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Modelling Glucose-Insulin Dynamics: Insights for Diabetes Management

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Abstract: *This study presents a comprehensive review and critical analysis of mathematical models used in glucose-insulin regulatory systems, with a focus on their application in diabetes research and clinical practice. The review highlights the strengths and limitations of existing models, emphasizing the need for further refinement and validation to enhance their predictive accuracy and clinical utility. Additionally, recommendations for future research directions are provided, emphasizing the importance of interdisciplinary collaborations and the translation of mathematical models into practical tools for personalized diabetes management. Overall, this work contributes to the advancement of mathematical modelling in diabetes research and underscores its potential to improve patient care and outcomes.*

Keywords: *Stability, Initial Conditions, Glucose-Insulin, Regulatory System, Diabetic Patient, Dynamical System*

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1.0 Introduction

Mathematical modelling and numerical simulation on glucose-insulin regulatory studies is not a new concept in diabetes epidemiology [Bergman (1980 and 2002), Bolie (1961), Derouch and Boutayeb (2002), Godsland (2003) and De Gaetano and Arino (2000), Amadi & Ekaka-a (2017)]. Analysis of insulin release models (Keener and Snyder (1998), Sturris *et al.*, (1991), Toffolo *et al.*, (1980), Engelborghs *et al.*, (2001), Bennett and Gourley (2004) and Bertram *et al.*, (2004). Stabilizing a mathematical model is fast-growing research in applied mathematics [(Yan *et al* (2008) and Yan *et al* (2009)]. Ekaka-a, *et al* (2013), have found alternative stabilizing methods for two controlled dis-similar biogas solids population systems with higher carrying capacities. Caumo *et al* (2000) explored the minimal model of glucose dynamics.

Kuperstein and Sasson (2000) conducted a controlled study of intravenous glucose tolerance test (IGTT) and blood pressure in obese patients. The impact of physical exercise on insulin and glucose dynamics using mathematical model parameters was investigated by Derouch and Boutayeb (2002). Similarly, Breen et al. (2011) investigated the effects of resistant exercise on the insulin sensitivity of healthy and normoglycemic adults using the experimental method. Furthermore, The necessity for the measurement of insulin secretion against insulin sensitivity in the evaluation of beta cell functioning has been reviewed by Ahren and Pacini (2004). Overgaard *et al.* (2005) have constructed a model known as the mean-field beta cell model which is an extension of the original minimal model of second-phase insulin secretion during the IVGTT. Cobelli *et al.* (2009) conducted a thorough and elaborate review of the glucose-insulin regulatory models Gyorgy *et al* (2009) focused their research on reviewing some earlier results obtained on glucose-insulin kinetics. Li *et al* (2006) proposed a model to study the ultradian oscillations of the regulatory system of glucose-insulin having utilized a two-time delay model system.

Tolic *et al* (2007) constructed a model to study the effects of an oscillatory supply of insulin in man in comparison with a constant supply of insulin at the same average rate. Randomski *et al.* (2010) proposed mathematical modelling to study changes in a very nonlinear glucose concentration using neural and fuzzy methods of modelling. Bergman *et al* (1981) conducted investigative research having applied the minimal model approach to study the effect of insulin action and insulin secretion on glucose concentration tolerance. Rao *et al.* (1997) have reviewed a set of four nonlinear differential equation models that imbibe beta-cell kinetics and a gastrointestinal absorption term into a glucose-insulin feedback system. To extend how we might interpret glucose-insulin regulation unique consideration was made to concentrating on stability.

2.0 Mathematical Formulation

The following multi-parameter system of nonlinear first-order ordinary differential equations indexed by the appropriate initial conditions, as given by De Gaetano and Arino (2000) and Makroglou *et al* (2006) has been considered:

$$\frac{dG(t)}{dt} = -[b_1 + X(t)]G(t) + b_1 G_b, \qquad G(0) = G_0 > 0, \qquad (1)$$

$$\frac{dX(t)}{dt} = -b_2 X(t) + b_3[I(t) - I_b], \qquad X(0) = X_0 > 0, \qquad (2)$$

where, $G(t)$ represents the blood glucose concentration at time t; $X(t)$ is the insulin-excitable tissue glucose uptake activity, $I(t)$ represents the blood insulin concentration; G_b is the subject's baseline glycemia; I_b is the subject's baseline insulinemia; b_1 is the glucose rate constant, that is the insulin-independent rate constant of tissue glucose uptake or glucose effectiveness; b_2 is the glucose rate constant expressing the spontaneous decrease of tissue glucose uptake activity; b_3 is the insulin-dependent increase in tissue glucose uptake activity per unit of insulin concentration excess over baseline insulin; b_4 is the rate of pancreatic release of insulin. b_5 is the pancreatic ''target glycemia''; b_6 is the first order decay rate constant for insulin in plasma.

2. 1 Determination of Steady-state Solution

At an arbitrary steady state, the following governing equations hold for the dynamical system:

$$-(b_1 + X_e)\,G_e + b_1 G_b = 0 \qquad (3)$$

$$-b_2 X_e + b_3(I_e - I_b) = 0 \qquad (4)$$

$$b_4(G_e - b_5)\,t - b_6\,(I_e - I_b) = 0 \qquad (5)$$

By expansion and simplification:

$$b_1 G_e + X_e G_e = b_1 G_b \qquad (6)$$

$$b_3 I_e - b_2 X_e = b_3 I_b \qquad (7)$$

$$b_4 t\, G_e - b_6 I_e = b_4 b_5 t - b_6 I_b \qquad (8)$$

To simplify the resulting system, the following substitutions are made:

$\rho_1 = b_1 G_b; \quad \rho_2 = b_3 I_b \;; \quad \rho_3 = b_4 b_5 t - b_6 I_b \;; \alpha_1 = b_4 t$

Also, dropping the subscripts and using the substitution above, the system becomes :

$$b_1 G + X\ G \ = \rho_1 \qquad (9)$$

$$b_3 I - b_2\ X \ = \rho_2 \qquad (10)$$

From equation (11),

$$I = \frac{\alpha_1 G - \rho_3}{b_6} \qquad (12$$

Substituting into equation

$$\frac{b_3}{b_6}(\alpha_1 G - \rho_3) - b_2 X = \rho_2 \qquad (13)$$

Let $\alpha_2 = \frac{b_3}{b_6}; \quad \alpha_3 = (\rho_2 + \frac{b_3 \rho_3}{b_6})$ in equation (13)

