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Adaptive Fuzzy Control of Blood Glucose Level in Patients with Type 1 Diabetes in Presence of Input Saturation

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ABSTRACT

In this research, an adaptive fuzzy controller is presented to regulate the blood glucose level of type 1 diabetic patients in the presence of input saturation. This controller along with an adaptive anti-windup compensator is considered to deal with the uncertainty of the Bergmann minimal nonlinear model parameters as well as the input saturation. Anti windup compensator is designed to prevent to saturation problems as hyperglycemia or hypoglycemia in regulating the blood glucose level of type 1 diabetes patients. The Bergman minimal model is used to mathematically model type 1 diabetes, depicting the dynamic behavior of the human body's blood glucose-insulin system. In the first step, the stability of the closed-loop system has been theoretically investigated and proved from the point of view of Lyapunov's theory. Next, to evaluate the effectiveness of the proposed method in regulating blood glucose levels, the proposed control system has been implemented in the presence of meal disturbances using the Simulink environment of MATLAB software. The implementation results show a lower control effort and less convergence time of the proposed method compared to the existing methods.

I. Introduction

Blood glucose level is one of the most important parameters that determines the health of the metabolic system. The normal function of this system is to maintain the blood glucose level in the range 70 to 110 mg/dl [1]. The amount of insulin secretion on the one hand and the amount of glucose received by the cells in response to insulin on the other hand are decisive in regulation of the blood glucose level.

Type 1 diabetes is originated by an autoimmune response in which the beta cells of the pancreas that are responsible for insulin production are attacked by the immune system. Consequently, insulin production will decrease [2, 3, 4, 5, 6] and blood glucose will increase.

Due to the complications caused by abnormal blood glucose levels, regulation of blood glucose concentration is very important and vital for patients. Therefore, many researches have been planned in recent years. Robust controllers [7, 8] and sliding mode control (SMC) [9, 10] are very popular. They can handle disturbances and uncertainties. However, a common drawback of SMC is the chattering phenomenon. To cope with this problem, higher order sliding mode controllers have been proposed. PID controllers [11, 12, 13, 14] need to be tuned for optimal performance. In addition, PID controllers are not able to cope with saturated insulin conditions. As a result, these controllers can lead to decrease blood glucose levels and hypoglycemia. Model predictive controllers [15, 16, 17] require a robust optimization scheme, which may be computationally expensive. In biomedicine, the accuracy of estimated models limits the performance of model-based predictive control methods. Moreover, providing a generally accurate model is difficult when the controlled subject is a human due to day-to-day and subject-to-subject variations.

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In [18], an observer-based adaptive controller is designed to deal with the patient parameter variations and lack of access to all state variables for measurement. In [19], an adaptive fuzzy integral sliding mode controller was proposed for regulating blood glucose levels. System dynamics were identified online using fuzzy logic systems. In [20], an adaptive backstepping control strategy is designed for a non-linear minimal Bergman model considering all the unknown parameters. In the aforementioned article, the control effort does not have a smooth behavior and also the problem of input saturation is not considered. In [21], the output-feedback continuous-twisting algorithm is applied to regulate the blood glucose concentration. The Robust output controller has been provided a practical criterion to tune the controller gains that may be used to individualize the insulin therapy. In [22], a positive input observer-based controller is designed for an Extended Bergman's Minimal Model. The backstepping approach is employed to design the feedback controller. The controller used the first state as feedback. The second state and the third states are estimated using the proposed observers. The controller is robust upon external disturbance and uncertainties in system parameters. In [23], a robust adaptive fractional sliding mode controller is studied for a nonlinear fractional order model of glucose insulin Systems. In [23], the unknown upper bound of model uncertainties and disturbances is obtained via a stable adaptive law and proposed controller was designed to stabilize a nonlinear affine fractional order system. In [24], robust fuzzy adaptive approach is considered to control the blood glucose level of type 1 diabetic patients in the presence of uncertainties. The proposed controller is based on the feedback linearization control approach and robust adaptive compensator confront with nonlinear dynamics, in which frequently involve uncertainties in system parameters and disturbance.

Due to physical constraints, most of control systems have limitations on the input signal (control signal) that may lead to input saturation. In this situation, if input saturation occurs, undesirable effects such as performance degradation or instability, known as windup phenomenon, will happen. Anti-windup is a method of preventing windup or recovering the unconstrained response after saturation has occurred by modifying the controller in a feedback loop. Anti-windup controllers have been studied in the literature extensively. In [25], adaptive fuzzy control is developed for a class of non-strict feedback systems with input saturation and output constraint. Combining fuzzy logic and adaptive back-stepping can solve input saturation and output limitation. In [26], a virtual saturation function and adaptive anti-windup compensator has been designed to deal with input saturation. In [27], the stability problem in systems with uncertainty and input saturation is investigated and an adaptive PID control method is proposed that uses both state-feedback and output-feedback methodologies. In [27], an adaptive anti-windup controller for chaos synchronization has been presented. The gain in the anti-windup compensator in [27] can be constant or variable and both of these strategies have been studied. The main controller is a PID controller with time-varying coefficients.

In order to highlight the superiority of the proposed controller in this paper, it must be mentioned that the problem of input saturation has not been considered in most of the previous related works [1-24]. Therefore, in the current research, the focus is on designing the controller to cope with input saturation as hyperglycemia or hypoglycemia in regulating the blood glucose level of type 1 diabetes patients and also determine the dose injected insulin to remain in appropriate range. For this purpose, an adaptive controller for regulation of blood glucose has been designed considering limitations on insulin injection. All uncertainties including parametric and non-parametric uncertainties are estimated and compensated using adaptive fuzzy systems. Similar to [27], two strategies have been adopted for the feedback gain in the anti-windup compensator. Based on the Lyapunov theorem, the adaptation rules for the fuzzy system and the gain of the anti-windup compensator are obtained. However, in comparison with [27], the number of virtual differential equations used in the controller design and stability analysis has been reduced which results in less computational complexity of the controller. In comparison with [20], the proposed controller is superior due to considering input saturation and more flexibility against uncertainties. In fact, in [20], parametric uncertainty has been considered which needs nominal model of the system. However, the proposed controller, compensates the lumped uncertainty. In other words, the proposed controller is model-free and can be used in the situations where the nominal model is not available. The novelties of the current work can be summarized as:

i. Designing adaptive fuzzy controller with adaptive anti-windup compensator for to regulate the blood glucose level of type 1 diabetic patients in the presence of input saturation has been studied in this paper, while the problem of input saturation has not been considered in most of the previous related works [1-24].

ii. In comparison with [27], the number of virtual control laws has been reduced which results in fewer adaptation laws.

iii. In comparison with [27], it must be mentioned that instead of PID controller, adaptive fuzzy controller has been designed in this paper. Adaptive fuzzy control is a more powerful strategy in uncertainty estimation and compensation.

iv. The need for Lipshitz property of the uncertainty function has been relaxed in the proposed method, while in [27], it is a necessary assumption.

