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Full Length Research Paper

Mathematical model of homogenious tumour growth with delay in time

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This paper consist of a problem of tumor growth with the function of phosphorous to both tumor cells and healthy cells. A detailed discussion about the growth of healthy cells and tumor cells was observed here. A consideration about the solution part of tumor micro vessels has been made here. The governing equations are than solved using MATLAB (a differential equation solver) and graphs are drawn which show the results to the problem under consideration.

Key words: Mathematical modeling, MATLAB, homogeneous tumour.

INTRODUCTION

Mathematical Modeling plays an important role in the area of Bio-Sciences especially tumour growth and allied areas. Mathematical Modeling is a standard process which has specific steps. When ever one has a real world problem (Physical Problem), first and foremost, it is converted to a mathematical equation or a set of equations, which is a very important step. One can play with these sets of equations accordingly and any standard mathematical or statistical process can be used to draw the results and can interpret the results suitably as attached with the real world problem. In a very concise form the simplified Mathematical Modeling may be represented in the form (Kapur, 1985, 1988, Figure 1).

Both tumor cells and normal cells needs nutrients like oxygen, sulpher etc, but other than that, an important element that is phosphorous is present every where in living cells and is a part of molecular systems that involves the genetic codes (DNA, RNA) and an important energy factor called (ATP). We know that the protein synthesis is very important for the cell division and many investigations prove that the conditions which favor hyper protein synthesis, increases the cell number to great extend. Therefore we can say that phosphorous play an important roll in cell division (Slatopolsky and Brown, 2001; Nystroem and Kjelleberg, 1989).

HOMOGENEOUS TUMOR

As we know that many types of mutuent cells may form the tumor but here we are discussing the tumor having only one type of mutuent cells. Let x and y be the mass of the healthy cells and tumor cells respectively at time t (assuming both masses in kilograms). Oxygen is supplied to tumor through blood vessels. We suppose that the mass of tumor vessels is z (in kilogram) and let V be the total mass of the phosphorous available to the organ.

Equation for the growth of the healthy cells (Yang et al., 2004)

The proliferation rate of cell depends on the phosphorous. Let us suppose that the healthy cells proliferate with their maximum per capita rate, that is, p

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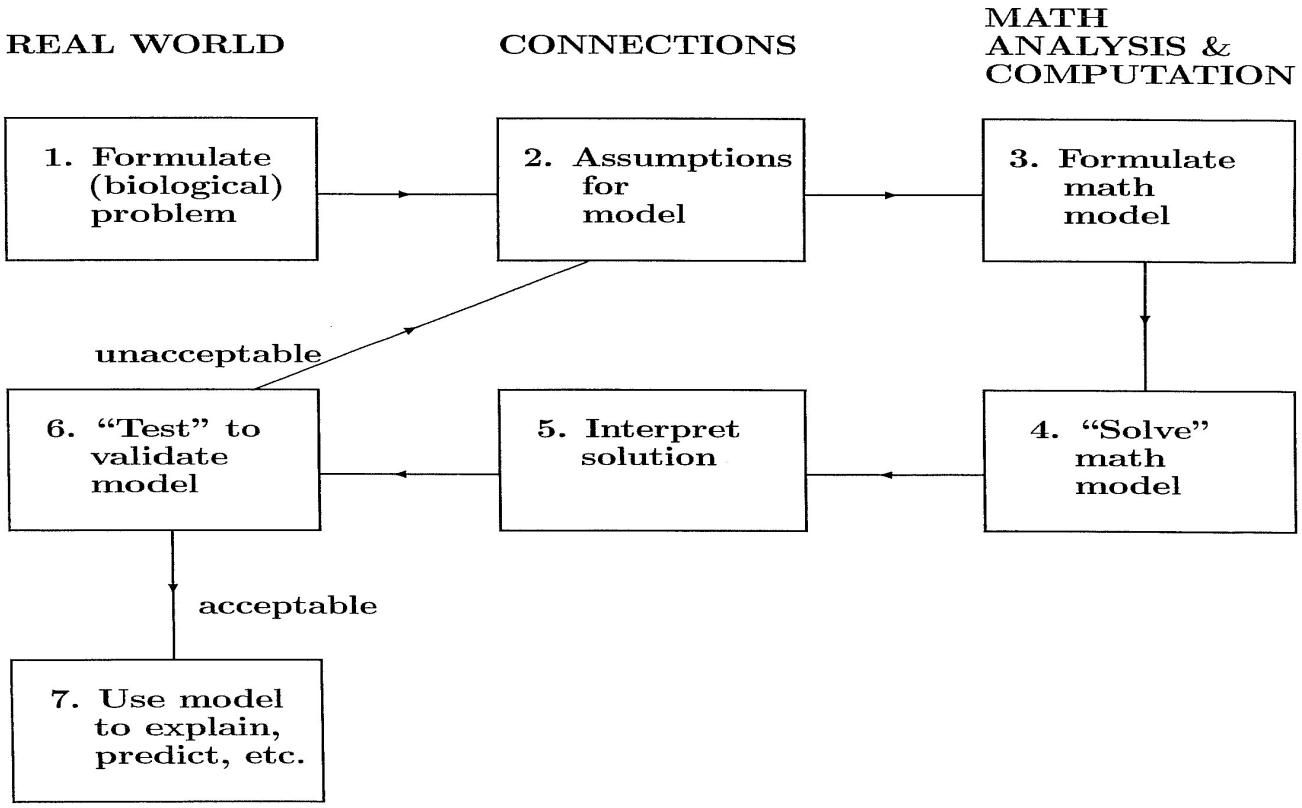

