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Some Control Policies for Control of Cancer

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Abstract

To control cancer, a patient goes through different treatment procedures such as surgery, drug therapy, radiotherapy and also sometimes integrated control of two or more therapy simultaneously. The treatment procedure depends solely upon the stage of cancer at the time of diagnosis. So the mathematical modeling of cancer under different control policy is very complex in nature. In this paper, an attempt has been made to formulate control policies to control cancer under drug therapy in the form of chemotherapy. The drug administered to a patient is assumed to be time dependent variable and primary assumption is that the drug kills both tumor and immune cells. The rate of drug administration at time t assumes to follow three different mathematical models such as (a) Exponential (b) logistic and (c) Oscillatory. The control variable $v(t)$ represents the drug administered at time *t.* Immune -Tumor cell growth are subjected to these drug models as mentioned above and the behavior of Tumor growth has been numerically analyzed A comparison on the behavior of tumor cell growth under these drug model give rise to a significant result and conclusion.

Mathematics Subject Classification: 92B05, 90-08, 65L07, 65L06

Keywords: Mathematical model, Tumor cell, Immune cell, Drug, Stability

1. Introduction

Like any other dynamical system representing physical and biological system, growth of cancer can be treated as a highly complex dynamical system. Many parameters need to be considered while formulating a reasonable and valid mathematical model of cancer. Mathematical modeling of cancer is analogous to formulate the growth of cancer causing tumor cells and its effect on normal cell and immune cell. Immune–Tumor mathematical model has already been researched in [1], [9], and [12]; between tumor and normal cells in [3], [6], [8]. Control of cancer includes treatment such as surgery, radiotherapy, drug therapy (Chemotherapy) [15], [20]. The behavior of tumor model under drug like chemotherapy is another important aspect of mathematical modeling of cancer which is extensively discussed in [2], [3], [6], [10], [11], [14], [16], [17], [21]. In many cases, an integrated control which includes one or more type of control policy used simultaneously to treat and control cancer. In the paper we have considered with three variable model with tumor (*T*), immune (*I*), under drug administration (*v*). The rate of drug applied is assumed to follow (a) Exponential (b) logistic and (c) Oscillatory behavior.

2 Model Description

2.1. Model Equation

Let *I*(*t*) denote the number of immune cell at time *t* that kill tumor cells, *T*(*t*) denote the tumor cells at time *t*. Immune and tumor cells together behaves as a predator-prey model of interacting species [19]. Immune cells in human body have a constant source and also get stimulated and recruited by the presence of tumor cells. Immune cells shows natural death at a rate d_1. Again the interaction of immune cells and tumor cells can result in either the death of tumor cells or the deactivation of immune cells, resulting in the two competition terms $-c_1 I(t)T(t)$ and $-c_2 I(t)T(t)$ where, $c_1$and c_2 represent the deactivation constants.
Hence the two variable growth model for immune – tumor cells can be modeled as

$$\frac{dI}{dt} = s + \frac{rI(t)T(t)}{\sigma + T(t)} - c_1 I(t)T(t) - d_1 I(t) \tag{2.1}$$

$$\frac{dT}{dt} = aT(t)\big(1 - bT(t)\big) - c_2 I(t)T(t), \tag{2.2}$$

where,
s =The constant immune cells present in the body.
σ= steepness coefficients.
r=recruitement rate of immune cells stimulated by the presence of tumor cells
d_1=natural death rate of immune cells.
a=intrinsic tumor growth rate

$\frac{1}{b}$=tumor population carrying capacity.

In the Immune Tumor model described by (2.1) and (2.2), the effect of drug is added to formulate a new mathematical model. The drug administration is assumed to follow three different rate equations, namely logistic growth, exponential and oscillatory. Let *v* (*t*) is the amount of drug administered at time *t*. Assumptions taken are:

- Drug kills both immune and tumor cells.
- The kill rate of immune cells and tumor cells by drug are different. Let $\beta_1$be the kill ratefor immune cells and $\beta_2$be the kill rate for tumor cells$\beta_1 \neq \beta_2$.

