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A DISCRETE MODEL OF GLUCOSE-INSULIN INTERACTION AND STABILITY ANALYSIS

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Abstract:

The stability of a discrete-time Glucose Insulin interaction system is considered in this paper. The system is modeled with difference equations. Local stability conditions about the equilibrium points are obtained. The phase portraits are obtained for different sets of parameter values. Also bifurcation diagrams are provided for selected range of parameter. Numerical simulations are carried out and graphs are also generated to indicate the role of insulin in the regulation process of glucose in the human body.

Introduction:

Diabetes is a metabolic disease characterized by high levels of blood glucose (blood sugar), which leads to severe damage to heart, blood vessels, eyes, kidneys, and nerves. It is a disease that occurs either because the pancreas does not produce enough insulin or because the body's cells cannot effectively use the insulin it produces. Type 1 diabetes is characterized by deficiency in insulin production and requires daily administration of insulin. Type 2 diabetes results from the body's inability to use insulin effectively. Diabetes is on the rise. The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. Diabetes caused 1.5 million deaths in 2012. Diabetes is an epidemic in India with more than 69.1 million diabetic individuals currently diagnosed with the disease. A body's homeostatic mechanism, when operating normally, restores the blood sugar level to a narrow range of about 4.4 to 6.1 mmol/L (79.2 to 110 mg/dL). For the majority of healthy individuals, normal blood sugar levels are as follows: between 4.0 to 6.0 mmol/L (72 to 108mg/dL) when fasting, up to 7.8 mmol/L (140 mg/dL) 2 hours after eating.

Mathematical models have been used to describe and understand diabetes dynamics. There are various models based on glucose and insulin distributions and those models have been used to explain glucose-insulin interaction. The most widely used model in the study of diabetes is the minimal model which is used in the interpretation of the intravenous glucose tolerance test (IVGTT) [2]. A glucose tolerance test measures how well a human body is able to break down glucose.

Model of Glucose and Insulin Interaction:

Sometimes, it is desirable to use a set of difference equations for which time is a discrete variable. Also, discrete time models governed by difference equations are more appropriate than continuous ones. Discrete time systems can also provide efficient computational models of continuous ones of numerical simulations. Several authors [1,3,5,6] have proposed more popular, general and realistic models with results consistent with physiology. The modeling of the glucose-insulin system has become an interesting topic and several models have been proposed and studied with the purpose of understanding the system better, investigating possible pathways to diabetes as well as providing better insulin administration practices. In the glucose regulatory system, insulin and glucagon play vital role in balancing metabolism. Insulin and glucagon act together to balance metabolism. Insulin helps control blood glucose levels by signaling the liver and muscle and fat cells to take in glucose from the blood. Glucose is stored in the body as glycogen. The liver is an important storage site for glycogen. In this paper, we consider the following system of difference equations as the discrete version of the model studied in [7].

$$\begin{aligned} x(n+1) &= (1-a)x(n) - bx(n)y(n) + c \\ y(n+1) &= (1-d)y(n) + ex(n) \end{aligned} \qquad (1)$$

where $x \geq 0, y \geq 0$.

Variables	Description
x	Glucose Concentration
y	Insulin Concentration
a	Insulin Independent Glucose Disappearance
b	Insulin Dependent Glucose Disappearance
c	Glucose Infusion Rate
d	Insulin Degradation
e	Insulin Production due to Glucose Stimulation

Equilibrium Points of the System:

In order to study the qualitative behavior of the solutions of the system of nonlinear Difference equations (1), we define the equilibrium points of the dynamic system as a non-negative fixed point of the map, i.e. the solutions of the following nonlinear algebraic system.

$$x = (1-a)x - bxy + c : y = (1-d)y + ex$$

The system (1) has two equilibrium points $E_0 = (0,0)$ and

$$E_1 = \left(\frac{-ad + \sqrt{a^2d^2 + 4bcde}}{2be}, \frac{-ad + \sqrt{a^2d^2 + 4bcde}}{2bd} \right).$$

In this discussion, we are interested in the interior positive equilibrium point E_1.

