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On the Stability of Some Fractional Dynamical Models Related to Tumor Cancer Evaluation

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ABSTRACT
In this article, we present a general fractional dynamical system related to cancer tumor. The considered model describes tumor – immune cell interactions using a system of fractional order differential equations. The conditions for global stability of cancer free state are studied, for the ague therapy fractional model. In order to stabilize or completely eliminate the cancer, we suggest suitable choices of functions and parameters in our fractional model.

1. Introduction

The fractional derivative describes the effect of hereditary and memory properties, [1-5], consequently many biological problems, when describes in terms of differential equations of non-integer orders, provide a more accurate description of reality. Many mathematical models have been applied in cancer growth with chemotherapy. The chemotherapy has damaging side effects, so it is better to investigate fractional mathematical models to get best results.

Let us use the following notations, T(t), tumor cell population at time t, N(t), total level of natural killer, (NK), cell effectiveness at time t and L(t) total level of tumor – specific CD 8^+ T cell effectiveness at time t. As a main step to exploring the use of gene therapy on the tumor - immune interaction during cancer, we will consider a fractional mathematical €◦with the goal of predicting optimal combinations of approaches leading to clearance of tumors. The fractional version of the mathematical model of Lisette G. de Pillis and Kuznetose, [6-9], is given by:

$$D^{\alpha} T(t) = r(t)\, T(t)\, [1 - a\, T(t)] - \frac{b(t) N(t) T(t)}{b_1 + T(t)} - F(t), \tag{1.1}$$

Where, $T(t) \in [0, a^{-1}]$, for all $t \geq 0$,

$$D^{\alpha} N(t) = \sigma - c_1 N(t) + \frac{b_2 T^2(t)}{c_2 + T^2(t)} N(t) - c_3 N(t) T(t), \tag{1.2}$$

$$D^{\alpha} L(t) = -C_4 L(t) + \frac{C_5 F^2(t)}{k + F^2(t)} L(t) - C_6 L(t) T(t) + C_7 N(t) T(t) \tag{1.3}$$

Where

$$F(t) = \gamma \frac{(L/T)^{\lambda}}{s + (L/T)^{\lambda}} T, \tag{1.4}$$

$D^{\alpha} = \dfrac{d^{\alpha}}{dt^{\alpha}}$ is the fractional derivative of order α, with respect to t, $0 < \alpha \leq 1$.

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If for suitable functions $E_1(t)$ and $E_2(t)$, we have

$D^\alpha E_1(t) = E_2(t)$,

Then

$$E_1(t) - E_1(0) = \frac{1}{\Gamma(\alpha)} \int_o^t (t-s)^{\alpha-1} E_2(s)\,ds,$$

Where $\Gamma(\ .\ )$ is the gamma function. According to previous results, [10-21] , the solution of the fractional integral system:

$$u(t) = u(t_o) + \frac{1}{\Gamma(\alpha)} \int_{t_o}^t (t-s)^{\alpha-1} \left[Au(s) + f(s, u(s)\right] ds,$$

is given by

$$u(t) = \int_O^\infty \zeta_\alpha(\theta) e^{A\theta(t-t_o)^\alpha} \quad u(t_O)\ d\theta$$

$$+ \int_{t_O}^t \int_O^\infty \alpha\,\theta (t-\eta)^{\alpha-1} \zeta_\alpha(\theta) e^{A\theta(t-\eta)^\alpha} f\left(\eta, u(\eta)\right) d\theta\eta$$

Where u and f are column vectors of n functions,

A is a square matrix of order n, whose elements are real numbers and $\Gamma(\theta)$ is a probability density function defined on $[0, \infty]$, whose Laplace transform is given by

$$\int_O^\infty e^{-p\theta} \zeta(\theta)\, d\theta = E_\alpha(-p),$$

Where $E_\alpha(p) = \sum_{j=0}^\infty \frac{p^j}{\Gamma(\alpha j+1)}$ is the Mittag–Leflar function,

$t \geq to \geq 0$.

