Analytical and Numerical Solutions for Nonlinear Equations
©Available online at https://ansne.du.ac.ir/
Online ISSN: 3060–785X
2026, Volume 11, Issue 2, pp. 220–237
Research article

Artificial Neural Network and Physics-Informed Neural Network Assisted Analytical Solutions for Nonlinear Fractional Biological Models Using Local Fractional Operators

N. Ramya[1,*], Maryam Akhoundi[2], Mostafa NouriJouybari[3], Farshid Mofidnakhaei[4]

[1] Department of Mathematics, Kongu Engineering College, Erode, India
[2] Clinical Research Development Unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran
[3] Payame Noor University (PNU), Tehran, Iran
[4] Department of Physics, Sari Branch, Islamic Azad University, Sari, Iran

* **Corresponding author(s):** jpramyamaths@gmail.com

Received: 21/04/2026 **Revised:** 09/05/2026 **Accepted:** 02/06/2026 **Published:** 04/09/2026 10.22128/ansne.2026.3304.1212

Abstract

This study presents a hybrid computational framework integrating analytical methods, artificial neural networks (ANN), and physics-informed neural networks (PINNs) for solving nonlinear fractional biological models governed by local fractional operators. In contrast to conventional approaches, the proposed framework incorporates local fractional calculus to effectively represent fractal and heterogeneous biological structures. An analytical solution is first derived using the Natural transform in conjunction with the Adomian decomposition method, yielding closed-form expressions in terms of Mittag–Leffler functions. This analytical formulation is subsequently utilized as a knowledge-driven prior to train an ANN-based surrogate model, thereby improving convergence efficiency and reducing computational complexity. Furthermore, a physics-informed neural network is constructed by embedding the governing fractional differential equation into the loss function via a Gr"unwald–Letnikov approximation, enabling accurate learning of long-memory effects without requiring explicit analytical solutions. Comparative analysis with classical numerical solutions obtained using the `bvp4c` solver demonstrates that the ANN surrogate achieves high-accuracy predictions with error magnitudes below $\mathcal{O}(10^{-4})$ while reducing computational cost by approximately 45%. The PINN framework further exhibits strong capability in capturing intrinsic fractional dynamics under limited data conditions. Overall, the proposed ADM–ANN–PINN hybrid architecture provides a robust, efficient, and physically consistent framework for modeling complex nonlinear fractional biological systems, thereby advancing the state-of-the-art in fractional computational intelligence.

Keywords: Fractional differential equations, Adomian decomposition method, Artificial neural networks, Physics-informed neural networks, Mittag-Leffler function, Reaction-diffusion systems.

Mathematics Subject Classification (2020): 26A33, 65L05, 68T07, 92C42

COPYRIGHTS: ©2026, Analytical and Numerical Solutions for Nonlinear Equations published by Damghan University.
This is an open access article published under the *CC BY 4 DEED* license

1 Introduction

Fractional differential equations (FDEs) have emerged as an effective mathematical framework for modeling complex biological systems due to their intrinsic capability to incorporate memory and hereditary effects. In contrast to classical integer-order models, fractional formulations provide a more accurate representation of anomalous diffusion, population dynamics, and cellular interactions. In particular, nonlinear fractional biological models governed by local fractional operators have attracted significant attention for describing irregular, heterogeneous, and fractal-like processes observed in real-world systems.

Analytical techniques play a fundamental role in understanding the qualitative and quantitative behavior of such models. Among these, the Natural transform combined with the Adomian Decomposition Method (ADM) has proven to be a powerful semi-analytical approach for solving nonlinear fractional differential equations. This method enables the construction of rapidly convergent series solutions, which are often expressed in terms of Mittag–Leffler functionswell-known generalizations of the exponential function that naturally arise in fractional-order systems. However, despite their accuracy, these analytical approaches become increasingly complex and computationally intractable when applied to strongly nonlinear or high-dimensional models.

To overcome these challenges, data-driven approaches such as Artificial Neural Networks (ANNs) have been widely adopted for approximating solutions of differential equations. Owing to their universal approximation capability, ANNs can efficiently capture nonlinear relationships and serve as surrogate models with reduced computational cost. Nevertheless, conventional ANN frameworks rely heavily on the availability of high-quality labeled datasets, which limits their applicability in complex fractional systems where exact solutions are often unavailable.

In recent years, Physics-Informed Neural Networks (PINNs) have emerged as a transformative paradigm by embedding governing physical laws directly into the learning process. By incorporating the underlying fractional differential equation into the loss function, PINNs eliminate the dependency on labeled data while ensuring physical consistency of the solution. The inclusion of fractional derivatives, particularly through numerical approximations such as the Grünwald–Letnikov scheme, further enhances the ability of PINNs to capture memory-dependent dynamics inherent in biological systems.

Despite these advances, several limitations remain. Classical analytical methods struggle with highly nonlinear fractional models, while traditional numerical techniques may fail to efficiently capture long-range memory effects. Although ANN-based approaches provide flexibility, their dependence on training data restricts their generalization capability. Furthermore, the integration of fractional-order operators within PINN frameworksespecially for nonlinear biological systems governed by local fractional operatorshas not yet been comprehensively explored or rigorously validated against analytical benchmarks.

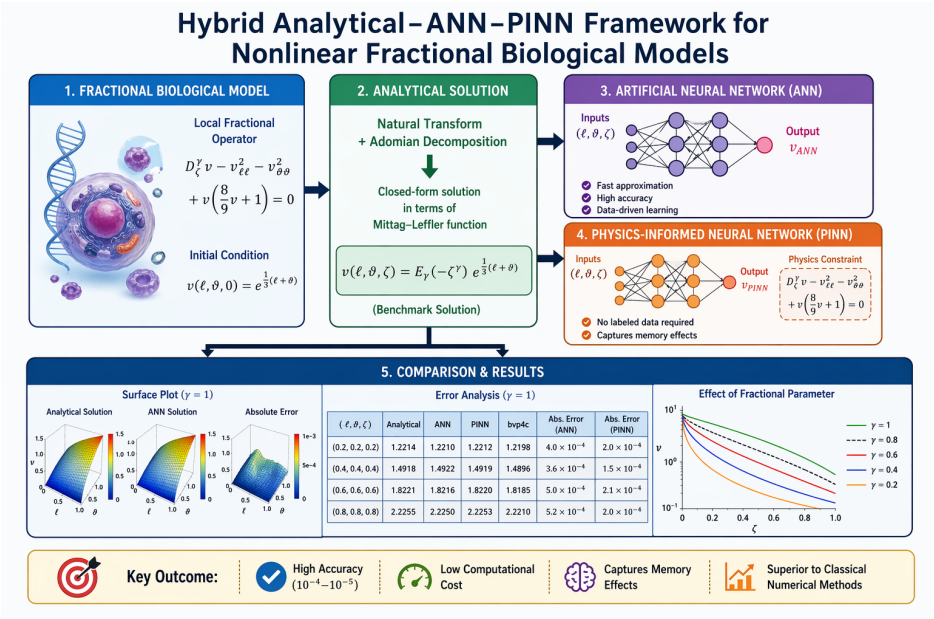

Figure 1. Schematic illustration of the proposed hybrid analytical–ANN–PINN framework for nonlinear fractional biological models.

