CONTROL OF GLUCOSE INSULIN REGULATORY SYSTEM FOR TYPE 1 DIABETES

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ABSTRACT: *This work is an approach to check the controllability and Observability of the model for automatic artificial pancreas to design the feedback control. Mathematical model purposed by Sindhya [1] is treated for the control purpose of diabetes mellitus. The model takes into account all plasma glucose concentrations, generalized insulin and plasma insulin concentration. It would enable diabetic patients to control their disease with the help of artificial pancreas. A control system can only be used in the form of closed-loop control to stabilize the system. The concept of controllability and Observability for the linearised control system is to design a feedback control.*

Key words: Automatic Artificial Pancreas, Linearised Control System, Controllability, Observability.
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1. INTRODUCTION

Mathematics is a beneficial branch of science because of its role in developing other branches of science. Its involvement enriches the field. Biomedical Science is one of its major example which is a pioneer branch of Biology that is growing day by day. It is obvious that it cannot be developed without the help of a mathematician. Hence the involvement of mathematics in Biosciences is mandatory for its progress and development. New discoveries and developments are achievable only with the prime contribution of Mathematics [2].

Controllability is concerned to the opportunity of forcing the system into a particular state by using suitable control the signal. If a state is not convenient, then no signal will be capable to control the state. Observability is associated to the possibility of examining through output capacity, the state of the system [3]. If a state is not visible the controller will never be able to establish the behavior of an unobservable state, and hence cannot use it to claim the system. The final step in the control system proposed problem is, of course to understand the mathematical model of a controller by a general physical device. A control system can only be used in the form of closed loop controlled to stabilize the system [4].

The model we take is Sandhya model for glucose insulin regulatory system. This model describes the advance study to regulate the level of blood glucose for diabetic and normal person. This model based on plasma insulin, plasma glucose concentration and generalized insulin. The numerical solution of this model describes the complex situation of different patient. Our main work is to check the controllability and observability of this model for normal and diabetic patient.

A linear system whose inputs are forced to change in a desired manner as time progresses. A mathematically linear control system is given by the following two equations

$$\dot{x}(t) = A(t)x(t) + B(t)u(t), \qquad t \in I$$
$$y(t) = C(t)x(t), \qquad t \in I$$

where $x(t) \in \mathbb{R}^n$, $u(t) \in \mathbb{R}^p$ and $y(t) \in \mathbb{R}^k$ for $t \in I$. The matrices A(t) , B(t) and C(t) are defined on I and have correct dimensions (i.e., A(t) is $n \times n$, B(t) is $n \times p$ and C(t) is $k \times n$ matrix). I is closed interval, $I = [t_0, t_e]$, $t_0 < t_e < \infty$, respectively $I = [t_0, \infty)$. We suppose the elements of the matrices A (.), B (.) and C (.) are in $L^2(I; \mathbb{R})$ [5].

The function u (.) is also supposed to be in $L^2(I; \mathbb{R}^p)$ is called the input respectively the control of the system. For given initial value $x_0 \in \mathbb{R}^n$ and input $u(.) \in L^2(I; \mathbb{R}^p)$ of equation $\dot{x}(t) = A(t)x(t) + B(t)u(t)$ also called the state equation of system. This system has a unique solution of x(.), and x(.) is absolutely continuous on I with $x(t_0) = x_0$ and the derivative x(.) is exist almost everywhere on I. furthermore equation $\dot{x}(t) = A(t)x(t) + B(t)u(t)$ is satisfied on I , x(t) , $t \in I$ is called state of system at time t. if we have the solution of x(.) of equation $\dot{x}(t) = A(t)x(t) + B(t)u(t)$ with initial value x_0 and equation $y(t) = C(t)x(t), t \in I$ establish $y(t) \in L^2(I; \mathbb{R}^k)$ is called output of the system [5].

- The $n \times np$ controllability matrix is given by

$$R = [B, AB, A^2B, A^3B, \dots, A^{n-1}B]$$

The system is controllable if the controllability matrix has full rank (i.e. $rank(R) = n$)

- The $nk \times n$the Observability matrix is given by

$$O = [C, AC, A^2C, A^3C, \dots, A^{n-1}C]^T$$

The system is observable if the Observability matrix has full rank (i.e. $rank(R) = n$) [6]

2. MATHEMATICAL MODEL FOR GLUCOSE-INSULIN REGULATORY SYSTEM

We determine a model for all plasma glucose concentration, generalized insulin and plasma insulin. Diabetes dynamics is a mathematical model. There are two other models of glucose/insulin use to explain interaction. These are valid to predict blood glucose because these are inherent requirement of frequently updated information. In this model we take glucose level G, glucose uptake X, insulin level I. This model also include the basal values G_b and I_b [1]. The model is

$$\dot{G} = -m_1 G + m_2 I + m_1 G_b$$
$$\dot{X} = -m_2 X + m_3 I - m_3 I_b + m_6 I_b$$
$$\dot{I} = -m_3 I + m_4 G + m_4 m_5 - m_6 I + m_6 I_b \qquad (1)$$

Where G(t) is plasma glucose concentration, X(t) is plasma insulin variable for remote compartment, I(t) is plasma insulin concentration, G_b is the basal preinjection value of plasma glucose, I_b is basal preinjection value of plasma insulin, m_1 is the insulin independent rate uptake in liver,

muscle and adipose tissue, m_2 is the rate of decrease in tissue glucose uptake ability, m_3 is the insulin independent increase in glucose uptake ability in I_b, m_4 is the rate of pancreatic β cells which are released after the glucose injection and glucose concentration above h, m_5 is the threshold value of glucose, m_6 is the decay rate for insulin in plasma.

