

Dynamical Behavior of Fractional Order Breast Cancer Model: an Analytical and Numerical Study

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Received: 25 Sep. 2022, Revised: 28 Dec. 2022, Accepted: 26 Jan. 2023

Published online: 1 Apr. 2024

Abstract: In this paper, we investigate the dynamical behavior of the fractional-order breast cancer model with modified parameters. In this fractional-order model (FOM), we replaced the integer-order derivatives with the fractional-order derivatives on both sides. In physics, this means that the memory of a biological process is examined and transferred from one part to another while maintaining balance. The positivity of solutions of this FOM is proved. Also, the equilibrium points and stability of disease-free and endemic cases for this FOM are studied. Furthermore, the basic reproduction number (R_0) is computed and sensitivity analysis concerning the parameters is achieved. We solve this FOM by two methods one of them gives an analytic-approximate solution called generalized Mittag-Leffler function method (GMLFM) and another method gives a numerical solution called predictor-corrector method (PCM). The simulations for the suggested model are presented to verify the obtained theoretical results.

Keywords: Breast cancer model, stability, fractional differential equations, Mittag-Leffler function, predictor-corrector method.

1 Introduction

A breast cancer disease (BCD) is the most common cancer diagnosed where can occur in both men and women, but its far more common in women, BCD is a cancer that forms in the cells of the breast [1]. The BCD occurs when some breast cells begin to grow abnormally, these cell divide more rapidly than healthy cell do and continue to accumulate forming a lump or mass may cell spread through your breast to your lymph nodes or to other parts of your body. The most common types of BCD are invasive ductal carcinoma, in this type the cancer cells grow outside the ducts into other parts of the breast tissue and Invasive lobular carcinoma, in this kind the cancer cells spread from the lobules to the breast tissue that is near it. There are different kinds of cancer treatments such as surgery, hormone therapy, radiotherapy, chemotherapy and targeted therapy. These treatments are used to kill cancer cells and remove them or prevent them from spreading. Usually, surgery is the first kind of treatment in use compared to other treatments. The target of BCD surgery is to discover the stage of the disease and remove cancer from the breast. Chemotherapy may be used if cancer has spread or there is a risk it will. Chemotherapy is dependent on many factors such as the number of lymph nodes involved, the size of cancer, and the presence of estrogen or progesterone receptors. Breast cancer treatment with chemotherapy has side effects on the heart is called cardiotoxicity [2]. The BCD has been studied in various ways by researchers in the literature (see e.g., [3, 4, 5, 6, 7, 8, 9]).

Mathematical models have been widely used to address the analysis of models that describe diseases such as bifurcation, extinction, the stability of solution and permanence of disease (see e.g., [10, 11, 12, 13, 14]). There are two kinds of mathematical models: the continuous-time models described by differential equations and the discrete-time models described by a difference equation. Moreover, there are different formulations to investigate continuous-time mathematical models, for instance, partial differential equations, ordinary differential equations and fractional-order differential equations (FODEs). The reason for using FODEs are very suitable tools related to systems with the memory and genetic effects of various processes and substances. A lot of models in interdisciplinary fields can be modeled by FODEs, such as epidemic [15], diffusion waves [16], nonlinear oscillation of earthquakes [17], viscoelastic material [18],

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hydrologic [19], wave propagation in nonlocal elastic continua [20], world economies [21], gyros [22], energy supply-demand [23] and muscular blood vessel [24]. Also, FODEs are closely related to fractals which are wide in biological systems. So, FODEs are more convenient than systems with integer order in biological, social and economic systems where memory has an important and effective role [25].

In consideration of epidemiological models, it is important to study the basic reproduction number which is defined as the expected number of secondary individuals produced by an individual in its lifetime and it is symbolized by the symbol R_0 [26, 27]. If $R_0 < 1$, then the free-disease equilibrium is locally asymptotically stable and the endemic equilibrium does not exist, also when $R_0 > 1$, then the free-disease equilibrium is unstable and the endemic equilibrium is stable [28, 29].

In this article, we consider the FOM for breast cancer as follows:

$$\begin{aligned}
 {}^C_0D_t^\alpha U &= \gamma_1^\alpha - \beta_1^\alpha U - \beta_2^\alpha U, \\
 {}^C_0D_t^\alpha V &= \gamma_2^\alpha + \beta_2^\alpha U - \xi_1^\alpha Z - \xi_2^\alpha V - \xi_3^\alpha V - \xi_4^\alpha V - \eta_1^\alpha V, \\
 {}^C_0D_t^\alpha W &= \gamma_3^\alpha + \xi_3^\alpha V + \delta_1^\alpha Z - \delta_2^\alpha W - \delta_3^\alpha W - \eta_2^\alpha W, \\
 {}^C_0D_t^\alpha Z &= \beta_1^\alpha U + \xi_2^\alpha V + \delta_2^\alpha W - \xi_1^\alpha Z - \delta_1^\alpha Z - \varepsilon_1^\alpha Z, \\
 {}^C_0D_t^\alpha M &= \varepsilon_1^\alpha Z + \delta_3^\alpha W + \xi_4^\alpha V - \eta_3^\alpha M,
 \end{aligned} \tag{1}$$

where U denote to the individuals who first received treatment, V refer to the individuals who were first treated at the hospital, W express to the individuals who are treated for the first time because the cancer has undergone metastasis, Z refer to the individuals number where disease-free can be increased, M denote to the individuals who experience cardiotoxic, γ_1 the rate of new patients diagnosed to suffer cancer, β_1 and β_2 represents the recovery and worse rate of the individuals who have been chemotherapy, respectively, γ_2 the individuals rate who were first treated at the hospital, both ξ_2 and ξ_3 were the recovery (disease-free) and the worse rate of the individuals after they used chemotherapy respectively, ξ_4 be the cardiotoxicity rate, η_1 the individuals death rate from cancer, δ_2 the recovery rate where the individuals become experience complete response, δ_3 the cardiotoxicity rate of cancer chemotherapy individuals who experience cardiotoxic, η_2 the death rate of stage W , ξ_1 the recovery rate of the individuals who back to V , δ_1 the recovery rate of individuals who back to stage W , ε_1 the recovery rate of the individuals who experience cardiotoxic and η_3 the death rate of cardiotoxic.

The main aim of this work is to formulate a fractional-order for the breast cancer model with modified parameters. Also, we investigate the stability analysis and their equilibria for the proposed FOM. Moreover, we solve this model analytically and numerically by two different methods. Additionally, the simulation for the obtained results is presented.