The drug equation as per logistic growth is as follows:

$$\frac{dv}{dt} = \alpha_3 v(t)\big(1 - \beta_3 v(t)\big) \tag{2.3}$$

The drug equation as per exponential growth is as follows:

$$\frac{dv}{dt} = \alpha_3 e^{-\beta_3 v(t)} - \gamma_3 \tag{2.4}$$

The drug equation as per oscillatory growth is as follows:

$$\frac{dv}{dt} = \alpha_3 \sin \beta_3 v(t) \tag{2.5}$$

Where, α_3 = intrinsic rate of drug application and $\frac{1}{\beta_3}$ = maximum drug carrying capacity, γ_3 = a constant rate of reduction of drug.

2.1.2 Immune-Tumor- Logistic Drug model (I-T-D_L)

Immune-Tumor-Drug model equation under logistic drug growth can be described as:

$$\frac{dI}{dt} = s + \frac{rI(t)T(t)}{\sigma + T(t)} - c_1 I(t)T(t) - d_1 I(t) - \beta_1 I(t)v(t) \tag{2.6}$$

$$\frac{dT}{dt} = aT(t)\big(1 - bT(t)\big) - c_2 I(t)T(t) - \beta_2 T(t)v(t) \tag{2.7}$$

$$\frac{dv}{dt} = \alpha_3 v(t)\big(1 - \beta_3 v(t)\big) \tag{2.8}$$

2.1.3 Immune-Tumor- Exponential Drug model (I-T-D_E)

Immune-Tumor-Drug model equation under exponential drug growth can be described as:

$$\frac{dI}{dt} = s + \frac{rI(t)T(t)}{\sigma + T(t)} - c_1 I(t)T(t) - d_1 I(t) - \beta_1 I(t)v(t) \tag{2.9}$$

$$\frac{dT}{dt} = aT(t)\big(1 - bT(t)\big) - c_2 I(t)T(t) - \beta_2 T(t)v(t) \quad (2.10)$$

$$\frac{dv}{dt} = \alpha_3 e^{-\beta_3 v(t)} - \gamma_3 \quad (2.11)$$

2.1.4 Immune-Tumor- Oscillatory Drug model (I-T-D$_O$)

Thus Immune-Tumor-Drug model equation under oscillatory drug growth can be described as:

$$\frac{dI}{dt} = s + \frac{rI(t)T(t)}{\sigma + T(t)} - c_1 I(t)T(t) - d_1 I(t) - \beta_1 I(t)v(t) \quad (2.12)$$

$$\frac{dT}{dt} = aT(t)\big(1 - bT(t)\big) - c_2 I(t)T(t) - \beta_2 T(t)v(t) \quad (2.13)$$

$$\frac{dv}{dt} = \alpha_3 \sin \beta_3 v(t) \quad (2.14)$$

The parameters are well defined.

3 Stability Analysis

3.1 Immune-Tumor- Logistic Drug model (I-T-D$_L$)

3.1.1 Equilibrium points

Immune-Tumor-Drug under logistic drug growth

$$\frac{dv}{dt} = \alpha_3 v(t)\big(1 - \beta_3 v(t)\big) \quad (3.1)$$

Leads to equilibrium points

$$v(t) = 0 \quad (3.2)$$

$$v(t) = \frac{1}{\beta_3} \quad (3.3)$$

Putting $v(t) = 0$ we get either $T(t) = 0$ or $T(t) = \frac{a - c_2 I}{ab}$

When $v(t) = 0, T(t) = 0$ then $I(t) = \frac{s}{d_1}$ and

For $v(t) = \frac{1}{\beta_3}, T(t) = 0$ then $I(t) = \frac{s}{d_1 + \frac{\beta_1}{\beta_3}}$

Hence here the equilibrium points are

- Tumor free drug free equilibrium $\left(\frac{s}{d_1}, 0, 0\right)$

- Tumor free drug equilibrium $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$

