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Fractional Order Derivative Glucose Insulin Model to Control the type 1 Diabetes Mellitus

Muhammad Umer Saleem
Department of Mathematics,
University of Education, Pakistan,
Email: umerlinks@ue.edu.pk

Muhammad Farman
Department of Mathematics and Statistics,
University of Lahore, Pakistan,
Email: farmanlink@gmail.com

Aqeel Ahmad
Department of Mathematics and Statistics,
University of Lahore, Pakistan,
Email: aqeelahmad.740@gmail.com

Muhammad Naeem
Division of Science and Technology,
University of Education, Pakistan,
Email: muhamamd.naeem@ue.edu.pk

Muhammad Ozair Ahmad
Department of Mathematics and Statistics,
University of Lahore, Pakistan,
Email: drchadury@yahoo.com

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Abstract. In this manuscript, Fractional-order derivatives are discussed for a comprehensive glucose insulin regulatory model. Observer is designed for approximating the structure of a blood glucose-insulin with glucose rate disorder to show the complete dynamics of the glucose-insulin system where the fractional-order at $\alpha \in (0, 1]$. The developed method provides the estimation algorithm for a glucose-insulin system with unknown time-varying glucose rate disturbance. Lyapunov function is used to check the stability analysis and input/output stability which play an important role in feedback control design for automatic control system. Numerical simulations are carried out to demonstrate our proposed results and show the nonlinear fractional-order glucose-insulin systems are at least stable in the existence of exogenous glucose infusion or meal disturbance. The concept of controllability and observability for the linearized

control system of human glucose insulin system is used so that we can have a feedback control for artificial pancreas.

AMS (MOS) Subject Classification Codes: 37C75,; 93B05; 93B07; 65L07
Key Words: Artificial pancreas; Caputo's derivative; fractional-order glucose insulin model; Lyapunov fractional; Laplace Adomian Decomposition Method.

1. INTRODUCTION

Diabetes Mellitus with interruptions of protein, Carbohydrate and fat metabolism arising from disabilities in insulin action, insulin secretion or both in a metabolic malady of multiple aetiologies featured by chronic hyperglycaemia. Diabetic's patients can be categorized in major two types, type 1 and type 2 diabetes. Insulin dependent diabetes, are caused by the absence of insulin secretion due to destruction of the $\beta-$cells of pancreas in type 1 diabetes. Insulin independent diabetes are caused by reduced action of insulin on the glucose or usually called insulin resistance in Type 2 diabetes [1,40]. From the big number of diabetics, type 1 diabetes only assigns for about 5 to 10% of all number of diabetes [40]. However, their occurrence continues to grow worldwide and it has a horrible short-term and long-term consequences. Treatment of type 1 diabetes requires a lot of concern to various aspects such as insulin administration, blood glucose monitoring and diabetes-related complications [20]. The goal of type 1 diabetes treatment is to regulate the blood glucose concentration within a normal range. This is to avoid the risks of hyperglycaemia (high blood glucose concentration) and hypoglycaemia (low blood glucose concentration). In normal healthy person, the natural internal control of blood glucose concentration is accomplished by a feedback control mechanism. In Type 1 diabetics, this mechanism must be employed by an external artificial control mechanism that controls the injection of the insulin with respect to the present blood glucose concentration which is must be very accurate and relatively high performance [8,33]. In Pakistan 6.9 million peoples suffers in cases of diabetes in 2014 and overall occurrence of diabetes as 11.47% (6.39-16.5%) according to World Health Organization (WHO) [30,6].

People of type 1 diabetes takes help to control their glucose level by wearing a continuous glucose monitor (CGM) [25]. However, it is also suggested that we can checked the correctness of the CGM amounts with a finger stick test [34]. The glucose sensor has a tiny needle that before sending information to the monitoring device and blood glucose level measures every time by CGM, it measure the glucose levels in tissue fluid [25]. It will give an alarm to the wearer, if the glucose levels are anomalous. If the glucose levels become very high then the CGM can also be amalgamated with an insulin pump that will vaccinate insulin [35]. Artificial pancreas is a innovation to preserve the typical blood glucose level in diabetes with a substitute endocrine work to pancreas. The task is lacking to oversee physically the blood glucose level with alone that is why the current treatment of affront substitution (Artificial Pancreas) is appreciated for its life sparing capability. This treatment can offer assistance in the hyperglycaemia state by catapulting more affront by the affront pump but in case of hypoglycaemia state this treatment will not work. Hypoglycaemia leads to neuroglycopenia and impacts can run from gentle dysphoria to more serious issues such as seizures, obviousness, harmful for brain cells and death.

Often, the behavior of a system is studied and described mathematically. This description is called a model and it should reproduce the outputs of a system based on the inputs as accurately as possible. However, quite often models are not capable of capturing the whole behavior of a system, either because it is too complex, or disturbances are too important. A system is called static if its outputs at a given time are influenced by the inputs at that time, only. In a dynamical system, however, the outputs are determined by current and past inputs. A controller is used to adjust a systems inputs, in order to obtain desired outputs. This system is called controlled system. A controller itself can be considered as a system, whose output is the controlled systems input. If the controllers inputs depend directly on the controlled systems outputs, then the controller is called a closed-loop controller, otherwise it is called an open-loop controller. The output value that a closed-loop control algorithm is intended to reach is called a set point [3].

