MATHEMATICAL MODELING APPROACH TO THE FRACTIONAL BERGMAN’S MODEL

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ABSTRACT. This paper presents the solution for a fractional Bergman’s minimal blood glucose-insulin model expressed by Atangana-Baleanu-Caputo fractional order derivative and fractional conformable derivative in Liouville-Caputo sense. Applying homotopy analysis method and Laplace transform with homotopy polynomial we obtain analytical approximate solutions for both derivatives. Finally, some numerical simulations are carried out for illustrating the results obtained. In addition, the calculations involved in the modified homotopy analysis transform method are simple and straightforward.

1. Introduction. Bergman’s minimal model consider a body as a compartment with a basal concentration of glucose and insulin. The minimal model has two variations, the first describes how blood glucose concentration reacts with blood insulin concentration, and the second describes how blood insulin concentration reacts with blood glucose concentration. The two models take glucose and insulin data as an input, and have mostly been used to interpret the kinetics during the glucose tolerance test [14]-[13].

Fractional Calculus (FC) describes the evolution of biological models with memory, this evolution is presented in the fractional exponent of the derivative. It implies the next state of a fractional system depends not only upon its current state but also upon all of its historical states. The fractional orders of differentiation highlight the intermediate behaviours that cannot be modeled by ordinary equations [28]-[26]. Atangana and Baleanu suggested a derivative in the Liouville-Caputo sense with non-singular and non-local kernel based in the generalized Mittag-Leffler law [10].

2010 Mathematics Subject Classification. Primary: 34A34, 65M12; Secondary: 26A33, 34A08, 65C20, 65P20.

Key words and phrases. Bergman’s model, fractional conformable derivative, Atangana-Baleanu fractional derivative, Laplace transform, modified homotopy analysis transform method.

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Khalil in [19] came up with an interesting idea that extends the familiar limit def-
nition of the derivatives of a function called conformable derivative. This derivative
is theoretically very easier to handle and also obeys some conventional properties
of classical calculus, for instance, the product rule, quotient rule or Rolle’s theo-
rem [8]- [9]. Iterating Riemann improper integrals, the authors in [18], proposed
new a fractional derivative in the Liouville-Caputo sense. This new fractional con-
formable operator has interesting properties, for instance, depend on two fractional
parameters, the first one involve the power law and the second one involve the
conformable derivative proposed by Khalil’s.

Fractional derivatives and fractional integrals are crucial subject matter in the
branch of FC. The fractional order differential equations are naturally related to sys-
tems with multiple timescale dynamics (related to the complexity of the medium),
memory effects and future dependence which exist in most biological systems, and
they have close relations to fractals, which are abundant in biological systems [23].

In [17], the authors obtained analytical solutions for the fractional Bergman’s min-
imal model involving the Adomian decomposition method. Alkahtani in [1] solved
the fractional Bergman’s minimal model using the Caputo-Fabrizio fractional-order
derivative. The existence and uniqueness of the solution were discussed.

The modified homotopy analysis transform method (MHATM) was proposed
in [20], this method is an analytical technique based on the combination of the
homotopy analysis method and Laplace transform with homotopy polynomial. In
this work, we formulate a fractional order Bergman’s minimal blood glucose-insulin
model with the aid of the MHATM using the fractional operators of Atangana-
Baleanu-Caputo fractional derivative and fractional conformable derivative in
Liouville-Caputo sense.

2. Fractional-order derivatives. The Atangana-Baleanu-Caputo fractional der-
vative (ABC) is presented as [10]

\[ \begin{align*}
\mathcal{A}^{\alpha}_{t_0} f(t) &= \frac{B(\alpha)}{1-\alpha} \int_{t_0}^{t} \frac{d}{dt} f(\tau) \frac{(t-\tau)^\alpha}{1-\alpha} \, d\tau, \quad n-1 < \alpha \leq n, \\
&= \frac{1}{\Gamma(n-\beta)} \int_{a}^{t} \left( \frac{(t-a)^\alpha - (x-a)^\alpha}{\alpha} \right)^{n-\beta-1} \frac{\mathcal{D}^\alpha_a f(x)}{(x-a)^{1-\alpha}} \, dx, \\
&= \frac{1}{\Gamma(n-\beta)} I^{n-\beta}_a \left( \mathcal{A}^{\beta}_a f(t) \right).
\end{align*} \]

where \( \alpha \in \mathbb{R} \), \( B(\alpha) \) denotes a normalization function \( B(0) = B(1) = 1 \) and \( E_\alpha(\cdot) \) denotes the Mittag-Leffler function.

The fractional integral associated to the ABC derivative with non-local kernel is
defined as

\[ \begin{align*}
\mathcal{A}^{\alpha}_{t_0} f(t) &= \frac{1}{\Gamma(n-\beta)} \int_{a}^{t} \left( \frac{(t-a)^\alpha - (x-a)^\alpha}{\alpha} \right)^{n-\beta-1} \frac{\mathcal{D}^\alpha_a f(x)}{(x-a)^{1-\alpha}} \, dx, \\
&= \frac{1}{\Gamma(n-\beta)} I^{n-\beta}_a \left( \mathcal{A}^{\beta}_a f(t) \right).
\end{align*} \]
3. Bergman’s minimal blood glucose-insulin model. The integer-order Bergman’s minimal blood glucose-insulin model is defined as

\[
\begin{align*}
D_t G(t) &= -(p_1 + X(t))G(t) + p_1 G_b, \\
D_t X(t) &= -p_2 X(t) + p_3 (I(t) - I_b), \\
D_t I(t) &= \eta t - p_4 (I(t) - I_b),
\end{align*}
\]

(4)

with initial conditions

\[
G(0) = G_0, \quad X(0) = X_0, \quad I(0) = I_0,
\]

(5)

where \(\eta = p_6 [G(t) - p_5]^+ = \max([G(t) - p_5], 0)\). The model assume that \(G(t)\) represent the blood glucose concentration measured in \(mg/dL\); \(X(t)\) represent the effect of active insulin measured in \(1/min\) and \(I(t)\) represent the blood insulin concentration measured in \(mU/L\). In the Table 1, we present the description of the parameters involved in the model [17]-[1].

| Parameter | Description | Unit |
|-----------|-------------|------|
| \(G_b\)  | Basal blood glucose concentration | \(mg/dL\) |
| \(I_b\)  | Basal blood insulin concentration | \(mU/L\) |
| \(p_1\)  | Insulin-independent glucose clearance rate | \(1/min\) |
| \(p_2\)  | Active insulin clearance rate | \(1/min\) |
| \(p_3\)  | Increase in uptake ability caused by insulin | \(L/min^2 \cdot mU\) |
| \(p_4\)  | Decay rate of blood insulin | \(1/min\) |
| \(p_5\)  | The target glucose level | \(mg/dL\) |
| \(p_6\)  | Pancreatic release rate after glucose bolus | \(mU\cdot dL/L \cdot mg \cdot min\) |

Table 1. Description of parameters in system (4).

In this model, the pancreas is the source of insulin [12]. The following function describe the reaction of the pancreas: \(\text{Pancreas}(t) = [G(t) - p_5]^+ + t\), where \([G(t) - p_5]^+ = \max([G(t) - p_5], 0)\), for more details see the references [17]-[1].

4. Implementation of the MHATM to Bergman’s model with fractional order derivatives. Following the methodology described in [20] we solved the time-fractional Bergman’s minimal blood glucose-insulin model via Atangana-Baleanu-Caputo derivative and fractional conformable derivative in Liouville-Caputo sense.