Figure 1. Simplified mathematical modeling.

and let us suppose that available phosphorous for the healthy cells is less than some threshold value *a,* then proliferation rate is given by:

$$p\frac{V}{aS_h g},$$

Where g is the fraction (about two- third) of the total fluid within the organ.

If λ_x is the death rate of healthy cell and τ_x is the time delay which is required by the healthy cells to divide, then $x(t-\tau_x)$ is the mass of the healthy cell at time $(t-\tau_x)$. Thus the growth rate for healthy cells is given by:

$$\frac{dx}{dt} = x(t-\tau_x)\Gamma - x\lambda_x - (x(t-\tau_x)p - x\lambda_x)\frac{x+y_0+z_0}{S_h} \quad (1)$$

$$\Gamma = \min\left\{1, p\frac{V}{aS_h g}\right\}.$$

Here we have taken the values y_0 and z_0 for y and z respectively.

Equation for the growth rate of tumor cells (Yang et al., 2004)

Here we assume that tumor can exceed to its maximum mass limit S_t (in kg.). Let tumor cells proliferate with their maximum per capita q but when the available amount is less than the certain limit says b for the tumor cells, than the proliferation rate is given by:

$$q\frac{V}{bS_t g}$$

Not only phosphorous is enough for the proliferation of tumor cells but also the growth of tumor very much depends on a process that is called the angiogenesis by which a tumor develops a blood supply. Small tumors can survive without networks o f blood vessels to deliver

oxygen and nutrients. When the amount of blood supply provided for the tumor cells is less than some threshold value than the proliferation rate of tumor cells slows up.

Now the growth rate is given by:

$$\frac{dy}{dt}=y(t-\tau_y)\Omega\Lambda-y\lambda_y-(y(t-\tau_y)p-x\lambda_y)\frac{y+z_0}{S_t} \quad (2)$$

Here λ_y is the death rate of tumor cells τ_y is the time delay that the tumor cell in time ($t-\tau_y$), also Ω is minimum of 1 and $q\frac{V}{bS_t g}$ i.e. $\Omega=\min\left\{1,q\frac{V}{bS_t g}\right\}$ and Λ is minimum of $k\frac{(z-hy)}{y}$ (in this expression h represents the mass of the cancer cells that one unit of blood vessels can just barely maintain and k represents sensitivity of tumor tissue due to lake of the blood vessels).

Equation of the growth rate of tumor micro vessels (Yang et al., 2004)

In order to grow larger and spread (metastasize), a tumor needs its own blood supply. Blood vessels supply to the tumor, the oxygen and nutrients, needed to maintain rapid growth of it. Blood vessels also offer access to other areas of the body without a blood supply. A tumor remains very small and localized if the growth rate of tumor micro vessels is not as complex. The tumor micro vessels first grow and take time for activation after which it starts growing the proliferation rate is given by

$$\frac{y(t-\tau_z)V}{aS_h g}r,$$

τ_z is the time delay, which the tumor micro vessels take from its birth to its activation. If r and λ_z is the maximum per capita rate for proliferation and death rate of tumor micro vessels respectively,

The growth rate of the tumor micro vessels is given by:

$$\frac{dz}{dt}=y(t-\tau_z)\Theta-z\lambda_z \quad (3)$$

Θ is the term of minimum of 1 and $\frac{y(t-\tau_z)}{aS_h g}r$,

That is, $\Theta=\min\left\{1,\frac{y(t-\tau_z)}{aS_h g}r\right\}$.

