AIMS Mathematics, 11(5): 13233–13256.
DOI: 10.3934/math.2026546
Received: 04 February 2026
Revised: 06 April 2026
Accepted: 20 April 2026
Published: 12 May 2026

https://www.aimspress.com/journal/Math

*Research article*

# Time-fractional optimal control in the Bergman model for type 1 diabetes

**Essamy Amina[1], Karim Marouane[2], Ferjouchia Hanane[1], M. Z. Youssef[3,*] and Mahmoud A. Zaky[3,*]**

[1] LAMS, Department of Mathematics and Computer Science, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco

[2] Multidisciplinary Research and Innovation Laboratory (LPRI), Moroccan School of Engineering Sciences (EMSI), Casablanca 20250, Morocco

[3] Department of Mathematics and Statistics, College of Science, Imam Mohammad Ibn Saud Islamic University (IMSIU), Riyadh 11566, Saudi Arabia

* **Correspondence:** Email: MZAbouelyamin@imamu.edu.sa, mibrahimm@imamu.edu.sa.

**Abstract:** This study investigates a time-fractional optimal control problem for the Bergman minimal model of type 1 diabetes by employing the Caputo derivative of order $q \in (0, 1)$ to incorporate memory effects into the glucose–insulin dynamics. First, the well-posedness of the fractional-order model is established by proving the existence, uniqueness, boundedness, and positivity of its solutions. Subsequently, an optimal control problem describing a normalized therapeutic intervention is formulated, and the existence of an optimal control is rigorously proved. By applying the fractional Pontryagin maximum principle, the corresponding optimality system is derived, and the optimal control law is explicitly characterized. The obtained results demonstrate that the proposed control strategy effectively stabilizes the glucose dynamics around the desired equilibrium while reducing excessive insulin administration. In comparison with the classical integer-order model, the fractional formulation provides a more realistic representation of delayed physiological responses. Finally, numerical simulations, carried out using a predictor–corrector scheme together with a forward–backward sweep algorithm, confirm the effectiveness and reliability of the proposed approach for blood glucose regulation.

**Keywords:** time fractional derivative; Bergman's minimal model; optimal control; type 1 diabetes
**Mathematics Subject Classification:** 49J15, 93B05, 92B05, 34A08

## 1. Introduction

Type 1 diabetes (T1D) is a chronic autoimmune disorder in which the immune system mistakenly attacks and destroys the insulin-producing beta cells of the pancreas. This destruction results in an absolute deficiency of insulin, thereby impairing the body's ability to regulate blood glucose levels. In the absence of sufficient insulin, glucose uptake by cells is severely reduced, leading to persistent hyperglycemia. The global burden of T1D continues to rise; in 2025, an estimated 9.5 million people were living with T1D, representing a 13% increase since 2021 [27]. This increase reflects a broader long-term trend in diabetes prevalence. The World Health Organization reported that the number of people living with diabetes increased from 108 million in 1980 to 830 million in 2022, while earlier projections identified diabetes as a major cause of global mortality by 2030 [25]. The management of T1D requires lifelong exogenous insulin therapy. In this context, mathematical modeling has become an essential tool for analyzing the complex dynamics of glucose–insulin regulation [24]. By representing physiological processes through systems of equations, such models allow researchers to simulate disease progression and evaluate insulin delivery strategies *in silico* before clinical implementation [15]. For instance, the minimal model of glucose–insulin dynamics [7] and more recent frameworks, such as GLUKINSLOOP [23], have played an important role in quantifying insulin sensitivity and improving insulin pump therapy. Beyond their descriptive value, these models support the design of closed-loop insulin delivery systems, commonly referred to as artificial pancreas systems, and enable the personalization of treatment strategies by accounting for inter-patient variability [13,31].

Fractional calculus extends classical calculus by introducing derivatives and integrals of non-integer order. It has become a powerful mathematical framework with broad applications in science and engineering [33]. Owing to its ability to capture memory and hereditary effects, fractional calculus is particularly suitable for modeling complex real-world phenomena [5, 12, 14, 20]. Foundational contributions by Caputo, Miller, Ross, Kilbas, Srivastava, and other researchers have substantially advanced the theory and applications of fractional operators [11], thereby promoting their increasing use in mathematical modeling. Building on this foundation, the present work employs fractional calculus to develop a more physiologically realistic model of glucose–insulin dynamics. Classical mathematical models of diabetes were initially formulated using systems of ordinary differential equations to describe the interaction between glucose and insulin. One of the earliest contributions was Bolie's pioneering linear model in 1961 [9], which provided a quantitative description of glucose–insulin regulation. Later, the minimal models developed by Bergman and Cobelli [7] became influential tools for studying insulin sensitivity and glucose disappearance. These models provided a basis for subsequent developments in diabetes modeling. Further refinements were introduced in later studies; for example, in 2006, a system-level model of oral glucose absorption was developed and validated using gold-standard data, yielding a more accurate description of meal absorption dynamics [22].

Fractional-order epidemic models have received considerable attention because they provide a flexible framework for describing disease-transmission dynamics. By incorporating fractional derivatives, these models can account for memory effects, meaning that the future evolution of a disease may depend on its previous states. This feature is especially relevant for diseases characterized by long incubation periods, waning immunity, or transmission processes affected by persistent behavioral and environmental factors [29, 30].

Recent studies have emphasized the usefulness of fractional calculus in describing the complex

glucose–insulin dynamics associated with type 1 diabetes. Fractional-order models offer a robust framework for representing the non-integer-order behavior of biological systems, particularly in relation to insulin delivery and glucose metabolism. By incorporating fractional derivatives, these models provide a more accurate description of the time-dependent evolution of glucose concentrations and improve the predictive capability of simulations of diabetic responses [19]. Comparative studies by Agilan et al. [1] and Vijayalakshmi et al. [32] further demonstrated the advantages of fractional-order models over classical integer-order formulations, particularly in capturing inter-patient variability and supporting more personalized treatment strategies. This growing body of research is consistent with the broader trends identified by Boutayeb et al. [10], whose systematic review of 85 mathematical models reported the increasing use of advanced mathematical techniques, including fractional calculus and optimal control, for studying diabetes dynamics and informing public-health strategies. These contributions help bridge the gap between mathematical theory and clinical application in diabetes management. They also show that fractional derivatives can extend classical modeling approaches and provide a more flexible representation of the nonlinear endocrine responses associated with insulin therapy.

Glucose–insulin regulation involves nonlinear interactions, compartmental effects, physiological delays, long-memory behavior, and pronounced interindividual variability. Mathematical analysis is therefore essential for clarifying these mechanisms and evaluating their implications for insulin-delivery and control strategies [18]. Recent studies incorporating fractional derivatives and time delays have shown that memory kernels and delayed responses may produce complex, and even chaotic, dynamics while also affecting stability properties. These findings indicate that classical integer-order models based on short-memory assumptions may be inadequate for capturing clinically relevant glucose–insulin dynamics [4, 21].

Fractional differential equations have received considerable attention because they provide a flexible framework for describing biological, physical, and engineering processes with memory and hereditary effects. Unlike classical integer-order models, fractional-order systems account for the influence of past states on present dynamics. This feature is particularly relevant to glucose–insulin regulation, where the current metabolic response depends not only on the instantaneous glucose concentration but also on previous insulin action, meal intake, and delayed physiological mechanisms. In diabetes modeling, fractional derivatives offer additional flexibility for capturing long-term dependencies and interindividual variability, and they may improve agreement with experimental and clinical observations. Consequently, fractional-order models have become increasingly important for studying glucose–insulin dynamics and developing effective strategies for diabetes management [2].

Many studies replace the classical derivative $\frac{d}{dt}$ with the Caputo fractional derivative $D^{\alpha}$, $0 < \alpha \leq 1$, in minimal or extended glucose–insulin systems. These formulations include both commensurate and incommensurate fractional orders, as well as explicit time delays, to examine stability behavior and Hopf bifurcations [3, 16]. Although fractional calculus has been applied to several physiological systems, including diabetes modeling, most existing studies focus on type 2 diabetes or simplified glucose-regulation models. Consequently, there remains a clear gap in the rigorous analysis and optimal control of fractional-order models specifically designed for type 1 diabetes. The present work addresses this gap by developing a comprehensive time-fractional optimal control framework for the Bergman model applied to T1D. This work develops a mathematical framework that combines theoretical analysis with practical control design for fractional-order type 1 diabetes modeling. More

precisely, the manuscript presents a complete study of a fractional Bergman model based on the Caputo derivative, including proofs of existence, uniqueness, boundedness, and positivity of solutions. These results establish both the mathematical well-posedness and the physiological consistency of the proposed model. In addition, we formulate an optimal control problem in which the control variable represents a therapeutic intervention acting on the glucose–insulin dynamics. The existence of an optimal control is established, and the associated first-order necessary optimality conditions are derived using a fractional version of Pontryagin's maximum principle. Another contribution of this work is the explicit characterization of the optimal control law, together with an analysis of how the fractional order influences the system dynamics. Finally, numerical simulations are conducted to compare the controlled and uncontrolled systems for different fractional orders. The results illustrate the role of memory effects and confirm the effectiveness of the proposed control strategy.