The main steps of this method are described as follows:

Step 1. Let us consider the following equation

\[
D_t^\alpha \{ u(x,t) \} + \Upsilon[x]u(x,t) + \Phi[x]u(x,t) = \Omega(x,t), \quad t > 0, \quad x \in \mathbb{R}, \quad 0 < \alpha \leq 1, \quad (6)
\]

where \(\Upsilon[x]\) is a bounded linear operator in \(x\). While the non-linear operator \(\Phi[x]\) in \(x\) is Lipschitz continuos and satisfying \(|\Phi(f) - \Phi(\phi)| \leq \vartheta |f - \phi|\), where \(\vartheta > 0\) and \(\Omega(x,t)\) is a continuos function. The boundary and initial conditions can be treated in a similar way.

Step 2. Applying the methodology proposed in [21]-[22] we get the following m-th order deformation equation
where the Laplace transform is applied in the Atangana-Baleanu and fractional con-
formable derivative in Liouville-Caputo sense and \( \Lambda_k \) is the homotopy polynomial
defined by Odibat in [25].

**Step 3.** The non-linear term \( \Phi[x]u(x,t) \) is expanded in terms of homotopy poly-
momials as

\[
\Phi[u(x,t)] = \Phi \left( \sum_{k=0}^{m-1} u_m(x,t) \right) = \sum_{m=0}^{\infty} \Lambda_m u^m. \tag{8}
\]

**Step 4.** Expanding the non-linear term in (7) as a series of homotopy polynomials,
we can calculate the various \( u_m(x,t) \) for \( m \geq 1 \) and the solutions of Eq. (6)
is considered as the summation of an infinite series which usually converges rapidly
to the exact solutions

\[
u(x,t) = \sum_{m=0}^{\infty} u_m(x,t). \tag{9}\]

Therefore, the series solution of Eq. (6) can be obtained as

\[
U_m(x,t) = \sum_{m=0}^{\infty} U_m(x,t). \tag{10}\]

The convergence analysis of the series solution is presented in [24]. Applying the
aforesaid technique, in this work, two fractional mathematical models are consid-
ered. The first one is based on the Atangana-Baleanu-Caputo fractional derivative.
The second one consider the fractional conformable derivative in Liouville-Caputo
sense.

**Atangana-Baleanu-Caputo sense.**

\[
^{ABC}D_t^\alpha G(t) = -(p_1 + X(t))G(t) + p_4 G_0, \quad 0 < \alpha < 1, \tag{11}\]

\[
^{ABC}D_t^\beta X(t) = -p_2 X(t) + p_3 (I(t) - I_0), \quad 0 < \beta < 1, \tag{12}\]

\[
^{ABC}D_t^\gamma I(t) = \eta t - p_4 (I(t) - I_0), \quad 0 < \gamma < 1, \tag{13}\]

with initial conditions

\[
G(0) = G_0, \quad X(0) = X_0, \quad I(0) = I_0, \tag{14}\]

where \( \eta = p_6 [G(t) - p_5]^+ = \max([G(t) - p_5], 0) \).

System (11)-(13) can be made more realistic considering three different orders
for the fractional differential operators \( \alpha \in (0, 1], \beta \in (0, 1] \) and \( \gamma \in (0, 1] \) for
the blood glucose concentration \( G(t) \), for the effect of active insulin \( X(t) \) and for the
blood insulin concentration \( I(t) \), respectively.

**Solution.** Applying Laplace transform to Eq. (11), and taking initial conditions
(14), we get
\[
\hat{G}(s) = \frac{G(0)}{s} + \frac{p_1 G_b (1 - \alpha)}{B(\alpha) s} + \frac{p_1 G_b \alpha}{B(\alpha) s^{\alpha+1}} - \frac{(1 - \alpha)s^\alpha + \alpha}{B(\alpha) s^\alpha} \mathcal{L}\{p_1 G(t) + X(t)G(t)\},
\]

(15)

applying the inverse Laplace transform to Eq. (15), we obtain

\[
G(t) = G_0 + \frac{p_1 G_b (1 - \alpha)}{B(\alpha) \Gamma(\alpha + 1)} + \frac{p_1 G_b \alpha t^\alpha}{B(\alpha) \Gamma(\alpha + 1)} - \mathcal{L}^{-1}\left\{\frac{(1 - \alpha)s^\alpha + \alpha}{B(\alpha) s^\alpha} \mathcal{L}\{p_1 G(t) + X(t)G(t)\}\right\}.
\]

(16)

In a similar way, for the Eqs. (12)-(13), we have

\[
X(t) = X_0 - \frac{p_3 I_b (1 - \beta)}{B(\beta)} - \frac{p_3 I_b \beta t^\beta}{B(\beta) \Gamma(\beta + 1)} - \mathcal{L}^{-1}\left\{\frac{(1 - \beta)s^\beta + \beta}{B(\beta) s^\beta} \mathcal{L}\{p_2 X(t) - p_3 I(t)\}\right\},
\]

(17)

\[
I(t) = I_0 + \frac{p_3 I_b (1 - \gamma)}{B(\gamma)} + \frac{\eta(1 - \gamma)t}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\gamma p_4 I_b t^\gamma}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\eta t^{\gamma+1}}{B(\gamma) \Gamma(\gamma + 2)} - \mathcal{L}^{-1}\left\{\frac{(1 - \gamma)s^\gamma + \gamma}{B(\gamma) s^\gamma} \mathcal{L}\{p_4 I(t)\}\right\}.
\]

(18)

We choose the linear operator as

\[
\mathfrak{F}[\phi_j(t; \eta)] = \mathcal{L}[\phi_j(t; q)], \quad j = 1, 2.
\]

With property \(\mathfrak{F}(c) = 0\), where \(c\) is a constant. Next, defining the system of nonlinear operators as

\[
N[\phi_1(t; \eta)] = \mathcal{L}[\phi_1(t; q)] - \left(\frac{G_0}{B(\alpha)} + \frac{p_1 G_b (1 - \alpha)}{B(\alpha) \Gamma(\alpha + 1)}\right) - \frac{(1 - \alpha)s^\alpha + \alpha}{B(\alpha) s^\alpha} \mathcal{L}\{p_1 \phi_1 + \Phi_2 \phi_1\},
\]

(19)

\[
N[\Phi_2(t; \eta)] = \mathcal{L}[\Phi_2(t; q)] - \left(\frac{X_0}{B(\beta)} - \frac{p_3 I_b (1 - \beta)}{B(\beta) \Gamma(\beta + 1)}\right) - \frac{(1 - \beta)s^\beta + \alpha}{B(\beta) s^\beta} \mathcal{L}\{p_2 \Phi_2 - p_3 \Phi_3\},
\]

(20)

\[
N[\Phi_3(t; \eta)] = \mathcal{L}[\Phi_3(t; q)] - \left(\frac{I_0}{B(\gamma)} + \frac{\eta(1 - \gamma)t}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\gamma p_4 I_b t^\gamma}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\eta t^{\gamma+1}}{B(\gamma) \Gamma(\gamma + 2)}\right) - \frac{(1 - \gamma)s^\gamma + \gamma}{B(\gamma) s^\gamma} \mathcal{L}\{p_4 \Phi_3\}.
\]

(21)

Now, we construct the so-called zeroth-order deformation equation of the following manner

\[
(1 - q) \mathfrak{F}[\phi_j(t; q) - u_0(t)] = q h N[\phi_j(t; q)], \quad j = 1, 2.
\]
when \( q = 0 \) and \( q = 1 \), we have

\[
\phi_j(t; 0) = u_0(t), \quad \phi_j(t; 1) = u(t), \quad j = 1, 2. \tag{22}
\]

