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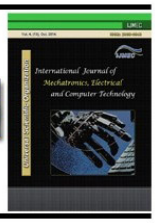

Blood Glucose Regulation Using Adaptive Fuzzy Sliding Mode Control in Type I Diabetic Patients

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Abstract

This paper presents a closed-loop control system to regulate blood glucose level of type I diabetic patients. The main goal of the controller is to avoid hypoglycemia or hyperglycemia. To fulfill this goal, a novel adaptive fuzzy sliding mode controller is developed and its performance is compared to the fuzzy logic controller using Bergman's minimal model for diabetic patients. In the first stage, the performance of the controller is tested against 4 perturbations (breakfast, lunch, dinner, and breakfast). In the second stage, the effect of the delay in the blood glucose sensor on regulation blood glucose is taken into consideration. In this study, we consider 14 minutes lag for the delay of the sensor. The results show that the designed adaptive fuzzy sliding mode controller can regulate the blood glucose level of all diabetic patients in an appropriate time and its results are superior to the fuzzy logic controller in terms of less fluctuation in blood glucose, better set-point tracking, lower risks for hypoglycemia and hyperglycemia, and lower root mean square error, all of which are essential factors for diabetic patients.

Keywords: *Sliding Mode Control, Blood Glucose Regulation, Hyperglycemia, Hypoglycemia.*

1. Introduction

As a disease which acts on the global scale, diabetes attracts the attention of researchers around the world. Diabetes is known to be caused by the improper control of blood glucose (BG) concentration in the body. BG levels are typically kept in normal ranges by two hormones, insulin, and glucagon, secreted by the pancreas. After a meal, the BG concentration increases, which stimulates β-cells in the pancreas to secrete insulin. Insulin causes most tissues of the body to absorb glucose and the excess glucose is stored, mainly in the liver and skeletal muscles, as glycogen. In contrast, between meals or in the state of sleep, the α-cells produce glucagon. Unlike insulin, glucagon acts as a mobilizer and circulates the stored glucose, fatty acids, and amino acids. Therefore, insulin decreases BG concentration and glucagon increases it. The BG concentration should be controlled within the range of 70-180 mg/dl (3.8-10 mmol/l) [14]. The state in which the BG concentration is less than 3.8 mmol/l, is known as hypoglycemia and the state, in which the BG concentration is greater than 10 mmol/l, is known as hyperglycemia [14]. In both states, patient safety is threatened seriously. In addition to diabetic patients, some patients who do not have diabetes but have experienced a surgery, suffer from bad performance of the BG concentration regulatory system in the body [20]. There are two kinds of diabetic patients, type I and type II. In type I, pancreas does not produce any insulin while in type II it

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produces an inadequate amount [20]. Type I diabetes occurs when the β-cells in the pancreatic islets of Langerhans are inactive [18].

There are two methods for regulating the BG levels in diabetic patients, including open-loop control and closed-loop control. In the first method, one should monitor BG concentration and then inject the appropriate dosage of insulin in the blood stream. Because this method is not continuous, it cannot ensure BG level is always closely tracking the normal level.

Closed-loop control has a wide variety of applications in biomedical engineering and modern medicine including robotic surgery, physiological systems, life support, image-guided therapy, and surgery. One aspect of using closed-loop control in drug delivery is insulin delivery in diabetic patients and propofol delivery for keeping anesthesia in the normal state [6], [12], [25]. Nowadays, there is a considerable interest in the regulation of BG concentration on a continuous basis which is known as the closed-loop method. In this method, BG concentration will be monitored continuously by a BG sensor and then a proper dosage of the required insulin needed will be calculated by a controller. This dosage of insulin will then be injected by an infusion pump. It is to say that the closed-loop system acts as an artificial pancreas.

There are many studies in which a closed-loop controller is used to keep the BG concentration of the diabetic patients within the appropriate range. One of the simple, yet efficient controllers which is used in these studies is the Proportional–Integral–Derivative (PID) controller. In [21] a closed-loop PID controller was used in real time for critically ill patients in the intensive care unit. In [22], it has been stated that the PID controller closely parallels the β-cell biphasic insulin response. One of its most important drawbacks of the PID controller is that it does not have good performance in the presence of disturbances and variability in the patient parameters. In order to compensate the effects of uncertainties and disturbances, it is necessary to use adaptive and robust control approaches such as fuzzy logic control, model predictive control (MPC), neural control, sliding mode control (SMC), and etc. Because of the simplicity and intuitiveness of PID controllers as well as the lack of precise information about the system which is being controlled, many researchers prefer using PID controllers and are working on ways to improve them. For this purpose, a genetic algorithm combined PID controller, an improved PID switching control, fuzzy-PID controller, and an adaptive PID controller, were used in [6], [16], [23], [33], [37], respectively.