3.1.2 Stability Analysis for $\left(\frac{s}{d_1}, 0,0\right)$

Linearizing around$\left(\frac{s}{d_1}, 0,0\right)$ give a linear system of equation

$$\begin{pmatrix} \dot{I} \\ \dot{T} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -d_1 & \frac{rs}{d_1\sigma} - \frac{c_1 s}{d_1} & \frac{-\beta_1 s}{d_1} \\ 0 & a - \frac{c_2 s}{d_1} & 0 \\ 0 & 0 & \alpha_3 \end{pmatrix} \begin{pmatrix} I - \frac{s}{d_1} \\ T \\ v \end{pmatrix} \tag{3.4}$$

With eigenvalues:

$$\lambda_1 = -d_1 \tag{3.5}$$

$$\lambda_2 = a - \frac{c_2 s}{d_1} \tag{3.6}$$

$$\lambda_3 = \alpha_3 \tag{3.7}$$

The model will be stable if

$$\lambda_1 < 0 \tag{3.8}$$
$$\lambda_2 < 0 \tag{3.9}$$
$$\lambda_3 < 0 \tag{3.10}$$

Which means

$$-d_1 < 0 \tag{3.11}$$

$$a - \frac{c_2 s}{d_1} < 0 \tag{3.12}$$

$$\alpha_3 < 0 \tag{3.13}$$

As the parameter α_3 is always positive contradicting the condition (3.13) so the system will not be stable around $\left(\frac{s}{d_1}, 0,0\right)$.

3.1.3 Stability Analysis for $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$

Linearizing the system around $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$ we get

$$\begin{pmatrix} \dot{I} \\ \dot{T} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -d_1 - \frac{\beta_1}{\beta_3} & \frac{rs}{\sigma(d_1 + \frac{\beta_1}{\beta_3})} & \frac{-\beta_1 s}{d_1 + \frac{\beta_1}{\beta_3}} \\ 0 & a - \frac{c_2 s}{(d_1 + \frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3} & 0 \\ 0 & 0 & -\alpha_3 \end{pmatrix} \begin{pmatrix} I - \frac{s}{d_1} \\ T \\ v - \frac{1}{\beta_3} \end{pmatrix} \quad (3.14)$$

Leads to the Eigen values

$$\lambda_1 = -d_1 - \frac{\beta_1}{\beta_3} \quad (3.15)$$

$$\lambda_2 = a - \frac{c_2 s}{(d_1 + \frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3} \quad (3.16)$$

$$\lambda_3 = -\alpha_3 \quad (3.17)$$

The model will be stable if

$$\lambda_1 < 0 \quad (3.18)$$

$$\lambda_2 < 0 \quad (3.19)$$

$$\lambda_3 < 0 \quad (3.20)$$

Which means

$$-d_1 - \frac{\beta_1}{\beta_3} < 0 \quad (3.21)$$

$$a - \frac{c_2 s}{(d_1 + \frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3} < 0 \quad (3.22)$$

$$-\alpha_3 < 0 \quad (3.23)$$

3.2 Immune-Tumor-Exponential Drug model (I-T-D_E)

3.2.1 Equilibrium points

Immune-Tumor-Drug under exponential drug growth

$$\frac{dv}{dt} = \alpha_3 e^{-\beta_3 v(t)} - \gamma_3 \quad (3.24)$$

Leads to equilibrium points

$$v(t) = \frac{1}{\beta_3} \log\left(\frac{\alpha_3}{\gamma_3}\right) = v^* \quad (3.25)$$

When $v(t) = \frac{1}{\beta_3} \log\left(\frac{\alpha_3}{\gamma_3}\right) = v^*$, then $T(t) = 0$ and $I(t) = \frac{s}{d_1 + \beta_1 v^*} = I^*$

Hence the equilibrium point is $\left(\frac{s}{d_1 + \beta_1 v^*}, 0, \frac{1}{\beta_3} \log\left(\frac{\alpha_3}{\gamma_3}\right)\right)$

