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Efficient Numerical Solutions for Breast Cancer Model

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Abstract. We know that mathematical modeling is a serious agent to realize the dynamics of Breast Cancer development, spread, and educe new therapeutic approaches. The main target of this study is to use Simpson's 1/3 rule as an efficient numerical scheme for integration to numerically treat the obtained fractional integral equations and reduce them to a set of algebraic equations. The fractional derivatives here are taken in the Caputo-Fabrizio (CF) sense. Particular assurance is located on elucidating the error analysis of the given scheme. The results acquired by implementing the Runge-Kutta method (RK4M) are compared to those obtained using the achieved results. The results explain that the implemented scheme offers a precise and effective agent for simulating this model. The primary benefit of the implemented method is that it relies on a small number of uncomplicated steps and does not have long-term effects.

2020 Mathematics Subject Classifications: 34A12, 41A30, 26C10, 47H10, 65N20

Key Words and Phrases: Breast Cancer, Caputo-Fabrizio fractional derivative, Numerical integration, RK4M

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1. Introduction

Breast Cancer (BC) is described and defined as a disease condition resulting from the uncontrolled proliferation of cells inside the breast tissue. Through the data supplied by the World Health Organization (WHO) on the global burden of cancer, we can find that the BC has the highest prevalence rate when assorted to other types of cancer [8]. Globally, through surveys conducted by WHO, which ranked BC in 2004 as the second most widespread form of cancer, we find that it represents a major potential threat to women, as it influenced approximately (8-9)% of women worldwide [1]. Despite all these meditations and numerous fulfillments, the exact reason of BC is still mysterious. It was also directly responsible for the deaths of 685,000 people in 2020, out of 2.3 million women affected, as indicated by the diagnosis of 7.8 million women during the previous 5-years. Breast cancer is most common in women after puberty and its incidence increases with age [1]. Based on all of the above considerations, we emphasize the need for an aggregate understanding of the epidemiology of BC and its effects on women's health, as it is of

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great importance in improving effective preventive and therapeutic methods all over the world ([11], [21]).

Scientists are currently studying more effective fractional operators ([5]-[23]). In order to address the issue of singularity and achieve accurate and reliable modeling outcomes, a more effective CF fractional derivative has been developed. This derivative incorporates a non-singular kernel, as proposed by Caputo and Fabrizio, leading to improved efficiency and robustness in recent years. The use of Laplace transformation to convert it to integer power is regarded as a constructive method. Consequently, in some scenarios, we can readily compute the precise solution. The citation for this information is [6]. The paper [16] explores the examination of fractional operators and presents novel characteristics associated with them. Fractional derivatives have acquired increasing leverage in the last few years, as they have greatly contributed to presenting the most difficult mathematical models in a clearer and more comprehensive manner, which in turn has helped researchers to obtain more accurate solutions to such models by applying appropriate numerical and approximate methods. The fundamental focus of the research [13] is the monotonicity theorem for Fractional Differential Equations (FDEs) in the Caputo form. A study [18] has devised a highly effective numerical technique, known as the iterative reproducing kernel algorithm, for computing approximate solutions to fractional Riccati and Bernoulli DEs while considering the CF-derivative. Furthermore, a work conducted in [7] has examined the intricate dynamics of the Omicron variant of COVID-19 by employing CF-fractional operators, and others [25]. In addition, a numerical method is created that includes an exponential law kernel to analyze and model the spread of the infection.

Many mathematicians find it challenging to create numerical and approximate solutions for the FDEs ([3]-[14]). The Adams-Bashforth method, incorporating the CF operator, is formulated in [22]. This method involves three steps and can be used to solve both linear/nonlinear FDEs. Additionally, it possesses diverse uses in resolving chaotic systems with fractional orders. The authors of [12] have developed a trapezoidal strategy to solve the FDEs efficiently. This scheme utilizes the CF operator and achieves a convergence order of two. Additionally, the convergence and stability of this technique have been thoroughly investigated. Inspired by this research, we devised Simpson's 1/3 scheme for solving FDEs. This method achieves a high level of accuracy, with an order of four, as detailed in our work. The proposed fractional Simpson's 1/3 approach offers superior accuracy compared to current methods and is straightforward to implement.

The novelty in the current research is the attempt to reach numerical simulations (through a good numerical method) to study the important system under consideration which is of interest to many researchers, so we presented by shedding some light on the convergence and calculating the resulting error as well as comparisons with the same method but in a less accurate case and finally the effect of the parameters in the system on the behavior of the solution to provide recommendations that can be used by those interested in studying this model medically or industrially. This work is devoted to giving a numerical solution for the fractional BC model. This is by using the Simpson's $\frac{1}{3}$ rule for CF-fractional integral.