Thus, we obtain the nth-order deformation equations as

\[
\mathcal{L}[G_m(t) - \chi_m G_{m-1}(t)] = h \, R_m(G_{m-1}^\rightarrow, t),
\]

\[
\mathcal{L}[X_m(t) - \chi_m X_{m-1}(t)] = h \, R_m(X_{m-1}^\rightarrow, t),
\]

\[
\mathcal{L}[I_m(t) - \chi_m I_{m-1}(t)] = h \, R_m(I_{m-1}^\rightarrow, t), \tag{23}
\]

applying the inverse Laplace transform to Eq. (23), we get

\[
G_m(t) = \chi_m G_{m-1}(t) + h \, R_m(G_{m-1}^\rightarrow, t),
\]

\[
X_m(t) = \chi_m X_{m-1}(t) + h \, R_m(X_{m-1}^\rightarrow, t),
\]

\[
I_m(t) = \chi_m I_{m-1}(t) + h \, R_m(I_{m-1}^\rightarrow, t), \tag{24}
\]

where

\[
R_m(G_{m-1}^\rightarrow, t) = \mathcal{L}[G_{m-1}(t)] - (1 - \chi_m)\left( G_0 + \frac{p_1 G_b (1 - \alpha)}{B(\alpha)} + \frac{p_1 G_b \alpha t^\alpha}{B(\alpha) \Gamma(\alpha + 1)} \right)
\]

\[
- \frac{(1 - \alpha) s^\alpha + \alpha}{B(\alpha) \, s^\alpha} \mathcal{L}[p_1 G_{m-1} + H_m],
\]

\[
R_m(X_{m-1}^\rightarrow, t) = \mathcal{L}[X_{m-1}(t)] - (1 - \chi_m)\left( X_0 - \frac{p_3 I_b (1 - \beta)}{B(\beta)} - \frac{p_3 I_b \beta t^\beta}{B(\beta) \Gamma(\beta + 1)} \right)
\]

\[
- \frac{(1 - \beta) s^\beta + \beta}{B(\beta) \, s^\beta} \mathcal{L}[p_2 X_{m-1} - p_3 I_{m-1}],
\]

\[
R_m(I_{m-1}^\rightarrow, t) = \mathcal{L}[I_{m-1}(t)]
\]

\[
- (1 - \chi_m)\left( I_0 + \frac{p_4 I_b (1 - \gamma)}{B(\gamma)} + \frac{\eta (1 - \gamma) t}{B(\gamma)} + \frac{\gamma p_4 I_b t^\gamma}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\eta t^{\gamma+1}}{B(\gamma) \Gamma(\gamma + 2)} \right)
\]

\[
- \frac{(1 - \gamma) s^\gamma + \gamma}{B(\gamma) \, s^\gamma} \mathcal{L}[p_4 I_{m-1}], \tag{25}
\]

Now, the solution of nth-order deformation equations (23) are given as

\[
G_m(t) = (\chi_m + h) G_{m-1} - h(1 - \chi_m) \left( G_0 + \frac{p_1 G_b (1 - \alpha)}{B(\alpha)} + \frac{p_1 G_b \alpha t^\alpha}{B(\alpha) \Gamma(\alpha + 1)} \right) -
\]

\[
- h \, \mathcal{L}^{-1} \left\{ \frac{(1 - \alpha) s^\alpha + \alpha}{B(\alpha) \, s^\alpha} \mathcal{L}[p_1 G_{m-1} + H_m] \right\},
\]

\[
X_m(t) = (\chi_m + h) X_{m-1} - h(1 - \chi_m) \left( X_0 - \frac{p_3 I_b (1 - \beta)}{B(\beta)} - \frac{p_3 I_b \beta t^\beta}{B(\beta) \Gamma(\beta + 1)} \right) -
\]

\[
- h \, \mathcal{L}^{-1} \left\{ \frac{(1 - \beta) s^\beta + \beta}{B(\beta) \, s^\beta} \mathcal{L}[p_2 X_{m-1} - p_3 I_{m-1}] \right\},
\]

\[
I_m(t) = (\chi_m + h) I_{m-1}
\]
Taking initial conditions and the iterative scheme (26), we obtain the following

\[-\hbar(1 - \chi_m) \left( I_0 + \frac{p_4 I_4 (1 - \gamma)}{B(\gamma)} + \frac{\eta (1 - \gamma) t}{B(\gamma)} + \frac{\gamma p_4 I_4 t^\gamma}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\eta g t^{\gamma + 1}}{B(\gamma) \Gamma(\gamma + 2)} \right) - \hbar L^{-1} \left\{ \frac{(1 - \gamma) s^\gamma + \gamma}{B(\gamma)} s^\gamma L \left[ p_4 I_{m - 1} \right] \right\}.\]

(26)

where

\[H_m = \frac{1}{\Gamma(m + 1)} \left[ \frac{d^m}{dq^m} N \left[ (q \Phi_2(t; q) \left( q \phi_1(t; q) \right) \right] \right]_{q=0}.\]

Taking initial conditions and the iterative scheme (26), we obtain the following iterations:

\[p^0: G_0(t) = G^0 + a_2 t^\alpha, \quad G^0 = G_0 + \frac{p_1 G_4 (1 - \alpha)}{B(\alpha)} \quad a_2 = \frac{p_1 G_4}{B(\alpha) \Gamma(\alpha + 1)},\]

\[X_0(t) = X^0 - a_1 t^\beta, \quad X^0 = X_0 - \frac{p_3 I_3 (1 - \beta)}{B(\beta)}, \quad a_1 = \frac{p_3 I_3}{B(\beta) \Gamma(\beta + 1)},\]

\[I_0(t) = I_0 + \frac{p_4 I_4 (1 - \gamma)}{B(\gamma)} + \frac{\eta (1 - \gamma) t}{B(\gamma)} + \frac{\gamma p_4 I_4 t^\gamma}{B(\gamma) \Gamma(\gamma + 1)} + \frac{\eta g t^{\gamma + 1}}{B(\gamma) \Gamma(\gamma + 2)},\]

\[p^1: G_1(t) = m_1 \left( (1 - \alpha) h + \frac{\alpha \hbar t^\alpha}{\Gamma(\alpha + 1)} \right) + m_2 \left( (1 - \alpha) h t^\alpha \Gamma(\alpha + 1) + \frac{\alpha \hbar t^{2\alpha}}{\Gamma(2\alpha + 1)} \right) - m_3 \left( \frac{(1 - \alpha) h \Gamma(\alpha + \beta + 1)}{\Gamma(\alpha + \beta + 1)} \right) - m_4 \left( \frac{(1 - \alpha) h \Gamma(2\alpha + \beta + 1)}{\Gamma(2\alpha + \beta + 1)} \right),\]

\[X_1(t) = m_5 \left( (1 - \beta) h + \frac{\beta \hbar t^\beta}{\Gamma(\beta + 1)} \right) - m_6 \left( \frac{(1 - \beta) h \Gamma(\beta + 1) + \beta \hbar t^{2\beta}}{\Gamma(2\beta + 1)} \right) - m_7 \left( (1 - \beta) h t + \frac{\beta \hbar t^{\beta + 1}}{\Gamma(\beta + 1)} \right),\]

