Closed-Loop Control of Blood Glucose Level in Type-1 Diabetics: A Simulation Study

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Abstract

Survey on diabetes is one of the popular fields of biomedical signal processing. In this paper, a closed-loop system which utilizes modified Stolwijk-Hardy glucose insulin interaction model is considered. The modified model was derived by adding an exogenous insulin infusion term. Two control algorithms are used for exogenous insulin infusion: a Mamdani type fuzzy logic controller (FLC), and a fuzzy-PID controller. Simulations are performed to assess control function in terms of keeping desired steady state plasma glucose level (0.81 mg/ml) against to exogenous glucose input. Simulation results are notable and significant in terms of controlling blood glucose level (BGL). The control algorithms that applied to the model are firstly proposed, therefore this study is made a contribution to the literature.

1. Introduction

Diabetes is a chronic illness of the glucose-insulin regulatory system which stemming from the failure of the pancreas in keeping the concentration of blood glucose between the range of 70-110 mg/dl (0.7–1.1 mg/ml). The World Health Organization (WHO) estimates that 347 million people throughout the world have diabetes and the diabetes is expected to be the 7th leading cause of death in 2030 [1, 2].

BGL is affected by food intake, digestion rate, exercise etc. After meals the BGL increases. The beta cells of the pancreas are stimulated to secrete insulin. The secreted insulin inhibits increasing of the glucose concentration excessively. This is succeeded by glucose consumption of muscle cells or conversion of glucose to glycogen molecules stored in the liver and muscle cells. On the other hand, in between meals or during sleep, the alpha cells of the pancreas secrete glucagon in order to avoid decreasing the BGL excessively. This interaction of insulin and glucagon regulates the BGL in the body[3, 4].

There are two types of diabetes, type-1 and type-2 diabetes. Destruction of beta cells by the immune system causes the type-1 diabetes. This type is more common in children and adolescents. On the other hand, more than 90 percent of diabetes patients are type-2 diabetes. In this type, the insulin produced by the pancreas does not function properly due to the resistance against insulin. There are some complications arising from diabetes; neuropathy, blindness, nephropathy, and other long-term vascular complications[5].

Since the pancreas does not produce insulin, high BGL is shown in type-1 diabetics. They need external insulin to support glucose uptake and consumption. External insulin should be infused at an appropriate rate to keep BGL in normal ranges[6, 7].

Measurements of BGL for three or four times in a day and injection of equal amount of insulin subcutaneously are proposed in the current medical treatments. But this method is unsuitable and painful. Moreover it is difficult to deliver the right amount and type of insulin. Promising that, nowadays plenty of researches are being performed to cope with the deficiencies of the current medical treatments. In this paper, we focused on closed-loop control algorithms for insulin injections. The closed-loop control system includes a glucose sensor, a controller and a mechanical pump. Measured BGL data from glucose sensor would be transmitted to a control system which determines the required insulin injection rate to maintain the BGL in a normal range. The desired insulin amount could be delivered by a mechanical pump. To maintain the BGL in normal ranges, the closed-loop system is more trustworthy since it simulates the normal pancreas behavior very closely[8-10]. The block diagram of closed-loop control of diabetic patients is shown in Fig. 1.

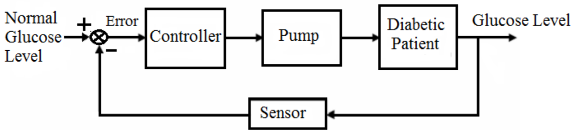


Fig. 1. Closed-loop control of diabetic patient

2. Mathematical Model

In the control terminology, the diabetic patient is identified as a system. So as to study and analyze the effect of glucose and insulin regulation, a model of pancreatic function is required. In this paper, modified Stolwijk-Hardy glucose insulin interaction model is used[11, 12]. The modified model was derived by adding a term for exogenous insulin infusion. Thus, the glucose dynamics are ruled by

$$\begin{aligned} C_G \frac{dG}{dt} &= U_G + Q_G - \lambda G\text{-}\nu GI, & G \le \theta \\ C_G \frac{dG}{dt} &= U_G + Q_G - \lambda G\text{-}\nu GI\text{-}\mu(G-\theta), & G > \theta \end{aligned} \quad (1)$$