The remainder of this research is organized as follows. In Section 2, we define some essential and important definitions and concepts of fractional calculus. We introduce the non-negative solution in Section 3. Also, the stability analysis of the system (1) and its equilibrium fixed points are investigated detailedly in Section 4. Additionally, our methods and its applications are introduced in Section 5. Numerical simulation is carried out to support the theoretical results in Section 6. Finally, we show our conclusion in Section 7.

2 Preliminaries

Here, we introduce some important definitions concerned to fractional calculus (see [30]).

Definition 1. The fractional integral of order $\alpha > 0$ in Riemann-Liouville sense is define by

$${}_aI_x^\alpha f(x) = \frac{1}{\Gamma(\alpha)} \int_a^x (x-\xi)^{\alpha-1} f(\xi) d\xi, \quad x > a,$$

$${}_aI_x^0 f(x) = f(x),$$

where $\Gamma(\alpha)$ is Euler Gamma function is defined as follows

$$\Gamma(z) = \int_0^\infty x^{z-1} e^{-x} dx, \quad \Re(z) > 0.$$

Definition 2. The Riemann-Liouville fractional derivatives is defined by

$${}_aD_x^\alpha f(x) = \begin{cases} \frac{1}{\Gamma(\alpha-n)} \frac{d^n}{dt^n} \int_a^t \frac{f(\xi)}{(t-\xi)^{\alpha-n+1}} d\xi, & n-1 < \alpha < n, n \in \mathbb{N}, \\ \frac{d^n f(x)}{dt^n}, & \alpha = n \in \mathbb{N}. \end{cases}$$

Definition 3. The Caputo fractional derivative of order $\alpha > 0$ is defined as follows

$${}^C D_x^\alpha f(x) = \begin{cases} \frac{1}{\Gamma(n-\alpha)} \int_a^x (x-\xi)^{n-\alpha-1} f^{(n)}(\xi) d\xi, & n-1 < \alpha < n, n \in \mathbb{N}, \\ \frac{d^n f(x)}{dt^n}, & \alpha = n \in \mathbb{N}. \end{cases}$$

Also, we present some properties of fractional calculus their detailedly explained in references [31, 32]

$${}^C D_x^\alpha {}^I_x^\alpha f(x) = f(x),$$

$${}^I_x^{\alpha c} {}^C D_x^\alpha f(x) = f(x) - \sum_{k=0}^{n-1} f^{(k)}(a) \frac{(x-a)^k}{\Gamma(k+1)}.$$

Definition 4. In (1902-1905), the Mittag-Leffler functions E_α and $E_{\alpha,\beta}$ defined by the power series as follows:

$$E_\alpha(x) = \sum_{n=0}^{\infty} \frac{x^n}{\Gamma(n\alpha + 1)}, \quad E_{\alpha,\beta}(x) = \sum_{n=0}^{\infty} \frac{x^n}{\Gamma(n\alpha + \beta)}, \quad \alpha, \beta > 0. \tag{2}$$

Therefore, the Caputo fractional derivative of the generalized Mittag-Leffler function (see e.g., [33, 34, 35, 36]) is given by

$${}^C D_t^\alpha E_\alpha(ax^\alpha) = \sum_{n=1}^{\infty} a^n \frac{x^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)}. \tag{3}$$

3 Non-Negative Solution

Let $R_+^5 = \{X \in R^5 : X \geq 0\}$, where $X(t) = (U, V, W, Z, M)^T$. In order to proceed, we introduce the following theorem and corollary.

Theorem 1. [37] (The mean value theorem). Suppose that $f(x) \in C(0, a]$ and $D^\alpha f(x) \in C(0, a]$, for $0 < \alpha \leq 1$. Then, we have

$$f(x) = f(0) + \frac{1}{\Gamma(\alpha)} (D^\alpha f)(\xi)(x)^\alpha,$$

with $0 \leq \xi \leq x, \forall x \in (0, a]$.

Corollary 1. [38] Assume that $f(x) \in C[0, a]$ and $D^\alpha f(x) \in C(0, a]$, for $0 < \alpha \leq 1$. It show that from Theorem 1 that if $D^\alpha f(x) \geq 0, \forall x \in (0, a]$, then $f(x)$ is non-decreasing and if $D^\alpha f(x) \leq 0, \forall x \in (0, a]$, then $f(x)$ is non-increasing $\forall x \in [0, a]$.

Theorem 2. There is a unique solution $X(t) = (U, V, W, Z, M)^T$ for (1) at $t \geq 0$ and the solution will remain in R_+^5 .

Proof. From [39], we can obtain the existence and uniqueness of the solution of the initial value problem (1) in $(0, \infty)$. Now we will show that R_+^5 is positively invariant domain. Then

$$\begin{aligned} {}^C D_t^\alpha U|_{U=0} &= \gamma_1^\alpha \geq 0, \\ {}^C D_t^\alpha V|_{V=0} &= \gamma_2^\alpha + \beta_2^\alpha U + \xi_1^\alpha Z \geq 0, \\ {}^C D_t^\alpha W|_{W=0} &= \gamma_3^\alpha + \xi_3^\alpha V + \delta_1^\alpha Z \geq 0, \\ {}^C D_t^\alpha Z|_{Z=0} &= \beta_1^\alpha U + \xi_2^\alpha V + \delta_2^\alpha W \geq 0, \\ {}^C D_t^\alpha M|_{M=0} &= \varepsilon_1^\alpha Z + \delta_3^\alpha W + \xi_4^\alpha V \geq 0. \end{aligned}$$

According to corollary 1, we will deduce that the solution remain in R_+^5 .

