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Blood glucose control using an ABC algorithm-based fuzzy-PID controller

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Abstract: In this paper, a Mamdani-type fuzzy controller is proposed as the controller part of an artificial pancreas. The controller is optimized with the artificial bee colony optimization algorithm. The glucose–insulin regulatory system, based on a nonlinear differential model in the presence of delay, is used both for virtual patient and healthy person data. The main target of the controller is to mimic a blood glucose concentration profile of the healthy person with exogenous insulin infusion. Simulations are performed to assess the control function in terms of tracking the blood glucose concentration profile of the healthy person and minimizing errors. To show robustness, a group of three tests are implemented. These tests include unusual glucose intake, sensor noise, and uncertainty in the clearance rate parameter. The simulation results demonstrate that the adopted method is more effective than similar studies in the literature.

Key words: Artificial bee colony algorithm, artificial pancreas, fuzzy control, Type 1 diabetes mellitus

1. Introduction

Diabetes mellitus (DM) is described as chronic hyperglycemia, caused by failure of the pancreas. The International Diabetes Federation reports that in 2013 there were almost 382 million patients with DM [1]. By 2035, the number of patients is expected to reach 592 million. In Type 1 diabetes mellitus (T1DM), the beta cells that produce insulin are destroyed by the immune system. This type is most common in children and adolescents. On the other hand, more than 90% of diabetic patients have Type 2 DM (T2DM). In T2DM, the insulin produced by the pancreas does not function properly due to resistance to the insulin. Especially for patients with T1DM, exogenous insulin should be infused at an appropriate rate in order to keep blood glucose concentration (BGC) in a normoglycemic range (70–180 mg/dL [2]). To infuse exogenous insulin at an appropriate rate, a closed-loop control system has been widely used [2–4], as illustrated in Figure 1. The closed-loop control system is also known as the artificial pancreas, which consists of a glucose sensor or continuous glucose monitor (CGM), a controller, and an insulin pump. The CGM signals are transmitted to the controller. The controller then uses a control algorithm to send the data of the proper insulin dose to the insulin pump.

Recently, studies on modeling the glucose–insulin regulatory system of the patient with T1DM have increased. These models have great importance in terms of understanding the system. Several of these models, such as Bergman's minimal model, the Hovorka model, and UVa/Padova's model, are very common [5–7].

Thanks to advances in modeling, control theory, and biomedical engineering, several control algorithms have been proposed to keep the BGC of the patients with T1DM in the normoglycemic range. These algorithms are mainly based on classical controllers [3,8,9], adaptive controllers [10], or robust controllers [4]. Although

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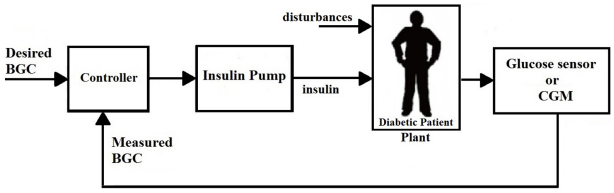

Figure 1. Block diagram of the closed-loop glucose control system [3,15].

these controllers have a good performance in simulation studies, they are unable to cope with the uncertainty and nonlinearity of biological systems, such as that of the glucose–insulin regulatory system [11,12].

Fuzzy logic (FL) is a promising approach to solving such complex control problems. FL allows the capture of valuable information about the behavior of the controlled variable, which can be a good guide that helps realize the artificial pancreas. FL is insensitive to the variability of system parameters and can overcome inter- and intrapatient variability [12]. In [13–16], fuzzy logic controllers (FLCs) showed relatively successful results in keeping the BGC of the patients with T1DM in a normoglycemic range. However, they have certain disadvantages [17,18]:

- Most depend on Bergman's minimal model, which may result in less efficient treatment, because the oscillatory nature of the glucose–insulin system is not accurately presented by the minimal model.
- The main purpose of these controllers is to keep BGC at a predetermined reference value. Therefore, the oscillatory nature of the glucose–insulin dynamics in healthy individuals is not imitated.
- In [13–15], the fuzzy rules and fuzzy membership functions (MFs) of the controllers are based on expert knowledge. Thus, it is quite difficult to get optimal control via tuning the MFs with a trial and error method.