The rest of the paper is organized as follows: Mathematical model is discussed in section 2. The controller design and stability analysis are presented in section 3. The simulation results of the control method are presented in Section 4 and finally, concluding remarks are given in Section 5.

II. Mathematical representation of glucose-insulin system

Bergman's minimal model is a mathematical model that illustrates the insulin-glucose system with some parameters [28, 29]. One of the main advantages of Bergman's minimal model is that it contains a minimal number of parameters. This model describes the interactions without biological complexity between the main components such as insulin and glucose concentration [30]. This model has a relative degree of three and consists of three differential equations that describe the insulin-glucose regulatory system with sufficient accuracy as follows [31]:

$$\dot{G}(t) = -p_1(G(t) - G_b) - G(t)X(t) + d(t) \tag{1}$$

$$\dot{X}(t) = -p_2X(t) + p_3(I(t) - I_b) \tag{2}$$

$$\dot{I}(t) = -p_4(I(t) - I_b) + \gamma(G(t) - h)^+ t + u(t) \tag{3}$$

The signals $G(t)$, $X(t)$, and $I(t)$ are the blood glucose concentration (mg/dl), the effect of insulin on glucose concentration reduction (min^{-1}), and the insulin concentration in plasma $(\mu U/ml)$, respectively. The parameter $G_b$represents the basal plasma glucose (mg/dl), I_b is the basal plasma insulin concentration $(\mu U/ml)$. The parameter p_1 denotes the insulin-independent glucose-utilization rate (min^{-1}), p_2 is the rate of decrease of the tissue glucose uptake ability (min^{-1}), p_3 denotes the insulin-dependent increase of glucose uptake ability $(\mu U/ml)^{-1}min^{-1}$, n is the first order decay rate for insulin blood (min^{-1}), γ is the rate of pancreatic release of insulin after bolus and h is the glucose threshold level for insulin secretion by the pancreas. The “+” sign in (3) indicates the positive reflection of glucose intake [20, 32] and "u” is the system input and actually the insulin injection rate. Also, d(t) represents a meal that is an external disturbance and is defined as follows

$$d(t) = \begin{cases} 0 & t < t_0 \\ A_1 exp\big(-B(t - t_0)\big) & t \geq t_0 \end{cases} \tag{4}$$

To describe what food intake will do to the concentration of glucose term. The coefficients A_1, and B have positive values

III. The proposed controller design

An adaptive fuzzy control structure and an adaptive anti-windup compensator are proposed to handle input saturation and compensate the lumped uncertainty. It is shown in the appendix that equations 1 to 3 can be converted to equation 5. Consider the following nonlinear model

$$\begin{aligned} \dot{x}_1 &= x_2 \\ \dot{x}_2 &= x_3 \\ &\vdots \\ \dot{x}_{n-1} &= x_n \\ \dot{x}_n = x^{(n)} &= f(x) + b(x)u \\ y &= Cx \end{aligned} \tag{5}$$

Where u is the control input, y is the desired output, $x = \left[x, \dot{x}, \dots, x^{(n-1)}\right]^T$ is the state vector, $f(x)$ and $b(x)$ are non-linear functions of are the state. The representation of state space (5) can be rewritten as:

$$\frac{d}{dt}\begin{bmatrix} x_1 \\ \dots \\ x_{n-1} \\ x_n \end{bmatrix} = \begin{bmatrix} x_2 \\ \dots \\ x_n \\ f(x) + b(x)u \end{bmatrix} \tag{6}$$

In the input-output linearization method, a controller is determined after establishing a linear input-output relationship. To explicitly relate output y and input u, the system output is differentiated n times if necessary (n denotes relative degree). The relative degree of the system is needed for controller design. The number of successive differentiations until the control appears in the equation will define the relative degree. The relative degree of this system is three.

For systems that can be represented in a conventional form of controllability using the following control input (assuming that b is opposite to zero).

$$bu + f = v \ , \qquad u = \frac{1}{b}(v - f) \tag{7}$$

Non-linearities can be removed and the following input-output relationship can be obtained.

$$y^{(n)} = v \tag{8}$$

Therefore, the control law

$$v = -k_0 y - k_1\dot{y} - \dots - k_{n-1}y^{(n-1)} \tag{9}$$

Choose k_i so that the roots of polynomial $p^n + k_{n-1}p^{n-1} + \dots + k_0$ have negative real parts, resulting in exponential stable dynamics.

$$y^{(n)} + k_{n-1}y^{(n-1)} + \dots + k_0 y = 0 \tag{10}$$

Which implies that $y(t) \to 0$. For tracking the desired output $y_d(t)$, the following control law

$$v = y_d^{(n)} - k_0 e - k_2\dot{e} - \dots - k_{n-1}e^{(n-1)} \tag{11}$$

Where $e(t) = y(t) - y_d(t)$ is the tracking error, it results in exponential convergence of tracking.

To design the controller, rewrite the system model with input saturation.

$$\begin{aligned} \dot{x} &= Ax + b(x)f(x) + b(x)sat(u) + b(x)d(t) \\ y &= cx \end{aligned} \tag{12}$$

$$A = \begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 0 \end{bmatrix} \; , \; b = \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix} \; , \qquad c = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix} \tag{13}$$

where $x \in R^n$, $u \in R$ and $y \in R$ are the state vector, input and output of the system respectively. Let f be a uniform vector field on R^n. $A \in R^{n \times n}$ and $b, c \in R^n$ are constant matrices of the system, (A, b) is controllable and $f(x)$ is the nonlinear vector function and $d(t)$ is an external disturbance in diabetic patients.