4 Stability and Equilibrium Points

To estimate the equilibrium points of the FOM (1), suppose that

$$\begin{aligned} {}_0^C D_t^\alpha U &= 0, \\ {}_0^C D_t^\alpha V &= 0, \\ {}_0^C D_t^\alpha W &= 0, \\ {}_0^C D_t^\alpha Z &= 0, \\ {}_0^C D_t^\alpha M &= 0. \end{aligned}$$

Then, we deduce that the model (1) has two equilibrium fixed points as follows:

–Free-disease equilibrium point $E_1 = (U_1, V_1, W_1, Z_1, M_1)$

$$= \left(\frac{\gamma_1^\alpha}{\beta_1^\alpha + \beta_2^\alpha}, 0, 0, \frac{\beta_1^\alpha U_1}{\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha}, \frac{\varepsilon_1^\alpha Z_1}{\eta_3^\alpha} \right).$$

–Endemic equilibrium point $E_* = (U_*, V_*, W_*, Z_*, M_*)$

$$= \left(\frac{\gamma_1^\alpha}{\beta_1^\alpha + \beta_2^\alpha}, \frac{\gamma_2^\alpha + \beta_2^\alpha U_* \xi_1^\alpha Z_*}{\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha}, \frac{\gamma_3^\alpha + \xi_3^\alpha V_* + \delta_1^\alpha Z_*}{\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha}, \frac{\beta_1^\alpha U_* + \xi_2^\alpha V_* + \delta_2^\alpha W_*}{\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha}, \frac{\varepsilon_1^\alpha Z_* + \delta_3^\alpha W_* + \xi_4^\alpha V_*}{\eta_3^\alpha} \right),$$

where

$$Z_* = \frac{\left(\xi_2^\alpha \left(1 - \frac{1}{R_0} \right) \right) \left[\beta_1^\alpha U_* (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) + 2\delta_2^\alpha \gamma_3^\alpha \right] + \left(\xi_3^\alpha \gamma_2^\alpha + \xi_3^\alpha \beta_2^\alpha U_* \right) \left[3\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha \right]}{\left(\xi_2^\alpha \left(1 - \frac{1}{R_0} \right) \right) \left[(\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) - 2\delta_2^\alpha \xi_1^\alpha \xi_3^\alpha + \delta_1^\alpha \right] - \xi_1^\alpha \xi_3^\alpha \left[3\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha \right]},$$

also R_0 [40] is given as follows:

$$R_0 = \rho(FV^{-1}) = \frac{-\xi_2^\alpha}{(\xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)},$$

where

$$F = \begin{pmatrix} -\xi_2^\alpha & 0 \\ \xi_3^\alpha & 0 \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha & 0 \\ -\xi_3^\alpha & \delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha \end{pmatrix}.$$

Stability Analysis of the Free-Disease Equilibrium Point E_1

We state the following theorem to discuss the local stability of the disease-free equilibrium fixed point E_1 of model (1).

Theorem 3. *The disease-free equilibrium E_1 is locally asymptotically stable if $R_0 < 1$, and it is unstable if $R_0 > 1$.*

Proof. The Jacobian matrix of the system (1) evaluated at an equilibrium fixed point E_1 is given by

$$J(E_1) = \begin{pmatrix} -(\beta_1^\alpha + \beta_2^\alpha) & 0 & 0 & 0 & 0 \\ \beta_2^\alpha & -(\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) & 0 & \xi_1^\alpha & 0 \\ 0 & \xi_3^\alpha & -(\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) & \delta_1^\alpha & 0 \\ \beta_1^\alpha & \xi_2^\alpha & \delta_2^\alpha & -(\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) & 0 \\ 0 & \xi_4^\alpha & \delta_3^\alpha & \varepsilon_1^\alpha & -\eta_3^\alpha \end{pmatrix}, \tag{4}$$

and the corresponding characteristic equation at the disease-free equilibrium E_1 is

$$(\beta_1^\alpha + \beta_2^\alpha + \lambda_1)(\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha + \lambda_2)(\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha + \lambda_3)(\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha + \lambda_4)(\eta_3^\alpha + \lambda_5) = 0. \tag{5}$$

Then, the eigenvalues of equation (5) are

$$\begin{aligned} \lambda_1 &= -(\beta_1^\alpha + \beta_2^\alpha) < 0, \\ \lambda_2 &= -(\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) < 0, \\ \lambda_3 &= -(\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) < 0, \\ \lambda_4 &= -(\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) < 0, \\ \lambda_5 &= -\eta_3^\alpha < 0. \end{aligned}$$

From the previous results of the eigenvalues, we note that the disease-free equilibrium E_1 is locally asymptotically stable.

Sensitivity Analysis of R_0

Here, we show that the sensitivity of R_0 at each parameters

$$\begin{aligned} \frac{\partial R_0}{\partial \xi_2^\alpha} &= \frac{-1}{(\xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)} < 0, \\ \frac{\partial R_0}{\partial \xi_3^\alpha} &= \frac{\xi_2^\alpha}{(\xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)^2} > 0, \\ \frac{\partial R_0}{\partial \xi_4^\alpha} &= \frac{\xi_2^\alpha}{(\xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)^2} > 0, \\ \frac{\partial R_0}{\partial \eta_1^\alpha} &= \frac{\xi_2^\alpha}{(\xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)^2} > 0. \end{aligned}$$

This refer to R_0 is increasing at $\xi_3^\alpha, \xi_4^\alpha, \eta_1^\alpha$ and decreasing at ξ_2^α .

5 Applications and Results

In this part, we show the efficiency and performance of the GMLFM as an analytic-approximate solution and the PCM as a numerical solution for solving FOM (1).

5.1 Implementing GMLFM on the Proposed Model

Here, we explain how use the GMLFM to solve the FOM (1). For more details of the analysis of GMLFM (see e.g., [33, 34, 35, 36]). Let

$$\begin{aligned} U &= \sum_{n=0}^{\infty} a^n \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, & V &= \sum_{n=0}^{\infty} b^n \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ W &= \sum_{n=0}^{\infty} c^n \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, & Z &= \sum_{n=0}^{\infty} d^n \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ M &= \sum_{n=0}^{\infty} l^n \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \end{aligned} \tag{6}$$

by using Eq.(3) we have

$$\begin{aligned} {}^C_0D_t^\alpha U &= \sum_{n=1}^{\infty} a^n \frac{t^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)} = \sum_{n=0}^{\infty} a^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ {}^C_0D_t^\alpha V &= \sum_{n=1}^{\infty} b^n \frac{t^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)} = \sum_{n=0}^{\infty} b^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ {}^C_0D_t^\alpha W &= \sum_{n=1}^{\infty} c^n \frac{t^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)} = \sum_{n=0}^{\infty} c^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ {}^C_0D_t^\alpha Z &= \sum_{n=1}^{\infty} d^n \frac{t^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)} = \sum_{n=0}^{\infty} d^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \\ {}^C_0D_t^\alpha M &= \sum_{n=1}^{\infty} l^n \frac{t^{(n-1)\alpha}}{\Gamma((n-1)\alpha + 1)} = \sum_{n=0}^{\infty} l^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha + 1)}, \end{aligned} \tag{7}$$

