Vol. 2, No. 3, 2012, 71–79

Shahrood University of Technology

Journal of Solid and Fluid Mechanics

Optimal intelligent control for glucose regulation

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Abstract

This paper introduces a novel control methodology based on fuzzy controller for a glucose-insulin regulatory system of type I diabetes patient. First, in order to incorporate knowledge about patient treatment, a fuzzy logic controller is employed for regulating the gains of the basis Proportional-Integral (PI) as a self-tuning controller. Then, to overcome the key drawback of fuzzy logic controller, i.e., the lack of systematic methods to define fuzzy rules and fuzzy membership functions, fuzzy PI controller are optimized by Particle Swarm Optimization with Linearly Decreasing Weight (LDW-PSO) algorithm, which is a novel evolutionary computation technique. Simulation results show the effectiveness of the proposed optimal fuzzy PI controller in terms of accuracy and time margin.

Keywords: Type 1 diabetes; Bergman model; Fuzzy logic control; Particle swarm optimization; PI controller.

1. Introduction

Diabetes is a group of diseases marked by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). There are three main types of diabetes. Type I diabetes, type II diabetes and gestational diabetes. Type I diabetes results from the body's failure to produce insulin, and presently requires the person to inject insulin. Type II diabetes results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. Gestational diabetes is occurred when pregnant women, who have never had diabetes before, have a high blood glucose level during pregnancy. It may precede development of type II diabetes; here the emphasis is on type II diabetes. As in 2000 was estimated at least 171 million people around the world suffer from diabetes [1].

Type II diabetes mellitus is determined by destruction of the insulin-producing beta cells of the islets of Langerhans in the pancreas resulting to insulin shortage. This type of diabetes can be further classified as immune-mediated or idiopathic. The majority of type II diabetes is of the immune-mediated nature, where beta cell dissipation is a T-cell mediated autoimmune assault [2]. There is no recognized preventive measure against type I diabetes, which causes nearly 10% of diabetes mellitus cases in North America and Europe. Most impressed individuals are otherwise healthy and of a normal weight when symptoms of diabetes are appeared. Sensitivity and reaction to insulin are generally regular, particularly in the primary steps. Type I diabetes can affect children or adults but was traditionally called "juvenile diabetes" because most patients with this type of diabetes are children. Brittle diabetes, also known as unstable diabetes or labile diabetes, relates to a type of insulin-affiliate diabetes determined by dramatic and frequent fluctuations in glucose levels, often happening for no specific reason. The outcome can be atypical and unexpected hyperglycemia, mostly with ketosis, and sometimes critical hypoglycemia. Brittle diabetes happens no more mostly than in 1% to 2% of diabetics [3].

Over time, diabetes can lead to side effects, specifically, diabetic retinopathy, diabetic neuropathy and diabetic nephropathy. Also there is an increasing risk of facing to heart failure and stroke in diabetic patients. Eventually, the general risk of death among individuals with diabetes is at least double the risk of people without diabetes. The World Health Organization (WHO) apprises that over 180 million

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people in the world have diabetes and this statistic is estimated to be 360 million people by 2030. In 2005, it has been estimated that 1.1 million people have died because of diabetes. When ranking diseases in terms of mortality, diabetes is the fifth cause of death, after communicable diseases, cardiovascular diseases, cancer and injury [4].

Medical sciences have more emphasis on prevention and in case of illness only offer a general treatment. In recent years to improve treatment of diabetes new instruments are designed by using biomedical engineering for instance insulin pump. The insulin pump is a medical device used for the administration of insulin in the treatment of diabetes mellitus, also known as continuous subcutaneous insulin infusion therapy. The insulin pump has application in the treatment of both types of diabetes [5–8], but what is important here is designing of an appropriate controller for insulin pump. The main features of the appropriate glucose controller are: 1) the controller should minimize the taken dosage of insulin. See [9, 10], 2) the controller should lower blood glucose level in the shortest possible time until its allowed range, i.e. among 70 mg/dl and 120 mg/dl before meals and under 180 mg/dl after meals [11]. See [12, 13] and 3) because of the diabetes model of every individual is exclusively for itself, the controller should have suitable performance for all diabetic patients. It means that the controller must have robust performance against parameter uncertainties that exist in parameters of diabetes model. See [14–16].

