

Examining of a tumor system with Caputo derivative

Esmehan UÇAR*

Balıkesir University Faculty of Arts and Sciences, Department of Mathematics, Cagis Campus, Balıkesir.

Geliş Tarihi (Received Date): 07.05.2022

Kabul Tarihi (Accepted Date): 06.10.2022

Abstract

Cancer is a disease that many people are exposed to, which results in the recovery of some and the death of others. For this reason, A system reflecting the relationship between immune system and tumor growth in this study is examined. This system is handled with the traditional Caputo fractional derivative. The stability analysis of equilibrium points and solution properties of this system is searched. Then, the conditions about the existence and uniqueness of the solution for this system are given. In conclusion, the fractional system is solved benefiting from Grünwald-Letnikov scheme.

Keywords: Caputo derivative, mathematical modeling, numerical solution.

Tümör sisteminin Caputo türev ile incelenmesi

Öz

Birçok insanın maruz kaldığı kanser, bazı hastaların iyileşmesi bazılarının ölmesi ile sonuçlanan bir hastalıktır. Bu nedenle bu çalışmada bağışıklık sistemi ile tümör büyümesi arasındaki ilişkiyi yansıtan bir sistem inceliyoruz. Söz konusu sistem, Caputo kesirli türevi ile ele alınacaktır. Bu sistemin denge noktalarının kararlılık analizini ve çözüm özelliklerini vereceğiz. Daha sonra bu sistem için çözüm özellikleri belirtilecektir. Son olarak, bu kesirli sistemi Grünwald-Letnikov nümerik metodunu kullanarak çözeceğiz.

Anahtar kelimeler: Caputo türev, matematiksel modelleme, nümerik çözüm.

*Esmehan UÇAR, esucarr@gmail.com, <http://orcid.org/0000-0003-0870-6270>

1. Introduction

Tumor diseases have killed many people around the world for centuries. For this purpose, a lot of scientists have analyzed immune system cells in order to cope with tumor growths in living beings. Normal cells grow in an orderly; they die when damaged or finish their job in people's bodies. When genes change, the cells in people's bodies grow out of control and cancer starts. Cancer cells multiply too much and grow uncontrolled and this situation causes a tumor growth. Scientists have begun to care of mathematical model of tumor and immune system such as [1-4].

Immune system is basic component for living's keeping alive. If immune system is weak, living's bodies may be open to attack from foreign matter. It can select tissue from foreign matter and the immune system identifies it via antigen. If immune system come across foreign matter, it analyse the cell's antigen and the antigen is foreign, immune system get alarmed and do best for run out of body. Dendritic cells initiate antigen for immune system. When the antigen is identified, CD4+T cells order alarm state and they spread IL-2. It is cause bodies reaction which is give rise to activate CD8+T cells which attack and destroy cancer cells. And we say that CD4+T cells coordinate immune response.

We study immune cells effected by cancer cells system which proposed in [1]. The system involves cancer cells, cytotoxic CD8+T cells, helper CD4+T cells, dendritic cells (DC) and cytokine interleukin-2 (IL-2).

Fractional calculus is more important real-life problems [5-14]. Recently, work on this subject has increased about physic, engineering, disease etc. (for more details one can see [15-16]). In this paper, we clarify that the quantity of tumor and tumor growth benefiting from Caputo derivative. The numerical solutions of the system is obtained by Grünwald-Letnikov method.

2. Basic definitions

Definition 2.1 [6] Let α , ($n-1 < \alpha < n$) is the order for the derivative and $g(t)$ be a function, then the definition of Caputo derivative is defined as:

$${}^C_0D_t^\alpha g(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t (t-\mu)^{n-\alpha-1} \left(\frac{d}{d\mu} \right) g(\mu) d\mu.$$

Definition 2.2 [17-19] We give the definition of Grünwald-Letnikov which is equivalent to the RL definition, is based on the finite-difference scheme and is defined as follows:. In this method $D^\alpha g(t)$ is approximated by

$$D^\alpha g(t) = h^{-\alpha} \sum_{j=0}^{\lceil t/h \rceil} (-1)^j \binom{\alpha}{j} g(t-jh). \quad (1)$$

Here $\lceil t \rceil$ denotes the integer part of t and h is step size and for $0 < \alpha < 1$,

$${}^C_0D_t^\alpha g(t) = D^\alpha g(t) - \frac{g(0)}{t^\alpha \Gamma(1-\alpha)}.$$

