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On Some Dynamical Systems of Controlling Tumor Growth

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***Abstract* – In this paper, and for the first time we solved a dynamical system of cancer disease that have been placed by the scientist Pillis in 2006, by using the constants and initial values of this model.**

For that purpose we used Adomian method decomposition in solving. Our aim was to study the evaluation of cancer during a specific period of time, in the same time study its behavior and figure out what will happen in future.

***Keywords* – Tumor Growth, Dynamical System, Adomian Decomposition Method.**

AMS Subject Classifications: 37C45, 92B05, 65Pxx.

I. INTRODUCTION

Cancer is a group of diseases characterized by hostile cells (which grow and divide without Borders), and the ability of these dividing cells to invade neighboring tissue and destroy it, or move to distant tissues in a process called metastasis by name. These capabilities are the characteristics of a malignant tumor on the opposite adenoma, which is characterized by specific growth and the inability to invasion and has no ability to move or transport. It can also adenoma evolved into a malignant cancer in some cases.

Cancer can affect all age groups even when human embryos, but the risk of infection increases as people age. The cause of cancer deaths by 13% of all deaths.And indicates the American Cancer Society ACS to 7.6 million people die of cancer patients in the world in 2007. The cancer affects the human forms of it infect animals and plants alike.

Mostly, due to healthy cells turning cancerous cells to changes in the genetic material / gene. These changes may cause carcinogenic factors such as smoking, or radiation or chemicals or infectious diseases (Kalasabh viruses)[26]. There are also encouraging factors for the occurrence of cancer, such as a random error or mutation in the DNA copy at cell division, or because of inheritance of this error or mutation of the mother cell.

At the moment most of the cancer treatment and may be cured, and this depends on the type of cancer, and its location, and stage. When the cancer is detected, treated with surgery, chemotherapy, and radiation therapy begins. Thanks to research advances, the production of drugs might be able to target the cancer cells to distinguish them at the molecular level, which reduces the possibility of targeting healthy cells.

Since cancerous tumors of the most deadly human diseases, so making fun of specialists and researchers of scientific studies and laboratory experiments in order to achieve an effective treatment for each of them, where they resorted to various branches of science in order to achieve this, and the science of mathematics, where specialists predict behavior cancerous tumor for the purpose of fighting it and eliminate it[13,14].

When was the hypotheses put methods of cancer treatment, it has become possible to develop a bio-mathematics predictive models, based on the way the cellular space. For example, you can see the growth of abnormal cells than healthy counterpart's rates through specific mutations coefficient. Has been employing such a model to predict the damage that mature cells continuously increases the chance of the formation of new abnormal cells, and thus the risk of cancer.

Different dynamics of the cancer development can be described in four states. They are included: Uncontrolled tumor growth, tumor dormancy (the populations of normal cells and malignant cells coexist together with blocked sizes in steady-state condition), tumor recurrence and tumor remission.

The mathematical modeling of tumor growth and treatment has been approached by a number of researchers over the past decades [10].

These models describe interaction and competition between tumor cells and immune cells [23,24,6,17,2,7,8,9,11,12,19,16].

Cancer research has undergone radical changes in the past few years. Producing information both at the basic and clinical levels is no longer the issue. Rather, how to handle this information has become the major obstacle to progress. Intuitive approaches are no longer feasible. The next big step will be to implement mathematical modeling approaches to interrogate the enormous amount of data being produced and extract useful answers (a “top-down” approach to biology and medicine).

This is an ongoing to find ways to resolve these mathematical models, or try to find logical solutions to benefit us in describing the course of the disease or even cure it.

The mathematical models we develop will enrich the study of cancer treatment and aid in hastening progress toward an increased understanding and more widespread availability of this new type of this new combination approach to cancer therapy.

II. SOLVING THE MATHEMATICAL MODEL BY DESCRIPTION OF THE ADOMIAN DECOMPOSITION METHOD

We shall denote by Natural killer (NK) cells are a type of non-specific white blood cells. Non-specific cells are the body’s first line of defense against disease and are always present in healthy individuals.

These cells travel through the bloodstream and lymph system to the extracellular fluid, where they find and destroy non-self cells, [26].

And we shall denote by CD8+ T-cells, Specific immune cells, such as CD8+ T immune cells, must be primed before they can attack.

CD8+ T cells are typically activated inside of lymph nodes, where they are presented with antigens. Because each primed T-cell is specific to a certain antigen, only a small [23, 22]. Those that do recognize an antigen presented to them are considered primed [26].

