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Cancer Modeling by Fractional Derivative Equation and Chemotherapy Stabilizing

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Abstract
This paper discusses the theme of cancer modeling and the control problem of chemotherapy. Cancer spread is modeled by fractional derivative equation and asymptotically stabilized by chemotherapy law. The model is converted by fractional complex transform into a simple partial derivative equation and associated with a viability problem, and the set-valued analysis is used to make the converted model viable by the regulation law of the regulation map. The regulation law is used to give the stabilizing chemotherapy control for a specific model of the glioblastomas multiforme (GBM) tumor concentration.

Keywords: Chemotherapy, Fractional derivative equation, Viability theory
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1. Introduction and Problem Statement

Fractional Differential Equations (FDEs) have more tendency in recent years to be an indispensable tool in various fields of oncology, notably in the modeling cancer cells growth (1.1), or cancer spread in tissues (1.2), even cancer spread and response to chemotherapy (1.3). The model (1.1) accounts for the fact that cancer cells have a memory of past events, such as exposure to chemotherapy, which can affect their growth. The fractional order derivative represents this memory effect by incorporating information from previous time points into the current growth rate. Several studies have been conducted on the model (1.1), especially the Logistic model (1.1a-1.1f). Tudor Alinei-Poiana et al. offered in [1] the minimum Mean Square Error. Nasser Sweilam et al. used in [2] finite difference method and variational iteration method to solve (1.1a-1.1f), and compared numerical solutions with the exact solution. Nadir Djeddi et al. solved (1.1a-1.1f) in [3] by reproducing kernel Hilbert space method, and compared numerical solutions with the exact solution. Adivi Kanth and Neetu Garg investigated in [4] computational simulations for analytical solution of (1.1a-1.1f). Sadia Arshad et al. approximated in [5] solution of (1.1a-1.1f) using Simpson's $1/3$ rule. Najla Varalta et al. applied in [6] Fractional calculus to solve (1.1a-1.1f). Francisco Ariza-Hernandez et al. given in [7] Bayesian estimation to derivative order of (1.1a-1.1f). Mohamed Meabed Khader and Mohammed Babatin expressed in [8] the solution of (1.1a-1.1f) as truncated Laguerre series. While Tudor Alinei-Poiana et al. considerd in [1] formal power series to obtain the solution of Allee logistic model (1.1a-1.1g), and Subhas Khajanchi et al. used in [9] non-singular kernel in the Caputo fractional derivative (1.1c) and calculated implicitly the analytical solutions of (1.1a-1.1g), and Souheyla Debbouche given in [10] the implicit solution of (1.1a-1.1g). Whereas Changdev Jadhav et al. solved in [11] the exponential model (1.1a-1.1e) using Elzaki and Sumudu transform. Finally Mesfin Etefa et al. generalized in [12] the fractional differential Cauchy problem (1.1a-1.1b) by κ-Hilfer fractional derivative, investigated the existence and

uniqueness of mild solutions, and established the stability in the sense of Ulam-Hyers-Rassias. Yeliz Karaca aimed in [13] to point on the importance of computational complexity to obtain the fractional-order derivative with the least complexity for optimal solution to (1.1a-1.1b). The model (1.2) accounts for the fact that cancer cells can spread through tissues by both diffusion and growth. The fractional order derivative again represents the memory effect of the cells, as they may remember previous times when they encountered resistance to their spread and adjust their growth and movement accordingly. Several approaches have been performed on this model. Zainouba Chebana et al. established in [14] the existence and uniqueness of the solution by Faedo-Galerkin method. Hamzeh Husni Zureigat et al. implemented in [15] explicit finite difference scheme for solving (1.2). Zeliha Körpınar et al. investigated in [16] solutions by using residual power series method. Rania Saadeh et al. examined in [17] analytical solutions by using Laplace residual power series method. Rakhi Singh et al. applied in [18] homotopy decomposition method to determine the solution. Belal Batiha et al. developed in [19] new iterative method to address (1.2), and compared solutions with those established by variational iteration method and Adomian decomposition method, as well as the exact solution. Najma Ahmed et al. studied (1.2) in [20] using the Laplace transform and numerical inversion. Roghayeh Moallem Ganji et al. founded in [21] numerical technique on operational matrix, and presented the solution as an expansion of the Bernoulli polynomials. Mohammad Partohaghighi et al. compared in [22] solutions by fictitious time integration method and reproducing kernel Hilbert space method as well as the exact solution. Fashareena Mohd et al. solved (1.2) in [23] using Laplace Adomian decomposition method. Hemant Gandhi et al. performed in [24] fractional reduced differential transform method to obtain the solution. Vineet Srivastava et al. solved (1.2) in [25] by fractional reduced differential transform method. Olaniyi Iyiola and Fiazuddin Zaman used in [26] q-homotopy analysis method for (1.2) to obtain analytical solution. Andrew Omame and Fiazuddin Zaman analytically solved (1.2) in [27] via the zeroth order finite Hankel transform. Simon Gimnitz et al. presented in [28] a series solution of the model (1.2) with its convergence analysis.