Considering these shortcomings, an optimized fuzzy-PID controller based on the nonlinear delay differential model of glucose–insulin is designed for regulating the BGC of patients with T1DM. The nonlinear delay differential model (i.e. the reference model) shows the glucose status in healthy individuals with scheduled insulin infusion. The purpose of the optimized controller is to mimic the glucose oscillation of the reference model. In order to achieve this, artificial bee colony (ABC) optimization algorithm is employed to select the optimum parameter values of the MFs of all fuzzy variables and the weighting factors.

2. Materials

2.1. Mathematical model of the glucose–insulin regulatory system

This study considers the glucose–insulin regulatory system, based on the nonlinear differential model in the presence of delay [19]. The dynamics of the model were studied both quantitatively and qualitatively. The insulin therapies were modeled to simulate the pancreatic insulin secretion of a healthy person. In [19], it was clearly demonstrated that the blood insulin concentration (BIC) profiles of the patient with T1DM are similar to those of the healthy person by modeling the external insulin therapies. The glucose and insulin dynamics under external insulin therapies for patients with T1DM are described by

$$\frac{dG}{dt} = G_{in}(t) - f_2(G(t)) - f_3(G(t))f_4(I(t-\tau_3)) + f_5(I(t-\tau_2)) \tag{1}$$

$$\frac{dI}{dt} = I_{in}(t) - d_i(I(t)), \tag{2}$$

where $I(t)$ and $G(t)$ represent BIC and BGC at time $t \geq 0$, respectively. $I_{in}(t)$ stands for the exogenous insulin infusion rate (in terms of mU/min) and $G_{in}(t)$ denotes the glucose intake rate (in terms of mg/dL.min), which are given in Eqs. (3) and (4), respectively.

$$I_{in}(t) = \begin{cases} 0.25, & 0 \leq t < 5(\text{min}), \\ 0.25 + (1 + \frac{t-30}{30-5}), & 5 \leq t < 30(\text{min}), \\ 0.25 + (1 - \frac{t-30}{120-30}), & 30 \leq t < 120(\text{min}), \\ 0.25, & 120 \leq t \leq 240(\text{min}). \end{cases} \tag{3}$$

$$G_{in}(t) = \begin{cases} 0.05 + \frac{5}{15}t, & 0 \leq t < 15(\text{min}), \\ 0.05 + 5\frac{45-t}{45-15}, & 15 \leq t < 45(\text{min}), \\ 0.05, & 45 \leq t \leq 240(\text{min}). \end{cases} \tag{4}$$

$f_2(G(t))$, given in Eq. (5), is the insulin-independent utilization of glucose, mostly by brain and nerve cells. The insulin-dependent utilization of the glucose is denoted by $f_3(G(t))\, f_4(I(t))$. The corresponding formulations of these functions are presented in Eqs. (6) and (7). $\tau_3 > 0$ is the time delay for insulin-dependent utilization by cells. $f_5(I(t))$ represents the glucose production function controlled by the insulin concentration, as in Eq. (8). $\tau_2 > 0$ stands for the time delay for hepatic glucose production. The insulin clearance rate is a constant and is denoted by $d_i > 0$.

$$f_2(G(t)) = U_b(1 - \exp(-G/(C_2V_g))) \tag{5}$$

$$f_3(G(t)) = G/(C_3V_g) \tag{6}$$

$$f_4(I(t)) = U_0 + (U_m - U_0)/(1 + \exp(-\beta \ln(I/C_4(1/V_i + 1/(0.2t_i))))) \tag{7}$$

$$f_5(I(t)) = R_g/(1 + \exp(\alpha(I/V_p - C_5))), \tag{8}$$

where U_b, C_2, V_g, C_3, U_0, U_m, β, C_4, V_i, t_i, R_g, α, V_p, and C_5 are fixed parameters, determined by experimental measurements taken from healthy individuals [19]. These parameters are given in Table 1.

