BULLETIN OF BIOMATHEMATICS

Bulletin of Biomathematics, 2024, 2(2), 162–181

https://www.bulletinbiomath.org
ISSN Online: 2980-1869 / Open Access
https://doi.org/10.59292/bulletinbiomath.2024007

RESEARCH PAPER

A stochastic approach to tumor modeling incorporating macrophages

Sümeyra Uçar [1,‡], **İlknur Koca** [2,‡], **Necati Özdemir** [1,*,‡] **and Tarık İnci** [3,‡]

[1]Department of Mathematics, Faculty of Science and Arts, Balıkesir University, 10145 Balıkesir, Türkiye, [2]Department of Economics and Finance, Fethiye Business Faculty, Muğla Sıtkı Koçman University, 48300 Muğla, Türkiye, [3]Department of Internal Medicine, Faculty of Medicine, Ege University, 35040 İzmir, Türkiye

[*] Corresponding Author
‡ sumeyraucar@balikesir.edu.tr (Sümeyra Uçar); ilknurkoca@mu.edu.tr (İlknur Koca); nozdemir@balikesir.edu.tr (Necati Özdemir); tarik.inci@ege.edu.tr (Tarık İnci)

Abstract

Macrophages are essential components of the immune system's response to tumors, engaging in intricate interactions shaped by factors such as tumor type, progression, and the surrounding microenvironment. These dynamic relationships between macrophages and cancer cells have become a focal point of research, as scientists seek innovative ways to harness the immune system, including macrophages, for cancer immunotherapy. In this study, we introduce a novel model that examines the interaction between tumor and macrophage cells. We provide an in-depth analysis of the equilibrium points and their stability, as well as a thorough investigation into the solution properties of the model. Moreover, by incorporating a stochastic approach, we account for inherent randomness and fluctuations within the system, offering a more comprehensive understanding of tumor-immune dynamics. Numerical simulations further validate the model, providing key insights into how stochastic elements may influence tumor progression and immune response.

Keywords: Stochastic differential equations; numerical approximations; tumor model; stability analysis

AMS 2020 Classification: 26A33; 34A34

1 Introduction

Tumor is the Latin word for swelling and is currently used to describe cancer. Cancer is a disease in which the body's own cells can grow uncontrollably, invade tissues, and cause specific problems. There are two subgroups of tumors called benign and malignant. Malignant tumors, widely

➤ **Received:** 04.06.2024 ➤ **Revised:** 30.09.2024 ➤ **Accepted:** 16.10.2024 ➤ **Published:** 31.10.2024

known as cancer, affect millions of people each year [1], and treatment regimens have diversified over decades. Yet, cancer and its treatments must be addressed to overcome this disease.
The healthy body is capable of defending against cancer cells. Our immune system is well-equipped to find and destroy cancerous cells before they progress to cancer. However, cancer cells acquire functions to evade the immune system, surviving and eventually leading to neoplastic or cancer growth in the body. Our immunity is composed of two different lines of defense. The first line of defense is the innate immune system, which takes action if a germ or unknown antigen is encountered in the body. Examples of the innate immune system include phagocytosis of bacteria, acid secretion in the stomach, skin resistance, neutrophils, macrophages, and natural killer cells [2–4].
Our tumor model introduces a significant advancement by capturing the complex interactions between tumor and macrophage cells. This model's novelty lies in its incorporation of stochastic differential equations, which account for biological variability and offer a more nuanced understanding of these interactions. By integrating these stochastic elements, our model provides a more realistic representation of the dynamic and often unpredictable nature of tumor growth and immune response, enhancing the accuracy and applicability of predictive simulations.
On the other hand, adaptive immunity takes over the process if the innate immune system cannot destroy the invaders. Acquired immunity is the process of generating a specific response to individual invading agents such as bacteria, viruses, toxins, foreign tissues, etc. In the case of reinfection with the same agents, this system generates quick responses. This system consists of B and T lymphocytes. B lymphocytes secrete small proteins called immunoglobulins, which can bind to and inactivate circulating antigens-substances found in foreign particles or germs that trigger an immune response. This is called B-cell-mediated immunity or humoral immunity. The other side of adaptive immunity is cell-mediated immunity, which is mediated by T lymphocytes. T lymphocytes continuously scan the body to find and eliminate emerging malignant cells [2, 5, 6].
One of the pathways cancerous cells use to evade the immune system is expressing the PD-L1 receptors on their surface. PD-L1 is a ligand found on cancer cells that binds to receptors on immune cells to inactivate them. It is one of the treatment options now in use for novel anticancer therapy. In Contrary to this phenomenon, cytotoxic T cells are proliferated by IL-10, despite its tumor-promoting effects. It is known that IL-10 has properties of both tumor-inhibiting and promoting effects through various mechanisms [7–9].
There have been few mathematical tools and concepts used to predict real-world problems in the last couple of decades, including classical differential and integral operators, fractional differential and integral operators, and stochastic differential equations. For classical mechanical problems with no memory, differentiation, and integration are used as a method of modeling. In fact, these two mathematical operators have been used to simulate many real-world phenomena with some limitations. Fractional calculus was introduced to replicate complex problems following power law processes, exponential decay rule, and memory effects. The concepts have been applied in particular to the modeling of real-life structures for example, understanding the dynamics of financial systems, ecosystems, population dynamics, the spread of diseases and many more [10–25].
A mathematical model that integrates uncertainty into its structure is called a stochastic system. The system's inherent complexity or external variables like noise may be the source of this uncertainty. The presence of random variables and probability distributions, which show the likelihood that various events will occur, are frequently characteristics of stochastic systems such as bacterial growth, electrical flows fluctuating due to thermal noise, or gas particles' moments. Stochastic activities can be used to model and understand a wide variety of phenomena, from chemical reactions to economics. They are also used to develop algorithms for predicting the

behavior of complex systems. For the study of stochastic techniques, one needs mathematical knowledge in probability, calculus, linear algebra, set theory, and topology, as well as branches of mathematical analysis such as real analysis and measure theory [26–30].

Ambient noise in the real world unavoidably affects the population system. The model's parameters might not be strictly constant and instead might vary within certain bounds. Environmental noise is thus an excellent way to describe these phenomena in disease models. In addition, stochastic differential equation models are a crucial type of model when considering population dynamics since they are more realistic than other models. There has been considerable research on biological and epidemiological stochastic models. These models provide insight into the spread of diseases and can help simulate clinical trials and other medical research [31–36].

The purpose of this work is to delve into a novel tumor model, a type of stochastic order model which, for the first time, was put forward in employing classical derivative to aim at a tumor model, based on more favorable stochastic theories. In [37], the authors present a system which generates anti-PD-L1 variables, IL-10, CD8+T cells, and cancer cell and demonstrate the critical role that IL-10 and anti-PD-L1 play in inactivating cancer cells, and the mechanism by which cancer cells are eliminated during the single-dose administration of these two medications. Motivating by this nice paper and, as explained above, macrophages and cancer cells are very closely related, herein, we give the following model in order to see the macrophage effects. The integer order differential equation the system that puts forth the tumor model can be seen below:

$$\begin{aligned}
\frac{dT(t)}{dt} &= a + bI(t)C(t)T(t)\left(1-\frac{T(t)}{p}\right) - cT(t),\\
\frac{dC(t)}{dt} &= kC(t)\left(1-\frac{C(t)}{q}\right) - eC(t)T(t)I(t) - zC(t)T(t)Z(t) - \widetilde{m}M(t)C(t),\\
\frac{dI(t)}{dt} &= -fI(t),\\
\frac{dZ(t)}{dt} &= -\gamma Z(t),\\
\frac{dM(t)}{dt} &= r_M\left(1-\frac{M(t)}{k_M}\right)M(t) + \widetilde{p}C(t)M(t) - \widetilde{d}M(t).
\end{aligned} \tag{1}$$

