Population Dynamics on Fractional Tumor System Using Laplace Transform and Stability Analysis

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ABSTRACT

Modeling is an effective way of using mathematical concepts and tools to represent natural systems and phenomena. Fractional calculus is an essential part of modeling a biological system. Recently, many researchers have been interested in modeling real-time problems mathematically and analyzing them. In this paper, the tumor system under fractional order is considered, and it comprises normal cells, tumor cells and effector-immune cells. By taking chemotherapy drugs into account, the toxicity of the drug and concentration of the drug is also studied in the model. The main objective of this work is to establish the solution for the model using Laplace transform and analyze the stability of the model. Laplace transform, a simple and efficient method, is used in solving the system that proves the existence and uniqueness of the solution. The boundedness of the system is also verified using the Lipschitz condition. Further, the system is solved for numerical values, and the population dynamics of cells are provided for different values of α as a graphical representation. Also, after analyzing the effect of chemotherapy drugs on tumor cells for different α's, which signifies that $\alpha = 0.9$ provides a sufficient decrease in the dynamics of tumor cells. The main and significant part of this work is presenting that the usage of chemotherapy drugs reduces the number of tumor cells. The importance of the work is that apart from the immune system, chemotherapy drugs play a significant role in destroying tumor cells. The Hyers Ulam stability has a significant application that one need not find the exact solution to when analyzing a Hyers Ulam stable system. Thus, the stability of this tumor model under Caputo fractional order is presented using Hyers-Ulam stability and Hyers-Ulam-Rassias stability.

1. Introduction

Cancer is the second most common cause of death in the world and a major global public health issue. Recently, due to the COVID-19 pandemic medical facilities closure, employment disruptions, health insurance coverage and concerns about exposure to COVID-19, have delayed the detection and treatment of cancer. Even though the COVID-19 peak was in mid-2020 which had the greatest impact, even now the delivery of healthcare facilities has not entirely recovered [1]. The origin of the term cancer dates back to 460-370 BC, which was credited to the Greek physician also known as Hippocrates. The words carcinos and carcinoma are coined by Hippocrates to describe ulcer and

non-ulcer forming tumors. These words denote a crab, in Greek, which is similar to cancer because the finger-like spreading pattern of cancer recollects the crab shape. Around 25 BC - 50 AD, the Roman physician Celsus translated the Greek word as the Latin word for crab, that is, cancer [2]. Later, a Greek physician, Galen around 130-200 AD, applied the term oncos to define tumors which interprets as the Greek word for swelling. The term that involves the crab analogy provided by Celsus and Hippocrates is still used to describe malignant tumors. And, Galen's term is used to denote cancer specialists – oncologists. Later in 1858, Rudolf Virchow presented the idea that the tumor-affected cells are the body's own cells. Several hypotheses were proposed to elaborate on the root of cancer cells and how they spread and develop [3]. The uncontrollable growth of cells and spreading to other parts of the body is the origin of cancer. Usually, normal human cells undergo cell division to form new cells where the dead cells are replaced by new ones. When this system disrupts, the damaged cells multiply irregularly which leads to the formation of lumps of tissue, known as a tumor. Tumor cells could be cancerous and also it may start anywhere in the human body. Chemotherapy treatment is a chemical drug therapy that eradicates rapidly growing cells and is used to handle cancer cells that grow and divide much faster than other cells. Chemotherapy is mostly used as a mixture of other therapies, such as hormones, surgery or radiation therapy. It has a successful rate of attacking cancer cells and also it has been a reliable therapy for decades.

The generalized concept of differential calculus is fractional calculus. It involves arbitrary order as a derivative of the function. Because of its significant nature, it has been used in various fields of Engineering and Science [4], [5] and [6]. Numerous researchers had considered uncertain fractional calculus especially, to take the fractional-order system under fuzzy initial conditions. Several fractional operators, such as Riemann-Liouville (R-L), Caputo, Hadamard, Grunwald-Letnikov (G-L), and Weyl, are used in fractional calculus, giving researchers the option to select the precise fractional operator for the given real-world situation. For this approach, the Laplace transform is effective [7].

Laplace transform is a powerful technique for solving the ordinary differential equation and partial differential equation with respect to time. It is a significant method as it converts the differential equations to a simple algebraic equation [16]. The generalized Laplace transform method was chosen by the author of [17] to analyse the Hilfer fractional integral and Caputo fractional derivative.

In recent years, mathematical modelling has developed into a crucial tool for both the analysis of outbreaks of diseases and the control strategy of contagious diseases [10] and [11]. It is also a useful tool for determining how well various infection-control measures work in a given population. Epidemiological modelling of infectious illnesses has had a growing impact on disease management and practice control in recent years [8] and [9]. While modelling a biological system such as cancer contributes to a different perception of the growth of tumor cells, their contact with immune cells and the effect of chemotherapeutic drugs on tumor cells in cancer patients. Efficient cancer therapy requires careful consideration of the drug delivery schedule. Modelling the treatment response and the population dynamics mathematically facilitates to classify and recognize the drug administration system. The author Michor [12] provided many insights on applying the mathematical model to the drug delivery concept. The nature of cancer is complex and is continuously evolving, thus it is difficult to recognize its physiological for various disease types and also develops interference in providing treatment effectively. In [13], the authors discussed biocomputational and mathematical modelling of cancer development and therapy. The authors Zhang [20] studied the stability and normalization of singular fractional order fuzzy systems. The fractional order SIR model is constructed by Kumar et al. [21] and the predictor corrector method of Adams-Bashforth–Moulton was considered in solving the system. In [14, 15], Ghaffari, constructed a model to examine the dynamics of tumor cells in different stages. Lyapunov stability was used to identify the optimal treatment. Later, the aforementioned model with the reliable controller was presented in [19] and the stability analysis for the system is performed with Lyapunov stability. One of the shortcomings of this approach is that finding a

suitable Lyapunov function is challenging. Hyers Ulam stability may be of aid in overcoming such shortcomings.