$D^\alpha g(t)$ can be replaced by $\sum_{j=0}^{\lceil t_n/h \rceil} w_j^\alpha g(t_{n-j})$, where $t_n = nh$ and w_j^α are the G-L coefficients which are defined by:

$$w_j^\alpha = h^{-\alpha} (-1)^j \binom{\alpha}{j}, \quad j=0,1,2,\dots$$

These coefficients can evaluate recursively:

$$w_0^\alpha = h^{-\alpha}, \quad w_j^\alpha = \left(1 - \frac{\alpha+1}{j}\right) w_{j-1}^\alpha, \quad j=1,2,3,\dots$$

3. System presented by Caputo fractional derivative

The ordinary differential equation (ODE) system of immune response to tumor growth which we use presented by [1]. The system consists of few key immune populations; helper CD4+T cells and cytotoxic CD8+T cells. The cytotoxic T cells able to recognize by dendritic cells (the best antigen tendering cells), make a good fist of killing since cancer cell distinguish on their face [20].

The fractional differential equation (FDE) of the system is given as follow:

$$\begin{aligned} {}^C_0D_t^\alpha H &= a_0 + b_0DH \left(1 - \frac{H}{f_0}\right) - c_0H, \\ {}^C_0D_t^\alpha C &= a_1 + b_1I(M + D) \left(1 - \frac{C}{f_1}\right) - c_1C, \\ {}^C_0D_t^\alpha M &= b_2M \left(1 - \frac{M}{f_2}\right) - d_2MC, \\ {}^C_0D_t^\alpha D &= -d_3DC, \\ {}^C_0D_t^\alpha I &= b_4DH - e_4IC - c_4I, \end{aligned} \tag{2}$$

where H are the helper CD4+T cells, C are the cytotoxic CD8+T cells, M are the cancer cells, D are the dendritic cells, I is the IL-2. The fundamental time unit is one hour and we neglect the effect of cross-activity of other cells.

We use $\alpha \in (0,1]$ and we use positive initial values are $H(0) = H_0, C(0) = C_0, M(0) = M_0, D(0) = D_0, I(0) = I_0$ which is given [1].

a_0 and c_0 represents helper cells birth and death rate, respectively. b_0 represents helper cells upon presentation of dendritic cells. a_1 and c_1 are cytotoxic cells birth and death rate, respectively, b_1 is proliferation rate. b_2 is saturation constant of tumor and d_2 is tumor rate killing by cytotoxic cells. d_3 is the rate of dendritic cells killed by cytotoxic cells. b_4, c_4 and e_4 are the rate of IL-2 production by helper cells, degradation and uptake by cytotoxic cells, respectively. f_0, f_1, f_2 are carrying capacity of helper cells, cytotoxic cells and tumor, respectively.

4. Stability of equilibria

Theorem 1 [21, 22] The system (2) has two equilibrium points $P_1 = \left(\frac{a_0}{c_0}, \frac{a_1}{c_1}, 0, 0, 0 \right)$ and

$P_2 = \left(\frac{a_0}{c_0}, \frac{a_1}{c_1}, f_2 \left(1 - \frac{a_1 d_2}{b_2 c_2} \right), 0, 0 \right)$. The stability of these equilibrium points depend on the sign of $a_1 d_2 - b_2 c_1$.

i) If $a_1 d_2 > b_2 c_1$, then P_1 is stable and P_2 is unstable.

ii) If $a_1 d_2 < b_2 c_1$, then P_1 is unstable and P_2 is stable.

Proof 1 We investigate the dynamic behaviour system and designate equilibrium point. Firstly, we write as follow:

$$a_0 + b_0 D H \left(1 - \frac{H}{f_0} \right) - c_0 H = 0,$$

$$a_1 + b_1 I (M + D) \left(1 - \frac{C}{f_1} \right) - c_1 C = 0,$$

$$b_2 M \left(1 - \frac{M}{f_2} \right) - d_2 M C = 0,$$

$$-d_3 D C = 0, b_4 D H - e_4 I C - c_4 I = 0,$$

with system parameters are given in [1]. There are two points $P_1 = (H_1, C_1, M_1, D_1, I_1)$ and $P_2 = (H_2, C_2, M_2, D_2, I_2)$ after the necessary operations are taken and defined by

$$H_1 = H_2 = \left(\frac{a_0}{c_0} \right), C_1 = C_2 = \left(\frac{a_1}{c_1} \right), M_1 = 0, M_2 = f_2 \left(1 - \frac{a_1 d_2}{b_2 c_2} \right),$$

$$D_1 = D_2 = 0, I_1 = I_2 = 0.$$

Hence, obtained $P_1 = \left(\frac{a_0}{c_0}, \frac{a_1}{c_1}, 0, 0, 0 \right)$ and $P_2 = \left(\frac{a_0}{c_0}, \frac{a_1}{c_1}, f_2 \left(1 - \frac{a_1 d_2}{b_2 c_2} \right), 0, 0 \right)$.