- Cancer cells growth modeling

$$\frac{d^{\alpha}u(t)}{dt^{\alpha}} = f(u(t)), \tag{1.1a}$$

with the initial condition

$$u(0) = u_0, \tag{1.1b}$$

and $\frac{d^{\alpha}u(t)}{dt^{\alpha}}$ is the fractional derivative of order $\alpha \in \mathbb{R}_+$, to the cancer cells concentration $u(t) \in \mathbb{R}_+$ at time $t \in \mathbb{R}_+$, so in the Caputo sense

$$\begin{cases} \dfrac{1}{\Gamma(m-\alpha)} \displaystyle\int_0^t (t-s)^{m-\alpha-1} \frac{d^m u(s)}{dt^m}\,\mathrm{d}s & \text{if } m-1 < \alpha < m \\ \dfrac{d^m u(t)}{dt^m} & \text{if } \alpha = m, m \in \mathbb{N} \end{cases}, \tag{1.1c}$$

where

$$u \in \mathscr{C}^m(\mathbb{R}_+, \mathbb{R}_+) \text{ and } m = \lceil \alpha \rceil,$$

while Γ is the Euler's *Gamma* function defined by the improper integral

$$\Gamma(\alpha) = \int_0^{+\infty} t^{\alpha-1} \exp(-s)\,\mathrm{d}s. \tag{1.1d}$$

With the classical sub-models

  - Exponential model [1]

$$f(u) = au. \tag{1.1e}$$

  - Logistic model [1]

$$f(u) = au\left(1 - \left(\frac{u}{k}\right)^b\right). \tag{1.1f}$$

  - Allee logistic model in [29] by Iván Area and Juan Nieto

$$f(u) = u(1-u)(u-a). \tag{1.1g}$$

– Gompertz model [1]

$$f(u) = au\ln\left(\frac{b}{u+c}\right).$$

– Bertalanffy-Pütter model, in generalized and particular form [1]

$$\begin{cases} f(u) = pu^a - qu^b & \text{for } a \neq b \\ f(u) = pu^a - q\ln(u)u^a & \text{for } a = b \end{cases}.$$

- Cancer spread modeling

$$\frac{\partial^\alpha u(x,t)}{\partial t^\alpha} = \nabla\cdot(D(x)\nabla u(x,t)) + f(u(x,t)), \tag{1.2a}$$

with the initial condition

$$u(x,0) = u_0(x), \tag{1.2b}$$

and $\dfrac{\partial^\alpha u(x,t)}{\partial t^\alpha}$ is the fractional time derivative of order $\alpha \in \mathbb{R}_+$, to the cancer cells concentration $u(x,t) \in \mathbb{R}_+$ at position $x \in \Omega \subset \mathbb{R}^n$ and time $t \in \mathbb{R}_+$, so in the Caputo sense

$$\begin{cases} \dfrac{1}{\Gamma(m-\alpha)}\displaystyle\int_0^t (t-s)^{m-\alpha-1}\frac{\partial^m u(x,s)}{\partial t^m}\,\mathrm{d}s & \text{if } m-1 < \alpha < m \\ \dfrac{\partial^m u(x,t)}{\partial t^m} & \text{if } \alpha = m, m \in \mathbb{N} \end{cases},$$

where

$$u \in \mathscr{C}^{2,m}(\Omega\times\mathbb{R}_+, \mathbb{R}_+) \text{ and } m = \lceil\alpha\rceil,$$

while $D(x)$ is the diffusion coefficient and ∇ is the nabla operator

$$\nabla u(x,t) = \left(\frac{\partial u(x,t)}{\partial x_1}, \cdots, \frac{\partial u(x,t)}{\partial x_n}\right)^\top,$$

and $f(u(x,t))$ is the reaction term.

