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Stability Analysis of a Fractional Order Mathematical Model of Leukemia

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Abstract. In this paper, we propose a fractional order model of leukemia in terms of a system of ordinary differential equations with the Caputo derivative that provides convenience for initial conditions of the differential equations. Firstly, we prove the global existence, positivity, and boundedness of solutions. The local stability properties of the equilibrium are obtained by using fractional Routh-Hurwitz stability criterion. Furthermore, a suitable Lyapunov functions are constructed to prove the global stability of equilibrium. Finally, numerical simulation of the model are presented to illustrate our theoretical results for different choices of fractional order of derivative α. Then, we can observe the impact of fractional derivative α on the evolution of the model states.

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1. Introduction

Among the non-communicable diseases, cancer is the second leading cause of death worldwide, accounting for 18.1 million new cases and 9.6 million deaths in 2018 [24]. Leukemia is a cancer of the bone marrow and blood. It results from an uncontrolled proliferation of abnormal white blood cells and appears when blood stem

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cells in the bone marrow undergo changes that make their behaviour abnormal. These abnormal cells are called leukemia cells; they gradually multiply and eventually invade the so-called "normal" blood cells which are then unable to perform their tasks. The four types of leukemia (acute lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia) are divided into two categories: acute and chronic [15]. Acute leukemia which is a clonal proliferation of immature stem hematological cells which are defined by cells unable to complete their maturation as well as a reduction of mature cells to cause of bone marrow, and leukemia frequently occurs in children. In chronic leukemia, the abnormal cells are partly mature and often appear normal. When these cells develop into leukemia cells, they dont fight off illness as well, and they survive longer than normal white blood cells, allowing them to build up in the blood.

Mathematical models have become one of the most important tools used to understand and predicate the evolution of diseases in such a way to prevent their spread. In the existing literature, most of the biological problems of leukemia are studies through the integer-order mathematical modeling by using ordinary differential equations, see for instance [1, 2, 9, 17, 18, 22, 29, 31]. See also [7, 23, 36] for the mathematical control models of leukemia.

Recently, much attentions have been given to fractional-order models with biological systems [8, 14, 16, 25]. This is due to the fact that fractional-order model is more accurate for the description of memory [6, 33] and hereditary properties of the system when compared with an integer-order model [11, 12, 27, 28, 30, 32, 34].

In this work, we introduce a fractional order for the model developed by [17], which describes the dynamics of leukemia. The model is constructed based on the characteristics of leukemia transmission in the blood. The model consists of three nonlinear ordinary differential equations. The three compartments are susceptible cells S, infected cells I and immune cells W. In these compartments which are not infected with leukemia disease but can be infected is defined as susceptible compartment denoted by S. The compartment which is infected with leukemia and able to transmit leukemia is defined as infective compartment and denoted by I. Again, recovered individuals are those who are removed from the susceptible-infective interaction by recovery with immunity, isolation by any process is defined as recovered compartment and denoted by W. Further, let Λ be the rate at which the susceptible blood cells entering into the circulatory blood from compartments like bone marrow, lymph nodes and thymus. Parameters μ_1, μ_2 and μ_3 are the natural mortality rate of susceptible blood cells, infected cells and immune cells respectively. The parameter β is the infection rate of susceptible blood cells. The rate at which the infected cells are recovered due to encounter with immune cells and it is denoted by γ . So this recovered term is added with the immune cells compartment. Our model is governed by the following equations:

$$\begin{cases} D^\alpha S = \Lambda - \beta SI - \mu_1 S, \\ D^\alpha I = \beta SI - (\mu_2 + \gamma) I, \\ D^\alpha W = \gamma I - \mu_3 W, \end{cases} \tag{1}$$

where $D^\alpha S, D^\alpha I$ and $D^\alpha W$ are the derivative of $S(t), I(t)$ and $W(t)$ respectively, of arbitrary order α (where $0 < \alpha \leqslant 1$) in the sense of Caputo.

A flowchart of our model is given in Figure 1.

The model (1) represents the classical SIW model studies in [17] when $\alpha = 1$. $S(0) > 0, I(0) \geqslant 0$ and $W(0) \geqslant 0$ are the given initial states.

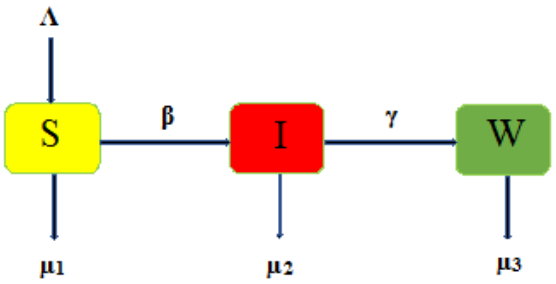


Figure 1. Flowchart of the model of leukemia transmission.

Table 1. Parameter and the values used in model (1).

