Model Based Simulation for Type I Diabetic Patients

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Abstract- **Maintaining the glucose level in normoglycaemic range is challenging in Type I diabetic patients. An attempt has been made in this paper to derive a control strategy for blood glucose regulation. Due to cost and complexity involved in testing the control algorithms to real patients, studies are done using a Type I diabetic patient model. Controller performance is assessed in terms of its ability to reject the effect of meal disturbance and to overcome the variability in the glucose-insulin dynamics from patient to patient. Computer simulations are used to evaluate the effectiveness of the proposed technique and to show its superiority in controlling hyperglycemia over other existing algorithms. A comparative study has been shown with the existing PID controllers and IMC controller.**

Keywords- Glucose Modeling; Insulin Dynamics; Insulin Modeling

I. INTRODUCTION

Anormal individual's blood glucose level is well-controlled by his/her pancreas. Diabetes is a disease in which the body does not produce or properly use insulin, a hormone that is needed to convert sugar, starches and other food into energy needed for daily life [1]. Diabetes is a chronic and potentially disabling disease that represents a major public health and clinical concern [2]. Diabetics are at increased risk of developing chronic complications such as heart attacks, strokes, amputations, kidney failure and blindness [2]. The majority of the diabetic population can be classified as either type I or type II. Type I, or Insulin-Dependent Diabetes Mellitus (IDDM), accounts for 5-10% of the diabetic population [1] and is characterized by insulin deficiency caused by autoimmune destruction of the ß cells in the pancreatic islets [3]. Type II, or Non-Insulin-Dependent diabetic population [1] and is characterized by insulin resistance and impaired insulin secretion [3]. Often type 2 diabetes can be controlled through losing weight, improved nutrition and exercise alone [1], but over time, many of these people will develop a dependency for insulin supplements to control their diabetes[33],[34].

Control strategies of diabetes treatment can be categorized as open loop control, semi closed-loop, and closed-loop control. Current treatment methods utilizing 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 sub-optimal and unable to accomplish the aforementioned normalization and also suffered from long sampling time problem of missing fast or accurate insulin level. This work deals with the design of controller for the delivery of insulin to the type I diabetic patient [32]. In this contribution, the control problem is reformulated by considering the rate of the blood glucose level.

Ultimate objective was to develop a closed loop control device consisting of three components: a glucose sensor, an insulin pump and a control algorithm. In this system, the glucose concentration will be measured by the glucose sensor and based on the measurement; the control algorithm will compute the optimal insulin delivery rate [30],[31]The mechanical pump will then infuse the computed amount of insulin.

II. MATHEMATICAL REPRESENTATION OF GLUCOSE-INSULIN SYSTEM

Since the 1960s, many mathematical models have been derived to represent the human glucose insulin interaction [14].These models have ranged from linear to non-linear, with increasing levels of complexity. Among the many mathematical models available, Ackerman's model [11], is one of the most frequently used linear models for simulation of glucose-insulin dynamics. Bergman's Minimal model [14] is the most popularly used non-linear model. While various modifications to Ackerman's original model and Bergman's non-linear model have been made in attempt to better approximate the metabolic interaction, other investigators have formulated their own mathematical model Cobelli [16] produced a comprehensive mathematical model of the glucose regulation system.

III. METHOD

Due to cost and complexity in implementing the control algorithm on real patients in this contribution algorithm is implemented on diabetic patient model. In order to achieve a realistic comparison of the performance of stochastic and deterministic optimal control profiles in the presence of parametric uncertainty, an analysis is performed using a more detailed compartmental model representing glucose–insulin system consisting of 19 differential equations and algebraic equations to represent the metabolic source and sink rates. This model was initially developed by Guyton et al. (1978) and updated by Sorensen (1985) and Parker et al. (2000).

This model, which we use as a proxy for real experiments, uses a six compartment representation for the internal organs that are the brain, heart/lungs, liver, gut, kidney and periphery. The combined effects of muscle and adipose tissue are represented by the periphery and the stomach and intestine effects are lumped into the gut compartment. The compartmental diagram for the glucose–insulin system is shown in Fig. 8 for this model.

