AIMS Mathematics

http://www.aimspress.com/journal/Math

AIMS Mathematics, 5(2): 1519–1531.
DOI:10.3934/math.2020104
Received: 29 October 2019
Accepted: 09 January 2020
Published: 21 January 2020

Research article

Investigating of an immune system-cancer mathematical model with Mittag-Leffler kernel

Necati Özdemir*and Esmehan Uçar

Department of Mathematics, Faculty of Science and Arts, Balıkesir University, Turkey

* **Correspondence:** Email: nozdemir@balikesir.edu.tr.

Abstract: Cancer that is difficult to treat, is a very common disease today and there are many types of cancer such as lung, colon, stomach. When cancer settles in the body, the immune system tries to resist it. In this study, the mathematical model of the interaction between immune system components and cancer is discussed and is modified by using Atangana-Baleanu derivative. After investigating the existence and uniqueness of the solution of the fractional immune system-cancer model, numerical simulations are given via predictor-corrector scheme.

Keywords: immune system-cancer; fractional calculus; Atangana-Baleanu derivative; dendritic cells and IL-2; fixed point theory
Mathematics Subject Classification: 34A08, 34A34, 47H10

1. Introduction

Cancer is one of the most frequently encountered diseases that can lead to the end of human life in spite of the advances in science and medicine. It is a multi-staged disease which occurs as a result of changes in DNA formation (mutation) of abnormal cells. Uncontrolled proliferation of the cells causes tumors and a great number cells mutate in the human body on a daily basis. While some of these mutated cells die, others continue to live and form cancerous cells. Cancer can occur when the immune system or other defensive mechanisms fail to protect the human body from these cells [1]. Cancer cells are different from normal cells due to their size, shape, number, differentiation, function, and ability to travel to distant tissues and organ systems [1]. The immune system recognizes cancer cells and tumors from their antigens [2].

Dendritic cells known as professional antigen-presenting cells, send tumor antigens to lymph nodes to activate T lymphocytes after recognizing cancer cells. CD4+T cells play a central role in the initiation and progression of immune responses [3] and also help CD8+T cells to activate and proliferate [4]. The basic mechanism of tumor immunity is to kill tumor cells by the help of CD8+T

cells. Immune reactions that provide protection against tumors, are typically the task of CD8+T cells. CD4+T cells also play a major role in these tasks [3]. Human CD4+T cells can identify tissue-specific antigens, common tumor antigens and viral antigens caused by tumor transformation [3]. Another task of CD4+T cells is to produce IL-2 as a result of antigen stimulation response. IL-2 has a potent T cell growth factor effect and it has been reported that the application of IL-2 seemingly leads to curative and persistent regressions in cancer patients [5].

Recently, interest in fractional has increased in order to clarify real life problems because of memory and hereditary property [6, 7, 8, 9, 10, 11, 12, 13, 14]. One of the most common fractional operators is Caputo, Riemann-Liouville (RL). However, these operators are considered weakness due to singularity problems caused by their kernel function. As a result of this weakness, Atangana felt the need to define Atangana-Baleanu (AB) derivative in [15] and [16, 17, 18, 19, 20, 21, 22, 23, 24, 25] are the some of the studies about AB derivative.

Mathematical modeling, known as the reinterpretation of real world problems with mathematical equations, has recently become one of the tools that scientists use to foresee the development of diseases that cause serious problems. [26, 27, 28, 29, 30] are some of the studies which attempt to show the relation between cancer and immune system by way of mathematical modeling.

The study is organized as: In section 2, some basic definitions and theorems to be used in study are briefly mentioned. In section 3, the existence and uniqueness of the solution of the fractional immune system-cancer model is given. The graphics of the numerical solution via predictor-corrector scheme is given in section 4 and comments is made on graphics. Lastly, we finalize our study in section 5. Briefly, the relationship between cancer cells and immune system cells will be examined with AB derivative and the effect of IL-2 and dendritic cells on cancer cells will be discussed using the integer form of model presented by Castiglione in [31].

Let us rearrange this model with fractional derivative:

$$\begin{aligned}
{}_0^{ABC}D_t^{\tau}\left(H\left(t\right)\right) &= a_0 + b_0 D\left(t\right) H\left(t\right)\left(1 - \frac{H\left(t\right)}{f_0}\right) - c_0 H\left(t\right), \\
{}_0^{ABC}D_t^{\tau}\left(C\left(t\right)\right) &= a_1 + b_1 I\left(t\right)\left(M\left(t\right) + D\left(t\right)\right) C\left(t\right)\left(1 - \frac{C\left(t\right)}{f_1}\right) - c_1 C\left(t\right), \\
{}_0^{ABC}D_t^{\tau}\left(M\left(t\right)\right) &= b_2 M\left(t\right)\left(1 - \frac{M\left(t\right)}{f_2}\right) - d_2 M\left(t\right) C\left(t\right), \\
{}_0^{ABC}D_t^{\tau}\left(D\left(t\right)\right) &= -d_3 D\left(t\right) C\left(t\right), \\
{}_0^{ABC}D_t^{\tau}\left(I\left(t\right)\right) &= b_4 D\left(t\right) H\left(t\right) - e_4 I\left(t\right) C\left(t\right) - c_4 I\left(t\right),
\end{aligned} \tag{1.1}$$

with the initial conditions $H\left(0\right) = 0, C\left(0\right) = 0, M\left(0\right) = 1, D\left(0\right) = 10, I\left(0\right) = 0$, where ${}_0^{ABC}D_t^{\tau}$ is AB derivative in Caputo sense and $\tau \in [0, 1]$. And H, C, M, D, I represent CD4+T (helper) cells, CD8+T (cytotoxic) cells, myeloid (cancer) cells, dendritic cells and IL-2, respectively.

