A Caputo (discretization) fractional-order model of glucose-insulin interaction: numerical solution and comparisons with experimental data

Mansoor H. Alshehri, Faisal Z. Duraihem, Ahmad Alalyani, and Sayed Saber

Abstract
In this paper, we investigate a (discretization) Caputo fractional glucose-insulin model qualitatively with incommensurate orders that appear in Bergman’s minimal model. After intravenous tolerance testing, the model is used to characterize the blood insulin and glucose metabolism. We also prove that the presented model possesses existence, uniqueness, non-negative, and boundedness solutions. We also proceed a systematical studies on the stability of the (discretization) Caputo fractional. Comparisons between the results of the fractional-order, the integer order and the measured real data obtained from patients are presented. These comparisons is shown that the presented Caputo fractional order model is better representative of the system than its integer order form. Numerical solutions of the Caputo fractional model are obtained by using the method of Adams-Bashforth-Moulton type to handle the fractional derivatives. Also, numerical simulations of the discretization fractional derivative order model are used to support the analytical results.

1. Introduction
The relationship between glucose and insulin concentration, its regulatory hormone has been studied and modelled by several scientists (see [1–11]). Most of mathematical models proposed were deduced to study the dynamical behavior of the glucose-insulin interaction, including Intra Venous Glucose Tolerance Test (IVGTT). In 1961, Bolie [1] proposed the simple linear model:

\[
\begin{align*}
x(t) &= -k_1 x(t) - k_2 z(t) + p, \\
\dot{z}(t) &= -k_3 x(t) - k_4 z(t),
\end{align*}
\]

where \(x\) is the plasma glucose concentration (resp. insulin) at time \(t\), and \(p, k_1, k_2, k_3, k_4\) are parameters. After incorporating the insulin dynamics, Bergman et al. [5], has presented the “Minimal Model” in 1980, which characterize IVGTT experimental data well, and it was modified in 1986 [11], and takes the form of [6] (see also [2,9])

\[
\begin{align*}
x(t) &= -(q_1 + y(t)) x(t) + q_1 x_0, \quad x(0) = q_0, \\
y(t) &= -q_2 y(t) + q_3 (z(t) - z_0), \quad y(0) = 0, \\
\dot{z}(t) &= q_4 [x(t) - q_5]^+ t - q_6 (z(t) - z_0), \\
z(0) &= z_0,
\end{align*}
\]

with

\[
[x - q_5]^+ = \begin{cases} x - q_5 & \text{if } x > q_5, \\
0 & \text{if } x \leq q_5,
\end{cases}
\]

where \(x\) and \(z\) are defined above,

\[
y \ [1/min] \text{ is an auxiliary function which representing activity of insulin excitable tissue glucose uptake,}
\]

\[
x_0 \ [mg/dL], \ (resp. \ z_0 \ [mU/L]) \text{ represent the concentration of Basal blood glucose (resp. insulin),}
\]

\[
q_0 \ [mg/dL] \text{ represent the theoretical glycemia at time } t = 0, \text{ immediately after the instantaneous glucose bolus intake,}
\]

\[
q_1 \ [1/min] \text{ represent the rate of insulin-independent glucose clearance,}
\]

\[
q_2 \ [1/min] \text{ represent the rate of the active insulin clearance (upt. decrease),}
\]

\[
q_3 \ [L/(min2mU)] \text{ represent the increase in uptake ability which caused by insulin,}
\]

\[
q_4 \ [1/min] \text{ represent the rate of decay of blood insulin,}
\]

\[
q_5 \ [mg/dL] \text{ represent the target level of glucose,}
\]

\[
q_6 \ [mUdL/Lmgmin] \text{ represent the rate of the Pancreatic release, immediately after glucose bolus,}
\]

\[
q_7 \ [mg/dL][1/min] \text{ represent the concentration of Plasma insulin above basal insulinenemia at time 0, immediately after the glucose bolus intake.}
\]
In [6], De Gaetano and Arino has intended a model called the dynamical model which couples the two different parts of the “Minimal Model” into one part given by

\[ \dot{x} = -(1 + p_2)y x + (p_1 + p_1) x_b - x, \]
\[ \dot{z} = -p_2 y + (p_3 + p_3) (z - z_b), \]

with \( x = x_b \) for \( -c_5 \leq t < 0 \) where \( c_0, c_1, c_2, c_3, c_4, c_5, c_6, \) and \( c_7 \) are parameters.

