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Mathematical Model of Glucose and Insulin Kinetics

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Abstract: *In this paper, we present a mathematical model of diabetes mellitus, which is a metabolic disease concerned with the regulation process of glucose in the body by the pancreatic insulin. This study presents variations of Glucose and Insulin verses time with different parameter values under different conditions. The phase plane diagrams also illustrated for different values of partial variations coefficients.*

Keywords: *Diabetes, Glucose, Insulin, Differential equations, phase-plane, Trajectories*.

1. Introduction

Mathematical modeling basically consists of translating real world problem into mathematical language, solving the mathematical problem [1]. Diabetes is a syndrome of metabolism which is characterized by too much sugar in the blood. Because of the lack of insulin, the patient's body is unable to burn off all its sugar, starches and carbohydrates. Insulin is the key hormone involved in the storage and controlled release within the body of the chemical energy available from the food. Blood glucose levels are closely regulated in heath and rarely stay outside range of 3.5-8.0 m mol/liter, despite its varying demand during food intake, fasting and exercise. At low insulin levels, glucose production is maximal and utilization is minimal, at high levels the situation is reversed [2].Among the earliest mathematical models, the simplified model proposed by Ackerman et al [3] and its modifications Ceresa et al[4], Norwich K.H [5] have been successful in describing the mathematical relation between the glucose and insulin in plasma. The glucose concentration (g) and insulin concentration (h) are difference from the corresponding fasting levels respectively which are consider in the basic equations by Gita Subba Rao [6].

2. Notations Applied

g = Deviation of glucose level from its fasting values

h = Deviation of insulin level from its fasting values

$m_i \, (i = 1, 2, 3, 4) =$ Positive constants representing the partial variation coefficients of production and secretion of glucose and insulin.

α , β = Roots of auxiliary equation.

Basic Equations: Governing the variation rates of glucose and insulin

$$\frac{dg}{dt} = -m_1 g - m_2 h$$

$$\frac{dh}{dt} = m_3 g - m_4 h \tag{1}$$

with the initial conditions g (0)= g_0 and h(0)= h_0 (2)

Eliminating h (t), we get the differential equation for g (t)

$$\left[D^2 + (m_1 + m_4)D + (m_1 m_4 + m_2 m_3)\right] g(t) = 0 \tag{3}$$

The auxiliary equation of (3) is

$$m^2 + (m_1 + m_4)m + (m_1 m_4 + m_2 m_3) = 0 \tag{4}$$

the roots of which are

$$(\alpha, \beta) = \frac{-(m_1 + m_4) \pm \sqrt{(m_1 + m_4)^2 - 4(m_1 m_4 + m_2 m_3)}}{2}$$

$$= \frac{-(m_1 + m_4) \pm \sqrt{(m_1 - m_4)^2 - 4 m_2 m_3}}{2} \tag{5}$$

The following cases would arise

Case (i):

If $(m_1 - m_4)^2 > 4m_2 m_3$

In this case roots (α, β) are real and distinct. The distribution of glucose and insulin are

$$g(t) = Ae^{\alpha t} + Be^{\beta t} \tag{6}$$

and

$$h(t) = \frac{-1}{m_2}\left[A(\alpha + m_1)e^{\alpha t} + B(\beta + m_1)e^{\beta t}\right] \tag{7}$$

Where A and B are constants chosen such that (6) and (7) satisfying the initial conditions

$$A = -\frac{h_0 m_2 + g_0(\beta + m_1)}{\alpha - \beta}$$

and

$$B = g_0 + \frac{h_0 m_2 + g_0(\beta + m_1)}{\alpha - \beta}$$

Substituting these values A and B in the equations (6) and (7), we get variations of glucose and insulin

$$g(t) = \left[-\frac{h_0 m_2 + g_0(\beta + m_1)}{\alpha - \beta}\right] e^{\alpha t} + \left[g_0 + \frac{h_0 m_2 + g_0(\beta + m_1)}{\alpha - \beta}\right] e^{\beta t} \tag{8}$$

and

$$h(t) = \left[\frac{h_0 m_2 + g_0(\beta + m_1)}{(\alpha - \beta) m_2}\right](\alpha + m_1)e^{\alpha t} - \left[g_0 + \frac{h_0 m_2 + g_0(\beta + m_1)}{\alpha - \beta}\right](\beta + m_1)e^{\beta t} \tag{9}$$