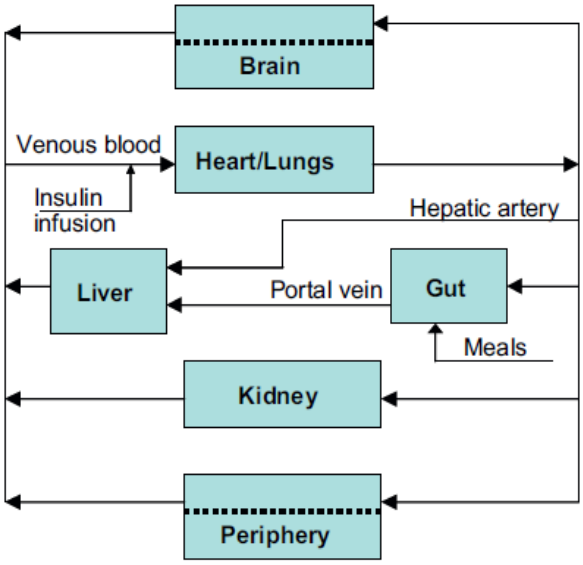


Figure1.Compartmental model of the Glucose-insulin system.

These threshold functions are of the form

$$\Gamma_e = E_{\Gamma_e}\left\{A_{\Gamma_e} - B_{\Gamma_e}\tanh[C_{\Gamma e}(x_i + D_{\Gamma_e})]\right\} \quad (1)$$

Inter or intra-patient variability is classified physiologically as either a receptor parameter (D_{Γ_e}) or post-receptor (E_{Γ_e}) parameter.

The threshold functions are used to describe the effects of insulin on peripheral glucose uptake (Γ_{EIPGU})and effect of glucose on peripheral glucose uptake(Γ_{EGPGU})

$$\Gamma_{EIPGU} = 1.0\left\{7.035 + 6.51623\tanh\left[0.33827\left(\frac{I_P^T}{5.304} - 5.82113\right)\right]\right\} \quad (2)$$

$$\Gamma_{EGHGU} = 1.0\left\{5.6648 + 5.6589\tanh\left[2.4375\left(\frac{G_L^C}{101} - 1.48\right)\right]\right\} \quad (3)$$

In these relations I_{P_T} is the state variable describing the insulin concentration in the peripheral tissue space and G_{L_C} is the state variable describing the glucose concentration in the liver capillaries.

Another important function that describe the liver clearance.

$$\Gamma_{LC} = F_{LC}(I_{HC}Q_A + I_{SC}Q_A + \Gamma_{PIR}) \quad (4)$$

Where F_{LC} is the fraction of hepatic insulin clearance, I_{HC} is the insulin concentration in the heart capillaries and I_{sc} is the insulin concentration in the gut capillaries Γ_{PIR} is the rate of pancreatic insulin release Q_S and Q_A are vascular plasma flow rate for the gut and hepatic artery respectively.

The three parameters which have the most significant effect on the glucose-insulin dynamics were EIPGU D_Γ (nominal =-5.82113), EGHGU D_Γ (nominal=-1.48) and F_{LC} (nominal =0.40).(Parker et al., 2000).

The performance of H_∞ controller is determined by using the reference model which was determined by using the Glucose Tolerance Curves of twenty two healthy subjects.