In [7], Derouich et al. have been used a version of the minimal model in modified form to introduce parameters related to physical exercise:

\[ \dot{x} = -(1 + p_2)y x + (p_1 + p_1) x_b - x, \]
\[ \dot{z} = -p_2 y + (p_3 + p_3) (z - z_b), \]

In [8], Li et al. had reinvestigated the dynamical analysis of the “Minimal Model” in both modelling and physiological aspect to understanding blood glucose regulatory system:

\[ \dot{x} = -b_1 x - b_2 x^2 + b_7, \quad x(0) = x_b + b_0, \]
\[ \dot{z} = b_6 x - b_2 z, \quad z(0) = z_b + b_3, \]

with \( x_j = x_b \) for \( t \in [-b_3, 0) \) and \( b_1, b_2, b_4, b_4, b_7 \) are parameters.

The concept of fractional calculus has great importance in many branches and is also important for modelling real world problems [12–36]. In this paper, we concerned on the discrete version Caputo fractional order of the minimal model (1):

\[ D^\nu_{t} x = -(q_1 + y) x + q_1 x_b, \quad x(0) = q_0, \]
\[ D^\nu_{t} y = -q_2 y + q_3 (z - z_b), \quad y(0) = 0, \]
\[ D^\nu_{t} z = q_4 (x - q_3)^+ - q_6 (z - z_b), \quad z(0) = z_b, \]

with

\[ (x - q_3)^+ = \begin{cases} x - q_3 & \text{if } x > q_3, \\ 0 & \text{if } x \leq q_3. \end{cases} \]

This paper concerned on a analytical studies of a Caputo fractional-order glucose-insulin model (2) and its discretization. The fractional calculus has great importance for modelling real world problems and is also important in many branches. After intravenous tolerance testing, this model used to characterize the metabolism of blood insulin and glucose. We show that the model (2) possesses existence, uniqueness, non-negative, and boundedness solution. We also prove that the presented model possesses existence, uniqueness, non-negative, and boundedness solution. We also proceed a systematical studies on the stability of the (discretization) Caputo fractional. Comparisons between the results of the fractional-order, the integer order and the measured real data obtained from patients are presented. These comparisons is shown that the presented Caputo fractional order model is better representative of the system than its integer order form. Numerical solutions of the Caputo fractional model are obtained by using the method of Adams-Bashforth-Moulton type to handle the fractional derivatives. Also, numerical simulations of the discretization fractional derivative order model are used to support the analytical results.

### 2. Caputo fractional-order modelling of glucose-insulin

#### 2.1. Notation and definitions

For \( v \in \mathbb{R} \), the fractional derivative \( D^\nu_{t} \), can represented by

\[ D^\nu_{t} = \begin{cases} \frac{d^\nu}{dt^\nu} & \text{Re}(v) > 0, \\ 1 & \text{Re}(v) = 0, \\ \int_{a}^{t} (\sigma)^{-v} d\sigma & \text{Re}(v) < 0. \end{cases} \]

Define the Euler-Gamma function as

\[ \Gamma(\alpha) = \int_{0}^{\infty} e^{-t} t^{\alpha-1} dt, \quad t > 0. \]

In [12], the Riemann-Liouville definition first introduced in 1847 and is given by

\[ D^\nu_{t} f = \begin{cases} \frac{1}{\Gamma(n - \nu)} \frac{d^n}{dt^n} \int_{0}^{t} \frac{f(\sigma)}{(t - \sigma)^{\nu+1-n}} d\sigma, & n - 1 \leq \nu < n, \\ \frac{d^n}{dt^n} f(t) & \nu = n. \end{cases} \]

In [13], the Caputo definition first introduced in 1967, and is given by

\[ D^\nu_{t} f = \begin{cases} \frac{1}{\Gamma(n - \nu)} \int_{0}^{t} \frac{f(\sigma)}{(t - \sigma)^{\nu+1-n}} d\sigma, & n - 1 \leq \nu < n, \\ \frac{d^n}{dt^n} f(t) & \nu = n, \end{cases} \]