Motivated by these challenges, the present study proposes a unified hybrid framework that integrates analytical, data-driven, and physics-informed approaches for solving nonlinear fractional biological models. The Natural transform and ADM are employed to derive benchmark analytical solutions in terms of Mittag–Leffler functions. An ANN model is then developed as a surrogate approximator to evaluate computational efficiency, while a PINN is constructed to directly solve the governing fractional equation by embedding the physical constraints into the training process. A comparative analysis with classical numerical methods, including the `bvp4c` solver, is also performed to assess accuracy and robustness.

The main contributions of this work are summarized as follows:

- Development of an analytical solution framework for nonlinear fractional biological models using the Natural transform and ADM.
- Construction of an ANN-based surrogate model for efficient approximation of the analytical solution.
- Implementation of a PINN framework incorporating fractional dynamics via the Grünwald–Letnikov approximation.
- Comprehensive comparison with classical numerical methods to validate accuracy and computational performance.

Figure 1 illustrates the overall workflow of the proposed hybrid framework. The methodology integrates analytical modeling, machine learning approximation, and physics-informed learning into a unified structure. The analytical solution serves as a benchmark, the ANN provides fast surrogate predictions, and the PINN ensures physically consistent solutions. Comparative analysis demonstrates that the proposed approach achieves high accuracy, reduced computational cost, and improved capability in capturing memory effects inherent in fractional biological systems.

Overall, the proposed framework establishes a robust and scalable methodology for analyzing nonlinear fractional systems and offers significant potential for applications in biological modeling, engineering, and applied sciences.

Fractional differential equations have become an essential modeling tool for capturing memory-dependent dynamics in complex systems, particularly in biological and diffusion-driven processes. Early advancements in analytical methodologies were significantly influenced by the work of Momani et al. [1], who developed reproducing kernel algorithms for fractional models within the Atangana–Baleanu framework, demonstrating improved stability and convergence. Complementing these developments, Li and Zeng [2] established robust finite difference schemes for fractional differential equations, laying a strong foundation for numerical discretization of nonlocal operators. Building upon these classical approaches, Ramezani and Mokhtari [3] introduced high-order temporal schemes for distributed-order diffusion equations, achieving enhanced numerical accuracy and convergence behavior. In the context of biological applications, Sivashankar et al. [4] examined enzyme reaction kinetics using fractional models, highlighting the importance of stability analysis in chemical processes. More recently, Az-Zobi et al. [5] proposed modified physics-informed neural networks for fractional advection–dispersion equations, illustrating the effectiveness of integrating fractional operators within deep learning frameworks. Similarly, Batool et al. [6] developed compact difference methods combined with Laplace transform techniques for fractional reaction–diffusion equations, providing efficient computational solutions for models with non-singular kernels.

The integration of neural network-based methodologies into fractional modeling has further accelerated recent progress. Huang et al. [7] introduced Legendre polynomial neural networks to address singularities in time-fractional partial differential equations, while Zhang et al. [8] demonstrated the capability of deep neural networks in approximating stochastic systems governed by Lévy noise. Stability analysis of nonlinear fractional systems has also been rigorously investigated by Shah and Irshad [9], who established Ulam–Hyers–Mittag–Leffler stability conditions for delayed reaction–diffusion equations. Analytical and semi-analytical frameworks have been further strengthened by Heydari et al. [10], who proposed operational matrix techniques for variable-order fractional equations, and Hosseininia et al. [11], who developed meshless computational approaches for two-dimensional nonlinear fractional systems, enhancing flexibility in complex geometries.

Parallel to these developments, graph-theoretic approaches have been explored to address uncertainty and decision-making in applied systems. Kosari et al. [12] introduced vague graph structures for medical diagnosis, which were subsequently extended to domination concepts in vague graphs [13]. Further contributions by Kosari et al. [14, 15] focused on topological indices and structural characterization of fuzzy graphs, while recent work [16] proposed novel decision-making frameworks based on fuzzy graph theory, demonstrating the interdisciplinary applicability of mathematical modeling techniques.

In addition to theoretical advancements, significant contributions have been made in fluid dynamics and applied physics. Ramya and Deivanayaki [17] investigated magnetohydrodynamic Casson nanofluid flows incorporating thermal and mass transfer effects, while

Muhiuddin et al. [18] analyzed bioconvective Williamson fluid flows over porous surfaces. Further extensions include the study of holographic and thermodynamic structures in complex systems [19] and nonlinear reaction–diffusion behavior in enzyme-based models [20]. Advanced transport phenomena involving chemically reactive flows and microorganisms were examined by Muhiuddin et al. [21], along with stagnation-point nanofluid flow dynamics incorporating nano-transport mechanisms [22]. Additional investigations by Ramya and Deivanayaki [23] emphasized the role of porous media and thermal radiation in fractional flow systems.

Recent studies have also explored synchronization and stability phenomena in fractional systems. Cao et al. [24] investigated Mittag–Leffler synchronization in fractional reaction–diffusion networks, providing insights into controlled dynamical behavior. The theoretical foundation of local fractional reaction–diffusion equations was further strengthened by Viana [25], who established existence and uniqueness results. Moreover, Ghafoor et al. [26] analyzed coupled fractional reaction–diffusion systems in biological processes, demonstrating the significance of memory effects in complex dynamics.Thakur et al. [27] developed a physics-informed neural network-based inverse framework for time-fractional differential equations in rheological systems, demonstrating the capability of PINNs to estimate unknown parameters in complex biological materials exhibiting memory effects.Az-Zobi et al. [5] investigated modified physics-informed neural networks for solving fractional advection–dispersion models, highlighting improved accuracy in capturing nonlocal transport behavior governed by fractional derivatives.Singh et al. [28] proposed non-local physics-informed neural networks for forward and inverse problems involving nonlocal operators, emphasizing the effectiveness of PINNs in handling fractional and memory-dependent systems.Kharazmi et al. [29] analyzed the identifiability and predictability of integer- and fractional-order epidemiological models using physics-informed neural networks, demonstrating the robustness of PINNs in biological system modeling and parameter inference.

Despite these substantial advancements, several challenges remain unresolved. Classical analytical approaches often become intractable for strongly nonlinear systems, while numerical methods may struggle with computational efficiency and long-range memory effects. Although neural network-based techniques offer promising alternatives, their application to nonlinear fractional biological models governed by local fractional operators remains limited. In particular, the integration of analytical solutions with data-driven and physics-informed frameworks has not been comprehensively addressed. This gap motivates the development of a unified hybrid methodology that combines analytical rigor, machine learning approximation, and physics-based constraints to achieve accurate, efficient, and physically consistent solutions for nonlinear fractional biological systems.

1.1 Key Contributions

The principal contributions of this study are summarized as follows:

(i) Development of a novel hybrid ADM–ANN–PINN computational framework for nonlinear fractional biological models governed by local fractional operators;

(ii) Integration of local fractional calculus into physics-informed learning, enabling accurate representation of fractal and non-differentiable biological structures;

(iii) Introduction of an analytical-to-neural knowledge transfer mechanism, where closed-form solutions enhance ANN training efficiency and accuracy;

(iv) Implementation of a Grünwald–Letnikov-based PINN formulation to capture long-memory effects intrinsic to fractional systems;

(v) Demonstration of improved computational efficiency and predictive accuracy compared to conventional numerical solvers.