- Cancer spread modeling with response to chemotherapy

$$\frac{\partial^\alpha u(x,t)}{\partial t^\alpha} = \nabla\cdot(D(x)\nabla u(x,t)) + f(u(x,t), c(x,t)), \tag{1.3a}$$

with the initial condition

$$u(x,0) = u_0(x), \tag{1.3b}$$

and $c(x,t) \in \mathbb{R}_+$ is the chemotherapy concentration, and f is the reaction-control function.

The set-valued methods developed to stabilize cancer cells concentration, to Ordinary Differential Equations (ODEs) models by Khalid Kassara in [30], Khalid Kassara and Amine Moustafid in [31], Lahoucine Boujallal et al. in [32], and Amine Moustafid in [33, 34, 35, 36, 37, 38], and to Partial Differential Equations (PDEs) models by Amine Moustafid in [39], is the motivation to prolong further theses methods here onto the FDE models (1.3) and stabilize the cancer cells concentration $u(x,t)$ in the sense of the following control problem, and not limit studies to analyze the solutions of uncontrollable FDE models (1.2).

Problem 1.1. *Find a chemotherapy concentration $c(x,t)$, to stabilize the cancer cells concentration $u(x,t)$, subject to the FDE* (1.3) *and the asymptotic sense*

$$\lim_{t\to+\infty} u(x,t) = 0, \text{ a. e. } x \in \Omega. \tag{1.4}$$

This paper is sectioned as follows: Section Introduction and Problem Statement presented the general cancer model by the FDE (1.3), and associated the control Problem 1.1 by chemotherapy. Section Fractional Complex Transform and Viability Analysis converts the FDE (1.3) into PDE model, and corresponds a viability problem, and gives the control solution by regulation law of regulation map. Section Chemotherapy Application carries out the obtained results on a particular model.

2. Fractional Complex Transform and Viability Analysis

This section uses the fractional complex transform (2.1c) in Proposition 2.1, to turn the FDE (1.3a) subject to the control Problem 1.1, into the PDE (2.1a) subject to the viability problem (2.3) in Theorem 2.3, and characterizes the control solution as regulation law (2.8) of the regulation map (2.6) by Corollary 2.6 under Assumption 2.5 of [40] by Jean-Pierre Aubin and Hélène Frankowska, then uses Lemma 2.7 of [34] by Amine Moustafid, to express the regulation law (2.8) by the explicit formula (2.10) in Corollary 2.8.

2.1 Fractional complex transform

Proposition 2.1. *The FDE* (1.3a) *can be converted into the PDE*

$$\frac{\partial U(x,\tau)}{\partial \tau} = \nabla \cdot (D(x)\nabla U(x,\tau)) + f(U(x,\tau),C(x,\tau)), \tag{2.1a}$$

with the initial condition

$$U(x,0) = u_0(x), \tag{2.1b}$$

by the fractional complex transform in [41] by Ji-Huan He and Zheng-Biao Li and in [42] by Rabha Ibrahim

$$\tau = \frac{t^\alpha}{\Gamma(1+\alpha)}, \tag{2.1c}$$

where the function Γ *is defined by* (1.1d)*,*
while

$$U(x,\tau) = u(x,t), \tag{2.1d}$$

and

$$C(x,\tau) = c(x,t). \tag{2.1e}$$

Proof.