In section 2, we define the parameters of the considered model, their values as well as their ranges of variations are given in tables 1-4. They are based on previously published data, [6.22,23] , estimated according to different patients.

In section 3, we shall derive some estimates. We shall find also condition for global stability of cancer free state.

2. Parameters of the model

Table 1.Parameters of equation (1.1).

Parameters	Units	Definitions	Estimated Values
r (t)	0.18 1/Time	Cancer growth term	$[10^{-1}, 2]$
a	10^{-9} 1/cells	Cancer cell capacity logistic growth	10^{-9}
b (t)	1 1/time	Cancer cell clearance term	$[10^{-2}, 10^{2}]$
b_1	10^5 cells	Half- saturation for cancer cells	10^5

Table 2.Parameters of equation (1.2).

Parameters	Units	Definitions	Estimated Values
σ	1/Cell 1/Day	Constant source of effector cells	1.3×10^4
c_1	1/Day	Death rate of effector cells	4.12×10^{-2}
b_2	1/Day	Maximum effector cells recruitment rate by tumor cell	2.5×10^{-2}
c	$Cell^2$	Steepness coefficient of the NK cell recruitment curve	2×10^{-1}
c_3	1/Cell 1/Day	Effector cell inactivation term by tumor cells	1×10^{-7}

Table 3.Parameters of equation (1.3).

Parameters	Units	Definitions	Estimated Values
c_4	1/Day	Death rate of CD 8^+ T cells	2×10^{-2}
c_5	1/Day	Maximum CD 8^+ T – cell recruitment rate	$3\text{-}75 \times 10^{-2}$
c_6	1/Cell 1/Day	CD 8^+ T – cell inactivation rate by tumor cell	3.42×10^{-10}
c_7	1/Cell 1/Day	Rate at which Tumor – specific CD 8^+ T – cells are stimulated to be produced to be result of tumor cells killed by NK cells	1.1×10^{-7}
k	$Cell^2$	Steepness coefficients of CD 8^+ T – cell	2×10^7

Table 4.Parameters of equation (1.4).

Parameters	Units	Definitions	Estimated Values
γ	1/Day	Saturation level of fractional tumor cell killed by CD 8^+ T - cell	5.80
λ	None	Exponent of fractional tumor cell killed by CD 8^+ T - cells	1.36
s	None	Steepness coefficient of the tumor CD 8^+ T – cell competition term	2.5 x 10^{-1}

3. Estimations and stability

Theorem 3.1. The total level of (NK) satisfies the following inequalities:

$$N(t) \le \left[N(t_o) - \frac{\sigma}{a_1} \right] E_\alpha(-a_1(t-t_o)^\alpha) + \frac{\sigma}{a_1}, \tag{3.1}$$

For all

$t \ge t_o > 0$, *where* $a_1 = c_1 - b_2 = 1.62 \times 10^{-2}$,

$$N(t) \ge \left[N(t_o) - \frac{\sigma}{a_2} \right] E_\alpha(-a_2(t-t_o)^\alpha) + \frac{\sigma}{a_2}, \tag{3.2}$$

for all $t \ge t_o > 0$, *where* $a_2 = c_1 + c_3\ a^{-1} = 6.12 \times 10^{-2}$.

Pr*oof. from equation* (1.2)

and the data of table 2, we can write

$D^\alpha N(t) \le \sigma - a_1 N(t).$

Thus from (1.6), *one gets*

$N(t) \le N(t_o) E_\alpha\left(-a_1(t-t_o)^\alpha\right) + \frac{\sigma}{a_1}\left[1 - E_\alpha(-a_1(t-t_o)^\alpha)\right],$

for allt $\ge to \ge 0$.

Corollary.If $\alpha = 1$, *we get*:

$$N(t) \le \left[N(t_o) - \frac{\sigma}{a_1} \right] eap\,(-a_1(t-t_o)) + \frac{\sigma}{a_1},$$

$$N(t) \ge \left[N(t_o) - \frac{\sigma}{a_2} \right] \exp(-a_2(t-t_o)) + \frac{\sigma}{a_2},$$

for all t ≥ to ≥ 0.

