

A TWO-STEP ADAMS–BASHFORTH SCHEME FOR THE FRACTIONAL-ORDER GLUCOSE–INSULIN MODEL: STABILITY AND CONVERGENCE

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Abstract The regulation of blood glucose and insulin in the human body is a highly non-linear physiological process influenced by hereditary memory, feedback mechanisms, and intrinsic delays. Classical integer-order models often fail to capture these memory-dependent and nonlocal effects. In this study, we introduce a novel fractional-order glucose–insulin regulatory model formulated with the Caputo–Fabrizio (CF) derivative, which employs a non-singular exponential kernel to describe fading memory effects more realistically. The model accounts for essential physiological parameters and incorporates the interplay between blood glucose concentration, insulin secretion, and an auxiliary control variable representing insulin action or resistance. We establish the well-posedness of the proposed CF-based system by proving existence and uniqueness of solutions via fixed-point theory under Lipschitz continuity and boundedness conditions on the nonlinear operators. To approximate the solution, we design a two-step Adams–Bashforth scheme tailored to the CF operator and provide a rigorous analysis of its convergence and stability. Numerical simulations confirm the accuracy and robustness of the method, demonstrating its ability to reproduce physiologically consistent glucose–insulin trajectories that outperform classical integer-order models. The results highlight the effectiveness of Caputo–Fabrizio fractional calculus in capturing hereditary and fading-memory effects in glucose–insulin dynamics, offering a robust mathematical framework for parameter estimation, optimal control, and personalized strategies in diabetes management.

Keywords Fractional-order model, Caputo–Fabrizio derivative, Adams–Bashforth scheme, glucose–insulin model, stability analysis.

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1. Introduction

The regulation of blood glucose and insulin represents a cornerstone of diabetes research, as disruptions in this delicate balance drive both the onset and progression of diabetes mellitus. The interaction between glucose concentration and insulin secretion is highly nonlinear, involving coupled feedback loops and delayed responses across multiple physiological pathways. The well-known minimal model introduced by Bergman and colleagues [12] provided a fundamental framework for interpreting intravenous glucose tolerance test (IVGTT) experimental data. This model, and its later refinements by De Gaetano and Arino [16], Li et al. [24], and Palumbo et al. [29], remains influential; however, it does not fully account for the hereditary and memory-dependent mechanisms intrinsic to biological regulation.

Fractional calculus has increasingly been employed to address these shortcomings by embedding memory and nonlocality into the governing equations [26, 27, 30]. Unlike classical integer-order operators, fractional derivatives incorporate past system states into present dynamics, thereby capturing hereditary effects. Traditional formulations such as the Caputo [13] and Riemann–Liouville derivatives rely on singular kernels, which can limit their physiological interpretability and pose numerical challenges [22]. In contrast, Caputo and Fabrizio [14] introduced a fractional derivative with a nonsingular exponential kernel that better reflects fading memory while maintaining numerical stability. This operator has since been successfully applied in physics, viscoelasticity, and biomedical modeling [2, 4, 9, 10, 25].

Recent studies have explored various fractional approaches to glucose–insulin dynamics. Ahmed et al. [2, 3] investigated different strategies for diabetes modeling using fractal–fractional derivatives and modified minimal models. Alhazmi and Saber [6] studied chaos control and stability analysis of the glucose–insulin regulatory system using Atangana–Baleanu fractal–fractional derivatives, while Alhazmi et al. [5] applied fractal–fractional operators with Adomian decomposition solutions. Saber and Alahmari [32] examined existence, stability, and control of glucose–insulin dynamics via Caputo–Fabrizio fractal–fractional operators. Furthermore, fractional-order approaches have been extended to other biological systems, including computer virus propagation [8, 33] and predator–prey dynamics [7, 20, 35].

In the context of glucose–insulin regulation, fractional-order models based on nonsingular kernels provide a promising framework to describe delayed insulin response, long-term adaptation, and nonlinear interactions that are difficult to capture using integer-order systems. Recent advances demonstrate the suitability of Caputo–Fabrizio and Atangana–Baleanu formulations in reproducing physiologically realistic glucose and insulin trajectories and in extending such models toward chaotic and complex dynamical regimes [1, 18, 19, 21, 28]. Moreover, the development of tailored numerical schemes, including Adams–Bashforth-type solvers, Newton polynomial approximations, and Laplace–Adomian decompositions [11, 17, 34], has facilitated stable and accurate simulations of fractional-order biomedical systems.

The classical mathematical model widely used in physiological research on glucose metabolism describes IVGTT experimental data using a small set of identifiable and physiologically meaningful parameters [12, 16, 24, 29]. The integer-order form of this model incorporating insulin dynamics is expressed as [16, 24]:

$$\begin{aligned}\frac{dx(t)}{dt} &= -[\tau_1 + y(t)]x(t) + \tau_1 y_b, \\ \frac{dy(t)}{dt} &= -\tau_2 y(t) + \tau_3 [z(t) - I_b],\end{aligned}\tag{1.1}$$

$$\frac{dz(t)}{dt} = \tau_4[x(t) - \tau_5]^+ - x_6[z(t) - I_b],$$

where

$$[x(t) - \tau_5]^+ = \begin{cases} x(t) - \tau_5, & \text{if } x(t) > \tau_5, \\ 0, & \text{if } x(t) \leq \tau_5. \end{cases}$$

The initial conditions are $y(0) = b_0$, $y(0) = 0$, and $z(0) = I_b$. Here, $x(t)$ [mg/dL] and $z(t)$ [mU/L] denote plasma glucose and insulin concentrations at time t [min], respectively; $y(t)$ [1/min] represents insulin-excitability tissue glucose uptake activity; y_b [mg/dL] and I_b [mU/L] are basal glucose and insulin levels; x_0 [mg/dL] is the theoretical glycemia at $t = 0$ after the glucose bolus; τ_1 [1/min] is the insulin-independent glucose clearance rate; τ_2 [1/min] is the active insulin clearance rate; τ_3 [L/(min² mU)] quantifies insulin-stimulated uptake ability; τ_4 [1/min] is the decay rate of blood insulin; τ_5 [mg/dL] is the target glucose level; x_6 [mU dL/(L mg min)] is the pancreatic release rate; and x_7 [mg/dL/min] represents the plasma insulin above basal at $t = 0$.

In this article, we introduce a novel glucose–insulin regulatory model formulated with the Caputo–Fabrizio (CF) operator, which explicitly incorporates fading memory effects without singular kernels. This work builds upon recent advances in fractional glucose–insulin modeling [5, 6, 32]. The system couples blood glucose concentration $x(t)$, insulin level $z(t)$, and an auxiliary control variable $u(t)$, with $y(t)$ representing insulin-mediated glucose uptake. The governing equations are given by

$$\begin{aligned} {}^{\text{CF}}\mathcal{D}_{0,t}^\varepsilon x(t) &= -(\tau_1 + y(t)) x(t) + \tau_1 x_b, \\ {}^{\text{CF}}\mathcal{D}_{0,t}^\varepsilon y(t) &= -\tau_2 y(t) + \tau_3(z(t) - z_b), \\ {}^{\text{CF}}\mathcal{D}_{0,t}^\varepsilon z(t) &= \tau_4[x(t) - \tau_5]^+ u(t) - \tau_6(z(t) - z_b), \\ {}^{\text{CF}}\mathcal{D}_{0,t}^\varepsilon u(t) &= 1 - \varrho u(t), \end{aligned} \tag{1.2}$$

with initial conditions $x(0) = b_0$, $y(0) = 0$, and $z(0) = I_b$. The threshold function $[x(t) - \tau_5]^+$ is defined as $x(t) - \tau_5$ if $x(t) > \tau_5$, and 0 otherwise, while $u(t) = (1 - e^{-\varrho t})/\varrho > 0$ represents an auxiliary control evolution.