The outline of the paper is given as follows: Section 2, presents some basic concepts of fractional calculus in sense of the Caputo and Fabrizio. Section 3, describes the breast cancer system in its fractional form. Section 4, derives the Simpson's-$\frac{1}{3}$ rule for CF-fractional integral. Section 5, outlines a numerical implementation for solving the model under study. Section 6, presents a numerical simulation for the model under study. Section 7, gives the conclusions and remarks.

2. Preliminaries

Mathematical models using more accurate fractional derivatives (FDs) have been used by taking advantage of a non-singular kernel. This approach enhances the system's ability to accurately represent and capture memory effects. In 2015, Caputo and Fabrizio successfully introduced CF-FD by substituting the singular kernel $(t-\tau)^{-\gamma}$ with $e^{\left(\frac{-\gamma(t-\tau)}{1-\gamma}\right)}$ in the Caputo derivative [6]. Here, we will provide a succinct overview of fundamental definitions pertaining to fractional calculus involving a non-singular kernel.

Definition 1.

For $\psi(t) \in \mathbb{H}^1(0,a), 0<\gamma<1$. Then the CF-FD ${}^{CF}D^{\gamma}\psi(t)$ and CF fractional integral ${}^{CF}I^{\gamma}\psi(t)$, respectively are defined by:

$$ {}^{CF}D^{\gamma}\psi(t) := \frac{1}{1-\gamma}\int_0^t \operatorname{Exp}\Big[-\frac{\gamma}{1-\gamma}(t-\tau)\Big]\dot{\psi}(\tau)d\tau, $$

$$ {}^{CF}I^{\gamma}\psi(t) := (1-\gamma)\psi(t) + \gamma\int_0^t \psi(\tau)d\tau. \tag{1} $$

3. Formulation of the model

As mentioned above, the mathematical modeling of the BC or any other biological phenomena has been an important tool for understanding the dynamics of tumor growth in the treatment process and solving epidemiological problems. This is evident from the studies previously done in [19]. Despite the large number of studies, none of the proposed mathematical models included a diet (ketogenic diet). Therefore, Oak et al. developed the model in [20], to include some of the control factors such as immune booster, anticancer drug, and ketogenic diet, in order to confirm that there is an interaction between cells due to the variation in the tumor cell DNA [9].

We study the following fractional forms of breast cancer ([2], [24]):

$$ \begin{aligned} {}^{CF}D^{\nu}\psi_1(t) &= \lambda_1\,\psi_1(t)\left(p_1-\beta_1\psi_1(t)-\alpha_1\,\psi_2(t)\right)-(1-p)\theta_1\,\psi_1(t)\psi_4(t),\\ {}^{CF}D^{\nu}\psi_2(t) &= \lambda_2\,\psi_2(t)\left(p_2d-\beta_2\psi_2(t)-\alpha_2\psi_3(t)\right)-\kappa\psi_2(t)+(1-p)\theta_1\psi_1(t)+\psi_2(t)\psi_4(t),\\ {}^{CF}D^{\nu}\psi_3(t) &= \sigma\rho+\lambda_1\,\psi_3(t)\left(p_3-\beta_3-\alpha_3\psi_2(t)\right)-(1-p)\theta_2\psi_3(t)\psi_4(t),\\ {}^{CF}D^{\nu}\psi_4(t) &= \alpha_4\psi_4(t)+\varrho(1-p), \end{aligned} \tag{2} $$

the corresponding I.Cs of this model are taken as follows:

$$\psi_1(0) = \hat{\psi}_1^0, \qquad \psi_2(0) = \hat{\psi}_2^0, \qquad \psi_3(0) = \hat{\psi}_3^0, \qquad \psi_4(0) = \hat{\psi}_4^0.$$

The description of the meaning of the included parameters ($\in \mathbb{R}^+$) of the system (2), will give in the Table 1 [20].

The stability analysis, equilibrium points, existence, & uniqueness, of the system under consideration are given in [24].

Table 1: The description of the included variables of the system (2).

Symbol	Description
$\psi_1(t)$	Normal cell population
$\psi_2(t)$	Luminal type tumor cells
$\psi_3(t)$	Class of immune response
$\psi_4(t)$	Estrogen compartment
λ_1	Growth rate of ψ_1
λ_2	Growth rate of ψ_2
p_i	Carrying capacity of ψ_i, $i = 1, 2, 3$
$(1 - p)$	Effectiveness of anti-cancer drugs
ϱ	Process of constantly replenishing excess estrogen
α_1	Inhibition rate of $\psi_1(t)$
α_2	Rate of the effectiveness of the immune system to the tumor cells
α_3	Rate of interaction between $\psi_2(t)$ and $\psi_3(t)$
θ_1	Tumor formation rate resulting from DNA mutation caused by the presence of excess estrogen
θ_2	Immune suppression rate
β_i	Logistic rate of ψ_i, $i = 1, 2, 3$
d	Ketogenic diet