$$\begin{aligned}
\frac{\partial^\alpha u(x,t)}{\partial t^\alpha} &= \frac{\partial u(x,t)}{\partial \tau} \times \frac{\partial^\alpha \tau(t)}{\partial t^\alpha} \\
&= \frac{\partial U(x,\tau)}{\partial \tau} \times \frac{1}{\Gamma(1+\alpha)} \times \frac{\partial^\alpha t^\alpha}{\partial t^\alpha} \\
&= \frac{\partial U(x,\tau)}{\partial \tau} \times \frac{1}{\Gamma(1+\alpha)} \times \Gamma(1+\alpha) \\
&= \frac{\partial U(x,\tau)}{\partial \tau}.
\end{aligned}$$

□

2.2 Viability problem

Definition 2.2. *Let the subset*

$$K = \{U \in L^2(\Omega), U \geq 0 \text{ and } \psi(U) \leq 0, \text{ a. e. } x \in \Omega\}, \tag{2.2a}$$

where the function ψ *expression is*

$$\psi(U)(x,\tau) = U(x,\tau) - u_0(x)\exp(-\tau). \tag{2.2b}$$

Theorem 2.3. *Let the initial state* $u_0 \in L^2(\Omega)$*. If the subset K is viable under* (2.1)*, in the sense that there exists a solution U such that*

$$\forall \tau \in [0,+\infty), U(\cdot,\tau) \in K, \tag{2.3}$$

then

$$\lim_{\tau \to +\infty} U(x,\tau) = 0, \text{ a. e. } x \in \Omega, \tag{2.4}$$

and by consequent u (2.1d) *is solution to the Problem 1.1.*

Proof.
By (2.2b) and (2.1b), a. e. $x \in \Omega$

$$\begin{aligned}\psi(U)(x,0) &= U(x,0) - u_0(x)\exp(0)\\ &= u_0(x) - u_0(x)\\ &= 0,\end{aligned}$$

then $u_0 \in K$.
By (2.2a) and (2.2b), a. e. $\tau \in [0,+\infty)$

$$\begin{aligned}U \in K &\implies \psi(U)(x,\tau) \leq 0\\ &\implies U(x,\tau) - u_0(x)\exp(-\tau) \leq 0\\ &\implies U(x,\tau) \leq u_0(x)\exp(-\tau)\\ &\implies \lim_{\tau\to+\infty} U(x,\tau) = 0. \quad (2.4)\end{aligned}$$

By (2.1d), a. e. $x \in \Omega$

$$\begin{aligned}\lim_{t\to+\infty} u(x,t) &= \lim_{\tau\to+\infty} U(x,\tau)\\ &= 0.\end{aligned}$$

□

Remark 2.4. *$u_0(x)$ is supposed regular enough (for example upper bounded) so that $u_0(x)\exp(-\tau)$ admits null limit 0.*

2.3 Set-valued analysis

Assumption 2.5. *The function f is continuous affine and linear growth to C*

$$\sup_U |f(U,C)| \leq \varsigma(|C|+1). \tag{2.5}$$

Corollary 2.6. *[40, Corollary 13.4.2] The subset K (2.2) is viable under (2.1) when and only when the regulation map*

$$R_K(U) = \{C \in L^2(\Omega), \nabla\cdot(D\nabla U) + f(U,C) \in T_K(U)\}, \tag{2.6}$$

where $T_K(U)$ is the contingent cone, enjoys non-emptiness property, in the sense that

$$\forall U \in K, R_K(U) \neq \emptyset, \tag{2.7}$$

and viable solution U is given by regulation law C

$$C(x,\tau) \in R_K(U(x,\tau)),\ a.e.\ (x,\tau) \in \Omega\times[0,+\infty). \tag{2.8}$$

Lemma 2.7. *[34, Lemma 3.3] The belonging of directions $\overline{U}$ in $T_K(U)$ is characterized by both inequalities*

$$\begin{cases} \overline{U} \geq 0 \text{ if } \quad U(x,\tau) = 0\\ D\psi(u(x,\tau))\overline{U} \leq 0 \text{ if } \psi(U(x,\tau)) = 0 \end{cases}, \tag{2.9}$$

where D denotes the differential operator.