Description	**Parameters**
Source term of susceptible population	Λ
Natural death rate of susceptible cells	μ_1
Infection rate of susceptible cells due to cancer cells	β
Natural death rate of infected cells	μ_2
Rate at which the infectious individuals recover for immunity	γ
Natural death rate of immune cells	μ_3

The rest of the paper is structured as follows : Section 2 presents some results and definitions on fractional calculus to be used in the next. In Section 3 we show that our model is biologically and mathematically well posed. Section 4 focuses on the problem of both local and global stability of equilibria by using Routh-Hurwitz criteria and the notion of Lyapunov function. Numerical simulations are performed in Section 5 to illustrate theoretical results. Finally, we conclude this paper in Section 6.

2. Definitions and preliminary results

In this section we introduce some definitions and proprieties which are used throughout this paper [26]:

(a) Let $f : \mathbb{R}_+ \to \mathbb{R}$ be a continuous function, then the Caputo fractional derivative of order $\alpha > 0$ of the function f is given by

$$D^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t (t-x)^{n-\alpha-1} f^n(x) dx, \tag{2}$$

where $D \doteq \dfrac{d}{dt}$, $n-1 < \alpha < n, n \in \mathbb{N}$ and $\Gamma(\cdot)$ is the gamma function. In particular, when $0 < \alpha < 1$, we get

$$D^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{f'(x)}{(t-x)^\alpha}. \tag{3}$$

(b) The Laplace transform of Caputo fractional derivative is given by

$$\mathcal{L}\left[D^\alpha f(t)\right] = \lambda^\alpha F(\lambda) - \sum_{k=0}^{n-1} f^k(0) \lambda^{\alpha-k-1}, \tag{4}$$

with $F(\lambda)$ the Laplace transform of $f(t)$.

(c) Let $\alpha, \beta > 0$. The Mittag-Leffler function $E_{\alpha,\beta}$ of parameter α and β is defined as follows:

$$E_{\alpha,\beta}(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k + \beta)}. \tag{5}$$

(d) The Laplace transform of the functions $t^{\beta-1}E_{\alpha,\beta}(\mp at^{\alpha})$ is

$$\mathcal{L}\left[t^{\beta-1}E_{\alpha,\beta}(\mp at^{\alpha})\right] = \frac{\lambda^{\alpha-\beta}}{\lambda^{\alpha} \pm a}, \tag{6}$$

for $\mathcal{R}e(\lambda) > |a|^{\frac{1}{\alpha}}$ and $\mathcal{R}e(\beta) > 0$.
(e) Let $\alpha, \beta > 0$ and $z \in \mathcal{C}$, then the Mittag-Leffler function satisfies the equality given by

$$E_{\alpha,\beta}(z) = zE_{\alpha,\alpha+\beta}(z) + \frac{1}{\Gamma(\beta)}. \tag{7}$$

(f) Let $f : \mathbb{R}^n \to \mathbb{R}^n$ with $n \geqslant 1$, and consider the following fractional-order system:

$$\begin{cases} D^{\alpha}x(t) = f(x), \\ x(t_0) = x_0, \end{cases} \tag{8}$$

with $0 < \alpha \leqslant 1, t_0 \in \mathbb{R}$ and $x_0 \in \mathbb{R}^n$.

To globalize the solution of system (8), we will use the following result which is a direct corollary from [20].

Lemma 2.1 *Assume that the function f satisfies the following conditions:*

(i) *f and $\dfrac{\partial f}{\partial x}$ are continuous on $\mathbb{R}^n$.*
(ii) *$\|f(x)\| \leqslant \omega + \lambda\|x\|$ for all $x \in \mathbb{R}^n$, where ω and λ are two positive constants.*

Then, system (8) has a unique solution on $[t_0, +\infty)$.

Lemma 2.2 *[10] Assume that $f \in \mathcal{C}^1$.*

(i) *If $D^{\alpha}f(t) \geqslant 0$ for all $t \in [a, b]$ and all $\alpha \in (\alpha_0, 1)$ with some $\alpha_0 \in (0, 1)$, then $f(t)$ is monotone increasing.*
(ii) *If $D^{\alpha}f(t) \leqslant 0$ for all $t \in [a, b]$ and all $\alpha \in (\alpha_0, 1)$ with some $\alpha_0 \in (0, 1)$, then $f(t)$ is monotone decreasing.*

Lemma 2.3 *[3, 35] Let $\psi : [0, \infty) \to \mathbb{R}_+$ be a continuous and derivable function. Then, for all $t \geqslant 0$,*

$$D_t^{\alpha}\left(\psi(t) - \psi^{\star} - \psi^{\star}\ln\frac{\psi(t)}{\psi^{\star}}\right) \leqslant \left(1 - \frac{\psi(t)}{\psi^{\star}}\right)D_t^{\alpha}\psi(t), \tag{9}$$

and

$$\frac{1}{2}D_t^{\alpha}\psi^2(t) \leqslant \psi(t)D_t^{\alpha}\psi(t), \tag{10}$$

where $\alpha \in (0, 1)$.