Because the BG regulatory system is a nonlinear system, researchers in [1] [8] [26] [27] [34] [41], employed MPCs to achieve an appropriate performance. The performance of these controllers is strongly dependent on the model which is being used. In the MPC method, the controller is designed based on the previous information about the system. In practical systems, there are challenges such as the lack of previous information, proofing asymptotic stability or guaranteeing performance, proofing of robustness of the performance, and on-line computation in real-time applications. For the above mentioned reasons, these controllers are not good choices. Another method that was used to regulate the BG levels is fuzzy logic control systems. In [18] and [10], fuzzy logic controllers (FLC) were designed because these type of controllers have the ability to deal with uncertainties and disturbances.

In designing phase of an FLC, it is necessary to select the membership functions, design fuzzy logic operators (ANDs and ORs), and make the rules which are complicated processes. Neural Network systems are another alternative approach to control blood glucose level. These systems have many applications in prediction and control of biological and nonlinear system's behavior [7], [11], [15], [30]. Neural network controllers have relatively good performances in the presence of inter-patient variability and disturbance. In [15] a neural network-based controller was presented to regulate BG level of diabetic patients. Training and finding the optimal structure of the neural network are challenges in designing neural controllers . Recently, SMC used to control biological systems and the results showed its suitable robustness against disturbances and variabilities in such systems [4], [30], [31], [40]. SMC was also used to maintain the optimal level of BG [2], [3], [5], [35], [38].

In this paper, we propose an adaptive fuzzy sliding mode controller (AFSMC) to regulate the BG concentration within the safety range. To deal with uncertainties and strong disturbances (meals) we use a novel reaching law in the design of AFSMC. In this study, the target BG range for a diabetic patient is considered between 3.8 to 10 mmol/l. Hypoglycemia and hyperglycemia are identified as a BG level below 3.8 mmol/l and a BG level above 10 mmol/l, respectively, and the desired value for BG level is considered 6.1 mmol/l (110 mg/dl) [14]. To evaluate performance of our controller, we have used indexes tabulated in Table 1.

This paper is organized as follows. The patient model and meal disturbances are described in section 2. Controller design and proof of its stability are shown in section 3. Section 4 represents the closed-loop simulation results, and finally, section 5 discusses the results.

2. Patient model

There are a large variety of models that describe the glucose-insulin system. Although complex models are accurate, in many cases, a simple model can predict the general behavior of the system accurately. A simple model was introduced by Richard N. Bergman and is called Bergman's minimal model. This model is a compartment model which is divided into three parts. The first part shows the glucose clearance and uptake. The second part describes the delay in the insulin, which affects the uptake of glucose by the tissues and the uptake and production by the liver. Finally, the third part demonstrates the insulin kinetics. The model equations are [36]:

$$\frac{dG(t)}{dt} = -p_1(G(t) - G_b)G(t) + D(t) \quad (1)$$

$$\frac{dx(t)}{dt} = -p_2 x(t) + p_3(I(t) - I_b) \quad (2)$$

$$\frac{dI(t)}{dt} = \gamma[G(t) - h]^+ t - n[I(t) - I_b] + u(t) \quad (3)$$

where $G(t)$ is the plasma glucose concentration above basal (mmol/l), G_b is the basal plasma glucose (mmol/l), $x(t)$ is the effect of active insulin (1/min), $I(t)$ is the insulin concentration over basal (mU/l), I_b is the basal insulin level (mU/l), $D(t)$ is the rate of glucose (mmol/l) that enters into the blood, $U(t)$ is the external insulin that is injected into blood (mU/l/min), and p_1, p_2, p_3, n, h, and γ are Bergman's minimal model parameters. γ is the rate of insulin that is released from pancreas after glucose bolus [(mU/l)(min)-1(mmol/l)-1]. n is decay rate of blood insulin (1/min), h is the rate of threshold value of BG above which pancreatic β-cells release insulin (mmol/l). The term $\gamma[G(t) - h]^+$ shows insulin secretion in the body which does not exist in type I diabetic patients. The clinical data demonstrates that the value of p_1 parameter in diabetic patients is low and can be approximated to zero.

A description for $D(t)$ was proposed by Fisher [29] and is shown in equation (4):

$$D(t) = Bexp(-at), B > 0 \quad (4)$$

3. Controller design

The block diagram of the closed-loop system is depicted in Figure 1. The dynamics of a typical single-input single-output time-varying nonlinear system can be described by the following second-order equation:

$$\ddot{x} = f(X) + g(X)\, u_1(t) \quad (5)$$

where $X = [x(t)\ \dot{x}(t)]^T$ is the system states vector, $f(X)$ and $g(X)$ are the unknown smooth functions, and $u_1(t)$ is the control input. The goal is to design a controller for the system described in (5) such that the system output $x(t)$ tracks a reference trajectory $x_d(t)$ and all closed loop variables of the system remain bounded. Throughout this paper we make the following assumption:

$$g(X) > \delta_0 > 0 \quad (6)$$

In order to design robust control system with the error convergence in a finite time, we define the following sliding mode function:

$$s(t) = \dot{e}(t) + \lambda e(t), \lambda > 0 \quad (7)$$

Table 1. Indices for evaluating the performance of contoller.

