© 2018 IJSRSET | Volume 4 | Issue 9 | Print ISSN: 2395-1990 | Online ISSN : 2394-4099
Themed Section : Engineering and Technology

A Mathematical Model for Glucose-Insulin Interaction under the Influence of Externally Ingested Glucose in Presence of Constant Amount of Glucose and Insulin in the Body

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ABSTRACT

Here, we prepare a mathematical model for glucose- insulin regulation having been influenced by externally ingested glucose. It is also assumed that constant amount of glucose and insulin are always present in the body. This model is a modification of the G-I-E model [14] considering the constant amount of insulin in the body. The stability of the model is analysed by construction of Lyapunov function and conditions for stability have been derived. The model is also analysed numerically to observe the behaviour of the glucose-insulin regulation.
Keywords: Modelling, Mathematical Modelling, Diabetes Mellitus, Glucose-Insulin Regulatory System, Stability, Lyapunov Function.

I. INTRODUCTION

Diabetes is a silent epidemic, rapidly increasing in many countries dramatically in low and middle income countries [15]. The drastic rise in the overall percentage of diabetic patients is normally due to rise in type2 diabetes. Type2 diabetes is derived by the factors overweight, obesity and hypertension, less physical work, wrong diet plan or due to some hereditary reasons. In 2030 diabetes will be the 7th leading cause of deaths.

The notion of mathematical modelling of different diseases was started in the beginning of 20th century. The diseases about which most of the mathematical models have been derived are Cancer, Asthma and Diabetes.. In last century many more clinical and non clinical models have been designed for diseases. Mathematicians have derived many models establishing the glucose and insulin dynamics. In few models few researchers introduced some control policies for recovering the complications of diabetes, cost of diabetes and cost effectiveness of strategies dealing with diabetes.

The first approach of mathematical modelling in diabetes was initiated by Himsworth and Ker (1939). Bolie (1961) is also one of the founders of the history of mathematical modelling. Later famous mathematicians Ackerman (1965, 1969), Bergman and Cobelli (1985) established and gave a new turn to the research of glucose-insulin dynamics through the evergreen Minimal model. Bergman was awarded the Banting madal by American diabetes association for his research work in Diabetes. Some remarkable research works in diabetes were done by Della et. al. (1970), Serge et al. (1973), Srinibasan et.al. (1970), Bergman et.al. 1981), Cobelli et.al(1983,1985,1987,1988,1989), Reaven et.al etc.

In last 25 years many mathematical, statistical models as well as computer algorithms were designed in different aspects of diabetes as described by Mokroglo et.al.(2011) and Boutayeb & Chetouni(2006).

II. MODEL DESCRIPTION

Let G(t) and I(t) denote the glucose and insulin concentration in the body at time t. Let E(t) is the externally ingested glucose at time t which is coming from the source of food to the body. Thus the model for Glucose-Insulin-Externally ingested glucose is a three variable model, with the following assumptions.

(a) Degradation of glucose from body is both insulin independent and insulin dependent with different rate.
(b) Degradation of insulin from the body is glucose independent.
(c) Secretion of insulin due to glucose stimulation.
(d) The externally ingested glucose is assumed to follow logistic growth model. There is increase of glucose level due this externally ingested glucose.
(e) There is no effect of externally ingested glucose on the level of insulin.
(f) A constant amount of glucose is always present in the body.
(g) A constant amount of insulin is always present in the body

III. MODEL EQUATIONS

With the above assumptions, the mathematical model for Glucose-Insulin-Ingested glucose regulatory system can be expressed by the following sets of differential equations $\dot{G} = -aG - bI + \alpha E + \delta$ (3.1)

$$\dot{I} = cG - dI + \eta \qquad (3.2)$$

$$\dot{E} = \beta E(1 - \gamma E) \qquad (3.3)$$

Where,

δ : Constant amount of glucose present in the body

η : Constant amount of insulin present in the body

a: Rate constant representing insulin independent glucose disappearance

b: Rate constant representing insulin dependent glucose disappearance

c: Rate constant representing insulin production due to glucose stimulation

d: Rate constant representing glucose independent insulin degradation

α: Rate constant representing increase of glucose level due to ingested glucose

β: Intrinsic growth constant of ingested glucose

$\frac{1}{\gamma}$: Carrying capacity of ingested glucose

IV. EQUILIBRIUM POINTS

The equilibrium points corresponding to the equations (2.1), (2.2), (2.3) can be determined by considering $\dot{G} = 0, \dot{I} = 0$ and $\dot{E} = 0$

