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Exploring a Mathematical Model for the Interaction Between Cancer Cells and Virotherapy Utilizing Fractional Derivative

Himani Agarwal, Manvendra Narayan Mishra and R. S. Dubey

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Abstract This treatise intends to examine the mathematical representation of the interplay between cancer cells and virotherapy, utilizing a mathematical model. This model will be further extrapolated to encompass a fractional mathematical paradigm through the incorporation of Atangana-Baleanu derivatives. Subsequently, we will provide evidence of the viability and distinctiveness of the solution to the augmented mathematical framework. Finally, we will apply numerical techniques to derive a numerical resolution of the fractional mathematical model.

1 Introduction

Whether it is a developed or developing nation, Cancer is amongst the most prevalent diseases. A study has shown that the countries having low and middle income do not have a designated care system for the cancer patients. According to statistics about 18.1million cancer cases were reported in 2020 (The most recent data available). The documented cases of cancer amounted to 18.1 million, with a disproportionate distribution of diagnoses between males (9.3 million) and females (8.8 million). The data indicates that the most ubiquitous forms of cancer worldwide are breast and lung cancers. Every year, a significant global population receives a cancer diagnosis, with a majority of those diagnosed ultimately succumbing to the disease. The total number of deaths globally due to cancer were recorded to be a devastating 10 million worldwide.
The origin of Cancer goes back to around 3000 BC, when it was first discovered in Egypt. The traces of cancer were found in fossils and human mummies in ancient Egypt. The designation "Cancer" was first introduced by the Greek medical practitioner, Hippocrates, widely regarded as the originator of the medical profession. The terms that Hippocrates propounded were ‘Carcinos’ referring to non-ulcer forming tumours and ‘Carcinoma’ referring to ulcer forming tumours. Later the Greek term was translated to the word ‘Cancer’ by Celsus, a Roman physician.
In cancer, cells within the body multiply uncontrollably and can disseminate to other areas. The fundamental process of cell division drives this proliferation, generating new cells as needed for bodily functions [19]-[21]. The old cells get damaged and eventually die. The new cells generated through cell division takes their place [20]. But sometimes this process is disrupted and the damaged cells continue to grow further and multiply in certain parts of the body giving rise to lumps of tissue called tumour. Tumours can be classified into ‘Cancerous’ and ‘Non-Cancerous’ [7]. Cancerous tumours invade other nearby tissues of the body while non-cancerous tumours don’t [1].
The current study is done with the use of mathematical modeling and fractional calculus. The use of fractional calculus in mathematical modelling has become more appropriate in recent years. Fractional calculus is one of the most significant and influential areas of mathematics because of its many useful operators and logical concepts. It produces more precise results because of the memory effect of its kernels. At the moment, fractional calculus is receiving much more attention from mathematicians and researchers than the integer order system because it allows for infinitely many points at which the results can be analysed, whereas the integer ordered system

limits us to integers. In this work we have tried to analyze the effect of virions and cancer cells over the period of time, means it is a strive to check the effect of virotheraphy in treatment of cancer.

In this research work, we are going to modify the mathematical model describing the cancer cells interaction with virotherapy which was proposed by Abernathy et al [2]. This model describes the relation between the uninfected cells of tumor U, the tumor with infected cells I, V represent Virions, and the Effector T cells E, given as

$$\begin{aligned}
\frac{dU}{dt} &= \theta U\left(1-\frac{I+U}{\delta}\right)-\beta\ V\ U-\alpha_1\ E\ U, & U(0)=U_0\\
\frac{dI}{dt} &= \beta\ U\ V-\alpha_2\ I\ E-\gamma_2\ I, & I(0)=I_0\\
\frac{dE}{dt} &= \lambda\ I-\gamma_3\ E, & E(0)=E_0\\
\frac{dV}{dt} &= A+\chi\ \gamma_2\ I-\gamma_4\ V, & V(0)=V_0
\end{aligned}$$

let θ denote the rate of uninfected tumor cell growth, δ represent the total carrying capacity of tumor cells, β stand for the infection rate of tumor cells, α_1 signify the rate at which uninfected cells decay via T-cells, α_2 denote the rate at which infected cells decay via T-cells, γ_2 indicate the rate of infected cell decay, γ_3 denote the rate of effector T-cell decay, γ_4 represent the rate of virion decay, A stand for the dosage of virotherapy, χ represent the number of virions released via infected cell lysis, and λ denote the rate of T-cell growth via infected tumor cells. In this study, we will enhance the previously mentioned mathematical model by incorporating the Atangana-Baleanu derivative to form a fractional mathematical model. The Atangana-Baleanu operator was chosen because of its special properties, which include a nonlocal and nonsingular kernel that is represented by the Mittag-Leffler function. The complex dynamics included in the model under study are ideally captured by this operator. This approach is beneficial as it accounts for memory and after-effects, which are often ignored in traditional models. This is due to the fact that many biological systems exhibit fractional electrical conductance in their cell membranes and can be categorized as non-integer models. Fractional calculus, with its advancements in fields such as physics, chemistry, biochemistry, biology, medicine, etc. (as seen in references ([9]-[11]), provides a deeper understanding of biological systems. The presence and distinctiveness of the solution are extensively elucidated, with numerical solutions for the mathematical model utilizing the Atangana-Baleanu derivative operator being derived. Due to its fractional order, this derivative provides more accurate findings than the exponential kernel derivative, making it a more generalised variant of the exponential kernel derivative. In this work, we will extend the above mentioned mathematical model to the fractional mathematical model using the Atangana-Baleanu derivative. Since the biological systems have memory or aftereffects and because of this reason the modeling of these biological systems using the concept of fractional order derivatives gives many advantages in which the effects like memory are neglected. It is also observed that there is fractional order electrical conductance in the cell membrane of many biological organisms and they are classified in groups of non integer models. Thus, fractional derivatives gives better understanding of these biological models. Fractional calculus has many developments in fields of physics, chemistry, biochemistry, biology, medicine etc. A detailed proof for the existence and the uniqueness of the solution is presented. The numerical solutions are presented for the fractional mathematical model in sense of the Atangana-Baleanu derivative operator.