Corollary 2.8. *The regulation law C (2.8) of the regulation map R_K is characterized by*

$$\nabla\cdot(D(x)\nabla U(x,\tau)) + f(U(x,\tau),C(x,\tau)) \geq 0, \tag{2.10a}$$

if

$$U(x,\tau) = 0,$$

and

$$D\psi(U(x,\tau))(\nabla\cdot(D(x)\nabla U(x,\tau)) + f(U(x,\tau),C(x,\tau)) \leq 0, \tag{2.10b}$$

if

$$\psi(U(x,\tau)) = 0.$$

Proof. By definition of the regulation map R_K (2.6)

$$C(x,\tau) \in R_K(U(x,\tau)),$$

if and only if

$$\nabla \cdot (D(x)\nabla U(x,\tau)) + f(U(x,\tau),C(x,\tau)) \in T_K(U(x,\tau)),$$

whence (2.10) by the characterization (2.9). □

3. Chemotherapy Application

To give an illustrative example of the theoretical results obtained in section 2, and their concordance with the numerical results, this section considers from [23] the following sub-model (3.1) of the general model (1.3) in section 1.

$$\frac{\partial^\alpha u(x,t)}{\partial t^\alpha} = \nabla \cdot (D(x)\nabla u(x,t)) + \rho u(x,t)\left(1 - \frac{u(x,t)}{u^{\max}}\right) - c(x,t)u(x,t), \tag{3.1a}$$

with the Gaussian initial condition

$$\begin{cases} u(x,0) = \dfrac{1}{\sqrt{2\pi}\varepsilon} \exp\left(-\dfrac{1}{2}\left(\dfrac{x-x_0}{\varepsilon}\right)^2\right), \\ x \in (0,50), x_0 = 25\,\text{mm}, \varepsilon = 0.01, \end{cases} \tag{3.1b}$$

which verifies the hypothesis of the Remark 2.4 on the initial state u_0.
$D(x)$ is the diffusion coefficient

$$D(x) = \begin{cases} 0.13\,mm^2/day, \text{if } 0\,mm \le x \le 7.2\,mm \text{ (grey region)}, \\ 0.65\,mm^2/day, \text{if } 7.2\,mm \le x \le 42.5\,mm \text{ (white region)}, \\ 0.13\,mm^2/day, \text{if } 42.5\,mm \le x \le 50\,mm \text{ (grey region)}, \end{cases}$$

ρ is the proliferation rate

$$\rho = 0.012\,day^{-1},$$

$u^{\max}$ is the carrying capacity

$$u^{\max} = 62.5\,\text{cells}/\text{mm}^3,$$

f is the continuous affine function

$$f(U,C) = \rho U\left(1 - \frac{U}{u^{\max}}\right) - CU,$$

and linear growth to C (2.5)

$$\sup_U |f(U,C)| \le u^{\max}(|C|+1),$$

which verifies the hypothesis of the Assumption 2.5 on the function f.

The *pdepe* function of MATLAB® programming solves the converting PDE of the FDE (3.1), while the function *quadprog* minimizes C under the constraints (2.10a) and (2.10b) to calculate the regulation law (2.8). The following figures illustrate the numerical results.

- Figure 3.1 represents uncontrolled cancer cells concentration $u(x,t)$ which seems diverging of 0.
- Figure 3.2 represents controlled cancer cells concentration $u(x,t)$, which seems converging to 0 in accordance with (1.4).
- Figure 3.3 represents the comparison between uncontrolled and controlled cancer cells concentrations.
- Figure 3.4 represents chemotherapy concentration $c(x,t)$ transformed by (2.1e), defined by the regulation law (2.8) of the regulation map (2.6) and characterized by (2.10), used to control cancer cells concentration $u(x,t)$.

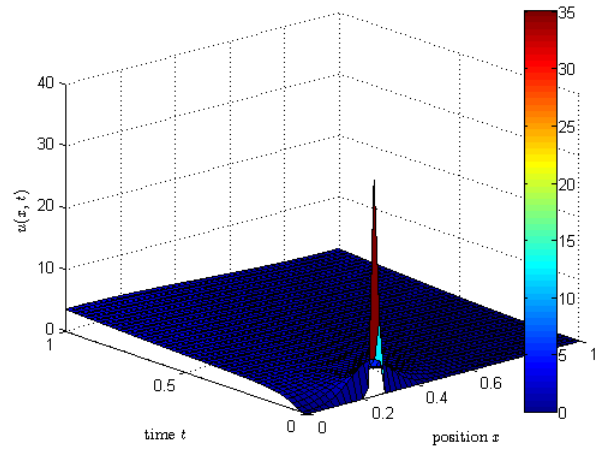

Figure 3.1. Cancer cells concentration $u(x,t)$ without chemotherapy.