4. Derivation Simpson's-1/3 rule for CF-fractional integral

This section presents the formulation of the fractional Simpson's-1/3 rule (FSR) for solving CF-FDEs [4]. Considering the subsequent γ-order FDE:

$$^{CF}D^{\gamma}u(t) = f(u(t)), \qquad u(0) = u_0, \tag{3}$$

whereas $f \in C[0, T]$ and satisfies the Lipschitz condition:

$$|f\,(u(t_1)) - f\,(u(t_2))\,| \leq \epsilon\,|u(t_1) - u(t_2)|, \qquad \epsilon > 0. \tag{4}$$

Applying CF-fractional integral operator on the IVP (3) and applying Proposition 3 in [2] and formula (1), we get:

$$u(t) = u_0 + {}^{CF}I^{\gamma} f\,(u(t)) = u_0 + (1 - \gamma) f(u(t)) + \gamma \int_0^t f(u(s))ds. \tag{5}$$

Theorem 1. *[17]*

Let us assume a continuous function f: $[0,T]\times\mathbb{R}\to\mathbb{R}$ with $\gamma\in(0,1)$ that satisfies the criterion (4). Then the IVP (3) has a unique solution on $C[0,T]$ under the condition:

$$\frac{(2(1-\gamma)+2\gamma T)\epsilon}{(2-\gamma)}<1.$$

Initially, we will employ a quadratic polynomial P_2 to estimate the integral function f in Equation (5). The function will be assessed at t_0, t_1, and t_2, where t_0 is less than t_1, and t_1 is less than t_2. The interval is partitioned into two subintervals, denoted as $t_1-t_0=t_2-t_1=h$, resulting in a combined width of $2h$. The integration of the quadratic polynomial P_2 can be computed as follows:

$$I_2f(u(t))=\int_a^b f(u(t))dt\approx\int_{t_0}^{t_2}P_2(u(t))dt=\int_{t_0}^{t_2}\left[\sum_{j=0}^{2}L_j(t)\,f\left(u\left(t_j\right)\right)\right]dt,$$

where the second-order Lagrange polynomials $L_0(t)$, $L_1(t)$, and $L_2(t)$ are defined as follows:

$$L_j(t)=\prod_{i=0,\,i\neq j}^{2}\frac{(t-t_i)}{(t_j-t_i)}.$$

Integrating the first interpolant function $L_0(t)$, by taking $h=\frac{t_2-t_0}{2}$ and substituting "$t=s+t_0$", gives us:

$$\begin{aligned}\int_{t_0}^{t_2}L_0(t)dt&=\frac{1}{2h^2}\int_{t_0}^{t_0+2h}\left(t-t_1\right)\left(t-t_2\right)dt=\frac{1}{2h^2}\int_0^{2h}\left(s+t_0-t_2\right)\left(s+t_0-t_1\right)ds\\&=\frac{1}{2h^2}\int_0^{2h}(s-2h)(s-h)ds=\frac{h}{3}.\end{aligned}$$

After making some simplifications to the rest of the terms, we have the following:

$$I_2(f)=\frac{h}{3}\left[f\left(u\left(t_0\right)\right)+4f\left(u\left(t_1\right)\right)+f\left(u\left(t_2\right)\right)\right].$$

Using Eq.(5), we get:

$$u\left(t_n\right)=u_0+(1-\gamma)f\left(u\left(t_n\right)\right)+\frac{h}{3}\left[f\left(u\left(t_0\right)\right)+4f\left(u\left(t_1\right)\right)+f\left(u\left(t_2\right)\right)\right],\quad n=0,1,2.$$

To improve the accuracy of numerical integration, we partition $[a,b]$ to n sub-intervals as follows:

For any even number $n\geq 2$, we establish the following definitions:

$$h=\frac{b-a}{n}=t_{k+1}-t_k,\quad k=0,1,2,\ldots,n.$$

Now, by using the quadrature rule for each pair of subintervals and implementing the Simpson's-1/3 rule to each of $\left[t_{2k}, t_{2(k+1)}\right], \quad k = 0, 1, 2, \ldots, \frac{n-2}{2}$, we can appoint the following formula:

$$I_n(f) = \sum_{k=0}^{\frac{n-2}{2}} \int_{t_{2k}}^{t_{2k+2}} f(u(t))dt = \sum_{k=0}^{\frac{n-2}{2}} \left(\frac{h}{3} \left[f\left(u\left(t_{2k}\right)\right) + 4f\left(u\left(t_{2k+1}\right)\right) + f\left(u\left(t_{2k+2}\right)\right) \right] \right).$$

By referring u_n as the approximate solution of $u\left(t_n\right)$ and using Eq.(5), we can write the FSR for the CF-FDE (3), for $n = 0[1](m-1)$:

$$u_{n+1} = u_0 + (1-\gamma) f\left(u_{n+1}\right) + \gamma \frac{h}{3} \left[f\left(u\left(t_0\right)\right) + 4 \sum_{i=2,4,6}^{n} f\left(u\left(t_i\right)\right) + 2 \sum_{j=1,3,5}^{n-1} f\left(u\left(t_j\right)\right) + f\left(u\left(t_{n+1}\right)\right) \right].$$

