Robust type-2 Fuzzy Control for Glucose-Level Regulation in Type-I Diabetic Patients

Razieh Zamani[1], Mehdi Siahi[2*], Amin Ramazani[3]

[1]Department of Electrical Engineering, Central Tehran Branch, Islamic Azad University, Tehran, Iran. raziza63.rz@gmail.com
[2]Department of Electrical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran, mehdi.siahi@srbiau.ac.ir
[3]Department of Electrical and Computer, University of Tarbiat Modares, Tehran, Iran, ramezani@modares.ac.ir

Abstract

In this paper, a Fractional Adaptive Fuzzy Controller is designed for controlling blood glucose levels in Type-I diabetic patients. Type 1 diabetes is a chronic disease. In people with type 1 diabetes, the pancreatic cells that make insulin are destroyed, and the body is unable to make insulin. Unlike previous works, the system dynamics is considered as undetermined and in the presence of noise. System dynamics is estimated using the type-2 fuzzy system to eliminate the estimation error through compensation. The adaptive rules for control signal parameters and fuzzy system parameters are determined using Lyapunov stability analysis. A modified Bergman model for a diabetic patient with different conditions is used for evaluating the performance of the proposed controller. Also in addition to the uncertainty of glucose-insulin dynamic, the effect of patient activity and disturbance in terms of lifestyle and type of food consumed is considered, The simulation results show that the proposed controller has very well performance.

Keywords: Diabetes, Insulin, Glucose level, Robust controller, Undetermined Dynamic, Stability
Article history: Received 02-Jul-2021; Revised 04-Jul-2021; Accepted 04-Aug-2021. Article Type: Research Paper

http://dx.doi.org/10.30495/ijsee.2021.683682

1. Introduction

Diabetes is a disorder in the metabolism of humans. Type-1 diabetes (T1D) is one of the variations of this condition. In this type of diabetes, the patients are incapable of producing insulin in their bodies, which can occur due the damage to the beta cells and obstruction of insulin pathways. In these cases, the required insulin is often supplied through insulin infusion. There are approximately 347 million diabetic patients worldwide, and around half of these patients are not informed regarding their disease [1]. Furthermore, around 4 million people lose their lives annually due to diabetes complications, which places this disease among the most dangerous diseases. Therefore, controlling diabetes is an important topic that has been investigated by various researchers. With the advancement of biosensor technology with MEMS dimensions and specifications and increase in the accuracy and speed of measurement for different parameters as well as improvements in optics and analysis of biological phenomena with high quality and efficiency, a movement has been created for combining control systems and biological technologies [2-4]. The control objective in this metabolism is regulation glucose concentration in to normal level. The control input in this bio system is the insulin infusion. To this day, various controllers have been designed for this problem. Some of these controllers use no sensors. These methods are known as programmed insulin infusion systems. In these systems, insulin infusion is carried out in a period of time on basis of the insulin variation graph obtained during one day. Due to their simplicity, these methods have sometimes seen practical applications [5-7]. These methods lack suitable performance because the changes in insulin level are not constant and can often change with respect to the changes in patient's activity.

In the closed-loop methods which require the use of glucose sensors, often, an automatic insulin infusion system is used, which carries out subcutaneous insulin infusions for the patient. For example, in reference [8], a pole placement technique is used in which the desired insulin level

is determined using the system model. The model parameters are determined by the relationship between insulin and glucose dynamics in a normal human. The main drawback is that; the model parameters are considered to be fixed. To solve this problem, adaptive control methods are used in some of the literature [9]. For example, in reference [10], some parameters are approximated, while in [11], a predictive method is suggested to forecast the necessary insulin level. Some other similar approaches, use the glucose metabolism for estimating desired insulin. the non-linear autoregressive (NARX) is One of the interesting models, which is a non-linear function on basis of glucose levels before and after the infusion of insulin dose. Another method used in predictive controllers for glucose level adjustment in various studies is the forecasting based on neural networks [12-14]. This model can be used when the patient suffers from other diseases resulting in an unusable or a very complex normal model. Neural network parameters can be determined using some measured data over a predefined period. These models are based on learning algorithms such as error back-propagation algorithm. Other approaches include a PID controller used in references [15-16] and the controller H_∞ used in [17].

Fuzzy control systems (FCS) have also been used in literature for controlling blood glucose level. For example, in [18], the glucose level is modelled using fuzzy logic and membership functions, and the controller is schemed using this model. In [19-21], the self-evolving PID controller using FCSs is proposed, determining controller parameters using the Cuckoo algorithm. One of the main disadvantages of this approach is the large calculation volume for the proposed explorer while also providing no guarantee of stability and resistance. The back stepping control system using sliding mode strategy is presented in [22-23]. In this work, the system's mathematical model is used for controller design. In [24], interval type-2 FCS is used for dynamic approximation of T1D patients. This work used a genetic algorithm for adjusting the parameters of the fuzzy system. In [25], the Takagi-Sugeno FCS is suggested as the controller. The main disadvantages of this method is that, the minimal Bergman model is employed, which ignores some of the dynamics acting as noise. The Nephropathy forecasting in T1D on basis of a type-2 FCS and the genetic tuning approach is suggested in reference [26]. Reference [27] uses a back stepping control approach on basis of non-linear glucose model. In [28], the FCS for adjustment of glucose concentration is implemented on FPGA boards. These methods often have high calculation volume and, therefore, limited practical applications. Based on the literature review, the most important disadvantages of the currently proposed methods include:

- Most studies use system models for controlled design. However, mathematical models are not very reliable for practical applications and can change due to various factors. This is especially important when the diabetic patient has other background conditions, which might mean that the model used for controller design is not accurate and ineffective.
- Some studies have attempted to replace the system model with controllers such as PID and fuzzy controllers. However, these methods also provide no guarantees for stability.
- Some of the proposed methods used adaptive algorithms for controller optimization, which not only offers no guarantee of stability but also results in large calculation volume [29].
- Other approaches use a stable and robust controller [30-31], such as sliding mode. Most of these approaches use minimal Bergman model which ignores some of the noise variations. Furthermore, the system model is also used in the controller design, which uses a set of undetermined parameters.

Based on the disadvantages mentioned above, the current study uses a modified Bergman model in the presence of undetermined values as well as resistance control for adjusting glucose levels. This article is organized as follows. Section 2 offers a description of the system and the general problem statement. Section 3 explains the details of the fuzzy system. In section 4, stability of closed-loop is analyzed. The controller based on the Bergman model is simulated for diabetic patients is presented in section 5. The conclusion is presented in section 6, and finally, references are provided in section 7.

