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Article

Mathematical Modelling for Detecting Diabetes

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Abstract: Diabetes is a disease of metabolism whose essential feature is excessive sugar in the blood and urine. Second order differential equation has been formulated to describe the performance of BGRS during GTT and its solution has been shown over here. Interesting point is that the sociological factors play an important role in the Blood Glucose Regulatory System.

Keywords: Mathematical Modelling, Diabetes, Glucose Tolerance Test

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1. Introduction

Diabetes is a disease of metabolism whose essential feature is excessive sugar in the blood and urine. In this disease the body is unable to burn off all it sugar, starches and carbohydrates which leads to serious pathological conditions.

To diagnose diabetes is by the Glucose Tolerance test (GTT) in which the patient is called to the hospital after overnight fasting. On his arrival, he is given a large dose of glucose (the form of sugar in which it occurs in the bloodstream) and then several measurements of the concentration of glucose in the patient's blood is taken during next 3 to 5 hours. Based on his measurements, the physician makes the diagnosis of diabetes which obviously depends on his interpretation of the results.

Realizing that a GTT may be looked upon as a representation of the behaviour of the bold glucose levels in response to a large dose of glucose, aim is to construct a differential equation model which would accurately describe the blood glucose regulatory system (BGRS) during a GTT and would identify one or two parameters to yield an analytical criteria for distinguishing normal individuals from mild diabetes.

To construct a mathematical model it is necessary to follow the following well known facts from the elementary biology.

(i) Glucose is a source of energy for all tissues and organs, and has an important role in the metabolism of any vertebrate. The blood glucose concentration has an optimal level for each individual, and any excessive departure from this optimal concentration causes severe pathological conditions, that may eventually result into death, the departure leads to Diabetes.

(ii) The blood glucose levels tend to be auto-regulatory but they are also susceptible to a wide variety of hormones and some hormones e.g. Insulin decrease the blood glucose concentration. Here we have mentioned two hormones due to their importance in BGRS.

(a) Insulin

This hormone is secreted by β -cells of the pancreas and dominates the performance of BGRS. It reduces the blood glucose concentration. It helps in the consumption of sugar in the facilities glucose uptake in muscles and tissues.

(b) Glycogen

This hormone is secreted by α -cells of the pancreas. Any excessive glucose is stored in the liver in the form of Glycogen. This glycogen is converted back into glucose in terms of need, for example, law blood sugar. The role of this hormone is to increase the rate of breakdown of glycogen into glucose.

2. Formulation of Mathematical Model

It has been formulated in two steps.

Step 1

In the first step, assumptions have been stated, have to identify suitable variables and give the law governing the performance of BGRS.

(i) It is assuming that the following two concentration adequately describe the performance of BGRS.

(1) Concentration of glucose in the blood(G).

(2) Net Hormonal concentration (H).

By net hormonal concentration, it means the cumulative effect of all the relevant hormones with the following sign convection: those hormones which decrease bold glucose concentration (BGC) for example Insulin, are regarded to increase H and hence their contribution to H is taken with positive sign while those hormones which increase BGC for example, Cortisol, contribute negatively to H.

(ii) Since, G and H changes with time, we are considering G and H as dependent variables while t as the independent variable.

(iii) From the elementary consideration of the biological facts, which is stated above, the logistic law which is governing the performance of BGRS may be written as

$$\frac{dG}{dt} = F_1(G,H) + E(t) \tag{1}$$

$$\frac{dH}{dt} = F_2(G,H) \tag{2}$$

Where $F_1 and\ F_2$ are some functions of G and H, while E(t) is the external rate at which the BGC is being increased.

<u>Step 2</u> (Construction of Mathematical Model)

Second order differential equation has been formulated to describe the performance of BGRS during GTT.

$G_0\ and\ H_0$ are the optimal values of G and H respectively. Here main interest is in studying the deviations of G and H from their optimal values therefore we have

$$g = G - G_0 \quad \text{and} \quad h = H - H_0 \tag{3}$$

Substituting these values in equations (1) and (2), and using Taylor's expansion,

We get,

$$\frac{dg}{dt} = \left[F_1(G_0, H_0) + g(\frac{\partial F_1}{\partial G})_0 + h(\frac{\partial F_1}{\partial H})_0 + C_1 \right] + E(t) \tag{4}$$

$$\frac{dh}{dt} = \left[F_2(G_0, H_0) + g(\frac{\partial F_2}{\partial G})_0 + h(\frac{\partial F_2}{\partial H})_0 + C_2 \right] \tag{5}$$

where $(\frac{\partial F_1}{\partial G})_0$ denotes $(\frac{\partial F_1}{\partial G})_{\substack{G=G_0\\H=H_0}}$ etc., and C_1 and C_2 contain terms of second and higher powers in *g* and *h*.

