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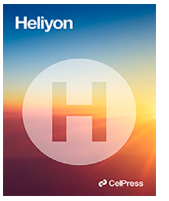

Research article

New solutions of time-fractional cancer tumor models using modified He-Laplace algorithm

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ABSTRACT

Cancer develops through cells when mutations build up in different genes that control cell proliferation. To treat these abnormal cells and minimize their growth, various cancer tumor samples have been modeled and analyzed in literature. The current study is focused on the investigation of more generalized cancer tumor model in fractional environment, where net killing rate is taken into account in different domains. Three types of killing rates are considered in the current study including time and position dependent killing rates, and concentration of cells based killing rate. A hybrid mechanism is proposed in which different homotopies are used with perturbation technique and Laplace transform. This leads to a convenient algorithm to tackle all types of fractional derivatives efficiently. The convergence and error bounds of the proposed scheme are computed theoretically by proving related theorems. In the next phase, convergence and validity is analyzed numerically by calculating residual errors round the fractional domain. It is observed that computed errors are very less in the entire fractional domain. Moreover, comparative analysis of Caputo, Caputo-Fabrizio (CF), and Atangana–Baleanu (AB) fractional derivatives is also performed graphically to discern the effect of different fractional approaches on the solution profile. Analysis asserts the reliability of proposed methodology in the matter of intricate fractional tumor models, and hence can be used to other complex physical phenomena.

1. Introduction

Cancer is a progressive disease that typically arises when body cells show mutations in the genes that control cell proliferation. The first step of cancer tumor formation is the alterations in certain genes known as tumor suppressor [1] and proto-oncogenes [2]. These cells with mutated genes have particular growth advantage over healthy cells. Their accumulation leads to increased genetic instability. As a result, they get more malignant and start invading the surrounding tissues. The challenges involved in understanding the spread of such tumors lead many researchers to model and analyze this disease. It aids in the development of efficient treatment plans and provides insight into the biological processes. To capture crucial elements including cell proliferation [3], mutations [4], and interactions [5], several differential models [6], agent-based models [7], and network models [8] have been employed in literature. There are many studies that discuss the treatment of cancer tumor cells. Some strategies are targeted therapies [9], immunotherapeutic

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approaches [10], and intervention strategies [11]. Their purpose is to target abnormal cells while keeping minimum harm to healthy cells. They also strengthen the body's protection against cancer cells.

The fractional modeling of cancer tumor differential equations has been a vast topic of interest in recent literature. There are several advantages of studying cancer tumor models in fractional version over their classical integer version. It enables a more detailed characterization of tumor at both spatial and temporal levels for precise simulation of tumor growth dynamics. It also provides a clearer picture of how different cell subpopulations respond to cancer therapy. Moreover, these models can be utilized by researchers and medical professionals to explore options and strategies for the treatment of tumors. Özköse et al. modeled fractional tumor-immune system related to lung cancer in [12]. Keshavarz et al. [13] solved cancer tumor model in fractional fuzzy environment using fuzzy integral transforms. Barbosa et al. [14] and Debbouche et al. [15] have taken an innovative approach in cancer tumor modeling to increase effects of anti-cancer drugs. Farman et al. analyzed time-fractional cancer tumor with respect to vaccination in [16]. Ucar and Ozdemir [17] examine the cancer immune system in respect of distinct fractional derivatives. Some cancer cell proliferation models are based on time or spatial growth for diverse constant rates [18]. In the current study, we consider both spatial and time dependencies for tumor cells concentration and killing rates. Burgess et al. [19] proposed a diffusion-based model whose governing equation is:

$$\frac{\partial \mathcal{P}(r,t)}{\partial t} - (\mathcal{D}/r^2)\frac{\partial}{\partial r}\left(r^2\frac{\partial \mathcal{P}(r,t)}{\partial r}\right) - \mathbb{L}\mathcal{P}(r,t) + \mathbb{K}\mathcal{P}(r,t) = 0,$$

where, cell concentration of tumor $\mathcal{P}$ is dependent upon time t at a position r. Moreover, $\mathcal{D}$, $\mathbb{L}$ and $\mathbb{K}$ are diffusivity coefficient, proliferation rate, and killing rate respectively. A one-dimensional variant of above model with varying killing rate is examined by Moyo and Leach [20] in which $\mathbb{K}$ is a function of both position and time. The fractional form of this model is:

$$\frac{\partial^\delta \mathcal{P}(r,t)}{\partial t^\delta} - \frac{\partial^2 \mathcal{P}(r,t)}{\partial r^2} + \mathbb{K}\mathcal{P}(r,t) = 0, \tag{1}$$

where, δ is the fractional parameter. Ali et al. [21], and Bokhari et al. [22] have taken killing rate $\mathbb{K}$ as a function of $\mathcal{P}$, leading to a non-linear model. As a result, different situations can be observed, ranging from the radially symmetric to the radially non-symmetric tumor model.

Fractional (non-integer) order derivatives have immense importance in modeling and simulation as it provides good tools that can be employed to describe real life phenomena with memory effects. Several types of fractional derivative have been utilized in literature including Caputo derivative [23], Caputo-Fabrizio derivative (CFD) [24], and Atangana–Baleanu derivative (ABD) [25]. These non-integer order derivatives also have great influence in the analysis of many diseases including cancer tumor. Korpinar et al. [26], Ghanbari [27], Arfan [28], and Ahmad et al. [29] are some of the researchers that have explored cancer tumor models in fractional form. Various techniques including Runge-Kutta method [30], Adomian decomposition method (ADM) [31], finite difference method (FDM) [32], shooting technique [33], optimal homotopy asymptotic method [34], homotopy analysis method [35], barrier Lyapunov function method [36], and homotopy perturbation method (HPM) [37] have been applied to calculate the solutions of fractional differential equations. HPM is a semi-analytical algorithm that uses homotopy and perturbation methods to solve non-linear differential problems. By combining Laplace transform and HPM, a highly productive technique known as He-Laplace method (HLM) [38] is obtained that can efficiently solve higher order fractional differential equations. Fractional differential properties of Laplace transform provide a convenient approach to tackle fractional derivatives involved in most of the FDEs. In current study, we are proposing fractional He-Laplace method (HLM) for the solution of the fractional diffusion cancer tumor model given in Eq. (1). Different fractional derivatives are also applied to study the memory effect in the model.