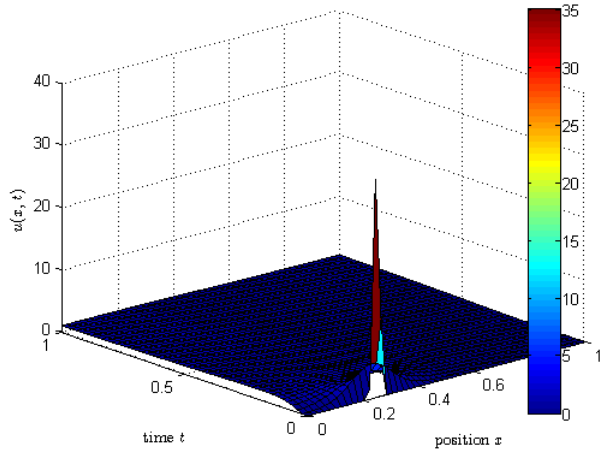

Figure 3.2. Cancer cells concentration $u(x,t)$ with chemotherapy concentration in Figure 3.4.

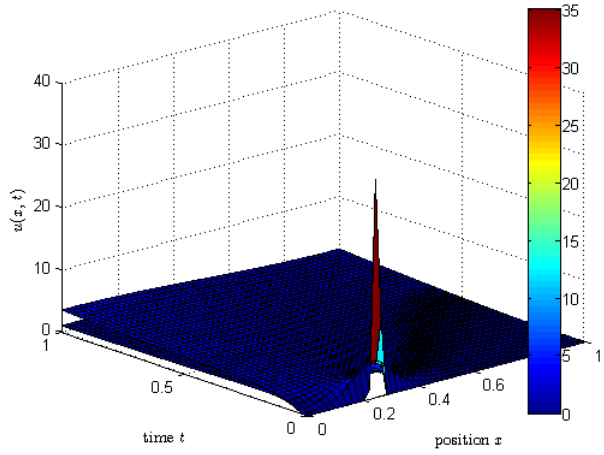

Figure 3.3. Cancer cells concentration $u(x,t)$ without chemotherapy in Figure 3.1 and with chemotherapy concentration in Figure 3.2.

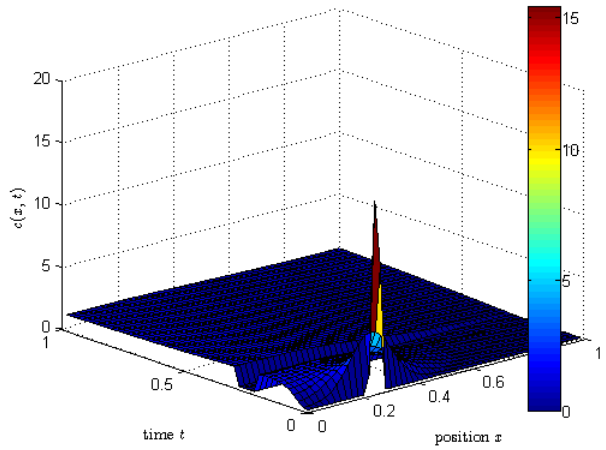

Figure 3.4. Chemotherapy concentration $c(x,t)$ transformed by (2.1e), defined by (2.8) of (2.6) and characterized by (2.10).

4. Conclusion

This paper solved the control Problem 1.1 of the cancer cells concentration $u(x,t)$. The fractional complex transform (2.1c) is used to translate the Problem 1.1 into the viability problem 2.3, which is approached by the set-valued analysis tool. The simulated FDE model (3.1) in the Figure 3.2, is stabilized in the sense (1.4) by the simulated chemotherapy concentration $c(x,t)$ in the Figure 3.4, which is transformed by (2.1e) and defined by the regulation law (2.8) of the regulation map (2.6) and characterized by (2.10). The prolonged set-valued method based on viability theory, conceives here chemotherapy protocol $c(x,t)$ at position x and time t, and on feedback state $u(x,t)$ dependence for any initial state $u_0 \in L^2(\Omega)$ in (1.3b), which is able to asymptotically stabilize the cancer cells concentration $u(x,t)$.