Stability Analysis:

In this section, we investigate the local behavior of the model around each fixed point. The local stability analysis of the model can be studied by computing the variation matrix corresponding to each fixed point [4]. The Jacobian matrix J for the system (1) is

$$J(x,y) = \begin{bmatrix} 1-a-by & -bx \\ e & 1-d \end{bmatrix} \qquad (2)$$

Trace $J(x,y) = 2-(a+d)-by$ and Det $J(x,y) = (1-a-by)(1-d) + bex$. For the system (1), we have the following analysis. From (2), using the equilibrium point E_0, Jacobian matrix for E_0 is given by

$$J(E_0) = \begin{bmatrix} 1-a & 0 \\ e & 1-d \end{bmatrix}$$

Trace $J(E_0) = 2-(a+d)$ and Det $J(E_0) = (1-a)(1-d)$. The Eigen values of the matrix J(E_0) are $\lambda_1 = 1-a$ and $\lambda_2 = 1-d$. Jacobian matrix for E_1 is given by

$$J(E_1) = \begin{bmatrix} 1 - \frac{a}{2} - \frac{A}{2d} & \frac{ad-A}{2e} \\ e & 1-d \end{bmatrix}$$

Where A=$\sqrt{a^2d^2 + 4bdce}$, Trace $J(E_1) = 2 - d - \frac{a}{2} - \frac{A}{2d}$ and Det $J(E_1) = (1-d) - \frac{a}{2} + A\left(1 - \frac{1}{2a}\right)$

Stability of Equilibrium Points:

The characteristic roots $\lambda_1$and λ_2 of p(λ) = 0 are called eigen values of the fixed point (x*, y*). Then the fixed point (x*,y*) is a sink if $|\lambda_{1,2}|$< 1. Hence the sink is locally asymptotically stable. The fixed point (x*, y*) is a source if $|\lambda_{1,2}|$> 1. The source is locally unstable. The fixed point (x*, y*) is a saddle if $|\lambda_1|$> 1 and $|\lambda_1|$< 1 (or $|\lambda_1|$<1 and

$|\lambda_1|> 1$). Finally (x^* y^*) is called non hyperbolic if either $|\lambda_1|$ = 1 or $|\lambda_2|$= 1. For the system (1), we have the following results [8, 9].

Proposition 1: The fixed point E_0 is a

- ✓ Sink if a > 0 and d > 0.
- ✓ Source if a < 0 and d < 0.
- ✓ Saddle if a > 0 and d < 0.

Proposition 2: The fixed point E_1 is a

- ✓ Sink if $\dfrac{d}{4be\left(1-\dfrac{1}{d}\right)^2}\left[3+\dfrac{2}{d}[(ad)^2+4(2-a)]\right]<c<\dfrac{(1+a)[a+d(1-a)]}{4be\left(1-\dfrac{1}{2d}\right)^2}$.
- ✓ Source if $c>\dfrac{d}{4be\left(1-\dfrac{1}{d}\right)^2}\left[3+\dfrac{2}{d}[(ad)^2+4(2-a)]\right]$ and $c>\dfrac{(1+a)[a+d(1-a)]}{4be\left(1-\dfrac{1}{2d}\right)^2}$.
- ✓ Saddle if $c<\dfrac{d}{4be\left(1-\dfrac{1}{d}\right)^2}\left[3+\dfrac{2}{d}[(ad)^2+4(2-a)]\right]$ and $c>\dfrac{(1+a)[a+d(1+a)]}{4be\left(1-\dfrac{1}{2d}\right)^2}$.

Numerical Simulations:

In this section, we provide the numerical simulations to illustrate the results of the previous sections. Mainly, we present the time plots of the solutions x and y with phase plane diagrams (around the equilibrium points) for the Glucose-Insulin systems. Dynamic nature of the system (1) about the equilibrium points under different sets of parameter values are presented in this section. Also the bifurcation diagram indicates the existence of chaos in both glucose and insulin interaction.

Example 1: For the values $a=0.99; b=0.001; c=0.0009; d=0.99; e=0.007$, it is the trivial fixed point. The Eigen values are $\lambda_{1,2}=0.01$ so that $|\lambda_{1,2}|=0.01<1$. Hence the trivial fixed point is stable. The time plot and the phase diagram are presented, see Figure – 1 & 2.