The remainder of the paper is organized as follows. Section 2 introduces the fractional Bergman model and establishes its fundamental analytical properties. Section 3 formulates the optimal control problem and proves the existence of an optimal control. Section 4 derives the associated necessary optimality conditions. Section 5 presents numerical simulations comparing the controlled and uncontrolled dynamics under different fractional orders. Finally, Section 6 concludes the paper with a discussion of the main findings and possible directions for future research.

## 2. The fractional Bergman model

This section begins by recalling the classical three-compartment Bergman minimal model in order to establish the underlying dynamical framework. We then introduce the fractional Bergman model formulated in the Caputo sense of order $q \in (0, 1)$.

### *2.1. Bergman's minimal model*

Bergman's minimal model [8] is a mathematical framework used to study glucose–insulin dynamics in the human body, particularly the roles of insulin sensitivity and glucose effectiveness in glucose regulation. The model provides insight into how efficiently the body controls blood glucose levels, which is a fundamental aspect of metabolic studies, especially in diabetes research.

Bergman's minimal model describes the glucose–insulin regulatory system through a set of coupled differential equations involving three compartments: the plasma glucose concentration $G(t)$, the plasma insulin concentration $I(t)$, and a remote insulin compartment $X(t)$, which accounts for the delayed peripheral effect of insulin on glucose utilization.

The dynamics of the system are governed by the following equations:

$$\begin{cases} \dfrac{dG(t)}{dt} = -p_1(G(t) - G_b) - X(t)\,G(t) + m(t), \\ \dfrac{dX(t)}{dt} = -p_2X(t) + p_3(I(t) - I_b), \\ \dfrac{dI(t)}{dt} = -nI(t) + u(t). \end{cases} \tag{2.1}$$

The definitions and physiological interpretations of the state variables and parameters appearing in the above system are summarized in Table 1.

**Table 1.** Description of the parameters and variables used in the Bergman model.

| Parameter | Unit | Description |
|---|---|---|
| $G(t)$ | [mg/dL] | Blood glucose concentration |
| $X(t)$ | [1/min] | Effect of active insulin |
| $I(t)$ | [mU/L] | Blood insulin concentration |
| $G_b$ | [mg/dL] | Basal blood glucose concentration |
| $I_b$ | [mU/L] | Basal blood insulin concentration |
| $p_1$ | [1/min] | Glucose clearance rate independent of insulin |
| $p_2$ | [1/min] | Clearance rate of active insulin (decrease in uptake effect) |
| $p_3$ | [L/(min$^2$ mU)] | Increase in glucose uptake induced by insulin |
| $n$ | [1/min] | Decay rate of blood insulin |
| $m(t)$ | [mg/dL/min] | Meal disturbance function |
| $u(t)$ | [mU/min] | Normalized combined therapeutic control |

### *2.2. The fractional Bergman model*

For the fractional Bergman model formulated in the Caputo sense of order $q \in (0, 1)$, consider the following system for $t > 0$:

$$\begin{cases} {}_0^C D_t^q G(t) = -p_1(G(t) - G_b) - X(t)G(t) + m(t), \\ {}_0^C D_t^q X(t) = -p_2 X(t) + p_3(I(t) - I_b), \\ {}_0^C D_t^q I(t) = -n(I(t) - I_b) + \gamma(G(t) - h)^+. \end{cases} \tag{1}$$

Here, $h$ represents the blood glucose threshold, and

$$(G(t) - h)^+ = \max(G(t) - h, 0)$$

is the threshold function.

If $G(t) \leq h$, then $(G(t) - h)^+ = 0$, and the insulin level decreases and converges to $I_b$, the basal level.

If $G(t) > h$, then the pancreas secretes insulin at a rate $\gamma > 0$.

The system is supplemented with the initial conditions

$$G(0) = G_0, \qquad X(0) = X_0, \qquad I(0) = I_0.$$

Define $y(t) = (G(t), X(t), I(t))^T \in \mathbb{R}^3$, and rewrite the system in the abstract form

$${}_0^C D_t^q y(t) = f(t, y(t)), \quad y(0) = y_0, \tag{2}$$

with

$$f(t, y) = \begin{pmatrix} -p_1(G - G_b) - XG + m(t) \\ -p_2 X + p_3(I - I_b) \\ -n(I - I_b) + \gamma(G - h)^+ \end{pmatrix}.$$

We impose the following hypotheses:

($H_1$): $m : [0, +\infty[ \to \mathbb{R}$ is continuous and bounded on every finite interval.

($H_2$): The parameters $p_1, p_2, p_3, n, \gamma > 0$, and $G_b, I_b, h \in \mathbb{R}$, are fixed.

($H_3$): The initial condition satisfies $y_0 \in \mathbb{R}^3$.

For $q \in (0, 1)$, problem (2), in the mild sense, is equivalent to the integral equation

$$y(t) = y_0 + \frac{1}{\Gamma(q)} \int_0^t (t - s)^{q-1} f(s, y(s))\, ds, \quad t \in [0, T]. \tag{3}$$

We denote this equation by $V_q$, where $\Gamma(q)$ is the gamma function.

We define the Banach space

$$X_T := C([0, T]; \mathbb{R}^3), \quad \|y\|_\infty := \sup_{t\in[0,T]} \|y(t)\|_{\mathbb{R}^3},$$

where $\|\cdot\|$ denotes the maximum norm on $\mathbb{R}^3$, that is, the maximum absolute value of the components. We denote $y = (G, X, I)^T$.

**Theorem 1.** *Under* ($H_1$) *and* ($H_3$)*, there exists* $T > 0$ *such that problem* (2) *admits a unique solution* $y \in C([0, T], \mathbb{R}^3)$.

*Proof.* 1. Regularity.

By ($H_1$), $m(\cdot)$ is continuous on every finite interval, and all other operations involved, namely sums and products, are continuous. Therefore, for every fixed $y$, the map $t \mapsto f(t, y)$ is continuous.

2. Local Lipschitz continuity with respect to $y$.

Fix $R > 0$. In the ball

$$B_R = \{y \in \mathbb{R}^3 : \|y - y_0\| \le R\},$$

all components satisfy

$$|G|, |X|, |I| < M_R = \|y_0\| + R.$$

For any $y = (G, X, I)$ and $\tilde{y} = (\tilde{G}, \tilde{X}, \tilde{I}) \in B_R$, and for any $t \in [0, T]$, we estimate each component separately.

For the first component,

$$\begin{aligned} |f_1(t, y) - f_1(t, \tilde{y})| &= | - p_1(G - \tilde{G}) - XG + \tilde{X}\tilde{G}| \\ &\le p_1|G - \tilde{G}| + |XG - \tilde{X}\tilde{G}| \\ &\le p_1|G - \tilde{G}| + |X||G - \tilde{G}| + |\tilde{G}||X - \tilde{X}| \\ &\le (p_1 + M_R)|G - \tilde{G}| + M_R|X - \tilde{X}| \\ &\le (p_1 + 2M_R)\|y - \tilde{y}\|_\infty. \end{aligned}$$

For the second component,

$$\begin{aligned} |f_2(t, y) - f_2(t, \tilde{y})| &= | - p_2(X - \tilde{X}) + p_3(I - \tilde{I})| \\ &\le p_2|X - \tilde{X}| + p_3|I - \tilde{I}| \\ &\le (p_2 + p_3)\|y - \tilde{y}\|_\infty. \end{aligned}$$

For the third component, using the fact that the function $u \mapsto (u - h)^+$ is Lipschitz continuous with constant 1, we obtain

$$|f_3(t, y) - f_3(t, \tilde{y})| = | - n(I - \tilde{I}) + \gamma\left((G - h)^+ - (\tilde{G} - h)^+\right)|$$

$$\begin{aligned}
&\leq n|I - \tilde{I}| + \gamma|(G - h)^+ - (\tilde{G} - h)^+| \\
&\leq n|I - \tilde{I}| + \gamma|G - \tilde{G}| \\
&\leq (n + \gamma)\|y - \tilde{y}\|_\infty.
\end{aligned}$$

Thus, on $B_R$, $f$ is Lipschitz continuous in $y$ with constant

$$L_R = \max\{p_1 + 2M_R,\ p_2 + p_3,\ n + \gamma\}.$$

3. Boundedness of the components.
For $t \in [0, T]$ and $y \in B_R$, we have the following bounds:

$$\begin{aligned}
|f_1(t, y)| &\leq p_1(|G| + |G_b|) + |X||G| + |m(t)| \\
&\leq p_1(M_R + |G_b|) + M_R^2 + m_T, \\
|f_2(t, y)| &\leq p_2|X| + p_3(|I| + |I_b|) \\
&\leq p_2 M_R + p_3(M_R + |I_b|), \\
|f_3(t, y)| &\leq n(|I| + |I_b|) + \gamma|(G - h)^+| \\
&\leq n(M_R + |I_b|) + \gamma(M_R + |h|),
\end{aligned}$$

where

$$m_T = \sup_{s\in[0,T]} |m(s)| < \infty \quad \text{by } (H_1).$$

Let

$$M_{R,T} = \max\left\{p_1(M_R + |G_b|) + M_R^2 + m_T,\ p_2 M_R + p_3(M_R + |I_b|),\ n(M_R + |I_b|) + \gamma(M_R + |h|)\right\}.$$