Homogeneous tumor with dietary regulation (Yang et al., 2004)

If we assume that the phosphorous depends on the diet which is ingested with food at the rate of $m(g/day)$ into the organ. We assume that the phosphorous is removed from the organ at the constant proportion; n the dead material hence the above model is modified by adding time variable phosphorous changes to:

$$\frac{dV}{dt}=m-n(a(\lambda_x x-\lambda_z z)+(x(t-\tau_z)p-x\lambda_x)ax\frac{x+y+z}{S_{h_h}}$$
$$+b\lambda_y y+(y(t-\tau_y)q-y\lambda_y)b\frac{y+z}{S_t} \quad (4)$$

Negative terms represents phosphorous liberated by dying cells, which is washed out of the tumor by the blood.

Finely writing all the differential equations representing model of the homogeneous tumors varying the total phosphorous

$$\frac{dx}{dt}=x(t-\tau_x)\Gamma-x\lambda_x-(x(t-\tau_x)p-x\lambda_x)\frac{x+y_0+z_0}{S_h} \quad (5)$$

$$\frac{dy}{dt}=y(t-\tau_y)\Omega\Lambda-y\lambda_y-(y(t-\tau_y)p-x\lambda_y)\frac{y+z_0}{S_t} \quad (6)$$

$$\frac{dy}{dt}=y(t-\tau_y)\Xi\Lambda-\eta\, y\lambda_y-(y(t-\tau_y)p-x\lambda_y)\frac{y+z_0}{S_t} \quad (*)$$

$$\frac{dz}{dt}=y(t-\tau_z)\Theta-z\lambda_z \quad (7)$$

$$\frac{dV}{dt}=m-n(a(\lambda_x x-\lambda_z z))+(x(t-\tau_x))p-x\lambda_x))ax\frac{x+y+z}{S_{h_h}}$$
$$+b\lambda_y y+(y(t-\tau_y)q-y\lambda_y)b\frac{y+z}{S_t} \quad (8)$$

Here an additional equation (*) is written in which η is

Table 1. The numerical parameters for the model.

Serial number	Parameter	Value of the parameter
1	p	3
2	a	10
3	b	20
4	V	150
5	S_h	8
6	q	5
7	S_t	2.5
8	g	.667
9	λ_x	1.2
10	λ_y	1.5
11	λ_z	05
12	τ_x	5
13	τ_y	5
14	τ_z	8
15	k	100
16	h	.05
17	x_0	7.2
18	y_0	.01
19	z_0	.001

an extra parameter which denotes effect of outside therapy or drug doses .Therefore when $\eta = 1$ it means that there is absence of the therapy, and Ξ is the minimum of 1 and $q\frac{V}{bS_t g}\alpha$ i.e. $\Xi = \min\left\{1, q\frac{V}{bS_t g}\alpha\right\}$ parameter α is artificially limiting phosphorous in such a way that making available to healthy cells and not to cancer cells by inhibiting membrane transport of phosphorous. When there is no such therapeutic intervention we take $\alpha = 1$ and when therapy is insuited we take α <1

Numerical solution

For numerical solution of the model under consideration we used the well known tool MATLAB. The numerical parameters (Yang et al., 2004) for this purpose are provided in Table 1.

Figure 2 gives the solution of Equation (1) which shows curve for healthy cells and it is clear that when time is lying between 1 and 7 days, healthy cells are approximately constant, as soon as time becomes approximately 7.5 days healthy cells increases rapidly after that cells increase slowly.

Figure 3 is the solution curve for tumor cells when $\eta = 1.5$ and $\alpha = 1.4$, and we observe that when time is up to approximately 8.5 days healthy cells remains constant and increases rapidly up to 9.25 days and after that tumor cells decreases slowly.

