# INTERNAL MODEL CONTROL DESIGN FOR BLOOD GLUCOSE REGULATION IN A TYPE 1 DIABETIC PATIENT

**[1]Araromi, D. O., Agarry, S. E., Onifade, D.V**

**Department of Chemical Engineering,**
**Ladoke Akintola University of Technology, Ogbomoso**

**Corresponding Author: doararomi@lautech.edu.ng**

*ABSTRACT*

***Internal Model Control (IMC) applied to the blood glucose regulation process in body of a type 1 diabetic patient in this study. Minimal Model (BMM) adopted as the type 1 diabetic patient was linearized using Taylor Series expansion to get appropriate transfer function. Insulin infusion rate was used as the manipulated variable to control the blood glucose concentration while glucose meal was used as disturbance variable. IMC algorithm was developed to control the process model using the IMC structure along with the Single Input Single Output (SISO) tool in MATLAB. Single parameter associated with IMC was tuned by using percentage of settling time (% OLST) for open the loop model representing the patient. The parameter equivalent to 5% OLST gave the best setting for full-order IMC with closed-loop settling time of 55.913 min, without violating input constraint. The parameter equivalent to 10% OLST gave the best setting for reduced-order IMC with closed-loop settling time of 93.788 min. The controllers gave good performance in term of set point tracking and disturbance attenuation. Comparison of IMC with PID controllers based on Zeigler-Nichols and Cohen-Coon indicated that IMC outperformed PID controllers.***

***Keyword***: Diabetics, Disturbance rejection, IMC, normoglycemia, PID, Set point tracking

## Introduction

Regulating blood glucose in diabetic patients has been one of the most challenging and socially important control problems in the field of biomedical systems. Before this time, the therapeutic system was based on open-loop strategies with some improvement by feed-forward actions and episodic finger-stick measures due to absence of reliable glucose sensors. Advancement in technology in recent time has given birth to minimally invasive subcutaneous (sc) Continuous Glucose Measurements (CGM) with implantable insulin infusion pumps and this gives way to complete automated closed-loop control strategies with assurance of normoglycemia to help prevent diabetic complications.

The blood glucose control regulation within 70-100 mg/dL (equivalent to 4-6 mmol/liter) is always a challenge. Whenever food containing carbohydrate is consumed, it is broken down by digestive system to glucose which is subsequently absorbed into blood stream to increase blood glucose level and this subsequently timulates insulin production from pancreas. The human body has many feedback control loops that regulate body system to function well. In human body, blood glucose level is regulated by manipulating the amount of insulin secreted through one of these feedback systems. People with lack of insulin production are named diabetic patients. They have reduced capability of producing insulin through pancreas. Diabetes is ranked the 8$^{th}$ leading cause of death worldwide with about 1.5 to 5.1 million deaths per year (International Diabetes Federation, 2013), and thus given rise to the need to devise a more accurate way of controlling it.

According to Sukha and Rubin (2007), the three main types of diabetes are Type 1 diabetes, Type 2 and Gestational diabetes (GDM). Type 1 diabetes also called juvenile-onset diabetes or Insulin Dependent Diabetes Mellitus (IDDM) is characterized by the insufficient secretion of insulin from the $\beta$-cells of pancreas caused by an auto-immune reaction where the body's defense system attacks the cells that produce insulin. Type 2 diabetes also called non-insulin dependent diabetes is characterized by insulin resistance and relative insulin deficiency, either or both of which may be present at the time diabetes is diagnosed. Gestational diabetes (GDM) which is a form of diabetes consisting of high blood glucose levels during pregnancy. Diabetes results in prolonged elevated blood glucose concentration and a clinical condition known as hyperglycemia (defined as

arterial glucose concentration > 120 mg/dl which is equivalent to 6.7mmol/liter) (Sukha and Rubin, 2007).

Different control systems have been developed in the past years to meet the need of blood glucose control such as therapeutic system based on open-loop strategies with some improvement by feed-forward actions and episodic finger-stick measures due to absence of reliable glucose sensors. In the recent times, model based and model free control algorithms methods have been tried to achieve different designs with implementations transitioning from in silico simulations to clinical evaluation stage with practical applications in mind (Clarke and Foster, 2012). Although, reduction in patient and health personnel intervention have been achieved through these techniques, there is a need to eliminate user intervention completely and this has built up tremendous motivation for the development of closed loop insulin delivery systems.

The ultimate purpose of developing better glucose monitoring and insulin delivery technologies is to combine these two processes by way of an algorithm, into an automatic closed-loop system (Klonoff, 2007). This closed loop sytem is currently reffered to as artificial pancreas and it comprises of a glucose monitoring sensor, an insulin pump, and a control algorithm to regulate the pump to deliver the insulin in order to maintain normoglycemia in presence of sensor measurements. These three components and how they are linked is shown in the schematic diagram in Figure 1 below.