In the recent year researcher takes interest and attention in fractional calculus in different aspects under consideration for research of the said subject [36,31,32]. In the last decade derivatives and integrals of fractional orders had notable development as revealed by several monographs dedicated to it [9,10], the plethora of research papers published in scientific journals [22] studied differential-difference equation of fractional order, [2] analyzed the Ebola epidemic model of fractional order, Carvalho and Pinto presented a delay mathematical model of fractional order to determine the co-infection of malaria and the human immunodeficiency virus [5], examined the local fractional diffusion and relaxation equations [37], a new fractional derivative and its application to explanation of polar bear hairs [11] , Wang and Liu [41,42] showed the applications of He's fractional derivative for non-linear fractional heat transfer equation, Hu et al. [12] studied fractal space-time and fractional calculus [23,24]. The fractional complex transform is used to con vert the fractal space-time to its continuous partner, and all known analytical methods can be directly ap plied to the resultant equations. This paper is an explanation of fractional calculus in a fractal frame [13,14]. The suggested fractal derivative is easy to be used for any discontinuous problems, and equations with fractal derivative can be easily solved used classical calculus [15,39]. This paper is an elementary introduction to fractal-Cantorian space time and fractional calculus. Particular attention is paid throughout the paper to giving an intuitive grasp for fractional derivatives, fractal derivatives and q-derivative. In other words, a (deterministic) fractal can be thought as an object, each part of which is a scaled copy of the whole, that differs from a regular geometrical shapes in its non integer scaling coefficient [4]. We showed that a relation between fractional calculus and fractal geometry exists, which is intimately related to the physical origins of the power-law long memory and hereditary properties observed in many natural phenomena, and that are the characteristic feature of fractional operators [16-18].

In this paper we find the equilibrium points of the model and check its stability analysis of the models by using Lyapunov equation. If the equilibrium point lies in the feasible region then by using the Jacobian, convert the nonlinear system of equation into linearized system and discussed the controllability and observability of the linearized system to design the close loop for automatic artificial pancreas. We proposed the fractional order glucose insulin model for healthy and type 1 diabetes and numerical simulations are carried out to support the analytical results.

2. MATHEMATICAL MODEL

Diabetes dynamics is a mathematical model in which two other models of glucose/insulin use to explain interaction. These are valid to predict blood glucose because these are inherent requirement of frequently updated information. In this model we take glucose level G, glucose uptake X, insulin level I. This model also include the basal values G_b and I_b [36]. The model is

$$\dot{G}(t) = -m_1 G + m_2 I + m_1 G_b \tag{2. 1}$$

$$\dot{X}(t) = -m_2 X + m_3 I - m_3 I_b + m_6 I_b \tag{2. 2}$$

$$\dot{I}(t) = -m_3 I + m_4 G + m_4 m_5 - m_6 I + m_6 I_b \tag{2. 3}$$

Here

$$G(0) = p_1 = 100, X(0) = p_2 = 0, I(t) = p_3 = I_b \tag{2. 4}$$

are used as initial condition, where $G(t)$ is plasma glucose concentration, $X(t)$ is plasma insulin variable for remote compartment, $I(t)$ is plasma insulin concentration, G_b is the basal preinjection value of plasma glucose, I_b is basal preinjection value of plasma insulin, m_1 is the insulin independent rate uptake in liver, muscle and adipose tissue, m_2 is the rate of decrease in tissue glucose uptake ability, m_3 is the insulin independent increase in glucose uptake ability in I_b, m_4 is the rate of pancreatic cells which are released after the glucose injection and glucose concentration above system, m_5 is the threshold value of glucose, m_6 is the decay rate for insulin in plasma [36].

2.1. **Stability Analysis and equilibria.**

Model after substituting parameters, we get

$$\dot{G}(t) = -0.0317000G + 0.0123I + 2.536 \tag{2. 5}$$

$$\dot{X}(t) = -0.0123X + 0.00000492I - 0.00000492 + 1.8613 \tag{2. 6}$$

$$\dot{I}(t) = -0.26590492I + 0.0039G + 2.1695 \tag{2. 7}$$

Substituting the left hand side of the system equal to zero and we get the values of G, X and I . Hence the equilibrium points is $(83.6417,\ 151.3288,\ 9.3817)$

Proposition 1: The linear $\dot{x}(t) = Ax$, where A continuous and bounded for $t \geq t_0$, is uniformly asymptotically stable if and only if given a positive definite real matrix A, there exists a symmetric positive definite real matrix P, which satisfies

$$\dot{P} + A^T P + PA = -Q, t \geq t_0$$

The linear time invariant system $\dot{x}(t) = Ax$ the corresponding equation to be used as $A^T P + PA + Q = 0$ this is called Lyapunov equation [24,18,29]. Here

$$A = \begin{bmatrix} -0.0317 & 0.0123 & 0 \\ 0 & -0.0123 & 1.1876 \\ 0.0039 & -0.2659 & 0 \end{bmatrix}$$

and substitute $Q = I_{3\times 3}$ in $A^T P + PA + Q = 0$, calculate P as

$$P = \begin{bmatrix} 16.0010 & 0.5880 & -2.2467 \\ 0.5880 & 219.0273 & 1.8475 \\ -2.2467 & 1.8475 & 49.0567 \end{bmatrix}$$

the Lyapunov equation has symmetric positive-definite solution P, then the eigen values of A are $(-0.0315, -0.0062 + 0.5619i, -0.0062 - 0.5619i)$ has negative real parts, so the system $\dot{x}(t) = Ax$ is asymptotically and uniformly stable.

3. Fractional Order Model

In this section, we give some fundamental results and definitions from fractional calculus. For detailed over view of the topic readers are referred to [38,21].