3.2.2 Stability Analysis for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right) = v^*\right)$

Linearizing the system around $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)\right)$ we get

$$\begin{pmatrix}\dot{I}\\ \dot{T}\\ \dot{v}\end{pmatrix} = \begin{pmatrix}-d_1-\beta_1 v^* & -c_1 I^* & -\beta_1 I^*\\ 0 & a-c_2 I^*-\beta_2 v^* & 0\\ 0 & 0 & -\alpha_3\beta_3 e^{-\beta_3 v^*}\end{pmatrix}\begin{pmatrix}I-\frac{s}{d_1+\beta_1 v^*}\\ T\\ v-\frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)\end{pmatrix} \tag{3.26}$$

Leads to the Eigen values

$\lambda_1 = -d_1 - \beta_1 v^*$ (3.27)

$\lambda_2 = a - c_2 I^* - \beta_2 v^*$ (3.28)

$\lambda_3 = -\alpha_3\beta_3 e^{-\beta_3 v^*}$ (3.29)

The model will be stable if

$\lambda_1 < 0$ (3.30)

$\lambda_2 < 0$ (3.31)

$\lambda_3 < 0$ (3.32)

Which means

$-d_1 - \beta_1 v^* < 0$ (3.33)

$a - c_2 I^* - \beta_2 v^* < 0$ (3.34)

$-\alpha_3\beta_3 e^{-\beta_3 v^*} < 0$ (3.35)

3.3 Immune-Tumor-Oscillatory Drug model (I-T-D_O)

3.3.1 Equilibrium points

Immune-Tumor-Drug under exponential drug growth

$\frac{dv}{dt} = \alpha_3 \sin\beta_3 v(t)$ (3.36)

Leads to equilibrium points

$v(t) = \frac{n\pi}{\beta_3} = v^*$ (3.37)

When $v(t) = \frac{n\pi}{\beta_3} = v^*$, then $T(t) = 0$ and $I(t) = \frac{s}{d_1+\beta_1 v^*} = I^*$

Hence the equilibrium point is $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$

3.3.2 Stability Analysis for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$

Linearizing the system around $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$ we get

$$\begin{pmatrix} \dot{I} \\ \dot{T} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -d_1 - \beta_1 v^* & -c_1 I^* & -\beta_1 I^* \\ 0 & a - c_2 I^* - \beta_2 v^* & 0 \\ 0 & 0 & \alpha_3 \beta_3 \cos(\beta_3 v^*) \end{pmatrix} \begin{pmatrix} I - \frac{s}{d_1+\beta_1 v^*} \\ T \\ v - \frac{n\pi}{\beta_3} \end{pmatrix} \tag{3.38}$$

Leads to the Eigen values

$$\lambda_1 = -d_1 - \beta_1 v^* \tag{3.39}$$

$$\lambda_2 = a - c_2 I^* - \beta_2 v^* \tag{3.40}$$

$$\lambda_3 = \alpha_3 \beta_3 \cos(\beta_3 v^*) \tag{3.41}$$

The model will be stable if

$$\lambda_1 < 0 \tag{3.42}$$
$$\lambda_2 < 0 \tag{3.43}$$
$$\lambda_3 < 0 \tag{3.44}$$

Which means

$$-d_1 - \beta_1 v^* \ < 0 \tag{3.45}$$

$$a - c_2 I^* - \beta_2 v^* \ < 0 \tag{3.46}$$

$$\alpha_3 \beta_3 \cos(\beta_3 v^*) < 0 \tag{3.47}$$

4. Analysis and Conclusion

Immune–Tumor model is subjected to three different drug models and the stability of the system has been analyzed around the equilibrium points. The stability conditions depend on the system parameters as well as the system equilibrium points. Model under tumor free-drug free equilibrium found to be unstable. Stability of all other models under the different system equilibrium are found to be conditional. Stability of the all three models can be summarized in the following table:

Table 4.1

Sl. No	Mathematical modeling	Equilibrium points	Condition For Stability
1	Immune-Tumor-Logistic Drug model (I-T-D_L)	Tumor free drug free equilibrium $\left(\frac{s}{d_1}, 0, 0\right)$	Not stable for any condition
		Tumor free drug equilibrium $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$	$a < \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$
2	Immune-Tumor-Exponential Drug model(I-T-D_E)	Tumor free drug equilibrium $\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$	$a < c_2 I^* - \beta_2 v^*$ Where, $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$
3	Immune-Tumor-Oscillatory Drug model(I-T-D_O)	Tumor free drug equilibrium $\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3}$	*i)* $a < c_2 I^* - \beta_2 v^*$ *ii)* $cos(\beta_3 v^*) < 0$ Where, $v^* = \frac{n\pi}{\beta_3}$ $I^* = \frac{s}{d_1+\beta_1 v^*}$

5. Numerical Analysis

The Immune –Tumor model under three different drug models has been analyzed numerically. Parameters are chosen to validate the condition of stability.