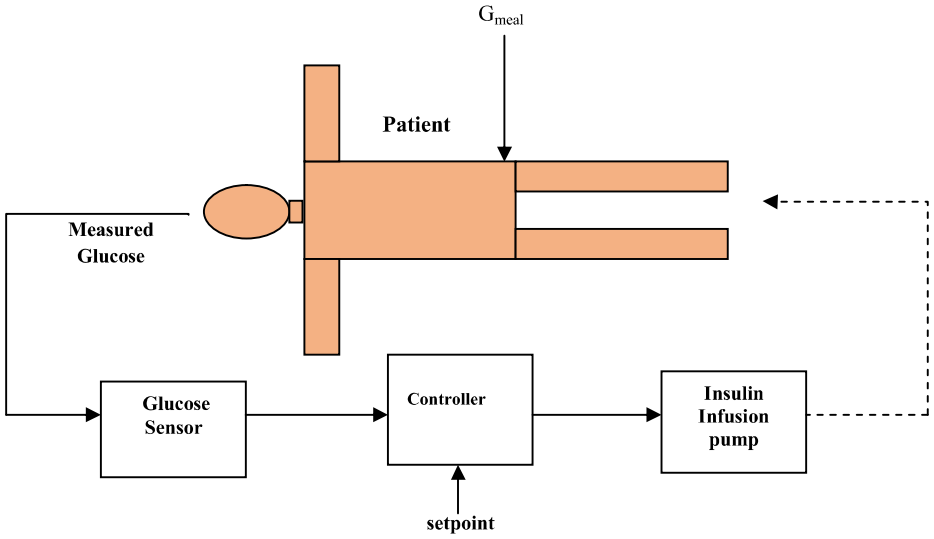


Fig. 1: Schematic Diagram of an artificial pancreas (Bequette *et. al*., 2002)

The main objective of this work is to design IMC control algorithm for blood glucose regulation in glycemic variability situation by using the Bergman Minimal Model (BMM). The model is suitable to test the effects of insulin infusion and glucose (meal) inputs on the blood glucose concentration.

Parker *et al.,* (1999) developed a model-based predictive control algorithm to maintain normoglycemic in the Type I diabetic patient using a closed-loop insulin infusion pump. A fundamental model of the diabetic patient was constructed utilizing compartmental modeling techniques. A linear model predictive controller (MPC) was developed and controller performance for unmeasured disturbance rejection (50 g oral glucose tolerance test) was examined. Under noise-free conditions, the model based predictive controller using state estimation was seen to outperform an internal model controller from literature. These results demonstrate the potential use of predictive algorithms for blood glucose control in an insulin infusion pump. MPC is sufficient for controlling blood glucose, but results in glucose concentrations near the output lower bound. The digital nature of the control algorithm allows potential implementation onto chip technology when sensors can guarantee long *in vivo* lifetimes.

Chase, *et al.*, (2002) developed a control method focusing on the rate of change of blood glucose level to utilize emerging technologies in blood glucose biosensors. The controller developed was found to provide tighter, more optimal control of blood glucose levels, while robustly handling variation in patient response and sampling rate. Particular emphasis was placed on the controller simplicity and robustness necessary for medical devices and implants. A PD controller with a heavily weighted derivative term was also found to outperform the more proportional-weighted

controllers in oral glucose tolerance testing. Simulation results showed reductions of over 50% in the magnitude and duration of blood glucose excursions from basal levels that were slightly better than normal non-diabetic response modeled. Comparison with normal response indicated that the physiological control system has some measure of both proportional and derivative control as the basis of glucose regulation

Van Herp *et al.*(2006) presented a modified minimal model to describe the glucose dynamics and the insulin kinetics of ICU patients. Simulations of their study showed that the modified model (ICU-MM) exhibits a similar glycemic behavior as that of the original minimal model (MM) and clinically more realistic insulin kinetics. Therefore, it is potentially more suitable for glycemia model predictive control (MPC). The modified model was also estimated on a real-life surgical ICU dataset. Although only two input variables were taken into account, the simulated glucose trajectories keep track of the general glycemia behaviour..

Sh.Yasini and Naghibi-Sistani, (2008) proposed a closed-loop control system based on fuzzy logic control for type I diabetic patients. A controller was designed using a Mamdani-type fuzzy scheme in order to incorporate knowledge about patient treatment. The controller can successfully tolerate dynamic uncertainty in patient model while rapidly rejecting meal disturbances and tracking the constant glucose reference. Robustness was tested over a group of three patients with model parameters varying considerably from the averaged model. They showed that the fuzzy logic framework has the potential to synthesize expert knowledge to treat diseases. Their simulation results proved that the fuzzy control method has preference over other conventional techniques in blood glucose control.