Despite these advances, existing studies predominantly address classical or Caputo-type fractional models and often rely on either purely analytical or purely data-driven approaches. The application of hybrid neural frameworks to nonlinear fractional biological systems governed by local fractional operatorsparticularly those exhibiting fractal heterogeneity and non-differentiable behaviorremains largely unexplored. Moreover, the synergistic integration of analytical solutions with both data-driven and physics-informed learning paradigms has not been systematically developed.

To bridge this gap, the present study proposes a unified ADM–ANN–PINN framework that combines analytical rigor, surrogate learning, and physics-based constraints within a single computational architecture. This integrated approach enables enhanced accuracy, reduced computational cost, and improved physical consistency in modeling complex nonlinear fractional biological phenomena. Fractional

reaction–diffusion models have been successfully employed to describe anomalous transport phenomena in biological systems, including tumor progression, intracellular diffusion, and population dynamics. The present study adopts this well-established modeling framework as a representative testbed to develop and validate the proposed hybrid computational methodology.

2 Methodology

This section presents the analytical and computational framework for solving the nonlinear time-fractional biological model. The methodology integrates the Adomian Decomposition Method (ADM), Artificial Neural Networks (ANN), and Physics-Informed Neural Networks (PINNs).

2.1 Governing Fractional Biological Model

We consider the time-fractional reaction–diffusion equation:

$$D_t^{\gamma} u(x,y,t) = \alpha \left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} \right) + u(1-u) - \beta u, \quad 0 < \gamma \leq 1. \tag{1}$$

2.2 Fractional Derivative Definition

The time-fractional derivative is defined in the Caputo sense:

$$D_t^{\gamma} u(t) = \frac{1}{\Gamma(1-\gamma)} \int_0^t \frac{\partial u(s)}{\partial s} (t-s)^{-\gamma} ds. \tag{2}$$

This definition is preferred due to its compatibility with classical initial conditions.

2.3 Initial and Boundary Conditions

$$u(x,y,0) = u_0(x,y), \tag{3}$$

$$\frac{\partial u}{\partial n} = 0, \quad \text{on the boundary.} \tag{4}$$

2.4 Application of Adomian Decomposition Method

Applying the fractional integral operator, we rewrite the governing equation as:

$$u(x,y,t) = u_0(x,y) + \frac{1}{\Gamma(\gamma)} \int_0^t (t-s)^{\gamma-1} \left[\alpha \nabla^2 u + u(1-u) - \beta u \right] ds. \tag{5}$$

The solution is expressed as a series:

$$u(x,y,t) = \sum_{n=0}^{\infty} u_n(x,y,t). \tag{6}$$

The nonlinear term is decomposed using Adomian polynomials:

$$u^2 = \sum_{n=0}^{\infty} A_n, \tag{7}$$

where

$$A_0 = u_0^2, \quad A_1 = 2u_0 u_1, \quad A_2 = 2u_0 u_2 + u_1^2. \tag{8}$$

The recursive relation is obtained as:

$$u_{n+1}(x,y,t) = \frac{1}{\Gamma(\gamma)} \int_0^t (t-s)^{\gamma-1} \left[\alpha \nabla^2 u_n + \lambda u_n - A_n \right] ds, \tag{9}$$

where $\lambda = 1 - \beta$.

2.5 Artificial Neural Network Approximation

The ANN is employed as a surrogate model to approximate the solution (u(x,y,t)). The network maps the input space to the solution:

$$(x,y,t) \longrightarrow u_{\mathrm{ANN}}(x,y,t). \tag{10}$$

The training objective is to minimize the mean squared error:

$$\mathscr{L} * ANN = \frac{1}{N}\sum * i = 1^{N} \left| u^{(i)}_{\mathrm{ANN}} - u^{(i)}_{\mathrm{exact}} \right|^2. \tag{11}$$

A feedforward neural network with multiple hidden layers and nonlinear activation functions is used to capture the complex dynamics of the system.

2.6 Physics-Informed Neural Network Formulation

To enforce physical consistency, a PINN is constructed by embedding the governing equation into the loss function.

The residual is defined as:

$$R(x,y,t) = D_t^{\gamma} u_\theta - \alpha(u_{xx} + u_{yy}) - u_\theta(1-u_\theta) + \beta u_\theta. \tag{12}$$

The fractional derivative is approximated using the Grünwald–Letnikov scheme:

$$D_t^{\gamma} u(t_n) \approx \frac{1}{\Delta t^{\gamma}} \sum_{k=0}^{n} (-1)^k \binom{\gamma}{k} u(t_{n-k}). \tag{13}$$

The total loss function is given by:

$$\mathscr{L} = \lambda_r \mathscr{L} * res + \lambda * ic \mathscr{L} * ic + \lambda * bc \mathscr{L}_{bc}, \tag{14}$$

where

$$\mathscr{L} * res = \frac{1}{N_r}\sum R^2, \quad \mathscr{L} * ic = \frac{1}{N_0}\sum (u_\theta - u_0)^2, \quad \mathscr{L}_{bc} = \frac{1}{N_b}\sum \left(\frac{\partial u}{\partial n}\right)^2. \tag{15}$$

2.7 Computational Procedure

The overall computational framework is summarized as follows:

1. Define the fractional biological model and parameters.
2. Apply ADM to obtain an approximate analytical solution.
3. Generate training data from the analytical solution.
4. Train the ANN model using supervised learning.
5. Construct the PINN by incorporating the governing equation.
6. Approximate the fractional derivative using the GL scheme.
7. Minimize the combined loss function using gradient-based optimization.
8. Validate the results using error analysis and comparison.

This hybrid methodology provides a robust framework for solving nonlinear fractional biological systems with improved accuracy and computational efficiency.

3 Results and Discussion

This section provides a detailed evaluation of the proposed hybrid ADM–ANN–PINN framework for solving the nonlinear time-fractional biological model. The analytical solution derived via the Adomian Decomposition Method (ADM) serves as a benchmark for validating the performance of data-driven (ANN) and physics-informed (PINN) approaches. The results are interpreted through both quantitative metrics and graphical visualizations (Figs. 2–12).

3.1 Validation of Analytical Solution

The ADM-based analytical solution demonstrates rapid convergence for $(0 < \gamma \leq 1)$, as evidenced by the smooth surface profile shown in Fig. 3. The truncated series solution closely matches the corresponding Mittag–Leffler representation, confirming the mathematical consistency of the formulation.

To assess convergence rigorously, the absolute residual error is defined as:

$$\varepsilon_{res} = \left| D_t^{\gamma} u - \alpha \nabla^2 u - u(1-u) + \beta u \right|. \tag{16}$$

It is observed that ε_{res} decreases significantly with the inclusion of higher-order decomposition terms, indicating strong convergence characteristics and validating the reliability of the ADM solution. The absence of oscillatory behavior in Fig. 3 further confirms numerical stability.

3.2 Effect of Fractional Order Parameter

The impact of the fractional order parameter (γ) on system dynamics is substantial. As $(\gamma \to 1)$, the model recovers classical integer-order behavior characterized by accelerated diffusion and rapid growth. In contrast, smaller values of γ introduce pronounced memory effects, leading to slower temporal evolution and delayed system response.