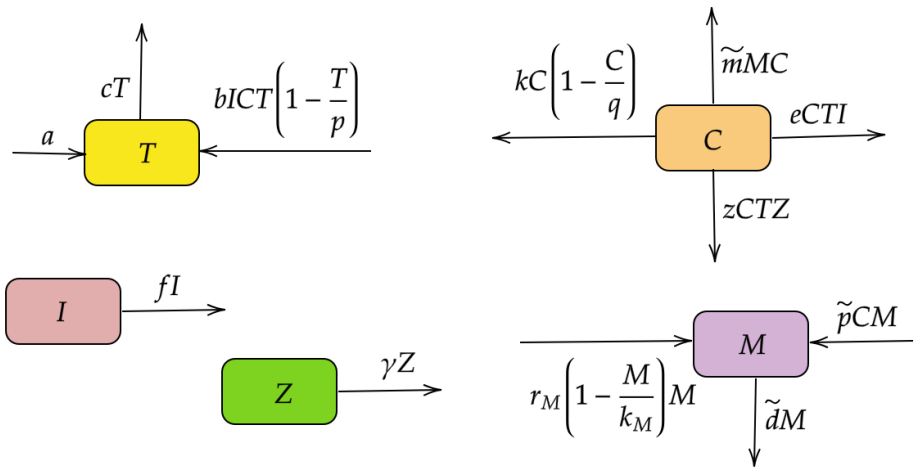


Figure 1. The transfer diagram of the tumor model

The variable factors concerning the model alter at time t as follows: $T(t)$, $C(t)$, $I(t)$, $Z(t)$, $M(t)$ characterize CD8+T lymphocytes, cancer cells, IL-10 cytokine, anti-PD-L1, makrophages in the order given. $\widetilde{p}$ is recruitment rate of macrophages, a is the initial density of CD8+T cells, b the reproduction rate of CD8+Tcells under the influence of IL-10, $\widetilde{d}$ shows death rate of macrophages, k_M display carrying capacity of macrophages, k is the tumor growth ratio, z the death rate of cancer cells under the influence of anti-PD-L1, f is the decay rate of IL-10, q present the carrying capacity of cancer cells, r_M show proliferation ratios of macrophages, γ is the decay ratios anti-PD-L1, $\widetilde{m}$ is tumor killing rate by $M(t)$, c refers to the carrying capacity of CD8+T cells, e is the death ratio of cancer cells under the influence of IL-10, p displays the carrying capacity of CD8+T cells.

The article is further structured with subdivisions specified below: The equilibrium points and their stability analysis are introduced in Section 2. Section 3 substantiates the existence and uniqueness of the solution for our novel model while we again rake through the model by means of the stochastic theory in Section 4. In Section 5, this model is depicted with respect to numerically so as to look over the entire effect. As a final step, we discuss our acquired outcomes and conclude our study.

2 Equilibrium points and stability analysis

Understanding equilibrium points helps analyze and predict the behavior of systems (physical, mathematical, or engineering). The stability of equilibrium points is an important consideration in determining the long-term behavior of a system. So in this section, we focus on the equilibrium points of the system. The equilibrium points are the solutions of the model as follows:

$$\begin{aligned}
a + bI(t)\,C(t)\,T(t)\left(1-\frac{T(t)}{p}\right) - cT(t) &= 0,\\
kC(t)\left(1-\frac{C(t)}{q}\right) - eC(t)\,T(t)\,I(t) - zC(t)\,T(t)\,Z(t) - \widetilde{m}M(t)\,C(t) &= 0,\\
-fI(t) &= 0,\\
-\gamma Z(t) &= 0,\\
r_M\left(1-\frac{M(t)}{k_M}\right)M(t) + \widetilde{p}C(t)\,M(t) - \widetilde{d}M(t) &= 0.
\end{aligned}$$

The disease-free equilibrium point

$$E^* = (T^*, C^*, I^*, Z^*, M^*) = \left(\frac{a}{c}, 0, 0, 0, \frac{k_M\left(r_M - \widetilde{d}\right)}{r_M}\right),$$

and the endemic equilibrium point

$$E^{**} = (T^{**}, C^{**}, I^{**}, Z^{**}, M^{**}) = \left(\frac{a}{c}, \frac{q\left(\widetilde{d}k_M\widetilde{m} + kr_M - k_M\widetilde{m}r_M\right)}{k_M\widetilde{m}\widetilde{p}q + kr_M}, 0, 0, \frac{dk_M\left(\widetilde{p}q + r_M - \widetilde{d}\right)}{k_M\widetilde{m}\widetilde{p}q + kr_M}\right).$$

Theorem 1 *The disease-free equilibrium point* $E^* = \left(\frac{a}{c}, 0, 0, 0, \frac{k_M\left(r_M-\widetilde{d}\right)}{r_M}\right)$ *is locally asymptotically stable if* $\widetilde{d} < r_M$ *and* $\frac{k_M\widetilde{m}\left(\widetilde{d}-r_M\right)}{r_M} + k < 0$.

Proof The Jacobian matrix at the disease-free equilibrium point E^* is

$$J(E^*) = \begin{pmatrix} -c & 0 & 0 & 0 & 0 \\ 0 & k + \frac{\tilde{m}k_M\left(\tilde{d}-r_M\right)}{r_M} & 0 & 0 & 0 \\ 0 & 0 & -f & 0 & 0 \\ 0 & 0 & 0 & -\gamma & 0 \\ 0 & \frac{\tilde{p}k_M\left(r_M-\tilde{d}\right)}{r_M} & 0 & 0 & -r_M + r_M\left(1+\frac{\tilde{d}-r_M}{r_M}\right) \end{pmatrix}.$$

The eigenvalues of this Jacobian matrix $J(E^*)$ are

$$\begin{aligned} \lambda_1 &= -f, \\ \lambda_2 &= \tilde{d} - r_M, \\ \lambda_3 &= \frac{k_M\tilde{m}\left(\tilde{d}-r_M\right)}{r_M} + k, \\ \lambda_4 &= -c, \\ \lambda_5 &= -\gamma. \end{aligned}$$

If $\tilde{d} < r_M$ and $\frac{k_M\tilde{m}\left(\tilde{d}-r_M\right)}{r_M} + k < 0$, then all eigenvalues are negative. So, from [38], the disease-free equilibrium point $E^* = \left(\frac{a}{c}, 0, 0, 0, \frac{k_M\left(r_M-\tilde{d}\right)}{r_M}\right)$ is locally asymptotically stable.

Theorem 2 *The endemic equilibrium point* $E^{**} = \left(\frac{a}{c}, \frac{q\left(\tilde{d}k_M\tilde{m}+dr_M-k_M\tilde{m}r_M\right)}{k_M\tilde{m}\tilde{p}q+dr_M}, 0, 0, \frac{kk_M\left(\tilde{p}q+r_M-\tilde{d}\right)}{k_M\tilde{m}\tilde{p}q+kr_M}\right)$ *is locally asymptotically stable if* $N^{\frac{1}{2}} < M$.

Proof The Jacobian matrix at the endemic equilibrium point E^{**} is

$$J(E^{**}) = \begin{pmatrix} -c & 0 & \frac{bq\left(\tilde{d}k_M\tilde{m}-k_M\tilde{m}r_M+kr_M\right)a\left(1-\frac{a}{cp}\right)}{\left(k_M\tilde{m}\tilde{p}q+kr_M\right)c} & 0 & 0 \\ 0 & \frac{k\left(-\tilde{d}\tilde{m}k_M+\tilde{m}k_Mr_M-dr_M\right)}{k_M\tilde{m}\tilde{p}q+kr_M} & -\frac{eqa\left(\tilde{d}k_M\tilde{m}-k_M\tilde{m}r_M+kr_M\right)}{\left(k_M\tilde{m}\tilde{p}q+kr_M\right)c} & -\frac{zqa\left(\tilde{d}k_M\tilde{m}-k_M\tilde{m}r_M+kr_M\right)}{\left(k_M\tilde{m}\tilde{p}q+kr_M\right)c} & -\frac{\tilde{m}q\left(\tilde{d}k_M\tilde{m}-k_M\tilde{m}r_M+kr_M\right)}{k_M\tilde{m}\tilde{p}q+kr_M} \\ 0 & 0 & -f & 0 & 0 \\ 0 & 0 & 0 & -\gamma & 0 \\ 0 & -\frac{\tilde{p}kk_M\left(-\tilde{p}q+\tilde{d}-r_M\right)}{k_M\tilde{m}\tilde{p}q+kr_M} & 0 & 0 & \frac{r_M\left(\tilde{p}\tilde{m}k_Mq-k\tilde{p}q+k\tilde{d}-\tilde{p}qk_M\tilde{m}r_M+\tilde{p}qkr_M-k\tilde{d}r_M\right)}{k_M\tilde{m}\tilde{p}q+kr_M} \end{pmatrix}.$$