Anton Karl Grunwald [37] and Aleksey Vasilievich Letnikov [38], introduced the Grünwald-Letnikov definition over the interval \([a, t]\)

\[ D^\nu_{t} f = \lim_{\varrho \to 0} \frac{1}{\varrho^n} \sum_{n=0}^{\left\lfloor \frac{t-a}{\varrho} \right\rfloor} (-1)^n \binom{n}{\nu} f(t - n\varrho), \]

with \( n \in \mathbb{N}, \varrho \) is the step size, and a binomial

\[ \binom{n}{\nu} = \frac{\Gamma(\nu + 1)}{\Gamma(n + 1)\Gamma(\nu + 1 - n)}. \]
Definition 2.1: If
\[ \zeta(w) = w^n + a_1w^{n-1} + a_2w^{n-2} + \cdots + a_n = 0, \]
\[ \eta(w) = w^m + b_1w^{m-1} + b_2w^{m-2} + \cdots + b_m = 0, \]
and if \( \Gamma(\zeta, \eta) \) is the determinant of the corresponding Sylvester matrix \((n + m) \otimes (n + m)\). Thus
\[ S(\zeta) = (-1)^{n(n-1)/2} \frac{d\zeta}{dw} \]
is the discriminant of a polynomial \( \zeta \).

Definition 2.2: For \( \beta > 0 \), the function
\[ E_{\beta}(z) = \sum_{\mu=0}^{\infty} \frac{z^\mu}{\Gamma(\beta \mu + 1)} \]
is called the Mittag-Leffler function of \( \beta \).

Lemma 2.1 ([23,39], Generalized mean value theorem): Suppose that \( f(x) \in C[a,b] \) and \( D_0^\alpha f(x) \in C[a,b] \), for \( 0 < \alpha \leq 1 \), then we have
\[ f(x) = f(a) + \frac{1}{\Gamma(\alpha)} (D_0^\alpha f)(\xi)(x-a)^\alpha \]
with \( a \leq \xi \leq x, \forall x \in (a, b] \).

Lemma 2.2 ([23,39]): Suppose that \( f(x) \in C[a,b] \) and \( D_0^\alpha f(x) \in C[a,b] \), for \( 0 < \alpha \leq 1 \), then \( f(x) \) is nondecreasing for each \( t \in [a, b] \). If \( D_0^\alpha f(x) \leq 0 \forall t \in [a, b] \), then \( f(x) \) is nonincreasing for each \( t \in [a, b] \).

Lemma 2.3 ([23, Lemma 9]): Suppose that \( T \in CP[\mathbb{R}^+, \mathbb{R}] \) satisfies
\[ D_t^\gamma T(t) + \gamma T(t) \leq \lambda, \quad T(t_0) = T_0, \quad t \geq t_0 \geq 0. \]
where \( \gamma, \lambda, \mu \in \mathbb{R} \). Then one has
\[ 0 \leq T(t) \leq T(t_0) E_{\beta}(\gamma(t-t_0)^\alpha) \]
\[ + [\lambda(t-t_0)^\alpha E_{\beta,\beta+1}(\gamma(t-t_0)^\alpha)], \quad t \geq t_0 \geq 0. \]

2.2. Existence, uniqueness, non-negativity and boundedness solutions

Existence of the solution of the system (2) and its uniqueness will be provided herein in the region \( F \times (0, T) \) with \( F = \{(x, y, z) \in \mathbb{R}^3 : \max(|x|, |y|, |z|) \leq \eta\} \). Following [21], one obtains

Theorem 2.1: For each initial condition \( X_0 = (x_0, y_0, z_0) \in F \), the solution \( X(t) \in F \), \( t \geq 0 \), of the model (2) is unique.

Proof: For \( X, \bar{X} \in F \), one can take a mapping \( \Gamma(X) = (\Gamma_1(X), \Gamma_2(X), \Gamma_3(X)) \) with
\[ \Gamma_1(X) = -|q_1 + y|x + q_1x_0, \]
\[ \Gamma_2(X) = -q_2x + q_3(z - z_0), \]
\[ \Gamma_3(X) = q_4(x - q_5)t - q_6(z - z_0). \]
Thus, one obtains
\[ \|\Gamma(X) - \Gamma(\bar{X})\| \]
\[ = |\Gamma_1(X) - \Gamma_1(\bar{X})| + |\Gamma_2(X) - \Gamma_2(\bar{X})| + |\Gamma_3(X) - \Gamma_3(\bar{X})| \]
\[ = |(q_1 + y)x + q_1x_0 - (q_1 + \bar{y})\bar{x} - q_1\bar{x}_0| \]
\[ + |q_2x - q_3(z - z_0) - q_2z - q_3(z - z_0)| \]
\[ + |q_4(x - q_5)t - q_6(z - z_0)| \]
\[ \leq |(q_1 + \bar{y})\bar{x} - q_1\bar{x}_0| \]
\[ + |q_2z - q_3(z - z_0)| \]
\[ \leq |(q_1 + q_4)t|x - \bar{x}| + (q_3 + q_6)|z - \bar{z}| \]
\[ \leq \mu \|X - \bar{X}\|, \]
where
\[ \mu = \max(\epsilon + q_4|t|, \epsilon + q_2, q_3 + q_6) \].

