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Blood Glucose Regulation in Diabetics Using H∞ Control Techniques

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ABSTRACT

This paper presents a control algorithm for insulin delivery in Type I diabetic patients. The control algorithm utilize a robust H∞ controller to regulate the blood glucose level in diabetic patients. Diabetes mellitus is a family of chronic metabolic ailment in which body's. In this study, Bergman's minimal model has been used as a base model, to reformulate dynamics of insulin and glucose concentrations in blood's plasma. To increase the functionalities of the glucose minimal model, some additions could be done. One of the additions is the exercise model. The performance of the resulting controller was tested on the nonlinear model of the process. The controller performance was evaluated in terms of its ability to mark a normoglycemic set point of 70mg/dl in presence of thrice daily meal disturbance and once daily exercise disturbance. A comparative study is given between our designed controller and the PID controller. The designed controller proved effective in achieving normoglycaemic and robust to meal and exercise disturbances.

Key words: Type I diabetes, Robust H∞ controller, Insulin Delivery rate, exercise model, Blood Glucose

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INTRODUCTION

Diabetes is a chronic metabolic disease that takes place when the body cannot produce enough or effectively use insulin [1]. At this production level the insulin cannot decrease the blood glucose level fast enough, when the person eats. The blood glucose rises even more because another missing functions of insulin, namely the function to stop the production of glucagon, when the blood glucose level is high. All this results in a very high blood glucose level, if not treated. The current medical treatments suggest three to four daily glucose measurements and an equivalent number of subcutaneous insulin injections [1]. An alternative approach is to deliver insulin continuously using a closed loop device like an insulin pump [2-4]. This closed loop device would include a glucose sensor that can measure blood glucose concentration. This information then would be passed to a control system that would calculate the necessary insulin delivery rate to keep the patient under metabolic control. Then a signal will be sent to a mechanical pump by the controller to deliver the desired amount of insulin. Fig (1) shows the block diagram of closed loop control of diabetic patients using insulin pumps.

In the closed-loop control system, one needs the use of a glucose sensor that can measure blood glucose level. This information then would be passed to a control 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.

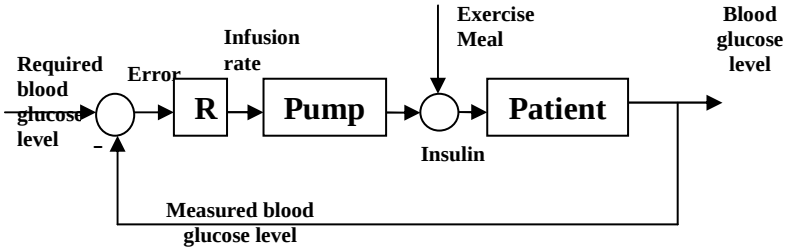

Fig.1 Closed-loop of diabetic patients

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 [5-21]. These models have ranged from linear to nonlinear with increasing the levels of complexity [8]. Employed controller in closed-loop system should be robust to physical disturbances like food intake. With availability of these mathematical models different algorithms based on control theory have been developed to optimize the insulin therapy of people with diabetes. Some of these algorithms include proportional-integral-derivative (PID) [9] and proportional-derivative (PD) [10], pole placement [11], and optimal control algorithms [12-13]. But full robustness cannot be achieved via these algorithms. Modeling the patients and the size and structure of the models, as well as nonlinear model against linear models has been addressed in various works. Robust control using the H∞ control methodology was the theme of the paper by Kientiz and Yoneyame [14]. In control theory field, the H∞ framework is well suited for blood glucose regulation, due to the ability to tune the controller to robustness to uncertainty while mathematically guarantying a certain degree of performance [15]. In this work, we use the Bergman's minimal model [7], which is one of the most distinguished travails in modeling of glucose insulin regulation in human body's to increase the functionalities of the glucose minimal model, some additions could be done. One of the additions is the exercise model [3].

This paper exploits the H∞ control method to regulate the blood glucose level of type I diabetes mellitus patient around euglycemia with a closed-loop system that is insensitive to internal and external disturbances, accuracy and robustness to uncertainty are the main features of the proposed algorithm. The paper is organized as follows. In section II the physiological model of glucose-insulin regulatory system in type I diabetes mellitus patient is introduced. Section III includes the synthesis of the H∞ control. Simulation results and concluding remarks are included respectively in sections IV and V.