Definition 3.1 The definitions of Laplace transform of Caputo's derivative and Mittag-Leffler function in two arguments is written as

$$\mathscr{L}\{D^{\alpha} f(t), s\} = s^{\alpha} F(s) - \Sigma_{i=0}^{n-1} s^{\alpha-i-1} f^{(i)}(0), (n-1 < \alpha \leq n);\ n \in N.$$

The fractional order extension of this model have been first studied in [12] and show the realistic biphasic decline behavior of infection of diseases but at a slower rate. The new diabetes mellitus model described in the form of fractional differential equations (FDEs) given as

$$D^{\alpha_1} G(t) = -m_1 G + m_2 I + m_1 G_b \tag{3. 8}$$

$$D^{\alpha_2} X(t) = -m_2 X + m_3 I - m_3 I_b + m_6 I_b \tag{3. 9}$$

$$D^{\alpha_3} I(t) = -m_3 I + m_4 G + m_4 m_5 - m_6 I + m_6 I_b \tag{3. 10}$$

with initial conditions $G(0) = p_1 = 100, p_2 = X(0) = 0, I(0) = p_3 = I_b$

4. The Laplace-Adomian Decomposition Method

Consider the fractional-order epidemic model $(3.8-3.10)$ subject to the initial condition (4). For $\alpha_1 = \alpha_2 = \alpha_3 = 1$ the fractional order model converts to the classical diabase model. Applying the Laplace transform on equation $(3.8 - 3.10)$, we get

$$\mathscr{L}\{D_t^{\alpha_1} G(t)\} = -m_1 \mathscr{L}\{G(t)\} + m_2 \mathscr{L}\{I(t)\} + \mathscr{L}\{m_1 G_b\} \tag{4. 11}$$

$$\mathscr{L}\{D_t^{\alpha_2} X(t)\} = -m_2 \mathscr{L}\{X(t)\} + m_3 \mathscr{L}\{I(t)\} - \mathscr{L}\{(m_3 I_b - m_6 I_b)\} \tag{4. 12}$$

$$\mathscr{L}\{D_t^{\alpha_3} I(t)\} = -(m_3 + m_6)\mathscr{L}\{I(t)\} + m_4 \mathscr{L}\{G(t)\} + \mathscr{L}\{(m_6 I_b + m_4 m_5)\} \tag{4. 13}$$

By applying the rule of Laplace transform, we get

$$S^{\alpha_1} \mathscr{L}\{G\} - S^{\alpha_1 - 1} G(0) = -m_1 \mathscr{L}\{G(t)\} + m_2 \mathscr{L}\{I(t)\} + \mathscr{L}\{m_1 G_b\} \tag{4. 14}$$

$$S^{\alpha_2} \mathscr{L}\{X\} - S^{\alpha_1 - 1} X(0) = -m_2 \mathscr{L}\{X(t)\} + m_3 \mathscr{L}\{I(t)\} - \mathscr{L}\{m_3 I_b - m_6 I_b\} \tag{4. 15}$$

$$S^{\alpha_3} \mathscr{L}\{I\} - S^{\alpha_1 - 1} I(0) = -(m_3 + m_6)\mathscr{L}\{I(t)\} + m_4 \mathscr{L}\{G(t)\} + \mathscr{L}\{m_6 I_b + m_4 m_5\} \tag{4. 16}$$

$$S^{\alpha_1} \mathscr{L}\{G\} = S^{\alpha_1 - 1} G(0) - m_1 \mathscr{L}\{G(t)\} + m_2 \mathscr{L}\{I(t)\} + \mathscr{L}\{m_1 G_b\} \tag{4. 17}$$

$$S^{\alpha_2} \mathscr{L}\{X\} = S^{\alpha_1 - 1} X(0) - m_2 \mathscr{L}\{X(t)\} + m_3 \mathscr{L}\{I(t)\} - \mathscr{L}\{m_3 I_b - m_6 I_b\} \tag{4. 18}$$

$$S^{\alpha_3}\mathscr{L}\{I\} = S^{\alpha_1-1}I(0) - (m_3+m_6)\mathscr{L}\{I(t)\} + m_4\mathscr{L}\{G(t)\} + \mathscr{L}\{m_6I_b + m_4m_5\} \tag{4. 19}$$

by using the initial conditions (2.4), we get

$$\mathscr{L}\{G\} = \frac{p_1}{S} + \frac{m_1G_b}{S^{\alpha_1+1}} + \frac{m_2}{S^{\alpha_1}}\mathscr{L}\{I(t)\} - \frac{m_1}{S^{\alpha_1}}\mathscr{L}\{G(t)\} \tag{4. 20}$$

$$\mathscr{L}\{X\} = \frac{p_2}{S} - \frac{m_3I_b - m_6I_b}{S^{\alpha_2+1}} - \frac{m_2}{S^{\alpha_2}}\mathscr{L}\{X(t)\} + \frac{m_3}{S^{\alpha_2}}\mathscr{L}\{I(t)\} \tag{4. 21}$$

$$\mathscr{L}\{I\} = \frac{p_3}{S} + \frac{m_6I_b + m_4m_5}{S^{\alpha_3+1}} - \frac{m_3+m_6}{S^{\alpha_3}}\mathscr{L}\{I(t)\} + \frac{m_4}{S^{\alpha_3}}\mathscr{L}\{G(t)\} \tag{4. 22}$$

4.1. **Case I for Normal Person.** First of all we study the glucose, plasma concentration and insulin for non-diabetic person for the period of 10 hours. The model show that when we give glucose to normal man then the level of glucose concentration is very high but after time passing it become stable [36]. The model after substituting the parameters values for case I.

$$\mathscr{L}\{G\} = \frac{p_1}{S} + \frac{2.536}{S^{\alpha_1+1}} + \frac{0.0123}{S^{\alpha_1}}\mathscr{L}\{I(t)\} - \frac{0.0317}{S^{\alpha_1}}\mathscr{L}\{G(t)\} \tag{4. 23}$$

$$\mathscr{L}\{X\} = \frac{p_2}{S} + \frac{1.861}{S^{\alpha_2+1}} - \frac{0.0123}{S^{\alpha_2}}\mathscr{L}\{X(t)\} + \frac{4.92\times10^{-6}}{S^{\alpha_2}}\mathscr{L}\{I(t)\} \tag{4. 24}$$

$$\mathscr{L}\{I\} = \frac{p_3}{S} + \frac{2.1696}{S^{\alpha_3+1}} - \frac{0.2659}{S^{\alpha_3}}\mathscr{L}\{I(t)\} + \frac{0.0039}{S^{\alpha_3}}\mathscr{L}\{G(t)\} \tag{4. 25}$$

with initial conditions $G(0) = p_1 = 100, p_2 = X(0) = 0, I(0) = p_3 = 7$ It should be assumed that method gives the solution as an infinite series

$$G = \sum_{k=0}^{\infty} G_k,\ X = \sum_{k=0}^{\infty} X_k,\ I = \sum_{k=0}^{\infty} I_k \tag{4. 26}$$