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References

[1] T. Alinei-Poiana, E. Dulf, L. Kovacs, *Fractional calculus in mathematical oncology*, Sci. Rep., **13** (2023), 10083.

[2] N. Sweilam, M. Khader, A. Mahdy, *Numerical studies for solving fractional-order logistic equation*, Int. J. Pure Appl. Math., **78** (2012), 1199-1210.

[3] N. Djeddi, S. Hasan, M. Al-Smadi, S. Momani, *Modified analytical approach for generalized quadratic and cubic logistic models with Caputo-Fabrizio fractional derivative*, Alex. Eng. J., **59** (2020), 5111-5122.

[4] A. Kanth, N. Garg, *Computational simulations for solving a class of fractional models via Caputo-Fabrizio fractional derivative*, Procedia Comput. Sci., **125** (2018), 476-482.

[5] S. Arshad, I. Saleem, A. Akgül, J. Huang, Y. Tang, S. Eldin, *A novel numerical method for solving the Caputo-Fabrizio fractional differential equation*, AIMS Math., **8** (2023), 9535-9556.

[6] N. Varalta, A. Gomes, R. Camargo, *A prelude to the fractional calculus applied to tumor dynamic*, TEMA Tend. Mat. Apl. Comput., **15** (2014), 211-221.

[7] F. Ariza-Hernandez, M. Arciga-Alejandre, J. Sanchez-Ortiz, A. Fleitas-Imbert, *Bayesian derivative order estimation for a fractional logistic model*, Mathematics, **8** (2020), 109.

[8] M. Meabed Khader, M. Babatin, *Others on approximate solutions for fractional logistic differential equation*, Math. Probl. Eng., **2013** (2013).

[9] S. Khajanchi, M. Sardar, J. Nieto, *Application of non-singular kernel in a tumor model with strong Allee effect*, Differ. Equ. Dyn. Syst., (2022), 1-6.

[10] S. Debbouche, *Implicit solution for logistic Caputo-Fabrizio fractional differential equation with Allee effect*, J. Fract. Calc. Nonlinear Syst., **4** (2023), 1-7.

[11] C. Jadhav, T. Dale, D. Chinchane, *A method to solve ordinary fractional differential equations using Elzaki and Sumudu transform*, J. Fract. Calc. Nonlinear Syst., **4** (2023), 8-16.

[12] M. Etefa, G. Guerekata, P. Ngnepieba, O. Iyiola, *On a generalized fractional differential Cauchy problem*, Malaya J. Mat., **11** (2023), 80-93.

[13] Y. Karaca, *Computational complexity-based fractional-order neural network models for the diagnostic treatments and predictive transdifferentiability of heterogeneous cancer cell propensity*, Chaos Theory Appl., **5** (2023), 34-51.

[14] Z. Chebana, T. Oussaeif, A. Ouannas, *Others solvability of Dirichlet problem for a fractional partial differential equation by using energy inequality and Faedo-Galerkin method*, Innovative J. Math. (IJM), **1** (2022), 34-44.

[15] H. Husni Zureigat, M. Al-Smadi, A. Al-Khateeb, S. Al-Omari, S. Alhazmi, *Numerical solution for fuzzy time-fractional cancer tumor model with a time-dependent net killing rate of cancer cells*, Int. J. Environ. Res. Public Health., **20** (2023), 3766.

[16] Z. Körpinar, M. Inc, E. Hınçal, D. Baleanu, *Residual power series algorithm for fractional cancer tumor models*, Alex. Eng. J., **59** (2020), 1405-1412.

[17] R. Saadeh, A. Qazza, K. Amawi, *A new approach using integral transform to Solve cancer models*, Fractal Fract., **6** (2022), 490.

[18] R. Singh, V. Gupta, J. Mishra, *An investigation of the complexities of a malignant tumor's fractional-order mathematical model*, Ann. Comput. Sci. Inf. Syst., **33** (2022), 207-211.