Some fractions of these cells become memory T-cells, which stay in the lymph nodes and allow the body to respond more quickly if a disease returns. Another large fraction become cytotoxic T-cells [22], multiplies, and then leaves the lymph node to find the source of the antigens [25].

The populations at time t are represented by:

Let T (t) is the population of tumor cell, N (t) is the total population of NK cell and L (t) is the total population of CD8+T cell.

The model of Pillis *et al*. [23],[24],is given by:

$$\begin{cases} \frac{dT}{dt} = aT(1-bT) - cNT - D \\ \frac{dN}{dt} = \delta - fN + g\frac{T^2}{h+T^2}N - pNT \\ \frac{dL}{dt} = -mL + j\frac{D^2}{k+D^2}L + rNT - qLT \end{cases} \quad (1)$$

Where

$$D = \frac{d\left(\frac{L}{T}\right)^l}{s+\left(\frac{L}{T}\right)^l}\,\mathrm{T}$$

Where the constants values is as follows:

$a = 5.14 \times 10^{-1} day^{-1}$, $b = 1.02 \times 10^{-9}$

$s = 2.5 \times 10^{-1}$, $c = 3.23 \times 10^{-7} day^{-1}$

$h = 2.02 \times 10^{7}$, $j = 3.75 \times 10^{-2} day^{-1}$

$f = 4.12 \times 10^{-2} day^{-1}$, $g = 2.5 \times 10^{-2} day^{-1}$

$q = 3.42 \times 10^{-10} cell^{-1} day^{-1}$, $m = 2 \times 10^{-2}$,

$d = 5.8\, day^{-1}$, $\delta = 1.3 \times 10^{4}$, $k = 2 \times 10^{7}$

$r = 1.1 \times 10^{-7} cell^{-1} day^{-1}$, $l = 1.36$, $p = 10^{-7}$

And initial densities:

T (0) = 1000, N (0) = 515530, L (0) = 1000 . [10] (2)

Operating with the integral operator L_t^{-1} to that the system (1) and using the initial data (2), we get:

$$\begin{cases} T(t) = 1000 + \int_0^t (aT(1-bT) - cNT - D)\, ds \\ N(t) = 515530 + \int_0^t \left(\delta - fN + g\frac{T^2}{h+T^2}N - pNT\right) ds \\ L(t) = 1000 + \int_0^t \left(-mL + j\frac{D^2}{k+D^2}L + rNT - qLT\right) ds \end{cases}$$

(3)

The linear functions $T(t)$, $N(t)$ and $L(t)$ can be decomposed by infinite series of components

$$\begin{cases} T(t) = \sum_{n=0}^{\infty} T_n(t) \\ N(t) = \sum_{n=0}^{\infty} N_n(t) \\ L(t) = \sum_{n=0}^{\infty} L_n(t) \end{cases} \quad (4)$$

Now substituting equations (4) in to equation (3) gives:

$$\sum_{n=0}^{\infty} T_n(t) = 1000 + \int_0^t \left(a\sum_{n=0}^{\infty} T_n\left(1 - b\sum_{n=0}^{\infty} T_n\right) - c\sum_{n=0}^{\infty} A_n - \sum_{n=0}^{\infty} D_n\right) ds$$

$$\sum_{n=0}^{\infty} N_n(t) = 515530 + \int_0^t \left(\delta - f\sum_{n=0}^{\infty} N_n(t) + g\frac{(\sum_{n=0}^{\infty} T_n(t))^2}{h + (\sum_{n=0}^{\infty} T_n(t))^2}\sum_{n=0}^{\infty} N_n(t) - p\sum_{n=0}^{\infty} A_n\right) ds$$

$$\sum_{n=0}^{\infty} L_n(t) = 1000 + \int_0^t \left(-m\sum_{n=0}^{\infty} L_n(t) + j\frac{(\sum_{n=0}^{\infty} D_n)^2}{k + (\sum_{n=0}^{\infty} D_n)^2}\sum_{n=0}^{\infty} L_n(t) + r\sum_{n=0}^{\infty} A_n - q\sum_{n=0}^{\infty} B_n\right) ds$$

Where A_n, B_n are Adomian polynomials for the nonlinear terms NT and LT respectively.

