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Evolution of Diabetic Control Identification in Lieu of Continuous Glucose Monitoring Technology- A Review

A. Alavudeen Basha[1] and Dr. S. Vivekanandan[2]

[1]Research Scholar, School of Electrical Engineering, VIT University, Vellore-632 014, Tamilnadu, India.

Orcid: 0000-0003-3930-483X

[2]Associate Professor, School of Electrical Engineering, VIT University, Vellore-632 014, Tamilnadu, India.

Abstract

Automatic infusion system is an indispensable tool for the regulation of blood glucose level for diabetic patient in present and future. To date, all the commercially available models considers plasma and insulin concentration of the human body and so this paper reviews three different modes such as Continuous glucose monitoring (CGM) system, the drug estimation techniques (PI, FUZZY and MPC) and to find the optimal control strategy for insulin approximation. The fine-tuned numerical value of insulin provides solution for complex situation of diabetic patients. The robustness of the projected controller performance is evaluated under dynamic conditions such as delayed meals, variability in the type of meal and metabolic uncertainty case. Therefore, we review the validation results based on that the results the new improved combine control strategies to achieve the controlled and optimized insulin rate for persistent glucose control compare then the reviewed methods. The MATLAB simulation is used to evaluate the effectiveness of the proposed work and obtain the results based on the proposed values.

Keywords: Automatic insulin infusion, Machine learning, Optimization techniques

INTRODUCTION

Diabetes is a major lifestyle disorder, the prevalence of which is increasing globally. Asian countries contribute to more than 60% of the world's diabetic population as the prevalence of diabetes is increasing in these countries [1]. Study on diabetes reveals that imbalance nutrition, obesity and improper diet are the main causes of disease [3]. A survey named prevalence of diabetes in age (2016) reports that most of middle and low-income countries has much prevalence compared to the other countries [1]. The health care budgets for the disease management are meager and India's pecuniary boom has been accompanied by a drastic increase in the number and the prevalence rates are up to 20% in some cities and recent figures showed surprisingly increased rates even in rural areas. Researchers prove that the prolonged diabetes will have other complications and leads to a high risk in heart [7], kidneys [3], eyes [1] and nerves problems [3] even develops skin infections too [1].

The type1 diabetic patient is totally dependent on an external source of insulin to be infused at an appropriate rate to maintain blood glucose level. The present medical treatments recommend to use three to four daily glucose measurements and an equivalent amount of subcutaneous insulin injections via manual dispersion. This method is not only inconvenient and painful but also unreliable due to the approximation involved in the amount and type of insulin delivered. Researchers have come up with many tools and approaches to diagnose and treat the disease [6], also they are focusing to develop the manifold of new techniques and feasible instrumentation to offer feasible solutions and improve the life of patients. Based on the discrepancy, researchers developed automatic insulin injection system that needs to calculate the insulin delivery rate to keep the blood glucose level in a stable range.

This paper reviews a continuous glucose level control based on the closed loop system which is designed and evaluated with high stability proportional-integral-derivative (PID) control along with model predictive and Fuzzy control. The difficulty in PID controller is the large delay of the subcutaneous sensing and actuation that can be achieved with the help of fuzzy controller which does not give perfect solution for all cases that has a main drawback of combining conjunctive or disjunctive clauses. In this case the model predictive control can be used to achieve the desired results with minimum time delay. The purpose of this work is to compare the existing control strategy for automatic insulin infusion system and based on the review a new proposal with combined control strategy that may improve the performance of automatic infusion in insulin dosage controller. The key idea of this assessment is to identify the proper design the controller for insulin evaluation that provides more stability and high performance guarantees.

AUTOMATED INSULIN DELIVERY SYSTEM

A fully automated closed-loop insulin delivery system could potentially be the ultimate answer for blood glucose (BG) control in diabetic patients [4]. This system can imitate the activity of human pancreas and it is capable of maintaining the glucose levels. The artificial pancreas is an integrated device, which substitute’s human pancreas by sensing plasma glucose concentration and calculates the amount of insulin needed to the human body and the level of accepted levels based on the pre calculated values and then delivering the correct amount of insulin. Such an artificial pancreas system can theoretically produce exact value of glucose without finger-stick, subcutaneous insulin injections, or hypo- glycemic/hyperglycemic events, thereby, drastically improves the quality of life.

