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An interactive Glucose- Insulin regulation under the influence of Externally Ingested Glucose $\left(G_{IG} - I - E\right)$ model

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Abstract

Here, we present a mathematical model for glucose (G)- insulin(I) regulatory system, where, the degradation of glucose from the body is assumed to be dependent on both insulin and glucose content in the body. It is also assumed that the body receives externally ingested glucose (E). The ingested glucose is the external source of glucose i.e. received by the body from the source of food intake and assumed to follow logistic growth. The three variable models thus defined analytically as well as numerically. The conditions for stability of the model is also established and validated numerically.

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1. INTRODUCTION

Research on diabetes has been going on from 1939, where Himsworth and Ker [5] introduce the first approach to measure insulin sensitively in VIVO. In 1960, Rosevear and Molnar of the Mayo clinic and Ackerman and Gatewood [6] of the University of Minnesota developed a simple model for blood glucose regulatory system (BGRS) where ‘g’ is taken to be excess glucose concentration and ‘h’ is excess insulin concentration at a time ‘t’ which is expressed as

$$\dot{g} = -a\,g - b\,h \tag{1.1}$$

$$\dot{h} = c\,g - d\,h \tag{1.2}$$

where *a, b, c* and *d* are constants.

Bolie [7] in 1961, modified the same model to incorporate additional variable to describe Glucose-Insulin system under the influence of external glucose intake in the form of source of food. Many other researchers [4]-[18] have also worked in the same field by modifying (1.1),(1.2). [3] is a research paper where author has developed a G-I-E model where externally ingested glucose is assumed to follow logistic growth and insulin is assumed to be glucose independent. The G-I-E model [3] is governed by the following equations.

$$\dot{G}(t) = -aG - bI + \alpha E + \delta \tag{2.1}$$

$$\dot{I}(t) = cG - dI \tag{2.2}$$

$$\dot{E}(t) = \beta E\left(1 - \gamma E\right) \tag{2.3}$$

Where,

δ : Constant amount of glucose 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 source of glucose

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

In this paper the G-I-E model as discussed in [3] and given by (2.1)-(2.3) is modified to a new model under the following assumptions:

I. Degradation of glucose from body is both insulin independent and insulin dependent with different rate.

II. Secretion of insulin due to glucose stimulation.

III. The externally ingested glucose is assumed to follow logistic growth. There is increase of glucose level due to this externally ingested glucose.

IV. There is no effect of externally ingested glucose on the level of insulin.

V. A constant amount of glucose is always present in the body.

VI. The degradation of glucose is dependent on glucose content of the body at a rate a.

VII. Also there is a degradation of glucose for the body which is defined by an interaction of glucose and insulin in the body at a rate b.

With the above assumptions the new model equations are,

$$\dot{G}(t) = -aG - bGI + \alpha E + \delta \tag{2.4}$$

$$\dot{I}(t) = cG - dI \tag{2.5}$$

$$\dot{E}(t) = \beta E\left(1 - \gamma E\right) \tag{2.6}$$

2. ANALYSIS OF THE MODEL:

2.1 Equilibrium points:

The equilibrium points corresponding to the equations (2.4), (2.5) and (2.6) are found by equating them to zero. i.e. $\dot{G}(t) = 0$, $\dot{I}(t) = 0$ and $\dot{E}(t) = 0$

(2.6) implies $E = 0$ and $E = \dfrac{1}{\gamma}$

For $E = 0$, equation (2.4) and (2.5) give,

$$G = \frac{-ad \pm \sqrt{a^2d^2 + 4bdc\delta}}{2bc} \quad \text{and} \quad I = \frac{-ad \pm \sqrt{a^2d^2 + 4bdc\delta}}{2bd}$$

Also, for $E = \dfrac{1}{\gamma}$, equation (2.4) and (2.5) give,

$$G = \frac{-ad\gamma \pm \sqrt{a^2d^2\gamma^2 + 4bd\gamma\left(c\alpha + \gamma\delta\right)}}{2bc\gamma}$$

$$I = \frac{-ad\gamma \pm \sqrt{a^2d^2\gamma^2 + 4bd\gamma\left(c\alpha + \gamma\delta\right)}}{2bd\gamma}$$