After studying Jacobian matrix $J(P)$, we find the eigenvalues as follow:

$$J(P_1) = \left(-c_0, -c_1, -\frac{a_1 d_2 - b_2 c_2}{c_1}, -\frac{a_1 d_3}{c_1}, -\frac{a_1 e_4 + c_1 c_4}{c_1} \right),$$

$$J(P_2) = \left(-c_0, -c_1, \frac{a_1 d_2 - b_2 c_2}{c_1}, -\frac{a_1 d_3}{c_1}, -\frac{a_1 e_4 + c_1 c_4}{c_1} \right).$$

Because system coefficients are positive, the eigenvalues are all negative but $-\frac{a_1 d_2 - b_2 c_2}{c_1}$

or $\frac{a_1 d_2 - b_2 c_2}{c_1}$. So, the stability of two equilibrium points connects with the sign of

$a_1 d_2 - b_2 c_1$. Thus, if $a_1 d_2 > b_2 c_1$, then P_1 is stable and P_2 is unstable. Otherwise,

$a_1 d_2 < b_2 c_1$, and P_1 is unstable and P_2 is stable. Considering parameters, it is concluded that P_1 is unstable and P_2 is stable.

5. The existence and uniqueness of the system

Let all parameters are positive and system Eq. (2) with the initial conditions $H(0) \geq 0$, $C(0) \geq 0$, $M(0) \geq 0$, $D(0) \geq 0$, $I(0) \geq 0$ where $0 < \alpha \leq 1$. Let

$$\eta = \begin{pmatrix} a_0 \\ a_1 \\ 0 \\ 0 \\ 0 \end{pmatrix}, F_1 = \begin{pmatrix} -c_0 & 0 & 0 & 0 & 0 \\ 0 & -c_1 & 0 & 0 & 0 \\ 0 & 0 & b_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -c_4 \end{pmatrix}, F_2 = \begin{pmatrix} 0 & 0 & 0 & b_0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b_4 & 0 \end{pmatrix},$$

$$F_3 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -d_3 & 0 \\ 0 & 0 & 0 & 0 & -e_4 \end{pmatrix}, F_4 = \begin{pmatrix} 0 & -d_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, F_5 = \begin{pmatrix} 0 & 0 & b_1 & b_1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$F_6 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{b_1}{f_1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, F_7 = \begin{pmatrix} 0 & 0 & -\frac{b_2}{f_2} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, F_8 = \begin{pmatrix} -\frac{b_0}{f_0} & 0 & 0 & 0 & 0 \\ \frac{f_0}{f_0} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

System (2) can be written in matrix form as follows where $t \in [0, \alpha]$

$$D_\alpha = F_1 K(t) + H F_2 K(t) + C F_3 K(t) + M F_4 K(t) + I C F_5 K(t) + I C (M + D) F_6 K(t) + M F_7 K(t) + D H F_8 K(t) + \eta. \tag{3}$$

We will give some definitions to use in the following which are given in [23–25].

Definition 3 Let $C^*[0, \alpha]$ be the class of continuous column vector $K(t)$ and $H(t)$, $C(t)$, $M(t)$, $D(t)$, $I(t)$ which are the components of $L(t)$ be the class of continuous functions on the interval $[0, \alpha]$. The norm of $K \in C^*[0, \alpha]$ is shown by a

$$\|L\| = \sup_t |Ke^{-Nt} H(t)| + \sup_t |Ke^{-Nt} C(t)| + \sup_t |Ke^{-Nt} M(t)| + \sup_t |Ke^{-Nt} D(t)| + \sup_t |Ke^{-Nt} I(t)|$$

if $t > \mu \geq 0$, we write $C_\mu^*[0, \alpha]$ and $C^*[0, \alpha]$.

Definition 4 $K \in C^*[0, \alpha]$ is a solution of the initial value problem in Eq.(3) if

- $(t, K(t)) \in B, t \in [0, \alpha]$ where $B = [0, \alpha] \times L, L = \{(H, C, M, D, I) \in R_+^5 : |H| \leq h, |C| \leq c, |M| \leq m, |d| \leq d |I| \leq i\}; h, c, m, d, i$ are positive constants.
- $X(t)$ verify in Eq.(3).

Theorem 2 The initial value problem Eq.(3) has a unique solution $K \in C^*[0, \alpha]$.