If we make the following assumptions:

$$\begin{aligned} L &= \frac{1}{2\left(k_M\tilde{m}\tilde{p}q+dr_M\right)}, \\ M &= -k\tilde{d}k_M\tilde{m} + kk_M\tilde{m}r_M - k\tilde{p}kr_M - k^2r_M + k\tilde{d}r_M - kr_M^2, \end{aligned}$$

$$N = \begin{pmatrix} -4k\widetilde{d}k_M^2\widetilde{m}^2\widetilde{p}^2q^2 + 4kk_M^2\widetilde{m}^2\widetilde{p}^2q^2r_M - 4k^2k_M\widetilde{m}\widetilde{p}^2q^2r_M \\ +4k\widetilde{d}^2k_M^2\widetilde{m}^2\widetilde{p}q - 8k\widetilde{d}k_M^2\widetilde{m}^2\widetilde{p}qr_M + 4kk_M^2\widetilde{m}^2\widetilde{p}qr_M^2 \\ +k^2\widetilde{d}^2k_M^2\widetilde{m}^2 - 2k^2\widetilde{d}k_M^2\widetilde{m}^2r_M + 2k^2\widetilde{d}k_M\widetilde{m}\widetilde{p}qr_M \\ +k^2k_M^2\widetilde{m}^2r_M^2 - 2k^2k_M\widetilde{m}\widetilde{p}qr_M^2 + k^2\widetilde{p}^2q^2r_M^2 \\ +2k^3\widetilde{d}k_M\widetilde{m}r_M - 2k^3k_M\widetilde{m}r_M^2 - 2k^3\widetilde{p}qr_M^2 \\ +2k^2\widetilde{d}^2k_M\widetilde{m}r_M - 4k^2\widetilde{d}k_M\widetilde{m}r_M^2 - 2k^2\widetilde{d}\widetilde{p}qr_M^2 \\ +2k^2k_M\widetilde{m}r_M^3 + 2k^2\widetilde{p}qr_M^3 + k^4r_M^2 + 2k^3\widetilde{d}r_M^2 \\ -2k^3r_M^3 + k^2\widetilde{d}^2r_M^2 - 2k^2\widetilde{d}r_M^3 + k^2r_M^4 \end{pmatrix}^{\frac{1}{2}},$$

then, the eigenvalues of this Jacobian matrix $J(E^{**})$ are

$$\begin{aligned} \lambda_1 &= -a\left(M + N^{\frac{1}{2}}\right), \\ \lambda_2 &= -a\left(M - N^{\frac{1}{2}}\right), \\ \lambda_3 &= -f, \\ \lambda_4 &= -c, \\ \lambda_5 &= -\gamma. \end{aligned}$$

If $M > N^{\frac{1}{2}}$, then all eigenvalues are negative. So, from [38], the endemic equilibrium point $E^{**} = \left(\frac{a}{c}, \frac{q\left(\widetilde{d}k_M\widetilde{m}+kr_M-k_M\widetilde{m}r_M\right)}{k_M\widetilde{m}\widetilde{p}q+kr_M}, 0, 0, \frac{kk_M\left(\widetilde{p}q+r_M-\widetilde{d}\right)}{k_M\widetilde{m}\widetilde{p}q+kr_M}\right)$ is locally asymptotically stable.

3 Existence and uniqueness analysis of tumor model

In this section, we give the existence and uniqueness theorems to guarantee the existence of solutions and we will present the conditions of existence and uniqueness for our model. Let us consider our model as taking the right side like below:

$$\begin{aligned} \frac{dT(t)}{dt} &= T_1(t,T), \\ \frac{dC(t)}{dt} &= T_2(t,C), \\ \frac{dI(t)}{dt} &= T_3(t,I), \\ \frac{dZ(t)}{dt} &= T_4(t,Z), \\ \frac{dM(t)}{dt} &= T_5(t,M). \end{aligned}$$

Here we consider

$$\begin{aligned} T_1(t,T) &= a + bI(t)C(t)T(t)\left(1 - \frac{T(t)}{p}\right) - cT(t), \\ T_2(t,C) &= kC(t)\left(1 - \frac{C(t)}{q}\right) - eC(t)T(t)I(t) - zC(t)T(t)Z(t) - \widetilde{m}M(t)C(t), \\ T_3(t,I) &= -fI(t), \\ T_4(t,Z) &= -\gamma Z(t), \end{aligned}$$

$$T_5(t,M) = r_M\left(1-\frac{M(t)}{k_M}\right)M(t)+\widetilde{p}C(t)M(t)-\widetilde{d}M(t).$$

For the existence and uniqueness of the model, we consider the following theorem [39]:

Theorem 3 *Assume that there are five positive constants t_1, t_2, t_3, t_4, t_5 and $\bar{t}_1,\bar{t}_2,\bar{t}_3,\bar{t}_4,\bar{t}_5$ such that*

i)

$$\begin{aligned}
|T_1(t,T)-T_1(t,T_1)|^2 &\leq t_1|T-T_1|^2,\\
|T_2(t,C)-T_2(t,C_1)|^2 &\leq t_2|C-C_1|^2,\\
|T_3(t,I)-T_3(t,I_1)|^2 &\leq t_3|I-I_1|^2,\\
|T_4(t,Z)-T_4(t,Z_1)|^2 &\leq t_4|Z-Z_1|^2,\\
|T_5(t,M)-T_5(t,M_1)|^2 &\leq t_5|M-M_1|^2.
\end{aligned}$$

ii)

$$\begin{aligned}
|T_1(t,T)|^2 &\leq \bar{t}_1(1+|T|^2),\\
|T_2(t,C)|^2 &\leq \bar{t}_2(1+|C|^2),\\
|T_3(t,I)|^2 &\leq \bar{t}_3(1+|I|^2),\\
|T_4(t,Z)|^2 &\leq \bar{t}_4(1+|Z|^2),\\
|T_5(t,M)|^2 &\leq \bar{t}_5(1+|M|^2).
\end{aligned}$$

Then, there exists a unique solution if the above conditions are verified. We start with the first equation of model $T_1(t,T)$. Then we verify first condition for equation $T_1(t,T)$ like below:

$$|T_1(t,T)-T_1(t,T_1)|^2 \leq t_1|T-T_1|^2.$$

Before we start the proof, let us define the following norm: $\|T\|_\infty = \sup_{t\in D_t}|T(t)|$, then we have $T, T_1 \in R^2$ and $t\in[0,T]$,

$$\begin{aligned}
|T_1(t,T)-T_1(t,T_1)|^2 &= \left|\begin{array}{c}\left(bI(t)C(t)-\frac{bI(t)C(t)}{p}\left(T(t)+T_1(t)\right)\right)\left(T(t)-T_1(t)\right)\\ -c\left(T(t)-T_1(t)\right)\end{array}\right|^2\\
&\leq \left|\left(\left(bI(t)C(t)\right)\left(1-\frac{T(t)+T_1(t)}{p}\right)-c\right)\left(T(t)-T_1(t)\right)\right|^2\\
&\leq \left(2b^2|I(t)|^2|C(t)|^2\left(1+\frac{|T(t)|^2+|T_1(t)|^2}{p}\right)+2c^2\right)|T(t)-T_1(t)|^2\\
&\leq \left(2b^2\sup_{t\in D_I}|I(t)|^2\sup_{t\in D_C}|C(t)|^2\left(1+\frac{\sup_{t\in D_T}|T(t)|^2+\sup_{t\in D_{T_1}}|T_1(t)|^2}{p}\right)+2c^2\right)\\
&\times |T(t)-T_1(t)|^2
\end{aligned}$$

$$\begin{aligned} &\leq \left(2b^2 \|I\|_\infty^2 \|C\|_\infty^2 \left(1 + \frac{\|T\|_\infty^2 + \|T_1\|_\infty^2}{p}\right) + 2c^2\right) |T(t) - T_1(t)|^2 \\ &\leq t_1 |T - T_1|^2, \end{aligned}$$

where

$$t_1 = \left(2b^2 \|I\|_\infty^2 \|C\|_\infty^2 \left(1 + \frac{\|T\|_\infty^2 + \|T_1\|_\infty^2}{p}\right) + 2c^2\right).$$

