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ARTIFICIAL PANCREAS BASED ON MODEL PREDICTIVE CONTROL

R. Helen
Department of Electrical and Electronics Engineering, Thaigarajar College of Engineering, Madurai, Tamil Nadu, India
E-Mail: rheee@tce.edu

ABSTRACT

Diabetes is recognized as a group of heterogeneous disorders with the common elements of high blood glucose concentration and glucose intolerance, due to insulin deficiency and impaired effectiveness of insulin action. The most common types of diabetes are diabetes mellitus type 1 and diabetes mellitus type 2, which does not necessarily require insulin injections. Type 2 constitutes about 85 to 95% of the approximately 246 million people worldwide with diabetes. The number of type 1 diabetics is estimated to be 10 to 20 million worldwide. Type 1 diabetes occurs when these beta cells are destroyed by the body's own immune system. So, the model is to be developed to recover from diabetes by means of MPC controller. This constrained robust control strategy is developed to reduce risks of hypo- and hyperglycemias (low and high blood glucose concentration). Here the role of controller is to regulate the blood glucose level by giving insulin. Closed-loop performance is evaluated through simulation studies of different controllers and it becomes human friendly.

Keywords: diabetes, artificial pancreas, model-predictive controller, robust controller.

1. INTRODUCTION

In the absence of insulin, the entry of glucose into skeletal, cardiac, smooth muscle and other tissues is decreased. Intestinal absorption of glucose is unaffected by insulin, as is glucose uptake by most of the brain and the red blood cells. When insulin is lacking for a longer period of time, the muscle and tissue cells will start using fat as energy source, instead of glucose from the blood stream. Oxidation of the resulting free fatty acids leads to production of ketone bodies that upset the chemical balance of the blood. This life threatening condition is called diabetic ketoacidosis, and can only be treated by insulin injections. Insulin is a hormone needed to enable glucose to enter the cells in the body in order to provide energy. In response to high levels of glucose in the blood, the artificial pancreas secretes insulin to maintain BG level. A normal blood glucose level is set by the WHO to be a fasting plasma glucose concentration of less than 6:1mmolL. One should take special notice of the fact that blood glucose values below 2:0 mmol/L is an acute and deadly condition, whereas concentrations up to 20mmol/L can be experienced without discomfort, at least for shorter periods of time. These results in a tight bound on the blood glucose concentration downwards, but some deviation can be tolerated for higher than normal blood glucose levels.

The disturbance of meal intake introduces large challenges to automatic blood glucose control. In normal functioning human glucose regulation, increased blood glucose Concentration after a meal is stimulus for prompt release of insulin from the pancreas. The relatively large time constants involved in external blood glucose measurement and insulin injections, makes a response close to the normal-functioning one hard to achieve in automatic diabetic treatment. Complicating matters further is the fact that the composition of food affects intestinal absorption rates. Also, fats and proteins cause delays in absorption of glucose from carbohydrates eaten at the same time. In addition to this, physical exercise affects the blood glucose regulation by reducing the need for insulin and for quite a long time after, work-out. Because working muscle has the ability to absorb some glucose without the help of insulin. Other factors that are even harder to measure, such as stress, physical illness and many more, are involved in the blood glucose regulation process, making accurate models, prediction of parameters and satisfactory closed-loop control hard to achieve.

In 2008, Gianni Marchetti *et al*, An improved PID control strategy for blood glucose control is proposed and critically evaluated in silico using a physiologic model of Hovorka [1].

In 2009 an artificial pancreas strategy using constrained model predictive control is developed to achieve closed-loop glucose control for type 1 diabetes. A system of meal detection and meal size estimation is also developed to automatically administer meal insulin boluses as feed-forward action to unmeasured meals [2].

In 2010, Amjad Abu-Rmileh *et al*, Designed the controller, model-based predictive control scheme has been applied to a newly developed diabetic patient model. The controller is provided with a feed forward loop to improve meal compensation, a gain-scheduling scheme to account for different BG levels, and an asymmetric cost function to reduce hypoglycemic risk [3].

In 2011, the system is developed based on a nonlinear model-predictive controller (NMPC) that uses a personalized glucose–insulin metabolism model, consisting of two compartmental models and a recurrent neural network. The model takes as input patient's information regarding meal intake, glucose measurements, and insulin infusion rates, and provides glucose predictions. The predictions are fed to the NMPC, in order for the latter to estimate the optimum insulin infusion rates. An algorithm based on fuzzy logic has been

developed for the online adaptation of the NMPC control parameters [4].