To achieve aforementioned objectives, some classical controllers have been proposed to control the blood glucose level in people with diabetes [17–22]. Despite the good performance of these controllers, they do not have the capabilities to deal with uncertainties that there are in biological models. Furthermore, the classical controllers cannot appropriately counter nonlinear and complex systems. As a result, if these controllers are used in practice it is likely that they would failed while applying to an actual patient.

In recent years, researchers have extensively used the fuzzy logic for modeling, identification, and control of highly nonlinear dynamic systems [23]. Many researchers tried to handle blood glucose regulation using fuzzy controller [24–27]. In [24], a comparative study between ordinary PID and a fuzzy logic controller with assumption of continuous insulin infusion has been represented whereas both controllers are designed for the purpose that maintaining blood glucose level around 60-100 mg/dL before eating and under 140 mg/dL after eating. In [25], a fuzzy controller based on ordinary PID controller is designed. In [26], the efficiency of fuzzy closed-loop controller has been compared to ordinary PID controller in presence of intense initial conditions including an unusual meal disturbance, variations in parameters of system and a white noise that indicates sensor's error. In [27], the optimal Linear Quadratic Regulator (LQR) and classical fuzzy logic controller has been proposed.

In this paper, the superiority of fuzzy-PI controller to the other controllers is shown. The proposed controller has the quickest response. It is capable to eliminate errors caused by the intense initial circumstances and the restore blood glucose level to its basal amount in duration of nearly an hour. The proposed controller among other controllers has the smallest overshoot when facing with a large disturbance due the exogenous glucose meal after accessing to its steady state.

Although there are a number of distinguished advantages of the fuzzy logic controllers over the classical controllers such as they are not so sensitive to the variation of system structure, parameters and operation points as well as can be easily implemented in a large scale nonlinear system, but, one drawback of them is the lack of systematic methods to define fuzzy rules and fuzzy membership functions. Most fuzzy rules are also based on human knowledge and differ among persons despite the same system performance. On the other hand, it is difficult to assume that the given expert’s knowledge captured in the form of the fuzzy controller leads to optimal control. Consequently, the effective approaches for tuning the membership function and control rules without a trial and error method are significantly required. Because of this, in this paper, the idea of employing Particle Swarm Optimization (PSO) algorithm to solve the combinatorial optimization problems is proposed.

Recently, Particle Swarm Optimization (PSO) algorithm has been becomes available and promising techniques for real world optimization problems [28]. Compared to GA, PSO takes less time for each function evaluation as it does not use many of GA operators like mutation, crossover and selection operator [29]. Due to the simple concept, easy implementation and quick convergence, nowadays PSO has gained much attention and wide applications in different fields [30].

The contribution of this paper is to propose a new approach based on the modified PSO algorithm, namely Particle Swarm Optimization with Linearly Decreasing Weight (LDW-PSO), for optimal design of a fuzzy logic based proportional integral controller in type I diabetes. This proposed approach, called the optimal fuzzy-PI controller, is utilized to obtain optimal solutions. This algorithm is utilized for learning the control rules of the fuzzy logic controller, and applied to optimize membership functions and control rules. Furthermore, the efficiency of the proposed controller will be demonstrated in this paper.

2. Insulin-glucose dynamical model

Bergman’s model is the most popularly utilized model in the literature, approximates the dynamic response of a diabetic patient’s blood glucose concentration to the insulin injection [31]. The model equation are given by [32]

$$dG/dt = -P_1(G - G_b) - XG + D(t)$$
$$dX/dt = -P_2X + P_3(I - I_b) \qquad (1)$$
$$dI/dt = -n(I - I_b) + \gamma(G - h)^+ + U(t)$$