INSULIN-GLUCOSE REGULATION MODEL

Bergman minimal model, which is a commonly referenced model in the literature, approximates the dynamic response of a diabetic patient's blood glucose concentration to the insulin injection. Bergman's minimal model is the most popularly used model in the literature which has the following advantages [7]:

- to be physiologically based,
- having parameters that can be estimated with a reasonable precision,
- parameters with values that are reasonable and have physiological interpretation,
- best able to simulate the dynamics of the system with the smallest number of identifiable parameters.

The Bergman minimal model, consists of three differential equations is as follows

$$\begin{aligned} \dot{G}(t) &= -p_1\left[G(t)-G_b\right]-X(t)G(t)+D(t) \\ \dot{X}(t) &= -p_2X(t)+p_3\left[I(t)-I_b\right] \\ \dot{I}(t) &= -n\left[I(t)-I_b\right]+\gamma\left[G(t)-h\right]^{+}t+u(t) \end{aligned} \tag{1}$$

Where $G(t)$ is the blood plasma glucose concentration (mg/dl), $X(t)$ the insulin's effect on the net glucose disappearance and referred to as the remote insulin concentration (1/min) and $I(t)$ is the insulin concentration in plasma at time t (μU/ml). G_b and I_b are respectively the basal pre-injection level of glucose and insulin, n is the first order decay rate for insulin in plasma (1/min), h is the threshold value of glucose above which the pancreatic β - cells release insulin (mg/dl) and γ is the rate of the pancreatic β- cells' release of insulin after the glucose injection with glucose concentration above the threshold [(μU/ml min $^{-2}$ (mg/dl) $^{-1}$], the term, $\gamma[G(t)-h]^{+}$ acts as an internal regulatory function that formulates the insulin secretion in the body, which does not exist in diabetic patients. It has been also argued in [17-18].The parameters of the model and their values are introduced in [17,18]. It is worth noting that all the values are calculated for a person of average weight and these are not constant numbers and vary from patient to patient.

To show the complete dynamics of the glucose-insulin regulatory system, two other terms are considered in equation (1). An critical set of assumptions in this computational study concerns the design of the glucose rate disturbance signal $D(t)$ that is used in the simulations. Since in diabetic patients, the normal insulin regulatory system does not exist, this glucose absorption is considered as a disturbance for the system dynamics presented in (1). Specifically, the following additive terms are incorporated into the disturbance signal $D(t)$. This disturbance can be modeled by a decaying exponential function of the following form:

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

- Terms of the exponential form $\gamma\cdot\exp(-0.05\cdot t)$, which represent the standard Fisher meals [18].
- Terms of the exponential form $\varepsilon\cdot\exp(-0.025\cdot t)$, which represent larger random effects due to factors such as exercise or strong emotions [3].

Where *t* is in min and *D(t)* is in (mg/dl/min). *u(t)* is the exogenous insulin infusion rate. The controller uses feedback loop that employs the blood glucose level *G(t)* and its derivative (*dG(t)/dt*), as sensor inputs, and the exogenous insulin infusion rate *u(t)* as the control output. The controller defines the insulin infusion rate, *u(t)* is to compensate the uncertainties and disturbances and stabilize blood glucose level of diabetic patient at basal level.

CLASSICAL H∞ CONTROLLER SYNTHESIS

For problem formulation of the present system in closed loop, let's consider the generalized block diagram shown in Fig. 2. P(s) and K(s) are the transfer matrices of the plant and the controller respectively, whose elements are assumed to be real, rational and proper transfer functions. The transfer matrix P(s) is assumed to be linear and time-invariant, and it is expressed as:

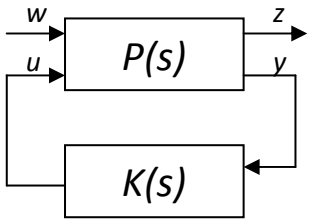

Fig 2 H∞ synthesis problem

$$P(s)=\begin{bmatrix} A & B_1 & B_2 \\ C_1 & D_{11} & D_{12} \\ C_2 & D_{21} & D_{22} \end{bmatrix}=\begin{bmatrix} P_{11} & P_{12} \\ P_{21} & P_{22} \end{bmatrix} \tag{3}$$

Which are compatible with the dimensions of exogenous input vector, $w \in \Re^d$ the control input $u \in \Re^q$ the regulated output vector $z \in \Re^p$, the controlled output $y \in \Re^p$ and the state $x \in \Re^n$.