Remark 1 Transformation of the Bergman's minimal model to (12) and (13) paves the way for designing adaptive anti-windup controller.

A. Input saturation

In equation (12), sat(u) is the saturation function [27]

$$sat\big(u(t)\big) = \begin{cases} u_{uppper} & u(t) \geq u_{uppper} \\ u(t) & u_{lower} < u(t) < u_{uppper} \\ u_{lower} & u(t) \leq u_{lower} \end{cases} \tag{14}$$

where $u_{uppper} > 0$ and $u_{lower} = 0$ are known constants and are defined as the upper and lower input saturation values of the system, respectively.

In order to design adaptive fuzzy control and anti-windup compensator to deal with input saturation and parameter uncertainty, the following assumptions are proposed:

Assumption 1: A_m is a satisfactory Horwitz matrix. $A_m^T P + P A_m = -Q$, P and Q are symmetric and positive definite matrices.

Assumption 2: Suppose there are constant vectors $K_1^{*T} \in R^n$ and $K_b \in R$ to satisfy the following equation

$$A_m = A + (1 - K_b) b K_1^{*T} u_{uppper} \tag{15}$$

B. Anti-windup compensation model

In the case that saturation occurs, a corrective feedback action $\mathrm{u_{aw}}(t)$ is needed as follows [27, 35].

$$u_{aw}(t) = K_b\big(sat(u) - u_c(t)\big) \tag{16}$$

Where K_b is the weighting factor for anti-windup.

Remark 2 There are two strategies for K_b. In the first strategy, the value of K_b remains unchanged and in the second strategy, K_b is variable and can be estimated online. Both of these strategies are studied in this paper.

C. The proposed controller design with constant K_b

The tracking error is defined as $\tilde{x} = G - G_{bref}$ and $G_{bref}{=}120exp(-\alpha t){+}80 \quad 0{<}\alpha{<}1$ is the reference value of glucose. Consider the following definitions:

$$\begin{aligned} \tilde{x}_1 &= G - G_{bref} \\ \dot{\tilde{x}}_1 &= \dot{G} - \dot{G}_{bref} \quad \tilde{x} = \begin{bmatrix} \tilde{x}_1 \\ \dot{\tilde{x}}_1 \\ \ddot{\tilde{x}}_1 \end{bmatrix} \\ \ddot{\tilde{x}}_1 &= \ddot{G} - \ddot{G}_{bref} \end{aligned} \tag{17}$$

$$\Delta u = sat(u) - u(t) \tag{18}$$

The equations of the closed-loop system (12) can be rewritten as follows

$$\begin{aligned} \dot{\tilde{x}} &= A\tilde{x} + bf(x) + bu + b\Delta u + bd \\ &\qquad - bv \quad , \quad v = \dddot{G}_{bref} \\ y &= c\tilde{x} \end{aligned} \tag{19}$$

$$\begin{aligned} \dot{\tilde{x}} &= A\tilde{x} + b\big(f(x) + u + \Delta u + d - \dddot{G}_{bref}\big) \\ y &= c\tilde{x} \end{aligned} \tag{20}$$

Now consider the control input u as below

$$u = u_c(t) + u_{aw}(t) + \dddot{G}_{bref} \tag{21}$$

Where u_c is the control input and u_{aw} is the anti-windup compensator. To remove the effect of the Δu term in equation (19), Δx is defined as the following differential equation

$$\dot{\Delta x} = A_m \Delta x + \widehat{K}_\Delta \Delta u \text{ ، } \Delta x(0) = 0 \tag{22}$$

Consider the following definitions.

$$\widetilde{K}_\Delta = b - \widehat{K}_\Delta \tag{23}$$

$$e = \tilde{x} - \Delta x \tag{24}$$

By replacing equations (20) in $\dot{\tilde{x}}$, (22) in $\dot{\Delta x}$ and also using the assumption two instead of A and the definition $\widetilde{K}_\Delta = b - \widehat{K}_\Delta$, The derivative of the Augmented error e is obtained as follows

$$\begin{aligned} \dot{e} = \dot{\tilde{x}} - \dot{\Delta x} = A_m e + bf(x) + bu + \widetilde{K}_\Delta \Delta u \\ + bd - b\dddot{G}_{bref} \\ - (1 - K_b) b K_1^{*T} \tilde{x} \end{aligned} \tag{25}$$

According to equation (16), $sat(u)$ is bounded and has an upper bound as follows [27]

$$|sat(u)| \leq L_1^* \tag{26}$$

Where L_1^* is a constant. The control input $\mathrm{u_c}$ is as follows

$$u_c = -\big(u_{fuzzy}/(1 - K_b)\big) + u_{classical} \tag{27}$$

Remark 3 The need for Lipshitz property of the uncertainty function has been relaxed in the proposed method, while in [27], it is a necessary assumption.

Remark 4 In comparison with [27], it must be mentioned that instead of PID controller, adaptive fuzzy controller has been designed in this paper. Adaptive fuzzy control is a more powerful strategy in uncertainty estimation and compensation.

The fuzzy IF-THEN rules that describe human control actions [33]

$$If \; x_1 \; is \; P_1^r \; and \ldots and \; x_n \; is \; P_n^r, then \; u \; is \; Q^r \tag{28}$$

where P_n^r and Q^r are fuzzy sets in R and $r = 1\text{،}2\text{،}\ldots\text{،}L_u$. The fuzzy controller should be designed in such a way that the rules (28) can be naturally incorporated [33]. To incorporate the rules (28), the fuzzy controller is as follows

$$u = u_{fuzzy}(X|\theta) \tag{29}$$

where u_{fuzzy} is a fuzzy system and θ is a set of adjustable parameters. Specifically, the fuzzy system $u_{fuzzy}(X|\theta)$ is constructed from the following two steps.

First step: for each variable x_i $(i = 1\text{،}2\text{،}\ldots\text{،}n)$, m_i the fuzzy set $A_i^{l_i}$ $(l_i = 1\text{،}2\text{،}\ldots\text{،}m_i)$ is defined, where P_n^r $(r = 1\text{،}2\text{،}\ldots.\text{،}L_u)$ in (28) as a special case.

