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Mathematical Model for Detecting Diabetes in the Blood

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Abstract

This study presents a new mathematical model for Blood Glucose Regulatory System(BGRS) which includes epinephrine as a third variable in the form, $\dot{Y} = AY$, and whose solution has been analyzed for equilibrium and stability to provide the blood glucose concentrations for diabetics and non-diabetics. We establish that the final model is asymptotically stable compared to the existing models, that is, the eigenvalues of the coefficient matrix are complex numbers with negative real parts. Furthermore, the resonance period for the final model, that is, $T_0 = 2.9847134$ hours, is far less than that of the existing model, showing that the glucose concentration returns to normal level within a shorter time.

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1 Introduction

Over the past years, mathematics has been used to understand and predict the spread of diseases, relating important public health questions to basic infection parameters. Diabetes Mellitus is a disease which is characterized by too high sugar levels in the blood and urine. It is usually diagnosed by means of a glucose tolerance test (GTT). Today, there are over 20 million diabetics in America, six million of whom must take injections of insulin daily, Reporter [25]. It was established by the Kenya Diabetes Management and Information Center during the free diabetes screening exercise at M. P. Shah hospital, Nairobi, Kenya that 3.3 million Kenyans suffer from diabetes, Okwemba [22]. Cases of diabetes in the country have increased from 3.5 to 10 per cent of the population in the past one year. Every 2 years 921 new cases are diagnosed in various clinics in Nairobi, Coast, Central, Nyanza, Eastern and Rift Valley provinces. Diabetic patients require supplement of insulin in the form of regular injections and tablets in addition to modified diet to regulate glucose input, Krimmel *et al* [20]. Glucose plays an important role in the food metabolism of any vertebrate tissue since it is a source of energy for all tissues and organs, Middleman [21]. The majority of mathematical models were devoted to the dynamics of glucose-insulin, including Intra Venous Glucose Tolerance Test (IVGTT), Oral Glucose Tolerance Test (OGTT) and Frequently Sampled Intra Venous Glucose Tolerance Test (FSIVGTT). So far, all the existing models were based on two variables only: glucose and insulin. In the GTT, an individual comes to the hospital after an overnight fast and is given a large dose of glucose (sugar in the form in which it usually appears in the bloodstream). During the next three to five hours several measurements are made on the concentration of glucose in the patient's blood and these measurements are used in the diagnosis of diabetes Mellitus, Eastham [14]. It is quite conceivable, therefore that the body will interpret this as an extreme emergency and thereafter the hormones epinephrine and glucagon come in play. After the ingestion of the glucose load a serious shortcoming of this simplified model was experienced because variables such as epinephrine and glucagon, which play an important role during this time of recovery phase of the GTT response were neglected. Epinephrine is secreted by the adrenal medulla in response to acute stress (fight or flight response), Duff and Jason [13]. Important effects of epinephrine, some of which are highlighted in the appendix, include;

(a) increased glucose production from glycogen breakdown

(b) increased glucose production from lactate and amino acids

(c) increased fat mobilization by stimulation of hormone sensitive lipase

(d) small net stimulation of insulin secretion from pancreatic β-cells

2 Preliminaries

Provided there is no recent digestion, glucose and insulin concentration will be in equilibrium.
If g is taken to be excess glucose concentration and h is excess insulin concentration at time t, then at equilibrium, $g = h = 0$; positive value of g or h corresponds to concentrations greater than the equilibrium values while negative values corresponds to concentrations less than equilibrium values.
If either h or g is a non-zero value then the body tries to restore the equilibrium. It is assumed that the rate of change of these quantities depend only on the values of g and h.
If there is an internal rate at which the blood glucose concentration is being increased, epinephrine is included as a separate variable in this model of blood glucose regulatory system. Thus, if it is assumed that there is no recent digestion, the following systems of differential equations results, Ackerman *et al* [1];

$$\begin{aligned} \dot{g} &= -ag - bh + fe \\ \dot{h} &= cg - dh + ke \\ \dot{e} &= -lg - mh + ne \end{aligned} \tag{1}$$

where e represents epinephrine.
Thus, a, b, c, d, f, k, l, m and n are constants.

3 Mathematical Model for Testing Diabetes

From the model in equation (1), differentiating

$$\frac{dg}{dt} = -ag - bh + fe$$

of equation (1) w.r.t t, we obtain;

$$\frac{d^2g}{dt^2} = -a\frac{dg}{dt} - b\frac{dh}{dt} + f\frac{de}{dt} \tag{2}$$

Substituting for

$$\frac{dh}{dt} = cg - dh + ke$$

and

$$\frac{de}{dt} = -lg - mh + ne$$

of equation (1) in equation (2) gives;

$$\frac{d^2g}{dt^2} + a\frac{dg}{dt} + (bc + fl)g + (bk - fn)e + (fm - bd)h = 0 \tag{3}$$

From equation (3), where

$$e = \frac{1}{f}(\frac{dg}{dt} + ag)$$

from equation (1), and assuming $h = 0$

$$\frac{d^2g}{dt^2} + (\frac{bk}{f} + a - n)\frac{dg}{dt} + (bc + fl + \frac{bka}{f} - na)g = 0$$