Thus the plant transfer matrix *P(s)* is related with the input and output vectors as:

$$\begin{bmatrix} z(s) \\ y(s) \end{bmatrix}=\begin{bmatrix} P_{11}(s) & P_{12}(s) \\ P_{21}(s) & P_{22}(s) \end{bmatrix}\begin{bmatrix} w(s) \\ u(s) \end{bmatrix} \tag{4}$$

A popular performance measure of a stable linear time invariant system is the H∞-norm of its transfer function. The controller synthesis for the suboptimal H∞ case is formulated as follows: given $\gamma > 0$, find an internally stabilizable controller *K(s)*, if there exists any, such that $\|G_{zw}\|_\infty \prec \gamma$ where G_{zw} is the closed-loop transfer matrix from *w* to *z* called Linear Fractional Transformation and it is given by:

$$G_{zw} = F_l(P,K) = P_{11} + P_{12}K(I - P_{22}K)^{-1}P_{21} \tag{5}$$

This problem can be solved by the methods of Ricatti equations. In order to find the controller, if there exists, *P(s)* should satisfy the following assumptions [19- 20]:

A1. (A, B_2) is stabilisable and (C_2, A) detectable;

A2. $D_{12} = [0\ I]^T$ and $D_{21} = [0\ I]$;

A3. $\begin{bmatrix} A - j\omega I_n & B_2 \\ C_1 & D_{12} \end{bmatrix}$ has full column rank for all ω;

A4. $\begin{bmatrix} A - j\omega I_n & B_1 \\ C_2 & D_{21} \end{bmatrix}$ has full row rank for all ω.

Assumption 1 is necessary for the existence of a stabilizing controller by output feedback. The assumption 2 guarantees a synthesized H∞ controller is proper. For the system in the present study this assumptions were satisfied. The system of two Riccati equations is solved through the γ-iteration technique.

Bergman mathematical model is a nonlinear model, which become linear around steady state values to design closed-loop controller of the model. An approximate transfer function for the nominal operating point of *G=Gb*, *X*=0 and *I=Ib* is given by:

$$G(s)=\frac{-0.001548}{s^3+0.30631s^2+0.01151s+9.92*10^{-5}}$$

Generalized plant *P(s)* is obtained according to block diagram in Fig 3 in which *G(s)* is the transfer function from blood glucose output to insulin input. To meet the desired performance goal it is important to design the weighting functions in a proper way, the weighting functions involved in the block diagram of Fig. 3 corresponds to the control input weight (*Wu*), meal disturbance weight (*Wm*), exercise disturbance weight (*Wex*) and performance weight (*Wp*). The control input weight is taken as *Wu*=1, which is reasonable for the present system [19]. We have not considered any weight (i.e. *W*=1) for the sensor noises as they are considered entirely white and Gaussian in nature and the intensity depends on the statistics of error in the device outputs. The *Wm* and *Wex* are described by the following first-order filters with the time constants depending on the dynamics how the deterministic disturbance inputs are absorbed in the process, where higher frequency variations have a lesser effect on the disturbance model input. The performance weight is chosen such that the controller will not track high frequency disturbance. The main object for the performance weight was in this case to design the rejection of the disturbance in the low frequency.

$$W_m(s)=\frac{1}{5s+1},\ W_{ex}(s)=\frac{1}{2s+1} \text{ and } \ W_p \text{ is selected to satisfy}$$

$$(1/|W_p|) \succ |SW_m| = |(1+GK)^{-1}W_m| \quad \forall\omega \text{ and } (1/|W_p|) \succ |SW_{ex}| = |(1+GK)^{-1}W_{ex}| \quad \forall\omega.$$

The weighted sensitivity SW_m and SW_{ex} are good measures of closed loop performances [19]. A first order $\boldsymbol{W_p}$ has been chosen:

$$W_p(s)=\frac{\frac{s}{M}+\omega_0}{s+\omega_0 A}=\frac{\frac{s}{2}+0.5}{s+0.05}$$

Here disturbance rejection at steady state is governed by *A* and *M* is taken as the least upper bound on the disturbance sensitivity and ω_0 is the desired bandwidth. The frequency ω_0 is used as a tuning parameter to trade-off aggressiveness and robustness of the controller.