Figure 4 is the solution curve for the tumor cells when we are considering $\alpha = 1$ and $\eta = 1.5$. Curve shows that when time is up to 5.5 days tumor cells remains constant approximately and as time is going on tumor cells increases exponentially.

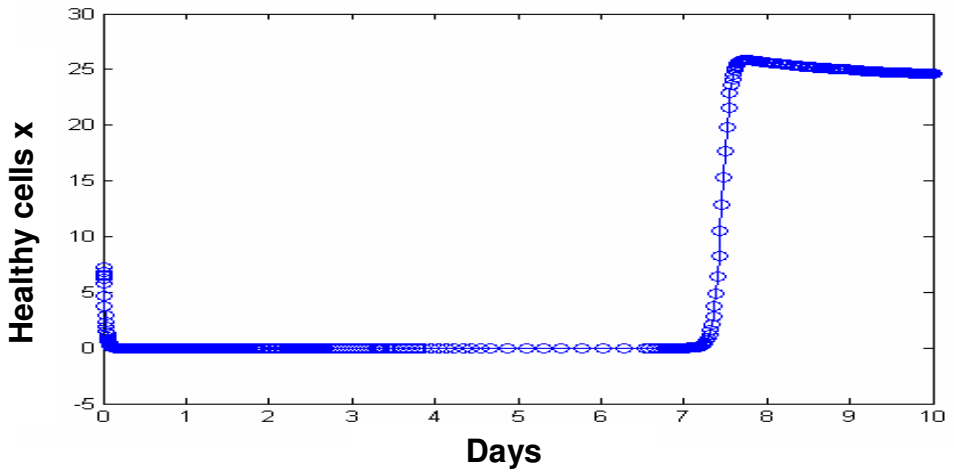

Figure 2. Solution curve for healthy cells with respect to days.

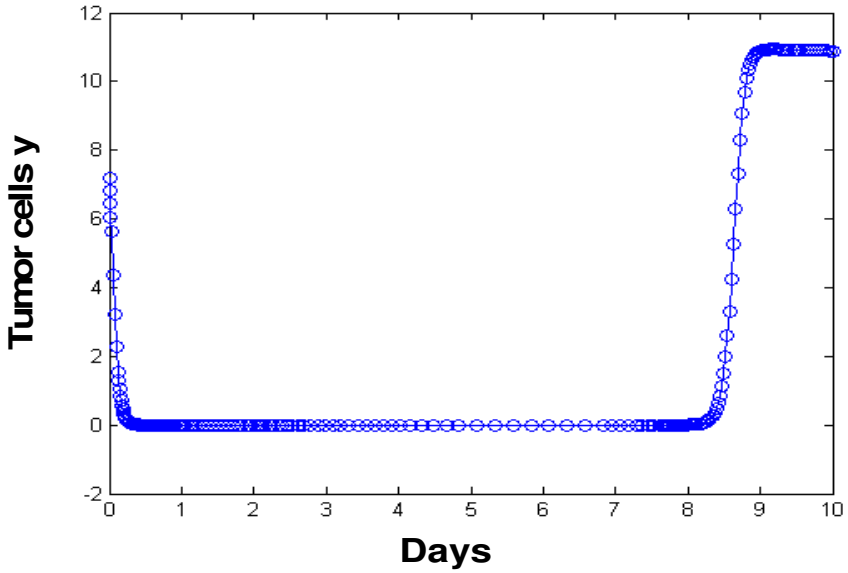

Figure 3. Solution curve for tumor cells with respect to days for parameters η=1.5 and $\alpha = 1.4$.

This is the solution curve for the tumor cells. By considering the value of $\alpha = 1.4$ and $\eta = 1$, curve shows that tumor cells remains constant up to 5 days approximately and as time is going on it increases rapidly up to 6.8 days and decreases onwards slowly.

Figure 5 is the solution curve for tumor cells also. Here the point to be noted is that this is also a solution curve for Equation (2) (when no therapy is used, since in this case both equations are same. We observe that changes are similar to a square curve.

This is the solution curve for the tumor micro vessels, showing that curves are similar to that of tumor cells when $\alpha = 1$ and $\eta = 1$ (when no therapy is used), both are like a square curve.