Now we proceed to show the second equation. If we have $C, C_1 \in R^2$ and $t \in [0, T]$, then

$$\begin{aligned} |T_2(t, C) - T_2(t, C_1)|^2 &= \left|(k - eT(t) I(t) - zT(t) Z(t) - \widetilde{m} M(t)) (C(t) - C_1(t)) - \frac{k}{q}\left(C^2(t) - C_1^2(t)\right)\right|^2 \\ &= \left| \begin{array}{c} \left((k - eT(t) I(t) - zT(t) Z(t) - \widetilde{m} M(t)) - \frac{k}{q}(C(t) + C_1(t))\right) \\ \times (C(t) - C_1(t)) \end{array} \right|^2 \\ &\leq \left(2\left(k^2 + e^2 |T(t)|^2 |I(t)|^2 + z^2 |T(t)|^2 |Z(t)|^2 + \widetilde{m} |M(t)|^2\right)\right. \\ &\left. + \frac{2k^2}{q^2}\left(|C(t)|^2 + |C_1(t)|^2\right)\right) \times |C(t) - C_1(t)|^2 \\ &\leq \left(\begin{array}{c} 2\left(k^2 + e^2 \sup_{t \in D_T} |T(t)|^2 \sup_{t \in D_I} |I(t)|^2 + z^2 \sup_{t \in D_T} |T(t)|^2 \sup_{t \in D_Z} |Z(t)|^2\right) \\ + 2\widetilde{m} \sup_{t \in D_M} |M(t)|^2 + \frac{2d^2}{q^2}\left(\sup_{t \in D_C} |C(t)|^2 + \sup_{t \in D_{C_1}} |C_1(t)|^2\right) \end{array} \right) \\ &\times |C(t) - C_1(t)|^2 \\ &\leq \left(2\left(k^2 + e^2 \|T\|_\infty^2 \|I\|_\infty^2 + z^2 \|T\|_\infty^2 \|Z\|_\infty^2 + \widetilde{m} \|M\|_\infty^2\right) + \frac{2k^2}{q^2}\left(\|C\|_\infty^2 + \|C_1\|_\infty^2\right)\right) \\ &\times |C(t) - C_1(t)|^2 \\ &\leq t_2 |C - C_1|^2, \end{aligned}$$

where

$$t_2 = \left(2\left(k^2 + e^2 \|T\|_\infty^2 \|I\|_\infty^2 + z^2 \|T\|_\infty^2 \|Z\|_\infty^2 + \widetilde{m} \|M\|_\infty^2\right) + \frac{2k^2}{q^2}\left(\|C\|_\infty^2 + \|C_1\|_\infty^2\right)\right).$$

We take two positive constants $I, I_1 \in R^2$ and $t \in [0, T]$, then

$$\begin{aligned} |T_3(t, I) - T_3(t, I_1)|^2 &= |-fI(t) + fI_1(t)|^2 \\ &\leq f^2 |I(t) - I_1(t)|^2 \\ &\leq t_3 |I - I_1|^2, \end{aligned}$$

where

$$t_3 = f^2.$$

We take two positive constants $Z, Z_1 \in R^2$ and $t \in [0, T]$, then

$$\begin{aligned} |T_4(t,Z) - T_4(t,Z_1)|^2 &= |-\gamma Z(t) + \gamma Z_1(t)|^2 \leq \gamma^2 |Z(t) - Z_1(t)|^2 \\ &\leq t_4 |Z - Z_1|^2, \end{aligned}$$

where

$$t_4 = \gamma^2.$$

Finally, if we take two positive constants $M, M_1 \in R^2$ and $t \in [0, T]$, then

$$\begin{aligned} |T_5(t,M) - T_5(t,M_1)|^2 &= \left| \left(r_M + \widetilde{p} C(t) - \widetilde{d} \right) (M(t) - M_1(t)) - \frac{r_M}{k_M} \left(M^2(t) - M_1^2(t) \right) \right|^2 \\ &= \left| \left(\left(r_M + \widetilde{p} C(t) - \widetilde{d} \right) - \frac{r_M}{k_M} (M(t) + M_1(t)) \right) (M(t) - M_1(t)) \right|^2 \\ &\leq \left(2 \left(r_M^2 + \widetilde{p}^2 |C(t)|^2 + \widetilde{d}^2 \right) + \frac{2 r_M^2}{k_M^2} \left(|M(t)|^2 + |M_1(t)|^2 \right) \right) \\ &\times |M(t) - M_1(t)|^2 \\ &\leq \left(2 \left(r_M^2 + \widetilde{p}^2 \sup_{t \in D_C} |C(t)|^2 + \widetilde{d}^2 \right) + \frac{2 r_M^2}{k_M^2} \left(\sup_{t \in D_M} |M(t)|^2 + \sup_{t \in D_{M_1}} |M_1(t)|^2 \right) \right) \\ &\times |M(t) - M_1(t)|^2 \\ &\leq \left(2 \left(r_M^2 + \widetilde{p}^2 \|C\|_\infty^2 + \widetilde{d}^2 \right) + \frac{2 r_M^2}{k_M^2} \left(\|M\|_\infty^2 + \|M_1\|_\infty^2 \right) \right) |M(t) - M_1(t)|^2 \\ &\leq t_5 |M - M_1|^2, \end{aligned}$$

where

$$t_5 = \left(2 \left(r_M^2 + \widetilde{p}^2 \|C\|_\infty^2 + \widetilde{d}^2 \right) + \frac{2 r_M^2}{k_M^2} \left(\|M\|_\infty^2 + \|M_1\|_\infty^2 \right) \right).$$

So condition (i) is satisfied.
Now we prove the second condition for the tumor model via the following condition:
$\forall (t, T) \in R^2 \times [t_0, T]$ then we will show that

$$\begin{aligned} |T_1(t,T)|^2 &= \left| a + bI(t) C(t) T(t) \left(1 - \frac{T(t)}{p} \right) - cT(t) \right|^2 \\ &\leq 4a^2 + 4b^2 |I(t)|^2 |C(t)|^2 |T(t)|^2 + 4b^2 |I(t)|^2 |C(t)|^2 \frac{\left| T^2(t) \right|^2}{p^2} + 4c^2 |T(t)|^2 \\ &\leq 4a^2 + 4b^2 \sup_{t \in D_I} |I(t)|^2 \sup_{t \in D_C} |C(t)|^2 |T(t)|^2 + 4b^2 \sup_{t \in D_I} |I(t)|^2 \sup_{t \in D_C} |C(t)|^2 \frac{\sup_{t \in D_T} \left| T^2(t) \right|^2}{p^2} \\ &\quad + 4c^2 |T(t)|^2 \end{aligned}$$

$$
\begin{aligned}
&\leq 4a^2+\frac{4b^2}{p^2}\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2\left\|T^2\right\|_\infty^2+\left(4b^2\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2+4c^2\right)|T|^2\\
&\leq \left(4a^2+\frac{4b^2}{p^2}\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2\left\|T^2\right\|_\infty^2\right)\left(1+\frac{4b^2\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2+4c^2}{4a^2+\frac{4b^2}{p^2}\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2\left\|T^2\right\|_\infty^2}|T|^2\right)\\
&\leq \bar{t}_1(1+|T|^2),
\end{aligned}
$$

where

$$
\bar{t}_1=\left(4a^2+\frac{4b^2}{p^2}\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2\left\|T^2\right\|_\infty^2\right),
$$

and with under condition

$$
\frac{4b^2\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2+4c^2}{4a^2+\frac{4b^2}{p^2}\left\|I\right\|_\infty^2\left\|C\right\|_\infty^2\left\|T^2\right\|_\infty^2}<1.
$$

Now we continue with the second equation.

$\forall(t,C)\in R^2\times[t_0,T]$ then we will show that

$$
\begin{aligned}
|T_2(t,C)|^2&=\left|kC(t)\left(1-\frac{C(t)}{q}\right)-eC(t)T(t)I(t)-zC(t)T(t)Z(t)-\widetilde{m}M(t)C(t)\right|^2\\
&\leq 2\left(k^2+e^2|T(t)|^2|I(t)|^2+z^2|T(t)|^2|Z(t)|^2+\widetilde{m}^2|M(t)|^2\right)|C(t)|^2+2\frac{k^2}{q^2}\left|C^2(t)\right|^2\\
&\leq 2\left(k^2+e^2\sup_{t\in D_T}|T(t)|^2\sup_{t\in D_I}|I(t)|^2+z^2\sup_{t\in D_T}|T(t)|^2\sup_{t\in D_Z}|Z(t)|^2+\widetilde{m}^2\sup_{t\in D_M}|M(t)|^2\right)|C(t)|^2\\
&+2\frac{k^2}{q^2}\sup_{t\in D_C}\left|C^2(t)\right|^2\\
&\leq 2\left(k^2+e^2\left\|T\right\|_\infty^2\left\|I\right\|_\infty^2+z^2\left\|T\right\|_\infty^2\left\|Z\right\|_\infty^2+\widetilde{m}^2\left\|M\right\|_\infty^2\right)|C|^2+2\frac{k^2}{q^2}\left\|C^2\right\|_\infty^2\\
&\leq 2\frac{k^2}{q^2}\left\|C^2\right\|_\infty^2\left(1+\frac{2\left(k^2+e^2\left\|T\right\|_\infty^2\left\|I\right\|_\infty^2+z^2\left\|T\right\|_\infty^2\left\|Z\right\|_\infty^2+\widetilde{m}^2\left\|M\right\|_\infty^2\right)}{2\frac{k^2}{q^2}\left\|C^2\right\|_\infty^2}|C|^2\right)\\
&\leq \bar{t}_2(1+|C|^2),
\end{aligned}
$$

where

$$
\bar{t}_2=2\frac{k^2}{q^2}\left\|C^2\right\|_\infty^2,
$$

and with under condition

$$
\frac{2\left(k^2+e^2\left\|T\right\|_\infty^2\left\|I\right\|_\infty^2+z^2\left\|T\right\|_\infty^2\left\|Z\right\|_\infty^2+\widetilde{m}^2\left\|M\right\|_\infty^2\right)}{2\frac{d^2}{q^2}\left\|C^2\right\|_\infty^2}<1.
$$