where G(t) shows the plasma glucose concentration at time t (mg/dl), X(t) is the generalized insulin variable for the remote compartment (1/min), I(t) is the plasma insulin concentration at time t (µU/ml), G_b is the basal value of plasma glucose (mg/dl), I_b is the basal value of plasma insulin (µU/ml). p_1, p_2, p_3, n, h, γ are parameters of Bergman minimal model. n is the first order decay rate for insulin in plasma (1/min), h is the threshold value of glucose above which pancreatic β-cells release insulin (mg/dl), and γ is the rate of the pancreatic β-cells' release of insulin after the glucose injection and with glucose concentration above h [(µU/ml) min^{-2} $(mg/dl)^{-1}$]. The term $\gamma[G(t)-h]^+$ in the third equation of the model acts as an internal regulatory function that formulates the insulin secretion in the body, which does not exist in diabetic patients. The available clinical data indicates that the value of p_1 parameter for diabetic patient will be significantly reduced and it can be approximated as zero [33]. Model parameters and their values are presented in reference [34]. It is noticeable that these values were calculated for a person of average weight and vary from patient to patient which makes the design of controller a more challenging task. Finally, *D*(t) represents the meal glucose disturbance and can be modeled by decaying exponential function of the following form [35]:

$$D(t) = 0.5exp(-0.5\,t)\,,\; t \geq 0 \qquad (2)$$

3. Sugeno Type Fuzzy Inference

In this section Sugeno method of deductive inference for fuzzy systems based on linguistic rules has been introduced. The Sugeno procedure was recommended in an endeavor to expand a systematic method to producing fuzzy rules from a certain input–output data collection. A generic rule in a Sugeno model, which has two-inputs *x* and *y*, and output *z*, is as follows:

IF *x* is A and *y* is B, THEN *z* is $z = f(x, y)$

where $z = f(x, y)$ is a crisp function as a result. Generally $f(x, y)$ is a polynomial function in the inputs *x* and *y*, but it can be any public function until it characterizes the output of the system inside the fuzzy area determined in the antecedent of the rule to which it is exerted. When $f(x, y)$ is a constant the inference system is known as a *zero-order Sugeno model*, which is a particular case of the Mamdani system in which each rule's resultant is determined as a fuzzy singleton. When $f(x, y)$ is a linear function of *x* and *y*, the inference system is known as a *first-order Sugeno model*, which has been used in this article. In [36] was indicated that the output of a zero-order Sugeno model is a flat function of its input variables until the neighbor membership functions in the antecedent have adequate overlap. Versus, the overlap of the membership functions as a result of a Mamdani model does not have a definitive efficacy on the flatness; it is the overlap of the antecedent membership functions that specifies the flatness of the resulting system conduct.

In a Sugeno model each rule has a crisp output, presented by a function; for this reason the total output is gained via a weighted average defuzzification (Eq. (3)). This procedure eschews the time consuming methods of defuzzification needed in the Mamdani model.

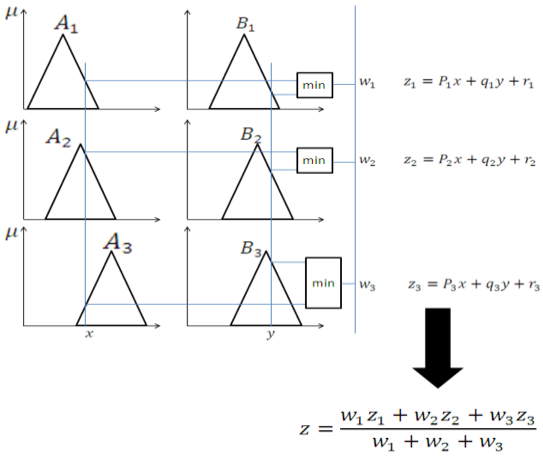

Fig. 1. The Sugeno fuzzy model

The weighted average method is the most repeatedly used in fuzzy usages since it is one of the more effective methods in terms of calculations. Unfortunately it is generally limited to symmetrical output membership functions. The algebraic expression is as follows:

$$Z^* = \frac{\sum \mu c(z)\,.\,z}{\sum \mu c(z)} \qquad (2)$$

where ∑ represents the algebraic sum while *z* is the centroid of each symmetric membership function. Linguistic variables used in fuzzy controller design are defined as follows:

Rule 1: *If glucose concentration is **Low** and glucose deviation rate is **Low** then insulin infusion rate is **Low**.*