This formula can be rewritten in a compact form as follows:

$$u_{n+1} = u_0 + (1-\gamma) f\left(u_{n+1}\right) + \gamma h \sum_{r=0}^{n+1} \xi_r f\left(u_r\right), \quad n = 0, 1, 2, \ldots, m-1, \tag{6}$$

where ξ_r are the weights of the FSR and defined as:

$$\xi_r = \begin{cases} 1/3, & r = 0, \; n+1, \\ 2/3, & r = 1, 3, 5, \ldots, \\ 4/3, & r = 2, 4, 6, \ldots. \end{cases}$$

Lemma 1. *[4]*

Suppose that $f(u(t)) \in C^4([a, b])$, then the error of numerical scheme (6) is estimated by:

$$\left| \int_{t_0}^{t_{n+1}} f(u(s))ds - \gamma h \sum_{i=0}^{n+1} \xi_i f\left(u(t_i)\right) \right| \leq h^4,$$

where $\hat{c} = \frac{(b-a) f^{(4)}(\zeta)}{180}$, for some constant $a < \zeta < b$, $h = \frac{b-a}{n}$, and $t_k = a + hk$, $k = 0, 1, \ldots, n+1$.
The stability and error analysis of the regulated numerical scheme are investigated and proved meanwhile the following theorems [4].

Theorem 2.

The newly designed fractional numerical technique (6) exhibits conditional stability.
Proof. The proof of this theorem can be found on [4].

Theorem 3.

The recently developed fractional numerical method exhibits conditional convergence of order 4, as stated in equation (6).

$$\|u(t_{n+1}) - u_{n+1}\| \leq \mathfrak{C}h^4,$$

where $\mathfrak{C} = \gamma \hat{c}\, c_h$.

Proof. The proof of this criterion can be found on [4].

5. Numerical implementation

Here in this section, we will try to treat the shortcomings of the existing numerical methods, which are represented by the slow convergence of most of them when solving this type of problem, which in turn leads to inaccurate approximations ([14], [15]). For this, we will use the FSR for numerical integration to calculate the resulting integral in the system of integral equations obtained from the same system of FDEs under study.

Now, we will numerically treat the BC system in its fractional form by creating a numerical scheme of it. For this purpose, let us reformulate the system (2) in an operator form as follows:

$$^{CF}D^{\nu}\,\bar{\Psi}(t) = \mathbb{F}(\bar{\Psi}(t), t), \tag{7}$$

where

$$\bar{\Psi}(t) = [\psi_1(t), \psi_2(t), \psi_3(t), \psi_4(t)]^T, \quad \mathbb{F}(\bar{\Psi}(t), t) = [\mathbf{f}_1, \mathbf{f}_2, \mathbf{f}_3, \mathbf{f}_4]^T, \quad \bar{\Psi}(0) = [\hat{\psi}_1^0, \hat{\psi}_2^0, \hat{\psi}_3^0, \hat{\psi}_4^0]^T, \tag{8}$$

where each one of the functions $\mathbf{f}_i(\psi_1, \psi_2, \psi_3, \psi_4, t)$, $i = 1(1)4$ is defined in the RHS of the four equations in (2), respectively.

Applying CF-fractional integral operator on the model (7) and implementing Proposition 3 in [2] and formula (1), we get:

$$\bar{\Psi}(t) = \bar{\Psi}(0) + {}^{CF}I^{\nu}\,\mathbb{F}(\bar{\Psi}(t), t) = \bar{\Psi}(0) + (1-\nu)\mathbb{F}(\bar{\Psi}(t), t) + \nu \int_0^t \mathbb{F}(\bar{\Psi}(s), s)ds. \tag{9}$$

Applying the derived FSR for the integration on the RHS of (9), to get the following numerical scheme as constructed in the formula (6):

$$\bar{\Psi}_{n+1} = \bar{\Psi}(0) + (1-\nu)\mathbb{F}(\bar{\Psi}_{n+1}, t_{n+1}) + \nu\, h \sum_{r=0}^{n+1} \xi_r\, \mathbb{F}(\bar{\Psi}_r, t_r), \quad n = 0, 1, 2, \ldots, m-1, \tag{10}$$

where the weights ξ_r, $r = 0, 1, ..., n+1$ of the FSR are defined in (6).

So, the system given in (10) transforms to an algebraic equations system as follows:

$$\begin{aligned} \psi_{k,n+1} = \psi_{k,0} &+ (1-\nu)\mathbf{f}_k(\psi_{1,n+1}, \psi_{2,n+1}, \psi_{3,n+1}, \psi_{4,n+1}, t_{n+1}) \\ &+ \nu\, h \sum_{r=0}^{n+1} \xi_r\, \mathbf{f}_k(\psi_{1,r}, \psi_{2,r}, \psi_{3,r}, \psi_{4,r}, t_r), \qquad k = 1(1)4, \end{aligned}$$

where the functions $\mathbf{f}_k$ are defined in (8).