Note that for $\alpha = 1$, the inequalities in Eqs (9) and (10) becomes equalities.

3. Analysis of the model

3.1 *Invariant region*

Theorem 3.1 *Let $\mu \doteq \min(\mu_1, \mu_2, \mu_3)$, then the feasible region Ω, defined by*

$$\Omega \doteq \left\{ (S, I, W) \in \mathbb{R}^3_+ \mid N = S + I + W \leqslant \frac{\Lambda}{\mu} \right\},$$

is positively invariant with respect to system (1).

Proof We will accomplish the proof through two steps:
Step 1: we will prove that the solution of system(1) states is always non-negative. According to system (1), we get easily

$$\begin{aligned} D^\alpha S|_{S=0} &= \Lambda > 0, \\ D^\alpha I|_{I=0} &= 0, \\ D^\alpha W|_{W=0} &= \gamma I \geqslant 0. \end{aligned}$$

From Lemma 2.2, we have $S(t), I(t), W(t) \geqslant 0$ for any $t \geqslant 0$. Then the solution of system (1) will remain in $\mathbb{R}^3_+$.
Step 2: The solution of the system(1) is bounded. Indeed, by adding all equations of the model (1), we have

$$D^\alpha N(t) \leqslant \Lambda - \mu N(t), \tag{11}$$

where $\mu \doteq \min(\mu_1, \mu_2, \mu_3)$. By applying the Laplace transform, we get

$$\lambda^\alpha \mathcal{L}(N(t)) - \lambda^{\alpha-1} N(0) \leqslant \frac{\Lambda}{\lambda} - \mu \mathcal{L}(N(t)).$$

According to e.q.(6) we deduce

$$N(t) \leqslant E_{\alpha,1}(-\mu t^\alpha) N(0) + t^\alpha E_{\alpha,\alpha+1}(-\mu t^\alpha)\Lambda.$$

By using e.q.(7), it follows that

$$N(t) \leqslant \left(N(0) - \frac{\Lambda}{\mu} \right) E_{\alpha,1}(-\mu t^\alpha) + \frac{\Lambda}{\mu}.$$

Since $E_{\alpha,1}(-\mu t^\alpha) \geqslant 0$ for any $t \geqslant 0$, then we have

$$N(t) \leqslant \frac{\Lambda}{\mu}, \ \forall t \geqslant 0,$$

provided that $N(0) \leqslant \dfrac{\Lambda}{\mu}$. This completes the proof. ■

By positivity means the population survives and boundedness refers as a natural restriction to growth as a consequence of limited resources. Since Ω

is positive invariant with respect to system (1), we only need to consider this system within Ω in the rest of the paper.

3.2 *Existence and uniqueness of global solution*

In order to prove the existence of unique global solution of the system (1), we will use the Lemma 2.1 in the following result:

Theorem 3.2 *The fractional order initial value system* (1) *has a unique global solution on* Ω.

Proof Let $X \doteq (S, I, W)'$, then system (1) can be rewritten as follows:

$$D^{\alpha} X = F(X), \tag{12}$$

where

$$F(X) \doteq \begin{pmatrix} \Lambda - \beta SI - \mu_1 S \\ \beta SI - (\mu_2 + \gamma) I \\ \gamma I - \mu_3 W \end{pmatrix}.$$

Firstly, it is easy to see that F satisfies the first condition of lemma 2.1. For the second condition, Let us rewrite the vector function F as follows

$$F(X) \doteq \bar{\Lambda} + (IA_1 + A_2)\, X,$$

where

$$\bar{\Lambda} = \begin{pmatrix} \Lambda \\ 0 \\ 0 \end{pmatrix}, A_1 = \begin{pmatrix} -\beta & 0 & 0 \\ \beta & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } A_2 = \begin{pmatrix} -\gamma & 0 & 0 \\ 0 & -(\mu_2 + \gamma) & 0 \\ 0 & \gamma & -\mu_3 \end{pmatrix}.$$

It follows that there exist

$$\omega \doteq \|\bar{\Lambda}\| \quad \text{and} \quad \theta \doteq |I|\|A_1\| + \|A_2\|$$

such that

$$\|F(X)\| \leqslant \omega + \theta \|X\|.$$

Then, system (1) has a unique solution on $[0, \infty)$. ■

4. Equilibria and stability analysis

In this section, we discuss the existence and local stability of equilibria for system (1). For this, we define the basic reproduction number of the model (1) by

$$\mathcal{R}_0 = \frac{\beta \Lambda}{\mu_1 (\mu_2 + \gamma)}.$$

This threshold is the average number of secondary cases produced by a single infective individual which is introduced into an entirely susceptible population.

