Active Insulin Infusion Using Fuzzy-Based Closed-loop Control

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Abstract

In this paper a closed-loop control algorithm is developed for blood glucose regulation in type I diabetes mellitus patients. The control technique incorporates expert knowledge about treatment of disease by using Mamdani-type fuzzy logic controller to stabilize the blood glucose concentration in normoglycaemic level of 70 mg/dl. Controller performance is assessed in terms of its ability to reject the multiple meal disturbances resulting from food intake, on an averaged nonlinear patient model. Robustness of the controller is tested over a group of patients with model parameter varying considerably from the average model. In addition, proposed controller provides the possibility of more accurate control of blood glucose level in the patient in spite of uncertainty in model and measurement noise. Simulation results show the superiority of the proposed scheme in terms of robustness to uncertainty in comparison with other researches.

1. Introduction

Diabetes mellitus is a metabolic disease caused by insufficient production or deficient responsiveness to insulin. The two types of diabetes are type I and type II. In this paper the focus is on type I diabetes. In type I diabetes the body immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin, which regulates blood glucose [1]. When glucose level remains high for extended periods of time the patient is at risk for neuropathy, nephropathy, blindness, and other long-term vascular complications. Since intensive insulin therapy in insulin-dependent diabetic patients can reduce the risk of developing complications [2]. Therefore, these patients are encouraged to have this kind of therapy prescribed by a continuous subcutaneous insulin infusion pump.

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Control strategies of diabetes treatment can be categorized as open loop control, semi closed-loop, and closed-loop control. The current treatment involves open loop control in which physicians inject a pre determined dose of insulin subcutaneously based on three or four time daily glucose measurements, usually by an invasive method of finger prick. This method not only is painful and inconvenient but also unreliable because of approximation involved in type and the amount of insulin delivered. In semi closed-loop control insulin infusion rate adjust according to intermittent blood glucose readings. This technique is also suffered from long sampling time problem of missing fast or inter-sample disturbances. However, closed-loop control method which acts as an artificial pancreas is the most effective way of diabetes treatment and could improve the quality of life and life expectancy of patients. As shown in figure 1, an artificial pancreas includes a blood glucose sensor, insulin pump, and appropriate glucose control algorithm. A control algorithm processes the information of the glucose sensor in real-time, and updates the insulin injection rate by the pump.

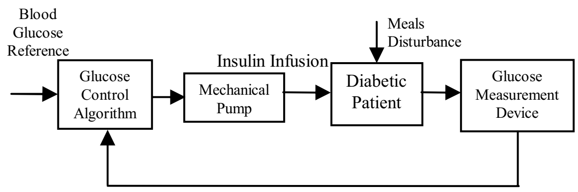

Figure 1. A closed-loop glucose control system.

Human bodies need to maintain a glucose concentration in narrow range of 70-110 mg/dl. When a normal person is subjected to a glucose meal, the glucose concentration in plasma increases from basal value and so the pancreatic β-cells secrete insulin. The insulin in plasma is hereby increased, and the glucose uptake in muscles, liver, and tissues is raised by the remote insulin in action. This lowers the glucose concentration in plasma to basal value. However, in

Type I diabetic patients whose pancreas does not release insulin, blood glucose level remains in much more than basal value for long period of time. Therefore, it is necessary to use an appropriate control strategy for these patients.

In testing the performance of the control algorithm a virtual patient need to be implemented using an appropriate mathematical model. During the last decades, many mathematical models have been derived to describe dynamics of glucose-insulin regulatory system [3]-[5]. These models have ranged from linear to nonlinear with increasing the levels of complexity [6]. Since, the parameters of these models are not constant and vary from patient to patient. Thus, designed controller should be robust to uncertainty in model parameters and meal disturbances.

With the availability of these mathematical models different algorithms based on control theory have been developed to control the blood glucose level in people with diabetes. Some of these algorithms include proportional-integral-derivative (PID) [7,8] and proportional-derivative (PD) [9], H_∞ [10], and optimal control algorithms [11,12]. However, the important point in most of these researches is that proposed controller has been designed with regard to mathematical model as a crisp model, and uncertainty in the model parameters has been not considered. Therefore, although these methods, would offer good responses in simulations, it is likely that they would not be successful in practice and failed while applying to an actual patient. A fuzzy controller to maintain a normoglycaemic average of blood glucose concentration was designed in [13]. Although, simulation results were promising for the nominal patient, but uncertainty in patient model parameters has not considered.