Proof 2 Considering characteristics of fractional calculus and Eq.(3), we have

$$I^{1-\tau} \frac{d}{dt} K(t) = F_1 K(t) + HF_2 K(t) + CF_3 K(t) + MF_4 K(t) + ICF_5 K(t) + IC(M + D)F_6 K(t) + MF_7 K(t) + DHF_8 K(t) + \eta.$$

We obtain with I^α

$$K(t) = K(0) + I^\alpha [F_1 K(t) + HF_2 K(t) + CF_3 K(t) + MF_4 K(t) + ICF_5 K(t) + IC(M + D)F_6 K(t) + MF_7 K(t) + DHF_8 K(t) + \eta]. \quad (4)$$

Let $F : C^*[0, \alpha] \rightarrow C^*[0, \alpha]$ hence by using F we get

$$FK(t) = K(0) + I^\tau [F_1 K(t) + HF_2 K(t) + CF_3 K(t) + MF_4 K(t) + IC(M + D)F_6 K(t) + MF_7 K(t) + DHF_8 K(t) + \eta]. \quad (5)$$

Then

$$\begin{aligned} e^{-Nt} (FK - FY) &= e^{-Nt} I^\alpha [F_1 K(t) + HF_2 (K - Y) + CF_3 (K - Y) + MF_4 (K - Y) + ICF_5 (K - Y) \\ &\quad + IC(M + D)F_6 (K - Y) + MF_7 (K - Y) + DHF_8 (K - Y) + \eta] \\ &\leq \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} e^{-N(t-s)} (K(s) - Y(s)) \times e^{-Ns} (F_1 + hF_2 + cF_3) \\ &\quad + mF_4 + icF_5 + ic(m+d)F_6 + mF_7 + dhF_8) ds \\ &\leq (F_1 + hF_2 + cF_3 + mF_4 + icF_5 + ic(m+d)F_6 + mF_7 + dhF_8) \\ &\quad \times \frac{1}{N^\alpha} \|K - Y\| \frac{1}{\Gamma(\alpha)} \int_0^t s^{\alpha-1} ds. \end{aligned}$$

We see that

$$\|FK - FY\| \leq (F_1 + hF_2 + cF_3 + mF_4 + icF_5 + ic(m+d)F_6 + mF_7 + dhF_8) \times \frac{1}{N^\alpha} \|K - Y\|.$$

If choose N following

$$N^\alpha \geq (F_1 + hF_2 + cF_3 + mF_4 + icF_5 + ic(m+d)F_6 + mF_7 + dhF_8)$$

then

$$\|FK - FY\| < \|K - Y\|.$$

So, the operator F with Eq. (5) has fixed point. Thus, Eq. (4) has a unique solution $K \in C^*[0, \alpha]$. We write from Eq. (4)

$$\begin{aligned} K(t) = & K(0) + \frac{t^\alpha}{\Gamma(\alpha+1)} \left[F_1K(0) + H(0)F_2K(0) + C(0)F_3K(0) + M(0)F_4K(0) \right. \\ & + I(0)C(0)(M(0) + D(0))F_6K(0) + M(0)F_7K(0) + D(0)H(0)F_8K(0) + \eta \left. \right] \\ & + I^{\alpha+1} \left[F_1K'(t) + H'(t)F_2K(t) + H'(t)F_2'(t) + C'(t)F_3K(t) + C(t)F_3K'(t) \right. \\ & + M'(t)F_4K(t) + M(t)F_4K'(t) + I'(t)C(t)F_5K(t) + I(t)C'(t)F_5K(t) + I(t)C(t)F_5K'(t) \\ & + I'(t)C(t)(M(t) + D(t))F_6K(t) + I(t)C'(t)(M(t) + D(t))F_6K(t) \\ & + I(t)C(t)(M'(t) + D'(t))F_6K(t) + I(t)C(t)(M(t) + D(t))F_6K'(t) \\ & + M'(t)F_7K(t) + M'(t)F_7K'(t) + D'(t)H(t)F_8K(t) + D(t)H'(t)F_8K(t) \\ & \left. + D(t)H(t)F_8K'(t)A_{13}K(t) + F(t)M'(t) \right], \end{aligned}$$

