONCLUSIONS

A new output feedback control scheme based on the TS fuzzy systems is introduced for the class of nonlinear differential equations with time-delay. We propose a new formulations and design conditions for T-S fuzzy dynamic output feedback tracking control problem in the presence of time-delay in the system dynamics. The proposed controller is utilized to adjust the amount of blood glucose by means of insulin injection as the control input. The dynamics behavior of the blood glucose/insulin metabolism is described by a single discrete-delay nonlinear differential equation system. Numerical simulations demonstrate that the proposed controller is effective and efficient to regulate the blood glucose level in the presence of time-delay in the dynamics model.

References

- [1] X. L. Luo, Q. K. Yan, Y. Wang, H. Fang, H. Y. Wang, Y. Bai, *et al.*, "Association between insulin dosage and insulin usage time, and coronary artery lesions in patients with type 2 diabetes and coronary heart disease," *Experimental and therapeutic medicine*, vol. 11, pp. 1767-1771, 2016.
- [2] J. A. Udell, M. A. Cavender, D. L. Bhatt, S. Chatterjee, M. E. Farkouh, and B. M. Scirica, "Glucose-lowering drugs or strategies and cardiovascular outcomes in patients with or at risk for type 2 diabetes: a meta-analysis of randomised controlled trials," *The Lancet Diabetes & Endocrinology*, vol. 3, pp. 356-366, 2015.
- [3] A. Basu, A. J. Jenkins, Y. Zhang, J. A. Stoner, R. L. Klein, M. F. Lopes-Virella, *et al.*, "Data on carotid intima-media thickness and lipoprotein subclasses in type 1 diabetes from the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC)," *Data in brief*, vol. 6, pp. 33-38, 2016.
- [4] S. Ligthart, T. T. van Herpt, M. J. Leening, M. Kavousi, A. Hofman, B. H. Stricker, *et al.*, "Lifetime risk of developing impaired glucose metabolism and eventual progression from prediabetes to type 2 diabetes: a prospective cohort study," *The lancet Diabetes & endocrinology*, vol. 4, pp. 44-51, 2016.