CONCLUSION

We solve the differential equations for healthy cells, tumor cells and micro vessels, by using MATLAB. Results are in the form of the some special types of the curves which are shown through Figures 2 to 7. Figure 2

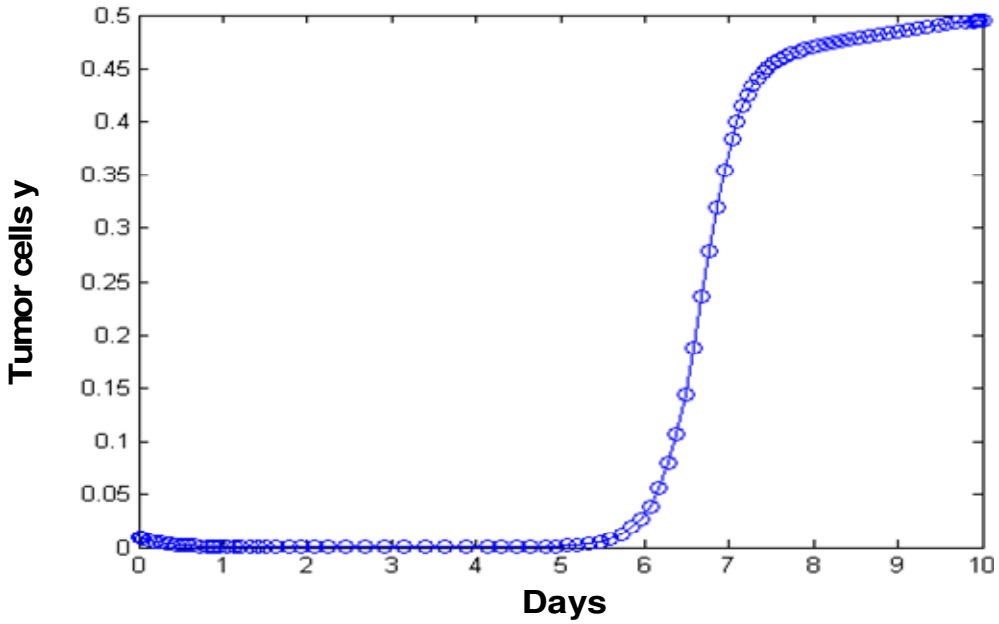

Figure 4. Solution curve for tumor cells with respect to days for parameters $\alpha = 1$ and $\eta = 1.5$.

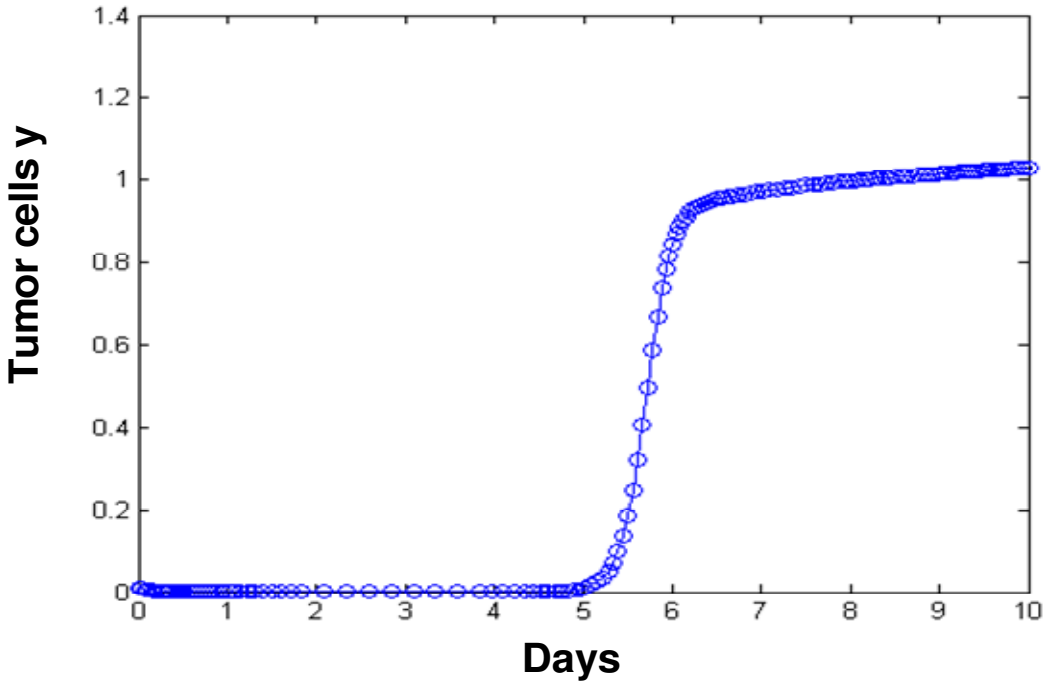

Figure 5. Solution curve for tumor cells with respect to days for parameters $\alpha = 1.4$ and $\eta = 1$.