Ibbini, (2008) demonstrated the superiority of using fuzzy logic control strategies for the case of regulating the normoglycemic average for type-I diabetic patients. The stability of the resulting system often encountered practical situations of severe initial conditions of hyperglycemic and sudden glucose meal intake was also demonstrated with computer simulations. The superiority of the FLC and PI-FLC controllers over other conventional (PID and PI) or optimal (LQR) techniques was also demonstrated and compared with computer simulations.

Sh Yasini and Naghibi-Sistani (2009) developed a consistent, robust controller for safe, predictable regulation of blood glucose levels in diabetic patients. The closed-loop control scheme incorporates expert knowledge about treatment by using Q-learning algorithm to maintain the normoglycemic average of 80 mg/dl and the normal condition for free plasma insulin concentration in severe initial state. Controller performance was 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 were used to evaluate the effectiveness of the proposed technique. The proposed controller was seen to successfully tolerate patient variability and dynamic uncertainty while rapidly rejecting meal disturbances and tracking the constant glucose reference.

Kamath (2014) derived a control strategy for blood glucose regulation. Controller performance was 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 were used to evaluate the effectiveness of the proposed technique and to show its superiority in controlling hyperglycemia over other existing algorithms. The performance and robustness characteristics of different PID controllers were obtained using four tuning methods. The performances of H∞ controller was compared with the performances of other two controllers such as PID and IMC controller. Shen and DMC-based tuning methods outperformed the other two tuning methods i.e. Cohen-Coon and IAE minimization methods and PID controller tuned by the Shen method was able to maintain the glucose concentration above the dangerous hypoglycemic range (< 60 mg/dL).

**Model Simulation**

The Bergman Minimal Model as employed in this paper is a three compartment model with one compartment each assigned to glucose and to insulin concentrations in the blood, and the third to the non-observable auxiliary variable $X(t)$, which creates the delay in the action of insulin on glucose (Bergman, 2005). The mathematical equations for the model includes:

$$\frac{dG}{dt} = -p_1(G - G_b) - X(G + G_b) + \frac{G_{input}}{V_1} \quad (1)$$

$$\frac{dX}{dt} = -p_2 X + p_3 I \quad (2)$$

$$\frac{dI}{dt} = -n(I + I_b) + \frac{U}{V_1} \quad (3)$$

The parameter definitions and their values used to simulate the model are presented in Table 1 (Bequette, 2002 and Sriram *et al.,* 2010).

Table 1 Parameters used in simulations

| | Variable Name | Value |
|---|---|---|
| $G_b$ | Basal Plasma Glucose | 4.5mmol/liter |
| $I_b$ | Basal Plasma Insulin | 4.5mU/liter |
| $V_1$ | Insulin Distribution Volume | 12liter |
| $p_1$ | Insulin Dependent constant | 1 $min^{-1}$ |
| $p_2$ | Delay in Insulin Action | 0.025 $min^{-1}$ |
| $p_3$ | the insulin-dependent increase in glucose uptake ability | 0.0013 $(mU.min/L)^{-1}$ |
| N | Fractional dissapearance rate of insulin | 5/54 $min^{-1}$ |
| G | Blood Glucose Concentration | 4.5mmol/liter |
| I | Insulin Concentration | 10.5mU/liter |
| X | Insulin Concentration (Remote Compartment) the insulin's seffect on the net glucose disappearance | 0.005461 $min^{-1}$ |

The set of non-linear equations were solved before using the model for controller design. Simulink Software in MATLAB was used to solve the model. The Simulink provides a graphical user interface (GUI) for building models as block diagram and it includes a comprehensive block library of sources, sinks, connectors along with linear and non-linear components. Simulation of then Bergman Minimal Model is shown in Figure 2.

