Model based Control of Artificial Pancreas under Meal Disturbances

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Abstract—**In this paper, a model based feedback control system equivalent to the functioning of a natural pancreas in human body is designed to monitor and control its blood glucose level (BGL). For a diabetic patient, an insulin dose is required to maintain the glycemic control. The idea of an artificial pancreas consists of a glucagon pump and an insulin infusion, through which glucagon/insulin is entered into the patient's body, based on the most recent blood glucose level (BGL) as sensed by the continuous blood glucose monitoring. Initially, the system response is tested by applying a step input and then a PID controller is tuned for keeping glucose level within the safe ranges. Multiple classical and advanced controllers have been tested to figure out the best result. Optimal performance requirements are achieved with an MPC controller and glucose level tracking is performed under unknown but realistic exogenous meal disturbance. The simulation results show that the patient safety can be enhanced through implementing a real-time MPC strategy.**

Keywords— ***Artificial Pancreas; Diabetes; Insulin Infusion; Glucagon Infusion; Simulation***

I. INTRODUCTION

The artificial pancreas is the technology controlling the BGL of diabetic patients by providing the insulin and glucose to avoid hyperglycemia and hypoglycemia state. Insulin as a vital hormone is secreted by the beta cells in the pancreas, which reduces the concentration of glucose in the blood by suppressing the production of sugar in the liver and promote the use of glucose [1]. On the other hand, by using the alpha cells, it secretes glucagon in the pancreas and increases the concentration of glucose in the blood by converting glycogen stores in the liver into glucose and release into the bloodstream. The second pump secretes glucagon by the alpha cells in the pancreas and increases the concentration of glucose in the blood by converting glycogen stores in the liver into glucose and release into the bloodstream. In healthy people, level of glucose in the blood is controlled tightly by these two hormones [2, 3].

Insulin therapy using pump was first proposed in late 1970s, in which fast-acting insulin is delivered continuously by a portable pump. Insulin is supplied in the subcutaneously via implanted thin cannula attached to a reservoir through a tube. The pump injects insulin in two ways. First, the basal delivery is a 24 hours continuous infusion, at a variable rate pre-programmed in the reservoir control pump and can be modified if necessary (for example, in the case of implementation) [4]. Basal insulin requirements differ from patient to patient and also at different instant of time on the same day.

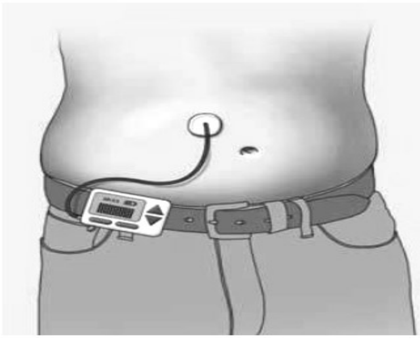

Figure 1: BGL monitoring system with implanted continous blood sensor

Fig. 1 shows the continuous feedback system to monitor the blood glucose level. There were different schemes in adjusting the monitoring tool with patients body for example, with the waist, or fastened with the arm. Several controllers have been proposed so far in the literature. For example in [5], a robust H-infinity based controller of blood sugar is proposed to withstand various disturbances. Though, the robust controller obtained by such methods is of higher order and it requires model order reduction to approximate it equal to the plant's order. Some researchers also proposed nonlinear and adaptive control algorithms as in [6], [7]. Such complex algorithms are not found suitable for real time precision control of biomedical systems. Some classical techniques e.g. PID control is also applied to this problem with some robust design techniques to ensure performance [8]. Some individual analysis includes design of PID and predictive controller as a separate effort [9-11]. However, a comparison of such approaches is found missing to evaluate the efficacy and performance of the blood sugar controller. We intend to propose a comparison of two popular algorithms i.e. proportional-integrator-derivative (PID) and model predictive control (MPC) so that a choice for real time control algorithm is evident from the simulation results.

This paper is organized as follows: Section 2 describes the dynamics of diabetes mellitus (DM); Section 3 defines the system model and basic parameters, Section 4 details about the control algorithm and simulation results. Section 5 compares the performance of PID and MPC controller under

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the meal disturbance effect, while Section 6 finally concludes the paper.