Substitute equations (4.26) in $(4.23-4.25)$, we have the followings results

$$\mathscr{L}\{G_0\} = \frac{p_1}{S} + \frac{2.536}{S^{\alpha_1+1}},\ \mathscr{L}\{X_0\} = \frac{p_2}{S} + \frac{1.861}{S^{\alpha_2+1}},\ \mathscr{L}\{I_0\} = \frac{p_3}{S} + \frac{2.1696}{S^{\alpha_3+1}} \tag{4. 27}$$

Similarly we have

$$\mathscr{L}\{G_1\} = \frac{0.0123}{S^{\alpha_1}}\mathscr{L}\{I_0\} - \frac{0.0317}{S^{\alpha_1}}\mathscr{L}\{G_0\},\ ...,\ \mathscr{L}\{G_{k+1}\} = \frac{0.0123}{S^{\alpha_1}}\mathscr{L}\{I_k\} - \frac{0.0317}{S^{\alpha_1}}\mathscr{L}\{G_k\} \tag{4. 28}$$

$$\mathscr{L}\{X_1\} = \frac{-0.0123}{S^{\alpha_2}}\mathscr{L}\{X_0\} + \frac{0.00000492}{S^{\alpha_2}}\mathscr{L}\{I_0\}, ..., \mathscr{L}\{X_{k+1}\} = \frac{-0.0123}{S^{\alpha_2}}\mathscr{L}\{X_k\} + \frac{0.00000492}{S^{\alpha_2}}\mathscr{L}\{I_k\} \tag{4. 29}$$

$$\mathscr{L}\{I_1\} = \frac{-0.2659}{S^{\alpha_3}}\mathscr{L}\{I_0\} + \frac{0.0039}{S^{\alpha_3}}\mathscr{L}\{G_0\}, ..., \mathscr{L}\{I_{k+1}\} = \frac{-0.2659}{S^{\alpha_3}}\mathscr{L}\{I_k\} +$$

$$\frac{0.0039}{S^{\alpha_3}}\mathscr{L}\{G_k\} \tag{4. 30}$$

The purpose of the work is to analysis the mathematical behaviour of the solution $G(t), X(t), I(t)$ for the different values of α. By applying the inverse laplace transform to both sides of the equation (4.27), we get the values of G_0, X_0, I_0 and used for further process. Putting the values of G_0, X_0, I_0 into the equations $(4.28-4.30)$ and get the values of G_1, X_1, I_1. Similarly we find the remaining term $G_2, G_3, G_4, ...$, $X_2, X_3, X_4, ...$ and $I_2, I_3, I_4, ...$ in the same manners. Solution can be written as

$$G(t) = G_0 + G_1 + G_2 + G_3 + G_4, ... \tag{4. 31}$$

$$X(t) = X_0 + X_1 + X_2 + X_3 + X_4, ... \tag{4. 32}$$

$$I(t) = I_0 + I_1 + I_2 + I_3 + I_4, ... \tag{4. 33}$$

by substituting the values of $G_0, X_0, I_0, G_1, X_1, I_1$ and $G_2, X_2, I_2, ...$, we get

$$G(t) = 100 - 0.547\frac{t^{\alpha_1}}{\alpha_1!} + 0.0267\frac{t^{\alpha_3}}{\alpha_3!} + 0.0174\frac{t^{2\alpha_1}}{2\alpha_1!} - 0.0190\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} -$$

$$0.0071\frac{t^{\alpha_1+2\alpha_3}}{(\alpha_1+2\alpha_3)!} + 0.00012\frac{t^{2\alpha_1+\alpha_3}}{(2\alpha_1+\alpha_3)!} + 0.0025\frac{t^{3\alpha_1}}{3\alpha_1!} \tag{4. 34}$$

$$X(t) = 1.86103\frac{t^{\alpha_2}}{\alpha_2!} - 1.92\times10^{-9}\frac{t^{2\alpha_2}}{2\alpha_2!} + 3.5\times10^{-6}\frac{t^{\alpha_2+\alpha_3}}{(\alpha_2+\alpha_3)!} + 0.00028\frac{t^{3\alpha_2}}{3\alpha_2!} +$$

$$1.3\times10^{-7}\frac{t^{2\alpha_2+\alpha_3}}{(2\alpha_2+\alpha_3)!} - 2.8\times10^{-6}\frac{t^{\alpha_2+2\alpha_3}}{(\alpha_2+2\alpha_3)!} + 4.87\times10^{-8}\frac{t^{\alpha_1+\alpha_2+\alpha_3}}{(\alpha_1+\alpha_2+\alpha_3)!} \tag{4. 35}$$

$$I(t) = 7 + 0.6983\frac{t^{\alpha_3}}{\alpha_3!} - 0.1856\frac{t^{2\alpha_3}}{2\alpha_3!} - 0.0021\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} - 0.1539\frac{t^{3\alpha_3}}{3\alpha_3!} -$$

$$0.0026\frac{t^{\alpha_1+2\alpha_3}}{(\alpha_1+2\alpha_3)!} - 0.00031\frac{t^{2\alpha_1+\alpha_3}}{(2\alpha_1+\alpha_3)!} \tag{4. 36}$$

4.2. **Case II for Type 1 Diabetes.** Now we study the model for diabetic patient for the period of 10 hours. The model show that at start time the level of glucose is very high but when we give glucose then his level of glucose does not fall. After time passing from $250mg/dl$ it fall only about $275mg/dl$ [36].
The fractional model after substituting the parameters values for case II.