Which implies, either or $E = 0$ or $E = \frac{1}{\gamma}$

For $E = 0$ equations (2.1) and (2.2) give the following results,

$$G = \frac{d\delta - b\eta}{bc + ad}, I = \frac{c\delta + a\eta}{bc + ad}$$

Hence the externally ingested glucose free equilibrium point for the model defined in (3.1), (3.2), and (3.3) is

$$(G_1, I_1, 0) = \left(\frac{d\delta - b\eta}{bc + ad}, \frac{c\delta + a\eta}{bc + ad}, 0 \right)$$

For $E = \frac{1}{\gamma}$ equations (2.1) and (2.2) give the following results,

$$G = \frac{d\alpha - b\gamma\eta}{bc\gamma + ad\gamma}, I = \frac{c\alpha + c\gamma\delta + a\gamma\eta}{bc\gamma + ad\gamma}$$

Hence the externally ingested glucose existing equilibrium point for model defined in (3.1), (3.2), and (3.3) is

$$(G_2, I_2, \frac{1}{\gamma}) = \left(\frac{d\alpha - b\gamma\eta}{bc\gamma + ad\gamma}, \frac{c\alpha + c\gamma\delta + a\gamma\eta}{bc\gamma + ad\gamma}, \frac{1}{\gamma} \right)$$

(4.1)

V. STABILITY OF THE MODEL

For the equilibrium point $(G_2, I_2, \frac{1}{\gamma})$, let us linearise the model as follows,

$$\begin{pmatrix} \dot{G} \\ \dot{I} \\ \dot{E} \end{pmatrix} = \begin{pmatrix} -a & -b & \alpha \\ c & -d & 0 \\ 0 & 0 & -\beta \end{pmatrix} \begin{pmatrix} G - G_2 \\ I - I_2 \\ E - \frac{1}{\gamma} \end{pmatrix}$$

Let us now use the transformations $G = X + G_2$, $I = Y + I_2$ and $E = Z + \frac{1}{\gamma}$ and we have,

$$\begin{pmatrix} \dot{X} \\ \dot{Y} \\ \dot{Z} \end{pmatrix} = \begin{pmatrix} -a & -b & \alpha \\ c & -d & 0 \\ 0 & 0 & -\beta \end{pmatrix} \begin{pmatrix} X \\ Y \\ Z \end{pmatrix}$$

Then we get the linearized system as,

$$\dot{X} = -aX - bY + \alpha Z$$
$$\dot{Y} = cX - dY$$
$$\dot{Z} = -\beta Z$$

(5.1)

Let us consider the Lyapunov function as $V = AX^2 + BY^2 + CZ^2 + 2DXZ$

Hence,

$$\dot{V} = 2AX\dot{X} + 2BY\dot{Y} + 2CZ\dot{Z} + 2DX\dot{Z} + 2DZ\dot{X}$$

$$\begin{aligned} &= -2AaX^2 - 2BdY^2 - (2C\beta - 2D\alpha)Z^2 \\ &-(2Ab - 2Bc)XY - 2DbYZ \\ &-(2Da + 2D\beta - 2A\alpha)XZ \end{aligned} \qquad (5.2)$$

Clearly the coefficients of, X^2 , Y^2 and YZ are negative definite, therefore considering other coefficients as zero we get the following equations,

$$2C\beta - 2D\alpha = 0$$

$$2Ab - 2Bc = 0$$
$$2Da + 2D\beta - 2A\alpha = 0$$

Now setting $D = 1$ in the above equations we have the following results,

$$A = \frac{a+\beta}{\alpha}, B = \frac{ab + b\beta}{c\alpha}, C = \frac{\alpha}{\beta} \qquad (5.3)$$

Hence, (5.2) implies,

$$\begin{aligned} \dot{V} &= -\left(\frac{2a^2 + 2a\beta}{\alpha} \right) X^2 \\ &-\left(\frac{2abd + 2b\beta d}{c\alpha} \right) Y^2 \\ &-\left(\frac{2a + 2\beta - 2ab - 2b\beta}{\alpha} \right) XY \\ &-2bYZ \end{aligned} \qquad (5.4)$$

Hence , (5.4) will be negative definite only when, $a + \beta > ab + b\beta \Rightarrow (1-b)(a+\beta) > 0$

$$\Rightarrow b < 1 \qquad (5.5)$$

Stability condition.