In 2012, B. Wayne Bequette, A closed-loop Artificial Pancreas (AP) with the use of meal feed forward control. In 2013, Matteo Ottavian *et al*, A novel automatic adaptive control strategy based on frequent glucose measurements and a self-tuning control technique is validated based on a simulation study for 200 virtual patients. The adaptive control strategy is shown to be highly effective in controlling blood glucose concentration [5].

2. PROBLEM DESCRIPTION

The controllers are both conventional and intelligent. But it holds only for linear setup of the system. While dealing with the non-linear system operations, the system should be first trimmed to a particular state and linearised. This linearised version of the non-near system could be precisely control using conventional intelligent controllers (i.e. robust controllers such as ANFIS, MPC).

3. METHODOLOGY

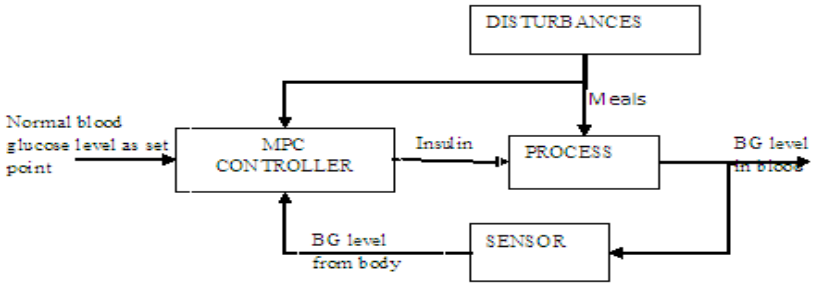


Figure-1. Methodologies for artificial pancreas.

Model Predictive Control (MPC) is a control strategy that offers attractive solutions, already successfully implemented in industry, for the regulation of constrained linear or nonlinear systems. In this method, the MPC controller design methodology will be employed for the regulation of constrained hybrid systems. One of the reasons for the success of MPC algorithms is their ability to handle hard constraints on state outputs and inputs shown in Figure-2. Stability and robustness are probably the most studied properties of MPC controllers, as they are indispensable to practical implementation. A complete theory on (robust) stability of MPC has been developed for linear and continuous nonlinear systems. However, these results do not carry over to hybrid systems easily.

As a starting point, the stability and input-to-state stability that allows for discontinuous and nonlinear system dynamics. These results act as the theoretical foundation of the thesis, enabling us to establish stability and robust stability results for hybrid systems in closed-loop with various model predictive control schemes. The (nominal) stability problem of hybrid systems in closed-loop with MPC controllers is shown in Figure-1.

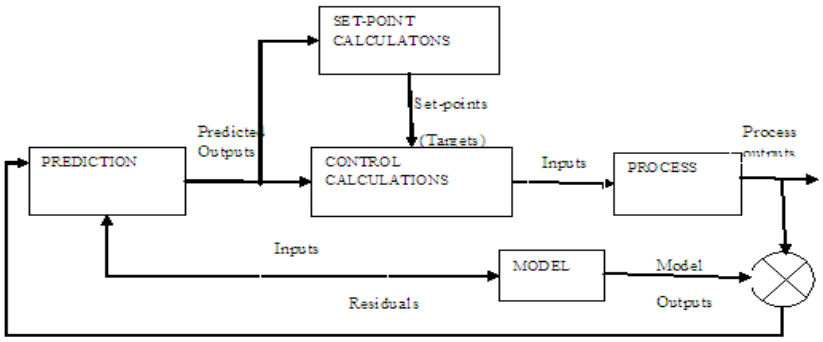


Figure-2. Model predictive controller for the system.