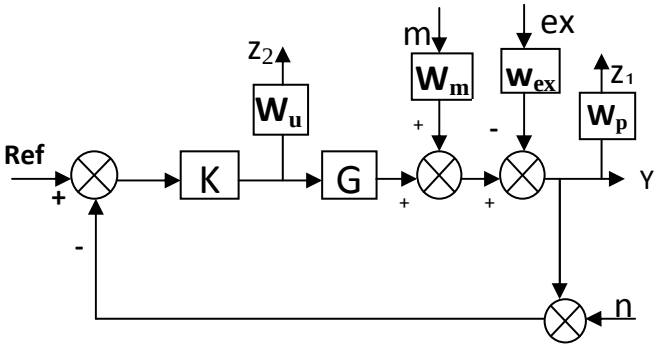

Fig.3. Standard feedback configuration with weights

SIMULATION RESULTS

In Fig.4 the blood glucose level of the patient is stabilized at the basal level, the response of PID control based on H-infinity control is very fast. It can be stable during about three hours. The patient model is subject to control the result of three meals, using Fisher's meal disturbance function and value of 60 (equivalent carbohydrate taken orally (CHO) for 15 min each (duration of meal ingestion) in a periodic manner i.e. at breakfast (8 am), lunch (2 pm) and dinner (8 pm) and an exercise disturbance of 0.05 arbitrary units at 5 pm for 20 min duration. The sensor noise is considered white and Gaussian and assuming ±10% deviation in the glucose sensor outputs as per sensor data available [19, 22], the particular noise intensity is taken as 0.01.The reference plasma BG level is considered as 4.5 mmol/l or 70mg/dl. Though the insulin dispensing device has a capacity of pumping rate 0 mU/min< u(k)< 133 mU/min as per device data [19], the controller design about the nominal point of 7 mU/ml with an upper bound of 44.6 mU/min is chosen to avoid over-delivery causing hypoglycaemia with a BG level <60mg/dl.

Fig. 6 and Fig .7 shows the 24-hour glucose-insulin profile in a patient with the output feedback H∞ control. From the G-I profile. In the presence of multiple meal disturbance at time *t*= 2100, *t*=4100 and *t*= 6100, patient's blood glucose concentration increases from goal level of 70 mg/dl and then is entirely stabilized at basal level in a reasonable time interval. When the patient is submitting to specific exercise disturbance, the glucose level falls to 67 mg/dl, which is also within satisfactory limit. The study with the impact of exercise input in closed loop control system in patient is an advantage and is a unique feature of this study, though perfect quantization of the activity input requires further study. The insulin dose is also well controlled between 0-36 mU/min so that the condition of hypoglycemia never appears at the same time device delivery restriction is maintained. The frequency response of the closed-loop system is shown in Fig.8.