INDEX	DESCRIPTION
Mean BG	Mean of BG level in the whole simulation time
% Below Target	% time in below the target BG value 6.1 *mmol/l*
% Above Target	% time in above the target BG value 6.1 *mmol/l*
% Within Target	% time within the 3.8-10 *mmol/l* target range
% Below 2.8 *mmol/l*	% of time in extreme hypoglycemia
% Below 3.8 *mmol/l*	% of time in hypoglycemia
% Above 10 *mmol/l*	% of time in hyperglycemia
% Above 16.7 *mmol/l*	% of time in extreme hyperglycemia
LBGI	Low Blood Glucose Risk Index [14]
HGI	High Blood Glucose Risk Index [14]
BGRI	BG Risk Index [14]
RMSE	Root mean square of tracking error

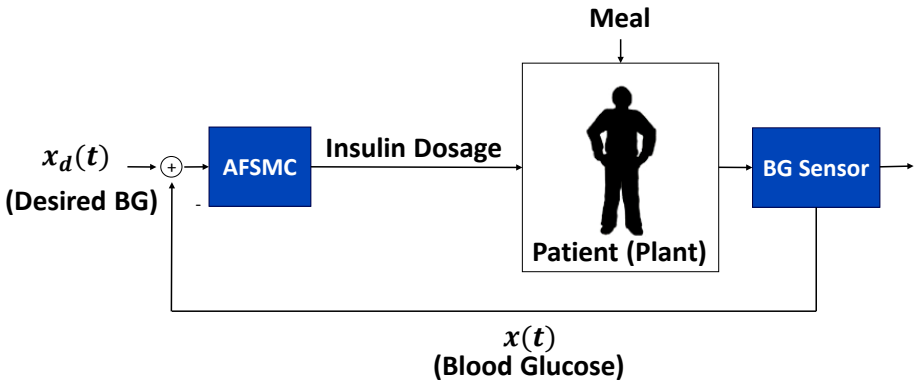

Figure 1. Closed-loop control system.

where $e(t) = x_d(t) - x(t)$ is tracking error. Then, from (6) and using (5), we get

$$\dot{s}(t) = \ddot{x_d}(t) + \lambda \dot{e}(t) - f(X) - g(X)\, u_1(t) \quad (8)$$

The reaching law that used in the design of the controller is in the following form

$$\dot{s}(t) = -k_1 s - k_2 |s|^{\alpha} sgn(s), \;\; k_1, k_2 > 0, 0 < \alpha < 1 \quad (9)$$

Using (8) and (9), we may write the equivalent control law as follows

$$u_{eq}(t) = g^{-1}(X)[-f(X) + \ddot{x_d}(t) + \lambda \dot{e}(t) + k_1 s + k_2 |s|^{\alpha} sgn(s)] \quad (10)$$

Since $f(X)$ and $g(X)$ are unknown (bounded) functions, these functions must be approximated. In this paper, based on the global approximation theorem for fuzzy systems, we used fuzzy logic to

approximate the aforementioned functions. Therefore, we may write the control law (10) as follows:

$$u_{eq}(t) = \hat{g}^{-1}(X)[-\hat{f}(X) + \ddot{x_d}(t) + \lambda\dot{e}(t) + k_1 s + k_2|s|^{\alpha} sgn(s)] \qquad (11)$$

Because the function $g(X)$ is estimated online, a singularity problem may occur. In order to avoid this problem, regularized inverse of $\hat{g}(X)$ can be defined as:

$$\hat{g}^{-1}(X) = \hat{g}(X)[\varepsilon_0 + \hat{g}(X)\hat{g}(X)]^{-1} \qquad (12)$$

where ε_0 is a positive constant. Substituting (12) into (11) can result in:

$$u_{eq}(t) = \hat{g}(X)[\varepsilon_0 + \hat{g}(X)\hat{g}(X)]^{-1}[-\hat{f}(X) + \ddot{x_d}(t) + \lambda\dot{e}(t) + k_1 s + k_2|s|^{\alpha} sgn(s)] \qquad (13)$$

By using the method which has been proposed in [3], the functions $f(X)$ and $g(X)$ can be approximated as

$$\hat{f}(X) = \theta_f^T \varphi_f(X) \qquad (14)$$
$$\hat{g}(X) = \theta_g^T \varphi_g(X) \qquad (15)$$

where $\varphi_f(X)$ and $\varphi_g(X)$ are fuzzy basis vectors fixed by the designer. θ_f and θ_g are adjustable parameters. The proper laws for adaptation of these parameters can be written as follows:

$$\dot{\theta_f}(X) = -\eta_f \varphi_f(X) s,\ \eta_f > 0 \qquad (16)$$
$$\dot{\theta_g}(X) = -\eta_g \varphi_g(X) s,\ \eta_g > 0 \qquad (17)$$

Because of the approximation error, the equation (13) cannot guarantee the stability of the closed-loop system. In order to guarantee the stability of the closed-loop system, we consider the control law as:

$$u_1(t) = u_{eq} + u_c \qquad (18)$$

where $u_c = \frac{s|s|(\overline{\varepsilon_f} + \overline{\varepsilon_g}|u_{eq}| + |u_0|)}{\delta_0 |s|^2}$ and $u_0 = \varepsilon_0[\varepsilon_0 + \hat{g}(X)\hat{g}(X)]^{-1}[-\hat{f}(X) + \ddot{x_d}(t) + k_1 s + k_2|s|^{\alpha} sgn(s)]$.