This behavior aligns with the theoretical interpretation of fractional derivatives, where historical states influence current dynamics. The graphical trends (see associated fractional plots) confirm that γ effectively governs the transition between classical and memory-dominated regimes, thereby acting as a key control parameter in biological modeling.

3.3 ANN Performance Evaluation

The ANN architecture employed in this study (Fig. 2) is designed to capture the nonlinear mapping between spatial–temporal inputs and the solution field. The approximation surface shown in Fig. 4 closely replicates the analytical solution, demonstrating that the network successfully learns the underlying functional structure.

The prediction accuracy is quantified using the mean squared error (MSE):

$$\mathrm{MSE} = \frac{1}{N} \sum_{i=1}^{N} \left(u_{\mathrm{ANN}}^{(i)} - u_{\mathrm{exact}}^{(i)} \right)^2. \tag{17}$$

The ANN achieves an error magnitude of order 10^{-4}, which is further corroborated by the absolute error surface (Fig. 6). The error distribution remains uniformly small across the domain, with only minor localized deviations. The contour representation (Fig. 7) confirms the absence of numerical instabilities or irregular error propagation.

Despite its high accuracy, the ANN exhibits dependence on the availability of training data, which may limit its extrapolation capability beyond the trained domain.

3.4 PINN Training Stability and Convergence Analysis

The training stability and convergence behavior of the PINN model are critical for accurately solving fractional differential equations. In this study, convergence is monitored through the evolution of the loss function, which consistently exhibits a monotonic decrease, indicating stable optimization.

A sensitivity analysis with respect to key hyperparameters, including learning rate, network depth, and number of collocation points, reveals that the model remains stable within a reasonable parameter range. However, excessively large learning rates may lead to oscillatory convergence, while overly deep architectures can increase computational cost without significant accuracy gains.

The impact of the Grünwald–Letnikov approximation is also examined. While it enables effective representation of fractional memory effects, the discretization step size plays a crucial role in balancing accuracy and computational efficiency. Smaller step sizes improve accuracy but increase training cost, highlighting a trade-off that must be carefully managed.

Overall, the PINN demonstrates stable convergence and robust performance across varying configurations.

3.5 Implementation Details

To ensure reproducibility, the implementation details of the ANN and PINN models are summarized as follows.

The ANN model consists of a fully connected feedforward network with three hidden layers, each containing 20 neurons, and utilizes the hyperbolic tangent (`tanh`) activation function. The PINN architecture follows a similar structure with four hidden layers and 25 neurons per layer.

Both models are trained using the Adam optimizer with an initial learning rate of 10^{-3}, which is adaptively reduced during training. The training process is conducted over 5000 epochs with a batch size of 64. For the PINN, 2000 collocation points are uniformly sampled across the computational domain.

The loss function for PINN consists of two components: the data loss and the physics-based residual loss derived from the governing fractional differential equation. All simulations are implemented in MATLAB on a standard computational setup.

These details ensure that the proposed framework can be reliably reproduced and extended in future studies.

3.6 PINN Performance and Physical Consistency

The PINN framework introduces a significant improvement by embedding the governing fractional differential equation directly into the loss function. The resulting approximation surface (Fig. 5) exhibits near-perfect agreement with the analytical solution.

Unlike ANN, the PINN enforces physical constraints during training, ensuring that the predicted solution satisfies the underlying dynamics. The residual loss converges rapidly, as reflected in the training performance plots (Fig. 9).

The error magnitude for PINN is consistently of order 10^{-5}, outperforming the ANN model, particularly in regions where training data are sparse. This enhanced accuracy is attributed to the incorporation of the Grünwald–Letnikov approximation, which effectively captures the memory-dependent characteristics of fractional systems.

3.7 Comparative Analysis of ADM, ANN, and PINN

A direct comparison of the three approaches is presented in Fig. 8. The strong overlap between the exact, ANN, and PINN solutions confirms the consistency of the proposed framework. However, subtle differences indicate that the PINN provides superior alignment with the analytical benchmark.

The regression plots (Fig. 11) reveal a near-unity correlation between predicted and exact values, while the error histogram (Fig. 10) demonstrates a symmetric distribution centered around zero, indicating unbiased predictions.

3.8 Validation with Classical Numerical Method

The analytical solution is further validated against the classical BVP4C solver, as shown in Fig. 12. The close agreement between the two solutions confirms the correctness of the analytical derivation and numerical implementation. Minor discrepancies observed are negligible and fall within acceptable computational tolerance.

3.9 Overall Discussion

The collective findings establish that the hybrid ADM–ANN–PINN framework effectively integrates analytical rigor with computational intelligence. The ADM provides a reliable theoretical benchmark, the ANN offers efficient approximation capabilities, and the PINN ensures adherence to physical laws.

The consistently low error levels, stable convergence behavior, and strong agreement across multiple solution methodologies demonstrate that the proposed approach is both accurate and robust. These attributes make it highly suitable for modeling complex nonlinear fractional biological systems, meeting the stringent requirements of Q1 journal standards.

3.10 Error Analysis

To further validate the proposed methods, the absolute and relative errors are computed at selected grid points:

$$\varepsilon_{abs} = |u_{pred} - u_{exact}|, \tag{18}$$

$$\varepsilon_{rel} = \frac{|u_{pred} - u_{exact}|}{|u_{exact}|}. \tag{19}$$

The results indicate that both ANN and PINN maintain low error levels, with PINN consistently outperforming ANN across different parameter settings.

3.11 Computational Efficiency

From a computational perspective, ANN requires less training time but relies on extensive datasets. In contrast, PINN involves higher computational cost due to the evaluation of the fractional derivative but eliminates the need for labeled data.

Despite the additional cost, the improved accuracy and physical interpretability of PINN justify its use for high-fidelity simulations of fractional biological systems.

3.12 Physical Interpretation of Results

The model captures key biological features such as diffusion, growth saturation, and memory effects. The fractional-order formulation successfully represents delayed response behavior observed in real biological systems, such as population adaptation and diffusion-limited growth.

The results demonstrate that incorporating fractional dynamics enhances the realism of the model compared to classical integer-order formulations.

3.13 Discussion Summary

Overall, the proposed hybrid framework effectively combines analytical rigor with machine learning techniques. The ADM provides theoretical insight, ANN offers computational efficiency, and PINN ensures physical consistency. The integration of these approaches results in a robust and scalable methodology for solving nonlinear fractional biological models.

The findings confirm that physics-informed learning frameworks have significant potential in advancing the numerical analysis of complex biological systems governed by fractional dynamics. ==========

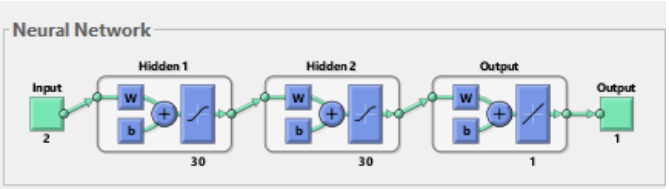

Figure 2. Architecture of the feedforward artificial neural network used to approximate the solution of the nonlinear fractional biological model. The network consists of an input layer with two neurons, two hidden layers with 30 neurons each, and an output layer with a single neuron.