2.2. Brief explanation of the ABC algorithm

The ABC algorithm, proposed by Karaboga [20], is a swarm-based global optimization algorithm that imitates the intelligent foraging behavior of honey bees. This algorithm stands out with its simplicity and robustness, and is one of the recently proposed algorithms [21].

The position of a food source is considered as a solution in the ABC algorithm. ABC is composed of onlooker, scout, and employed bees. The classification of the bees is determined by the selection method of the food source. The number of solutions in the population is equal to the population of either employed or

Table 1. Parameters of the functions in Eqs. (5)–(8) [19].

Parameters	Units	Values	Parameters	Units	Values
U_b	mg.min^{-1}	72	C_4	m.U.L^{-1}	80
C_2	mg.L^{-1}	144	V_i	L	11
V_g	L	10	t_i	min	100
C_3	mg.L^{-1}	1000	R_g	mg.min^{-1}	180
U_0	mg.min^{-1}	40	α	L.m.U^{-1}	0.29
U_m	mg.min^{-1}	940	V_p	l	3
β	–	1.77	C_5	m.U.L^{-1}	26

onlooker bees. Employed bees provide information to the onlooker bees about the quality of the food source site. Thanks to this information, onlooker bees select profitable food source regions, whereas scout bees explore new rich food sources [22]. A detailed description of the algorithm, including its main steps and mathematical infrastructure, can be found in [20–22].

Recently, the ABC algorithm has been widely used for optimization problems. Compared to particle swarm optimization (PSO) and the genetic algorithm (GA), ABC has the ability to get out of a local minimum and perform global and local search processes in a balanced manner, due to the selection strategies and neighbor production mechanisms used. Moreover, ABC has fewer control parameters (colony size, maximum cycle, and limit) than PSO and GA, which are independent from complexity or problem type [23,24].

3. Control method

3.1. General structure of the fuzzy-PID controller

The block diagram of the optimized Mamdani-type fuzzy-PID controller for the regulation of the BGC of the virtual patient is presented in Figure 2. The system is designed based on a Mamdani-type fuzzy architecture. The error signal (e) and its rate of change (e_c) are the input variables. The insulin infusion rate (u) is the output variable. The error signal (e) represents the difference between the measured BGC of the virtual patient under the control system and the set point value, i.e. 110 mg/dL. The MFs of the Mamdani-type fuzzy controller comprise three and five linguistic variables for input and output, respectively. Gaussian MFs are used for all linguistic variables. Each function has the following form:

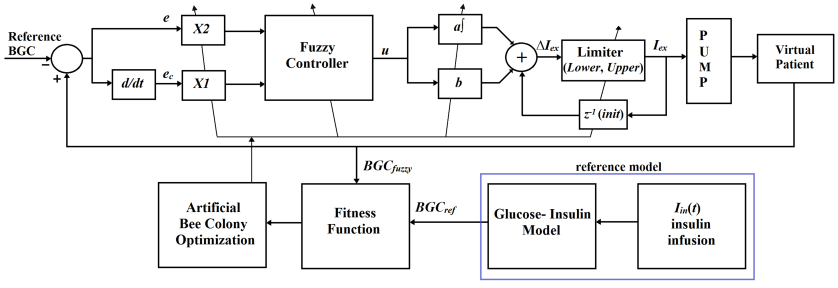

Figure 2. Block diagram of the optimized fuzzy-PID controller.

$$\mu(z) = \exp\left(\frac{(z-c)^2}{2\sigma}\right), \tag{9}$$

where the parameters σ and c are the variance and the mean of each MF, respectively. Parameter z represents the crisp input, and $\mu(z)$ is its MF degree in the interval [0 1]. Table 2 shows the meanings of all linguistic variables. A total of nine IF-THEN rules are demonstrated in Table 3.

Table 2. Meaning of input and output membership functions.