The rest of the manuscript is organized as: preliminaries containing important definitions are in Section 2, whereas the proposed methodology is given in Section 3. Section 4 contains theoretical convergence and error analysis of He-Laplace method. Application of HLM to cancer tumor model is given in Section 5. The discussion of results is in Section 6, while the conclusion of study is in Section 7.

2. Preliminaries

Definition 1 *([39]).* For a function $\mathcal{P}(r,t)$, the time-fractional derivative in **Caputo sense** ${}^C\mathbb{D}_t^\delta$ is

$${}^C\mathbb{D}_t^\delta \mathcal{P}(r,t) = \frac{1}{\Gamma(\vartheta-\delta)}\int_0^t (t-\chi)^{\vartheta-\delta-1}\mathcal{P}^{(\vartheta)}(r,\chi)d\chi, \qquad \vartheta-1<\delta\le\vartheta. \tag{2}$$

Definition 2 *([40]).* The Laplace transform $\mathbb{L}$ connected with Caputo sense time-fractional derivative (2) can be expressed by

$$\mathbb{L}\{{}^C\mathbb{D}_t^\delta \mathcal{P}(r,t)\} = s^\delta \mathbb{L}\{\mathcal{P}(r,t)\} - \sum_{w=0}^{\vartheta-1} s^{\delta-w-1}\mathcal{P}^{(w)}(r,0), \qquad \vartheta-1<\delta\le\vartheta. \tag{3}$$

Definition 3 *([24])*. The time-fractional derivative in **Caputo-Fabrizio sense** ${}^{CF}\mathbb{D}_t^{\delta}$ of a function $\mathcal{P}(r,t)$ is given as

$$ {}^{CF}\mathbb{D}_t^{\delta}\mathcal{P}(r,t) = \frac{1}{1-\delta}\int_0^t e^{\frac{-\delta(t-\chi)}{1-\delta}}\frac{\partial \mathcal{P}(r,\chi)}{\partial \chi}d\chi, \qquad 0<\delta<1. \tag{4}$$

Definition 4 *([41])*. Laplace transform $\mathbb{L}$ of Caputo-Fabrizio sense time-fractional derivative (4) is defined in the form

$$ \mathbb{L}\{{}^{CF}\mathbb{D}_t^{\delta}\mathcal{P}(r,t)\} = \frac{s\mathbb{L}\{\mathcal{P}(r,t)\}-\mathcal{P}(r,0)}{s+\delta(1-s)}, \qquad 0<\delta<1.$$

Definition 5 *([42])*. A function $\mathcal{P}(r,t)$ in sense of **Atangana–Baleanu time-fractional derivative** ${}^{AB}\mathbb{D}_t^{\delta}$ can be described by

$$ {}^{AB}\mathbb{D}_t^{\delta}\mathcal{P}(r,t) = \frac{K(\delta)}{1-\delta}\int_0^t E_{\delta}\left[-\frac{\delta(t-\chi)^{\delta}}{1-\delta}\right]\frac{\partial \mathcal{P}(r,\chi)}{\partial \chi}d\chi \qquad 0<\delta\leq 1. \tag{5}$$

where, $K(\delta)$ represents the normalization function that shows $K(0)=K(1)=1$.

Definition 6 *([25])*. Atangana–Baleanu time-fractional derivative (5) has Laplace transform $\mathbb{L}$ defined as

$$ \mathbb{L}\{{}^{AB}\mathbb{D}_t^{\delta}\mathcal{P}(r,t)\} = K(\delta)\frac{s^{\delta}\mathbb{L}\{\mathcal{P}(r,t)\}-s^{\delta-1}\mathcal{P}(r,0)}{s^{\delta}(1-\delta)+\delta}, \qquad 0<\delta\leq 1.$$

3. Proposed methodology

Consider a general non-linear time-fractional partial differential equation

$$ \mathbb{D}_t^{\delta}\mathcal{P}(r,t)+\mathrm{L}[\mathcal{P}(r,t)]+\mathrm{N}[\mathcal{P}(r,t)]-g(r,t)=0, \qquad t>0,\ \vartheta-1<\delta\leq\vartheta, \tag{6}$$

that has initial conditions

$$ \mathcal{P}^{\vartheta}(r,0)=\mathcal{K},$$

where, the unknown function $\mathcal{P}$ depends on time t and space r with $\mathbb{D}_t^{\delta}$ as its time-fractional derivative and $g(r,t)$ is a known function. δ, L and N are symbols representing fractional parameter, linear and non-linear operators respectively. In some cases of highly non-linear problems containing transcendental functions, HLM does not prove to be as effective. However, fractional differential properties of Laplace transform provide a convenient approach to tackle fractional derivatives involved in most of the FDEs. Thus, by utilizing Laplace transform '$\mathbb{L}$' on given equation (6), we obtain

$$ \mathbb{L}\{\mathbb{D}_t^{\delta}\mathcal{P}(r,t)\}+\mathbb{L}\{\mathrm{L}[\mathcal{P}(r,t)]+\mathrm{N}[\mathcal{P}(r,t)]-g(r,t)\}=0,$$

By Caputo's fractional derivative (2)

$$ \mathbb{L}\{\mathcal{P}(r,t)\}-\left(\frac{1}{s^{\delta}}\right)\sum_{w=0}^{\vartheta-1}s^{\delta-w-1}\mathcal{P}^{(w)}(r,0)+\left(\frac{1}{s^{\delta}}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}(r,t)]+\mathrm{N}[\mathcal{P}(r,t)]-g(r,t)\}=0, \tag{7}$$

The homotopy of equation (7) is

$$ \begin{aligned}\mathbb{H}:(1-q)(\mathbb{L}\{\mathcal{P}(r,t)\}-\mathcal{P}_0(r,t))+q(\mathbb{L}\{\mathcal{P}(r,t)\}-\left(\frac{1}{s^{\delta}}\right)\sum_{w=0}^{\vartheta-1}s^{\delta-w-1}\mathcal{P}^{(w)}(r,0)+\\ \left(\frac{1}{s^{\delta}}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}(r,t)]+\mathrm{N}[\mathcal{P}(r,t)]-g(r,t)\}),\end{aligned} \tag{8}$$

where, $\mathcal{P}_0(r,t)$ represents the initial guess.