$$\mathscr{L}\{G\} = \frac{p_1}{S} + \frac{0.017}{S^{\alpha_1}}\mathscr{L}\{I(t)\} \tag{4. 37}$$

$$\mathscr{L}\{X\} = \frac{p_2}{S} + \frac{3.9599}{S^{\alpha_2+1}} - \frac{0.017}{S^{\alpha_2}}\mathscr{L}\{X(t)\} + \frac{5.3\times10^{-6}}{S^{\alpha_2}}\mathscr{L}\{I(t)\} \tag{4. 38}$$

$$\mathscr{L}\{I\} = \frac{p_3}{S} + \frac{4.297}{S^{\alpha_3+1}} - \frac{0.264}{S^{\alpha_3}}\mathscr{L}\{I(t)\} + \frac{0.0042}{S^{\alpha_3}}\mathscr{L}\{G(t)\} \tag{4. 39}$$

with initial conditions $G(0) = p_1 = 240, p_2 = X(0) = 0, I(0) = p_3 = 15$. We computed first three terms by using the L-ADM for the equations $(4.37 - 4.39)$. We have followings series solution

$$G(t) = 240 + 0.255\frac{t_1^{\alpha}}{\alpha_1!} + 0.0228\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} - 0.0193\frac{t^{\alpha_1+2\alpha_3}}{(\alpha_1+2\alpha_3)!}, \tag{4. 40}$$

$$X(t) = 3.9606\frac{t^{\alpha_2}}{\alpha_2!} - 0.067314\frac{t^{2\alpha_2}}{(2\alpha_2)!} + 6.8\times10^{-5}\frac{t^{\alpha_2+\alpha_3}}{(\alpha_2+\alpha_3)!} + 0.0011\frac{t^{3\alpha_2}}{3\alpha_2!} - 0.0000039\frac{t^{2\alpha_2+\alpha_3}}{(2\alpha_2+\alpha_3)!} - 0.00006\frac{t^{\alpha_2+2\alpha_3}}{(\alpha_2+2\alpha_3)!}, \tag{4. 41}$$

$$I(t) = 15 + 1.645\frac{t^{\alpha_3}}{\alpha_3!} - 0.3551\frac{t^{2\alpha_3}}{2\alpha_3!} + 0.2994\frac{t^{3\alpha_3}}{3\alpha_3!} + 0.0011\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} + 0.00031\frac{t^{\alpha_1+2\alpha_3}}{(\alpha_1+2\alpha_3)!} \tag{4. 42}$$

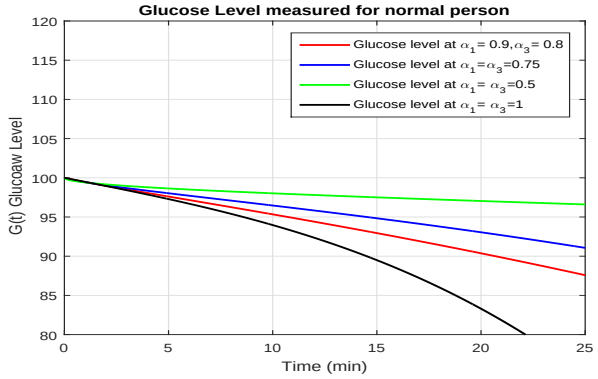

Figure 1: Numerical solution of Glucose level of normal person at different values of α

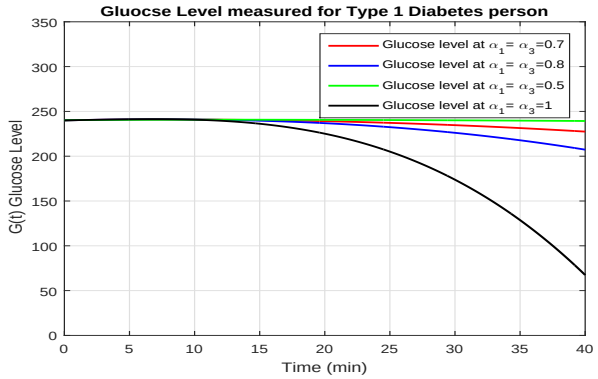

Figure 2: Numerical solution of Glucose level of type 1 diabetes at different values of α

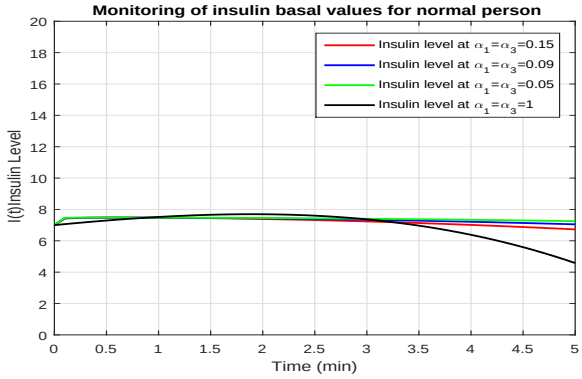

Figure 3: Behavior of insulin in normal person at different values of α

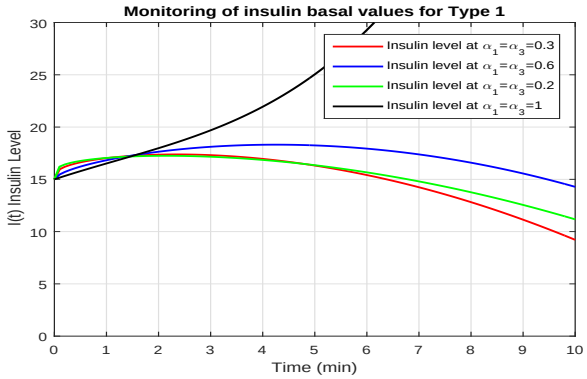

Figure 4: Behavior of insulin in type 1 diabetes at different values of α

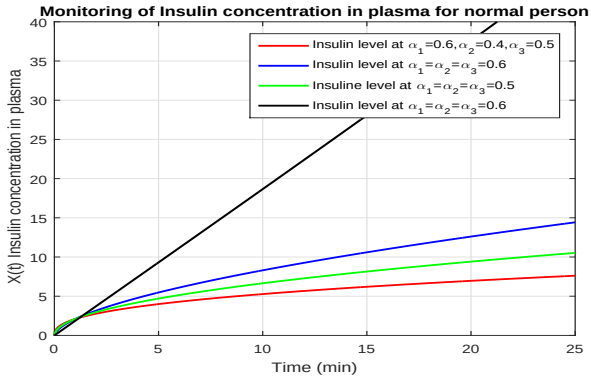

Figure 5: Numerical solution of insulin concentration in plasma of normal person at different values of α