Then

$$|f(t, y)| \leq M_{R,T} \quad \text{for all } (t, y) \in [0, T] \times B_R.$$

Define $\Phi : X_T \to X_T$ by

$$(\Phi y)(t) = y_0 + \frac{1}{\Gamma(q)} \int_0^t (t - s)^{q-1} f(s, y(s))\, ds.$$

The operator $\Phi$ is well defined, and $\Phi y \in C([0, T])$ by the continuity of $f$.
Fix $R > 0$. For $y \in B_R = \{z \in X_T : \|z - y_0\|_\infty \leq R\}$, we have

$$\begin{aligned}
\|\Phi y - y_0\|_\infty &\leq \frac{1}{\Gamma(q)} \sup_{t\in[0,T]} \int_0^t (t - s)^{q-1} |f(s, y(s))|\, ds \\
&\leq \frac{M_{R,T}}{\Gamma(q)} \sup_{t\in[0,T]} \int_0^t (t - s)^{q-1} ds \\
&= \frac{M_{R,T} T^q}{\Gamma(q + 1)}.
\end{aligned}$$

Therefore, if

$$\frac{M_{R,T} T^q}{\Gamma(q + 1)} \leq R, \tag{4}$$

then $\Phi(B_R) \subset B_R$.

We now study the contraction property for sufficiently small $T$.

For $y, z \in X_T$,

$$\|(\Phi y)(t) - (\Phi z)(t)\| \leq \frac{1}{\Gamma(q)} \int_0^t (t-s)^{q-1} |f(s, y(s)) - f(s, z(s))|\, ds \leq \frac{L_R}{\Gamma(q)} \int_0^t (t-s)^{q-1} \|y(s) - z(s)\|\, ds.$$

Hence,

$$\|(\Phi y)(t) - (\Phi z)(t)\| \leq \frac{L_R}{\Gamma(q)} \|y - z\|_\infty \int_0^t (t-s)^{q-1} ds = \frac{L_R T^q}{\Gamma(q+1)} \|y - z\|_\infty.$$

Thus, $\Phi$ is a contraction whenever

$$\frac{L_R T^q}{\Gamma(q+1)} < 1. \tag{5}$$

Choose $R > 0$, for example,

$$R = 1 + \|y_0\|_\infty.$$

Fix $T \leq 1$, and let

$$\overline{m} = \sup_{s \in [0,T]} |m(s)|.$$

Define

$$M_R' = \max \left\{ p_1(M_R + |G_b|) + M_R^2 + \overline{m},\ p_2 M_R + p_3(M_R + |I_b|),\ n(M_R + |I_b|) + \gamma(M_R + |h|) \right\}.$$

Then $M_{R,T} \leq M_R'$ for all $T \in (0, 1]$. It is therefore sufficient to impose

$$\frac{T^q}{\Gamma(q+1)} M_R' \leq R \quad \text{and} \quad \frac{L_R T^q}{\Gamma(q+1)} < 1.$$

A possible choice is

$$T \leq \min \left\{ \left( \frac{R\Gamma(q+1)}{2M_R'} \right)^{1/q}, \left( \frac{\Gamma(q+1)}{2L_R} \right)^{1/q}, 1 \right\}.$$

This choice ensures (4) and (5). Therefore, for this $T$, $\Phi$ is a contraction mapping from $B_R$ into itself.

Thus, the Banach fixed-point theorem guarantees the existence of a unique fixed point $y \in B_R \subset X_T$. This proves the existence and uniqueness of a solution to system (2). Hence, problem (2) admits a unique solution $y \in C([0, T]; \mathbb{R}^3)$.

□

**Theorem 2** (Local boundedness)**.** *Let $T > 0$ be such that the Picard operator associated with* (1) *is well defined and maps the closed ball*

$$B_R := \left\{ y \in X_T = C([0, T]; \mathbb{R}^3) : \|y - y_0\|_\infty \leq R \right\}$$

*into itself for some $R > 0$. Then the unique solution $y(t) = (G(t), X(t), I(t))^T$ of* (1) *on $[0, T]$ is bounded on $[0, T]$. More precisely, there exists a constant $C > 0$, depending only on $R$, $y_0$, the model parameters, $T$, and $\sup_{s \in [0,T]} |m(s)|$, such that*

$$\|y(t)\| \leq C, \qquad \forall t \in [0, T].$$

*In particular,*

$$\sup_{t\in[0,T]} \|y(t)\| \le C.$$

*Proof.* We work in the Banach space

$$X_T = C([0,T];\mathbb{R}^3), \qquad \|y\|_\infty := \sup_{t\in[0,T]} \|y(t)\|.$$

Recall that the solution of (1) satisfies the equivalent Volterra integral equation

$$y(t) = y_0 + \frac{1}{\Gamma(q)} \int_0^t (t-s)^{q-1} f(s, y(s))\, ds, \qquad t \in [0,T].$$

Accordingly, we define the Picard operator $\Phi : X_T \to X_T$ by

$$(\Phi y)(t) := y_0 + \frac{1}{\Gamma(q)} \int_0^t (t-s)^{q-1} f(s, y(s))\, ds.$$

Let $R > 0$ and consider the closed ball

$$B_R := \{y \in X_T : \|y - y_0\|_\infty \le R\}.$$

Assume that $T > 0$ is chosen so that $\Phi(B_R) \subset B_R$. By the fixed-point argument established in the existence theorem, $\Phi$ admits a unique fixed point $y \in B_R$, which is precisely the unique local solution of (1) on $[0,T]$.

Since $y \in B_R$, by the definition of the ball, we have

$$\|y - y_0\|_\infty \le R.$$

Therefore, for every $t \in [0,T]$,

$$\|y(t) - y_0\| \le R.$$

Using the triangle inequality, we immediately obtain

$$\|y(t)\| \le \|y(t) - y_0\| + \|y_0\| \le R + \|y_0\|, \qquad \forall t \in [0,T].$$

Hence,

$$\sup_{t\in[0,T]} \|y(t)\| \le \|y_0\| + R.$$

Thus, the solution is bounded on $[0,T]$. We may therefore take

$$C := \|y_0\| + R.$$

It remains to clarify the dependence of the constant $C$. The radius $R$ is chosen so that the closed ball $B_R$ is invariant under the Picard operator. More precisely, from the estimate used in the existence proof, there exists a constant $M_{R,T} > 0$, depending on the parameters of the system, on $T$, on $R$, and on $\sup_{s\in[0,T]} |m(s)|$, such that

$$\|\Phi y - y_0\|_\infty \le \frac{M_{R,T} T^q}{\Gamma(q+1)}, \qquad \forall y \in B_R.$$

Hence, if $T$ is chosen so that

$$\frac{M_{R,T}T^q}{\Gamma(q+1)} \le R,$$

then $\Phi(B_R) \subset B_R$, and the above estimate yields the boundedness of the fixed-point solution. Consequently, the bound

$$\|y(t)\| \le C := \|y_0\| + R, \qquad \forall t \in [0,T],$$

holds, where $C$ depends on $y_0$, $R$, $T$, the model parameters, and $\sup_{s\in[0,T]} |m(s)|$.

This proves the local boundedness of the solution on the interval $[0,T]$. □

**Theorem 3** (Positivity of the state variables)**.** *Let $q \in (0,1)$, $G_0 \ge 0$, $X_0 > 0$, $I_0 > I_b > 0$, and assume that $m(t) \ge 0$ for all $t \in [0,T]$. Then the local solution $y(t) = (G(t), X(t), I(t))^T$ satisfies*

$$G(t) \ge 0, \qquad X(t) \ge 0, \qquad I(t) \ge I_b > 0, \qquad \forall t \in [0,T].$$

*Proof.* We divide the proof into three steps.