by substituting from Eqs.(6) and (7) in model (1), we get

$$\left\{ \begin{array}{l} \sum_{n=0}^{\infty} a^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} = \gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha) \sum_{n=0}^{\infty} a^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)}, \\ \sum_{n=0}^{\infty} b^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} = \gamma_2^\alpha + \beta_2^\alpha \sum_{n=0}^{\infty} a^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \xi_1^\alpha \sum_{n=0}^{\infty} d^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) \sum_{n=0}^{\infty} b^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)}, \\ \sum_{n=0}^{\infty} c^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} = \gamma_3^\alpha + \xi_3^\alpha \sum_{n=0}^{\infty} b^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \delta_1^\alpha \sum_{n=0}^{\infty} d^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) \sum_{n=0}^{\infty} c^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)}, \\ \sum_{n=0}^{\infty} d^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} = \beta_1^\alpha \sum_{n=0}^{\infty} a^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \xi_2^\alpha \sum_{n=0}^{\infty} b^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \delta_2^\alpha \sum_{n=0}^{\infty} c^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} - (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) \sum_{n=0}^{\infty} d^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)}, \\ \sum_{n=0}^{\infty} l^{n+1} \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} = \varepsilon_1^\alpha \sum_{n=0}^{\infty} d^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \delta_3^\alpha \sum_{n=0}^{\infty} c^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} + \xi_4^\alpha \sum_{n=0}^{\infty} b^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)} - \eta_3^\alpha \sum_{n=0}^{\infty} l^n \frac{t^{n\alpha}}{\Gamma(n\alpha+1)}, \end{array} \right. \quad (8)$$

after calculate the summations of equation (8), we obtain

$$\left\{ \begin{array}{l} \sum_{n=0}^{\infty} \left(\frac{a^{n+1}}{\Gamma(n\alpha+1)} + (\beta_1^\alpha + \beta_2^\alpha) \frac{a^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} = \gamma_1^\alpha, \\ \sum_{n=0}^{\infty} \left(\frac{b^{n+1}}{\Gamma(n\alpha+1)} - \beta_2^\alpha \frac{a^n}{\Gamma(n\alpha+1)} - \xi_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} + (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) \frac{b^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} = \gamma_2^\alpha, \\ \sum_{n=0}^{\infty} \left(\frac{c^{n+1}}{\Gamma(n\alpha+1)} - \xi_3^\alpha \frac{b^n}{\Gamma(n\alpha+1)} - \delta_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} + (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) \frac{c^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} = \gamma_3^\alpha, \\ \sum_{n=0}^{\infty} \left(\frac{d^{n+1}}{\Gamma(n\alpha+1)} - \beta_1^\alpha \frac{a^n}{\Gamma(n\alpha+1)} - \xi_2^\alpha \frac{b^n}{\Gamma(n\alpha+1)} - \delta_2^\alpha \frac{c^n}{\Gamma(n\alpha+1)} + (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) \frac{d^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} = 0, \\ \sum_{n=0}^{\infty} \left(\frac{l^{n+1}}{\Gamma(n\alpha+1)} - \varepsilon_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} - \delta_3^\alpha \frac{c^n}{\Gamma(n\alpha+1)} - \xi_4^\alpha \frac{b^n}{\Gamma(n\alpha+1)} + \eta_3^\alpha \frac{l^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} = 0. \end{array} \right. \quad (9)$$

By taking the first limit of the equation (9) we deduce that

$$\begin{aligned} a^1 &= \gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha) a^0, \\ b^1 &= \gamma_2^\alpha + \beta_2^\alpha a^0 + \xi_1^\alpha d^0 - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) b^0, \\ c^1 &= \gamma_3^\alpha + \xi_3^\alpha b^0 + \delta_1^\alpha d^0 - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) c^0, \\ d^1 &= \beta_1^\alpha a^0 + \xi_2^\alpha b^0 + \delta_2^\alpha c^0 - (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha) d^0, \\ l^1 &= \varepsilon_1^\alpha d^0 + \delta_3^\alpha c^0 + \xi_4^\alpha b^0 - \eta_3^\alpha l^0. \end{aligned} \quad (10)$$

From Eq.(10), then Eq.(9) transformed to

$$\left\{ \begin{aligned} \sum_{n=1}^{\infty} \left(\frac{a^{n+1}}{\Gamma(n\alpha+1)} + (\beta_1^\alpha + \beta_2^\alpha) \frac{a^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} &= 0, \\ \sum_{n=1}^{\infty} \left(\frac{b^{n+1}}{\Gamma(n\alpha+1)} - \beta_2^\alpha \frac{a^n}{\Gamma(n\alpha+1)} - \xi_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} + (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) \frac{b^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} &= 0, \\ \sum_{n=1}^{\infty} \left(\frac{c^{n+1}}{\Gamma(n\alpha+1)} - \xi_3^\alpha \frac{b^n}{\Gamma(n\alpha+1)} - \delta_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} + (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) \frac{c^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} &= 0, \\ \sum_{n=1}^{\infty} \left(\frac{d^{n+1}}{\Gamma(n\alpha+1)} - \beta_1^\alpha \frac{a^n}{\Gamma(n\alpha+1)} - \xi_2^\alpha \frac{b^n}{\Gamma(n\alpha+1)} - \delta_2^\alpha \frac{c^n}{\Gamma(n\alpha+1)} + (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha) \frac{d^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} &= 0, \\ \sum_{n=1}^{\infty} \left(\frac{l^{n+1}}{\Gamma(n\alpha+1)} - \epsilon_1^\alpha \frac{d^n}{\Gamma(n\alpha+1)} - \delta_3^\alpha \frac{c^n}{\Gamma(n\alpha+1)} - \xi_4^\alpha \frac{b^n}{\Gamma(n\alpha+1)} + \eta_3^\alpha \frac{l^n}{\Gamma(n\alpha+1)} \right) t^{n\alpha} &= 0. \end{aligned} \right. \tag{11}$$

From Eq.(11), we note that $t^{n\alpha}$ is impossible equal to zero but the coefficients that equal to zero and we can obtain values of the constants a^n, b^n, c^n, d^n, l^n , and $n = 1, 2, 3, \dots$.