while the insulin dynamics are ruled by

$$C_I \frac{dI}{dt} = U_I - \alpha I, \qquad G \le \varphi \qquad (2)$$

$$C_I \frac{dI}{dt} = U_I - \alpha I + \beta (G - \varphi), \qquad G > \varphi$$

where

$G(t)$: Instantaneous BGL in mg/ml
$I(t)$: Instantaneous blood insulin level mU/ml
$U_G(t)$: Exogenous glucose infusion in mg/h
$U_I(t)$: Exogenous insulin infusion in mU/h
C_G : Glucose capacitance in the extracellular space
C_I : Insulin capacitance in the extracellular space
$Q_G(t)$: Glucose inflow into blood in mg/h
λ : Tissue usage rate of glucose that is independent of $I(t)$
ν : Tissue usage rate of glucose that is dependent on $I(t)$
α : Insulin destruction rate
β : Insulin production rate by the pancreas
θ : Threshold for renal discharge of glucose
φ : Threshold for pancreatic production of insulin
μ : Glucose excretion rate

There are two ways of glucose inflow into the blood, glucose produced from the liver or glucose absorbed from the gastrointestinal tract. Additively, as it can be shown from parameters above, coefficients are related to physiology and vary according to the condition of patient. The used parameter values are given in [8, 12]. In this model, volume of plasma and interstitial fluid are given in a single compartment (3l+12l, in healthy adult). Steady state concentrations of glucose and insulin in this compartment are 0.81 mg/ml and 0.055 mU/ml, respectively. For type-1 diabetic patients the main problem is the inadequacy of beta cells to produce the necessary amount of insulin. This situation is modeled by reducing the sensitivity of insulin response to glucose. From this modeling for type-1 diabetic patient, glucose and insulin concentrations can be found as 1.28 mg/ml and 0.029 mU/ml in the steady state, respectively[12].

2.1. Simulation with the model

Using Matlab/Simulink, the glucose-insulin regulation model is examined and performed without exogenous insulin infusion $U_I(t)$. Simulink model is presented in Fig. 2[12]. Control studies related to the exogenous insulin infusion $U_I(t)$ will take place in the next section of this paper.

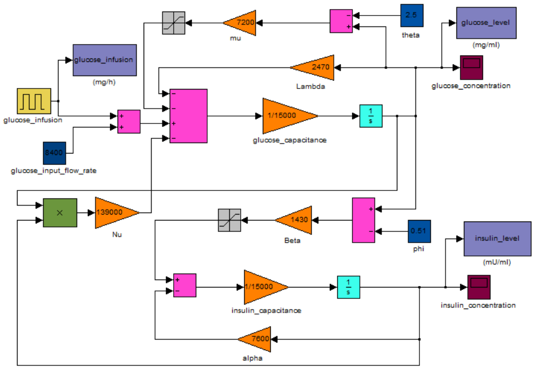


Fig. 2. Simulink model of glucose-insulin regulation system[12]

Glucose infusion $U_G(t)$ into the model considered as a step input is used as infusion of 40 g of glucose for 25 minutes. Furthermore, simulation study was evaluated through reducing the sensitivity of insulin response to glucose for type-1 diabetes.

The blood glucose concentration and the blood insulin concentration are shown in Fig. 3 and Fig. 4, respectively.

In the Fig. 3, it can be seen that the abrupt rise in glucose level with glucose infusion which is considered as food intake. Then, it settles down to the steady state after a certain time. Secreted level of insulin is altered according to the BGL. It is shown in Fig. 4.

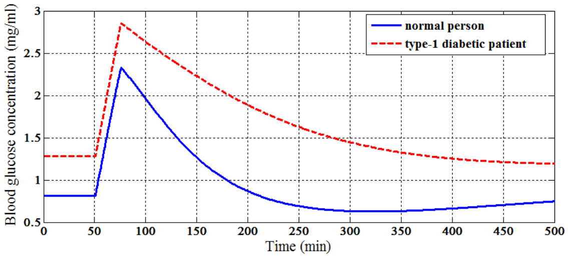


Fig. 3. Blood glucose concentration

It can be obviously seen in Fig. 3, the steady state BGL of type-1 diabetic patient is higher than normal person. Furthermore, for type-1 diabetic patient the blood glucose and insulin levels reach steady state slower than normal subject.

