Differential Equations and Dynamical Systems
https://doi.org/10.1007/s12591-022-00622-x

ORIGINAL RESEARCH

Application of Non-singular Kernel in a Tumor Model with Strong Allee Effect

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Dedicated to the memory of Professor H. I. Freedman.

Accepted: 7 December 2022

Abstract
We obtain the analytical solutions in implicit form of a tumor cell population differential equation with strong Allee effect. We consider the ordinary case and then a fractional version. Some particular cases are plotted.

Keywords Tumor growth model · Allee effect · Caputo-Fabrizio fractional derivative · Non-singular kernel

Introduction

The mathematical modeling and analysis of tumor growth is a crucial point to understand different aspects of cancer and to discover potential treatments [1–4]. Prof. H.I. Freedman has made important contributions in tumor-immune competitive systems and their application to chemotherapy [5, 6].

In this paper, we investigate a tumor model with strong Allee effect in the following form [7]

$$\frac{dT}{dt} = \alpha T\left(1 - \frac{T}{k}\right)\left(T - c\right), \tag{1}$$

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Published online: 19 December 2022

with initial size of the tumor population is $T(0) = T_0 \geq 0$. We assume that tumor cells grow logistically as tumor growth slows down due to insufficient nutrients. Here, α represents the intrinsic growth rate and k is the maximum carrying capacity of tumor cells [8]. It can be observed that 0, k and c are constant solutions. The parameter $c \geq 0$ represents the strong Allee threshold. The growth of population subject to Allee effects is reduced at low density and it is related to the existence of a threshold size for the visibility of that population and they may altered the long-term persistence of the population. Note that for T between 0 and k, T is increasing if $T > c$, and T is decreasing if $T < c$.

There is a long history of fractional order derivative and it plays a vital role in nonlinear mathematical model. There are some limitations in integer derivatives of nonlinear models. Therefore the application of fractional order derivative is very important in the mathematical model. In fractional order differential equation, there are mainly two types of derivatives known as Caputo-Fabrizio derivative and Riemann-Liouville derivative. In our study, we used Caputo-Fabrizio fractional order derivative.

The following fractional derivative of the model (1) has been considered as

$$D^{\lambda}T(t) = \alpha T\left(1 - \frac{T}{k}\right)\left(T - c\right), \tag{2}$$

with $\lambda \in (0, 1)$ and D^{λ} the Caputo fractional derivative of a C^1 function and T is defined as

$$D^{\lambda}T(t) = \frac{1}{\Gamma(1-\lambda)}\int_0^t (t-x)^{-\lambda}T'(x)dx.$$

In this paper, we investigate the fractional version of the model (1)

$$\mathbb{D}^{\lambda}T(t) = \alpha T\left(1 - \frac{T}{k}\right)\left(T - c\right), \tag{3}$$

where $\mathbb{D}$ is the Caputo-Fabrizio fractional derivative [9–11] and in the line of [12].

The paper is organized in the following way. We investigate the Caputo-Fabrizio fractional order derivative and its corresponding fractional integral in the Sect. 2. We implicitly solved the Caputo-Fabrizio fractional derivative with order $\lambda \in (0, 1)$ of the proposed model (1) in the next Section. In the same Section, we plot the fractional Caputo-Fabrizio logistic equation with strong Allee effect (7) for different values of λ by using MATHEMATICA. The paper ends with a brief conclusion.

Fractional Calculus with Non-singular Kernel

Let us assume that $\lambda \in (0, 1)$. The classical Riemann-Lioville fractional integral is given by

$$J^{\lambda}T(t) = \frac{1}{\Gamma(\lambda)}\int_0^t (t-x)^{\lambda-1}T(x)dx.$$

We have [13],

$$D^{\lambda}J^{\lambda}T(t) = T(t),$$

and

$$J^{\lambda}D^{\lambda}T(t) = T(t) + K_1,$$

where K_1 is an arbitrary constant. For real smooth function g, the Caputo-Fabrizio fractional derivative is given by

$$\mathbb{D}^{\lambda} g(t) = \frac{1}{1-\lambda} \int_0^t e^{-\frac{\lambda}{1-\lambda}(t-x)} g'(x) dx. \tag{4}$$

It is corresponding to the Caputo fractional derivative replacing the constant $\frac{1}{\Gamma(1-\lambda)}$ by $\frac{1}{1-\lambda}$ and the singular kernel

$$m(t,x) = (t-x)^{-\lambda}$$

by another kernel

$$n(t,x) = e^{-\frac{\lambda}{1-\lambda}(t-x)}.$$

Thus, the corresponding fractional integral [14, 15] of the function h is given by

$$\mathbb{I}^{\lambda} h(t) = (1-\lambda)[h(t) - h(0)] + \lambda \int_0^t h(x) dx. \tag{5}$$