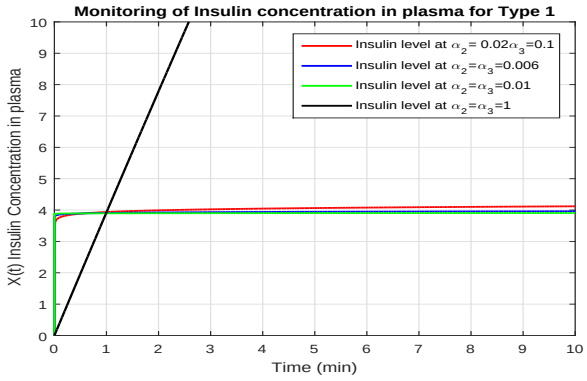

Figure 6: Numerical solution of insulin concentration in plasma of type 1 diabetes at different values of α

5. He-Laplace Method

It is worth mentioning that He-Laplace method is an elegant combination of the Laplace transformation, the homotopy perturbation method and He's polynomials [7, 26-28]. Consider the system $(3.8 - 3.10)$ with initial condition in equation (2.4), By applying the He-Laplace Method method subject to the in condition, we have

$$\mathscr{L}\{G\} = \frac{p_1}{S} + \frac{m_1 G_b}{S^{\alpha_1+1}} + \frac{m_2}{S^{\alpha_1}}\mathscr{L}\{I(t)\} - \frac{m_1}{S^{\alpha_1}}\mathscr{L}\{G(t)\} \tag{5. 43}$$

$$\mathscr{L}\{X\} = \frac{p_2}{S} - \frac{m_3 I_b - m_6 I_b}{S^{\alpha_2+1}} - \frac{m_2}{S^{\alpha_2}}\mathscr{L}\{X(t)\} + \frac{m_3}{S^{\alpha_2}}\mathscr{L}\{I(t)\} \tag{5. 44}$$

$$\mathscr{L}\{I\} = \frac{p_3}{S} + \frac{m_6 I_b + m_4 m_5}{S^{\alpha_3+1}} - \frac{m_3 + m_6}{S^{\alpha_3}}\mathscr{L}\{I(t)\} + \frac{m_4}{S^{\alpha_3}}\mathscr{L}\{G(t)\} \tag{5. 45}$$

The inverse Laplace transform implies that

$$G = 100 + \frac{2.536 t^{\alpha_1}}{\alpha_1!} + p\mathscr{L}^{-1}\left(\frac{m_2}{S^{\alpha_1}}\mathscr{L}\{I(t)\} - \frac{m_1}{S^{\alpha_1}}\mathscr{L}\{G(t)\}\right) \tag{5. 46}$$

$$X = \frac{1.861 t^{\alpha_1}}{\alpha_1!} + p\mathscr{L}^{-1}\left(-\frac{m_2}{S^{\alpha_2}}\mathscr{L}\{X(t)\} + \frac{m_3}{S^{\alpha_2}}\mathscr{L}\{I(t)\}\right) \tag{5. 47}$$

$$I = 7 + \frac{2.1696 t^{\alpha_3}}{\alpha_3!} + p\mathscr{L}^{-1}\left(-\frac{m_3 + m_6}{S^{\alpha_3}}\mathscr{L}\{I(t)\} + \frac{m_4}{S^{\alpha_3}}\mathscr{L}\{G(t)\}\right) \tag{5. 48}$$

Now apply Homotopy Perturbation Method [7,19], we have

$$\sum_{k=0}^{\infty} p^n G_n(t) = 100 + \frac{2.536t^{\alpha_1}}{\alpha_1!} + p\mathscr{L}^{-1}(\frac{m_2}{S^{\alpha_1}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n I_n(t)\} - \frac{m_1}{S^{\alpha_1}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n G_n(t)\}) \quad (5.\ 49)$$

$$\sum_{k=0}^{\infty} p^n X_n(t) = \frac{1.861t^{\alpha_1}}{\alpha_1!} + p\mathscr{L}^{-1}(-\frac{m_2}{S^{\alpha_2}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n X_n(t)\} + \frac{m_3}{S^{\alpha_2}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n I_n(t)\}) \quad (5.\ 50)$$

$$\sum_{k=0}^{\infty} p^n I_n(t) = 7 + \frac{2.1696t^{\alpha_3}}{\alpha_3!} + p\mathscr{L}^{-1}(-\frac{m_3+m_6}{S^{\alpha_3}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n I_n(t)\} + \frac{m_4}{S^{\alpha_3}}\mathscr{L}\{\sum_{k=0}^{\infty} p^n G_n(t)\}) \quad (5.\ 51)$$

where $G_n(t)$, $X_n(t)$, $I_n(t)$, are He's polynomials. The first few component of He's polynomials Comparing the coefficient of like powers of p, we have

$$G(t) = 100 - 0.5479\frac{t^{\alpha_1}}{\alpha_1!} + 0.094\frac{t^{2\alpha_1}}{2\alpha_1!} + 0.026686\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} + ... \quad (5.\ 52)$$

$$X(t) = 1.861\frac{t^{\alpha_1}}{\alpha_1!} + 0.00003444\frac{t^{\alpha_2}}{(\alpha_2)!} + 0.0228903\frac{t^{\alpha_1+\alpha_2}}{(\alpha_1+\alpha_2)!} + 0.00001067\frac{t^{\alpha_2+\alpha_3}}{(\alpha_2+\alpha_3)!} + ... \quad (5.\ 53)$$

$$I(t) = 7 + 2.1696\frac{t^{\alpha_3}}{\alpha_3!} + 2.0381\frac{t^{\alpha_3}}{\alpha_3!} + 0.0989\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} - 0.5769\frac{t^{2\alpha_3}}{2\alpha_3!} \quad (5.\ 54)$$