Expanding $\mathcal{P}(r,t)$ in Taylor series form with q gives

$$ \mathcal{P}(r,t)=\sum_{i=0}^{\infty}q^i\mathcal{P}_i, \tag{9}$$

In the next step equation (9) is substituted in (8). Equating same coefficients of q leads to

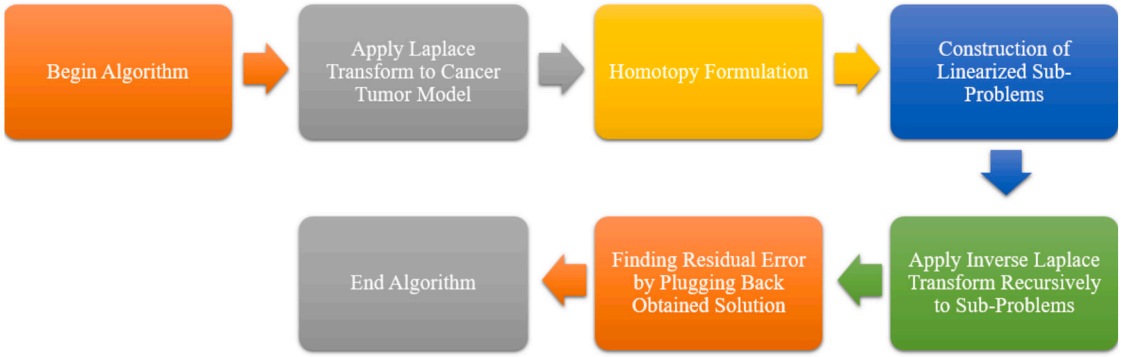


Fig. 1. Block diagram of HLM.

At first order:

$$\mathbb{L}\{\mathcal{P}_1(r,t)\} + \mathcal{P}_0(r,t) - \left(\frac{1}{s^\delta}\right)\sum_{w=0}^{\vartheta-1} s^{\delta-w-1}\mathcal{P}^{(w)}(r,0) + \left(\frac{1}{s^\delta}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}_0(r,t)] + \mathrm{N}[\mathcal{P}_0(r,t)] - g(r,t)\} = 0,$$

$$\mathcal{P}_1^{\vartheta}(r,0) = 0,$$

Inverse of Laplace transform leads to

$$\mathcal{P}_1(r,t) + \mathbb{L}^{-1}\left\{\mathcal{P}_0(r,t) - \left(\frac{1}{s^\delta}\right)\sum_{w=0}^{\vartheta-1} s^{\delta-w-1}\mathcal{P}^{(w)}(r,0)\right\} + \mathbb{L}^{-1}\left\{\left(\frac{1}{s^\delta}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}_0(r,t)] + \mathrm{N}[\mathcal{P}_0(r,t)] - g(r,t)\}\right\} = 0,$$

In general, at m^{th} order we have

$$\mathbb{L}\{\mathcal{P}_m(r,t)\} + \left(\frac{1}{s^\delta}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}_{m-1}(r,t)] + \mathrm{N}[\mathcal{P}_{m-1}(r,t)]\} = 0,$$

$$\mathcal{P}_m^{\vartheta}(r,0) = 0,$$

Inverse Laplace transform gives

$$\mathcal{P}_m(r,t) + \mathbb{L}^{-1}\left\{\left(\frac{1}{s^\delta}\right)\mathbb{L}\{\mathrm{L}[\mathcal{P}_{m-1}(r,t)] + \mathrm{N}[\mathcal{R}_{m-1}(r,t)]\}\right\} = 0,$$

The required approximate series solution of equation (6) is obtained by adding all order deformation equations as

$$\tilde{\mathcal{P}} = \mathcal{P}_0(r,t) + \mathcal{P}_1(r,t) + \mathcal{P}_2(r,t) + \mathcal{P}_3(r,t) + \mathcal{P}_4(r,t) + \ldots, \tag{10}$$

Substitution of equation (10) in the given fractional differential equation (6) gives residual function

$$\mathbb{R} = \mathbb{D}_\tau^\delta[\tilde{\mathcal{P}}] + \mathrm{L}[\tilde{\mathcal{P}}] + \mathrm{N}[\tilde{\mathcal{P}}] - g(r,t).$$

The block diagram of proposed methodology is given in Fig. 1. The same procedure is applied for CF and AB type fractional derivatives.

4. Convergence and error estimation

4.1. Convergence

Theorem 1. *If a Banach space $(\mathscr{B}[0,\mathbf{T}], \|\,.\,\|)$ has functions $\mathcal{P}_i(r,t)$ and $\mathcal{P}(r,t)$ defined in it, then, the series solution given in equation (10) converges towards the solution of (6) with constant $c \in (0,1)$ [43].*

4.2. Error estimation

Theorem 2. *For a general fractional partial differential equation (6), the maximum absolute truncation error of its solution (10) is [43]*

$$\left|\mathcal{P}(r,t) - \sum_{h=0}^{j}\mathcal{P}_h(r,t)\right| \le \frac{c^{j+1}}{1-c}\,\|\,\mathcal{P}_0(r,t)\,\|\,.$$

5. Application of fractional He-Laplace method to cancer tumor model

In this section, three cases will be considered of the killing rate of cancer cells $\mathbb{K}$ in equation (1).