Hence, we have:

$$\alpha_2 G - b_2 X = \alpha_3 \qquad (14)$$

$$X = \frac{\alpha_2 G - \alpha_3}{b_2} \qquad (15)$$

$$b_1 G + (\frac{\alpha_2 G - \alpha_3}{b_2})G = \rho_1 \qquad (16)$$

$$b_1 b_2 G + \alpha_2 G^2 - \alpha_3 G = b_2 \rho_1 \qquad (17)$$

Rearranging and simplifying:

$$\alpha_2 G^2 + (b_1 b_2 - \alpha_3)\ G - b_2 \rho_1 = 0 \qquad (18)$$

This is a quadratic equation hence, the roots:

$$G = \left\{ \frac{-(b_1 b_2 - \alpha_3) \pm \sqrt{(b_1 b_2 - \alpha_3)^2 + 4\alpha_2 b_2}}{2\alpha_2} \right\} \qquad (19)$$

From equation (6),

$$X = \left\{ \frac{\alpha_2}{b_2} \left[\frac{-(b_1 b_2 - \alpha_3) \pm \sqrt{(b_1 b_2 - \alpha_3})^2 + 4\alpha_2 b_2}{2\alpha_2} \right] - \frac{\alpha_3}{b_2} \right\} \qquad (20)$$

From equation (7),

$$I = \left\{ \frac{\alpha_1}{b_6} \left[\frac{-(b_1 b_2 - \alpha_3) \pm \sqrt{(b_1 b_2 - \alpha_3})^2 + 4\alpha_2 b_2}{2\alpha_2} \right] - \frac{\rho_3}{b_6} \right\} \qquad (21)$$

Hence, the steady-state solutions at any given time t are the pairs of triples (G_1, X_1, I_1) and (G_2, X_2, I_2).

where,

$\rho_3 = b_4 b_5 t - b_6 I_6,\quad \alpha_1 = b_4 t,\quad \alpha_2 = \frac{b_3 b_4 t}{b_6},$

$\alpha_3 = b_3 I_b + \frac{b_3}{b_6}\left(b_4 b_5 t - b_6 I_b\right).$

Substituting these values into equations (1), (2), and (3) yields:

$$G = \left\{ \frac{-(b_1 b_2 - (b_3 I_b + \frac{b_3}{b_6}(b_4 b_5 t - b_6 I_b) \pm \sqrt{(b_1 b_2 - \alpha_3)^2 + 4\alpha_2 b_2}}{\frac{2 b_3 b_4 t}{b_6}} \right\} \quad (22)$$

$$X = \left\{ \begin{array}{l} \frac{b_3 b_4 t}{b_2 b_6}\left[\frac{-(b_1 b_2 - (b_3 I_b + \frac{b_3}{b_6}(b_4 b_5 t - b_6 I_b)) \pm \sqrt{(b_1 b_2 - (b_3 I_b + \frac{b_3}{b_6}(b_4 b_5 t - b_6 I_b)))^2 + \frac{4 b_2 b_3 b_4 t}{b_6}}}{2\frac{b_3 b_4 t}{b_6}} \right] \\ \qquad - \frac{b_3 b_6 I_b + b_3 (b_4 b_5 t - b_6 I_b)}{b_2 b_6} \end{array} \right\} \quad (23)$$

$$I = \left\{ \begin{array}{l} \frac{b_4 t}{b_6}\left[\frac{-(b_1 b_2 - (b_3 I_b + \frac{b_3}{b_6}(b_4 b_5 t - b_6 I_b)) \pm \sqrt{(b_1 b_2 - (b_3 I_b + \frac{b_3}{b_6}(b_4 b_5 t - b_6 I_b)))^2 + \frac{4 b_2 b_3 b_4 t}{b_6}}}{2\frac{b_3 b_4 t}{b_6}} \right] \\ \qquad - \frac{b_4 b_5 t - b_6 I_6}{b_6} \end{array} \right\} \quad (24)$$

Substituting the model parameter values and solving gives the pair of triple
(G_1, X_1, I_1) = (0.178064286289873, 0.178064286289873, 1.173970742841688)
(G_2, X_2, I_2) = (- 0.121088108233883, -0.121088108233883, -1.692102198240748)
Therefore,

$F_{GX\,I}(G_1, X_1, I_1,)$

is a non-negative equilibrium point,

$\left(0.178064286289873,\ \ 0.178064286289873,\ \ 1.173970742841688)\right),$

is a possible steady-state solution.

3.0 Characterization of the Steady-state Solution

In this method, consideration is given to the method of solving a system of nonlinear first-order ordinary differential equations which takes the following mathematical structure:
Let the continuous and partially differentiable interaction functions F_1, F_2 and F_3 at an arbitrary steady-state solution (G_e, X_e, I_e) be

$$F_1(G_e, X_e, I_e) = -b_1 G_e - X_e G_e + b_1 G_b \quad (25)$$

$$F_2(G_e, X_e, I_e) = -b_2 X_e + b_3 I_e - b_3 I_b \quad (26)$$

$$F_3(G_e, X_e, I_e) = b_4 G_e t - b_4 b_5 t - b_6 I_e + b_6 I_b \quad (27)$$

Where, $F_1, F_2, and\ F_3$ are continuous functions of variables, $G, X, and\ I$.