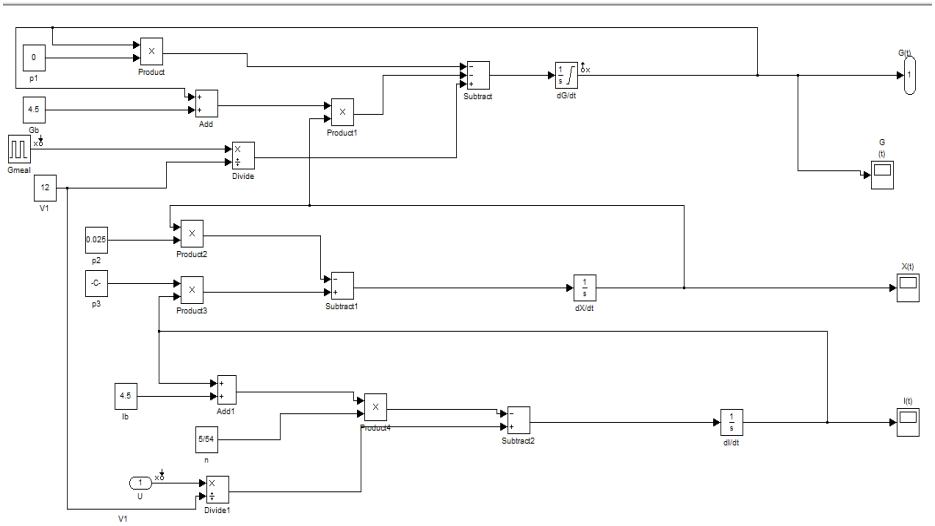


Figure 2 Simulink Model of the Blood Glucose Regulation process

The meal disturbance was represented by a pulse input with amplitude of 0.18. The linearization points were also specified with Gmeal and U as inputs and G(t) as the output.

**Model Linearization**

The control and estimation tools manager in MATLAB SIMULINK gave the following state space representation of the model:

$$A = \begin{bmatrix} -1.0055 & -4.5000 & 0 \\ 0 & -0.0250 & 0.0013 \\ 0 & 0 & -0.0926 \end{bmatrix}$$

$$B = \begin{bmatrix} 0 & 0.4630 \\ 0 & 0 \\ 0.0833 & 0 \end{bmatrix}$$

$$C = [1 \quad 0 \quad 0] \qquad D = [0 \quad 0]$$

The transfer function that shows relationship between controlled variable (blood glucose concentration, G) and manipulated input (insulin infusion rate, u) was derived according to

$$g_p = C(sI - A)^{-1}B \tag{4}$$

Evaluation of Eq. 4 leads to the following

$$g_p = \frac{-3.7810}{(40.0s+1)(10.8s+1)(0.9948s+1)} \tag{5}$$

The transfers function from the disturbance input (Glucose meal, $G_{meal}$) otherwise known as the disturbance transfer function was derived as:

$$g_d = \frac{8.3340}{s+1.005} \tag{6}$$

**IMC Design Procedure**

The IMC design procedure is a design process to provide a suitable tradeoff between performance and robustness. It refers to systematic procedure for control system design based on the Q-

parameterization concept that is the basis for any modern control techniques. Aside from controller design, IMC has been found to be helpful in assessing the fundamental requirements associated with feedback control such as determining the effect of non-minimum phase elements (delays and Right Hand Plane (RHP) zeros) on achievable control performance (Rivera and Flores, 2004). Two types of IMC design are common. In the first type, the plant is approximated as a first-order model with a time delay and PID parameters is computed using Skogestad design rules (Skogestad, 2003). In the second type, a full-order feedback controller is generated using Q-parameterization concept to guarantee closed-loop stability when there is no model error and integrator is included to guarantees zero steady-state offset for plants without a free differentiator.

The IMC design structure based on Q-parameterization concept used for the feedback control is shown in Fig. 3.

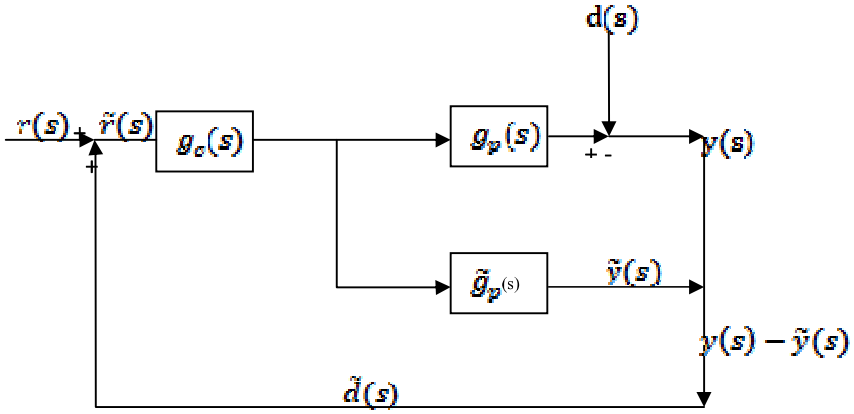


Fig. 3: IMC Design Structure

The transfer function and variables represented in Fig. 3 are:

d(s) = disturbance; $\tilde{d}(s)$ = estimated disturbance; $g_p(s)$ = plant;

$\tilde{g}_p(s)$ = process model; $g_c(s)$ = internal model controller; r(s) = set point

$\tilde{r}(s)$ = modified setpoint (corrects for model error and disturbances)

u(s) = manipulated input (controller output); y(s) = measured process output

$\tilde{y}(s)$ = model output.