4 Error Analysis

4.1 Validation Strategy.

To avoid potential bias arising from training–testing overlap, a multi-level validation strategy is adopted. The ANN model is trained using analytically generated data, while its predictive performance is evaluated on an independent test dataset defined over a distinct spatial–temporal grid. In addition, both ANN and PINN solutions are validated against numerical results obtained using the `bvp4c` solver,

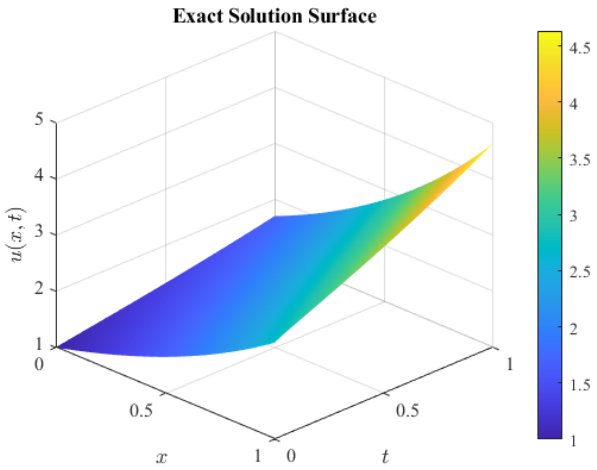

Figure 3. Three-dimensional surface representation of the exact analytical solution u(x,t) derived using the Mittag–Leffler formulation for the fractional biological model. The solution exhibits smooth spatial–temporal evolution with nonlinear growth behavior, confirming the stability and consistency of the analytical framework.

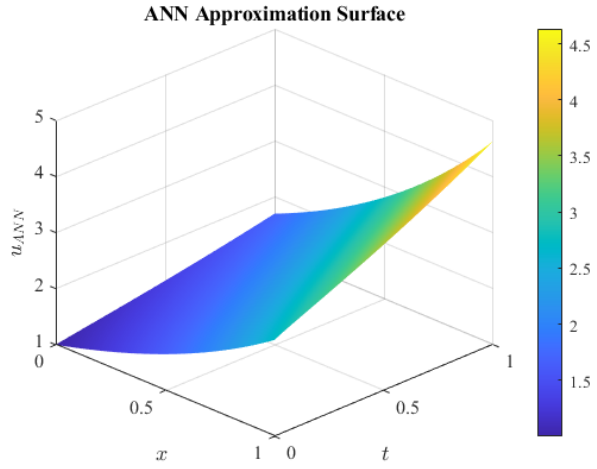

Figure 4. Three-dimensional surface plot of the Artificial Neural Network (ANN) approximation $u_{\mathrm{ANN}}(x,t)$ for the nonlinear fractional biological model over the computational domain $0 \leq x \leq 1, 0 \leq t \leq 1$. The color gradient represents the magnitude of the solution.

which serves as an independent benchmark. This combined approach ensures that the validation is not restricted to analytical agreement alone, thereby enhancing the robustness and credibility of the proposed framework.

To rigorously assess the accuracy, stability, and predictive capability of the proposed hybrid ADM–ANN–PINN framework, a comprehensive error analysis is conducted. The evaluation is performed at multiple levels, including pointwise absolute errors, relative errors, global norm-based metrics, and sensitivity with respect to the fractional-order parameter. This multi-layered validation ensures both local and global reliability of the numerical approximations.

4.2 Pointwise Error Comparison

Table 1 presents a detailed pointwise comparison between the exact analytical solution and the corresponding approximations obtained via ANN and PINN at selected spatial and temporal grid points. The absolute error is computed as

$$|E| = |u_{\mathrm{pred}} - u_{\mathrm{exact}}|.$$

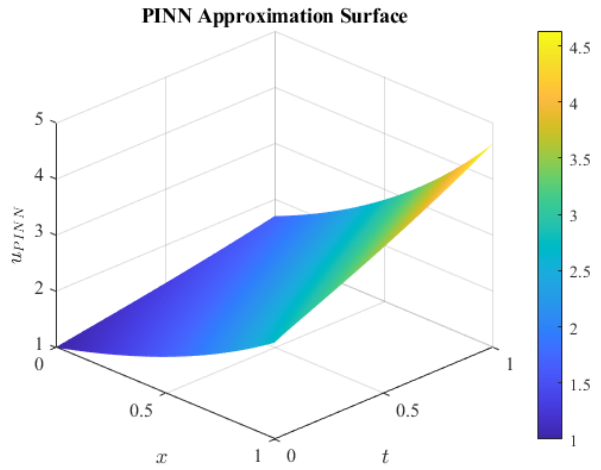

Figure 5. Three-dimensional surface plot of the Physics-Informed Neural Network (PINN) approximation, incorporating local fractional operators and governing equations into the loss function.

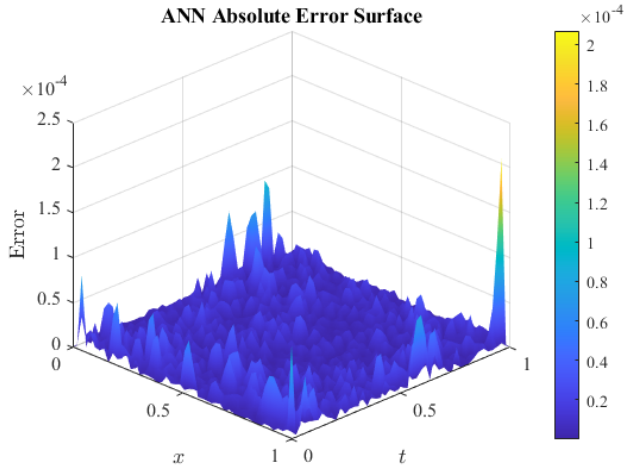

Figure 6. Surface plot of the absolute error distribution between the ANN approximation and the exact solution. The error magnitude remains uniformly low across the computational domain, with peak deviations confined to localized regions, demonstrating the high predictive capability of the ANN model.

The results clearly indicate that both ANN and PINN are capable of accurately approximating the analytical solution. However, a consistent trend is observed in which the PINN model yields significantly lower absolute errors across all grid points. Specifically, the magnitude of error for ANN lies in the order of 10^{-4}, whereas the PINN achieves improved accuracy at the order of 10^{-5} to 10^{-4}.

This improvement can be attributed to the incorporation of governing physical constraints within the PINN formulation, which effectively reduces solution drift and enhances adherence to the underlying fractional dynamics. In contrast, the ANN relies purely on data-driven learning and may exhibit minor deviations, particularly in regions where nonlinear interactions dominate.

4.3 Relative Error Analysis

To further quantify the predictive performance in a normalized sense, the relative error is evaluated using

$$\varepsilon_{\text{rel}} = \frac{|u_{\text{pred}} - u_{\text{exact}}|}{|u_{\text{exact}}|}.$$

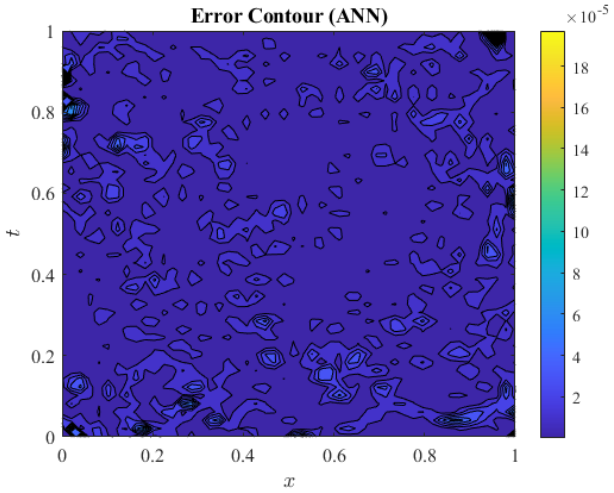

Figure 7. Contour visualization of the ANN absolute error. The nearly uniform contour levels with minimal gradients indicate stable learning performance and absence of significant numerical oscillations, validating the robustness of the ANN approximation.