The global stability of this system is analysed using Hyers Ulam and Hyers Ulam Rassias stability. In the mathematical modelling of biological systems finding an exact solution is complicated. The main benefit of Hyers Ulam and Hyers Ulam Rassias stability is that it is sufficient to determine the approximate solution of the system rather than finding the exact solution. Also, in proving this stability, it does not involve complicated calculations and challenging computations. A Cauchy problem based on fuzzy fractional derivative was taken by Chaharpashlou et al. [22] and the stability was analysed by uncertain Ulam-Hyers-Rassias stability for the same. The fractional order of the coronavirus model was formulated and the uniqueness and existence of the solution were examined. Its local and global stability was analysed by the authors Akindeinde et al. [23] and a numerical simulation was provided. The Hyers-Ulam stability was studied for the Caputo q-fractional differential equation in [24]. The stability for the nonlinear differential equation was studied using Banach's contraction principle in [25]. With the application of Pachpatte's inequality in Hermite's differential equation, the stability of the equation was investigated in [26] using Hyers-Ulam-Rassias stability.

Inspired by the above works, the tumor system under chemotherapy treatment is considered and the solution for the system is obtained through an effective method, Laplace transform. The notable advancement in this paper are enumerated below:

1. The tumour-immune system taken under chemotherapy is solved using Laplace transform method and its uniqueness is proved.

2. The population dynamics of each parameter for different values of α are presented graphically.

3. The impact of chemotherapeutic drugs on tumour cells is investigated and graphical solutions are presented.

4. The global stability of the system is analysed using Hyers-Ulam stability and Hyers-Ulam-Rassias stability.

This paper is systematized as follows: In Section (2) the preliminaries, properties and basic results are embedded. The model formulation and parameter description are contained in Section (3.1). Section (4) is devoted to the existence and uniqueness of the solution and some necessary theorems. The numerical simulation of the model including the graph is provided in the Section (5). Finally, the global stability was analysed using Hyers-Ulam and Hyers-Ulam-Rassias stability concepts in Section (6).

2. Preliminaries

The necessary and useful definitions, results and fundamental facts applied throughout the paper are discussed in this section.

Definition 1. *The Caputo derivative of f(t) under fractional order α is as follows*

$$^{C}D^{\alpha}f(t) = \frac{1}{\Gamma(k-\alpha)} \int_{a}^{t} (s-t)^{k-\alpha-1} D^{k}f(s)ds, \quad k-1 < \alpha < k, \quad t > a, \quad k \in \mathbb{N}$$

where the function $f : [a,b] \to \mathbb{R}$ and $D^{k}f(s)$, for all k, are integrable. The Euler gamma function $\Gamma(\alpha)$ for $\alpha > 0$ is denoted as:

$$\Gamma(\alpha) = \int_{0}^{\infty} t^{\alpha-1}e^{-t}dt \tag{1}$$

Definition 2. *Let the function $f : [a, b] \to \mathbb{R}$, the Riemann-Liouville fractional order integral of f(t) for α is provided as*

$$I_a^\alpha f(t) = \frac{1}{\Gamma(\alpha)} \int_a^t (t-s)^{\alpha-1} f(s) ds, \quad I_a^0 f(t) = f(t).$$

where, Γ denotes Euler gamma function.

Few properties of fractional calculus related to Caputo fractional differential equations and integral equations required for computations are provided,

1. $^C D^\alpha Y(t) = I_a^{k-\alpha} D^k Y(s) ds,$

2. $I_a^{\alpha C} D^\alpha Y(t) = Y(t) - Y(a) \quad$ for $0 < \alpha < 1.$

Lemma 1. *[27] Let $\alpha \geq 0$ and $k=\lfloor\alpha\rfloor + 1$. Then*

$$I_a^{\alpha C} D^\alpha Y(t) = Y(t) - \sum_{p=0}^{k-1} \frac{Y^p(0)}{p!} t^p \tag{2}$$

Differential equations, both ordinary and partial, are used to describe how specific quantities change over time. The Laplace transform, which literally converts the original differential equation into a simple algebraic expression, is a particularly effective method for overcoming these issues. Then the latter (algebraic expression) can then be easily changed once more into the answer to the first issue. For solving such fractional order differential equation, Laplace transform is an easy handling as well as efficient method. Even though iteration method can be used in solving the fractional order differential equation, but it is more effective for simple equations [28]. On the other hand, the Laplace transform can be easily solved without complex derivations.

Definition 3. *The laplace transform for the function $f(t)$ is provided by the following formula:*

$$L[f(t)] = F(s) = \int_0^\infty e^{-st} f(t) dt$$
$$L[f(t)] = \lim_{\tau \to \infty} \int_0^\tau e^{-st} f(t) dt \tag{3}$$

If the limit of (3) exist, then the integral converges. If the limit does not exist, then the integral diverges. The interested reader can refer to [29] for the related properties based on Laplace transform.

3. Method

3.1. Model Formulation

The mathematical model that involve tumor-immune system is considered as our proposed model and it is referred from [15]. In this section, the population of normal cells $N(t)$, the population of tumor cells $T(t)$, the population of Effector Immune cells $I(t)$, the drug toxicity $T_x(t)$ and the drug concentration $M(t)$ of chemotherapy with time t are considered. In the proposed model is the

formulation of tumor system in regard to chemotherapy is explained with its parameters.

$$
\begin{aligned}
{}^{C}D^{\alpha}N &= r_2 N(1 - b_2 N) - c_4 NT, \\
{}^{C}D^{\alpha}T &= r_1 T(1 - b_1 T) - c_2 IT - c_3 NT - a_2 MT, \\
{}^{C}D^{\alpha}I &= s - d_1 I + \sigma \frac{T}{c_5 + T} I - c_1 IT, \\
{}^{C}D^{\alpha}T_x &= M - \phi T_x, \\
{}^{C}D^{\alpha}M &= -\gamma M.
\end{aligned}
\tag{4}
$$

where ${}^{C}D^{\alpha}$ represents the Caputo derivative of order $0 < \alpha < 1$. The parameters of the model and their description are given as the table in (Table 1).