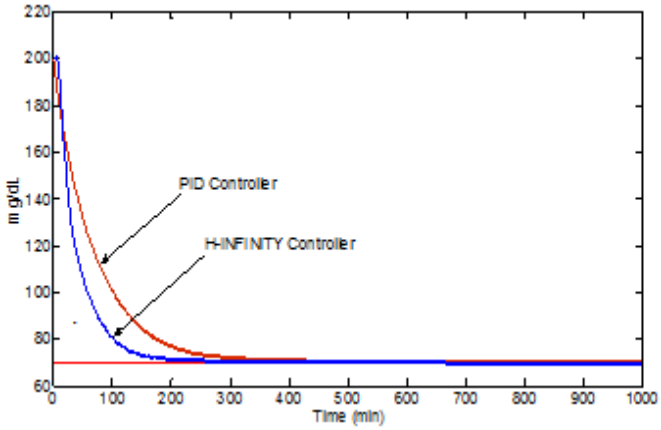

Fig.4 Glucose regulatory profiles of patient using the proposed controller

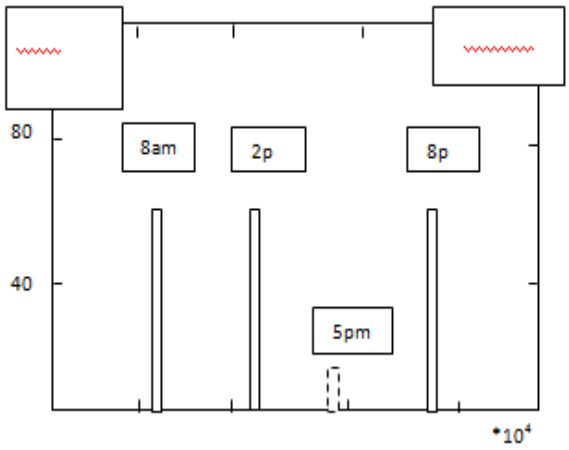

Fig.5 Meal and Exercise input

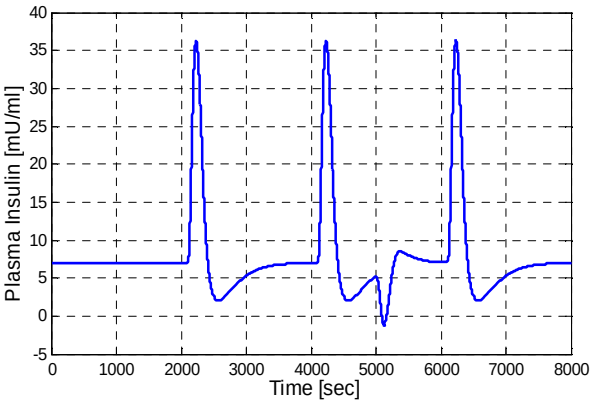

Fig.6 Insulin Infusion response of the closed loop system

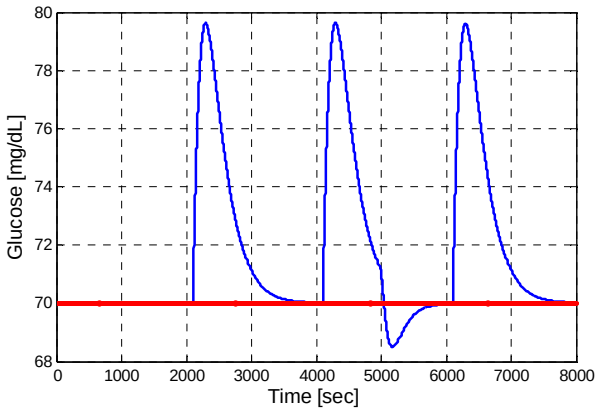

Fig.7 BG response of the closed loop system

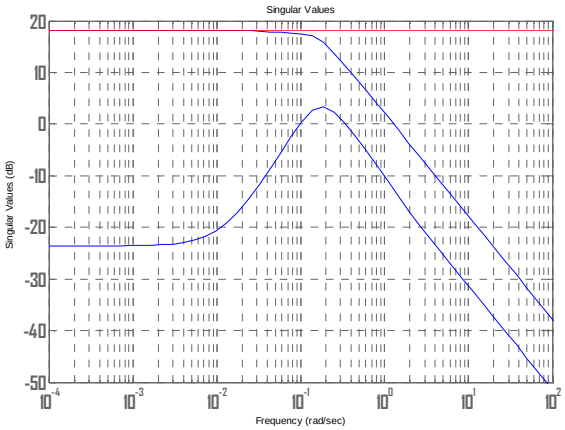

Fig.8. Frequency response of the closed-loop system

CONCLUSION

Diabetes management is one of important issues in the field of human regulatory systems, which is discussed in recent years. In this paper we propose a closed-loop H∞ controller able to guarantee the robust stability of the system as well as the robust performance of normoglycemic average for diabetic patients of type I. The performance objective was to regulate the glucose level in face to disturbances represented by known meals and exercise. The glucose-insulin response has shown very close regulation of BG level with minimum overshoots and undershoots and acceptable limits of insulin infusion rate as compared to the earlier studies with similar nonlinear model. The modeling of the peripheral activity and study of exercise input is a unique feature of this work, though the proper measurement and quantization of exercise input and its significance require further study. Future work is conducted to the employing of the μ analysis and synthesis approach in designing a controller for blood glucose regulation in diabetic patients.

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