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Stability Analysis of Mathematical Model of Virus Therapy for Cancer

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Abstract. In this paper, we have analyzed a mathematical model for the study of interaction between tumor cells and oncolytic viruses. The model is analyzed using stability theory of differential equations. We gain some conditions for global stability of trivial and interior equilibrium point.

Keywords: Tumor, Oncolytic virus, Stability, Asymptotic stability.

2000 Mathematics subject classification: 34A34, 34D20, 34D23.

1. Introduction

Cancer is one of the dangerous illnesses causing many death each year. Up to now, many efforts have been done for the treatment of cancer. Specially it is important if the tumor can be treated or controlled medically in order to avoid an unnecessary surgery. In the middle of last century, a novel method was tried by direct injection of virus into tumor [12, 9, 13, 6, 16, 17]. The first viruses implemented in this regards, were found in the nature, but the immune response began to destroy them and prevented them from destroying the cancer [9, 5, 13]. To overcome this problem, genetic researchers altered the viruses in the laboratory and created new ones which were useful for cancer therapy. Of course, this prevented the immune system to distinguish the virus in first

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injection, but the problem was still remained for further injections. Later, the virus was intellectually chosen such that it will infected and kill the tumor cells but it did not effect normal cells [11, 4]. This method is known today as cancer viral therapy and the special virus type is called oncolytic virus [8, 2].

The relation between the effect of virus and tumor growth is very complex. For having a better understanding of the connection between them, many mathematicians performed the modeling of their interactions with ordinary differential equations. This leads us to better understanding and analyzing of the treatment method. Several mathematical models that described these methods were recently developed [19, 20, 10, 14, 15].

Our analyzed model is the Wodarz's model [18]. Wodarz presented a mathematical model which described the interaction between two types of tumor cells (the cells that are not infected but are susceptible to be infected so far as they have the cancer phenotype) with ratio dependent functional response between them.

This paper is organized as follows: In Section 2, the model is outlined. Section 3 contains boundedness of solutions of the system which proves that system is meaningful in biology. In Section 4, conditions for existence of equilibrium points in natural phenomena are obtained. Sections 5 deals with the local stability analysis of equilibrium points; furthermore, in this section we will conclude that the existence of Hopf bifurcation at interior equilibrium point is meaningless. In Section 6, we determine the conditions for global stability of two important equilibrium points, and we explain interaction between equilibrium points. Section 7 presents the numerical results and finally, conclusions are given in Section 8.

2. Mathematical Model

The model contains two types of tumor cells x and y that respectively are the size of uninfected tumor cells and infected tumor cells by the virus. It is explained schematically in Figure 1. In this model r is growth rate of tumor in a logistic fashion, d is death rate. The maximum size or space that tumor is allowed to occupy is given by its carrying capacity k. Parameter β is spread rate of virus in tumor cells (this parameter can be viewed as summarizing the replication rate of the virus). Death rate of infected tumor cells by virus represents by a; moreover, s shows growth rate in a logistic fashion. Based on these assumption model is given the following form [18]:

$$\begin{aligned} \dot{x} &= rx(1-\frac{x+y}{k}) - dx - \beta xy, \\ \dot{y} &= \beta xy + sy(1-\frac{x+y}{k}) - ay. \end{aligned} \tag{2.1}$$

With the conditions $x(0) = x_0 > 0$ and $y(0) = y_0 > 0$.
Agarwal and Bhadauria [1] considered the model that Novozhilov [10] presented

and analyzed it. The model that we considered is a little easier but more accurate, because death rate of the uninfected cells exists.

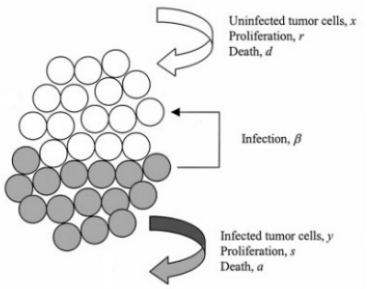

FIGURE 1. Interactions between the virus and the tumor cells [18].