In this study, the results of AFSMC is compared to FLC designed in [10] because this type of controller has a good performance in the presence of nonlinearities and uncertainties. The controller was designed with Mamdani type fuzzy structure in MATLAB® using two inputs including error and its derivative, and one output including the dosage of insulin. By the definition of inputs and output fuzzy sets, a total of 49 IF-THEN rules were defined.

3.1. Proof of stability

Consider the following Lyapunov function candidate:

$$V = \frac{1}{2}(s^2 + \frac{1}{\eta_f}\tilde{\theta}_f^T \tilde{\theta}_f + \frac{1}{\eta_g}\tilde{\theta}_g^T \tilde{\theta}_g) \qquad (19)$$

where $\tilde{\theta}_g = \theta_g^* - \theta_g$, $\tilde{\theta}_f = \theta_f^* - \theta_f$ are the estimation errors, and θ_f^* and θ_g^* are the optimum parameters of fuzzy approximator. We can write the time derivative of (19) as the following form:

$$\dot{V} = s\dot{s} - \frac{1}{\eta_f}\tilde{\theta}_f^T\dot{\theta}_f - \frac{1}{\eta_g}\tilde{\theta}_g^T\dot{\theta}_g \tag{20}$$

The time derivative of (7) can be written as follows:

$$\dot{s} = \ddot{x_d} + \lambda\dot{e} - f(X) - \big(g(X) - \hat{g}(X)\big)u_{eq} - \hat{g}(X)u_{eq} + g(X)u_c \tag{21}$$

By considering equation (12) and the fact that $\hat{g}(X)\hat{g}(X)[\varepsilon_0 + \hat{g}(X)\hat{g}(X)]^{-1} = 1 - \varepsilon_0[\varepsilon_0 + \hat{g}(X)]^{-1}$, we have:

$$\dot{s} = -k_1 s - k_2|s|^{\alpha}sgn(s) - \Big(f(X) - \hat{f}(X)\Big) - \big(g(X) - \hat{g}(X)\big)u_{eq} - g(X)u_c + u_0 \tag{22}$$

We can define the following equations:

$$f(X) - \hat{f}\big(X,\theta_f\big) = \hat{f}\big(X,\theta_f^*\big) - \hat{f}\big(X,\theta_f\big) + \varepsilon_f(X) \tag{23}$$

$$g(X) - \hat{g}\big(X,\theta_f\big) = \hat{g}\big(X,\theta_g^*\big) - \hat{g}\big(X,\theta_g\big) + \varepsilon_g(X) \tag{24}$$

If we rewrite equation (22) using equations (23) and (24), we have:

$$\dot{s} = -k_1 s - k_2|s|^{\alpha}sgn(s) - \Big(\hat{f}^*(X) - \hat{f}(X)\Big) - (\hat{g}^*(X) - \hat{g}(X))u_{eq} - g(X)u_c + u_0 - \varepsilon_f(X) - \varepsilon_g(X)u_{eq} \tag{25}$$

If we multiply the two sides of equation (25) by s, we have:

$$s\dot{s} = -k_1 s^2 - k_2|s|^{\alpha+1} - \Big(\hat{f}^*(X) - \hat{f}(X)\Big)s - (\hat{g}^*(X) - \hat{g}(X))u_{eq}s - g(X)u_c s + u_0 s - \varepsilon_f(X)s - \varepsilon_g(X)u_{eq}s \tag{26}$$

We can write (26) as:

$$s\dot{s} = -k_1 s^2 - k_2|s|^{\alpha+1} + \dot{V}_1 + \dot{V}_2 \tag{27}$$

In which, we have:

$$\dot{V}_1 = -\tilde{\theta}_f^T\left(\varphi_f(X)s + \frac{1}{\eta_f}\dot{\theta}_f\right) - \tilde{\theta}_g^T\left(\varphi_g(X)u_{eq}s + \frac{1}{\eta_g}\dot{\theta}_g\right) \tag{28}$$

$$\dot{V}_2 = -g(X)u_c s - \varepsilon_f(X)s - \varepsilon_g(X)su_{eq} + su_0 \tag{29}$$