2. Basic definitions

In this part, some definitions and properties that will be helpful in this work is given.

Definition 2.1. *Suppose that $g \in H^1\left(a, b\right)$, $a < b$ be a function and $\tau \in [0, 1]$. The AB derivative in*

Caputo sense of order τ of g is given by [15]

$$ {}^{ABC}_{a}D^{\tau}_{t}\left[g\left(t\right)\right]=\frac{F\left(\tau\right)}{1-\tau}\int_{a}^{t}g'\left(y\right)E_{\tau}\left[-\tau\frac{\left(t-y\right)^{\tau}}{1-\tau}\right]dy \tag{2.1} $$

where E_τ is the Mittag-Leffler function and $F(\tau)$ is a normalization function with $F(0)=F(1)=1$.

Definition 2.2. *Assume that $g\in H^{1}(a,b)$, $a<b$ be a function and $\tau\in[0,1]$. The AB derivative in RL sense of order E_τ of g is given by [15]:*

$$ {}^{ABR}_{a}D^{\tau}_{t}\left[g\left(t\right)\right]=\frac{F\left(\tau\right)}{1-\tau}\frac{d}{dt}\int_{a}^{t}g\left(y\right)E_{\tau}\left[-\tau\frac{\left(t-y\right)^{\tau}}{1-\tau}\right]dy. \tag{2.2} $$

Definition 2.3. *The fractional integral is given by [15]:*

$$ {}^{AB}_{a}I^{\tau}_{t}\left[g\left(t\right)\right]=\frac{1-\tau}{F\left(\tau\right)}g\left(t\right)+\frac{\tau}{F\left(\tau\right)\Gamma\left(\tau\right)}\int_{a}^{t}g\left(\lambda\right)\left(t-\lambda\right)^{\tau-1}d\lambda. \tag{2.3} $$

Theorem 2.1. *[15] Let g on $[a,b]$ is a continuous function. Given the following inequality holds on $[a,b]$:*

$$ \left\|{}^{ABR}_{0}D^{\tau}_{t}\left[g\left(t\right)\right]\right\|<\frac{F\left(\tau\right)}{1-\tau}\left\|g\left(t\right)\right\|, \tag{2.4} $$

where $\left\|g\left(t\right)\right\|=\max\limits_{a\leq t\leq b}\left|g\left(t\right)\right|$.

Theorem 2.2. *The AB derivative in Caputo and RL sense satisfy Lipschitz condition [15]:*

$$ \left\|{}^{ABC}_{0}D^{\tau}_{t}\left[g\left(t\right)\right]-{}^{ABC}_{0}D^{\tau}_{t}\left[h\left(t\right)\right]\right\|\leq H\left\|g\left(t\right)-h\left(t\right)\right\| \tag{2.5} $$

and

$$ \left\|{}^{ABR}_{0}D^{\tau}_{t}\left[g\left(t\right)\right]-{}^{ABR}_{0}D^{\tau}_{t}\left[h\left(t\right)\right]\right\|\leq H\left\|g\left(t\right)-h\left(t\right)\right\|. \tag{2.6} $$

Theorem 2.3. *The fractional ordinary differential equation*

$$ {}^{ABC}_{0}D^{\tau}_{t}\left(h\left(t\right)\right)=s\left(t\right) $$

has a unique solution given as [15]

$$ h\left(t\right)=\frac{1-\tau}{F\left(\tau\right)}s\left(t\right)+\frac{\tau}{F\left(\tau\right)\Gamma\left(\tau\right)}\int_{a}^{t}s\left(\lambda\right)\left(t-\lambda\right)^{\tau-1}d\lambda. $$

3. Existence and uniqueness

Let $\mathcal{P}=C\left(K\right)\times C\left(K\right)\times C\left(K\right)\times C\left(K\right)\times C\left(K\right)$ and $C\left(K\right)$ be a Banach space of continuous $\mathbb{R}\to\mathbb{R}$ valued functions on the interval K with the norm

$$ \left\|\left(H,C,M,D,I\right)\right\|=\left\|H\right\|+\left\|C\right\|+\left\|M\right\|+\left\|D\right\|+\left\|I\right\|, $$

where $\|H\| = sup\{|H(t)| : t \in K\}$, $\|C\| = sup\{|C(t)| : t \in K\}$, $\|M\| = sup\{|M(t)| : t \in K\}$, $\|D\| = sup\{|D(t)| : t \in K\}$, $\|I\| = sup\{|I(t)| : t \in K\}$.