The structure of the article is given as follows: Section 1 is about introduction and some prerequisites. Section 2 is about the mathematical model under consideration. Part 3 is having the numerical scheme used in analysis while next section is about the graphical and numerical solution of the problem. In section 5, we have concluded the article.

Definition 1.1. Consider a function μ integrable on $\mathbb{R}$, and suppose $0<\eta<1$. The Atangana-Baleanu derivative [24] of fractional order can then be expressed as follows:

$${}_0^{FAB}\zeta_t^{\eta}(\mu(t))=\frac{K(\eta)}{1-\eta}\int_0^t \mu'(\tau)E_{\eta}\left[-\eta\frac{(t-\tau)^{\eta}}{1-\eta}\right]d\tau. \tag{1.1}$$

The expression for the A-B derivative of fractional order η, in the Caputo sense, is represented by ${}_0^{FAB}\zeta t^{\eta}$. The derivative is accompanied by the Mittag Leffler function $E\eta$ and normalization $K(\eta)$ function such as $K(0) = 1 = K(1)$.

Definition 1.2. The Atangana-Baleanu integral of order η of the integrable function μ on $\mathbb{R}$ is defined as follows

$$\mathcal{I}^{\mathcal{FAB}\eta}_{t}(\mu(t)) = \frac{1-\eta}{K(\eta)}\mu(t) + \frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^t \mu(\tau)(t-\tau)^{\eta-1}d\tau. \tag{1.2}$$

Theorem 1.3. *Let us consider*

$$\mathcal{I}^{\mathcal{FAB}\eta}_{t}(\mu(t)) = f(t),$$

possesses a solution defined as

$$\mu(t) = \frac{1-\eta}{K(\eta)}f(t) + \frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^t f(\tau)(t-\tau)^{\eta-1}d\tau,$$

for more details (see [3]–[6]).

2 Fractional Mathematical Model of Cancer Cell with Its Interaction With Virotheraphy and it's Analysis

We proceed to expand the mathematical model into the fractional framework for the interaction between Cancer Cells and Virotherapy, employing the AB derivative operator. Moreover, to maintain dimensional consistency between the right and left sides of the resultant fractional model, parameters with units of $(time)^{-1}$ are elevated to the power of η.

$$\begin{aligned}
{}_0^{\mathcal{FAB}}\zeta_t^{\eta}U(t) &= \theta^{\eta}\,U\left(1-\frac{U+I}{\delta}\right) - \beta^{\eta}\;U\;V - \alpha_1^{\eta}\;U\;E, & U(0) = U_0\\
{}_0^{\mathcal{FAB}}\zeta_t^{\eta}I(t) &= \beta^{\eta}\;U\;V - \alpha_2^{\eta}\;I\;E - \gamma_2^{\eta}\;I, & I(0) = I_0\\
{}_0^{\mathcal{FAB}}\zeta_t^{\eta}E(t) &= \lambda^{\eta}\;I - \gamma_3^{\eta}\;E, & E(0) = E_0\\
{}_0^{\mathcal{FAB}}\zeta_t^{\eta}V(t) &= A + \chi\;\gamma_2^{\eta}\;I - \gamma_4^{\eta}\;V, & V(0) = V_0
\end{aligned} \tag{2.1}$$

here, the AB fractional derivative of order η is represented by $0^{\mathcal{FAB}}\zeta t^{\eta}$.

2.1 preliminary results

Given that the non-negative initial conditions hold for define system, we observe that the system remains invariant in the non-negative orthant. Furthermore, owing to the vector field's continuous differentiability, the Picard-Lindel theorem guarantees the presence of a distinct outcome for given equations, when non-negative initial conditions are applied.

2.2 Boundedness

To ensure our model doesn't anticipate unrestrained cell proliferation, we verify that the cell populations remain constrained. Specifically, regarding the uninfected tumor cells:

$$\begin{aligned}
{}_0^{FAB}\zeta_t^{\eta}U(t) &= \theta^{\eta}U\left(1-\tfrac{U+I}{\delta}\right) - \beta^{\eta}VU - \alpha_1^{\eta}EU,\\
&\leq \theta^{\eta}\left(1-\tfrac{U}{\delta}\right)U,\\
&< 0,\ if\ \tfrac{U}{\delta} > 1.
\end{aligned}$$

Thus, $\lim_{t\to\infty} sup\ U(t) \leq 1$. We can obtain an upper limit for the population of infected tumor cells by utilizing this upper bound. Referring to above model, we have:

$$
\begin{aligned}
{}_0^{FAB}\zeta_t^{\eta}\,(U+I) &= \theta^{\eta}\left(1-\tfrac{U+I}{\delta}\right)U-\alpha_1^{\eta}EU-\alpha_2^{\eta}EI-\gamma_2^{\eta}I,\\
&\leq \theta^{\eta}\left(1-\tfrac{U+I}{\delta}\right)U,\\
&< 0, \quad if\ \tfrac{U+I}{\delta}>1.
\end{aligned}
$$

It follows that $\lim_{t\to\infty} supI(t) \leq 1$. Utilizing the asymptotic upper bound of the infected tumor cells, for effector T-cells we have ${}_0^{FAB}\zeta_t^{\eta}E(t) = \lambda^{\eta}-\gamma_3^{\eta}E$. By standard comparison theory, it follows that $\lim\limits_{t\to\infty} supE(t) \leq \frac{\lambda^{\eta}}{\gamma_3^{\eta}}$. Similarly, for the virion population, we have $\lim\limits_{t\to\infty} supV(t) \leq \frac{A+\chi\gamma_2^{\eta}}{\gamma_4^{\eta}}$.