The objectives of this study are twofold: (i) To establish the existence and uniqueness of solutions to system (1.2) via fixed-point arguments, and (ii) to design and analyze a two-step Adams–Bashforth numerical method tailored to the CF operator, including convergence and stability results. Finally, numerical simulations are presented to validate the theoretical framework and illustrate the physiological relevance of CF-based fractional modeling in capturing glucose–insulin dynamics.

The remainder of this paper is structured as follows. Section 2 presents essential preliminaries and mathematical definitions related to the Caputo–Fabrizio (CF) fractional derivative and its associated integral operator. In Section 3, we establish the existence and uniqueness of solutions for the proposed CF-based glucose–insulin model using fixed-point theory under suitable Lipschitz and boundedness conditions. Section 4 introduces the numerical formulation based on a two-step Adams–Bashforth scheme adapted to the CF operator, while Section 5 provides a detailed convergence and stability analysis of the proposed algorithm. In Section 6, a stochastic extension of the CF model is developed to incorporate physiological randomness arising from meal intake and hormonal variability. Section 7 illustrates computational experiments and numerical results demonstrating the impact of the fractional order on glucose–insulin dynamics.

Finally, Section 8 discusses the biological and computational implications of the results, and Section 9 concludes the paper with key findings and future research directions.

2. Preliminaries

Let us begin by recalling the Caputo fractional derivative of order $\alpha \in (n-1, n)$ for $n \in \mathbb{N}$, as formulated in [31]. For a function $f(t)$ possessing sufficient smoothness, the classical Caputo derivative is defined by

$${}^C \mathcal{D}_t^\alpha (f(t)) = \frac{1}{\Gamma(n-\alpha)} \int_0^t \frac{f^{(n)}(\vartheta)}{(t-\vartheta)^{\alpha-n+1}} d\vartheta.$$

Now, let $\mathcal{L}^2(c, d)$ denote the Hilbert space of square-integrable functions over the interval (c, d) . The Sobolev space $\mathcal{H}^1(c, d)$ is defined as:

$$\mathcal{H}^1(c, d) = \{f \in \mathcal{L}^2(c, d) \mid f' \in \mathcal{L}^2(c, d)\}.$$

Assume $f \in \mathcal{H}^1(c, d)$ and $0 < \varepsilon < 1$. The Caputo–Fabrizio (CF) fractional derivative, as introduced in [14], is expressed by:

$${}^{\text{CF}} \mathcal{D}_t^\varepsilon (f(t)) = \frac{M(\varepsilon)}{1-\varepsilon} \int_c^t f'(\vartheta) \exp\left(-\frac{\varepsilon(t-\vartheta)}{1-\varepsilon}\right) d\vartheta,$$

where $M(\varepsilon)$ is a normalization function satisfying $M(0) = M(1) = 1$.

In the case that $f \notin \mathcal{H}^1(c, d)$, the CF derivative is defined using an alternative integral form:

$${}^{\text{CF}} \mathcal{D}_t^\varepsilon (f(t)) = \frac{\varepsilon M(\varepsilon)}{1-\varepsilon} \int_c^t (f(t) - f(\vartheta)) \exp\left(-\frac{\varepsilon(t-\vartheta)}{1-\varepsilon}\right) d\vartheta.$$

Remark 2.1 ([14]). By introducing the transformation $\varepsilon = \frac{1}{1+\eta}$ with $\eta > 0$, the above representation simplifies, and the CF derivative becomes

$${}^{\text{CF}} \mathcal{D}_t^\varepsilon (f(t)) = \frac{N(\varepsilon)}{\varepsilon} \int_c^t f'(\vartheta) \exp\left(-\frac{\varepsilon(t-\vartheta)}{1-\varepsilon}\right) d\vartheta,$$

where $N(\varepsilon) = M(\varepsilon)/(1-\varepsilon)$ is the rescaled normalization satisfying $N(0) = N(\infty) = 1$.

Remark 2.2 ([14]). It is known that the exponential kernel in the CF derivative reduces to the Dirac delta function as $\varepsilon \rightarrow 0$, i.e.,

$$\lim_{\varepsilon \rightarrow 0} \frac{1}{\varepsilon} \exp\left(-\frac{t-\vartheta}{\varepsilon}\right) = \delta(t-\vartheta),$$

where $\delta(\cdot)$ denotes the Dirac distribution.

A modified form of the CF derivative, developed by Losada and Nieto [25], is given by:

$${}^{\text{CF}} \mathcal{D}_t^\varepsilon (f(t)) = \frac{(2-\varepsilon)M(\varepsilon)}{2(1-\varepsilon)} \int_c^t f'(\vartheta) \exp\left(-\frac{\varepsilon(t-\vartheta)}{1-\varepsilon}\right) d\vartheta.$$

For $0 < \varepsilon < 1$, the associated fractional integral is defined as:

$${}^{\text{CF}} I_t^\varepsilon (f(t)) = \frac{2(1-\varepsilon)}{(2-\varepsilon)M(\varepsilon)} f(t) + \frac{2\varepsilon}{(2-\varepsilon)M(\varepsilon)} \int_0^t f(\vartheta) d\vartheta.$$

From the requirement that ${}^{\text{CF}}I_t^\varepsilon$ inverts ${}^{\text{CF}}\mathcal{D}_t^\varepsilon$, it follows that:

$$\frac{2(1-\varepsilon)}{(2-\varepsilon)M(\varepsilon)} + \frac{2\varepsilon}{(2-\varepsilon)M(\varepsilon)} = 1,$$

leading to the simplification $M(\varepsilon) = \frac{2}{2-\varepsilon}$ for $\varepsilon \in (0, 1)$.

Remark 2.3. Substituting $M(\varepsilon) = 2/(2-\varepsilon)$ into the Losada–Nieto definitions yields the compact, singularity-free formulations below.