If we put equations (16) and (17) in (28), considering that $\dot{V}_1 = 0$. Using (6), we have:

$$g(X) \geq \delta_0 \rightarrow sg(X)s \geq \delta_0|s|^2 \tag{30}$$

If we multiply the two sides of equation (30) by $\frac{|s|(\bar{\varepsilon}_f + \bar{\varepsilon}_g|u_{eq}| + |u_0|)}{\delta_0|s|^2}$, we have:

$$sg(X)s\frac{|s|(\bar{\varepsilon}_f+\bar{\varepsilon}_g|u_{eq}|+|u_0|)}{\delta_0|s|^2}\geq\delta_0|s|^2\frac{|s|(\bar{\varepsilon}_f+\bar{\varepsilon}_g|u_{eq}|+|u_0|)}{\delta_0|s|^2} \qquad (31)$$
$$sg(X)u_c\geq|s|(\bar{\varepsilon}_f+\bar{\varepsilon}_g|u_{eq}|+|u_0|)$$

Using equations (29) and (31), we have $\dot{V}_2\leq 0$. By considering equation (27), $\dot{V}_1=0$ and $\dot{V}_2\leq 0$, we can conclude that:

$$\dot{V}\leq -k_1s^2-k_2|s|^{\alpha+1} \qquad (32)$$

Using the Lyapunov stability theorem and the fact that $\dot{V}\leq 0$, we conclude that the system is stable and the proof is completed.

4. Results

In this section, the results of the applications of FLC and AFSMC are reported and compared with each other. To evaluate the results of controllers' performance, important indices from [14] have been considered (Table 1). To test the robustness of the controllers against uncertainties and intra-patient variability, 14 patients with different parameters [24] [36] [39] have been selected. There were two different tests for evaluating the robustness of the controllers. In the first stage, the performance of the controllers against 4 perturbations (breakfast, lunch, dinner, breakfast) was tested. We simulated the breakfast meal two times in our simulation to evaluate the blood glucose of patients during sleeping time at night. This is because the risk of hypoglycemia will increase during that time more than any other times during the day. The meal sizes (*gram CHO*) for all patients were 60 *grams* for breakfast, 90 *grams* for lunch and 80 *grams* for dinner. In the second stage, the effect of sensor's delay on the BG regulation has been considered. This dynamic is related to the diffusion of glucose across the capillary endothelial barrier and the glucose rate-limiting membrane. The intrinsic electrochemical sensor's lag is 1-2 minutes, whereas the physiologic lag is 3-12 minutes [17]. In this study we considered 14 minutes lag for sensor's delay and the performance of AFSMC was evaluated. The controllers were tuned for patient 9 and tested on other patients.

Figure 2 shows the results of the BG regulation for 4 patients among the 14 patients. The 12 indices including mean of BG during simulation time, the time in which the BG is below 6.1 *mmol/l* (reference value for BG concentration level), the time in which the BG is above 6.1 *mmol/l*, the time in which the BG is within target range (3.8-10 *mmol/l*), the time in which the BG is below 2.8 *mmol/l* (extreme hypoglycemia), the time in which the BG is below 3.8 *mmol/l* (hypoglycemia), the time in which the BG is above 10 *mmol/l* (hyperglycemia), the time in which the BG is above 16.7 *mmol/l* (extreme hyperglycemia), LBGI, HGI, BGRI, and RMSE were calculated to evaluate the results. LBGI and HGI are indexes that determine the risk of hypoglycemia and hyperglycemia, respectively. Higher LBGI and HGI indicate more hypoglycemia and hyperglycemia, respectively. The LBGI is an excellent predictor for detecting hypoglycemia while the HGI is related to the risk of hyperglycemia and hemoglobin. These indices are computed as follows.

For any BG reading, first we compute:

$$f(BG)=1.509\times[(\ln(BG)\times 18)^{1.084}-5.381],(BG\ is\ in\frac{mmol}{l}) \qquad (33)$$

Then the BG risk function is calculated as follows:

$$r(BG)=10\times f(BG)^2 \qquad (34)$$

Then, the right and left part is separated as follows:

$$rl(BG) = r(BG), if\ f(BG) < 0\ and, 0\ otherwise$$
$$rh(BG) = r(BG), if\ f(BG) > 0\ and, 0\ otherwise \quad (35)$$

$$LBGI = \frac{1}{N}\sum_{i=1}^{N} rl(BG_i)\ , HGI = \frac{1}{N}\sum_{i=1}^{N} rh(BG_i)\ , BGI = LBGI + HGI \quad (36)$$

To compute the root mean square error, for error of tracking, we use the following equation:

$$RMS = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(BG - BG_d)^2} \quad (37)$$

where BG is the measured output that was regulated by FLC or AFSMC, and BG_d is 6.1 *mmol/l* and N is the number of the data points of BG.

Table 2 shows the average of indices that were considered to evaluate the performance of FLC and AFSMC according to Table 1. As it can be seen in Figure 2 and Table 2, the performance of AFSMC is superior to that of FLC in terms of less fluctuation in BG concentration, better setpoint tracking, lower hypoglycemia and hyperglycemia risks, and lower RMSE.