2.3 Existence of equilibrium

To establish equilibrium [12]-[18] of (2.1), we must solve the following system of equations:

$$\theta^{\eta}U^*\left(1-\frac{U^*+I^*}{\delta}\right)-\beta^{\eta}V^*U^*-\alpha_1^{\eta}E^*U^*=0, \tag{2.2}$$

$$\beta^{\eta}V^*U^*-\alpha_2^{\eta}I^*E^*-\gamma_2^{\eta}I^*=0, \tag{2.3}$$

$$\lambda^{\eta}I^*-\gamma_3^{\eta}E^*=0, \tag{2.4}$$

$$A+\chi\gamma_2^{\eta}I^*-\gamma_4^{\eta}V^*=0. \tag{2.5}$$

If we consider $U^*=0$, we get $I^*=E^*=0$ and $V=\frac{A}{\gamma_4^{\eta}}$. Hence we get the cure state equilibrium points $p_0=(0,0,0,\frac{A}{\gamma_4^{\eta}})$.

Although if we assume $U^*\neq 0$, we obtain the values of U^*,E^*,V^* from above equations depending on I^*:

$$
\begin{aligned}
E^* &= \tfrac{\lambda^{\eta}I^*}{\gamma_3^{\eta}},\\
V^* &= \tfrac{A+\chi\gamma_2^{\eta}I^*}{\gamma_4^{\eta}},\\
U^* &= \delta-I^*-\tfrac{\delta\beta^{\eta}}{\theta^{\eta}}V^*-\tfrac{\delta\alpha_1^{\eta}}{\theta^{\eta}}E^*,
\end{aligned}
$$

or

$$U^*=\delta-I^*-\frac{\delta\beta^{\eta}}{\theta^{\eta}}\left(\frac{A+\chi\gamma_2^{\eta}I^*}{\gamma_4^{\eta}}\right)-\frac{\delta\alpha_1^{\eta}}{\theta^{\eta}}\left(\frac{\lambda^{\eta}I^*}{\gamma_3^{\eta}}\right).$$

Substituting these expression into (3) leaves us with a polynomial in I^*, denoted by $f(I^*)$:

$$
\begin{aligned}
f(I^*) &= \beta^{\eta}U^*V^*-\alpha_2^{\eta}I^*E^*-\gamma_2^{\eta}I^*,\\
&= \beta^{\eta}\left(\delta-I^*-\tfrac{\delta\beta^{\eta}}{\theta^{\eta}}\tfrac{A+\chi\gamma_2^{\eta}I^*}{\gamma_4^{\eta}}-\tfrac{\delta\alpha_1^{\eta}}{\theta^{\eta}}\tfrac{\lambda^{\eta}I^*}{\gamma_3^{\eta}}\right)\left(\tfrac{A+\chi\gamma_2^{\eta}I^*}{\gamma_4^{\eta}}\right)-\alpha_1^{\eta}I^*\left(\tfrac{\lambda^{\eta}I^*}{\gamma_3^{\eta}}\right)-\gamma_2^{\eta}I^*\\
&= -\left(\tfrac{\theta^{\eta}\beta^{\eta}\chi\gamma_2^{\eta}\gamma_4^{\eta}+\delta(\beta^{\eta})^2\chi^2(\gamma_2^{\eta})^2}{\theta^{\eta}(\gamma_4^{\eta})^2}+\tfrac{\theta^{\eta}\lambda^{\eta}\alpha_1^{\eta}\gamma_4^{\eta}+\delta\beta^{\eta}\chi\lambda^{\eta}\alpha_1^{\eta}\gamma_2^{\eta}}{\theta^{\eta}\gamma_3^{\eta}\gamma_4^{\eta}}\right)I^{*2}\\
&\quad -\left(\gamma_2^{\eta}+\tfrac{A\beta^{\eta}}{\gamma_4^{\eta}}+\tfrac{2A(\beta^{\eta})^2\delta\chi\gamma_2^{\eta}}{\theta^{\eta}(\gamma_4^{\eta})^2}+\tfrac{A\delta\beta^{\eta}\lambda^{\eta}\alpha_1^{\eta}}{\theta^{\eta}\gamma_3^{\eta}\gamma_4^{\eta}}-\tfrac{\chi\beta^{\eta}\delta\gamma_2^{\eta}}{\gamma_4^{\eta}}\right)I^*+\tfrac{A\beta^{\eta}\delta\left(\gamma_4^{\eta}-\frac{A\beta^{\eta}}{\theta^{\eta}}\right)}{(\gamma_4^{\eta})^2}.
\end{aligned}
$$

The number of internal equilibria is thus determined by the number of the solutions to $f(I^*)=0$. We first note that $f(I^*)$ is a quadratic function and that the coefficient on I^{*2} is negative. We also note that the constant term is positive if and only if $\gamma_4^{\eta}>\frac{A\beta^{\eta}}{\theta^{\eta}}$. by Descartes' Rule of Signs, it follows that there exists one unique positive real root for $f(I^*)$. Since I^* is positive and real, U^*,E^* , and V^* must also be positive and real. We conclude that there exists a unique cancer persistence state of the form $P^*=(U^*,I^*,E^*,V^*)$ when $\gamma_4^{\eta}>\frac{A\beta^{\eta}}{\theta^{\eta}}$. We summarize these results in the following theorem:

Theorem 2.1. *1. We have the only one state of the form* $P_0 = (0, 0, 0, \frac{A}{\gamma_4^\eta})$.
2. When $\frac{A\beta^\eta}{\theta^\eta} < \gamma_4^\eta$*,there exists a unique cancer persistence state of the form* $P^* = (U^*, I^*, E^*, V^*)$.

2.4 Stability of the cure state

In this section, we explore the stability of the cure state equilibrium $P_0 = (0, 0, 0, \frac{A}{\gamma_4^\eta})$.We note that the nonzero virion population in the cure state results from assuming a continuous constant dosage treatment. Furthermore, the lack of effector T-cells in the cure state represents there no longer being a need for an immune response due to cancer clearance.