Example 2: For the values $a=1.9; b=1.9; c=1.19; d=1.25; e=0.65$, we obtain $E_1=(0.43, 0.22)$ which is an interior fixed point. The eigen values are $\lambda_{1,2}=-0.8210\pm i0.5369$ so that $|\lambda_{1,2}|=0.9809<1$. Hence the fixed point is stable. The time plot and the phase diagram are provided in Figure – 3 & 4.

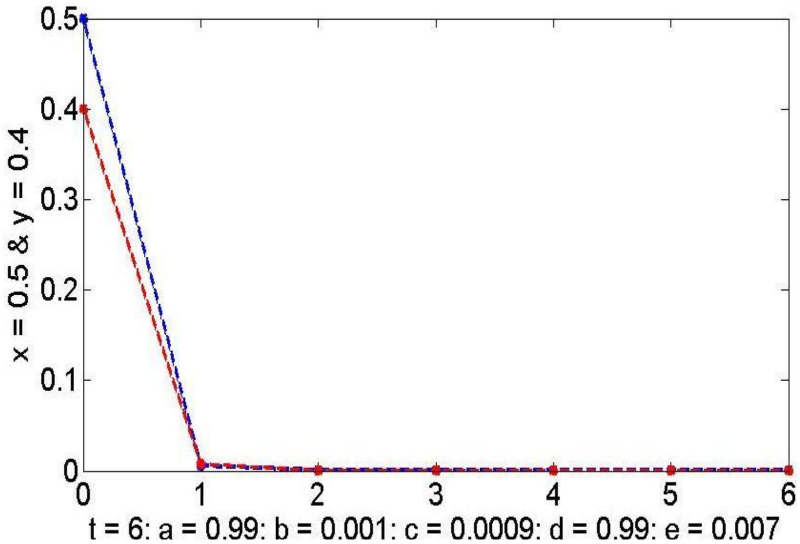

Figure 1: Time Plot for E_0 for system (1)

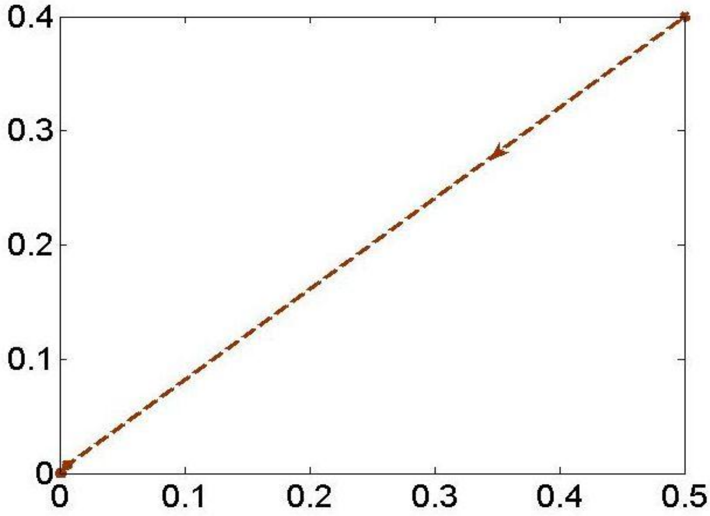

Figure2: Phase Portrait E_0 for system(1)

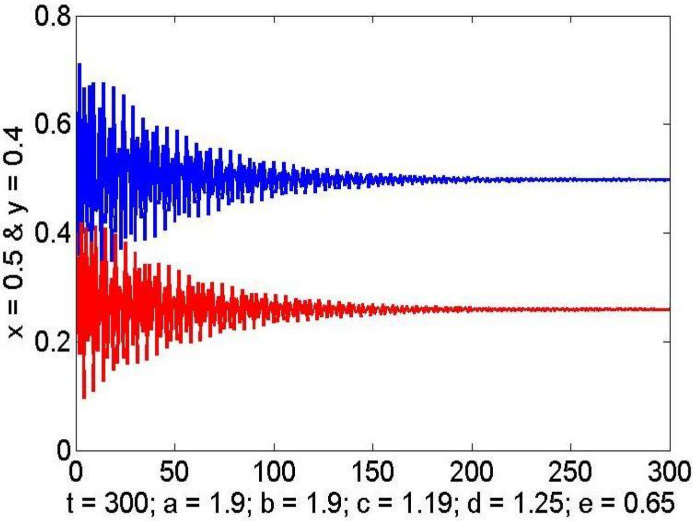

Figure 3: Time Plot for E_1 for system (1)