Definition 2.1 ([25]). Let $0 < \varepsilon < 1$ and $c = 0$ for the initial value problem considered in this work. The Caputo–Fabrizio fractional derivative without singular kernel is given by

$${}^{\text{CF}}\mathcal{D}_t^\varepsilon(f(t)) = \frac{1}{1-\varepsilon} \int_0^t f'(\vartheta) \exp\left(-\frac{\varepsilon(t-\vartheta)}{1-\varepsilon}\right) d\vartheta, \quad t \geq 0,$$

and the corresponding fractional integral is

$${}^{\text{CF}}I_t^\varepsilon(f(t)) = (1-\varepsilon)f(t) + \varepsilon \int_0^t f(\vartheta) d\vartheta, \quad t \geq 0.$$

3. Existence and uniqueness of solutions

Consider the nonlinear Caputo–Fabrizio fractional system (1.2), describing the dynamics of $x(t), y(t), z(t), u(t)$. For convenience, define the nonlinear operators:

$$\begin{aligned} \omega_1(x, y, t) &= -(\tau_1 + y(t))x(t) + \tau_1 x_b, \\ \omega_2(y, z, t) &= -\tau_2 y(t) + \tau_3(z(t) - z_b), \\ \omega_3(x, z, u, t) &= \tau_4[x(t) - \tau_5]^+ u(t) - \tau_6(z(t) - z_b), \\ \omega_4(u, t) &= 1 - \varrho u(t). \end{aligned}$$

Here, τ_i ($i = 1, \dots, 6$) are positive system parameters, while x_b, z_b are baseline constants. The operator $[\cdot]^+$ denotes the positive part.

3.1. Lipschitz and boundedness properties

(i) **For ω_1 .** Assume $y(t)$ is bounded, i.e. $|y(t)| \leq M_y$. For any x_1, x_2 ,

$$\begin{aligned} \|\omega_1(x_1, y, t) - \omega_1(x_2, y, t)\| &= \|-(\tau_1 + y(t))(x_1 - x_2)\| \\ &\leq (\tau_1 + M_y) \|x_1 - x_2\|. \end{aligned}$$

Hence, ω_1 is Lipschitz in x with constant $L_1 = \tau_1 + M_y$. Since $x(t)$ is bounded, ω_1 is also bounded: $\|\omega_1\| \leq k_1$.

(ii) **For ω_2 .** If $z(t)$ is bounded, then for any y_1, y_2 ,

$$\|\omega_2(y_1, z, t) - \omega_2(y_2, z, t)\| = \tau_2 \|y_1 - y_2\|.$$

Thus ω_2 is Lipschitz in y with constant $L_2 = \tau_2$ and bounded by k_2 .

(iii) **For ω_3 .** If $x(t), u(t)$ are bounded, then for any z_1, z_2 ,

$$\|\omega_3(x, z_1, u, t) - \omega_3(x, z_2, u, t)\| = \tau_6 \|z_1 - z_2\|.$$

So ω_3 is Lipschitz in z with constant $L_3 = \tau_6$ and bounded by k_3 .

(iv) **For ω_4 .** For any u_1, u_2 ,

$$\|\omega_4(u_1, t) - \omega_4(u_2, t)\| = \varrho \|u_1 - u_2\|.$$

Thus ω_4 is Lipschitz in u with constant $L_4 = \varrho$ and bounded by k_4 .

3.2. Picard operators and contraction mapping

Define the Banach space $\mathcal{X} = C([0, T]; \mathbb{R}^4)$ equipped with the supremum norm $\|\cdot\|_\infty$. Using the Caputo–Fabrizio fractional integral operator ${}^{\text{CF}}I_t^\varepsilon$, we define the Picard operators:

$$\begin{aligned}\mathcal{P}_1 x(t) &= x(0) + {}^{\text{CF}}I_t^\varepsilon \omega_1(x, y, t), \\ \mathcal{P}_2 y(t) &= y(0) + {}^{\text{CF}}I_t^\varepsilon \omega_2(y, z, t), \\ \mathcal{P}_3 z(t) &= z(0) + {}^{\text{CF}}I_t^\varepsilon \omega_3(x, z, u, t), \\ \mathcal{P}_4 u(t) &= u(0) + {}^{\text{CF}}I_t^\varepsilon \omega_4(u, t).\end{aligned}$$

For any two functions (x_1, y_1, z_1, u_1) and (x_2, y_2, z_2, u_2) in $\mathcal{X}$, using the Lipschitz properties and the CF integral representation, we obtain for the combined operator $\mathcal{P} = (\mathcal{P}_1, \mathcal{P}_2, \mathcal{P}_3, \mathcal{P}_4)$:

$$\|\mathcal{P}(\mathbf{Y}_1) - \mathcal{P}(\mathbf{Y}_2)\|_\infty \leq \frac{2L}{M(\varepsilon)} \left(\frac{1 - \varepsilon + \ell\varepsilon}{2 - \varepsilon} \right) \|\mathbf{Y}_1 - \mathbf{Y}_2\|_\infty,$$

where $L = \max\{L_1, L_2, L_3, L_4\}$ and L is a constant depending on the time horizon T .

Theorem 3.1. *Under the assumptions of boundedness and Lipschitz continuity of ω_i for $i = 1, \dots, 4$, the Caputo–Fabrizio system (1.2) admits a unique solution on $[0, T]$ for any finite $T > 0$, provided that*

$$\frac{2L}{M(\varepsilon)} \left(\frac{1 - \varepsilon + \ell\varepsilon}{2 - \varepsilon} \right) < 1.$$

The proof relies on Banach’s fixed point theorem applied to the Picard operator $\mathcal{P}$ constructed above.

Proof. The Picard operator $\mathcal{P}$ maps the complete metric space $\mathcal{X}$ into itself. For sufficiently small T (or under the contraction condition), $\mathcal{P}$ is a contraction. Banach’s fixed point theorem guarantees the existence of a unique fixed point, which corresponds to the unique solution of system (1.2). The contraction condition ensures uniqueness globally on $[0, T]$. $\square$

4. Numerical Caputo–Fabrizio algorithm

In this section, we present a computational scheme to approximate the solution of the nonlinear system (1.2) involving the Caputo–Fabrizio (CF) fractional derivative. Each equation can be rewritten using the fundamental theorem of calculus for CF operators as

$$\begin{aligned}x(t) - x(0) &= (1 - \varepsilon) \omega_1(x, y, t) + \varepsilon \int_0^t \omega_1(x, y, \xi) d\xi, \\ y(t) - y(0) &= (1 - \varepsilon) \omega_2(y, z, t) + \varepsilon \int_0^t \omega_2(y, z, \xi) d\xi,\end{aligned}$$

$$\begin{aligned} z(t) - z(0) &= (1 - \varepsilon) \omega_3(x, z, u, t) + \varepsilon \int_0^t \omega_3(x, z, u, \xi) d\xi, \\ u(t) - u(0) &= (1 - \varepsilon) \omega_4(u, t) + \varepsilon \int_0^t \omega_4(u, \xi) d\xi, \end{aligned}$$

where the nonlinearities are explicitly

$$\begin{aligned} \omega_1(x, y, t) &= -(\tau_1 + y(t)) x(t) + \tau_1 x_b, \\ \omega_2(y, z, t) &= -\tau_2 y(t) + \tau_3 (z(t) - z_b), \\ \omega_3(x, z, u, t) &= \tau_4 [x(t) - \tau_5]^+ u(t) - \tau_6 (z(t) - z_b), \\ \omega_4(u, t) &= 1 - \varrho u(t). \end{aligned}$$