$$\begin{aligned} a^{n+1} &= -(\beta_1^\alpha + \beta_2^\alpha)a^n, \\ b^{n+1} &= \beta_2^\alpha a^n + \xi_1^\alpha d^n - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)b^n, \\ c^{n+1} &= \xi_3^\alpha b^n + \delta_1^\alpha d^n - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)c^n, \\ d^{n+1} &= \beta_1^\alpha a^n + \xi_2^\alpha b^n + \delta_2^\alpha c^n - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha)d^n, \\ l^{n+1} &= \epsilon_1^\alpha d^n + \delta_3^\alpha c^n + \xi_4^\alpha b^n - \eta_3^\alpha l^n, \end{aligned} \tag{12}$$

at $n = 1$ we get the following relation

$$\left\{ \begin{aligned} a^2 &= -(\beta_1^\alpha + \beta_2^\alpha)(\gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha)a^0), \\ b^2 &= \beta_2^\alpha (\gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha)a^0) + \xi_1^\alpha (\beta_1^\alpha a^0 + \xi_3^\alpha b^0 + \delta_2^\alpha c^0 - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha)d^0) \\ &\quad - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha) (\gamma_2^\alpha + \beta_2^\alpha a^0 + \xi_1^\alpha d^0 - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)b^0), \\ c^2 &= \xi_3^\alpha (\gamma_2^\alpha + \beta_2^\alpha a^0 + \xi_1^\alpha d^0 - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)b^0) + \delta_1^\alpha (\beta_1^\alpha a^0 + \xi_3^\alpha b^0 + \delta_2^\alpha c^0 - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha)d^0) \\ &\quad - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha) (\gamma_3^\alpha + \xi_3^\alpha b^0 + \delta_1^\alpha d^0 - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)c^0), \\ d^2 &= \beta_1^\alpha (\gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha)a^0) + \xi_2^\alpha (\gamma_2^\alpha + \beta_2^\alpha a^0 + \xi_1^\alpha d^0 - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)b^0) \\ &\quad + \delta_2^\alpha (\gamma_3^\alpha + \xi_3^\alpha b^0 + \delta_1^\alpha d^0 - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)c^0) - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha) (\beta_1^\alpha a^0 + \xi_3^\alpha b^0 + \delta_2^\alpha c^0 - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha)d^0), \\ l^2 &= \epsilon_1^\alpha (\beta_1^\alpha a^0 + \xi_3^\alpha b^0 + \delta_2^\alpha c^0 - (\xi_1^\alpha + \delta_1^\alpha + \epsilon_1^\alpha)d^0) + \delta_3^\alpha (\gamma_3^\alpha + \xi_3^\alpha b^0 + \delta_1^\alpha d^0 - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)c^0) \\ &\quad + \xi_4^\alpha (\gamma_2^\alpha + \beta_2^\alpha a^0 + \xi_1^\alpha d^0 - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)b^0) - \eta_3^\alpha (\epsilon_1^\alpha d^0 + \delta_3^\alpha c^0 + \xi_4^\alpha b^0 - \eta_3^\alpha l^0), \end{aligned} \right. \tag{13}$$

By substituting from equations (10) and (13) into Eq.(6) we obtain the following expression in the infinite series form as

$$U = a^0 + a^1 \frac{t^\alpha}{\Gamma(\alpha + 1)} + a^2 \frac{t^{2\alpha}}{\Gamma(2\alpha + 1)} + a^3 \frac{t^{3\alpha}}{\Gamma(3\alpha + 1)} + a^4 \frac{t^{4\alpha}}{\Gamma(4\alpha + 1)} + a^5 \frac{t^{5\alpha}}{\Gamma(5\alpha + 1)} + \dots,$$

$$V = b^0 + b^1 \frac{t^\alpha}{\Gamma(\alpha + 1)} + b^2 \frac{t^{2\alpha}}{\Gamma(2\alpha + 1)} + b^3 \frac{t^{3\alpha}}{\Gamma(3\alpha + 1)} + b^4 \frac{t^{4\alpha}}{\Gamma(4\alpha + 1)} + b^5 \frac{t^{5\alpha}}{\Gamma(5\alpha + 1)} + \dots,$$

$$W = c^0 + c^1 \frac{t^\alpha}{\Gamma(\alpha + 1)} + c^2 \frac{t^{2\alpha}}{\Gamma(2\alpha + 1)} + c^3 \frac{t^{3\alpha}}{\Gamma(3\alpha + 1)} + c^4 \frac{t^{4\alpha}}{\Gamma(4\alpha + 1)} + c^5 \frac{t^{5\alpha}}{\Gamma(5\alpha + 1)} + \dots,$$

$$Z = d^0 + d^1 \frac{t^\alpha}{\Gamma(\alpha + 1)} + d^2 \frac{t^{2\alpha}}{\Gamma(2\alpha + 1)} + d^3 \frac{t^{3\alpha}}{\Gamma(3\alpha + 1)} + d^4 \frac{t^{4\alpha}}{\Gamma(4\alpha + 1)} + d^5 \frac{t^{5\alpha}}{\Gamma(5\alpha + 1)} + \dots,$$

$$M = l^0 + l^1 \frac{t^\alpha}{\Gamma(\alpha + 1)} + l^2 \frac{t^{2\alpha}}{\Gamma(2\alpha + 1)} + l^3 \frac{t^{3\alpha}}{\Gamma(3\alpha + 1)} + l^4 \frac{t^{4\alpha}}{\Gamma(4\alpha + 1)} + l^5 \frac{t^{5\alpha}}{\Gamma(5\alpha + 1)} + \dots$$

5.2 Implementing PCM on the Proposed Model

We apply the PCM or Predict, Evaluate, Correct, Evaluate (PECE) method ([41,42,43,44,45]) on the fractional-order breast cancer model (1) to illustrate the theoretical analysis. We explain the approximate solution of the FODEs by given this algorithm in the following approach.