Label	Meaning
E-N	Error negative
E-Z	Error zero
E-P	Error positive
EC-N	Error change negative
EC-Z	Error change zero
EC-P	Error change positive
NM	Negative medium
NS	Negative small
Z	zero
PS	Positive small
PM	Positive medium

Table 3. Fuzzy IF-THEN rules.

		Error change (e_c)		
		EC-N	EC-Z	EC-P
Error (e)	E-N	NM	NS	Z
	E-Z	NS	Z	PS
	E-P	Z	PS	PM

Each fuzzy rule, R_i, consists of two parts: if-part and then-part. If-part involves the input variables e and e_c, and then-part involves output variable u. In this study, the antecedent part is performed by the *MIN* operator and the aggregation part is executed by the *SUM* operator. The output is obtained as follows:

$$u = (defuz_*(fuz(X1_*e, X2_*e_c))), \tag{10}$$

where *fuz* and *defuz* are the fuzzification and defuzzification operations, respectively. *X1* and *X2* are gain scales of the error and the error change rate, respectively. In the design of the controller, the center of gravity defuzzifier is used. ΔI_{ex} is the output of the fuzzy-PID controller given in Eq. (11):

$$\Delta I_{ex} = a \int udt + bu \tag{11}$$

Furthermore, a saturation block is used to protect the patient's body against extreme decrease or increase in the injected insulin dose. The total output of the controller is expressed as follows:

$$I_{ex}(G(t)) = \begin{cases} Upper, & I_{ex} \geq Upper \\ I_{ex}(G(t-1)) + \Delta I_{ex}(G(t)), & Lower < I_{ex} < Upper \\ Lower, & I_{ex} \leq Lower \end{cases}, \tag{12}$$

where *Lower* and *Upper* are the lower and upper limits of the saturation block. Current and previous exogenous insulin amounts at $G(t)$ and $G(t-1)$ are represented by $I_{ex}(G(t))$ and $I_{ex}(G(t-1))$, respectively. $\Delta I_{ex}(G(t))$

provides a change in the amount of insulin injection depending on BGC. The proposed controller operates in the range of [*Lower*, *Upper*] mU/min. The total amount of insulin at $t = 0$ is obtained as follows:

$$I_{ex}(G(0)) = \Delta I_{ex}(G(0)) + init, \tag{13}$$

where *init* is the injected amount of insulin from the insulin pump at $t = 0$, which plays an important role in mimicking the reference model at the beginning of the simulation.

3.2. Optimization of the controller by ABC

The ABC algorithm is used for determining the parameters by minimizing an objective function. The difference between the amount of BGC of the reference model (BGC_{ref}) and the BGC of the virtual patient (BGC_{fuzzy}), i.e. output of the controlled glucose–insulin system, is considered as an error. Based on this, the mean absolute percentage error (MAPE), as given by Eq. (14), is used as the objective function for the optimization process. The aim of ABC is to minimize the MAPE as in [17,18,25].

$$MAPE = \frac{1}{n}\sum_{t=0}^{n}\left|\frac{BGC_{ref} - BGC_{fuzzy}}{BGC_{ref}}\right|, \tag{14}$$

where n is the duration of the simulation.

Optimization is performed on all the MFs described in Eq. (9) and the weighting parameters, i.e. *X1*, *X2*, a, and b. Additionally, the parameter *init* is optimized for choosing the optimal amount of the injected insulin at the beginning of the simulation. Moreover, the parameters *Upper* and *Lower* are determined by the ABC algorithm. The control parameter values of ABC are given as follows: *Colony size is 60*, *maximum cycle is 100*, *and Limit is 870*. Matlab/Optimization Toolbox is used for the optimization process.

In order to obtain minimum MAPE value, the ABC algorithm is run 30 times by using different search intervals. The obtained search intervals are given in Table 4.

Table 4. Search intervals.