The process model obtained after linearization is given as:

$$\frac{-0.0088}{s^3+1.123s^2+0.1205\,s+0.002327} \qquad (7)$$

The idealized IMC controller was formed using $q(s) = g_p^{-1}(s)$

$$q(s) = g_p^{-1}(s) = \frac{s^3+1.123s^2+0.1205\,s+0.002327}{-0.0088}$$

A filter of the form $\frac{1}{(\lambda s+1)^n}$ was cascaded in order to make the controller proper (such that the order of the denominator of the controller transfer function will be at least as great as the order of its numerator). To avoid controller with high order we choose *n* to be 3. Thus, the feedback controller is given as

$$g_c(s) = g_p^{-1}(s)\frac{1}{(\lambda s+1)^3} \qquad (9)$$

The controller has one parameter setting, $\lambda$ which can be adjusted to vary the speed of response. The parameter, $\lambda$ was adjusted by using percentage of open-loop settling time (% OLST) of the patient model represented by transfer function in Eq. 5.

**Proportional Integral Derivative Controller Tunings**

The performance of IMC scheme was compared with conventional PID controllers. The PID controllers used is of the form (Bequette, 2002):

$$C(s) = K_c\left[\frac{\tau_D\tau_I s^2+\tau_I s+1}{\tau_I s}\right]\left[\frac{1}{0.1\tau_D s+1}\right] \qquad (10)$$

where, $K_c$= Controller gain, $\tau_D$=derivative time and $\tau_I$=integral time

The value of the controller parameters were obtained by using Ziegler-Nichols open-loop tuning parameter (Eqn. 11) and Cohen-Coon tuning parameters (Eqn. 12) from model parameters (Bequette, 2002).

$$K_c = \frac{1.2\tau_p}{k_p t_d},\ \tau_I = 2t_d,\ \tau_n = 0.5t_d \qquad (11)$$

$$K_c = \frac{\tau_p}{k_p t_d}\left[\frac{4}{3}+\frac{t_d}{4\tau_p}\right],\ \tau_I = t_d\left[\frac{32+\frac{6t_d}{\tau_p}}{13+\frac{8t_d}{\tau_p}}\right],$$

$$\tau_D = \frac{4t_d}{11+\frac{2t_d}{\tau_p}} \qquad (12)$$

The third order transfer function in Eqn. 5 was reduced to first order transfer function with delay given by Eqn. (13) using half-rule technique proposed by (Skogestad, 2003) in order to evaluate the settings represented by Eqn. 11 and Eqn. 12 to give

$$g_p = \frac{K_p e^{-t_d}}{(\tau s+1)} \qquad (13)$$

**Results and Discussion**

The blood glucose regulation process was simulated in MATLAB Simulink. The equations for the internal model control algorithm was written in MATLAB and executed on a PC with 2.1GHz and 4GB RAM. The turning parameters were set using percentage of open-loop settling time (% OLST). The full-order feedback controllers obtained for 2.5%, 5%, 10%, 15% and 20% of the open-loop settling time are presented in Table 2. The table also contains corresponding reduced order controllers obtained after the full-order controllers were subjected to balanced residualization technique implemented in MATLAB software. Order reduction on the full-order controllers was carried out in order to simplify the controllers because practical implementation of high order control laws is prohibitive. The full-order was successfully reduced to second order. Further reduction to first order turned the closed loop system to become unstable.

Servo responses for full-order and reduced order controllers are presented in Fig. 4 and Fig. 5, respectively. Increase in the %OLST makes the response to be more sluggish for both full-order and reduced-order controllers. Setting with 2.5% and 5%OLST are able to track the set point of 80mg/dcliter blood glucose concentration within 100 min. For instance, the settling time with full-order controllers for 2.5% and 5% OLST setting are 17.887 min and 55.913 min, respectively while the settling time with reduced-order controllers are 28.474 min and 80.891min, respectively. Settling times for all the settings are presented in Table 3.

Table 2: Full-order and reduced –order IMC controllers based on percentage open-loop settling time (%OLST)

| % OLST | Full-order feedback controllers | Reduced order controllers |
|---|---|---|
| 2.5% | $\frac{-1.482s^3 - 1.665s^2 - 0.1787s - 0.00345}{s^3 + 0.7055s^2 + 0.1659s - 8.348e-018}$ | $\frac{-2.367s^2 - 0.2571s - 0.00497}{s^2 + 0.239s - 1.327e-017}$ |
| 5% | $\frac{-0.1853s^3 - 0.2081s^2 - 0.02234s - 0.0004313}{s^3 + 0.3528s^2 + 0.04148s - 1.043e-018}$ | $\frac{-0.03082s^2 - 0.6986s - 0.0159}{s^2 \mid 1.539s \quad 3.395e \quad 016}$ |
| 10% | $\frac{-0.02316s^3 - 0.02601s^2 - 0.002792s - 5.391e-005}{s^3 + 0.1764s^2 + 0.01037s - 1.304e-019}$ | $\frac{-0.00957s^2 - 0.03092s - 0.0007393}{s^2 + 0.1422s - 1.974e-018}$ |
| 15% | $\frac{-0.006863s^3 - 0.007707s^2 - 0.0008273s - 1.597e-005}{s^3 + 0.1176s^2 + 0.004609s + 1.71e-020}$ | $\frac{0.001333s^2 - 0.009148s - 0.0002162}{s^2 + 0.0624s + 4.33e-019}$ |
| 20% | $\frac{-0.002895s^3 - 0.003252s^2 - 0.000349s - 6.739e-006}{s^3 + 0.08819s^2 + 0.002593s - 1.63e-020}$ | $\frac{0.005773s^2 - 0.004334s - 9.76e-005}{s^2 + 0.03755s - 2.443e-019}$ |