- Fluctuation in BG concentration: The results showed that the minimum and maximum of BG concentration among 14 patients during simulation time for FLC are 3.2-16.5 *mmol/l*, and for AFSMC are 4.4-13.4 *mmol/l*. As a result, the SMC controller can regulate the BG level in a narrower range.
- Setpoint tracking: According to Table 2, the mean of BG concentration using the AFSMC is 6.7 *mmol/l* while it is 7 *mmol/l* using the FLC. This shows that the mean of BG concentration using the AFSMC is closer to 6.1 *mmol/l* (reference value for BG concentration level) and as a result, this controller has a better setpoint tracking.
- The Risk of hyperglycemia: The numerical results in Table 2 show that none of the patients reach severe hyperglycemia (BG>16.7 *mmol/l*). If we compare the average value of HGI in FLC and AFSMC, it is clear that AFSMC can achieve a lower HGI in comparison to FLC. Although, the results show that the time in which the BG concentration is above the target is higher in the case of using AFSMC than FLC, we observe that the sharp decrease of BG concentration in the case of FLC can result in an undershoot in BG concentration and as a result, the probability of hypoglycemia will increase.
- Risk of hypoglycemia: As it is shown in Figure 2, using FLC for patient 4 can result in hypoglycemia (minimum of BG is 3.2 *mmol/l*), but in the case of using AFSMC, the hypoglycemia was not observed and the indices showed that the BG concentrations of all patients are within the safe range. When we compared the value of LBGI in patient 4 for FLC with AFSMC, we found it to be 0.36 for AFSMC and 1.78 for FLC, which is much closer to 2.5 (limit of hypoglycemia risk) [9],[13].

In the second stage, the effect of the delay on the BG regulation has been considered. In this study, the performance of AFSMC is evaluated while the lag for the sensor's delay is 14 minutes. The simulation results of 4 patients have been shown in Figure 3. As it can be observed, the AFSMC has a robust performance against the considered delay. None of the patients reach the hypoglycemic or hyperglycemic range, and the BG concentrations of all patients are within the safety range. The average results of the parameter indices which were considered for 14 patients have been shown in Table 3.

As it can be observed, the results of Table 3 have a high similarity with that of Table 2. The BG concentration of all patients is in the safe range, and none of the patients face hypoglycemia or hyperglycemia risks. The simulation results showed that the designed AFSMC has the ability to regulate the BG levels of all the patients in an appropriate manner. In other words, it is robust against external disturbance (meal entrances), intra-patient variability, and delay of the sensor.

Discussion

In this study, a novel robust control strategy for control of BG level in type I diabetic patients has been proposed, incorporating the SMG with a new reachability condition and adaptive fuzzy control, and its results were compared to FLC. Robustness of these controllers was evaluated by a group of diabetic patient models with different parameters. It should be noted that the resulting insensitivity of the proposed AFSMC to the plant parameters considerably increases the applicability of the system in controlling glucose levels due to the fact that patient parameters vary from one subject to the other. Here, based on Lyapunov stability analysis, adaptive laws was derived for online adaptation of the parameters in the model, guaranteeing the closed-loop stability and asymptotic convergence to zero for the error and its derivatives. One of the major contributions of this study is that the proposed control algorithm can operate precisely without the need for offline calibration or identifications. i.e. the model adapts online without any need for pre-known parameters or offline adjustments. The new reaching law increases the convergence speed when the state is far away from the sliding surface (s(t)=0) and reduces convergence speed when the state is close to the sliding surface. As a result, the system will have a fast reaching mode with low chattering. Since reaching mode is fast in the new reaching law, the AFSMC can regulate the BG level of all diabetic patients in an appropriate time, and also faster than FLC.

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In the first stage, the performance of controllers against 4 perturbations (breakfast, lunch, dinner, breakfast) was tested. When we compared the value of LBGI in patient 4 using FLC and AFSMC, we observed that this value is 0.36 for AFSMC, while it is 1.78 for FLC, which is much closer to the 2.5 limit of hypoglycemia risk (LBGI, Minimal (LBGI ≤1.1), Low (1.1<LBGI ≤2.5), Moderate (2.5<LBGI≤5), and High (LBGI >5.0)18; HGI, Low (HGI ≤4.5), Moderate (4.5<HGI ≤9.0), and High (HGI >9.0) [37]). The results showed that the AFSMC can regulate the BG levels of all diabetic patients in an appropriate time, and its performance is superior to FLC in terms of less fluctuation in BG levels, better setpoint tracking, lower hypoglycemia and hyperglycemia risks, and lower RMS.

