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MATHEMATICAL MODELLING OF THE IMPACT OF CHEMOTHERAPY ON THE STATE OF A CANCEROUS TUMOR BASED ON FRACTIONAL CALCULUS

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Abstract. The article is dedicated to constructing difference approximations of fractal operators in a mathematical model of the impact of chemotherapy on the state of a cancerous tumor, based on fractional calculus using the Caputo derivative. A mathematical model of stem cells and chemotherapy is presented. Numerical algorithms for implementing fractional-order mathematical models have been developed using the Atangana-Toufik method. The UML diagram of the software application and its development process are described. The impact of fractal characteristics (long-term memory) of chemotherapy on the state of a cancerous tumor is analysed. The presence of a fractional-order time derivative as a parameter of the solutions provides important information for predicting the effects of chemotherapy on the tumor's state.

Keywords: fractional order model, fractional operators, atangana–toufik method, cancer tumor python, R language.

Introduction

The investigation of interactions between immune cells and tumor cells seeks to elucidate how the immune system engages with cancer cells to develop more effective treatments for oncological diseases. The study of these interactions necessitates the use of diverse methodologies to examine the complexity of these relationships [1,2]. A significant challenge arises when cancer cells attempt to divide and proliferate, sustaining themselves by forming new blood vessels, a process known as angiogenesis. In doing so, the tumor compromises surrounding healthy tissues and may disseminate throughout the body via a process referred to as metastasis.

Mathematical modelling plays a pivotal role in forecasting tumor progression and evaluating the efficacy of therapeutic interventions based on available data concerning the behaviour of immune and cancer cells. The modelling of the metastatic process represents a sophisticated scientific approach, enabling the exploration of the mechanisms by which cancer cells spread from the primary tumor to other organs and tissues. This is a critical phase in cancer research, as metastasis constitutes the principal cause of cancer-related mortality. To model metastasis, various experimental, computational, and mathematical techniques are employed, alongside both in vitro and in vivo models.

Mathematical models are utilised to describe and predict the spread of metastases. These models often involve differential equations that characterise the growth rate of the primary tumor, cellular invasion, migration, colonisation, and the expansion of metastatic sites. The development of such models is also integral to the creation of computer simulation systems, which enable the construction of virtual tumor

models. These models are instrumental in assessing the potential efficacy of therapeutic interventions and in studying the interactions between tumor cells and the tumor microenvironment.

Thus, metastasis modelling is a multifaceted approach that combines cell-level experiments, innovative mathematical models, and computer simulations. This comprehensive strategy not only enhances the understanding of the mechanisms driving cancer dissemination but also facilitates the development of therapeutic strategies aimed at preventing the progression of metastasis.

Fractal models are crucial for simulating complex processes such as metastasis, due to their ability to describe the dynamics of systems with memory and multi-scale time layers, which are characteristic of biological systems, particularly in tumor growth and metastasis spread.

Fractional calculus plays a significant role in modelling the process of metastasis, as it allows for the consideration of the intricate dynamics of biological processes, such as the dissemination of tumor cells and their interaction with the organism. One of the key advantages of fractional derivatives is their ability to model processes with "memory," accounting for all previous states of the system. This is particularly important for complex phenomena like metastasis [3]. Conventional mathematical models often fail to capture all influences that accumulate over time, whereas fractional calculus can provide more accurate predictions regarding tumor progression and response to treatment.

The use of fractional derivatives enables the modelling of anomalous diffusion processes in tumor cells within tissues, accounting for variations in their movement when the cells do not follow classical Brownian diffusion laws. This is characteristic of the spread of cancer cells through blood or lymphatic vessels [4]. Moreover, fractional models can incorporate information on pharmacokinetics and pharmacodynamics, allowing for the prediction of the efficacy of various treatment methods, such as chemotherapy or immunotherapy, and facilitating personalised approaches in medicine.

Research in this field encompasses the application of fractional calculus to model the evolution of cancer cells and to predict treatment efficacy [5]. This article presents an overview of the application of fractional calculus in cancer research, particularly in the modelling of tumor growth and metastasis spread. Mathematical models that account for the complex dynamics of tumor processes and their interactions with the microenvironment are considered. For instance, the development of models to study metastases in bone tissues using fractional derivatives allows for a more precise assessment of therapy's impact on various types of cancer. This approach enables the tailoring of individual treatment protocols for each patient, considering the specific progression of their disease. Thus, the development of fractal mathematical models that can aid in predicting chemotherapy efficacy and optimising treatment regimens is of great importance.