Prevent violations of input and output constraints drive some output variables to their optimal set points, while maintaining other outputs within specified range. Prevent excessive movement of the input variables. Future values of output variables are predicted using a dynamic model of the process and current measurements. Unlike time delay compensation methods, the predictions are made for more than one time delay ahead. The control calculations are based on both future predictions and current measurements. The manipulated variables, $u(k)$, at the k-th sampling instant are calculated so that they minimize an objective function J. Here the Unconstrained Optimal Control, Computation of Cost Function, Unconstrained Optimal Control, RICATTI Equation,

Constrained Optimal Control Problem, (Quadratic Performance Index), Constrained Optimal Control and the

Constrains: $\begin{cases} u_{min} \le u(t) \le u_{max} \\ y_{min} \le y(t) \le y_{max} \end{cases}$ (1)

4. MATHEMATICAL MODELLING AND SIMULATION FOR ARTIFICIAL PANCREAS

The model used in this thesis is an expanded version of the minimal model developed by Bergman which is tabulated in Table-1. The elements that added to the original minimal model equations are from (1)-(17) The model equations are given as:

$$\frac{dI(t)}{dt} = \frac{1}{T_{xi}}[-I(t) + K_i S(t)] \quad (2)$$

$$\frac{dX(t)}{dt} = \frac{1}{T_m}[-X(t) + I(t)] \quad (3)$$

$$\frac{dS(t)}{dt} = \frac{1}{T_i}[-S(t) + U(t)] \quad (4)$$

$$\frac{dG(t)}{dt} = \frac{G(t)}{T_{YG}} + \frac{Y(t)}{T_{GY}} + \frac{1}{V_G}[E_g(t) + E_b(t)] - E_r(t) \quad (5)$$

$$\frac{dY(t)}{dt} = K_{YG}\left[\frac{G(t)}{T_{YG}} - \frac{Y(t)}{T_{GY}}\right] - K_{is}X(t)Y(t) \quad (6)$$

Equations (2-4) →Insulin kinetics, third order, linear system and (5- 6) →Glucose kinetics, second order, non linear system.

4.1 Insulin Kinetics

X1=I (t), X2=X (t), X3=S (t). (7)

The general matrix is,

$$\begin{bmatrix} \dot{X}_1 \\ \dot{X}_2 \\ \dot{X}_3 \end{bmatrix} = \begin{bmatrix} -\frac{1}{T_{xi}} & 0 & \frac{K_i}{T_{xi}} \\ \frac{1}{T_m} & -\frac{1}{T_m} & 0 \\ 0 & 0 & -\frac{1}{T_i} \end{bmatrix} \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ \frac{1}{T_i} \end{bmatrix} U(t) \quad (8)$$

The insulin kinetics sub model simulation is shown in Figure-1.

4.2 Glucose Kinetics

X_4=G (t), X_5=Y (t). (9)

The matrix is,

$$\begin{bmatrix} \dot{X}_4 \\ \dot{X}_5 \end{bmatrix} = \begin{bmatrix} -\frac{1}{T_{YG}} & \frac{1}{T_{GY}} \\ \frac{K_{YG}}{T_{YG}} & -\frac{K_{YG}}{T_{YG}}\left(\frac{K_{YG}}{T_{YG}} + K_{is}X(t)\right) \end{bmatrix} \begin{bmatrix} X_4 \\ X_5 \end{bmatrix} \quad (10)$$

The glucose sub model consists of the blood plasma and subcutaneous compartment. This is because the glucose monitor measures glucose concentrations in the subcutaneous compartment Y (t), even though this value lags some time behind the actual blood glucose concentration G (t).

The modelled parameters are used for the calculated equations to simulate the sub models.

$$E_b = Q_r - Q_c \quad (11)$$

$$E_{rel} = \frac{14}{I} - 0.17 \quad (12)$$

$$Q_r = \begin{cases} 0.88 & \text{if } E_{rel} > 0.88 \\ E_{rel} & \text{if } 0.88 \ge E_{rel} \ge 0 \\ 0 & \text{else} \end{cases} \quad (13)$$

$$Q_g = \begin{cases} 0.061G - 0.25 \text{ if } 0.061G - 0.25 \ge 0.23 \\ 0.23 \text{ else} \end{cases} \quad (14)$$

$$Q_c = 0.25E_g + Q_g \quad (15)$$

$$E_m = 0.117\left(0.87 + \tanh 0.0045(G - 175)\right) \quad (16)$$

$$E_r = \begin{cases} E_m \text{ if } E_m \ge 0 \\ 0 \text{ else} \end{cases} \quad (17)$$

The renal clearance and hepatic balance from equation (11-17) was designed to reduce the measured disturbances.

From the non-linear system output, the values are taken from the workspace. So, the known input and known output are given as known parameter to the system identification toolbox. It gives best fit transfer function by assuming the number of poles and zeroes to linearise the system which is shown in Figure-3.