Similarly, for case II, we have following series solution

$$G(t) = 240 + 0.255\frac{t_1^{\alpha}}{\alpha_1!} + 0.073049\frac{t^{\alpha_1+\alpha_3}}{(\alpha_1+\alpha_3)!} - 0.0193\frac{t^{\alpha_1+2\alpha_3}}{(\alpha_1+2\alpha_3)!} + ... \quad (5.\ 55)$$

$$X(t) = 3.9599\frac{t^{\alpha_2}}{\alpha_2!} - 0.067314\frac{t^{2\alpha_2}}{(2\alpha_2)!} + 7.9\times10^{-5}\frac{t^{\alpha_2}}{\alpha_2!} + 0.00002277\frac{t^{\alpha_2+\alpha_3}}{(\alpha_2+\alpha_3)!} + (5.\ 56)$$

$$I(t) = 15 + 1.345\frac{t^{\alpha_3}}{\alpha_3!} - 1.13441\frac{t^{2\alpha_3}}{2\alpha_3!} + ... \quad (5.\ 57)$$

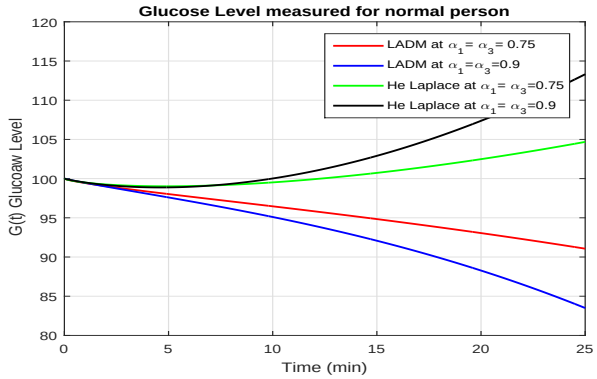

Figure 7: Comparison with He Laplace and LADM, $G(t)$ of normal person at α

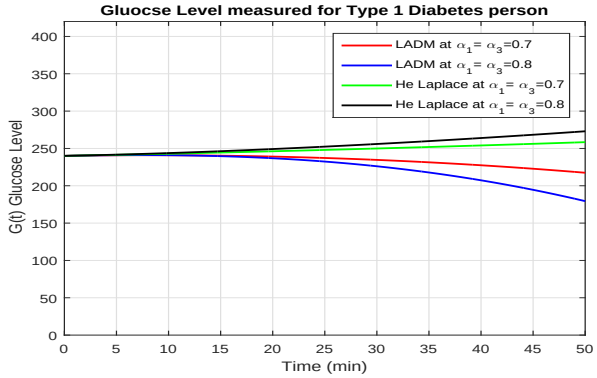

Figure 8: Comparison with He Laplace and LADM, $G(t)$ of type 1 diabetes at α

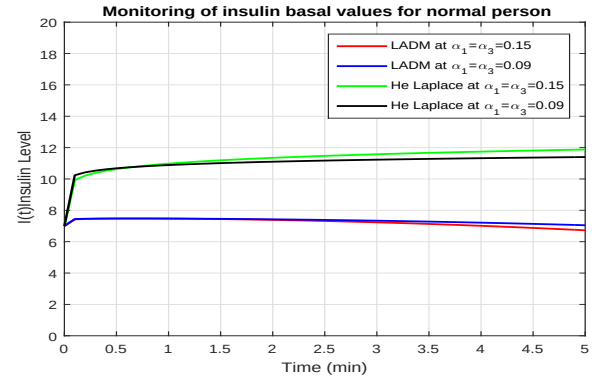

Figure 9: Comparison with He Laplace and LADM, $I(t)$ in normal person at α

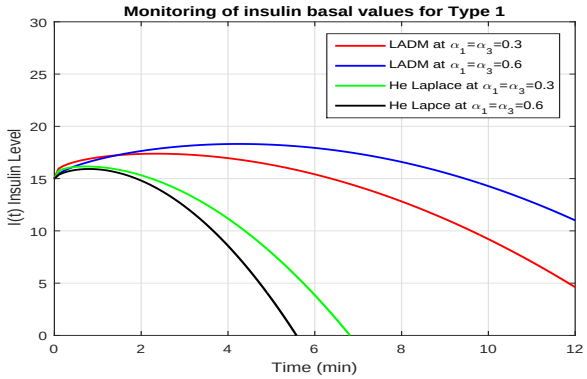

Figure 10: Comparison with He Laplace and LADM, $I(t)$ in type 1 diabetes at α

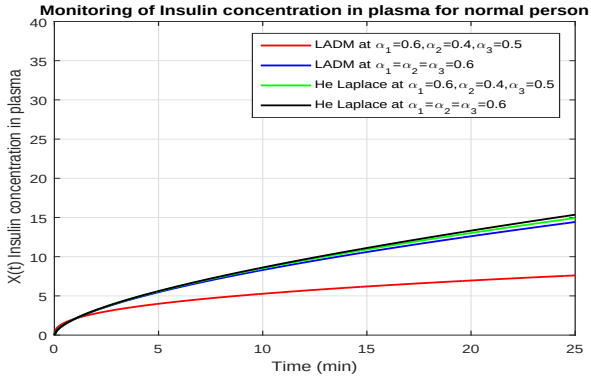

Figure 11: Comparison with He Laplace and LADM, $X(t)$ of normal person at α

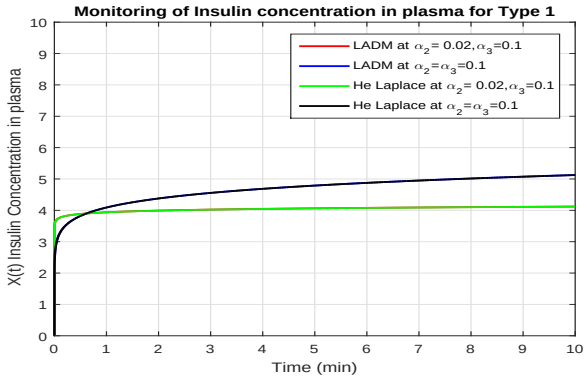

Figure 12: Comparison with He Laplace and LADM, $X(t)$ of type 1 diabetes at α

6. Numerical Results and Discussion

The analytical solution of fractional order model consist of nonlinear system of fractional differential equation has been presented by using Laplace Adomian decomposition method. To observe the effects of the parameter on the dynamics of the fractional-order model $(3.8 - 3.10)$, we conclude several numerical simulations varying the value of parameter given in table 1 with time 20 to 40 minutes. These simulations reveals that a change of the value affects the dynamics of the model . In figure 1 and 2 clearly shows the bounded solution according to normal values of glucose level for normal person and type 1 diabetes. In figure 3 and 4 basal values of insulin properly rise and bounded according to inial conditions and approach to zero when no insulin injected nor produced in human body. Figure 5 represent the insulin concentration in plasma with effect of glucose level. Figure 6 represents no insulin produce in human body caused by type 1 diabetes with passage of time. The system gives the solution at fractional derivative on non integer values which are more appropriate and accurate values in given domain. Glucose level increase in figure 2 due to cause of type 1 diabetes which control with suitable input values of insulin to normalize the glucose level. For GIS system given in figure (1-6), we observe that the classical system(i.e $\alpha_1 = \alpha_2 = \alpha_3 = 1$) fail to stable the glucose insulin system for normal as well as type-1 diabetics mellitus and do not fulfill the condition and maintenance of close loop design for an artificial pancreas. it can be easily observe that in figure (1-6) fractional order values maintain the stability gulose insulin system. In figure(7-12), the comparison of fractional order model made with Adomian decomposition Method with Laplace transform and He laplace method for normal person and type -1 diabetics mellitus. It should be observe that the behavior of the glucose insulin system is almost same but LADM gives more appropriate and comfortable behavior in system.