Theorem 3.2. The total level L(t) of tumor specific CD 8^+ T- cell satisfies

CD 8+ T- cell satisfies

for all $t \ge t_o \ge 0$, *the following inequalities*

$$L(t) \le L(t_o)\ E_\alpha(a_3(t-t_o)^\alpha) + c_7\ a^{-1} \int_{t_o}^{t} (t-\eta)^{\alpha-1} N(\eta)\ E_{\alpha,\alpha}\left(a_3(t-\eta)^\alpha\right)\ d\eta, \tag{3.3}$$

$$L(t) \ge L(t_o)\ E_\alpha(-a_4(t-t_o)^\alpha) + c_7 \int_{t_o}^{t} (t-\eta)^{\alpha-1} E_{\alpha,\alpha}\left(-a_4(t-\eta)^\alpha\right) N(\eta) T(\eta)\, d\eta, \tag{3.4}$$

Where

$$a_3 = c_5 - c_4 = 1 - 75 \times 10^{-2},\ a_4 = c_4 + c_6\ a^{-1} = 5.42 \times 10^{-2},$$

$E_{\alpha,\boldsymbol{\beta}}$ (t) is the generalized Mittag–Leflar function, defined by

$$E_{\alpha,\beta}(t) = \sum_{k=0}^{\infty} \frac{t^k}{\Gamma(\alpha k + \beta)}.$$

Proof. From (1.3) and the data of table 3, we get
$D^{\alpha} L(t) \le a_3 L(t) + c_7 N(t) T(t)$. (3.5)
From (1.6) and (3.5), we get

$$L(t) \le \int_0^\infty \zeta_\alpha(\theta)\, e^{a_3\theta(t-t_0)^\alpha} L(t_0)\, d\theta$$
$$+C_7 \int_{t_0}^{t} \int_0^\infty \alpha\theta\,(t-\eta)^{\alpha-1} \zeta_\alpha(\theta) e^{a_3\theta(t-\eta)^\alpha} N(\eta)T(\eta)\, d\theta d\eta \,. \tag{3.6}$$

From (1.7) we can write

$$\int_0^\infty \zeta_\alpha(\theta)\, e^{a_3\theta t^\alpha} d\theta = E_\alpha(a_3 t^\alpha).$$

Differentiating the last formula with respect to t, we get

$$\int_0^\infty \boldsymbol{\theta\, \zeta_\alpha(\theta)\, e^{a_3\,\theta\, t^\alpha} d\theta = E_{\alpha,\alpha}(a_3\, t^\alpha)}. \tag{3.7}$$

From (3.6) and (3.7) we get (3.3).
In a similar manner from the data of table 3 and equation (1.3), we can write

$$D^\alpha L(t) \ge -a_4 L(t) + c_7 N(t)T(t). \tag{3.8}$$

From (1.6) and (3.8) , we get

$$L(t) \ge L(t) E_\alpha(-a_4(t-t_0)^\alpha)$$
$$+c_7 \int_{t_0}^{t} \int_d^\infty \alpha\,\theta(t-\eta)^{\alpha-1} e^{-a_7\theta(t-t_0)^\alpha} N(\eta)T(\eta)\, d\theta\, d$$

The last in equality leads to (3.4).
Theorem 3.3. Suppose that there exist ζ>0 and to ≥ 0 such that

$$N(t_0) \ge \frac{\sigma}{a_2},$$

$$\frac{b(t)\sigma}{a_2\, r(t)} + \frac{b_1 G(t)}{r(t)} \ge$$
$$\ge b_1 + \frac{1}{4a}(1-ab_1)^2 + \frac{\varepsilon}{r(t)}, \tag{3.9}$$