Problem Statement

The object of the study is the process of chemotherapy's impact on the state of a cancerous tumor. The subject of the study is the mathematical and software tools for modelling the effect of chemotherapy on the state of a cancerous tumor using fractal methods.

Aim of the work: The construction of a mathematical model using fractal analysis methods and the development of software-algorithmic support to assess the impact of chemotherapy on the state of a cancerous tumor. Objective: To build a mathematical model using fractal analysis methods and to develop software and algorithmic support for the effect of chemotherapy on the state of a cancerous tumor.

The achievement of the objective includes the following tasks. Analysis of fractal mathematical models of the effect of chemotherapy on the state of a cancerous tumor, taking into account long-term memory. Analysis of the mathematical model of the effect of chemotherapy on the state of a breast cancer tumor, taking into account the effect of long-term memory. Construction of difference approximations of fractal operators of the model. Development of algorithmic software. Software implementation of the model.

Validation of the mathematical model. Analysis of the influence of the fractal characteristic (long-term memory) of chemotherapy on the state of a cancerous tumor.

Practical significance. The synthesised mathematical models and software-algorithmic tools can assist physicians and researchers in predicting the effectiveness of chemotherapy for individual cancer

patients. This can aid in selecting an optimal treatment regimen and improving treatment outcomes. Moreover, the analysis of the tumor's fractal characteristics and its changes under the influence of chemotherapy may reveal new patterns and features that will contribute to the further development of therapeutic strategies. Thus, this work can help enhance the efficacy of chemotherapy and improve the quality of life for cancer patients.

Review of Modern Information Sources on the Subject of the Paper

Chemotherapeutic drugs are cycle-specific, meaning they destroy cells at specific phases of their cycles. Some drugs act during the gap period (G1 phase) and the synthetic period (replication phase, S). Other drugs act during mitosis (M phase) or the second gap period (G2 phase). In the paper [10] studied mathematical linear and nonlinear models of cycle-specific chemotherapy, where he examined the advantages of shorter dosing periods. A mathematical model with constraint equations, describing the effect of drugs on sensitive normal tissue, based on impulse and piecewise-continuous chemotherapeutic effects, was explored in paper [13]. They determined the optimal period required for maximum tumor reduction.

Panetta developed a mathematical model that accounts for treatment-sensitive cells (proliferating cells) and quiescent cells (G0 phase), which are resistant to treatment. Model parameters were evaluated for breast cancer, ovarian cancer, and bone marrow. Liu [12] and others studied the effect of an M-phase-specific drug on cancer progression, incorporating the G0 quiescent phase and the immune response. In their model, the authors included a time delay for transitioning through interphase and assumed that immune cells interact with all cancer cells. The authors found that the dynamics of the G0 phase dictate the overall cancer dynamics.

In papers [11, 13] investigated a cell-cycle-specific chemotherapy model by reformulating the model's differential equations as time-dependent Schrödinger equations. The effect of chemotherapy on cyclic tumor cells was treated as an exponentially decaying function, and the potential function was modelled as a Morse-type potential. Through numerical modelling [14] developed a model of interactions between tumor cells, immune system cells, and drug response systems.

In the paper [15] presented a set of mathematical models on cancer cell plasticity, specifically the process by which, due to genetic and epigenetic changes, cancer cells survive in hostile environments and migrate to more favourable ones, contributing to tumor growth and invasion. In paper [16] developed a mathematical model to investigate the effects of toxic drugs on tumor growth to achieve more effective chemotherapy. In paper [17] formulated a mathematical model to describe radiovirotherapy, a combination of virotherapy with radiation, used to eliminate tumors when virotherapy alone is insufficient. This model is based on population dynamics, encompassing the key elements of radiovirotherapy. The authors explored the existence of equilibrium points associated with partial/complete cure and therapy failure.

Mathematical models described by ordinary differential equations, algebraic equations, and partial differential equations used to characterize tumor burden dynamics have been presented by the paper [18] . The authors also discussed stochastic and deterministic models of tumor resistance evolution and highlighted the possibility of developing a new model that includes both tumor dynamics and the evolution of resistance.

Other researchers, such as Wang and Schattler [19], considered cancer chemotherapy as an optimal control problem. They created a mathematical model to find optimal conditions under which the tumor size and side effects of chemotherapy can be minimized over a certain treatment period.