\[I_1(t) = m_{10} \left( (1 - \gamma) h + \frac{\gamma \hbar t^\gamma}{\Gamma(\gamma + 1)} \right) + m_{11} \left( (1 - \gamma) h t + \frac{\gamma \hbar t^{\gamma + 1}}{\Gamma(\gamma + 1)} \right) + m_{12} \left( \frac{(1 - \gamma) h \Gamma(\gamma + 1) + \gamma \hbar t^{2\gamma}}{\Gamma(2\gamma + 1)} \right) + m_{13} \left( \frac{(1 - \gamma) h \Gamma(\gamma + 1) + \gamma \hbar t^{2\gamma + 1}}{\Gamma(2\gamma + 2)} \right),\]

\[p^2: G_2(t) = m_1 \left( (1 - \alpha) h (1 + h) + \frac{\alpha \hbar (1 + h) t^\alpha}{\Gamma(\alpha + 1)} \right) + m_2 \left( \frac{(1 - \alpha) h (1 + h) t^\alpha}{\Gamma(\alpha + 1)} + \frac{\alpha \hbar (1 + h) t^{2\alpha}}{\Gamma(2\alpha + 1)} \right) - m_3 \left( \frac{(1 - \alpha) h (1 + h) t^\beta}{\Gamma(\beta + 1)} + \frac{\alpha \hbar (1 + h) t^{\alpha + \beta}}{\Gamma(\alpha + \beta + 1)} \right).\]
\[-m_4 \left( \frac{(1-\alpha)h(1+h)t^{\alpha+\beta}}{\Gamma(\alpha+\beta+1)} + \frac{\alpha h(1+h)t^{2\alpha+\beta}}{\Gamma(2\alpha+\beta+1)} \right) + \frac{1}{B(\alpha)} \left( m_1(1-\alpha)(X^0 + p_1) \right) + G^0(1-\beta)(m_5 - m_7) \left( (1-\alpha)h^2 + \frac{\alpha h^2 t^\alpha}{\Gamma(\alpha+1)} \right) + \frac{1}{B(\alpha)} \left( X^0 (am_1 + m_2(1-\alpha)) + a_2 m_5 (1-\beta) \Gamma(\alpha+1) \right)
\]
\[+ p_1 (m_1 \alpha + m_2(1-\alpha)) \left( \frac{(1-\alpha)h^2 t^{\alpha}}{\Gamma(\alpha+1)} + \frac{\alpha h^2 t^{2\alpha}}{\Gamma(2\alpha+1)} \right) - \frac{1}{B(\alpha)} \left( (1-\alpha)(X^0 m_3 + a_1 m_1) - G^0(m_5 \beta - m_6(1-\beta)) - m_5 a_2 \beta \right) + p_1 m_3 (1-\alpha) \left( \frac{(1-\beta)h^2 t^{\beta}}{\Gamma(\beta+1)} + \frac{\alpha h^2 t^{2\beta}}{\Gamma(2\beta+1)} \right) \]
\[+ \frac{1}{B(\alpha)} \left( a m_2 X^0 + p_1 \right) \left( \frac{(1-\alpha)h^2 t^{2\alpha}}{\Gamma(2\alpha+1)} + \frac{\alpha h^2 t^{3\alpha}}{\Gamma(3\alpha+1)} \right) + \frac{1}{B(\alpha)} \left( a_1 m_3 (1-\alpha) - G^0 m_6 \beta \right) \left( \frac{(1-\alpha)h^2 t^{2\beta}}{\Gamma(2\beta+1)} + \frac{\alpha h^2 t^{3\beta}}{\Gamma(3\beta+1)} \right) \]
\[- \frac{1}{B(\alpha)} \left( a \left( \frac{X^0 m_3}{\Gamma(\alpha+\beta+1)} + \frac{a_1 m_1}{\Gamma(\alpha+1)} \right) + (1-\alpha) \left( \frac{X^0 m_4}{\Gamma(\alpha+\beta+1)} \right) \right) + \frac{a_1 m_2}{\Gamma(\alpha+1)} + \frac{p_1}{\gamma(\alpha+\beta+1)} \left( m_3 \alpha + m_4(1-\alpha) \right) + \frac{a_2 m_6 (1-\beta)}{\Gamma(\beta+1)} \left( (1-\alpha) h^2 t^{\alpha+\beta} \right) \]
\[+ \frac{a \Gamma(\alpha+\beta+1)}{\Gamma(2\alpha+\beta+1)} h^2 t^{2\alpha+\beta} + \frac{\alpha \Gamma(2\alpha+\beta+1)}{\Gamma(3\alpha+\beta+1)} h^2 t^{3\alpha+\beta} \]
\[+ \frac{1}{B(\alpha) \Gamma(\alpha+\beta+1)} \left( a_1 m_3 \alpha + a_1 m_4(1-\alpha) - \frac{a_2 m_6 \beta \Gamma(\alpha+\beta+1)}{\Gamma(2\beta+1)} \right) \times \left( (1-\alpha) h^2 t^{\alpha+2\beta} + \frac{a \Gamma(\alpha+2\beta+1)}{\Gamma(2\alpha+2\beta+1)} h^2 t^{2\alpha+2\beta+1} \right) \]
\[+ \frac{a_1 m_4 \alpha}{B(\alpha)} \left( \frac{(1-\alpha) h^2 t^{2\alpha+\beta}}{\Gamma(2\alpha+\beta+1)} + \frac{\alpha h^2 t^{3\alpha+\beta}}{\Gamma(3\alpha+\beta+1)} \right) - \frac{G^0 m_7 \beta}{B(\alpha)} \left( \frac{(1-\alpha) h^2 t^{\beta+1}}{\Gamma(\beta+2)} \right) \]
\[+ \frac{\alpha h^2 t^{\alpha+\beta+1}}{\Gamma(\alpha+\beta+2)} - \frac{G^0 m_6 (1-\beta)}{B(\alpha)} \left( \frac{(1-\alpha) h^2 t^{\gamma+1}}{\Gamma(\gamma+2)} + \frac{\alpha h^2 t^{\alpha+\gamma+1}}{\Gamma(\alpha+\gamma+2)} \right) \]
\[- \frac{G^0 m_8 \beta}{B(\alpha)} \left( \frac{(1-\alpha) h^2 t^{\beta+\gamma+1}}{\Gamma(\beta+\gamma+2)} + \frac{\alpha h^2 t^{\alpha+\beta+\gamma+1}}{\Gamma(\alpha+\beta+\gamma+2)} \right) \]
\[- \frac{G^0 m_9 (1 - \beta)}{B(\alpha)} \left( \frac{(1 - \alpha) h^2 t^\gamma}{\Gamma(\gamma + 1)} + \frac{\alpha h^2 t^{\alpha + \gamma}}{\Gamma(\alpha + \gamma + 1)} \right)\]

\[- a_2 m_7 (1 - \beta) \frac{\Gamma(1 - \alpha) h^2 t^{\alpha + 1}}{\Gamma(2 \alpha + 2)} + \frac{\alpha \Gamma(\alpha + 2) h^2 t^{2\alpha + 1}}{\Gamma(2 \alpha + 2)}\]

\[- a_2 m_7(1 - \beta) \frac{\Gamma(1 - \alpha) h^2 t^{\alpha + \beta + 1}}{\Gamma(2 \alpha + 2)} + \frac{\alpha \Gamma(\alpha + 2) h^2 t^{2\alpha + \beta + 1}}{\Gamma(2 \alpha + 2)}\]

\[- a_2 m_8 (1 - \beta) \frac{\Gamma(1 - \alpha) h^2 t^{\alpha + 1}}{\Gamma(2 \alpha + 2)} + \frac{\alpha \Gamma(\alpha + 2) h^2 t^{2\alpha + 1}}{\Gamma(2 \alpha + 2)}\]