and we have

$$\begin{aligned} e^{-Nt} K'(t) = & e^{-Nt} \left[\frac{t^{\alpha-1}}{\Gamma(\alpha)} \left[F_1K(0) + H(0)F_2K(0) + C(0)F_3K(0) + M(0)F_4K(0) \right. \right. \\ & \left. \left. + I(0)C(0)(M(0) + D(0))F_6K(0) + M(0)F_7K(0) + D(0)H(0)F_8K(0) + \eta \right] \right. \\ & + I^\alpha \left[F_1K'(t) + H'(t)F_2K(t) + H'(t)F_2'(t) + C'(t)F_3K(t) + C(t)F_3K'(t) \right. \\ & + M'(t)F_4K(t) + M(t)F_4K'(t) + I'(t)C(t)F_5K(t) + I(t)C'(t)F_5K(t) + I(t)C(t)F_5K'(t) \\ & + I'(t)C(t)(M(t) + D(t))F_6K(t) + I(t)C'(t)(M(t) + D(t))F_6K(t) \\ & + I(t)C(t)(M'(t) + D'(t))F_6K(t) + I(t)C(t)(M(t) + D(t))F_6K'(t) \\ & + M'(t)F_7K(t) + M'(t)F_7K'(t) + D'(t)H(t)F_8K(t) + D(t)H'(t)F_8K(t) \\ & \left. \left. + D(t)H(t)F_8K'(t)A_{13}K(t) + F(t)M'(t) \right] \right]. \end{aligned}$$

Using Eq. (4) it is said that $K' \in C_\mu^*[0, \alpha]$. Again, from Eq. (4), get

$$\frac{dL(t)}{dt} = \frac{d}{dt} I^\alpha \left[F_1K(t) + HF_2K(t) + CF_3K(t) + MF_4K(t) \right]$$

$$+IC(M + D)F_6K(t) + MF_7K(t) + DHF_8K(t) + \eta].$$

Hence, it is obtained

$$I^{1-\alpha} \frac{dL(t)}{dt} = I^{1-\alpha} \frac{d}{dt} I^\alpha [F_1K(t) + HF_2K(t) + CF_3K(t) + MF_4K(t) + IC(M + D)F_6K(t) + MF_7K(t) + DHF_8K(t) + \eta],$$

and

$$D^\alpha K(t) = F_1K(t) + HF_2K(t) + CF_3K(t) + MF_4K(t) + IC(M + D)F_6K(t) + MF_7K(t) + DHF_8K(t) + \eta.$$

So, we get

$$K(0) = K_0 + I^\alpha [F_1K(0) + HF_2K(0) + CF_3K(0) + MF_4K(0) + IC(M + D)F_6K(0) + MF_7K(0) + DHF_8K(0) + \eta] = K_0.$$

Consequently, Eq.(4) is equivalent to the initial value problem Eq. (3).

6. Numerical solution and results

To solve the FDE system in (2) we should discretize it. For this aim, we can use Grünwald-Letnikov method. Benefiting from G-L method in the system (2), we obtain

$$\begin{aligned} \sum_{k=0}^n w_k H_{n-k} - \frac{H(0)}{t^\alpha \Gamma(1-\alpha)} &= a_0 + b_0 D_n H_n \left(1 - \frac{H_n}{f_0}\right) - c_0 H_n, \\ \sum_{k=0}^n w_k C_{n-k} - \frac{C(0)}{t^\alpha \Gamma(1-\alpha)} &= a_1 + b_1 I_n (M_n + D_n) \left(1 - \frac{C_n}{f_1}\right) - c_1 C_n, \\ \sum_{k=0}^n w_k M_{n-k} - \frac{M(0)}{t^\alpha \Gamma(1-\alpha)} &= b_2 M_n \left(1 - \frac{M_n}{f_2}\right) - d_2 M_n C_n, \\ \sum_{k=0}^n w_k D_{n-k} - \frac{D(0)}{t^\alpha \Gamma(1-\alpha)} &= -d_3 D_n C_n, \\ \sum_{k=0}^n w_k I_{n-k} - \frac{I(0)}{t^\alpha \Gamma(1-\alpha)} &= b_4 D_n H_n - e_4 I_n C_n - c_4 I_n. \end{aligned} \tag{6}$$

We have used initial values $H_0 = 0$, $C_0 = 0$, $M_0 = 1$, $D_0 = 10$, $I_0 = 0$, parameters $a_0 = 10^{-4}$, $b_0 = 10^{-1}$, $f_0 = 1$, $c_0 = 0.005$, $a_1 = 10^{-4}$, $b_1 = 10^{-2}$, $f_1 = 1$, $c_1 = 0.005$, $b_2 = 0.02$, $f_2 = 1$, $d_2 = 0.1$, $d_2 = 0.1$, $d_3 = 0.1$, $b_4 = 10^{-2}$, $e_4 = 10^{-7}$, $c_4 = 10^{-2}$ and Eq.(6) and get results are illustrated about helper, cytotoxic, myeloid (tumor) and dendritic cells, IL-2 in Fig. 1-5 especially fractional order $\alpha = 0.7, 0.65, 0.6$. We see that via Fig. 3, tumor cells

are rapidly decreasing but fractional order α close to 0.7, the decreasing is more slowly. It is seen that via Fig. 1 and 2, the immune system cells are rapidly increasing simultaneously tumor cells. Because tumor mass in the system causes the immune system cells to raise rapidly. Especially, the level of tumor cells at fractional order $\alpha=0.7$ is higher than if $\alpha=0.6$ because fractional calculus has hereditary property.