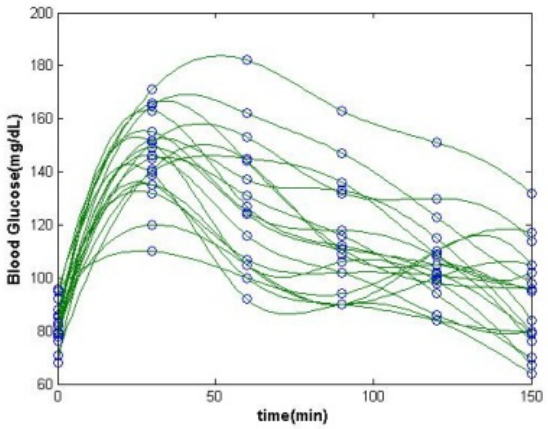


Figure 2. Overall Glucose Tolerance Curves of twenty two healthy subjects

IV. RESULTS AND DISCUSSIONS

A. *Sensitivity function*

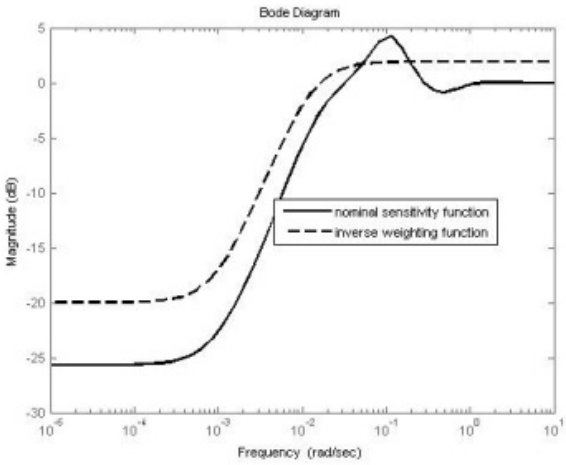


Figure 3. Sensitivity function vs inverse weighting function

Figure 3 shows the variation of sensitivity function and the weighting function used for design of robust controller for blood glucose regulation.

Table I.Variation of different uncertainty parameters within a specified range

Uncertainty Parameters	Variations				
	-20%	-40%	Normal	+20%	+40%
EIPGU(D_Γ)	-3.492	-4.656	-5.82113	-6.984	-8.148
EGHGU(D_Γ)	-0.888	-1.184	-1.48	1.736	2.072
FHIC(F_{sc})	0.36	0.32	0.4	0.44	0.48

B. *Robust performance*

In addition to the robust stability, the closed-loop system, for all $P_p = F_U(P, \Delta)$ must satisfy the performance criterion

$$\left\| \begin{bmatrix} W_P(I+P_pK)^{-1} \\ W_uK(I+P_pK)^{-1} \end{bmatrix} \right\|_\infty < 1 \quad (5)$$

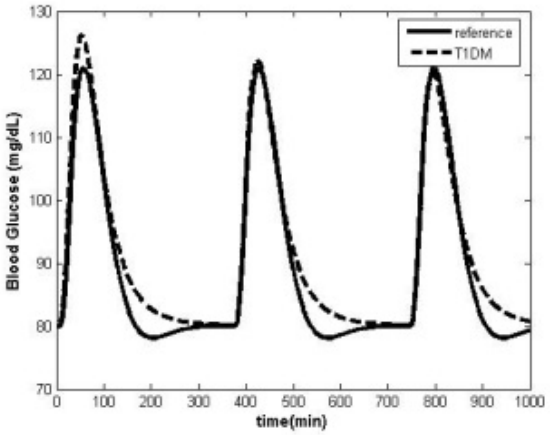


Figure4. BG response with uncertainty parameter EIPGU-(D_Γ) = -3.492

By incorporating above mentioned uncertainties the Blood Glucose response shown in Figure 4 is obtained , which shows the Type I diabetic patient model curve tracks well with the reference Glucose curve of healthy subjects.

V. COMPARISON WITH EXISTING CONTROLLERS

Table 2. Performances of PID controllers tuned by four methods on the nominal patient model

Tuning	K_p	K_I	K_D	Overshoot(mg/dL)	Undershoot(mg/dL)
IAE minimization	-1.23	-0.055	-6.034	20.32	10.1
Cohen-Coon	-1.35	-0.046	-6.076	20	6.54
DMC Based	-0.84	-0.007	-6.724	4	0.001
Shen	-3.87	-0.08	-36.5	4	0.01

The performances of the PIDs in rejecting, according to the four tuning methods, a 50 g meal taken by a nominal patient are depicted in Figures 5-8 .

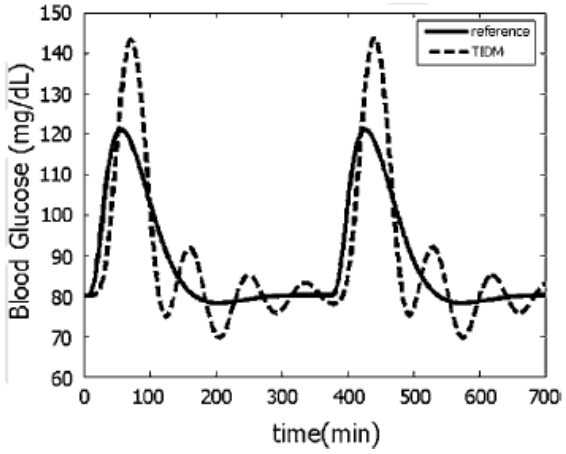


Figure 5. Performance of IAE based tuned PID controller

From the performance of IAE minimization it is observed that there is a overshoot of around 20.32 mg/dL and undershoot of 10.1mg/dL. This leads to corresponding hyperglycaemia and hypoglycaemic effects.