Let the temporal mesh be $\{t_m = m\Delta : m = 0, 1, 2, \dots\}$ with step size Δ . At t_{m+1} we obtain

$$x(t_{m+1}) - x(0) = (1 - \varepsilon) \omega_1(x_m, y_m, t_m) + \varepsilon \int_0^{t_{m+1}} \omega_1(\cdot) d\xi,$$

and similarly for y, z, u . Subtracting the corresponding relations at t_m yields

$$\begin{aligned} x_{m+1} - x_m &= (1 - \varepsilon) \left(\omega_1(x_m, y_m, t_m) - \omega_1(x_{m-1}, y_{m-1}, t_{m-1}) \right) \\ &\quad + \varepsilon \int_{t_m}^{t_{m+1}} \omega_1(\cdot) d\xi, \\ y_{m+1} - y_m &= (1 - \varepsilon) \left(\omega_2(y_m, z_m, t_m) - \omega_2(y_{m-1}, z_{m-1}, t_{m-1}) \right) \\ &\quad + \varepsilon \int_{t_m}^{t_{m+1}} \omega_2(\cdot) d\xi, \\ z_{m+1} - z_m &= (1 - \varepsilon) \left(\omega_3(x_m, z_m, u_m, t_m) - \omega_3(x_{m-1}, z_{m-1}, u_{m-1}, t_{m-1}) \right) \\ &\quad + \varepsilon \int_{t_m}^{t_{m+1}} \omega_3(\cdot) d\xi, \\ u_{m+1} - u_m &= (1 - \varepsilon) \left(\omega_4(u_m, t_m) - \omega_4(u_{m-1}, t_{m-1}) \right) \\ &\quad + \varepsilon \int_{t_m}^{t_{m+1}} \omega_4(\cdot) d\xi. \end{aligned}$$

Approximating the integrals by the two-step Adams–Bashforth formula,

$$\int_{t_m}^{t_{m+1}} \omega_i(\cdot) d\xi \approx \frac{3\Delta}{2} \omega_i(\cdot, t_m) - \frac{\Delta}{2} \omega_i(\cdot, t_{m-1}), \quad i = 1, \dots, 4,$$

we obtain the final update scheme

$$\begin{aligned} x_{m+1} &= x_m + \Lambda \omega_1(x_m, y_m, t_m) + \Gamma \omega_1(x_{m-1}, y_{m-1}, t_{m-1}), \\ y_{m+1} &= y_m + \Lambda \omega_2(y_m, z_m, t_m) + \Gamma \omega_2(y_{m-1}, z_{m-1}, t_{m-1}), \\ z_{m+1} &= z_m + \Lambda \omega_3(x_m, z_m, u_m, t_m) + \Gamma \omega_3(x_{m-1}, z_{m-1}, u_{m-1}, t_{m-1}), \\ u_{m+1} &= u_m + \Lambda \omega_4(u_m, t_m) + \Gamma \omega_4(u_{m-1}, t_{m-1}), \end{aligned}$$

with coefficients

$$\Lambda = (1 - \varepsilon) + \frac{3\varepsilon\Delta}{2}, \quad \Gamma = (1 - \varepsilon) - \frac{\varepsilon\Delta}{2}.$$

This scheme constitutes a stable and efficient two-step predictor of Adams–Bashforth type tailored to the CF operator, suitable for simulating the nonlinear glucose–insulin dynamics described by system (1.2).

5. Convergence and stability analysis

This section establishes convergence and stability of the two-step CF–Adams–Bashforth scheme derived for (1.2). Let the exact solution be $(x(t), y(t), z(t), u(t))$ and recall the nonlinearities

$$\begin{aligned}\omega_1(x, y, t) &= -(\tau_1 + y(t)) x(t) + \tau_1 x_b, \\ \omega_2(y, z, t) &= -\tau_2 y(t) + \tau_3 (z(t) - z_b), \\ \omega_3(x, z, u, t) &= \tau_4 [x(t) - \tau_5]^+ u(t) - \tau_6 (z(t) - z_b), \\ \omega_4(u, t) &= 1 - \varrho u(t).\end{aligned}$$

Let $M_y := \sup_{t \in [0, T]} |y(t)|$ and assume the solution remains in a compact, positively invariant set so that the following hold with constants independent of $t \in [0, T]$:

(A1) ω_i are uniformly bounded: $|\omega_i| \leq N$ for $i = 1, \dots, 4$.

(A2) Lipschitz continuity in their state arguments on that set:

$$\begin{aligned}\|\omega_1(\mathbf{Y}) - \omega_1(\mathbf{Z})\| &\leq L_1 \|\mathbf{Y} - \mathbf{Z}\| \quad \text{in } x, \quad L_1 = \tau_1 + M_y, \\ \|\omega_2(\mathbf{Y}) - \omega_2(\mathbf{Z})\| &\leq L_2 \|\mathbf{Y} - \mathbf{Z}\| \quad \text{in } y, \quad L_2 = \tau_2, \\ \|\omega_3(\mathbf{Y}) - \omega_3(\mathbf{Z})\| &\leq L_3 \|\mathbf{Y} - \mathbf{Z}\| \quad \text{in } z, \quad L_3 = \tau_6, \\ \|\omega_4(\mathbf{Y}) - \omega_4(\mathbf{Z})\| &\leq L_4 \|\mathbf{Y} - \mathbf{Z}\| \quad \text{in } u, \quad L_4 = \varrho.\end{aligned}$$

Let the temporal grid be $t_m = m\Delta$ with step size $\Delta > 0$. The two-step scheme reads

$$\begin{aligned}x_{m+1} &= x_m + \Lambda \omega_1(x_m, y_m, t_m) + \Gamma \omega_1(x_{m-1}, y_{m-1}, t_{m-1}) + \tau_1^m, \\ y_{m+1} &= y_m + \Lambda \omega_2(y_m, z_m, t_m) + \Gamma \omega_2(y_{m-1}, z_{m-1}, t_{m-1}) + \tau_2^m, \\ z_{m+1} &= z_m + \Lambda \omega_3(x_m, z_m, u_m, t_m) + \Gamma \omega_3(x_{m-1}, z_{m-1}, u_{m-1}, t_{m-1}) + \tau_3^m, \\ u_{m+1} &= u_m + \Lambda \omega_4(u_m, t_m) + \Gamma \omega_4(u_{m-1}, t_{m-1}) + \tau_4^m,\end{aligned}\tag{5.1}$$

where

$$\Lambda = (1 - \varepsilon) + \frac{3\varepsilon\Delta}{2}, \quad \Gamma = (1 - \varepsilon) - \frac{\varepsilon\Delta}{2},$$

and τ_i^m denote local truncation terms.

Let $\mathbf{Y}(t) = (x, y, z, u)^\top$ be the exact solution evaluated at the grid. Define the local truncation error vector $\boldsymbol{\tau}^m = (\tau_1^m, \tau_2^m, \tau_3^m, \tau_4^m)^\top$ as the defect obtained by inserting $\mathbf{Y}(t_m)$ and $\mathbf{Y}(t_{m-1})$ into (5.1). Then, by the CF reformulation and the two-step Adams–Bashforth quadrature,

$$\|\boldsymbol{\tau}^m\|_\infty \leq C_{\text{loc}} \Delta^2, \quad C_{\text{loc}} = \varepsilon \max_{t \in [0, T]} \|\partial_t \omega(\mathbf{Y}(t), t)\|.$$

Hence, the scheme is *second-order consistent*.