Define

$$Z(t) := I(t) - I_b.$$

Then $Z(0) = I_0 - I_b > 0$, and $Z$ satisfies

$${}_0^C D_t^q Z(t) = -nZ(t) + \gamma(G(t) - h)^+.$$

Since $(G(t) - h)^+ \ge 0$, the variation-of-constants formula gives

$$Z(t) = E_q(-nt^q)Z(0) + \gamma \int_0^t (t-s)^{q-1} E_{q,q}(-n(t-s)^q)(G(s) - h)^+ \, ds.$$

For $q \in (0,1)$ and $n > 0$, the Mittag–Leffler functions satisfy

$$E_q(-nt^q) \ge 0, \qquad E_{q,q}(-nt^q) \ge 0, \qquad \forall t \ge 0.$$

Hence, both terms in the above representation are nonnegative. Since $Z(0) > 0$, we obtain

$$Z(t) \ge E_q(-nt^q)Z(0) > 0, \qquad \forall t \in [0,T].$$

Therefore,

$$I(t) = Z(t) + I_b > I_b > 0, \qquad \forall t \in [0,T].$$

The equation for $X$ is

$${}_0^C D_t^q X(t) = -p_2 X(t) + p_3(I(t) - I_b).$$

Since $I(t) - I_b \ge 0$, the variation-of-constants formula yields

$$X(t) = E_q(-p_2 t^q)X_0 + p_3 \int_0^t (t-s)^{q-1} E_{q,q}(-p_2(t-s)^q)(I(s) - I_b) \, ds.$$

Again, the Mittag–Leffler kernels are nonnegative, and $X_0 > 0$. Consequently,

$$X(t) \ge E_q(-p_2 t^q)X_0 > 0, \qquad \forall t \in [0,T].$$

In particular,

$$X(t) \geq 0, \qquad \forall t \in [0, T].$$

Finally, suppose, for contradiction, that there exists $t_1 \in (0, T]$ such that

$$G(t_1) < 0.$$

Since $G$ is continuous and $G(0) = G_0 \geq 0$, there exists a point $t_* \in (0, T]$ such that

$$G(t_*) = \min_{t \in [0, t_1]} G(t) < 0.$$

By the fractional minimum principle for the Caputo derivative, we have

$${}_0^C D_t^q G(t_*) \leq 0.$$

On the other hand, from the equation

$${}_0^C D_t^q G(t) = -p_1(G(t) - G_b) - X(t)G(t) + m(t),$$

we obtain at $t = t_*$,

$${}_0^C D_t^q G(t_*) = -p_1(G(t_*) - G_b) - X(t_*)G(t_*) + m(t_*).$$

Since $G(t_*) < 0$, $X(t_*) \geq 0$, $G_b \geq 0$, and $m(t_*) \geq 0$, we have

$$-p_1(G(t_*) - G_b) > 0, \qquad -X(t_*)G(t_*) \geq 0, \qquad m(t_*) \geq 0.$$

Therefore,

$${}_0^C D_t^q G(t_*) > 0,$$

which contradicts the fractional minimum principle. Hence,

$$G(t) \geq 0, \qquad \forall t \in [0, T].$$

Combining the above three steps, we conclude that

$$G(t) \geq 0, \qquad X(t) \geq 0, \qquad I(t) \geq I_b > 0, \qquad \forall t \in [0, T].$$

This completes the proof. □

## 3. Optimal control problem

Consider the state vector $y = (G, X, I)^T$ governed by the fractional-order system, with order $q \in (0, 1)$,

$$\begin{cases} {}_0^C D_t^q G(t) = -p_1(G(t) - G_b) - X(t)G(t) + (1 - u(t))m(t), \\ {}_0^C D_t^q X(t) = -p_2 X(t) + p_3(I(t) - I_b), \\ {}_0^C D_t^q I(t) = -n(I(t) - I_b) + \gamma(G(t) - h)^+ + u(t), \end{cases} \tag{3.1}$$

with initial conditions

$$G(0) = G_0 \geq 0, \quad X(0) = X_0 \geq 0, \quad I(0) = I_0 \geq 0.$$

The control variable $u(t) \in [0, 1]$ is interpreted as a dimensionless combined therapeutic control representing the overall treatment intensity, including both dietary regulation and insulin support. Within this normalized framework, $u(t)$ simultaneously reduces the effective glucose disturbance through $(1-u(t))m(t)$ and enhances insulin action through the term $+u(t)$, thereby providing a consistent biological and mathematical interpretation.

The cost functional is designed to achieve optimal glycemic management while minimizing clinical risks and treatment burden:

$$J(u) = \int_0^T \left(\alpha G(t) + \beta I(t) - \rho X(t) + \frac{A}{2}u(t)^2\right) dt.$$

Based on the previous section, we assume:

1. $m \in C([0, T])$ is bounded.
2. All parameters are fixed and positive, that is, $p_i, n, \gamma, \alpha, \beta, \rho, A > 0$.
3. There exists a nonempty, compact, and convex set $U \subset \mathbb{R}$, and the admissible control set is defined by
$$\mathcal{U}_{ad} = \{u : [0, T] \to U \text{ measurable}\}.$$
Thus, $u \in \mathcal{U}_{ad}$ satisfies $u(t) \in U$ for almost every $t \in [0, T]$. The set $\mathcal{U}_{ad}$ is closed under weak-$*$ convergence, since its values lie in a compact convex set.
4. The nonlinearity in $y$ is locally Lipschitz continuous.
5. The integrand $L(t, y, u) = \alpha G + \beta I - \rho X + \frac{A}{2}u^2$ is continuous in $(y, u)$ and convex in $u$.

**Theorem 4.** *Under assumptions* 1–5*, there exists an optimal control* $u^* \in \mathcal{U}_{ad}$ *such that*

$$J(u^*) = \min_{u \in \mathcal{U}_{ad}} J(u).$$

*Proof.* For each admissible control $u \in \mathcal{U}_{ad}$, the state equation admits a unique solution $y_u \in C([0, T], \mathbb{R}^3)$. Moreover, since $u(t) \in U$ is bounded and $m$ is bounded, we obtain a uniform bound on the family of trajectories:

$$\sup_{t \in [0,T]} \|y_u(t)\| \leq M$$

for some $M > 0$.

Furthermore, we have

$$y_u(t) = y_0 + \frac{1}{\Gamma(q)} \int_0^t (t - s)^{q-1} f(s, y_u(s), u(s))\, ds.$$

In addition, we derive a uniform equicontinuity estimate. For $0 \leq s < t \leq T$,

$$\|y_u(t) - y_u(s)\| \leq C|t - s|^q,$$

since

$$\int_s^t (t - \tau)^{q-1}\, d\tau = \frac{\Gamma(q)}{\Gamma(q + 1)}(t - s)^q.$$

Thus, the family $\{y_u : u \in \mathcal{U}_{ad}\}$ is uniformly bounded and equicontinuous. By the Arzelà–Ascoli theorem, it is relatively compact in $C([0,T],\mathbb{R}^3)$.

Let $(u_n) \subset \mathcal{U}_{ad}$ be a minimizing sequence, that is,

$$J(u_n) \to \inf_{u\in\mathcal{U}_{ad}} J(u).$$

Since each $u_n(t) \in U$ is bounded, $(u_n)$ is bounded in $L^\infty([0,T])$. By the Banach–Alaoglu theorem, there exists a subsequence $u_{n_k}$ and $u^* \in L^\infty([0,T])$ such that

$$u_{n_k} \rightharpoonup^* u^* \quad \text{in } L^\infty([0,T]).$$

Moreover, since $u_n(t) \in U$ almost everywhere and $U$ is closed and convex, the limit satisfies $u^*(t) \in U$ almost everywhere. Hence, $u^* \in \mathcal{U}_{ad}$.

Next, consider the convergence of the associated trajectories. Let $y_n = y_{u_n}$ be the trajectory corresponding to $u_n$. The family $\{y_n\}$ is uniformly bounded and equicontinuous. By the Arzelà–Ascoli theorem, we may extract a subsequence, still denoted by $y_n$, such that

$$y_n \to y^* \quad \text{uniformly on } [0,T],$$

for some $y^* \in C([0,T],\mathbb{R}^3)$.

We now show that the pair $(u^*, y^*)$ satisfies the state equation. Starting from the integral form satisfied by $y_n$,

$$y_n(t) = y_0 + \frac{1}{\Gamma(q)}\int_0^t (t-s)^{q-1} f(s, y_n(s), u_n(s))\, ds,$$

we write

$$y_n(t) - \left(y_0 + \frac{1}{\Gamma(q)}\int_0^t (t-s)^{q-1} f(s, y^*(s), u^*(s))\, ds\right) = I_{1,n}(t) + I_{2,n}(t),$$

where

$$I_{1,n}(t) = \frac{1}{\Gamma(q)}\int_0^t (t-s)^{q-1}\left(f(s, y_n(s), u_n(s)) - f(s, y^*(s), u_n(s))\right) ds,$$
$$I_{2,n}(t) = \frac{1}{\Gamma(q)}\int_0^t (t-s)^{q-1}\left(f(s, y^*(s), u_n(s)) - f(s, y^*(s), u^*(s))\right) ds.$$

For $I_{1,n}(t)$, using the Lipschitz continuity of $f$ with respect to $y$, we have

$$\|I_{1,n}(t)\| \le \frac{L}{\Gamma(q)}\int_0^t (t-s)^{q-1}\|y_n(s) - y^*(s)\| ds.$$

By the uniform convergence $y_n \to y^*$, this bound converges uniformly to 0 on $[0,T]$.