2. System Description and Problem Statement

Various models are proposed for diabetic patients in order to evaluate proposed control methods. One of the essential such models used in many studies for design and testing of controllers is the minimal and modified Bergman model. The current study uses the modified Bergman model, which has a complete structure and includes variations such as a change in glucose level with patients' daily activities. The system dynamics based on modified Bergman model is as (1). Where i =1, 2, 3, I_b, K_f, P_i, and G_b are positive variables. G shows the patient's blood glucose concentration in mg/dL; X is the time of infused insulin, affecting glucose in minutes; I, is the blood insulin concentration in mIU (mIU is milli-international units for pharmaceutical applications equal to 0.0347 milligrams of insulin). I_b and G_b are the ideal

insulin and glucose levels, respectively and R_a is the glucose metabolism rate. Other parameters are constant values that differ from one person to the next.

$$\begin{aligned}
\frac{dG}{dt} &= P_1 G_b + R_a - (P_1 + X)G \\
\frac{dX}{dt} &= -P_2 X + (I - I_b)P_3 \\
\frac{dI}{dt} &= b_f U_1 + I_b k_f \\
\frac{dU_1}{dt} &= -U_1 k_s + u \\
\frac{dR_1}{dt} &= -(R_1 - d)C_1 \\
\frac{dR_2}{dt} &= -(R_2 - R_1)C_2
\end{aligned} \quad (1)$$

The block diagram of the control method is presented in figure (1) and, the system dynamics can be rewritten as follows:

$$\begin{aligned}
&\dot{x}_1 = f_1 + \varepsilon_1 - x_1 x_2, f_1 = -P_1(x_1 - G_b), \varepsilon_1 = w_1 + k_{gr} x_5 \\
&\dot{x}_2 = f_2 + \varepsilon_2 + P_3 x_3, f_2 = -P_2 x_2 - P_3 I_b, \varepsilon_2 = w_2 \\
&\dot{x}_3 = f_3 + \varepsilon_3 + b_f x_4, f_3 = -k_f x_3, \varepsilon_3 = w_3 \\
&\dot{x}_4 = f_4 + \varepsilon_4 + u, f_4 = -k_s x_4, \varepsilon_4 = w_4
\end{aligned} \quad (2)$$

Where x_5 is defined $a x_5 = K_{gr} R_2$ s the variation created due to carbohydrate introduction to the body and w_i, i =1,…,5 is the noise. System dynamics can be estimated as follows:

$$\begin{aligned}
&\hat{x}_1^{(4)} = \hat{f}(\chi|\theta) - \hat{g} x_1 u \\
&-\zeta_1 \dddot{\hat{e}} - \zeta_2 \ddot{\hat{e}} - \zeta_3 \dot{\hat{e}} - \zeta_4 \hat{e}
\end{aligned} \quad (3)$$

Where $\hat{f}(x|\theta)$ is the proposed fuzzy system and $\chi = \left[x_1, D_t^q x_1\right]^T$ is the input vector of the fuzzy system, $D_t^q x_1$ is the Fractional derivative of the glucose level, and q is the fractional-order which is a number between 0 and 1. The $\zeta_i, i = 1, \ldots . 4$ parameters are determined so that the $s^4 + \zeta_1 s^3 + \zeta_2 s^2 + \zeta_3 s + \zeta_4$ polynomial is Hurwitz Stable. The estimated error is defined as $\hat{e} = \hat{x}_1 - x_1$. The control signal is defined as that output of system is stabilized at its normal value of 100 (Glucose level). Figure (1) shows the block diagram of the proposed method.

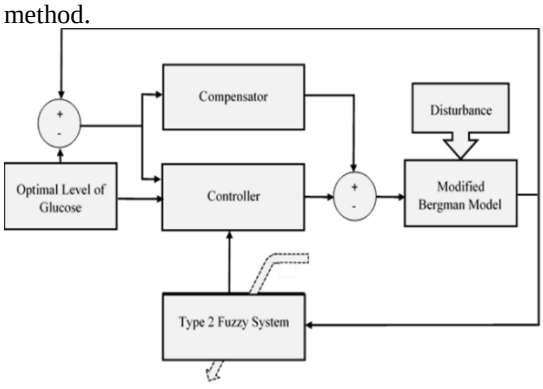

Fig. 1. Block diagram of the proposed method

3. Design of type-2 fuzzy system

As explained in the previous section, the glucose-insulin dynamics are estimated using a fuzzy system. The structure of the proposed fuzzy system with full details are provided in this section. The schematic of the structural diagram of the type-2 fuzzy system with two inputs is presented in figure (2), while the output of each layer is explained in the following part.

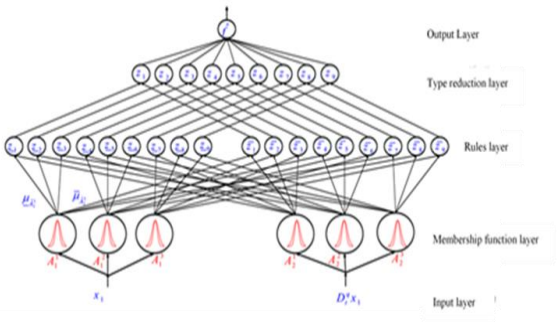

Fig. 2. Structure of the fuzzy system

Input layer: the inputs for the fuzzy system include $x_1(t)$ and $D_t^q x_1(t)$. Membership function layer: In this layer, each node is a membership function. For each input, three membership functions with constant mean and varying widths are used, as shown in figure (3). Consider the membership function A_i^j, $i = 1,2$ $j = 1,2,3$ (the j_{th} membership function for the i_{th} input); the degrees of membership for upper and lower boundaries are calculated as follows:

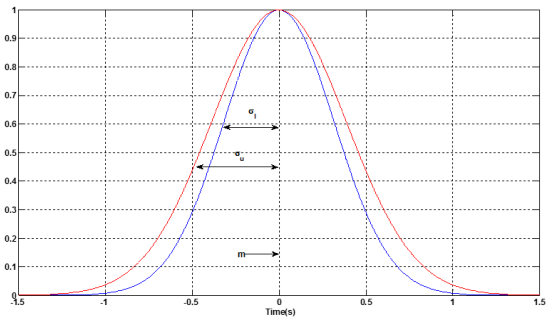

Fig. 3. The type-2 membership function graph with constant mean and varied width

$$\begin{aligned}
\bar{\mu}_{\tilde{A}_1^1}(x_1(t)) &= exp\left(-\frac{1}{2}\left(\frac{x_1(t) + \bar{x}_1}{\bar{\sigma}^2}\right)^2\right) \\
\bar{\mu}_{\tilde{A}_1^2}(x_1(t)) &= exp\left(-\frac{1}{2}\left(\frac{x_1(t)}{\bar{\sigma}^2}\right)^2\right) \\
\bar{\mu}_{\tilde{A}_1^3}(x_1(t)) &= exp\left(-\frac{1}{2}\left(\frac{x_1(t) - \underline{x}_1}{\bar{\sigma}^2}\right)^2\right)
\end{aligned} \quad (4)$$

$$\begin{aligned}
\underline{\mu}_{\tilde{A}_2^1}\left(D_t^q x_1(t)\right) &= exp\left(-\frac{1}{2}\left(\frac{D_t^q x_1(t) + \bar{x}_1'}{\bar{\sigma}^2}\right)^2\right) \\
\underline{\mu}_{\tilde{A}_2^2}\left(D_t^q x_1(t)\right) &= exp\left(-\frac{1}{2}\left(\frac{D_t^q x_1(t)}{\bar{\sigma}^2}\right)^2\right)
\end{aligned} \quad (5)$$

$$\underline{\mu}_{A_2^3}\left(D_t^q x_1(t)\right) = exp\left(-\frac{1}{2}\left(\frac{D_t^q x_1(t) - \underline{x}_1'}{\bar{\sigma}^2}\right)^2\right)$$

Where $\overline{x_1}\,\underline{x_1}$ and are the upper and lower boundaries of glucose level while $\overline{x'}\ \underline{x'}$ and are the fractional derivative of upper and lower boundaries of glucose level. Rules layer: The nodes in this layer are the rules. There is a total of 9 rules in this layer. The output of this layer is as follows:

$$\begin{aligned}&\underline{z}_1 = \underline{\mu}_{A_1^1}\underline{\mu}_{A_2^1}, \underline{z}_2 = \underline{\mu}_{A_1^1}\underline{\mu}_{A_2^2}, \underline{z}_3 = \underline{\mu}_{A_1^1}\underline{\mu}_{A_2^3}\\ &\underline{z}_4 = \underline{\mu}_{A_1^2}\underline{\mu}_{A_2^1}, \underline{z}_5 = \underline{\mu}_{A_1^2}\underline{\mu}_{A_2^2}, \underline{z}_6 = \underline{\mu}_{A_1^2}\underline{\mu}_{A_2^3}\\ &\underline{z}_7 = \underline{\mu}_{A_1^3}\underline{\mu}_{A_2^1}, \underline{z}_8 = \underline{\mu}_{A_1^3}\underline{\mu}_{A_2^2}, \underline{z}_9 = \underline{\mu}_{A_1^3}\underline{\mu}_{A_2^3}\end{aligned} \quad (6)$$

The upper limit of fire degrees is calculated as follows:

$$\begin{aligned}&\bar{z}_1 = \bar{\mu}_{A_1^1}\bar{\mu}_{A_2^1}, \bar{z}_2 = \bar{\mu}_{A_1^1}\bar{\mu}_{A_2^2}, \bar{z}_3 = \bar{\mu}_{A_1^1}\bar{\mu}_{A_2^3}\\ &\bar{z}_4 = \bar{\mu}_{A_1^2}\bar{\mu}_{A_2^1}, \bar{z}_5 = \bar{\mu}_{A_1^2}\bar{\mu}_{A_2^2}, \bar{z}_6 = \bar{\mu}_{A_1^2}\bar{\mu}_{A_2^3}\\ &\bar{z}_7 = \bar{\mu}_{A_1^3}\bar{\mu}_{A_2^1}, \bar{z}_8 = \bar{\mu}_{A_1^3}\bar{\mu}_{A_2^2}, \bar{z}_9 = \bar{\mu}_{A_1^3}\bar{\mu}_{A_2^3}\end{aligned} \quad (7)$$

Type reduction layer: This layer uses the Nie-Tan type reduction operator. The output of this layer as follows:

$$z_l = \frac{\bar{z}_l + \underline{z}_l}{\sum_{l=1}^{M} \bar{z}_l + \underline{z}_l}, l = 1, \ldots, M \quad (8)$$

Where M is the number of rules.The output layer: The final output is calculated as follows:

$$\hat{f} = \sum_{l=1}^{M} z_l \theta_l \quad (9)$$

In which $\theta_l, l = 1,\ldots,9$ are the lower section parameters. In other words, these parameters indicate the mean of singleton output membership functions.

4. Controller design

The main results can be summarized in the following theorem:

Theorem: by considering the control signal of (10) and adaptive rules of (11), the closed-loop glucose-insulin system is Asymptotic stable.

$$u = -\frac{1}{\hat{g}x_1}\left(-\hat{f} + r^{(4)} - \lambda_1\ddot{e} - \lambda_2\ddot{e} - \lambda_3\dot{e} - \lambda_4 e - u_c\right) \quad (10)$$

$$\begin{aligned}&\dot{\theta} = \gamma\hat{\underline{e}}^T P_2 b Z\\ &\dot{\hat{g}} = \gamma\hat{\underline{e}}^T P_2 b x_1 u\end{aligned} \quad (11)$$

Where γ is the matching rate and between 0 and 1; r is the reference signal, and P_i, $i = 1,2$ are positive symmetrical determined matrices and $\lambda_i, i = 1,..,4$ parameters are determined so that the polynomial $s^4 + \lambda_1 s^3 + \lambda_2 s^2 + \lambda_3 s + \lambda_4$ is Hurwitz Stable. u_c is the compensator which is calculated as follows:

$$u_c = tanh(\underline{e}^T P_1 b)\frac{|\hat{\underline{e}}^T P_2 b||\bar{\varepsilon}|}{|\underline{e}^T P_1 b| + \delta} \quad (12)$$