Following Leticia and Oleka (2016), at a steady-state solution, all rates of change are simultaneously equal to zero. That is, at a steady-state solution, equations (13) – (15) become:
By differentiating (25) – (27) the following Jacobian elements are obtained:

$$J_{11}=\frac{\partial F_1}{\partial G}=-b_1-X_e \qquad J_{12}=\frac{\partial F_1}{\partial X}=-G_e \qquad J_{13}=\frac{\partial F_1}{\partial I}=0$$

$$J_{21}=\frac{\partial F_2}{\partial G}=0 \qquad J_{22}=\frac{\partial F_2}{\partial X}=-b_2 \qquad J_{23}=\frac{\partial F_1}{\partial I}=b_3 \tag{29}$$

$$J_{31}=\frac{\partial F_3}{\partial G}=b_4t \qquad J_{32}=\frac{\partial F_1}{\partial X}=0 \qquad J_{33}=\frac{\partial F_1}{\partial I}=-b_6$$

The Jacobian matrix

$$J_1=\begin{bmatrix}-b_1-X_e & -G_e & 0\\ 0 & -b_2 & b_3\\ b_4\ t & 0 & -b_6\end{bmatrix} \tag{30}$$

The characteristic equation

$$(J-\lambda I)=0 \tag{31}$$

$$\det\left[\begin{pmatrix}-b-X_e & -G_e & 0\\ 0 & -b_2 & b_3\\ b_4\ t & 0 & -b_6\end{pmatrix}-\lambda\begin{pmatrix}1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 1\end{pmatrix}\right]=0 \tag{32}$$

$$=-(b_1+X_e+\lambda)\left[(\left(b_2+\lambda\right)\left(b_6+\lambda\right))+0\right]+G_e\left[0-b_3b_4t\right]+0\left[0+b_4(b_2+\lambda)\right]=0 \tag{33}$$

$$=-(b_1+X_e+\lambda)\left[\left(b_2+\lambda\right)\left(b_6+\lambda\right)\right]-Gb_3b_4t=0 \tag{34}$$

$$=(b_1+X_e+\lambda)\left[b_2b_6+b_2\lambda+b_6\lambda+\lambda^2\right]=-G_eb_3b_4t \tag{35}$$

$$\lambda^3+(X_e+b_1+b_2+b_6)\ \lambda^2+(b_1b_2+b_1b_6+b_2X_e+b_6X_e+b_2b_6)\ \lambda+b_2b_6X_e+b_1b_2b_6+G_eb_3b_4t=0 \tag{36}$$

The parameter values used are: $b_0 = 1$, $b_1 = 0.233$, $b_2 = 0.044$, $b_3 = 0.213$, $b_4 = 0.594$, $b_5 = 0.062$, $b_6 = 0.062$, $G_b = 0.072$, $I_b = 0.074$

This is a cubic function (third-degree polynomial) whose solution takes a longer calculation time. However, substituting the values of the model parameters and the initial conditions of the state variables at time t=1 gives:

$$\lambda^3+(0.2+0.233+0.044+0.062)\ \lambda^2+[(0.233)(0.044)+(0.233)(0.062)+(0.044)(0.2)+(0.062)(0.2)$$

$$+(0.044)(0.062)\ \lambda+(0.044)(0.062)(0.2)+(0.233)(0.044)(0.062)+(0.4)(0.213)(0.594)(1)=0$$

Solving gives the roots of the polynomial as:

$$\lambda_1=-0.6014, \quad \lambda_2=0.0312+0.2918\,i, \quad \lambda_3=0.0312-0.2918\,i$$

This implies that the coexistence steady- state solutions,

$$F_{GXI}(G_e, X_e, I_e), \quad \frac{dG}{dt}=0, \quad \frac{dX}{dt}=0, \quad \frac{dI}{dt}=0, \quad G\neq 0, \quad X\neq 0, \quad I\neq 0$$

will be unstable.

Based on the theory of stability of a steady-state-solution, through the process of linearization at each steady-state-solution and setting up a Jacobian matrix as explained above (Nafo and Ekaka-a, 2012), three eigenvalues of which one is a real and negative λ_1= -0.6014 whereas the other two are complex numbers with positive real parts: 0.2918 and 0.2918 respectively has been calculated. Therefore, instability is concluded for the steady-state solution $S_1(G_e, X_e, I_e)$.

Next, we consider

$F_G(G_e, 0, 0)$ at the equilibrium point $\left(\dfrac{b_1 G_b}{b_1}, 0, 0\right)$,

Therefore,

$F_G(G_e, 0, 0) = F_G(0.072, 0, 0)$ is a non-negative equilibrium point and hence, a possible steady state solution.

Next, we evaluate the steady-state solution:

$F_X(0, X_e, 0,)$ at the equilibrium point $\left(0, -\dfrac{b_1 I_b}{b_2}, 0, \right)$

Hence,

$F_G(0, \; X_e, \; 0) = F_G(0, -0.391864, \; 0)$

is a negative equilibrium point and hence not a possible steady-state solution.

Next, we evaluate the steady-state solution:

$F_X(0, \; 0, \; I_e,)$ at the equilibrium point $\left(0, 0, \dfrac{b_6 I_b - b_4 b_5 t}{b_6}\right)$,

Therefore,

$F_X(0, \; 0, \; I,) = (0, \; 0, -0.589412)$

is a negative equilibrium point and hence not a possible steady-state solution.

Next, we evaluate the steady-state solution:

$F_{GX}(G_e, X_e, 0,)$ at the equilibrium point $\left(\dfrac{b_1 b_2 G_b}{b_1 b_2 - b_3 I_b}, \; \dfrac{-b_3 I_b}{b_{2,}}, \; 0\right)$,

Therefore,

$F_{GX}(G_e, X_e, 0,) = (-0.133396, \; -0.35823, 0)$

has negative coordinates in its equilibrium point and hence not a possible steady-state solution.

Next, we evaluate the steady-state solution:

$F_{GI}(G_e, 0, I_e,)$ at the equilibrium point $\left(G_b, \; 0, \dfrac{b_4 G_b t - b_4 b_5 t + b_6 I_b}{b_6}\right)$,

Therefore,

$F_{GI}(G_e, 0, I_e,) = (0.072, \; 0, \; 0.16981)$

is a non-negative equilibrium point and hence a possible steady-state solution.

Lastly, we evaluate

$F_{XI}(0, X_e, I_e)$

at the equilibrium point $\left(0, \; \dfrac{b_3 b_6 I_b - b_3 b_4 b_5 t + b_3 I_b}{b_6}, \; \dfrac{-(b_4 b_5 t + b_6 I_b}{b_6}\right)$.

Therefore,

$F_{XI}(0, X_e, I_e,) = (0,\ \ 0.247359,\ \ 0.133)$

is a non-negative equilibrium point and hence a possible steady-state solution.

4.0 Results and Discussion

This article showed an analytical solution to the formulated problem and numerical simulation done using MATLAB ODE45 numerical scheme. The parameter values used are: $b_0 = 1$, $b_1 = 0.233$, $b_2 = 0.044$, $b_3 = 0.213$, $b_4 = 0.594$, $b_5 = 0.062$, $b_6 = 0.062$, $G_b = 0.072$, $I_b = 0.074$.