Table 1. Parameter Description

Parameter	Description
a_2	Fractional tumor cells killed using chemotherapy
b_1	$1/b_1$ is Tumor cells carrying capacity
b_2	$1/b_2$ is Normal cells carrying capacity
c_1	Fractional Effector Immune Cells killed by Tumor cells
c_2	Fractional Tumor Cells killed by Effector Immune cells
c_3	Fractional Tumor Cells killed by Normal cells
c_4	Fractional Normal Cells killed by Tumor cells
r_1	Growth rate of Tumor cells
r_2	Growth rate of Normal cells
d_1	Death rate of Effector Immune cells
s	Constant source of Effector Immune cells
c_5	Steepness coefficient of Effector Immune cells recruitment curve
σ	Maximum Effector Immune cells recruitment rate by Tumor cells
ϕ	Rate at which drug toxicity decay
γ	Rate at which chemotherapy drug decay
α	Order of the given system

The flow chart diagram of the proposed model is provided as the following diagram (Fig. 1). The rate of change of the normal cell population is represented in first equation. It is presumed that normal cell population will increase logistically and the mass-action dynamic is used by tumor cells to kill normal cells. The rate of change of the tumor cell population is represented in second equation. The interaction of tumor cells with immune cells and normal cells leads to the death of tumor cells. Also, chemotherapy impacts tumour cell population through a mass-action dynamic. The third equation represents the immune cell population's rate of change. While the death of immune cells is proportional to immune cell population, source rate of immune cell is constant. Moreover, tumour cells are engaged with immune cells by using the term $\sigma \frac{IT}{c_5 + T}$, which can provide a saturation effect. Upon interaction with tumour cells, a mass-action dynamic results in the inactivation of immune cells.

The aforementioned mathematical model is expanded for Equation (4), as it describes the relationship between the cumulative drug toxicity T_x and the drug concentration M within the body. The cumulative drug toxicity rises with drug concentration, and falls with the rate of metabolism of drug within the body. It is presumed that the rate of drug metabolism within the body is directly proportional to the cumulative drug toxicity, with a proportion constant ϕ. Drug concentration is anticipated to decay exponentially. The variation in drug concentration is described in Equation (5). The halflife of the drug is represented by γ, which is dependent on the biochemical property of the drug. The system is constructed based on certain assumptions which are explained in [15]. Let $Y(t)$ denote the

$(N, T, I, T_x, M)^T$ and $\mathcal{S}(t, Y(t)) = (\eta_i)^T$ where $i = 1, 2, 3, 4, 5$. The η_i's are classified as follows,

$$\eta_1 = r_2 N(1 - b_2 N) - c_4 NT,$$
$$\eta_2 = r_1 T(1 - b_1 T) - c_2 IT - c_3 NT - a_2 MT,$$
$$\eta_3 = s - d_1 I + \sigma \frac{T}{c_5 + T} I - c_1 IT,$$
$$\eta_4 = M - \phi T_x,$$
$$\eta_5 = -\gamma M.$$

with initial condition $Y(0) = Y_0 \geq 0, \quad t \geq 0$ and of order $0 < \alpha < 1$. The aforementioned equations are represented dynamically as the following,

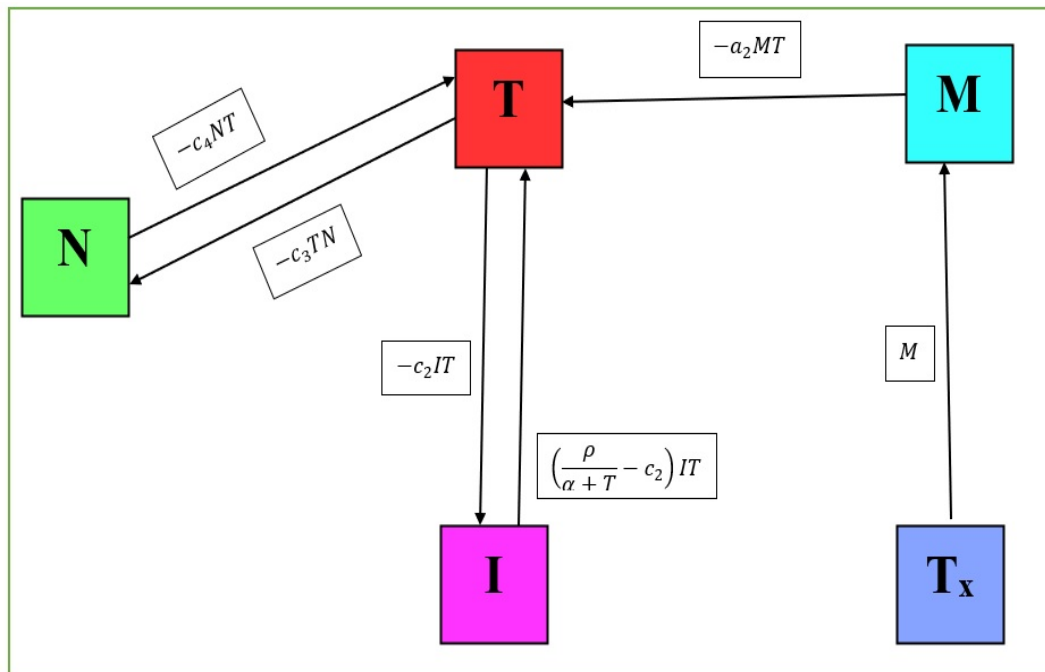$$^C D^\alpha Y(t) = \mathcal{S}(t, Y(t)). \tag{5}$$

Fig. 1. Model Formulation

4. Qualitative Properties of Solution

In this section, the existence and uniqueness of the solution and the boundedness of the system are discussed. The solution for the above system is derived by Laplace transform, which is an easily applicable method. Because of its hereditary property and the generalization of the order of the derivative, the fractional order differential equations are applied frequently in major sectors. The articulation of the research methodology is provided in this flowchart (Fig. 2).