Where δ is a small positive number $|\overline{\varepsilon}|$ is the upper boundary of the estimation error and we have:

$$A^T P_1 + P_1 A = -Q_1 \quad (13)$$

$$\Lambda^T P_2 + P_2 \Lambda = -Q_2 \quad (14)$$

$$\Lambda = \begin{bmatrix} 0 & 1 & 0 & 0\\ 0 & 0 & 1 & 0\\ 0 & 0 & 0 & 1\\ -\zeta_4 & -\zeta_3 & -\zeta_2 & -\zeta_1 \end{bmatrix} \quad (15)$$

$$A = \begin{bmatrix} 0 & 1 & 0 & 0\\ 0 & 0 & 1 & 0\\ 0 & 0 & 0 & 1\\ -\lambda_4 & -\lambda_3 & -\lambda_2 & -\lambda_1 \end{bmatrix} \quad (16)$$

$$b = \begin{bmatrix} 0\\ 0\\ 0\\ 1 \end{bmatrix} \quad (17)$$

$$\underline{e} = \begin{bmatrix} e\\ \dot{e}\\ \ddot{e}\\ \dddot{e} \end{bmatrix} \quad (18)$$

$$\hat{\underline{e}} = \begin{bmatrix} \hat{e}\\ \dot{\hat{e}}\\ \ddot{\hat{e}}\\ \dddot{\hat{e}} \end{bmatrix} \quad (19)$$

$$e = \hat{x}_1 - r \quad (20)$$

By differentiating the output, we can write:

$$\ddot{x}_1 = -P_1\dot{x}_1 - \dot{x}_1 x_2 - x_1(-P_2 x_2 + P_3 x_3 - P_3 I_b) - \varepsilon_2 x_1 \quad (21)$$

Using the third-order derivate of the output we have:

$$\begin{aligned}\dddot{x}_1 = &-\dddot{x}_1(P_1 + x_2) - \dot{x}_1\dot{x}_2 + P_2\dot{x}_1 x_2 + P_2 x_1\dot{x}_2\\ &+P_3 I_b\dot{x}_1 - P_3\dot{x}_1 x_3 - P_3 x_1\left(-k_f x_3 + b_f x_4\right) - \varepsilon_2\dot{x}_1 - P_3 x_1\varepsilon_3\end{aligned} \quad (22)$$

By replacing (21) in (22), we can write:

$$\begin{aligned}\dddot{x}_1 = &[P_1\dot{x}_1 + \dot{x}_1 x_2 + x_1(-P_2 x_2 + P_3 x_3 - P_3 I_b)]\\ &(P_1 + x_2) - \dot{x}_1\dot{x}_2 - P_2\dot{x}_1 x_2 - P_2 x_1\dot{x}_2\\ &+P_3 I_b\dot{x}_1 - P_3\dot{x}_1 x_3 - P_3 x_1\left(-k_f x_3 + b_f x_4\right) - \varepsilon_2\dot{x}_1\\ &-P_3 x_1\varepsilon_3 + \varepsilon_2 x_1(P_1 + x_2)\end{aligned} \quad (23)$$

In the next step, the 4^{th} order derivate of the output is calculated:

$$\begin{aligned}x_1^{(4)} = &-\ddot{\ddot{x}}_1(P_1 + x_2) - 2\ddot{x}_1\dot{x}_2 - \dot{x}_1\ddot{x}_2 + P_2\ddot{x}_1 x_2 +\\ &2P_2\dot{x}_1\dot{x}_2 + P_2 x_1\ddot{x}_2 + P_3 I_b\ddot{x}_1 - P_3\ddot{x}_1 x_3\\ &-P_3\dot{x}_1\dot{x}_3 - P_3\dot{x}_1\left(-k_f x_3 + b_f x_4 + \varepsilon_3\right)\\ &-P_3 x_1\left(-k_f\dot{x}_3 + b_f\dot{x}_4\right) - \varepsilon_2\ddot{x}_1\end{aligned} \quad (24)$$

Now, by replacing $\dot{x}_4$ with its value we have:

$$\begin{aligned}x_1^{(4)} = &-\ddot{\ddot{x}}_1(P_1 + x_2) - 2\ddot{x}_1\dot{x}_2 - \dot{x}_1\ddot{x}_2 - P_2\ddot{x}_1 x_2 -\\ &2P_2\dot{x}_1\dot{x}_2 - P_2 x_1\ddot{x}_2 + P_3 I_b\ddot{x}_1 - P_3\ddot{x}_1 x_3 -\\ &P_3\dot{x}_1\dot{x}_3 - P_3\dot{x}_1\left(-k_f x_3 + b_f x_4 + \varepsilon_3\right)\\ &-P_3 x_1\left(-k_f\dot{x}_3 + b_f[-k_s x_4 + \varepsilon_4 + u]\right) - \varepsilon_2\ddot{x}_1\end{aligned} \quad (25)$$

Simplification of equation (25) results in:

$$\begin{aligned}x_1^{(4)} = &-\ddot{\ddot{x}}_1(P_1 + x_2) - 2\ddot{x}_1\dot{x}_2 - \dot{x}_1\ddot{x}_2 - P_2\ddot{x}_1 x_2 -\\ &2P_2\dot{x}_1\dot{x}_2 - P_2 x_1\ddot{x}_2 + P_3 I_b\ddot{x}_1 - P_3\ddot{x}_1 x_3 -\\ &P_3\dot{x}_1\dot{x}_3 - P_3\dot{x}_1\left(-k_f x_3 + b_f x_4 + \varepsilon_3\right) -\\ &P_3 x_1\left(-k_f\dot{x}_3 - b_f k_s x_4 + b_f\varepsilon_4\right) - \varepsilon_2\ddot{x}_1 - P_3 b_f x_1 u\end{aligned} \quad (26)$$

Finally, equation (26) can be simplified as follows:

$$x_1^{(4)} = f - P_3 b_f x_1 u \tag{27}$$

In which:

$$\begin{aligned} f = &-\dddot{x}_1(P_1 + x_2) - 2\ddot{x}_1\dot{x}_2 - \dot{x}_1\ddot{x}_2 - P_2\ddot{x}_1 x_2 \\ &-2P_2\dot{x}_1\dot{x}_2 - P_2 x_1\ddot{x}_2 + P_3 I_b\ddot{x}_1 - P_3\ddot{x}_1 x_3 \\ &-P_3\dot{x}_1\dot{x}_3 - P_3\dot{x}_1(-k_f x_3 + b_f x_4 + \varepsilon_3) \\ &-P_3 x_1(-k_f\dot{x}_3 - b_f k_s x_4 + b_f\varepsilon_4) - \varepsilon_2\ddot{x}_1 \end{aligned} \tag{28}$$