Additionally, a mathematical model was developed to study the impact of immunotherapy, chemotherapy, and their combinations, as well as vaccine therapy on the immune response against cancer. This model, proposed by the paper [20], allows for the analysis of vaccine therapy effectiveness depending on tumor size, immune system status, and the body's response to vaccination. The effect of vaccine therapy was considered as a perturbing parameter in the model.

Objectives and Problems of Research

Since most biological systems possess memory or after-effects—such as the delay associated with the incubation period when carriers become infectious—modeling biological systems using fractional differential equations is more advantageous than classical modeling, which neglects memory effects. Recently, various fractional-order operators (Riemann-Liouville, Caputo, Caputo-Fabrizio, Atangana-Baleanu, etc.) have been used in the mathematical modeling of processes that have "memory" and multilayered time scales, which is characteristic of tumors and their interaction with chemotherapy. For accurate modeling using fractional differential equations, it is necessary to define the order of the fractional derivative, which can vary depending on various factors (type of tumor, state of the microenvironment, individual responses to therapy). Choosing this parameter is a complex task and requires additional experimental data. This work is also dedicated to the software implementation of algorithms using fractal operators.

Main Material Presentation

Formulation of the Fractal Mathematical Model

The mathematical framework of fractional differentiation includes fractional derivatives, which generalise ordinary derivatives to non-integer orders. Fractional derivatives are initially divided into two main types. Those with a singular kernel include the Riemann-Liouville (RL) and Caputo derivatives [6]. One of the most widely used types of fractional derivatives is the Caputo derivative [6]. It reflects the contribution of previous values of the function and its derivative in the computation of the fractional derivative. The Caputo kernel $\kappa(t,\alpha)$ is employed in the formula for calculating the Caputo derivative:

$$\left({}^{c}D_{t}^{\alpha}\psi\right)(t)=\kappa(t,\alpha)*\dot{\psi}(t)=\int_{0}^{t}\kappa(t-\tau,\alpha)\dot{\psi}(\tau)d\tau\,, \tag{1}$$

where $\dot{\psi}(\tau)$ - the ordinary derivative of a function $\psi(t)$ and for T > 0 is differentiable by ψ: $[0,T]\to C$.

The Caputo kernel is defined as follows:

$$\kappa(t,\alpha)=\begin{cases}t^{-\alpha}/\Gamma(1-\alpha),0\le\alpha<1\\ \delta(t),\alpha=1\end{cases}, \tag{2}$$

where Γ(·) indicates the gamma function, and δ(·) represents the Dirac delta function.

The derivative of $N(t)$ with respect to the Liouville-Caputo operator of order r is defined by the formula:

$${}_{0}^{C}D_{t}^{r}N(t)=\frac{1}{\Gamma(q-r)}\int_{0}^{t}(t-\delta)^{q-r-1}N^{r}(\delta)d\delta,t>0\,, \tag{3}$$

where $q-1<r\le q,q\in\mathrm{N}$.

For $N:R^{+}\to R$ and $r\in(0,1)$ the Riemann-Liouville fractional integral is defined as:

$${}_{0}^{RL}I_{t}^{r}N(t)=\frac{1}{\Gamma(r)}\int_{0}^{t}(t-\delta)^{r-1}N(\delta)d\delta,t>0\,, \tag{4}$$

In this work, we use the mathematical model [2], which considers three populations: tumor cells T(t), effector cells of the immune system E(t), stem cells S(t) and the concentration of the chemotherapeutic drug M(t).

We express the mathematical model [2] using the Liouville-Caputo fractional derivative:

$$\begin{cases} {}_0^C D_t^\alpha S(t) = \gamma_1 S(t) = k_S M(t) S(t) \\ {}_0^C D_t^\alpha E(t) = a - \mu E(t) + \dfrac{p_1 E(t) S(t)}{(S(t)+1)} - p_2 \big(T(t)+M(t)\big) E(t) \\ {}_0^C D_t^\alpha T(t) = r(1-bT(t))T(t) - \big(p_3 E(t) + k_T M(t)\big) T(t) \\ {}_0^C D_t^\alpha M(t) = -\gamma_2 M(t) + V(t) \end{cases}, \tag{5}$$

with initial conditions:

$S_0(t) = S(0), E_0(t) = E(0), T_0(t) = T(0), M_0(t) = M(0),$

where $M(t)$ is the concentration of the chemotherapeutic drug, $E(t)$ is the concentration of effector cells, $T(t)$ - is the concentration of tumor cells, $S(t)$ is the concentration of stem cells, γ_1 is the decay rate of stem cell concentration, k_s is the fraction of stem cells killed by chemotherapy, α is the rate of effector cell production, μ is the natural death rate of effector cells, b is the carrying capacity related to dead cells, p_1 is the maximum proliferation rate of effector cells, r is the growth rate of tumor cells, p_2 is the rate at which effector cells and chemotherapy kill tumor cells, k_t is the fraction of tumor cells killed by chemotherapy, p_3 is the decay rate of tumor cells killed by effector cells, γ_2 is the decay rate of the chemotherapeutic drug, and $V(t)$ represents the time-dependent external influx of the chemotherapeutic drug. Other characteristics and their interrelations are provided in [7].

In model (5), the first equation reflects the interaction between stem cells and the chemotherapeutic drug, acknowledging the ability of stem cells to transform into specific cells cultivated from them. They lose concentration over time at a rate γ_1. Additionally, chemotherapy negatively affects the concentration of stem cells at a rate k_s. In the second equation, effector cells have a constant production rate $\alpha = \alpha_1 + \alpha_2$; where α_1 s the natural production rate of effector cells and α_2 is the rate of effector cell production from the transformation of stem cells. The second term represents the mortality rate, which is proportional to the effector cell population. In the third equation, the first term is the growth rate of tumor cells, while the second term represents the decay of tumor cells due to interaction with effector cells and the chemotherapeutic drug at rates p_3, and k_T respectively. The fourth equation describes the rate of change of the concentration of the chemotherapeutic drug.

Finite Difference Approximations of Fractal Operators

Since the given mathematical model is nonlinear, obtaining an exact solution may be difficult. Therefore, we will use finite difference approximations of the fractal operators of model (5) based on the Atangana-Toufik scheme [8]. Additionally, the fundamental theorem of fractional calculus [9] can be applied at a given point $t = t_{j+1}, j = 0,1,2,...$, and a two-step Lagrange polynomial interpolation [4,5] can be utilized within the interval $[t_m, t_{m+1}]$. Then, the function $f(\theta, y(\theta))$ can be approximated within the interval $[t_m, t_{m+1}]$

$$g_{j+1} = g_0 + \frac{1}{\Gamma(\alpha)} \sum_{m=0}^{j} \left(\frac{f(t_m, g_m)}{h} \int_{t_m}^{t_{m+1}} (t - t_{m-1})(t_{m+1} - t)^{\alpha-1} dt - \right. \\ \left. - \frac{f(t_{m-1}, g_{m-1})}{h} \int_{t_m}^{t_{m+1}} (t - t_m)(t_{m+1} - t)^{\alpha-1} dt \right), \tag{6}$$

Let us define the following expressions:

$$A_{\alpha,m,1} = h^{\alpha+1} \frac{(j+1-m)^\alpha (j-m+2+\alpha) - (j-m)^\alpha (j-m+2+2\alpha)}{\alpha(\alpha+1)}, \tag{7}$$

$$A_{\alpha,k,2} = h^{\alpha+1}\frac{(j+1-m)^{\alpha+1} - (j-m)^{\alpha}(j-m+1+\alpha)}{\alpha(\alpha+1)}, \tag{8}$$

Thus, the general numerical algorithm for implementing mathematical models with the Liouville-Caputo fractional derivative has the form:

$$g_{j+1} = g(0) + \frac{1}{\Gamma(\alpha)}\sum_{m=0}^{j}\left(\frac{h^{\alpha} f(t_m, g_m)}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha}(j-m+2+\alpha) - (j-m)^{\alpha}\times\right.\right.$$
$$\left.\left.\times(j-m+2+2\alpha)\right) - \frac{h^{\alpha} f(t_{m-1}, g_{m-1})}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha+1} - (j-m)^{\alpha}(j-m+1+\alpha)\right)\right), \tag{9}$$