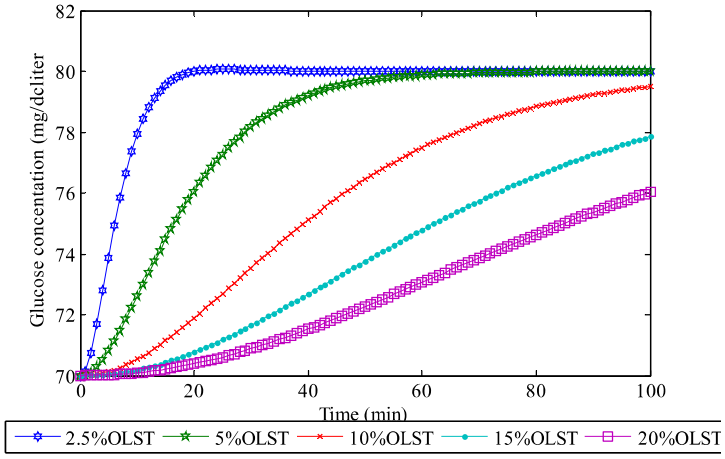


Figure 3: Closed-loop response with full-order controllers at different parameter settings for set point of 10 mg/dcliter step change

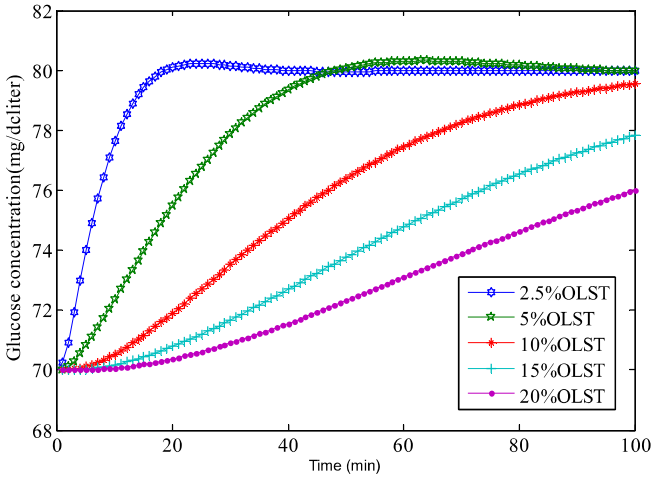


Figure 4: Closed-loop response with reduced-order controllers at different parameter settings for set point of 10 mg/dcliter step change

Table 3: Performance metrics for Full-order IMC (FOIMC) and reduced-orders IMC (ROIMC) for set point tracking

| % OLST | Settling time(min) for FOIMC | Settling Time(min) for ROIMC | Range of insulin infusion rate (mU/min) for FOIMC | Range of insulin infusion rate (mU/min) for ROIMC |
|---|---|---|---|---|
| 2.5% | 17.887 | 28.474 | (-87.096, 19.619 ) | (-148.994, 16.478) |
| 5% | 55.913 | 80.891 | (3.699, 14.019) | (-12.418, 14.513) |
| 10% | 93.486 | 93.788 | (13.598, 15.049) | (13.635, 16.000) |
| 15% | 98.112 | 98.175 | (13.997, 16.190) | (13.986, 16.763) |
| 20% | 99.115 | 99.103 | (14.285, 16.467) | (14.457, 17.432) |

Comparative study of the settling times for all the settings indicate that closed-loop systems with full-order controllers are faster than the corresponding closed- loop responses with reduced-order controllers except to 20% OLST setting in which response with reduced-order controller is slightly faster than the response with full-order controller. It seems that 2.5% (OLST) setting is the best in term of speed of response for closed-loop system with both full-order and reduced-order controllers however, input (insulin infusion rate which must not be negative) constraint must be satisfied before concluding. Table 3 which also show the ranges of insulin infusion rate for the closed loop system for the two controller types indicates that 5% -20% OLST

settings satisfy the input constraint for full-order controller while 10%-20% OLST settings satisfy the constraint for reduced-order controller. To this end, the best choice is the full-order controller resulting from 5% OLST setting in term the speed of response. However, if ease of implementation is given priority, then reduced-order emanating from 10% OLST setting may be considered.