2.5 Local stability of the cure state

We first consider the local stability of the cure state equilibrium P_0 .Recall that our non-dimensionalized model is

$$\begin{aligned}
&{}_0^{FAB}\zeta_t^\eta U(t) = \theta^\eta U\left(1 - \tfrac{U+I}{\delta}\right) - \beta^\eta U V - \alpha_1^\eta U E,\\
&{}_0^{FAB}\zeta_t^\eta I(t) = \beta^\eta U V - \alpha_2^\eta I E - \gamma_2^\eta I,\\
&{}_0^{FAB}\zeta_t^\eta E(t) = \lambda^\eta I - \gamma_3^\eta E,\\
&{}_0^{FAB}\zeta_t^\eta V(t) = A + \chi\gamma_2^\eta I - \gamma_4^\eta V.
\end{aligned}$$

Evaluating the Jacobian matrix at P_0 yields

$$J\left(0, 0, 0, \frac{A}{\gamma_4^\eta}\right) = \begin{bmatrix} \theta^\eta - \frac{\beta^\eta A}{\gamma_4^\eta} & 0 & 0 & 0 \\ \frac{A}{\gamma_4^\eta} & -\gamma_2^\eta & 0 & 0 \\ 0 & \lambda^\eta & -\gamma_3^\eta & 0 \\ 0 & \chi\gamma_2^\eta & 0 & -\gamma_4^\eta \end{bmatrix},$$

with eigenvalues $\frac{-\beta^\eta A + \theta^\eta\ \gamma_4^\eta}{\gamma_4^\eta}, -\gamma_2^\eta, -\gamma_3^\eta, -\gamma_4^\eta$. Thus, we find the local stability condition for the cure state to be $\beta^\eta A > \theta^\eta\gamma_4^\eta$. If this condition is not met, the cure state is unstable.
Now we are going to discuss about the existence and oneness of the solution. We have many ways to show the existence and oneness of the solution (see [17]–[22]).

2.6 Existence and Oneness

Theorem 2.2. *Let us consider the functions as follows*

$$\begin{aligned}
H_1(t, U) &= \theta^\eta\ U\left(1 - \frac{U+I}{\delta}\right) - \beta^\eta\ U\ V - \alpha_1^\eta\ U\ E,\\
H_2(t, I) &= \beta^\eta\ U\ V - \alpha_2^\eta\ I\ E - \gamma_2^\eta\ I,\\
H_3(t, E) &= \lambda^\eta\ I - \gamma_3^\eta\ E,\\
H_4(t, V) &= A + \chi\ \gamma_2^\eta\ I - \gamma_4^\eta\ V,
\end{aligned} \tag{2.6}$$

satisfy the Lipschitz condition; moreover, contract when:

(i) $0 < h_1 < 1$,

(ii) $0 < h_2 < 1$,

(iii) $0 < h_3 < 1$,

(iv) $0 < h_4 < 1$.

Proof. Let

$$H_2(t, I) = \beta^\eta\ U\ V - \alpha_2^\eta\ I\ E - \gamma_2^\eta\ I$$

Let I_1 and I_2 be two functions, then

$$\begin{aligned}\|H_2(t,I_1)-H_2(t,I_2)\| &= \left\|\alpha_2^\eta E\,(I_1-I_2)+\gamma_2^\eta\,(I_1-I2)\right\| \\ &\leq (\alpha_2^\eta\|E\|+\gamma_2^\eta)\,\|I_1(t)-I_2(t)\|. \end{aligned} \tag{2.7}$$

Let $p_1 = sup_t\|U(t)\|$, $p_2 = sup_t\|I(t)\|$, $p_3 = sup_t\|E(t)\|$, $p_4 = sup_t\|V(t)\|$ hence

$$\|H_2(t,I_1)-H_2(t,I_2)\| \leq h_2\|I_1(t)-I_2(t)\|,$$

where

$$h_2 = \alpha_2^\eta p_3 + \gamma_2^\eta.$$

Therefore, $H_2(t,U)$ satisfies Lipschitz's condition and if $0 < h_2 < 1$, it also meets the requirement for contraction. The same can be shown to be true for $H_1(t,I)$, $H_3(t,E)$, and $H_4(t,V)$.

Theorem 2.3. *An extended mathematical model that encompasses fractional dimensions for the study of cancer cells and their interaction with virotherapy*

$$\begin{aligned}
{}_0^{\mathcal{FAB}}\zeta_t^\eta U(t) &= \theta^\eta\,U\left(1-\frac{U+I}{\delta}\right)-\beta^\eta\;U\;V-\alpha_1^\eta\;U\;E, & U(0)=U_0\\
{}_0^{\mathcal{FAB}}\zeta_t^\eta I(t) &= \beta^\eta\;U\;V-\alpha_2^\eta\;I\;E-\gamma_2^\eta\;I, & I(0)=I_0\\
{}_0^{\mathcal{FAB}}\zeta_t^\eta E(t) &= \lambda^\eta\;I-\gamma_3^\eta\;E, & E(0)=E_0\\
{}_0^{\mathcal{FAB}}\zeta_t^\eta V(t) &= A+\chi\;\gamma_2^\eta\;I-\gamma_4^\eta\;V. & V(0)=V_0
\end{aligned} \tag{2.8}$$

Finds a singular solution within the constraints by searching for a value of t_{max} that meets the requirements.

$$\frac{1-\eta}{K(\eta)}h_i+\frac{t_{max}^\eta}{K(\eta)\Gamma(\eta)}h_i<1,\quad for\ i=1,2,3,4. \tag{2.9}$$

where, $k_1 = d+n_1$, $k_2 = s$, $k_3 = \delta$.