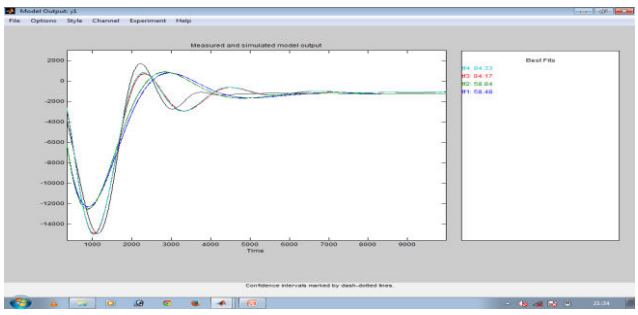
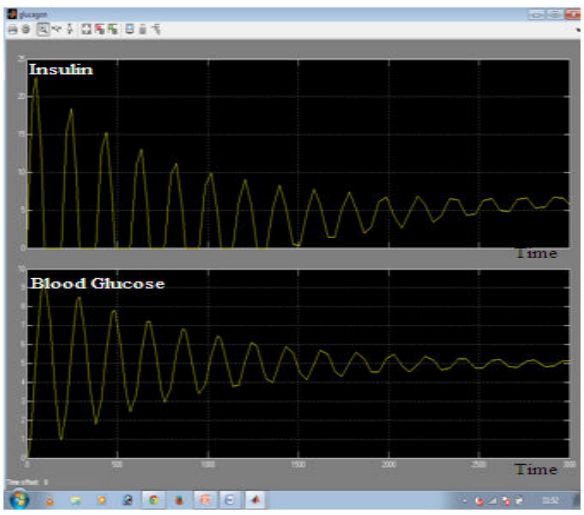


Figure-3. System Identification result.

The obtained transfer function is used to linearise the plant and the model is designed to simulate the system shown in Figure-4. It helps to tune the controller to get the reference input.



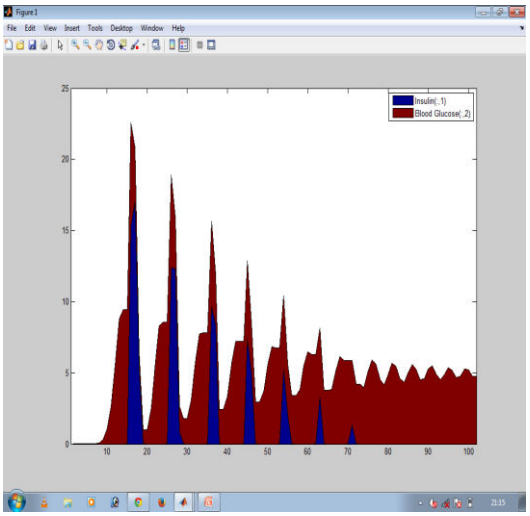


Figure-4. **Figure-5.**

Figure-4. Input glucagon to output blood glucose for tuned linear model. **Figure-5.** Ares plot for linear model tuned with PI controller.

5. RESULT OF ROBUST CONTROLLER

5.1 MPC controller

After tuning the PID controller, the system is clearly checked and evaluates the performance. But, the time taken is infinite and the process is not settled for the expected output. So, the robust controller (MPC) is connected instead of PID. The MPC have several options that have easily designed the controlled variables and model output. Second option is to already store the identified parameter values and linear model inside the MPC controller GUI toolbox. The inbuilt designed MPC controller had model which is shown in Figure-6.