Let the global error be $\mathbf{e}_m = \mathbf{Y}(t_m) - \mathbf{Y}_m$. Subtracting the numerical update from the exact CF integral form and using (A2) yields the vector inequality

$$\|\mathbf{e}_{m+1}\|_\infty \leq (1 + L\Lambda) \|\mathbf{e}_m\|_\infty + L\Gamma \|\mathbf{e}_{m-1}\|_\infty + C_{\text{loc}} \Delta^2,$$

where $L := \max\{L_1, L_2, L_3, L_4\}$. A standard two-step discrete Grönwall argument implies:

Theorem 5.1 (Convergence and stability of the CF–AB2 scheme). *Under assumptions (A1)–(A2) and for sufficiently small Δ so that*

$$1 - (L\Lambda + L\Gamma) > 0,$$

the numerical solution produced by (5.1) is stable in the uniform norm and converges to the exact solution with order $\mathcal{O}(\Delta^2)$:

$$\max_{0 \leq m \leq T/\Delta} \|\mathbf{e}_m\|_\infty \leq C \Delta^2,$$

for a constant C independent of Δ .

Proof. Iterate the two-step error recurrence. Since $\Lambda = (1 - \varepsilon) + \mathcal{O}(\Delta)$ and $\Gamma = (1 - \varepsilon) + \mathcal{O}(\Delta)$, pick Δ small enough such that $L(\Lambda + \Gamma) < 1$. Then the homogeneous part is root-stable and the forced part accumulates as $\mathcal{O}(\Delta^2)$. The discrete Grönwall inequality yields the stated bound. $\square$

Corollary 5.1 (Successive differences). *There exists $C_\varepsilon > 0$ such that, for each m ,*

$$\begin{aligned} \|x_{m+1} - x_m\|_\infty &\leq (1 - \varepsilon) \|\omega_1(x_m, y_m, t_m) - \omega_1(x_{m-1}, y_{m-1}, t_{m-1})\|_\infty + C_\varepsilon \Delta^2, \\ \|y_{m+1} - y_m\|_\infty &\leq (1 - \varepsilon) \|\omega_2(y_m, z_m, t_m) - \omega_2(y_{m-1}, z_{m-1}, t_{m-1})\|_\infty + C_\varepsilon \Delta^2, \\ \|z_{m+1} - z_m\|_\infty &\leq (1 - \varepsilon) \|\omega_3(x_m, z_m, u_m, t_m) - \omega_3(x_{m-1}, z_{m-1}, u_{m-1}, t_{m-1})\|_\infty + C_\varepsilon \Delta^2, \\ \|u_{m+1} - u_m\|_\infty &\leq (1 - \varepsilon) \|\omega_4(u_m, t_m) - \omega_4(u_{m-1}, t_{m-1})\|_\infty + C_\varepsilon \Delta^2. \end{aligned}$$

If the differences of the evaluated nonlinearities converge to 0 as $m \rightarrow \infty$, then the successive state increments also vanish: $\|x_{m+1} - x_m\|_\infty \rightarrow 0$, etc., and the numerical trajectory is Cauchy.

Remark (Step-size admissibility). A sufficient practical condition is $L(\Lambda + \Gamma) < 1$, i.e.

$$L(2(1 - \varepsilon) + \varepsilon\Delta) < 1,$$

which holds for all sufficiently small Δ . Since $L_1 = \tau_1 + M_y$, $L_2 = \tau_2$, $L_3 = \tau_6$, $L_4 = \varrho$, one may take $L = \max\{\tau_1 + M_y, \tau_2, \tau_6, \varepsilon\}$.

6. Stochastic extension of the CF model

Physiological glucose–insulin regulation is inherently influenced by random fluctuations arising from meal intake, hormonal variability, and sensor noise. To incorporate these stochastic effects, we extend the deterministic Caputo–Fabrizio (CF) system (1.2) into a stochastic fractional framework driven by Gaussian white noise. This approach builds upon recent stochastic fractional modeling efforts [8, 33].

6.1. Itô integration with the CF kernel

The interaction between the Itô stochastic integral and the CF fractional derivative requires careful treatment. Since the CF kernel is exponential (nonsingular) and the Itô integral is defined with respect to the Wiener process, the stochastic CF model can be interpreted as a system of stochastic integral equations where the deterministic fractional part (expressed via

the CF kernel) and the stochastic Itô term are additive. The exponential kernel ensures that the memory decays smoothly, and the Itô isometry can be applied in the analysis of mean-square convergence. Specifically, for the stochastic process $x(t)$ satisfying

$$x(t) = x(0) + (1 - \varepsilon)\omega_1(x, y, t) + \varepsilon \int_0^t \omega_1(x, y, s) ds + \int_0^t \sigma_1 x(s) dW_s,$$

the Itô integral $\int_0^t \sigma_1 x(s) dW_s$ is well-defined in the mean-square sense, and the CF memory operators are deterministic and differentiable, allowing standard fixed-point arguments in L^2 spaces.

6.2. Stochastic model formulation

Let $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathbb{P})$ be a complete probability space supporting a one-dimensional Wiener process W_t . The stochastic CF glucose–insulin model takes the form

$$\begin{cases} {}^{CF}D_t^\varepsilon x(t) = -(\tau_1 + y(t))x(t) + \tau_1 x_b + \sigma_1 x(t) \dot{W}_t, \\ {}^{CF}D_t^\varepsilon y(t) = -\tau_2 y(t) + \tau_3(z(t) - z_b) + \sigma_2 y(t) \dot{W}_t, \\ {}^{CF}D_t^\varepsilon z(t) = \tau_4[x(t) - \tau_5]^+ u(t) - \tau_6(z(t) - z_b) + \sigma_3 z(t) \dot{W}_t, \\ {}^{CF}D_t^\varepsilon u(t) = 1 - \varrho u(t) + \sigma_4 u(t) \dot{W}_t, \end{cases} \quad (6.1)$$

where $\sigma_i \geq 0$ ($i = 1, \dots, 4$) represent the intensities of multiplicative noise acting on the respective physiological processes. The terms $\dot{W}_t$ denote the formal time derivatives of Wiener processes, interpreted in the Itô sense. Setting $\sigma_i = 0$ for all i retrieves the deterministic CF system (1.2).

6.3. Existence and uniqueness for the stochastic system

The stochastic integral form of the CF derivative reads

$$x(t) = x(0) + (1 - \varepsilon)\omega_1(x, y, t) + \varepsilon \int_0^t \omega_1(x, y, s) ds + \int_0^t \sigma_1 x(s) dW_s,$$

and similarly for (y, z, u) . Applying standard fixed-point arguments in $L^2(\Omega; C([0, T]; \mathbb{R}^4))$, and under the same Lipschitz and boundedness assumptions on ω_i as in Section 3, together with

$$\mathbb{E} \|\sigma_i(Y_1) - \sigma_i(Y_2)\|^2 \leq L_{\sigma_i} \mathbb{E} \|Y_1 - Y_2\|^2,$$

the stochastic CF system (6.1) admits a unique mean-square continuous solution on $[0, T]$. The proof parallels Theorem 3.1, enhanced by the Itô isometry.