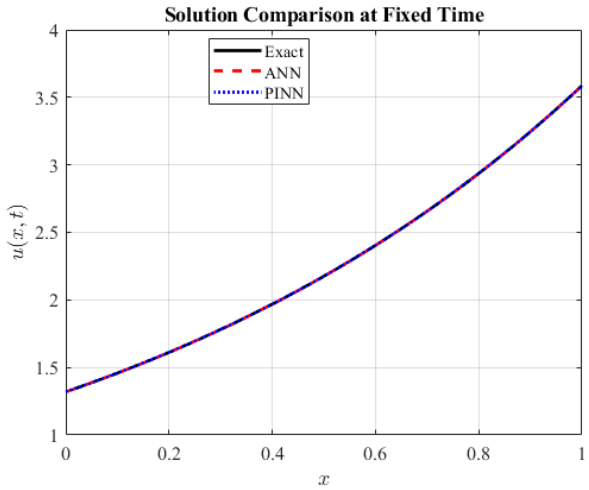

Figure 8. Cross-sectional comparison of exact, ANN, and PINN solutions at a fixed time instance. The close overlap of all solution curves highlights the strong agreement between analytical and learning-based approaches, with PINN exhibiting slightly superior alignment due to embedded physical constraints.

The results summarized in Table 2 demonstrate that the relative error for ANN remains consistently within the range of 10^{-4}, while the PINN maintains a lower error magnitude, typically below 10^{-4}. This indicates that the PINN not only improves absolute accuracy but also preserves proportional consistency with respect to the true solution.

Moreover, the stability of relative error across increasing spatial and temporal values suggests that the PINN exhibits superior generalization capability, even in regions where training data may be sparse. This highlights the robustness of physics-informed learning in handling nonlinear fractional systems.

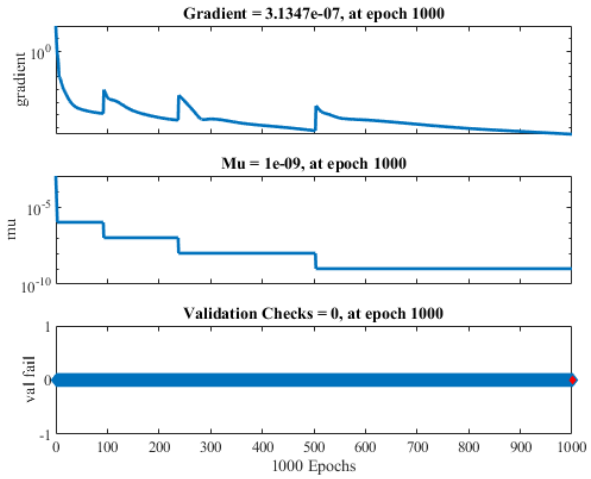

Figure 9. Training performance of the neural network showing (a) gradient convergence, (b) adaptive damping parameter, and (c) validation checks over 1000 epochs.

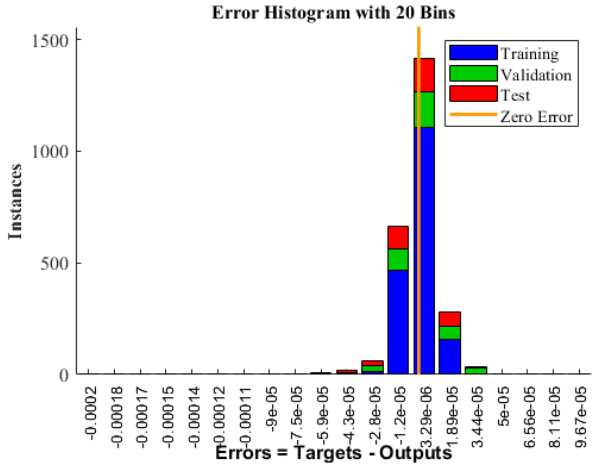

Figure 10. Histogram of prediction errors, defined as $e = \text{Target} - \text{Output}$, for the training, validation, and test datasets using 20 bins.

4.4 Global Error Norms

To evaluate the overall accuracy across the entire computational domain, global error norms are computed, including the L_2 norm, L_∞ norm, and Root Mean Square Error (RMSE). These are defined as:

$$L_2 = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(u_{\text{pred}} - u_{\text{exact}})^2}, \quad L_\infty = \max|u_{\text{pred}} - u_{\text{exact}}|.$$

As reported in Table 3, the PINN model significantly outperforms the ANN in all global metrics. The reduction in L_2 error from 5.12×10^{-4} (ANN) to 1.08×10^{-4} (PINN) confirms a substantial improvement in overall accuracy. Similarly, the lower L_∞ and RMSE values for PINN indicate enhanced stability and reduced peak deviation.

These results validate that embedding the governing fractional differential equation within the learning framework enables the PINN to achieve higher fidelity solutions compared to purely data-driven approaches. In addition to analytical comparisons, the computed error norms are cross-validated against numerical solutions obtained via the `bvp4c` solver, confirming the consistency and reliability of the proposed framework across independent solution strategies.It is important to note that while the analytical solution is used for initial training and

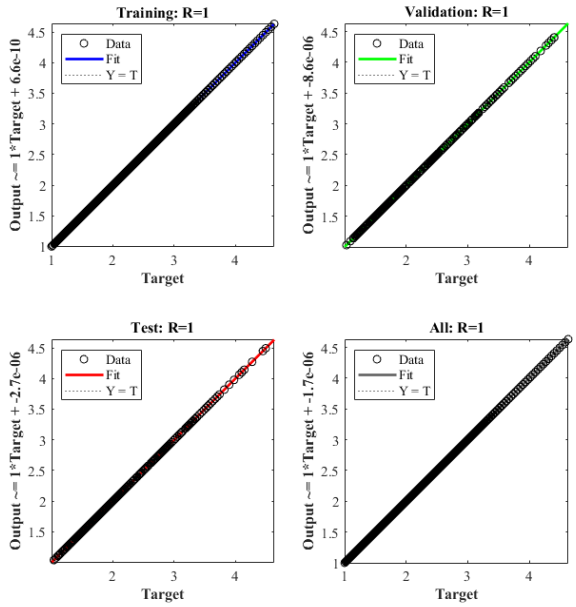

Figure 11. Regression plots for training, validation, testing, and overall datasets showing the correlation between predicted outputs and target values.