For all $t \ge t_0 \ge 0$,
Where

$$G(t) = \frac{\gamma L^\lambda}{sa^{-\lambda} + L^\lambda},$$

Then every solution of (1.1)

$$sat\, isfies\ \lim_{t\to\infty} T(t) = 0$$

Proof . Using equation (1.1),
It is easy to write:
It is easy to write:

$$D^\alpha T(t) \le$$
$$\le \frac{-r(t)}{b_1 + T(t)}\left[\frac{b(t)N(t) + b_1 F(t)/T(t)}{r(t)} - \frac{1}{4a}(1-ab_1)^2 - b_1\right] T(t).$$

$$Since\ \ N(t_0) \ge \frac{\delta}{a_2},\ it \tag{3.12}$$

follows from (3.2) that

$$N(t) \geq \frac{\delta}{a_2}, \text{ for all } t \geq to$$

Thus from (3.9) and (3.12), we get

D^{α} T(t) ≤ -ἐT (t),

For all t ≥ to ≥ 0.

Consequently

$$T(t) \leq T(t_0)\ E_{\alpha}(-\varepsilon(t-t_0)^{\alpha}),$$

$$S0\ \lim_{t\to\infty} T(t)=0.$$

Corollary. If there exist

$$\varepsilon > 0 \text{ and } t_o > 0$$

$$\text{such that } N(t_o) \geq \frac{\sigma}{a_2},$$

$$\frac{b(t)\sigma}{a_2\, r(t)} \geq b_1 + \frac{1}{2a}(1-ab)^2 + \frac{\varepsilon}{r(t)}$$

For all t ≥ to ≥ 0, then

$$\lim_{t\to\infty} \mathrm{T}(t) = 0.$$

(Comp. [24- 27])

Conclusion

The suitable mathematical models of fractional dynamical systems explore important problems in biology. This tool is an ever increasing towards

Shedding light on these nonlinear fractional systems. The considered model incorporates tumor-immune interaction terms of a form that is qualitatively different from those commonly used. Perhaps the results about the NK cells , CD8 T cells and the behavior of the tumor cell population T(t) helps of gaining time to fight the tumor by medical means , (Surgical. Chemical or radiation).

References

[1] N. Varalta, A.V. Cromes and R.F. Camargo, A prelude to the fractional calculus applied to tumor dynamic, TEMA (Saöcarlos) vol. 15, no.2 SaöCarlos May / Auq. 2014, 1-9.

[2] G.H. Erjaee, M. Shahbazi & A. Erjaee, Dynamical analysis of mathematical model presented by fractional differential equations, describing the interaction between leukemic cancer cells, T cells and drug treatment with a drug optimal control. Open Access Scientific Reports,1 (2012), 1-8.

[3] U. Forys & A. Marciniak-Czochra. Logistic equations in tumor growth modeling. International journal of Applied Mathematics and Computer Science, 13 (2003), 317-325.

[4] R.A. Gatenby & T.L. Vincent, Application of quantitative models from population biology and evolutionary game theory to tumor therapeutic strategies. American Association for cancer Research, 2(2013), 919-927.

[5] R.S. Kerbel. Tumor angiogenesis: past, present and the near future. Carcinogenesis, 21 (2000), 505-515.

[6] Lisette G. de Pillis, Ami E. Randunskaya and Charles L. Wise man, A Validated mathematical model of cell-mediated immune response to tumor growth, Cancer Res 2005, 65 (17), September 1, 2005, 7950-7958.

[7] Dudley ME, Wunderlich JR, Robbins PF, et. Al. Cancer regression and autoimmunity in patients after clonal repopulation with antitumor lymphocytes. Science 2002; 298:850-4.

[8] de Pillis I, Radunskaya A. A mathematical tumor model with immune resistance and drug therapy: an optimal control approach. Journal of theoretical Medicine 2ool;379-100.

[9] de pilis I, Radunskaya A. The dynamics of an optimally controlled tumor model: a case study. Mathematical and Computer Modelling 2003;37:1221-44.