Variables and parameters	Search interval
E-N, EC-N, NM, NS	[–1 0]
E-P, EC-P, PM, PS	[0 1]
E-Z, EC-Z, Z	[–0.5 0.5]
Variance of all Gaussian MFs (σ)	[0 1]
Lower	[0 0.45]
Upper	[0.5 2]
X1, *X2*	[0 0.5]
a, b, *init*	[0 2]

4. Simulation results

The reference model, defined in Eqs. (1)–(8), is generated via MATLAB/Simulink. In addition, the virtual patient is obtained without using the exogenous insulin infusion rate $I_{in}(t)$, which is specified in Eq. (3). Simulations are performed for 1440 min (24 h) to assess the controller in terms of mimicking the reference model. In order to demonstrate the performance of the controller, two types of simulations are performed.

4.1. Simulations without uncertainty

As mentioned before, the main purpose of the optimization process is to tune the parameters in order that the BGC profile of the virtual patient converges to BGC profile of the reference model. After the optimization process, the obtained MFs of the input and output linguistic variables are shown in Figures 3–5, respectively.

Table 5. Obtained parameter values.

Parameter	Value
X1	0.1387
X2	0.4904
a	0.1167
b	1.9594
Upper (mU/min)	0.9882
Lower (mU/min)	0.2513
init	0.2608

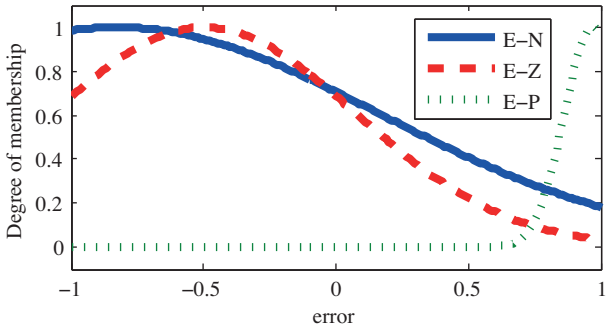

Figure 3. Obtained MFs of input 1 (e) after optimization by ABC.

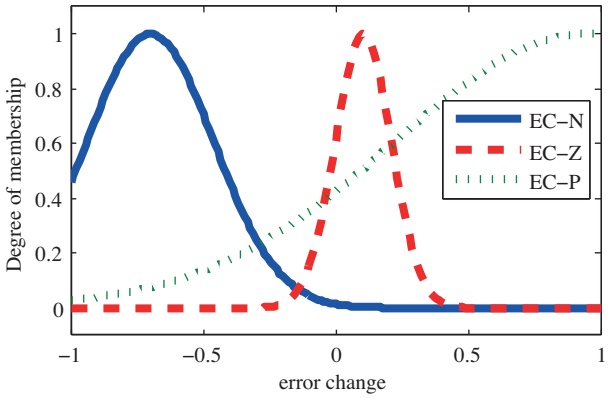

Figure 4. Obtained MFs of input 2 (e_c) after optimization by ABC.

The BGC and BIC profiles of the reference model and the controlled virtual patient are presented in Figures 6 and 7, respectively. Furthermore, the parameter values obtained with the ABC algorithm are listed in Table 5. Finally, the performance comparison of the proposed controller and similar studies in the literature are given in Table 6.

Table 6. Comparison of the studies in terms of performance analysis.

	Objective function value (%)	Mean value of the BGC ($mg.dL^{-1}.min^{-1}$)	Daily infusion (mU/day)
Proposed controller	0.7822	106.11	695.75
SOTFC in [18]	1.235	104.6055	707.595
Controller in [17]	1.3787	106.3488	708.8412
Controller in [25]	1.4136	-	708.1953
Reference model	-	107.38	705.25

It should be emphasized that the obtained simulation results are more successful than those obtained in [17], [18], and [25]. The controller has several advantages and superiority over the mentioned studies, which are summarized below:

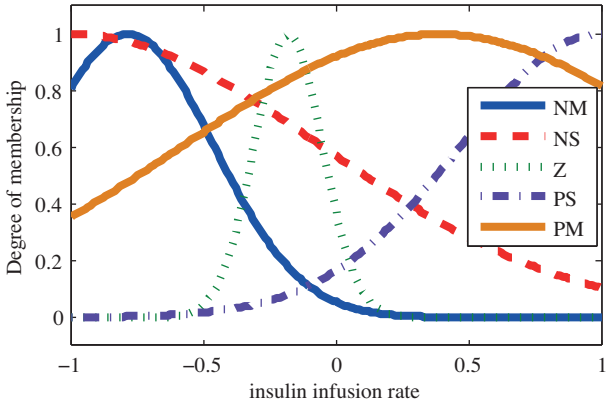

Figure 5. Obtained MFs of output (u) after optimization by ABC.