6. Experimental results

Now, we are going to test the precision of the resulting numerical scheme by introducing numerical simulation on some cases in $[0, 3]$ for the proposed model (2). The behavior of $\psi_k(t)$, $k = 1, 2, 3, 4$ are presented in Figures 1-5 at different values of some parameters (ν, ϱ, p, m).

We approach the system under study (2) with the following values for the parameters contained in it [10]:

$$\theta_1 = 0.2, \quad \theta_2 = 0.02, \quad \lambda_1 = 0.3, \quad \lambda_2 = 0.4, \quad d = 0.5, \quad \alpha_1 = 6 \times 10^{-8}, \quad \alpha_2 = 3 \times 10^{-7},$$

$$\alpha_3 = 1\times10^{-7}, \quad \alpha_4 = 0.97, \quad \rho = 0.01, \quad \kappa = 2, \quad \beta_1 = 0.15, \quad \beta_2 = 0.7, \quad \beta_3 = 0.1, \quad p = 0.5,$$

$$\sigma = 0.1, \quad p_1 = 0.1, \quad p_2 = 0.2, \quad p_3 = 0.3, \quad \varrho = 0.8,$$

with the initial conditions (I.Cs) $\psi_i(0) = 0.2$, $i = 1, 2, 3, 4$. Figures 1-5 display a numerical simulation for the system under investigation by applying the given procedure.

(i) Figure 1 outlines the solution via various values of ν = 1.0, 0.95, 0.85, 0.75, at $h = 0.01$.

(ii) Figure 2 gives the solution for distinct values of $m = 5, 10, 15$.

(iii) Figure 3 shows the solution for distinct values of the estrogen source rate ϱ = 0.8, 1.4, 2.0, 2.6.

(iv) Figure 4 depicts the effect of p (= 0.25, 0.5, 0.75, 1.0) on the approximate solution.

(v) Figure 5 presents a comparison between the solution created by the obtained approach with that numerical solution by implementing RK4M [14] with the same parameters and I.Cs.

The behavior of the approximate solution is based on ν, m, ϱ, p, as shown in Figures 1-4, respectively. From Figures 3 and 4, we can confirm that the behavior of the solution consists with the nature effect of the parameters ϱ, and p, respectively. From Figures 2 and 5, we can point out that the proposed method has been well implemented to solve the model under study. Hence, we can verify that the expected behavior of the disease has been obtained, which means that we have provided an evident simulation of the proposed system that can be used by the relevant authorities to treat this deadly cancer.