6.4. Numerical approximation: CF–ABM scheme

To approximate (6.1), we adopt a *stochastic Caputo–Fabrizio Adams–Bashforth–Milstein (CF–ABM) scheme*. For step size h and grid points $t_n = nh$, we have

$$x_{n+1} = x_n + \Lambda \omega_1(x_n, y_n, t_n) + \Gamma \omega_1(x_{n-1}, y_{n-1}, t_{n-1}) + \sigma_1 x_n \Delta W_n + \frac{1}{2} \sigma_1^2 x_n [(\Delta W_n)^2 - h],$$

and analogously for $y_{n+1}, z_{n+1}, u_{n+1}$,

(6.2)

where $\Lambda = (1 - \varepsilon) + \frac{3\varepsilon h}{2}$, $\Gamma = (1 - \varepsilon) - \frac{\varepsilon h}{2}$, and $\Delta W_n = W_{t_{n+1}} - W_{t_n}$. The first two deterministic terms correspond to the CF two-step Adams–Bashforth coefficients (Λ, Γ) , while the Itô–Milstein correction ensures strong mean-square convergence of order $\mathcal{O}(h)$.

6.5. Physiological interpretation

The stochastic extension models spontaneous variability in glucose uptake and insulin secretion resulting from random dietary, hormonal, and measurement fluctuations. Small noise amplitudes ($\sigma_i \ll 1$) preserve deterministic equilibrium stability, whereas moderate noise levels induce intermittent oscillations or altered convergence rates—consistent with observed physiological variability. Hence, the stochastic CF framework offers a realistic and robust representation of metabolic regulation that bridges deterministic memory effects and physiological randomness.

Future work may integrate hybrid stochastic–optimal control strategies for system (6.1), estimate noise intensities σ_i from clinical data, and investigate stochastic stability through Lyapunov functionals compatible with the CF kernel. Extending the formulation to time-varying delays or random fractional orders $\varepsilon(t)$ could further enhance model flexibility and predictive accuracy.

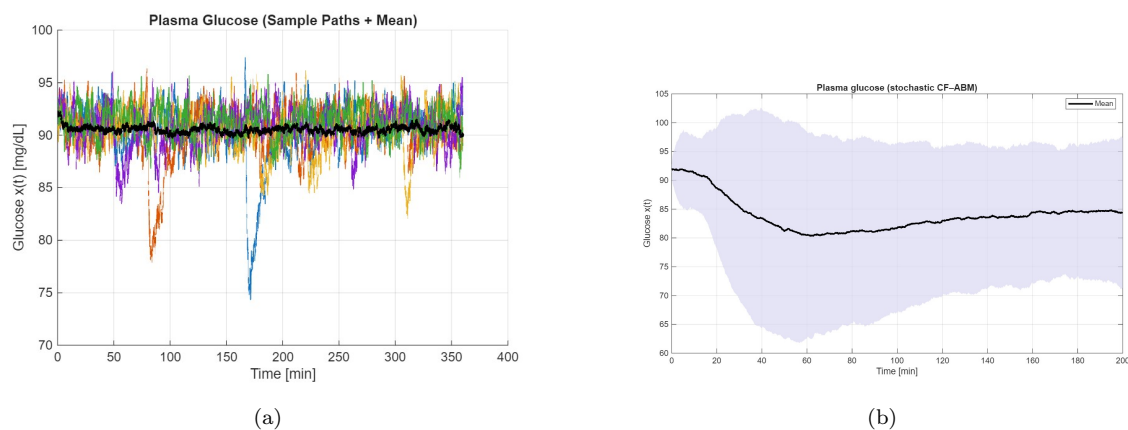


Figure 1. Stochastic CF simulation under mild noise $\sigma_i = 0.1$ showing glucose and insulin trajectories.

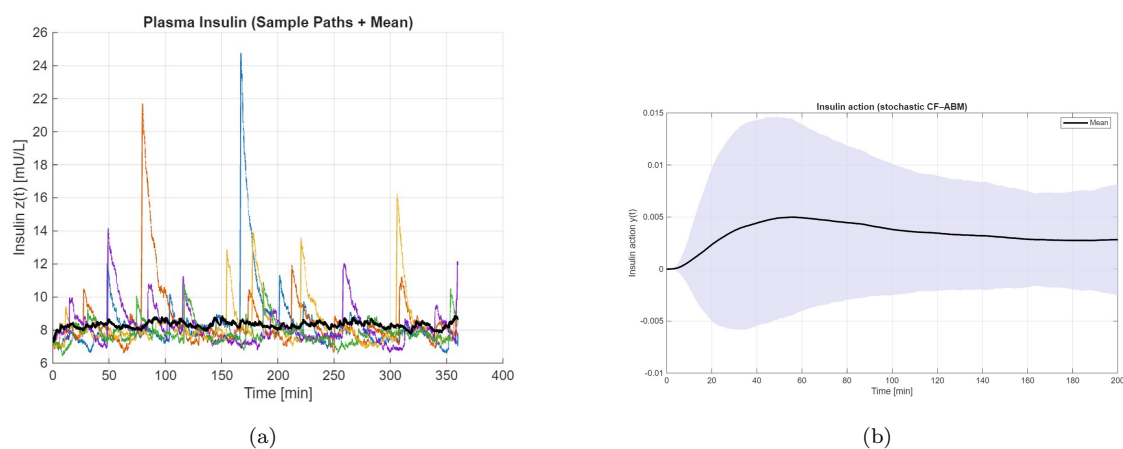


Figure 2. Influence of moderate stochastic intensity $\sigma_i = 0.3$ on system dynamics.

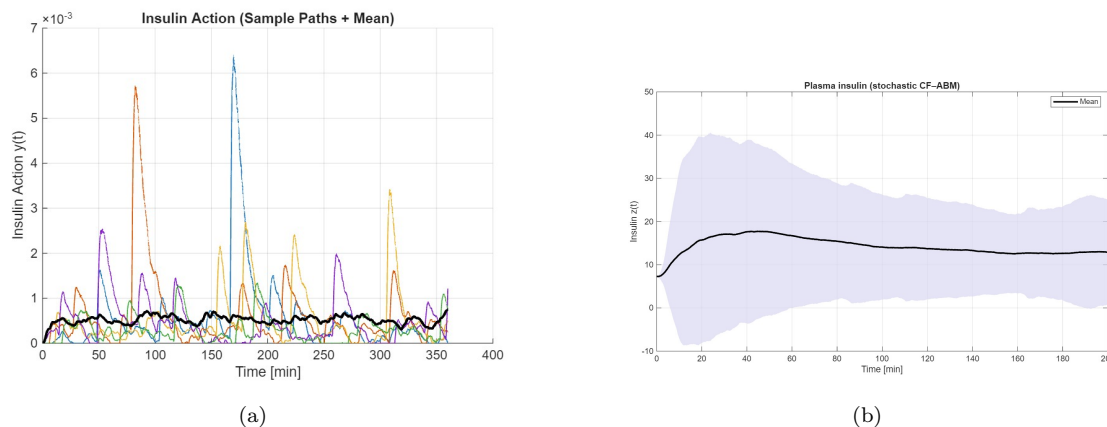


Figure 3. Emergence of intermittent oscillations for $\sigma_i = 0.6$.