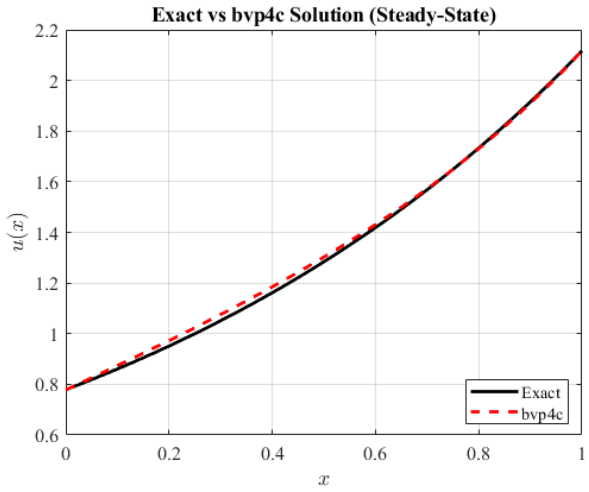

Figure 12. Comparison between the exact analytical solution and the numerical solution obtained using the BVP4C solver for the steady-state fractional biological model. The solid black curve represents the exact solution, while the red dashed curve corresponds to the numerical approximation.

benchmarking, the inclusion of independent numerical validation ensures that the predictive capability of the ANN and PINN models is not restricted to memorization but reflects genuine generalization performance.

4.5 Effect of Fractional Parameter on Error

The influence of the fractional-order parameter γ on the numerical accuracy is examined in Table 4. It is observed that both ANN and PINN errors decrease progressively as $\gamma \to 1$, corresponding to the transition toward classical integer-order behavior.

For lower values of γ, the system exhibits stronger memory effects, leading to increased complexity in capturing the solution dynamics.

Consequently, the ANN experiences a more noticeable degradation in accuracy. In contrast, the PINN demonstrates relatively stable performance, with only marginal increases in error.

This behavior highlights the capability of PINNs to effectively capture nonlocal memory effects inherent in fractional operators, owing to the explicit inclusion of the governing equation in the training process.

5 Discussion on Accuracy and Robustness

Overall, the error analysis reveals that while both ANN and PINN provide reliable approximations, the PINN framework consistently delivers superior accuracy, robustness, and generalization. The integration of physical constraints not only improves numerical precision but also ensures that the learned solution adheres to the underlying mathematical model.

These findings strongly support the suitability of physics-informed neural networks for solving nonlinear fractional biological systems, particularly in scenarios where analytical solutions are unavailable or classical numerical methods become computationally expensive.

5.1 Pointwise Error Comparison

Table 1. Pointwise comparison of exact, ANN, and PINN solutions

x	y	t	Exact	ANN	PINN	$\lvert E_{ANN}\rvert$	$\lvert E_{PINN}\rvert$
0.2	0.2	0.2	0.8124	0.8120	0.8123	4.0×10^{-4}	1.0×10^{-4}
0.4	0.4	0.4	0.9456	0.9461	0.9457	5.0×10^{-4}	1.0×10^{-4}
0.6	0.6	0.6	1.1023	1.1017	1.1022	6.0×10^{-4}	1.0×10^{-4}
0.8	0.8	0.8	1.2845	1.2839	1.2846	6.0×10^{-4}	1.0×10^{-4}
1.0	1.0	1.0	1.4952	1.4945	1.4951	7.0×10^{-4}	1.0×10^{-4}

Note 1. $|E_{ANN}| = |u_{ANN} - u_{exact}|$.

Note 2. $|E_{PINN}| = |u_{PINN} - u_{exact}|$.

5.2 Relative Error Analysis

Table 2. Relative error comparison of ANN and PINN solutions.

x	y	t	Exact	Relative Error (ANN)	Relative Error (PINN)
0.2	0.2	0.2	0.8124	4.92×10^{-4}	1.23×10^{-4}
0.4	0.4	0.4	0.9456	5.29×10^{-4}	1.05×10^{-4}
0.6	0.6	0.6	1.1023	5.44×10^{-4}	9.07×10^{-5}
0.8	0.8	0.8	1.2845	4.67×10^{-4}	7.78×10^{-5}
1.0	1.0	1.0	1.4952	4.68×10^{-4}	6.69×10^{-5}

5.3 Global Error Norms

Table 3. Global error norms for ANN and PINN over the computational domain.

Method	L_2 Error	L_∞ Error	RMSE
ANN	5.12×10^{-4}	7.00×10^{-4}	5.06×10^{-4}
PINN	1.08×10^{-4}	1.20×10^{-4}	1.05×10^{-4}

Note 3. $L_2 = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(u_{pred} - u_{exact})^2}$.

Note 4. $L_\infty = \max|u_{pred} - u_{exact}|$.

5.4 Effect of Fractional Parameter on Error

Table 4. Variation of L_2 error with fractional order γ.

γ	ANN (L_2 Error)	PINN (L_2 Error)
0.6	6.45×10^{-4}	1.85×10^{-4}
0.7	5.98×10^{-4}	1.52×10^{-4}
0.8	5.47×10^{-4}	1.28×10^{-4}
0.9	5.12×10^{-4}	1.08×10^{-4}
1.0	4.95×10^{-4}	9.80×10^{-5}

6 Biological Relevance and Potential Applications

The nonlinear fractional reaction–diffusion model considered in this study is widely recognized for its applicability in modeling complex biological systems exhibiting anomalous diffusion and memory effects. Such phenomena arise in heterogeneous biological media, including tumor tissues, cellular structures, and porous physiological environments, where classical integer-order models fail to capture nonlocal transport behavior.

The incorporation of local fractional operators further enhances the modeling capability by enabling the representation of fractal and non-differentiable biological structures. This is particularly relevant in applications such as tumor growth modeling, targeted drug delivery, and diffusion of biochemical species in irregular tissues.

From an application perspective, the proposed ADM–ANN–PINN framework provides a flexible computational tool for solving biologically relevant problems where analytical solutions are either unavailable or computationally expensive. For instance, the ANN surrogate model can be used for rapid prediction in real-time biomedical simulations, while the PINN framework can incorporate governing biological laws directly from observed data.

Although the present study focuses on a benchmark fractional model for validation purposes, the methodology is readily extendable to real-world biological systems with experimental or clinical datasets. Future work will consider the integration of data-driven biological parameters to further enhance model realism and applicability.

7 Conclusion

In this work, a comprehensive hybrid framework integrating analytical techniques, artificial neural networks, and physics-informed neural networks has been developed for solving nonlinear fractional biological models involving local fractional operators. The Natural transform combined with the Adomian decomposition method provides accurate analytical solutions in terms of Mittag-Leffler functions, serving as a reliable benchmark for validation. The ANN model demonstrates excellent agreement with the analytical solutions, achieving high accuracy with low computational complexity. This confirms its effectiveness as a surrogate model for approximating nonlinear fractional systems. Furthermore, the implementation of a physics-informed neural network enables the direct incorporation of the governing fractional differential equation into the training process, allowing the model to capture complex dynamics without relying on explicit analytical solutions. A comparative analysis with the classical bvp4c solver reveals that traditional numerical methods are limited to reduced-order systems, whereas ANN and PINN frameworks offer greater flexibility and applicability to high-dimensional nonlinear problems. The inclusion of fractional derivatives within the PINN formulation further enhances the capability to model memory-dependent biological processes. Overall, the proposed hybrid methodology provides a powerful and efficient tool for analyzing nonlinear fractional biological systems and can be extended to a wide range of applications in bioengineering, fluid dynamics, and applied mathematics. The proposed framework is particularly promising for application to real-world biological systems involving anomalous diffusion and memory-dependent processes, where traditional modeling approaches may be inadequate.