It can be see easily that system (1) has two equilibrium points:

- Disease free equilibrium of the form $E_0 = \left(\frac{\Lambda}{\mu_1}, 0, 0\right)$. This equilibrium corresponds to the case when there are non leukemia in the cell population.
- Disease endemic equilibrium point, if $\mathcal{R}_0 > 1$, given by $E^\star = (S^\star, I^\star, W^\star)$, where

$$S^\star = \frac{\mu_2 + \gamma}{\beta}, I^\star = \frac{\mu_1(\mathcal{R}_0 - 1)}{\beta} \text{ and } W^\star = \frac{\gamma\mu_1(\mathcal{R}_0 - 1)}{\beta\mu_3}.$$

4.1 *Local stability*

In this section we will establish the local stability of both free equilibrium E_0 and endemic equilibrium $E^\star$.

Theorem 4.1 *The disease free equilibrium E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable whenever $\mathcal{R}_0 > 1$.*

Proof The jacobian matrix at E_0 is given by

$$J_{E_0} = \begin{pmatrix} -\mu_1 & -\frac{\Lambda\beta}{\mu_1} & 0 \\ 0 & \frac{\beta\Lambda}{\mu_1} - (\mu_2 + \gamma) & 0 \\ 0 & \gamma & -\mu_3 \end{pmatrix}.$$

Therefore eigenvalues of the characteristic equation of J_{E_0} are

$$\begin{aligned} &\lambda_1 = -\mu_3 < 0, \\ &\lambda_2 = -\mu_1 < 0, \\ &\lambda_3 = (\mu_2 + \gamma)(\mathcal{R}_0 - 1). \end{aligned}$$

Hence, all eigenvalues of the characteristic equation are negative if $\mathcal{R}_0 < 1$. Thus $|\arg(\lambda_i)| = \pi > \frac{\alpha\pi}{2}$ for $i = 1, 2, 3$. Consequently, by the Routh-Hurwitz fractional order condition [21], the equilibrium point E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. ■

Theorem 4.2 *If $\mathcal{R}_0 > 1$, then the endemic equilibrium $E^\star$ is locally asymptotically stable*

Proof The jacobian matrix at $E^\star$ is given by

$$J_{E^\star} = \begin{pmatrix} -\gamma - \mu_1(\mathcal{R}_0 - 1) & -(\mu_2 + \gamma) & 0 \\ \mu_1(\mathcal{R}_0 - 1) & 0 & 0 \\ 0 & \gamma & -\mu_3 \end{pmatrix}.$$

Its characteristic equation is

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{13}$$

where

$$\begin{aligned} a_1 &= \gamma + \mu_2 + \mu_1(\mathcal{R}_0 - 1), \\ a_2 &= \mu_3\gamma + \mu_1(\mu_2 + \gamma + \mu_3)(\mathcal{R}_0 - 1), \\ a_3 &= \mu_1\mu_3(\mu_2 + \gamma)(\mathcal{R}_0 - 1). \end{aligned}$$

If $\mathcal{R}_0 > 1$ then $a_1 > 0, a_2 > 0, a_3 > 0$ and $a_1a_2 - a_3 > 0$. Hence, the Routh-Hurwitz conditions are satisfied. ■

Let $D(Q)$ denote the discriminant of the polynomial $Q(\lambda)$ given by e.q.(13), then

$$D(Q) = -\begin{vmatrix} 1 & a_1 & a_2 & a_3 & 0 \\ 0 & 1 & a_1 & a_2 & a_3 \\ 3 & 2a_1 & a_2 & 0 & 0 \\ 0 & 3 & 2a_1 & a_2 & 0 \\ 0 & 0 & 3 & 2a_1 & a_2 \end{vmatrix}$$

$$= 4a_1^3a_3 - a_1^2a_2^2 - 18a_1a_2a_3 + 4a_2^3 + 27a_3^2.$$

According to [4, 5], we can state the following result

Theorem 4.3 *Assume that $\mathcal{R}_0 > 1$.*

(i) *If $D(Q) > 0$ and $0 < \alpha \leqslant 1$, then $E^\star$ is locally asymptotically stable.*
(ii) *If $D(Q) < 0$ and $\alpha \leqslant 2/3$, then $E^\star$ is locally asymptotically stable.*

4.2 *Global stability*

Now, we investigate the global asymptotic stability of both equilibrium.