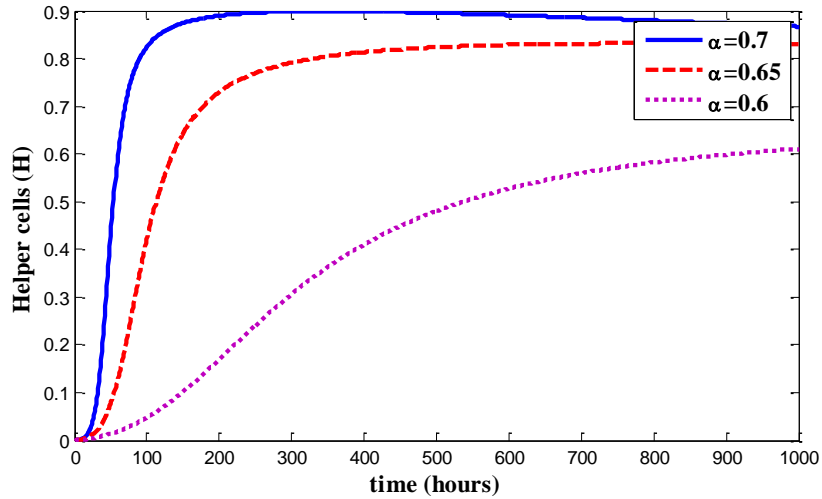


Figure 1. Figures of helper cells for changing α .

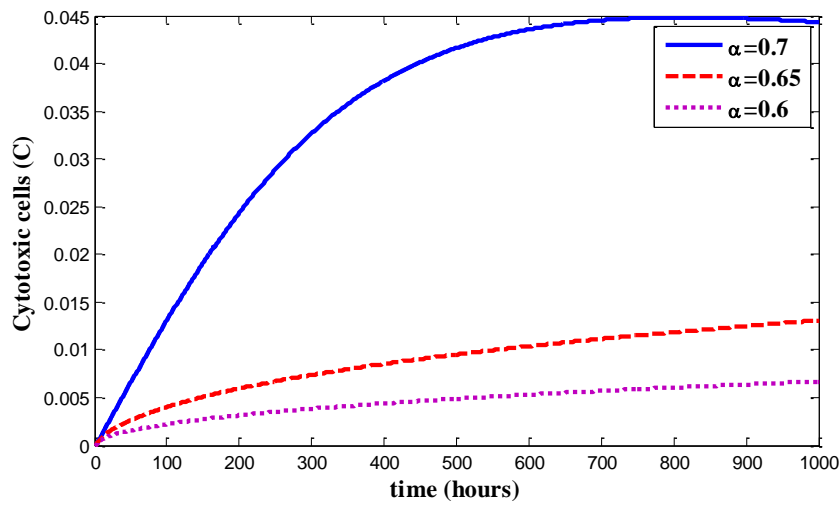


Figure 2. Figures of cytotoxic cells for changing α .

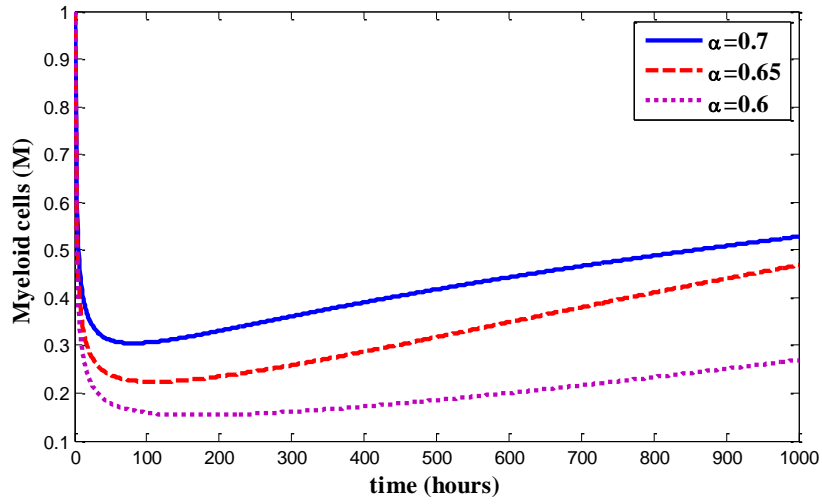


Figure 3. Figures of myeloid (tumor) cells for changing α .