In the control theory, the fuzzy logic has emerged as a powerful tool to employ expert knowledge about the systems for implementing an appropriate control low [14].

This work employs fuzzy logic control scheme to stabilize the blood glucose concentration of type I diabetic patients around normal value, where a Mamdani-type of fuzzy controller is designed by using expert knowledge about diabetes mellitus treatment. Insensitive to typical error in commercial device and multiple meal disturbances, accuracy, robustness to model parameter variations and appropriate settling time are main features of proposed algorithm. The text is organized as follows.

In section 2 the physiological model of glucose-insulin regulatory system in type I diabetes mellitus patient is introduced. Section 3 includes the design of knowledge-based fuzzy controllers. Simulation results are included in section 4. Finally, the paper is closed with the interpretation and discussion of the results.

2. Glucose-insulin regulatory system model

Complex models though are accurate for regimen evaluation but are generally unsuited for real-time control due to they need several time points of input to produce the insulin infusion profile. Additionally, they are not generic requiring the data of a specific patient and known glucose inputs. Against, simple models capture essential dynamics behaviors and provide a more suitable foundation for real-time control design. Bergman's minimal model is the most popularly used model between simple inadequate and comprehensive not identifiable models which has the minimum number of parameters and captures the essential dynamics of glucose-insulin regulatory system. The model equations are [5]:

$$\begin{aligned} \dot{G}(t) &= -p_1[G(t)-G_b] - X(t)G(t) + D(t) \\ \dot{X}(t) &= -p_2 X(t) + p_3[I(t)-I_b] \\ \dot{I}(t) &= -n[I(t)-I_b] + \gamma[G(t)-h]^+ t + u(t) \end{aligned} \tag{1}$$

In the above equations $G(t)$ represents 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} $(\text{mg/dl})^{-1}$]. 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 [12]. Model parameters and their values are presented in reference [5,12]. Note 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.

$D(t)$ shows the meal glucose disturbance and can be modeled by decaying exponential function of the following form [12]:

$$D(t) = A\exp(-Bt),\ \ B > 0 \tag{2}$$

Table 1. Characteristics of input variables.

input variables	interval	membership functions						
Glucose level *G(t)*	[40 400] mg/dl	Negative big	Negative small	Normal	Positive small	Positive medium	Positive big	Positive large
Glucose deviation *dG/dt*	[-20 20] mg/dl	Negative	Zero	Positive				

Table 2. Output variable characteristics.

output variables	interval	membership functions						
Insulin Infusion u(t)	[-1 4] [µU/mg/min2]	Negative big	Negative small	Zero	Positive small	Positive medium	Positive big	Positive large

Where t is in min and $D(t)$ is in (mg/dl/min). $u(t)$ is the exogenous insulin infusion rate. The model is simple, yet accurately represents the essential dynamics of the human glucose-insulin regulatory system. The controller uses a feedback loop that employs the blood glucose level G, and its derivative (dG/dt), as sensor inputs, and the exogenous insulin infusion rate $u(t)$ as the control output.

3. Controller synthesis

The controller is structured with a Mamdani-type fuzzy architecture with two input linguistic variables and one output variable. The input variables are the plasma glucose concentration $G(t)$ and its rate of change dG/dt, and the output variable is the exogenous insulin infusion rate. The characteristics of the input and output variables are given in table 1 and 2, respectively. The types of membership functions applied in the design are chosen triangular membership functions for simplicity. These membership functions were selected according with the fuzzy classification of the input and output variables. The shapes of inputs membership functions are presented in figure 2. The output membership function is then shown in figure 3.

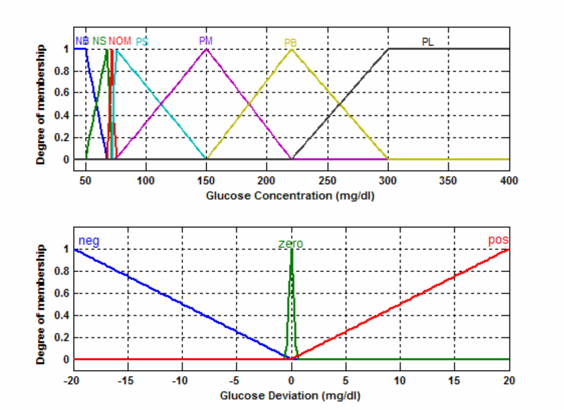

Figure 2. Input membership functions.