gives the curves for healthy cells which show that cells remains constant up to 7 days and increases rapidly at 7.5 days. Figures 3 to 7 shows curves for tumor cells in different conditions. Figure 7 shows the curve for tumor micro vessels. Change in the concentration of tumor cells is different for different parameters. Concentration of

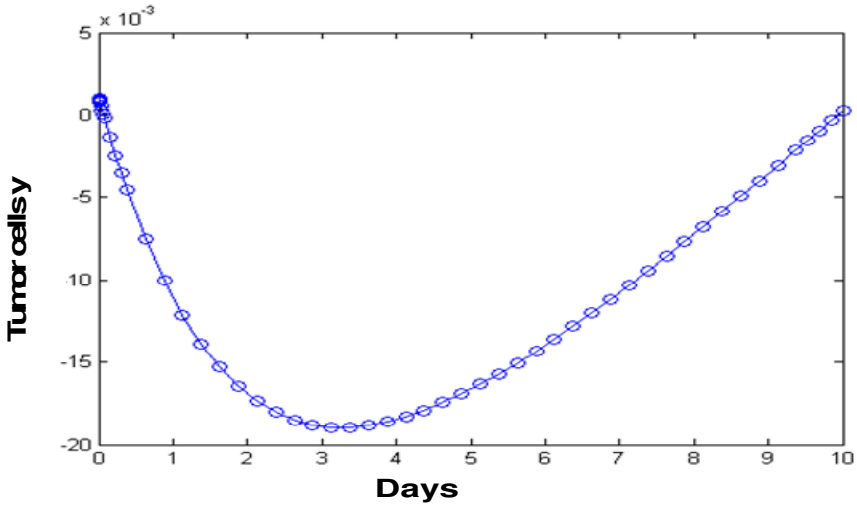

Figure 6. Solution curve for tumor cells with respect to days for parameters $\alpha = 1$ and $\eta = 1$.

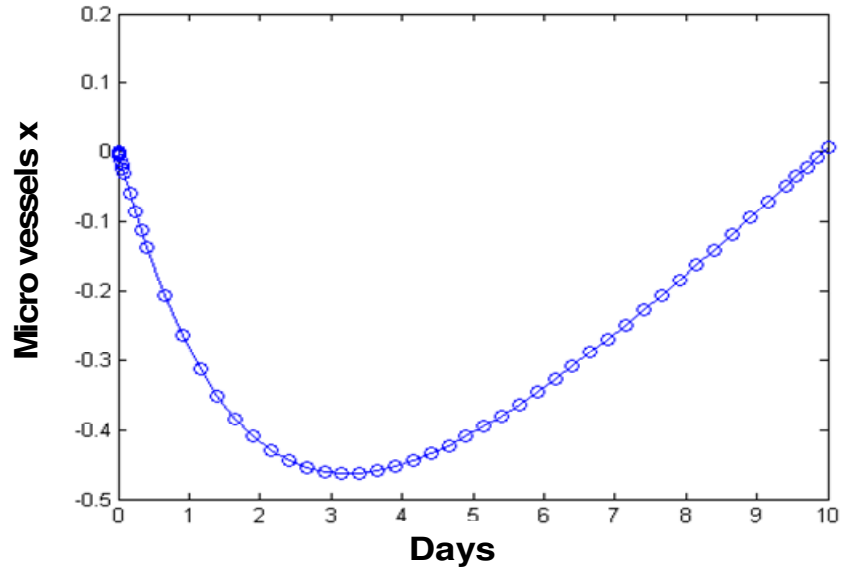

Figure 7. Solution curve for tumor micro vessels with respect to days.

tumor micro vessels with respect to days, changes like a square curve. Initially concentration of tumor micro vessels decreases, and when time is between 3 and 4 days, it started to increase.

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