

Optimal PID Insulin Injection Control For Blood Glucose Regulation in IDDM Patient

A K Patra¹, R K Samantaray², (DR) J K Maharana^{3*}

1. Department of Electrical & Electronics Engineering, I.T.E.R, 'SOA' University, Odisha, India

2. Department of ECE, REC, Bhubaneswar, odisha, india

3. Dept of EEE, GITA, Bhubaneswar, Odisha, India

hiakp@yahoo.com, samantaray.ranjan75@gmail.com

Abstract: This paper address the design of output feedback PID controller to deliver insulin via an implantable micro insulin dispenser for insulin dependent diabetes mellitus (IDDM) patients. For synthesis of the controller, a 9th order linear state space model of the multivariable nonlinear dynamic glucose insulin process of the IDDM patient has been used. The performance of the resulting controller was tested on the nonlinear model of the process in simulation platform implants of the insulin pump & glucose sensor. The controller performance was assessed in terms of its ability to track a normoglycemic set point of 81 mg/dl in presence of once daily meal disturbance & once daily exercise disturbance with other stochastic noises. With an appropriate patient model, simulation studies have shown that the controller could correct the BG deviation using clinically acceptable insulin delivery rates.

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I. INTRODUCTION

In modern fast life style pattern, for the intensive treatment of type-1 or insulin dependent diabetes mellitus (IDDM) patient, continuous & controlled release of insulin to the blood stream is necessary to maintain a specific level of Blood glucose (BG) in presence of normal meal & activity disturbances [1,2]. Effective & successful control of biological processes is a meticulous & non – trivial task over it's complete operating range & patient variations. The complex nonlinear process of glucose metabolism is linked to a number of internal factors, which are not always measurable. With accessible information like occasional blood glucose sensing, amount of food intake & other activity conditions, the system appears highly stochastic. The closed loop control involves interplay between the nonlinear dynamics of the physiological process, the stochastic nature of the disturbances & the insulin command with on-line & implantable sensor & actuating devices [3 - 5].

BG regulation is necessary in physiological process in presence of process & sensor noises, where it is very difficult to establish a priori the exact relationship amongst the interacting sub-processes due to dynamic nonlinearities & parameter variations from patient to patient. The classical control objectives like noise rejection, shaping of open loop response can be expressed in terms of PID performance & well tackled by PID synthesis [8 - 9]. This paper addresses the patient model showing linear & nonlinear physiological blocks & the design

of a PID controller for closed loop BG regulation by output feedback [8].

A 9th order linear state space model from the first principle nonlinear model [6,10,11] of process has been considered for the design. Performance in the bandwidth region, defined as the portion of the frequency spectrum in which control is effective, was tested on the simulated nonlinear process with deterministic meal & exercise inputs in presence of other noises. The section II describes the function of glucose, insulin & their interaction processes. Section III gives the idea of classical PID controller synthesis. In section IV, the response & the performance characteristics of the patient model (open loop system) is presented. In section V, the response & the characteristic of the resulting controller for BG regulation in an IDDM patient is presented.

II. SYSTEM OVERVIEW

The closed loop drug delivery system for BG regulation necessarily requires a patient model, which is simulated from the equations relating the nonlinear dynamics of physiological process [4,5] in presence of uncertainties & disturbances as shown in block diagram of figure-1.

For IDDM patient model, u = actuator signal (insulin dose), y = glucose level error, z_1 = plasma glucose level, z_2 = insulin infusion rate, w_1 = reference glucose, w_2 = meal disturbance, w_3 = exercise disturbance, w_4 = actuator noise & w_5 = sensor noise.

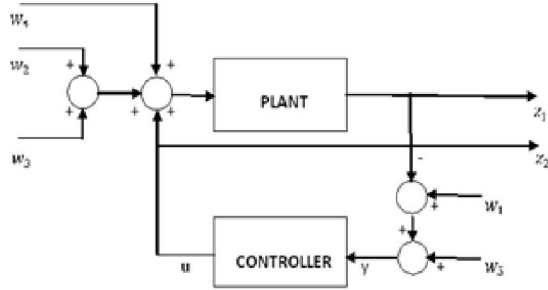


Fig1. Block diagram of IDDM patient model with closed loop control

A. The physiological process:

Diabetes Mellitus is a chronic disorder of metabolism process caused by the inability of the pancreas to produce sufficient amount of insulin or resistance of insulin action or both. Which leads to uncontrolled increase of BG level exceeding 144mg/dl, called **hyperglycemia**. The glucose metabolisms in a healthy are maintained within tight tolerances & are controlled by the secretion of insulin. Treatment of IDDM patient to maintain normal range of BG level (**normoglycaemia**) is mainly done by administering insulin intermittently through subcutaneous injection or through an implantable insulin pump in closed loop [1-2].