The disturbance attenuating capability of both full-order controllers and reduced-order controllers emanating from the considered % OLTS settings was considered in the design. Fig. 4 and Fig. 5 show the close-loop responses with Full-order controllers and reduced-order controllers, respectively disturbance attenuation. Each of these system was subjected a pulse meal consumption of 50 g glucose at t=0 min under closed-loop. In case of full-order controllers, the highest peak blood glucose concentration ( Fig. 4) is found to be 7.45 mg/dclilter which is still within normoglycemic range (70-100 mg/dl) and this occurs for the controller obtained from 2.5% OLST setting. Fig.4 indicates that, the higher the % OLST setting used in controller designed the peak blood sugar level and the speed of response. The ranges of % OLST settings that satisfy the input constraint (i.e, non-negative insulin delivery rate) are 10%- 20% OLST (Table 4). The same pattern observed in closed-loop response with full-order controllers was observed for the case of closed-loop response with reduced-order controllers with a slight difference in term settling times (see Table 4).

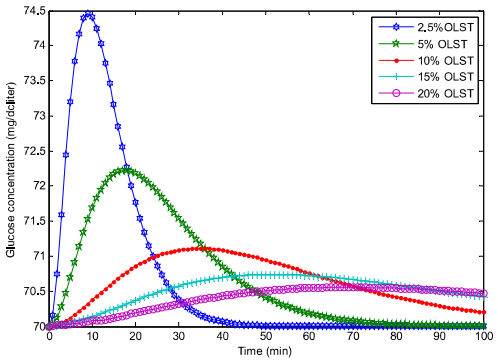


Figure 5: Closed-loop response for disturbance rejection with full-order controllers for different settings

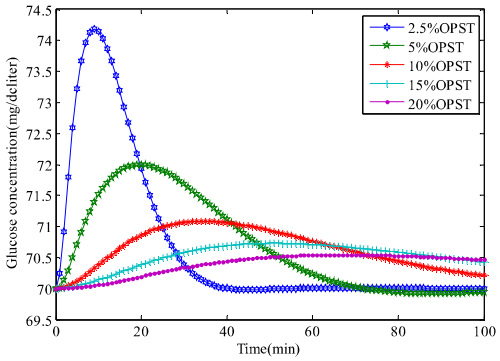


Figure 6: Closed-loop response for disturbance rejection with reduced-order controllers for different settings

Table 4: Performance metrics for Full-order IMC (FOIMC) and Reduced-orders IMC (ROIMC) for disturbance rejection

| % OLST | Settling time(min) for FOIMC | Settling Time(min) for ROIMC | Range of insulin infusion rate (mU/min) for FOIMC | Range of insulin infusion rate (mU/min) for ROIMC |
|---|---|---|---|---|
| 2.5% | 36.763 | 39.272 | (-87.096,32.721) | (-148.994, 36.333) |
| 5% | 74.424 | 76.022 | (3.699, 17.854) | (-12.418, 17.179) |
| 10% | 99.001 | 98.764 | (15.049, 16.721) | (13.635, 16.714) |
| 15% | 99.899 | 99.958 | (16.188, 16.660) | (13.986, 16.763) |
| 20% | 98.681 | 98.819 | (16.428, 16.612) | (14.298, 17.074) |

Servo closed-loop responses for IMC, PID controllers based on Zeigler-Nichols setting and Cohen-Coon setting are shown in Fig. 7 and the corresponding performance metrics are shown in Table 5. Both PID controllers have aggressive responses with faster rising and with overshoot. This means both will have damping factor less than unity and implication of the overshoot is that there is possibility of patient to experience hyperglycemic condition if such control scheme is used in artificial pancreas. Similarly, both PID controllers give negative insulin infusion rate which is not realistic and poor performances are also indicated with larger settling time.