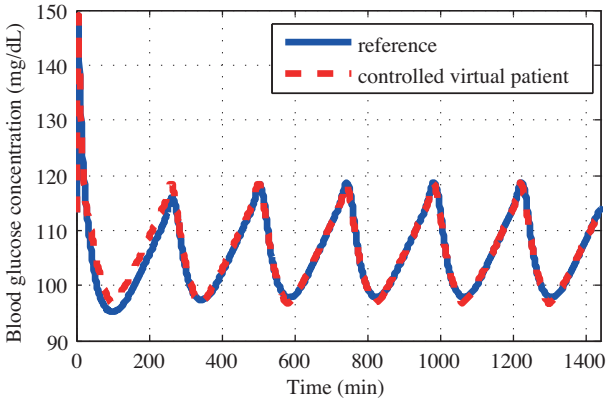

Figure 6. BGC profiles of the reference model and the controlled virtual patient.

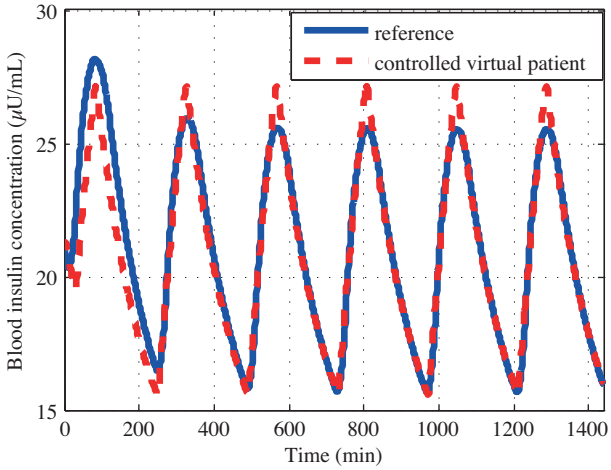

Figure 7. BIC profiles of the reference model and the controlled virtual patient.

i) The proposed controller satisfies the design requirements with only 9 rules. In [17] and [25], however, 49 rules are defined. In [18], the swarm optimization-tuned Mamdani fuzzy controller (SOTFC) also has 9 rules.

ii) As seen in Table 6, the objective function value is only 0.7822%. In [17], the best value for the objective function is 1.3787%. In [25], it is 1.4136%, and in [18], it is 1.235%.

iii) The proposed controller performed the control function with the minimum insulin infusion. Particularly during the first hours of the simulation, the controller provides less insulin than the reference model. Given the entire duration of the simulation, it can be said that the controller is starting to follow the glucose oscillation of the reference model earlier. Figures 6 and 7 clearly demonstrate this situation.

4.2. Robustness tests of the controller

To show the robustness of the controller, three different tests are implemented: 1) unusual glucose intake, 2) sensor noise, and 3) uncertainty in the clearance rate parameter. As mentioned before, the normoglycemic

range of BGC is considered as 70–180 mg/dL. In each case, the results are compared in a similar way to the simulations without uncertainty.

4.2.1. Unusual glucose intake

Normally, the highest rate of glucose intake is 5 (mg/dL)/min. In this case, a value equal to 15 (mg/dL)/min glucose is added to the model at a time interval between 735 and 740 min. The amount considered here is 5 (mg/dL)/min larger than the amount in [17], [18], and [25] for the same situation. The total absorbed glucose intake can reach 20 (mg/dL)/min with this unexpected glucose absorption. The highest recorded BGC within the time interval of applying the disturbance is only 121.2 mg/dL. On the other hand, the obtained highest BGC values for the same situation are 130.9063 mg/dL in [18], 126.7097 mg/dL in [17], and approximately 131 mg/dL in [25]. Figure 8 demonstrates a satisfactory performance of the proposed controller in this case.