And the system dynamics can be estimated as follows:

$$\begin{aligned} &\hat{x}_1^{(4)} = \hat{f}(\chi|\theta) - \hat{g}x_1 u \\ &-\zeta_1\dddot{\hat{e}} - \zeta_2\ddot{\hat{e}} - \zeta_3\dot{\hat{e}} - \zeta_4\hat{e} \end{aligned} \tag{29}$$

In which $\hat{f}(x|\theta)$ is the proposed fuzzy system, $\chi = [x_1, D_t^q x_1]^T$ is the input vector of the fuzzy system, $D_t^q x_1$ is the fractional derivative order of the glucose level, and q is the fractional-order which is a number between 0 and 1. The $\zeta_i, i = 1,..,4$ parameters are determined so that the polynomial $s^4 + \zeta_1 s^3 + \zeta_2 s^2 + \zeta_3 s + \zeta_4$ is Hurwitz Stable. The estimation error is defined as $\hat{e} = \hat{x}_1 - x_1$.

By subtracting (32) and (29), the estimation error can be calculated as follows:

$$\begin{aligned} &\hat{e}_1^{(4)} = \hat{f}(\chi|\theta) - f + (g - \hat{g})x_1 u - \\ &\zeta_1\dddot{\hat{e}} - \zeta_2\ddot{\hat{e}} - \zeta_3\dot{\hat{e}} - \zeta_4\hat{e} \end{aligned} \tag{30}$$

By adding and subtracting the optimum fuzzy system in equation (30) we have:

$$\begin{aligned} &\hat{e}_1^{(4)} = \hat{f}^*(\chi|\theta^*) - f + \hat{f}(\chi|\theta) - \hat{f}^*(\chi|\theta^*) \\ &+(g - \hat{g})x_1 u - \zeta_1\dddot{\hat{e}} - \zeta_2\ddot{\hat{e}} - \zeta_3\dot{\hat{e}} - \zeta_4\hat{e} \end{aligned} \tag{31}$$

Which can be rewritten as follows:

$$\begin{aligned} &\hat{e}_1^{(4)} = \varepsilon + \tilde{\theta}^T Z + \tilde{g}x_1 u \\ &-\zeta_1\dddot{\hat{e}} - \zeta_2\ddot{\hat{e}} - \zeta_3\dot{\hat{e}} - \zeta_4\hat{e} \end{aligned} \tag{32}$$

In which, ε is the estimation error defined as follows:

$$\varepsilon = \hat{f}^*(\chi|\theta^*) - f \tag{33}$$

The $\tilde{\theta}$ and Z parameters are defined as follows:

$$\tilde{\theta} = \theta - \theta^* \tag{34}$$

$$Z = [z_1, \ldots, z_M]^T, z_l = \frac{\bar{z}_l + \underline{z}_l}{\sum_{l=1}^{M} \bar{z}_l + \underline{z}_l}, l = 1, \ldots, M \tag{35}$$

By replacing the control rule in equation (27) we have:

$$e^{(4)} + \lambda_1\dddot{e} + \lambda_2\ddot{e} + \lambda_3\dot{e} + \lambda_4 e = -u_c \tag{36}$$

In the vector format of equations (32) and (36) we have:

$$\dot{\underline{e}} = A\underline{e} - bu_c \tag{37}$$

$$\dot{\underline{\hat{e}}} = \Lambda\underline{\hat{e}} - b\tilde{\theta}^T Z + b\tilde{g}x_1 u + b\varepsilon \tag{38}$$

Where:

$$\Lambda = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ -\zeta_4 & -\zeta_3 & -\zeta_2 & -\zeta_1 \end{bmatrix} \tag{39}$$

$$A = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ -\lambda_4 & -\lambda_3 & -\lambda_2 & -\lambda_1 \end{bmatrix} \tag{40}$$

$$b = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \tag{41}$$

$$\underline{e} = \begin{bmatrix} e \\ \dot{e} \\ \ddot{e} \\ \dddot{e} \end{bmatrix} \tag{42}$$

$$\underline{\hat{e}} = \begin{bmatrix} \hat{e} \\ \dot{\hat{e}} \\ \ddot{\hat{e}} \\ \dddot{\hat{e}} \end{bmatrix} \tag{43}$$

$$e = \hat{x}_1 - r \tag{44}$$

$$\hat{e} = \hat{x}_1 - x_1 \tag{45}$$

For stability analysis, we use the following Lyapunov function:

$$V = \frac{1}{2}\underline{e}^T P_1\underline{e} + \frac{1}{2}\underline{\hat{e}}^T P_2\underline{\hat{e}} + \frac{1}{2\gamma}\tilde{\theta}^T\tilde{\theta} + \frac{1}{2\gamma}\tilde{g}^2 \tag{46}$$

In which:

$$A^T P_1 + P_1 A = -Q_1 \tag{47}$$

$$\Lambda^T P_2 + P_2\Lambda = -Q_2 \tag{48}$$

$$\tilde{g} = g - \hat{g} \tag{49}$$

$$\tilde{\theta} = \theta - \theta^* \tag{50}$$

By derivation of Lyapunov function we have:

$$\begin{aligned} &\dot{V} = \frac{1}{2}\dot{\underline{e}}^T P_1\underline{e} + \frac{1}{2}\underline{e}^T P_1\dot{\underline{e}} + \frac{1}{2}\dot{\underline{\hat{e}}}^T P_1\underline{\hat{e}} + \\ &\frac{1}{2}\underline{\hat{e}}^T P_1\dot{\underline{\hat{e}}} + \frac{1}{\gamma}\tilde{\theta}^T\dot{\theta} - \frac{1}{\gamma}\dot{\hat{g}} \end{aligned} \tag{51}$$

By replacing (37) and (38), we have:

$$\begin{aligned} &\dot{V} = \frac{1}{2}\underline{e}^T(A^T P_1 + P_1 A)\underline{e} + \frac{1}{2}\underline{\hat{e}}^T(\Lambda^T P_2 + P_2\Lambda)\underline{\hat{e}} \\ &-\underline{e}^T P_1 b u_c - \underline{\hat{e}}^T P_2 b\tilde{\theta}^T Z + \underline{\hat{e}}^T P_2 b\tilde{g}x_1 u + \underline{\hat{e}}^T P_2 b\varepsilon \\ &+\frac{1}{\gamma}\tilde{\theta}^T\dot{\theta} - \frac{1}{\gamma}\dot{\hat{g}} \end{aligned} \tag{52}$$