Table 1: Predicting the type of stability on the variation of time for every week for the initial condition: [1.2, 0.6, 0.72] using MATLAB ODE45 numerical method

Example	Time (weeks)	G_e	X_e	I_e	λ_1	λ_2	λ_3	TOS
1	1	1.2000	0.6000	0.7200	-1.0017	0.0314	0.0314	Unstable
2	2	1.1051	0.6117	0.7805	-1.0005	0.0249	0.0249	Unstable
3	3	1.0165	0.6247	0.8353	-1.0008	0.0186	0.0186	Unstable
4	4	0.9339	0.6386	0.8846	-1.0027	0.0125	0.0125	Unstable
5	5	0.8569	0.6535	0.9289	-1.0060	0.0067	0.0067	Unstable
6	6	0.7852	0.6693	0.9686	-1.0106	0.0012	0.0012	Unstable
7	7	0.7185	0.6857	1.0039	-1.0039	-0.0040	-0.0040	Stable
8	8	0.6565	0.7028	1.0352	-1.0239	-0.0089	-0.0089	Stable
9	9	0.5988	0.7205	1.0627	-1.0324	-0.0135	-0.0135	Stable
10	10	0.5452	0.7385	1.0869	-1.0421	-0.0177	-0.0177	Stable
11	11	0.4958	0.7571	1.1078	-1.0528	-0.0216	-0.0216	Stable
12	12	0.4503	0.7759	1.1258	-1.0646	-0.0252	-0.0252	Stable
13	13	0.4084	0.7950	1.1409	-1.0773	-0.0284	-0.0284	Stable
14	14	0.3700	0.8144	1.1536	-1.0908	-0.0313	-0.0313	Stable
15	15	0.3346	0.8339	1.1641	-1.1051	-0.0339	-0.0339	Stable
16	16	0.3021	0.8535	1.1725	-1.1200	-0.0362	-0.0362	Stable
17	17	0.2723	0.8731	1.1790	1.1790	-0.0383	-0.0383	Stable
18	18	0.2450	0.8928	1.1839	1.1839	-0.0402	-0.0402	Stable
19	19	0.2203	0.9125	1.1871	1.1871	-0.0418	-0.0418	Stable
20	20	0.1978	0.9322	1.1890	1.1890	-0.0432	-0.0432	Stable
21	21	0.1775	0.9518	1.1895	1.1895	-0.0445	-0.0445	Stable
22	22	0.1592	0.9713	1.1888	1.1888	-0.0456	-0.0456	Stable
23	23	0.1426	0.9908	1.1872	1.1872	-0.0466	-0.0466	Stable
24	24	0.1277	1.0101	1.1846	1.1846	-0.0474	-0.0474	Stable
25	25	0.1142	1.0292	1.1812	-1.2719	-0.0481	-0.0481	Stable
26	26	0.1021	1.0482	1.1771	-1.2896	-1.2896	-1.2896	Stable
27	27	0.0913	1.0669	1.1724	-1.3073	-0.0493	-0.0493	Stable
28	28	0.0817	1.0855	1.1670	-1.3249	-0.0498	-0.0498	Stable
29	29	0.0731	1.1040	1.1611	-1.3425	-0.0502	-0.0502	Stable
30	30	0.0655	1.1221	1.1548	-1.3600	-0.0506	-0.0506	Stable
31	31	0.0587	1.1401	1.1482	-1.3774	-0.0509	-0.0509	Stable

32	32	0.0527	1.1579	1.1579	-1.3946	-0.0511	-0.0511	Stable
33	33	0.0474	1.1754	1.1338	-1.4116	-0.0514	-0.0514	Stable
34	34	0.0427	1.1927	1.1263	-1.4285	-0.0516	-0.0516	Stable
35	35	0.0386	1.2097	1.1185	-1.4452	-0.0517	-0.0517	Stable
36	36	0.0349	1.2265	1.1106	-1.4618	-0.0519	-0.0519	Stable
37	37	0.0317	1.2431	1.1024	-1.4781	-0.0520	-0.0520	Stable
28	38	0.0289	1.2594	1.0942	-1.4942	-0.0521	-0.0521	Stable
39	39	0.0264	1.2755	1.0859	-1.5100	-0.0522	-0.0522	Stable
40	40	0.0243	1.2913	1.0774	-1.5257	-0.0523	-0.0523	Stable
41	41	0.0224	1.3068	1.0690	-1.5411	-0.0524	-0.0524	Stable
42	42	0.0207	1.3222	1.0604	-1.5563	-0.0524	-0.0524	Stable
43	43	0.0193	1.3372	1.0518	-1.5713	-0.0525	-0.0525	Stable
44	44	0.0180	1.3521	1.0432	-1.5860	-0.0525	-0.0525	Stable
45	45	0.0169	1.3666	1.0346	-1.6005	-0.0526	-0.0526	Stable
46	46	0.0160	1.3809	1.0259	-1.6148	-0.0526	-0.0526	Stable
47	47	0.0151	1.3950	1.0173	-1.6288	-0.0526	-0.0526	Stable
48	156	0.0081	1.8220	0.3027	-2.0552	-0.0529	-0.0529	Stable

$\lambda_1, \lambda_2, \lambda_3 = eigen\ values,$ **TOS =Type of stability**

Table 2: Predicting the type of stability on the variation of time for every week for the initial condition: [3.6, 1.8, 2.16] using MATLAB ODE45 numerical method

