International Journal of Pure and Applied Mathematical Sciences.
ISSN 0972-9828 Volume 13, Number 1 (2020), pp. 1-10

http://www.ripublication.com/ijpams.htm

Fractional Order Differential Equations for Glucose-insulin Interaction

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Abstract

In this paper we consider the fractional-order glucose-insulin model. A discretization process is applied to obtain its discrete version. The stability of equilibrium points is studied. Numerical solutions of this model are given.

1. INTRODUCTION

Fractional derivatives have a long mathematical history and it is a 300 year old topic. A property of these fractional models is their nonlocal property which does not exist in integer order differential equations. Nonlocal property means that the next state of a model depends not only upon its current state, but also upon all of its historical status as the case in epidemics. Fractional-order differential equations can be used to model phenomena which cannot be adequately modeled by integer-order differential equations. An excellent literature of this can be found in [1]-[10]. On the other hand, discrete-time models are more accurate to describe epidemics than the continuous-time models because statistical data on epidemics is collected in discrete time. Recalling the basic definitions (Caputo) and properties of fractional order differentiation and integration

Definition 1.1 *The fractional integral operator of order $\alpha \in \mathbb{R}^+$ of the function $f(t)$, $t > 0$ is defined as*

$$I^{\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} f(s) ds,$$

where $\Gamma(z) = \int_0^{\infty} e^{-t} t^{z-1} dt$ is the Euler gamma function.

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*The research contained in this report has been supported by the University of Al-Baha, Saudi Arabia.

Definition 1.2 *[2] The Caputo fractional derivative of order $\alpha > 0$, $n-1 < \alpha < n$, $n \in N$ is defined as*

$$D^{\alpha} f(t) = \begin{cases} \frac{1}{\Gamma(n-\alpha)} \int_0^t \frac{f^{(n)}(s)}{(t-s)^{\alpha+1-n}} ds, & n-1 < \alpha < n, \\ \frac{d^n}{dt^n} f(t) & \alpha = n. \end{cases}$$

Lemma 1.1 *([7]) Considering the following fractional differential system with Caputo derivative*

$$D^{\alpha} x = Ax; \;\; x(0) = x_0$$

with $\alpha \in (0,1]$, $x \in R^n$ and $A \in R^{n\times n}$. The characteristic equation of the system is det$|s^{\alpha} I - A| = 0$. If all of the roots of the characteristic equation have negative real parts, then the zero solution of the system is asymptotically stable.

Lemma 1.2 *([11]) The equilibrium point $E_1 = (x^*, y^*)$ of the fractional differential system*

$$D^{\alpha} x(t) = f_1(x,y), \; \alpha \in (0,1]$$
$$D^{\alpha} y(t) = f_2(x,y), \; t \in [0,T].$$

with initial data:

$$x(0) = x_0, \; y(0) = y_0,$$

is locally asymptotically stable if and only if all eigenvalues λ_i of the Jacobian matrix

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial x} & \frac{\partial f_1}{\partial y} \\ \frac{\partial f_2}{\partial x} & \frac{\partial f_2}{\partial y} \end{bmatrix}.$$

evaluated at the equilibrium point E_1, satisfy the condition that $|arg(\lambda_i)| > \frac{\alpha\pi}{2}$.

Here we propose a discretization process to obtain the discrete version of fractional order differential equations. Mean while, we apply the same discretization process to discretize the fractional order of the discrete-time generalist glucose-insulin dynamics model with fractional order:

$$\begin{aligned} D^{\alpha} x(t) &= -ax(t) - bx(t)y(t) + c, \; t \in [0,T], \\ D^{\alpha} y(t) &= dx(t) - ey(t), \; t \in [0,T]. \end{aligned} \tag{1.1}$$

with initial data:

$$x(\theta) = \phi(\theta), \; \theta < 0, y(\theta) = \psi(\theta), \; \theta < 0.$$

where

$x \geq 0$ represents glucose concentration,

$y \geq 0$ represents insulin concentration,

a is the rate constant which represents insulin-independent glucose disappearance,

b is the rate constant which represents insulin-dependent glucose disappearance,

c is the glucose infusion rate,

d is the rate constant which represents insulin production due to glucose stimulation,

e is the rate constant which represents insulin degradation.

The model (1.1) was considered in [12] in the case $\alpha = 1$.