Two recursive relations can be contracted from equations (3) given by:

$$T_0 = 1000$$

$$T_{k+1}(t) = \int_0^t (aT_k(1-bT_k) - cA_k - D_k)\, ds \quad (5)$$

$$N_0 = 515530$$

$$N_{k+1}(t) = \int_0^t \left(\delta - fN_k + g\frac{{T_k}^2}{h+{T_k}^2}N_k - pA_k\right) ds \quad (6)$$

$$L_0 = 1000$$

$$L_{k+1}(t) = \int_0^t \left(-mL_k + j\frac{{D_k}^2}{k+{D_k}^2}L_k + rA_k - qB_k\right) ds \quad (7)$$

We list the first three Adomian polynomials as follows for NT we find:

$A_0 = N_0T_0$

$A_1 = N_1T_0 + N_0T_1$

$A_1 = N_2T_0 + N_1T_1 + N_0T_2$

For LT we find:

$B_0 = L_0T_0$

$B_1 = L_1T_0 + L_0T_1$

$B_1 = L_2T_0 + L_1T_1 + L_0T_2$

Notice that

$$D_0 = \frac{d\left(\frac{L_0}{T_0}\right)^l}{s + \left(\frac{L_0}{T_0}\right)^l} \mathrm{T}_0 = 4.64 * 10^3$$

Using the derived Adomian polynomials into equations (5), (6) and (7) we obtain:

$T_0 = 1000$

$$T_1(t) = \int_0^t (aT_0(1 - bT_0) - cA_0 - D_0)\, ds$$

$$= \int_0^t (a * 10^3(1 - b * 10^3) - cN_0T_0 - 4.64 * 10^3)\, ds$$

$$= \int_0^t (a * 10^3(1 - b * 10^3) - c * 515530 * 10^3 - 4.64 * 10^3)\, ds$$

$$= (a * 10^3 - ab * 10^6 - c * 515530 * 10^3 - 4.64 * 10^3)t$$

$$= \beta t$$

Where

$$\beta = a * 10^3 - ab * 10^6 - c * 515530 * 10^3 - 4.64 * 10^3$$

$$T_2(t) = \int_0^t (aT_1(1 - bT_1) - cA_1 - D_1)\, ds$$

$$= \int_0^t (as\beta(1 - bs\beta) - c\rho s * 10^3 * + c\beta s^2 * 515530 - D_1)\, ds$$

Where

$$\rho = \delta - f * 515530 + g\frac{10^6}{h + 10^6} * 515530 - p * 515530 * 10^3$$

We notice that

$$D_1 = \frac{d\left(\frac{L_1}{T_1}\right)^l}{s + \left(\frac{L_1}{T_1}\right)^l} \mathrm{T}_1 = \frac{d(\frac{\theta}{\beta})^l}{s + (\frac{\theta}{\beta})^l} * \beta t$$

Where

$$\theta = -m * 10^3 + j\frac{(4.64 * 10^3)^2}{k + (4.64 * 10^3)^2} * 10^3 + r * 515530 - q * 10^6$$

Set

$$\gamma = \frac{d\left(\frac{\theta}{\beta}\right)^l}{s + \left(\frac{\theta}{\beta}\right)^l} * \beta$$

Then

$D_1 = \gamma t$

Now

$$T_2 = \int_0^t (as\beta(1 - bs\beta) - cs\rho * 10^3 + cs^2 * 515530 * \beta - \gamma s)\, ds$$

$$= \int_0^t (a\beta s - ab\beta^2 s^2 - c\rho s * 10^3 + 515530 * c\beta s^2 - \gamma s)ds$$

$$= (a\beta - c\rho * 10^3 - \gamma)\frac{t^2}{2} - (ab\beta^2 + 515530 * c\beta s^2)\frac{t^3}{3}$$

Now

$N_0 = 515530$

$$N_1 = \int_0^t \left(\delta - fN_0 + g\frac{{T_0}^2}{h + {T_0}^2}N_0 - pA_0\right) ds$$

$$= \int_0^t \left(\delta - f * 515530 + g\frac{10^6}{h + 10^6} * 515530 - p * 515530 * 10^3\right) ds$$

$$= \left(\delta - f * 515530 + g\frac{10^6}{h + 10^6} * 515530 - p * 515530 * 10^3\right) t$$

$$= \rho t$$

$$N_2 = \int_0^t \left(\delta - fN_1 + g\frac{{T_1}^2}{h + {T_1}^2}N_1 - pA_1\right) ds$$

$$= \int_0^t [\,\delta - f\rho s + g\frac{(\beta s)^2}{h + (\beta s)^2} * \rho s - ps(\rho * 10^3 + 515530 * \beta)]ds$$

$$= \delta t - [f\rho + p(\rho * 10^3 + 515530 * \beta)]\frac{t^2}{2} + g\rho * \frac{\beta^2 t^2 - h \ln\left|\frac{h + \beta^2 t^2}{h}\right|}{2\beta^2}$$