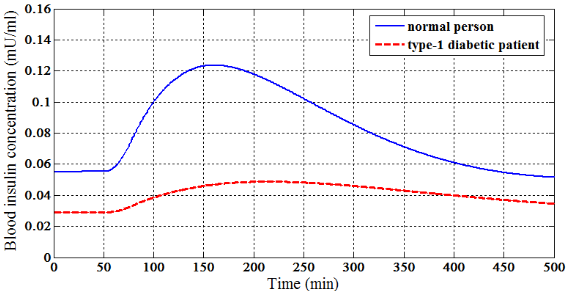


Fig. 4. Blood insulin concentration

3. Control Studies

For any normal person or diabetics, the steady state BGL in the person's blood is determined by existing amount of insulin. So, insulin injection is required to lower the BGL in diabetics. Therefore, the controller determines the insulin infusion rate based on the measured glucose concentration. The exogenous insulin infusion $U_I(t)$, which is mentioned above, is added to the model to keep under control the BGL in a tight range around the steady state BGL of normal adults.

Many different algorithms have been proposed to control the BGL in diabetics through the usability of mathematical models. Some of these algorithms employ proportional-integral-derivative (PID) [13, 14], proportional-derivative (PD) [10]. On the other hand, these proposed controllers have been formed with regard to mathematical model as a crisp model. Biomedical systems like this are often related with inaccuracy and ambiguity in model parameters. As a result, it can be claimed that, classical control techniques are inadequate for controlling such systems. These techniques are unrealizable in practice and inapplicable to a real patient[15]. This complex control problem could be solved by the help of fuzzy logic. Fuzzy logic allows capturing more valuable information about the behavior of the controlled variable and it can be good guide that helps us to discover artificial pancreas. Furthermore, fuzzy logic controllers have shown relatively successful results comparing with the renowned classical controllers such as PID [16, 17]. Fuzzy based controllers to maintain normal range of BGL were designed in [18].

In the following paragraphs, design of the FLC and the fuzzy-PID controller are introduced.

3.1. Fuzzy Logic Controller (FLC) Design

Closed-loop feedback control system with the proposed FLC is depicted in Fig. 5.

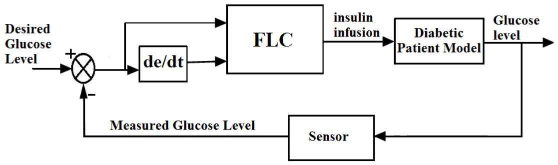


Fig. 5. Fuzzy logic control block diagram

The controller for exogenous insulin infusion is designed with a Mamdani-type fuzzy architecture which has two input and one output variables. While the plasma glucose concentration *G(t)* and its derivative *dG(t)/dt* are the input variables, the insulin infusion rate $U_I(t)$ is output variable.

Membership functions of input and output variables are shown in Fig. 6 and Fig. 7, respectively.

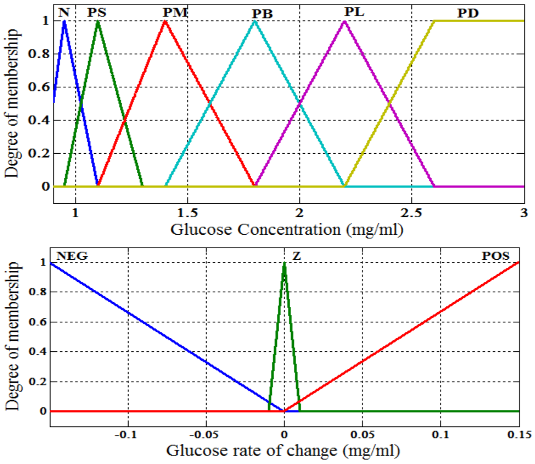


Fig. 6. Input membership functions

Normal(N), Positive Extremely Small(PXS), Positive Small(PS), Positive Medium(PM), Positive Big(PB), Positive Large(PL), Positive Danger(PD), Negative(NEG), Zero(Z), and Positive(POS) are determined as the fuzzy sets of the variables.

The types of membership functions applied in the design are chosen mostly triangular membership functions for simplicity. Also, trapezoidal membership function is used in order to increase the level of insulin infusion as possible when the blood glucose concentration reaches dangerous high levels.

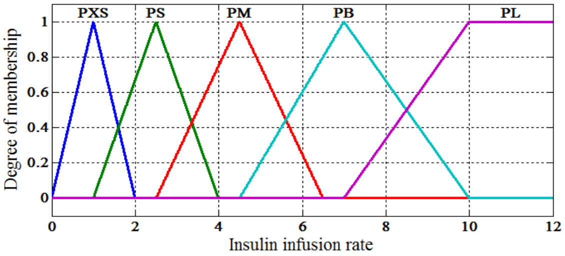


Fig. 7. Output membership function

By the definition of the input and output membership functions, 18 IF-THEN rules were defined. Those linguistic rules are given in Table 1. Each rule output is computed by MIN-MAX law. And CENTROID defuzzification method is used for crisp system output.