For clarity, we rewrite the model (1.1) of the following form:

$$\begin{aligned} {}_0^{ABC}D_t^{\tau}(H(t)) &= N_1(t,H), \\ {}_0^{ABC}D_t^{\tau}(C(t)) &= N_2(t,C), \\ {}_0^{ABC}D_t^{\tau}(M(t)) &= N_3(t,M), \\ {}_0^{ABC}D_t^{\tau}(D(t)) &= N_4(t,D), \\ {}_0^{ABC}D_t^{\tau}(I(t)) &= N_5(t,I). \end{aligned} \tag{3.1}$$

Using Theorem 2.3, the system (3.1) can be written as:

$$\begin{aligned} H(t) - H(0) &= \frac{1-\tau}{F(\tau)}N_1(t,H) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_1(\lambda,H)\,d\lambda, \\ C(t) - C(0) &= \frac{1-\tau}{F(\tau)}N_2(t,C) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_2(\lambda,C)\,d\lambda, \\ M(t) - M(0) &= \frac{1-\tau}{F(\tau)}N_3(t,M) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_3(\lambda,M)\,d\lambda, \\ D(t) - D(0) &= \frac{1-\tau}{F(\tau)}N_4(t,D) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_4(\lambda,D)\,d\lambda, \\ I(t) - I(0) &= \frac{1-\tau}{F(\tau)}N_5(t,I) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_5(\lambda,I)\,d\lambda. \end{aligned} \tag{3.2}$$

Theorem 3.1. *If the following inequality holds*

$$0 \le b_0\psi_4 + \frac{b_0}{f_0}\psi_4(\psi_1+\omega_1) + c_0 < 1,$$

then the kernel N_1 satisfies the Lipschitz condition and contraction.

Proof. Let H and H_1 be two functions, then we have

$$\begin{aligned} & \|N_1(t,H) - N_1(t,H_1)\| \\ = & \left\| -b_0 D(t)(H(t) - H_1(t)) - \frac{b_0}{f_0}D(t)\left(H^2(t) - H_1^2(t)\right) - c_0(H(t) - H_1(t)) \right\| \\ \le & \left(b_0\|D(t)\| + \frac{b_0}{f_0}\|D(t)\|\|H(t) + H_1(t)\| + c_0 \right)\|H(t) - H_1(t)\| \\ \le & A_1\|H(t) - H_1(t)\|. \end{aligned} \tag{3.3}$$

Taking $A_1 = b_0\psi_4 + \frac{b_0}{f_0}\psi_4(\psi_1+\omega_1) + c_0$ where D, H and H_1 are bounded functions such that $\|D(t)\| \le \psi_4$, $\|H(t)\| \le \psi_1$, $\|H_1(t)\| \le \omega_1$ then we have

$$\|N_1(t,H) - N_1(t,H_1)\| \le A_1\|H(t) - H_1(t)\|. \tag{3.4}$$

Hence, the Lipschitz condition is fulfilled for N_1 and $0 \leq b_0\psi_4 + \frac{b_0}{f_0}\psi_4(\psi_1 + \omega_1) + c_0 < 1$ implies N_1 is also contraction. □

Similarly, the other kernels N_2, N_3, N_4 and N_5 satisfy Lipschitz condition and contraction. Consider the system (3.2) in the following recursive formula:

$$\begin{aligned}
H_n(t) &= \frac{1-\tau}{F(\tau)}N_1(t, H_{n-1}) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_1(\lambda, H_{n-1})\, d\lambda,\\
C_n(t) &= \frac{1-\tau}{F(\tau)}N_2(t, C_{n-1}) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_2(\lambda, C_{n-1})\, d\lambda,\\
M_n(t) &= \frac{1-\tau}{F(\tau)}N_3(t, M_{n-1}) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_3(\lambda, M_{n-1})\, d\lambda,\\
D_n(t) &= \frac{1-\tau}{F(\tau)}N_4(t, D_{n-1}) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_4(\lambda, D_{n-1})\, d\lambda,\\
I_n(t) &= \frac{1-\tau}{F(\tau)}N_5(t, I_{n-1}) + \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1} N_5(\lambda, I_{n-1})\, d\lambda,
\end{aligned} \tag{3.5}$$

with the initial conditions

$$H_0(t) = H(0), C_0(t) = C(0), M_0(t) = M(0), D_0(t) = D(0), I_0(t) = I(0).$$

We find the difference between the successive terms in the expressions:

$$\begin{aligned}
\Phi_{1n}(t) = H_n(t) - H_{n-1}(t) &= \frac{1-\tau}{F(\tau)}\left[N_1(t, H_{n-1}) - N_1(t, H_{n-2})\right]\\
&+ \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1}\left[N_1(\lambda, H_{n-1}) - N_1(\lambda, H_{n-2})\right] d\lambda,
\end{aligned}$$

$$\begin{aligned}
\Phi_{2n}(t) = C_n(t) - C_{n-1}(t) &= \frac{1-\tau}{F(\tau)}\left[N_2(t, C_{n-1}) - N_2(t, C_{n-2})\right]\\
&+ \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1}\left[N_2(\lambda, C_{n-1}) - N_2(\lambda, C_{n-2})\right] d\lambda,
\end{aligned}$$

$$\begin{aligned}
\Phi_{3n}(t) = M_n(t) - M_{n-1}(t) &= \frac{1-\tau}{F(\tau)}\left[N_3(t, M_{n-1}) - N_3(t, M_{n-2})\right]\\
&+ \frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1}\left[N_3(\lambda, M_{n-1}) - N_3(\lambda, M_{n-2})\right] d\lambda,
\end{aligned}$$

$$\Phi_{4n}(t) = D_n(t) - D_{n-1}(t) = \frac{1-\tau}{F(\tau)}\left[N_4(t, D_{n-1}) - N_4(t, D_{n-2})\right]$$
$$+\frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1}\left[N_4(\lambda, D_{n-1}) - N_4(\lambda, D_{n-2})\right]d\lambda,$$

$$\Phi_{5n}(t) = I_n(t) - I_{n-1}(t) = \frac{1-\tau}{F(\tau)}\left[N_5(t, I_{n-1}) - N_5(t, I_{n-2})\right]$$
$$+\frac{\tau}{F(\tau)\Gamma(\tau)}\int_0^t (t-\lambda)^{\tau-1}\left[N_5(\lambda, I_{n-1}) - N_5(\lambda, I_{n-2})\right]d\lambda. \tag{3.6}$$

