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Existence and Uniqueness of Glucose-Insulin model Using Caputo-Fabrizio Fractional Derivative

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Abstract:- In this article, we aim to examine glucose concentration for type I diabetic patient to strengthen diabetic's research. Firstly, the model is integrated into the Caputo-Fabrizio fractional derivative with a non-singular kernel in order to subdue the limitations of the conventional Riemann-Liouville and Caputo fractional derivatives. After that, the presented mathematical model is reviewed for the existence of system solutions in detail by applying the fixed-point postulate. We ascertain the conditions under which the uniqueness of this system of solutions can be obtained.

Keywords: *Fractional-Order Differential Equations, Fixed-Point Theorem, Caputo-Fabrizio Derivative, Glucose-Insulin Concentration.*

1. Introduction

Mathematical modeling is a powerful tool due to its manifest importance and multifaceted uses against real-world problems in engineering, finance, social sciences and biology. Models have been formulated using classical derivatives. The modeling concept was extended to the novel approach, applying fractional derivatives [2–4]. The basics of the fractional derivative, Caputo-Fabrizio, are given in [5-6 & 26-27]. Thus, some of the studies focused on the multiple applications of fractional operator, Caputo-Fabrizio derivatives, without a singular kernel. A variety of Fractional Models investigation is given in [7-13&25].

The glucose in human blood is the main source of energy and comes from the food insulin, a hormone made by the pancreas, which helps glucose from food to get into our cells and to use it for energy. Insulin also controls and adjusts the quantity of sugar in human body [14]. When a human body is unable to make the desired amount of insulin or is not able to use it well, then the glucose doesn't reach the cells and stays in the blood. Frequent urination (polyurea), feeling more thirsty and hungry (polydipsia and polyphagia) are the symptoms which the patients having high blood sugar typically experience. Diabetes is known as a Raj Rog (meaning "kingship disease" or "royalty disease") in ancient India, that is, a disease which affects those people having lots of wealth and lives a comfortable prosperous life by using servants for doing their works and chores. But, in recent years, it has become a problem which affects the whole society. In ancient times, this problem was seen in the age group above 70 years, but (in today's era) it is a problem of all age groups. And, in very short time period, it has become a problem of the whole world. The issue is very serious and researchers are doing their best to control this problem. Generally, Type I diabetes requires a daily dose of insulin taken by the patient to regulate the amount of glucose in blood. Non-access of insulin leads to certain complications or danger to the patient's life.

Previously, some feedback controllers for insulin delivery have been investigated such as Fractional-Order (FO) proportional–integral–derivative control for diabetes patients using Bergman minimal model (BMM) [15]. In [16] adaptive FO Sliding Mode Control (SMC) for glucose concentration level of diabetic patients in the presence of the parameters uncertainty and multiple meal disturbances is used. A non-linear delay differential model of the glucose–insulin regulation system was studied and then an intelligent Mamdani-type fuzzy controller is proposed. In [22], the theoretical model of nonlinear differential equations having three variables (glucose, Insulin, β-cell mass) with thirteen parameters has been discussed. The homotopy perturbation method (HPM) was used to find analytical expressions of the glucose, Insulin, and β -cell mass respectively. Also, HPM methods are also used in various other models [23 & 24]. Recently, various models based on FDDEs such as glucose-insulin interaction model [1 & 17-21] and so on have been discussed in the literature. The organization of this paper is as follows. Next section 2, contains background on definitions related to the Caputo-Fabrizio derivative. Section 3 includes mathematical model of glucose regulatory system for type-1 diabetic patient including the impact of carbohydrate by different food items on glucose level in the blood with Caputo-Fabrizio derivative whereas section 4 deals with theorems to prove existence and uniqueness of the solution using the fixed-point postulate. Lastly section 5 provides a conclusion.

Background for Caputo-Fabrizio fractional derivative

Definition 1: The Riemann – Liouville (R-L) fractional integral operator of order $\theta > 0$, of function $f \in L^1(\mathbb{R}^+)$ is defined as

$$D^{\theta} f(t) = \frac{1}{\Gamma(\theta)} \int_0^t (t-s)^{\theta-1} f(s) ds, \qquad 1.1$$

where is $\Gamma(\theta)$the Euler gamma function.