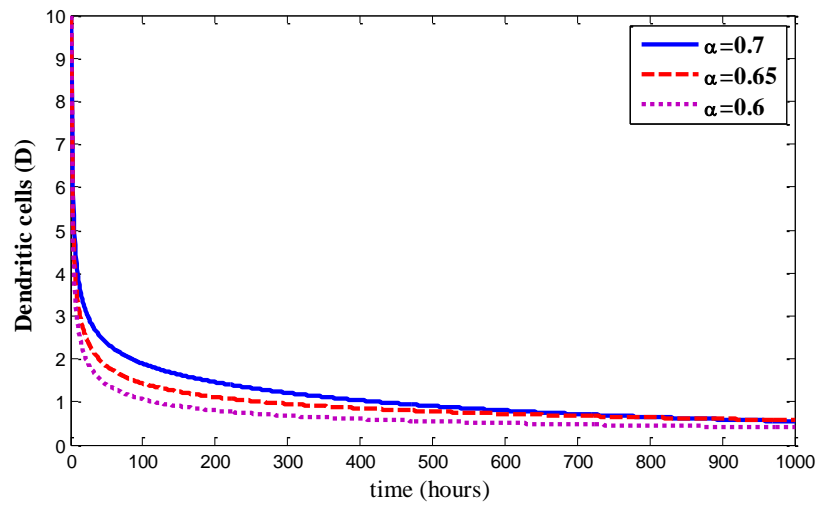


Figure 4. Figures of dendritic cells for changing α .

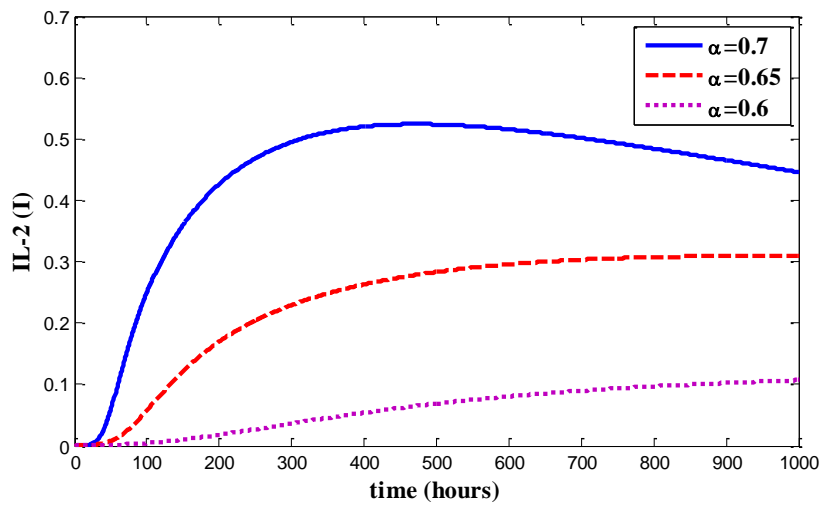


Figure 5. Figures of IL-2 for changing α .

7. Conclusion

In this study, we give brief information about response immune system to tumor growth and Caputo fractional derivative. We give some detail of equilibrium point and numerical solution of the system (2), then, we deeply analyse the solution properties of the fractional order system. Lastly, we give some numerical results and see that these graphics of the FDE system are very interesting. This effect is due to the fact that FDE is non-local and the FDE is more appropriate real-life problem.