Example	Time (weeks)	G_e	X_e	I_e	λ_1	λ_2	λ_3	TOS
1	1	3.6000	1.8000	2.1600	-2.1378	-0.0006	-0.0006	Stable
2	2	2.9337	1.8384	2.3363	-2.1554	-0.0110	-0.0110	Stable
3	3	2.3814	1.8799	2.4754	-2.1796	-0.0197	-0.0197	Stable
4	4	1.9250	1.9239	2.5840	-2.2093	-0.0268	-0.0268	Stable
5	5	1.5495	1.9697	2.6674	-2.2436	-0.0326	-0.0326	Stable
6	6	1.2427	2.0169	2.7298	-2.2816	-0.0372	-0.0372	Stable
7	7	0.9910	2.0650	2.7757	-2.3224	-0.0408	-0.0408	Stable
8	8	0.7870	2.1137	2.8078	-2.3654	-0.0437	-0.0437	Stable
9	9	0.6228	2.1628	2.8287	-2.4100	-0.0459	-0.0459	Stable
10	10	0.4905	2.2120	2.8408	-2.4557	-0.0476	-0.0476	Stable
11	11	0.3845	2.2611	2.8458	-2.5023	-0.0489	-0.0489	Stable
12	12	0.3004	2.3101	2.8452	-2.5492	-0.0499	-0.0499	Stable
13	13	0.2340	2.3588	2.8401	-2.5964	-0.0507	-0.0507	Stable
14	14	0.1816	2.4072	2.8316	-2.6436	-0.0513	-0.0513	Stable
15	15	0.1406	2.4551	2.8204	-2.6907	-0.0517	-0.0517	Stable
16	16	0.1087	2.5026	0.8070	-2.7375	-0.0520	-0.0520	Sable
17	17	0.0840	2.5495	2.7922	-2.7839	-0.0523	-0.0523	Stable
18	18	0.0649	2.5959	2.7761	-2.8300	-0.0525	-0.0525	Stable
19	19	0.0503	2.6418	2.7591	-2.8756	-0.0526	-0.0526	Stable
20	20	0.0391	2.6871	2.7414	-2.9207	-0.0527	-0.0527	Stable

21	21	0.0306	2.7318	2.7233	-2.9652	-0.0528	-0.0528	Stable
22	22	0.0241	2.7759	2.7049	-3.0092	-0.0528	-0.0528	Stable
23	23	0.0193	2.8194	2.6862	-3.0527	-0.0529	-0.0529	Stable
24	24	0.0156	2.8623	2.6675	-3.0956	-0.0529	-0.0529	Stable
25	25	0.0129	0.0129	2.6486	-3.1379	-0.0529	-0.0529	Stable
26	26	0.0108	0.0108	2.6297	-3.1796	-0.0529	-0.0529	Stable
27	27	0.0082	0.0082	2.5920	-3.2613	-0.0529	-0.0529	Stable
28	28	0.0073	0.0073	2.5732	-3.3013	-0.0530	-0.0530	Stable
29	29	0.0073	0.0073	2.5732	-3.3013	-0.0530	-0.0530	Stable
30	30	0.0067	0.0067	2.5545	-3.3408	-0.0530	-0.0530	Stable
31	31	0.0062	0.0062	2.5359	-3.3797	-0.0530	-0.0530	Stable
32	32	0.0058	0.0058	2.5174	-3.4180	-0.0530	-0.0530	Stable
33	33	0.0056	3.2226	2.4989	-3.4557	-0.0530	-0.0530	Stable
34	34	0.0053	3.2598	2.4806	-3.4929	-0.0530	-0.0530	Stable
35	35	0.0052	3.2965	2.4623	-3.5295	-0.0530	-0.0530	Stable
36	36	0.0050	3.3326	2.4442	-3.5656	-0.0530	-0.0530	Stable
37	37	0.0049	3.3681	2.4262	-3.6012	-0.0530	-0.0530	Stable
28	38	0.0048	3.4031	2.4083	-3.6362	-0.0530	-0.0530	Stable
39	39	0.0048	3.4376	2.3905	-3.6707	-0.0530	-0.0530	Stable
40	40	0.0047	3.4716	2.3727	-3.7046	-0.0530	-0.0530	Stable
41	41	0.0046	3.5050	2.3551	-3.7380	-0.0530	-0.0530	Stable
42	42	0.0046	3.5379	2.3376	-3.7709	-0.0530	-0.0530	Stable
43	43	0.0045	3.5703	2.3203	-3.8033	-0.0530	-0.0530	Stable
44	44	0.0045	3.6022	2.3030	-3.8352	-0.0530	-0.0530	Stable
45	45	0.0044	3.6336	2.2858	-3.8666	-0.0530	-0.0530	Stable
46	46	0.0044	3.6644	2.2687	-3.8975	-0.0530	-0.0530	Stable
47	47	0.0044	3.6948	2.2517	-3.9278	-0.0530	-0.0530	Stable
48	155	0.0033	4.8277	0.9065	-5.061	-0.0530	-0.0530	Stable

$\lambda_1, \lambda_2, \lambda_3 = eigen\ values,$ TOS =Type of stability

From Table 1, we have made the following observations: As the independent variable time (t) in the unit of weeks ranges from week one (1) to week six (6), we have found six (6) valid steady states solutions which are dominantly unstable because of the existence of two positive eigenvalues and one negative eigenvalue. Therefore, based on the sign method of stability the six (6) steady-state solutions are considered unstable. The two (2) positive eigenvalues contribute to the unbounded growth of the solution trajectories whereas the negative eigenvalues contribute to the decaying behaviour of the solution trajectories over time. We have also observed that the earlier observed instability changes to dominant stability ranging from the seventh (7^{th}) week to one hundred and fifty-sixth (156^{th}) week. In this context, the bifurcation intervals have occurred between the sixth (6^{th}) and seventh (7^{th}) week. These observations are specific to the initial condition: [1.2, 0.6, 0.72].

From Table 2, as the independent variable time (t) in the unit of weeks ranges from week one (1) to one hundred and fifty-sixth (156^{th}) week, we have found one hundred and fifty-six (156) valid steady states solutions which are dominantly stable because of the existence of three negative eigenvalues.