Theorem 4.4 *The disease free equilibrium E_0 is globally asymptotically stable whenever $\mathcal{R}_0 \leqslant 1$.*

Proof Consider the Lyapunov function $V : \Omega \to \mathbb{R}$ such that

$$V(S, I) = \frac{1}{2}(S - S_0 + I)^2 + \frac{\mu_1 + \mu_2 + \gamma}{\beta} I.$$

Then, by calculating the fractional time derivative of V along the solution of system (1), we get

$$D^\alpha V(S, I) \leqslant -\mu_1(S - S_0)^2 - (\mu_2 + \gamma)I^2 - \frac{(\mu_1 + \mu_2 + \gamma)(\mu_2 + \gamma)}{\beta}(1 - \mathcal{R}_0)I.$$

Thus $D^\alpha(S, I) \leqslant 0$ for $\mathcal{R}_0 \leqslant 1$. Furthermore, the largest invariant set of $\left\{(S, I) \in \mathbb{R}_+^2 : D^\alpha V(S, I) = 0\right\}$ is only the singleton $\{E_0\}$. Consequently, by LaSalle's invariance principle [19], the free equilibrium E_0 is globally asymptotically stable. ■

Theorem 4.5 *If $\mathcal{R}_0 > 1$, then the endemic equilibrium $E^\star$ is globally asymptotically stable.*

Proof Let $V : \Omega \to \mathbb{R}$ be a Lyapunov function such that

$$V(S, I) = S - S^\star \ln\left(\frac{S}{S^\star}\right) + I - I^\star \ln\left(\frac{I}{I^\star}\right).$$

Its fractional time derivative along the solution of system (1) implies that

$$D^{\alpha}V(S,I) \leqslant S^{\star}\left(1-\frac{S}{S^{\star}}\right)D^{\alpha}\left(\frac{S}{S^{\star}}\right)+I^{\star}\left(1-\frac{I}{I^{\star}}\right)D^{\alpha}\left(\frac{I}{I^{\star}}\right)$$

$$\leqslant \left(1-\frac{S}{S^{\star}}\right)D^{\alpha}S+\left(1-\frac{I}{I^{\star}}\right)D^{\alpha}I.$$

Using e.q.(1) and the expressions of the coordinates of the equilibrium point $E^{\star}$, we get

$$D^{\alpha}V(S,I) \leqslant -\frac{\Lambda(S-S^{\star})}{SS^{\star}} \leqslant 0.$$

Furthermore, the largest invariant set of $\left\{(S,I)\in\mathbb{R}^2_+ \ : \ D^{\alpha}V(S,I)=0\right\}$ is only the singleton $\{E^{\star}\}$. By LaSalle's invariance principle, $E^{\star}$ is globally asymptotically stable.

■

5. Numerical simulations

In this section; we perform some numerical simulations of leukemia transmission model(1) to illustrate our theoretical results discussed in the previous sections. The simulation is performed using fde12 solver written in Matlab by Garrappa [13]. Graphical results are displayed using the initial conditions: $S_0 = 1.95, I_0 = 8.6, W_0 = 12.9$ and all the parameters showed in Table 1.

By choosing $\Lambda = 1.5$ cells $\mu\ell^{-1}$ day^{-1}, $\beta = 0.0005\mu\ell$cells^{-1} day^{-1}, $\mu_1 = 0.01$ day^{-1}, $\mu_2 = 0.003$ day^{-1}, $\gamma = 0.09\mu\ell$ cells^{-1} day^{-1}, $\mu_3 = 0.03$ day^{-1}, $t_f = 200$ day and different values of α, we get the disease free equilibrium point $E_0 = (150, 0, 0)$ and $\mathcal{R}_0 = 0.8065 < 1$. Then, according to Theorem 4.4, the disease free equilibrium point E_0 is globally asymptotically stable on Ω (see Figure 2).

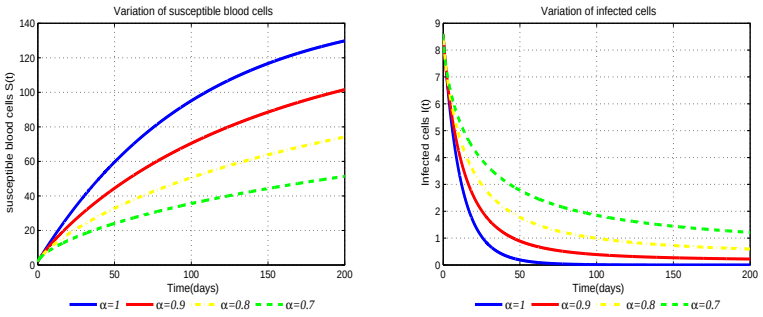
For different values of initial conditions and for fixed value of α, Figure 3 shows that solutions of system (1) converge to the disease free equilibrium E_0 when $\mathcal{R}_0 < 1$, which implies that the disease free equilibrium E_0 of system (1) is globally asymptotically stable on Ω.

Now, we present in Figure 4 the graphic representation of the solutions of the system (1) with the same parameters values given above and for different values of α except $\gamma = 0.03\mu\ell$ cells^{-1} day^{-1}. In this case $\mathcal{R}_0 = 57.6923 > 1$ and the endemic equilibrium point $E^{\star} = (2.6, 113.3846, 37.7949)$, then, according to Theorem 4.5, the endemic equilibrium point $E^{\star}$ of system (1) is globally asymptotically stable on Ω.