The second step: construct the fuzzy system $u_{fuzzy}(X|\theta)$ from following $\prod_{i=1}^{n} m_i$ rules.

$$\begin{aligned}&If\ x_1\ is\ A_1^{L_1}\ and \ldots and\ x_n\ is A_n^{L_n}, then\\ &u_{fuzzy} is\ S^{L_1 \ldots L_n}\end{aligned} \tag{30}$$

where $l_i = 1\text{،}2\text{،}\ldots\text{،}m_i$, $i = 1\text{،}2\text{،}\ldots\text{،}n$, and $S^{L_1 \ldots L_n}$ will be equivalent to Q^r in equation (28), so that the part if the equation (30) with the part If equation (28) agrees; Otherwise, it is equivalent to an arbitrary fuzzy set. Specifically, by using the product fuzzy inference engine the singleton fuzzifier and the center average de-fuzzifier, the following relationship will be obtained [33].

$$u_{fuzzy}(X|\theta) = \frac{\sum_{l_1=1}^{m_1} \cdots \sum_{l_n=1}^{m_n} \bar{y}_u^{l_1 \ldots l_n} \left[\prod_{i=1}^{n} \mu_{A_i}^{l_i(x_i)}\right]}{\sum_{l_1=1}^{m_1} \cdots \sum_{l_n=1}^{m_n} \left[\prod_{i=1}^{n} \mu_{A_i}^{l_i(x_i)}\right]} \tag{31}$$

where $\bar{y}_u^{l_1 \ldots l_n}$ are selected as adjustable parameters and these parameters are collected in the vector $\theta \epsilon R^{\prod_{i=1}^{n} m_i}$. The fuzzy controller u_{fuzzy} is defined as below [33]

$$u_{fuzzy} = \hat{\theta}^T \zeta(x) \tag{32}$$

where $\zeta(x)$ is the vector of the fuzzy basis function and θ is the adjustable parameter.

Also, $u_{classical}$, which is used for system stability as follows

$$u_{classical} = \hat{K}_1^T \tilde{x} - \frac{K_b}{1 - K_b} \hat{L}_1 sgn(e^T Pb) \tag{33}$$

where $\hat{K}_1$ is the estimate of classical control gain K_1. By substituting equations (32) and (33) into equation (27) and also by substituting equations (27) and (15) into equation (21) and by using equation (21) into equation (25), the derivative of the augmented error e as follows

$$\begin{aligned}\dot{e} = A_m e + bf(x) + (1 - K_b)b \Big[\hat{K}_1^T \tilde{x} &\\ - \frac{K_b}{1 - K_b} \hat{L}_1 sgn(e^T Pb) &\\ - \left(\hat{\theta}^T \zeta(x)/(1 - K_b)\right)\Big] &\\ + \qquad K_b bsat(u) + \tilde{K}_\Delta \Delta u &\\ + bd - (1 - K_b) b K_1^{*T} \tilde{x} &\end{aligned} \tag{34}$$

By definition

$$\acute{f}(x) = f(x) + d \ = \theta^T \zeta(x) \tag{35}$$

$$\tilde{K}_1 = \hat{K}_1 - K_1^*, \qquad \tilde{\theta} = \hat{\theta} - \theta \tag{36}$$

By Substituting equations (35) and (36) into equation (34), the derivative of the augmented error e is defined as follows

$$\begin{aligned}\dot{e} = A_m e + K_b bsat(u) + \tilde{K}_\Delta \Delta u &\\ + (1 - K_b) b \tilde{K}_1^T \tilde{x} - b\tilde{\theta}^T \zeta(x) &\\ - bK_b \hat{L}_1 sgn(e^T Pb) &\end{aligned} \tag{37}$$

To remove the effect of the term K_b in equation (37), Δe is defined as the following differential equation

$$\dot{\Delta e} = A_m \Delta e + u_e \ , \qquad \Delta e(0) = 0 \tag{38}$$

The u_e is defined as follows

$$u_e = \ \hat{K}_{be} bsat(u) \tag{39}$$

By defining $\tilde{K}_{be} = K_b - \hat{K}_{be}$ and using equation (37) instead of $\dot{e}$ and replacing equation (39) in equation (38) and also using equation (38) instead of $\dot{\Delta e}$, the derivative of the augmented error $e_1 = e - \Delta e$, will be as follows

$$\begin{aligned}\dot{e_1} = \dot{e} - \dot{\Delta e} = A_m e_1 - \tilde{K}_{be} b\big(sat(u)\big) + \tilde{K}_\Delta \Delta u &\\ + (1 - K_b) b \tilde{K}_1^T \tilde{x} - b\tilde{\theta}^T \zeta(x) &\\ - \ bK_b \hat{L}_1 sgn(e^T Pb) &\end{aligned} \tag{40}$$

According to equation (40) and to substitute equations (32) and (33) into equation (27) and also to substitute equations (27) and (15) into equation (21), the adaptive laws are derived as

$$\dot{\tilde{K}}_1 = -\gamma_1 {e_1}^T Pb\tilde{x} \tag{41}$$

$$\dot{\tilde{K}}_\Delta^T = -\gamma_2 {e_1}^T Pb\Delta u \tag{42}$$

$$\dot{\tilde{K}}_{be} = \gamma_3 {e_1}^T Pbsat(u) \tag{43}$$

$$\dot{\tilde{\theta}} = \gamma_4 {e_1}^T P\zeta \tag{44}$$

$$\dot{\tilde{L}}_1 = \gamma_5 |{e_1}^T Pb| \tag{45}$$

where $\tilde{L}_i = \hat{L}_i - L_i^*$, γ_j $j = 1,2,3, \ldots$ are positive constant coefficients.