5.1 Analysis of I-T-D_L Model:

(i)It has been seen that, the system is unstable for tumor free-drug free equilibrium [Fig-5.1] for any condition of stability.

(ii)When the parameters are selected in such a way that the stability condition $a < \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$ is satisfied, the numerical result shows the validity of the condition. Rate of drug administered under logistic model is given in Fig-5.2. The growth of tumor under logistic drug model also shows stability given in Fig-5.3. With same parameters and satisfying conditions of stability, we can observe the stability for immune cell growth also in Fig-5.4

(iii) System parameters are chosen in such a way that, the stability condition is not satisfied. That means $a > \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$. The numerical result also shows instability of tumor growth in Fig-5.5.

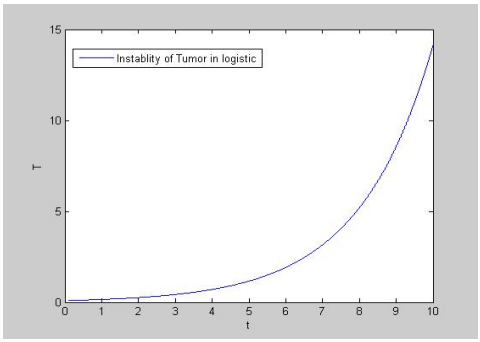

Fig-5.1: Instability of Tumor for drug free equilibrium $\left(\frac{s}{d_1}, 0,0\right)$

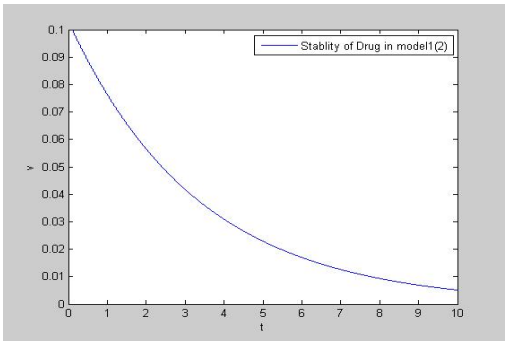

Fig-5.2: Stability of drug administered for $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$

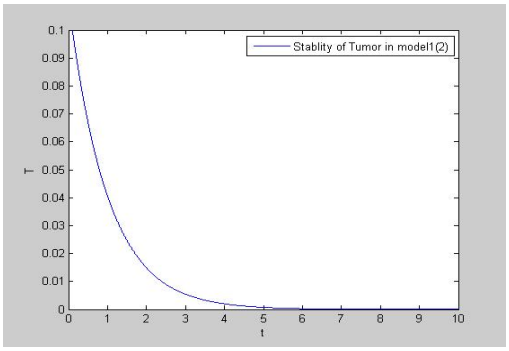

Fig-5.3: Stability of Tumor for $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$ **satisfying condition** $a < \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$

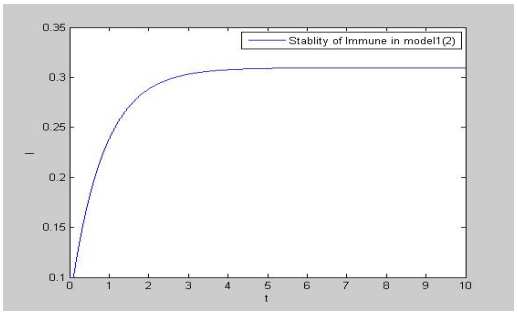

Fig-5.4: Stability of Immune for $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$ **satisfying condition of stability** $a < \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$