B. Function of Glucose:

Glucose is absorbed in the circulation from food (mainly carbohydrate) at various parts of our digestive systems, generally termed as 'gut'. This is the "external" source of blood glucose. The venous blood draining gut absorbs glucose & transports to the liver where glucose is stored as **glycogen** & released again into the circulation by the process of gluconeogenesis when BG level drops too low between the meals. This is the 'internal' source of glucose. Inside a cell, with the help of oxygen, glucose is metabolized into water, carbon dioxide & produces energy [1]. It is utilized in adipose tissues, RBCs, central nervous system (CNS) & also cleared by the kidney when it's level exceeds renal threshold [2].

C. Function of insulin:

Insulin is the key hormone, synthesized in the β -cells of the "Islets of langerhans" in the pancreas, involved in the storage of controlled release of chemical energy in the cells. The function of insulin is two folds: (1) it is carried to the liver through portal circulation helping the liver to take up glucose to store as glycogen, shuts off excess

'internal sugar' production In liver & muscle when glucose level is high at meal times; & (ii) insulin as a catalyst, forms a complex that promotes glucose uptake in muscles & 'periphery' for energy [1,2].

D. Glucose – Insulin interaction process:

In IDDM, the patient is completely lacking the endogenous insulin production & a single glucose pool represents the extra-cellular glucose. Both of the above functions of insulin are absent; cells do not get energy, but liver produces 'internal' sugar resulting in uncontrolled rise of BG concentration. In modern intensive therapy, arterial glucose concentration is regulated (to 81mg/dl or 4.5 mmol/l) by the controlled infusion of 'fast acting' insulin (over a basal dose of 22.3 mU/min) through the implanted insulin pump [3,4] at a regular time interval by adjusting the dosage adaptively to the daily schedule of meals & exercise.

The compartmental model of the Glucose-Insulin (GI) process given by Lehmann et al. [5], is mostly followed in BG regulation problem, which uses the **pharmacokinetic** model of insulin action & **pharmacodynamics** of glucose model. The model uses the underlying patho-physiology of insulin action and carbohydrate absorption in terms of insulin sensitivity. Volume of glucose & insulin, dynamic nonlinear sub processes like gastric emptying rate, peripheral utilization, net hepatic glucose balance (NHGB), renal excretion rate etc. RBC & central nervous system takes up glucose independent of insulin present in the circulation. The various blocks of the nonlinear model shown in figure – 2 have been realized [7] in SIMULINK to illustrate the dynamics of glucose production & utilization in various organs & insulin action on it including that of insulin dispenser system.

E. linearized State space model of physiological process:

The 'patient model' of glucose-insulin process of figure -2 is a non-linear one with five inputs & two outputs. Our purpose in this section is to find a linear state space model for blood glucose regulation process. The state space model of the corresponding LTI system is expressed as

$$\dot{x} = A x + B u + G w$$

$$Y = C x + D u$$

Where A, B, C, G & D are the system matrices of appropriate order, x is the state space vector of the process, u is the insulin infusion input & w is the disturbance input vector.