In addition, we can observe in Figure 5 that for fixed value of $\alpha = 0.9$ and for different initial conditions the solution of system (1) converge to the endemic equilibrium point $E^{\star}$. Finally, from all of these Figures, we can remark the impact of fractional derivative α on the evolution of the model states.

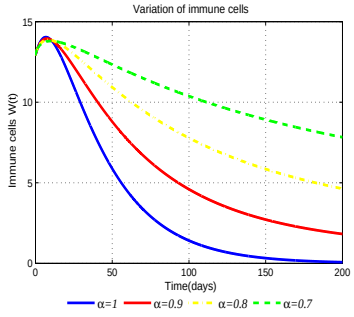
6. Conclusion

In the present work, we have proposed and studied a new fractional order model that describes the spread of leukemia with Caputo fractional derivative. Initially, we have established the existence and the boundedness of non-negative solutions. By using the Routh-Hurwitz criteria and constructing Lyapunov functions, the



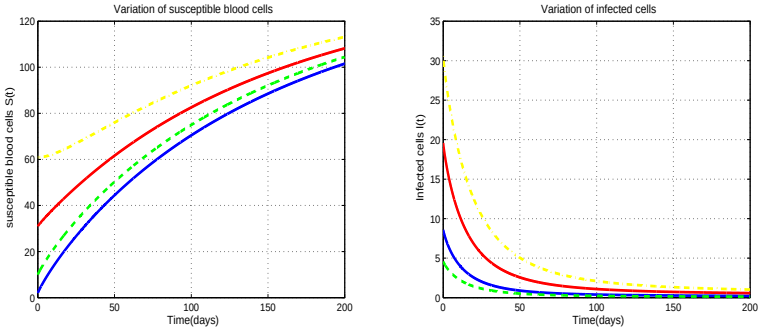
(a)

(b)



(c)

Figure 2. Stability of the disease free equilibrium E_0 for different values of α.



(a)

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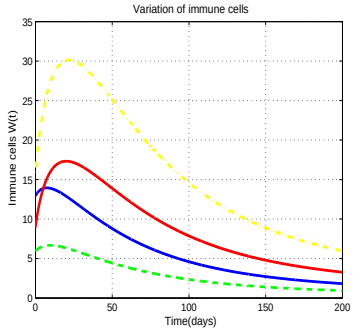

(c)

Figure 3. Stability of the disease free equilibrium E_0 for different initial values for each variable of state and with fixed value of $\alpha = 0.9$.

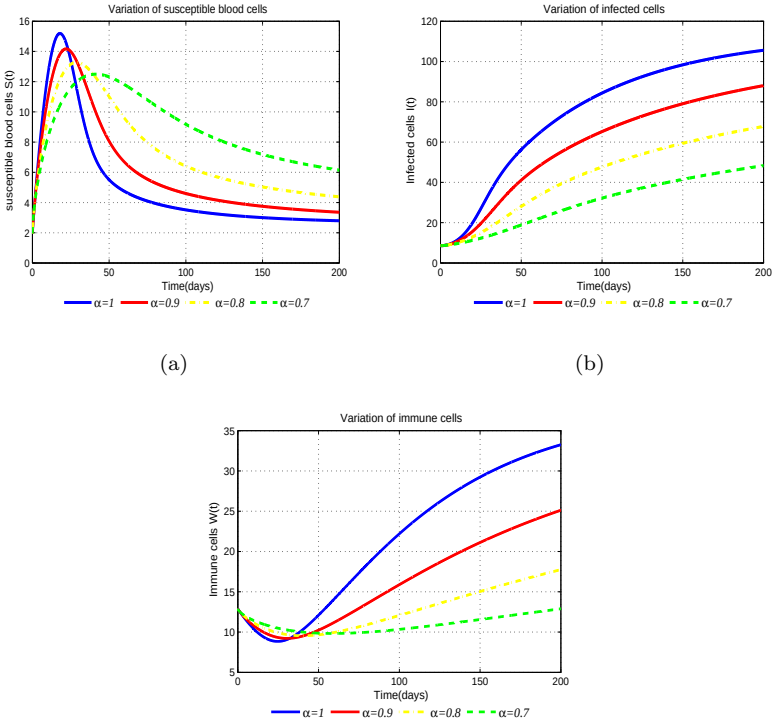

Figure 4. Stability of the endemic equilibrium $E^\star$ for different values of α.