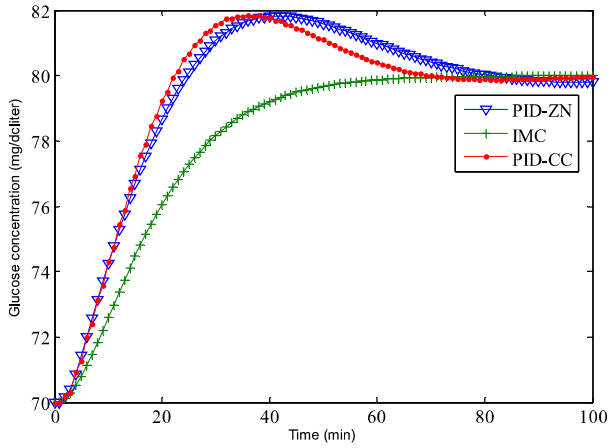


Figure 7: Closed-loop response for set point of 10 step change under different control schemes

Table 4: Performance metrics for different control schemes for setp point tracking.

| Performance | IMC | PID_ZN controller | PID_CC controller |
|---|---|---|---|
| Overshoot (%) | 0 | 2.533 | 2.362 |
| Settling Time(min) | 55.9131 | 81.738 | 65.481 |
| Range of insulin infusion rate (mU/min) | (3.699, 14.019) | (-91.897, 109.14) | (-91.27, 14.671) |

**Conclusions**

IMC was successfully applied to a blood glucose regulation in a patient with diabetic type-1. Parameter tuning for the IMC was based on percentage settling time (% OLST) of the open loop model representing the diabetic patient. It was found that the larger the % OLST the more sluggish is the response. The parameter setting that gave reasonable is response 5% OLST without violating input constraint (no negative insulin infusion rate). The reduced-order controller gave slower response when compared full-order controller while PID controllers from Zeigler-Nichols and Cohen-Coon gave aggressive response with overshoot and both violate input constraint. We therefore conclude that IMC scheme outperform PID schemes based on conventional tuning parameters.

**REFERENCES**

Bequette, B. W. (2002). *Process Control: Modeling, Design, and Simulation.* New Jersey: Prentice Hall PTR.

Bergman, N. R. (2005). Minimal Model. *Hormone Research* , 64 (supl 3):9-15.

Boiroux, D., Schmidt, S., Madsen, H., & Madsbad, S. (2012). Control of Blood Glucose for People with Type 1 Diabetes. *Seventeenth Nordic Process Control Workshop* (pp. 133-140). Denmark: Kgs Lyngby.

Chase, G. J., Lam, Z. H., J.Y., L., & Hwang, K. (2002). Active Insulin Infusion Control of the Blood Glucose Derivative. *Seventh International Conference on Control, Automation, Robotics and Vision*, (pp. 1162-1167). Singapore.

Clarke, S. F., & Foster, J. (2012). A history of Blood Glucose Meters and their Role in Self Monitoring of Diabetes Mellitus. *British Journal of Biomedical Science* , 69(2): 83-93.

Doyle, F., Jovanovic, L., & Seborg, D. (2007). Glucose control strategies for treating type 1 diabetes. *Journal of Process Control* , 572-576.

Ibbini, M. S. (2008). Comparative Study of Different Control Techniques. *International Conference on Biomedical Electronics and Biomedical Informatics* (pp. 106-110). Rhodes: Ramtha-Irbid.

International Diabetes Federation(IDF). (2013). *Diabetes Mellitus.* Retrieved from IDF website : www.idf.org

Kamath, S. (2014). Model Based Simulation for Type I Diabetic Patients. *Journal of Control Engineering and Technology* , 17-21.

Klonoff, C. D. (2007). The Artificial Pancreas:How Sweet Engineering will olve Bitter Problems. *Journal of Diabetes Science and Technology* , 72-81.

Parker, R. S., Doyle, F. J., & Peppas, N. A. (1999). A Model-Based Algorithm for Blood Glucose Control in Type I Diabetic Patients. *IEEE Transactions on Biomedical Engineering* , 148-157.

Rivera, D. E., & Flores, M. E. (2004). Internal Model Control. *Control System, Robotics anc Automation* , 25-33.

Sh Yasini, M., & Naghibi-Sistani, A. K. (2009). Agent-based Simulation for Blood Glucose. *International Journal of Applied Science, Engineering and Technology* , 40-47.

Sh. Yasini, M. B., & Naghibi-Sistani, A. K. (2008). Active Insulin Infusion Using Fuzzy-Based Closed-loop Control. *International Conference on Intelligent System and Knowledge Engineering*, (pp. 429-434). Iran.

Skogestad, S. (2003). Simple analytic rules for model reduction and PID controller tuning. *Journal of Process Control , 13* , 291–309.

Sukha, A. Y. and Rubin, A. (2007). Definition, classification and visual aspects of diabetes mellitus, diabetic retinopathy and diabetic macular edema. *The South African Optometrist* , 120-31.

Van Herpe, T., Pluymers, B., Espinoza, M., Van den Berghe, G., & De Moor, B. (2006). A minimal model for glycemia control in critically ill patients. *EMBS Annual International Conference*, (pp. 5432-5435). New York.

World Health Organization. (1999). *Definition, Diagnosis.* Genev.

Youssef, E. J., Castle, J., & Ward, W. K. (2009). A Review of Closed-Loop Algorithms for Glycemic Control in. *Algorithms* , 518-532.