Proof. Consider

$${}_0^{\mathcal{FAB}}\zeta_t^\eta U(t) = \theta^\eta\,U\left(1-\frac{U+I}{\delta}\right)-\beta^\eta\;U\;V-\alpha_1^\eta\;U\;E, \qquad U(0)=U_0 \tag{2.10}$$

let

$$H_1(t,U) = \theta^\eta\,U\left(1-\frac{U+I}{\delta}\right)-\beta^\eta\;U\;V-\alpha_1^\eta\;U\;E$$

.
Subsequently, equation (2.10) can be expressed as:

$${}_0^{\mathcal{FAB}}\zeta_t^\eta U(t) = H_1(t,U). \tag{2.11}$$

Using theorem 1.3, we get

$$U(t) = U_0+\frac{1-\eta}{K(\eta)}H_1(t,U(t))+\frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^t(t-\rho)^{\eta-1}H_1(\rho,U(\rho))d\rho. \tag{2.12}$$

Let us consider $Z=(0,T)$ which is define for operator $G:\ \mathcal{C}(Z,\mathbb{R}^4)\longrightarrow\mathcal{C}(J,\mathbb{R}^4)$ such that

$$Y[U(t)] = U_0+\frac{1-\eta}{K(\eta)}H_1(t,U(t))+\frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^t(t-\rho)^{\eta-1}H_1(\rho,U(\rho))d\rho. \tag{2.13}$$

So we have that (2.12) can be like $Z[U(t)] = U(t)$. Now define norm on Z as $\|U\| = Sup_{t\in Z}|U(t)|$. Then $\mathcal{C}(Z,\mathbb{R}^4)$ and $\|.\|$ defines a Banach Space. Consider

$$G[U_1(t)] - G[U_2(t)] = \frac{1-\eta}{K(\eta)}\left(H_1(t,U_1(t)) - H_1(t,U_2(t))\right) + \frac{\zeta}{K(\eta)\Gamma(\eta)}\int_0^t (t-\rho)^{\eta-1}\left(H_1(\rho,U_1(\rho)) - H_1(\rho,U_2(\rho))\right)d\rho. \quad (2.14)$$

By taking the modulus of equation (2.14) and applying the triangle inequality, we arrive at

$$|G[U_1(t)] - G[U_2(t)]| \leq \frac{1-\eta}{K(\eta)}\left|(H_1(t,U_1(t)) - H_2(t,U_2(t)))\right| + \frac{\eta}{k(\eta)\Gamma(\eta)}\int_0^t \left|(t-\rho)^{\eta-1}\left(H_1(\rho,U_1(\rho)) - H_1(\rho,U_2(\rho))\right)d\rho\right|. \quad (2.15)$$

As the function $H_1(t,U(t))$ agrees with the Lipschitz condition, we have

$$|G(U_1) - G(U_2)| \leq \left(\frac{1-\eta}{K(\eta)}h_1 + \frac{t_{max}^{\eta}}{K(\eta)\Gamma(\eta)}h_1\right)|U_1 - U_2|. \quad (2.16)$$

Also equation (2.16) will be a contraction only if

$$\frac{1-\eta}{K(\eta)}h_1 + \frac{t_{max}^{\eta}}{K(\eta)\Gamma(\eta)}h_1 < 1. \quad (2.17)$$

The utilization of the Banach Fixed Point theorem has enabled us to definitively control the presence of a solitary solution for extended SEIR model, with the purpose of surmising the Omicron variant through the lens of the AB derivative operator.

□

3 Development of Numerical Method

Toufik and Atangana [8] defined a numerical approach for calculating derivatives of fractional order with non singular and non local kernels [22]-[25]. Consider

$${}_0^{FAB}\zeta_t^{\eta}\mu(t) = d(t,\mu(t)), \quad t \geq 0, \quad \mu(0) = \mu_0. \quad (3.1)$$

The above equation can be rephrased by utilizing Theorem (1),

$$\mu(t) - \mu(0) = \frac{1-\eta}{K(\eta)}d(t,\mu(t)) + \frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^t (t-\tau)^{\eta-1}d(\tau,\mu(\tau))d\tau. \quad (3.2)$$

We have at $t = t_{m+1}$, the above equation (3.2) reduces in to the following equation

$$\mu(t_{n+1}) - \mu(0) = \frac{1-\eta}{K(\eta)}d(t_m,\mu(t_m)) + \frac{\eta}{K(\eta)\Gamma(\eta)}\int_0^{t_{m+1}} (t_{m+1}-\tau)^{\eta-1}d(\tau,\mu(\tau))d\tau, \quad (3.3)$$

or

$$\mu_{m+1} = \mu(t_{m+1}) = \mu(0) + \frac{1-\eta}{K(\eta)}d(t_m,\mu(t_m)) + \frac{\eta}{K(\eta)\Gamma(\eta)}\sum_{j=0}^{m}\int_{t_j}^{t_{j+1}} (t_{m+1}-\tau)^{\eta-1}d(\tau,\mu(\tau))d\tau. \quad (3.4)$$

Considering d(τ, $\mu(\tau)$) through Lagrange polynomial interpolation,

$$q_n = d(\tau,\mu(\tau)) = \frac{\tau - t_{i-1}}{t_i - t_{i-1}}d(t_i,\mu_{t_i}) + \frac{\tau - t_i}{t_{i-1} - t_i}d(t_{i-1},\mu_{t_{i-1}}). \quad (3.5)$$

Substituting the value of $d(\tau,\mu(\tau))$ in equation (3.4), we get

$$\mu_{m+1} = \mu(0) + \frac{1-\eta}{K(\eta)} d(t_m, \mu(t_m)) + \frac{\eta}{K(\eta)\Gamma(\eta)} \sum_{i=0}^{m} \left(\frac{d(t_i, \mu(t_i))}{l} \int_{t_i}^{t_{i+1}} (t - t_{i-1})(t_{m+1} - t)^{\eta-1} dt - \frac{d(t_{i-1}, \mu(t_{i-1}))}{l} \int_{t_i}^{t_{i+1}} (t - t_{i-1})(t_{m+1} - t)^{\eta-1} dt \right). \quad (3.6)$$