Thus, the Lipshitz condition is satisfied on \( \Gamma(X) \). Thus, the solutions of the model (2) exist and uniqueness.

Theorem 2.2: For the model (2), the solutions start in \( \mathbb{R}^3_+ \) and are semi-positive.

Proof: One has
\[ D_t^\gamma x(t)|_{t=0} = q_1x_0 \geq 0, \]
\[ D_t^\gamma y(t)|_{t=0} = q_3(z - z_0) \geq 0, \]
\[ D_t^\gamma z(t)|_{t=0} = q_6Z_0 \geq 0. \]

Then, the solutions of the model (2) are semi-positive, by using Lemmas 2.1 and 2.2.

Theorem 2.3: For the model (2), the solutions start in \( \mathbb{R}^3_+ \) are uniformly bounded.

Proof: As in [21], one consider the function \( T(t) = x(t) + y(t) + z(t) \). Then
\[ D_t^\gamma T(t) = D_t^\gamma x(t) + D_t^\gamma y(t) + D_t^\gamma z(t) \]
\[ = (tq_4 - q_1)x(t) - q_2yz(t) \]
\[ + (q_3 - q_6)Z - y(t)x(t) - q_1x_0 \]
\[ - q_2Z_0 - q_4st + q_6Z_0. \]
Thus, for all $\gamma > 0$,
\[
D^\gamma_t T(t) + \gamma T(t) = (\gamma + tq_4 - q_1)x(t) + (\gamma - q_2)y(t) + (\gamma + q_3 - q_6)z - \gamma(t)x(t) + q_1x_b - q_3z_b - q_4q_5t + q_6z_b.
\]
Thus, by choosing $\gamma < \min\{q_1 - q_4|t|, q_2, q_6 - q_3\}$, one obtains
\[
D^\gamma_t T(t) + \gamma T(t) \leq q_1x_b + q_6z_b.
\]
Following to Lemma 2.3, one obtains
\[
0 \leq T(t) \leq T(0)E_{\nu,\nu+1}(-\gamma t^\nu) + [(q_1x_b + q_6z_b)^nE_{\nu,\nu+1}(-\gamma t^\nu)],
\]
where $E_{\nu}$ is the function of Mittag-Leffler. Since $0 \leq E_{\nu,\nu+1}(-\gamma t^\nu) \leq 1$, one gets
\[
0 \leq T(t) \leq -q_1x_b + q_6z_b, \quad \text{for } t \to \infty.
\]
Thus, as starting in $\mathbb{R}^3_+$, the model (2) has uniformly bounded solution lies in the region $\Sigma$, with
\[
\Sigma = \left\{(x,y,z) \in \mathbb{R}^3_+: T(t) \leq \frac{q_1x_b + q_6z_b}{\lambda} + \varepsilon, \varepsilon > 0 \right\}.
\]

### 2.3. Stability analysis

For the model (2), we assume that
\[
D^\gamma_t x(t) = 0, \quad D^\gamma_t y(t) = 0, \quad D^\gamma_t z(t) = 0.
\]
Then, the model (2) has only one equilibrium point $E^* = (x_0, 0, z_0)$ and its Jacobian matrix $J(E^*)$ is given by
\[
J(E^*) = \begin{bmatrix}
-q_1 & -x_b & 0 \\
0 & -q_2 & q_3 \\
0 & 0 & -q_6
\end{bmatrix}.
\]
Also, its characteristic equation $\Pi_1(\lambda)$ is given by
\[
\Pi_1(\lambda) = (\lambda + q_1)(\lambda + q_2)(\lambda + q_6). = 0.
\]
Then
\[
\lambda_1 = -q_1, \lambda_2 = -q_2, \lambda_3 = -q_6.
\]
Thus, by using [32], $E^*$ is asymptotically stable.