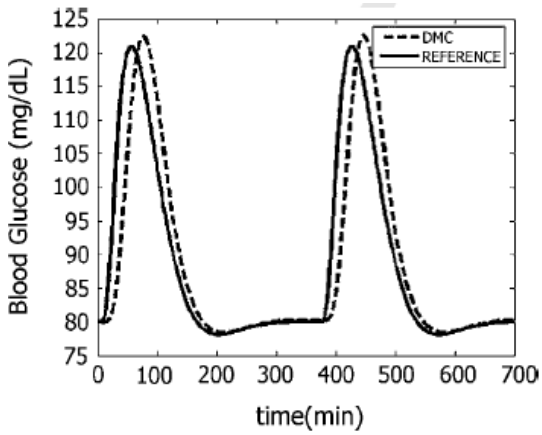


Figure 6. Performance of DMC based tuned PID controller

An over-shoot of 4mg/dL can be observed from the performances of DMC-based tuned PID controller shown in Fig.6

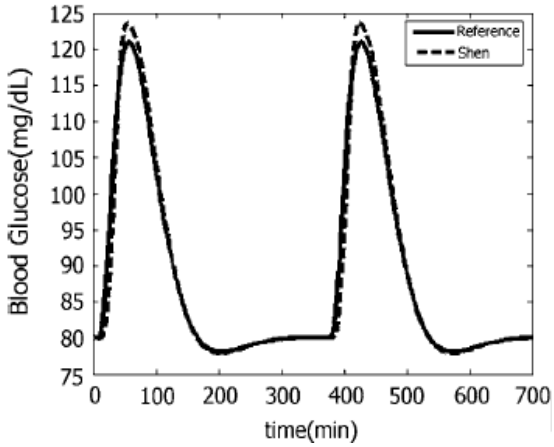


Figure 7. Performance of Shen based tuned PID controller

Shen tuned PID controller shows an overshoot of 2mg/dL and an undershoot of 0.01mg/dL (Fig.7).But from the performance of Cohen-Coon tuning one can observe that an approximately 20 mg/dL of overshoot and 5mg/ dL of undershoot (Fig.8).

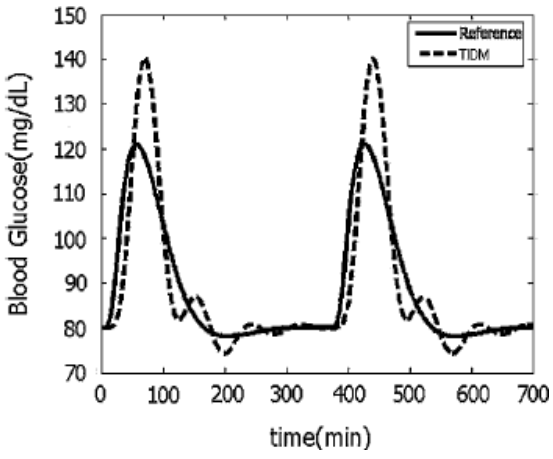


Figure 8. Performance of Cohen Coon based tuned PID controller

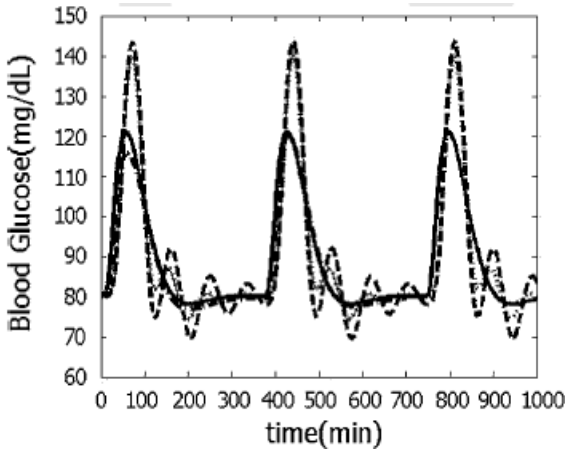


Figure 9..Performances of PID controllers tuned by four methods on the nominal patient model