Definition 2: From [5], Let $\Xi \in H^1(b,c)$, $c > b$, $\lambda \in [0,1]$ then, the definition of the arbitary order Caputo-Fabrizio fractional derivative is given by

$$ {}_{b}^{CF}D_t^{\lambda} (\Xi(t)) = \frac{\mathcal{M}(\lambda)}{1-\lambda} \int_b^t \Xi'(z) \exp\left[-\lambda \frac{t-z}{1-\lambda}\right] dz. \qquad 1.2$$

In the equation (1.2), $\mathcal{M}(\lambda)$ represents normalization function with conditions
$\mathcal{M}(\lambda) = \mathcal{M}(0) = 1.$

Definition 3: From [6] Assume $0 < \lambda < 1$, hence fractional order integral of order λ for function Ξ (z) is denoted as

$$P_t^{\lambda}(\Xi(t)) = \frac{2(\lambda-1)}{(\lambda-2)\mathcal{M}(\lambda)} g(t) + \frac{2\lambda}{(2-\lambda)\mathcal{M}(\lambda)} \int_0^t \Xi(s)\, ds, t \geq 0. \qquad 1.3$$

$$\frac{2}{2\mathcal{M}(\lambda) - \lambda\mathcal{M}(\lambda)} = 1 \qquad 1.4$$

We get $\mathcal{M}(\lambda) = \frac{2}{(2-\lambda)}$, and with order $0 < \lambda < 1$.
The authors in [6] represent the new Caputo derivative in another form as

$$ {}_{b}^{CF}D_t^{\lambda} (\Xi(t)) = \frac{\mathcal{M}(\lambda)}{1-\lambda} \int_0^t \Xi'(z) \exp\left[-\lambda \frac{t-z}{1-\lambda}\right] dz. \qquad 1.5$$

2. Objectives

Mathematical model of glucose regulatory system for type-1 diabetic patient including the impact of carbohydrate by different food items on glucose level

In this section, we present the fractional mathematical model of glucose regulatory system for type-1 diabetic patient including the impact of carbohydrate by different food items on glucose level with CF derivative which includes Blood Glucose Concentration denoted by G(t), Blood Insulin Concentration denoted by I(t) and Epinephrine denoted by E(t) respectively e_G= Effect of physical exercise in increasing the utilization of Glucose, e_I = Effect of physical exercise in accelerating the utilization of Insulin, G_{ext} = Output of carbohydrate metabolism system V = Volume distribution space are the positive real-valued model parameters. $m_1, m_2, m_3, \dots, m_9$ are the constants. FODEs model presented in (2.3) includes assumptions and descriptions of parameters as per the ordinary differential equation mathematical model presented in the paper [21]. Fractional mathematical model of glucose regulatory system for type-1 diabetic patient including the impact of carbohydrate by different food items on glucose level with CF derivative is represented as ODE Model is represented by:

$$\frac{dG}{dt} = -(m_1 + e_G)G - m_2 I + m_3 E + \frac{G_{ext}}{V},$$

$$\frac{dI}{dt} = m_4 G - (m_5 + e_I)I + m_6 E,$$

$$\frac{dE}{dt} = m_7 G - m_8 I + m_9 E. \qquad 2.1$$

For Simplification we can let

$$-(m_1 + e_G) = \theta_1 \,, -m_2 = \theta_2, m_3 = \theta_3, \frac{G_{ext}}{V} = \theta_4$$

$$m_4 = \theta_5, -(m_5 + e_I) = \theta_6, m_6 = \theta_7$$

$$m_7 = \theta_8, -m_8 = \theta_9, m_9 = \theta_{10}. \qquad 2.2$$

Now instead of derivative of order 1 in ordinary differential equation model represented by (2.2) we taker order of α to change the model into fractional order differential equation by using Caputo Fabrizio fractional derivative of order α from 0 to $t$we get,CF Fractional model is given by equation (2.3) below,

$${}^{CF}_{0}G^{\alpha}_{t} = \theta_1 G + \theta_2 I + \theta_3 E + \theta_4,$$

$${}^{CF}_{0}I^{\alpha}_{t} = \theta_5 G + \theta_6 I + \theta_7 E,$$

$${}^{CF}_{0}E^{\alpha}_{t} = \theta_8 G - \theta_9 I + \theta_{10} E. \qquad 2.3$$

By using Caputo-Fabrizio fractional integral operator on the above system of equation (2. 3), we get

$$G(t) - G(0) = {}^{CF}_{0}\mathcal{J}^{\alpha}_{t}\{\theta_1 G + \theta_2 I + \theta_3 E + \theta_4\},$$

$$I(t) - I(0) = {}^{CF}_{0}\mathcal{J}^{\alpha}_{t}\{\theta_5 G + \theta_6 I + \theta_7 E\},$$

$$E(t) - E(0) = {}^{CF}_{0}\mathcal{J}^{\alpha}_{t}\{\theta_8 G - \theta_9 I + \theta_{10} E\}. \qquad 2.4$$