4.1. Existence of the Solution

In a mathematical analysis, a complete normed vector space is referred to as a Banach space. In other words, as the sequence continues, the distance between the vectors decreases. A normed vector space called a Banach space is used in functional analysis to calculate the vector length. Each vector other than the zero vector has a length greater than zero when the vector space is normed. Hence, it
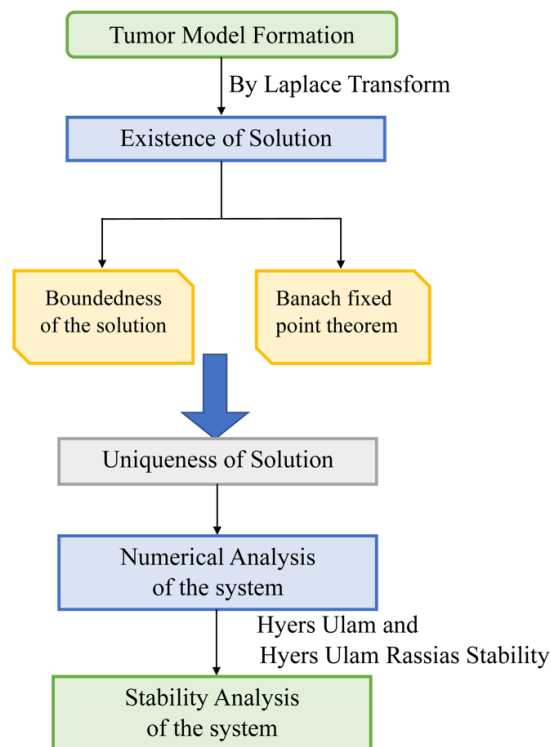
Fig. 2. Research Methodology

is easy to determine the length and distance between two vectors. If a Cauchy sequence of vectors in the space converge towards a limit, then the vector space is complete. The vectors arbitrarily get closer together as the sequence progresses. In this paper, the notation $\mathcal{D} = C([0, b]; \mathbb{R})$ is denoted for all continuous function from $[0, b]$ to $\mathbb{R}$ in banach space with the norm $\|Y\|_{\mathcal{D}} = \sup|Y(t)|, t \in [0, b]$ where

$$|Y(t)| = |N(t)| + |T(t)| + |I(t)| + |T_x(t)| + |M(t)|$$

Also, note that $N, T, I, T_x, M \in C([0, b])$. The existence of solution for the proposed system is proved by the Lemma 9.

Lemma 2. *Let $t \geq 0$ and α is defined as $0 < \alpha < 1$. There exist a solution $Y(t)$ for the system (5) under the initial conditions $Y(0) = Y_0$ that satisfies $Y_0 \geq 0$.*

Proof. The solution for the Caputo fractional order differential equation is derived through Laplace transform as,

$$^C D^\alpha Y(t) = \mathcal{S}(t, Y(t))$$

Applying the Laplace transform on both sides,

$$L[^C D^\alpha Y(t)] = L[\mathcal{S}(t, Y(t))]$$

By applying Laplace transform and its properties for $0 < \alpha < 1$,

$$Y(t) = \int_0^t \frac{(t-s)^{\alpha-1}}{\Gamma(\alpha)} \mathcal{S}(s, Y(s))ds + Y_0. \tag{6}$$

Thus, Equation (6) provides the solution for the tumor-immune fractional order system (5). $\square$

Also, an operator $\mathcal{T}$ is specified as $\mathcal{T} : \mathcal{D} \to \mathcal{D}$ by

$$(\mathcal{T}Y)(t) = \int_0^t \frac{(t-s)^{\alpha-1}}{\Gamma(\alpha)} \mathcal{S}(s, Y(s))ds + Y_0. \tag{7}$$

As the continuity of $\mathcal{S}$ is an obvious condition, it implies that the operator $\mathcal{T}$ is well-defined.

4.2. Uniqueness of the Solution

This section is devoted to prove the uniqueness of the solution obtained for the proposed system. Further the boundedness is proved using Lipschitz condition. The lemmas and theorems to support the uniqueness of solution are presented as follows.

Lemma 3. *Consider* $\bar{Y} = (\bar{N}, \bar{T}, \bar{I}, \bar{T}_x, \bar{M})$. *The function* $\mathcal{S}$ *defined as* $\mathcal{S}(t, Y(t)) = (\eta_i)^T$ *for* $L_\mathcal{S} > 0$ *satisfies the equation*

$$\|\mathcal{S}(t, Y(t)) - \mathcal{S}(t, \bar{Y}(t))\|_\mathcal{D} \le L_\mathcal{S}\|Y - \bar{Y}\|_\mathcal{D}.$$

Proof. The first part of $\mathcal{S}$ is examined, that is η_1 is derived as the following,

$$\begin{aligned}\eta_1(t, Y(t)) - \eta_1(t, \bar{Y}(t)) &= r_2 N(1 - b_2 N) - c_4 NT - r_2 \bar{N}(1 - b_2 \bar{N}) - c_4 \bar{N}\bar{T}, \\ &= r_2[N(1 - b_2 N) - \bar{N}(1 - b_2 \bar{N})] - c_4[NT - \bar{N}\bar{T}], \\ &= r_2[1 - b_2 N - b_2 \bar{N}](N - \bar{N}) - c_4 N(T - \bar{T}) - c_4 \bar{T}(N - \bar{N})\end{aligned}$$

By taking modulus on both sides,

$$\begin{aligned}|\eta_1(t, Y(t))| - |\eta_1(t, \bar{Y}(t))| &= r_2[1 - b_2|N| - b_2|\bar{N}|](|N - \bar{N}|) \\ &\quad - c_4|N|(|T - \bar{T}|) - c_4|\bar{T}|(|N - \bar{N}|), \\ &\le r_2 f_1(t)(|N - \bar{N}|) + c_4 f_2(t)(|T - \bar{T}|) + c_4 f_3(t)|(|N - \bar{N}|),\end{aligned}$$

where the notations f_1, f_2 and f_3 are employed as,

$$f_1 = [1 - b_2|N| - b_2|\bar{N}|], \quad f_2 = |N|, \quad f_3 = |\bar{T}|.$$

Finally, the equation that implies the boundedness of η_1 is obtained,

$$\begin{aligned}|\eta_1(t, Y(t))| - |\eta_1(t, \bar{Y}(t))| &\le (r_2 f_1(t) + c_4 f_3(t))|N - \bar{N}| + c_4 f_2(t)|T - \bar{T}| \\ &\le L_1(|N - \bar{N}| + |T - \bar{T}|),\end{aligned}$$

where the constant L_1 is denoted by, $L_1 = \sup_{t \in [0,b]} \{r_2 f_1(t) + c_4 f_3(t) + c_4 f_2(t)\}$.