$\forall (t, I) \in R^2 \times [t_0, T]$

$$|T_3(t, I)|^2 = |-fI(t)|^2 \leq 1 + f^2 |I(t)|^2 \leq \bar{t}_3(1 + |I|^2),$$

where

$$\bar{t}_3 > 0,$$

and with under condition

$$f^2 < 1.$$

$\forall (t, Z) \in R^2 \times [t_0, T]$

$$|T_4(t, Z)|^2 = |-\gamma Z(t)|^2 \leq 1 + \gamma^2 |Z(t)|^2 \leq \bar{t}_4(1 + |Z|^2),$$

where

$$\bar{t}_4 > 0,$$

and with under condition

$$\gamma^2 < 1.$$

$\forall (t, M) \in R^2 \times [t_0, T]$

$$\begin{aligned}
|T_5(t, M)|^2 &= \left| r_M \left(1 - \frac{M(t)}{k_M}\right) M(t) + \widetilde{p} C(t) M(t) - \widetilde{d} M(t) \right|^2 \\
&\leq 4r_M^2 |M(t)|^2 + 4\frac{r_M^2}{k_M^2} \left| M^2(t) \right|^2 + 4\widetilde{p}^2 |C(t)|^2 |M(t)|^2 + 4\widetilde{d}^2 |M(t)|^2 \\
&\leq \left(4r_M^2 + 4\widetilde{p}^2 |C(t)|^2 + 4\widetilde{d}^2\right) |M(t)|^2 + 4\frac{r_M^2}{k_M^2} \left| M^2(t) \right|^2 \\
&\leq \left(4r_M^2 + 4\widetilde{p}^2 \sup_{t \in D_C} |C(t)|^2 + 4\widetilde{d}^2\right) |M(t)|^2 + 4\frac{r_M^2}{k_M^2} \sup_{t \in D_M} \left| M^2(t) \right|^2 \\
&\leq \left(4r_M^2 + 4\widetilde{p}^2 \|C\|_\infty^2 + 4\widetilde{d}^2\right) |M(t)|^2 + 4\frac{r_M^2}{k_M^2} \left\| M^2 \right\|_\infty^2 \\
&\leq 4\frac{r_M^2}{k_M^2} \left\| M^2 \right\|_\infty^2 \left(1 + \frac{4r_M^2 + 4\widetilde{p}^2 \|C\|_\infty^2 + 4\widetilde{d}^2}{4\frac{r_M^2}{k_M^2} \|M^2\|_\infty^2} |M|^2\right) \\
&\leq \bar{t}_5(1 + |M|^2),
\end{aligned}$$

where

$$\bar{t}_5 = 4\frac{r_M^2}{k_M^2}\left\|M^2\right\|_\infty^2,$$

and with under condition

$$\frac{4r_M^2 + 4\widetilde{p}^2\left\|C\right\|_\infty^2 + 4\widetilde{d}^2}{4\frac{r_M^2}{k_M^2}\left\|M^2\right\|_\infty^2} < 1.$$

So, if the conditions below are satisfied, then the model has a unique solution

$$\max\left\{\begin{array}{c} \frac{4b^2\|I\|_\infty^2\|C\|_\infty^2+4c^2}{4a^2+\frac{4b^2}{p^2}\|I\|_\infty^2\|C\|_\infty^2\left\|T^2\right\|_\infty^2}, \\ \frac{2\left(k^2+e^2\|T\|_\infty^2\|I\|_\infty^2+z^2\|T\|_\infty^2\|Z\|_\infty^2+\widetilde{m}^2\|M\|_\infty^2\right)}{2\frac{k^2}{q^2}\left\|C^2\right\|_\infty^2}, \\ f^2, \\ \gamma^2, \\ \frac{4r_M^2+4\widetilde{p}^2\|C\|_\infty^2+4\widetilde{d}^2}{4\frac{r_M^2}{k_M^2}\left\|M^2\right\|_\infty^2}, \end{array}\right\} < 1.$$

By the above theorem, we can say that the model has a unique solution.

4 Stochastic model

In this section, we add to the model under investigation some environmental noise. The idea was suggested by Atangana, where randomness was added to some models [40]. In this section, we convert the deterministic model to the following stochastic system:

$$\begin{aligned}
dT(t) &= \left(a + bI\left(t\right)C\left(t\right)T\left(t\right)\left(1-\frac{T\left(t\right)}{p}\right) - cT\left(t\right)\right) + \sigma_1 T(t)dB_1(t), \\
dC(t) &= \left(\begin{array}{c} kC\left(t\right)\left(1-\frac{C(t)}{q}\right) - eC\left(t\right)T\left(t\right)I\left(t\right) \\ -zC\left(t\right)T\left(t\right)Z\left(t\right) - \widetilde{m}M\left(t\right)C\left(t\right) \end{array}\right) + \sigma_2 C(t)dB_2(t), \\
dI(t) &= \left(-fI\left(t\right)\right) + \sigma_3 I(t)dB_3(t), \\
dZ(t) &= \left(-\gamma Z\left(t\right)\right) + \sigma_4 Z(t)dB_4(t), \\
dM(t) &= \left(r_M\left(1-\frac{M\left(t\right)}{k_M}\right)M\left(t\right) + \widetilde{p}C\left(t\right)M\left(t\right) - \widetilde{d}M\left(t\right)\right) + \sigma_5 M(t)dB_5(t), \\
T(0) &= T_0,\ C(0) = C_0,\ I(0) = I_0,\ Z(0) = Z_0 \text{ and } M\left(0\right) = M_0.
\end{aligned}$$

The existence of a unique solution to a general equation has been presented. Besides this, we have presented the conditions under which the deterministic model admits a unique system of solutions. Now we can present a numerical solution of the model by converting the stochastic model into an integral system below:

$$T(t) - T(0) = \int_0^t T_1(T,C,I,Z,M,\tau)d\tau + \sigma_1\int_0^t T_{11}(T,\tau)dB_1(\tau),$$

$$
\begin{aligned}
C(t)-C(0) &= \int_0^t T_2(T,C,I,Z,M,\tau)d\tau+\sigma_2\int_0^t T_{21}(C,\tau)dB_2(\tau),\\
I(t)-I(0) &= \int_0^t T_3(T,C,I,Z,M,\tau)d\tau+\sigma_3\int_0^t T_{31}(I,\tau)dB_3(\tau),\\
Z(t)-Z(0) &= \int_0^t T_4(T,C,I,Z,M,\tau)d\tau+\sigma_4\int_0^t T_{41}(Z,\tau)dB_4(\tau),\\
M(t)-M(0) &= \int_0^t T_5(T,C,I,Z,M,\tau)d\tau+\sigma_5\int_0^t T_{51}(M,\tau)dB_5(\tau).
\end{aligned}
$$

If we choose to apply the classical Adams-Bashforth to the first component of the system, we have

$$
\begin{aligned}
T_{n+1} &= T_n+\frac{3}{2}\Delta t T_1(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_1(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_1\int_{t_n}^{t_{n+1}} T_{11}(T,\tau)dB_1(\tau),\\
C_{n+1} &= C_n+\frac{3}{2}\Delta t T_2(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_2(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_2\int_{t_n}^{t_{n+1}} T_{21}(C,\tau)dB_2(\tau),\\
I_{n+1} &= I_n+\frac{3}{2}\Delta t T_3(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_3(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_3\int_{t_n}^{t_{n+1}} T_{31}(I,\tau)dB_3(\tau),\\
Z_{n+1} &= Z_n+\frac{3}{2}\Delta t T_4(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_4(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_4\int_{t_n}^{t_{n+1}} T_{41}(Z,\tau)dB_4(\tau),\\
M_{n+1} &= M_n+\frac{3}{2}\Delta t T_5(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_5(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_5\int_{t_n}^{t_{n+1}} T_{51}(M,\tau)dB_5(\tau).
\end{aligned}
$$