4.2.2. Sensor noise

A white Gaussian noise with a mean equal to 0 and variance equal to 0.3 is assumed as the effect of measurement noise, which is more severe than the conditions given in [17,18,25]. BGC profiles in the presence of sensor noise are demonstrated in Figure 9. As shown in Figure 9, the controller gives highly effective results in dealing with sensor noise. Obtained BGC by the controller is in the range of 93.87–118.75 mg/dL. Consequently, these results are promising in terms of practical applications such as an insulin pump, by means of the efficacious performance of the proposed controller.

4.2.3. Uncertainty in the clearance rate parameter

In real life, insulin absorption varies from patient to patient. To simulate this situation, the clearance rate parameter given in Eq. (2), d_i, is assumed to be uncertain. The nominal value of d_i is 0.0076. If d_i is decreased, the insulin degradation rate decreases; in other words, less external infused insulin is required to

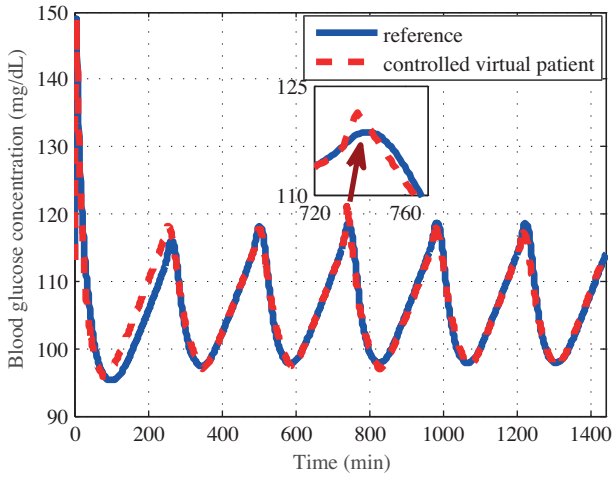

Figure 8. BGC profiles of the reference model and the controlled virtual patient in the presence of unusual glucose intake.

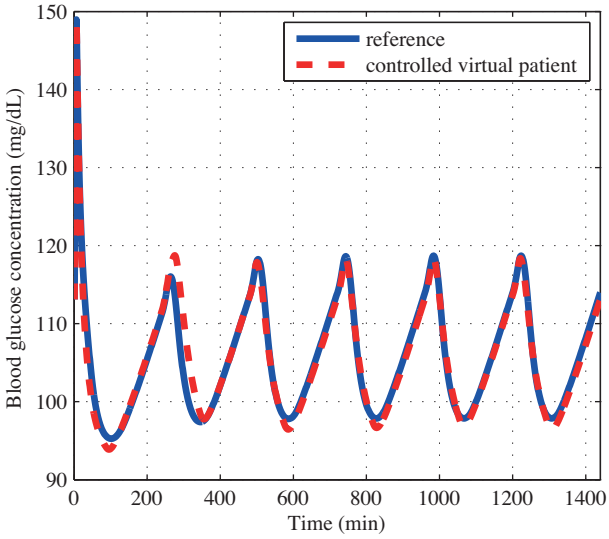

Figure 9. BGC profiles of the reference model and the controlled virtual patient in the presence of sensor noise.

keep BGC in the normoglycemic range and vice versa. The BGC profiles obtained under this condition are shown in Figures 10 and 11. A comparative list of the amounts of insulin injected via the insulin pump is shown in Table 7. As in [17,18,25], it is assumed that the parameter d_i is changed by $\pm 20\%$:

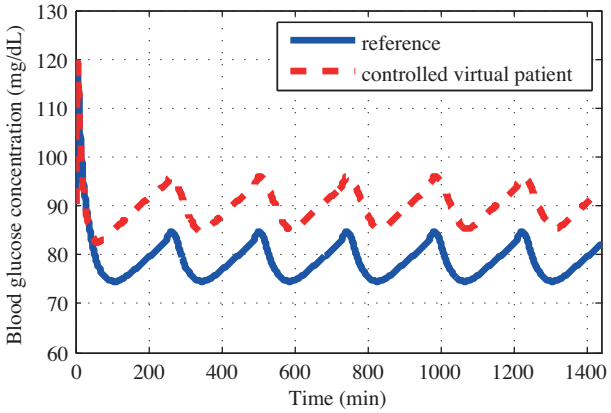

Figure 10. BGC profiles of the reference model and the controlled virtual patient when the clearance rate parameter $d_i = d_i\,LOWER$.

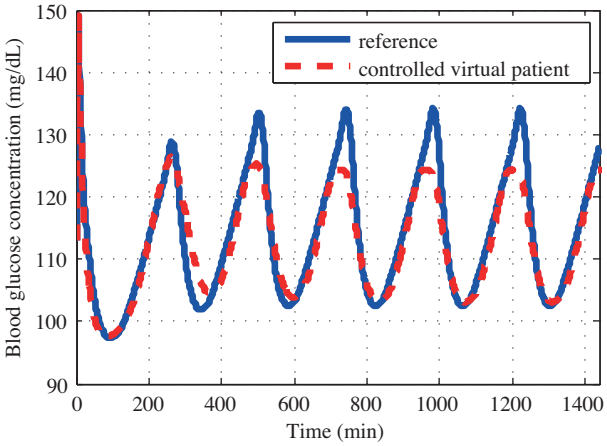

Figure 11. BGC profiles of the reference model and the controlled virtual patient when the clearance rate parameter $d_i = d_i\,UPPER$.

$$d_i LOWER = 0.8 d_i \tag{15}$$

$$d_i UPPER = 1.2 d_i \tag{16}$$

When $d_i\,LOWER$ is used, BIC degrades slowly. This means that the patient is faced with a reduced BGC. Nearly 2 h after beginning the simulation, the BIC profiles of the virtual patient and the reference model are in the range of [15.55 22.16] μU/mL and [20.63 30.72] μU/mL, respectively. Moreover, the BGC profiles of the virtual patient and the reference model are in the range of [84.79 95.91] mg/dL and [74.56 84.85] mg/dL, respectively.

Table 7. Injected insulin amounts in the presence of uncertainty in the clearance rate.

	When $d_i = d_i LOWER$ (mU/day)	When $d_i = d_i UPPER$ (mU/day)
Proposed controller	467.7585	723.5896
SOTFC in [18]	597.8805	826.9351
Controller in [17]	601.2317	832.345
Controller in [25]	599.5973	833.381

When $d_i\,UPPER$ is used, BIC degrades fast. The patients with $d_i\,UPPER$ will face increased BGC, i.e. hyperglycemia. About 2 h after the beginning of the simulation, BGC reached the range of [104.56 126.47] mg/dL for the virtual patient, which is in the normoglycemic range. The BIC values of the virtual patient are similarly in the range of [13.85 21.61] μU/mL.

5. Conclusion

In this study, a closed-loop control system, based on the Mamdani-type fuzzy controller, is proposed to imitate the glucose profile of the healthy person. On the basis of the controller, the ABC optimization algorithm

is employed to obtain optimal parameters for input and output MFs, and weighting parameters through the objective function. Numerical simulations cover 24-h daily life and include robustness tests such as unusual glucose intake, sensor noise, and uncertainty in the clearance rate parameter. As can be clearly seen from Tables 6 and 7, the proposed controller has the lowest objective function value among the mentioned studies, and performed the control function with the minimum insulin infusion. It is revealed from the numerical results that the proposed controller outperforms the compared studies and is able to keep BGC in the normoglycemic range. Future works may include testing the proposed controller on more rigorous models that contain entire dynamics of real patients with T1DM.

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