Thus for the second parameter η_2, the following equations are obtained as,

$$\begin{aligned}\eta_2(t, Y(t)) - \eta_2(t, \bar{Y}(t)) &= r_1 T(1 - b_1 T) - c_2 IT - c_3 NT - a_2 MT - [r_1 \bar{T}(1 - b_1 \bar{T}) - c_2 \bar{I}\bar{T} \\ &\quad - c_3 \bar{N}\bar{T} - a_2 \bar{M}\bar{T}] \\ &= [r_1(1 - b_1 T - b_1 \bar{T}) - c_2 I - c_3 N - a_2 M](T - \bar{T}) - c_2 \bar{T}(I - \bar{I}) \\ &\quad - c_3 \bar{T}(N - \bar{N}) - a_2 \bar{T}(M - \bar{M})\end{aligned}$$

$$|\eta_2(t, Y(t)) - \eta_2(t, \bar{Y}(t))| \le L_2(|T - \bar{T}| + |I - \bar{I}| + |N - \bar{N}| + |M - \bar{M}|) \tag{8}$$

where the notations g_1 and g_2 are given as,

$$g_1 = r_1(1 - b_1 T - b_1 \bar{T}) - c_2 I - c_3 N - a_2 M, \quad g_2 = |\bar{T}|$$

and the constant L_2 is provided as,

$$L_2 = \sup_{t \in [0,b]} \{g_1(t) + c_2 g_2(t) + c_3 g_2(t) + a_2 g_2(t)\}$$

The third parameter η_3 of $\mathcal{S}$ is solved as,

$$\eta_3(t, Y(t)) - \eta_3(t, \bar{Y}(t)) = -d_1(I - \bar{I}) + \sigma\left[\frac{T}{c_5 + T} - \frac{\bar{T}}{c_5 + \bar{T}}\right] - c_1(IT - \bar{I}\bar{T}) \qquad (9)$$

Here, by simplifying a part in (9),

$$\left[\frac{T}{c_5 + T} - \frac{\bar{T}}{c_5 + \bar{T}}\right] = \left[\frac{c_5(T - \bar{T})}{(c_5 + T)(c_5 + \bar{T})}\right]$$

where, we take the parameter h_1 as, $h_1 = |I|$. Taking modulus on both sides of the equation the following are obtained as,

$$|\eta_3(t, Y(t)) - \eta_3(t, \bar{Y}(t))| \le d_1|I - \bar{I}| + \sigma c_5|T - \bar{T}| + c_1 h_1|T - \bar{T}| + c_1 g_2|I - \bar{I}|$$
$$\le L_3(|I - \bar{I}| + |T - \bar{T}|)$$

where the constant L_3 is given as,

$$L_3 = d_1 + \sigma c_5 + \sup_{t \in [0,b]} \{c_1 h_1(t) + c_1 g_2(t)\}$$

Similarly, the other parameters η_4 and η_5 of $\mathcal{S}$ proceeded as,

$$|\eta_4(t, Y(t)) - \eta_4(t, \bar{Y}(t))| \le L_4(|M - \bar{M}| + |T_x - \bar{T}_x|),$$
$$|\eta_5(t, Y(t)) - \eta_5(t, \bar{Y}(t))| \le L_5|M - \bar{M}|$$

where the constants L_4 and L_5 are taken as,

$$L_4 = 1 - \eta, \qquad L_5 = \gamma.$$

Thus, the Lipschitz condition of the function $\mathcal{S}(t, Y(t))$ is proved as,

$$\|\mathcal{S}(t, Y(t)) - \mathcal{S}(t, \bar{Y}(t))\|_{\mathcal{D}} = \sup_{t \in [0,b]} \sum_{i=1}^{5} |\eta_i(t, Y(t)) - \eta_i(t, \bar{Y}(t))|,$$
$$\le L_{\mathcal{S}}\|Y - \bar{Y}\|_{\mathcal{D}},$$

where $L_{\mathcal{S}} = L_1 + L_2 + L_3 + L_4 + L_5$.   □

In $\mathbb{R}$, the Banach fixed point theorem is frequently used to refer to the contraction mapping concept. One of the most useful mathematical methods for analysing nonlinear equations, including algebraic, integral, and differential equations, is the contraction mapping principle. A fixed point theorem known as the mapping principle guarantees that a contraction mapping of the complete metric space has an unique fixed point. The fixed point can be calculated numerically using this theory, which is also known as a constructive fixed point theorem.

Theorem 1 (Banach Fixed Point Theorem)**.** *[18] Consider a banach space Y and $\mathcal{Z} : Y \to Y$ be a contraction mapping. Then $\mathcal{Z}$ has a fixed point.*

$$\mathcal{Z}y = y \qquad (10)$$

for all $y \in Y$

Lemma 4. *The Caputo fractional order tumor system model (4) has unique solution if the above Lemma (3) and $\Phi L_{\mathcal{S}} < 1$ holds where Φ is an arbitrary constant.*

Proof. The uniqueness of the model shall be proved by applying Banach contraction mapping principle on the operator $\mathcal{T}$. Based on the above Lemma (3) and the Theorem 4.3 of [23], it is obvious that the solution of the model (4) under the operator $\mathcal{T}$ is unique. □

5. Numerical Results and Discussion

This section involves a numerical example to display the efficiency of the method. Since the model is related to the human body cells, all the parameters are non-negative. The numerical values of the parameters involved in the model are referred from [19] and it is tabulated as Table 2. The initial conditions for the model (4) are provided as $N(0) = 1, T(0) = 0.25, I(0) = 0.1$. Under the initial conditions the solution path for the system is plotted.