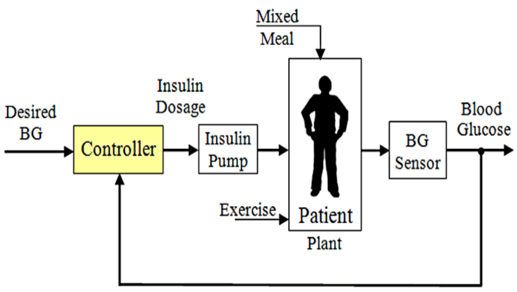

Figure 1: Block Diagram Automatic Infusion Delivery system

In the closed-loop control system, the system needs a glucose sensor to measure the blood glucose level and the sensed information then would be passed to a control system (PID or Fuzzy or MPC or other newly identified controller for automatic infusion system) that would calculate the necessary insulin delivery rate to keep the blood glucose level in a stable range. Then a mechanical pump can deliver the desired amount of insulin. In general, the closed-loop method is more reliable in maintaining the level of blood glucose and also is close to the normal pancreas [8]. Figure 1 shows the block diagram of closed-loop control of diabetic patients.

THE MATHEMATICAL MODEL OF DIABETES

In order to have a reliable automatic insulin delivery system under various physiological conditions, a model must be created to predict glucose which includes all the major energy providing substrates at rest and during physical activity. In the glucose based existing mathematical model [6], contribution of free fatty acid (FFA) metabolism is the important source of energy for the body. It is important to consider these metabolic interactions in order to characterize the endogenous energy production of a healthy or a deceased. Furthermore, physiological exercises are taken into account to induce the fundamental metabolic changes in the body. Figure 2 shows the simulation of a composite model that is capable of predicting FFA-glucose-insulin dynamics during rest and exercise [3]. Mixed meal model was employed to capture the absorption of carbohydrates (CHO), proteins, and FFA from the gut into the circulatory system [12]. An exercise model was used to incorporate the effects of exercise on glucose and insulin dynamics to capture the changes in glucose and insulin dynamics during and after mild-to-moderate exercise [4]. The mixed meal, and exercise models served as a disturbance to the proposed model [6]. The overall diabetic plant comprises of 34 differential algebraic equations, which describe 20 states. The diabetic plant includes the composite model, and its disturbances (mixed meal, and exercise models). The model successfully captured the FFA-glucose interactions at the systemic level, and also effectively predicted mild-to-moderate exercise effects on glucose and FFA dynamics. Accordingly, this composite model was selected. In this work to provide a plat- form for the development of closed-loop controllers to maintain glucose homeostasis of a diabetic patient.

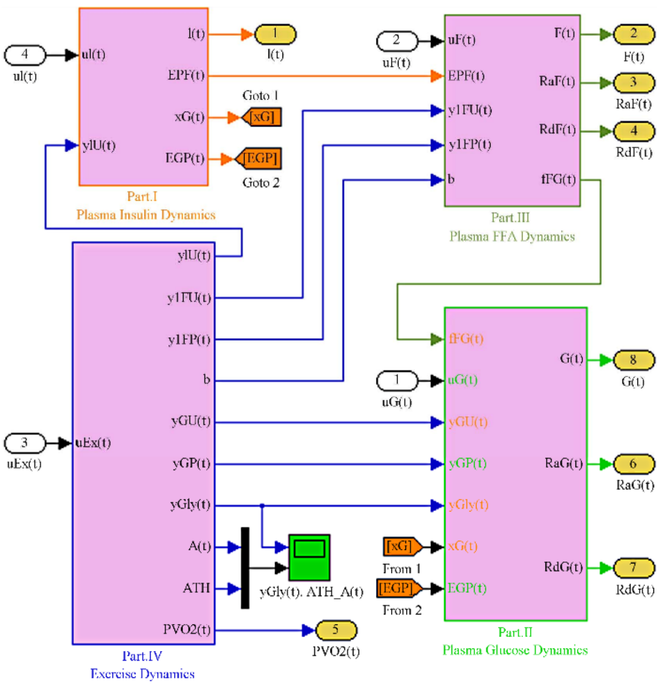

Figure 2: Composite Model simulation of Diabetic Patient

CONTROLLERS DESIGN AND SIMULATION

Various types of control algorithms for blood glucose control have been reported in the literature. Some of these algorithms include: PID control [5, 6], and fuzzy logic control [7] and model predictive control [4].