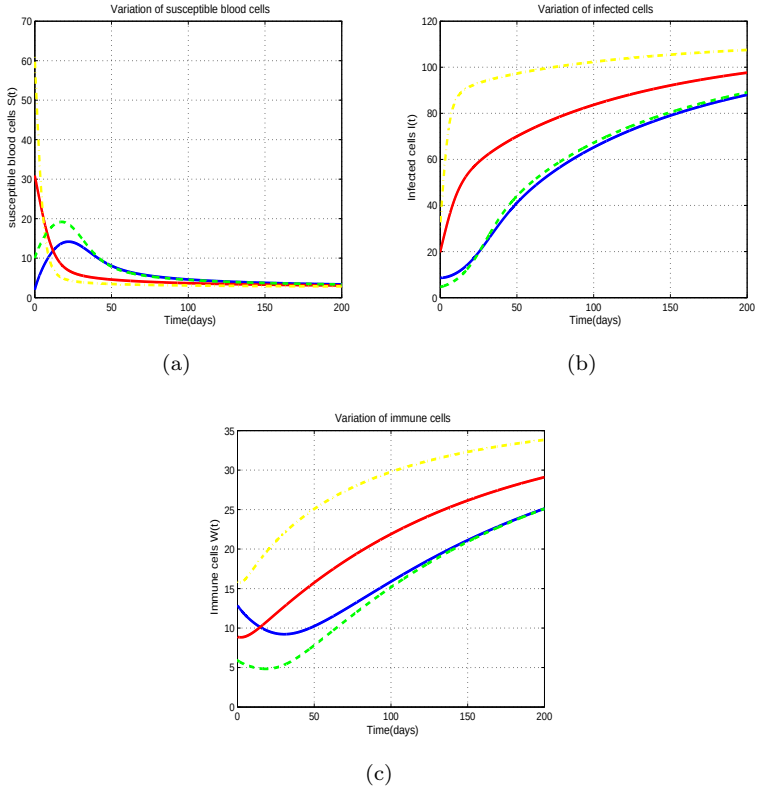

Figure 5. Stability of the endemic equilibrium $E^\star$ for different initial values for each variable of state and with fixed value of $\alpha = 0.9$.

local and the global stability of disease-free equilibrium and endemic equilibrium are established. The numerical simulation was carried out for different values of parameter α and we have remarked that this parameter has impact on the evolution of the model states.

References

[1] E. K. Afenya and D. E. Bentil, Some perspectives on modeling leukemia, Mathematical Biosciences, **150** (1998) 113–130.

[2] M. Agarwal and A. S. Bhadauria, Mathematical modeling and analysis of leukemia: Effect of external engineered T cells infusion, Applications & Applied Mathematics, **10 (1)** (2015) 249–266.

[3] N. Aguila-Camacho, M. A. Duarte-Mermoud and J. A. Gallegos, Lyapunov functions for fractional order systems, Communications in Nonlinear Science and Numerical Simulation, **19** (2014) 2951–2957.

[4] E. Ahmed, A. El-Sayed and H. A. El-Saka, On some routh–hurwitz conditions for fractional order differential equations and their applications in lorenz, rössler, chua and chen systems, Physics Letters A, **358** (2006) 1–4.

[5] E. Ahmed, A. El-Sayed and H. A. El-Saka, Equilibrium points, stability and numerical solutions of fractional-order predator–prey and rabies models, Journal of Mathematical Analysis and Applications, **325** (2007) 542–553.

[6] O. Balatif, L. Boujallal, A. Labzai and M. Rachik, Stability analysis of a fractional-order model for abstinence behavior of registration on the electoral lists, International Journal of Differential Equations, **2020** (2020), Article ID 4325640, doi:10.1155/2020/4325640.

[7] L. Berezansky, S. Bunimovich-Mendrazitsky and A. Domoshnitsky, A mathematical model with time-varying delays in the combined treatment of chronic myeloid leukemia, Advances in Difference Equations, **2012** (2012), doi:10.1186/1687-1847-2012-217.

[8] F. Bozkurt, T. Abdeljawad and M. Hajji, Stability analysis of a fractional order differential equatin model of a brain tumor growth depending on the density, Applied and Computational Mathematics, **14 (1)** (2015) 50-62.

[9] G. Clapp and D. Levy, A review of mathematical models for leukemia and lymphoma, Drug Discovery Today: Disease Models, **16** (2015) 1–6.

[10] K. Diethelm, Monotonicity of functions and sign changes of their caputo derivatives, Fractional Calculus and Applied Analysis, **19** (2016) 561–566.

[11] S. Fahmy, A. M. El-Geziry, E. Mohamed, A. M. AbdelAty and A. G. Radwan, Fractional-order mathematical model for chronic myeloid leukaemia, in 2017 European Conference on Circuit Theory and Design (ECCTD), IEEE, (2017) 1–4, doi:10.1109/ECCTD.2017.8093247.

[12] M. F. Farayola, S. Shafie, F. M. Siam and I. Khan, Numerical simulation of normal and cancer cells populations with fractional derivative under radiotherapy, Computer Methods and Programs in Biomedicine, **187** (2020) 105202, doi:10.1016/j.cmpb.2019.105202.