Table 2. Numerical values of Parameters

| Parameter	Numerical value	Parameter	Numerical value
a_2	$0.3 \ day^{-1}$	b_1	$1 \ cell^{-1}$
b_2	$1 \ cell^{-1}$	c_1	$1 \ cell^{-1}day^{-1}$
c_2	$0.5 \ cell^{-1}day^{-1}$	c_3	$1 \ cell^{-1}day^{-1}$
c_4	$1 \ cell^{-1}day^{-1}$	r_1	$1.5 \ day^{-1}$
r_2	$1 \ day^{-1}$	d_1	$0.2 \ day^{-1}$
s	$0.33 \ cellday^{-1}$	c_5	$0.3 \ cell$
σ	$0.01 \ day^{-1}$	ϕ	$0.5 \ day^{-1}$
γ	$0.9 \ day^{-1}$	α	0.99

5.1. Graphical Representation

The population dynamics of the normal cells, tumor cells, effector immune cells are represented graphically when α = 0.5, 0.6, 0.7, 0.8, 0.9. By observing the graph Fig. 3(a) and Fig. 3(b) for different values of α, we can conclude that, as the numerical value of α increases for a fixed time period, the dynamics of normal cells and effector immune cells gradually increases. Similarly, the dynamics of tumor cells gradually decreases in the graph Fig. 3(c).

Further, the impact of chemotherapy drug on tumor cells is analysed in (4). The rate at which tumor cells are killed by chemotherapy are denoted as a_2 which is analysed in this part. For this analysis, we consider the fractional order $\alpha = 0.5, 0.7, 0.9$ which provides significant change in the dynamics. When a_2 becomes zero, it implies the dynamics tumor cells without chemotherapy. By observing Fig. 4(a), the dynamics of tumor system increases for $a_2 = 0$. In observing Fig. 4(b) and Fig. 4(c) when $a_2 = 0.5$ and 1, the dynamics of tumor system decreases. In $a_2 = 1$, the dynamics of tumor system decreases faster than $a_2 = 0.5$. From the above analysis, it is implied that the greater the amount of a_2 that is, greater the tumor cells are killed by chemotherapy, will lead to reduction in tumor cells. Thus, when a_2 increases, the dynamics of tumor cells decreases. Also, note that the time t is considered as same interval for all the three conditions of a_2.

6. Global Stability

The global stability of the proposed model is analysed using Hyers-Ulam stability and Hyers-Ulam-Rassias stability in this section. In 1940, at Winscosin University, Ulam delivered a talk, which formed the basis for the Hyers-Ulam stability. Themistocles M. Rassias in 1978, worked to weaken

(a) Normal cells N(t)

(b) Tumor cells T(t)

(c) Effector immune cells I(t)
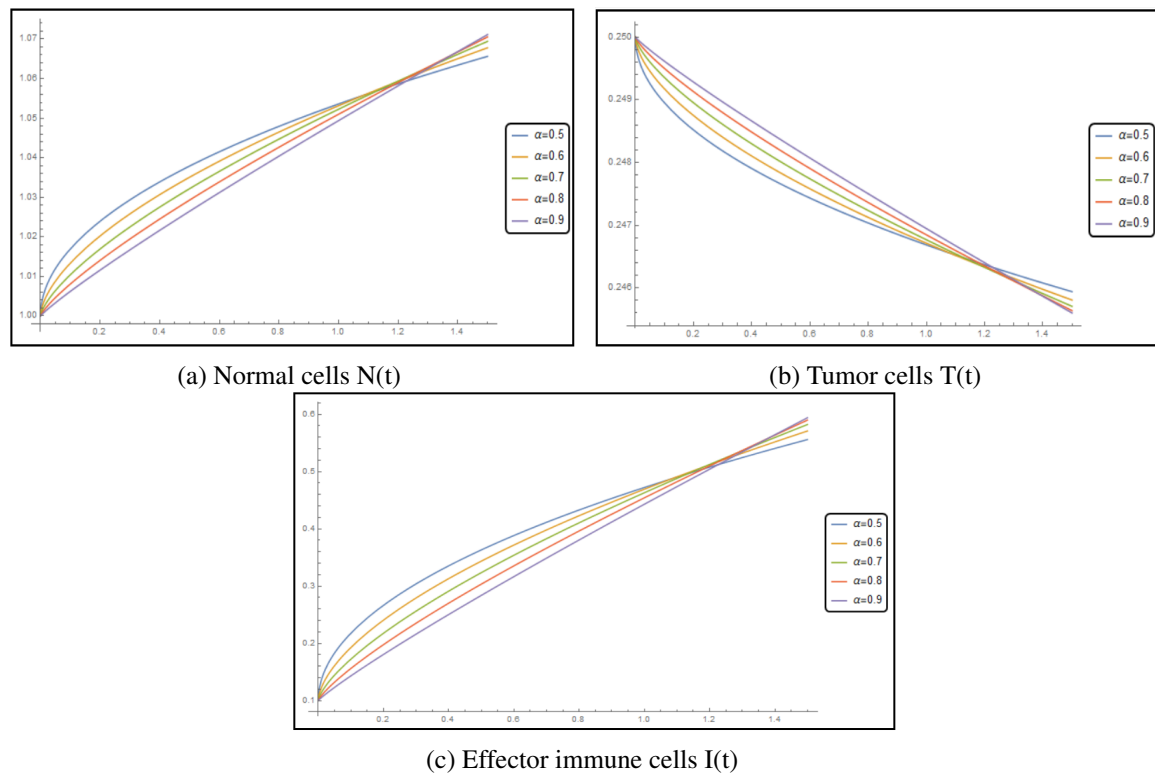
Fig. 3. Population Dynamics of cells for different fractional order α