II. DIABETIES MELLITUS AND ITS CONTROL

Diabetes is a life-long chronic disease and leading a cause of death [12]. It deals with high blood sugar and a lack of insulin as shown in Fig. 2.

- Type 1: In this case, the patients are not able to produce insulin. Type 1 is only found in about 5% of people of with diabetes.
- Type 2: For such patients counting approximately 95% of DM, they are able to produce insulin; however, their bodies build up a resistance towards the insulin secretion. Therefore, it is not sufficient to control BGL within the good ranges.

It is important to note that for both Type 1 and Type 2 patients, medicines (or insulin) are required to control glucose level in the body. However, as there is no permanent healing from diabetes, the medication must be continued life time which is troublesome as injecting the insulin twice daily is painful to most of the diabetic patients. Scientists and researchers have recommended an autonomous pancreas for the convenience of diabetic patients. However, since the healthcare products need a much stringent requirements to pass various tests on patients before they are available in the market, the need to obtain a safe and deterministic control performance is a mandatory. This opens the research area to test and verify various algorithms for the control of artificial pancreas.

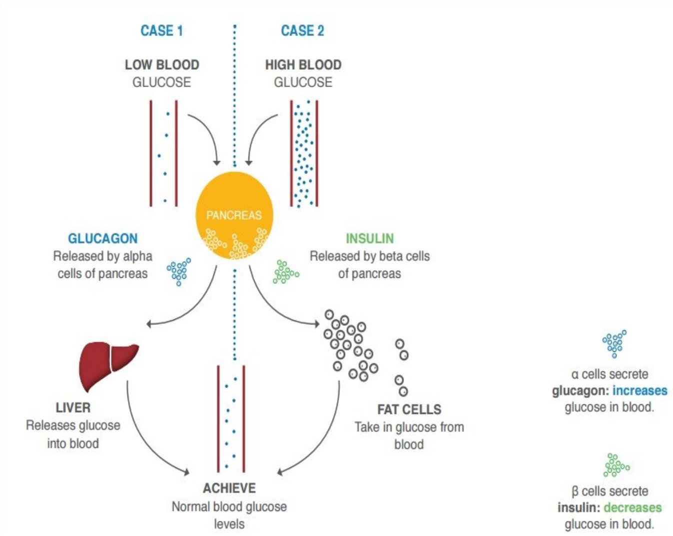

Figure 2: Working of natural pancreas to maintain normal blood glucose level

Although, the sensors and pump technologies are progressing well, the gross challenge is to combine the two in an automated manner. Delivery of closed-loop systems (often called "artificial pancreas") regulate glucose levels through a combination of the two devices through sports dosing algorithm. It is altered insulin delivery every 1-15 minutes by controlling glucose sensor based on the levels of glucose in a manner algorithm continuously in response aimed at levels glycemic glucose [13]. Closed-loop systems have the prospective to transform diabetic care to next level and improve the quality of life for diabetic patients as shown in Fig. 3 [14].

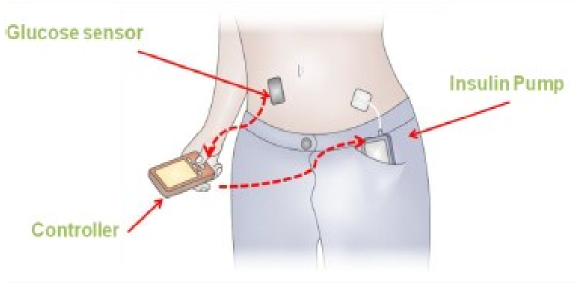

Figure 3: Closed-loop delivery system

The method commonly used to check BGL is that the patients prick themselves to check their blood sugar levels. The closest thing to the artificial pancreas is an insulin pump.