Discretization of the Fractal Model

To discretize the fractal model (5), we use the numerical scheme (9) [8]. We obtain the numerical solution of the equations of model (5) as follows:

$$S_{j+1} = S_0 + \frac{1}{\Gamma(\alpha)}\sum_{m=0}^{j}\left(\frac{h^{\alpha} f_1(t_m, S_m, E_m, T_m, M_m)}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha}(j-m+2+\alpha) - \right.\right.$$
$$\left.\left.-(j-m)^{\alpha}(j-m+2+2\alpha)\right) - \frac{h^{\alpha} f_1(t_{m-1}, S_{m-1}, E_{m-1}, T_{m-1}, M_{m-1})}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha} - (j-m)^{\alpha}(j-m+1+\alpha)\right)\right), \tag{10}$$

$$E_{j+1} = E_0 + \frac{1}{\Gamma(\alpha)}\sum_{m=0}^{j}\left(\frac{h^{\alpha} f_2(t_m, S_m, E_m, T_m, M_m)}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha}(j-m+2+\alpha) - \right.\right.$$
$$\left.\left.-(j-m)^{\alpha}(j-m+2+2\alpha)\right) - \frac{h^{\alpha} f_2(t_{m-1}, S_{m-1}, E_{m-1}, T_{m-1}, M_{m-1})}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha} - (j-m)^{\alpha}(j-m+1+\alpha)\right)\right), \tag{11}$$

$$T_{j+1} = T_0 + \frac{1}{\Gamma(\alpha)}\sum_{m=0}^{j}\left(\frac{h^{\alpha} f_3(t_m, S_m, E_m, T_m, M_m)}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha}(j-m+2+\alpha) - \right.\right.$$
$$\left.\left.-(j-m)^{\alpha}(j-m+2+2\alpha)\right) - \frac{h^{\alpha} f_3(t_{m-1}, S_{m-1}, E_{m-1}, T_{m-1}, M_{m-1})}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha} - (j-m)^{\alpha}(j-m+1+\alpha)\right)\right), \tag{12}$$

$$M_{j+1} = M_0 + \frac{1}{\Gamma(\alpha)}\sum_{m=0}^{j}\left(\frac{h^{\alpha} f_4(t_m, S_m, E_m, T_m, M_m)}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha}(j-m+2+\alpha) - \right.\right.$$
$$\left.\left.-(j-m)^{\alpha}(j-m+2+2\alpha)\right) - \frac{h^{\alpha} f_4(t_{m-1}, S_{m-1}, E_{m-1}, T_{m-1}, M_{m-1})}{\alpha(\alpha+1)}\left((j+1-m)^{\alpha} - (j-m)^{\alpha}(j-m+1+\alpha)\right)\right), \tag{13}$$

where

$$f_1(t, S(t), E(t), T(t), M(t)) := \gamma_1 S(t) - k_S M(t) S(t)$$
$$f_2(t, S(t), E(t), T(t), M(t)) := \alpha - \mu E(t) + \frac{p_1 E(t) S(t)}{(S(t)+1)} - p_2\left(T(t) + M(t)\right)E(t)$$
$$f_3(t, S(t), E(t), T(t), M(t)) := r(1 - bT(t))T(t) - (p_3 E(t) + k_T M(t))T(t)$$
$$f_4(t, S(t), E(t), T(t), M(t)) := -\gamma_2 M(t) - V(t)$$

Software implementation

Using the procedure described above, a software implementation of the discrete model with Liouville-Caputo fractional derivatives (10-13) has been carried out. The main idea of the algorithm is the iterative calculation of the values $T(t)$, $E(t)$, $S(t)$, and $M(t)$ at specified time intervals. The execution of the algorithm involves the following steps:

1. Initialization of parameter values: : y1, y2, α , μ , p_1, p_2, p_3, r, b, k_s , k_t , V(t).

2. Initialization of the Treatment Period and Partitioning the Interval: Divide the treatment period into finite segments with a certain step size.

3. Determination of Initial Conditions: Set the initial conditions of the system of nonlinear equations

4. Iterative Computation: Iteratively calculate the values of T(t), E(t), S(t) and M(t) at each step of the interval.

For the implementation of the algorithm, the corresponding coefficients of model (5) are used: $S_0 = 1$, $E_0 = 1$, $T_0 = 1$, γ_1 = -0.02825, α - 0.17, $\mu = 0.03$, b = 10-9, $k_s = 1$, $p_1 = 0.1245$, r = 0.18, $p_2 = 1$, $k_t = 0.9$, $p_3 = 0.9$, $\gamma_2 = 6.4$, V(t) = 1.

Figure 1 presents the UML diagram of the software application. Let's describe each of the classes.

BaseAlgorithm: This is the base class that represents the general algorithm for computing the mathematical model. When this class is created, the parameter values and the initial conditions of the system are initialized. The equations of the mathematical model are also presented in this class as methods.