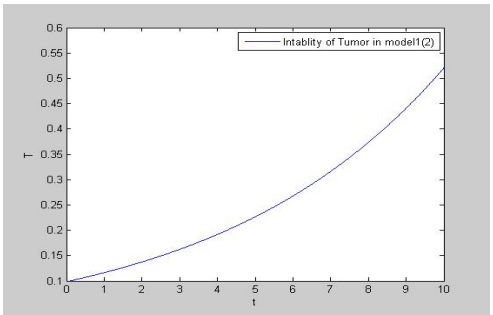

Fig-5.4: Instability of Tumor for $\left(\frac{s}{d_1+\frac{\beta_1}{\beta_3}}, 0, \frac{1}{\beta_3}\right)$ **satisfying condition of instability i.e** $a > \frac{c_2 s}{(d_1+\frac{\beta_1}{\beta_3})} - \frac{\beta_2}{\beta_3}$

5.2 Analysis of I-T-D$_E$ Model :

(i)There is no drug free –tumor free equilibrium for I-T-D$_E$ Model.

(ii) Stability analysis around the equilibrium point $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)_3}\right) = v^*\right)$ gives rise to the stability condition $a < c_2 I^* - \beta_2 v^*$ with $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$. When the parameters are selected in such a way that the given stability condition is satisfied, then the stable rate of drug administered under exponential model is given in Fig-5.6. The growth of tumor under exponential drug model also shows stability given in Fig-5.7. With same parameters and satisfying conditions of stability, we can observe the stability for immune cell growth also in Fig-5.8.
(iii) System parameters are chosen in such a way that, the stability condition is not satisfied. That means $a > c_2 I^* - \beta_2 v^*$ The numerical result also shows instability of tumor growth in Fig-5.9.

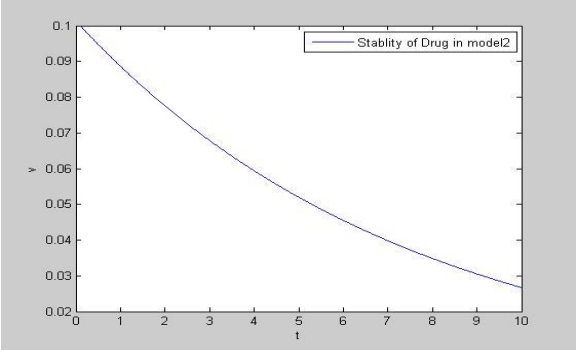

Fig-5.6: Stability of Drug administered for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\beta_3}\right) = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ with $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$

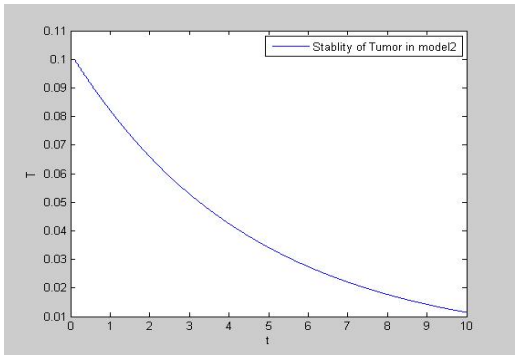

Fig-5.7: Stability of Tumor for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\beta_3}\right) = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ with $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$

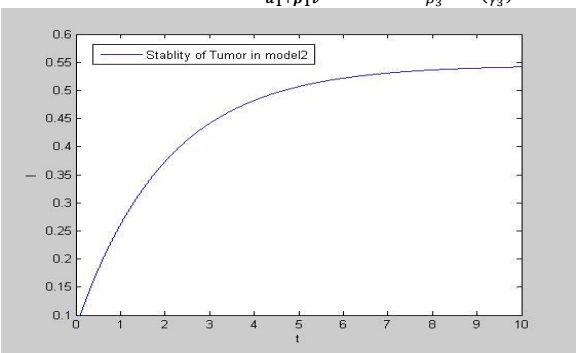

Fig-5.8: Stability of Immune for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\beta_3}\right) = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ with $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$