2.1.1 Existence of equillibrium points:

Ignoring the negative signs before redical signs we get the equillibrium points as follows:

For $E = 0$, $G = \frac{-ad + \sqrt{a^2d^2 + 4bdc\delta}}{2bc} = G_1$ (say) and $I = \frac{-ad + \sqrt{a^2d^2 + 4bdc\delta}}{2bd} = I_1$ (say)

i.e the first equilibrium point is $\left(G_1, I_1, 0\right)$

And for $E = \frac{1}{\gamma}$,

$G = \frac{-ad\gamma + \sqrt{a^2d^2\gamma^2 + 4bd\gamma\left(c\alpha + \gamma\delta\right)}}{2bc\gamma} = G_2$ (say) and $I = \frac{-ad\gamma + \sqrt{a^2d^2\gamma^2 + 4bd\gamma\left(c\alpha + \gamma\delta\right)}}{2bd\gamma} = I_2$ (say)

i.e the 2nd equilibrium point is $\left(G_2, I_2, \frac{1}{\gamma}\right)$

3. STABILITY OF THE MODEL

Linearising the model around the equilibrium point $\left(G_1, I_1, 0\right)$ we get,

$$\begin{pmatrix} \dot{G} \\ \dot{I} \\ \dot{E} \end{pmatrix} = \begin{pmatrix} -a & -bG_1 & \alpha \\ c & -d & 0 \\ 0 & 0 & \beta \end{pmatrix} \begin{pmatrix} G - G_1 \\ I - I_1 \\ E \end{pmatrix}$$

The eigen values are: $\lambda_1 = \beta$ and $\lambda_{2,3} = \frac{-\left(a+d\right) \pm \sqrt{\left(a-d\right)^2 - 4bc\,G_1}}{2}$

Since $\lambda_1 > 0$, therefore the model is unstable at $\left(G_1, I_1, 0\right)$.

Linearising the model around the equilibrium point $\left(G_2, I_2, \frac{1}{\gamma}\right)$ we get,

$$\begin{pmatrix} \dot{G} \\ \dot{I} \\ \dot{E} \end{pmatrix} = \begin{pmatrix} -a & -bG_2 & \alpha \\ c & -d & 0 \\ 0 & 0 & -\beta \end{pmatrix} \begin{pmatrix} G - G_2 \\ I - I_2 \\ E - \frac{1}{\gamma} \end{pmatrix}$$

The eigen values are: $\lambda_1 = -\beta$ and $\lambda_{2,3} = \dfrac{-\left(a+d\right) \pm \sqrt{\left(a-d\right)^2 - 4bc\, G_2}}{2}$

Since $\lambda_1 = -\beta < 0$, therefore the stability of the model depends on λ_2 and λ_3.

Case 1: Let, $\lambda_2 = \dfrac{-\left(a+d\right) - \sqrt{\left(a-d\right)^2 - 4bc\, G_2}}{2}$

(a) If $\left(a-d\right)^2 - 4bc\, G_2 < 0$, then λ_2 is imaginary and has negative real part.

(b) If $\left(a-d\right)^2 - 4bc\, G_2 > 0$, then λ_2 is purely negative .

Hence the eigen value λ_2 satisfies the stbility condition always.

Case 2: Let, $\lambda_3 = \dfrac{-\left(a+d\right) + \sqrt{\left(a-d\right)^2 - 4bc\, G_2}}{2}$

(a) If $\left(a-d\right)^2 - 4bc\, G_2 < 0$, then λ_3 is imaginary and has negative real part, hence the model is stable.