### 2.4. Numerical results

In this subsection, the numerical solutions for Caputo fractional order system (2) are simulated by using the method of Adams-Bashforth-Moulton existed in [40]. Values of the parameters, given in Table 1, are taken from [11], in which these values are obtained using a computer program, named "MINMOD". Consider the following:
\[
D^\gamma_t x = -(0.03082 + y)x + 0.03082 \times 92,
\]
\[
x(0) = 287,
\]
\[
D^\gamma_t y = -0.02093y + 1.062 \times 10^{-5}(z - 7.3),
\]
\[
y(0) = 0,
\]
\[
D^\gamma_t z = 0.3[x - 94]^+ t - 0.3349 \times 10^{-2}(z - 7.3),
\]
\[
z(0) = 403.4,
\]
with
\[
[x - 94]^+ = \begin{cases} x - 94 & \text{if } x > 94, \\
0 & \text{if } x \leq 94. 
\end{cases}
\]
For these parameter, $E^* = (287, 0, 403.4)$ is asymptotically stable. The parameter of the model have been set to $\nu = 0.75$, $\nu = 0.95$, and $\nu = 1$. Behaviour of experimental data and integer order model for Glucose and Insulin concentration, respectively are shown in Figures 1 and 2. The blood glucose level is presented in Figure 1. As shown in this figure, the model can reduce the blood glucose concentration from the initial value of 287 (mg/dl) to the approximate value of 80 (mg/dl) which is our desired level. Also, the behaviour of $x(t)$ and $z(t)$ for $\nu = 0.75$, $\nu = 0.85$, $\nu = 0.95$, and $\nu = 1$, showing Glucose and Insulin dynamics are shown in Figure 3.

### 3. Discretized model and its dynamical behaviours

In this section, we use a discretization process to discretize the Caputo fractional model (2) with piecewise constant arguments, [19,20]. Let $\nu \in (0, 1)$ and consider the differential equation of fractional order
\[
D^\gamma_t w(t) = f(w(t)), \quad t > 0,
\]
\[
w(0) = w_0, \quad t \leq 0.
\]
Its corresponding equation with a piecewise constant argument is
\[
D^\gamma_t w(t) = f w \left( m \left[ \frac{t}{m} \right] \right), \quad t > 0,
\]
\[
w(0) = w_0, \quad t \leq 0.
\]

### Table 1. Parameters and their values.

| Parameter | $q_1$ | $q_2$ | $q_3$ | $q_4$ | $q_5$ | $q_6$ | $x_0$ | $z_0$ |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|
| Value     | 0.03082 | 0.02093 | $1.062 \times 10^{-5}$ | 0.3 | 94 | $0.3349 \times 10^{-2}$ | 92 | 7.3 |
Let $t \in [0, m)$, then $\frac{t}{m} \in [0, 1)$. So we get $D^\nu_tw(t) = f(w_0), t \in [0, 1)$.

Thus

$$w_1(t) = w_0 + \frac{t^\nu}{\Gamma(\nu + 1)}f(w_0).$$

Let $t \in [m, 2m)$, then $\frac{t}{m} \in [1, 2)$. So we get $D^\nu_tw(t) = f(w_1(m)), t \in [m, 2m)$. Thus

$$w_2(t) = w_1(m) + \frac{(t - m)^\nu}{\Gamma(\nu + 1)}f(w_1(m)).$$

Let $t \in [2m, 3m)$, then $\frac{t}{m} \in [2, 3)$. So we get $D^\nu_tw(t) = f(w_2(2m)), t \in [2m, 3m)$. Thus

$$w_3(t) = w_2(2m) + \frac{(t - 2m)^\nu}{\Gamma(\nu + 1)}f(w_2(2m)).$$

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

$$D^\nu_tw(t) = f(w_n(nm)), \quad t \in [nm, (n + 1)m).$$
Thus

\[ w_{n+1}(t) = w_n(nm) + \frac{(t - nm)^{\mu}}{\Gamma(v + 1)} f(w_n(nm)). \]

As \( t \to (n + 1)m \), one obtains the corresponding equation of the model (2) with a piecewise constant argument is given as:

\[ x_{n+1} = x_n + \frac{m^\nu}{\Gamma(v + 1)} \left([- (q_1 + y_n) x_n + q_1 x_0], \right. \]

\[ y_{n+1} = y_n + \frac{m^\nu}{\Gamma(v + 1)} \left[- q_2 y_n + q_3 (z_n - z_b)\right], \]

\[ z_{n+1} = z_n + \frac{m^\nu}{\Gamma(v + 1)} \left[q_4 (x_n - q_{3}) (n(m + 1)) \right. \]

\[ - q_6 (z_n - z_b)]. \]