By replacing (47) and (48), $\dot{V}$ can be written as follows:

$$\begin{aligned} &\dot{V} = -\frac{1}{2}\underline{e}^T Q_1\underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2\underline{\hat{e}} \\ &-\underline{e}^T P_1 b u_c - \underline{\hat{e}}^T P_2 b\tilde{\theta}^T Z + \underline{\hat{e}}^T P_2 b\tilde{g}x_1 u + \underline{\hat{e}}^T P_2 b\varepsilon \\ &+\frac{1}{\gamma}\tilde{\theta}^T\dot{\theta} - \frac{1}{\gamma}\dot{\hat{g}} \end{aligned} \tag{53}$$

Equation (53) can be rewritten as follows:

$$\dot{V} = -\frac{1}{2}\underline{e}^T Q_1 \underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} \\ \tilde{\theta}^T\left(\frac{1}{\gamma}\dot{\theta} - \underline{\hat{e}}^T P_2 b Z\right) + \tilde{g}\left(-\frac{1}{\gamma}\dot{\hat{g}} + \underline{\hat{e}}^T P_2 b x_1 u\right) \\ -\underline{e}^T P_1 b u_c + \underline{\hat{e}}^T P_2 b\varepsilon \quad (54)$$

By replacing adaption rules form (11) we have:

$$\dot{V} = -\frac{1}{2}\underline{e}^T Q_1 \underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} - \underline{e}^T P_1 b u_c + \underline{\hat{e}}^T P_2 b\varepsilon \quad (55)$$

Using equation (55), we can write:

$$\dot{V} \le -\tfrac{1}{2}\underline{e}^T Q_1 \underline{e} - \tfrac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} - \underline{e}^T P_1 b u_c + |\underline{\hat{e}}^T P_2 b||\bar{\varepsilon}| \quad (56)$$

Which $|\bar{\varepsilon}|$ is the upper boundary of estimation error. By replacing the compensator form (12) we have:

$$\dot{V} \le -\frac{1}{2}\underline{e}^T Q_1 \underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} \\ -\underline{e}^T P_1 b\left(tanh(\underline{e}^T P_1 b)\frac{|\underline{\hat{e}}^T P_2 b||\bar{\varepsilon}|}{|\underline{e}^T P_1 b|+\delta}\right) + |\underline{\hat{e}}^T P_2 b||\bar{\varepsilon}| \quad (57)$$

Equation (57) can be simplified as follows:

$$\dot{V} \le -\frac{1}{2}\underline{e}^T Q_1 \underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} \\ +|\underline{\hat{e}}^T P_2 b||\bar{\varepsilon}|\left(1 - \frac{[\underline{e}^T P_1 b\, tanh(\underline{e}^T P_1 b)]}{|\underline{e}^T P_1 b| + \delta}\right) \quad (58)$$

Since $\underline{e}^T P_1 b \tanh\left(\underline{e}^T P_1 b\right) \approx \left|\underline{e}^T P_1 b\right|$ we can write:

$$\frac{[\underline{e}^T P_1 b\, tanh(\underline{e}^T P_1 b)]}{|\underline{e}^T P_1 b| + \delta} \approx 1 \quad (59)$$

Therefore, we have:

$$\dot{V} \le -\frac{1}{2}\underline{e}^T Q_1 \underline{e} - \frac{1}{2}\underline{\hat{e}}^T Q_2 \underline{\hat{e}} \quad (60)$$

Due to the error signal being bounded, Barbalat's lemma can be used to prove Asymptotic stability.

5. Simulation

In this section, the schemed controller is applied to the Bergman model of several diabetic patients. In table (1), there is the information of Bergman model for patients [11]. Figure (5) shows the glucose level changes in patients without controlling the conditions in patients. As can be observed, the glucose level increases rapidly and moves past the acceptable range. For each patient, various initial conditions (initial blood glucose levels) of 20, 80, and 200 were used. The output glucose levels have presented figures (5), (6), and (7) for the first, second, and third patients. As can be seen, the suggested controller has managed to stabilize glucose levels in an acceptable range. In the next step, in order to better evaluate the performance of the proposed controller, variations in the form of white noise were introduced to the system. It is worth noting that these variations are different from the variations of the Bergman model used. The results of controller performance under these conditions have presented in figures (8), (9), and (10) for first, second and third patients. In order to show the performance of the proposed method, its results are compared to several other control methods in the table (2). The proposed controller's RMSE value is suitable, and the performance of suggested method is better compared to other similar control methods.

Furthermore, many previous studies have used constant and defined versions of the Bergman method to evaluate controller performance. However, in this study, other than the undefined model, model parameters change over time. Finally, the simulation results show that the performance of proposed model is excellent and can be considered for practical applications. The proposed model is applied to the modified Bergman model of a diabetic patient in order to evaluate its performance. The Bergman model date for these patients is presented in table (1) [32]. Various initial conditions (initial glucose levels) such as 20 and 200 are used for this patient. The output glucose level, along with the controller signal, is presented in figure 2 and figure 3. As it can be observed, the controller has successfully managed to stabilize the glucose level in the acceptable range.

Table.1.
The Bergman model data for several diabetic patients [11]

Adult	k_{gr}	C_2	C_1
I	1.1e-3	2.4e-2	9.93e-2
II	4.1e-3	6.2e-3	9.23e-2
III	1.6e-3	7.3e-3	9.31e-2

Adult	b_f	K_s	G_b	I_b
I	1.78e-4	6.7e-3	76.5	25.1
II	4.9e-4	5.67e-2	80.1	28.5
III	9.37e-4	1.35e-2	75.2	31

Adult	P_1	P_2	P_3	K_f
I	3.1e-3	1.55e-2	1.25e-6	3.83e-2
II	1.31e-2	5.3e-3	1.44e-6	1.3e-2
III	3.9e-3	5.53e-3	5.48e-7	6.68e-2

