

## Numerical Solution for Fractional-Order Mathematical Model of Immune-Chemotherapeutic Treatment for Breast Cancer Using Modified Fractional Formula

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**Abstract.** Cancer is a complex and diverse group of diseases characterized by the uncontrolled growth and spread of abnormal cells in the body. Tumors, which are commonly associated with cancer, refer to abnormal masses of tissue that can develop in various organs or tissues. Cancer can arise from almost any cell type in the body and can affect different organs and systems. The disease occurs when the normal processes of cell division and growth go awry, leading to the formation of malignant tumors. These tumors have the potential to invade nearby tissues and spread to distant parts of the body through a process known as metastasis. In this paper, we aim to present a numerical solution for a recent fractional-order model related to Immune-Chemotherapeutic Treatment for Breast Cancer (ICT) using a novel numerical scheme called the Modified Fractional Euler Method (MFEM). We will also compare our proposed scheme with the traditional numerical scheme, Fractional Euler Method (FEM), through numerical simulations.

### 1. Introduction

Mathematical modeling plays a crucial role in understanding and studying cancer tumors. Mathematical models are used to describe and simulate the growth, development, and behavior of tumors,

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as well as their interactions with the surrounding tissues and the immune system. These models help researchers and clinicians gain insights into the underlying mechanisms of tumor growth, predict treatment outcomes, and optimize therapeutic strategies see [1, 3].

There are several mathematical models used in cancer research, such as Growth Models: these models describe the growth dynamics of tumors over time. They incorporate factors such as cell proliferation, cell death, nutrient supply, and oxygen levels to simulate tumor growth patterns. Pharmacokinetic Models: these models focus on how drugs are absorbed, distributed, metabolized, and eliminated in the body. They help in understanding drug concentrations at tumor sites and predicting drug effectiveness. Spatial Models: tumors often exhibit spatial heterogeneity, meaning that their characteristics vary in different regions. Spatial models consider the spatial distribution of tumor cells, nutrients, oxygen, and other factors, allowing researchers to study the impact of spatial organization on tumor growth and treatment response. Immune Response Models: These models capture the interactions between the tumor and the immune system. They help investigate how the immune system recognizes and responds to tumor cells, and how immunotherapies can be used to enhance immune responses against cancer. Evolutionary Models: Tumors can undergo genetic and phenotypic changes, leading to the development of drug resistance and disease progression. Evolutionary models simulate the evolutionary dynamics within a tumor population, helping to understand the emergence and spread of resistant cell populations see [5, 7].

These mathematical models are typically based on differential equations, cellular automata, agent-based models, or other mathematical frameworks. They are often calibrated and validated using experimental data and can provide valuable insights into tumor behavior, treatment response, and the effectiveness of various therapeutic interventions. It's important to note that mathematical models are simplifications of the complex biological reality, and their predictions should be interpreted with caution. However, they serve as powerful tools for hypothesis generation, guiding experimental design, and aiding in clinical decision-making in the field of cancer research and treatment see [9, 11].

Overall, the mathematical system divides the fractional-order breast cancer mathematical model among four manifestations: normal cell population  $S$ , tumor cells  $R$ , immune response class  $N$  and estrogen compartment  $Z$ , ( $SRNZ$ ).

The fractional-order ICT model represents a promising approach for improving the diagnosis and treatment of this devastating disease. However, further research is needed to fully validate the model and to translate its findings into clinical practice. The objective of this paper is to develop a numerical solution for the fractional-order differential system associated with ICT. We will employ a numerical scheme, the Modified Fractional Euler Method (MFEM), to solve this system and obtain numerical results see [2, 6, 8, 10]. Anyhow, the ICT model can be described in the following manner:

$$\begin{aligned} D^\mu S(t) &= S(t)\rho_1(k_1 - \varsigma_1 S(t) - \gamma_1 R(t)) - (1 - k)\psi_1 S(t)Z(t), \\ S(0) &= S_0, \end{aligned} \tag{1.1}$$

$$D^\mu R(t) = R(t)\rho_2(k_2d - s_2R(t) - \gamma_2N(t)) - \delta R(t) + (1 - k)\psi_1S(t)R(t)Z(t),$$

$$R(0) = R_0,$$

$$D^\mu N(t) = \eta\lambda + N(t)\rho_1(k_3 - s_3 - \gamma_3R(t)) - (1 - k)\psi_2N(t)Z(t),$$