However, our studies have focused on using the successfully captured FFA-glucose-insulin dynamics combined model presented in section two, which has never been used before for control purposes, to developing two control algorithms: the PID and the fuzzy logic controllers using Mat lab/Simulink. The target blood glucose range that the controllers were supposed to attain and maintain is similar to healthy blood-glucose levels. The proposed blood-glucose range is between 70 mg/dl and 120 mg/dl before meals and less than 180 mg/dl after meals [5], and the maximum insulin infusion rate is con- strained to 100 mU/min.

The PID Controller

The most traditional of all controllers is probably the proportional integral derivative (PID) controller. A PID controller uses a proportional term, an integral term, and a derivative term, each with a coefficient that provides a weight for that term. In many processes, especially industrial, PID controllers are used to keep some kind of a steady state. The controller takes a measurement from a plant process (diabetic mathematical model) and com- pares it with a set-point (reference) value of BG concentration. The difference (or “error” signal) is then used to adjust the input to the plant in order to bring the measured value back to its desired set-point. PID controller can adjust process outputs based on the history and rate of change of the error signal. The schematic diagram of the PID controller used with the composite model is shown in Figure 3.

The general equation of the PID error controller is given as:

$$U(t) = Kp * e(t) + Ki \int_0^t e(\tau)d\tau + Kd \frac{d}{dt}e(t) \qquad (1)$$

Where

KP = Proportional gain, Ki = Integral gain,

KD = Derivative gain, e: - Error = Set point Measured value, t= time, τ = variable of integration.

From the equation the transfer function of the PI controller is

$$\mathrm{Gc(s)} = \mathrm{Kp}\left(1 + \frac{1}{\mathrm{s\ Ti}} + \mathrm{s\ Td}\right)(2)$$

Where

Ti= integral time and Td= derivative time.

The KP and the timing constraints of integral systems is finding using Routh array method. Based on the simulation the transfer function modeling of diabetes patient is designed and the artificial designed pancreas model produces the insulin result as like real patient. To estimate percentage of insufficient insulin to the patient body this output is connected with PI controller. For the case study the P and I value is obtained from reference paper [3]. From the PI controller output and necessary constant to get the result value of insulin required for diabetes patient

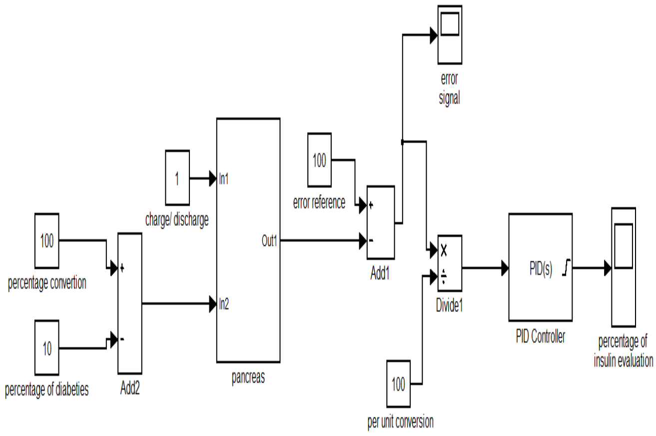

Figure 3: Simulation diagram for PID Controller

The Fuzzy Logic Controller (FLC)

In the control theory field, fuzzy logic has appeared as a powerful tool to integrate an expert knowledge about systems into the controllers design. In particular, the ability of synthesizing expert knowledge in the fuzzy logic context has raised a lot of consideration in different engineering fields. In this research, a control algorithm was developed to incorporate “formalize” expert knowledge about the treatment of diabetes using fuzzy logic controller [6]. This controller should be able to regulate the blood glucose (BG) level when the diabetic patient is subjected to a mixed meal disturbance or fluctuations in the measured glucose level due to error or noise in the measuring instrument. The intelligent controller (FUZZY LOGIC) was instigated to evaluate the insulin level for diabetes. The transfer function modeling of diabetes patient is same as chosen for PI controller modeling Fuzzy logic control is furthermore an advanced process control, which imitates the logic of human thought and much less rigid than calculations that computers generally perform. There are three steps for the process of a fuzzy logic algorithm: fuzzification, rules, and defuzzification. In this case, it is assumed that there are two different inputs of fuzzy logic controller: the glucose con- centration and the rate of change in glucose concentration, and one output of the dose of insulin.