Notice that

$$\begin{aligned} H_n(t) &= \sum_{k=1}^{n}\Phi_{1k}(t), \\ C_n(t) &= \sum_{k=1}^{n}\Phi_{2k}(t), \\ M_n(t) &= \sum_{k=1}^{n}\Phi_{3k}(t), \\ D_n(t) &= \sum_{k=1}^{n}\Phi_{4k}(t), \\ I_n(t) &= \sum_{k=1}^{n}\Phi_{5k}(t). \end{aligned} \tag{3.7}$$

Taking the norm on both sides of the Eq. (3.6) and applying triangular identity, we find

$$\begin{aligned} &\|\Phi_{1n}(t)\| = \|H_n(t) - H_{n-1}(t)\| \\ &\leq \frac{1-\tau}{F(\tau)}\|[N_1(t, H_{n-1}) - N_1(t, H_{n-2})]\| \\ &+\frac{\tau}{F(\tau)\Gamma(\tau)}\left\|\int_0^t (t-\lambda)^{\tau-1}\left[N_1(\lambda, H_{n-1}) - N_1(\lambda, H_{n-2})\right]d\lambda\right\| \end{aligned}$$

Because the kernel N_1 satisfy Lipschitz condition proved in Eq. (3.4), we have

$$\begin{aligned} \|\Phi_{1n}(t)\| &= \|H_n(t) - H_{n-1}(t)\| \\ &\leq \frac{1-\tau}{F(\tau)}A_1\|H_{n-1} - H_{n-2}\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_1\int_0^t (t-\lambda)^{\tau-1}\|H_{n-1} - H_{n-2}\|d\lambda \end{aligned}$$

and

$$\|\Phi_{1n}(t)\| \leq \frac{1-\tau}{F(\tau)}A_1\left\|\Phi_{1(n-1)}(t)\right\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_1\int_0^t (t-\lambda)^{\tau-1}\left\|\Phi_{1(n-1)}(\lambda)\right\|d\lambda \tag{3.8}$$

Analogously, we have the following results:

$$\begin{aligned}
\|\Phi_{2n}(t)\| &\leq \frac{1-\tau}{F(\tau)}A_2\left\|\Phi_{2(n-1)}(t)\right\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_2\int_0^t (t-\lambda)^{\tau-1}\left\|\Phi_{2(n-1)}(\lambda)\right\|d\lambda,\\
\|\Phi_{3n}(t)\| &\leq \frac{1-\tau}{F(\tau)}A_3\left\|\Phi_{3(n-1)}(t)\right\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_3\int_0^t (t-\lambda)^{\tau-1}\left\|\Phi_{3(n-1)}(\lambda)\right\|d\lambda,\\
\|\Phi_{4n}(t)\| &\leq \frac{1-\tau}{F(\tau)}A_4\left\|\Phi_{4(n-1)}(t)\right\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_4\int_0^t (t-\lambda)^{\tau-1}\left\|\Phi_{4(n-1)}(\lambda)\right\|d\lambda,\\
\|\Phi_{5n}(t)\| &\leq \frac{1-\tau}{F(\tau)}A_5\left\|\Phi_{5(n-1)}(t)\right\| + \frac{\tau}{F(\tau)\Gamma(\tau)}A_5\int_0^t (t-\lambda)^{\tau-1}\left\|\Phi_{5(n-1)}(\lambda)\right\|d\lambda.
\end{aligned} \tag{3.9}$$

In the light of the results in hand, we give the below theorem.

Theorem 3.2. *The fractional model given in (1.1) has a solution, if we can find t_0 satisfying the equation*

$$\frac{1-\tau}{F(\tau)}A_i + \frac{t_0^{\tau}}{F(\tau)\Gamma(\tau)}A_i < 1$$

for $i = 1, 2, 3, 4, 5$.

Proof. We know that $H(t)$, $C(t)$, $M(t)$, $D(t)$ and $I(t)$ are bounded functions and satisfy Lipschitz condition. From the Eqs. (3.8) and (3.9), we obtain the succeeding relations:

$$\begin{aligned}
\|\Phi_{1n}(t)\| &\leq \|H_n(0)\|\left[\frac{1-\tau}{F(\tau)}A_1 + \frac{t^{\tau}}{F(\tau)\Gamma(\tau)}A_1\right]^n,\\
\|\Phi_{2n}(t)\| &\leq \|C_n(0)\|\left[\frac{1-\tau}{F(\tau)}A_2 + \frac{t^{\tau}}{F(\tau)\Gamma(\tau)}A_2\right]^n,\\
\|\Phi_{3n}(t)\| &\leq \|M_n(0)\|\left[\frac{1-\tau}{F(\tau)}A_3 + \frac{t^{\tau}}{F(\tau)\Gamma(\tau)}A_3\right]^n,\\
\|\Phi_{4n}(t)\| &\leq \|D_n(0)\|\left[\frac{1-\tau}{F(\tau)}A_4 + \frac{t^{\tau}}{F(\tau)\Gamma(\tau)}A_4\right]^n,\\
\|\Phi_{5n}(t)\| &\leq \|I_n(0)\|\left[\frac{1-\tau}{F(\tau)}A_5 + \frac{t^{\tau}}{F(\tau)\Gamma(\tau)}A_5\right]^n.
\end{aligned} \tag{3.10}$$