Table 1 Blood sugar reference ranges in fasting and random [6]

mg/dl	Fasting	After Eating	2-3 hours after Eating
Normal	80-100	170-200	120-140
Impaired Glucose	101-230	190-230	140-160
Diabetic	126+	220-300	200+

Where, the artificial pancreas takes the insulin pump to a new level by adding real-time monitoring systems [15] , [16]. Table 1 shows the reference values for blood sugar level in healthy persons. Fig. 4 provides a graphical representation of this variation for diabetic patients as compared to normal persons.

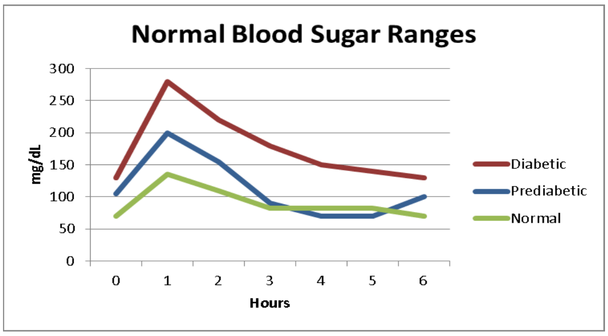

Figure 4: Normal Blood Glucose Ranges & Blood Glucose Chart

The closed loop system shown in Fig. 3 uses a computer attached to the insulin pump to continuously measure glucose in the blood and insulin in the body. The artificial pancreas is going to make the lives of diabetes much more manageable. It then uses algorithms to increase the insulin levels as the body needs it. The artificial pancreas has four major parts including glucose sensors and transmitter that measures the level of glucose concentration in the body. The information is then transmitted to a receiver that displays the glycemic levels for the patients. An embedded controller calculates in real time, the required dose of insulin which is needed to compensate the increase in glycemic level. Furthermore, the embedded controller actuates the insulin pump via Bluetooth to release the appropriate dose of insulin into the patient [17], [18].

Table 2: Modified Bergman Model Parameters

Parameters	Values
p_1	0.0337 min^{-1}
p_2	0.0209 min^{-1}
p_3	$7.5\times10^{-6}(\mu U/ml)^{-1}$
$\overline{X}$	$0.0054\mu\frac{U}{ml}$
$\overline{G}$	0.81 mg/ml
G_b	0.811 mg/ml
N	0.214 min^{-1}
T	5 min

III. System Model

There are many researchers who have proposed the insulin-glucose model of a human body. Bergman minimal model equations are used to define relationship b/w concentration of insulin, glucose and BGL [19].

$$\frac{dG(t)}{dt} = -p_1[G(t)-G_b] - X(t)G(t) + [D(t)+C(t)] .....(1)$$

$$\frac{dX(t)}{dt} = -p_2X(t) + p_3[I(t)+I_b] .....(2)$$

$$\frac{dI(t)}{dt} = -n[I(t)-I_b] + \Upsilon[G(t)+h]^{t} t + r(t) ......(3)$$

Where:

- G(t): Instantaneous glucose concentration
- X(t): Effective amount of insulin used
- I(t): Instantaneous insulin concentration
- G_b and I_b: Concentration of glucose
- P_1, P_2, and P_3: Model parameters
- n: Rate at which insulin is being injected
- h: Lowest value of blood sugar
- Y: Rate of endogenous release of insulin

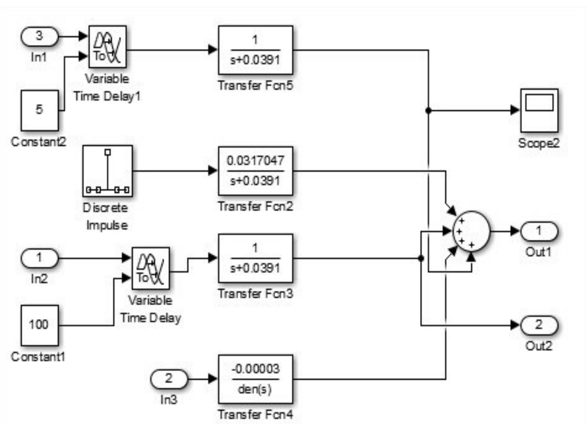

Figure 5: Simulink Block Diagram

The simulation model is developed by taking values shown in Table 2. Using these values and adjusting the delays, an effort is made to make the plant more realistic/equivalent to the real human body.