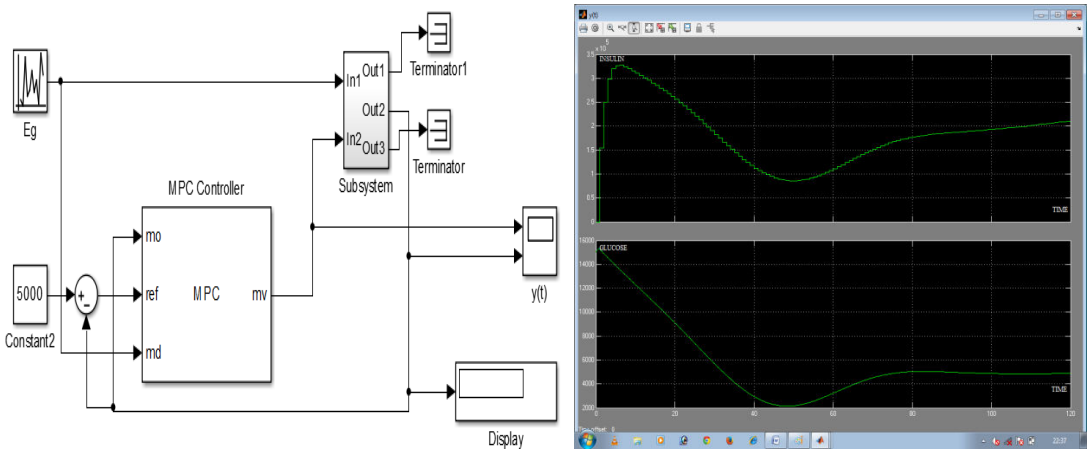


Figure-6. Non Linear-Controller with MPC controller and its corresponding result.

5.2 ANFIS controller

ANFIS stands for Adaptive Neural Fuzzy Inference System. Using a given input/output data set, the toolbox function ANFIS constructs a Fuzzy Inference System (FIS) whose membership function parameters are tuned (adjusted) using either a back propagation algorithm alone, or in combination with a least squares type of method. This allows your fuzzy systems to learn from the data they are modelling. Creates a fuzzy decision tree to classify the data into one of 2n linear regression models to minimize the Sum of Squared Errors (SSE):

$$sse = \sum_j e_j^2 \quad (18)$$

Where

- ej is the error between the desired and the actual output
- p is the number of fuzzy partitions of each variable
- n is the number of input variables

Expert knowledge can increase learning speed and estimation accuracy. From this, the result from the program is shown in Figure-7. This technique gives a fairly good estimate of the speed and is robust to parameter variation

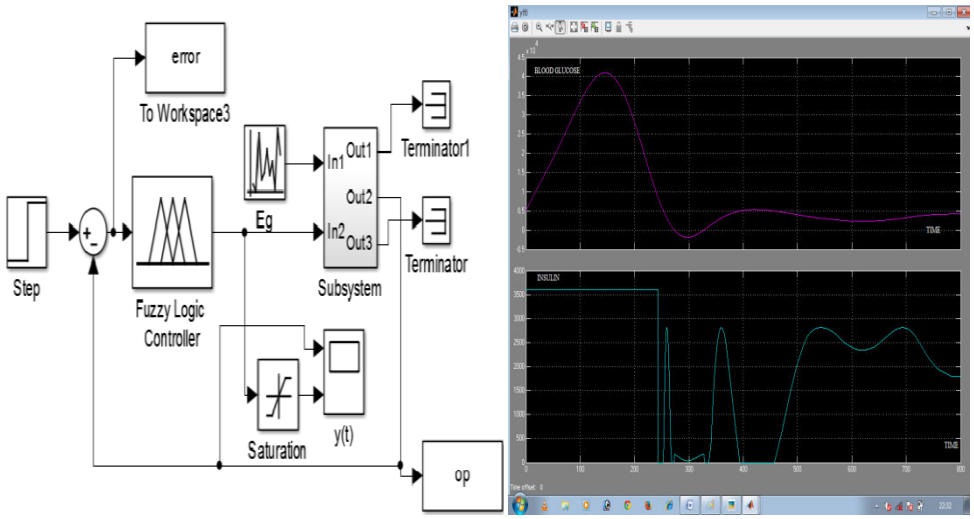


Figure-7. Non Linear-Controller with ANFIS controller and its corresponding result.

6. DISCUSSIONS AND CONCLUSIONS

An intelligently developed back-propagation algorithm could be used for NN training for the proper selection of the rule base. Here, we have formulated this complex control strategy for the diabetic control, which yielded excellent result compared to the other methods mentioned in the literature survey. But, compared with MPC, it still lags in time. The MPC is more robust and time efficient.

The simulation results presented above prove that if the designed control is more effective, it has faster response times or settling times. The sudden fluctuation or change in input and its effect on the various parameters of the dynamic system are also considered in this work. The designed controller not only takes care of the sudden perturbations in process, but also brings back the parameters to the reference or the set value in a few minutes, thus exhibiting the robustness in behaviour. In other words, the designed controller is robust to parametric variations. A reasonable accuracy in this system could be observed using this robust control scheme.

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