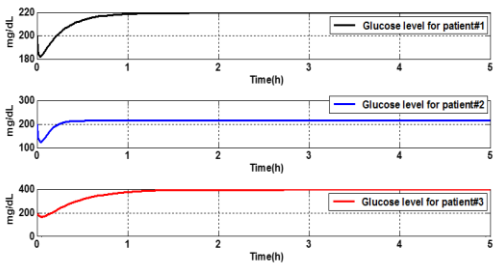

Fig. 4. Blood glucose level in patients in uncontrolled conditions

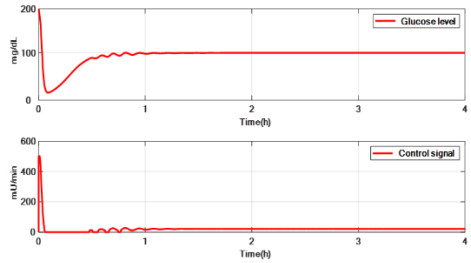

Fig. 5. Tracking optimum glucose level for an initial glucose level of 200 for the first patient

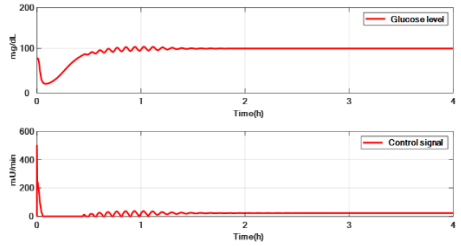

Fig. 6. Tracking optimum glucose level for an initial glucose level of 80 for the second patient

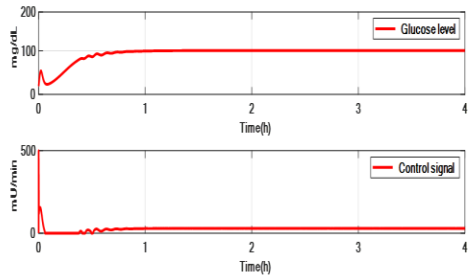

Fig. 7. Tracking optimum glucose level for an initial glucose level of 20 for the third patient

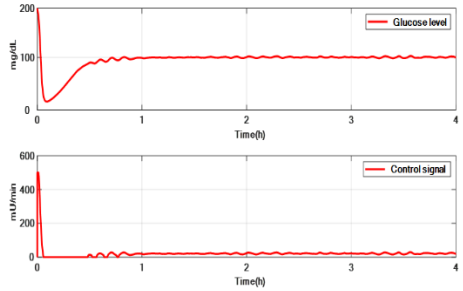

Fig. 8. Tracking optimum glucose level in the presence of noise for the first patient

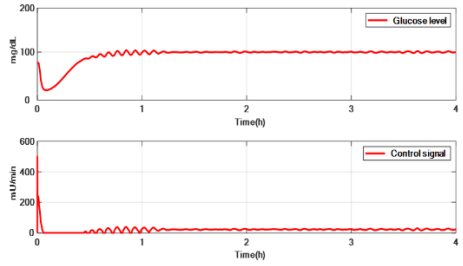

Fig. 9. Tracking optimum glucose level in the presence of noise for the second patient

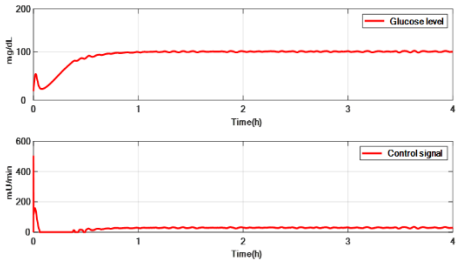

Fig. 10. Tracking optimum glucose level in the presence of noise for the third patient

Table.2.
Comparison of the proposed method with other control methods

11.0135	Proposed method
15.1064	Proportional-derivative-integral fuzzy control [33]
12.0287	Fuzzy self-adjusting control [34]

6. Conclusion

In this study, a robust controller for regulation the blood glucose level of T1D patients was proposed. This controller was designed based on Lyapunov stability. To evaluate the regulation performance of the suggested controller, diabetic patients with different initial conditions were used. The modified Bergman model was used in simulations. The results of simulation indicated that the performance of offered controller is excellent and can be considered for practical applications. Future studies include the feasibility study for the implementation of the proposed control method.

References

[1] W. H. Organization and W. H. Organization, "Diabetes fact sheet No. 312," Geneva, Switzerland URL: http://www. who.int/mediacentre/factsheets/fs312/en/index. html [accessed 2013-02-12][WebCite Cache ID 6ENYIOJ6e], 2013.

[2] F. S. Grodins, Control theory, and biological systems. Columbia University Press, 1963.

[3] M. C. Khoo, Physiological control systems: analysis, simulation, and estimation. Wiley Online Library, 2000.

[4] P. A. Iglesias and B. P. Ingalls, Control theory, and systems biology. MIT Press, 2010.

[5] W. Spencer, "A review of programmed insulin delivery systems," IEEE Transactions on Biomedical Engineering, no. 3, pp. 237-251, 1981.

[6] M. Franetzki, K. Prestele, and H. Kresse, "Technological problems of miniaturized insulin dosing devices and some approaches to clinical trials," Hormone and metabolic research. Supplement series, no. 8, pp. 58-65, 1979.

[7] J.-L. Hauser, "Programmable portable infusion pump system," ed: Google Patents, 1995.

[8] S. Shimoda et al., "Closed-loop subcutaneous insulin infusion algorithm with a short-acting insulin analog for long-term clinical application of a wearable artificial endocrine pancreas," Frontiers of medical and biological engineering: the international journal of the Japan Society of Medical Electronics and Biological Engineering, vol. 8, no. 3, pp. 197-211, 1997.

[9] R. Zamani Forooshani, M. Siahi & A. Ramezani (2019) Adaptive Type-2 Fuzzy Control for Regulation of Glucose Level

in Type 1 Diabetes, IETE Journal of Research, DOI: 10.1080/03772063.2019.1595183

[10] R. S. Parker, F. J. Doyle, and N. A. Peppas, "A model-based algorithm for blood glucose control in type I diabetic patients," IEEE Transactions on biomedical engineering, vol. 46, no. 2, pp. 148-157, 1999.

[11] R. Dudde, T. Vering, G. Piechotta, and R. Hintsche, "Computer-aided continuous drug infusion: setup and test of a mobile closed-loop system for the continuous automated infusion of insulin," IEEE Transactions on Information Technology in Biomedicine, vol. 10, no. 2, pp. 395-402, 2006.