Thus, the existence and continuity of the above solutions are proved. Our goal is to show that the above functions are solutions of Eq. (1.1), assume that

$$H(t) - H(0) = H_n(t) - K_{1n}(t),$$

$$\begin{aligned} C(t) - C(0) &= C_n(t) - K_{2n}(t), \\ M(t) - M(0) &= M_n(t) - K_{3n}(t), \\ D(t) - D(0) &= D_n(t) - K_{4n}(t), \\ I(t) - I(0) &= I_n(t) - K_{5n}(t). \end{aligned} \tag{3.11}$$

Then,we have

$$\begin{aligned} \|K_{1n}(t)\| &= \left\| \frac{1-\tau}{F(\tau)} [N_1(t,H) - N_1(t,H_{n-1})] \right. \\ &\left. + \frac{\tau}{F(\tau)\Gamma(\tau)} \int_0^t (t-\lambda)^{\tau-1} [N_1(\lambda,H) - N_1(\lambda,H_{n-1})]\, d\lambda \right\| \\ &\leq \frac{1-\tau}{F(\tau)} \|N_1(t,H) - N_1(t,H_{n-1})\| \\ &+ \frac{\tau}{F(\tau)\Gamma(\tau)} \int_0^t (t-\lambda)^{\tau-1} \|N_1(\lambda,H) - N_1(\lambda,H_{n-1})\, d\lambda\| \\ &\leq \frac{1-\tau}{F(\tau)} A_1 \|H - H_{n-1}\| + \frac{t^\tau}{F(\tau)\Gamma(\tau)} A_1 \|H - H_{n-1}\|. \end{aligned} \tag{3.12}$$

By continuing this method recursively, it gives at t_0

$$\|K_{1n}(t)\| \leq \left(\frac{1-\tau}{F(\tau)} + \frac{t_0^\tau}{F(\tau)\Gamma(\tau)} \right)^{n+1} A_1^{n+1} a. \tag{3.13}$$

As n approaches to ∞, $\|K_{1n}(t)\|$ tends to 0. In an analogous way, it can be shown $\|K_{2n}(t)\| \to 0$, $\|K_{3n}(t)\| \to 0$, $\|K_{4n}(t)\| \to 0$ and $\|K_{5n}(t)\| \to 0$. □

It is another matter to demonstrate the uniqueness of the solutions of the Eq. (1.1). Suppose that there exist another set of solutions $H_1(t)$, $C_1(t)$, $M_1(t)$, $D_1(t)$ and $I_1(t)$, we find

$$\begin{aligned} H(t) - H_1(t) &= \frac{1-\tau}{F(\tau)} [N_1(t,H) - N_1(t,H_1)] + \frac{\tau}{F(\tau)\Gamma(\tau)} \\ &\quad \times \int_0^t (t-\lambda)^{\tau-1} [N_1(\lambda,H) - N_1(\lambda,H_1)]\, d\lambda \end{aligned} \tag{3.14}$$

Applying the norm to the Eq. (3.14) and because the kernel satisfies the Lipschitz condition, we find

$$\begin{aligned} \|H(t) - H_1(t)\| &\leq \frac{1-\tau}{F(\tau)} A_1 \|H(t) - H_1(t)\| \\ &+ \frac{t^\tau}{F(\tau)\Gamma(\tau)} A_1 \|H(t) - H_1(t)\| \end{aligned} \tag{3.15}$$

This gives

$$\|H(t) - H_1(t)\| \left(1 - \frac{1-\tau}{F(\tau)} A_1 - \frac{t^\tau}{F(\tau)\Gamma(\tau)} A_1\right) \leq 0. \tag{3.16}$$

Clearly $H(t) = H_1(t)$, if the following inequality holds

$$\left(1 - \frac{1-\tau}{F(\tau)} A_1 - \frac{t^\tau}{F(\tau)\Gamma(\tau)} A_1\right) > 0, \tag{3.17}$$

Using the same attitude, we obtain

$$C(t) = C_1(t), M(t) = M_1(t), D(t) = D_1(t), I(t) = I_1(t).$$

4. Numerical simulations

In this section, graphs obtained by using predictor-corrector numerical scheme given in [32] of fractional mathematical model in Eq. (1.1) is given. Our aim is to observe how cancer cells and immune system cells change as fractional order changes. In addition, the interaction between cancer cells and immune system cells can be observed by means of graphs. We use the initial conditions $(0, 0, 1, 10, 0)$ for H, C, M, D, I, respectively and use parameters $a_0 = 10^{-4}$, $b_0 = 10^{-1}$, $f_0 = 1$, $c_0 = 0.005$, $a_1 = 10^{-4}$, $b_1 = 10^{-2}$, $f_1 = 1$, $c_1 = 0.005$, $b_2 = 0.02$, $f_2 = 1$, $d_2 = 0.1$, $d_3 = 0.1$, $b_4 = 10^{-2}$, $e_4 = 10^{-7}$, $c_4 = 10^{-2}$ given in [31]. Figures 1–3 represents that the action of the fractional cancer-immune system model constituent for distinct values of τ and it can be seen that as the fractional order τ is decreased, the number of helper, cytotoxic, dendritic cells and IL-2 are increased, while the cancer cells is declined. In other words, when $\tau = 0.98$, approximately 60 percent of cancer cells die, while $\tau = 0.65$, about 90 percent die. Moreover, Figures 4–5 represents that numerical simulations for the Eq. (1.1) at $\tau = 0.9$, $\tau = 0.8$, $\tau = 0.7$ and $\tau = 0.6$, respectively.