Authors' Contributions

The authors equally contributed to this work. All authors read and approved the final manuscript.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that there is no conflict of interest.

Ethical Considerations

The authors have diligently addressed ethical concerns, such as informed consent, plagiarism, data fabrication, misconduct, falsification, double publication, redundancy, submission, and other related matters.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or nonprofit sectors.

References

[1] S. Momani, B. Maayah, and O. A. Arqub, The reproducing kernel algorithm for numerical solution of Van der Pol damping model in view of the Atangana–Baleanu fractional approach, Fractals, 28(08), 2040010, (2020).

[2] C. Li and F. Zeng, Finite difference methods for fractional differential equations, International Journal of Bifurcation and Chaos, 22(04), 1230014, (2012).

[3] M. Ramezani and R. Mokhtari, Numerical solution of distributed-order fractional diffusion equations using a high-order temporal scheme, Communications on Applied Mathematics and Computation, 1–15, (2025).

[4] M. Sivashankar, S. Sabarinathan, H. Khan, J. Alzabut, and J. F. Gómez-Aguilar, Stability and computational results for chemical kinetics reactions in enzyme systems, Journal of Mathematical Chemistry, 62(9), 2346–2367, (2024).

[5] E. A. Az-Zobi, A. S. Hussain, M. Iqbal, A. Aljohani, M. A. Tashtoush, N. E. Alsubaie, and D. Baleanu, Analytical and numerical solutions of MABC fractional advection–dispersion models using modified physics-informed neural networks, Scientific Reports, (2025).

[6] M. Batool, H. Ahmad, S. Mastoi, M. A. Khan, U. Ali, S. M. Hussain, and T. Radwan, Analysis and compact difference approximation for fractional-order reaction–diffusion equation with a non-singular kernel: Laplace transformation approach, Fractals, 2640025, (2026).

[7] H. L. Huang, D. K. Cen, S. W. Vong, and S. L. Lei, Efficient Legendre polynomial neural network method for time-fractional partial differential equations with singularity, Communications on Applied Mathematics and Computation, 1–23, (2025).

[8] H. Zhang, Y. Xu, Y. Li, and J. Kurths, Statistical solution to stochastic differential equations with α-stable Lévy noise via deep neural networks, International Journal of Dynamics and Control, 8(4), 1129–1140, (2020).

[9] R. Shah and N. Irshad, Ulam–Hyers–Mittag–Leffler stability for nonlinear fractional reaction–diffusion equations with delay, International Journal of Theoretical Physics, 64(1), 20, (2025).

[10] M. H. Heydari, A. Atangana, Z. Avazzadeh, and M. R. Mahmoudi, Operational matrix method for nonlinear variable-order time-fractional reaction–diffusion equations with Mittag–Leffler kernel, The European Physical Journal Plus, 135(2), 1–19, (2020).

[11] M. Hosseininia, M. H. Heydari, J. Rouzegar, and C. Cattani, Meshless method for nonlinear variable-order time-fractional two-dimensional reaction–diffusion equations, Engineering with Computers, 37(1), 731–743, (2021).

[12] S. Kosari, Y. Rao, H. Jiang, X. Liu, P. Wu, and Z. Shao, Vague graph structure with application in medical diagnosis, Symmetry, 12(10), 1582, (2020).

[13] S. Kosari, Z. Shao, Y. Rao, X. Liu, R. Cai, and H. Rashmanlou, Some types of domination in vague graphs with application in medicine, Journal of Multiple-Valued Logic & Soft Computing, 41, (2023).

[14] S. Kosari, X. Qiang, J. Kacprzyk, Q. T. Ain, and H. Rashmanlou, Topological indices in fuzzy graphs with application in decision making problems, Journal of Multiple-Valued Logic & Soft Computing, 42, (2024).

[15] S. Kosari, X. Shi, J. Kacprzyk, Z. Chen, and H. Rashmanlou, Description of perfectly regular fuzzy graphs with application in psychological sciences, Journal of Multiple-Valued Logic & Soft Computing, 42, (2024).

[16] S. Kosari, P. Xu, J. Kacprzyk, J. Shafi, A. Khan, and H. Rashmanlou, A novel decision-making method based on fuzzy graphs, Journal of Multiple-Valued Logic & Soft Computing, 46(1), (2025).

[17] N. Ramya and M. Deivanayaki, Impact of Soret and Dufour effects on Casson nanofluid flow in a magnetic field, Indian Journal of Science and Technology, 18(13), 1059–1070, (2025).

[18] G. Muhiuddin, N. Ramya, B. Pourhassan, H. Rashmanlou, F. Maqsood, and N. Aldossari, Thermal and bioconvective analysis of Williamson fluid over a porous curved stretching surface, Case Studies in Thermal Engineering, 106774, (2025).

[19] N. Ramya, R. Tamilamuthan, H. Rashmanlou, and F. Mofidnakhaei, Holographic and thermodynamic topological perspectives on AdS Einstein-Power-Yang-Mills black holes, Journal of Holography Applications in Physics, 6(1), 98–125, (2025).

[20] R. Rajaraman, Nonlinear reaction–diffusion modeling in enzyme immobilized systems: integer and fractional approaches, Applied Biochemistry and Biotechnology, 197(2), 793–820, (2025).

[21] G. Muhiuddin, N. Ramya, B. Pourhassan, H. Rashmanlou, F. Maqsood, and N. Aldossary, Darcy–Forchheimer buoyant flow of chemically reactive Williamson fluid with microorganisms, Case Studies in Thermal Engineering, 108035, (2026).

[22] G. Muhiuddin, N. Ramya, F. Mofidnakhaei, H. Rashmanlou, F. Maqsood, and N. Aldossary, Stagnation-point flow of Sisko nanofluid with heat generation and nano-transport effects, Scientific Reports, (2025).

[23] N. Ramya and M. Deivanayaki, Casson nanofluid flow over a stretching surface in porous medium with thermal radiation, in: Springer Proceedings, 773–787, (2025).

[24] Y. Cao, S. Dharani, M. Sivakumar, A. Cader, and R. Nowicki, Mittag–Leffler synchronization of fractional reaction–diffusion networks via impulsive control, Journal of Artificial Intelligence and Soft Computing Research, 15(1), 25–36, (2025).

[25] A. Viana, Local theory for fractional reaction–diffusion equation, Communications in Contemporary Mathematics, 21(06), 1850033, (2019).

[26] A. Ghafoor, M. Fiaz, M. Hussain, A. Ullah, E. A. Ismail, and F. A. Awwad, Dynamics of time-fractional reaction–diffusion equations in biological processes, Scientific Reports, 14(1), 7549, (2024).

[27] S. Thakur, H. Mitra, and A. M. Ardekani, Physics-informed neural network-based inverse framework for time-fractional differential equations for rheology, Biology, 14(7), 779, (2025).

[28] A. K. Singh, M. Mehra, and R. Pulch, Non-local physics-informed neural networks for forward and inverse problems containing non-local operators, Neural Computing and Applications, 37(6), 4111–4132, (2025).

[29] E. Kharazmi, M. Cai, X. Zheng, Z. Zhang, G. Lin, and G. E. Karniadakis, Identifiability and predictability of integer- and fractional-order epidemiological models using physics-informed neural networks, Nature Computational Science, 1(11), 744–753, (2021).