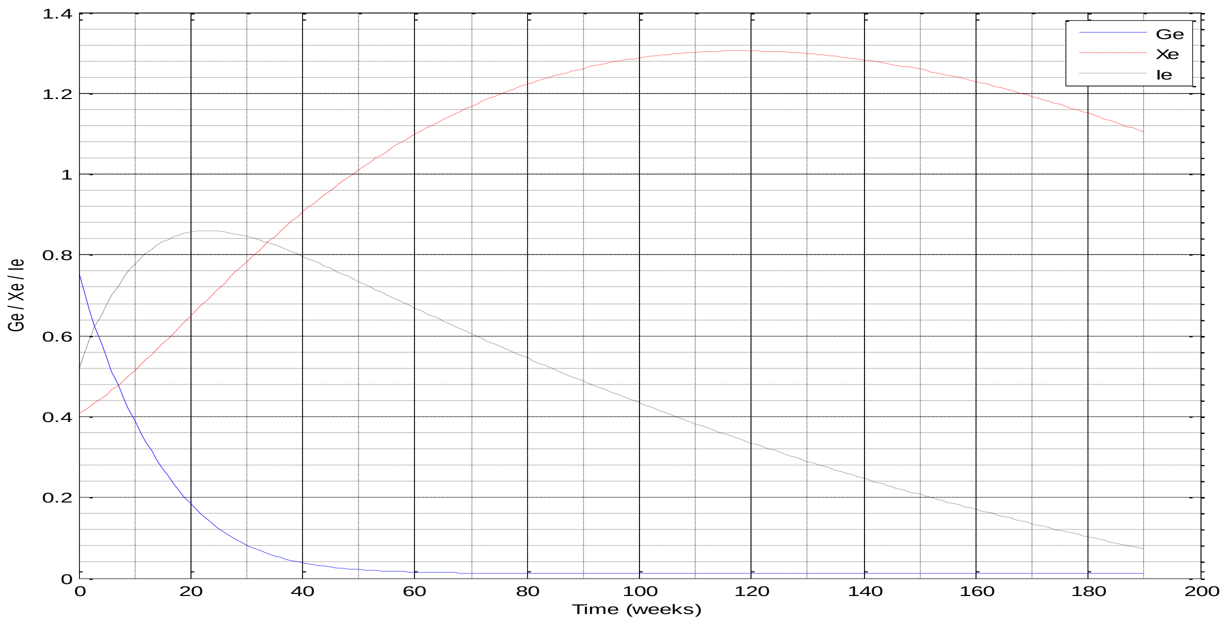

Fig. 1: Predicted stability due to variation in time for every week for the condition:[0.7, 0.4, 0.48] with steady-state solution

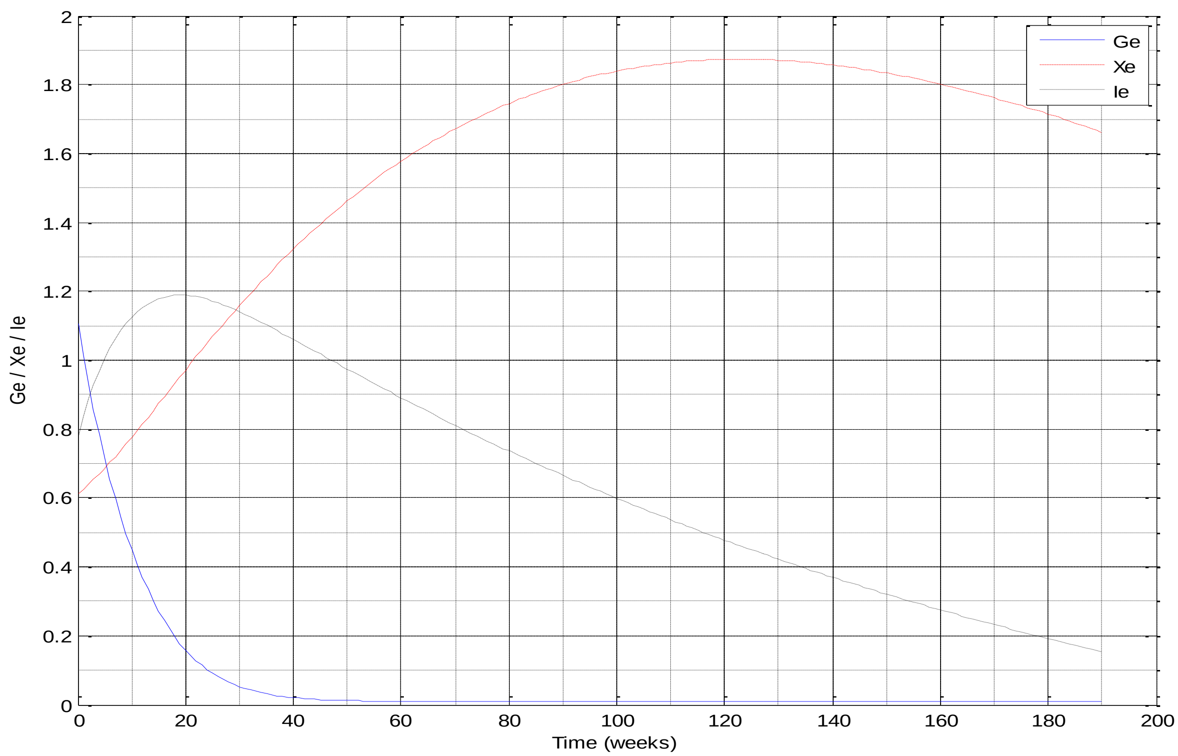

Fig. 2: Predicted stability due to variation in time for every week for the initial condition: [1.1, 0.6, 0.82] with steady-state solution