3. Boundedness of Solutions

Boundedness may be interpreted as a natural restriction to grew because of limited resources. To establish the biological validity of the system, we have to show that the solutions of system (2.1) are bounded. For this, we find the region of attraction in the following lemma.

Lemma 3.1. *All the solutions of (2.1) starting in the positive orthant* $(\mathbb{R}_0^+)^2$ *either approaches, enter or remain in the subset of* $(\mathbb{R}_0^+)^2$ *defined by*

$$\Omega = \{(x, y) \in (\mathbb{R}_0^+)^2 : 0 < x + y \leq k\}$$

where $(\mathbb{R}_0^+)^2$ *denote the non-negative cone of* $\mathbb{R}^2$ *including its lower dimensional faces.*

Proof. From system (2.1) we get:

$$\begin{aligned} \dot{x} + \dot{y} &= (rx + sy)(1 - \frac{x+y}{k}) - dx - ay, \\ \dot{x} + \dot{y} &\leq \delta(x + y)(1 - \frac{x+y}{k}) \end{aligned}$$

where $\delta = max(r, s)$. If we consider $z(t) = x(t) + y(t)$; therefore, $\dot{z} = \dot{x} + \dot{y} \leq \delta(x + y)(1 - \frac{x+y}{k}) = \delta z(1 - \frac{z}{k})$. Hence, we consider $\dot{U} = \delta U(1-\frac{U}{k})$, with solving this differential equation we have $U(t) = (\frac{k}{1-e^{k t_0 - \delta t}})$, which gives $\limsup_{t\to\infty} U(t) = k$. On the other hand, we know that $\dot{z}(t) \leq \dot{U}(t)$; then, By usual comparison theorem [7], because $z(t) \leq U(t)$, it implies that $\limsup_{t\to\infty} z(t) \leq \limsup_{t\to\infty} U(t) = k$. Hence, we get the following expression as $t \to \infty$,

$$\limsup_{t\to\infty} x(t) + y(t) \leq k.$$

Thus, it is sufficient to consider solutions in the region Ω. Solutions of the initial value problem starting in Ω and defined by (2.1) exist and are unique on a maximal interval [3]. Since solutions remain bounded in the positively invariant region Ω , the maximal interval is well posed both mathematically and epidemiologically. □

4. Admissibility of Equilibriums in Relation

System (2.1) have the following equilibrium points

$$E_0 = (0,0),$$
$$E_1 = (\frac{k(r-d)}{r}, 0), \tag{4.1}$$
$$E_2 = (0, \frac{k(s-a)}{s}), \tag{4.2}$$
$$E_3 = (\frac{\beta k(a-s)+ar-sd}{\beta(\beta k+r-s)}, \frac{\beta k(r-d)+sd-ar}{\beta(\beta k+r-s)}) := (x^*, y^*).$$

The equilibriums of E_1 and E_2 are biologically admissible if and only if $r > d$ and $s > a$ respectively. For stability of E_3 we have following theorem;

Theorem 4.1. *equilibrium E_3 exists if and only if one of the following conditions holds:*

(i) $\quad \beta k < s < \beta k + r$ *and* $max\{\frac{a-\beta k}{s-\beta k}r, 0\} < d < \beta k(\frac{a}{s}-1)+\frac{a}{s}r,$

(ii) $\quad s < \beta k$ *and* $0 < d < min\{\frac{a-\beta k}{s-\beta k}r, \beta k(\frac{a}{s}-1)+\frac{a}{s}r\},$

(iii) $\quad s > \beta k + r$ *and* $max\{\beta k(\frac{a}{s}-1)+\frac{a}{s}r, 0\} < d < \frac{a-\beta k}{s-\beta k}r.$

Proof. At first, we suppose $\beta k + r - s > 0$; therefore,

$$\beta k(a-s)+ar-ds > 0, \tag{4.3}$$
$$\beta k(r-d)+ds-ar > 0. \tag{4.4}$$

From (4.3) we have $d < \big(\beta k(a-s)+ar\big)/s$; also, with the help of (4.4) we gain $d(s-\beta k) > (a-\beta k)r$. It means that if $s > \beta k$, then $d > \frac{a-\beta k}{s-\beta k}r$. Because of positivity of d we have $max\{\frac{a-\beta k}{s-\beta k}r, 0\} < d$. Although, we get $d < \frac{a-\beta k}{s-\beta k}r$ if $s < \beta k$. Because d is positive, we gain $d < min\{\frac{a-\beta k}{s-\beta k}r, \beta k(\frac{a}{s}-1)+\frac{a}{s}r\}$.