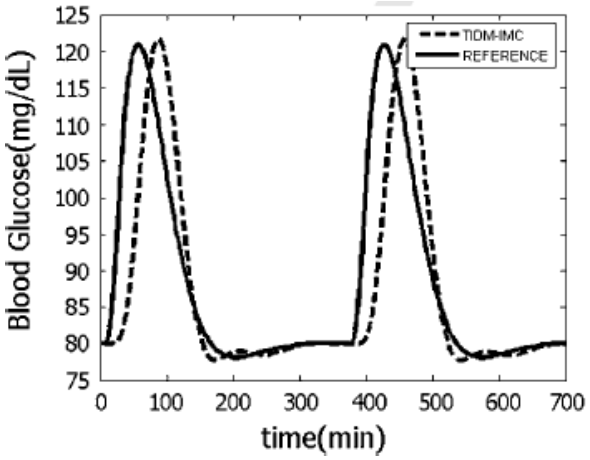
From the overall response it is evident that the performance of the PID controller with the Shen and DMC method of tuning is better than the performances of the controllers designed by the other two methods in terms of the lowest and highest glucose concentrations observed in the rejection of the meal disturbance.

PERFORMANCE OF IMC CONTROLLER

Based on the FOPDT approximation of the nominal diabetic model, IMC controller was developed for the regulation of glucose level in diabetics. The various parameters such as, K_C, τ_I and τ_D can be evaluated by using following formulae:

$$K_c = \frac{2\tau + \tau_d}{2(\lambda + \tau_d)} \quad \tau_I = \tau + (\tau/2) \text{ and } \tau_D = \frac{\tau\tau_d}{2\tau + \tau_d}$$

From the above mentioned FOPDT model the different parameters are $\theta = 20.32, K = -7.31,$ *and* $\tau = 73.14$.



Figue 10. Performance of IMC controller

Figure 10 shows the response of IMC controller for nominal patient to 50 g meal disturbance. Compared to PID and H∞ controller we can observe that output of controller will not be well tracked by the input.

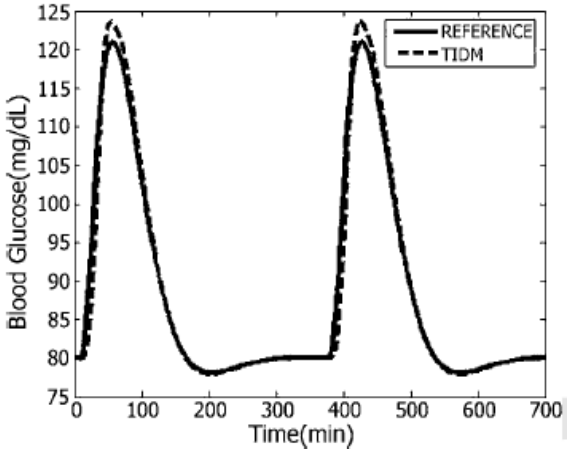


Figure 11. BG response for the TIDM patient using H∞ controller

Figure 11 shows the simulation of the BG response of a TIDM patient under a meal, at t = 0 min and at t = 370 min. The controller used for this simulation is resulted by H∞ approach. The maximum difference between the BG reference and the glucose level of the diabetic patient is 3.5 mg/dL. Here, as it was mentioned above, the insulin delivered to patient $i(t)$ (mU/min) is given by

$$i(t) = u(t) + 22 \tag{6}$$

Where $u(t)$ is the insulin portion calculated by the controller.Hence, from the above discussion it is clear that the response of H∞ approach shows more satisfactory tracking response than the other mentioned controllers.

VI. CONCLUSION

The performance and robustness characteristics of different PID controllers obtained using four tuning methods were investigated for maintaining blood glucose concentration in diabetic patients. The performances of H∞ controller was compared with the performances of other two controllers such as PID and IMC controller. Controller parameters were determined using a FOPDT approximation of a detailed first principles physiological model representing a nominal diabetic patient. Among four different PID controllers the Shen and DMC tuning methods outperformed the other two tuning methods i.e Cohen-Coon and IAE minimization method. The PID controller tuned by the Shen method is able to maintain the glucose concentration above the dangerous hypoglycemic range (<60 mg/dL).

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