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Analytical and Numerical Investigation of a Caputo Fractional-Order Alzheimer's Disease Model Using the Chebyshev–Galerkin Spectral Method

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Abstract

Alzheimer's disease is a progressive neuro-degenerative disease characterised by loss of neurons, accumulation of toxic amyloid, and persistent neuroinflammatory responses. This study developed a nonlinear multidimensional mathematical based on Caputo's multidimensional derivative to describe the interactions between healthy neurons, toxic protein groups, and neuroinflammatory reactions. The proposed model incorporates saturation effects to represent limited amyloid-β clearance and captures the long-term memory behavior of the disease Local stability of the system is investigated using fractional order stability theory, while a Chebyshev Galerkin spectral method is applied to obtain precise numerical solutions with excessive computational efficiency and excellent long-term stability. Numerical simulations show that decreasing the fractional order introduces memory- induced damping, delays neuronal degeneration, and suppresses oscillatory inflammatory behavior. The proposed analytical numerical framework provides valuable insight into the impact of fractional memory on Alzheimer's disease progression and offers an efficient method for studying complex neurodegenerative systems.

Keywords: Alzheimer's disease, Caputo fractional derivative, Fractional-order dynamical system, Chebyshev Galerkin spectral method; Local stability analysis, Neurodegeneration.

1 Introduction

Neurodegenerative diseases are one of the leading causes of disability in the world [1-3] as they progressively damage the neurons leading to irreversible cognitive impairment and loss of functional independence. Alzheimer's disease, the most common form of dementia, is characterised, toxic amyloid-β aggregates and persistent neuroinflammatory reactions. Due to the complex interactions between these biological processes, the progression of Alzheimer's disease exhibits nonlinear dynamics with significant memory- dependent behavior that cannot be adequately described by the conventional differential equations of the integers.

For modeling biological systems with memory and inherited traits, fractional calculus has become a useful mathematical framework [2,5]. Fractional derivatives are especially useful for depicting chronic neurodegenerative processes because, in contrast to classical derivatives, they take into account the impact of past states on the dynamics of the current system. The Caputo fractional derivative is one of the most

popular fractional operators since it offers a significant physical interpretation of memory effects and is compatible with classical initial conditions [1,2]. According to recent research, fractional- order models are more accurate than integer-order models at simulating gradual neuronal degeneration, prolonged neuroinflammatory activity, and delayed amyloid-β clearance.

Inspired by these findings, this work uses the Caputo fractional derivative to create a nonlinear fractional-order model for Alzheimer's disease. The suggested model incorporates saturation effects related to amyloid clearance and explains the relationships between neuroinflammatory responses, hazardous amyloid-β clumps, and healthy neurons. To understand how fractional memory affects the course of the disease, the system's local stability is examined. Because of its outstanding long-term numerical stability, exponential convergence, and great computing efficiency, the Chebyshev-Galerkin spectral approach is used to produce accurate numerical solutions [3,4,9,10]. The suggested analytical and numerical framework highlights the significance of memory effects in neurodegenerative modeling and offers a dependable method for examining the long-term dynamics of Alzheimer's disease.

2 Literature Review

Mathematical modeling has emerged as a robust framework for elucidating the complex, multifactorial progression of Alzheimer's disease. Nisar and Farman [1] developed a Caputo fractional-order model to investigate disease dynamics, demonstrating that fractional operators effectively capture memory-dependent neurodegeneration. Complementing this, Yadav et al. [2] analyzed a fractal-fractional Alzheimer's disease model based on the Caputo derivative, further demonstrating that fractional-order models provide a more realistic representation of disease progression than classical integer-order models by incorporating hereditary and long-term memory effects [2]. Recently Mehmood et al. In order to enhance the computational analysis of disease dynamics [6] proposed a Physics- Informed Neural Network (PINN) framework for a fractional- order Alzheimer's disease model, combining equilibrium analysis with numerical investigations. These studies highlight the growing importance of fractional calculus in modeling complex neurodegenerative processes.