Since α and β are both negative, g (t) $\to 0$ and h (t) $\to 0$ as $t \to \infty$

The variations of glucose (g) and insulin (h) verses time (t) for the initial values as follows

For the initial values g (0) =75 and h (0) = 100 are illustrated in figure1 and 2

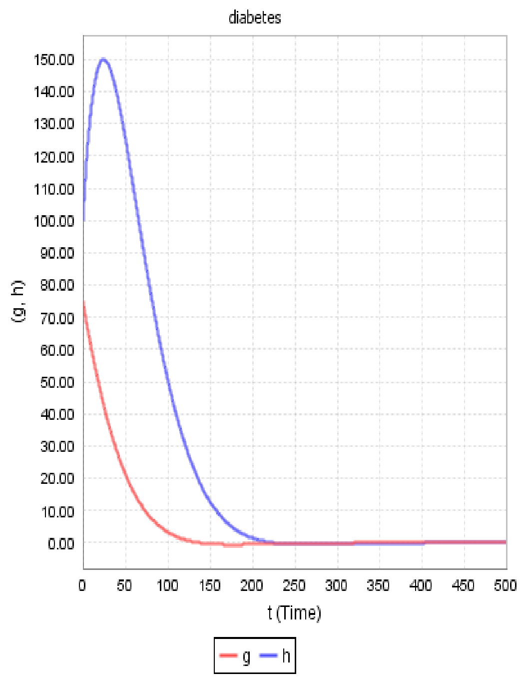

Fig 1. $m_1= .018, m_2=.002, m_3=.105, m_4=.03$

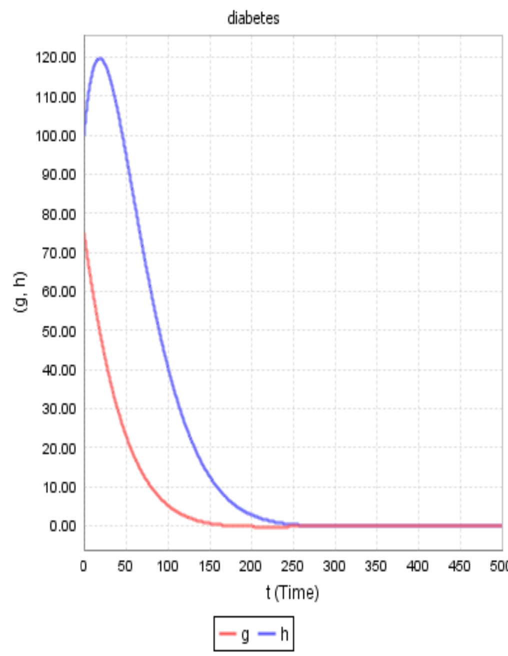

Fig 2. $m_1= .018, m_2= .002, m_3=.072, m_4=.03$

Case (ii):

If $(m_1 - m_4)^2 = 4m_2 m_3$

In this case roots (α , β) are real and equals each to α (say):

$$\alpha = -\left(\frac{m_1 + m_4}{2}\right) < 0$$

Variations of glucose and insulin are

$$g(t) = \left[g_0 - \left\{ h_0 + g_0 \left(\alpha + \frac{m_1}{m_2} \right) \right\} t \right] e^{\alpha t} \tag{10}$$

$$h(t) = -\left[\left(g_0 + \left\{ h_0 + g_0 \left(\alpha + \frac{m_1}{m_2} \right) t \right\} \right) \left(\alpha + \frac{m_1}{m_2} \right) - \left\{ h_0 + g_0 \left(\alpha + \frac{m_1}{m_2} \right) \right\} \right] e^{\alpha t} \tag{11}$$

which satisfying the initial conditions.

It is noticed that

g (t) $\to 0$ and h(t) $\to 0$ as $t \to \infty$

For different constant values the trajectories of g (glucose) and h (insulin) verses time (t) for the initial values g(0)=75 and h(0)=100 as follows.