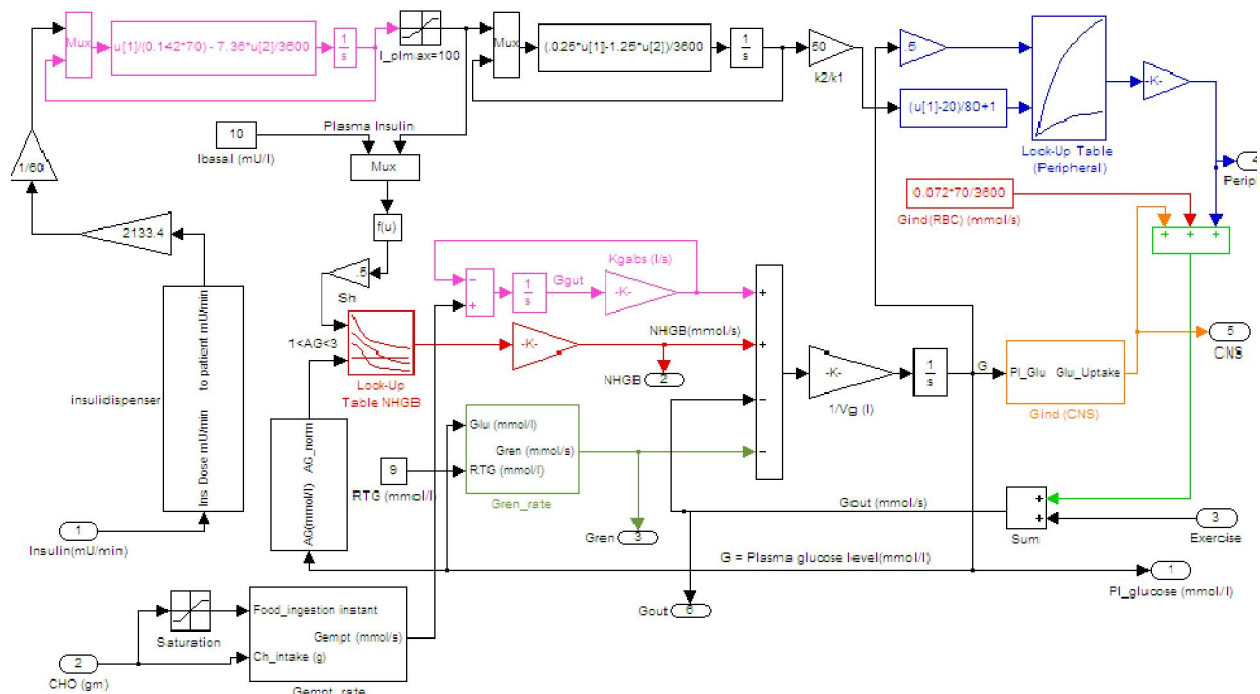


Figure-2 ‘Patient model’ showing linear & nonlinear patho - physiological blocks

The linearized model of the system is obtained by using *linmod* command of MATLAB on the SIMULINK block ‘patient model’ with five inputs & two outputs. The continuous time system matrices of equation (1) for the linear model of present process & implantable pump with fixed parameters, thus obtained are;

$$A = \begin{bmatrix} -0.0001 & 0.000016 & -0.00008 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -0.0003 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -0.002 & 0 & 0 & 11447 & 0 & 0 & 0 \\ 0 & 0 & 0.000007 & -0.0003 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -240 & -2560 & 0 & 0 & 0.125 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -125 & -72.67 & -33.335 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

$$B = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad G = \begin{bmatrix} 0 & -0.057143 \\ 1 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

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

$$D = [0]$$

III. CLASSICAL PID CONTROLLER SYNTHESIS

A PID controller system is shown in figure -1. Where it can be seen that in a PID controller, the

error signal $y(t)$ is used to generate the proportional, integral & derivative actions with the resulting signals weighted & summed to form the control signal $u(t)$ is applied to the patient model. The transfer function of PID controller looks like the following [14 - 19].

$$T.F = K_p + \frac{K_I}{s} + k_D s = \frac{K_D s^2 + K_P s + K_I}{s} \quad (2)$$

A mathematical description of the PID controller is

$$u(t) = K_p y(t) + K_I \int y(t) dt + K_D \frac{dy(t)}{dt} \quad (3)$$

$$u(t) = K_p \left[y(t) + \frac{1}{T_I} \int y(t) dt + T_D \frac{dy(t)}{dt} \right] \quad (4)$$

Where $u(t)$ is control input to the plant model, $y(t)$ is the error which is difference between the actual output $z_1(t)$ & reference input $w_1(t)$, K_p is proportional gain, K_I is integral gain, K_D is the derivative gain, T_I is integral time constant & T_D is derivative time constant.

A. The characteristics of P, I & D Controllers:

A proportional controller (K_p) will have the effect of reducing the rise time & will reduce but never eliminate the steady state error. An integral control (K_I) will have the effect of eliminating steady state error but it may make the transient response worse. A derivative control (K_D) will have the effect of increasing the stability of the system, reducing the overshoot & improving the transient response. Effect of each controller K_p , K_D & K_I on a closed loop system are summarized in the Table shown below [12 - 14].