(a) Dynamics of $T(t)$ when $a_2 = 0$

(b) Dynamics of $T(t)$ when $a_2 = 0.5$

(c) Dynamics of $T(t)$ when $a_2 = 1$
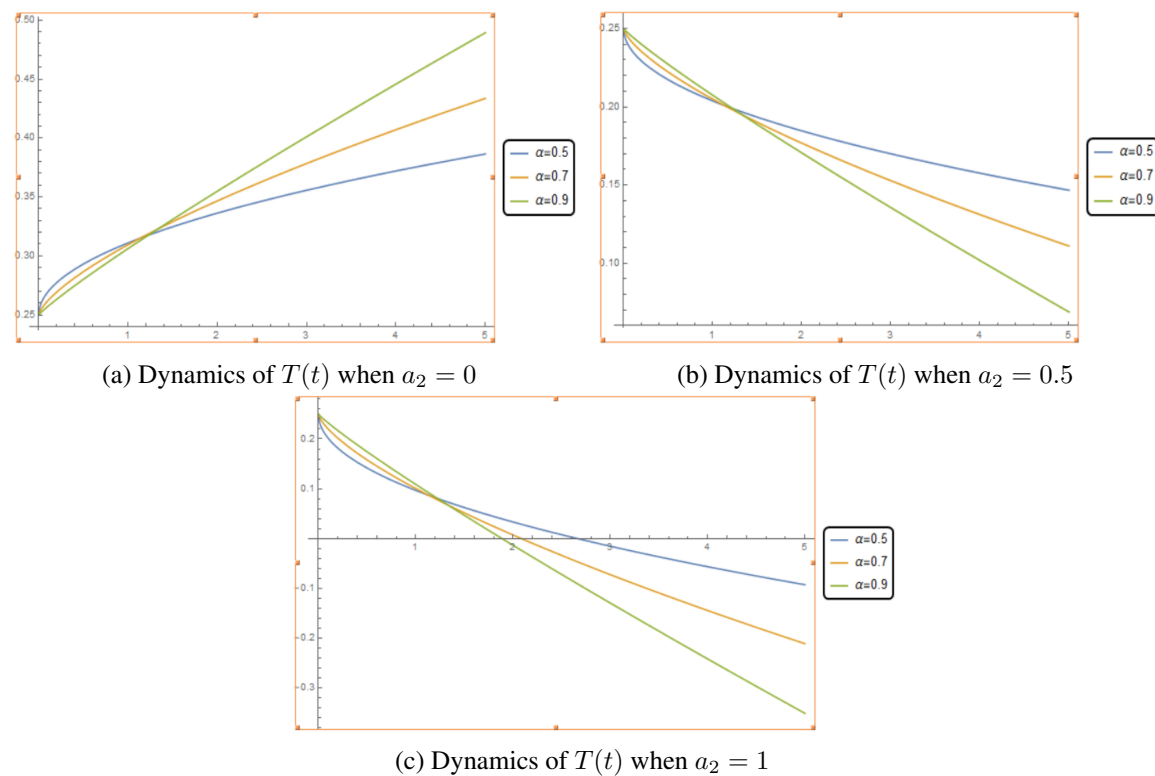
Fig. 4. Effect of chemotherapy on tumor cells for different fractional order $\alpha = 0.5, 0.7, 0.9$

the bound condition of the Cauchy difference norm and contributed a more generalized result than

Hyers [30]. Thus, Hyers-Ulam-Rassias stability emerged and inspired numerous mathematician to investigate and examine the stability problem.

The Hyers Ulam stability possess great importance since it suggests that while analysing a Hyers Ulam stable system, one need not identify a precise solution. It is helpful in a various challenging fields where it can be difficult to obtain an exact solution, such as numerical analysis, optimization, biology, economics, etc., The stability analysis of the fractional dominating system of equations is effecctively performed using the Hyers-Ulam-Rassias stability criteria.

Assumption 1. *(A1) For $t \in [0, b]$ and $\epsilon > 0$, $|^C D^\alpha Y(t) - \mathcal{S}(t, Y(t))| \le \epsilon$.*

Definition 4. *The Caputo fractional order tumor model is Hyers-Ulam stable (4), if there is a constant $\mathcal{C_D} > 0$ s.t. for all $\epsilon > 0$ and for every solution $\bar{Y}(t)$ in $\mathcal{D}$, satisfying (A1) then there exist a solution $Y(t)$ in $\mathcal{D}$ satisfying*

$$\|\bar{Y}(t) - Y(t)\| \le \mathcal{C_D}\epsilon \tag{11}$$

6.1. Hyers Ulam Stability

Theorem 2. *[23] Let (1) and the result of Lemma 1 hold. Assume that $\mathrm{C} = \dfrac{b^\alpha}{\Gamma(\alpha + 1)}$ and also $1 - \mathrm{C}L_\mathcal{S} > 0$. Then the Caputo fractional order tumor system based on Chemotherapy is Hyers-Ulam Stable.*