[12] Z. Trajanoski and P. Wach, "Neural predictive controller for insulin delivery using the subcutaneous route," IEEE Transactions on Biomedical Engineering, vol. 45, no. 9, pp. 1122-1134, 1998.

[13] Scott M. Pappada, Brent D. Cameron, Paul M. Rosman, Raymond E. Bourey, Thomas J. Papadimos, William Olorunto, and Marilyn J, " Neural Network-Based Real-Time Prediction of Glucose in Patients with Insulin-Dependent Diabetes " Borst.Diabetes Technology & Therapeutics.Feb 2011.135-141. Volume: 13 Issue 2: February 1, 2011.

[14] Nesreen Samer El_Jerjawi, and Samy S. Abu-Naser, " Diabetes Prediction Using Artificial Neural Network," International Journal of Advanced Science and Technology, Vol.121 (2018), pp. 55-64

[15] Stuart A. Weinzimer, Garry M. Steil, Karena L. Swan, Jim Dziura, Natalie Kurtz, " Fully Automated Closed-Loop Insulin Delivery Versus Semiautomated Hybrid Control in Pediatric Patients With Type 1 Diabetes Using an Artificial Pancreas, American Diabetes Association, ISSN 0149-5992, April 29, 2008.

[16] D. N. M. Abadi, M. H. Khooban, A. Alfi, and M. Siahi, "Design of optimal self-regulation Mamdani-type fuzzy inference controller for type I diabetes mellitus," Arabian Journal for Science and Engineering, vol. 39, no. 2, pp. 977-986, 2014.

[17] G. Steil, K. Rebrin, and J. J. Mastrototaro, "Metabolic modeling and the closed-loop insulin delivery problem," Diabetes research and clinical practice, vol. 74, pp. S183-S186, 2006.

[18] M. F. Alamaireh, "A Predictive Neural Network Control Approach in Diabetes Management by Insulin Administration," 2006 2nd International Conference on Information & Communication Technologies, Damascus, 2006, pp. 1618-1623, doi: 10.1109/ICTTA.2006.1684626.

[19] C. Li and R. Hu, "Fuzzy-PID Control for the Regulation of Blood Glucose in Diabetes," 2009 WRI Global Congress on Intelligent Systems, Xiamen, 2009, pp. 170-174, doi: 10.1109/GCIS.2009.280.

[20] Sakthivel, R., Raajananthini., Kwon, O.M. and Mohanapriya, S., 2019. Estimation and disturbance rejection performance for fractional order fuzzy systems. ISA transactions, 92, pp.65-74.

[21] Sakthivel, R., Karthick.S.A, Kaviarasan, B. and Alzahrani, F., 2018. Dissipativity-based non-fragile sampled-data control design of interval type-2 fuzzy systems subject to random delays. ISA transactions, 83, pp.154-164.

[22] Heydarinejad, H., Delavari, H. & Baleanu, D. Fuzzy type-2 fractional Backstepping blood glucose control based on sliding mode observer. Int. J. Dynam. Control 7, 341–354 (2019). https://doi.org/10.1007/s40435-018-0445-8

[23] Sakthivel, R.,Kaviarasan, B., Selvaraj, P. and Karimi, H.R., 2019. EID-based sliding mode investment policy design for fuzzy stochastic jump financial systems. Nonlinear Analysis: Hybrid Systems, 31, pp.100-108.

[24] T.-C. Lin, Y.-J. Huang, I. Josephine, J. Lin, V. E. Balas, and S. Srinivasan, "Genetic algorithm-based interval type-2 fuzzy model identification for people with type-1 diabetes," in Fuzzy Systems (FUZZ-IEEE), 2017 IEEE International Conference on, 2017, pp. 1-6: IEEE.

[25] Arash Sharifi, Asiyeh Vosolipour, Mahdi Aliyari Sh ; Mohammad Teshnehlab, " Hierarchical Takagi-Sugeno type fuzzy system for diabetes mellitus forecasting," 2008 International Conference on Machine Learning and Cybernetics: IEEE.

[26] N. S. Bajestani, A. V. Kamyad, E. N. Esfahani, and A. Zare, "Nephropathy forecasting in diabetic patients using a GA-based type-2 fuzzy regression model," Biocybernetics and Biomedical Engineering, vol. 37, no. 2, pp. 281-289, 2017.

[27] Iftikhar Ahmad, FaysalMunir, Muhammad FaizanMunir, " An adaptive backstepping based non-linear controller for artificial pancreas in type 1 diabetes patients," Biomedical Signal Processing and Control Volume 47, January 2019, Pages 49-56.

[28] R. HariKumar, V.K. Sudhaman, C.Ganesh Babu, " FPGA Synthesis of Fuzzy (PD and PID) Controller for Insulin Pumps in Diabetes Using Cadence," International Journal of Soft Computing and Engineering (IJSCE) ISSN: 2231-2307, Volume-1, Issue-6, January 2012

[29] H. Taghavifar, A. Mardani, C. Hu and Y. Qin, "Adaptive Robust Nonlinear Active Suspension Control Using an Observer-Based Modified Sliding Mode Interval Type-2 Fuzzy Neural Network," in IEEE Transactions on Intelligent Vehicles, vol. 5, no. 1, pp. 53-62, March 2020, doi: 10.1109/TIV.2019.2955365.

[30] Kavikumar,R., Sakthivel, R., Kwon.O.M. and Kaviarasan, B., 2020. Robust model reference tracking control for interval type-2 fuzzy stochastic systems. IET Control Theory & Applications, 14(9), pp.1123-1134.

[31] Mohammadzadeh, A., Taghavifar, H. A robust fuzzy control approach for path-following control of autonomous vehicles. Soft Comput 24, 3223–3235 (2020).

[32] M. Penet. Robust Nonlinear Model Predictive Control based on Constrained Saddle Point Optimization : Stability Analysis and Application to Type 1 Diabetes. PhD thesis, Sup´elec, 2013.

[33] Y. Ramprasad, G. P. Rangaiah, and S. Lakshminarayanan, " Robust PID Controller for Blood Glucose Regulation in Type I Diabetics," Industrial & Engineering Chemistry Research 2004, 43, 26, 8257-8268, November 30, 2004.

[34] D. N. M. Abadi, M. H. Khooban, A. Alfi, M. J. A. J. f. S. Siahi, and Engineering, "Design of optimal self-regulation Mamdani-type fuzzy inference controller for type I diabetes mellitus," vol. 39, no. 2, pp. 977-986, 2018