Substituting $l = t_i - t_{i-1}$ and on simplification, we get

$$\mu_{m+1} = \mu_0 + \frac{1-\eta}{K(\eta)} d(t_m, \mu(t_m)) + \frac{\eta}{K(\eta)} \sum_{i=0}^{m} \left[\frac{l^\eta \; d(t_i, \mu_{t_i})}{\Gamma(\eta+2)} \left((m-i+1)^\eta \; (m+2-i+\eta) - (m-i)^\eta (m+2-i+2\eta) \right) - \frac{l^\eta \; d(t_{i-1}, \mu(t_{i-1}))}{\Gamma(\eta+2)} \left((m+1-i)^{\eta+1} \; - (m-i)^\eta \; (m+1-i+\eta) \right) \right]. \quad (3.7)$$

The numerical method for the fractional model of cancer cells, incorporating the A-B derivative operator, is demonstrated using the previously outlined numerical technique.

$$U_{m+1} = U_0 + \frac{1-\eta}{K(\eta)} H_1(t_m, U(t_m)) + \frac{\eta}{K(\eta)} \sum_{i=0}^{m} \left[\frac{l^\eta \; H_1(t_i, U_{t_i})}{\Gamma(\eta+2)} \left((m+1-i)^\eta \; (m+2-i+\eta) - (m-i)^\eta (m+2-i+2\eta) \right) - \frac{l^\eta \; H_1(t_{i-1}, U(t_{i-1}))}{\Gamma(\eta+2)} \left((m+1-i)^{\eta+1} \; - (m-i)^\eta \; (m+1-i+\eta) \right) \right], \quad (3.8)$$

where,

$$H_1(t, U) = \theta^\eta \, U \left(1 - \frac{I+U}{\delta} \right) - \beta^\eta \; V \; U - \alpha_1^\eta \; E \; U.$$

And

$$I_{m+1} = I_0 + \frac{1-\eta}{K(\eta)} H_2(t_m, I(t_m)) + \frac{\eta}{K(\eta)} \sum_{i=0}^{m} \left[\frac{l^\eta \; H_2(t_i, I_{t_i})}{\Gamma(\eta+2)} \left((m+1-i)^\eta \; (m-i+2+\eta) - (m-i)^\eta (m-i+2+2\eta) \right) - \frac{l^\eta \; H_2(t_{i-1}, I(t_{i-1}))}{\Gamma(\eta+2)} \left((m+1-i)^{1+\eta} \; - (m-i)^\eta \; (m+1+\eta-i) \right) \right], \quad (3.9)$$

where,

$$H_2(t, I) = \beta^\eta \; U \; V - \alpha_2^\eta \; I \; E - \gamma_2^\eta \; I.$$

Also

$$E_{m+1} = E_0 + \frac{1-\eta}{K(\eta)} H_3(t_m, E(t_m)) + \frac{\eta}{K(\eta)} \sum_{i=0}^{m} \left[\frac{l^\eta \; H_3(t_i, E_{t_i})}{\Gamma(\eta+2)} \left((m-i+1)^\eta \; (m+2-i+\eta) - (m-i)^\eta (m+2-i+2\eta) \right) - \frac{l^\eta \; H_3(t_{i-1}, E(t_{i-1}))}{\Gamma(2+\eta)} \left((m+1-i)^{\eta+1} \; - (m-i)^\eta \; (m+1+\eta-i) \right) \right], \quad (3.10)$$

where,

$$H_3(t, E) = \lambda^\eta \; I - \gamma_3^\eta \; E.$$

Also, we get the relation for V,

$$V_{m+1} = V_0 + \frac{1-\eta}{K(\eta)} H_4(t_m, V(t_m)) + \frac{\eta}{K(\eta)} \sum_{i=0}^{m} \left[\frac{l^\eta \ H_4(t_i, V_{t_i})}{\Gamma(\eta+2)} \left((m-i+1)^\eta \ (m+2-i+\eta) - (m-i)^\eta (m+2-i+2\eta) \right) - \frac{l^\eta \ H_4(t_{i-1}, V(t_{i-1}))}{\Gamma(2+\eta)} \left((m-i+1)^{1+\eta} \ - (m-i)^\eta \ (m+1-i+\eta) \right) \right]. \quad (3.11)$$

where,

$$H_4(t, V) = A + \chi \ \gamma_2^\eta \ I - \gamma_4^\eta \ V.$$

4 Numerical and Graphical Results

In this section, now we are going to find the graphical results of the cancer model under consideration. We have used following parameters with their numeric values [26]:

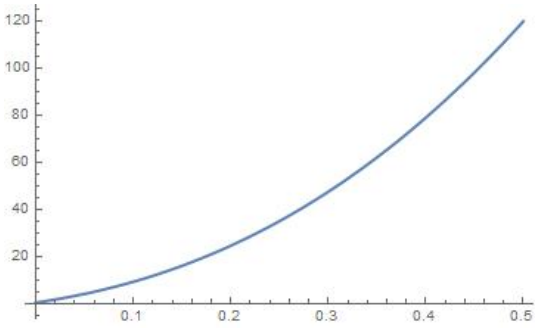
Parameter	Value
δ	3×10^9
λ	2.9
β	8.9×10^{-13}
θ	0.31
α_1	1.5×10^{-7}
α_2	1.5×10^{-7}
γ_3	0.35
γ_2	1
γ_4	2.3
χ	3500

By using the numerical technique discussed in section 3 and above parameters, we have got following graphs for various factors defined in the given mathematical model:

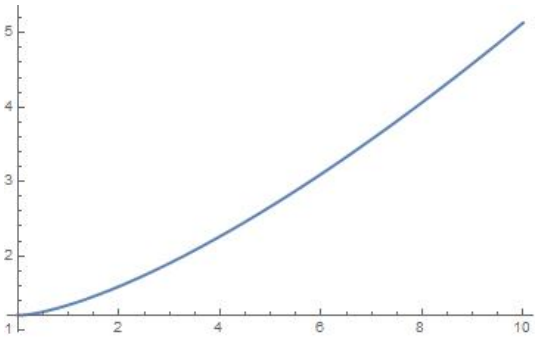
5 Conclusion

The objective of this work is to investigate the mathematical model of the interaction between cancer cells and virotherapy. In order to do this, a mathematical model that describes the dynamics of this interaction is put forward. Moreover, by adding Atangana-Baleanu derivatives, we expand this model to include a fractional mathematical paradigm and offer a more realistic depiction of the intricate dynamics of cancer cells and virotherapy. The findings show that the solution to the expanded mathematical framework is both unique and feasible. Study also show that the increasing number of virions results the increasing number of effective cells which is quite high than the increasing rate of tumor as well as infected cells. The numerical methods also yield a numerical solution for the fractional mathematical model. The results of this study might have a significant impact on how cancer immunotherapy therapies are developed and optimized.