\[- a_2 m_8 (1 - \beta) \frac{\Gamma(1 - \alpha) h^2 t^{\alpha + \beta + 1}}{\Gamma(2 \alpha + 2)} + \frac{\alpha \Gamma(\alpha + 2) h^2 t^{2\alpha + \beta + 1}}{\Gamma(2 \alpha + 2)}\]

\[X_2(t) = m_2 \left( (1 - \beta) h(1 + h) + \frac{\beta h(1 + h) t^\beta}{\Gamma(\beta + 1)} \right)\]

\[- m_6 \left( (1 - \beta) h(1 + h) t^\beta + \frac{\beta h(1 + h) t^{2\beta}}{\Gamma(2 \beta + 1)} \right)\]

\[- m_7 \left( (1 - \beta) h(1 + h) t^{\beta + 1} + \frac{\beta h(1 + h) t^{\beta + 2}}{\Gamma(2 \beta + 1)} \right)\]

\[- m_8 \left( (1 - \beta) h(1 + h) t^{\beta + 1} + \frac{\beta h(1 + h) t^{\beta + 2}}{\Gamma(2 \beta + 1)} \right)\]

\[- m_9 \left( (1 - \beta) h(1 + h) t^\gamma + \frac{\beta h(1 + h) t^{\beta + \gamma}}{\Gamma(2 \beta + 1)} \right)\]

\[\frac{1}{B(\beta)} \left( p_2 m_5 (1 - \beta) - p_3 m_{10} (1 - \gamma) \right) \left( (1 - \beta) h^2 + \frac{\beta h^2 t^\beta}{\Gamma(\beta + 1)} \right)\]

\[\frac{1}{B(\beta)} \left( p_2 m_7 (1 - \beta) + p_3 m_{11} (1 - \gamma) \right) \left( (1 - \beta) h^2 t^\beta + \frac{\beta h^2 t^{\beta + 1}}{\Gamma(\beta + 1)} \right)\]

\[\frac{1}{B(\beta)} \left( p_2 (m_7 \beta - m_6 (1 - \beta)) \right) \left( (1 - \beta) h^2 t^\beta + \frac{\beta h^2 t^{2\beta}}{\Gamma(\beta + 1)} \right)\]

\[- \frac{1}{B(\beta)} \left( p_2 m_9 (1 - \beta) + p_3 m_{10} \gamma + p_3 m_{12} (1 - \gamma) \right) \left( (1 - \beta) h^2 t^\gamma + \frac{\beta h^2 t^{\gamma + \beta}}{\Gamma(\gamma + 1) \Gamma(\beta + 1)} \right)\]

\[- \frac{1}{B(\beta)} \left( p_2 m_8 (1 - \beta) + p_3 m_{11} \gamma + p_3 m_{11} (1 - \gamma) \right) \left( (1 - \beta) h^2 t^{\gamma + 1} + \frac{\beta h^2 t^{\gamma + \beta + 1}}{\Gamma(\gamma + 1) \Gamma(\beta + 1)} \right)\]
\[- \frac{p_2 m_8 \beta}{B(\beta)} \left( \frac{(1 - \beta) \hbar^2 t^{\beta + \gamma + 1}}{\Gamma(2 \beta + \gamma + 1)} + \frac{\beta \hbar^2 t^{2 \beta + 1}}{\Gamma(2 \beta + 2)} \right) - \frac{p_2 m_9 \beta}{B(\beta)} \left( \frac{(1 - \beta) \hbar^2 t^{\beta + \gamma}}{\Gamma(\beta + \gamma + 1)} + \frac{\beta \hbar^2 t^{2 \beta + \gamma}}{\Gamma(2 \beta + \gamma + 1)} \right) - \frac{p_2 m_{10} \gamma}{B(\beta)} \left( \frac{(1 - \beta) \hbar^2 t^{\beta + \gamma}}{\Gamma(2 \beta + 1)} + \frac{\beta \hbar^2 t^{2 \beta + \gamma}}{\Gamma(\beta + \gamma + 1)} \right) - \frac{p_2 m_{11} \gamma}{B(\beta)} \left( \frac{(1 - \beta) \hbar^2 t^{2 \gamma + 1}}{\Gamma(2 \gamma + 2)} + \frac{\beta \hbar^2 t^{2 \beta + 2 \gamma}}{\Gamma(\beta + 2 \gamma + 2)} \right) \]

\[I_2(t) = m_{10} \left( (1 - \gamma) \hbar (1 + \hbar) + \frac{\gamma \hbar (1 + \hbar) t^{\gamma}}{\Gamma(\gamma + 1)} \right) \]

\[+ m_{11} \left( (1 - \gamma) \hbar (1 + \hbar) t + \frac{\gamma \hbar (1 + \hbar) t^{\gamma + 1}}{\Gamma(\gamma + 2)} \right) \]

\[+ m_{12} \left( (1 - \gamma) \hbar (1 + \hbar) t^{\gamma} + \frac{\gamma \hbar (1 + \hbar) t^{2 \gamma}}{\Gamma(2 \gamma + 1)} \right) \]

\[+ m_{13} \left( (1 - \gamma) \hbar (1 + \hbar) t^{\gamma + 1} + \frac{\gamma \hbar (1 + \hbar) t^{2 \gamma + 1}}{\Gamma(2 \gamma + 2)} \right) \]

\[+ \frac{1}{B(\gamma)} p_4 \ m_{10} (1 - \gamma) \left( (1 - \gamma) \hbar^2 + \frac{\gamma \hbar^2 t^\gamma}{\Gamma(\gamma + 1)} \right) \]

\[+ \frac{1}{B(\gamma)} p_4 \ m_{11} (1 - \gamma) \left( (1 - \gamma) \hbar^2 t + \frac{\gamma \hbar^2 t^{\gamma + 1}}{\Gamma(\gamma + 2)} \right) \]

\[+ \frac{1}{B(\gamma)} \left( p_4 \ m_{10} \gamma + p_4 \ m_{12} (1 - \gamma) \right) \left( \frac{(1 - \gamma) \hbar^2 t^{\gamma}}{\Gamma(\gamma + 1)} + \frac{\gamma \hbar^2 t^{2 \gamma}}{\Gamma(2 \gamma + 1)} \right) \]

\[+ \frac{1}{B(\gamma)} \left( p_4 \ m_{11} \gamma + p_4 \ m_{13} (1 - \gamma) \right) \left( \frac{(1 - \gamma) \hbar^2 t^{\gamma + 1}}{\Gamma(\gamma + 2)} + \frac{\gamma \hbar^2 t^{2 \gamma + 1}}{\Gamma(2 \gamma + 2)} \right) \]

\[+ \frac{1}{B(\gamma)} p_4 \ m_{12} \gamma \left( \frac{(1 - \gamma) \hbar^2 t^{2 \gamma}}{\Gamma(2 \gamma + 1)} + \frac{\gamma \hbar^2 t^{3 \gamma}}{\Gamma(3 \gamma + 1)} \right) \]

\[+ \frac{1}{B(\gamma)} p_4 \ m_{13} \gamma \left( \frac{(1 - \gamma) \hbar^2 t^{3 \gamma + 1}}{\Gamma(2 \gamma + 2)} + \frac{\gamma \hbar^2 t^{3 \gamma + 1}}{\Gamma(3 \gamma + 2)} \right) \]

where \( m_j, \ j = 1, 2 \ldots, 7 \), are given by

\[m_1 = \frac{1}{B(\alpha)} \left( p_1 G^0 + X^0 G^0 \right), \quad m_7 = \frac{p_3 \eta (1 - \gamma)}{B(\beta) B(\gamma)}, \quad m_{13} = \frac{p_4 \eta \gamma}{B(\gamma)^2}. \]
Consider Example. Numerical Simulations.