(i) Here we can note that $F_1(G_0, H_0) = 0,\ F_2(G_0, H_0) = 0$ because it is assumed that G and H have assumed their optimal values G_0 and H_0 respectively by the time the fasting patient arrives at the hospital, and

(ii) $E_1\ and\ E_2$, being small quantities, may be neglected; for the case of mild diabetes, g and h are small. With these conditions, eq. (4) and (5) becomes

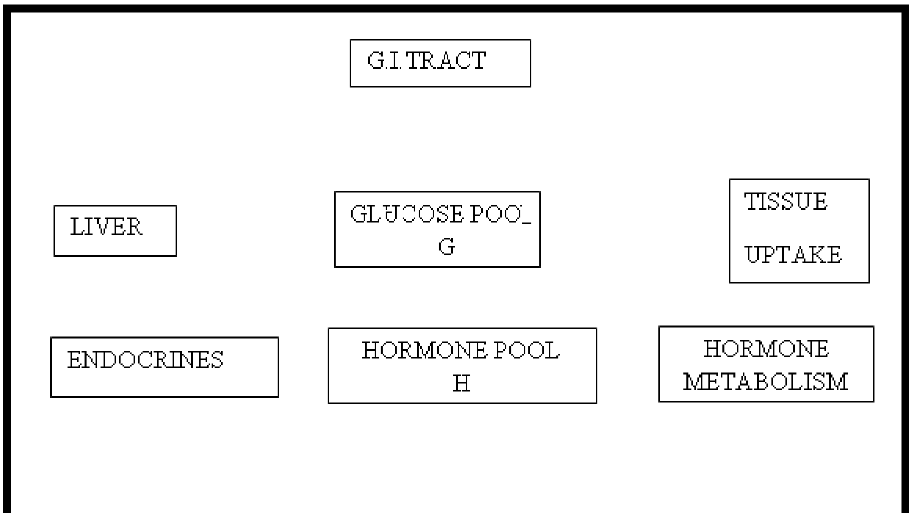
$$\frac{dg}{dt} = \left[g(\frac{\partial F_1}{\partial G})_0 + h(\frac{\partial F_1}{\partial H})_0 \right] + E(t) \tag{6}$$

$$\frac{dh}{dt} = \left[g(\frac{\partial F_2}{\partial G})_0 + h(\frac{\partial F_2}{\partial H})_0 \right] \tag{7}$$

There are a priori no methods to find the values of the numbers $(\frac{\partial F_1}{\partial G})_0$, $(\frac{\partial F_1}{\partial H})_0$, $(\frac{\partial F_2}{\partial G})_0$ and $(\frac{\partial F_2}{\partial H})_0$, but it is possible to, ascertain their signs in the following way:

(a) Sign of $(\frac{\partial F_1}{\partial G})_0$

For this purpose, it is considering g>0, h=0 (excessive glucose). It follows from the fig. That BGC will be decreasing on account of the tissue uptake of glucose and the storing of excess glucose in the form of glycogen, that is, $\frac{dg}{dt}$ <0. In turn, equation (6) implies that $(\frac{\partial F_1}{\partial G})_0$ must be negative.



SCHEMATIC DIAGRAM OF BGRS SYSTEM

(b) Sign of $(\frac{\partial F_1}{\partial H})_0$

For this purpose, it is considering h>0, g=0 (excessive insulin). In this case, $\frac{dh}{dt}$ <0 because excessive insulin will decrease BGC by facilitating tissue uptake of glucose and by increasing the rate at which glucose is converted to glycogen. In turn, equation (6) implies that $(\frac{\partial F_1}{\partial H})_0$ must be negative.

(c) Sign of $(\frac{\partial F_2}{\partial G})_0$

Here, it is considering that g>0, h=0 (excessive glucose). It is well known that after we eat any carbohydrates, our processes G.I. tract sends a signal to the pancreas to decrease more insulin and thus $\frac{dg}{dt}$ >0. In turn it follows equation (7) that $(\frac{\partial F_2}{\partial G})_0$ must be positive.

(d) Sign of $(\frac{\partial F_2}{\partial H})_0$

It is considering h>0, g=0 (excessive insulin). In this case, the hormone concentration decreases due to hormone metabolism. So equation (7) implies that $(\frac{\partial F_2}{\partial H})_0$ must be negative.

With the consideration of above signs equations (6) and (7) can rewrite as

$$\frac{dg}{dt} = -\theta_1 g - \theta_2 h + E(t) \tag{8}$$

$$\frac{dh}{dt} = \theta_3 g - \theta_4 h \tag{9}$$

Where $\theta_1, \theta_2, \theta_3$ *and* θ_4 are all positive constants.