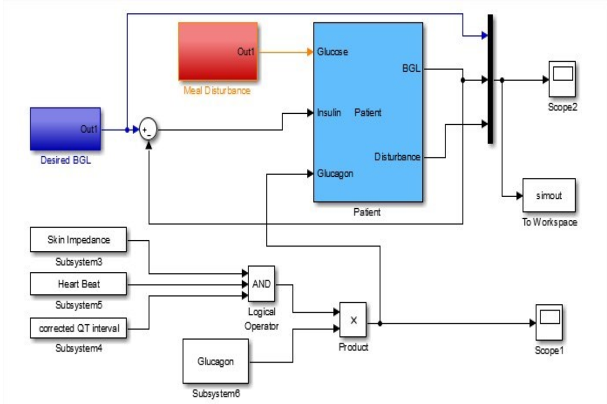

Figure 6: Block Diagram of Equivalent System with Disturbance

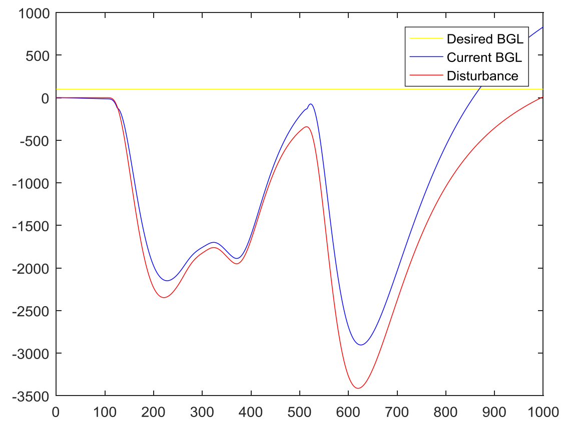

Figure 7: Step Response of the System with disturbance

IV. Controller Design

In literature, various control algorithms exist which were aimed to control the BGL level in closed loop. These algorithms have been tested in simulations and a few on animals and on diabetic patients [20]. To control the response of plant/patient's glucose level, closed loop control is needed. This controller will help to normalize the BGL in certain limits and continuously monitor the output. The closed loop diagram of an artificial pancreas with insulin and plant is shown in Fig. 10.

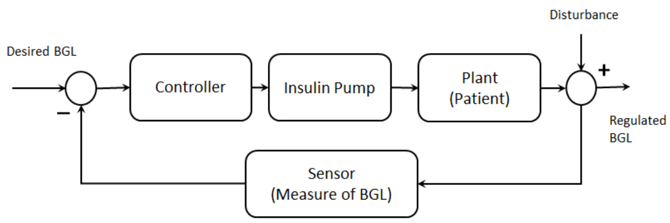

Figure 8: Closed loop Diagram

In the present work, we consider the generalized continuous time system in state space form as:

$$\dot{x}_m(t) = A_m x_m(t) + B_m u(t) \qquad \ldots\ldots. (4)$$
$$y = C_m x_m(t)$$

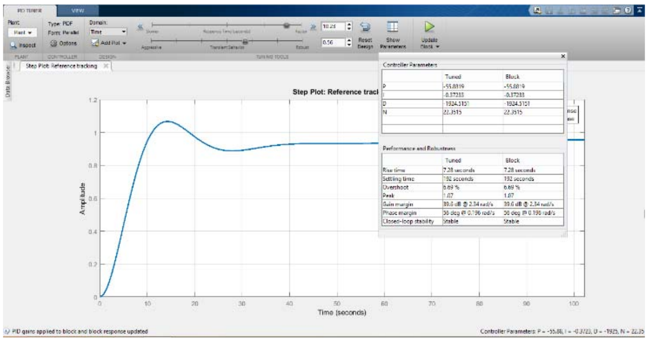

Figure 9: PID Auto-tune Parameters

a) PID Controller:

PID controller is an all-purpose feedback control mechanism which is widely used in multiple applications. The purpose of the PID control algorithm for artificial pancreas is to control the insulin delivery rate by calculating glucose level from three aspects namely the proportional component which is directly related to the error term, the integral component which sums up the error and the derivative component which handles the rate of change of the error. Matlab offers PID auto-tune GUI for designers as shown in Fig. 9. Some controllers include only a subset of the modules [21], [20]. The generalized formula for the continuous time controller is given as in Eq. 4.

$$PID = K_p\left(1 + \frac{1}{T_i} + T_d\right) \qquad \ldots\ldots. (5)$$

Table 3: Summary of PID Controller Parameters

Parameter	Value
P	51.16
I	0.7589
D	860.22
N	12.2
Rise time (sec)	12.5
Settling time (sec)	38.9
Overshoot (%)	6.52
Peak value	1.07
Gain Margin (dB)	40.3
Phase Margin (deg)	63
Closed loop stability	Stable

b) Model Predictive Control (MPC)

MPC controller offers several additive advantages as it performs many important tasks by respecting the input and output constraints of the system, prevention against extreme movement of the input variables as well as optimal set points for controlled state variables, while retaining other outputs within preset limits [7]. Since, it is an estimation based controller, it can be used for diagnosis and control reconfiguration when a sensor or actuator is not available [9].

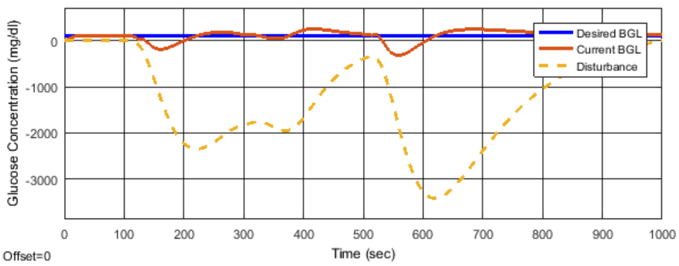

Figure 10: PID controller response with disturbance

Considering the general system representation in Eq. 4, we assume a linear time invariant (LTI) system, which when disturbed converges to zero; after the transient period, showing the global asymptotical stability. The closed loop system with initial conditions $x(t_i)$ is observed as:

$$x(\tau) = e^{(A-BK)\tau} x(t_i)$$
$$\dot{u}(\tau) = -Ke^{(A-BK)\tau} x(t_i) \qquad \ldots.. (6)$$

Suppose that the 'K' is selected such that the system is stable with all eigenvalues of the closed loop system $A_{cl} = (A - BK)$ placed in the stable left half of the s-plane by applying a finite $u(\tau)$ such that $\dot{u}(\tau)$ decays to zero exponentially. Since the control is based on a predictor estimator, we assume that at time every instant t_i, the state variable $x(t_i)$ is available as follows:

$$x(t_i + \tau | t_i) = e^{A\tau} x(t_i) + \int_0^{\tau} e^{A(t-\tau)} B\dot{u}(\gamma)d\gamma \quad \ldots\ldots (7)$$

Whereas, the zero mean random disturbances (including the deterministic and stochastic disturbances) have zero expected effect in the future prediction. Using the predicted values of the state variable, the output prediction at time τ is:

$$y(t_i + \tau | t_i) = Ce^{A\tau} x(t_i) + C\phi(\tau)^T \eta \quad \ldots\ldots (8)$$

It is desired to minimize the cost function J, which results in an optimal controller within the moving window which is expected to take the form:

$$J = \int_0^{T_p} \left(x(t_i + \tau | t_i)^T Q x(t_i + \tau | t_i) + \dot{u}(\tau)^T R \dot{u}(\tau) \right) d\tau \quad \ldots\ldots (9)$$

Where, $x\ (t_i)$ describes the state's initial conditions. 'Q' and 'R' are semi-positive definite weights describing the optimal performance such that $Q, R \geq 0$.

c) MPC Design Results

The model predictive controller is designed to realize a closed loop control. In this paper, working and results of MPC controller is shown. MPC is a model based technique that uses a generalized patient model to predict the correction for the glycemic levels. In order to find out the correct insulin dosage, the MPC algorithm uses an optimized controller calculated at each sampling instant by minimizing a quadratic cost function.