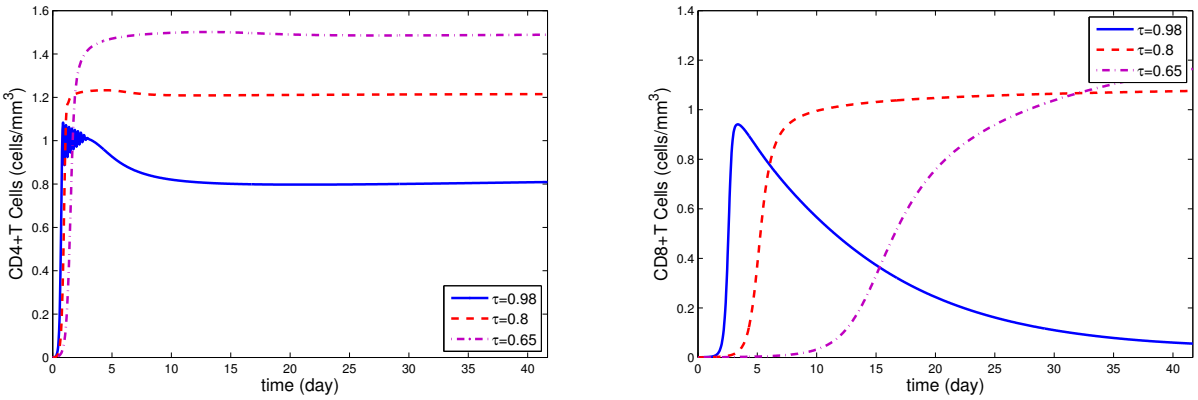

Figure 1. The action of T cells which are constituent of the fractional cancer-immune system model for distinct values of τ.

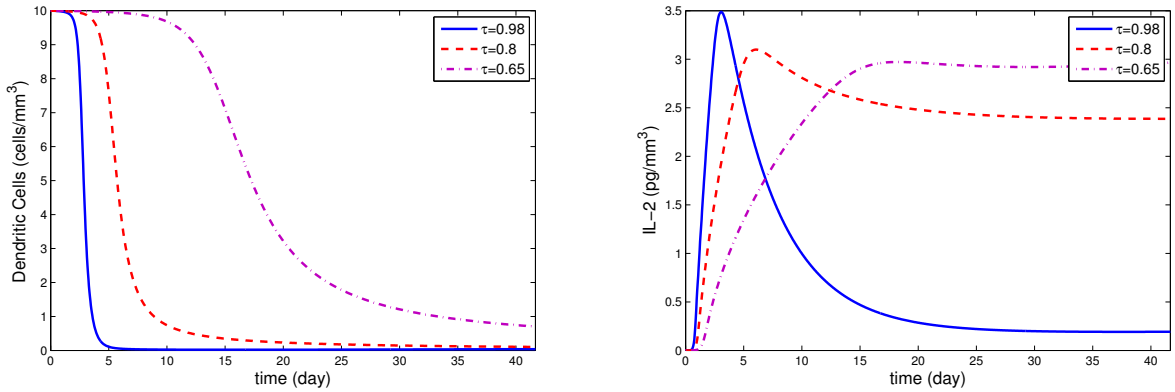

Figure 2. The action of dendritic cells and IL-2 which are constituent of the fractional cancer-immune system model for distinct values of τ.

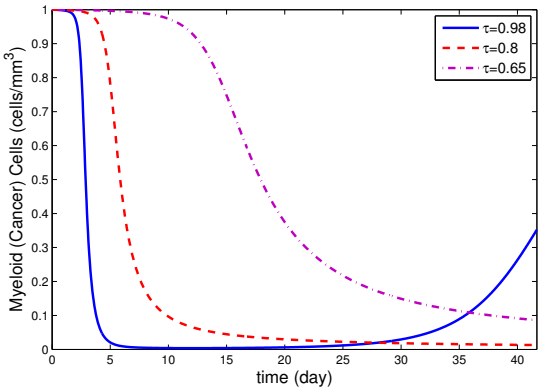

Figure 3. The action of cancer cells which are constituent of the fractional cancer-immune system model for distinct values of τ.

