

Simulation of Multiple Delay based Blood Glucose Metabolism using Dynamic Matrix Control

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Abstract - The presented paper deals with a multiple delay glucose-insulin regulatory system, analysis and the methodology of control strategy with Dynamic Matrix Control. The intent of the work is to avoid risk of patients with Type I diabetes mellitus by predicting the future *glucose* concentrations based on the model.

Key Words: Model Predictive Controller (MPC), Dynamic Matrix Control (DMC), hyperglycemia

1. INTRODUCTION

Diabetes Mellitus is a chronic, lifelong, metabolic disorder which affects human health. Diabetes includes both micro vascular and macro vascular diseases. Varying exogenous & endogenous disturbances are the main reason for the disease which includes food intake, exercise etc. Tight control of blood glucose levels overcomes prolonged complications. Current medical treatment procedure consists of insulin delivery and frequent exercise. Diabetes Mellitus is mainly classified into two major groups: Type I and Type II diabetes. Major difference between type I (insulin dependent) and type II diabetes (non-insulin dependent) is that the former is juvenile onset and the latter is adult onset[1]. Mathematical model helps us to approximate the actual, physiologic & metabolic processes of the system.

1.1 Insulin-glucose regulatory system

Diabetes Mellitus increases blood glucose concentration. Endocrine hormones namely insulin and glucagon maintains glucose homeostasis in our blood. In Pancreatic duct there is a cluster of cells called Islets of Langerhans which consists of β -cells, responsible for the production of insulin in our body. As glucose level increases, β -cells release insulin causing huge intake of glucose by fat cells and muscles. Insulin also stimulates liver cells to absorb the left over glucose.[2] α -cells of the pancreas releases glucagon when the glucose level is too low. Glucagon stimulates liver cells to release the left over glucose providing enough insulin-glucose regulation in our body. If the level of glucose persistently increases in the range of 70-110mg/dl results in hyperglycemia progressively leading to diabetes. Fig.1 shows the glucose-insulin feedback methodologies.

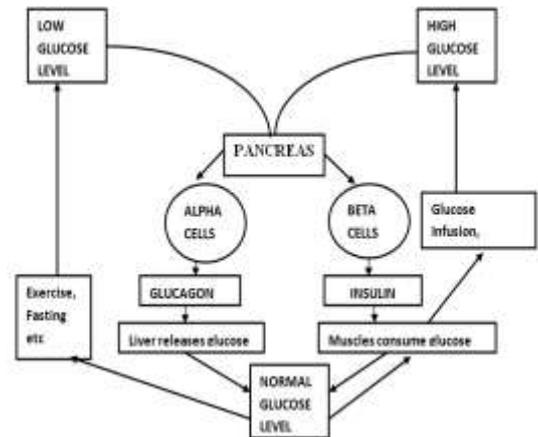


Fig -1: Physiological Insulin Glucose Regulatory System

2. MULTIPLE DELAY MODEL

2.1 Three Main Delays

Elevated glucose concentrations lead to slow oscillations in liver and pancreas. Oscillations are of two types namely: Rapid Oscillations (5-15min) [3], Ultradian Oscillations (50-150min) leaving behind a fact of instability in glucose-insulin endocrine metabolic systems. Oscillations perform delayed effect.

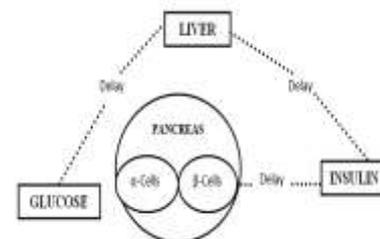


Fig.2. Multiple Delay based glucose insulin metabolism-proposed model

One is due to pancreatic β -cells during the production of insulin. Second delay represents insulin effect on hepatic glucose. Third delay is on the production of residual glucose by liver cells. Fig.2. illustrates the proposed model. Multiple Delay based glucose insulin metabolism includes two equations of the form:

$$\frac{dG(t)}{dt} = G_\gamma - f_2(G(t)) - f_3(G(t))f_4(I(t - \tau_2)) + f_5(I(t - \tau_0)) \quad (1)$$

$$\frac{dI_p(t)}{dt} = bf_1(G(t - \tau_1)) - \frac{I_i}{t_i} \frac{dI_i(t)}{dt} \quad (2)$$

G specifies glucose concentration in both plasma and intercellular space, I_i specifies insulin concentration in intercellular space, I_p Specifies insulin concentration in plasma, $f_1(G)$ and $f_4(I)$ represents first order polynomial, $f_2(G)$ and $f_3(G)$ denotes constant, $f_5(I)$ represents third order polynomial, τ_0, τ_1, τ_2 are the delays with rate of infusion $216\text{mg}\cdot\text{min}^{-1}$. Fig.3, Fig.4 depicts Simulink output for glucose and insulin profiles with single delays ([4], Wang *et al.*, 2007) & Fig.5, Fig.6 depicts Simulink output for glucose and insulin profiles with multiple delays respectively. Insulin degradation occurs in liver and Kidney. Source of glucose are carbohydrates, sugar, fibers etc.