GUI: This class is responsible for interaction with the user interface. It receives as input the initial values T(0), E(0), S(0) , and M(0), as well as a number of parameters such as y1, y2, α , μ , p_1, p_2, p_3, r, b, k_s , k_t , V(t). Upon clicking the "Run Simulation" button, it initiates the computation of the selected algorithms of the corresponding classes. This class is also responsible for displaying the results in a graphical representation.

RiemannLiouvilleAlgorithm: This class, like the previous one, solves the fractional-order Liouville-Caputo problem based on the Atangana-Toufik method.

RungeKuttaAlgorithm: This class is responsible for computing the integer-order results of the mathematical model using the Runge-Kutta method. This algorithm is applied in the software implementation of the mathematical model to compare the integer-order and fractional-order results.

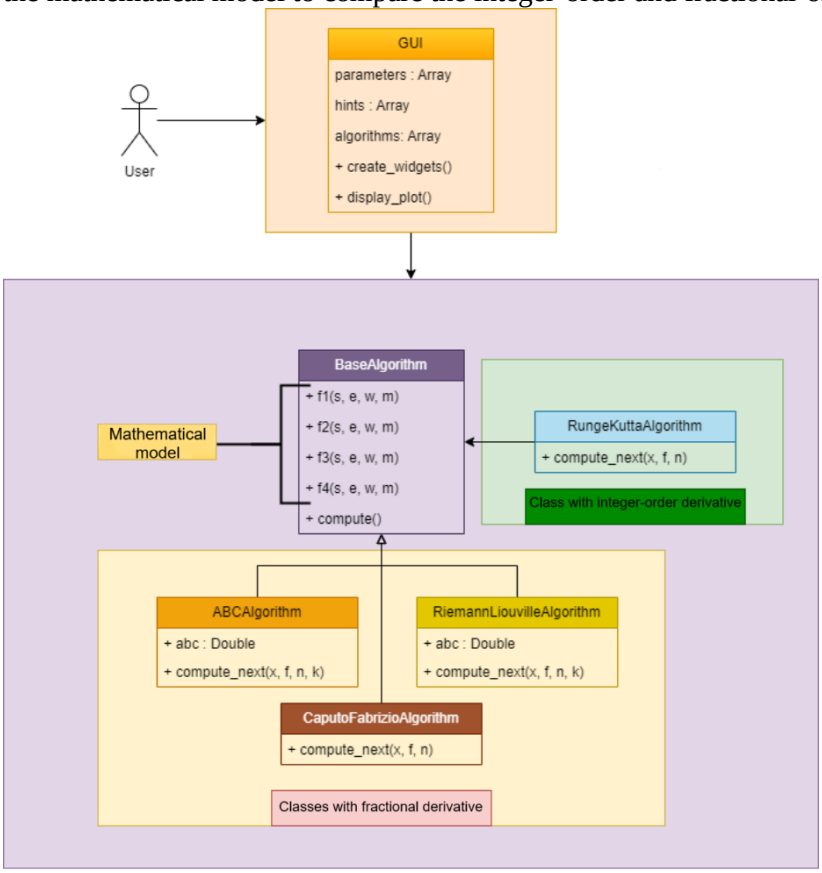

Fig. 1. UML diagram of the software application

Results and Discussion

The obtained graphical results are presented in Figures 2 to 3, using α = 1, 0.98, 0.96, 0.92. Figure 4 shows the dependencies of the concentrations of tumor cells T(t) (yellow line), effector immune cells E(t) (red line), stem cells S(t) (blue line), and the chemotherapeutic drug M(t) (purple line).