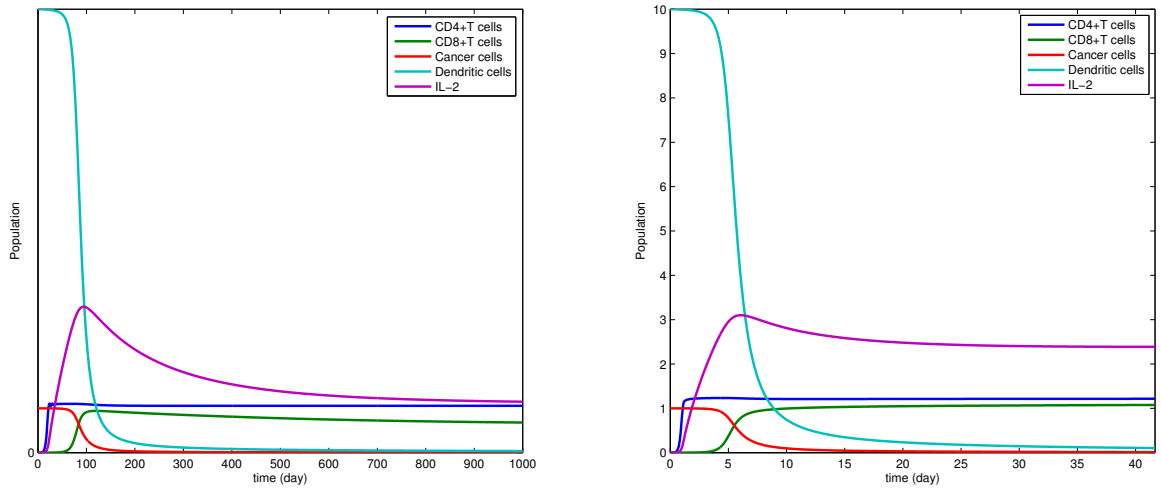

Figure 4. Numerical simulations for the Eq. (1.1) at $\tau = 0.9$ and $\tau = 0.8$, respectively.

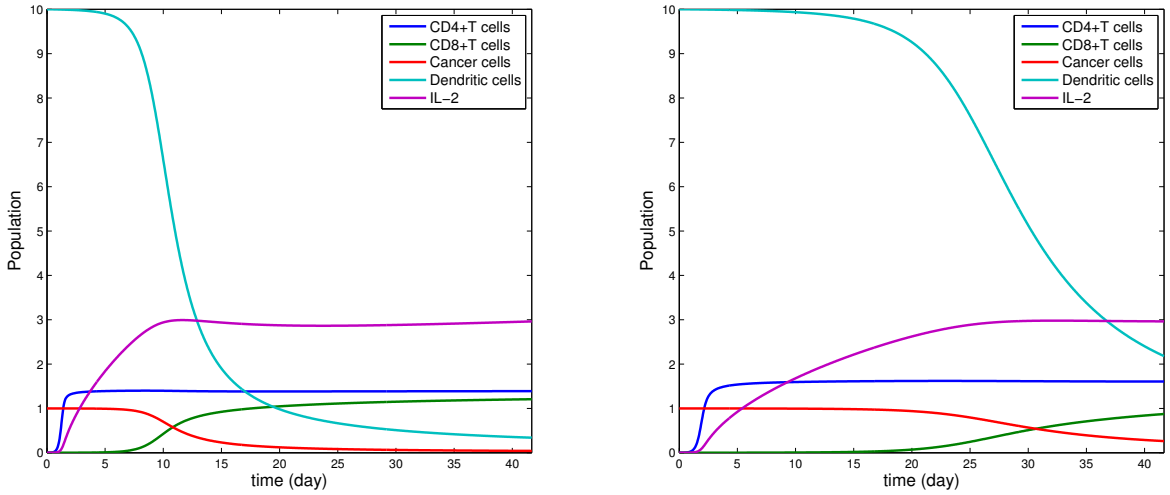

Figure 5. Numerical simulations for the Eq. (1.1) at $\tau = 0.7$ and $\tau = 0.6$, respectively.

5. Conclusions

Cancer is an issue that needs to be addressed when because of affects many people's lives directly and indirectly. How does the body respond to cancer? The answer to the question can be made more effective in the fight against cancer. So, the integer order cancer-immune system model given in [31] is studied in this paper. Firstly, the cancer-immune system model is modified by AB derivative and then the existence and uniqueness of numerical solution of this model is given. After obtaining graphs related to the model with predictor-corrector numerical method, these graphs is interpreted briefly it can be seen that as τ is increased, it is observed that immune system cells eliminate cancer cells less in these graphs. Apparently, because of the hereditary property of fractional derivative, the fractional derivative is more suitable for real life events.

Conflict of interest

The authors declare that no conflicts of interest in this paper.

References

1. L. Marsha, K. R. Conroy, J. L. Davis, et al. *Atlas Pathophysiology*, Lippincott Williams & Wilkins, 2010.
2. V. Kumar, A. Abbas, J. Aster, *Robbins and cotran pathologic basis of disease*, Canada: Elsevier, 2014.
3. M. Zanetti, *Tapping CD4 T cells for cancer immunotherapy: The choice of personalized genomics*, J. Immunol., **194** (2015), 2049–2056.
4. D. Cassell, J. Forman, *Linked recognition of helper and cytotoxic antigenic determinants for he generation of cytotoxic T lymphocytes*, Ann. N. Y. Acad. Sci., **532** (1998), 51–60.

