

## Model Based Control for Insulin Infusion System in Postoperative Diabetic Patients: A Novel Approach

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**Key words:** Diabetic infusion system, minimal model, model predictive control, internal model control, blood glucose, infusion system

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**Abstract:** In post-operative period, the variation of the blood glucose level is one of the important complications to be controlled which avoid abnormal conditions like hypo/hyper glycaemia that leads to emergency situation. To overcome this condition the closed loop control strategy is used to infuse the insulin to the human body as a continuous infusion system that stabilizes its level. In this study two different model based controllers (Model predictive control and Internal model control) were designed and their performances were observed. The output of the controller were compared and tested with Bergman minimal model in normal condition and even with series disturbance like meal and exercise. The results clearly predict that model predictive controller performance is better and meets the target.

## INTRODUCTION

The increment or decrement to the basal value is called hypo/hyper glycemia state which is dangerous of that hypoglycemia is a more serious and it can cause coma or may be even fatal. Hypoglycemia is a well-known complication for cardiac surgery patients and a study clearly depicts that the glucose levels were high which was reviewed from 1,586 patients of vascular surgery 560 (36%) persons, 227 (14%) had colon related surgery and 779 (50%) were part of surgical procedure (Anonymous, 2012 a, b). The literature survey portrays that researches have made an attempt to find various methods to treat the post-operative patients and one of the common traditional method is closed loop insulin delivery system (Artificial pancreas) that is capable of maintaining glucose level for diabetic patient with the desired level of insulin delivery (Cobelli *et al.*, 2011).

The insulin infusion system is an integrated system contains synthetic materials as per the medical standards which will substitute the pancreas with sensing the blood glucose and calculate the desired amount of insulin required and deliver the desired amount to the human body with the help of insulin pump. Figure 1 shows the basic architecture of the closed loop insulin control

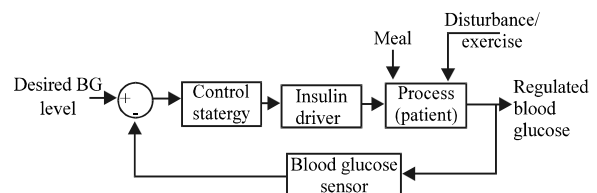


Fig. 1: Closed loop drug delivery control structure

system in which the controller regulates the details between the sensor input and desired insulin range (Bergman *et al.*, 1979).

The control algorithm is used based on the optimal requirement and the controller input given to insulin pump with the help of syntactic micro needle. In this study the proposed closed loop control strategy will produce the output equal to the pancreas and this research is keen to develop the system which will produce the optimal insulin infusion.

## MATERIALS AND METHODS

The mathematical model describes the dynamics of the human diabetic system that helps to find the correlation between the insulin and its resistance also,

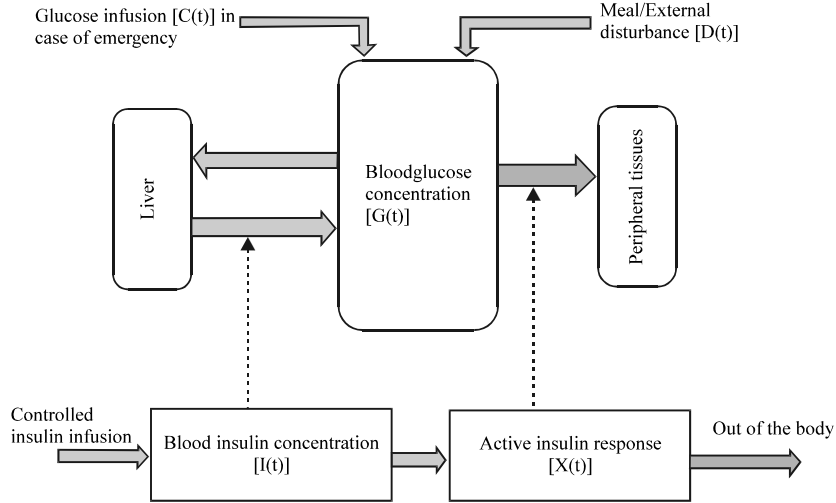


Fig. 2: Bergman minimum model system architecture

helps to design the control system based on standard rules and measures (Vivekanandan and Devanand, 2015). Basically the human body is a nonlinear stochastic and intrinsic system of that pancreas is an independent system that controls the blood glucose level. When pancreas does not work properly, insulin has to be pumped artificially to the patient which plays an important role called artificial pancreas (Basha and Vivekanandan, 2017a, b). During the last decades an interesting number of mathematical models has been developed based on the non-exhaustive criteria (Shah *et al.*, 2014), the different aspects of diabetes (Basha and Vivekanandan, 2017a,b) including glucose-insulin dynamics, beta-cell function (Bergman and Urquhart, 1971), epidemiology of diabetes (Lehman and Deutsch, 1992) management and the burden of diabetes and its complications (Bergman *et al.*, 1979). Bergman an awardee of the Anonymous (2015) for his achievements in the development of the famous minimal model, Fig. 2 for diabetes that indicates the importance of mathematical model in the basis of diabetes and its management.