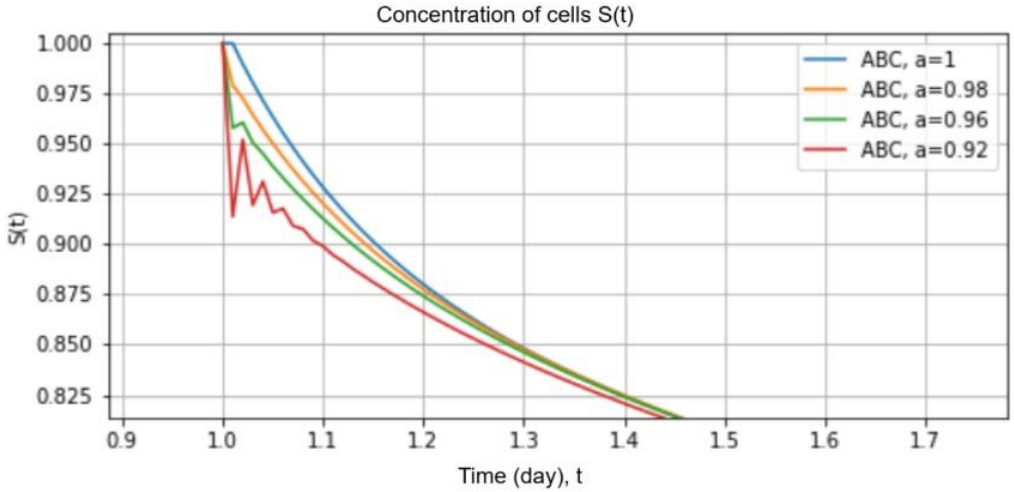

Fig. 2. Variation of the function S(t) for different values of the fractional parameter a

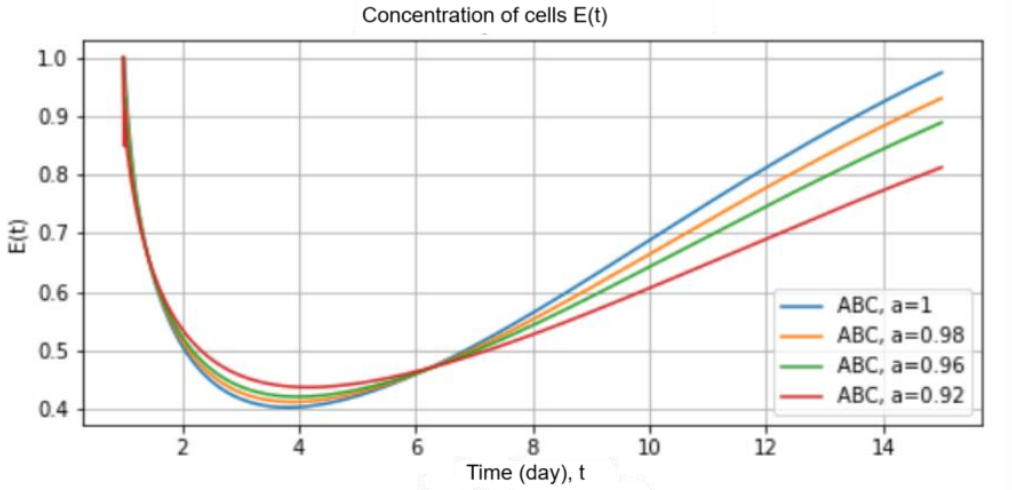

Fig. 3. Variation of the function E(t) for different values of the fractional parameter a

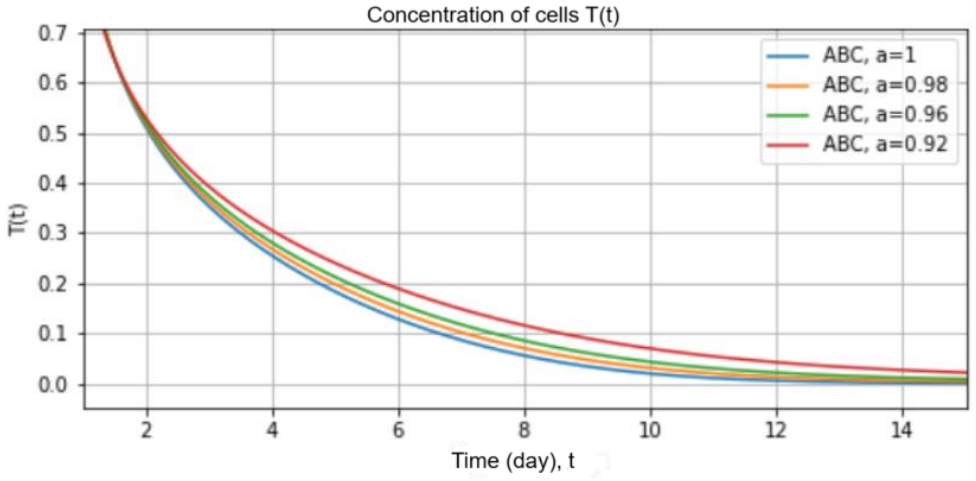

Fig. 4. Variation of the function T(t) for different values of the fractional parameter a