For $I_{2,n}(t)$, we use the specific structure of $f$, namely its affine dependence on $u$. The dependence on $u$ appears only in the first and third components of $f$. Specifically,

$$f(s,y,u) = \begin{pmatrix} -p_1(G-G_b) - XG + (1-u)m(s) \\ -p_2 X + p_3(I - I_b) \\ -n(I-I_b) + \gamma(G-h)^+ + u \end{pmatrix}.$$

Thus, we may write

$$f(s, y, u) = f_0(s, y) + uf_1(s),$$

where

$$f_0(s, y) = \begin{pmatrix} -p_1(G - G_b) - XG + m(s) \\ -p_2X + p_3(I - I_b) \\ -n(I - I_b) + \gamma(G - h)^+ \end{pmatrix}, \qquad f_1(s) = \begin{pmatrix} -m(s) \\ 0 \\ 1 \end{pmatrix}.$$

Then,

$$I_{2,n}(t) = \frac{1}{\Gamma(q)} \int_0^t (t - s)^{q-1}(u_n(s) - u^*(s))f_1(s)\, ds.$$

For each fixed $t$, the function

$$s \mapsto (t - s)^{q-1} f_1(s)$$

belongs to $L^1([0, t])$, since $(t - s)^{q-1}$ is integrable and $f_1$ is bounded. Since $u_n \rightharpoonup^* u^*$ in $L^\infty([0, T])$, we have, for each $t$,

$$\int_0^t (u_n(s) - u^*(s)) \Big((t - s)^{q-1} f_1(s)\Big)\, ds \to 0.$$

Hence, $I_{2,n}(t) \to 0$ pointwise for each $t \in [0, T]$. Moreover, since the integrand is uniformly bounded, the convergence is uniform on $[0, T]$. Therefore, $I_{2,n} \to 0$ uniformly.

Combining the convergences $y_n \to y^*$, $I_{1,n} \to 0$, and $I_{2,n} \to 0$, and passing to the limit in the integral representation, we obtain

$$y^*(t) = y_0 + \frac{1}{\Gamma(q)} \int_0^t (t - s)^{q-1} f(s, y^*(s), u^*(s))ds.$$

Thus, $y^*$ is the trajectory associated with the control $u^*$, and $(u^*, y^*)$ is an admissible pair.

Finally, it remains to prove that

$$J(u^*) \leq \liminf_{n\to\infty} J(u_n).$$

We have $y_n \to y^*$ uniformly and $u_n \rightharpoonup^* u^*$ in $L^\infty([0, T])$. The integrand

$$L(t, y, u) = \alpha G + \beta I - \rho X + \frac{A}{2}u^2$$

is continuous in $y$ and convex in $u$. Therefore, by the theorem of Fleming and Rishel [17], it is lower semicontinuous with respect to the above convergence. Equivalently, the same conclusion follows from a direct lower semicontinuity argument under the weak convergence of $u_n$ and the uniform convergence of $y_n$. Hence,

$$J(u^*) \leq \liminf_{n\to\infty} J(u_n) = \inf_{u\in\mathcal{U}_{ad}} J(u).$$

Therefore, $u^*$ is an optimal control. □

## 4. Necessary optimality conditions

Let $y = (G, X, I)^T$ be the state vector, let $\lambda = (\lambda_1, \lambda_2, \lambda_3)^T$ be the adjoint vector, and let $u \in \mathcal{U}_{ad}$. Define the Hamiltonian

$$\begin{aligned} H(t, y, u, \lambda) = \alpha G + \beta I - \rho X + \frac{A}{2}u^2 \\ + \lambda_1 \left(-p_1(G - G_b) - XG + (1 - u)m(t)\right) \\ + \lambda_2 \left(-p_2 X + p_3(I - I_b)\right) \\ + \lambda_3 \left(-n(I - I_b) + \gamma(G - h)^+ + u\right). \end{aligned}$$

**Theorem 5.** *Suppose that $u^*$ is an optimal control and $y^*(t)$ is the associated state trajectory. Then there exists an absolutely continuous adjoint vector $\lambda(t) = (\lambda_1, \lambda_2, \lambda_3)^T$ satisfying the backward adjoint equation*

$$ {}_t^C D_T^q \lambda(t) = -\nabla_y H(t, y^*(t), u^*(t), \lambda(t)), $$

*with the terminal transversality conditions*

$$ \lambda_i(T) = 0, \qquad \text{for } i = 1, 2, 3. $$

*Explicitly, the adjoint equations are*

$$\begin{aligned} {}_t^C D_T^q \lambda_1(t) &= -\frac{\partial H}{\partial G} = -\alpha + (p_1 + X^*(t))\lambda_1(t) - \gamma s(t)\lambda_3(t), \\ {}_t^C D_T^q \lambda_2(t) &= -\frac{\partial H}{\partial X} = \rho + G^*(t)\lambda_1(t) + p_2\lambda_2(t), \\ {}_t^C D_T^q \lambda_3(t) &= -\frac{\partial H}{\partial I} = -\beta - p_3\lambda_2(t) + n\lambda_3(t), \end{aligned}$$

*with $\lambda(T) = 0$, where $s(t) \in \partial(G^*(t) - h)^+$ is the subgradient of the threshold function*

$$ s(t) = \begin{cases} 1, & \text{if } G^*(t) > h, \\ 0, & \text{if } G^*(t) < h, \\ [0, 1], & \text{if } G^*(t) = h. \end{cases} $$

*Moreover, the optimal control satisfies the minimization condition*

$$ u^*(t) \in \operatorname{argmin}_{u \in \mathcal{U}_{ad}} H(t, y^*(t), u, \lambda(t)) \quad \text{for a.e. } t \in [0, T]. $$

*Since the Hamiltonian is strictly convex in u, the optimal control is given by*

$$ u^*(t) = \mathcal{P}_{[0, U_{\max}]}\left(\frac{\lambda_1(t)m(t) - \lambda_3(t)}{A}\right), $$

*where $\mathcal{P}_{[0,U_{\max}]}$ denotes the projection onto the interval $[0, U_{\max}]$.*

*Proof.* The proof follows from Pontryagin's maximum principle for fractional optimal control problems [6, 28]. The adjoint equations are derived by differentiating the Hamiltonian with respect to the state variables:

$$\frac{\partial H}{\partial G} = \alpha - p_1\lambda_1 - X\lambda_1 + \gamma s(t)\lambda_3,$$
$$\frac{\partial H}{\partial X} = -\rho - G\lambda_1 - p_2\lambda_2,$$
$$\frac{\partial H}{\partial I} = \beta + p_3\lambda_2 - n\lambda_3.$$

The backward adjoint equations then follow from the principle

$${}_t^C D_T^q \lambda(t) = -\nabla_y H(t, y^*(t), u^*(t), \lambda(t)).$$

The terminal condition $\lambda(T) = 0$ follows from the free terminal state. The optimality condition for the control is obtained from

$$\frac{\partial H}{\partial u} = Au - \lambda_1 m(t) + \lambda_3 = 0,$$

which gives

$$u^*(t) = \frac{\lambda_1(t)m(t) - \lambda_3(t)}{A}.$$

Since $u$ must belong to $\mathcal{U}_{ad} = [0, U_{\max}]$, we project this expression onto the admissible set:

$$u^*(t) = \max\left(0, \min\left(U_{\max}, \frac{\lambda_1(t)m(t) - \lambda_3(t)}{A}\right)\right).$$

This completes the proof of the necessary optimality conditions. □

## 5. Numerical simulations

This section presents numerical simulations validating the theoretical results of the fractional optimal control approach. While clinical variability poses challenges for universal parameterization in Type 1 diabetes, we adopt physiologically plausible parameters from the classical Bergman model [7], ensuring consistency with established basal values ($G_b = 92$ mg/dL, $I_b = 7.3$ mU/dL). The primary objective is to illustrate how the fractional order $q \in (0, 1)$ influences the system dynamics and the performance of the optimal control strategy, rather than to provide patient-specific calibrations. Simulations were implemented in MATLAB using a Grünwald–Letnikov discretization scheme for the Caputo derivative with step size $\Delta t = 0.01$. The fractional Pontryagin system was solved iteratively using a forward–backward sweep method [26] with convergence tolerance $\varepsilon = 10^{-6}$.

The fractional Pontryagin optimality system is solved numerically by means of a forward–backward sweep method combined with a predictor–corrector scheme for the fractional state and adjoint equations. The main steps of the procedure are summarized in Algorithm 1.