Based on the observation the parameters has taken for an steady state process with approximate parameters and the model designed based on the selected approximate values also these models limited with real time prediction of the glucose measurement. The observation of frequently measured data with insulin availability, glucose compactness along with sensor system errors (Shah *et al.*, 2014):

$$\frac{dG_m(t)}{dt} = -p_1[G_m(t)-G_b]-x(t)G_m(t)+[d(t)+C(t)] \quad (1)$$

$$\frac{dX}{dt} = -p_2X(t)+p_3I \quad (2)$$

$$\frac{dI_d(t)}{dt} = -n[I(t)-I_b]+\gamma[G_m(t)-h]+r(t) \quad (3)$$

In the model  $G_m(t)$  is noted as plasma glucose concentration (mg/dL) and  $I(t)$  denotes insulin concentration ( $\mu\text{U}/\text{mL}$ ). The  $I_b$  is considered as basal value of insulin level (mU/L) and  $X_i(t)$  is observed as insulin in plasma glucose,  $U(t)$  is called as external input insulin (mU/min) and  $D_i(t)$  is external input glucose of the human body (mm/min).  $I_b$  and  $G_b$  are glucose and insulin concentration before infusion of the insulin. The  $P_1$ - $P_3$  are patient parameters taking as random and 'n' is change in rate of insulin which is used in plasma layer ( $\text{Min}^{-1}$ ). Bergman theory denotes the values of the parameters (Basha and Vivekanandan, 2017a, b),  $P_1$ - $P_3$  may be regulates based on the different conditions the values are  $P_1 = 0$ ,  $P_2 = 0.025$ ,  $P_3 = 0.000013$  and for type 1 diabetic patient and the values can be identified as follows P for normal person, the values are  $P_1 = 28/1000$ ,  $P_2 = 25/1000$ ,  $P_3 = 0.000013$  (Shah *et al.*, 2014; Bergman *et al.*, 1979; Basha and Vivekanandan, 2017a, b; Bergman and Urquhart, 1971).

Based on the values and equations, Lynen and Bequette developed a diabetic model process transfer Eq. 6 along with the process parameters (Morari and Zafiriou, 1989):

$$Gp_g(s) = \frac{-3.79}{(40s+1)(10.8s+1)} \quad (4)$$

Also, the transfer function with meal to be consider as follows:

$$Gd_m(s) = \frac{8.44}{s(20s+1)} \quad (5)$$

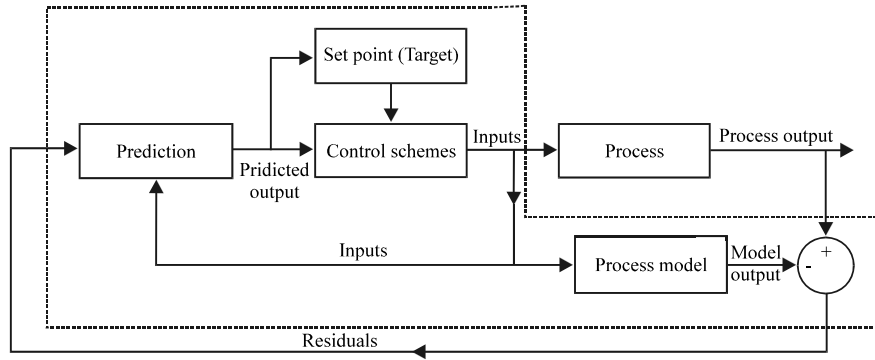


Fig. 3: Architecture of model predictive control system

The meal difference is consider as pulse value, the 5 g glucose meal consumed in 15 min tile lag, the pulse is developed with the scale of 3.33 g/min with the same duration.

#### Controller scheme

**Model predictive controller:** Model Predictive Controller (MPC) is an advanced control technique used in process industries, since, 1980. As MPC offers several important advantages such as fast response, accurate model prediction, multiple input/output processes in a systematic manner, controlled optimal set point, dynamic model relay and dynamic principles these controllers are used in bio control field (Lehman and Deutsch, 1992).

MPC can handle the constraints of the process variables and it can be manipulated and controlled by the variables in a systematic manner for an multivariable control problems naturally, also it is an easy to tune method (Breithaupt, 2010) it is a totally open methodology based on certain basic principles which allow for future extensions (Chen *et al.*, 2007). The controller schemes are based on the running process of the measurement and the process output is to beresponsible on the predictions of the values in future condition. The MPC controller calculations are based on predicted system variables at present condition with the sequence of regulated changes and the controlled changes has been manipulated in the prediction and it will move the set point in an optimal manner and the control technique is shown in Fig. 3.