5. H. Choudhry, N. Helmi, W. H. Abdulaal, et al. *Prospects of IL-2 in cancer immunotherapy*, BioMed Res. Int., **2018** (2018), 9056173.
6. A. A. Kilbas, H. M. Srivastava, J. J. Trujillo, *Theory and applications of fractional differential equations*, Elsevier, 2006.
7. D. Baleanu, K. Diethelm, E. Scalas, et al. *Fractional calculus models and numerical methods*, World Scientific, 2012
8. N. Özdemir, D. Karadeniz, B. B. Iskender, *Fractional optimal control problem of a distributed system in cylindrical coordinates*, Phys. Lett. A, **373** (2009), 221–226.
9. F. Evirgen, N. Özdemir, *Multistage adomian decomposition method for solving NLP problems over a nonlinear fractional dynamical system*, J. Comput. Nonlinear Dyn., **6** (2011), 21003.
10. F. Evirgen, *Analyze the optimal solutions of optimization problems by means of fractional gradient based system using VIM*, An International Journal of Optimization and Control: Theories & Applications (IJOCTA), **6** (2016), 75–83.
11. Z. Hammouch, T. Mekkaoui, *Circuit design and simulation for the fractional-order chaotic behavior in a new dynamical system*, Complex Intell. Syst., **4** (2018), 251–260.
12. E. Bonyah, A. Atangana, M. A. Khan, *Modeling the spread of computer virus via Caputo fractional derivative and the beta derivative*, Asia Pacific Journal on Computational Engineering, **4** (2017), 1–15.
13. N. Özdemir, M. Yavuz, *Numerical solution of fractional Black-Scholes equation by using the multivariate pade approximation*, Acta Phys. Pol. A., **132** (2017), 1050–1053.
14. E. Uçar, N. Özdemir, E. Altun, *Fractional order model of immune cells influenced by cancer cells*, Math. Model. Nat. Phenom., **14** (2019), 308.
15. A. Atangana, D. Baleanu, *New fractional derivatives with non-local and non-singular kernel: theory and applications to heat transfer model*, Therm. Sci., **20** (2016), 763–769.
16. M. Yavuz, N. Özdemir, H. M. Baskonus, *Solutions of partial differential equations using the fractional operator involving Mittag-Leffler kernel*, Eur. Phys. J. Plus, **133** (2018), 215.
17. V. F. Morales-Delgadoa, J. F. Gomez-Aguilar, M. A. Taneco-Hernandez, et al. *Mathematical modeling of the smoking dynamics using fractional differential equations with local and nonlocal kernel*, J. Nonlinear Sci. Appl., **11** (2018), 994–1014.
18. N. A. Asif, Z. Hammouch, M. B. Riaz, et al. *Analytical solution of a Maxwell fluid with slip effects in view of the Caputo-Fabrizio derivative*, Eur. Phys. J. Plus, **133** (2018), 272.
19. I. Koca, *Analysis of rubella disease model with non-local and non-singular fractional derivatives*, Int. J. Optim. Control Theor. Appl. IJOCTA, **8** (2018), 17–25.
20. D. Avcı A. Yetim, *Analytical solutions to the advection-diffusion equation with the Atangana-Baleanu derivative over a finite domain*, J. BAUN Inst. Sci. Technol., **20** (2018), 382–395.
21. S. Uçar, E. Uçar, N. Özdemir, et al. *Mathematical analysis and numerical simulation for a smoking model with Atangana-Baleanu derivative*, Chaos, Solitons & Fractals, **118** (2019), 300–306.
22. D. Baleanu, A. Fernandez, *On some new properties of fractional derivatives with Mittag-Leffler kernel*, Commun. Nonlinear Sci. Numer. Simulat., **59** (2018), 444–462.

23. A. Fernandez, D. Baleanu, H. M. Srivastava, *Series representations for fractional-calculus operators involving generalised Mittag-Leffler functions*, Commun. Nonlinear Sci. Numer. Simulat., **67** (2019), 517–527.

24. S. Uçar, *Existence and uniqueness results for a smoking model with determination and education in the frame of non-singular derivatives*, Discrete Continuous Dyn. Syst. Ser. S, in press.

25. F. Evirgen, S. Uçar, N. Özdemir, et al. *System response of an alcoholism model under the effect of immigration via non-singular kernel derivative*, Discrete Continuous Dyn. Syst. Ser. S, in press.

26. J. E. Solis-Perez, J. F. Gomez-Aguilar, A. Atangana, *A factional mathematical model of breast cancer competition model*, Chaos, Solitons and Fractals, **127** (2019), 38–54.

27. V. F. Morales-Delgado, J. F. Gomez-Aguilar, K. Saad, et al. *Application of the Caputo-Fabrizio and Atangana-Baleanu fractional derivatives to mathematical model of cancer chemotherapy effect*, Math. Methods Appl. Sci., **42** (2019), 1167–1193.

28. P. Vereesha, D. G. Prakasha, H. M. Baskonus, *New numerical surfaces to the mathematical model of cancer chemotherapy effect in Caputo fractional derivatives*, CHAOS, **29** (2019), 1–13.

29. A. Minelli, F. Topputo, F. Bernelli, *Controlled drug delivery in cancer immunotherapy: Stability, optimization and monte carlo analysis*, SIAM J. Appl. Math., **71** (2011), 2229–2245.

30. L. G. De Pillis, A. Radunskaya, *A mathematical tumour model with immune resistance and drug therapy: An optimal control approach*, Journal of Theoretical Medicine, **3** (2001), 79–100.

31. F. Castiglione, B. Piccoli, *Cancer immunotheraphy, mathematical modeling and optimal control*, J. Theor. Biol., **247** (2007), 723–732.

32. D. Baleanu, A. Jajarmi, M. Hajipour, *On the nonlinear dynamical systems within the generalized fractional derivatives with Mittag-Leffler kernel*, Nonlinear Dyn., **94** (2018), 397–414.

AIMS Press