Secondly, if $\beta k + r - s < 0$; thus,

$$\beta k(a-s)+ar-ds < 0,$$
$$\beta k(r-d)+ds-ar < 0.$$

Because of $s > \beta k + r > \beta k$, we get $d > \big(\beta k(a-s)+ar\big)/s$ and $d < \frac{a-\beta k}{s-\beta k}r$. □

Consequently, all situation for existence of equilibrium points were obtained.

5. Local Stability Analysis of Equilibrium Points

An equilibrium point is locally asymptotically stable if all solutions of the system approach it as $t \to \infty$. To discuss the local stability of equilibrium points we compute the variational matrix of system (2.1). The signs of real parts of eigenvalues of the variational matrix evaluated at a given equilibrium point determine its stability. The entries of general variational matrix are given by differentiating the right hand side of system (2.1) with respect to x and y. The variational matrix is given by

$$V(E) = \begin{bmatrix} A & B \\ C & D \end{bmatrix}$$

where

$$\begin{aligned} A &= r(1 - \frac{x+y}{k}) - \frac{r}{k}x - \beta y - d, \\ B &= -\beta x - \frac{r}{k}x, \\ C &= \beta y - \frac{s}{k}y, \\ D &= s(1 - \frac{x+y}{k}) - \frac{s}{k}y + \beta x - a. \end{aligned}$$

We denote the variational matrix corresponding to E_i by $V(E_i)$, $i = 0, 1, 2, 3$.

5.1. **Local stability analysis of E_0.** To explore local stability of trivial equilibrium point, we compute variational matrix of E_0. The variational matrix of equilibrium point E_0 is given by

$$V(E_0) = \begin{bmatrix} r-d & 0 \\ 0 & s-a \end{bmatrix}.$$

Eigenvalues of $V(E_0)$ are given by $\lambda_1 = r - d$ and $\lambda_2 = s - a$. E_0 is a stable equilibrium point if and only if E_1 and E_2 do not exist.
Biological interpretation: In this case both infected and uninfected cells destroyed and it means that therapy is successful.

5.2. **Local stability analysis of E_1.** Now, to study the stability behavior of E_1, we compute the variational matrix $V(E_1)$ corresponding to E_1 as follows:

$$V(E_1) = \begin{bmatrix} d-r & \frac{(d-r)(\beta k+r)}{r} \\ 0 & \frac{ds-ar+\beta k(-d+r)}{r} \end{bmatrix}.$$

We observe that eigenvalues of the matrix $V(E_1)$ are given by $\lambda_1 = d - r$ and $\lambda_2 = \big(\beta k(r-d) + ds - ar\big)/r$. Thus E_1 is a stable equilibrium point if $a > (\beta k(r-d)+ds)/r$; furthermore, E_1 is a saddle point if $a < (\beta k(r-d)+ds)/r$.
Biological interpretation: In this case, uninfected cells exist and do not destroy which means after virus injection, all viruses destroy but tumor still exists. Hence, stability of this point is not useful for cancer therapy.

5.3. **Local stability analysis of E_2.** The variational matrix of equilibrium point E_2 is given by

$$V(E_2) = \begin{bmatrix} \frac{\beta k(a-s)+ar-ds}{s} & 0 \\ \frac{(a-s)(s-\beta k)}{s} & a-s \end{bmatrix}.$$

We observe that eigenvalues of the matrix $V(E_2)$ are given by $\lambda_1 = a - s$ and $\lambda_2 = \big(\beta k(a-s) + ar - sd\big)/s$. Thus E_2 is a stable equilibrium point if $a < [s(\beta k + d)]/(\beta k + r)$; in addition, E_2 is a saddle point if $a > [s(\beta k + d)]/(\beta k + r)$.