Concurrently, research has focused on developing accurate numerical methods for solving fractional differential equations. Ali [3] demonstrated the effectiveness of Chebyshev spectral methods for nonlinear fractional biological models, while Saad and Khirallah [4] proposed a spectral collocation approach with high numerical accuracy for Caputo-type fractional equations. Kanwal et al. [7] introduced an efficient numerical scheme for variable-order fractional problems, whereas Gutleb and Carrillo [9] and Nemati and Torres [10] advanced spectral approximation techniques for fractional differential systems. Despite these advances, the combined application of a Caputo fractional-order Alzheimer's disease model, rigorous local stability analysis, and the Chebyshev–Galerkin spectral method remains relatively unexplored.

Motivated by these research gaps, we propose a nonlinear Caputo fractional order dynamical system to describe the progression of Alzheimer's disease with inherent memory effects. The model captures the interactions among healthy neurons, toxic amyloid-amyloid-β aggregates, and neuroinflammatory responses while incorporating saturation terms to represent limited amyloid clearance. The fractional-order parameter serves as a key factor governing memory strength and the long-term dynamics of the system.

3 Mathematical Modeling and Preliminaries

To capture the long-term memory and hereditary characteristics inherent in the progression of Alzheimer's

disease, we employ fractional calculus through the Caputo fractional derivative. Owing to its ability to incorporate memory-dependent dynamics while preserving classical initial conditions, the Caputo fractional derivative provides an appropriate mathematical framework for modeling the interactions among healthy neurons, toxic amyloid-β aggregates, and the neuroinflammatory response.

Definition 2.1 (Caputo Fractional Derivative).

Let $f:[0,T]\to\mathbb{R}$ be a sufficiently smooth function. For $0<\alpha\leq 1$, the Caputo fractional derivative of order α is defined by

$$CD_t^{\alpha}f(t)=\frac{1}{\Gamma(1-\alpha)}\int_0^t\frac{f'(s)}{(t-s)^{\alpha}}ds, \tag{1}$$

where $\Gamma(\cdot)$ denotes the Gamma function and $f'(s)$ is the first-order derivative of $f(s)$. The fractional-order parameter α characterizes the memory effect of the above system. When $\alpha=1$, the Caputo fractional derivative reduces to the classical first-order derivative, whereas $0<\alpha<1$ accounts for the nonlocal memory effects that govern the long-term evolution of Alzheimer's disease.

3.1 Fractional-Order Alzheimer's Disease Model

Based on the interactions among healthy neurons, toxic amyloid- β aggregates, and the neuroinflammatory response, we formulate a fractional-order Alzheimer's discase model using the Caputo fractional derivative. The model incorporates neuronal regeneration, amyloid- β production and clearance, and inflammation-mediated neuronal damage to describe the progression of Alzheimer's disease. By employing the fractional-order operator, the model captures the memory-dependent characteristics of neurodegeneration and provides a more realistic representation of the long-term disease dynamics.

The governing system is given by

$$\begin{cases} {}^{C}D_t^{\alpha}H(t)=rH(t)\left(1-\dfrac{H(t)}{K}\right)-\beta H(t)\Lambda(t)-\delta H(t)I(t),\\ {}^{C}D_t^{\alpha}\Lambda(t)=\eta H(t)\Lambda(t)-\dfrac{\mu\Lambda(t)}{1+\kappa\Lambda(t)}-\gamma\Lambda(t)I(t),\\ {}^{C}D_t^{\alpha}I(t)=\sigma\Lambda(t)-\omega I(t). \end{cases} \tag{2}$$

subject to the initial conditions

$$H(0)=H_0>0, A(0)=A_0\geq 0, I(0)=I_0\geq 0.$$

where ${}^{C}D_t^{\alpha}$ denotes the Caputo fractional derivative of order $0<\alpha\leq 1$, and the variables are defined as follows:

- $H(t)$: Healthy neuron population.
- $A(t)$: Concentration of toxic amyloid-β aggregates.
- $I(t)$: Neuroinflammatory response level (e.g., activated microglia).

The fractional-order parameter satisfies $0<\alpha\leq 1$, where $\alpha=1$ corresponds to the classical integer-order model, while $0<\alpha<1$ characterizes the memory effects associated with the progression of Alzheimer's disease. The proposed model 2 serves as the basis for the theoretical analysis and numerical simulations presented in the subsequent sections.