Proof: With $0 < K_b < 1$, the positive definite Lyapunov function can be considered as follows

$$\begin{aligned}V = {e_1}^T Pe_1 + (1 - K_b)\gamma_1^{-1} \tilde{K}_1^T \tilde{K}_1 + \gamma_2^{-1} \tilde{K}_\Delta^T \tilde{K}_\Delta &\\ + \gamma_3^{-1} \tilde{K}_{be}^2 + \gamma_4^{-1} \tilde{\theta}^T \tilde{\theta} &\\ + K_b \gamma_5^{-1} \tilde{L}_1^2 &\end{aligned} \tag{46}$$

The derivative of the Lyapunov function is

$$\dot{V} = \dot{e_1}^T P e_1 + e_1^T P \dot{e_1} + 2(1 - K_b)\gamma_1^{-1}\widetilde{K}_1^T \dot{\widetilde{K}}_1 + 2\gamma_2^{-1}\widetilde{K}_\Delta^T \dot{\widetilde{K}}_\Delta + 2\gamma_3^{-1}\widetilde{K}_{be}\dot{\widetilde{K}}_{be} + 2\gamma_4^{-1}\tilde{\theta}^T\dot{\tilde{\theta}} + 2\gamma_5^{-1}K_b\tilde{L}_1\dot{\tilde{L}}_1 \tag{47}$$

By substituting equations (40) - (45) respectively instead of $\dot{e_1}$, $\dot{\widetilde{K}}_1$, $\dot{\widetilde{K}}_\Delta$, $\dot{\widetilde{K}}_{be}$, $\dot{\tilde{\theta}}$, and $\dot{\tilde{L}}_1$ in equation (47), by using the assumption of one and two in equation (47) and also $e_1^T Pbsgn(e_1^T Pb) = |e_1^T Pb|$ [34]. Finally, we have

$$\dot{V} \le -\tilde{x}^T Q \tilde{x} \tag{48}$$

D. *The proposed controller design with variable K_b*

Considering K_b as the controlling variable coefficient, the second assumption should be modified as follows [27].

Third assumption: Suppose there is a constant vector K_1^* so that the following equation is satisfied [27].

$$A_m = A + bK_1^{*T} \tag{49}$$

Assuming that K_b is variable, equation (15) can be written as follows [27]

$$u_{aw}(t) = \widehat{K}_b\big(sat(u) - u_c(t)\big) \tag{50}$$

The u_c control input is as follows

$$u_c = -u_{fuzzy} + u_{classical} \tag{51}$$

The fuzzy controller $u_{fuzzy}$is defined as follows

$$u_{fuzzy} = \hat{\theta}^T\zeta(x) \tag{52}$$

$\zeta(x)$ is a fuzzy basis function vector and θ is an adjustable parameter. Also, $u_{classical}$ is used for system stability, as follows

$$u_{classical} = \widehat{K}_1^T\tilde{x} - \hat{L}_1 sgn(e^T Pb) \tag{53}$$

By substituting equations (52) and (53) in equation (51) and also by substituting (50), (51) in equation (21), also by substituting equation (21) in equation (19) and by considering the third assumption, $\dot{\tilde{x}}$ is obtained

$$\begin{aligned}\dot{\tilde{x}} &= A\tilde{x} + bf(x) + bu + b\Delta u + bd - b\dddot{G}_{bref} \\ &= (A_m - bK_1^{*T})\tilde{x} + bf(x) \\ &\quad + b\Big(\widehat{K}_b\big(sat(u) - u_c(t)\big) \\ &\quad - \hat{\theta}^T\zeta(x) + \widehat{K}_1^T\tilde{x} \\ &\quad - \hat{L}_1\|x\|sgn(e^T Pb) \\ &\quad - \hat{d}sgn(e^T Pb) + \dddot{G}_{bref}\Big) \\ &\quad + b\Delta u + bd - b\dddot{G}_{bref}\end{aligned} \tag{54}$$

By definition

$$\acute{f}(x) = f(x) + d = \theta^T\zeta(x) \tag{55}$$

By placing equations (55) in equation (54) and using the definitions $\widetilde{K}_1^T = \widehat{K}_1^T - K_1^{*T}$ and $\tilde{\theta} = \hat{\theta} - \theta$, equation (54) can be written as follows

$$\begin{aligned}\dot{\tilde{x}} &= A_m\tilde{x} + b\widetilde{K}_1^T x - b\tilde{\theta}^T\zeta(x) + b\Delta u \\ &\quad + b\widehat{K}_b\big(sat(u) - u_c(t)\big) \\ &\quad - b\hat{L}_1 sgn(e^T Pb)\end{aligned} \tag{56}$$

To remove the effect of some terms, Δx is defined as the following differential equation [27]

$$\dot{\Delta x} = A_m\Delta x + u_x \text{ ، } \Delta x(0) = 0 \tag{57}$$

The virtual control u_x is defined as follows

$$\begin{aligned}u_x &= K_b b\big(sat(u) - u_c(t)\big) + \widehat{K}_\Delta\Delta u, \\ &\Delta x(0) = 0\end{aligned} \tag{58}$$

Remark 5 The number of virtual systems such as (57) has been reduced in the proposed method in comparison with [27].

By substituting equation (56) in $\dot{\tilde{x}}$, substituting equation (58) in equation (57), substituting equation (57) in $\dot{\Delta x}$ and also using the third assumption $A_m + bK_1^{*T}$ instead of A and using the definitions $\widetilde{K}_\Delta = b - \widehat{K}_\Delta$ and $\widetilde{K}_b = \widehat{K}_b - K_b$, the augmented error derivative of the equation $e = \tilde{x} - \Delta x$ is obtained as follows

$$\begin{aligned}\dot{e} = \dot{\tilde{x}} - \dot{\Delta x} &= A_m e + b\widetilde{K}_1^T\tilde{x} - b\tilde{\theta}^T\zeta(x) \\ &\quad + \widetilde{K}_\Delta\Delta u \\ &\quad + b\widetilde{K}_b\big(sat(u) - u_c(t)\big) \\ &\quad - b\hat{L}_1 sgn(e^T Pb)\end{aligned} \tag{59}$$