Now

$$L_0(t) = 1000$$

$$L_1(t) = \int_0^t \left(-mL_0 + j\frac{{D_0}^2}{k+{D_0}^2}L_0 + rA_0 - qB_0\right)ds$$

$$= \int_0^t \left(-mL_0 + j\frac{{D_0}^2}{k+{D_0}^2}L_0 + rN_0T_0 - qL_0T_0\right)ds$$

$$= \int_0^t \left(-m*10^3 + j\frac{(4.64*10^3)^2}{k+(4.64*10^3)^2}*10^3 + r*515530*10^3 - q*10^6\right)ds$$

$$= \left(-m*10^3 + j\frac{(4.64*10^3)^2}{k+(4.64*10^3)^2}*10^3 + r*515530*10^3 - q*10^6\right)t$$

$$= \theta t$$

$$L_2(t) = \int_0^t \left(-mL_1 + j\frac{{D_1}^2}{k+{D_1}^2}L_1 + rA_1 - qB_1\right)ds$$

$$= \int_0^t \left(-mL_1 + j\frac{{D_1}^2}{k+{D_1}^2}L_1 + r(N_1T_0 + N_0T_1) - q(L_1T_0 + L_0T_1)\right)ds$$

$$= \int_0^t \left(-m\theta s + j\frac{(\gamma s)^2}{k+(\gamma s)^2}*\theta s + rs(\rho*10^3 + 515530*\beta) - qs(\theta+\beta)*10^3\right)ds$$

$$= (-m\theta + r\rho*10^3 + 515530*r\beta - q\{\theta+\beta\}*10^3)\frac{t^2}{2} + j\theta*\frac{\gamma^2t^2 - k\ln\left|\frac{k+\gamma^2t^2}{k}\right|}{2\gamma^2}$$

And so on ……..

The solutions $T(t), N(t), L(t)$ in a series form are given by:

$$T(t) = 1000 + \beta t + (a\beta - c\rho*10^3 - \gamma)\frac{t^2}{2} - (ab\beta^2 + 515530*c\beta s^2)\frac{t^3}{3} + \cdots$$

$$N(t) = 515530 + \rho t + \delta t - [f\rho + p(\rho*10^3 + 515530*\beta)]\frac{t^2}{2} + g\rho*\frac{\beta^2t^2 - h\ln\left|\frac{h+\beta^2t^2}{h}\right|}{2\beta^2} + \cdots$$

$$L(t) = 1000 + \theta t + \left(\begin{matrix}-m\theta + r\rho*10^3 + \\ 515530*r\beta - q\{\theta+\beta\}*10^3\end{matrix}\right)\frac{t^2}{2} + j\theta*\frac{\gamma^2t^2 - k\ln\left|\frac{k+\gamma^2t^2}{k}\right|}{2\gamma^2} + \cdots$$

And using MATLAB software and its application to the solutions that we have obtained from the system we got the following results shown in Table1.1for a period of70 day, which shows that the population of tumor cell is decreasing to get to the50daysandthenbeganincreasingwith the total population of NK cell increasing and decreasing the total population of CD8+T cell.

Table 1.1: The population of tumor cell is decreasing to get to the 50 days and then began increasing with the total population of NK cell increasing and decreasing the total population of CD8+T cell.

Time	$T(t)$	$N(t)$	$L(t)$
1	1000	5.1553e+05	1000
2	-4379.3	5.2109e+05	877.37
3	-11873	5.2702e+05	510.48
4	-21391	5.3327e+05	-100.66
5	-32845	5.3986e+05	-956.05
6	-46144	5.4678e+05	-2055.7
7	-61201	5.5404e+05	-3399.6
8	-77925	5.6164e+05	-4987.8
9	-96227	5.6958e+05	-6820.2
10	-1.1602e+05	5.7787e+05	-8896.9
11	-1.3721e+05	5.865e+05	-11218
12	-1.5971e+05	5.9547e+05	-13783
13	-1.8343e+05	6.0479e+05	-16592
14	-2.0828e+05	6.1446e+05	-19646
15	-2.3418e+05	6.2447e+05	-22944
16	-2.6103e+05	6.3482e+05	-26486
17	-2.8874e+05	6.4553e+05	-30273
18	-3.1722e+05	6.5657e+05	-34303
19	-3.4639e+05	6.6797e+05	-38578
20	-3.7616e+05	6.797e+05	-43098
.			
.			
.			
47	-1.0785e+06	1.1275e+06	-2.5744e+05
48	-1.0887e+06	1.149e+06	-2.688e+05
49	-1.0969e+06	1.1707e+06	-2.8041e+05
50	-1.103e+06	1.1929e+06	-2.9225e+05
51	-1.1069e+06	1.2153e+06	-3.0434e+05
52	-1.1086e+06	1.2382e+06	-3.1668e+05
.			
.			
.			