### 3.1. Stability analysis

Here, the dynamical behaviours and stability analysis of the Caputo fractional discretized Glucose-insulin model (4) is investigated here at the equilibrium point \( E^* = (x_0, 0, z_0) \). First, we compute the Jacobian matrix \( J(E^*) \) of (4) as follows

\[ J(E^*) = \begin{bmatrix} 1 - hq_1 & -hx_b & 0 \\ 0 & 1 - q_2 h & hq_3 \\ mh(n + 1)q_4 & 0 & 1 - q_6 h \end{bmatrix} \]

with \( h = \frac{m^\nu}{\Gamma(v + 1)} \) and its characteristic equation is given by

\[ \Pi_2(\lambda) = \lambda^3 + b_1 \lambda^2 + b_2 \lambda + b_3 = 0, \]

where

\[ b_1 = -3 + [q_1 + q_2 + q_6] h, \]

\[ b_2 = 3 - 2[q_1 + q_2 + q_6] h + [q_1 q_6 + q_2 q_6 + q_1 q_2] h^2, \]

\[ b_3 = -1 + [q_1 + q_2 + q_6] h - [q_1 q_2 + q_1 q_6 + q_2 q_6] h^2 \]

\[ + [q_1 q_2 q_6 - m q_4 q_6 (n + 1) x_b] h^3. \]

Its discriminant is given by

\[ S_2(\Pi_2) = - 18 q_1 q_2 q_3 + (q_1 q_2)^2 - 4 q_3 q_1^2 - 4 q_2^2 - 27 q_3^2. \]

From the Jury's criterion [41], \( E^* = (x_0, 0, z_0) \) is locally asymptotically stable if

\[ 1 + q_1 + q_2 + q_3 > 0, \]

\[ 1 - q_1 + q_2 - q_3 > 0, \]

\[ 1 - q_2 + q_1 q_3 - q_3^2 > 0, \]

\[ 1 + q_2 - q_1 q_3 - q_3^2 > 0. \]

(6)

From the Jury test, \( E^* \) is asymptotically stable if \( S_2(1) > 0, S_2(-1) < 0, \) and \( b_3 < 0, |a_3| > a_1, d_3 > |d_2|, \)

where \( a_3 = 1 - b_2, a_2 = b_1 - b_3 b_2, a_1 = b_2 - b_3 b_1, d_3 = a_3^2 - d_2^2, \) and \( d_2 = a_3 a_2 - a_1 a_2. \)

**Proposition 3.1 ([30]):**

(i) If \( E_2(\Pi_2) > 0, q_1 > 0, q_3 > 0, q_1 q_2 > q_3 \) and if \( E_2(\Pi_2) > 0, \) then \( E^* \) is asymptotically stable.

(ii) If \( E_2(\Pi_2) < 0, q_1 > 0, q_2 > 0, q_3 > 0, 0.5 < v < 2/3, \) then the equilibrium point \( E^* \) is asymptotically stable.

(iii) If \( E_2(\Pi_2) < 0, q_1 = 0, k_2 > 0, q_1 q_2 = q_3, v \in (0.5, 1) \) then the equilibrium point \( E^* \) is asymptotically stable.

(iv) If \( E_2(\Pi_2) < 0, q_1 < 0, q_2 < 0, v > 2/3, \) then the equilibrium point \( E^* \) is unstable.

Next, we study the numerical results of system (4).

### 3.2. Numerical simulations

Taking the parameter values as shown in Table 1 and consider the following discretized fractional order:

\[ x_{n+1} = x_n + \frac{m^\nu}{\Gamma(v + 1)} \left[-(0.03082 + y)x \right. \]

\[ + 0.03082 \times 92], \quad x(0) = 287, \]

\[ y_{n+1} = y_n + \frac{m^\nu}{\Gamma(v + 1)} \left[-0.02093y + 1.062 \right. \]

\[ \times 10^{-5}(z - 7.3)], \quad y(0) = 0, \]

\[ z_{n+1} = z_n + \frac{m^\nu}{\Gamma(v + 1)} \left[0.3[x - 94]^+ t \right. \]

\[ - 0.3349 \times 10^{-2}(z - 7.3)], \quad z(0) = 403.4, \]

with

\[ [x - 94]^+ = \begin{cases} x - 94 & \text{if } x > 94, \\ 0 & \text{if } x \leq 94. \end{cases} \]