According to equation (59) and to substitute equations (52) and (53) in equation (51) and also to substitute equations (50) and (51) in equation (21), the adaptive laws are derived as

$$\dot{\widetilde{K}}_1 = -\gamma_1 e^T Pb\tilde{x} \tag{60}$$

$$\dot{\widetilde{K}}_\Delta^T = -\gamma_2 e^T P\Delta u \tag{61}$$

$$\dot{\widetilde{K}}_b = -\gamma_3 e^T Pb\big(sat(u) - u_c(t)\big) \tag{62}$$

$$\dot{\tilde{\theta}} = -\gamma_4 e^T Pb\zeta \tag{63}$$

$$\dot{\tilde{L}}_1 = \gamma_5|e_1^T Pb| \tag{64}$$

Where γ_j $j = 1,2,3,\dots$ are positive constant coefficients

Proof: The following Lyapunov function candidate is chosen

$$\begin{aligned}V &= e^T Pe + \gamma_1^{-1}\widetilde{K}_1^T\widetilde{K}_1 + \gamma_2^{-1}\widetilde{K}_\Delta^T\widetilde{K}_\Delta + \gamma_3^{-1}\widetilde{K}_b^2 \\ &\quad + \gamma_4^{-1}\tilde{\theta}^T\tilde{\theta} + \gamma_5^{-1}\tilde{L}_1^2\end{aligned} \tag{65}$$

The derivative of the Lyapunov function is

$$\begin{aligned}\dot{V} &= \dot{e}^T Pe + e^T P\dot{e} + 2\gamma_1^{-1}\widetilde{K}_1^T\dot{\widetilde{K}}_1 + 2\gamma_2^{-1}\widetilde{K}_\Delta^T\dot{\widetilde{K}}_\Delta \\ &\quad + 2\gamma_3^{-1}\widetilde{K}_b\dot{\widetilde{K}}_b + 2\gamma_4^{-1}\tilde{\theta}^T\dot{\tilde{\theta}} \\ &\quad + 2\gamma_5^{-1}\tilde{L}_1\dot{\tilde{L}}_1\end{aligned} \tag{66}$$

By substituting equations (59) - (64) instead of $\dot{e}$, $\dot{\tilde{K}}_1$, $\dot{\tilde{K}}_\Delta$, $\dot{\tilde{K}}_b$, $\dot{\tilde{\theta}}$, $\dot{\tilde{L}}_1$ and also by replacing the assumption of $A_m^T P + PA_m = -Q$ in equation (66), the derivative of the Lyapunov function is obtained as follows

$$\begin{aligned}\dot{V} = -e^TQe - 2e^TPb\hat{L}_1\|x\|sgn(e^TPb) \\ + 2\tilde{L}_1|{e_1}^TPb|\|x\|\end{aligned} \tag{67}$$

Finally, using $e^TPbsgn(e^TPb) = |e^TPb|$, the derivative of the Lyapunov function will be as follows

$$\dot{V} \leq -\tilde{x}^TQ\tilde{x} \tag{68}$$

IV. Simulation results

In this section, the simulation results of the fuzzy adaptive controller with input saturation in the Simulink environment of MATLAB software are presented. In this simulation, the initial values of the Bergman model state variables $\boldsymbol{G(t)}$, $\boldsymbol{X(t)}$, and $\boldsymbol{I(t)}$ are considered to be 200, 0, and 50, respectively and $\boldsymbol{0 \leq u(t) \leq 60\quad \mu U/ml/min}$ [32]. Bergman model simulation parameters for two patients and a normal person are used according to Table 1.

TABLE 1 PARAMETERS OF BERGMAN MODEL [20]

Parameters	Normal	Patient 1	Patient 2	Units
$\boldsymbol{p_1}$	0.0317	0	0	min^{-1}
$\boldsymbol{p_2}$	0.0123	0.0142	0.02	min^{-1}
$\boldsymbol{p_3}$	4.92e − 06	1.54e − 05	5.3e − 06	$(\mu\mathrm{U/ml})^{-1}\mathrm{min}^{-1}$
$\boldsymbol{\gamma}$	0.0039	0	0	$(\mu\mathrm{U/ml})(\mathrm{mg/dl})^{-1}\mathrm{min}^{-2}$
$\boldsymbol{n}$	0.2659	0.2814	0.3	min^{-1}
$\boldsymbol{h}$	79.035	_	_	mg/dl
$\boldsymbol{G_b}$	80	80	80	mg/dl
$\boldsymbol{I_b}$	7	7	7	μU/ml
$\boldsymbol{A_1}$	1	1	1	_
$\boldsymbol{B}$	0.05	0.05	0.05	_
$\boldsymbol{t_0}$	450	450	450	min
$\boldsymbol{p_1}$	0.0317	0	0	min^{-1}

The open-loop simulation of Bergman's minimal model has been presented. In the open-loop simulation, the behavior of a diabetic patient and a healthy person have been compared. In Fig. 1, the blood glucose for a healthy person and two patients without insulin injection have been shown. It is easy to see that the blood glucose level of a healthy person will eventually be at the base level, but the patient's blood glucose level cannot reach the desired value and remains out of range.

In order to compare the performances of the different controllers, consider Fig. 3. As shown in this figure, the proposed controller with variable K_b approach can reduce the patient's blood glucose level to the desired value faster than other approaches. Also, it can be seen that using anti-windup compensator in the constant K_b structure will lead to superior results in comparison with the case where no anti-windup compensation is used.

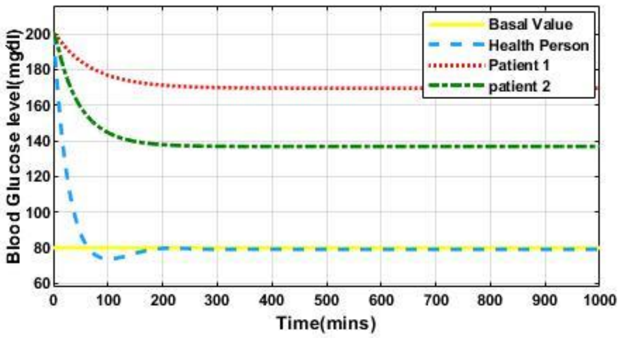


Fig. 1. Blood glucose concentration of patients and a healthy person in open loop simulation

In Fig. 2, the performance of the proposed controller in a diabetic patient and a healthy person have been investigated. In this simulation, the proposed controller can reduce the blood glucose level of type 1 diabetic patients to the desired basal level.