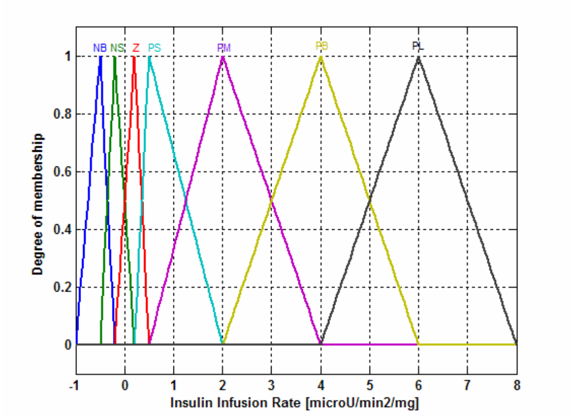

Figure 3. Output membership function.

By the definition of the input and output fuzzy sets, a total of 21 IF-THEN rules were defined. These rules were of AND (minimum) type antecedent. The output (defuzzification method) is calculated by the CENTROID method. The linguistic rules are detailed in table 3.

Figure 4. shows the output surface of the controller. It is obvious that controller inputs change with the output in a piecewise linear fashion.

Table 3. Fuzzy IF-THEN rules.

	Glucose Rate of Change		
Glucose	Negative	Zero	Positive
Positive Large	PL	PL	PL
Positive Big	PB	PB	PL
Positive Medium	PM	PM	PM
Positive Small	PS	PS	PS
Normal	Z	Z	Z
Negative Small	NB	NS	NS
Negative Big	NB	NB	NB

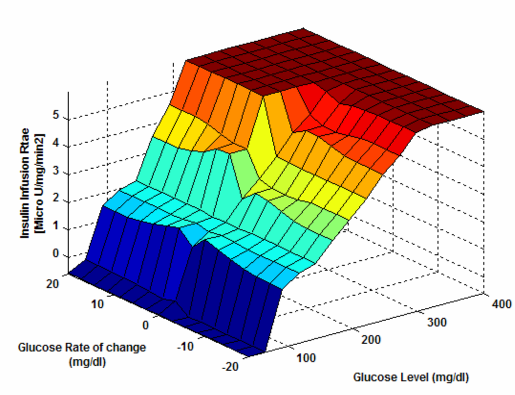

Figure 4. Control action surface.

4. Simulation results

To verify the physiological model the controller output *u(t)* is set to zero and the response of a healthy person and diabetic patient is obtained to demonstrate the difference between their glucose regulatory systems. As seen in figure 5, a healthy person's blood glucose value is stabilized in normal value in spite of meal disturbance, but a patient's glucose level remains in much more than basal value.

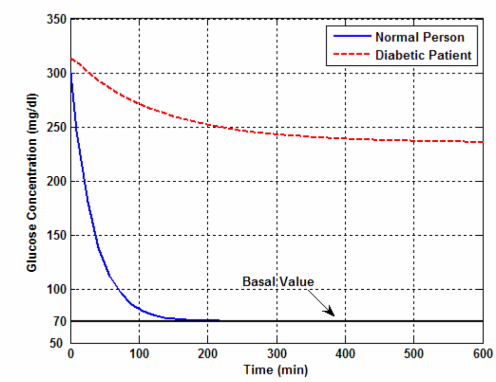

Figure 5. Healthy person and diabetic patient glucose regulatory system.

To validate the proposed algorithm, designed fuzzy logic controller is applied to the original nonlinear model in equation (1) and patient's response obtained in presence of meal disturbance. To consider the variations in model parameters three sets of parameters for three different patients are used. Figure 6 shows closed-loop glucose regulatory system of the patients. Proposed controller acts successfully in controlling the blood glucose level in presence of multiple meal disturbance at time t=0 and t=360 min. It is obvious that the transient responses of the different patients to the same controller are different, but in all cases, the glucose is completely stabilized at the basal level with an appropriate settling time. The controller performance demonstrates superiority of using fuzzy logic control and shows more effective results in terms of settling time and uncertainty in the model parameters, comparing with the results discussed in [13,7,10].