**Algorithm 1** Forward–backward sweep method for the fractional optimal control problem

1: Choose an initial guess $u^{(0)}(t)$ on the interval $[0, T]$.
2: Set the convergence tolerance $\varepsilon = 10^{-6}$.
3: Initialize the iteration counter $k = 0$.
4: Set $E^{(0)} = 1$.
**while** $E^{(k)} > \varepsilon$ **do**
**end**
5: Solve the fractional state system forward in time using a predictor–corrector method with the control $u^{(k)}(t)$.
6: Solve the fractional adjoint system backward in time using the state trajectory obtained in the previous step.
7: Update the control by

$$u^{(k+1)}(t) = \mathcal{P}_{[0,U_{\max}]}\left(\frac{\lambda_1^{(k)}(t)m(t) - \lambda_3^{(k)}(t)}{A}\right).$$

8: Compute the error

$$E^{(k+1)} = \max_{t\in[0,T]} \left|u^{(k+1)}(t) - u^{(k)}(t)\right|.$$

9: Set $k \leftarrow k + 1$.
10: Return the optimal control $u^*(t)$, the optimal state trajectory $y^*(t)$, and the adjoint variables $\lambda^*(t)$.

The comparison between Figures 1 and 2 clearly demonstrates the effectiveness of the optimal control strategy. Without control, the glucose level $G(t)$ exhibits significant and sustained elevation over the 24-hour period. In contrast, the application of the control law successfully regulates the system, leading to a substantial reduction in glucose levels and maintaining them closer to the basal state $G_b$. These results confirm that the designed time-fractional optimal control effectively manages the glucose concentration in the proposed model.

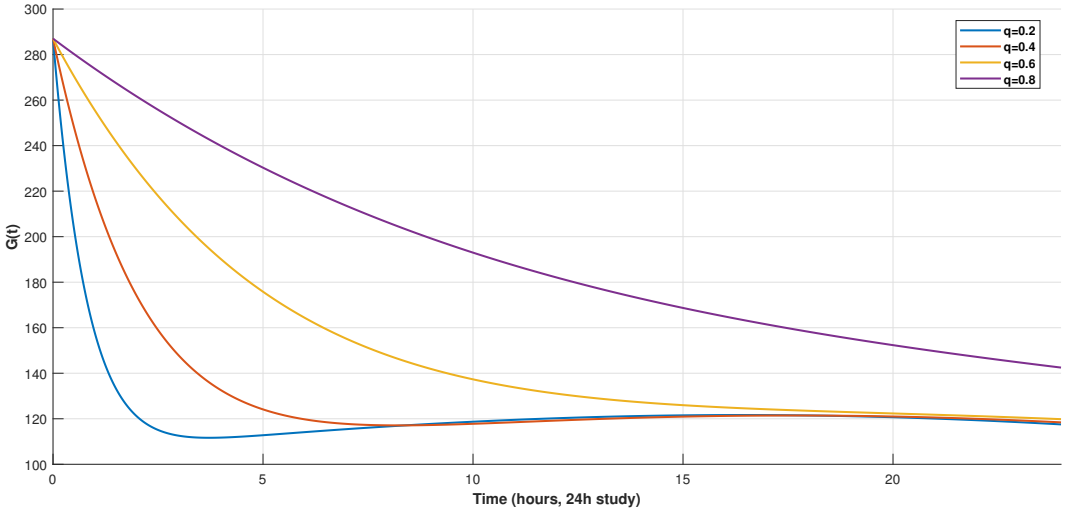


**Figure 1.** Evolution of the glucose function $G(t)$ over time without control.

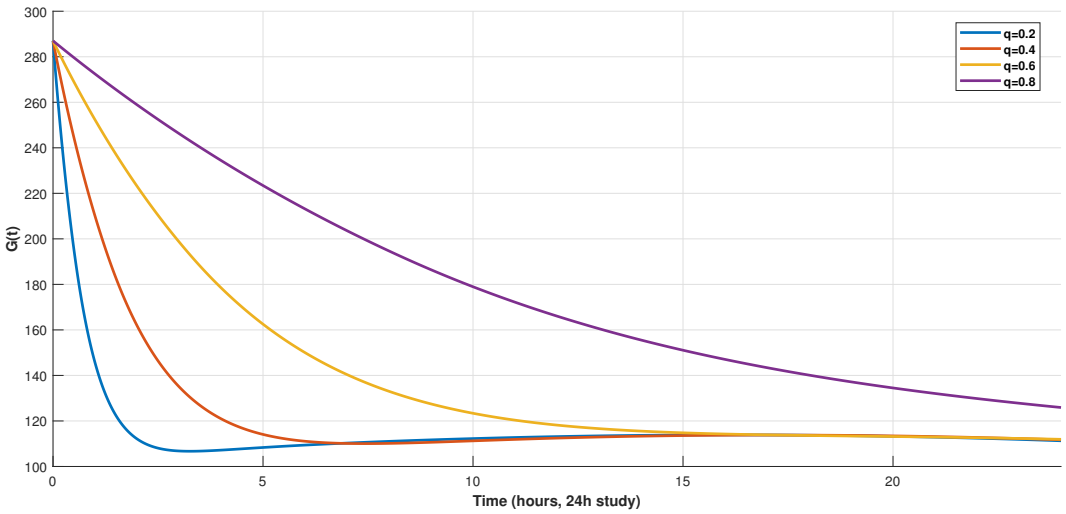


**Figure 2.** Evolution of the glucose function $G(t)$ over time with control.

Without control, Figure 3 shows that $X(t)$ displays unregulated fluctuations, indicating unstable insulin–glucose dynamics. With control, as illustrated in Figure 4, the optimal control stabilizes $X(t)$, leading to a smoother and more physiologically plausible profile.

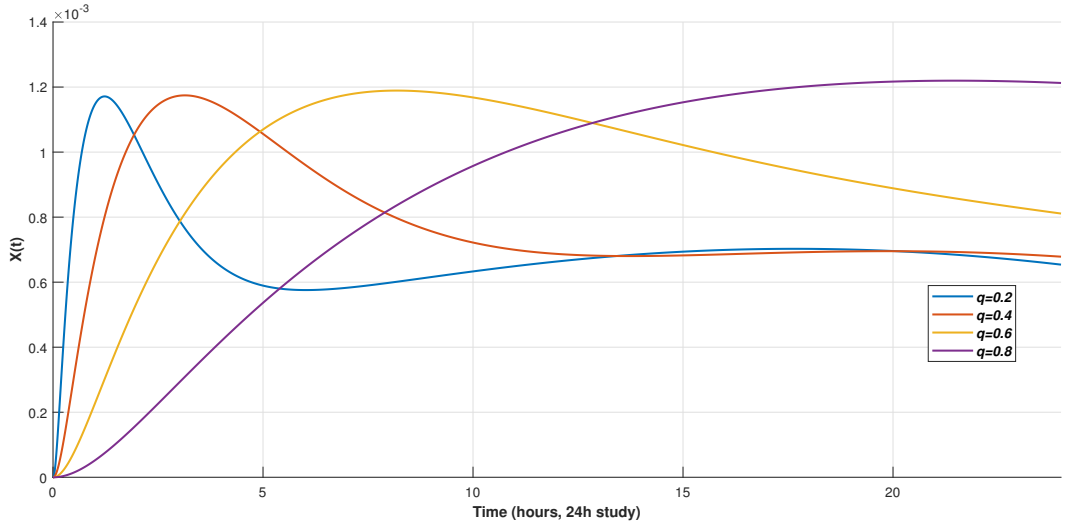


**Figure 3.** Evolution of active insulin $X(t)$ over time without control.

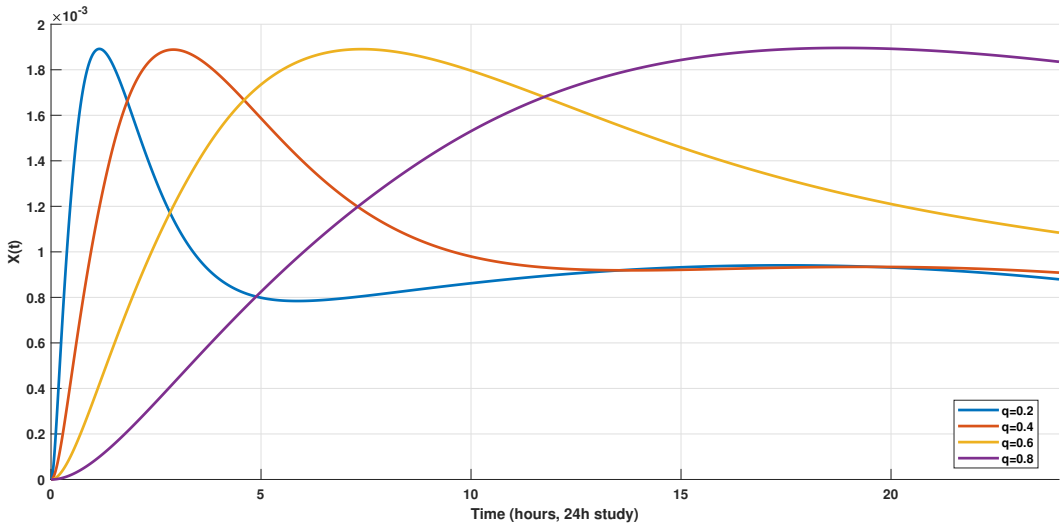


**Figure 4.** Evolution of active insulin $X(t)$ over time with control.

Without control, Figure 5 shows that $I(t)$ exhibits large oscillations, frequently deviating from the basal level $I_b$. With control, Figure 6 demonstrates that the optimal control maintains $I(t)$ near $I_b$, reducing variability and improving regulation.