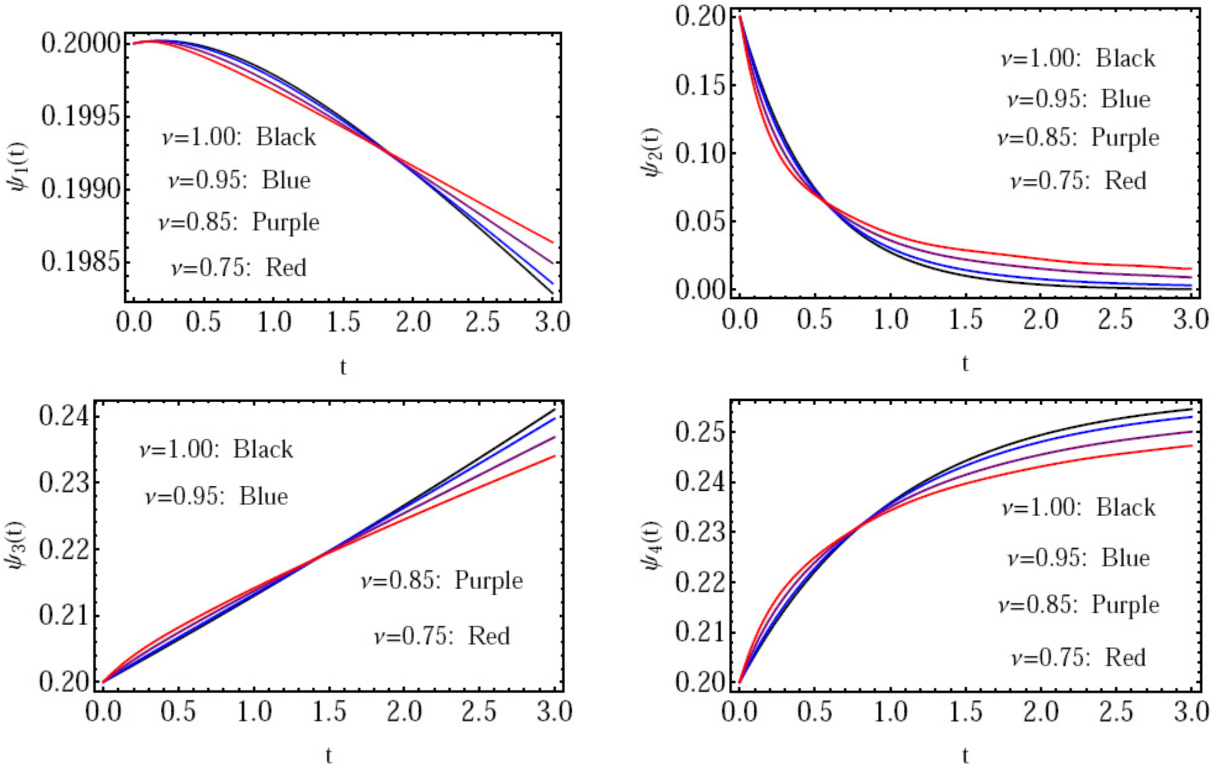

Figure 1. The solution $\psi_i(t)$ via various values of ν.

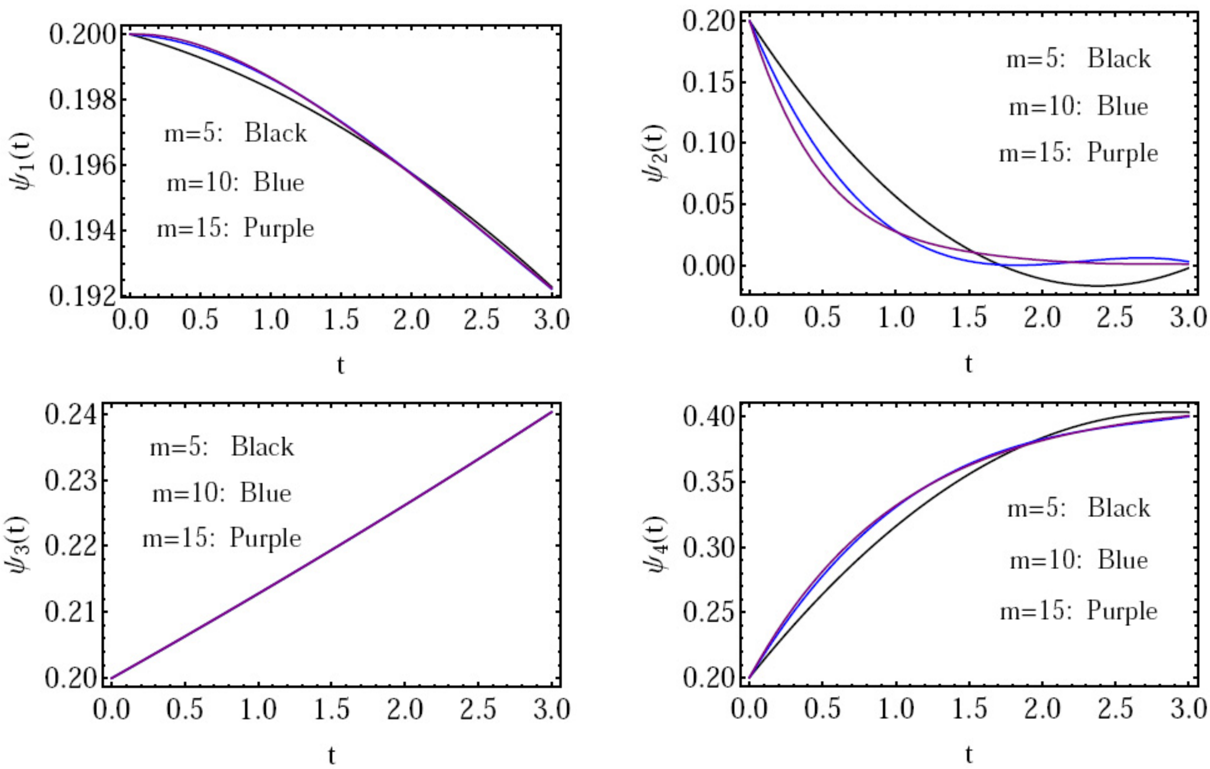

Figure 2. The solution $\psi_i(t)$ via various values of m.