Table 1. Fuzzy IF-THEN rules

	Glucose rate of change		
Glucos	**NE**	**Z**	**PO**
N	PXS	PXS	PS
PS	PS	PS	PM
PM	PM	PM	PB
PB	PB	PB	PL
P	PL	PL	PL
PD	PL	PL	PL

3.2. Fuzzy-PID Controller Design

The proposed fuzzy-PID control system is shown in Fig. 8.

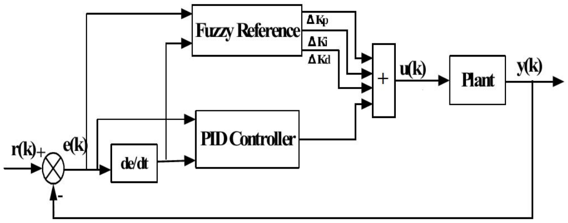


Fig. 8. The Fuzzy-PID control system

The fuzzy-PID controller is adapted from classical PID control algorithm. By using fuzzy inference system (FIS), system error and its change maintain an online adjustment in the PID parameters (kp, ki, kd). Two-input three-output controller is used as the fuzzy controller. The two linguistic inputs are e(k) and Δe(k); the three outputs are the change of PID parameters (Δkp, Δki, Δkd). The universe of discourse of input and output variables are as follows:

e(k) = [0.7, 3]
Δe(k) = [-0.15, 0.15]
Δkp = [-0.2, 0.6]
Δki = [-0.1, 0.2]
Δkd = [0, 0.8]

Negative Medium(NM), Negative Small(NS), Zero(Z), Positive Small(PS), Positive Medium(PM), Positive Big(PB), and Positive Large(PL) are determined as the fuzzy sets of the variables. Due to design simplicity and used commonly in literature the membership functions are selected as triangular and trapezoidal membership functions. The shapes of input variables are presented in Fig. 9. The output membership functions are then shown in Fig. 10.

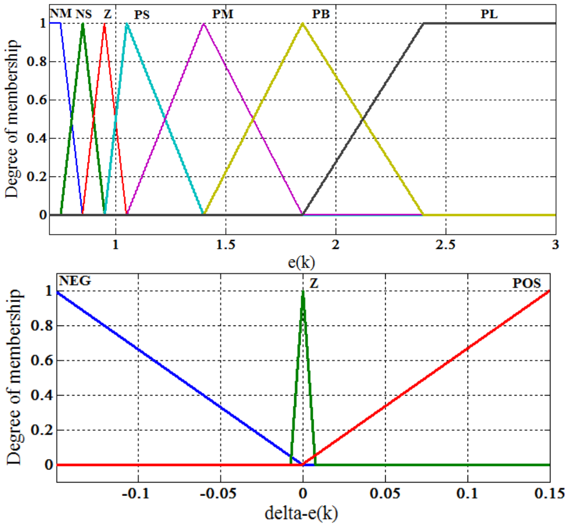
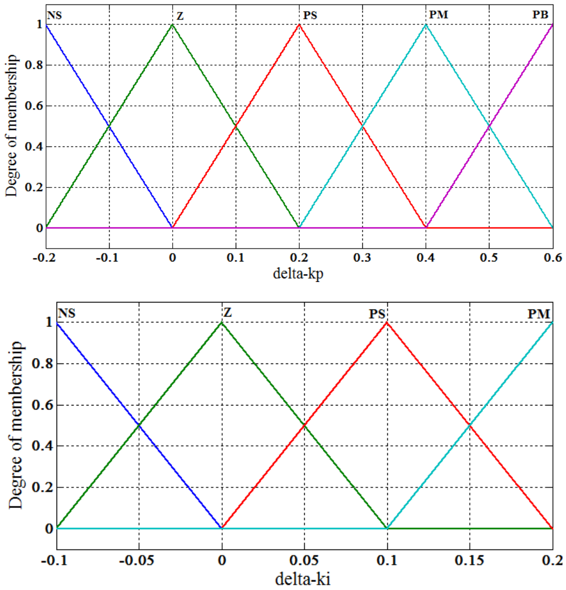


Fig. 9. Input membership functions

Robustness of the controller is characterized by some specifications in the classical PID controller. Some of these specifications are rise time, settling time, overshoot, stability, and steady-state error. Furthermore, these specifications are affected by the PID parameters kp, ki and kd[19, 20]. The individual effects of these three terms on the closed-loop performance are summarized in Table 2.