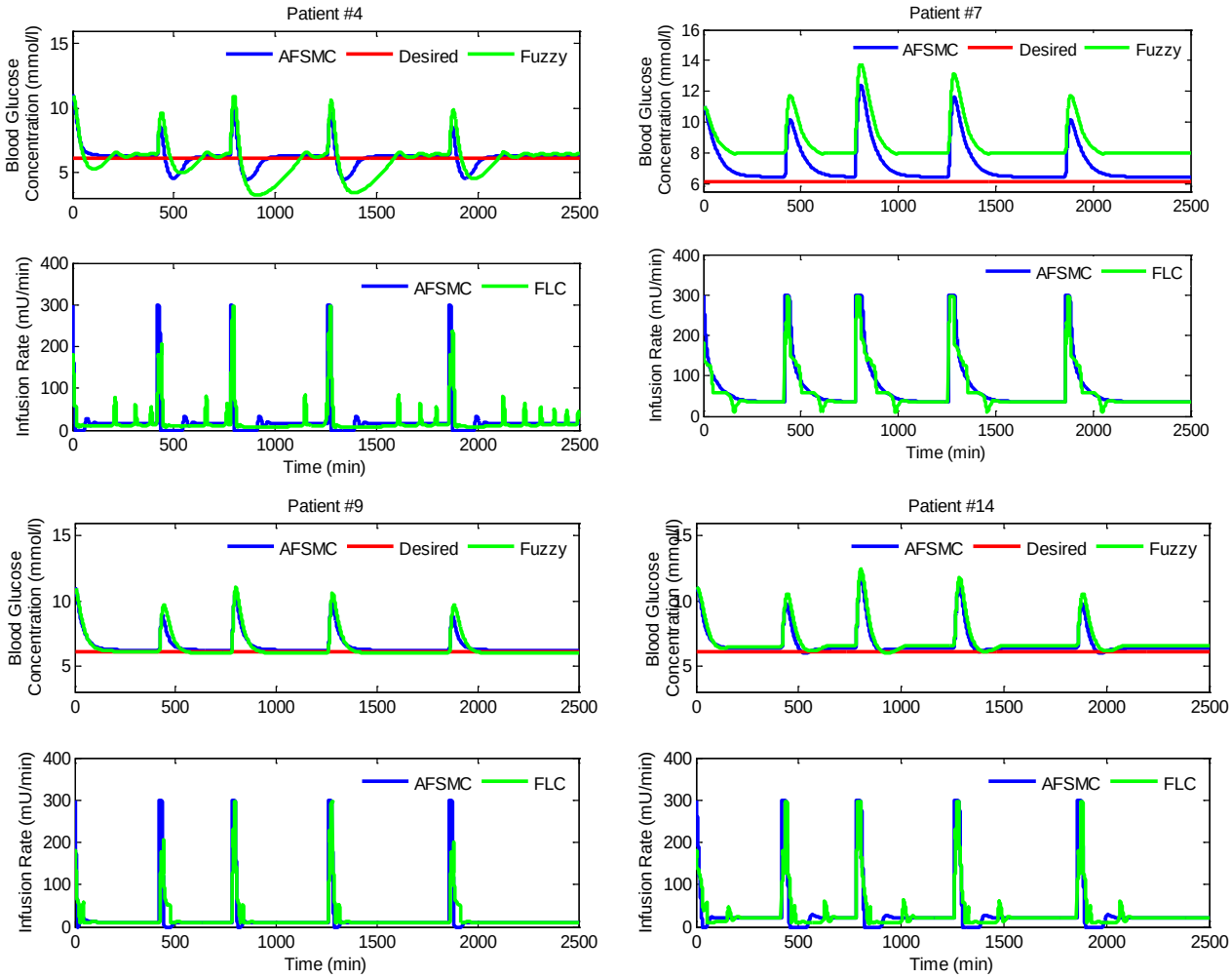

Figure 2. The result of BG regulation and insulin infusion using FLC and AFSMC for 4 patients. In each figure, the top plot is related to BG concentration and the bottom plot is related to insulin infusion rate.

One of the important points that need to be considered for a blood glucose controller is its ability to stop the BG level from dropping to the hypoglycemic interval, which would be caused by a rapid fall of the glucose level [28]. The results of Table 2 exemplifies that the value of LBGI, which shows the risk of hypoglycemia, is much lower when the AFSMC is used.

Table 2. Average of indices that are considered to evaluate the performance of controllers over 14 patients.

Controller	Mean *(mmol/l)*	Below target	Above target	Within target	Blow 50 *mg/dl*	Blow 70 *mg/dl*	Above 180 *mg/dl*	Above 300 *mg/dl*	LBGI	HGI	BGRI	RMSE
AFSMC	6.7	8.78	91.22	96.11	0	0	3.89	0	0.04	0.81	0.85	1.25
FLC	126.8	20.80	79.19	92.54	0	0.72	6.73	0	0.17	1.46	1.63	1.7