The condition from Lyapunov stability is not a sufficient condition to state the stability behaviour. That is why a phase diagram using some values of the parameter satisfying the condition (5.5) is drwan. The phase portrait of Glucose and Insulin is drawn under the stability condition.

The phase portrait of Glucose-Insulin under the condition $b < 1$ is shown in Fig.4 which shows stability.

The above constraint guarantees the positive definiteness of V and negative definiteness of its derivative which indicates that the model is locally assymptotically stable for co-existing equilibrium point.

VI. ANALYSIS AND CONCLUSION

It is interesting to observe that the model is stable under the condition b<1. The influence of neither other parameters of the model or the constant amount of insulin and glucose plays any significant role on the condition of stability.

The mathematical model defined by (3.1)-(3.3) is analysed numerically. Fig.1 shows the growth of externally ingested glucose which shows a logistic growth as described. The comparision between the Glucose-Insulin regulation is described in Fig.2 under the condition of stability and shows stability. Fig.3 compares the behaviou of Glucose, Insulin and Externally ingested glucose under the

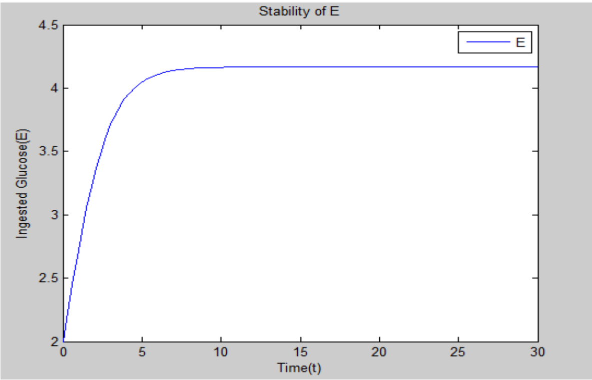

Figure 1

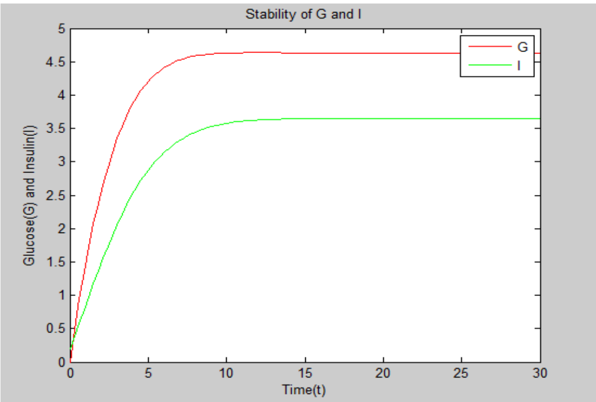

Figure 2

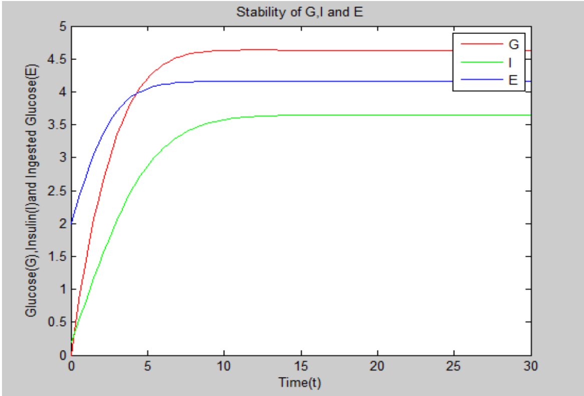

Figure 3

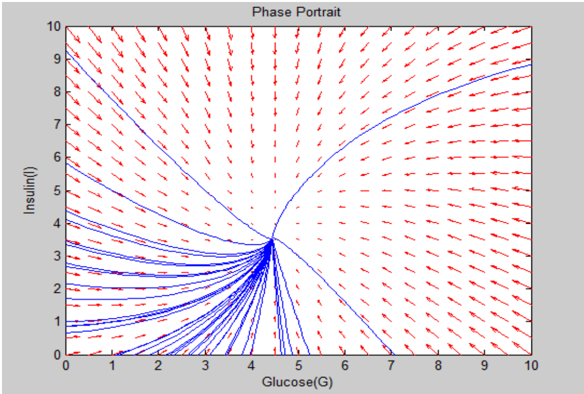

Figure 4

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