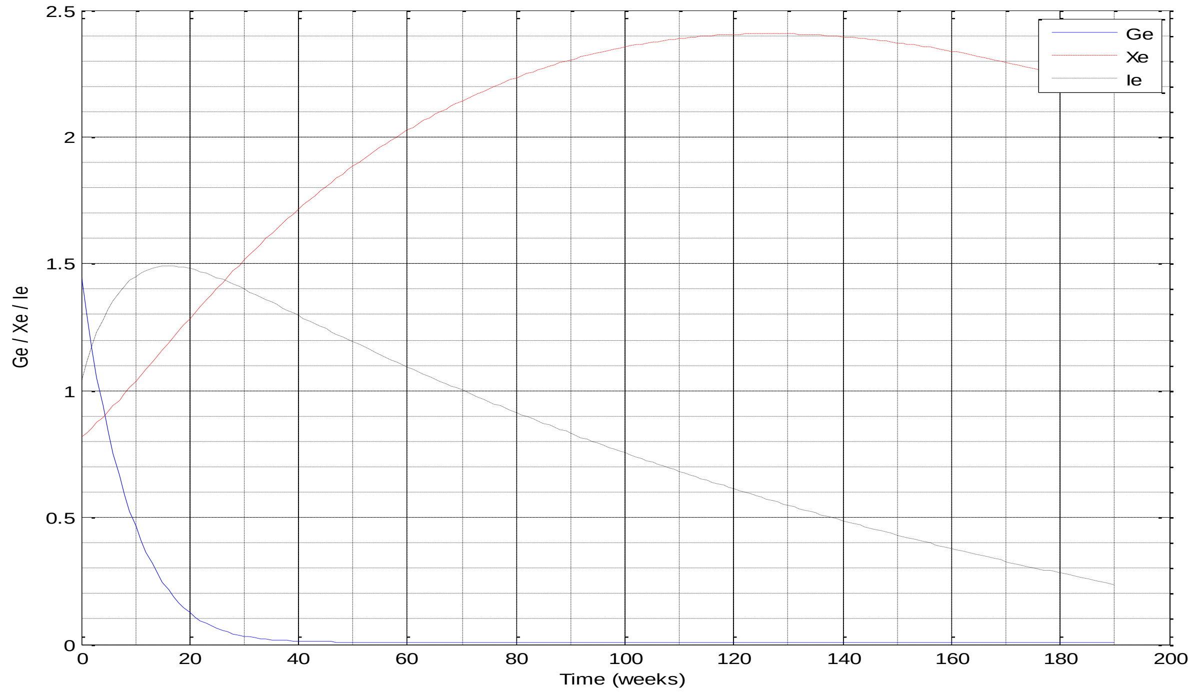

Fig. 3: The variation of initial condition: [1.4, 0.8, 1.0] with steady-state solution for time t = 156 weeks and for fixed values of other model parameters.

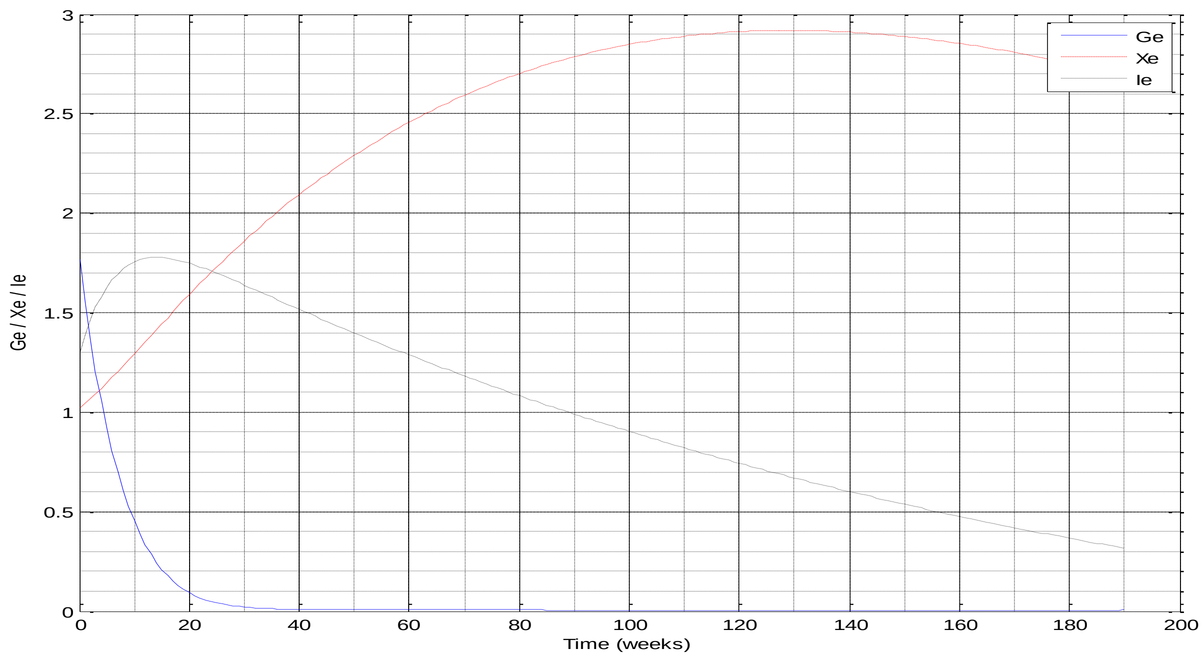

Fig. 4: Predicted stability due to variation in time for every week for the initial condition:[1.7, 1.0, 1.40].

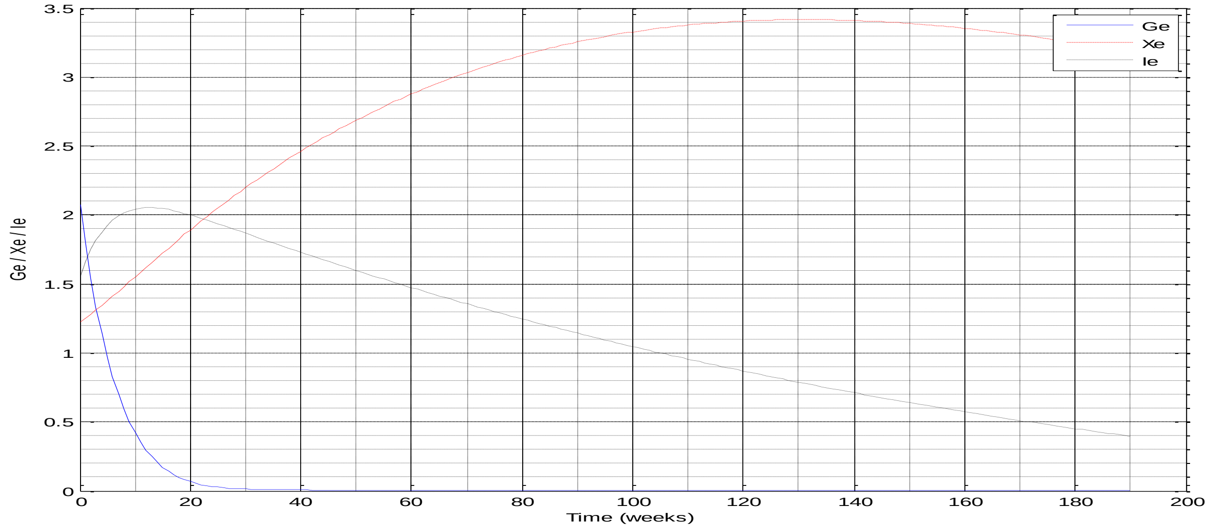

Fig. 5: Predicted stability due to variation in time for every week for the initial condition: [2.0, 1.2, 1.60]