2. DISCRETIZATION PROCESS

In [13, 14], a discretization process is introduced to discretize the fractional order logistic differential equations. When the fractional order parameter $\alpha \longrightarrow 1$, Euler's discretization method is obtained. Let $\alpha \in (0,1)$ and consider the differential equation of fractional order

$$D^{\alpha}x(t) = f(x(t)), \;\; t > 0,$$
$$x(0) = x_0, \;\; t \leq 0.$$

The corresponding equation with a piecewise constant argument

$$\begin{aligned} D^{\alpha}x(t) =& f\left(x\left(r\left[\frac{t}{r}\right]\right)\right), \;\; t > 0, \\ x(0) =& x_0, \;\; t \leq 0. \end{aligned}$$

Let $t \in [0, r)$, then $\frac{t}{r} \in [0, 1)$. So we get $D^{\alpha}x(t) = f(x_0), \;\; t \in [0, 1)$. Thus

$$x_1(t) = x_0 + \frac{t^{\alpha}}{\Gamma(\alpha+1)} f(x_0).$$

Let $t \in [r, 2r)$, then $\frac{t}{r} \in [1, 2)$. So we get $D^{\alpha}x(t) = f(x_1(r)), t \in [r, 2r)$. Thus

$$x_2(t) = x_1(r) + \frac{(t-r)^{\alpha}}{\Gamma(\alpha+1)} f(x_1(r)).$$

Let $t \in [2r, 3r)$, then $\frac{t}{r} \in [2, 3)$. So we get $D^{\alpha}x(t) = f(x_2(2r)), t \in [2r, 3r)$. Thus

$$x_3(t) = x_2(2r) + \frac{(t-2r)^{\alpha}}{\Gamma(\alpha+1)} f(x_2(2r)).$$

Repeating the process, we get when $t \in [nr, (n+1)r)$, then $\frac{t}{r} \in [n, n+1)$ so we get

$$D^{\alpha}x(t) = f(x_n(nr)), \;\; t \in [nr, (n+1)r).$$

Thus

$$x_{n+1}(t) = x_n(nr) + \frac{(t-nr)^{\alpha}}{\Gamma(\alpha+1)} f(x_n(nr)).$$

3. MODEL DESCRIPTION AND DISCRETIZATION

We are interested in applying the discretizations method to the fractional glucose-insulin dynamics model (1.1). The discretization of system (1.1) with piecewise constant arguments is given as

$$\begin{aligned} D^a x(t) &= -ax\left(r\left[\frac{t}{r}\right]\right) - bx\left(r\left[\frac{t}{r}\right]\right) y\left(r\left[\frac{t}{r}\right]\right) + c, \\ D^a y(t) &= dx\left(r\left[\frac{t}{r}\right]\right) - ey\left(r\left[\frac{t}{r}\right]\right), \end{aligned} \tag{3.1}$$

with initial condition $x(0) = x_0$, $y(0) = y_0$. The proposed discretization method has the following steps:

Step 1. Let $t \in [0, r)$, then $\frac{t}{r} \in [0, 1)$. So we get

$$\begin{aligned} D^\alpha x_1 &= ax_0 - bx_0 y_0 + c, \\ D^\alpha y_1 &= dx_0 - ey_0, \end{aligned}$$

and the solution of (3.1) is given by

$$\begin{aligned} x_1(t) &= x_0 + \frac{r^\alpha}{\Gamma(\alpha+1)}(ax_0 - bx_0 y_0 + c) \\ y_1(t) &= y_0 + \frac{r^\alpha}{\Gamma(\alpha+1)}(dx_0 - ey_0) \end{aligned}$$

Step 2. Let $t \in [r, 2r)$,then $\frac{t}{r} \in [1, 2)$. So we get

$$\begin{aligned} D^\alpha x_2(t) &= ax_1(r) - bx_1(r)y_1(r) + c, \\ D^\alpha y_2(t) &= dx_1(r) - ey_1(r), \end{aligned}$$

and the solution of (3.1) is given by

$$\begin{aligned} x_2(t) = x_1(r) &= x_1(r) + \frac{(t-r)^\alpha}{\Gamma(\alpha+1)}(ax_1(r) - bx_1(r)y_1(r) + c) \\ y_2(t) &= y_1(r) + \frac{(t-r)^\alpha}{\Gamma(\alpha+1)}(dx_1(r) - ey_1(r)). \end{aligned}$$