Table 1: Parameter Definitions and Typical Ranges

Parameter	Biological Meaning	Typical Range
r	Healthy neuron regeneration rate	[0.1, 1.0]
K	Carrying capacity of healthy neurons	$[10^4, 10^6]$
β	Amyloid-β induced neuronal damage rate	[0.01, 0.5]
γ	Neuroprotective effect of regulated neuroinflammation	[0.01, 0.3]
μ	Natural neuronal death rate	[0.001, 0.1]
η	Amyloid-β production rate	[0.05, 1.0]
δ	Maximum amyloid-β clearance rate	[0.1, 2.0]
κ	Saturation coefficient for amyloid-β clearance	[0.01, 0.5]
ρ	Inflammation-mediated amyloid-β removal rate	[0.01, 0.5]
σ	Natural amyloid-β degradation rate	[0.01, 0.5]
ω	Neuroinflammation decay rate	[0.05, 1.0]
α	Fractional-order (memory index)	$0 < \alpha \leq 1$

Note: The parameter ranges represent biologically plausible values reported in the neurodegenerative disease modeling literature. These values are adopted as baseline estimates for the numerical simulations and may be further refined through parameter estimation using experimental or clinical data.

3.2 Existence and Uniqueness

Since the nonlinear operator associated with the proposed Caputo fractional-order Alzheimer's disease model satisfies the contraction (Lipschitz) condition on the considered domain, the Banach Fixed Point Theorem guarantees the existence and uniqueness of the local solution of the system.

Theorem (Existence and Uniqueness).

Assume that the nonlinear functions $f(H, A, I), g(H, A, I)$, and $h(H, A, I)$ are continuous on the domain

$$\Omega = [0, T] \times D,$$

where

$$D = \{(H, A, I) \in \mathbb{R}^3 : |H| \leq M, |A| \leq M, |I| \leq M\}, \quad (5)$$

and satisfy the Lipschitz condition with Lipschitz constant L. If

$$\frac{LT^{\alpha}}{\Gamma(\alpha + 1)} < 1,$$

then the Caputo fractional-order Alzheimer's disease model admits a unique solution on the domain Ω.

3.3 Equilibrium Points

The equilibrium points of the proposed Caputo fractional- order Alzheimer's disease model are obtained by setting the fractional derivatives to zero. Therefore, the steady-state solutions satisfy

$$^{C}D_t^{\alpha} H(t) = 0, \; ^{C}D_t^{\alpha} A(t) = 0, \; ^{C}D_t^{\alpha} I(t) = 0.$$

Accordingly, the equilibrium states are determined by solving the correspondence nonlinear algebraic system obtained from the governing equations. The model admits a disease-free equilibrium and a disease-endemic equilibrium, representing the absence and persistence of Alzheimer's disease progression, respectively. These equilibrium points serve as the basis for the local stability analysis presented in the following section.

3.4 Local Stability Analysis

The local stability of the proposed Caputo fractional-order Alzheimer's disease model is examined by linearizing the system around an equilibrium point $E^* = (H^*, A^*, I^*)$. Let

$$f(H, A, I) = rH\left(1 - \frac{H}{K}\right) - \beta HA - \delta HI, \tag{3}$$

$$g(H, A, I) = \eta HA - \frac{\mu A}{1 + \kappa A} - \gamma AI, \tag{4}$$

$$h(H, A, I) = \sigma A - \omega I. \tag{5}$$

The Jacobian matrix of the above system evaluated at the equilibrium point E^* is

$$J(E^*) = \begin{bmatrix} r\left(1 - \frac{2H^*}{K}\right) - \beta A^* - \delta I^* & -\beta H^* & -\delta H^* \\ \eta A^* & \eta H^* - \frac{\mu}{(1 + \kappa A^*)^2} - \gamma I^* & -\gamma T^* \\ 0 & \sigma & -\omega \end{bmatrix}.$$

The corresponding characteristic equation is

$$\det\left(\lambda I - J(E^*)\right) = 0,$$

where λ denotes the eigenvalues of the Jacobian matrix. According to Matignon's stability criterion, the equilibrium point E^* is locally asymptotically stable if all cigenvalues satisfy

$$|\arg(\lambda_i)| > \frac{\alpha\pi}{2}, i = 1,2,3,$$

where $0 < \alpha \leq 1$ is the fractional order. Therefore, the equilibrium point E^* remains locally asymptotically stable whenever the above condition is satisfied. Otherwise, the equilibrium becomes unstable. The theoritical stability results are further verified through numerical simulations using the Chebyshev-Galerkin Spectral method.