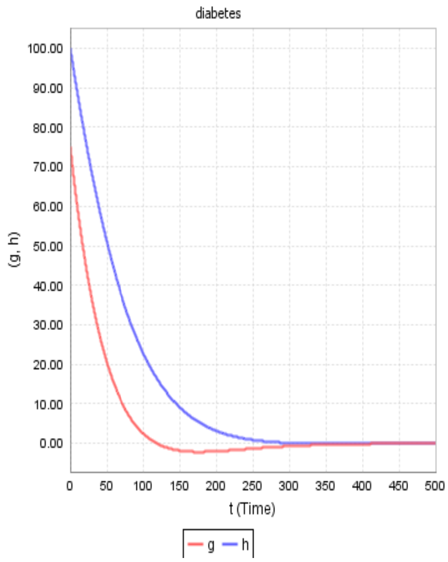

Fig 3. *m_1= .015, m_2= .006, m_3=.008, m_4=.018*

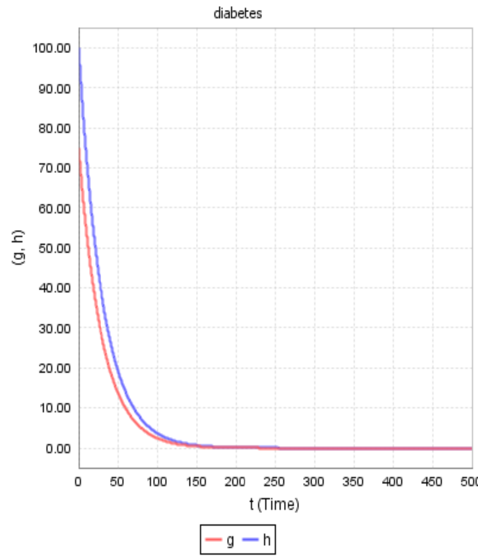

Fig 4. *m_1= .02, m_2= .01, m_3=.01, m_4=.04*

Case (iii):

If $(m_1 - m_4)^2 < 4m_2m_3$

In this case roots are complex p+iq (say):

Here $p = -\left(\frac{m_1 + m_4}{2}\right) < 0\,, \quad q = \frac{\sqrt{(m_1 - m_4)^2 - 4m_2m_3}}{2}$

Variations of glucose and insulin are

$$g(t) = \left(g_0 \cos qt - \frac{g_0(\alpha + m_1) + m_2 h_0}{q} \sin qt \right) e^{pt} \tag{12}$$

and

$$h(t) = \begin{pmatrix} \{2g_0(\alpha + m_1) + m_2 h_0\} \cos qt \\ + \left\{ q g_0 + \left(\frac{\alpha + m_1}{q}\right)\left(g_0(\alpha + m_1) + m_2 h_0\right)\right\} \sin qt \end{pmatrix} e^{pt} \tag{13}$$

which satisfying the initial conditions.

For different constant values the trajectories of g (glucose) and h (insulin) verses time (t) for the initial values g (0) = 75 and h (0) = 100 as follows