[19] B. Batiha, A. Al-khateeb, H. Zureigat, *Improving numerical solutions for the generalized Huxley equation: The new iterative method (NIM)*, Appl. Math., **17** (2023), 423-427.

[20] N. Ahmed, N. Shah, S. Taherifar, F. Zaman, *Memory effects and of the killing rate on the tumor cells concentration for a one-dimensional cancer model*, Chaos, Solitons & Fractals, **144** (2021), 110750.

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

[22] M. Partohaghighi, A. Akgül, E. Akgül, N. Attia, M. Sen, M. Bayram, *Analysis of the fractional differential equations using two different methods*, Symmetry, **15** (2023), 65.

[23] F. Mohd, H. Sulaiman, N. Alias, *Modified Swanson's equation to detect the growth of glioblastomas multiforme (GBM) tumour*, Int. J. Adv. Res. Engineering Innovation, **3** (2021), 1-18.

[24] H. Gandhi, A. Tomar, D. Singh, *A predicted mathematical cancer tumor growth model of brain and its analytical solution by reduced differential transform method*, TCCE 2019, (2021), 203.

[25] V. Srivastava, S. Kumar, M. Awasthi, B. Singh, *Two-dimensional time fractional-order biological population model and its analytical solution*, Egypt. J. Basic Appl. Sci., **1** (2014), 71-76.

[26] O. Iyiola, F. Zaman, *A fractional diffusion equation model for cancer tumor*, AIP Adv., **4** (2014), 107121.

[27] A. Omame, F. Zaman, *Analytic solution of a fractional order mathematical model for tumour with polyclonality and cell mutation*, Partial Differ. Equ. Appl. Math., (2023), 100545.

[28] S. Gimnitz, B. Bira, D. Zeidan, *Optimal systems, series solutions and conservation laws for a time fractional cancer tumor model*, Chaos, Solitons & Fractals, **169** (2023), 113311.

[29] I. Area, J. Nieto, *On the fractional Allee logistic equation in the Caputo sense*, Ex. Countex., **4** (2023), 100121.

[30] K. Kassara, *A unified set-valued approach to control immunotherapy*, SIAM J. Control Optim., **48** (2009), 909-924.

[31] K. Kassara, A. Moustafid, *Angiogenesis inhibition and tumor-immune interactions with chemotherapy by a control set-valued method*, Math. Biosci., **231** (2011), 135-143.

[32] L. Boujallal, M. Elhia, O. Balatif, *A novel control set-valued approach with application to epidemic models*, J. Appl. Math. Comput., **65** (2021), 295-319.

[33] A. Moustafid, *General chemotherapy protocols*, J. Appl. Dynamic Syst. Control., **4** (2021), 18-25.

[34] A. Moustafid, *Set-valued control of cancer by combination chemotherapy*, J. Math. Sci. Model., **6** (2023), 7-16.

[35] A. Moustafid, *Viability control of chemo-immunotherapy and radiotherapy by set-valued analysis*, Int. J. Inform. Appl. Math., **6** (2023), 40-56.

[36] A. Moustafid, *Set-valued analysis of anti-angiogenic therapy and radiotherapy*, Math. Modelling Numer. Simul. Appl., **2** (2022), 187-196.

[37] A. Moustafid, *General anti-angiogenic therapy protocols with chemotherapy*, Int. J. Math. Model. Comput., **11** (2021).

[38] A. Moustafid, *Feedback protocols for anti-angiogenic therapy in the treatment of cancer tumors by chemotherapy*, Int. J. Optim. Appl., **2** (2022), 17-24.

[39] A. Moustafid, *Set-valued stabilization of reaction-diffusion model by chemotherapy and or radiotherapy*, Fun. J. Math. Appl., **6** (2023), 147-156.

[40] J. P. Aubin, H. Frankowska, *Set-valued Analysis*, Springer Science & Business Media, 2009.

[41] J. H. He, Z. B. Li, *Converting fractional differential equations into partial differential equations*, Therm. Sci., **16** (2012), 331-334.

[42] R. Ibrahim, *Fractional complex transforms for fractional differential equations*, Adv. Difference Equ., **2012** (2012), 1-12.