(b) When $\left(a-d\right)^2 - 4bc\, G_2 > 0$, then the model will be stable if

$$\frac{-\left(a+d\right) + \sqrt{\left(a-d\right)^2 - 4bc\, G_2}}{2} < 0$$

$$\Rightarrow \frac{ad}{bc} > -G_2 \tag{3.1.1}$$

Using the value of G_2, (3.1.1) implies:

$a\,d\,\gamma > -\sqrt{a^2d^2\gamma^2 + 4bd\gamma\left(c\alpha + \gamma\delta\right)}$, which indicates that the model is stable for any values of the parameters $a, b, c, d, \alpha, \gamma, \delta$.

4. ANALYSIS AND CONCLUSION:

The stability of the $\left(\mathbf{G_{IG} - I - E}\right)$ model has been analysed numericaly.The model shows instability in the ingested glucose free equillibrium points. The instability is shown (Fig. 1) arround externally ingested free equillibrium point $\left(G_1, I_1, 0\right)$. However the model is stable in glucose-insulin-externally ingested glucose existing equillibrium point $\left(G_2, I_2, \frac{1}{\gamma}\right)$. Fig.2 stability for externally ingested glucose (E). Stability of glucose and insulin is observed in Fig.3. Comparison of behaviour of glucose and insulin under the influence of externally ingested glucose is seen in Fig. 4. Both glucose and insulin became stable after certain period of time under co-existing equillibrium point. Behaviour of glucose and insulin arround the co-existing equillibria can be observed in the phase portrait given in Fig.5. The phase portrait has been drawn taking the following parameters values.

Parameters	a	b	c	d	α	β	γ	δ
values	0.0354	0.0213	0.756	0.0713	0.0132	0.200	0.0124	0.016