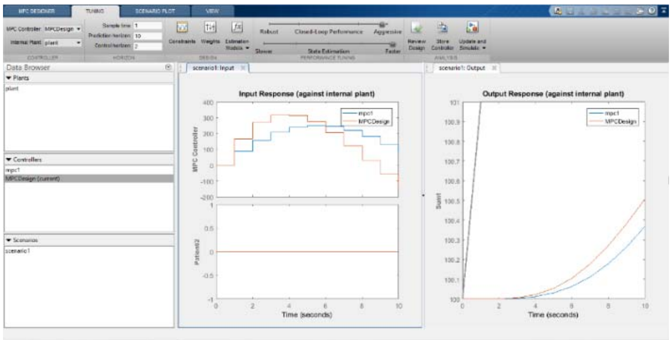

Figure 11: MPC Parameters selection

This cost function includes the term that adjusts the set point i.e. the difference b/w the future value prediction for the blood glucose level, the desired set point as well as the insulin required rate [22]. The prime benefit of this control scheme is that unlike PID, it can predict future glucose excursion and able to act in a proactive fashion to evade the stage of hypoglycemic and hyperglycemic ensuring safety.

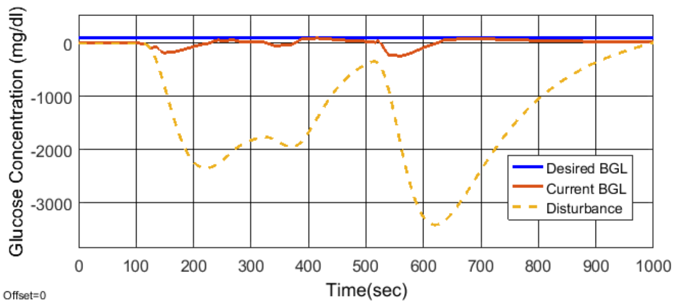

Figure 12: MPC Results

Furthermore, MPC allows the control of the input and output constraints. Whereas, in design review, MPC auto-generated tests shows the controller's internal stability, closed loop nominal stability, closed loop steady state gains and memory size for MPC data. If limits exceed in designing, than the status of test performed changes to warning/fail otherwise it shows 'Pass' in the status and results can be seen by simulating this controller. Fig. 12 depicts the response of the BGL control with MPC algorithm when a meal disturbance is applied. The prediction horizon is selected as 30 samples while control horizon is 2 samples for faster correction in real time.

V. Performance Comparison

Various control algorithms have been proposed including classical controllers for linear systems e.g. PID, Lead/Lag compensators as well as advanced optimal/robust control algorithms such as H-infinity, MPC, H_2 optimal controller, sliding mode control and some soft algorithms like fuzzy and neural network control. PID controllers are the most powerful controller in classical control algorithms and widely used in controlling glucose level abnormalities. Generally, PID operates on input tracking by finding the output error, i.e. difference b/w desired BGL and current BGL. In the PID control, the integral part affects the amount of delivered insulin at much higher stage causing the over-dozed effect and increases the risk of hypoglycemia. Thus, in critical biomedical applications such as the one under consideration, the glucagon insulation is required which is considered as the unnecessary loss of glucagon [23]. The limitation of classical approach algorithms (PID) indicate the need for advanced control algorithms.

The anticipated performance for the two control methods using a PID controller and an MPC is presented. Fig. 11 presents an optimized PID tuning results for BGL control in the presence of disturbance. When compared with Fig. 12, it is evident that the MPC controller offers less fluctuation in the controlled variable and perfectly limits the disturbance.

VI. Conclusion

The paper presents a comparison of PID and MPC for the application of an artificial pancreas. The results show that the MPC algorithm is more favorable and safe for the glycemic control under fasting and overnight conditions in T1DM patients as it offers prediction based control of BGL and real time adaptation in case of meal disturbances which provides better regulation as compared to a fixed parameter PID controller.

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