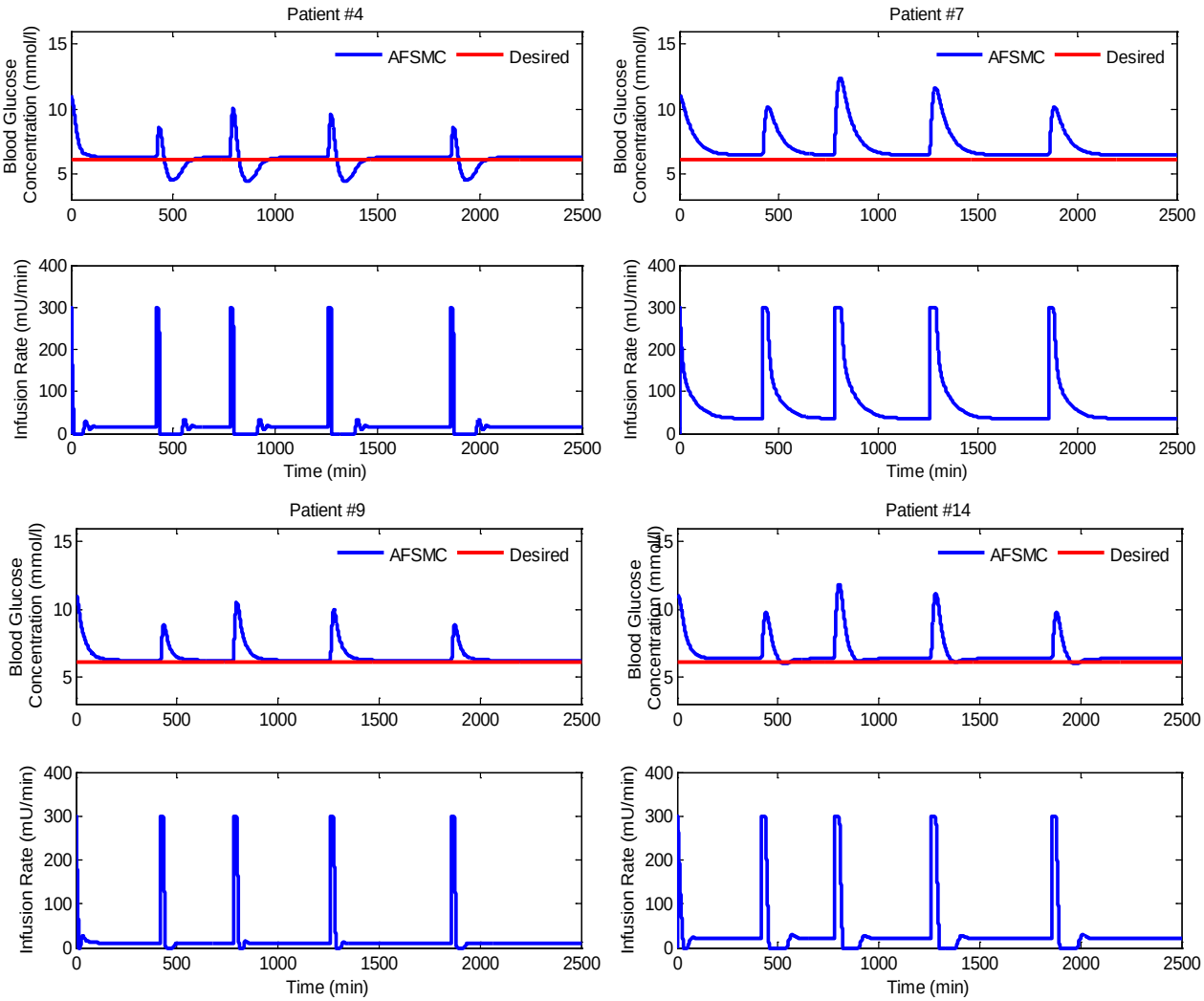

Figure 3. The results of BG regulation and insulin infusion using AFSMC for 4 patients in the presence of sensor's delay. In each figure, the top plot is related to BG concentration and the bottom plot is related to insulin infusion rate.

Table 3. Average of indices that are considered to evaluate the performance of AFSMC in the presence of delay.

Controller	Mean *(mmol/l)*	Below target	Above target	Within target	Blow 50 *mg/dl*	Blow 70 *mg/dl*	Above 180 *mg/dl*	Above 300 *mg/dl*	LBGI	HGI	BGRI	RMSE
AFSMC	6.7	8.98	91.01	96.08	0	0	3.91	0	0.05	0.81	0.86	1.25

Insulin sensitivity is defined as the decrease in BG level per unit of insulin injection. When we calculated insulin sensitivity for all 14 patients, we observed that this value is high for patient 4. As a result, this patient is more likely to face hypoglycemia. According to Figure 2, the AFSMC is robust against insulin sensitivity and it can regulate the BG concentrations of this patient as well.

In the second stage, the effect of the delay on the BG regulation was considered. This dynamic is related to the diffusion of glucose across the capillary endothelial barrier and the glucose rate-limiting

membrane. In this study, the performance of AFSMC is evaluated for 14 minute lag. As it can be observed in Table 3, the AFSMC shows a desirable performance against the considered delay. None of the patients reach the hypoglycemic or hyperglycemic range and the BG concentrations of all patients are within the safety range.

In conclusion, it is clear that the AFSMC is robust against external disturbances (meal entrances), intra-patient variability, and delay in the sensor. Although according to simulation results, the performance of AFSMC is acceptable, and even promising. More investigation is required before utilizing this strategy in clinical applications [19], [32].

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