Case 1: Time dependent killing rate [44] For this case consider

$$\frac{\partial^\delta \mathcal{P}(r,t)}{\partial t^\delta} - \frac{\partial^2 \mathcal{P}(r,t)}{\partial r^2} + t^2 \mathcal{P}(r,t) = 0, \qquad 0 < \delta \leq 1,$$

with condition

$$\mathcal{P}(r,0) = e^{lr},$$

where, l is a constant.

Solution: Initiating Laplace transform on Eq. (6) and then using definition (3) we get

$$\mathbb{L}\{\mathcal{P}(r,t)\} - \left(\frac{1}{s}\right) e^{lr} + \left(\frac{1}{s^\delta}\right) \mathbb{L}\left\{ - \frac{\partial^2 \mathcal{P}(r,t)}{\partial r^2} + t^2 \mathcal{P}(r,t) \right\} = 0,$$

which leads to homotopy equation

$$\mathbb{H} : (1-q)(\mathbb{L}\{\mathcal{P}(r,t)\} - \mathcal{P}_0(r,t)) + q\left(\mathbb{L}\{\mathcal{P}(r,t)\} - \left(\frac{1}{s}\right) e^{lr} + \left(\frac{1}{s^\delta}\right) \mathbb{L}\left\{ - \frac{\partial^2 \mathcal{P}(r,t)}{\partial r^2} + t^2 \mathcal{P}(r,t) \right\} \right),$$

with initial approximation $\mathcal{P}_0(r,t) = e^{lr}$.

By putting Eq. (9) in above equation and equating same coefficient of q, we have At first order:

$$\mathbb{L}\{\mathcal{P}_1(r,t)\} + e^{lr} - \left(\frac{1}{s}\right) e^{lr} + \left(\frac{1}{s^\delta}\right) \mathbb{L}\left\{ - \frac{\partial^2 \mathcal{P}_0(r,t)}{\partial r^2} + t^2 \mathcal{P}_0(r,t) \right\} = 0,$$
$$\mathcal{P}_1(r,0) = 0,$$

Application of inverse Laplace transform gives

$$\mathcal{P}_1(r,t) = -e^{lr} t^\delta \left(\frac{2t^2}{\Gamma(\delta+3)} - \frac{l^2}{\Gamma(\delta+1)} \right),$$

At second order:

$$\mathbb{L}\{\mathcal{P}_2(r,t)\} + \left(\frac{1}{s^\delta}\right) \mathbb{L}\left\{ - \frac{\partial^2 \mathcal{P}_1(r,t)}{\partial r^2} + t^2 \mathcal{P}_1(r,t) \right\} = 0,$$
$$\mathcal{P}_2(r,0) = 0,$$

Inverse Laplace transform leads to

$$\mathcal{P}_2(r,t) = -e^{lr} t^{2\delta} \left(-\frac{l^4}{\Gamma(2\delta+1)} + \frac{l^2 t^2 (2\Gamma(\delta+1) + \Gamma(\delta+3))}{\Gamma(\delta+1)\Gamma(2\delta+3)} - \frac{2t^4 \Gamma(\delta+5)}{\Gamma(\delta+3)\Gamma(2\delta+5)} \right),$$

Hence in this way we have solution at fifth approximation

$$\tilde{\mathcal{P}} = \sum_{i=0}^{5} \mathcal{P}_i(r,t).$$

Case 2: Position dependent killing rate [44]

$$\frac{\partial^\delta \mathcal{P}(r,t)}{\partial t^\delta} - \frac{\partial^2 \mathcal{P}(r,t)}{\partial r^2} + \frac{2}{r^2} \mathcal{P}(r,t) = 0, \qquad 0 < \delta \leq 1,$$

with condition

$$\mathcal{P}(r,0) = \frac{A}{r} + Br^2,$$

where, A and B are constants.

Solution: Applying Laplace transform and using definition (3) leads to homotopy equation

$$\mathbb{H}:(1-q)(\mathbb{L}\{\mathcal{P}(r,t)\}-\mathcal{P}_0(r,t))+q\Bigg(\mathbb{L}\{\mathcal{P}(r,t)\}-\frac{1}{s}\left(\frac{A}{r}+Br^2\right)+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}(r,t)}{\partial r^2}+\frac{2}{r^2}\mathcal{P}(r,t)\right\}\Bigg),$$

with initial approximation $\mathcal{P}_0(r,t)=\frac{A}{r}+Br^2$.

Using Eq. (9) we have different order deformation equations. At first order:

$$\mathbb{L}\{\mathcal{P}_1(r,t)\}+\frac{A}{r}+Br^2-\frac{1}{s}\left(\frac{A}{r}+Br^2\right)+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}_0(r,t)}{\partial r^2}+\frac{2}{r^2}\mathcal{P}_0(r,t)\right\}=0,\qquad \mathcal{P}_1(r,0)=0,$$

At second order:

$$\mathbb{L}\{\mathcal{P}_2(r,t)\}+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}_1(r,t)}{\partial r^2}+\frac{2}{r^2}\mathcal{P}_1(r,t)\right\}=0,\qquad \mathcal{P}_2(r,0)=0,$$

At third order:

$$\mathbb{L}\{\mathcal{P}_3(r,t)\}+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}_2(r,t)}{\partial r^2}+\frac{2}{r^2}\mathcal{P}_2(r,t)\right\}=0,\qquad \mathcal{P}_3(r,0)=0,$$

Continuing this way inverse Laplace transform gives the analytical solution

$$\tilde{\mathcal{P}}=\sum_{i=0}^{5}\mathcal{P}_i(r,t)=\frac{A}{r}+Br^2.$$

Case 3: Cells concentration dependent killing rate [44]

$$\frac{\partial^\delta\mathcal{P}(r,t)}{\partial t^\delta}-\frac{\partial^2\mathcal{P}(r,t)}{\partial r^2}-\frac{2}{r}\frac{\partial\mathcal{P}(r,t)}{\partial r}+\mathcal{P}^2(r,t)=0,\qquad 0<\delta\le 1,$$

with condition

$$\mathcal{P}(r,0)=r^\sigma,$$

where, σ is a constant.