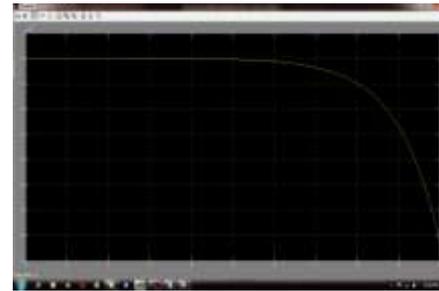


Fig.6. Insulin profile with multiple delay

Step response in Fig.7 tells the ability to reach stationary point of the system. Impulse response (fig.7) explains the output in time domain. Bode plot can easily find frequency range for system dynamics. Fig.8. infers bode plot with first two dimensions of magnitude and phase as equal to 1. The frequency is measured to be 33. Nyquist Plot (Fig.8) shows the real and imaginary part of the model with real values in the range of $1.0336\text{e-}30$, $4.1344\text{e-}30$, 104.6805 etc. and imaginary values in the range of $6.7520\text{e-}05$, $1.6880\text{e-}04$, 0.0017 etc.

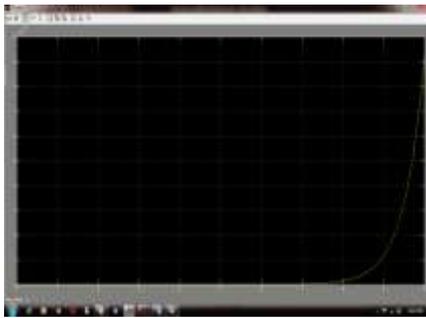


Fig.3. Glucose profile with single delay



Fig.4. Insulin profile with single delay

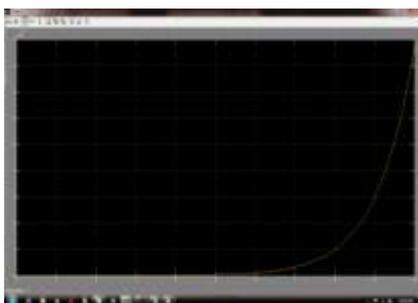
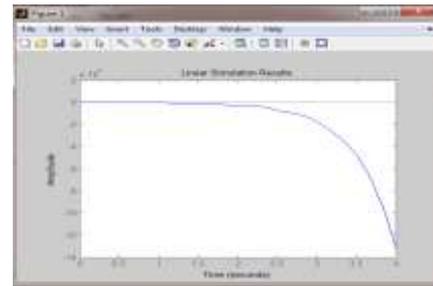
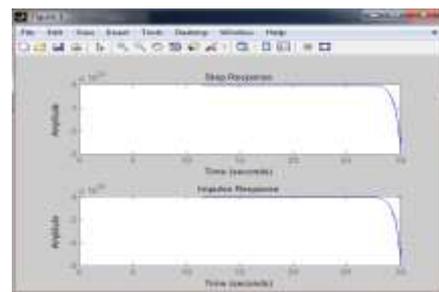


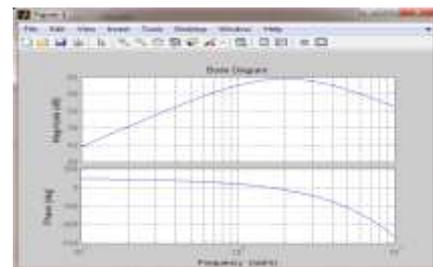
Fig.5. Glucose profile with multiple delay



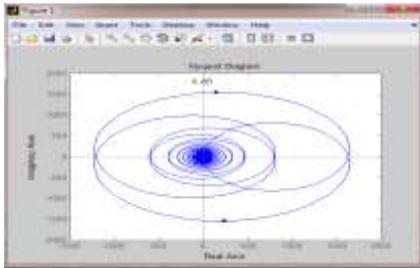
7(a)



7(b)



7(c)



7(d)

Fig.7(a)&(b) Linearization, Step & impulse response of the proposed model Fig.7(c) &(d) Bode plot and Nyquist plot of the proposed model

3. MODEL PREDICTIVE CONTROLLER(MPC)

Model Predictive Controller optimizes insulin infusion rate. MPC handles constraints properly with a deep estimate about the future. MPC includes parameters such as receding horizon, preceding horizon, optimization problem having objective functions like step and impulse response, Cost function.