Differentiating equation (8) w.r.t. time gives,

$$\frac{d^2 g}{dt^2} = -\theta_1 \frac{dg}{dt} - \theta_2 \frac{dh}{dt} + \frac{dE}{dt} \tag{10}$$

Substituting the value of $\frac{dh}{dt}$ from equation (9) we get,

$$\frac{d^2 g}{dt^2} = -\theta_1 \frac{dg}{dt} - \theta_2\theta_3 g + \theta_2\theta_4 h + \frac{dE}{dt} \tag{11}$$

Now substituting the value of $\theta_2 h$ from equation (8) in equation (11), and rearranging the term we get,

$$\frac{d^2 g}{dt^2} + 2\alpha \frac{dg}{dt} + w_0^2 g = M(t) \tag{12}$$

Where $2\alpha = (\theta_1 + \theta_4), w_0^2 = (\theta_1\theta_4 + \theta_2\theta_3)$ *and* $M(t) = \theta_4 E(t) + \frac{dE}{dt}$

Equation (12) is a second order differential equation with constant co-efficient which governs the BGRS after a heavy load of glucose is ingested.

If M(t) $\neq$ 0, M(t)= e^{-at} where a is constant adoption rate then equation (12) becomes

$$\frac{d^2g}{dt^2}+2\alpha\frac{dg}{dt}+w_0^2g=e^{-at}$$

Here first main in studying the basic system and if t = 0 is defined to be the instant when the glucose load is completely ingested, then equation (12) will be

$$\frac{d^2g}{dt^2}+2\alpha\frac{dg}{dt}+w_0^2g=0 \qquad (13)$$

Equation (13) may be identified as the standard equation governing damped free vibrations [1]. Now analyzing the model in two steps. In first step solution is obtained and in second step Interpretation of the result has been discussed.

3. Analysis of the Model

We have analyzed the model in two step.

Step I: Solution

The auxiliary equation of (13) is

$m^2+2\alpha m+w_0^2=0$, whose roots are given by $m=\alpha\pm\sqrt{\alpha^2-w_0^2}$.

Three cases can be considered about $\begin{matrix}\alpha^2-w_0^2\leq 0\\ \alpha^2-w_0^2\geq 0\end{matrix}$.

And it is fact that when equation (13) approaches to 0 as $t\to\infty$ and so our model confirms to reality in predicting that the BGC tends to return ultimately to its optimal concentration. So it passes the test of consistency.

For the case $\alpha^2-w_0^2<0$ then

g(t)= $g(t)=Ae^{-\alpha t}\cos\left(wt-\delta\right)$, (14)

where $w^2=w_0^2-\alpha^2$

and for particular integral

P.I. = $\dfrac{1}{D^2+2\alpha D+w_0^2}e^{-at}$

P.I. = $\dfrac{1}{a^2+w_0^2-2\alpha a}e^{-at}$

and in the original variable equation (14) will be

$$G(t) = G_0 + Ae^{-\alpha t}\cos(wt - \delta) + \frac{1}{a^2 + w_0^2 - 2\alpha a}e^{-at} \tag{15}$$

Equation (15) have 6 unknowns viz., $G_0, \alpha, w_0, A, \delta \, and \, a; G_0$, being Blood Glucose Concentration before the glucose load is ingested, can be determined by measuring the patients blood glucose concentration immediately upon his arrival at the hospital. The remaining unknowns can be finding through the equations

$$G_j = G_0 + Ae^{-\alpha t_j}\cos(wt_j - \delta) + \frac{1}{a^2 + w_0^2 - 2\alpha a}e^{-at_j}, \text{ j= 1,2,3,4,5} \tag{16}$$

By taking five measurements of $G_1, G_2, G_3, G_4 \, and \, G_5$ of the patients BGC at time $t_1, t_2, t_3, t_4 \, and \, t_5$ respectively.

Step II: Interpretation

i. From equation (13), it is found that there are two system parameters viz $\alpha \, and \, w_0$; out of them which is a more suitable is depend on the response of Blood Glucose Regulatory System to a Glucose Tolerance Test.
ii. Based numbers of experiments, Ackerman et al [2] has concluded that a slight error in the measurement of G causes a very significant error in the value of α while the parameter w_0 was relatively insensitive to the error in G.
iii. In solution (15), *a* also plays an important role because it is also adoption rate so it also make effect on the response of BGRS during GTT.
iv. w_0 may be regarded as more faithful parameter for diagnosis of diabetes.
v. Corresponding period has been defined by $T_0 = \frac{2\pi}{w_0}, w_0$ is the natural frequency of the system and here it is considered T_0 as a suitable parameter for diagnosis of diabetes.
vi. It has been concluded that a value of less than four hours for T_0 indicated normalcy while appreciably more than four hours implied mild diabetes.
vii. Looking over these all points, interesting point is that the sociological factors play a important role in the Blood Glucose Regulatory System.

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