7. Computational experiments

We report numerical simulations of the fractional-order glucose–insulin model (1.2) using the discretization scheme from Section 4. Unless stated otherwise, the fractional order satisfies $\varepsilon \in (0, 1)$, the step size $h > 0$, and the initial data are prescribed as

$$x(0) = x_0, \quad y(0) = y_0, \quad z(0) = z_0, \quad u(0) = u_0,$$

with baseline levels x_b and z_b and physiological parameters $\tau_1, \dots, \tau_6 > 0$.

Table 1. Assigned parameters for simulation.

Symbol	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	x_0	z_0
Preset value	0.03082	0.02093	1.062×10^{-5}	0.3	94	0.3349×10^{-2}	92	7.3

Discrete procedure. Given two consecutive time steps $(x_{n-1}, y_{n-1}, z_{n-1}, u_{n-1})$ and (x_n, y_n, z_n, u_n) , the next state $(x_{n+1}, y_{n+1}, z_{n+1}, u_{n+1})$ is computed via the Caputo–Fabrizio Adams–Bashforth discretization derived in Section 4, where the threshold operator is defined by

$$[x_n - \tau_5]^+ = \max\{x_n - \tau_5, 0\}.$$

For clinically meaningful parameter sets, the system admits a stable equilibrium near $(x_b, 0, z_b)$ with $u \approx 1/\varepsilon$, confirming that the CF memory kernel yields smooth exponential decay and stable convergence toward the basal steady state.

Numerical setup. Simulations were performed for fractional orders $\varepsilon = 1, 0.98, 0.95, 0.9, 0.85$ (note: $\varepsilon = 1$ corresponds to the integer-order case), illustrating how decreasing ε intensifies the memory effect, delays the response, and smooths the oscillatory transients in glucose and insulin levels. Each simulation was conducted for a time horizon of $T = 200$ minutes with step size $h = 0.01$.

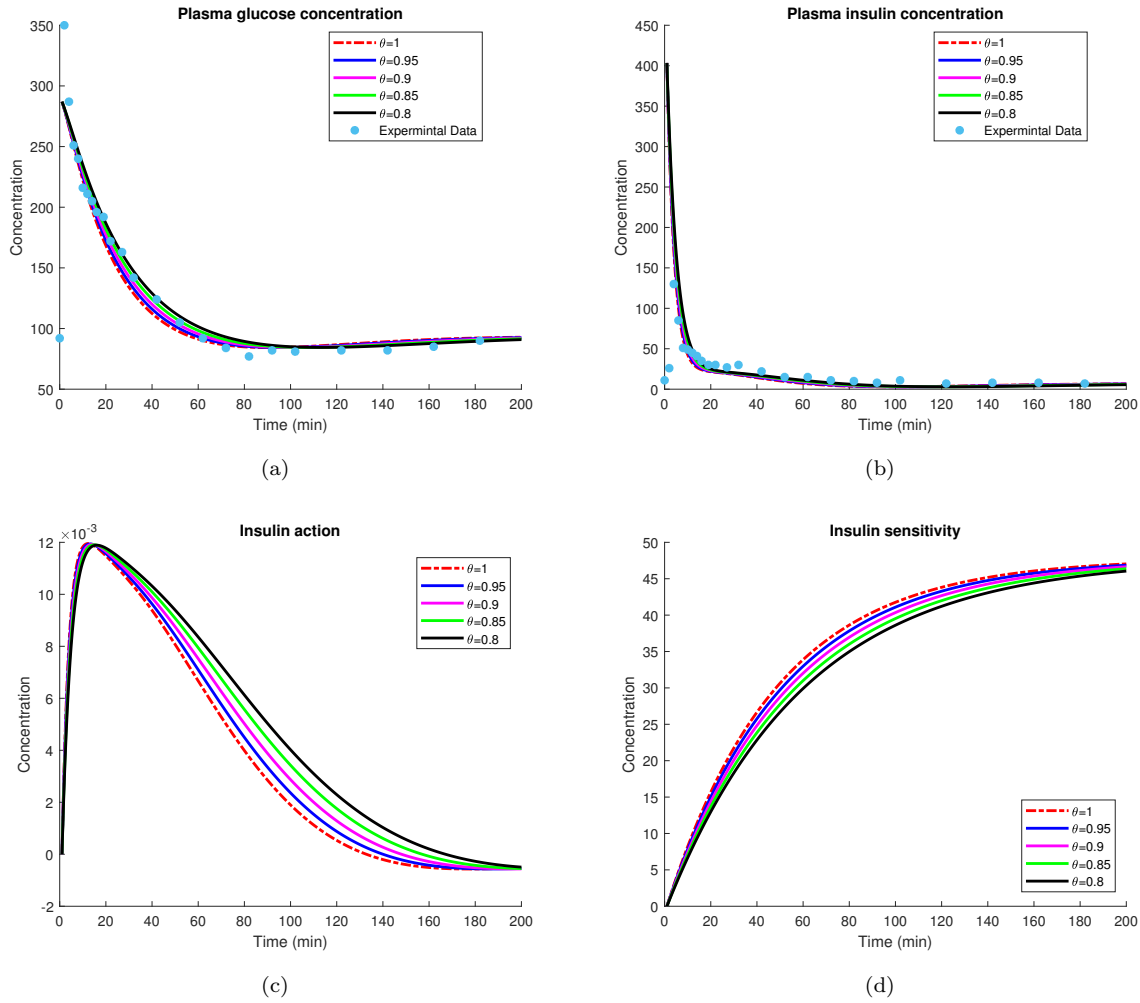


Figure 4. Time evolution of the state variables (a) plasma glucose $x(t)$ [mg/dL], (b) plasma insulin $z(t)$ [mU/L], (c) insulin action $y(t)$ [1/min], and (d) auxiliary control $u(t)$ for Subject 1 under different fractional orders $\varepsilon = 1, 0.98, 0.95, 0.9$. The fractional memory attenuates peak amplitudes and delays the return to equilibrium, reflecting realistic metabolic adaptation.

Decreasing the fractional order ε enhances the system's memory and smoothness, producing delayed glucose decay and prolonged insulin activity. For $\varepsilon \rightarrow 1$, the model reproduces classical integer-order dynamics, while smaller ε values exhibit persistent tails and slower recovery, in alignment with experimental glucose tolerance data. These findings validate the Caputo–Fabrizio framework's ability to model fading memory and physiological hysteresis more accurately than integer-order formulations.