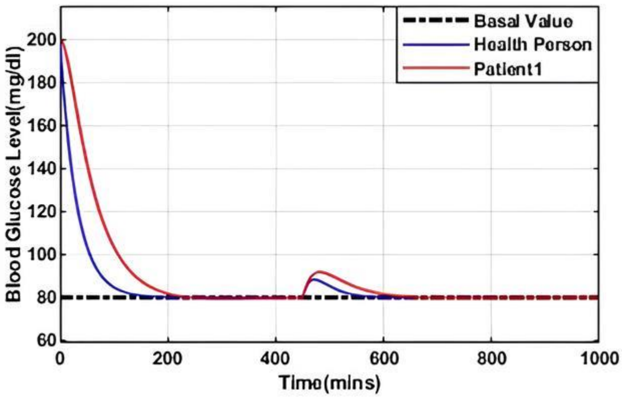


Fig. 2. Blood glucose concentration of patient and a healthy person using the proposed controller

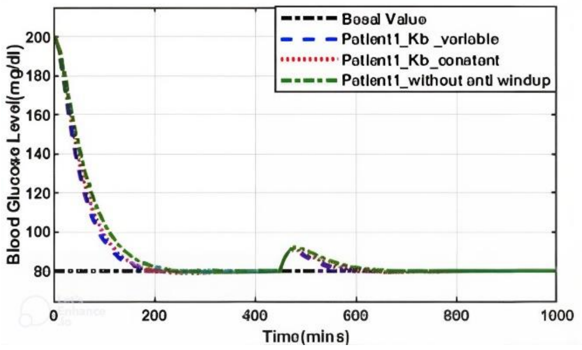


Fig. 3. Comparison of blood glucose level using different controllers

The ideal plasma insulin concentration level is around $7\,(\mu U/ml)$. Fig. 4 shows a comparison between different controllers for plasma insulin concentration. The simulation shows that the insulin concentration converges to the desired level of plasma insulin but variable K_b approach is faster.

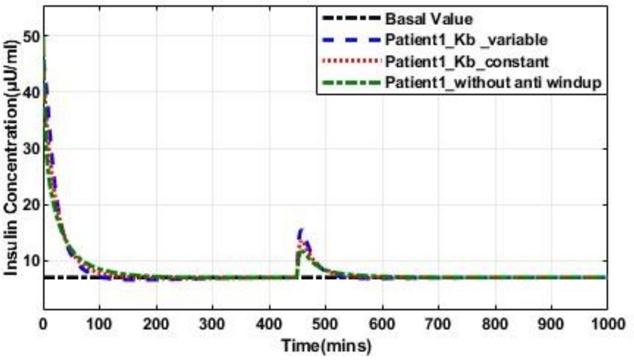


Fig. 4. Comparison of plasma insulin concentration for different controllers

Fig. 5. shows insulin injected by an insulin pump using different controllers. According to this figure, the proposed controller with variable K_b approach has a faster performance than other controllers.

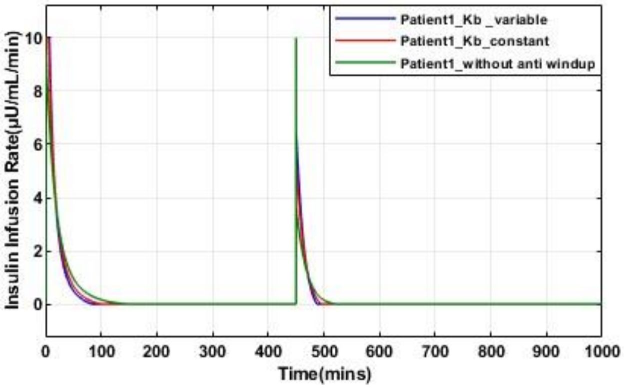
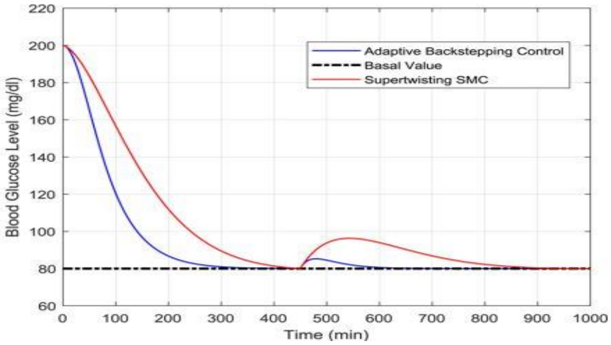


Fig. 5. Comparison of control input (insulin injection rate) using different controllers



In Fig. 6. the convergence of blood glucose level of two different patients are shown. As shown in this figure, for both patients, variable K_b controller is faster.

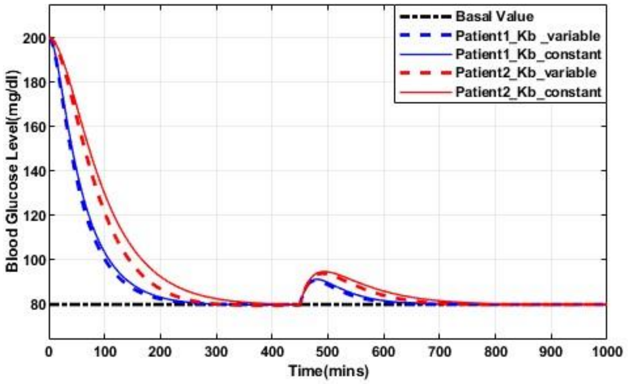


Fig. 6. Comparison of blood glucose levels for two different patients

Comparison of the anti-windup compensator with constant and variable K_b approaches for insulin requirements of two patients is presented in Fig. 7. According to this figure, in both patients, variable K_b controller is faster.