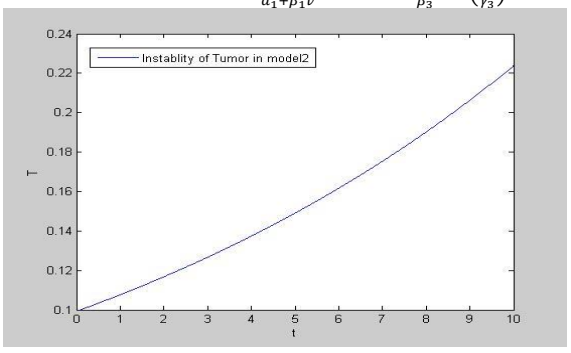

Fig-5.9: Instability of Tumor for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\beta_3}\right) = v^*\right)$ violating condition of stability i.e $a > c_2 I^* - \beta_2 v^*$ with $I^* = \frac{s}{d_1+\beta_1 v^*}$ and $v^* = \frac{1}{\beta_3}\log\left(\frac{\alpha_3}{\gamma_3}\right)$

5.3 Analysis of I-T-D$_0$ Model:

(i)There is no drug free –tumor free equilibrium for I-T-D$_o$ Model.

(ii) Stability analysis around the equilibrium point $\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3}$ gives rise to the stability condition $a < c_2 I^* - \beta_2 v^*$ and $cos(\beta_3 v^*) < 0$,Where, $v^* = \frac{n\pi}{\beta_3}$ and $I^* = \frac{s}{d_1+\beta_1 v^*}$. When the parameters are selected in such a way that the above stability condition is satisfied, then the stable rate of drug administered under oscillatory drug model is given in Fig-5.10. The growth of tumor under oscillatory drug model also shows stability given in Fig-5.11. With same parameters and satisfying conditions of stability, we can observe the stability for immune cell growth also in Fig-5.11.

(iii) System parameters are chosen in such a way that, the stability condition is not satisfied. That means $a > c_2 I^* - \beta_2 v^*$ The numerical result also shows instability of tumor growth in Fig-5.9.

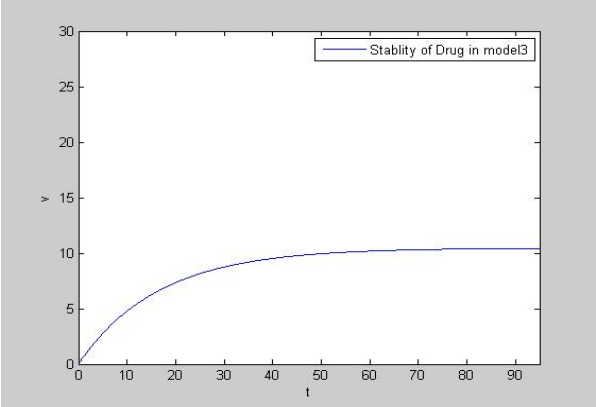

Fig-5.10: Stable rate of Drug administered for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ and $cos(\beta_3 v^*) < 0$,Where, $v^* = \frac{n\pi}{\beta_3}$ and $I^* = \frac{s}{d_1+\beta_1 v^*}$

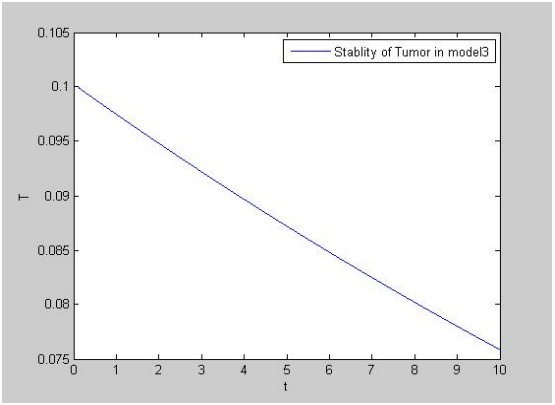

Fig-5.11: Stability of Tumor for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ and $cos(\beta_3 v^*) < 0$,Where, $v^* = \frac{n\pi}{\beta_3}$ and $I^* = \frac{s}{d_1+\beta_1 v^*}$