Using a sequence of partition of the interval $[t_n, t_{n+1}]$, the last integrals can be approximated to

$$
\begin{aligned}
T_{n+1} &= T_n+\frac{3}{2}\Delta t T_1(T_n,C_n,I_n,Z_n,M_n,t_n)\\
&\quad -\frac{\Delta t}{2}T_1(T_{n-1},C_{n-1},I_{n-1},Z_{n-1},M_{n-1},t_{n-1})+\sigma_1\sum_{i=n-1}^{n} T_{11}(T_i,c_i)\left[B_1(t_{i+1})-B_1(t_i)\right],
\end{aligned}
$$

$$
\begin{aligned}
C_{n+1} &= C_n + \frac{3}{2}\Delta t T_2(T_n, C_n, I_n, Z_n, M_n, t_n) \\
&\quad -\frac{\Delta t}{2} T_2(T_{n-1}, C_{n-1}, I_{n-1}, Z_{n-1}, M_{n-1}, t_{n-1}) + \sigma_2 \sum_{i=n-1}^{n} T_{21}(C_i, c_i)\left[B_2(t_{i+1}) - B_2(t_i)\right], \\
I_{n+1} &= I_n + \frac{3}{2}\Delta t T_3(T_n, C_n, I_n, Z_n, M_n, t_n) \\
&\quad -\frac{\Delta t}{2} T_3(T_{n-1}, C_{n-1}, I_{n-1}, Z_{n-1}, M_{n-1}, t_{n-1}) + \sigma_3 \sum_{i=n-1}^{n} T_{31}(I_i, c_i)\left[B_3(t_{i+1}) - B_3(t_i)\right], \\
Z_{n+1} &= Z_n + \frac{3}{2}\Delta t T_4(T_n, C_n, I_n, Z_n, M_n, t_n) \\
&\quad -\frac{\Delta t}{2} T_4(T_{n-1}, C_{n-1}, I_{n-1}, Z_{n-1}, M_{n-1}, t_{n-1}) + \sigma_4 \sum_{i=n-1}^{n} T_{41}(Z_i, c_i)\left[B_4(t_{i+1}) - B_4(t_i)\right], \\
M_{n+1} &= M_n + \frac{3}{2}\Delta t T_5(T_n, C_n, I_n, Z_n, M_n, t_n) \\
&\quad -\frac{\Delta t}{2} T_5(T_{n-1}, C_{n-1}, I_{n-1}, Z_{n-1}, M_{n-1}, t_{n-1}) + \sigma_5 \sum_{i=n-1}^{n} T_{51}(M_i, c_i)\left[B_5(t_{i+1}) - B_5(t_i)\right],
\end{aligned}
$$

where $c_i \in (t_n, t_{n+1})$.

5 Numerical simulations

Deterministic and stochastic modeling are two different approaches used in mathematical modeling to represent and analyze systems. Stochastic modeling of tumors provides insight into the inherent uncertainties and complexities associated with cancer biology. It allows researchers to better understand the range of possible outcomes so in this section, we show the numerical simulations for the considered stochastic tumor model which is given by

$$
\begin{aligned}
dT(t) &= \left(a + bI(t)C(t)T(t)\left(1 - \frac{T(t)}{p}\right) - cT(t)\right) + \sigma_1 T(t) dB_1(t), \\
dC(t) &= \begin{pmatrix} kC(t)\left(1 - \frac{C(t)}{q}\right) - eC(t)T(t)I(t) \\ -zC(t)T(t)Z(t) - \widetilde{m}M(t)C(t) \end{pmatrix} + \sigma_2 C(t) dB_2(t), \\
dI(t) &= (-fI(t)) + \sigma_3 I(t) dB_3(t), \\
dZ(t) &= (-\gamma Z(t)) + \sigma_4 Z(t) dB_4(t), \\
dM(t) &= \left(r_M\left(1 - \frac{M(t)}{k_M}\right)M(t) + \widetilde{p}C(t)M(t) - \widetilde{d}M(t)\right) + \sigma_5 M(t) dB_5(t), \\
T(0) &= T_0,\ C(0) = C_0,\ I(0) = I_0,\ Z(0) = Z_0 \text{ and } M(0) = M_0.
\end{aligned}
$$

For the numerical simulations of the system, we consider the values of the parameters as follows:

$a = 10^{-4}$, $b = 0.175$, $c = 5 * 10^{-3}$, $k = 0.02$, $e = 0.15$, $f = 0.01$, $p = 1$, $q = 1$, $z = 1$, $\gamma = 0.001925$, $r_M = 0.64$, $k_M = 3.39$, $\widetilde{p} = 4.5 * 10^{-9}$, $\widetilde{d} = 0.55$, $\widetilde{m} = 1.8 * 10^{-5}$.

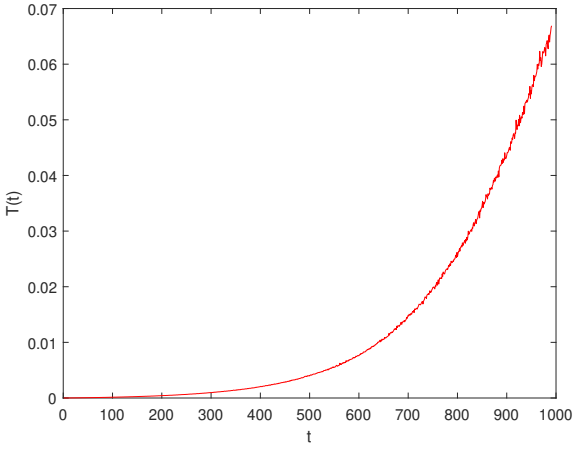
The initial conditions are given as follows:

$$T(0) = 0,\ C(0) = 1,\ I(0) = 4,\ Z(0) = 2 \text{ and } M(0) = 3.$$

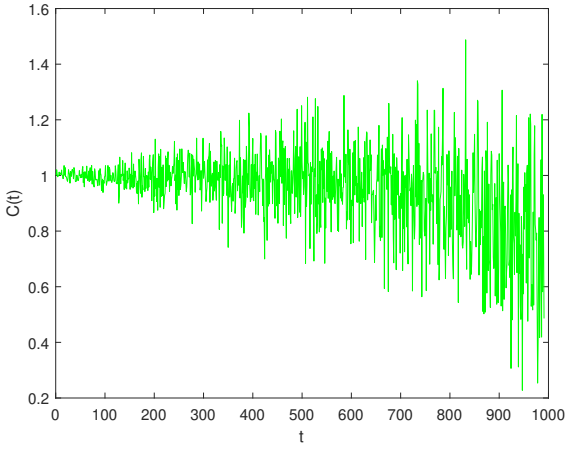
In the model, the densities of randomness values are given as figures

$$\sigma_1 = 0.001,\ \sigma_2 = 0.015,\ \sigma_3 = 0.012,\ \sigma_4 = 0.013,\ \sigma_5 = 0.014.$$

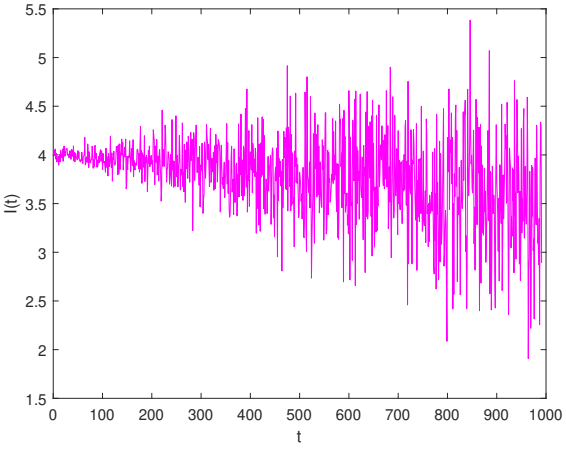
Tumors are influenced by a multitude of factors that exhibit probabilistic behavior. It is now strongly believed that even micro-biota have a role in cancer development and treatment. Chemotherapy, radiotherapy, and targeted drug therapy along with surgery are used to treat cancer caused by factors such as the likelihood of benefit from treatment, stage of cancer, cytogenetic of tumor, comorbidities and patients' performance status. Considering these complex behaviours of tumors, we observe that a more accurate depiction of the model's complexity arises when we examine the densities of randomness in the stochastic tumor model. These models assist researchers and clinicians in understanding the variety of tumor characteristics and developing strategies for tailored and adaptive cancer therapy by simulating a range of potential outcomes. Tumors are influenced by a multitude of factors that exhibit probabilistic behavior. Chemotherapy, radiotherapy, and drug therapy are used to treat cancer caused by factors such as genetics, environmental factors, lack of exercise, and stress. Cancer is a complex and dynamic system influenced by a multitude of factors so stochastic modeling provides a more realistic representation of these processes.