Let considered the general FODEs as the following

$$D_t^\alpha y(t) = f(t, y(t)), \quad 0 \leq t \leq T, \tag{15}$$

$$y^{(k)}(0) = y_0^{(k)}, \quad k = 0, 1, 2, \dots, [\alpha] - 1,$$

is equivalent to the Volterra integral equation

$$y(t) = \sum_{k=0}^{[\alpha]-1} y_0^{(k)} \frac{t^k}{k!} + \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha-1} f(y(\tau)) d\tau. \tag{16}$$

Assume that $h = \frac{T}{N}$, $t_n = nh$, $n = 0, 1, \dots, N \in \mathbb{Z}^+$. Then, Eq.(16) take the form as follows:

$$y_n(t_{n+1}) = \sum_{k=0}^{[\alpha]-1} y_0^{(k)} \frac{t_{n+1}^k}{k!} + \frac{h^\alpha}{\Gamma(\alpha + 2)} f(y_n^P(t_{n+1})) + \frac{h^\alpha}{\Gamma(\alpha + 2)} \sum_{j=0}^n a_{j,n+1} f(y_n(t_j)). \tag{17}$$

Where

$$a_{j,n+1} = \begin{cases} n^{\alpha+1} - (n - \alpha)(n + 1)^\alpha & \text{if } j = 0, \\ (n - j + 2)^{\alpha+1} + (n - j)^{\alpha+1} - 2(n - j + 1)^{\alpha+1} & \text{if } 0 \leq j \leq n, \\ 1 & \text{if } j = n + 1. \end{cases} \tag{18}$$

Also, the predicted value $y_n^P(t_{n+1})$ is determined by

$$y_n^P(t_{n+1}) = \sum_{k=0}^{[\alpha]-1} y_0^{(k)} \frac{t_{n+1}^k}{k!} + \frac{1}{\Gamma(\alpha)} \sum_{j=0}^n b_{j,n+1} f(y_n(t_j)), \tag{19}$$

where

$$b_{j,n+1} = \frac{h^\alpha}{\alpha} ((n-j+1)^\alpha - (n-j)^\alpha). \quad (20)$$

This is show that the PCM is an approximation for the fractional-order integration. By applying the above approach, system (1) transformed to

$$\left\{ \begin{array}{l} U_{n+1} = U_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} [\gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha)U_{n+1}^P] + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=0}^n a_{j,n+1} [\gamma_1^\alpha - (\beta_1^\alpha + \beta_2^\alpha)U_j], \\ V_{n+1} = V_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} [\gamma_2^\alpha + \beta_2^\alpha U_{n+1}^P + \xi_1^\alpha Z_{n+1}^P - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)V_{n+1}^P] \\ \quad + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=0}^n a_{j,n+1} [\gamma_2^\alpha + \beta_2^\alpha U_j + \xi_1^\alpha Z_j - (\xi_2^\alpha + \xi_3^\alpha + \xi_4^\alpha + \eta_1^\alpha)V_j], \\ W_{n+1} = W_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} [\gamma_3^\alpha + \xi_3^\alpha V_{n+1}^P + \delta_1^\alpha Z_{n+1}^P - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)W_{n+1}^P] \\ \quad + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=0}^n a_{j,n+1} [\gamma_3^\alpha + \xi_3^\alpha V_j + \delta_1^\alpha Z_j - (\delta_2^\alpha + \delta_3^\alpha + \eta_2^\alpha)W_j], \\ Z_{n+1} = Z_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} [\beta_1^\alpha U_{n+1}^P + \xi_2^\alpha V_{n+1}^P + \delta_2^\alpha W_{n+1}^P - (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha)Z_{n+1}^P] \\ \quad + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=0}^n a_{j,n+1} [\beta_1^\alpha U_j + \xi_2^\alpha V_j + \delta_2^\alpha W_j - (\xi_1^\alpha + \delta_1^\alpha + \varepsilon_1^\alpha)Z_j], \\ M_{n+1} = M_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} [\varepsilon_1^\alpha Z_{n+1}^P + \delta_3^\alpha W_{n+1}^P + \xi_4^\alpha V_{n+1}^P - \eta_3^\alpha M_{n+1}^P] \\ \quad + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=0}^n a_{j,n+1} [\varepsilon_1^\alpha Z_j + \delta_3^\alpha W_j + \xi_4^\alpha V_j - \eta_3^\alpha M_j]. \end{array} \right. \quad (21)$$

6 Numerical Simulation

In this section, the dynamical behavior of system (1) is investigated numerically to confirm our analytical results. So, the numerical simulation for to suggested methods is considered by the following value of parameters $\gamma_1 = 5, \gamma_2 = 20, \gamma_3 = 11, \beta_1 = 0.63, \beta_2 = 0.56, \xi_1 = 0.36, \xi_2 = 0.35, \xi_3 = 0.62, \xi_4 = 0.30, \eta_1 = 0.5, \eta_2 = 0.8, \eta_3 = 0.4, \delta_1 = 0.42, \delta_2 = 0.10, \delta_3 = 0.30, \varepsilon_1 = 0.30$, with initial conditions $U(0) = 14, V(0) = 30, W(0) = 20, Z(0) = 10, M(0) = 10$.

Figure 1 (a) and (b) shows that the first stage of breast cancer patients U descended from 14 to 4 patients in equilibrium conditions. Similarly, the second stage of sub-populations V dropped from 30 to 14 patients in equilibrium conditions. At stage 3 the sub-population changes from 20 patients according to the initial condition to 19 patients, also stage 4 which is called disease-free occurs slightly changes concerning stage 3 such that sub-populations change from 10 to 8 patients. This shows that conditions of relative constant occur in stage 3 and disease-free sub-populations where in these cases, no significant change in population. Furthermore, in the experience of cardiotoxic M , the population increased from the initial condition of 10 patients to 32 patients in equilibrium conditions considering the equilibrium conditions at all stages occur from the 7th time period.

Figures 2 (a) and (b) are carried out by reducing the value of the relapse rate ξ_1 and δ_1 to 0.1 such that in this case deduce that the free-disease sub-population Z increased to 19 patients and the cardiotoxic sub-population M arisen to 37 patients at equilibrium conditions but the other sub-populations U, V and W are relatively stable at the same as initial conditions.

In Figures 3 (a) and (b), we display the simulation of reducing the cardiotoxic rate ξ_4 and δ_3 to 0.1. We observed that the free-disease sub-population increased slightly to 10 patients but the cardiotoxic sub-population decreased to 18 patients at the same time of equilibrium. Additionally, at stage 3 note that sub-population increased slightly compared to the initial simulation given in Figure 1. Finally, in Figures 4 and 5, we show that the simulation results of populations at different values of α .