$$N(0) = N_0,$$

$$D^\mu Z(t) = \gamma_4Z(t) + (1 - k)v,$$

$$Z(0) = Z_0.$$

In which the parameters are positive real values. This model 1.1 explains the relation between normal cell population ( $S$ ), tumor cells ( $R$ ), immune response class ( $N$ ), and estrogen compartment ( $Z$ ). Where Caputo fractional derivative  $D^\mu$  with a fractional order  $\mu$ , where  $0 < \mu < 1$ , is applied to the temporal derivative in the system. The system involves several positive constants as parameters, including  $\rho_1, \rho_2, \gamma_1, \gamma_2, \gamma_3, \gamma_4, s_1, s_2, \psi_1, \psi_2, \delta, k, v$ . These parameters govern various aspects of the model such as the Fractional cell kill, Carrying capacity, Competition term, Death rate, and Per capita growth rate respectively. Overall, the system involves various parameters that govern the dynamics of different cell populations in the context of breast cancer, and the numerical solution using the MFEM will provide insights into the behavior of the system under different conditions.

## 2. Modified Fractional Euler Method

We introduce fundamental definitions and theorems related to fractional calculus, including Riemann-Liouville integral and derivative, Caputo derivative and other relevant concepts [4].

**Definition 2.1.** *The fractional Riemann-Liouville integral of a function  $f(t)$  of order  $0 < \mu \leq 1$  is initially defined by*

$$J^\mu f(t) = \frac{1}{\Gamma(\mu)} \int_0^t f(\tau)(t - \tau)^{\mu-1} d\tau, \quad t > 0, \quad \mu > 0. \quad (2.1)$$

Some of the properties of the Riemann-Liouville integral are given below for completeness:

$$J^0 f(t) = f(t). \quad (2.2)$$

$$J^\mu(t - a)^\gamma = \frac{\Gamma(\gamma + 1)}{\Gamma(\mu + \gamma + 1)}(t - a)^{\mu+\gamma}, \quad \gamma \geq -, a \in \mathbb{R}. \quad (2.3)$$

$$J^\mu J^\beta f(t) = J^\beta J^\mu f(t), \quad \mu, \beta \geq 0. \quad (2.4)$$

$$J^\mu J^\beta f(t) = J^{\mu+\beta} f(t), \quad \mu, \beta \geq 0. \quad (2.5)$$

**Definition 2.2.** *The Caputo fractional derivative of a real-valued function  $f(t)$  of order  $0 < \alpha \leq 0$  is defined as*

$${}^c D_*^\alpha f(t) = \frac{1}{\Gamma(1 - \alpha)} \int_0^t \frac{f'(\tau)}{(t - \tau)^\alpha} d\tau, \quad (2.6)$$

where  $0 < \alpha < 1$  and  $t > 0$ .

Some of the characteristics of the Caputo derivative are listed below:

- ${}^C D_*^\alpha c = 0$ , where  $c$  is constant.
- For  $a \in \mathbb{R}$  we have

$${}^C D_*^\alpha (t-a)^\rho = \begin{cases} \frac{\Gamma(\rho+1)}{\Gamma(\rho-\alpha+1)} (t-a)^{\rho-\alpha}, & \rho > \alpha - 1, \\ 0, & \text{otherwise.} \end{cases}$$

- ${}^C D_*^\alpha$  is a linear operator, i.e.,

$${}^C D_*^\alpha (\mu f(t) + \omega k(t)) = \mu {}^C D_*^\alpha (f(t)) + \omega {}^C D_*^\alpha (k(t)),$$

where  $\mu$  and  $\omega$  are constants.

In addition, we need to recall the following basic property for their significance:

$$J^\alpha {}^C D_*^\alpha f(t) = f(t) - \sum_{i=1}^n f^i(0^+) \frac{t^i}{i!}, \quad t > 0, \quad (2.7)$$

where  $m-1 < \alpha \leq m$  such that  $m \in \mathbb{N}$ .

**Definition 2.3.** The Caputo fractional derivative operator  ${}^C D_*^\alpha$  can be defined in terms of the Riemann-Liouville fractional integral operator as follows:

$${}^C D_*^\alpha f = J^{m-\alpha} D^m f. \quad (2.8)$$

where  $\alpha \in \mathbb{R}^+$  and  $m = \lceil \alpha \rceil$ .