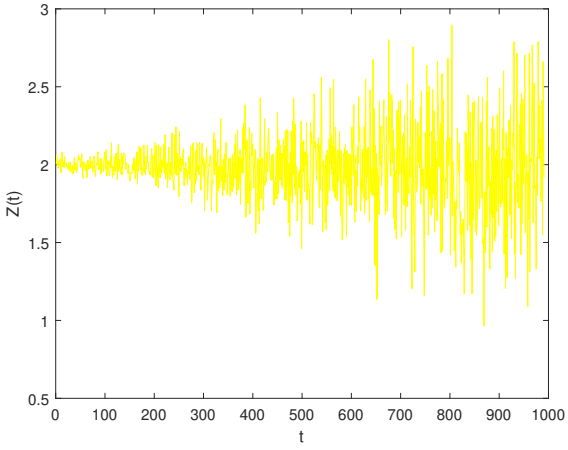
(a) Numerical simulation for CD8+T lymphocytes $T(t)$



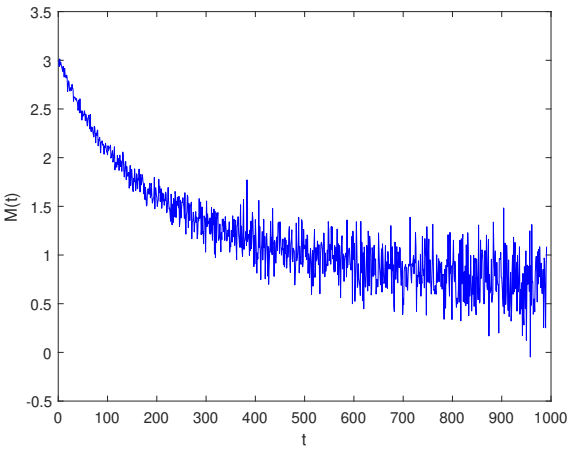
(b) Numerical simulation for cancer cells $C(t)$



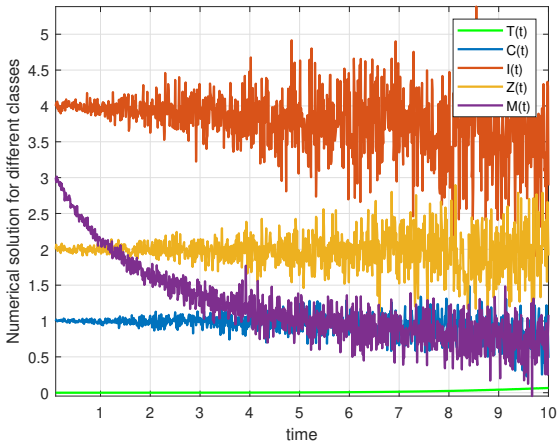
(c) Numerical simulation for IL-10 cytokine $I(t)$



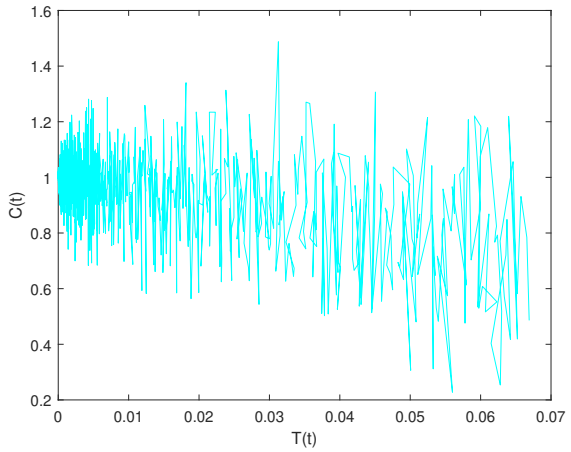
(d) Numerical simulation for anti-PD-L1 $Z(t)$



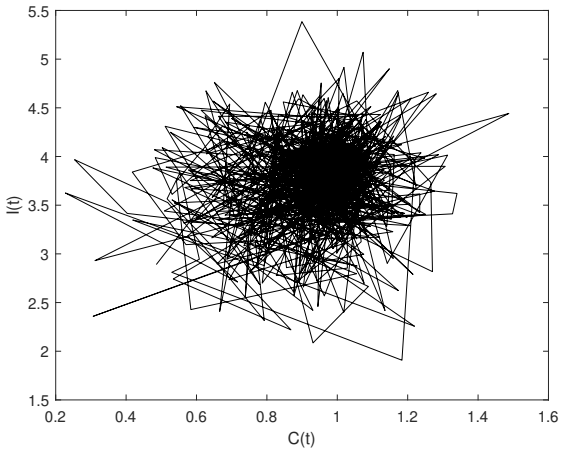
(e) Numerical simulation for makrophages $M(t)$



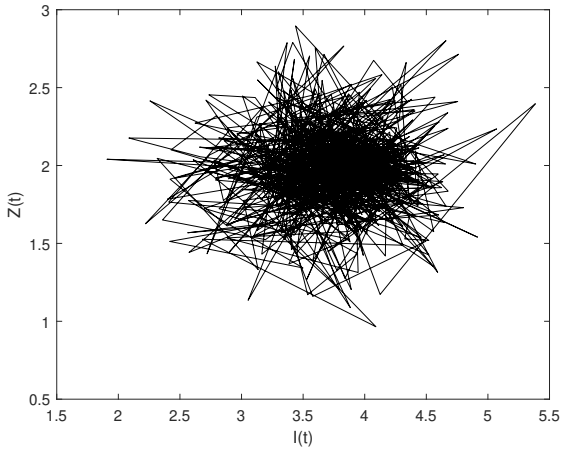
(f) Numerical simulation results of system for all classes $T(t)$, $C(t)$, $I(t)$, $Z(t)$, $M(t)$



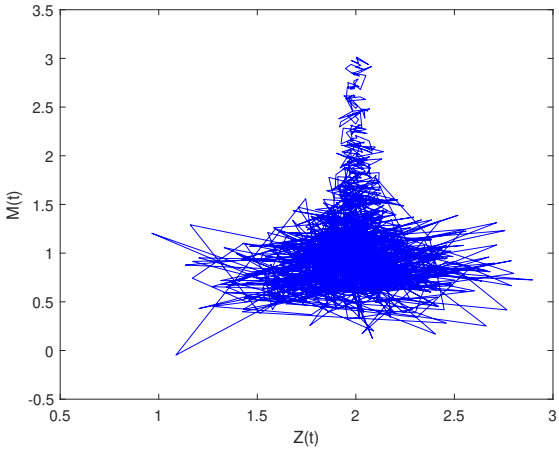
(g) Numerical simulation for $T - C$ phase



(h) Numerical simulation for $C - I$ phase



(i) Numerical simulation for $I - Z$ phase



(j) Numerical simulation for $Z - M$ phase

6 Conclusions

One important class of white blood cells in the immune system are macrophages. They are a component of the body's primary defense against diseases and foreign invaders which is the innate immune system. Also, macrophages are essential for both immune response and infection defense because they clear pathogens and detritus from the body and coordinate the intricate interactions between various immune system components. Given the importance of macrophage cells to the body, this study includes a discussion of a novel tumor model and monitored the propagation of the tumor model more comprehensively. The equilibrium points are produced and the conditions proving the solution's existence and exclusivity in relation to this tumor model become clear. Then, the model is scrutinized carefully in terms of stochastic theory. In the end, a number of numerical outputs for this model pertaining to the aforementioned stochastic model are presented here.

Declarations

Use of AI tools

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

Data availability statement

All data generated or analyzed during this study are included in this article.

Ethical approval

The authors state that this research complies with ethical standards. This research does not involve either human participants or animals.

Consent for publication

Not applicable

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

Not applicable

Author's contributions

N.Ö and İ.K.: Conceptualization, S.U. and T.İ.: Supervision, Investigation. N.Ö and İ.K.: Formal Analysis. İ.K.: Software. İ.K., S.U. and T.İ.: Validation. N.Ö., İ.K., S.U. and T.İ.: Writing-Review and Editing. The authors have read and agreed to the published version of the manuscript.

Acknowledgements

Not applicable

References

[1] Global Cancer Observatory (GCO), Cancer Today, (2022). https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets

[2] Guyton, A.C. and Hall, J.E. *Textbook of Medical Physiology*. Elsevier: Pennsylvania, USA, (2006).