References

- [1] Castiglione, F. and Piccoli, B., Cancer immunotherapy, mathematical modeling and optimal control, **Journal of Theoretical Biology**, 247, 723-732, (2007). Pillis, L.G. and Radunskaya A., A mathematical tumor model with immune resistance and drug therapy: an optimal control approach, **Journal of Theoretical Medicine**, 3, 79-100, (2000).
- [2] Kirschner, D. and Panetta, J.C., Modelling immunotherapy of tumor-immune interaction, **Journal of Mathematical Biology**, 37, 235-252, (1998).
- [3] Arshad, S., Baleanu, D., Huang, J., Tang, Y. and Qurashi, M.M.A. Dynamical analysis of fractional order model immunogenic tumors, **Advances in Mechanical Engineering**, 8, 1-13, (2016).
- [4] Kilbas, A.A and Marzan, S.A., Nonlinear differential equations with the Caputo fractional derivative in the space of continuously differentiable functions, **Differential Equations**, 41, 82-89, (2005).
- [5] Podlubny, I., **Fractional Differential Equations**, Academic Press, New York, (1999).
- [6] Fernandez, A., Uçar, S. and Özdemir, N., Solving a well-posed fractional initial value problem by a complex approach, **Fixed Point Theory and Algorithms for Sciences and Engineering**, 1, 1-13, (2021).
- [7] Uçar, E., Uçar, S, Evirgen, F. and Özdemir, N., A Fractional SAIDR Model in the Frame of Atangana–Baleanu Derivative, **Fractal and Fractional**, 5, 32, (2021).
- [8] Uçar, S., Özdemir, N., Koca, İ., and Altun, E., Novel analysis of the fractional glucose–insulin regulatory system with non-singular kernel derivative, **The European Physical Journal Plus**, 135, 1-18, (2020).
- [9] Koca, i., Analysis of rubella disease model with non-local and non-singular fractional derivatives, **An International Journal of Optimization and Control Theories & Applications (IJOCTA)**, 8, 17-25, (2018).
- [10] Hristov, J., Magnetic field diffusion in ferromagnetic materials: fractional calculus approaches, **An International Journal of Optimization and Control Theories & Applications (IJOCTA)**, 12, 20-38, (2022).
- [11] Hammouch, Z., Yavuz, M., and Özdemir, N., Numerical solutions and synchronization of a variable-order fractional chaotic system, **Mathematical Modelling and Numerical Simulation with Applications**, 1(1), 11-23, (2021).
- [12] Veerasha, P., Yavuz, M., and Baishya, C., A computational approach for shallow water forced Korteweg–De Vries equation on critical flow over a hole with three fractional operators, **An International Journal of Optimization and Control: Theories & Applications (IJOCTA)**, 11(3), 52-67, (2021).
- [13] Özköse, F., Şenel, M. T., and Habbireeh, R., Fractional-order mathematical modelling of cancer cells-cancer stem cells-immune system interaction with

- chemotherapy, **Mathematical Modelling and Numerical Simulation with Applications**, 1(2), 67-83, (2021).
- [14] Baleanu, D., Güvenç, Z. and Teenreriro Machado, J.A. **New trends in nanotechnology and fractional calculus applications**, Springer, (2010).
- [15] Pinto, C.M.A. and Carvalho, A. R. M., Fractional modeling of typical stages in HIV epidemics with drug-resistance, **Progress in Fractional Differentiation and Applications an International Journal**, 2, 111-122, (2015).
- [16] Momani, S. and Odibat, Z., Numerical comparison of methods for solving linear differential equations of fractional order. **Chaos, Solitons Fractals**, 131, 1248-1255 (2007).
- [17] Özdemir, N., Avcı, D. And İskender, B. B., The numerical solutions of a two-dimensional-space-time Riesz-Caputo fractional diffusion equation, **An International Journal of Optimization and Control Theories & Applications (IJOCTA)**, 1, 17-26, (2011).
- [18] Scherer, R., Kalla, S. L., Yang, Y., and Huang, J., The Grunwald-Letkinov method for fractional differential equations, **Computers Mathematics with Applications**, 62, 902-917, (2011).
- [19] Kumar, V., Abbas, A. and Aster, J., **Robbins and cotran pathologic basis of disease**, Elsevier, (2014).
- [20] Minelli, A., Topputo, F. and Bernelli F., Controlled drug delivery in cancer immunotherapy: stability, optimization and monte carlo analysis, **SIAM Journal on Applied Mathematics**, 71, 2229-2245, (2011).
- [21] Ahmed E., El-Sayed A. M. A., El-Saka H. A. A., Equilibrium points, stability and numerical solutions of fractional-order predator-prey and rabies models, **Journal of Mathematical Analysis and Applications**, 325, 542-553, (2007).
- [22] Ahmed, E., El-Sayed, A. M. A. and El-Saka, H. A. A., Equilibrium points, stability and numerical solutions of fractional-order predator-prey and rabies models, **Journal of Mathematical Analysis and Applications**, 325, 542-553, (2007).
- [23] Bozkurt, F., Stability analysis of fractional-order differential equation system of a GBM-IS interaction depending on the density, **Applied Mathematics and Information Sciences**, 8, 1021-1028, (2014).
- [24] El-Sayed A. M. A., El-Mesiry, A. E. M. and El-Saka, H. A. A., On the fractional-order logistic equation, **Applied Mathematics Letters**, 20, 817-823, (2007).