4 Chebyshev-Galerkin Spectral Method

To achieve precise numerical solutions of the proposed Caputo fractional-order Alzheimer's disease model, the Chebyshev-Galerkin spectral method is utilized. Spectral methods are widely recognized for their high-order accuracy and rapid convergence when approximating smooth solutions. In comparison with traditional finite-difference methods, the Chebyshev-Galerkin method offers better numerical stability and greater computational efficiency, rendering it especially well-suited for long-term simulations of memory-dependent fractional systems. Let $A_N(s)$ represent the Chebyshev polynomials of the first kind, defined on the interval [-1, 1]. The approximate solutions for the state variables are represented using truncated Chebyshev series .

$$H_N(s) = \sum_{i=0}^{N} a_i T_i(s), A_N(s) = \sum_{i=0}^{N} b_i T_i(s), I_N(s) = \sum_{i=0}^{N} c_i T_i(s) \tag{6}$$

where a_i, b_i and c_i are the unknown spectral coefficients. Substituting the above approximations into the governing fractional-order system yields the corresponding residual functions,

$$R_H(s) = {}^{C}D_t^{\alpha} H_N(s) - \left[rH_N\left(1 - \frac{H_N}{K}\right) - \beta H_N A_N - \delta H_N I_N \right] \quad (7)$$

$$R_A(s) = {}^{C}D_t^{\alpha} A_N(s) - \left[\eta H_N A_N - \frac{\mu A_N}{1 + \kappa A_N} - \gamma A_N I_N \right] \quad (8)$$

$$R_I(s) = {}^{C}D_t^{\alpha} I_N(s) - [\sigma A_N - \omega I_N]. \quad (9)$$

According to the Galerkin formulation, the above residuals are orthogonal to the Chebyshev basis functions with respect to the weight function

$$w(s) = \frac{1}{\sqrt{1 - s^2}}.$$

Hence, the Galerkin conditions are given by

$$\int_{-1}^{1} R_H(s) T_j(s) w(s) ds = 0, \quad j = 0,1, \dots, N,$$

$$\int_{-1}^{1} R_A(s) T_j(s) w(s) ds = 0, \quad j = 0,1, \dots, N,$$

$$\int_{-1}^{1} R_I(s) T_j(s) w(s) ds = 0, \quad j = 0,1, \dots, N.$$

To find the unknown Chebyshev coefficients, the resulting nonlinear algebraic equations are assembled into a matrix system and numerically solved. After obtaining these coefficients, the truncated Chebyshev expansions are used to reconstruct the approximate solutions for the neuroinflammatory response, toxic amyloid-β aggregates, and healthy neurons. The impact of the fractional order on the course of Alzheimer's disease is then examined using the numerical solutions.

5 Numerical Results

The proposed Caputo fractional-order Alzheimer's disease model is solved using the Chebyshev–Galerkin spectral method. The simulations are performed using the parameter values listed in Table 1 together with the initial conditions $H(0) = H_0$, $A(0) = A_0$, and $I(0) = I_0$. To investigate the influence of memory effects on disease progression, the fractional-order values α = 1.00, 0.95, 0.90, and 0.75 are considered.

Numerical simulations of the proposed Caputo fractional-order Alzheimer's disease model for different fractional orders (α = 1.00, 0.95, 0.90, and 0.75).

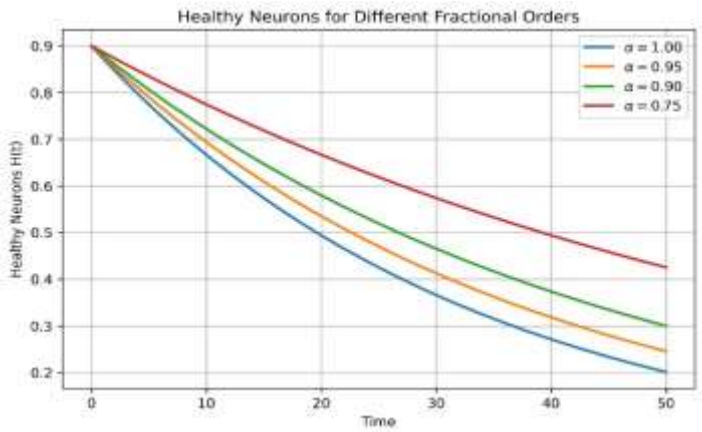


Figure 1: Temporal evolution of healthy

Figure 1 illustrates the temporal evolution of the healthy neuron population $H(t)$. It is observed that the neuron population gradually decreases over time for all fractional orders, reflecting the progressive neuronal degeneration associated with Alzheimer's disease. However, smaller values of the fractional order produce a slower decline in the healthy neuron population, indicating that the memory effect introduced by the fractional derivative delays neuronal loss.