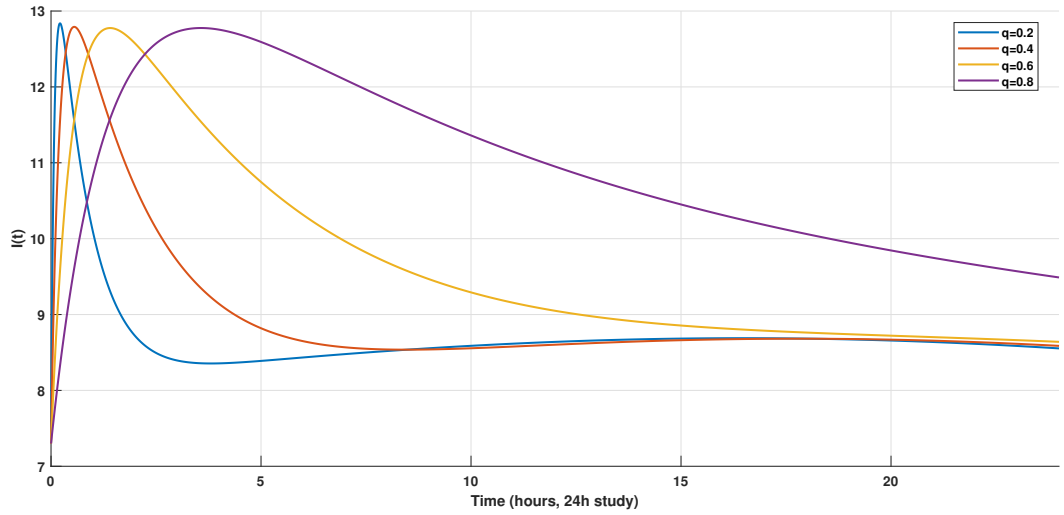


**Figure 5.** Evolution of the insulin concentration $I(t)$ over time without control.

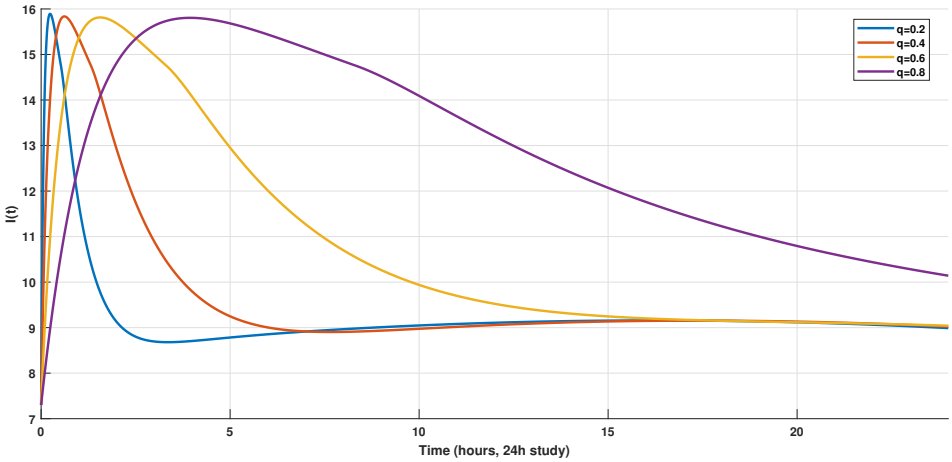


**Figure 6.** Evolution of the insulin concentration $I(t)$ over time with control.

*Remark* 1. The proposed control strategy is expected to remain effective for a broader range of initial conditions and operating scenarios, since the theoretical analysis is not restricted to a particular initial state. In particular, the existence, uniqueness, and stability results established in this work remain valid for arbitrary admissible initial conditions.

*Interpretation of the numerical results*

The numerical simulations presented in this study provide a compelling validation of the proposed time-fractional optimal control framework for the Bergman model of Type 1 diabetes. The comparative analysis between the uncontrolled and controlled scenarios demonstrates the efficacy of the derived control law in regulating the complex glucose–insulin dynamics.

The key findings can be summarized as follows:

- **Glycemic control:** The optimal control strategy successfully mitigates hyperglycemia, driving the glucose concentration $G(t)$ toward the basal level $G_b$ and maintaining it within a physiologically desirable range. This is in stark contrast to the uncontrolled case, where $G(t)$ exhibits sustained and clinically dangerous elevation.
- **System stabilization:** The controller effectively stabilizes the auxiliary variable $X(t)$, which represents active insulin. The transition from unregulated, nonphysiological fluctuations to a smooth, stable profile underscores the controller's ability to dampen inherent instabilities in the system.
- **Insulin regulation:** The plasma insulin concentration $I(t)$ is maintained close to its basal level $I_b$, with a significant reduction in oscillatory behavior. This suggests that the control law provides a stable and sustainable insulin infusion profile, minimizing large deviations that could lead to secondary complications.

Beyond merely replicating the performance of integer-order controllers, this work highlights the significant influence of the fractional order $q$. The Caputo derivative, by incorporating memory effects, allows the model to capture the historical dependence of metabolic processes. This results in a control response that is not solely reactive to the current state but is also informed by the system's trajectory,

leading to a more nuanced and potentially more robust regulatory strategy.

Despite the promising results obtained in this work, several limitations should be acknowledged. First, the proposed model relies on a simplified representation of glucose–insulin dynamics. In particular, it does not explicitly account for delays in insulin absorption, variability in insulin sensitivity, or the influence of other physiological hormones such as glucagon. These factors may play a significant role in real clinical settings and could affect the accuracy of the model predictions.

Second, the assumption of a bounded and known meal disturbance function $m(t)$ may not fully reflect real-life conditions, where meal intake is often uncertain and subject to abrupt variations. Incorporating stochastic effects or uncertain inputs would provide a more realistic framework for practical applications.

Third, the fractional-order formulation introduces additional modeling flexibility, but it also raises challenges in terms of parameter identification and clinical interpretability. Estimating the fractional order and associated parameters from patient data remains a nontrivial task and may limit the direct applicability of the model without further validation.

These limitations suggest several directions for future research, including the integration of more detailed physiological mechanisms, uncertainty modeling, and data-driven parameter estimation.

In conclusion, the numerical results confirm the theoretical foundations of the model and the optimal control approach. They demonstrate that the fractional-order framework is not only mathematically sound but also functionally superior for capturing the essential dynamics of glucose homeostasis. This work thereby establishes a robust foundation for the development of next-generation, personalized artificial pancreas systems that can account for the long-memory effects and interindividual variability inherent in Type 1 diabetes.

## 6. Conclusions

This study presented a fractional optimal-control framework for the Bergman glucose–insulin model associated with Type 1 diabetes. By integrating fractional-order modeling with optimal control theory, the proposed formulation captures hereditary and memory-dependent effects that arise naturally in metabolic regulation.

The theoretical analysis confirmed the well-posedness of the fractional dynamical system through the establishment of existence, uniqueness, boundedness, and positivity of its solutions. Subsequently, an optimal control problem was formulated, and the existence of an admissible optimal control was demonstrated. Using the fractional Pontryagin maximum principle, we derived the corresponding first-order necessary optimality conditions and obtained an explicit representation of the optimal therapeutic control.

The numerical results demonstrate that the proposed control strategy can effectively regulate glucose concentration while maintaining physiologically reasonable insulin dynamics. The simulations also show that the fractional order has a noticeable impact on the system behavior, indicating that the fractional model offers greater flexibility than its classical integer-order counterpart in describing glucose–insulin interactions.

Despite these contributions, the present model has some limitations. It remains a simplified representation of the physiological process and does not include several relevant effects, such as stochastic perturbations, time-delay mechanisms, variations in meal intake, or uncertainty in patient-

dependent parameters. Moreover, in strict Type 1 diabetes, the endogenous insulin secretion term may be negligible, which corresponds to setting the associated parameter equal to zero. The numerical experiments are also primarily illustrative and do not yet provide a detailed quantitative comparison among different treatment strategies or fractional-order values.

Future research may address these limitations by developing more realistic fractional models involving delays, random effects, adaptive patient-specific control laws, and multi-objective optimization criteria that balance glucose regulation, insulin administration, and hypoglycemia prevention. A further important direction is the calibration and validation of the proposed model using real clinical data. Such extensions would improve the applicability of the framework to diabetes treatment planning and artificial pancreas systems.

## Author contributions

All authors have worked equally.

## Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

## Funding statement

This work was supported and funded by the Deanship of Scientific Research at Imam Mohammad Ibn Saud Islamic University (IMSIU) (grant number IMSIU-DDRSP2602).