Table 1. K_p , K_D & K_I on a closed loop system

CL Response	Rise Time	Over shoot	Setting time	S.S error
K_p	Decrease	Increase	Small change	Decrease
K_I	Decrease	Increase	Increase	Eliminate
K_D	Small change	Decrease	Decrease	Small change

B. General Tips for designing a PID controller:

When you are adjusting a PID controller for a given system, follow the steps shown below to obtain a desired response.

1. Obtain an open loop response & determine what needs to be improved.
2. Add a proportional control to improve the rise time.
3. Add a derivative control to improve the overshoot.
4. Add a integral control to eliminate the steady state error.
5. Adjust each of K_p , K_I & K_D until you obtain a desired overall response, you can always refer to the table shown in this document to find out which controller controls what characteristics.

IV. THE RESPONSE & PERFORMANCE OF THE “PATIENT MODEL” (OPEN LOOP)

Before we design the compensator for the patient model, it is expected to analyze the pure dynamics. In this section, we study the transient response of blood glucose level for an uncontrolled process (SIMULINK diagram for nonlinear ‘patient model’, open loop, figure-3) with constant insulin infusion of 22.3mU/min (basal dose) for specified disturbances. At $t = 40000s$ meal is applied to ‘patient model’, meal is converted to glucose by digestive system (generally termed as ‘Gut’), then glucose is added to venous blood, that response of Gut rate (mmol/s) is shown in figure 4(e). Response of glucose level (mg/dl) in venous blood with application of 60 gm meal at $t = 40000s$ & exercise at $t = 80000s$ is shown in figure – 4(a). It is seen that glucose level is increased in uncontrolled manner due to shortage of insulin dose in patient model. In diabetics patient, pancreas is unable to produce sufficient amount of insulin when meal is injected to it, that response of insulin dose is shown in figure – 4(b). Due to shortage of insulin in ‘patient model’, glucose level is increased in uncontrolled manner, when that level exceeds renal threshold value, when that level exceeds renal threshold value, that extra amount glucose is injected outside through urine by help of kidney, that response of GRen rate (mmol/s) is shown in figure – 4(d). Since insulin level is very low in ‘patient model’, internal sugar production in liver can not be stopped, that response of NHGB rate (mmol/s) is shown in figure – 4(c). It shows a large effect of meal disturbance (w_2) on the glucose level than the other disturbances.

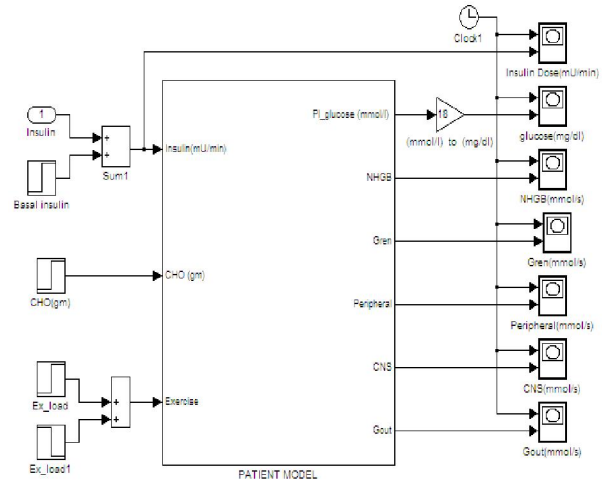


Figure-3 SIMULINK diagram of non-linear ‘patient model’

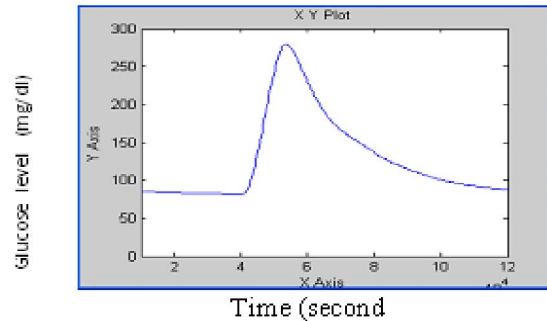


Figure-4 (a) Response of glucose level (mg/dl)

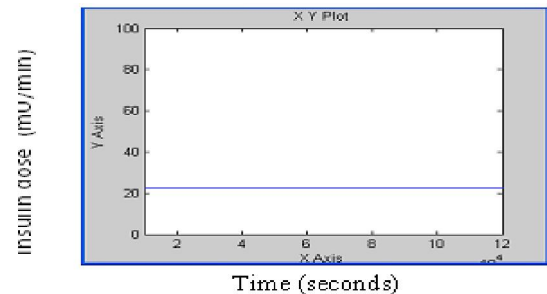


Figure-4 (b) Response of insulin dose (mU/min)