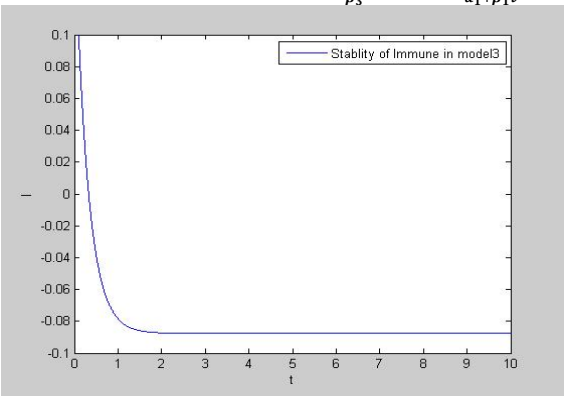

Fig-5.12: Stability of Immune for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$ satisfying condition of stability $a < c_2 I^* - \beta_2 v^*$ and $cos(\beta_3 v^*) < 0$,Where, $v^* = \frac{n\pi}{\beta_3}$ and $I^* = \frac{s}{d_1+\beta_1 v^*}$

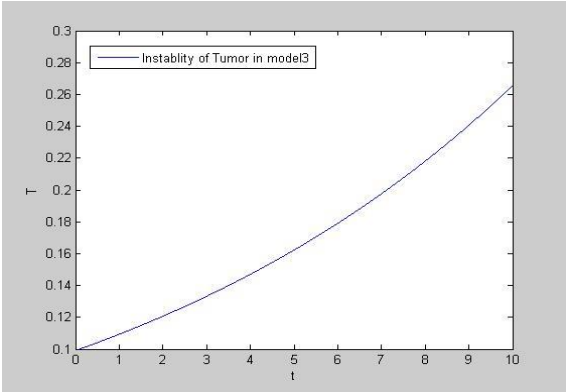

Fig-5.13: Instability of Tumor for $\left(\frac{s}{d_1+\beta_1 v^*}, 0, \frac{n\pi}{\beta_3} = v^*\right)$ violating condition of stability $a < c_2 I^* - \beta_2 v^*$ and $cos(\beta_3 v^*) < 0$,Where, $v^* = \frac{n\pi}{\beta_3}$ and $I^* = \frac{s}{d_1+\beta_1 v^*}$

5.4 Tumor growth under the three drug model : A comparison

The growth of tumor cell under all three types of drug model has been analyzed under the condition of stability. Figure -5.14 gives a comparison of the growth of tumor cells under all three types of drug model satisfying stability conditions. It is observed that, the growth of tumor decreases under application of all types of drug models. However, Immune – Tumor -Drug model under Logistic drug (**I-T-D_L**) shows the reduction of tumor cell quicker than the exponential or oscillatory model. The oscillatory drug administration shows slow recovery.

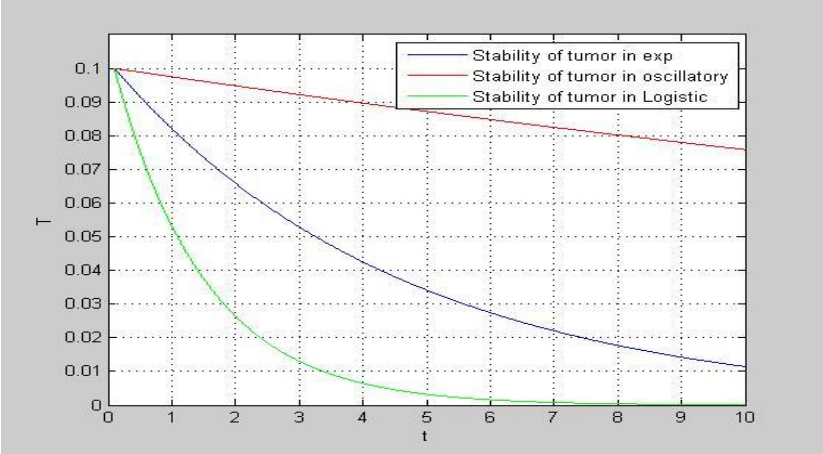

Figure-5.14

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