**Definition 2.4.** [4] The Mittag-Leffler function of two parameters  $\alpha$  and  $\beta$  is outlined by the following series:

$$E_{\alpha,\beta}(t) = \sum_{k=0}^{\infty} \frac{t^k}{\Gamma(\alpha k + \beta)},$$

where  $\alpha, \beta > 0$  and  $t \in \mathbb{C}$ .

**Theorem 2.1.** [4] (Generalized Taylor's formula) Suppose that  ${}^C D_*^{k\alpha} f(x) \in C(0, b]$  for  $k = 0, 1, 2, \dots, n+1$ , where  $0 < \alpha \leq 1$ . Then we can expand the function  $f$  about the node  $x_0$  as follows:

$$f(x) = \sum_{i=0}^n \frac{(x-x_0)^{i\alpha}}{\Gamma(i\alpha+1)} ({}^C D_*^{i\alpha} f)(x_0) + \frac{(x-x_0)^{(n+1)\alpha}}{\Gamma((n+1)\alpha+1)} ({}^C D_*^{(n+1)\alpha} f)(\xi), \quad (2.9)$$

with  $0 < \xi < x$ ,  $\forall x \in (0, b]$ .

This section will recall some existing numerical methods to deal with the fractional initial value IVP problem formulated in the sense of Caputo fractional differentiator [4]. Such a problem has the form:

$$D^\alpha y(t) = f(t, y(t)), \quad (2.10)$$

with the initial condition:

$$y(0) = y_0, \quad (2.11)$$

where  $0 < \alpha \leq 1$ . The authors in [12] developed a generalization of the classical Euler method called the Fractional Euler Method (FEM) by proposing a general formula for solving fractional IVPs (2.10-2.11). This formula has the following form:

$$\begin{aligned} w_0 &= y_0 \\ w_{i+1} &= w_i + \frac{h^\alpha}{\Gamma(\alpha + 1)} f(t_i, w_i), \end{aligned} \quad (2.12)$$

for  $i = 0, 1, \dots, k - 1$ . Note that  $w_i$  denotes the numerical solution of problem (2.10-2.11) at  $t_i$ .

More recently, the authors in [2] have successfully developed a new further modification for the FEM, called MFEM for solving fractional IVP (2.10-2.11). This formula has the form:

$$\begin{aligned} w_0 &= y_0 \\ w_{i+1} &= w_i + \frac{h^\alpha}{\Gamma(\alpha + 1)} f\left(t_i + \frac{h^\alpha}{2\Gamma(\alpha + 1)}, w_i + \frac{h^\alpha}{2\Gamma(\alpha + 1)} f(t_i, w_i)\right), \end{aligned} \quad (2.13)$$

for  $i = 0, 1, 2, \dots, k - 1$ .

### 3. Solving fractional-order cancer tumor disease model

In this section, we intend to employ MFEM to obtain a numerical solution of the fractional-order ICT model 1.1. This method represents a fractional version of the traditional Euler method. Therefore, to obtain a full overview of this method, the reader may refer to [2]. From now, we endeavor to apply MFEM to the fractional-order ICT model 1.1. For this purpose, we can consider such a model again as follows:

$$\begin{aligned} D^\mu S(t) &= d_1(t, S(t), R(t), N(t), Z(t)), \\ D^\mu R(t) &= d_2(t, S(t), R(t), N(t), Z(t)), \\ D^\mu N(t) &= d_3(t, S(t), R(t), N(t), Z(t)), \\ D^\mu Z(t) &= d_4(t, S(t), R(t), N(t), Z(t)), \end{aligned} \quad (3.1)$$

where

$$\begin{aligned} d_1(t, S(t), R(t), N(t), Z(t)) &= S(t)\rho_1(k_1 - s_1S(t) - \gamma_1R(t)) - (1 - k)\psi_1S(t)Z(t), \\ d_2(t, S(t), R(t), N(t), Z(t)) &= R(t)\rho_2(k_2d - s_2R(t) - \gamma_2N(t)) - \delta R(t) + (1 - k)\psi_1S(t)R(t)Z(t), \\ d_3(t, S(t), R(t), N(t), Z(t)) &= \eta\lambda + N(t)\rho_1(k_3 - s_3 - \gamma_3R(t)) - (1 - k)\psi_2N(t)Z(t), \\ d_4(t, S(t), R(t), N(t), Z(t)) &= \gamma_4Z(t) + (1 - k)v. \end{aligned} \quad (3.2)$$