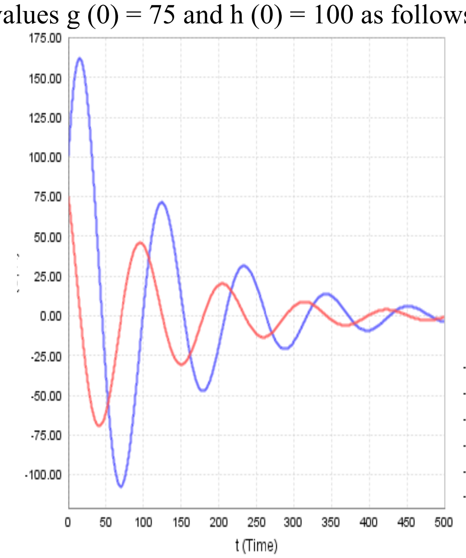

Fig5. *m_1= .012,m_2= .03 ,m_3=.111,m_4=.003.*

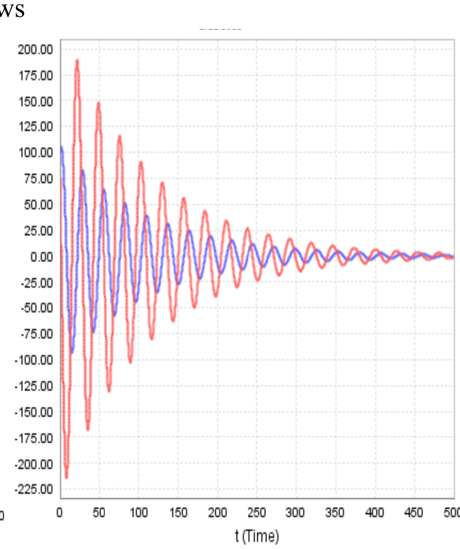

Fig6. *m_1=.01, m_2=.5,m_3=.108, m_4=.003.*

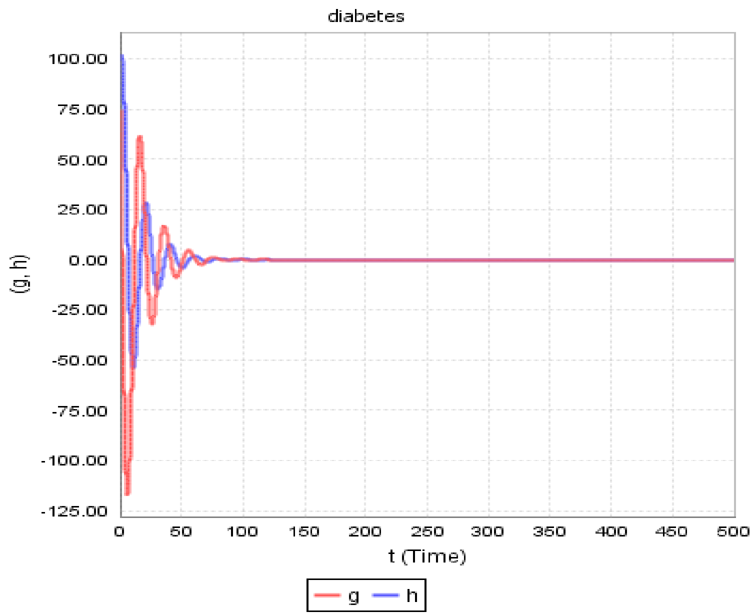

Fig7. *m_1= .051, m_2= .5020, m_3=.198,m_4=.078*

3. Conclusion

Glucose (g) and insulin (h) reach zero values as time (t) increases. It is noticed that glucose and insulin are oscillates with decreasing amplitude (since p is negative). Alternating rise and fall of the glucose and insulin levels are noticed and this would indicate the chronic state of the disease. The oscillations g and h die out faster as m_1, m_2, m_3, m_4 increases.

Phase-plane (Trajectories in the g-h plane):

From the basic equations (1) we obtain the differential equations in the phase- plane:

$$\frac{dg}{dh} = \frac{-m_1 g - m_2 h}{m_3 g - m_4 h} \tag{14}$$

Using the transformation g (t) = v (t) h (t) (15)

The equation (14) gets transformed as

$$\frac{dv}{h} = \frac{-m_3 v^2 + (m_4 - m_1)v - m_2}{(m_3 v - m_4)}$$

After the separation of variables this reduces to

$$\frac{dh}{h} = \frac{(m_3 v - m_4)dv}{-m_3 v^2 + (m_4 - m_1)v - m_2} \tag{16}$$

Taking integration on (16), we obtain after some simplification

$$\Rightarrow \log h = -\frac{1}{2}\log\left[-m_3 v^2 + (m_4 - m_1)v - m_2\right] + \frac{m_1 + m_4}{2m_3}\int \frac{dv}{\left[v - \left(\frac{m_4 - m_1}{2m_3}\right)\right]^2 + K^2} \tag{17}$$

where

$$K^2 = \frac{m_2}{m_3} - \left(\frac{m_4 - m_1}{2m_3}\right)^2 = \frac{4m_2 m_3 - (m_4 - m_1)}{4m_3^2} \tag{18}$$

The following cases would arrive

Case (i):

$If\ 4m_2m_3 > (m_4 - m_1)^2$

Then

$$\int \frac{dv}{\left[v - \left(\frac{m_4 - m_1}{2m_3}\right)\right]^2 + K^2} = \frac{1}{K}\tan^{-1}\left[\frac{\frac{g}{h} - \frac{m_4 - m_1}{2m_3}}{K}\right] + const. \tag{19}$$

Therefore from the result (17) will be

$$\Rightarrow \log h = -\frac{1}{2}\log\left[-m_3\left(\frac{g}{h}\right)^2 + (m_4 - m_1)\frac{g}{h} - m_2\right] + \frac{m_4 + m_1}{2m_3K}\tan^{-1}\left[\frac{\frac{g}{h} - \frac{m_4 - m_1}{2m_3}}{K}\right] + const \tag{20}$$