[3] Hanahan, D. and Weinberg, R.A. Hallmarks of cancer: the next generation. *Cell,* 144(5), 646-674, (2011). [CrossRef]

[4] Marsha, L., Conroy, K.R., Davis, J.L. and Embree, B.M. *Atlas Pathophysiology*. Lippincott Williams & Wilkins: Pennsylvania, USA, (2010).

[5] Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K. and Walter, P. *Molecular Biology of the Cell*. Garland Science: New York, (2002).

[6] Kumar, V., Abbas, A.K. and Aster, J.C. *Robbins Basic Pathology.* Elsevier: Netherlands, (2017).

[7] Dennis, K.L., Blatner, N.R., Gounari, F. and Khazaie K. Current status of interleukin-10 and regulatory T-cells in cancer. *Current Opinion in Oncology*, 25(6), 637-645, (2013). [CrossRef]

[8] Sheikhpour, E., Noorbakhsh, P., Foroughi, E., Farahnak, S., Nasiri, R. and Neamatzadeh, H. A Survey on the Role of Interleukin-10 in Breast Cancer: A Narrative. *Reports of Biochemistry and Molecular Biology*, 7(1), 30-37, (2018). [CrossRef]

[9] Sheergojri, A.R., Iqbal, P., Agarwal, P. and Özdemir, N. Uncertainty-based Gompertz growth model for tumor population and its numerical analysis. *An International Journal of Optimization and Control: Theories & Applications*, 12(2), 137-150, (2022). [CrossRef]

[10] 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). [CrossRef]

[11] Uçar, E. and Özdemir, N. New fractional cancer mathematical model via IL-10 cytokine and anti-PD-L1 inhibitor. *Fractal and Fractional*, 7(2), 151, (2023). [CrossRef]

[12] Alla Hamou, A., Azroul, E., Diki, G. and Guedda, M. Effect of family and public health education in drug transmission: an epidemiological model with memory. *Modeling Earth Systems and Environment*, 9, 2809-2828, (2023). [CrossRef]

[13] Evirgen, F. Transmission of Nipah virus dynamics under Caputo fractional derivative. *Journal of Computational and Applied Mathematics*, 418, 114654, (2023). [CrossRef]

[14] Atede, A.O., Omame, A. and Inyama, S.C. A fractional order vaccination model for COVID-19 incorporating environmental transmission: a case study using Nigerian data. *Bulletin of Biomathematics*, 1(1), 78-110, (2023). [CrossRef]

[15] Özdemir, N. and Uçar, E. Investigating of an immune system-cancer mathematical model with Mittag-Leffler kernel. *AIMS Mathematics*, 5(2), 1519-1531, (2020). [CrossRef]

[16] Uçar, S., Evirgen, F., Özdemir, N. and Hammouch, Z. Mathematical analysis and simulation of a giving up smoking model within the scope of non-singular derivative. *Proceedings of the Institute of Mathematics and Mechanics*, 48, 84-99, (2022). [CrossRef]

[17] Guo, Y., Fan, L. and Wang, X. Mathematical investigation of the role of re-polarisation of M2 in cancer therapy. *Discrete and Continuous Dynamical Systems - Series B,* 28(4), 2718-2744, (2023). [CrossRef]

[18] Aguiar, M., Pinto C., Nieto, J.J. and Ribeiro, R.M. New trends on mathematical modeling and simulation of biological systems. *Chaos Solitons and Fractals*, 172, 113568, (2023). [CrossRef]

[19] Yavuz, M., Ozdemir, N. and Okur, Y.Y. Generalized differential transform method for fractional partial differential equation from finance. In Proceedings, *International Conference on Fractional Differentiation and its Applications (ICFDA)*, pp. 778-785, Novi Sad, Serbia, (2016, July).

[20] Ucar, E., Özdemir, N. and Altun, E. Fractional order model of immune cells influenced by

cancer cells. *Mathematical Modelling of Natural Phenomena*, 14(3), 308, (2019). [CrossRef]

[21] Paul, S., Mahata, A., Mukherjee, S., Das, M., Mali, P.C., Roy, B. et al. Study of fractional order SIR model with MH type treatment rate and its stability analysis. *Bulletin of Biomathematics*, 2(1), 85-113, (2024). [CrossRef]

[22] Paul, S., Mahata, A., Karak, M., Mukherjee, S., Biswas, S. and Roy, B. A fractal-fractional order Susceptible-Exposed-Infected-Recovered (SEIR) model with Caputo sense. *Healthcare Analytics*, 5, 100317, (2024). [CrossRef]

[23] Paul, S., Mahata, A., Mukherjee, S., Mali, P.C. and Roy, B. Dynamical behavior of fractional order SEIR epidemic model with multiple time delays and its stability analysis. *Examples and Counterexamples*, 4, 100128, (2023). [CrossRef]

[24] Mahata, A., Roy, B., Mondal, S.P. and Alam, S. Application of ordinary differential equation in glucose-insulin regulatory system modeling in fuzzy environment. *Ecological Genetics and Genomics*, 3-5, 60-66, (2017). [CrossRef]

[25] Evirgen, F. and Özdemir, N. A fractional order dynamical trajectory approach for optimization problem with HPM. In *Fractional Dynamics and Control* (pp. 145–155). New York: Springer, (2012). [CrossRef]

[26] Ross, S.M. *Stochastic Processes*. Wiley: New York, (1996).

[27] Burdzy, K. *Brownian Motion and its Applications to Mathematical Analysis*. Springer: Switzerland, (2014). [CrossRef]

[28] Brown, R. XXVII. A brief account of microscopical observations made in the months of June, July and August 1827, on the particles contained in the pollen of plants; and on the general existence of active molecules in organic and inorganic bodies. *The Philosophical Magazine*, 4(21), 161-173, (1828). [CrossRef]

[29] Ikram, R., Khan, A., Zahri, M., Saeed, A., Yavuz, M. and Kumam, P. Extinction and stationary distribution of a stochastic COVID-19 epidemic model with time-delay. *Computers in Biology and Medicine*, 141, 105115, (2022). [CrossRef]

[30] Beghin L. and Caputo, M. Stochastic applications of Caputo-type convolution operators with nonsingular kernels. *Stochastic Analysis and Applications*, 41(2), 377-393, (2023). [CrossRef]

[31] Koca, I. and Atangana, A. Theoretical and numerical analysis of a chaotic model with nonlocal and stochastic differential operators. *An International Journal of Optimization and Control: Theories & Applications*, 13(2), 181-192, (2023). [CrossRef]

[32] Okuonghae, D. Analysis of a stochastic mathematical model for tuberculosis with case detection. *International Journal of Dynamics and Control*, 10, 734-747, (2022). [CrossRef]

[33] Liping, C., Khan, M.A., Atangana, A. and Kumar, S. A new financial chaotic model in Atangana-Baleanu stochastic fractional differential equations. *Alexandria Engineering Journal*, 60(6), 5193-5204, (2021). [CrossRef]

[34] Ali, I. and Khan, S.U. A dynamic competition analysis of stochastic fractional differential equation arising in finance via pseudospectral method. *Mathematics*, 11(6), 1328, (2023). [CrossRef]

[35] Naim, M., Sabbar, Y. and Zeb, A. Stability characterization of a fractional-order viral system with the non-cytolytic immune assumption. *Mathematical Modelling and Numerical Simulation with Applications*, 2(3), 164-176, (2022). [CrossRef]

[36] Tadmon, C. and Njike Tchaptchet, E.R. Impact of Financial Crisis on Economic Growth: A

Stochastic Model. *Stochastics and Quality Control*, 37(1), 45-63, (2022). [CrossRef]

[37] Uçar, E., Özdemir, N. and Altun, E. Qualitative analysis and numerical simulations of new model describing cancer. *Journal of Computational and Applied Mathematics*, 422, 114899, (2023). [CrossRef]

[38] 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(1), 542-553, (2007). [CrossRef]

[39] Atangana, A. Mathematical model of survival of fractional calculus, critics and their impact: How singular is our world. *Advances in Difference Equations*, 2021(403), 1-59, (2021). [CrossRef]

[40] Atangana, A. Extension of rate of change concept: From local to nonlocal operators with applications. *Results in Physics*, 19, 103515, (2020). [CrossRef]

Bulletin of Biomathematics (BBM)
(https://bulletinbiomath.org)

How to cite this article: Uçar, S., Koca, İ., Özdemir, N. & İnci, T. (2024). A stochastic approach to tumor modeling incorporating macrophages. *Bulletin of Biomathematics*, 2(2), 162-181. https://doi.org/10.59292/bulletinbiomath.2024007