\[ \gamma \]

\[ \eta \]

\[ \frac{\alpha G^\gamma \Gamma(\beta + 1)}{B(\alpha)} \]

\[ \frac{\alpha_2 G^\gamma \Gamma(\alpha + \beta + 1)}{B(\alpha)} \]

\[ \frac{1}{B(\alpha)} \left( p_2 X^0 - p_3 I_0 - \frac{p_4 I_b(1 - \gamma)}{B(\gamma)} \right) \]

\[ \frac{p_2 p_3 \beta I_b}{B(\beta)^2} \]

Finally the solutions of Eqs. (11)-(13) are given by

\[ G(t) = G_0(t) + G_1(t) + G_2(t) + \cdots = \sum_{m=0}^{\infty} G_m(t), \]

\[ X(t) = X_0(t) + X_1(t) + X_2(t) + \cdots = \sum_{m=0}^{\infty} X_m(t), \]

\[ I(t) = I_0(t) + I_1(t) + I_2(t) + \cdots = \sum_{m=0}^{\infty} I_m(t). \]

Numerical Simulations.

**Example.** Consider \( G_b = 90 \text{ mg/dL}, I_b = 7.1 \text{ mU/L}, p_1 = 0.02079 \text{ 1/min}, p_2 = 0.01875 \text{ 1/min}, p_3 = 0.00001013 \text{ L/min}^2\text{mU}, p_4 = 0.4 \text{ 1/min}, p_5 = 88.7 \text{ mg/dL} \) and \( p_6 = 0.003271 \text{ mU\cdot dL/L-mg-min}, \) with initial conditions \( G(0) = 281 \text{ mg/dL}, X(0) = 0 \text{ mg/DL}, I(0) = 401.2 \text{ mg/DL}, \) and different particular cases of \( \alpha, \beta \) and \( \gamma, \) arbitrarily chosen. The numerical results given in Figs. 2a-2c show numerical simulations for the blood glucose concentration \( G(t), \) the effect of active insulin \( X(t) \) and the blood insulin concentration \( I(t). \)

**Fractional conformable derivative in Liouville-Caputo sense.**

\[ C^\beta D_t^{\alpha_1} G(t) = -\left( p_1 + X(t) \right) G(t) + p_1 G_b, \quad 0 < \alpha_1 < 1, \]

\[ C^\beta D_t^{\alpha_2} X(t) = -p_2 X(t) + p_3 \left( I(t) - I_b \right), \quad 0 < \alpha_2 < 1, \]

\[ C^\beta D_t^{\alpha_3} I(t) = \eta t - p_4 \left( I(t) - I_b \right), \quad 0 < \alpha_3 < 1, \]

with initial conditions

\[ G(0) = G_0, \quad X(0) = X_0, \quad I(0) = I_0, \]

where \( \eta = p_6 \left[ G(t) - p_5 \right]^+ = \max\{ [G(t) - p_5], 0 \}. \)

System (28)-(30) can be made more realistic considering three different orders for the fractional differential operators \( \alpha_1 \in (0, 1], \alpha_2 \in (0, 1] \) and \( \alpha_3 \in (0, 1] \) for the blood glucose concentration \( G(t), \) for the effect of active insulin \( X(t) \) and for the blood insulin concentration \( I(t), \) respectively.
Solution. Applying Laplace transform to Eq. (28), we get
\[
\frac{\alpha_1 \Gamma(1 - \alpha_1 \beta)}{\Gamma(1 - \alpha_1)} \left( s^{\alpha_1 \beta} \hat{G}(s) - s^{\alpha_1 \beta - 1} G(0) \right) = \frac{p_1 G_b}{s} - \mathcal{L} \left\{ p_1 G(t) + X(t)G(t) \right\}.
\]
Taking initial conditions (31) and simplifying, we get
\[
\hat{G}(s) = \frac{G_0}{s} + \frac{p_1 G_b}{a_1 s^{\alpha_1 \beta + 1}} - \frac{1}{a_1 s^{\alpha_1 \beta}} \mathcal{L} \left\{ p_1 G(t) + X(t)G(t) \right\}.
\]
Applying the inverse Laplace transform to Eq. (32), we obtain
\[
G(t) = G_0 + \frac{p_1 G_b t^{\alpha_1 \beta}}{a_1 \Gamma(\alpha_1 \beta + 1)} - \mathcal{L}^{-1} \left\{ \frac{1}{a_1 s^{\alpha_1 \beta}} \mathcal{L} \left\{ p_1 G(t) + X(t)G(t) \right\} \right\}.
\]
In a similar way, for the Eqs. (29)-(30), we have
\[
X(t) = X_0 - \frac{p_2 I_b t^{\alpha_2 \beta}}{a_2 \Gamma(\alpha_2 \beta + 1)} - \mathcal{L}^{-1} \left\{ \frac{1}{a_2 s^{\alpha_2 \beta}} \mathcal{L} \left\{ p_2 X(t) - p_3 I(t) \right\} \right\},
\]
where

\[ a_i = \frac{\alpha_i^\beta (1 - \alpha_i^\beta)}{\Gamma(1 - \alpha_i)} , \quad i = 1, 2, 3. \] (34)

We choose the linear operator as

\[ \mathcal{F}[\phi_j(t; q)] = \mathcal{L}[\phi_j(t; q)] , \quad j = 1, 2. \]

With property \( \mathcal{F}(c) = 0 \), where \( c \) is a constant. Next, defining the system of nonlinear operators as

\[
N[\phi_1(t; q)] = \mathcal{L}[\phi_1(t; q)] - \left( G_0 + \frac{p_1 G_y t^\alpha_{1,\beta}}{a_1 \Gamma(\alpha_{1,\beta} + 1)} \right) - \frac{1}{a_1} \frac{\eta t^{\alpha_{3,\beta} + 1}}{\Gamma(\alpha_{3,\beta} + 1)} \mathcal{L}\{p_1 \phi_1 + \Phi_2 \phi_1\},
\]

\[ N[\Phi_2(t; q)] = \mathcal{L}[\Phi_2(t; q)] - \left( X_0 - \frac{p_3 I_y t^\alpha_{2,\beta}}{a_2 \Gamma(\alpha_{2,\beta} + 1)} \right) - \frac{1}{a_2} \frac{\eta t^{\alpha_{3,\beta} + 1}}{\Gamma(\alpha_{3,\beta} + 1)} \mathcal{L}\{p_2 \Phi_2 - p_3 \Phi_3\}, \]

\[ N[\Phi_3(t; q)] = \mathcal{L}[\Phi_3(t; q)] - \left( I_0 + \frac{p_4 I_y t^\alpha_{3,\beta}}{a_3 \Gamma(\alpha_{3,\beta} + 1)} + \frac{\eta t^{\alpha_{3,\beta} + 1}}{\Gamma(\alpha_{3,\beta} + 2)} \right) \]

\[- \frac{1}{a_3} \frac{\eta t^{\alpha_{3,\beta} + 1}}{\Gamma(\alpha_{3,\beta} + 1)} \mathcal{L}\{p_4 \Phi_3\}.
\]

Now, we construct the so-called zeroth-order deformation equation of the following manner

\[(1 - q) \mathcal{F}[\phi_j(t; q) - u_0(t)] = q \ h \ N[\phi_j(t; q)] , \quad j = 1, 2.\]

when \( q = 0 \) and \( q = 1 \), we have

\[ \phi_j(t; 0) = u_0(t), \quad \phi_j(t; 1) = u(t), \quad j = 1, 2. \] (38)