If the process is probably accurate with the dynamic model of the system and the model, current measurements can be used to predict the values of the process output. The attained changes may be an individual input variables of process model (Magni *et al.*, 2007). MPC is implemented based on discrete time nonlinear process models, so, the mathematical description can be represented:

$$x_{k+1} = f(x_k, u_k) \quad (6)$$

The MPC control problem is as follows with the knowledge of current output  $y_k$ :

$$J = \phi(y_k + N_k) + \sum_{j=0}^{N-1} L(y_k + j|k, u_k + j|k, \Delta u_k + j|k) \quad (7)$$

The variable N-move is the control sequence that minimizes the objectives and the measurement is available the parameters of the problem are updated and a new optimization problem is formulated whose solution provides the next control. This recurrent optimization is using to obtain the function and modified through the entire process feedback of MPC to control the variables.

**Internal model control:** The Internal Model Control (IMC) is an advanced control strategy commonly used in industrial application and controller algorithm is simple and robust to handle the nonlinear and inaccuracies in the process. The IMC controller is contain the specific locating process of the controller performance also the controller is taking the specific control track of the process for an set point of the process also the IMC controller is contain the explicit filter technique to reject the disturbance for the steady state processes (Man *et al.*, 2006). The internal model control system structure shown in Fig. 4 with three different positions. The main part of the controller is used to forecast the process output (Bequette, 2003) of the system. The following is the internal loop which is used to differentiate the process output and the internal model output. To end, the third position of the controller can be used to control the error to compute the upcoming values of the process outputs (Rivals and Personnaz, 2000).

The difference between the output of the internal model and the process output is fed back to produce the error, used by the controller. This helps to reduce the effect of disturbances on the system (Breithaupt, 2010). In

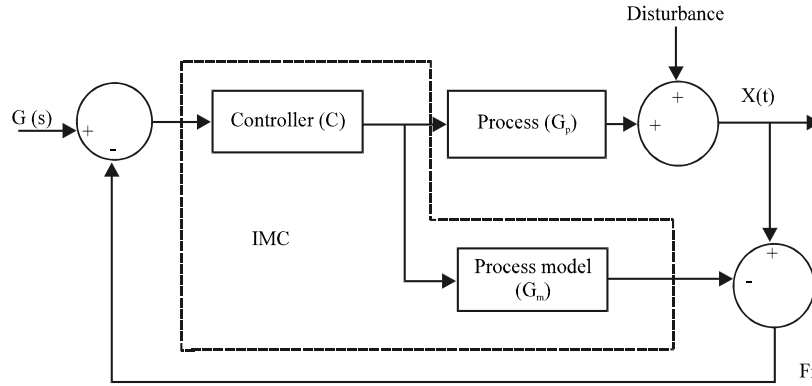


Fig. 4: Diagram of IMC structure

this model we have implemented the IMC developed by Garcia and his co-researchers (Rivals and Personnaz, 2000) on the patient model proposed by slate and his co-researchers (Rivera *et al.*, 1986). The IMC has been to control of blood glucose by Jingkun (2003). The conventional IMC structure is shown in Fig. 4 in that the parameter  $G_p$  is the plant to be controlled and  $G_m$  is a applied plant model of the process, C is the controller based on model control and  $x(t)$  is the system output and D is the external disturbance of the system. Based on the parameters the formulae evaluated as follows:

$$K_{cp} = \frac{2\tau + \tau_d}{2(\tau + \tau_d)} \quad (8)$$

Where:

$$\tau_d = \frac{\tau \tau_d}{2\tau + \tau_d}$$

## RESULTS AND DISCUSSION

The results obtained from MPC and IMC controllers were simulated, tested and compared that predicts and evaluates the optimal infusion of insulin to the human body.

The simulation has been carried out with the help of MATLAB with virtual patient model to regulate the desired optimal level of infusion along with the meal disturbance. The IMC and MPC controllers were verified based on the designed parameters and the response of each model was obtained in the presence of disturbances along with meal input. These results are shown (Table 1 and 2), the performance of the controllers are satisfied with both the MPC and IMC controller with the desired level of infusion control. However, the settling time for the IMC control of the patient's responses are shorter than with MPC, especially, the multiple disturbance response which has a minimum settling time hat offered by the IMC controller.