## Conflict of interest

All authors declare no conflicts of interest in this paper.

## References

1. K. Agilan, S. Naveen, S. Suganya, V. Parthiban, Analysis of variable-order fractional enzyme kinetics model with time delay, *Sci. Rep.*, **15** (2025), 34255. https://doi.org/10.1038/s41598-025-16382-x
2. A. Ahmad, M. Farman, P. A. Naik, E. Hincal, F. Iqbal, Z. Huang, Bifurcation and theoretical analysis of a fractional-order Hepatitis B epidemic model incorporating different chronic stages of infection, *J. Appl. Math. Comput.*, **71** (2025), 1543–1564. https://doi.org/10.1007/s12190-024-02301-2
3. A. B. A. Al-Hussein, F. Rahma, S. Jafari, Hopf bifurcation and chaos in time-delay model of glucose-insulin regulatory system, *Chaos Soliton. Fract.*, **137** (2020), 109845. https://doi.org/10.1016/j.chaos.2020.109845
4. A. Alalyani, On the solution of a nonlinear fractional-order glucose-insulin system incorporating $\beta$-cells compartment, *Malays. J. Math. Sci.*, **17** (2023), 1–12. https://doi.org/10.47836/mjms.17.1.01

5. D. Baleanu, K. Diethelm, E. Scalas, J. J. Trujillo, *Fractional calculus: Models and numerical methods*, World Scientific, **3** (2012). https://doi.org/10.1142/8180
6. R. Banerjee, R. K. Biswas, Fractional optimal control of compartmental SIR model of COVID-19: Showing the impact of effective vaccination, *Ifac-papersonline*, **55** (2022), 616–622. https://doi.org/10.1016/j.ifacol.2022.04.101
7. R. N. Bergman, C. Cobellit, G. Toffolo, Minimal models of glucose/insulin dynamics in the intact organism: A novel approach for evaluation of factors controlling glucose tolerance, *T. I. Meas. Control*, **3** (1981), 207–216. https://doi.org/10.1016/0376-6349(81)90014-6
8. R. N. Bergman, L. S. Phillips, C. Cobelli, Physiologic evaluation of factors controlling glucose tolerance in man: Measurement of insulin sensitivity and beta-cell glucose sensitivity from the response to intravenous glucose, *J. Clin. Invest.*, **68** (1981), 1456–1467. https://doi.org/10.1172/JCI110398
9. V. W. Bolie, Coefficients of normal blood glucose regulation, *J. Appl. Physiology*, **16** (1961), 783–788. https://doi.org/10.1152/jappl.1961.16.5.783
10. A. Boutayeb, M. E. N. Lamlili, W. Boutayeb, A systematic review of mathematical models dealing with diabetes population dynamics, *Comput. Math. Model. Diabetes*, 2025, 3–95. https://doi.org/10.1007/978-981-96-1925-2_1
11. M. Caputo, M. Fabrizio, A new definition of fractional derivative without singular kernel, *Prog. Fract. Differ. Appl.*, **1** (2015), 73–85. http://dx.doi.org/10.12785/pfda/010201
12. V. B. L. Chaurasia, R. S. Dubey, F. B. M. Belgacem, Fractional radial diffusion equation analytical solution via Hankel and Sumudu transforms, *Int. J. Math. Eng. Sci. Aerospace*, **3** (2012), 1–10.
13. C. Cobelli, C. D. Man, G. Toffolo, R. Basu, A. Vella, R. Rizza, The oral minimal model method, *Diabetes*, **63** (2014), 1203–1213. https://doi.org/10.2337/db13-1198
14. R. S. Dubey, P. Goswami, F. B. M. Belgacem, Generalized time-fractional telegraph equation analytical solution by sumudu and fourier transforms, *J. Fract. Calc. Appl.*, **5** (2014), 52–58.
15. P. G. Fabietti, V. Canonico, M. Orsini-Federici, E. Sarti, M. Massi-Benedetti, Clinical validation of a new control-oriented model of insulin and glucose dynamics in subjects with type 1 diabetes, *Diabetes Technol. The.*, **9** (2007),327–338. https://doi.org/10.1089/dia.2006.0030
16. B. Fernández-Carreón, J. M. Munoz-Pacheco, E. Zambrano-Serrano, O. G. Félix-Beltrán, Analysis of a fractional-order glucose-insulin biological system with time delay, *Chaos Theory Appl.*, **4** (2022), 10–18. https://doi.org/10.51537/chaos.988758
17. W. H. Fleming, R. W. Rishel, *Deterministic and stochastic optimal control*, Springer Science & Business Media, **1** (2012).
18. M. M. A. Hasan, A. M. Alghanmi, S. M. Al-Mekhlafi, H. Al Ali, Z. Mukandavire, A novel crossover dynamics of variable-order fractal-fractional stochastic diabetes model: Numerical simulations, *J. Math.*, **2025** (2025), 2986543. https://doi.org/10.1155/jom/2986543
19. M. M. A. Hasan, N. H. Sweilam, Numerical studies of the fractional optimal control problem of awareness and trial advertising model, *Prog. Fract. Differ. Appl.*, **8** (2022), 509–524. https://doi.org/10.18576/pfda/080405
20. M. Karim, I. Khaloufi, S. B. Rhila, M. A. Zaky, M. Z. Youssef, M. Rachik, Optimal regional control of a time-fractional spatiotemporal sir model with vaccination and treatment strategies, *Fractal Fract.*, **9** (2025), 382. https://doi.org/10.3390/fractalfract9060382

21. N. Lekdee, S. Sirisubtawee, S. Koonprasert, Bifurcations in a delayed fractional model of glucose–insulin interaction with incommensurate orders, *Adv. Differ. Equations*, **2019** (2019), 318. https://doi.org/10.1186/s13662-019-2262-6
22. C. D. Man, M. Camilleri, C. Cobelli, A system model of oral glucose absorption: Validation on gold standard data, *IEEE T. Biomed. Eng.*, **53** (2006), 2472–2478. https://doi.org/10.1109/TBME.2006.883792
23. L. Marchetti, F. Reali, M. Dauriz, C. Brangani, L. Boselli, G. Ceradini, et al., A novel insulin/glucose model after a mixed-meal test in patients with type 1 diabetes on insulin pump therapy, *Sci. Rep.*, **6** (2016), 36029. https://doi.org/10.1038/srep36029
24. A. Mari, A. Tura, E. Grespan, R. Bizzotto, Mathematical modeling for the physiological and clinical investigation of glucose homeostasis and diabetes, *Front. Physiol.*, **11** (2020), 575789. https://doi.org/10.3389/fphys.2020.575789
25. C. D. Mathers, D. Loncar, Projections of global mortality and burden of disease from 2002 to 2030, *PLoS Med.*, **3** (2006), e442. https://doi.org/10.1371/journal.pmed.0030442
26. M. McAsey, L. Mou, W. Han, Convergence of the forward-backward sweep method in optimal control, *Comput. Optim. Appl.*, **53** (2012), 207–226. https://doi.org/10.1007/s10589-011-9454-7
27. G. D. Ogle, F. Wang, A. Haynes, G. A. Gregory, T. W. King, K. Deng, et al., Global type 1 diabetes prevalence, incidence, and mortality estimates 2025: Results from the international diabetes Federation Atlas, and the T1D index version 3.0, *Diabetes Res. Clin. Pr.*, **225** (2025), 112277. https://doi.org/10.1016/j.diabres.2025.112277
28. L. S. Pontryagin, *Mathematical theory of optimal processes*, Routledge, 2018.
29. S. Soulaimani, A. Kaddar, F. A. Rihan, A spatio-temporal infection epidemic model with fractional order, general incidence, and vaccination analysis, *Sci. Afr.*, **26** (2024), e02349. https://doi.org/10.1016/j.sciaf.2024.e02349
30. S. Soulaimani, A. Kaddar, F. A. Rihan, Analysis of a fractional endemic seir model with vaccination and time delay, *Eur. Phys. J.-Spec. Top.*, **234** (2025), 1935–1951. https://doi.org/10.1140/epjs/s11734-024-01267-3
31. G. M. Steil, Algorithms for a closed-loop artificial pancreas: The case for proportional-integral-derivative control, *J. Diabetes Sci. Techn.*, **7** (2013), 1621–1631. https://doi.org/10.1177/193229681300700623
32. G. M. Vijayalakshmi, P. R. Besi, A. Akgül, Fractional commensurate model on COVID-19 with microbial co-infection: An optimal control analysis, *Optim. Contr. Appl. Met.*, **45** (2024), 1108–1121. https://doi.org/10.1002/oca.3093
33. M. A. Zaky, I. G. Ameen, A priori error estimates of a Jacobi spectral method for nonlinear systems of fractional boundary value problems and related Volterra-Fredholm integral equations with smooth solutions, *Numer. Algorithms*, **84** (2020), 63–89. https://doi.org/10.1007/s11075-019-00743-5


AIMS Press