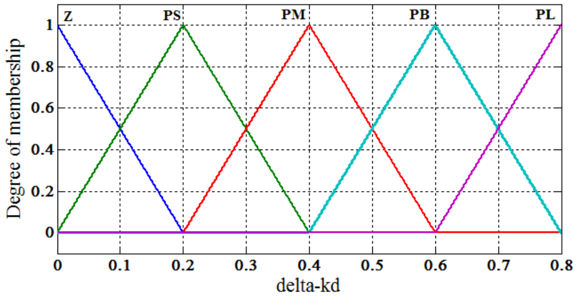


Fig. 10. Output membership functions

Table 2. Effects of independent P, I, and D tuning on closed-loop response[19]

Closed-Loop Response	Rise Time	Overshoot	Settling Time	Steady-State Error	Stability
Increasing K_P	Decrease	Increase	Small Increase	Decrease	Degrade
Increasing K_I	Small Decrease	Increase	Increase	Large Decrease	Degrade
Increasing K_D	Small Decrease	Decrease	Decrease	Minor Change	Improve

Considering of the individual effects of PID parameters'(kp, ki, kd) on the closed-loop response, the control knowledge is determined. Using the fuzzy sets and universe of discourse of the variables as defined above, control rules are composed through the control knowledge. 21 IF-THEN rules were defined for each output (Δkp, Δki, Δkd). Each rule output is computed by using MIN-MAX law. The CENTROID defuzzification method is employed for crisp system output.

4. Results and Conclusions

In this study, the closed-loop control of pancreatic model is designed, conducted and analyzed with the aid of Matlab/Simulink for the management of the glucose-insulin regulation. The closed-loop control techniques are firstly evaluated to the Stolwijk-Hardy glucose-insulin model in this paper. Proposed and simulated design could be a scientific background for the design of robust insulin pump. The results obtained with the help of Matlab for above-mentioned closed loop control methods that applied to keep the blood glucose concentration at the level of steady-state for type 1 diabetic patient are presented. For the simulations of the Fuzzy-PID control, PID parameters were taken from [13]. The blood glucose concentration results are shown in Fig. 11. The blood insulin concentration results are then presented in Fig. 12. The results include the FLC, the fuzzy-PID controller along with the shapes of type 1 diabetic patient and normal person for comparison.

By comparing the simulation results it can be clearly seen that the Fuzzy-PID controller gives more effective results than the FLC in terms of the regulation of the blood glucose level. BGL is better controlled with the Fuzzy-PID controller and the profile of the blood glucose concentration approaches a normal adult. Furthermore, comparing the Fuzzy-PID controller and FLC, the Fuzzy-PID controller comes into prominence in terms of overshoot, settling time and steady state error.

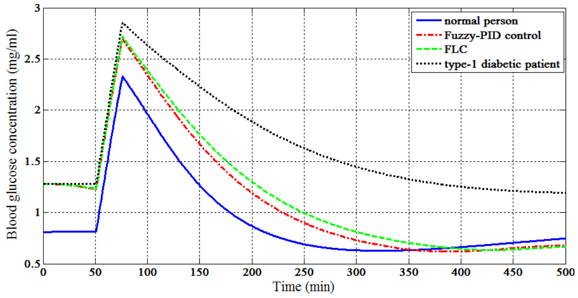


Fig. 11. The results of blood glucose concentration

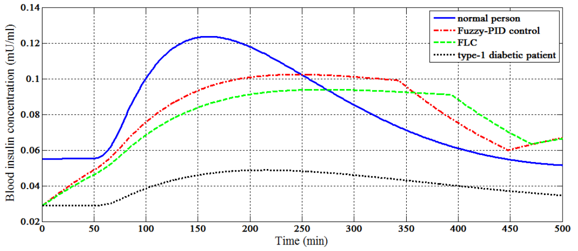


Fig. 12. The results of blood insulin concentration

Nowadays, with the aid of insulin pump, control algorithm that developed for the regulation of blood glucose concentration is an area that needs attention especially for the treatment of type 1 diabetes. In this context, researching the model that gives interaction and the pharmacokinetics of glucose-insulin in the best way and working on the control methods which improve the quality of life of patients with type-1 diabetes are crucial.

5. References

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