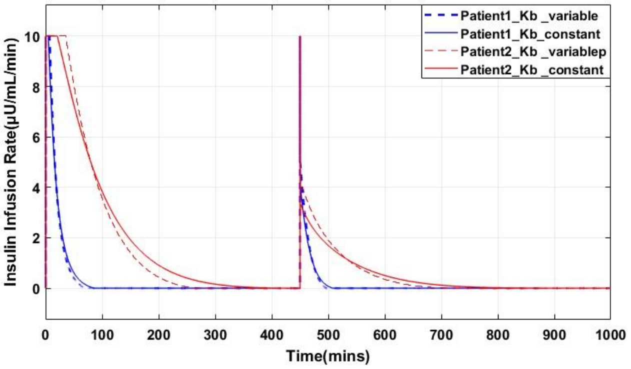
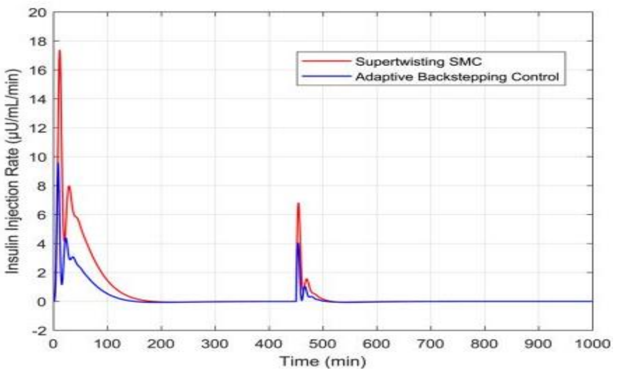


Fig. 7. Comparison of control input for two patients with constant and variable K_b approaches

In Fig. 8, a comparison of blood glucose level and control effort of the adaptive back-stepping and the super twisting SMC has been depicted [20]. It should be mentioned that in these controllers, the limitation on the control effort has not been considered and therefore, the saturation phenomenon in practical implementation may happen. It is obvious that the system operates in an open loop in the presence of saturation for a while. As a result, satisfactory performance of the sliding mode controller and the adaptive back-stepping controller in achieving the desired blood glucose level and dealing with saturation are not guaranteed. According to Fig. 3, Fig. 5 and Fig. 8, it is evident that the proposed controller outperforms the sliding mode controller and the adaptive back-stepping controller in terms of faster output tracking. Moreover, the proposed controllers require less control effort and exhibit faster convergence time.

(a) Blood glucose level



(b) Control effort

Fig. 8. Blood glucose level and control effort using adaptive back-stepping controller and super twisting SMC [20]

In order to have a quantitative comparison, the integral of squared error between the desired glucose and the patient glucose level has been selected as a cost function. The results are presented in Table 2. According to this table, for both patients, the variable K_b approach outperforms the constant K_b approach. Moreover, the controller with constant K_b is superior to the controller with no anti-windup compensation.

TABLE 2 COMPARISON OF COST FUNCTION

Controller	The integral of squared error for patient 1	The integral of squared error for patient 2
variable K_b approach	8.217×10^4	2.846×10^5
Constant K_b approach	1.022×10^5	3.721×10^5
Without anti-windup	1.552×10^5	5.213×10^5

V. Conclusions

In this paper, an adaptive fuzzy controller with anti-windup compensator has been designed to prevent saturation problems in regulating the blood glucose level of type 1 diabetes patients. Bergman's minimal model is considered in this paper for simulations. Stability analysis has been presented based on Lyapunov theorem. Adaptive fuzzy systems have been used to estimate uncertainties. In comparison with previous related works on adaptive anti-windup controllers, the proposed method is simpler with less adaptation laws and less virtual differential equations. Simulation results show the superiority of the proposed method in regulating the blood glucose level of type 1 diabetes patients. According to simulation results, using anti-windup compensator with constant gain results in better performance in comparison with the controller without anti-windup compensator. Also, the controller with variable anti-windup compensator gain outperforms the controller with constant anti-windup compensator gain. For future work, the dynamic anti-windup compensator can be considered as a topic to deal with input saturation in regulating the blood glucose level of type 1 diabetes patients.

APPENDIX

In this article, equation 5 is used to design the parameter $v = \dddot{G}_{bref}$ based on feedback linearization to simplify the structure of the proposed nonlinear control law.

The output is considered as follows

$$y = cx = G \tag{69}$$

By taking time derivative of eq (69), we have

$$\dot{y} = \dot{G} = -p_1(G(t) - G_b) - G(t)X(t) + d(t) \tag{70}$$

The second derivative is given by

$$\begin{aligned}\ddot{y} = \ddot{G} = p_1^2(G(t) - G_b) &+ p_1 X(t)(G(t) - G_b) \\ &+ \big(p_1 + X(t)\big)X(t)G(t) \\ &- \big(p_1 + X(t)\big)d(t) \\ &+ p_2 G(t)X(t) \\ &- p_3 G(t)\big((I(t) - I_b)\big)\end{aligned} \tag{71}$$

The control input did not appear in the second derivative. So, the third derivative must be computed:

$$\begin{aligned}\dddot{y} = \dddot{G} = G(t)[-p_1(p_1^2 + 3p_3 I_b) & \\ &- p_3 I_b(p_2 + p_4) \\ &- p_3\gamma(G(t) - h)^+ t] \\ &+ X(t)[-p_1^2(1 + G_b) \\ &+ p_1 p_2(2G_b - 1) \\ &+ 2d(t)(p_1 + p_2)] \\ &+ I(t)\big[-2p_3\big(p_1 + d(t)\big)\big] \\ &+ G(t)X(t)[-(p_1 + p_2)^2 \\ &- 3p_3 I_b] \\ &+ G(t)I(t)[p_3(3p_1 + p_2 \\ &+ p_4)] \\ &+ G(t)X(t)^2[-3(p_1 + p_2)] \\ &+ X(t)^2\big(p_1 G_b + d(t)\big) \\ &+ 3p_3 G(t)X(t)I(t) \\ &- G(t)X(t)^3 + \ddot{d}(t) \\ &+ \big(p_1 G_b + d(t)\big)(p_1^2 \\ &+ 2p_3 I_b) - p_3 G(t)u(t) \\ &= f(x) + b(x)u\end{aligned} \tag{72}$$

The control input u appears for the first time at the third derivative. So, the relative degree of the system is 3. The state variables are considered as follows

$$\begin{aligned}x_1 &= G - G_{bref} \\ \mathrm{x}_2 &= \dot{G} - \dot{G}_{bref} \\ \mathrm{x}_3 &= \ddot{G} - \ddot{G}_{breff}\end{aligned} \qquad x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} \tag{73}$$

Then, the stste space equations are given by:

$$\begin{aligned}\dot{x}_1 &= \dot{G} - \dot{G}_{bref} \\ \dot{x}_2 &= \dot{G} - \dot{G}_{bref} \\ \dot{x}_3 &= \dddot{G} - \dddot{G}_{bref} = f(x) + b(x)u\end{aligned} \tag{74}$$

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