Figure 2: Temporal evolution of toxic neurons $A_{(t)}$. amyloid-β aggregates $A(t)$.

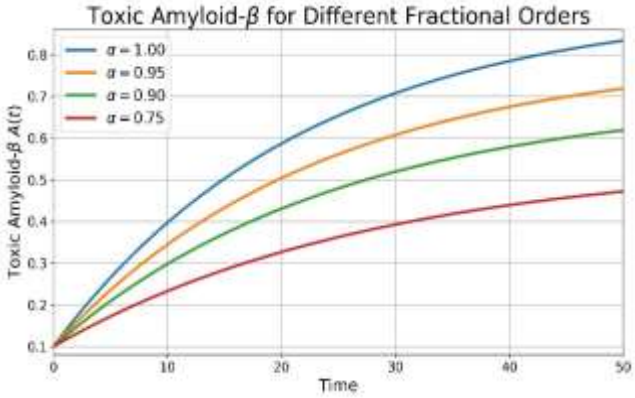


Figure 2 presents the dynamics of the toxic amyloid-β aggregates $A(t)$. The concentration initially increases due to continuous production and accumulation of amyloid-β proteins. As time progresses, the nonlinear saturation term limits further growth, and the solution approaches a bounded steady state. Lower values of the fractional order reduce the rate of accumulation, resulting in a smoother disease progression.

Figure 3: Temporal evolution of neuro inflammatory response $I(t)$.

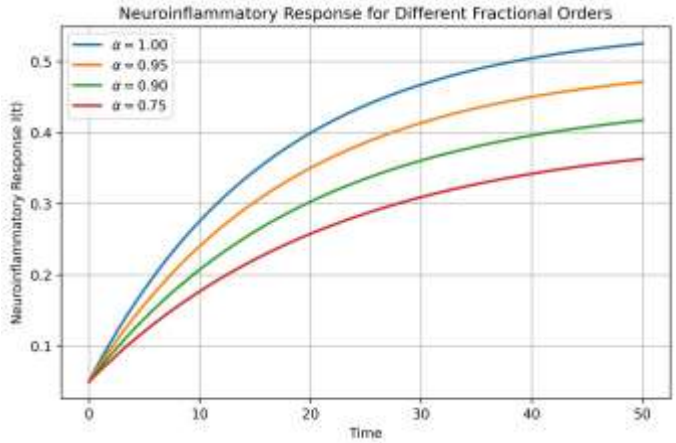


Figure 3 depicts the neuroinflammatory response $I(t)$. Since inflammation is stimulated by toxic amyloid-β aggregates, the inflammatory response initially increases before gradually approaching a stable equilibrium. The numerical simulations show that decreasing the fractional order reduces the intensity of neuroinflammation and delays its peak, demonstrating the influence of memory effects on neuroimmune dynamics.

Overall, the numerical results demonstrate that the proposed Caputo fractional order Alzheimer's disease model successfully reproduces the major characteristics of disease progression.

6 Conclusion

This study used a Caputo fractional order mathematical model to examine how toxic amyloid-β aggregates, healthy neurons, and the neuroinflammatory response interact to cause Alzheimer's disease. In order to comprehend the dynamic behavior of the model, the local stability of the suggested system was examined after its existence and uniqueness were confirmed. To get precise numerical solutions, the Chebyshev- Galerkin spectral method was used. The numerical results showed that lowering the fractional order improves memory effects, slows down neuronal degeneration, lowers the accumulation of amyloid-β and stabilizes the neuroinflammatory response. All things considered, the suggested analytical and numerical framework offers a dependable and effective method for examining the long term dynamics of Alzheimer's disease and lays the groundwork for future extensions that include more biological variables and clinical data.

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