Solution: Following the same procedure as in Section 3 gives

$$\mathbb{H}:(1-q)(\mathbb{L}\{\mathcal{P}(r,t)\}-\mathcal{P}_0(r,t))+q\Bigg(\mathbb{L}\{\mathcal{P}(r,t)\}-\left(\frac{1}{s}\right)r^\sigma+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}(r,t)}{\partial r^2}-\frac{2}{r}\frac{\partial\mathcal{P}(r,t)}{\partial r}+\mathcal{P}^2(r,t)\right\}\Bigg),$$

with initial approximation $\mathcal{P}_0(r,t)=r^\sigma$.

Different order deformation equations are At first order:

$$\mathbb{L}\{\mathcal{P}_1(r,t)\}+r^\sigma-\frac{1}{s}(r^\sigma)+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}_0(r,t)}{\partial r^2}-\frac{2}{r}\frac{\partial\mathcal{P}_0(r,t)}{\partial r}+\mathcal{P}_0^2(r,t)\right\}=0,\qquad \mathcal{P}_1(r,0)=0,$$

Inverse Laplace transform gives

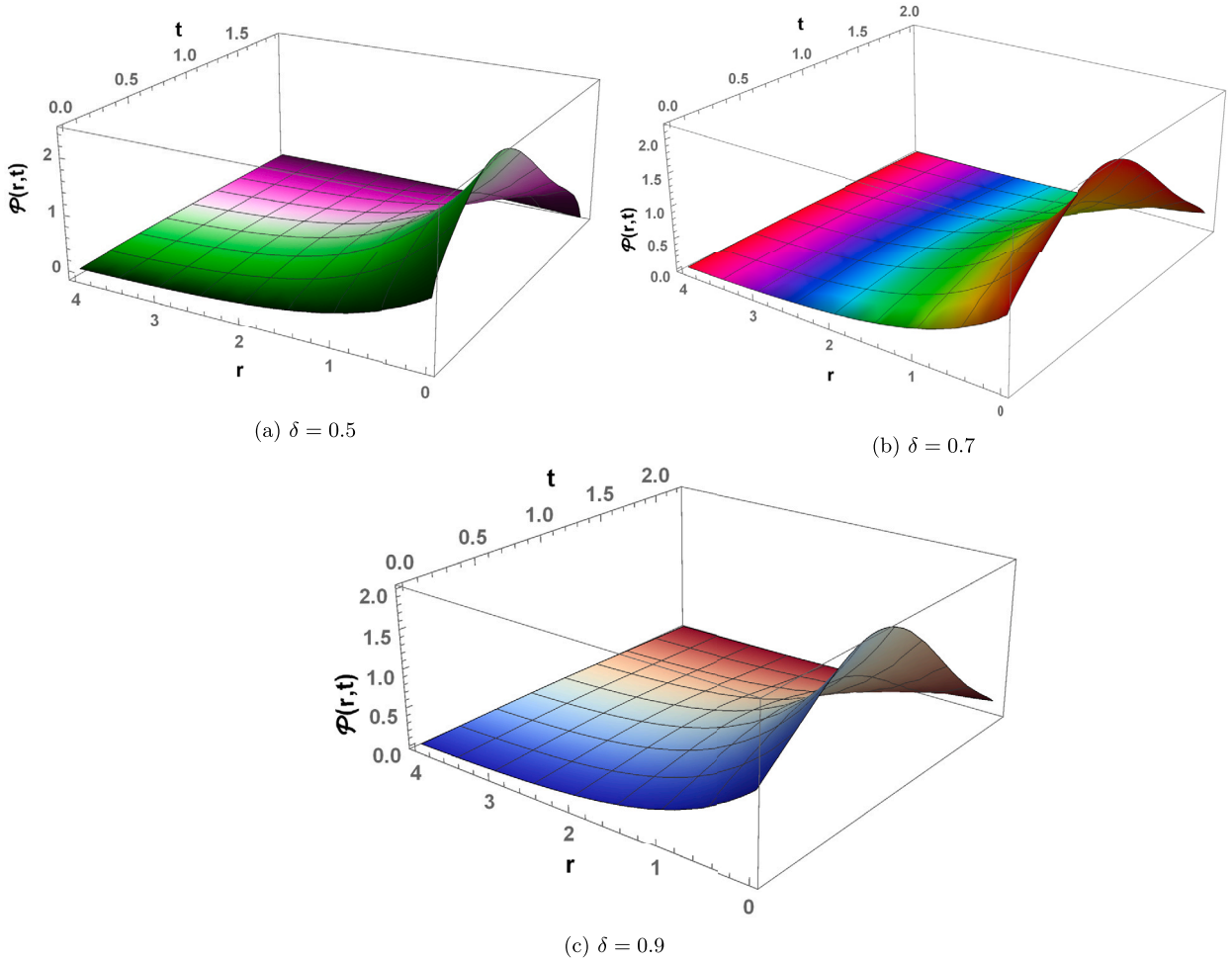
$$\mathcal{P}_1(r,t)=-\frac{t^\delta\left(-\sigma^2r^{\sigma-2}-\sigma r^{\sigma-2}+r^{2\sigma}\right)}{\Gamma(\delta+1)},$$

At second order:

$$\mathbb{L}\{\mathcal{P}_2(r,t)\}+\left(\frac{1}{s^\delta}\right)\mathbb{L}\left\{-\frac{\partial^2\mathcal{P}_1(r,t)}{\partial r^2}-\frac{2}{r}\frac{\partial\mathcal{P}_1(r,t)}{\partial r}+\mathcal{P}_1^2(r,t)\right\}=0,\qquad \mathcal{P}_2(r,0)=0,$$