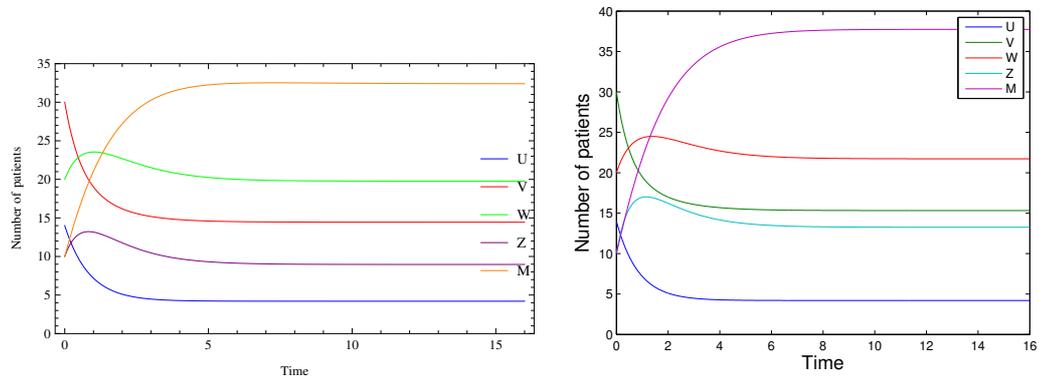


Fig. 1: The behavior of all breast cancer patients for the FOM (1) when $\alpha = 1$, the left plot using GMLFM and the right plot using PCM.

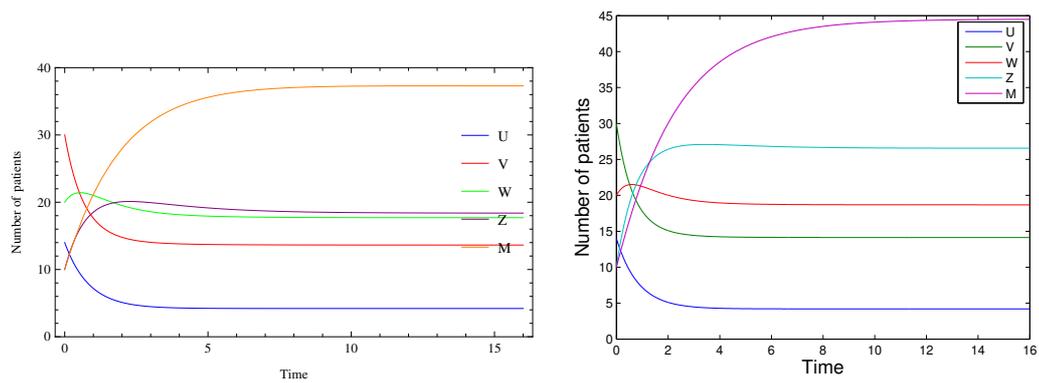


Fig. 2: The behavior of all breast cancer patients for the FOM (1) at $\alpha = 1$ and $\xi_1 = \delta_1 = 0.1$, the left plot using GMLFM and the right plot using PCM.

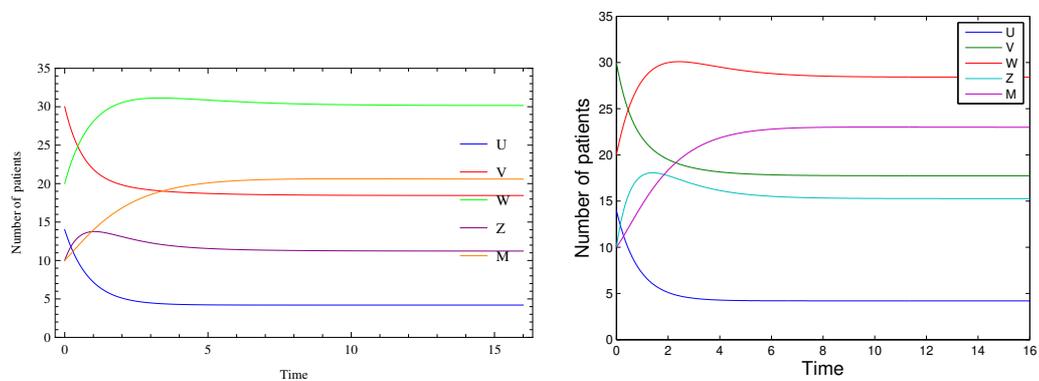


Fig. 3: The behavior of breast cancer patients of the FOM (1) at $\alpha = 1$ and $\xi_4 = \delta_3 = 0.1$, the left plot using GMLFM and the right plot using PCM.