For instance, to generate the set of points  $(t_k, S(t_k))$  of the class  $S$  formulated in such a system, we have to assume that each of  $S(t)$ ,  $D^\mu S(t)$  and  $D^{2\mu} S(t)$  are continuous on  $(0, T]$ . In this regard, if one supposes that:

$$d_1(t, S(t), R(t), N(t), Z(t)) = \rho S(t) + r_1 S(t)(k_1 - \beta_1 S(t)) - \gamma S(t)R(t) - d_1 S(t) - \tau_1 S(t)N(t),$$

so that

$$D^\mu S(t) = d_1(t, S(t), R(t), N(t), Z(t)),$$

then by using formula (2.13), we can have the following expression:

$$S(t_{i+1}) = S(t_i) + \frac{h^\mu}{\Gamma(\mu+1)} d_1 \left( t_i + \frac{h^\mu}{2\Gamma(\mu+1)}, S(t_i) + \frac{h^\mu}{2\Gamma(\mu+1)} d_1(t_i, S(t_i), R(t_i), N(t_i), Z(t_i)) \right), \quad (3.3)$$

where  $i = 0, 1, 2, \dots, k-1$ .

Similarly, the procedure outlined above can be used to get approximate numerical solutions for the remaining classes. Ultimately, we can deduce the following recursive states that represent the whole approximate numerical solution of system (1.1):

$$\begin{aligned} S(t_{i+1}) &= S(t_i) + \frac{h^\mu}{\Gamma(\mu+1)} d_1 \left( t_i + \frac{h^\mu}{2\Gamma(\mu+1)}, S(t_i) + \frac{h^\mu}{2\Gamma(\mu+1)} d_1(t, S(t_i), R(t_i), N(t_i), Z(t_i)) \right), \\ R(t_{i+1}) &= R(t_i) + \frac{h^\mu}{\Gamma(\mu+1)} d_2 \left( t_i + \frac{h^\mu}{2\Gamma(\mu+1)}, E(t_i) + \frac{h^\mu}{2\Gamma(\mu+1)} d_2(t, S(t_i), R(t_i), N(t_i), Z(t_i)) \right), \\ N(t_{i+1}) &= N(t_i) + \frac{h^\mu}{\Gamma(\mu+1)} d_3 \left( t_i + \frac{h^\mu}{2\Gamma(\mu+1)}, I(t_i) + \frac{h^\mu}{2\Gamma(\mu+1)} d_3(t, S(t_i), R(t_i), N(t_i), Z(t_i)) \right), \\ Z(t_{i+1}) &= Z(t_i) + \frac{h^\mu}{\Gamma(\mu+1)} d_4 \left( t_i + \frac{h^\mu}{2\Gamma(\mu+1)}, R(t_i) + \frac{h^\mu}{2\Gamma(\mu+1)} d_4(t, S(t_i), R(t_i), N(t_i), Z(t_i)) \right), \end{aligned} \quad (3.4)$$

where  $d_1, d_2, d_3, d_4$  are defined in (3.2)  $i = 0, 1, 2, \dots, k-1$ .

#### 4. Numerical results

In this part, we offer some numerical findings using the technique described in the preceding section. We examine an ICT interaction's fractional-order differential system and for more, we recommend [15–19]. For this purpose, we consider the values of the parameters  $M = 20, L = 15, \psi_1 = 0.1, \psi_2 = 0.1, \psi_3 = 0.1, \rho_1 = 0.3, \rho_2 = 0.4, d_1 = 0.5, \gamma_1 = 6 * 10^{-8}, \gamma_2 = 3 * 10^{-7}, \gamma_4 = 0.97, \nu = 1, \lambda = 0.01, \delta = 2, \varsigma_1 = 0.2, \varsigma_2 = 0.002, k = 0.5, \eta = 1.3 * 10^2, k_1 = 1.232, k_2 = 1.75, k_3 = 0.15$ . For the given parameter values, we plot the numerical solution of the considered model in Figures 1-2-3 and 4. This solution represents the numerical solution curves of the fractional-order differential system of ICT. In particular, in Figure 1 we use the FEM and MFEM to show the size of the normal cells with  $\mu = 0.8, 0.9, 1$ . In Figure 2 we use the FEM and MFEM to show the size of the tumor cells, with  $\mu = 0.8, 0.9, 1$ . In Figure 3 we use the FEM and MFEM to show the size of the

immune cells, with  $\mu = 0.8, 0.9, 1$ . In Figure 4 we use the FEM and MFEM to show the size of the chemotherapeutic drugs with  $\mu = 0.8, 0.9, 1$ .