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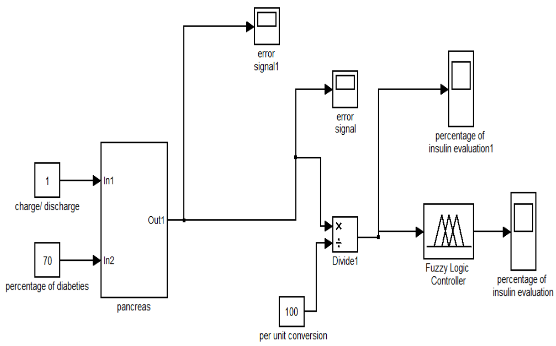

Figure 4: Simulation Diagram for Fuzzy Controller

The Model Predictive Controller (MPC)

In MPC controller the generalized control framework is proposed with the same function, an MPC, a state estimator, an optimizer or a second MPC [4] and a scheduling level. In an effort to develop delivery systems the custom-made infusion of an patient is having two general strategies based on the proposed framework are investigated: i) a systematic strategy which aims towards an individualized closed loop insulin delivery and ii) an "approximation" strategy which aims towards a generalized applicability of the closed loop system because this controller has in-built predefined disturbance rejection problem as a personalized nonlinear optimization [14].

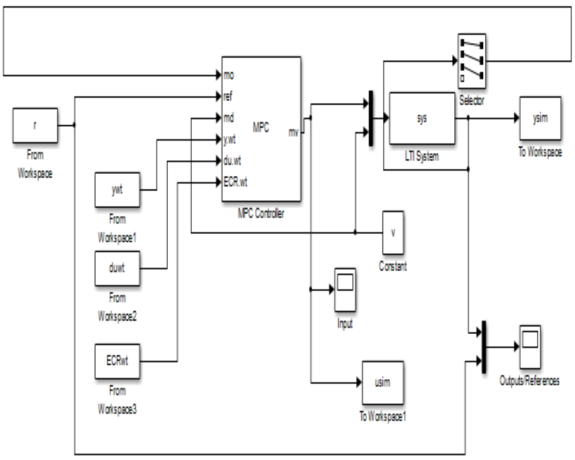

Figure 5: The Model Predictive Controller (MPC)

The proposed control design are validated in difference of values for the diabetic model and the detailed evaluation of MPC performance during the tests and this evaluation of predictive accuracy has shown that the predictive plasma glucose up to 60 min ahead with an error comparable to the measurement error. The results for predicting 60 min ahead are excellent with predicting 120 min ahead still clinically good. This good predictive accuracy is a necessary condition for good performance of the controller [10]. The model controller tests have shown to recognize special conditions and recover from this purpose, based on the study the safety schemes have been implemented with the aim of preventing serious hypoglycemia events resulting from insulin overdosing. Hypoglycemia is potentially a life-threatening condition and occurs more often during intensified insulin therapy. Thus every means needs to be employed to facilitate the prevention.

DISCUSSION

In the observation the results of all three different controllers were analyzed with their response. The following table 1 shows the results of the simulation for the three controllers with mixed meal for the said reference [5, 6, 7].