Availability of statistics and materials: Availability of statistics is already cited in article.
Statement of disagreement: Researchers state that there aren't any conflicts of interest with the article that is being discussed.
Author's Contribution: The study was directed by Ravi Shanker Dubey, who also constructed the study map, analysed the findings, and organised the necessary research materials. Himani Agarwal summarised the data into tables and formatted the final paper while Manvendra Narayan Mishra prepared the article and carried out all the mathematical computations. The draught was read, corrected, and polished by all authors.

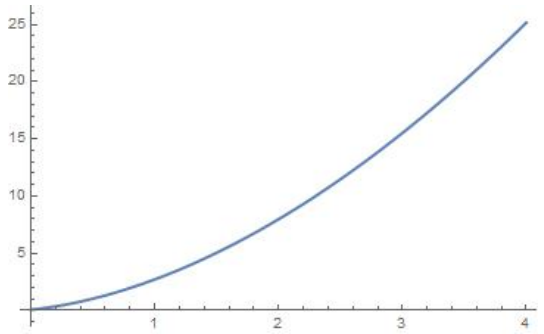


(a) For $\eta = 0.7$

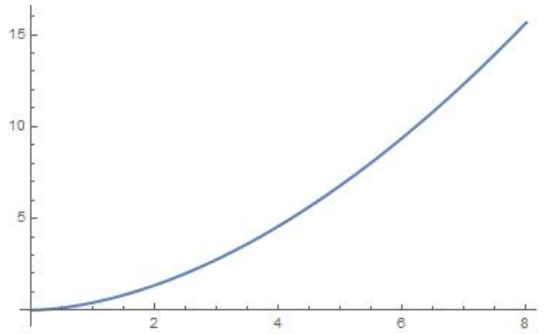


(b) For $\eta = 0.9$

Figure 1: Growth rate of uninfected tumor cells

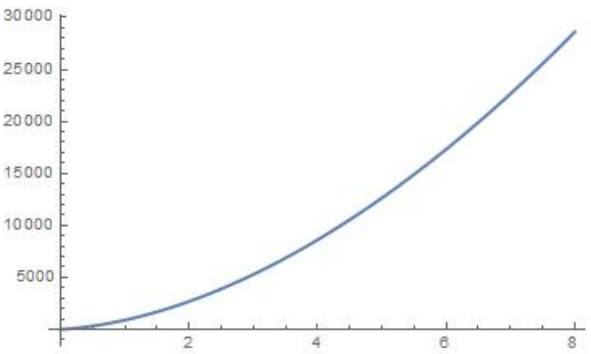


(a) For $\eta = 0.7$

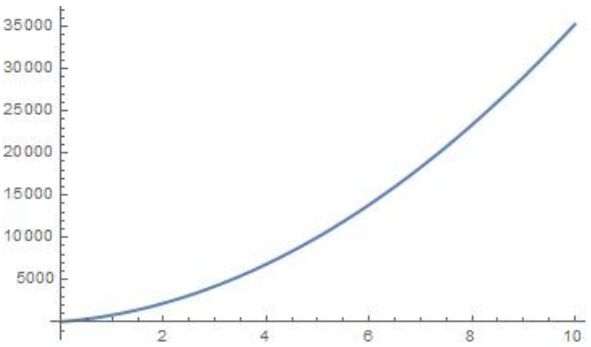


(b) For $\eta = 0.9$

Figure 2: Growth rate of infected tumor cells

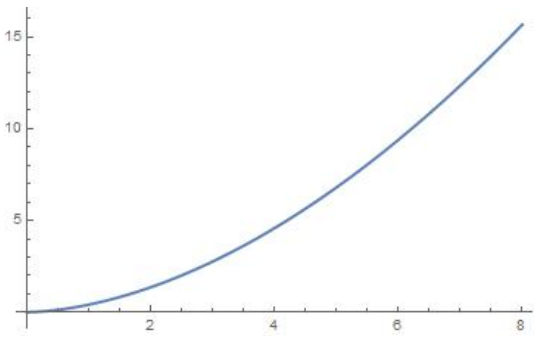


(a) For $\eta = 0.7$

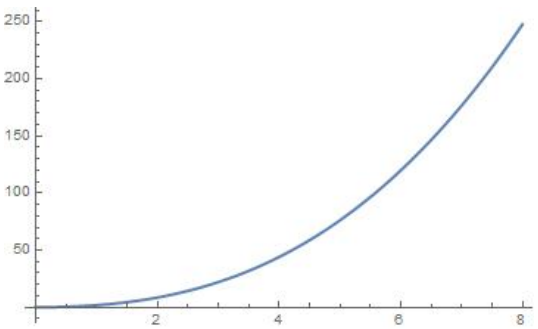


(b) For $\eta = 0.9$

Figure 3: Growth rate of effector T cells



(a) For $\eta = 0.7$



(b) For $\eta = 0.9$

Figure 4: Growth rate of virions

References

[1] US Department of Health and Human Services, Nci dictionary of cancer terms, Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=457964

[2] Z. Abernathy, K. Abernathy and J. Stevens, *A mathematical model for tumor growth and treatment using virotherapy*, AIMS Mathematics, **5**(5), 4136–4150, (2020).