Rule 2: *If glucose concentration is **Medium** and glucose deviation rate is **Medium** then insulin infusion rate is **Medium.***

Rule 3: *If glucose concentration is **High** and glucose deviation rate is **High** then insulin infusion rate is **High.***

As shown in Fig. 1, the above three IF-THEN rules are combined together in the form of *first-order Sugeno model.*

4. Particle Swarm Optimization

PSO is a subset of inspired algorithms that model biological processes to optimize highly complex cost functions. PSO algorithm allows a population composed of numerous individuals to evolve under specified selection rules to a state that maximizes/minimizes the fitness function/cost function.

The main advantages of PSO are as follows:

1) Optimizes with continuous/ discrete parameters

2) Does not require derivative information

3) Does not get stuck into so called local optima

In PSO, each candidate solution is called "Particle". Each particle in the swarm represents a candidate solution to the optimization problem, and if the solution is made up of a set of variables, the particle can correspondingly be a vector of variables. In PSO, each particle is flown through the multidimensional search space, adjusting its position in search space according to their momentum and both individual and global memories. The particle therefore makes use of the best position encountered by itself and that of its neighbors to position itself toward an optimal solution. The fitness of each particle can be evaluated according to the objective function of optimization problem. At each iteration, the velocity of every particle will be calculated as follows:

$$v_i(t+1) = \omega v_i(t) + c_1 r_1 (p_{id} - x_i(t)) + c_2 r_2 (p_{gd} - x_i(t)) \qquad (3)$$

where t is the current step number, ω the inertia weight, c_1 and c_2 are the acceleration constants, r_1 and r_2 are two random numbers in the range [0,1], $x_i(t)$ is the current position of the particle, p_{id} is the best one of the solutions this particle has reached, p_{gd} is the best one of the solutions all the particles have reached. After calculating the velocity, the new position of every particle can be worked out

$$x_i(t+1) = x_i(t) + v_i(t+1) \qquad (4)$$

The PSO algorithm is repeated using equations of Eqs. (2) and (3) which are updated at each iteration, until the pre-specified number of generations G is reached.

Although Standard PSO (SPSO) involves some important advances by providing high speed of convergence in specific problems, it does exhibit some shortages. It is found that SPSO has a poor ability to search at a fine grain because it lacks velocity control mechanism. Many approaches are attempted to improve the performance of SPSO by variable inertia weight. The inertia weight is critical for the performance of PSO, which balances global exploration and local exploitation abilities of the swarm. A big inertia weight facilitates exploration, but it makes the particle long time to converge. Conversely, a small inertia weight makes the particle fast converge, but it sometimes leads to local optimum. Hence several inertia weight adaptation algorithms have been proposed in the literatures [37]. One of the most well-known algorithms is the Linearly Decreasing Inertia Weight PSO (LDW-PSO). In LDW-PSO, the inertia weight is adapted linearly as follows [38]:

$$\omega^t = \omega_{\min} + \frac{iter_{\max} - t}{iter_{\max}}.(\omega_{\max} - \omega_{\min}) \qquad (5)$$

where $iter_{max}$ is the maximal number of iterations, t is the current number of iterations. So as iterations go, ω decreases linearly from ω_{max} to ω_{min}.

5. The Proposed control method

In order to design the optimal fuzzy-PI controller, at first fuzzy PD controller is introduced. Fig. 2 shows the controller including two inputs and one output. The two inputs of controller are the error ***e*** and the change rate of error ė, respectively and the output of controller is ***U*** [39]**.** In fact, the parameter ***e*** represents the difference between measured blood glucose level and its basal level and the parameter ***ė*** represents return speed of blood glucose to its basal level.

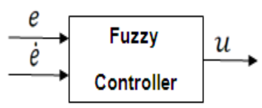

Fig. 2. Fuzzy-PD controller

Based on fuzzy-PD controller above, we can create the optimal fuzzy-PI controller as:

$$\begin{aligned} u_1 &= \alpha \int (A + PK_1 e + D\,K_2 \dot{e})dt \\ &= \alpha At + \alpha K_2 De + \alpha K_1 P \int e\,dt \end{aligned} \qquad (6)$$

where α is the integral constant and K_1 and K_2 are weighting parameters for ***e*** and ***ė***, respectively. Therefore, the fuzzy controller becomes a parameter varying PI controller, its tantamount proportional control and integral control components are $\alpha K_2 D$, $\alpha K_1 P$ [39].