Thus, we obtain the mth-order deformation equations as

\[
\mathcal{L}[G_m(t) - \chi_m G_{m-1}(t)] = h \ R_m(G_{m-1}^\gamma, t) ,
\]

\[
\mathcal{L}[X_m(t) - \chi_m X_{m-1}(t)] = h \ R_m(X_{m-1}^\gamma, t) ,
\]

\[
\mathcal{L}[I_m(t) - \chi_m I_{m-1}(t)] = h \ R_m(I_{m-1}^\gamma, t) ,
\] (39)

applying the inverse Laplace transform to Eq. (39), we get

\[ G_m(t) = \chi_m G_{m-1}(t) + h \ R_m(G_{m-1}^\gamma, t) ,
\]

\[ X_m(t) = \chi_m X_{m-1}(t) + h \ R_m(X_{m-1}^\gamma, t) ,
\]

\[ I_m(t) = \chi_m I_{m-1}(t) + h \ R_m(I_{m-1}^\gamma, t) ,
\] (40)

where

\[
R_m(G_{m-1}^\gamma, t) = \mathcal{L}[G_{m-1}(t)] - (1 - \chi_m) \left( G_0 + \frac{p_1 G_y t^\alpha_{1,\beta}}{a_1 \Gamma(\alpha_{1,\beta} + 1)} \right) \]

\[- \frac{1}{a_1} \frac{\eta t^{\alpha_{1,\beta} + 1}}{\Gamma(\alpha_{1,\beta} + 1)} \mathcal{L}\{p_1 G_{m-1} + H_m\} ,
\]
\[ R_m(X_{m-1}, t) = \mathcal{L}[X_{m-1}(t)] - (1 - \chi_m)X_0 - \frac{p_3I_3t^{\alpha_3\beta}}{a_2\Gamma(\alpha_2\beta + 1)} \]
\[ - \frac{1}{a_2s^{\alpha_2\beta}} \mathcal{L}[p_2 X_{m-1} - p_3 I_{m-1}], \]
\[ R_m(I_{m-1}, t) = \mathcal{L}[I_{m-1}(t)] - (1 - \chi_m)\left(I_0 + \frac{p_4I_bt^{\alpha_3\beta}}{a_3\Gamma(\alpha_3\beta + 1)} + \frac{\eta t^{\alpha_3\beta + 1}}{a_3\Gamma(\alpha_3\beta + 2)}\right) \]
\[ - \frac{1}{a_3s^{\alpha_3\beta}} \mathcal{L}[p_4 I_{m-1}]. \]

Now, the solution of \( m \)-th order deformation equations (39) are given as

\[ G_m(t) = (\chi_m + h)G_{m-1} - h(1 - \chi_m) \left(G_0 + \frac{p_1G_b t^{\alpha_1\beta}}{a_1\Gamma(\alpha_1\beta + 1)}\right) - \]
\[ - h \mathcal{L}^{-1}\left\{ \frac{1}{a_1s^{\alpha_1\beta}} \mathcal{L}[P_1 G_{m-1} + H_m]\right\}, \]
\[ X_m(t) = (\chi_m + h)X_{m-1} - h(1 - \chi_m) \left(X_0 - \frac{p_3I_3t^{\alpha_2\beta}}{a_2\Gamma(\alpha_2\beta + 1)}\right) - \]
\[ - h \mathcal{L}^{-1}\left\{ \frac{1}{a_2s^{\alpha_2\beta}} \mathcal{L}[p_2 X_{m-1} - p_3 I_{m-1}]\right\}, \]
\[ I_m(t) = (\chi_m + h)I_{m-1} - h(1 - \chi_m) \left(I_0 + \frac{p_4I_b t^{\alpha_3\beta}}{a_3\Gamma(\alpha_3\beta + 1)} + \frac{\eta t^{\alpha_3\beta + 1}}{a_3\Gamma(\alpha_3\beta + 2)}\right) - \]
\[ - h \mathcal{L}^{-1}\left\{ \frac{1}{a_3s^{\alpha_3\beta}} \mathcal{L}[p_4 I_{m-1}]\right\}, \]

(41)

where

\[ H_m = \frac{1}{\Gamma(m + 1)} \left[ \frac{d^m}{dq^m}N [(q \Phi_2(t; q)) (q \phi_1(t; q))] \right]_{q=0}^m. \]

Taking initial conditions and the iterative scheme (42), we obtain the following iterations

\[ p^0 : G_0(t) = G_0 + \eta_1 t^{\alpha_1\beta}, \quad \eta_1 = \frac{p_1G_b}{a_1\Gamma(\alpha_1\beta + 1)}; \]
\[ X_0(t) = X_0 - \eta_2 t^{\alpha_2\beta}, \quad \eta_2 = \frac{p_3I_b}{a_2\Gamma(\alpha_2\beta + 1)}; \]
\[ I_0(t) = I_0 + \frac{p_4I_b t^{\alpha_3\beta}}{a_3\Gamma(\alpha_3\beta + 1)} + \frac{\eta_3 t^{\alpha_3\beta + 1}}{a_3\Gamma(\alpha_3\beta + 2)}, \]
\[ p^1 : G_1(t) = \frac{1}{a_1} \left[ G_0(p_1 + X_0) \frac{t^{\alpha_1\beta}}{\Gamma(\alpha_1\beta + 1)} + \eta_1 (p_1 + X_0) \frac{\Gamma(\alpha_1\beta + 1) t^{2\alpha_1\beta}}{\Gamma(2\alpha_1\beta + 1)} \right] \]
\[ - G_0 \eta_2 \frac{\Gamma(\alpha_2\beta + 1) t^{\beta(\alpha_1 + \alpha_2)}}{\Gamma(\beta(\alpha_1 + \alpha_2) + 1)} - \eta_1 \eta_2 \frac{\Gamma(\beta(\alpha_1 + \alpha_2) + 1) t^{\beta(2\alpha_1 + \alpha_2)}}{\Gamma(\beta(2\alpha_1 + \alpha_2) + 1)} \right] \h \]
\[ X_1(t) = \frac{1}{a_2} \left[ (p_2X_0 - p_3G_0) \frac{t^{\alpha_2\beta}}{\Gamma(\alpha_2\beta + 1)} \right] \]
\[-(p_2 \eta_2 + p_3 \eta_1) \frac{\Gamma(\beta(\alpha_1 + \alpha_2))t^{\beta(\alpha_1 + 2\alpha_2)}}{\Gamma(\beta(\alpha_1 + 2\alpha_2) + 1)} \eta,\]

\[I_1(t) = \frac{1}{a_3} \left[p_4 I_0 \frac{t^{\alpha_3 \beta}}{\Gamma(\alpha_3 \beta + 1)} + \frac{p_2^2 I_0 t^{2\alpha_3 \beta}}{a_3 \Gamma(2\alpha_3 \beta + 1)} + \frac{p_4 \eta t^{2\alpha_3 \beta + 1}}{a_3 \Gamma(2\alpha_3 \beta + 2)} \right] \eta,\]

Finally the solutions of Eqs. (28)-(30) are given by

\[G(t) = G_0(t) + G_1(t) + G_2(t) + \cdots = \sum_{m=0}^{\infty} G_m(t),\]

\[X(t) = X_0(t) + X_1(t) + X_2(t) + \cdots = \sum_{m=0}^{\infty} X_m(t),\]

\[I(t) = I_0(t) + I_1(t) + I_2(t) + \cdots = \sum_{m=0}^{\infty} I_m(t).\] (43)

Numerical Simulations.