Table 1: Glucose prediction level for IMC and MPC controller

Meal duration	IMC controller (mg/dL)	MPC controller (mg/dL)
Break fast	93-138	85-132
Lunch	80-139	82-128
Dinner	85-148	85-135

Table 2: Insulin infusion level for IMC and MPC controller

Meal duration	IMC controller (mU/min)	MPC controller (mU/min)
Break fast	1.2-5	1.3-5
Lunch	0.6-5	0.8-5
Dinner	1.2-5	0.8-5

The tuning parameters are injected in IMC and MPC controllers which is used to control the blood glucose system. Figure 5 shows the glucose and insulin outputs of IMC controller, based on the output response, the blood glucose increases depends on the meal inputs, similarly the insulin also increases to bring back the blood glucose level to normal condition in that scenario the response time is lagging due to controller action with the disturbed output, similarly this trend continues for multiple meals and the insulin level also, changes and reaches the maximum level. To overcome the disturbance model predictive controller is used, the glucose and insulin response are shown in Fig. 6. The MPC allows the disturbance and minimize the sudden change and it bring backs the blood glucose concentration in minimum level with optimal glucose infusion at the desired level.

As per the design the MPC controller maintain the glucose in the desired level while it increases after the surgical procedures and it will control naturally with pancreas to inject the insulin to our body to maintain the glucose level with the proper controlled delivery whereas his trend continues for multiple meals and the insulin level also changes and reaches the desired level. Figure 7 and 8 shows the comparison of IMC and MPC controller glucose level and insulin responses in this the MPC controller gives minimum time to reach the measurement and the controller taken the lesser time to regulate the blood glucose based on the optimal insulin infusion rate.

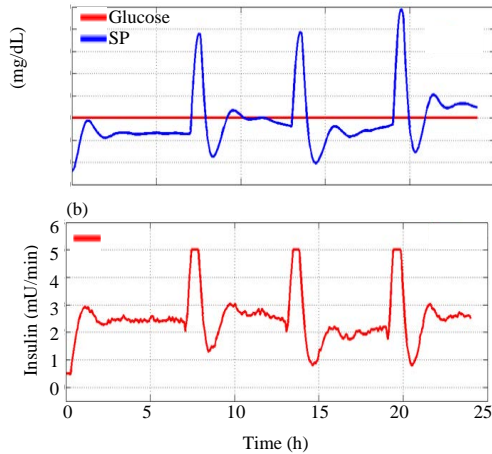


Fig. 5: Response of glucose vs. Insulin evaluation for controller IMC

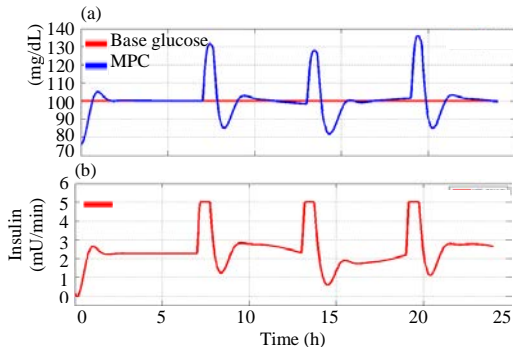


Fig. 6: Of glucose vs. Insulin evaluation for MPC controller

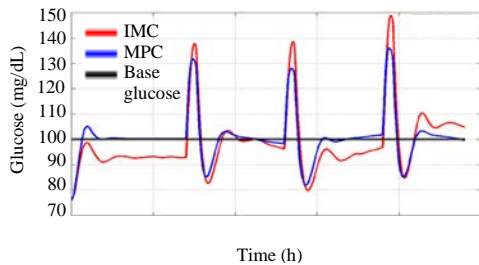


Fig. 7: Response of MPC and IMC controller glucose estimation

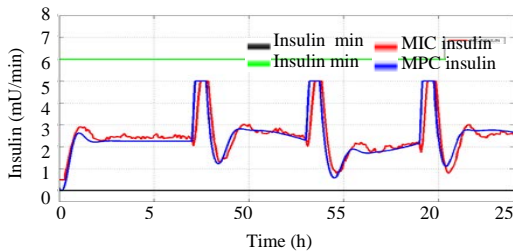


Fig. 8: Response of insulin infusion for MPC and IMC controller

## CONCLUSION

In this study the IMC and MPC controllers were proposed for control the blood glucose system for post-operative patients. The simulation was carried out with reference to diabetic model from which glucose and insulin kinetics were referred with the help of new control strategy carried out and developed, the meal (glucose) is taken as a disturbance and based on the feedback the controlled insulin is infusing to the patient which maintains the glucose level in the body. The simulation of the physiological results of the IMC and MPC controllers are compared and identified the superiority of characteristics are shown and discussed. The optimal selection of parameters in MPC regulates the blood glucose level effectively compared with IMC controller. The controller settings are adopted using a self-tuning strategy and the settings has been simulated with the minimal model.

This output is a major exertion to develop the model based strategy of continuous glucose control for insulin pumps. The MPC is an effective model based control which requires exact model of blood glucose system and it will vary patient to patient based on the modelling.

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