Table 1
Numerical errors at different value of δ (fractional parameter) in Case 1 when $t = 0.3$ and $l = 0.01$.

r	$\delta = 0.22$	$\delta = 0.47$	$\delta = 0.69$	$\delta = 0.85$	$\delta = 1.0$
1	1.88×10^{-8}	3.52×10^{-10}	9.18×10^{-12}	5.99×10^{-13}	4.39×10^{-14}
2	1.90×10^{-8}	3.55×10^{-10}	9.27×10^{-12}	6.05×10^{-13}	4.43×10^{-14}
3	1.92×10^{-8}	3.59×10^{-10}	9.36×10^{-12}	6.11×10^{-13}	4.48×10^{-14}
4	1.94×10^{-8}	3.62×10^{-10}	9.46×10^{-12}	6.17×10^{-13}	4.52×10^{-14}
5	1.96×10^{-8}	3.66×10^{-10}	9.55×10^{-12}	6.23×10^{-13}	4.57×10^{-14}



(a) $\delta = 0.5$ (b) $\delta = 0.7$

(c) $\delta = 0.9$

Fig. 2. 3D solutions (Case 1) across various values of δ when $l = -1$.

Taking inverse Laplace transform

$$\mathcal{P}_2(r,t) = \frac{t^{2\delta} r^{\sigma-4}\left(\sigma\left(\sigma^3 - 2\sigma^2 - \sigma + 2\right) - 2\sigma(3\sigma+2)r^{\sigma+2} + 2r^{2\sigma+4}\right)}{\Gamma(2\delta+1)},$$

Final approximate solution can be determined by $\sum_{i=0}^{5} \mathcal{P}_i(r,t)$.

6. Discussion of results

This manuscript presents investigation of time-fractional cancer tumor model with three different killing rates. In Case 1, residual errors are calculated at both fractional and integer order. The comparison of these errors is shown in Table 1 with fractional parameter $\delta = 0.22$, 0.47, 0.69, 0.85, and 1.0. As can be observed from this table, the value of errors decreased as the value of δ increased across the domain. Furthermore, the effectiveness of HLM for the entire fractional domain is deduced from these errors. Three-

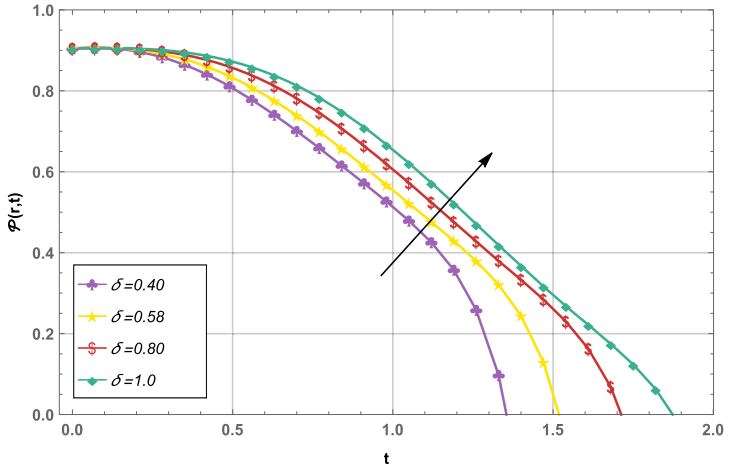


Fig. 3. 2D graphics of cell concentration w.r.t. time t (Case 1) when $r = 1$ and $l = -0.1$.

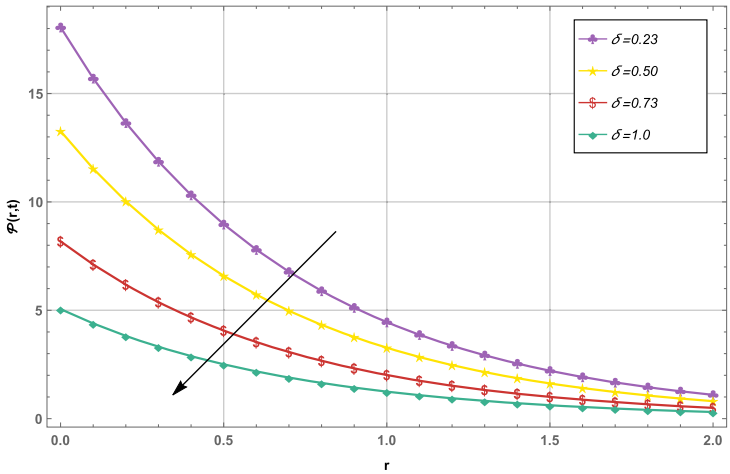


Fig. 4. 2D graphics of cell concentration w.r.t. position r (Case 1) when $t = 1$ and $l = -1.4$.

Table 2
Numerical errors at different value of δ in Case 3 when $t = 15$ and $\sigma = -4$.

t	$\delta = 0.22$	$\delta = 0.47$	$\delta = 0.69$	$\delta = 0.85$	$\delta = 1.0$
0.1	5.01×10^{-10}	1.04×10^{-11}	2.15×10^{-13}	1.05×10^{-14}	9.76×10^{-18}
0.3	1.67×10^{-9}	1.37×10^{-10}	9.55×10^{-12}	1.12×10^{-12}	7.11×10^{-15}
0.5	2.94×10^{-9}	4.58×10^{-10}	5.56×10^{-11}	9.85×10^{-12}	1.52×10^{-13}
0.7	4.26×10^{-9}	1.00×10^{-9}	1.77×10^{-10}	4.11×10^{-11}	1.14×10^{-12}
0.9	5.61×10^{-9}	1.82×10^{-9}	4.22×10^{-10}	1.19×10^{-10}	5.18×10^{-12}

dimensional representations of the solutions for $\delta = 0.50$, 0.70, and 0.90 are shown in Fig. 2a-2c. According to these diagrams, cell concentration drops to zero as the value of time and position increases which indicates that the tumor is shrinking. Fig. 3 and 4 depicts the concentration of tumor cells in two-dimensional diagram with regard to time and space respectively. It can be noted through Fig. 3 that the tumor cells concentration increases with increase in fractional parameter in case 1, in contrast, for Fig. 4, tumor cells concentration shows decline with increase in fractional parameter in case 2. The results of the acquired solutions through Caputo, Caputo-Fabrizio, and Atangana-Baleanu at $\delta = 0.24$ are also compared (see Fig. 5), and it can be observed that the tumor is getting smaller for all derivatives. Moreover, Caputo derivative depicts highest and Atangana-Baleanu derivative shows least cell concentration in contrast.