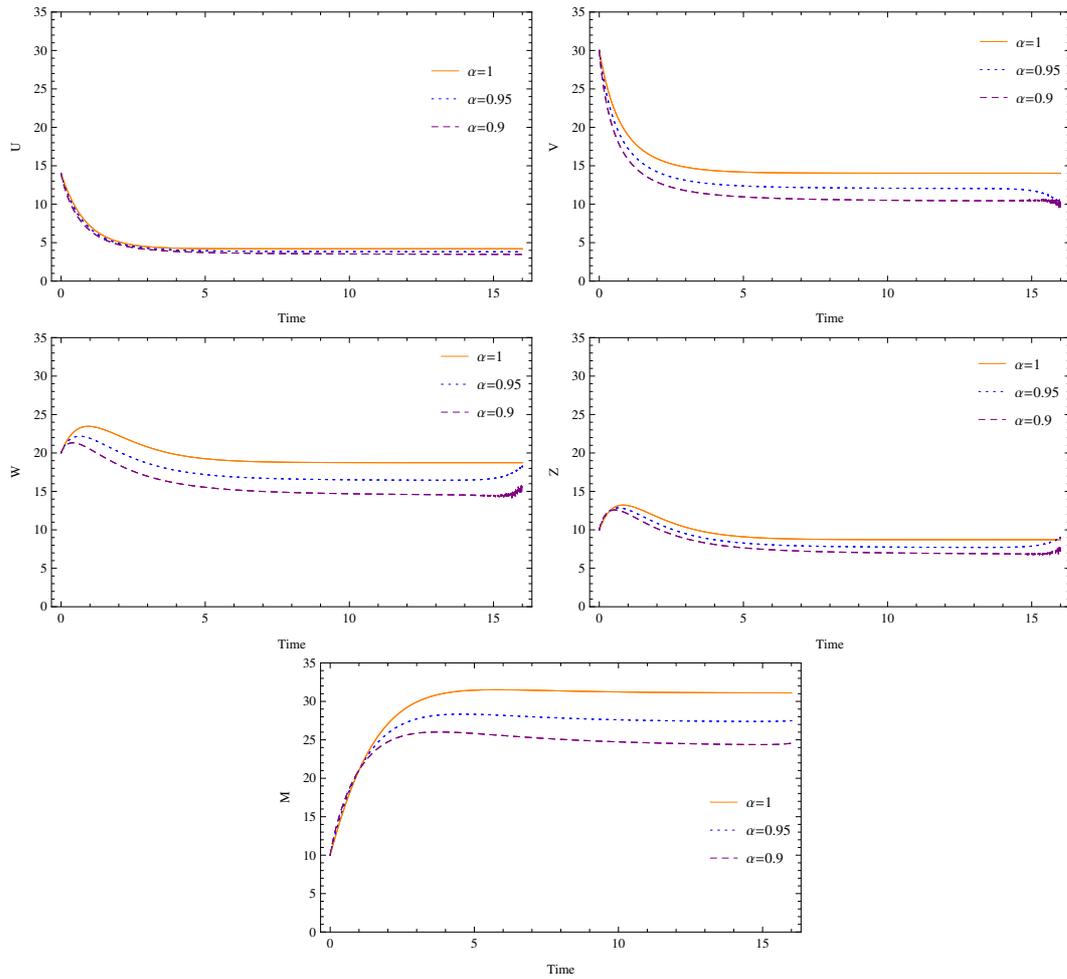


Fig. 4: Simulation result for system (1) at $\alpha = 1, 0.95, 0.9$ using GMLFM.

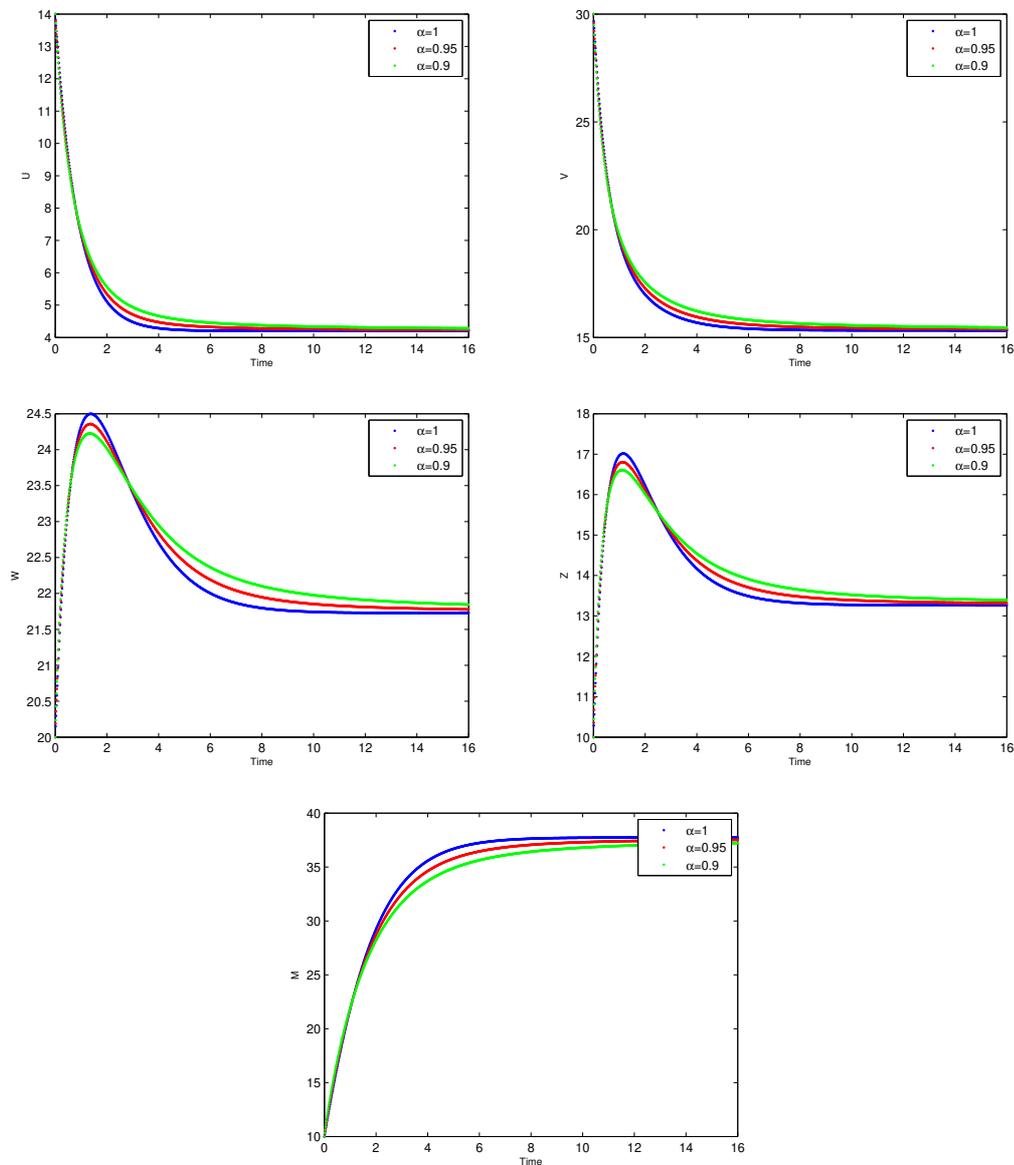


Fig. 5: Simulation result for system (1) at $\alpha = 1, 0.95, 0.9$ using PCM.

7 Conclusion

In this paper, we have proposed an FOM with modified parameters that describes BCD. We have deduced the stable equilibria for the fractional-order breast cancer system. We have illustrated the importance of the basic reproduction number and its effects on this FOM. Moreover, we have analyzed the suggested model using an approximate method (i.e., GMLFM) and the numerical method (i.e., PCM). Furthermore, we have investigated change effective on the number of patients when reducing both the disease-free patients rate who relapse back to sub-population V , the disease-free patients rate who relapse back to sub-population W , the rate of stage V cancer chemotherapy patients who experience cardiotoxic and the rate of stage W cancer chemotherapy patients who experience cardiotoxic. Our obtained results offer that the fractional-order α plays a significant role in the dynamics behavior of the system (1). The numerical simulations have been illustrated to confirm our obtained theoretical results.

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