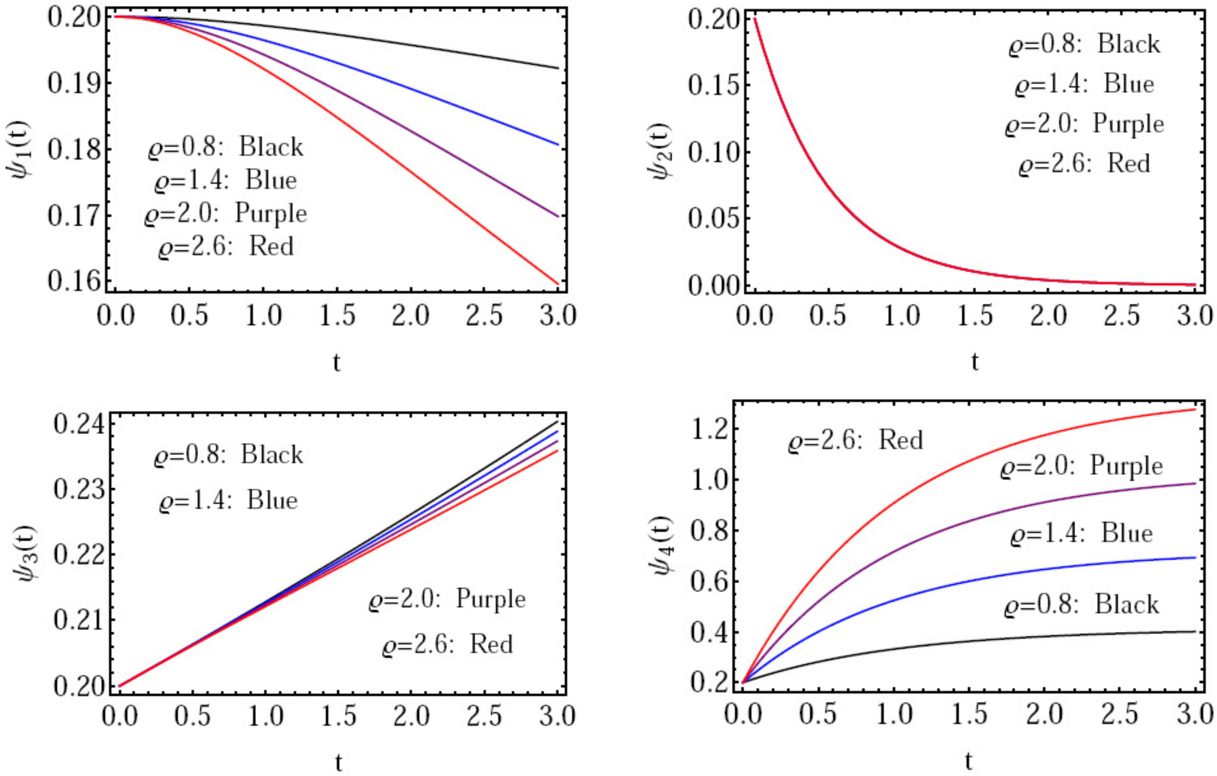

Figure 3. The solution $\psi_i(t)$ via various values of ϱ.