Case (ii):

$If\ 4m_2m_3 = (m_4 - m_1)^2$

Then

$$\int \frac{dv}{\left[v - \left(\frac{m_4 - m_1}{2m_3}\right)\right]^2 + K^2} = \frac{1}{v - \left(\frac{m_4 - m_1}{2m_3}\right)} + const. \tag{21}$$

Therefore from the result (17) will be

$$\Rightarrow \log h = -\frac{1}{2}\log\left[-m_3\left(\frac{g}{h}\right)^2 + (m_4 - m_1)\frac{g}{h} - m_2\right] - \frac{(m_4 + m_1)h}{2m_3g - (m_4 - m_1)h} + const \tag{22}$$

Case (iii) : $If\ 4m_2m_3 = (m_4 - m_1)^2$

Then

$$\int \frac{dv}{\left[v - \left(\frac{m_4 - m_1}{2m_3}\right)\right]^2 + K^2}. = \frac{1}{2K}\log\left[\frac{\frac{g}{h} - \left(\frac{m_4 - m_1}{2a_3}\right) - K}{\frac{g}{h} - \left(\frac{m_4 - m_1}{2m_3}\right) + K}\right] + const. \tag{23}$$

Therefore from the result (17) will be

$$\Rightarrow \log h = -\frac{1}{2}\log\left[-m_3\left(\frac{g}{h}\right)^2 + (m_4 - m_1)\frac{g}{h} - m_2\right] + \frac{m_4 + m_1}{4m_3K}\log\left[\frac{\frac{g}{h} - \left(\frac{m_4 - m_1}{2m_3}\right) - K}{\frac{g}{h} - \left(\frac{m_4 - m_1}{2m_3}\right) + K}\right] + const \tag{24}$$

For different constant values of m_1, m_2, m_3 and m_4, trajectories g (glucose) verses h (insulin) for the initial values g (0) =75, h (0) = 100 illustrated through Fig 8 to Fig 9

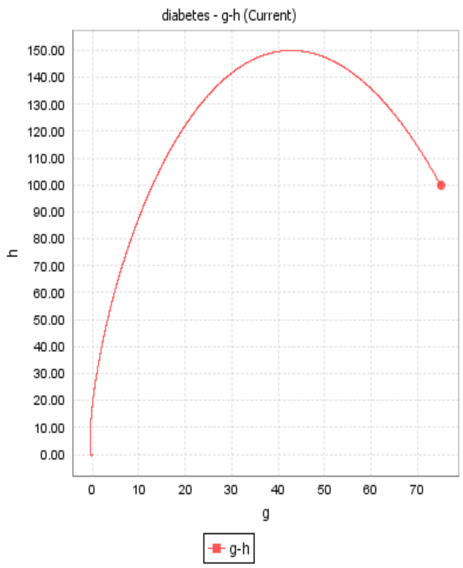

Fig8. *m_1= .018, m_2= .002, m_3=.105,m_4=.03*

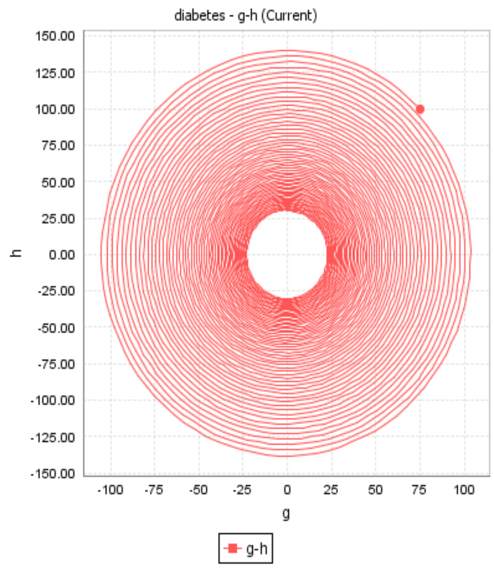

Fig9. *m_1= .0001, m_2= .5140,m_3=.9, m_4=.006*

Fig 8 explains the rise and fall of insulin as glucose increases. This shows the rise and fall of insulin as glucose increases.

Fig 9 illustrates the orbits around the equilibrium points for the values m_1= .0001, m_2= .5140, m_3=.9, m_4=.006 exhibiting the prolonged chronic state of disease.

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