For simplicity we let the kernels of the above equations in the form mentioned below

$$K_1 = \{\theta_1 G + \theta_2 I + \theta_3 E + \theta_4\},$$

$$K_2 = \{\theta_5 G + \theta_6 I + \theta_7 E\},$$

$$K_3 = \{\theta_8 G - \theta_9 I + \theta_{10} E\} \qquad 2.5$$

The definition of CF integral [5,6] is given by

$${}^{CF}_{0}\mathcal{J}^{\alpha}_{t}F(t) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}F(t) + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t F(y)dy$$

We will apply this definition on equation (4) by taking the kernels$K_i, for\ i = 1,2,3$. Then we will get

$$G(t) - G(0) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_1(y,G)\}dy,$$

$$I(t) - I(0) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_2(t,I)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_2(y,I)\}dy,$$

$$E(t) - E(0) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_3(t,E)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_3(y,E)\}dy \qquad 2.6$$

3. Methods

Existence of solution for glucose regulatory system for type-1 diabetic patient including the impact of carbohydrate by different food items on glucose level FODEs mathematical model

Now we will assume that G, I and $E$are the non-negative bounded functions, such that $\|G(t)\| \leq \beta_1$, $\|I(t)\| \leq \beta_2$ and $\|E(t)\| \leq \beta_3$ where β_1, β_2, β_3 are the positive constants. Now we do the existence and uniqueness theorems.

First theorem we will prove that the kernels satisfy Lipschitz and contraction mapping.

Theorem 1: If the following inequality holds then kernels satisfy the Lipschitz condition and contraction mapping $0 \leq M = maximum\ value\ of\ \{\gamma_1, \gamma_2, \gamma_3\} < 1$.

Proof: We take the first kernel K_1. Let G and G_1 be any two functions.

If we put those in first kernel K_1 and taking norm we get.

Now we apply the triangular inequality, we get

$$\|K_1(t,G) - K_1(t,G_1)\| \leq \|\theta_1(G(t) - G_1(t))\| + \|\theta_2 I\| + \|\theta_3 E\| + \|\theta_4\|$$

$$\|K_1(t,G) - K_1(t,G_1)\| \leq \theta_1\|(G(t) - G_1(t))\| + \theta_2\|I\| + \theta_3\|E\| + \theta_4$$

$$\|K_1(t,G) - K_1(t,G_1)\| \leq \theta_1\|(G(t) - G_1(t))\| + \theta_2\beta_2 + \theta_3\beta_3 + \theta_4$$

$$\|K_1(t,G) - K_1(t,G_1)\| \leq \theta_1\|(G(t) - G_1(t))\|$$

Now $\theta_1 = \gamma_1$ such that $0 \leq \gamma_1 < 1$ hence Lipschitz condition and contraction mapping for the kernel K_1.Similar way we can prove other two kernels also. Now let us take equation (2.6) and shift the G(0), I(0) And E(0) on the right hand side, We get

$$G(t) = G(0) + \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_1(y,G)\}dy,$$

$$I(t) = I(0) + \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_2(t,I)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_2(y,I)\}dy,$$

$$E(t) = E(0) + \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_3(t,E)\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_3(y,E)\}dy. \qquad 3.1$$

Using this equation (3.1) we can apply the recursive formula for the nth term and taking the initial values $G(0) = G_0(t)$, $I(0) = I_0(t)$, $E(0) = E_0(t)$ we get

$$G_n(t) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G_{n-1})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_1(y,G_{n-1})\}dy,$$

$$I_n(t) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_2(t,I_{n-1})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_2(y,I_{n-1})\}dy,$$

$$E_{n(t)} = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_3(t,E_{n-1})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_3(y,E_{n-1})\}dy. \qquad 3.2$$

The successive term difference for above system is

$$\Phi_n(t) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G_{n-1}) - K_1(t,G_{n-2})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_1(y,G_{n-1}) - K_1(y,G_{n-2})\}dy,$$

$$\Psi_n(t) = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_2(t,I_{n-1}) - K_2(t,I_{n-2})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_2(y,I_{n-1}) - K_2(y,I_{n-2})\}dy,$$

$$\Xi_{n(t)} = \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_3(t,E_{n-1}) - K_3(t,E_{n-2})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_3(y,E_{n-1}) - K_3(y,E_{n-2})\}dy \qquad 3.3$$

Now the summation of all the differences can be written as

$$G_n(t) = \sum_{i=1}^{n} \Phi_i(t)$$

$$I_n(t) = \sum_{i=1}^{n} \Psi_i(t)$$

$$E_n(t) = \sum_{i=1}^{n} \Xi_i(t) \qquad 3.4$$

Now the norm

$$\|\Phi_n(t)\| = \|G_n(t) - G_{n-1}(t)\|$$

From equation (3.3)

$$\|\Phi_n(t)\| = \left\|\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G_{n-1}) - K_1(t,G_{n-2})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_1(y,G_{n-1}) - K_1(y,G_{n-2})\}dy\right\| \qquad 3.5$$