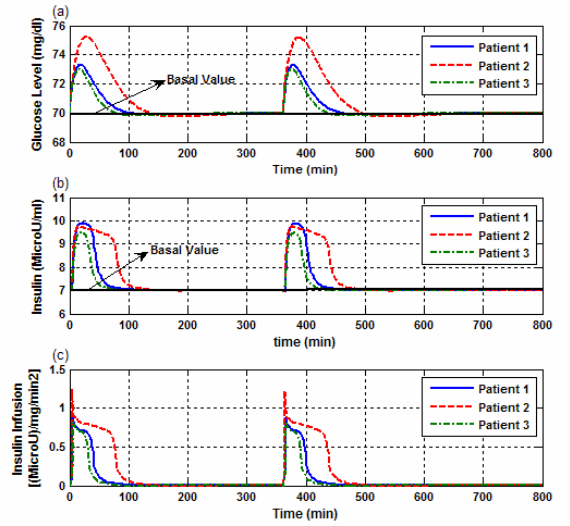

Figure 6. Blood glucose regulation under two meals, at time t=0 and t=360 min. (a) Plasma glucose concentration with initial state of 70 (mg/dl) (b) Plasma insulin concentration with initial state of 7 (MicroU/ml) (c) Exogenous insulin infusion rate.

In the next set of simulations, to consider the effect of sensor noise, a white-disturbance (an error) with the amplitude of 0.15 in each of the glucose measurements is assumed. Figure 7 demonstrates that the fuzzy logic controller remains close to normoglycaemic average in presence of error in measurements.

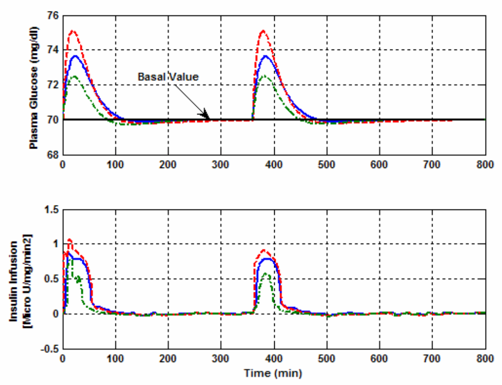

Figure 7. Closed-loop glucose response when subjected to error in glucose measurements.

Figure 8 demonstrates that the fuzzy logic controller work slightly better than a normal person in terms of peak reduction and settling time. These simulations show that a feedback scheme is the best choice for the blood glucose regulation.

The values of the model parameters that have been used in implementing the controller are given in table 4.

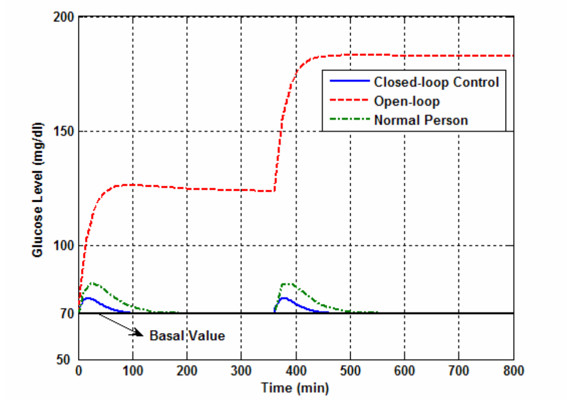

Figure 8. Comparison of feedback and open-loop glucose regulatory systems.

5. Conclusion

In This work, a closed-loop control system based on fuzzy logic control for type I diabetic patients has been proposed. In order to incorporate knowledge about patient treatment, the controller is designed using a Mamdani-type fuzzy scheme. It is important to mention that the control algorithm is essence model-free. The proposed controller can successfully tolerate dynamic uncertainty in patient model while rapidly rejecting meal disturbances and tracking the constant glucose reference. Robustness was tested over a group of three patients with model parameters varying considerably from the averaged model. As shown in this paper, the fuzzy logic framework has the potential to synthesize expert knowledge to treat diseases. In addition, it is proved that this method has preference over other conventional techniques in blood glucose control. The suggested scheme is expected to enhance the automation of insulin delivery in Type I diabetic patients.

Table 4. Parameter values.

	Normal	Patient 1	Patient 2	Patient 3
p_1	0.0317	0	0	0
p_2	0.0123	0.02	0.0072	0.0142
p_3	4.92×10^{-6}	5.3×10^{-6}	2.16×10^{-6}	9.94×10^{-6}
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_0	291.2	220	200	180
I_0	364.8	50	55	60

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