Again, we have

$$\mathbb{I}^{\lambda} \mathbb{D}^{\lambda} g(t) = g(t) + K_1, \tag{6}$$

K_1 is an arbitrary constant. Due to [15], we point out that

$$\mathbb{D}^{\lambda} \mathbb{I}^{\lambda} g(t) = g(t) - g(0) e^{-\frac{\lambda}{1-\lambda} t}.$$

This is quite different to the first order integral and derivative, the Caputo fractional derivative and the Riemann-Liouville fractional derivative and integral.

Solution for the Fractional Differential Equation

Assume that T is a solution of (3). Integration leads to

$$\mathbb{I}^{\lambda} \mathbb{D}^{\lambda} T(t) = \mathbb{I}^{\lambda} P(t),$$

where

$$P(t) = \alpha T(t) \left(1 - \frac{T(t)}{k}\right)\left(T(t) - c\right).$$

Therefore by (6), we get

$$\begin{aligned} T(t) - T_0 =& (1-\lambda)\left[\alpha T(t)\left(1 - \frac{T(t)}{k}\right)\left(T(t) - c\right) - \alpha T_0 \left(1 - \frac{T_0}{k}\right)\left(T_0 - c\right)\right] \\ & + \lambda \int_0^t \alpha T(s) \left(1 - \frac{T(s)}{k}\right)\left(T(s) - c\right) ds, \end{aligned}$$

where $T(0) = T_0$ is the initial value. Taking derivative both sides of the above equation leads to

$$\begin{aligned}T'(t) =&(1-\lambda)\left[\alpha T(t)\left(1-\frac{T(t)}{k}\right)T'(t)+\alpha(T(t)-c)\left(T'(t)-\frac{2T(t)T'(t)}{k}\right)\right]\\&+\lambda\alpha T(t)\left(1-\frac{T(t)}{k}\right)\left(T(t)-c\right).\end{aligned} \tag{7}$$

We notice that if $\lambda = 1$ then we recover the Allee model (1). After some algebraic manipulation, for $0 < \lambda < 1$ equation (7) becomes

$$\begin{aligned}T'(t) &= \frac{\alpha\lambda}{3(\lambda-1)}\cdot\frac{T^3(t)-a_1T^2(t)+a_2T(t)}{T^2(t)-\frac{2}{3}a_1T(t)+a_3}\\ \Rightarrow l &= T'(t)\frac{T^2(t)-\frac{2}{3}a_1T(t)+a_3}{T^3(t)-a_1T^2(t)+a_2T(t)},\end{aligned}$$

with

$$\begin{aligned}a_1 &=(k+c),\\ a_2 &=kc,\\ a_3 &=\frac{1+\alpha c(1-\lambda)}{3\alpha(1-\lambda)}k,\\ l &= \frac{\alpha\lambda}{3(\lambda-1)}.\end{aligned}$$

Solving above equation by integration, we get

$$\begin{aligned}lt+c_1 =&\frac{1}{3}\ln|T_2(t)|+\left(\frac{a_3}{a_2}-\frac{1}{3}\right)\ln|T(t)|+\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)\ln|T_3(t)|\\&+\left(\frac{a_1a_3}{2a_2}-\frac{a_1}{6}\right)\frac{1}{c-k}(\ln|T(t)-c|-\ln|T(t)-k|),\quad [c_1 \text{ is an integral constant.}]\\ \Rightarrow \exp(lt+c_1) =&(T_2(t))^{\frac{1}{3}}(T(t))^{\left(\frac{a_3}{a_2}-\frac{1}{3}\right)}(T_3(t))^{\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)}\left(\frac{T(t)-c}{T(t)-k}\right)^{\frac{3a_1a_3-a_1a_2}{6a_2(c-k)}},\end{aligned}$$

where

$$\begin{aligned}T_2(t) &= T^3(t)-a_1T^2(t)+a_2T(t),\\ T_3(t) &= T^2(t)-a_1T(t)+a_2.\end{aligned}$$