Repeating the process, we can easily deduce that the solution of (3.1) is given by

$$\begin{aligned} x_{n+1}(t) &= x_n(nr) + \frac{(t-nr)^\alpha}{\Gamma(\alpha+1)}\left[ax_n(nr) - bx_n(nr)y_n(nr) + c\right] \\ y_{n+1}(t) &= y_n(nr) + \frac{(t-nr)^\alpha}{\Gamma(\alpha+1)}\left[dx_n(nr) - ey_n(nr)\right]. \end{aligned}$$

Hence the discrete version is

$$\begin{aligned} x_{n+1} &= x_n + \frac{r^\alpha}{\Gamma(\alpha+1)}\left[ax_n - bx_n y_n + c\right] \\ y_{n+1} &= y_n + \frac{r^\alpha}{\Gamma(\alpha+1)}[dx_n - ey_n] \end{aligned} \tag{3.2}$$

4. FIXED POINT AND STABILITY OF EQUILIBRIA

Now we analyze the stability of the fixed points of the system (1.1) which has the following two fixed equilibrium points: $E_0 = (0, 0)$, $E_1 = (x^*, y^*)$, where

$$x^* = \frac{-ad + \sqrt{(ad)^2 + 4becd}}{2dc},$$
$$y^* = \frac{-ad + \sqrt{(ad)^2 + 4becd}}{2eb}.$$

For the system (3.2), the Jacobian matrix J at the equilibrium point E_1 is

$$J = \begin{bmatrix} 1 + ah - by^* & -bx^*h \\ hd & 1 - eh \end{bmatrix},$$

where $h = \frac{r^\alpha}{\Gamma(\alpha+1)}$ and its eigenvalues are

$$\lambda_{1,2} = \frac{1}{2}\left(tr(J) \pm \sqrt{tr^2(J) - 4\Delta}\right)$$

where

$$tr(J) = 2 + h(a - y^* - e)$$

and

$$\Delta = (bdx^* - ae)h^2 + (bey^* + a)h + 1 - eh - by^*.$$

A sufficient condition for the local asymptotic stability of the equilibrium point E_1 is

$$|arg(\lambda_1)| > \frac{\alpha\pi}{2}, \ \ |arg(\lambda_2)| > \frac{\alpha\pi}{2},$$

i.e.,

$$\left|\frac{\sqrt{4\Delta - tr^2(J)}}{tr(J)}\right| > tan\frac{\alpha\pi}{2},$$

then

$$\left|\frac{\sqrt{4[(bdx^* - ae)h^2 + (bey^* + a)h + 1 - eh - by^*] - (2 + h(a - y^* - e))^2}}{2 + h(a - y^* - e)}\right| > tan\frac{\alpha\pi}{2}$$

and the hopf bifurcation occurs when

$$|arg(\lambda_1)| = \frac{\alpha\pi}{2}, \ \ |arg(\lambda_2)| = \frac{\alpha\pi}{2}$$

i.e.,

$$\left|\frac{\sqrt{4\Delta - tr^2(J)}}{tr(J)}\right| = tan\frac{\alpha\pi}{2},$$

then

$$\left|\frac{\sqrt{4[(bdx^* - ae)h^2 + (bey^* + a)h + 1 - eh - by^*] - (2 + h(a - y^* - e))^2}}{2 + h(a - y^* - e)}\right| = tan\frac{\alpha\pi}{2}.$$

For E_0, we have

$$J = \begin{bmatrix} 1 + ah & 0 \\ hd & 1 - eh \end{bmatrix}.$$

its eigenvalues are

$$\lambda_{1,2} = \frac{1}{2}\left(tr(J) \pm \sqrt{tr^2(J) - 4\Delta}\right)$$

where

$$tr(J) = 2 + h(a - e)$$

and

$$\Delta = -aeh^2 + ah + 1 - eh.$$

A sufficient condition for the local asymptotic stability of the equilibrium point $E_0 = (0, 0)$ is

$$\left|\frac{\sqrt{-4aeh^2 + 4ah + 4 - 4eh - (2 + h(a - e))^2}}{2 + h(a - e)}\right| > tan\frac{\alpha\pi}{2}$$

and the hopf bifurcation occurs when

$$\left|\frac{\sqrt{-4aeh^2 + 4ah + 4 - 4eh - (2 + h(a - e))^2}}{2 + h(a - e)}\right| = tan\frac{\alpha\pi}{2}.$$