Table 1: Simulation of insulin Results

Parameter	PID	FLC	MPC
Maximum glucose (mg/dl)	186.5	194.5	180
Minimum glucose (mg/dl)	88.97	89.58	89.61
Duration of Hyperglycemia (min)	0	0	0
Duration of Hypoglycemia (min)	0	0	0
Total infused insulin (U)	20.49	18.92	16.9
Infused insulin above basal (U)	10.26	8.537	6.9

The PID controller in daily life test has a proper response where soon after the overshoot that happened due to the ingestion of mixed meal, the BG level returned back to the basal level. However, the overshoot in the FLC is little more than that what happened in the PID controller, where the effect of long time of high over- shoot has a long term effect on the life of the patient. In the stage of steady state, both controllers have the basal level of BG concentration, and basal level of insulin infusion. However there is no case of hyperglycemia (BG more than 270 mg/dl) or hypoglycemia (BG less than 60 mg/dl) as presented in Figure.7.

In the test, the blood glucose level drastically decreased below the target line in PID controller as shown in the Figure 6 which results wrong insulin dosage and life causing danger to the patient. In contrast, the overshoot of blood glucose concentration in the FLC is a little more than that of PID controller which is shown in Figure 7.

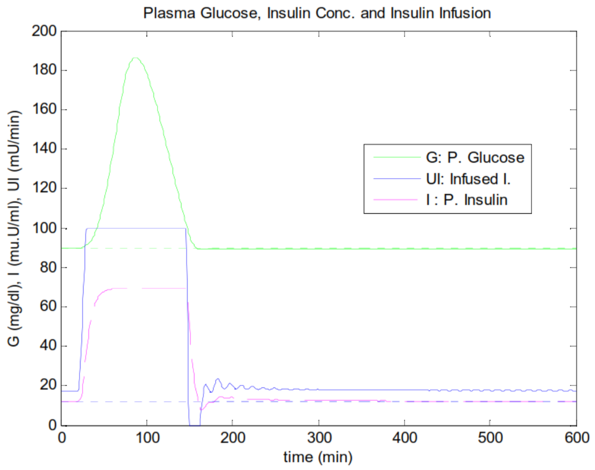

Figure 6: PID Controller Results

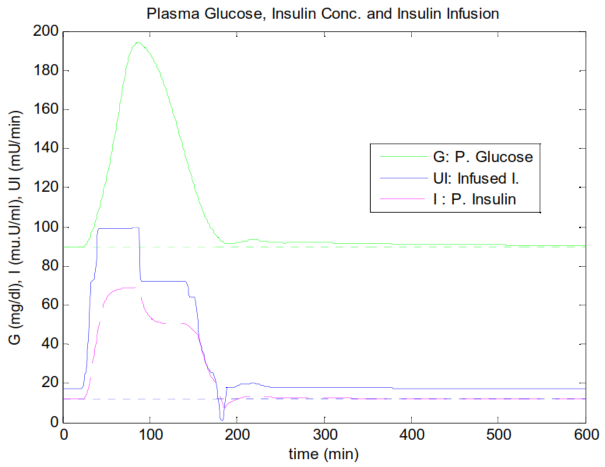

Figure 7: FLC Controller Results

Figure 8 shows the steady state response is stable with the basal level of the blood glucose and the controller response of MPC is stable compared with FLC controller. Thus, the insulin dosage by the MPC is less than that of PID and FLC controller as presented in Table 1. However, resulting tables and figures have shown that the MPC controller is more reliable, safer and has less insulin consumption than the PID and FLC controller. Consequently the FLC and MPC are well suited to control glucose concentration during all conditions in subjects with type 1 diabetes mellitus and will give predictive accuracy of glucose sampling and subcutaneous insulin infusion and it would be preferable and advisable when it comes to critical diabetes cases.

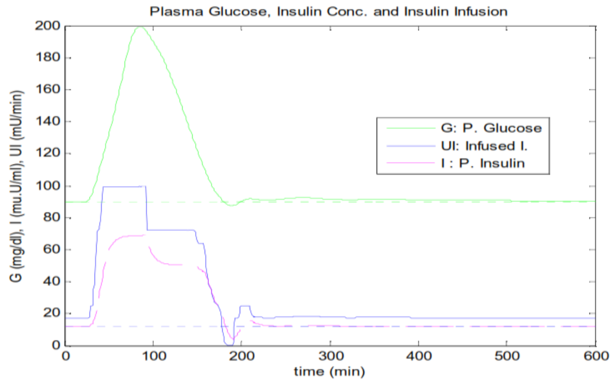

Figure 8: MPC Controller Results

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