[3] K.S. Miller and B. Ross, *An introduction to the fractional calculus and fractional differential equations*, A Wiley-Interscience Publication, New York, 366, (1993).

[4] A. Kilbas, *Fractional calculus of the generalized Wright function*, Fractional Calculus and Applied Analysis, Institute of Mathematics and Informatics Bulgarian Academy of Sciences, **8**(2), 113-126, (2005).

[5] A.A. Kilbas, H.M. Srivastava and J.J. Trujillo,*"Theory and applications of fractional differential equations*, North-Holland Mathematics Studies, Elsevier, 523, (2006).

[6] I. Podlubny, *Fractional differential equations. An introduction to fractional derivatives, fractional differential equations, to methods of their solution and some of their applications*, Mathematics in Science and Engineering, Academic Press, 340, (1999).

[7] Sachin Kumar and Abdon Atangana,*A numerical study of the nonlinear fractional mathematical model of tumor cells in presence of chemotherapeutic treatment*, International Journal of Biomathematics, **13**(3), 2050021, (2020).

[8] M. Toufik and A. Atangana, *New numerical approximation of fractional derivative with non-local and non-singular kernel*, The European Physical Journal Plus, **132**, 444, (2017).

[9] M. Areshi, P. Goswami and M. N. Mishra, *Comparative study of blood sugar–insulin model using fractional derivatives*, Journal of Taibah University for Science, **18**(1), 2339009, (2024).

[10] Ibtehal Alazman, M. N. Mishra, Badr Saad Alkahtani, and Pranay Goswami, *Computational analysis of rabies and its solution by applying fractional operator*, Applied Mathematics in Science and Engineering **32** (1), 2340607, (2024).

[11] S. S. Alzaid, B. T. S. Alkahtani, S. Sharma and R. S. Dubey, *Numerical solution of fractional model of HIV-1 infection in framework of different fractional derivatives*, J Funct Spaces, Article ID 6642957, (2021).

[12] X.J. Yang, M. Abdel-Aty and C. Cattani, *A new general fractional order derivative with Rabotnov fractional -exponential kernel applied to model the anomalous heat*, Thermal Science, **23**(3A), 1677-1681,(2019).

[13] Behzad Ghanbari, Sunil Kumar and Ranbir Kumar, *A study of behaviour for immune and tumor cells in immunogenetic tumour model with non-singular fractional derivative*, Chaos, Solitons and Fractals, **133**, 109619, (2020).

[14] A. Atangana and D. Baleanu, *New fractional derivatives with non-local and non-singular kernel: Theory and application to heat transfer model*, Thermal Science, **20**(2): 763-769, (2016).

[15] H. Agarwal, M. N. Mishra and R. S. Dubey, *On fractional Caputo operator for the generalized glucose supply model via incomplete Aleph function*, International Journal of Mathematics for Industry, 2450003, (2024).

[16] K.M. Altaf and A. Atangana, *Dynamics of Ebola Disease in the framework of different fractional derivatives*, Entropy, (2019).

[17] A.M. Alqahtani and M.N. Mishra, *Mathematical Analysis of Streptococcus Suis Infection in Pig-Human Population by Riemann-Liouville's Fractional Operator*, Progress in Fractional Differentiation and Applications, **10**(1), 119-135, (2024).

[18] R. S. Dubey, P. Goswami, H. M. Baskonus and A. Gomati Tailor ,*On the existence and uniqueness analysis of fractional blood glucose-insulin minimal model*, International Journal of Modeling, Simulation, and Scientific Computing, (2022).

[19] R. M. Ganji, H. Jafari, S. P. Moshokoa and N. S. Nkomo, *A mathematical model and numerical solution for brain tumor derived using fractional operator*, Results in Physics **28**, 104671, (2021).

[20] M. N. Mishra and A.F. Aljohani, *Mathematical modelling of growth of tumour cells with chemotherapeutic cells by using Yang–Abdel–Cattani fractional derivative operator*, Journal of Taibah University for Science, **16**(1), 1133-1141, (2022).

[21] Ausif Padder, Laila Almutairi, Sania Qureshi, Amanullah Soomro, Afroz Afroz, Evren Hincal, and Asifa Tassaddiq, *Dynamical analysis of generalized tumor model with Caputo fractional-order derivative*, Fractal and Fractional **7**(3), 258, (2023).

[22] Nikita Kumawat, A. Shukla, M. N. Mishra, Rahul Sharma and R. S. Dubey, *Khalouta Transform and Applications to Caputo-Fractional Differential Equations*, Frontiers in Applied Mathematics and Statistics, **10**, 1-10, (2024).

[23] H.M. Shrivastava, R.S. Dubey and M. Jain, *A Study of the Fractional-Order Mathematical Model of Diabetes and its Resulting Complications*, Mathematical Methods in the Applied Sciences, (2019).

[24] Awatif Muflih Alqahtani and Akanksha Shukla, *Computational analysis of multi-layered Navier–Stokes system by Atangana–Baleanu derivative*, Applied Mathematics in Science and Engineering, **32**(1), 2290723, (2017).

[25] Rania Saadeh, Ahmad Qazza and Kawther Amawi, *A new approach using integral transform to solve cancer models*, Fractal and Fractional, **6**(9), 490, (2022).

[26] Zachary Abernathy, Kristen Abernathy and Jessica Stevens, *A mathematical model for tumor growth and treatment using virotherapy*, AIMS Math, **5**(5), 4136-4150, (2020).

Author information

Himani Agarwal, Department of Mathematics, Suresh Gyan Vihar University, Jaipur, Rajasthan, India.
E-mail: himani1961994@gmail.com

Manvendra Narayan Mishra, Department of Mathematics, Suresh Gyan Vihar University, Jaipur, Rajasthan, India.
E-mail: manvendra.mishra22187@gmail.com

R. S. Dubey, Department of Mathematics, Amity University Rajasthan, India, India.
E-mail: ravimath13@gmail.com

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