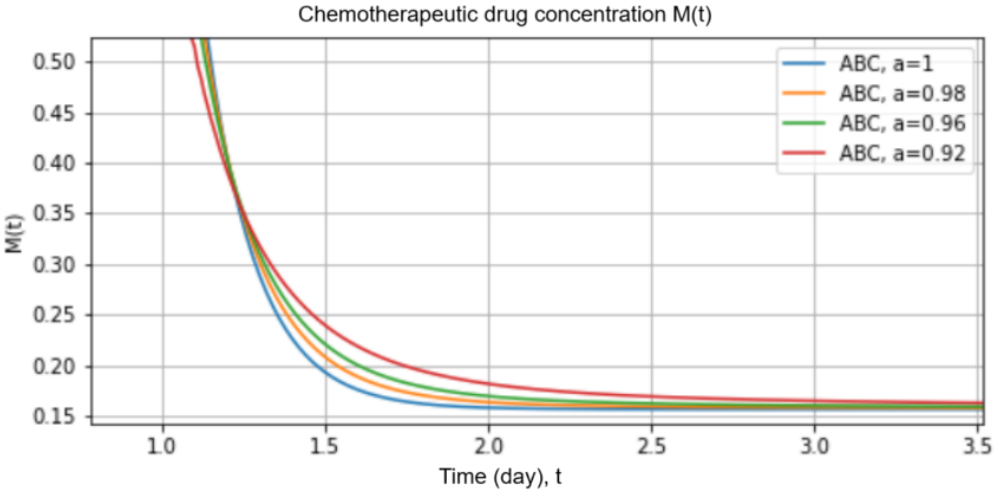

Fig. 5. Variation of the function M(t) for different values of the fractional parameter a

From these figures, it can be seen that fractional models can produce cases where the studied functions decrease even in the interval where the drug is inactive ($t > t_0$). Such behavior is not observed in the ordinary case, which corresponds to $\alpha = 1$. In the case of the fractional model, one can select a convenient value of the fractional parameter so that at the end of the active period or at the end of the total treatment period, the desired function attains a given value. Such a choice can suggest certain forms of treatment.

Analysis of the obtained data indicates that the concentration of cancer cells decreases over time and approaches zero at a death rate of p3 = 0.9 and given initial conditions. The growth rate of tumor cells is less than the rate of interaction between tumor cells and effector cells, which are supported by stem cells and the concentration of the chemotherapeutic drug; therefore, the immune system is modified. Thus, the combination of stem cell therapy and chemotherapy allows us to hope for recovery from cancer and improvement in the quality of life.

Conclusions

In this work, mathematical models have been synthesized using fractal analysis methods, and software algorithms have been developed to assess the impact of chemotherapy on the state of a cancerous tumor, taking into account the effect of long-term memory. The considered mathematical model of the influence of chemotherapy on the tumor state has been investigated based on the Liouville-Caputo derivatives. To implement the fractal model of chemotherapy influence, the Atangana-Toufik numerical scheme was used. Finite difference approximations of the fractal operators of the mathematical models have been constructed. Additionally, one of the main stages of the work was the software implementation of the model, development of the interface, and visualization of the results. The numerical results obtained using the software are presented in the form of graphical illustrations. The use of the fractional model shows that the time evolution of the concentrations of tumor cells, effector cells of the immune system, and stem cells is significantly influenced by their history. The presence of a fractional-order time derivative as a parameter in the solutions provides important information for predicting the impact of chemotherapy on the state of the cancerous tumor. Furthermore, considering the fractal structure of the tumor and its changes under the influence of chemotherapy allows for the discovery of new patterns and features.

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МАТЕМАТИЧНЕ МОДЕЛЮВАННЯ ВПЛИВУ ХІМІОТЕРАПІЇ НА СТАН РАКОВОЇ ПУХЛИНИ НА ПІДСТАВІ АПАРАТУ ДРОБОВОГО ДИФЕРЕНЦІЮВАННЯ

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Анотація. Стаття присвячена побудові різницевих апроксимацій фрактальних операторів математичної моделі впливу хіміотерапії на стан ракової пухлини на підставі апарату дробового диференціювання з використанням похідної Капуто. Представлено математичну модель стовбурових клітин і хіміотерапії. Побудовано числові алгоритми для реалізації математичних моделей дробового порядку з використанням методу Атангана-Туфіка. Описано UML-діаграму програмного застосунку та процес його розробки.Проведено аналіз впливу фрактальних характеристик (довготривалої пам’яті) хіміотерапії на стан ракової пухлини . Наявність дробового порядку похідної за часом як параметра розв’язків дає важливу інформацію про прогнозування впливу хіміотерапії на стан ракової пухлини

Ключові слова: модель дробового порядку, дробові оператори, метод Атангана–Туфіка, ракова пухлина, python, мова R.