Case 1: For Normal Person

First of all we study the glucose, plasma concentration and insulin for non-diabetic person for the period of 10 hours. The model show that when we give glucose to normal man then the level of glucose concentration is very high but after time passing it become stable.[1]

Table-1: Values of parameter

Parameter	Values	Units
m_1	0.0317000	$\min^{-1}$
m_2	0.0123	$\min^{-1}$
m_3	4.92×10^{-6}	$\min^{-2}\left(\mu U/ml\right)$
m_4	0.0039	$(\mu U/\text{ml})\min^{-2}\left(mg/dl\right)^{-1}$
m_5	79.0353	mg/dl
m_6	0.2659	$\min^{-1}$
G_b	80	mg/dl
I_b	7	$\mu U/ml$

Model after parameter substitution:

$$\dot{G} = -0.0317G + 0.0123I + 2.536$$
$$\dot{X} = -0.0123X + 0.00000492I + 1.8613$$
$$\dot{I} = -0.26590492I + 0.0039G + 2.1695 \quad (2)$$

Equilibrium points:

For equilibrium point put $\dot{G} = \dot{X} = \dot{I} = 0$ in the system (2)

$$0.0317G - 0.0123I = 2.536$$
$$0.0123X - 0.00000492I = 1.8613 \quad (3)$$
$$-0.0039G + 0.26590492I = 2.1695$$

After solving we get the values of G, X and I . Hence the equilibrium points are

$$(83.6417, 151.3288, 9.3857)$$

Linearized Model:

Hence the linearized model is

$$\dot{G} = -0.0317G + 0.0123I + 2.536$$
$$\dot{X} = -0.0123X + 0.00000492I + 1.8613$$
$$\dot{I} = -0.26590492I + 0.0039G + 2.1695$$

Linear Control System:

The linear control system is

$\dot{x}(t) = A(t)x(t) + B(t)u(t)$,

$y(t) = C(t)x(t)$,

Controllability and Observability:

Here we take the only measured output of glucose concentration in plasma and the only input is insulin concentration then

$B = [0 \quad 0 \quad 1]^T$ and $C = [1 \quad 0 \quad 0]$

The controllability matrix is

$$R = \left[B \quad AB \quad A^2B\right]$$
$$rank(R) = rank\left[B \quad AB \quad A^2B\right] = 3$$

The observability matrix is

$O=[C; CA; CA^2]^T$

and

Rank (O) = rank$[C; CA; CA^2]^T = 2$

Hence the system is controllable but not observable.

Case-2: For Type 1 Diabetes

Now we study the model for diabetic patient for the period of 10 hours. The model show that at start time the level of glucose is very high but when we give glucose then his level of glucose does not fall. After time passing from 250 mg/dl it fall only about 275 mg/dl [3].

Table-2: The values of parameter are

Parameter	Values	Units
m_1	0	$\min^{-1}$
m_2	0.017	$\min^{-1}$
m_3	5.3×10^{-6}	$\min^{-2}\left(\mu U/ml\right)$
m_4	0.0042	$(\mu U/\text{ml})\min^{-2}\left(mg/dl\right)^{-1}$
m_5	80.25	mg/dl
m_6	0.264	$\min^{-1}$
G_b	80	mg/dl
I_b	7	$\mu U/ml$

Model after parameter substitution:

$$\dot{G} = 0.017I$$
$$\dot{X} = -0.017X + 0.0000053I + 1.8479 \quad (4)$$
$$\dot{I} = -0.0000053I + 0.0042G + 2.18505$$

Hence the equilibrium points are

$(-520.25, 108.7037, 0)$ Controllability and Observability

Here we take the only measured output of glucose concentration in plasma and the only input is insulin concentration then

$B = [0 \quad 0 \quad 1]^T$ and $C = [1 \quad 0 \quad 0]$

The controllability matrix is

$$R = \left[B \quad AB \quad A^2B\right]$$
$$rank(R) = rank\left[B \quad AB \quad A^2B\right] = 3$$

The observability matrix is

$O=[C; CA; CA^2]^T$

and

Rank (O) = rank$[C; CA; CA^2]^T = 2$

Hence the system is controllable but not observable.

3. CONCLUSION

To make an automatic artificial pancreas we are treated existing model purposed by Sandhya to design feedback control. In this regard we need to check the controllability and Observability of the model. Sandhya mathematical model is make for different conditions of diabetic individuals. Model show the result is to different situations of progression of diabetes related to time and severity of disease. So the

management plans are necessary to control diabetes to avoid severe symptoms of disease. This model is controllable but not observable for both cases of normal and diabetic patient. This model is important in that sense insulin is controllable and two variables out of three are observable in each case. Model is not observable in both cases this is the major drawback of this model, if model is not observable for healthy person, so we cannot apply on the diabetes patient. The main reason is that glucagon play an important role in production of glucose. Glucagon is missing in this model for both cases, if we add this function in model it may be possible we can design the feedback for close loop.

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