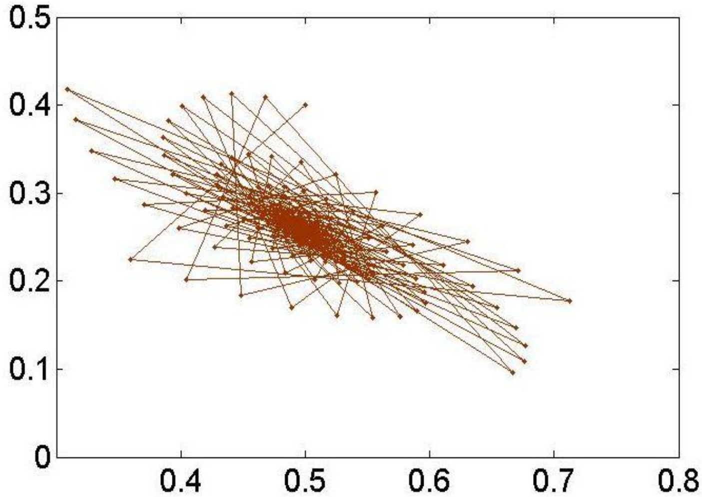

Figure 4: Phase Portrait E_1 for system (1)

Studies in population dynamics aims at identifying qualitative changes in the long-term dynamics predicted by the model. Bifurcation theory deals with classifying, ordering and studying the regularity in the dynamical changes. Bifurcation diagrams provide information about abrupt changes in the dynamics and the values of parameters at which such changes occur. Also they provide information about the dependence of the dynamics on a certain parameter. Qualitative changes are tied with bifurcation see Figure – 5 & 6.

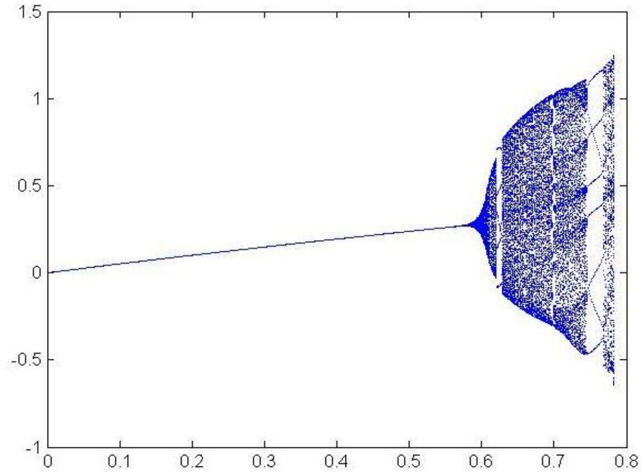

Figure 5: Bifurcations for Glucose system

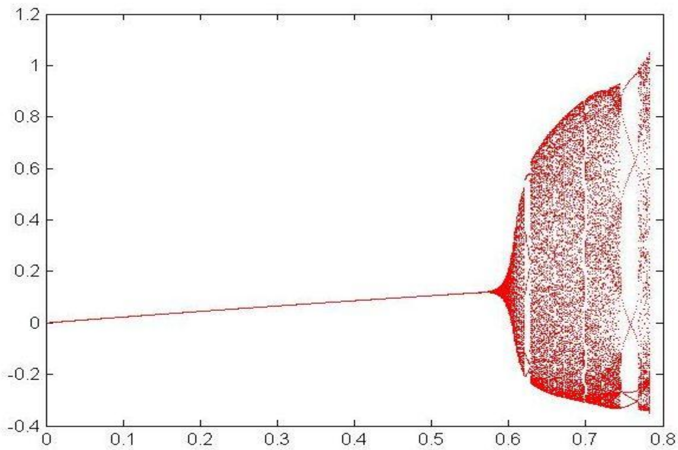

Figure 6: Bifurcation for Insulin system

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