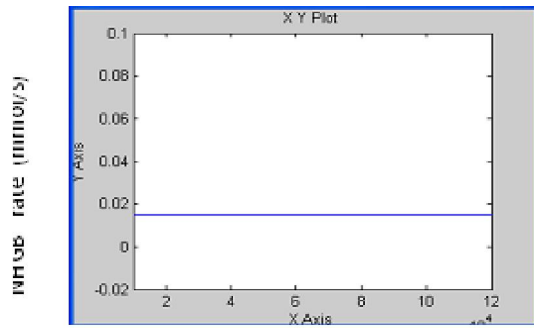


Figure-4 (c) Response of NHGB rate (mmol/s)

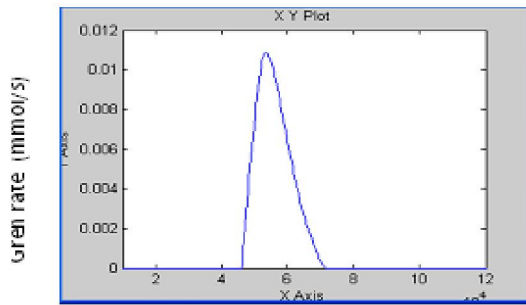


Figure-4(d) Response of Gren rate (mmol/s)

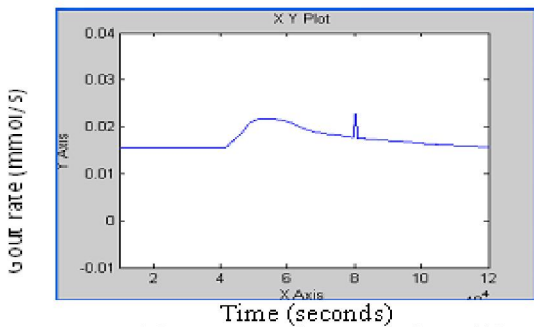


Figure 4 (e) Response of Gut rate (mmol/s).

V. THE RESPONSE & PERFORMANCE OF THE “PATIENT MODEL” WITH PID CONTROL:

In this section, we study the response of the glucose insulin process with PID control for the process of 60 gm meal at $t = 40000s$ & exercise of 0.005 arbitrary units at $t = 80000s$ along with additive sensor noises. PID controller design has been applied on the simulated non-linear ‘patient model’ & data from linearized system matrices have been used for on-line design of closed system [20-21] as shown in figure - 5. The PID controller gains (K_p , K_I & K_D) have been computed by using MATLAB routines. The ‘patient model’ block in figure-5 represents combination of the physiological process & the implanted insulin delivery device. The closed loop system compares the output plasma BG level with reference glucose level of 4.5 mmol/l (81mg/dl) &

PID controller generates insulin, correction over the nominal (basal) rate 22.3mU/min to maintain normoglycemia. The model has been tested in closed loop by varying glucose intake & exercise. In this section we study the transient response of blood glucose level for a controlled process with constant insulin infusion of 22.3mU/min (basal dose) for selected disturbances.

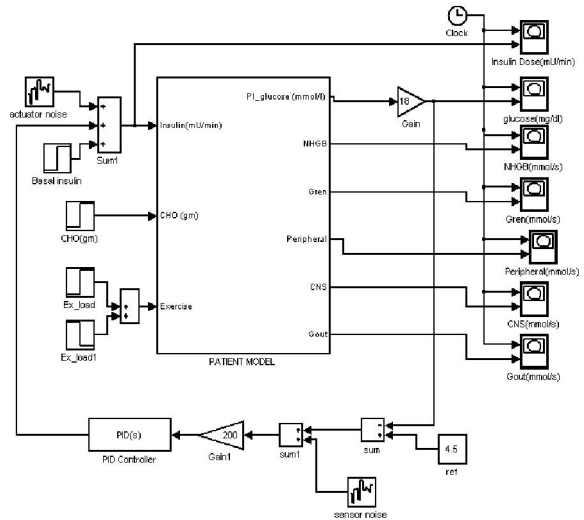


Figure-5 SIMULINK diagram of ‘Patient model’ with PID controller

The response of Glucose level (mg/dl), Insulin dose (mU/min), NHGB rate (mmol/s), Gren rate (mmol/s), Gut rate (mmol/s) with application of 60 gm meal at $t = 40000s$ & exercise at $t = 80000s$ are shown in figure-6 at optimal values of controller gains ($K_p = -0.00081501426299255$, $K_I = -4.58670797308168e-008$ & $K_D = 0.91008840596103$).