**Example.** Consider \(G_b = 90\) mg/dL, \(I_b = 7.1\) mU/L, \(p_1 = 0.02079\) 1/min, \(p_2 = 0.01875\) 1/min, \(p_3 = 0.0001013\) L/min^2·mU, \(p_4 = 0.4\) 1/min, \(p_5 = 88.7\) mg/dL and \(p_6 = 0.003271\) mU·dL/L-mg·min, with initial conditions \(G(0) = 281\) mg/dL, \(X(0) = 0\) mg/dL, \(I(0) = 401.2\) mg/dL, and different particular cases of \(\alpha_1 - \beta,\) \(\alpha_2 - \beta\) and \(\alpha_3 - \beta,\) arbitrarily chosen. The numerical results given in Figs. 2a-2c show numerical simulations for the blood glucose concentration \(G(t),\) the effect of active insulin \(X(t)\) and the blood insulin concentration \(I(t)\).

**5. Conclusions.** In this paper we investigated the time fractional Bergman’s minimal blood glucose-insulin model involving operators of type Atangana-Baleanu-Caputo fractional derivative and fractional conformable derivative in Liouville-Caputo sense. For both derivatives, analytical approximate solutions were obtained with the MHATM for the Bergman’s minimal blood glucose-insulin model. The basic characters of this technique were presented in detail. To present the effect of fractional order some numerical simulations are performed. These novel behaviors are showed for the first time in this work.

**Acknowledgments.** José Francisco Gómez Aguilar acknowledges the support provided by CONACyT: Cátedras CONACyT para jóvenes investigadores 2014. José Francisco Gómez Aguilar and Marco Antonio Taneco Hernández acknowledges the support provided by SNI-CONACyT.

**REFERENCES**

[1] B. S. Alkahtani, O. J. Algahtani, R.S. Dubey and P. Goswami, The solution of modified fractional bergman’s minimal blood glucose-insulin model, *Entropy*, 19 (2017), 114.

[2] A. Atangana, *Derivative with a New Parameter: Theory, Methods and Applications*, Academic Press, New York, 2016.

[3] A. Atangana, *Fractional Operators with Constant and Variable Order with Application to Geo-Hydrology*, Academic Press, London, 2018.

[4] A. Atangana and K. M. Owolabi, New numerical approach for fractional differential equations, *Mathematical Modelling of Natural Phenomena*, 13 (2018), 1–21.
Figure 2. Numerical simulations for the blood glucose concentration $G(t)$, the effect of active insulin $X(t)$ and the blood insulin concentration $I(t)$ for several values of $\alpha_1 - \beta$, $\alpha_2 - \beta$ and $\alpha_3 - \beta$.

[5] A. Atangana, Blind in a commutative world: Simple illustrations with functions and chaotic attractors, Chaos, Solitons & Fractals, 114 (2018), 347–363.

[6] A. Atangana, Non validity of index law in fractional calculus: A fractional differential operator with Markovian and non-Markovian properties, Physica A: Statistical Mechanics and its Applications, 505 (2018), 688–706.

[7] A. Atangana, J. F. Gómez Aguilar, Decolonisation of fractional calculus rules: Breaking commutativity and associativity to capture more natural phenomena, The European Physical Journal Plus, 133 (2018), 1–23.

[8] A. Atangana and E. F. D. Goufo, On the mathematical analysis of Ebola hemorrhagic fever: Deothery infection disease in West African countries, BioMed Research International, 2014 (2014), Article ID 261383, 7 pages.

[9] A. Atangana and B. S. T. Alkahtani, Modeling the spread of Rubella disease using the concept of with local derivative with fractional parameter, Complexity, 21 (2016), 442–451.

[10] A. Atangana and D. Baleanu, New fractional derivatives with nonlocal and non-singular kernel: Theory and application to heat transfer model, Therm Sci., 20 (2016), 763–769.

[11] R. N. Bergman, Y. Z. Ider, C. R. Bowden and C. Cobelli, Quantitative estimation of insulin sensitivity, American Journal of Physiology-Endocrinology And Metabolism, 236 (1979), 667–677.

[12] A. Caumo, C. Cobelli and M. Omenetto, Overestimation of minimal model glucose effectiveness in presence of insulin response is due to under modeling, American Journal of Physiology, 278 (1999), 481–488.
A. De Gaetano and O. Arino, Mathematical modelling of the intravenous glucose tolerance test, *Journal of Mathematical Biology*, 40 (2000), 136–168.

L. C. Gatewood, E. Ackerman, J. W. Rosevear, G. D. Molnar and T. W. Burns, Tests of a mathematical model of the blood-glucose regulatory system, *Computational Biomedical Research*, 2 (1968), 1–14.

A. Fabre and J. Hristov, On the integral-balance approach to the transient heat conduction with linearly temperature-dependent thermal diffusivity, *Heat and Mass Transfer*, 53 (2017), 177–204.

J. Hristov, Steady-state heat conduction in a medium with spatial non-singular fading memory: derivation of Caputo-Fabrizio space-fractional derivative with Jeffrey’s kernel and analytical solutions, *Thermal Science*, 1 (2016), 115–115.

R. Jain, K. Arekar and R. Shanker Dubey, Study of Bergman’s minimal blood glucose-insulin model by Adomian decomposition method, *Journal of Information and Optimization Sciences*, 38 (2017), 133–149.

F. Jarad, E. Ugurlu, T. Abdeljawad and D. Baleanu, On a new class of fractional operators, *Advances in Difference Equations*, 2017 (2017), Paper No. 247, 16 pp.

R. Khalil, M. Al Horani, A. Yousef and M. Sababheh, A new definition of fractional derivative, *Journal of Computational and Applied Mathematics*, 264 (2014), 65–70.

S. Kumar, A. Kumar and I. K. Argyros, A new analysis for the Keller-Segel model of fractional order, *Numerical Algorithms*, 75 (2017), 213–228.

S. Kumar, A new analytical modelling for telegraph equation via Laplace transform, *Appl. Math. Modell.*, 38 (2014), 3154–3163.

S. Kumar and M. M. Rashidi, New analytical method for gas dynamic equation arising in shock fronts, *Comput. Phy. Commun.*, 185 (2014), 1947–1954.

G. A. Losa, On the fractal design in human brain and nervous tissue, *Applied Mathematics*, 5 (2014), 1725–1732.

V. F. Morales-Delgado, J. F. Gómez-Aguilar, S. Kumar and M. A. Taneco-Hernández, Analytical solutions of the Keller-Segel chemotaxis model involving fractional operators without singular kernel, *The European Physical Journal Plus*, 133 (2018), 200.

Z. Odibat and A. S. Bataineh, An adaptation of homotopy analysis method for reliable treatment of strongly nonlinear problems: Construction of homotopy polynomials, *Math. Meth. Appl. Sci.*, 38 (2015), 991–1000.

K. M. Owolabi, Robust and adaptive techniques for numerical simulation of nonlinear partial differential equations of fractional order, *Communications in Nonlinear Science and Numerical Simulation*, 44 (2017), 304–317.

K. M. Owolabi and A. Atangana, Numerical solution of fractional-in-space nonlinear Schrödinger equation with the Riesz fractional derivative, *The European physical Journal Plus*, 131 (2016), 335.

I. Podlubny, *Fractional Differential Equations: An Introduction to Fractional Derivatives, Fractional Differential Equations, to Methods of Their Solution and some of Their Applications*, Academic Press, San Diego, California, USA, 1999.

Received June 2018; revised August 2018.

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