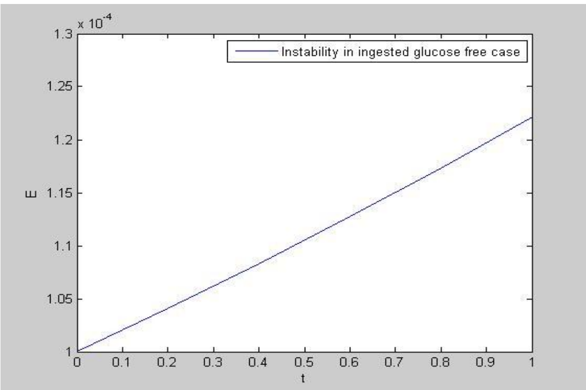

Fig1. Instability of E for $\left(G_1, I_1, 0\right)$

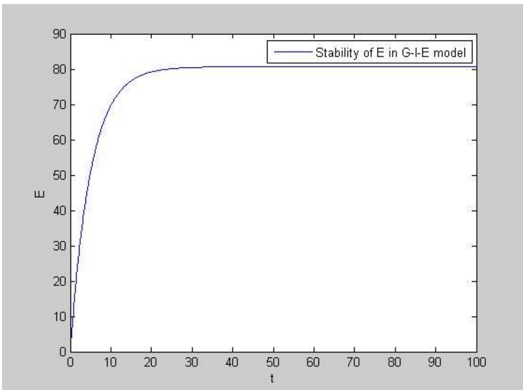

Fig2. Stability of E for $\left(G_2, I_2, \frac{1}{\gamma}\right)$

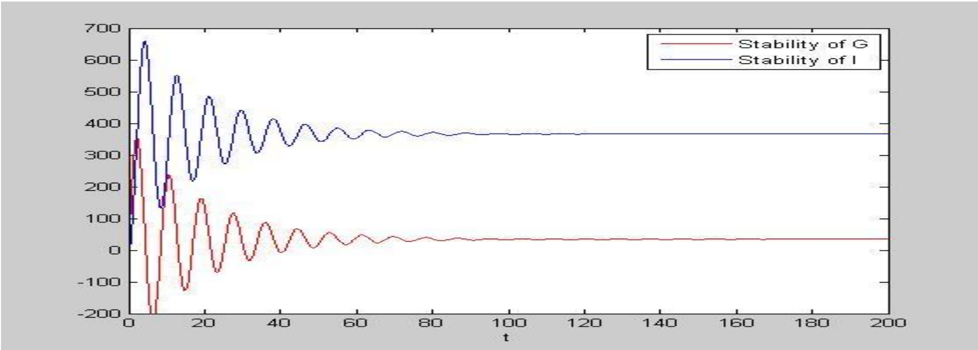

Fig3. Stability of G and I for $\left(G_2, I_2, \frac{1}{\gamma}\right)$

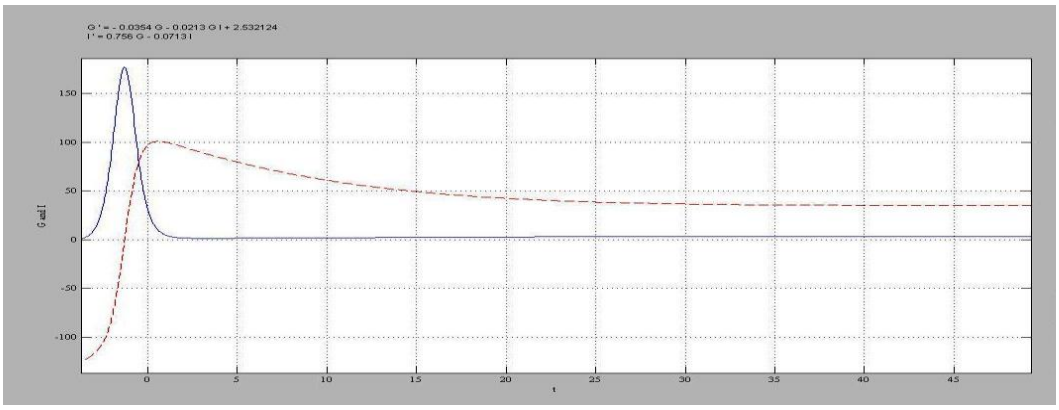

Fig4. Glucose Insulin Plot (t vs G,I)

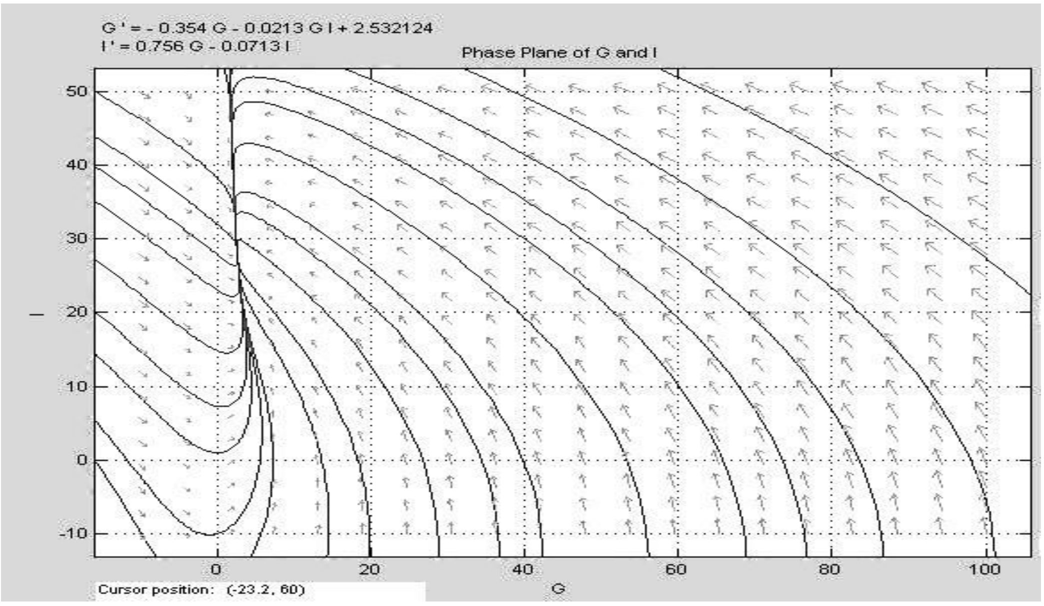

Fig4. Phase portrait for G-I interaction

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