3.1 Dynamic Matrix Control(DMC)

Dynamic Matrix Control(DMC) is a form of model predictive controller. The performance evaluation is done by Objective function[5]. The quadratic objective function is given by Performance is measured with prediction horizon 3 and control horizon 2.

$$\Phi = (R_{K+1} - \hat{Y}_{K+1})^2 + (R_{K+2} - \hat{Y}_{K+2})^2 + (R_{K+3} - \hat{Y}_{K+3})^2 + w\Delta U_K^2 + w\Delta U_{K+1}^2 \tag{3}$$

Entire Optimization is performed using DMC. Simulation results exhibit robustness, stability against parameter changes. Least mean square is the commonly used optimization function. Minimization of objective function leads to optimization. Prediction horizon and control horizon vary in their length with Prediction horizon as a larger value.

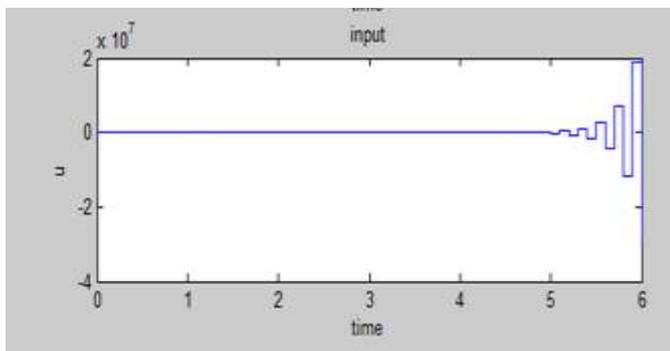


Fig.8. Dynamic control input

DMC uses step response model to predict future values of output. The model provides input in the form of step signal, with linear response relating output as a sum of weighted past values. Weight matrix (W) specifies control action.

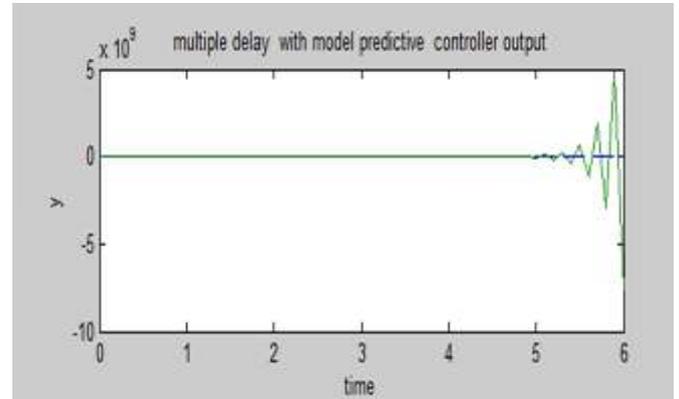


Fig.9. Multiple delay with Dynamic control MPC output

If Prediction horizon is too short uncertainty[6] occurs. Introduction of noise, input and output disturbances adds the offset tracking. Fig.10. shows the input with noise added.

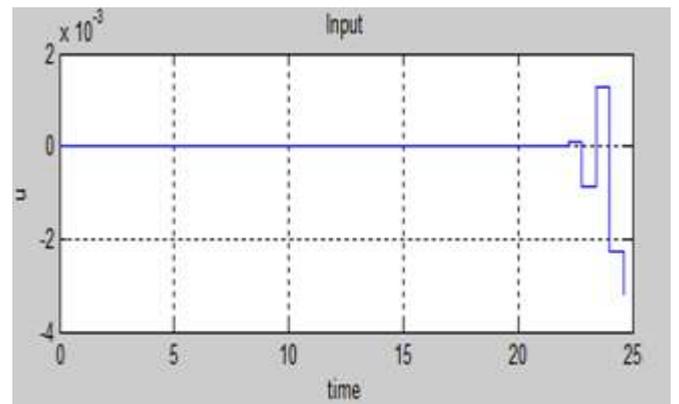


Fig.10. Input with added noise

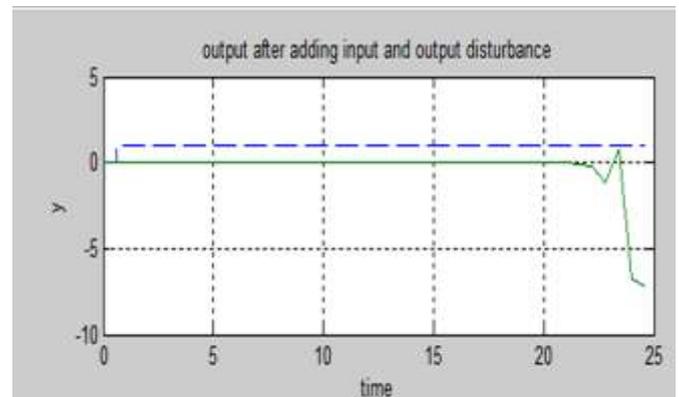


Fig.11. Output of DMC with added noise

4. Conclusion & future work

Multiple delay with Model Predictive Controller optimizes and stabilizes glucose-insulin metabolism. Multiple delay gives robustness in the estimation of diabetes. This is an ongoing research work and extension aims at implementation using FPGA.

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