Putting $t = 0$ in the above equation, we have

$$\exp(c_1) = (T_2(0))^{\frac{1}{3}}T_0^{\left(\frac{a_3}{a_2}-\frac{1}{3}\right)}(T_3(0))^{\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)}\left(\frac{T_0-c}{T_0-k}\right)^{\frac{3a_1a_3-a_1a_2}{6a_2(c-k)}},$$

where

$$\begin{aligned}T_2(0) &= T_0^3-a_1T_0^2+a_2T_0,\\ T_3(0) &=T_0^2-a_1T_0+a_2.\end{aligned}$$

Hence, we obtained the solution in an implicit form as

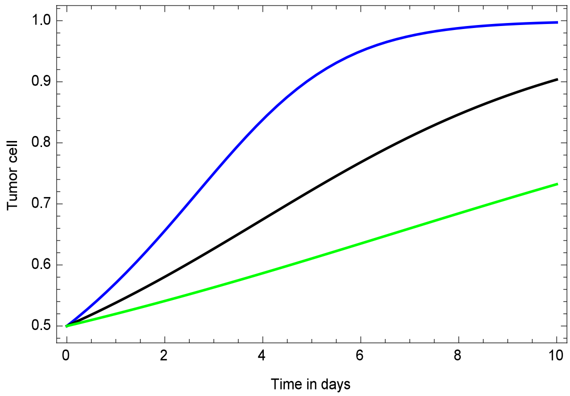

Fig. 1 Solution of the ordinary logistic differential equation with strong Allee effect for the initial value $T_0 = 0.5$. Classical logistic equation with strong Allee effect (blue colour), fractional Caputo-Fabrizio logistic equation with strong Allee effect (7) for $\lambda = 1/2$ (black) and for $\lambda = 1/4$ (green)

$$e^{lt} \cdot (T_2(0))^{\frac{1}{3}} T_0^{\left(\frac{a_3}{a_2}-\frac{1}{3}\right)} (T_3(0))^{\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)} \left(\frac{T_0 - c}{T_0 - k}\right)^{\frac{3a_1a_3-a_1a_2}{6a_2(c-k)}} = (T_2(t))^{\frac{1}{3}} (T(t))^{\left(\frac{a_3}{a_2}-\frac{1}{3}\right)} \cdot (T_3(t))^{\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)} \left(\frac{T(t) - c}{T(t) - k}\right)^{\frac{3a_1a_3-a_1a_2}{6a_2(c-k)}},$$

$$\Rightarrow \exp(lt) = \left(\frac{T_2(t)}{T_2(0)}\right)^{\frac{1}{3}} \left(\frac{T(t)}{T_0}\right)^{\left(\frac{a_3}{a_2}-\frac{1}{3}\right)} \left(\frac{T_3(t)}{T_3(0)}\right)^{\left(\frac{1}{6}-\frac{a_3}{2a_2}\right)} \left(\frac{(T(t)-c)(T_0-k)}{(T(t)-k)(T_0-c)}\right)^{\frac{3a_1a_3-a_1a_2}{6a_2(c-k)}}. \tag{8}$$

We plot the solutions of the proposed model (7) by choosing a suitable set of parameter values and for different values of λ. To numerically plot the solutions of (7), we use the initial size of the tumor cell population is $T_0 = 0.5$. To compare the solution of the classical ($\lambda = 1$) logistic differential equation with Allee effect (1), and the Caputo-Fabrizio fractional logistic equation with Allee effect (7) for $\lambda = 1/2$ and $\lambda = 1/4$. See the Fig. 1. Rest of the parameter values are chosen as $\alpha = 1$, $k = 1$ and $c = 0.25$. The solution of the classical logistic equation with strong Allee effect is above the solution of the fractional order Caputo-Fabrizio logistic equation with strong Allee effect (7) and above all the solution of the Caputo-fractional logistic differential equation.

Conclusions

In this paper, we proposed a mathematical model of tumor cell population with strong Allee effect, which is constructed by Sardar et al. [7] . Then we introduce fractional order derivative in our model. To solve the fractional logistic differential equation with Allee effect, we use fractional calculus with non-singular kernel. We calculate the analytical solutions in implicit form of the tumor cell population with strong Allee effect. Finally, we plot our solutions for different values of λ.

Acknowledgements The research of Juan J. Nieto has been partially supported by the Agencia Estatal de Investigación (AEI) of Spain under grant PID2020-113275GB-I00, and by Xunta de Galicia, grant ED431C 2019/02. Subhas Khajanchi acknowledges the financial support from the Department of Science and Technology (DST), Govt. of India, under the Scheme “Fund for Improvement of S &T Infrastructure (FIST)” [File No. SR/FST/MS-I/2019/41].

Funding Open Access funding provided thanks to the CRUE-CSIC agreement with Springer Nature.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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