Proof. Let $\bar{Y}(t)$ be the solution of (1) and Y(t) is the solution of (5). For $\epsilon > 0$, and by taking Laplace transform provides the following,

$$\|\bar{Y} - Y\|_\mathcal{D} = \sup_{t \in [0,b]} |\bar{Y}(t) - Y(t)|,$$

$$= \sup_{t \in [0,b]} |\bar{Y}(t) - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds - Y_0|$$

$$= \sup_{t \in [0,b]} |\bar{Y}(t) - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds - Y_0$$

$$\pm \int_0^t (t-s)^{\alpha-1} \frac{1}{\Gamma(\alpha)} \mathcal{S}(s, \bar{Y}(s)) ds|$$

$$\le \mathrm{C}\epsilon + \frac{L_\mathcal{S}}{\Gamma(\alpha)} \sup_{t \in [0,b]} \int_0^t (t-s)^{\alpha-1} |\bar{Y}(s) - Y(s)| ds,$$

$$\le \mathrm{C}\epsilon + \mathrm{C}L_\mathcal{S} \|\bar{Y} - Y\|_\mathcal{D}$$

$$\|\bar{Y} - Y\|_\mathcal{D} \le \frac{\mathrm{C}}{1 - \mathrm{C}L_\mathcal{S}} \epsilon \le \mathcal{K}\epsilon.$$

where $\mathcal{K} \le \dfrac{\mathrm{C}}{1 - \mathrm{C}L_\mathcal{S}}$.   □

6.2. Hyers Ulam Rassias Stability

Definition 5. *The differential equation Y(t), satisfying*

$$|^C D^\alpha Y(t) - \mathcal{S}(t, Y(t))| \le \epsilon\psi(t), \quad t \in [0, b] \tag{12}$$

is Hyers-Ulam Rassias stable, if there is a constant $\mathcal{C_D} > 0$ and also a function $\psi : [0, b] \to [0, \infty)$ such that for any solution $\bar{Y}(t)$ of the fractional differential Equation (4) such that

$$\|\bar{Y}(t) - Y(t)\| \le \mathcal{C_D}\epsilon\psi(t) \tag{13}$$

Theorem 3. [24] *Assume the function $\mathcal{S}$ and ψ are continuous and defined as $\mathcal{S} : [0, b] \times \mathbb{R}^5 \to \mathbb{R}^5$ and $\psi : \mathbb{R} \to \mathbb{R}$. Let $\mathrm{K} \leq 1 - \mathrm{CL}_{\mathcal{S}}$. Then the Caputo fractional order tumor system based on Chemotherapy is Hyers-Ulam-Rassias Stable.*

Proof. $\bar{Y}(t)$ is the solution of the inequality (12). Thus,

$$-\epsilon\psi(t) \leq {}^C D^\alpha Y(t) - \mathcal{S}(t, Y(t)) \leq \epsilon\psi(t)$$

Applying Laplace transform, we obtain,

$$L[-\epsilon\psi(t)] \leq L[{}^C D^\alpha Y(t) - \mathcal{S}(t, Y(t))] \leq L[\epsilon\psi(t)],$$

$$-\epsilon\Psi(s) \leq Y(t) - Y_0 - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds \leq \epsilon\Psi(s),$$

$$\left| Y(t) - Y_0 - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds \right| \leq \epsilon\Psi(s).$$

Consider,

$$\|\bar{Y} - Y\|_{\mathcal{D}} = \sup_{t \in [0,b]} \left| \bar{Y}(t) - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds - Y_0 \right|$$

$$= \sup_{t \in [0,b]} \left| \bar{Y}(t) - \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathcal{S}(s, Y(s)) ds - Y_0 \right.$$

$$\left. \pm \int_0^t (t-s)^{\alpha-1} \frac{1}{\Gamma(\alpha)} \mathcal{S}(s, \bar{Y}(s)) ds \right|$$

$$\|\bar{Y} - Y\|_{\mathcal{D}} \leq \epsilon\Psi(s) + \mathrm{CL}_{\mathcal{S}} \leq \mathrm{K}\epsilon\Psi(s)$$

$\square$

Nonlinear dynamical system stability is crucial for both scientists and engineers. Over the past ten years, fractional dynamics have become increasingly utilised to describe the behaviour of complex systems. In this work, the Hyer Ulam stability was extended for Caputo type fractional-order nonlinear systems which is solved using Laplace transform. The main findings of the present study is to establish the solution for the system, numerically verify whether chemotherapy drug has effect on tumor cells and stability analysis. Compared to method of successive approximation [23], Laplace transform requires less process to find the solution. Also, in Lyapunov stability finding the lyapunov function is challenging part. Rather than the previous method, Hyers Ulam stability involves simple steps and finding approximate solution is sufficient for proving the stability. The implication of this method is commonly used in real time model or biological model can be verified for stability using Hyers Ulam stability. Also, the limitation of this work is that the data needs to be more precise to obtain more effective results.

7. Conclusion

Many successful conclusions and efficient ways of treating disease have been achieved by mathematically modelling the disease. In this paper, the mathematical model of drug administration during chemotherapy for cancer is considered.

1. Laplace transform significantly reduces the complicated process of differentiation and integration to multiplication and division, respectively. By applying the Laplace transform for the system, the solution for the model is derived.

2. Also, a lemma which proves the Lipschitz condition of the parameter is provided and the uniqueness of the solution for the system is proved.

3. The numerical example is solved for the system and the graph for different values of α are plotted. The effect of chemotherapy drug on tumor cells is analyzed, from this we can observe that chemotherapy treatment plays a vital role in decreasing the tumor cells.

4. Finally, Since the exact solution is not necessary in proving the Hyer Ulam stability, it is a significant and effective method in proving the stability. The global stability of this model is proved by using Hyers-Ulam and Hyers-Ulam Rassias Stability,

The above system and model may vary based on numerous factors such as demographic, climate, social factors, etc., These variations may have impact on dynamics of cells and can modify the effect of chemotherapy drug acting on the cells. As far as the data is accurate the result will be effective which is a slight downside of this work. Thus, the future path of this research will be in the direction as follows:

1. To include and analyze other parameters such as the variations based on food intake and side-effects of the drug given to patients. Since, this work is framed based on killing the tumor cells using chemotherapy drugs, other than drugs healthy food intake also plays the role of destroying the tumor cells.

2. Estimation of model parameters using a wide range of data.

3. To compare the solution and the stability with different methods to estimate its effectiveness compared to other methods.

Case study or modelling research provides effective approaches for understanding the characteristics that facilitate improvement. Even if they are valuable on their own, such techniques also present a chance to complement more standard methods of evaluating interventions by illuminating why some are ineffective or why they appear to function well in some situations but not others. Modelling methodologies offer a reliable method of directing the application of successful approaches.

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