This is in the form of;

$$\frac{d^2g}{dt^2} + 2\alpha\frac{dg}{dt} + \omega_0^2 g = 0 \tag{4}$$

$$\Rightarrow \alpha = \frac{1}{2}(\frac{bk}{f} + a - n)$$

and

$$\omega_0^2 = (\frac{1}{f}bka + bc + fl - na)$$

where the value of ω_0, which is the system natural frequency is the basic descriptor of the response to a GTT.
The model certainly conforms to reality in predicting that the blood glucose concentration tends to return eventually to its optimal concentration (1). It is assumed that $\alpha^2 - \omega_0^2$ is negative, so $\alpha^2 - \omega_0^2 < 0$. This means that characteristic equation of (2) has complex roots.
If $\alpha^2 - \omega_0^2 > 0$, then $g(t)$ drops very rapidly from a fairly high values to negative ones below the equilibrium value. The body will interpret this as an extreme emergency and large amounts of epinephrine will be secreted (2).

4 Verification of the model

From equation (1), the model is in the form of;

$$\begin{bmatrix} \dot{g} \\ \dot{h} \\ \dot{e} \end{bmatrix} = \begin{bmatrix} -2.92 & -4.34 & 1.24 \\ 0.208 & -0.78 & 0.14 \\ -2.94 & -0.98 & 0.53 \end{bmatrix} \begin{bmatrix} g \\ h \\ e \end{bmatrix} \tag{5}$$

where the constants given by 2.92, 4.34, 0.208, 0.78, 1.24, 0.14, 2.94, 0.98 and 0.53 respectively are secondary values, Paolo *et al*[24].
This system of equations can be expressed in the matrix vector form as

$$\dot{\mathbf{Y}} = \mathbf{AY}.$$

Using MATLAB, the eigenvalues are, $\lambda_1 = -1.5825 + 1.5754i$,
$\lambda_2 = -1.5825 - 1.5754i$ and $\lambda_3 = -0.0050$. Since the eigenvalues are complex numbers with negative real parts, the system is asymptotically stable. This is a situation where the individual is normal.
From the relation;

$$\omega_0^2 = (\frac{1}{f}bka + bc + fl - na)$$

$\omega_0^2 = (1.4308 + 0.90272 + 3.6456 - 1.5476)$.
$\Rightarrow \omega_0^2 = 4.43152$
$\Rightarrow \omega_0 = 2.1051176$.
From the relation;

$$T_0 = \frac{2\pi}{\omega_0}$$

and by substituting ω_0,

$$T_0 = \frac{2\pi}{2.1051176}$$

$\Rightarrow T_0 = 2.9847134$
Since the resonance period is far less than 4 hours, the individual is said to be normal. From the results, it was shown that by employing the model, the blood glucose concentrations were corrected to normal levels in hyperglycaemic situations.
Table (3.1): Blood glucose concentrations after Insulin infusion and corresponding concentrations with Epinephrine, in mmol/L.

Glucose	**Insulin**	**Epinephrine**	**Glucose**	**Insulin**	**Epinephrine**
Initial	Control	Control	Initial	Control	Control
26.00	6.8	3.0634	30.00	9.0	3.6495
18.30	11.3	7.9093	18.60	7.9	3.2156
22.00	8.0	3.0831	21.84	7.2	2.5910
25.00	7.0	3.6415	27.20	4.3	3.9789
17.30	5.7	2.4745	20.70	7.1	2.9385
18.00	6.9	2.7898	18.46	6.7	2.5910
20.20	8.0	2.9766	18.10	7.2	2.2616

For individuals presenting with very low blood sugar, that is hypoglycaemic patients, secondary values and raw data of blood glucose concentrations before

and after intravenous (IV) bolus of 50 percent dextrose were used to correct the blood glucose concentrations as shown in table (3.2) below.
Table (3.2): Blood glucose concentrations before and after intravenous (IV) bolus of 50 percent dextrose.

Fasting blood sugar(mmol/L)	**Corrected blood sugar(mmol/L)**
2.2	6.8
1.8	5.0
1.5	7.1
2.1	5.6
1.9	4.1
1.0	4.8
2.0	5.6
2.3	6.1
1.7	4.3
1.1	5.2

Similarly from the results, it is shown that by employing the model, the blood glucose concentrations were corrected to normal levels in hypoglycaemic states.

5 Conclusion and recommendation

This paper presents a model for detecting diabetes Mellitus in the blood described by equation (5). Epinephrine has been successfully incorporated as a third variable in this model of blood glucose regulatory system (BGRS). The importance of this third variable lies in its ability to help in conducting a reliable test for detecting diabetes in the blood. This leads to a system of linear homogenous equations, which are expressed in the form $\dot{Y} = AY$ and whose solution provides the blood glucose concentrations for diabetics and non diabetics. This is exemplified by the sample results considered in Table (3.1) and Table (3.2). This model has been found to be asymptotically stable since the eigenvalues of the coefficient matrix are complex numbers with negative real parts. Furthermore the resonance period for this model which is $T_0 = 2.9847134$ hrs, is far less than $T_0 = 3.5232581$ hrs for the existing model. This shows that the glucose concentration returns to normal level within a shorter time. It is worth noting that the model developed in this study only considered an internal rate at which the blood glucose concentration is being increased. Future research may take into consideration an external rate at which the blood glucose concentration is being increased.

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