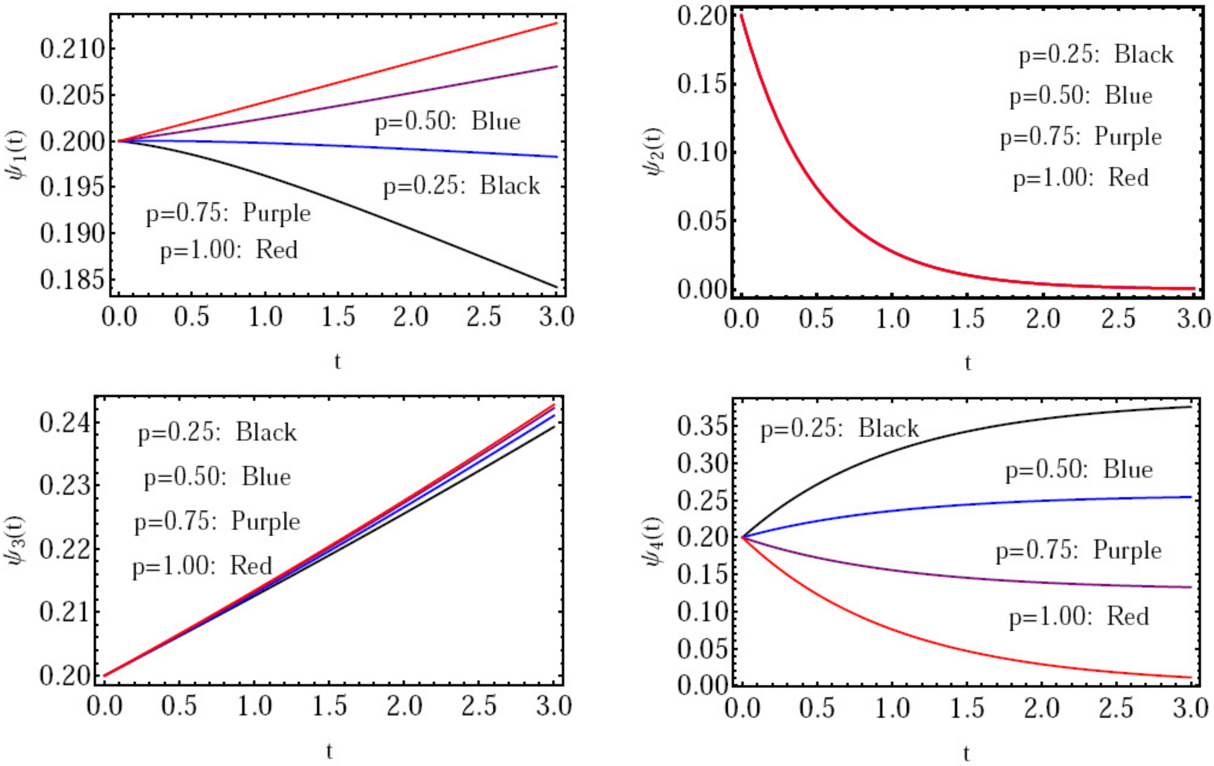

Figure 4. The solution $\psi_i(t)$ via various values of p.

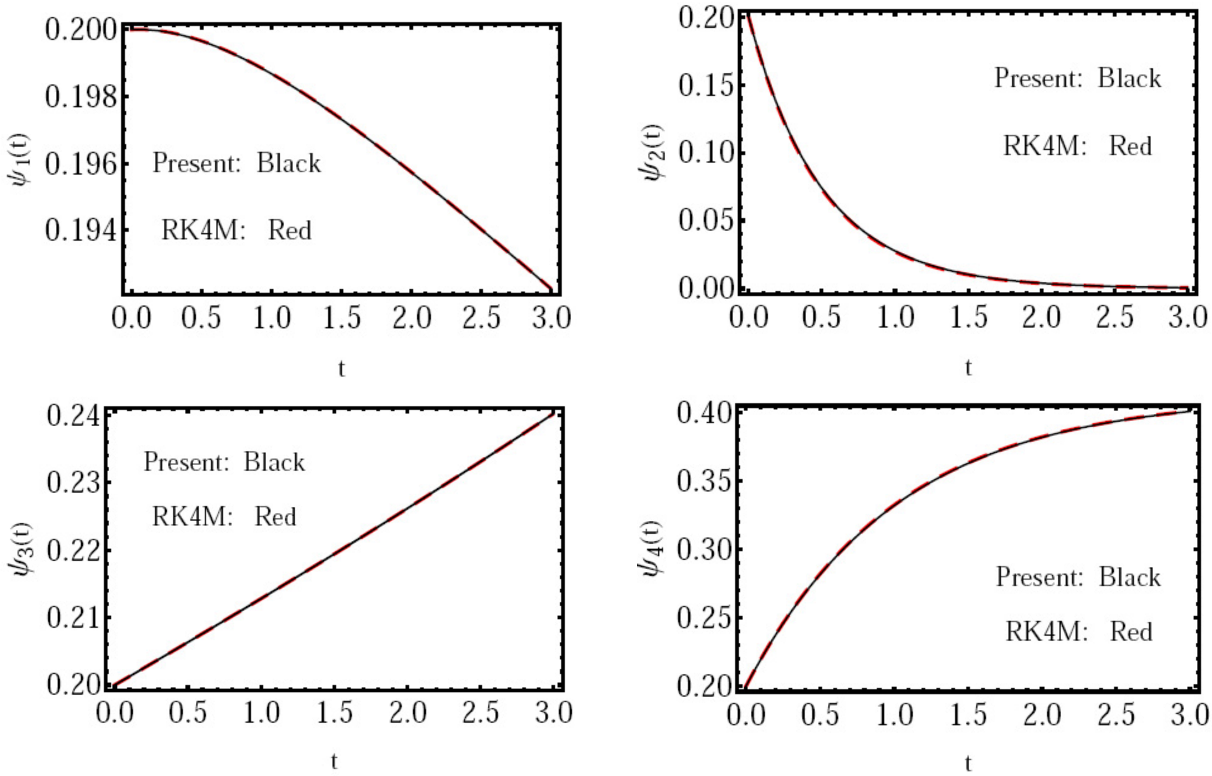

Figure 5. Comparison the solution obtained by proposed method and RK4M.

7. Conclusions and remarks

This study aims to utilize an efficient and accurate method to gain numerical solutions for the CF-fractional BC mathematical system. Simpson's rule 1/3 was applied in its fractional form in computing the resulting integral within the system of fractional integral equations corresponding to the FDEs expressing mathematically the BC model to achieve fourth-order accuracy for the resulting solutions. This study utilized several values of the fractional order ν and ϱ, m, p to derive solutions for the model being examined. Also, we have determined that the proposed approach is remarkably effective in analyzing this system. Furthermore, reducing the value of h allows us to control the accuracy of the numerical solution. From the obtained solutions, we can confirm that the offered approach is surprisingly successful in simulating the BC model, as well as demonstrating the accuracy and computational effectiveness of this method. Finally, the present study may contribute to providing more robust physical explanations for future theoretical and computational studies on the same topic.

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