5. NUMERICAL SIMULATIONS

In this section, we present some examples and numerical simulations to verify our theoretical results proved in the previous sections by using matlab programm. We consider the system:

$$\begin{aligned} D^\alpha x(t) &= -ax(t) - bx(t)y(t) + c, \\ D^\alpha y(t) &= dx(t) - ey(t). \end{aligned} \tag{5.1}$$

Example 1 *Let us consider the parameter values* $a = 0.20626$*;* $b = 2.80e - 08$*;* $c = 1.956$*;* $d = 0.0222$*;* $e = 0.011437$*,* $s = 0.980$*. For these parameter the corresponding eigenvalues are* $\lambda_1 = -0.0750$*,* $\lambda_1 = -15.8520$ *for* $\alpha = 0.99$*, which satisfy conditions* $|arg(\lambda)| = 3.1416 > \alpha\pi/2 = 1.555$*. It means the system (1.1) is stable on* $E^* = (120.2304, 2.8182)$*, Fig-1.*

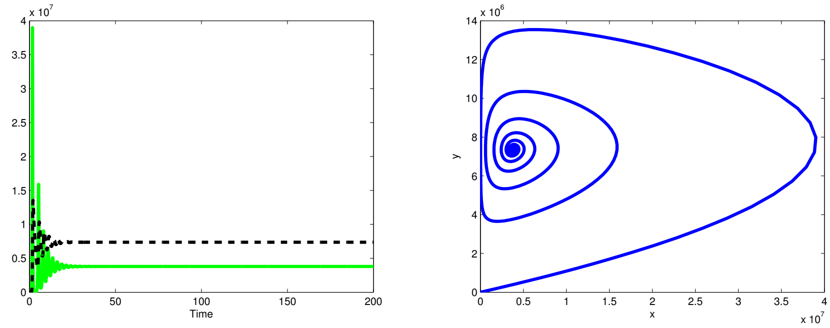

Figure 1: Glucose-Insulin dynamics and phase plain of the Glucose-Insulin dynamics for $a = 0.20626$; $b = 2.80e - 08$; $c = 1.956$; $d = 0.0222$; $e = 0.011437$, $s = 0.980$, $\alpha = 0.99$

Example 2 *Let us consider the parameter values* $a = 0.20626$; $b = 3.80e - 08$; $c = 1.956$; $d = 0.00322$; $e = 0.011437$, $s = 0.980$. *For these parameter the corresponding eigenvalues are* $\lambda_1 = -0.2181 + 1.0686i$, $\lambda_2 = -0.2181 - 1.0686i$ *for* $\alpha = 0.99$, *which satisfy conditions* $|arg(\lambda)| = 1.6920 > \alpha\pi/2 = 1.4923$. *It means the system (1.1) is stable on* $E^* = (33.6828, 2.6699)$, *Fig-2.*

Example 3 *Let us consider the parameter values* $a = 0.10626$; $b = 3.80e - 08$; $c = 0.956$; $d = 0.0022$; $e = 0.01437$, $s = 0.0280$. *For these parameter the corresponding eigenvalues are* $\lambda_1 = 0.0889 + 0.9974i$, $\lambda_2 = 0.0889 - 0.9974i$ *for* $\alpha = 0.99$, *which satisfy conditions* $|arg(\lambda)| = 1.4819 > \alpha\pi/2 = 1.5551$. *It means the system (1.1) is unstable on* $E^* = (1.2926, 62.6206)$, *Fig-3.*

Example 4 *Let us consider the parameter values* $a = 0.10626$; $b = 3.80e - 08$; $c = 0.956$; $d = 0.000022$; $e = 0.01437$, $s = 0.0280$. *For these parameter the corresponding eigenvalues are* $\lambda_1 = 1.0011 + 0.02001i$, $\lambda_2 = 1.0011 + 0.02001i$ *for* $\alpha = 0.99$, *which satisfy conditions* $|arg(\lambda)| = 0.0199 > \alpha\pi/2 = 1.5551$. *It means the system (1.1) is unstable on* $E^* = (1.2926, 62.6206)$, *Fig-4.*

6. CONCLUSION

In this paper, we considered and investigated the fractional-order glucose-insulin model. We applied a simple discretization scheme to discretize fractional-order differential equations. Chaos and bifurcation of the resulting discrete system were numerically investigated by varying the system parameters and the fractional-order parameter α. Also we provided numerical simulations exhibiting dynamical behavior and stability around equilibria of the system.