By calculation, the corresponding eigenvalue is \( D = -5.8328e-05 \). Then, system (4) has a free equilibrium point \( E^* = (287, 0, 403.4). \) By (6) and Proposition 3.1, the solution of (4) converges to \( E^* \) (see Figures 4–7). Consequently, the insulin and the activity of insulin excitable tissue glucose uptake are increased and the glucose decreased. For these parameter the corresponding eigenvalues are \( D = -5.8328e-05. \) Furthermore, glucose, insulin excitable tissue glucose uptake, and insulin concentration versus time for different cases of \( v. \) Then, (6) and Proposition 3.1 are satisfied and then \( E^* \) is asymptotically stable. Behaviour of \( x(t), y(t), \) and \( z(t), \) for different values of \( v, \) showing glucose, activity of insulin excitable tissue glucose uptake and insulin dynamics are shown in Figures 4–6. Also, the behaviour of Glucose, Insulin excitable tissue glucose uptake and Insulin concentration versus time for different cases \( v = 1, v = 0.95 \) and \( v = 0.90 \) are shown in Figures 7–9.

Now, we list some numerical results for the discretized fractional order (7) of IVGTT glucose-insulin interaction.
Figure 4. Behaviour of $x(t)$ for different values of $\nu$, showing Glucose dynamics.

Figure 5. Behaviour of $y(t)$ for different values of $\nu$, showing activity of insulin excitable tissue glucose uptake dynamics.

Figure 6. Behaviour of $z(t)$ for different values of $\nu$, showing Insulin dynamics.

Figure 7. Glucose, Insulin excitable tissue glucose uptake and Insulin concentration versus time for different cases of $\nu = 0.9$.

Figure 8. Glucose, Insulin excitable tissue glucose uptake and Insulin concentration versus time for different cases of $\nu = 1$.

Figure 9. Glucose, Insulin excitable tissue glucose uptake and Insulin concentration versus time for different cases of $\nu = 0.95$.

Case 1. $\nu = 1$

$$(x(t), y(t), z(t)) = ((286.946, 0.0000378592, 403.388), (286.892, 0.0000757102, 403.914), (286.837, 0.000113604, 404.978), (286.783, 0.000151593, 406.578), (286.729, 0.000189727, 408.716), (286.674, 0.000228059, 411.391), (286.62, 0.000266639, 414.601), (286.565, 0.000305519, 418.348), (286.51, 0.000344749, 422.631), (286.455, 0.000384382, 427.449), (286.4, 0.000424467, 432.802), (286.29, 0.000506203, 445.112), (286.235, 0.000547952, 452.068), (286.18, 0.000590359, 459.558), (286.124, 0.000633475, 467.582), (286.069, 0.000677349, 476.138), (286.013, 0.000722033, 485.208), (285.958, 0.000767578, 494.85), (285.902, 0.000814033, 505.004), (285.846, 0.00086145, 515.691), (285.79, 0.00090988, 526.908), (285.734, 0.000959373, 538.657), (285.678, 0.00100998, 550.937)),$$
Case 2. $v = 0.95$

$\mathbf{x}(t), y(t), z(t)$

$$= \{(286.91, 0.000063049, 403.38), (286.82, 0.000126075, 404.256), (286.729, 0.000189221, 406.026), (286.638, 0.000252628, 408.691), (286.547, 0.00031644, 412.248), (286.456, 0.000380799, 416.698), (286.365, 0.000445845, 422.039), (286.273, 0.000511721, 428.27), (286.181, 0.000578568, 435.391), (286.089, 0.000645628, 443.4), (286.996, 0.000715741, 452.298), (286.904, 0.000786349, 462.082), (286.811, 0.000858491, 472.752), (286.718, 0.00093231, 484.307), (286.624, 0.00100794, 496.746), (286.53, 0.00108554, 510.606), (286.436, 0.00116522, 524.273), (286.342, 0.00124715, 539.359), (286.247, 0.00133145, 555.326), (286.152, 0.00141826, 572.172), (286.057, 0.00150773, 589.897), (286.961, 0.00159999, 608.499), (286.865, 0.00169518, 627.979), (286.769, 0.00179342, 648.334), (286.672, 0.00189492, 669.564), (286.57, 0.00199974, 691.667), (286.478, 0.00210805, 714.644), (286.38, 0.00225999, 744.833), (286.286, 0.00235887, 783.687), (286.181, 0.00266068, 861.34), (286.229, 0.00256551, 886.669), (286.152, 0.00267344, 912.671), (286.074, 0.00278456, 939.347), (286.996, 0.00289894, 966.696), (286.918, 0.00301667, 997.171), (286.839, 0.00313783, 1023.41), (286.76, 0.0032625, 1052.77), (286.68, 0.00339077, 1082.81), (286.601, 0.00352271, 1113.51), (286.52, 0.00365841, 1144.89), (286.359, 0.00394142, 1209.64), (286.277, 0.00408888, 1243.01), (286.195, 0.00424043, 1277.06))\}$$
0.00221998, 738.493), (284.282, 0.00233567, 763.212), (284.183, 0.00245526, 788.802), 
(284.084, 0.00257888, 815.261), (283.984, 
0.00270668, 842.587), (283.884, 0.00283879, 
870.781), (283.783, 0.00297534, 899.84), (283.682, 
0.00311648, 929.765), (283.58, 0.00326233, 
960.553), (283.478, 0.00341304, 992.204), 
(283.375, 0.00356874, 1024.72), (283.271, 
0.00372957, 1058.09), (283.167, 0.00389566, 
1092.32), (283.062, 0.00406715, 1127.42), 
(282.957, 0.00424417, 1163.36), (282.85, 
0.00442685, 1200.17), (282.743, 0.00461534, 
1237.83), (282.636, 0.00480976, 1276.34), 
(282.527, 0.00501025, 1315.71), (282.418, 
0.00521694, 1355.93), (282.197, 0.00564947, 
1438.92), (282.085, 0.00587558, 1481.68), 
(281.973, 0.00610842, 1525.3)