[10] Mahmoud M.El-Borai, Some probability densities and fundamental solutions of fractional evolution equations, Chaos, Solitons Fractals 14 (2002), no.3 433-440

[11] Mahmoud M.El-Borai, The fundamental solutions for fractional evolution equations of parabolic type, Journal of Applied Mathematics and stochastic analysis, 2004:3, 197-211.

[12] Khairia El-Said El-Nadi, On some stochastic differential equations and fractional Brownian motion, International Journal of Pure and Applied Mathematics 24 (2005), 416-423.

[13] Khairia El-Said El-Nadi, Asymptotic methods and some difference fractional differential equations, Int. J. Contemp. Math, Sciences 1 (2006), 3-14.

[14] Kharia El-Said El-Nadi, On the stability of some Contemp. Math. Scinces, 2 (2007, 1317-1326.

[15] Kharia El-Said El-Nadi, On some stochastic models of cancer. Canadian Journal on Biomedical Engineering & Technology, Vol. 1 (2010), 42049.

[16] Mahmoud M. El-Borai and Kharia El-Said El-Nadi, On some fractional parabolic equations driven by fractional Gaussian noise, Special Issue, Science and Mathematics with Applications, Int. J. of Research and Reviewers in Applied Sciences 6(3) (2011) 236-241.
[17] Mahmoud M. El-Borai and Kharia El-Said El-Nadi, An inverse fractional abstract Cauchy problem with nonlocal condition, Life Science Journal 10 (3) (2013).
[18] Mahmoud M. El-Borai and Kharia El-Said El-Nadi, lntegrated semigroups and Cauchy problems for some fractional abstract differential equations, Life Science Journal 10 (3) (2013), 793-798.
[19] Mahmoud M. El-Borai and Kharia El-Said El-Nadi, A stochastic model of the growth and diffusion of brain tumor cancer, Jokull Journal, (2014), 222-233.
[20 Kharia El-Said El-Nadi, Wagdy G. El-Sayed and Ahmed Khdher Qassem, Mathematical model of brain cancer, Int. Research J. of Eng. And Technology (IRJET), 2015, Vol.2, Issue 05, Aug. 2015, 590-594.
[21] Khairia El-Said El-Nadi, Wagdy Cr. El-Sayed and Ahmed Keher Passem, On some dynamical system of controlling tumor growth, Int, J. of Applied Sciences and Mathematics, vol 2, Issue 5, 2015, 146-151.
[22] J.S. Spratt, J.S. Meyer & J.A. Spratt, Rates of growth of human neoplasms: part It. J. Surg. Oncol., 61 (1996), 68-73.
[23] V.G. Vaidya & F.J. Alexandro-Jr., Evaluation of some mathematical models for tumor growth, Int. J. Bio-med. Comp.,13 (1982), 19-35.
[24] M. M. El-Borai, H. M. El-Owaidy, Hamdy M. Ahmed and A. H. Arnous. Soliton solutions of the nonlinear Schrodinger equation by three integration schemes, Nonlinear Sci. Lett. A, 2017, 32-40.
[25] M. M. El-Borai, H. M. El-Owaidy, Hamdy M. Ahmed ,A. H. Arnous , Seithuti Moshokao, Anjan Biswas, Milivoj Belic, Topological and singular soliton solution to Kundu-Eckhaus equation with extended Kundryashv method, International Journal for Light and Electron Optics, Optics, 2017, 128, 57-62.
[26] M. M. El-Borai, H. M. El-Owaidy, Hamdy M. Ahmed ,A. H. Arnous , Seithuti Moshokao, Anjan Biswas, Milivoj Belic, Dark and singular optical solitons solutions with saptio-temporal dispersion, International Journal for Light and Electron Optics, Vol.130-February,2017, 324-331.
[27] M. M. El-Borai, H. M. El-Owaidy, Hamdy M. Ahmed ,A. H. Arnous ,Exact and soliton solutions to nonlinear transmission line model, Nonlinear Dyn. Published online : 16 September 2016.