- [5] S. Sen, R. Chakraborty, and B. De, "Diabetes Mellitus in 21st Century," 2016.
- [6] D. P. Lavin, M. F. White, and D. P. Brazil, "IRS proteins and diabetic complications," *Diabetologia*, vol. 59, pp. 2280-2291, 2016.
- [7] R. N. Bergman, Y. Z. Ider, C. R. Bowden, and C. Cobelli, "Quantitative estimation of insulin sensitivity," *American Journal of Physiology-Endocrinology And Metabolism*, vol. 236, p. E667, 1979.
- [8] A. Caumo and C. Cobelli, "Hepatic glucose production during the labeled IVGTT: estimation by deconvolution with a new minimal model," *American Journal of Physiology-Endocrinology And Metabolism*, vol. 264, pp. E829-E841, 1993.
- [9] J. T. Sorensen, "A physiologic model of glucose metabolism in man and its use to design and assess improved insulin therapies for diabetes," Massachusetts Institute of Technology, 1985.
- [10] A. De Gaetano and O. Arino, "Mathematical modelling of the intravenous glucose tolerance test," *Journal of mathematical biology*, vol. 40, pp. 136-168, 2000.
- [11] I. M. Tolić, E. Mosekilde, and J. Sturis, "Modeling the insulin–glucose feedback system: the significance of pulsatile insulin secretion," *Journal of theoretical biology*, vol. 207, pp. 361-375, 2000.
- [12] J. Li, Y. Kuang, and C. C. Mason, "Modeling the glucose–insulin regulatory system and ultradian insulin secretory oscillations with two explicit time delays," *Journal of Theoretical Biology*, vol. 242, pp. 722-735, 2006.
- [13] F. Chee and T. Fernando, *Closed-loop control of blood glucose* vol. 368: Springer Science & Business Media, 2007.
- [14] G. Marchetti, M. Barolo, L. Jovanovic, H. Zisser, and D. E. Seborg, "An improved PID switching control strategy for type 1 diabetes," *IEEE Transactions on Biomedical Engineering*, vol. 55, pp. 857-865, 2008.
- [15] A. K. Patra and P. K. Rout, "Optimal H_∞ insulin injection control for blood glucose regulation in IDDM patient using physiological model," *International Journal of Automation and Control*, vol. 8, pp. 309-322, 2014.
- [16] P. Dua, F. J. Doyle, and E. N. Pistikopoulos, "Model-based blood glucose control for type 1 diabetes via parametric programming," *IEEE Transactions on Biomedical Engineering*, vol. 53, pp. 1478-1491, 2006.
- [17] B. Gopakumaran, H. M. Duman, D. P. Overholser, I. F. Federiuk, M. J. Quinn, M. D. Wood, et al., "A Novel Insulin Delivery Algorithm in Rats With Type 1 Diabetes: The Fading Memory Proportional-Derivative Method," *Artificial organs*, vol. 29, pp. 599-607, 2005.
- [18] P. Palumbo, P. Pepe, S. Panunzi, and A. De Gaetano, "Robust closed-loop control of plasma glycemia: a discrete-delay model approach," in *Decision and Control, 2008. CDC 2008. 47th IEEE Conference on*, 2008, pp. 3330-3335.
- [19] S. Yasini, A. Karimpour, and M. B. Naghibi Sistani, "Knowledge-based closed-loop control of blood glucose concentration in diabetic patients and comparison with H_∞ control technique," *IETE Journal of Research*, vol. 58, pp. 328-336, 2012.
- [20] M. Goharimaneh, A. Lashkaripour, and A. Akbari, "A Comparison of Fuzzy Types 1 and 2 in Diabetics Control, Based on Augmented Minimal Model," *Diabetes*, vol. 1, p. 2, 2015.
- [21] N. Duangpim and W. Assawinchaichote, "Fuzzy Control Design for Blood Glucose and Free Fatty Acid Regulation in Diabetes Patients," *Procedia Computer Science*, vol. 86, pp. 104-107, 2016.
- [22] P. Palumbo, S. Panunzi, and A. De Gaetano, "Qualitative behavior of a family of delay-differential models of the glucose-insulin system," *DISCRETE AND CONTINUOUS DYNAMICAL SYSTEMS SERIES B*, vol. 7, p. 399, 2007.
- [23] S. Panunzi, P. Palumbo, and A. De Gaetano, "A discrete single delay model for the intra-venous glucose tolerance test," *Theoretical Biology and Medical Modelling*, vol. 4, p. 35, 2007.
- [24] P. Palumbo, P. Pepe, S. Panunzi, and A. De Gaetano, "Time-delay model-based control of the glucose–insulin system, by means of a state observer," *European Journal of Control*, vol. 18, pp. 591-606, 2012.
- [25] D. Saifia, M. Chadli, S. Labiod, and T. M. Guerra, "Robust H_∞ static output feedback stabilization of TS fuzzy systems subject to actuator saturation," *International Journal of Control, Automation and Systems*, vol. 10, pp. 613-622, 2012.
- [26] T. Zhao, J. Xiao, L. Han, C. Qiu, and J. Huang, "Static Output Feedback Control for Interval Type-2 T-S Fuzzy Systems Based on Fuzzy Lyapunov Functions," *Asian Journal of Control*, vol. 16, pp. 1702-1712, 2014.
- [27] J. Qiu, S. X. Ding, H. Gao, and S. Yin, "Fuzzy-Model-Based Reliable Static Output Feedback H_∞ Control of Nonlinear Hyperbolic PDE Systems," *IEEE Transactions on Fuzzy Systems*, vol. 24, pp. 388-400, 2016.
- [28] K. Tanaka and H. O. Wang, *Fuzzy control systems design and analysis: a linear matrix inequality approach*: John Wiley & Sons, 2004.
- [29] H. D. Tuan, P. Apkarian, T. Narikiyo, and Y. Yamamoto, "Parameterized linear matrix inequality techniques in fuzzy control system design," *IEEE Transactions on fuzzy systems*, vol. 9, pp. 324-332, 2001.
- [30] Y.-H. Lan and Y. Zhou, "Non-fragile observer-based robust control for a class of fractional-order nonlinear systems," *Systems & Control Letters*, vol. 62, pp. 1143-1150, 2013.
- [31] J. F. Sturm, "Using SeDuMi 1.02, a MATLAB toolbox for optimization over symmetric cones," *Optimization methods and software*, vol. 11, pp. 625-653, 1999.