The main shortage of the optimal fuzzy-PI controller is the lack of systematic approaches to define fuzzy rules and fuzzy membership functions. As we know, most fuzzy rules are based on human knowledge and differ among persons despite the same system performance. Because of this, it is complex to assume that the given expert's knowledge captured in the form of the fuzzy controller leads to optimal control. Therefore, the efficient approaches for tuning the membership function and control rules without a trial and error method are significantly required. Because of this, the idea of employing LDW-PSO algorithm to achieve best robustness, smallest settling time and the minimum insulin dosage is represented. The parameters of the signal builder, the parameters of fuzzy-PI controller and the parameters of input and output membership functions are optimized simultaneously.

Table 1. Optimal Parameters of Triangular Membership Functions

input variables	Membership functions	interval
Glucose Concentration	Low	[65.54 135.6 148.4]
	Medium	[161.8 175.9 230.4]
	High	[269 271.6 292]
Glucose Deviation Rate	Low	[5.525 7.774 12.39]
	Medium	[9.819 17.84 20.64]
	High	[17.83 31.99 34.17]
parameters of crisp Polynomial functions	Low	[1.0991 0.9704 1.2233]
	Medium	[1.5787 1.1441 1.3791]
	High	[0.6737 2.0464 1.9973]

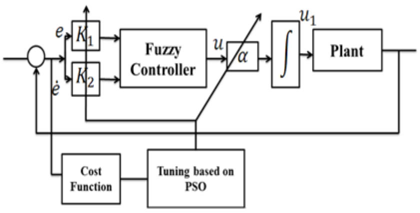

Fig. 3. Fuzzy-PI controller

First-order Sugeno model is used in the proposed optimal fuzzy-PI controller with two inputs and one output. Linguistic entrance variables are plasma glucose deviation *G(t)* (mg/dL) and its changes rate, i.e. *dG/dt*, and the only output variable is the exogenous insulin injection rate, *U(t)* [(μU/ml min $^{-2}$ (mg/dl) $^{-1}$]. This parameter is also considered as a control variable. Triangular membership functions, because of their simple application, are used in the design process. These membership functions are chosen with respect to fuzzy clustering of inputs and output. Best locations of the left and right "feet" or base points of the triangle and also best location of the triangle peak are set by LDW-PSO. The membership functions forms of inputs are given in Fig. 4.

5. Simulation and Result

In order to simulate the proposed optimal fuzzy-PI controller, MATLAB software is applied. Utmost generally accessible glucose measurement instruments acting by measuring the blood glucose content of a

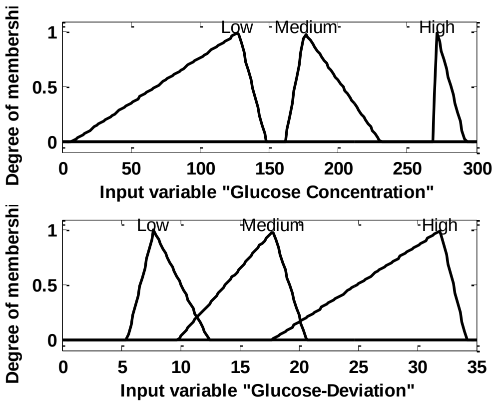

Fig. 4. Input membership functions

small finger-prick blood instance, a nettlesome procedure upon repeated application. Consequently, some diabetic persons gage blood sugar as rarely as once per day, or less. Although last progresses have led to semi-aggressive systems, for example, the GlucoWatch Biographer from Cygnus [40]. This instrument offers sampling rates up to one readership every 20 minutes, and can gage and save data constantly for up to 12 hours before new sensor pads are needed. Due to the existence limitations in measurement rate of blood glucose level we can't have continuous insulin infusion and the maximum injection rate according to existing technology is once every twenty minutes. What is not considered in [34, 41]. In this paper, the sampling period of 20 minutes is chosen and with the aid of applied parameters in [34, 41] the simulation has been done. With the difference that the initial level of glucose is considered much more severe than used values in [34, 41]. In addition, in order to evaluate the robust performance of controller against parametric uncertainties that exist in Bergman model, three sets of parameters have been used that relate to three different patients. Numerical values of the parameters are given in Table 2 [34].