[13] R. Garrappa, On linear stability of predictor–corrector algorithms for fractional differential equations, International Journal of Computer Mathematics, **87** (2010) 2281–2290.

[14] M. Hassouna, A. Ouhadan and E. El Kinani, On the solution of fractional order sis epidemic model, Chaos, Solitons & Fractals, **117** (2018) 168–174.

[15] T. In, Facts & figures 2019: Us cancer death rate has dropped 27% in 25 years, (2019).

[16] C. Ionescu, A. Lopes, D. Copot, J. T. Machado and J. Bates, The role of fractional calculus in modeling biological phenomena: A review, Communications in Nonlinear Science and Numerical Simulation, **51** (2017) 141–159.

[17] M. S. Khatun and M. H. A. Biswas, Mathematical analysis and optimal control applied to the treatment of leukemia, Journal of Applied Mathematics and Computing, **64** (2020) 331–353.

[18] M. S. Khatun and M. H. A. Biswas, Modeling the effect of adoptive t cell therapy for the treatment of leukemia, Computational and Mathematical Methods, **2** (2020) e1069, doi:10.1002/cmm4.1069.

[19] J. P. La Salle, The Stability of Dynamical Systems, SIAM, (1976).

[20] W. Lin, Global existence theory and chaos control of fractional differential equations, Journal of Mathematical Analysis and Applications, **332** (2007) 709–726.

[21] D. Matignon, Stability results for fractional differential equations with applications to control processing, in Computational Engineering in Systems Applications, vol. 2, Lille, France, (1996) 963–968.

[22] H. Moore and N. K. Li, A mathematical model for chronic myelogenous leukemia (cml) and t cell interaction, Journal of Theoretical Biology, **227** (2004) 513–523.

[23] S. Nanda, H. Moore and S. Lenhart, Optimal control of treatment in a mathematical model of chronic myelogenous leukemia, Mathematical Biosciences, **210** (2007) 143–156.

[24] W. H. Organization et al., Latest global cancer data: Cancer burden rises to 18.1 million new cases and 9.6 million cancer deaths in 2018, International Agency for Research on Cancer. Geneva: World Health Organization, (2018).

[25] I. Öztürk and F. Özköse, Stability analysis of fractional order mathematical model of tumor-immune system interaction, Chaos, Solitons & Fractals, **133** (2020) 109614, doi:10.1016/j.chaos.2020.109614.

[26] I. Podlubny, Fractional Differential Equations, Elsevier Science, (1998).

[27] J. K. Popović, D. T. Spasić, J. Tošić, J. L. Kolarović, R. Malti, I. M. Mitić, S. Pilipović and T. M. Atanacković, Fractional model for pharmacokinetics of high dose methotrexate in children with acute lymphoblastic leukaemia, Communications in Nonlinear Science and Numerical Simulation, **22** (2015) 451–471.

[28] F. Rihan and G. Velmurugan, Dynamics of fractional-order delay differential model for tumor-immune system, Chaos, Solitons & Fractals, **132 (C)** (2020), doi:10.1016/j.chaos.2019.109592.
[29] D. S. Rodrigues, P. F. Mancera, T. Carvalho and L. F. Gonçalves, A mathematical model for chemoimmunotherapy of chronic lymphocytic leukemia, Applied Mathematics and Computation, **349** (2019) 118–133.
[30] J. G. Silva, A. C. Ribeiro, R. F. Camargo, P. F. Mancera and F. L. Santos, Stability analysis and numerical simulations via fractional calculus for tumor dormancy models, Communications in Nonlinear Science and Numerical Simulation, **72** (2019) 528–543.
[31] T. Stiehl and A. Marciniak-Czochra, Mathematical modeling of leukemogenesis and cancer stem cell dynamics, Mathematical Modelling of Natural Phenomena, **7** (2012) 166–202.
[32] N. Sweilam, S. AL-Mekhlafi, A. Alshomrani and D. Baleanu, Comparative study for optimal control nonlinear variable-order fractional tumor model, Chaos, Solitons & Fractals, **136 (C)** (2020), doi:10.1016/j.chaos.2020.1098.
[33] V. E. Tarasov, Generalized memory: Fractional calculus approach, Fractal and Fractional, **2 (4)** (2018), doi:10.3390/fractalfract2040023.
[34] E. Ucar, N. Özdemir and E. Altun, Fractional order model of immune cells influenced by cancer cells, Mathematical Modelling of Natural Phenomena, **14 (3)** (2019), doi:10.1051/mmnp/2019002.
[35] C. Vargas-De-León, Volterra-type lyapunov functions for fractional-order epidemic systems, Communications in Nonlinear Science and Numerical Simulation, **24** (2015) 75–85.
[36] A. Zenati, M. Chakir and M. Tadjine, Global stability analysis and optimal control therapy of blood cell production process (hematopoiesis) in acute myeloid leukemia, Journal of Theoretical Biology, **458** (2018) 15–30.