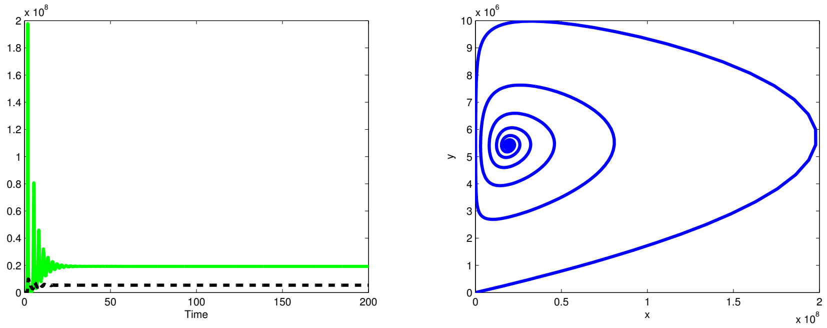

Figure 2: Glucose-Insulin dynamics and phase plain of the Glucose-Insulin dynamics for $a = 0.20626$; $b = 3.80e - 08$; $c = 1.956$; $d = 0.00322$; $e = 0.011437$, $s = 0.980$, $\alpha = 0.99$

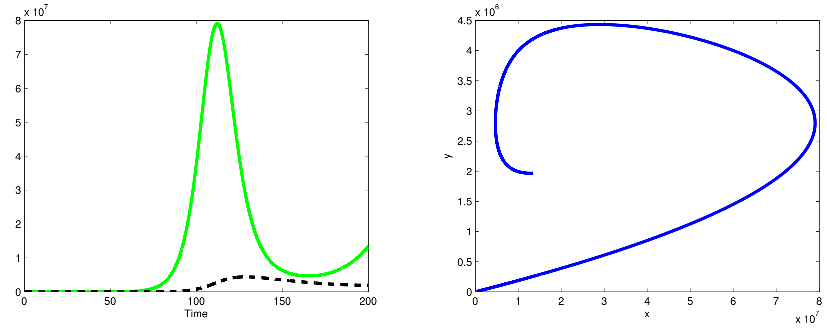

Figure 3: Glucose-Insulin dynamics and phase plain of the Glucose-Insulin dynamics for $a = 0.10626$; $b = 3.80e - 08$; $c = 0.956$; $d = 0.0022$; $e = 0.01437$, $s = 0.0280$, $\alpha = 0.99$

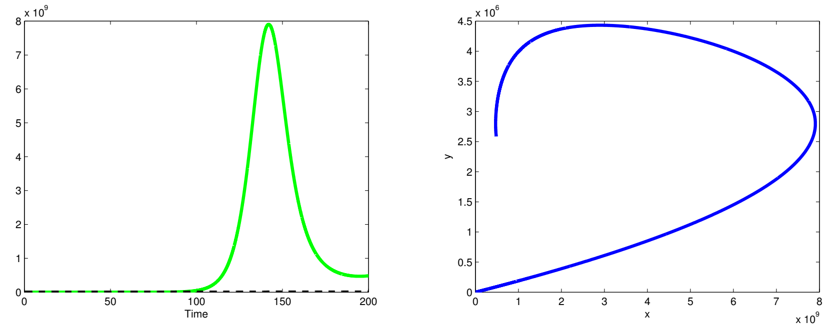

Figure 4: Glucose-Insulin dynamics and phase plain of the Glucose-Insulin dynamics for $a = 0.10626$; $b = 3.80e - 08$; $c = 0.956$; $d = 0.000022$; $e = 0.01437$, $s = 0.0280$, $\alpha = 0.99$

ACKNOWLEDGMENT

This research is a part of a project entitled ”Different Strategies for Diabetes Diseases in Al-Baha region, Saudi Arabia by Mathematical Modelling”. This project was funded by the Deanship of Scientific Research, Albaha University, KSA (Grant No. 1439/019). The assistance of the deanship is gratefully acknowledged.

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