8. Discussion

The Caputo–Fabrizio (CF) derivative furnishes a nonsingular, exponentially fading memory that aligns naturally with physiological lags in glucose uptake and insulin action. Within the proposed system (1.2), this memory structure yields responses that are both numerically stable and biologically interpretable: Insulin reacts to excursions in $x(t)$ in a delayed yet smooth

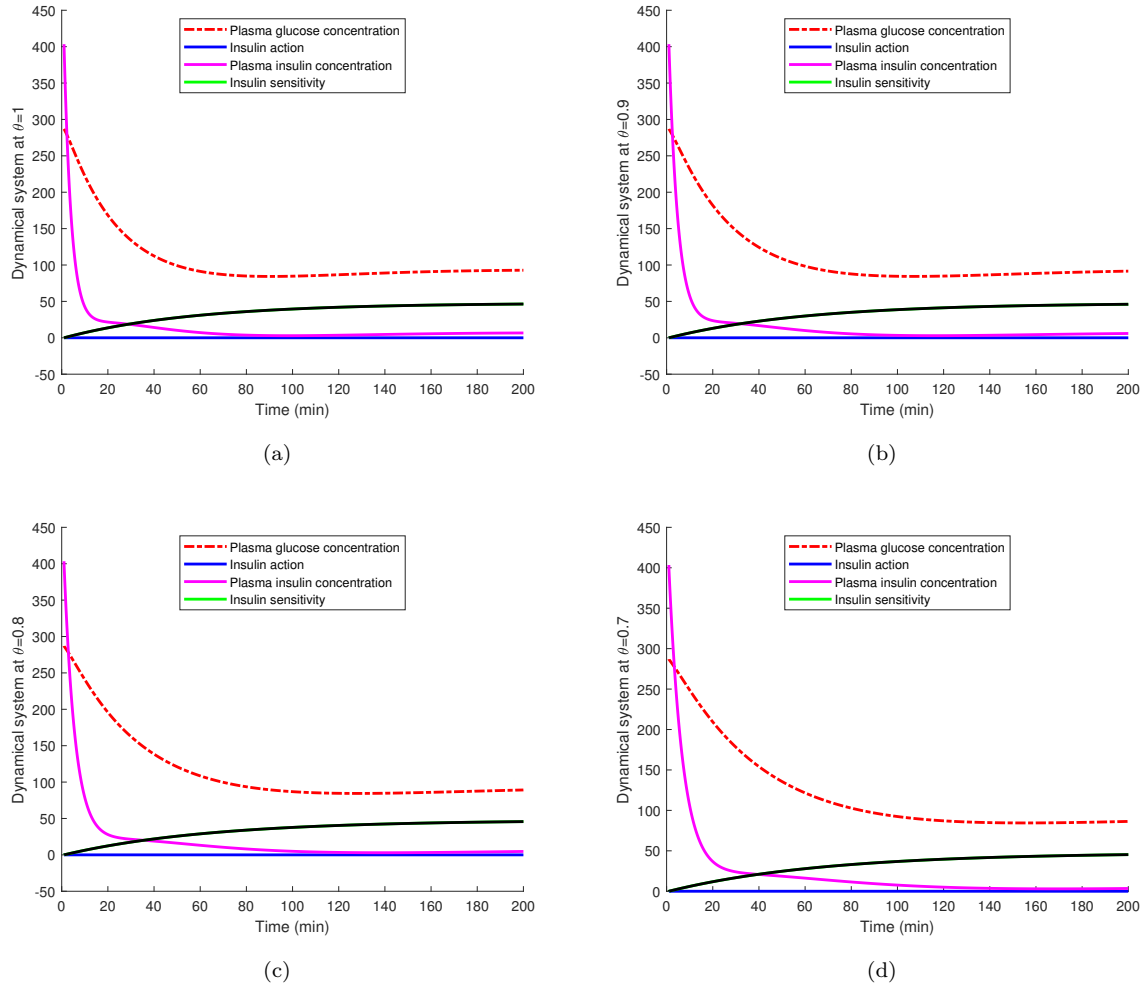


Figure 5. Global dynamical behavior of model (1.2) for fractional orders (a) $\varepsilon = 1.0$, (b) $\varepsilon = 0.95$, (c) $\varepsilon = 0.9$, and (d) $\varepsilon = 0.85$. The results confirm that decreasing ε increases memory depth, delays transient decay, and produces smoother, physiologically realistic trajectories.

manner, while glucose decays without the spurious stiffness often induced by power-law kernels. Parameter groupings admit clear physiological meanings—for example, τ_1 governs basal glucose turnover toward x_b , τ_2 and τ_3 couple insulin and z -dynamics to deviations from z_b , and (τ_4, τ_5, τ_6) regulate the activation threshold and clearance in the z -equation—facilitating model calibration and sensitivity analysis.

On the numerical side, the tailored two-step Caputo–Fabrizio Method discretization preserves the CF memory through the coefficients Λ and Γ , while achieving second-order accuracy with respect to the time step. Under the mild admissibility condition $L(\Lambda + \Gamma) < 1$ (where $L = \max\{\tau_1 + M_y, \tau_2, \tau_6, \varepsilon\}$ and $M_y = \sup_t |y(t)|$), the scheme is zero-stable and convergent, as verified through error recursion and discrete Grönwall analysis. In practical terms, this ensures robust numerical performance across a wide range of $\varepsilon \in (0, 1)$ and parameter values, enabling reliable downstream tasks such as patient-specific parameter estimation, feedback or optimal control (through $u(t)$), and comparative analysis of therapeutic strategies.

The stochastic extension presented in Section 6 provides a natural framework for incorpo-

rating physiological randomness. The interaction between the Itô integral and the CF kernel is well-defined due to the exponential memory structure, which ensures that the deterministic fractional part and the stochastic Itô term are additive. This allows the application of standard stochastic analysis techniques while preserving the biological interpretability of the model. Recent studies have successfully applied similar stochastic fractional approaches to various biological systems [8, 33].

Taken together, the CF formulation offers an effective balance between physiological fidelity—via smooth fading memory and interpretable thresholds—and computational tractability—through explicit two-step updates and $\mathcal{O}(h^2)$ convergence. This synergy supports model-based personalization and control synthesis while avoiding numerical artifacts commonly encountered in singular-kernel fractional models. Future research may extend this framework by incorporating stochastic forcing, time-varying parameters, or optimal-control constraints, thereby further bridging model predictions with clinical and experimental observations.

9. Conclusion

In this study, we have applied the Caputo–Fabrizio (CF) fractional derivative within a two-step Adams–Bashforth formulation to model glucose–insulin dynamics as described in system (1.2). The resulting numerical scheme preserves the exponential memory kernel intrinsic to the CF operator, thereby capturing smooth fading-memory effects while avoiding singular behavior typical of power-law kernels. The discretization was proven to be consistent, second-order accurate in the time step h , and stable under a mild admissibility condition.

Numerical experiments confirmed that the proposed method reproduces physiologically realistic trajectories for glucose $x(t)$, insulin $z(t)$, insulin action $y(t)$, and the auxiliary control variable $u(t)$. These results highlight that CF-based fractional modeling provides both theoretical rigor and practical reliability in simulating metabolic regulation.

The stochastic extension demonstrates how physiological randomness can be incorporated into the CF framework, with the exponential kernel ensuring a well-defined interaction with Itô calculus. This opens avenues for more realistic patient-specific modeling.

Overall, the developed framework offers a promising computational tool for parameter estimation, patient-specific personalization, and the design of optimal therapeutic control strategies. Future research will focus on extending this deterministic framework to stochastic CF models, incorporating measurement noise and time-varying parameters, thereby enhancing its predictive and clinical applicability.

Data availability. The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests. The authors declare that they have no competing interests.

Authors' contributions. All authors read and approved the final manuscript.

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