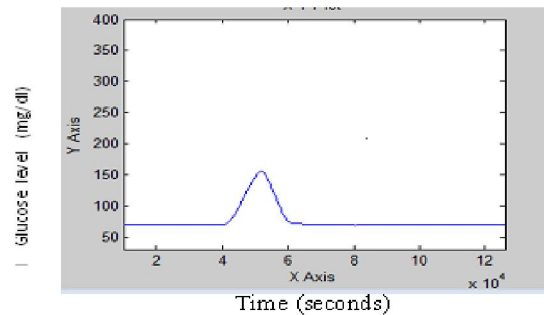


Figure -6 (a) Response of Glucose level (mg/dl)

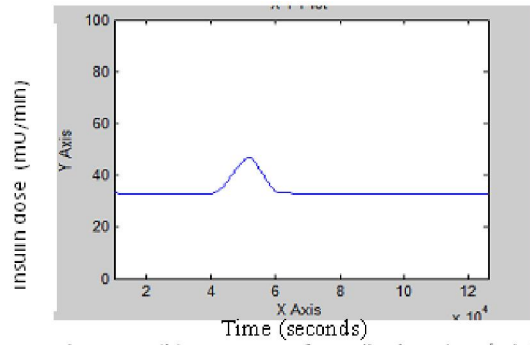


Figure – 6 (b) Response of Insulin dose (mU/min)

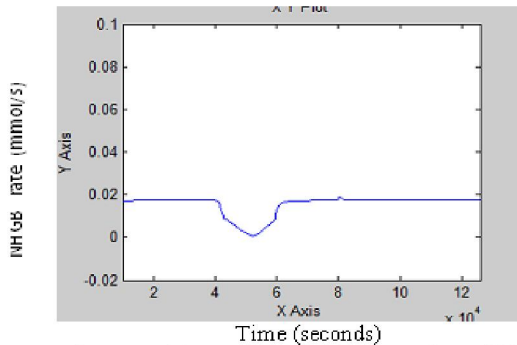


Figure – 6 (c) Response of NHGB rate (mmol/s)

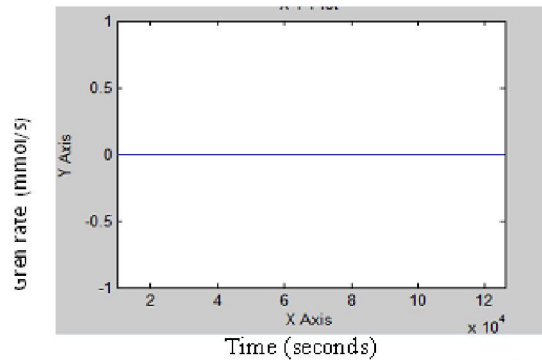


Figure – 6 (d) Response of GRen rate (mmol/s)

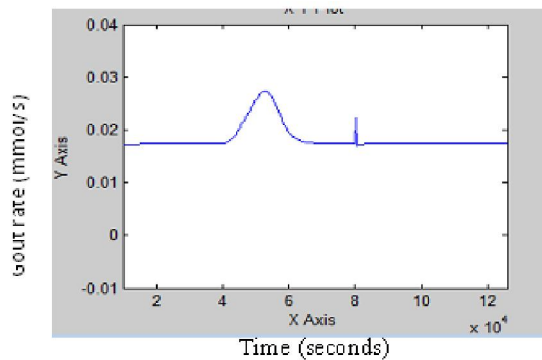


Figure – 6 (e) Response of Gut rate (mmol/s)

VI. CONCLUSION:

Designed optimal PID controller gives a good performance, create poor robustness & high exceeding. It is obvious that in case of few parameter changes of the plant led to decline of the performance of the PID controller drastically. Thus it is not enough to control process dynamics swimmingly although it is good start to tune PID parameters. The present study is focused on the modeling & identification of the physiological process of Glucose-Insulin interaction in Type-1 diabetes patient & design of optimal PID controller for implantable insulin delivery system in all possible physiological conditions & disturbances of type-1 diabetes patient.

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