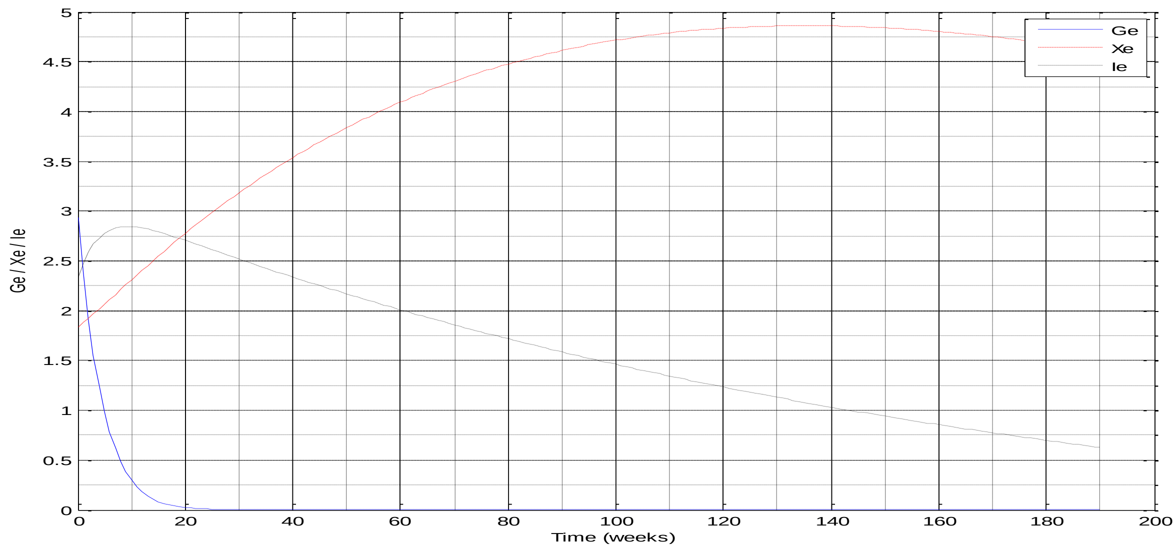

Fig 6: Predicted stability due to variation in time for every week for the initial condition: [2.9, 1.8, 2.80]

Therefore, based on the sign method of stability, the forty-seven (47) steady-state solutions are considered stable. The three (3) negative eigenvalues contribute to the decaying behaviour of the solution trajectories over time. These observations are specific to the initial condition: [3.6, 1.8, 2.16].

Fig 1 shows the predicted stability due to time variation for the initial condition [0.7. 0.4, 0.48] with a steady-state solution. At this initial condition, G_e shows a falling pattern from 0.7 to 0.02 and then stabilizes. Also, it is seen that X_e rises from the value of 0.4 to the value of 1.25 and falls from the value of 1.25 to the value of 1.06 extendedly. Similarly, I_e rises from the value of 0.5 to the value of 0.82 and then falls to the value of 0.08. Fig 2 demonstrates the predicted stability due to time variation for the initial condition [1.1, 0.6, 0.82] with a steady-state solution. At this initial condition, G_e shows a falling and stabilizing pattern whereas X_e and I_e show a rising and then falling trend. Fig 3 demonstrates the predicted stability due to time variation for the initial condition [1.4, 0.8, 1.0] with a steady-state solution. At this initial condition, G_e shows a falling and stabilizing pattern whereas X_e and I_e shows a rising and then falls. Fig 4 illustrates the predicted stability due to time variation for the initial condition [1.7, 1.0, 1.40] with a steady-state solution. At this initial condition, G_e shows a falling and stabilizing pattern whereas X_e and I_e a shows a rising and then falls. Fig 5 illustrates the predicted stability due to time variation for the initial condition [2.0, 1.2, 1.60] with a steady-state solution. At this initial condition, G_e shows a falling and stabilizing pattern whereas X_e and I_e a show a rising and then falling trend. Fig 6 illustrates the predicted stability due to time variation for the initial condition [2.9, 1.8, 2.80] with a steady-state solution. At this initial condition, G_e shows a falling and stabilizing pattern whereas X_e and I_e shows a rising and falling trend.

5.0 Conclusion

The work presented offers a comprehensive analysis of mathematical modelling and numerical simulation concerning glucose-insulin regulatory studies in the context of diabetes epidemiology. By reviewing previous literature and utilizing advanced mathematical formulations, the study delves into understanding the dynamics of glucose-insulin regulation, offering insights into stability and behaviour and under various conditions. The investigation begins by establishing the foundation laid by previous researchers, acknowledging the significance of mathematical models in studying glucose-insulin kinetics. Notably, the work integrates findings from a plethora of studies, highlighting the continuous evolution of this field over decades. The mathematical formulation section presents a detailed model of glucose-insulin regulation, comprising nonlinear ordinary differential equations. Through rigorous mathematical analysis, including the determination of steady-state solutions and characterization of stability, the study provides a solid framework for understanding system behaviour. The results and discussion section further enriches the study by offering insights gained from numerical simulations. The analysis of stability over time, as depicted in Tables 1 and 2 and the corresponding figures, provides a nuanced understanding of system behaviour under different initial conditions. The observation of transitions from unstable to stable states underscores the dynamic nature of glucose-insulin regulation.

Based on the results, findings and scope and limitations of the study, the following suggestions are recommended

(i) Condition of further research for refining the mathematical model and numerical simulation techniques to enhance the accuracy of predictions and stability assessments in glucose-insulin regulatory studies.

(ii) Future studies could explore the impact of various interventions, such as dietary changes or medication, on glucose-insulin dynamics using advanced mathematical modelling and simulation methods.

(iii) Researchers are encouraged to investigate the applicability of the developed models in clinical settings to assist in personalized diabetes management and treatment strategies.

(iv) Collaboration between mathematicians, clinicians, and biomedical engineers should be promoted to ensure the translation of mathematical models into practical tools for improving diabetes care and patient outcomes.

(v) Efforts should be directed towards validating the mathematical models against clinical data to establish their reliability and efficacy in real-world scenarios.

(vi) Continuous refinement and validation of mathematical models are necessary to account for the complexity and variability of glucose-insulin dynamics in diverse populations and clinical conditions.

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Compliance with Ethical Standards Declarations

The authors declare that they have no conflict of interest.

Data availability

All data used in this study will be readily available to the public.

Consent for publication

Not Applicable

Availability of data and materials

The publisher has the right to make the data public.

Competing interests

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Authors' Contributions

All the aspects of the work were done by the author