Table 2. Parameters Values

	Normal	Patient 1	Patient 2	Patient 3
P_1	0.0317	0	0	0
P_2	0.0123	0.2	0.0072	0.0142
P_3	4.92×10^{-6}	5.3×10^{-6}	2.16×10^{-6}	9.94×10^{-5}
γ	0.0039	0.005	0.0038	0.0046
n	0.2659	0.3	0.2465	0.2814
h	79.0353	78	77.5783	82.9370
G_b	70	70	70	70
I_b	7	7	7	7
G_o	291.2	290	270	250
I_o	364.8	50	55	60

The used parameters of LDW-PSO are also listed in Table 3.

Table 3. The Used Parameters of LDW-PSO

Popsize	Size of the Swarm	50
Npar	Dimension of Problem (Number of Parameters to be Estimated)	35
Maxit	Maximum Number Of Intrations	100
C_1	Cognitive Parameter	1
C_2	Social Parameter	1
C	Construction Factor	1

In order to obtain the best response the objective function is defined as the Least Mean Square (LMS). In [41] the initial state of plasma glucose concentration is considered 70 (mg/dl) for all three patients that seems irrational and also the initial conditions in [34] were considered 180, 200, and 220 (mg/dl) for patients 1, 2, and 3 respectively, while in our paper much more severe initial conditions of blood glucose level were selected, i.e. 290, 270, and 250 (mg/dl) for patients 1, 2, and 3 respectively. The maximum insulin dosage rate in [34] were obtained 10, 4.4, and 2.8 [(μU/ml min^{-2} (mg/dl)$^{-1}$] for patients 1, 2, and 3 respectively, while in our paper were selected 1.4, 1.3, and 1.2 [(μU/ml min^{-2} (mg/dl)$^{-1}$] for patients 1, 2, and 3 respectively. It is noteworthy that if the simulations had been done with sampling rate of less than 20 minutes better responses will be achieved, this subject shows the superiority of our method in optimization of insulin infusion rate than proposed method in [34]. Blood glucose level in diabetic patients should never be less than 70 (mg/dL) while according to Figure (3) in [34] the basal value of blood glucose level is considered 60 (mg/dL) and in interval 50 (min) until 250 (min) is even less than 60 (mg/dL). In relation with linguistic rules, 3 linguistic rules are used whereas in comparison with [41] less IF-THEN rules are used. It means that the optimal fuzzy-PI controller is less complicated than the proposed controller in [41]. In order to evaluate performance of optimal fuzzy-PI controller in terms of settling time, the parameter *TM* (Time Margin) is introduced. *TM* parameter is the amount of time (min) that it takes the blood glucose level to reach the normal limits of 70-110. In [34] the amount of parameter *TM* for patients 1,2 and 3 are obtained approximately 60,50 and 40 (min) respectively, however, by applying proposed optimal fuzzy-PI controller these parameters are 40,45 and 20 (min) for patients 1,2 and 3 respectively.

Figure 5 shows the difference between glucose profile of a healthy person and glucose profiles of three patients; figure 6 shows the obtained glucose profiles of 3 patients using the proposed fuzzy-PI controller and figures 7, 8 and 9 show exogenous insulin infusion rates for patients 1, 2 and 3 respectively.