In Case 2, analytical solution is obtained through HLM that illustrates the convergence of proposed technique. The obtained solution is demonstrated through Fig. 6, which shows that a high tumor concentration is present at the initial time 't' and position 'r'. However, as the therapy progressed, the tumor began to contract and gradually converged towards zero. Table 2 of Case 3 displays residual errors at different fractional orders. This table presents that when δ increases through the domain, the values of errors reduces.

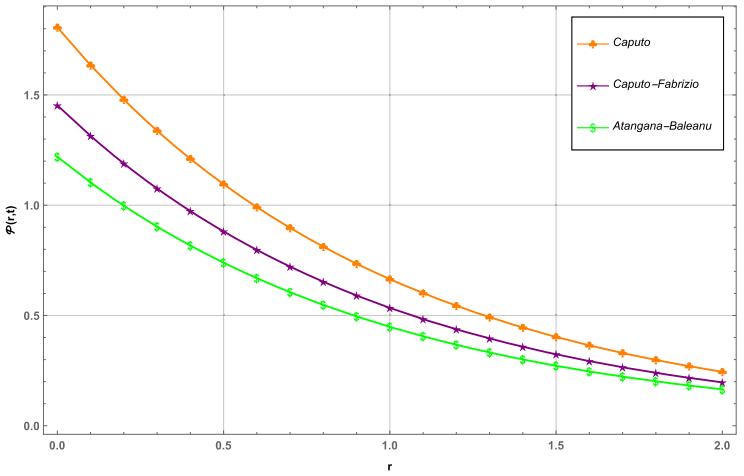


Fig. 5. Effect of Caputo, CF, and AB derivative approaches (Case 1) when $\delta = 0.24$, $t = 1$ and $l = -1$.

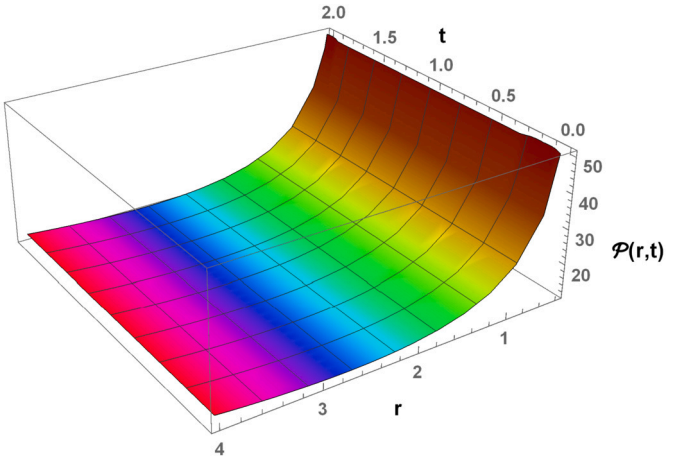
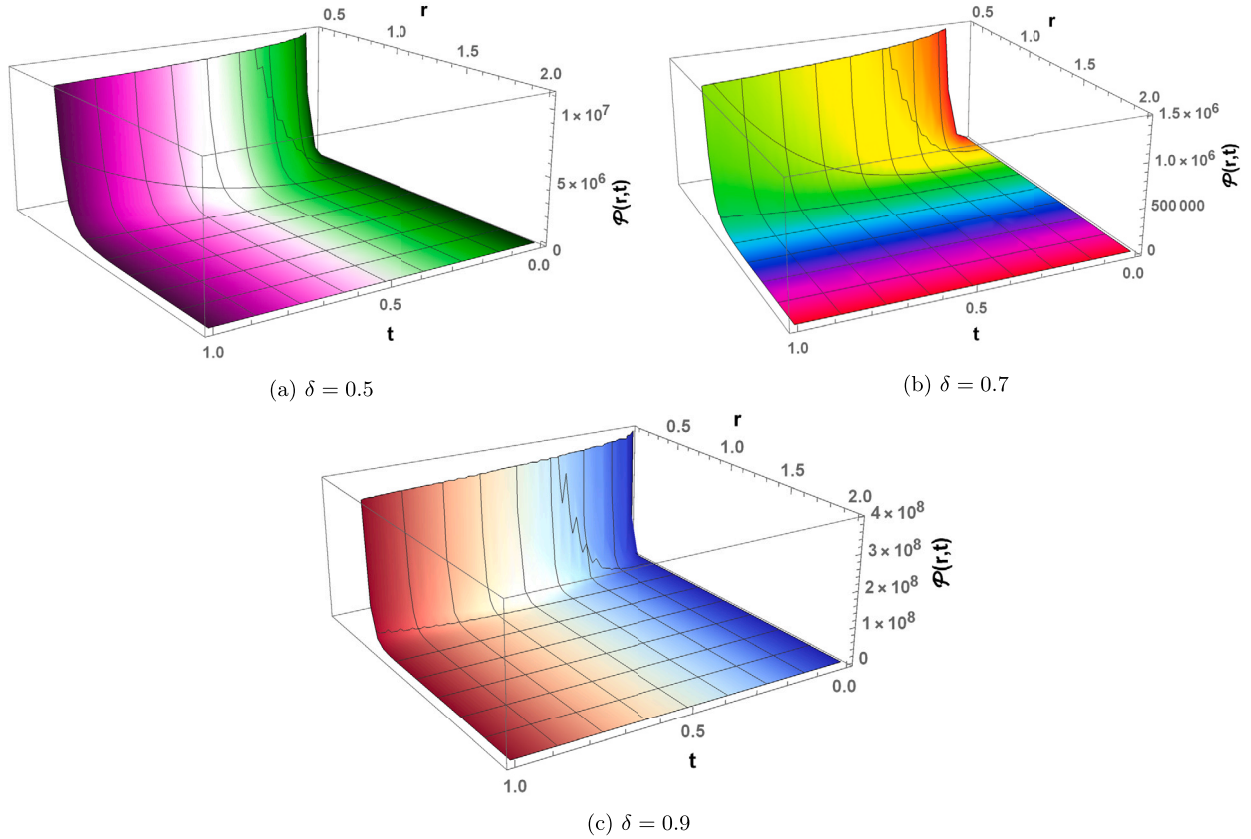