Now using the above two equations we can get

$$\|G_n(t) - G_{n-1}(t)\| = \left\|\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G_{n-1}) - K_1(t,G_{n-2})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_1(y,G_{n-1}) - K_1(y,G_{n-2})\}dy\right\| \qquad 3.6$$

Now Appling triangular inequality

$$\|\Phi_n(t)\| = \|G_n(t) - G_{n-1}(t)\|$$

$$\leq \left\|\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G_{n-1}) - K_1(t,G_{n-2})\}\right\| + \left\|\frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \{K_1(y,G_{n-1}) - K_1(y,G_{n-2})\}dy\right\|$$

$$\|G_n(t) - G_{n-1}(t)\| \leq \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\|\{K_1(t,G_{n-1}) - K_1(t,G_{n-2})\}\| + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t \|K_1(y,G_{n-1}) - K_1(y,G_{n-2})\|dy$$

Now as we know the kernel K_1 satisfy the Lipschitz condition and contraction for γ_1 we get,

$$\|G_n(t) - G_{n-1}(t)\| \leq \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\|\{G_{n-1}(t) - G_{n-2}(t)\}\| + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\int_0^t \|\{G_{n-1}(y) - G_{n-2}(y)\}\|dy$$

Thus we obtain

$$\|\Phi_n(t)\| \leq \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\|\{\Phi_{n-1}(t)\}\| + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\int_0^t\|\Phi_{n-1}(y)\|dy \quad 3.7$$

Similarly we can do for others parts of the equation. Now we will use this result in next theorem.

Theorem 2: If for $t_0 > 0$ and the inequalities below holds

$$\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 t_0 < 1$$

Then a solution exists

Proof: Since all G, I, E are the bounded functions and kernels fulfill Lipschitz condition which shows existence and smoothness of the functions. To complete the proof we prove the convergence of $G_n(t),\ I_n(t),\ E_n(t)$ is the solution of the CF model. Let $B_n(t),\ C_n(t),\ D_n(t)$ as $G(t) - G(0) = G_n(t) - B_n(t)$ and for others also.

Now

$$\|B_n(t)\| = \left\|\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G) - K_1(t,G_{n-1})\} + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_1(y,G) - K_1(y,G_{n-1})\}dy\right\|$$

Applying triangular inequality, we get

$$\|B_n(t)\| \leq \left\|\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\{K_1(t,G) - K_1(t,G_{n-1})\}\right\| + \left\|\frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\int_0^t\{K_1(y,G) - K_1(y,G_{n-1})\}dy\right\|$$

$$\|B_n(t)\| \leq \frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\|G - G_{n-1}\| + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1\int_0^t\|G - G_{n-1}\|dy \quad 3.8$$

Applying the process recursively we get

$$\|B_n(t)\| \leq \left[\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 t\right]^{n+1}$$

At $t = t_0$

$$\|B_n(t)\| \leq \left[\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 t_0\right]^{n+1} \quad 3.9$$

Now applying limits as $n \to \infty$, we get

$$\|B_n(t)\| \to 0 \quad 3.10$$

Similarly, we can do for other parts of the models equations I and E.

Theorem 3: CF Model have a unique solution if

$$\left(1 - \left[\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 t\right]\right) > 0$$

Proof: Assume $G_1(t)$ is the other solution of the equation of the CF model

Then

$$\|G(t) - G_1(t)\| \left(1 - \left[\frac{2(1-\rho)}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 + \frac{2\rho}{(2-\rho)\mathcal{M}(\rho)}\gamma_1 t\right]\right) \leq 0$$

Hence,

$$G(t) = G_1(t)$$

Similarly,

$$I(t) = I_1(t)$$

$$E(t) = E_1(t) \qquad 3.11$$

4. Results

The glucose regulatory system for type-1 diabetic patient has been validated using Existence and Uniqueness Theorem using fixed point postulate. The Caputo Fabrizio Fractional Derivative has been used in proving the theorems where the kernel satisfies Lipschitz condition.

5. Discussion

For achieving better quality of life in diabetic patients it is necessary to pay attention towards a preventive and personalized approach of treatment. Mathematical modeling of diabetic condition and its associated complications provides a deep and clear understanding about the diverse and complex mechanism involved. A differential equation model has been proposed in this work with fractional derivative. Glucose-insulin concentration in blood model is extended to fractional calculus by using the CF fractional derivative and validation by uniqueness and existence of solution is shown with Lipschitz condition. The existence and uniqueness of the solution is found by employing the fixed-point theorem. Non-integer values of α the fractional parameter of CF fractional derivative create a significant mathematical model. This model will benefit diabetics' research by substantially minimizing the cost of care. For future research a similar comparative analysis can also be undertaken of other integer order disease models.

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