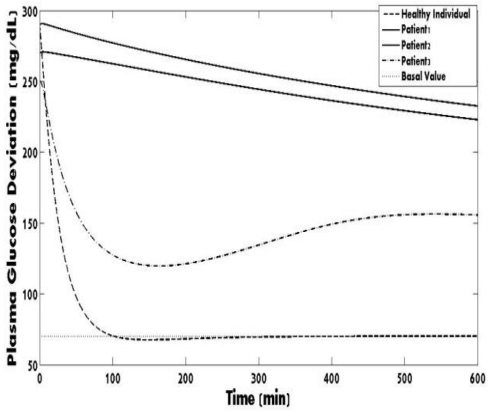

Fig. 5. Comparison between a healthy person and glucose profiles of three patients

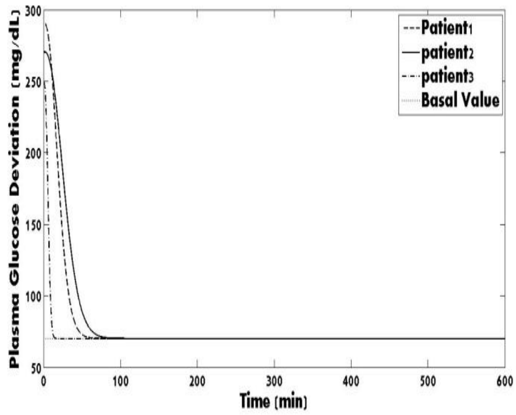

Fig. 6. Glucose profiles of 3 patients using the proposed controller

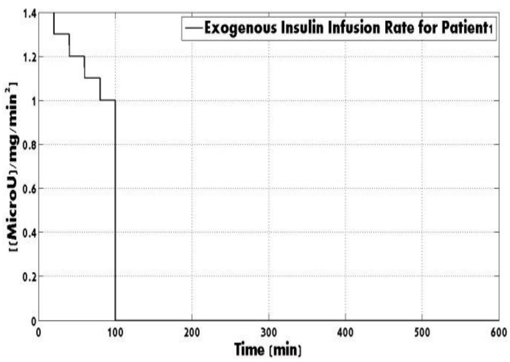

Fig. 7. Exogenous Insulin Infusion Rate of Patient 1

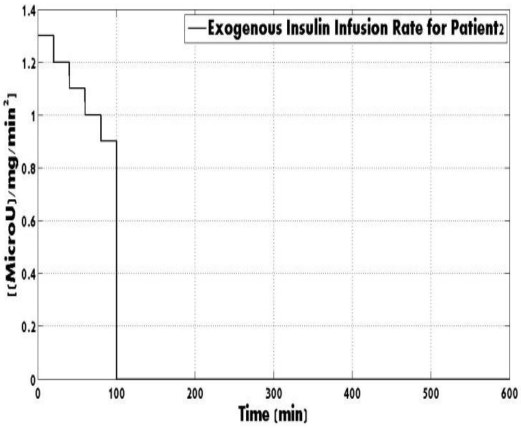

Fig. 8. Exogenous Insulin Infusion Rate of Patient 2

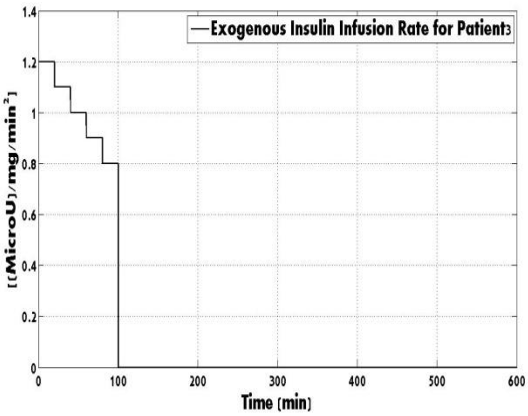

Fig. 9. Exogenous Insulin Infusion Rate of Patient 3

7. Conclusion

The main goal of this paper is to design an optimal fuzzy-PI controller base on first-order Sugeno model for blood glucose in diabetic patient. In the core of the proposed controller, a heuristic algorithm, namely Particle Swarm Optimization with Linearly Decreasing Weight (LDW-PSO), is utilized to optimize the membership functions, PI controller and insulin infusion signal simultaneously. To evaluate the performance of proposed controller, it is tested by three different sets of parameters that relate to three different patients. With regard to existing limitations in insulin injection rate the proposed controller has minimized the insulin injection rate. The simulation results depicted that the proposed controller has much better potential in terms of solution accuracy and better convergence speed in comparison with other methods despite of existent uncertainties in parameters of model.

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