Fig. 6. 3D solution (Case 2) where $A = 20$ and $B = 0.5$.

3D depiction of cell concentration in Fig. 7a-7c at $\delta = 0.50, 0.70$, and 0.90 exhibit that the tumor quickly reduces in size with both position and time. Moreover, the tumor cells in a 2D diagram (see Fig. 8) with constant time and variable position, diminishes as the fractional parameter value rises. Fig. 9 demonstrates the impact of Caputo, CF, and AB derivatives on tumor cells. It is evident that CF derivative has lower tumor cells accumulation in comparison with Caputo and AB derivative.

7. Conclusion

The objective of this manuscript is the analysis of fractional cancer tumor model with different net killing rates. A hybrid methodology is proposed for obtaining new solutions. Fractional cancer tumor model is taken in three different scenarios related to killing rate of the tumor. Firstly (Case 1), killing rate is time dependent, then secondly (Case 2) it is dependent on position, and lastly (Case 3) it is solely dependent on the concentration of cells. The proposed algorithm provides series form approximate solutions for Case 1 and 3, while analytical solution is achieved in Case 2. Error estimation over the entire fractional domain is performed by finding residual errors numerically which proves legitimacy of the given method. The effect of varying fractional parameter value on the solution profile is analyzed graphically through 2D and 3D plots. Change in concentration of tumor cells is observed against position and time to determine the effectiveness in different killing rates. It is observed in all cases that killing rate therapy decreases the concentration of tumor cells and ultimately, they tend to zero. Graphical analysis of different fractional derivatives including Caputo, CF, and AB on the cell concentration shows similar effects. Hence, it is concluded that proposed algorithm is highly efficient and can be easily extended to other non-linear influential physical problems. Since in most cases homotopy based algorithms are not greatly productive for the solutions of exponential type functions, so in future work we will utilize the proposed methodology to tackle exponential differential systems arising in various fields of science and engineering.



(a) $\delta = 0.5$ (b) $\delta = 0.7$

(c) $\delta = 0.9$

Fig. 7. 3D solutions for different values of δ in Case 3 when σ = -2.

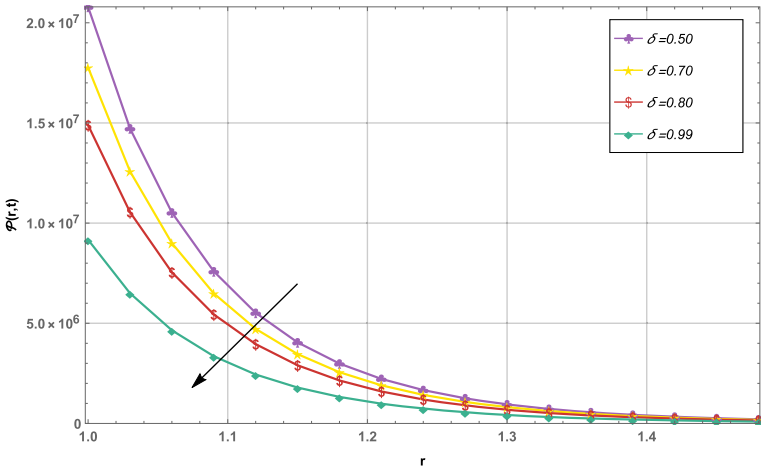


Fig. 8. Change in concentration of tumor cells with position r (Case 3) when t = 3 and σ = -2.5.

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CRediT authorship contribution statement

Mubashir Qayyum: Supervision, Conceptualization, Methodology, Formal analysis, Data curation. **Efaza Ahmad:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Mohamed R. Ali:** Supervision, Project administration, Investigation, Software, Resources, Funding acquisition.

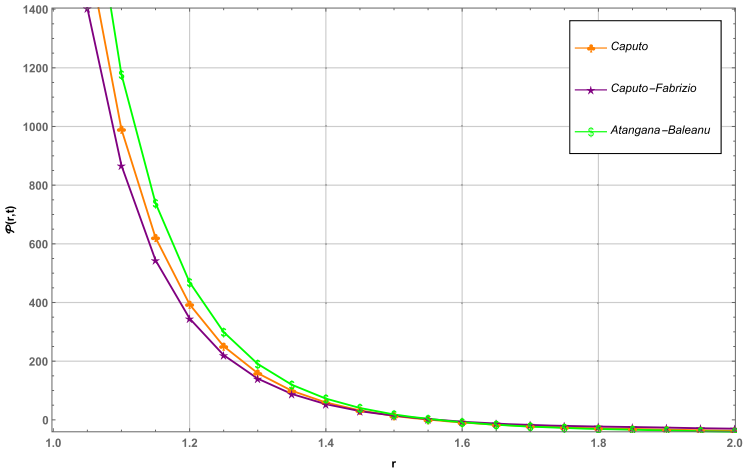

Fig. 9. Comparison of Caputo, CF, and AB derivative (Case 3) when $\delta = 0.24$, $t = 1$ and $\sigma = 0.1$.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data included in article/supp. material/referenced in article.

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