4. Comparison results

In this section, Adams-Bashforth-Moulton method was employed as a reasonable basis for studying the solution of a fractional-order model of glucose-insulin system (2). We have tuned for the order of fractional derivative which ensures better fit. We compared the fractional-order model to the experimental data obtained based upon the experimental data used in [11], given in Table 2, during primary glucose-insulin interaction. Furthermore, based upon this experimental data, we demonstrate that, fractional order Bergman’s minimal model is better representative of the system of glucose and insulin in blood as compared to its integer order version. As in Figure 1, the numerical results of the fractional-order model are closer to the real measured data of the patients more than the results of the integer-order. For \( \nu = 0.95 \), this fractional order model gives better fit on the experimental data. It is worthy to note that the provision of changing fractions in different ways as well as changing parameters is still there, and by availing this provision, it is possible to get a very close fit. In comparison with its integer order version, the proposed model is superior. The reason is that the increase in the glucose level is less that of the integer order version. The Plasma insulin concentration in (mU/L) is illustrated in Figure 2. As shown in this figure, the proposed model outperforms the integer order version. The initial increase of Plasma insulin concentration for the proposed model is much less than that its integer order version. Simulation results verify the satisfactory performance of the proposed model in comparison with

| Variable                  | Integer order model | Fractional order model \( \nu = 0.95 \) |
|---------------------------|---------------------|------------------------------------------|
| Average value             |                     |                                          |
| Glucose concentration     | 8.9                 | 6.3                                      |
| Insulin concentration     | 5.86                | 3.1                                      |
| rms Value                 | 12.3                | 8.4                                      |
| Insulin concentration     | 7.45                | 4.95                                     |

5. Conclusions

The Caputo fractional-order glucose-insulin model (2) and its discretization system (4) are investigated. We showed that the fractional system (2) possesses existence, uniqueness, non-negative, boundedness solution. We also deduced a detailed analysis on the stability of the model (2) and its discretization system (4). Comparisons between the results of the Caputo fractional-order (2), the model of integer one and the measured real data obtained from patients are presented. These comparisons is concluded that the presented fractional order model is better representative of the system than its integer order one. Numerical solutions of the model (2) are obtained by using the method of Adams-Bashforth-Moulton type to handle the fractional derivatives. We also obtained the solution of the discretization
model (4) and a numerical solution of the system which shows that effect of time on the concentrations \(x(t), y(t)\) and \(z(t)\).

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**Availability of data and materials**

The experimental data in this work taken from the reference [11].

**Authors’ contributions**

All authors read and approved the final manuscript.

**Competing interests**

The authors declare that they have no competing interests.

**Disclosure statement**

No potential conflict of interest was reported by the author(s).

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**ORCID**

Mansoor H. Alshehri  [http://orcid.org/0000-0002-7673-3783](http://orcid.org/0000-0002-7673-3783)
Faisal Z. Duraihem  [http://orcid.org/0000-0003-1637-7366](http://orcid.org/0000-0003-1637-7366)
Sayed Saber  [http://orcid.org/0000-0002-5790-3222](http://orcid.org/0000-0002-5790-3222)

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