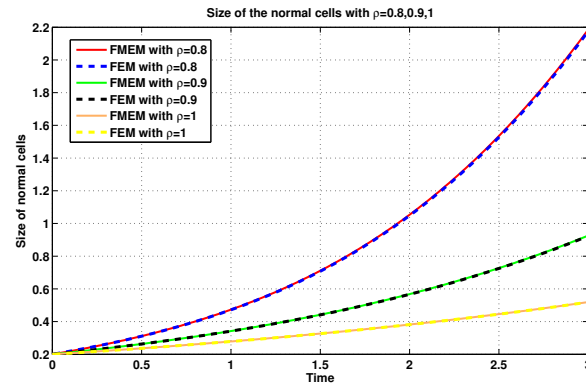


Figure 1. Size of the normal cells with  $\rho = 0.8, 0.9, 1$

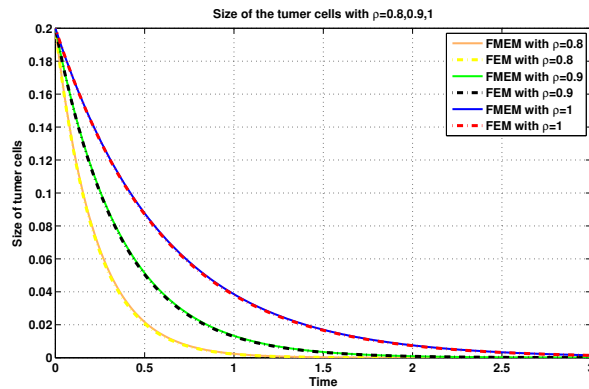


Figure 2. Size of the tumor cells with  $\rho = 0.8, 0.9, 1$

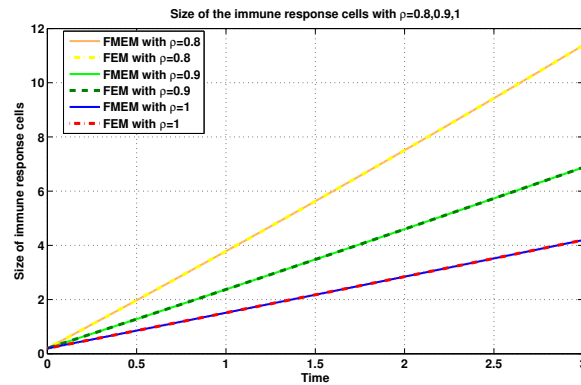


Figure 3. Size of the immune cells, with  $\rho = 0.8, 0.9, 1$

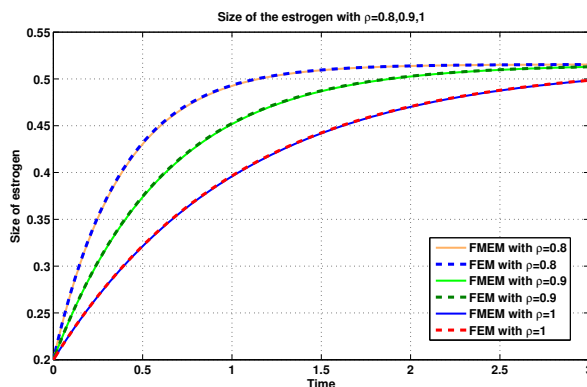


Figure 4. Size of the chemotherapeutic drugs with  $\rho = 0.8, 0.9, 1$

One might observe that the above numerical simulations illustrate the system's dynamic behavior and stability around equilibria. Based on these simulations it can be determined that the fractional-order version of the differential system of the ICT carried out by the two numerical methods (FEM and MFEM) are completely considered. For more about fractional calculus and its applications, the reader may refer to [6, 8, 10, 13, 14].

## 5. Conclusion

The Modified Fractional Euler Method (MFEM) has been employed in this paper to investigate a fractional-order version of the differential system of ICT. The utilization of this powerful numerical scheme has yielded impressive results, demonstrating the high efficiency of the algorithm. The obtained numerical results open up possibilities for conducting further research in this field and showcasing additional findings in the future.

**Conflicts of Interest:** The authors declare that there are no conflicts of interest regarding the publication of this paper.

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