6.1. **Input and output Stability.** Stability is a main anxiety in feedback control design in engineering for automatic control systems because a feedback control law can stabilize and also can destabilize a system. We use Lyapunov's indirect method [29] to examine the system stability $(2.1 - 2.3)$. The system equilibrium points depends on the steady state of glucose and insulin concentration in plasma. The blood glucose level has the steady state $100(mg/dl)$ and the steady state of insulin in the system $(2.1 - 2.3)$ with the feedback infusion rates and the values of parameters are given in Tables 1 . Equilibrium point by using Matlab as $(83.6417, 151.3288, 9.3857)$. Suppose the linear system

$$\dot{x}(t) = Ax + B,\ y(t) = Cx \tag{6. 58}$$

where $x = [G, I, X]^T$ $B = [0, 0, 1]^T$ and $C = [1, 0, 0]$ and A is the Jacobian matrix at the equilibrium. We find the following eigenvalues of A by using the MATLAB are as follows $(-0.0315, -0.0062 + 0.5619i, -0.0062 - 0.5619i)$, Since the eigen values of the system are negative real parts, it satisfied the inputoutput stability theorem.

6.2. **Controllability and observability.** The dynamical system has physical properties Controllability and observability that represents the effect of regulatory system of blood glucose in human. The system (6.58) is controllable if for any initial state x_0 and any desired state x_f , there exists a control of insulin such that $x(T) = x_f$ for some $T > 0$. The system (6.58) is observable if any initial state can be uniquely determined by the output Glucose (blood glucose) over $(0, T)$ for some $T > 0$. To check the controllability

of (6.58), it suffices to examine the rank of the Kalman controllability matrix [29,31]. $C = [B|AB|A^2B]$. Here we take the only measured output of glucose and the only input is insulin. we compute the determinant of the matrix $det(C) = 0.0245$. Therefore C has the full rank of 3 and then the system (6.58) is controllable. In the same way, $O = [C^T|A^TC^T|(A^T)^2C]$ and $det(O) = -2.3574e^{005}$ we can has the full rank of 3 and then the system (6.58) is observable. Hence the system is controllable and observable. Similarly for case II, the system is controllable but not observable.

7. CONCLUSIONS

This paper presented a theoretical and numerical investigation of the bio-medical glucose insulin model. It shows the controllability and applicability of the model for the control of the blood glucose concentration in normal person and type 1 diabetes. For the purpose of automatic artificial pancreas in the glucose regulatory system, we discuss fractional order glucose insulin model. The model is stable by using the lyapunov equation and input/output stability is also satisfied for automatic control. Hence the model is stable in each case to design the close loop for artificial pancreas. System is controllable and observable for case 1. For case II, the system is controllable but not observable according to the given parameters values.

It is important to note that Adomian Decomposition method with laplace transform is for mathematical models based on system of fractional order differential equations are more powerful approach to compute the convergent solutions. The constructed series by Laplace adomian decomposition method and He Laplace method for type 1 diabetes model show a good agreement to control the glucose insulin system. The model provide the continues glucose measuring in limited time and solutions are bounded in normal values for healthy person and type 1 diabetes. This is perhaps due to development in the biological approach for the new model: e.g the hypothesis associated to internal insulin creation through a time dependent model. Our results show that the fractional-order models can give enhanced turns to the data than integer-order models in some cases, it is clear that for the satisfactory turns, the models need additional improvement and insertion of these changes should greatly improve future models.

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