64	-9.1945e+05	1.539e+06	-4.8376e+05
65	-8.8356e+05	1.5664e+06	-4.9927e+05
66	-8.4416e+05	1.594e+06	-5.1502e+05
67	-8.0115e+05	1.622e+06	-5.3102e+05
68	-7.5445e+05	1.6504e+06	-5.4726e+05
69	-7.0397e+05	1.6791e+06	-5.6375e+05
70	-6.4963e+05	1.7082e+06	-5.8048e+05

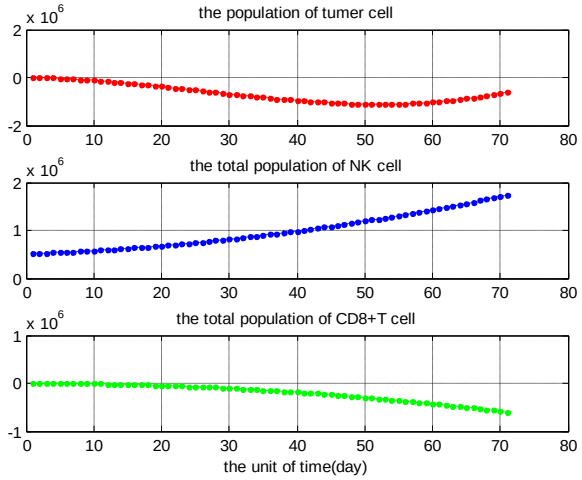

Fig.1.1. The population of tumor cell is decreasing to get to the50daysandthenbeganincreasingwith the total population of NK cell increasing and decreasing the total population of CD8+T cell.

CONCLUSION

The solution to any system of cancer helps doctors seeing how much resistance the patient and the disease in order to know when they can increase or decrease the size of the tumor without waiting to see it; and then can gain time to fight the tumor by medical means were either surgical or chemical or Radiation.

APPENDIX

```
clc;
clear; close all
jk=0;
 a=5.14*10^(-1);b=0;s=2.5*10^(-1);c=0;h=2.02*10^(7);
 j=3.75*10^(-2);f=4.12*10^(-2);g=2.5*10^(-2);          q=0;
m=2*10^(-2);
 d=5.8;
 S=1.3*10^(4);    %sigma
 k=2*10^(7);r=0;l=1.36;p=0;
 B=a*10^(3)-a*b*10^(6)-c*515530*10^(3)-4.64*10^(3);
%beta
 R=S-f*515530+g*(10^(6)/(h+10^(6)))*515530-
p*515530*10^(3);    %ro
 o=-
m*10^(3)+j*((4.64*10^(3))^2/(k+(4.64*10^(3))^2))*10^(
3)+r*515530-q*10^(6);   %theta
 Y=((d*(o/B)^l)/(s+(o/B)^l))*B;      %gama
for t=0:150
 T=1000+B*t+(a*B-c*R*10^(3)-Y)*(t^(2)/2)-
(a*b*B^(2)+515530*c*B*s^(2))*(t^(3)/3);
 N=515530+R*t+S*t-
(f*R+p*(R*10^(3)+515530*B))*(t^(2)/2)+g*R*(B^(2)*t^
(2)-....
h*log(abs((h+B^(2)*t^(2))/h)))/(2*B^(2));
 L=1000+o*t+(-m*o+r*R*10^(3)+515530*r*B-
q*(o+B)*1000)*(t^2/2)+j*o.....
    *(Y^(2)*t^(2)-
k*log(abs((k+Y^(2)*t^(2))/k)))/2*Y^(2);

jk=jk+1;
e(jk)=jk;
e1(jk)=T;e2(jk)=N;e3(jk)=L;
end
Rs=[e' e1' e2' e3']
figure(1)
subplot(3,1,1)
plot(e1,'.--r')
title ('the population of tumer cell')
grid
subplot(3,1,2)
plot(e2,'.--')
title ('the total population of NK cell')
grid
subplot(3,1,3)
plot(e3,'.--g')
title ('the total population of CD8+T cell')
grid
xlabel('the unit of time(day)')
grid
grid
```

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