Biological interpretation: In this case, infected cells exist and do not destroy which means after virus injection, all tumor cells infected but did not disappear. Hence, stability of this point is not useful for cancer therapy.

5.4. **Local stability analysis of E_3.** Variational matrix of E_3 is given by

$$V(E_3) = \begin{bmatrix} A^* & B^* \\ C^* & D^* \end{bmatrix} \tag{5.1}$$

where

$$\begin{aligned} A^* &= \frac{r\big(s(d+\beta k) - a(\beta k + r)\big)}{\beta k(\beta k + r - s)}, \quad B^* = \frac{(\beta k + r)\big(s(d+\beta k) - a(\beta k + r)\big)}{\beta k(\beta k + r - s)}, \\ C^* &= \frac{(s - \beta k)\big(\beta k(d-r) + ar - ds\big)}{\beta k(\beta k + r - s)}, \quad D^* = \frac{s\big(\beta k(d-r) + ar - ds\big)}{\beta k(\beta k + r - s)}. \end{aligned}$$

From variational matrix $V(E_3)$, we find that eigenvalues are $\lambda_\pm$ where

$$\begin{aligned} \lambda_\pm &= \frac{ds - ar}{2\beta k} \\ &\pm \sqrt{(\frac{ds-ar}{2\beta k})^2 + \frac{(\beta k(d-r) + ar - ds)(\beta k(a-s) + ar - ds)}{\beta k(\beta k + r - s)}} \\ &= \frac{1}{2\beta k}(A \pm \sqrt{A^2 - 4\beta^3 k(\beta k + r - s)x^* y^*}) \end{aligned}$$

where $A = ds - ar$. Studying stability of E_3 two cases will happen:

Case1 $s < r + \beta k$**:** In this case if $A > 0$ then E_3 is source, and if $A < 0$, then E_3 is locally asymptotically stable,

Case2 $s > r + \beta k$**:** In this case E_3 is a saddle point.

One of the important subjects that affects on the stability of E_3 is the possibility of existence for Hopf bifurcation. If we wanted to have a Hopf bifurcation in E_3, there should be a pair of pure imaginary eigenvalues.

For existence of Hopf bifurcation in $E_3 := (x^*, y^*)$, trace of (5.1) must be equal to zero and determinant of (5.1) must be positive. Therefore, we must have $(-ar + ds)/(\beta k) = 0$; then, $ds = ar$. Moreover, $-\frac{\beta k(d-r)^2 s}{r(\beta k + r - s)}$ must be positive; then, $\beta k + r - s < 0$ which means there is a $\delta > 0$ that $s = \beta k + r + \delta$. With this assumption, we have $E_3 = (-\frac{k(d-r)(\beta k + r + \delta)}{r\delta}, \frac{k(d-r)}{\delta})$; it means that

E_3 does not exist because one of the components is negative. Hence, as we said in introduction, Hopf bifurcation in E_3 does not mean in biology.
Biological interpretation: In this cases two infected and uninfected cells exist but if this equilibrium point is stable it means that size of tumor is constant and will not grow.

6. Interaction Between Equilibrium Points

In section 5, we showed that E_3 did not pass through a Hopf bifurcation. This means that any change in the stability of E_3 causing by change in the sign of $Rel(\lambda_{\pm})$, does not cause a limit cycle. Now we are going to determine the way that stabilities of equilibrium points effect on the system. In this section we will study global stability of E_0 and E_3 and relevance of equilibrium points with each other. An equilibrium point is globally stable if a solution of system always approaches to it, regardless of its initial position. For equilibrium E_0 we construct Lyapunov functions that enable us to find biologically realistic conditions sufficient to ensure of a globally stable equilibrium state. Global stability of the trivial equilibrium point of system (2.1) is determined in the below theorem:

Theorem 6.1. *If E_1, E_2 and E_3 do not exist then E_0 is globally stable.*

Proof. Since E_1 and E_2 do not exist, so from (4.1) and (4.2) we have $r-d<0$ and $s-a<0$. Now consider the Lyapunov's function $V=x+y$. It must be noticed that the first region of the x,y plane is positively invariant for (2.1), so $V(t)=x(t)+y(t)$ is positively defined in the first region of the coordinate plane. Since E_3 does not exists; hence, for $x>0$ and $y>0$, we have $\frac{dx}{dt}\neq 0$ and $\frac{dy}{dt}\neq 0$. Therefore, computing the derivative of V with respect to t, from (2.1), we get

$$\frac{dV}{dt}=\frac{dx}{dt}+\frac{dy}{dt}=\frac{kx(r-d)+y(s-a)-(x+y)(rx+sy)}{k}<0.$$

□

We know E_3 means both of uninfected and infected cells exist. This case happens in nature, and is important in biology, so in the rest of this section we suppose E_3 exists. We see $\beta k+r-s$ has a virtual role for determining kind of E_3. Consequently, we have following theorem;

Theorem 6.2.
(i) *If E_3 is a saddle point, then E_1 and E_2 exist and are stable point. Also, E_0 is source.*
(ii) *If E_3 is source, then E_1 and E_2 do not exist, and E_0 is a stable point.*
(iii) *If E_3 is a stable point, then E_1 exist and is a saddle point. In this case, if E_2 does not exist, then E_0 is a saddle point, and if E_2 exists, then it is a saddle point, and E_0 is source.*

Proof. First, E_3 is a saddle point if and only if $\beta k + r - s$ is negative. From existence of E_3 we should have

$$\beta k(a-s) - A < 0, \qquad \beta k(r-d) + A < 0. \tag{6.1}$$

Thus, we gain

$$a - s < \frac{A}{\beta k} < d - r. \tag{6.2}$$

Because $\beta k + r - s < 0$ we get $\beta k < \beta k + r < s$ and with the help of (6.1) we have

$$\frac{a(r+\beta k)}{s} - \beta k < d < \frac{r(a-\beta k)}{s-\beta k}. \tag{6.3}$$

As a result, we have $\frac{a(r+\beta k)}{s} - \beta k - \frac{r(a-\beta k)}{s-\beta k} < 0$; therefore, $\frac{(a-s)(s-r-\beta k)}{s(s-\beta k)} < 0$ which means that $a < s$. Therefore, E_2 always exists. Although, with the help of (6.3) and $a < s$ we have $d < \frac{r(a-\beta k)}{s-\beta k} < \frac{r(s-\beta k)}{s-\beta k} = r$ which means E_1 exists. Existence of E_1 and E_2 imply that E_0 is source; also, (6.1) proves that E_1 and E_2 are stable points. Determining stability type of all equilibrium points we can draw phase space, so we have figure $2(a)$. In this case we can not have a periodic solution and therapy fails.

Secondly, if $\beta k + r - s$ is positive, then E_3 might be a stable or an unstable point which stability of it depends on sign A. We know that switches from unstability to stability or vice versa is not a result of Hopf bifurcation here because we showed that E_3 did not have Hopf bifurcation. For existence of E_3 we should have

$$\beta k(a-s) - A > 0, \qquad \beta k(r-d) + A > 0. \tag{6.4}$$

Thus, we have

$$d - r < \frac{A}{\beta k} < a - s. \tag{6.5}$$

If A is positive, then E_3 is source, so E_2 and E_1 do not exist. Because existence of E_2 implies $a - s < 0$, noticing positivity of A, it has a contradiction with (6.5). Thus, $a > s$, and if E_1 exists, then $r > d$, the result will be $ar > ds$ that is a contradiction with positivity of A. The absence of E_1 and E_2 imply E_0 is a stable point. Phase space is shown in Figure 2(b), and cancer completely treated. Virus therapy will be succeed in condition that parameters of system are as what we explain before.

Now we suppose A is negative, result is stability of E_3; also, equilibrium points E_1 and E_2 will be saddle points from (6.4) if they exist. In this case, E_1 should exist because non-existence of E_1 implies $a - r > 0$, we know $A < 0$, therefore, we have a contradiction with (6.5), but for equilibrium E_2 we assume that two conditions: i) We suppose E_2 does not exist; hence, E_0 is a saddle point, and phase space is shown in Figure 2(c). ii) If all equilibrium points exist, then E_0 is source, and we see phase space in Figure 2(d).

□

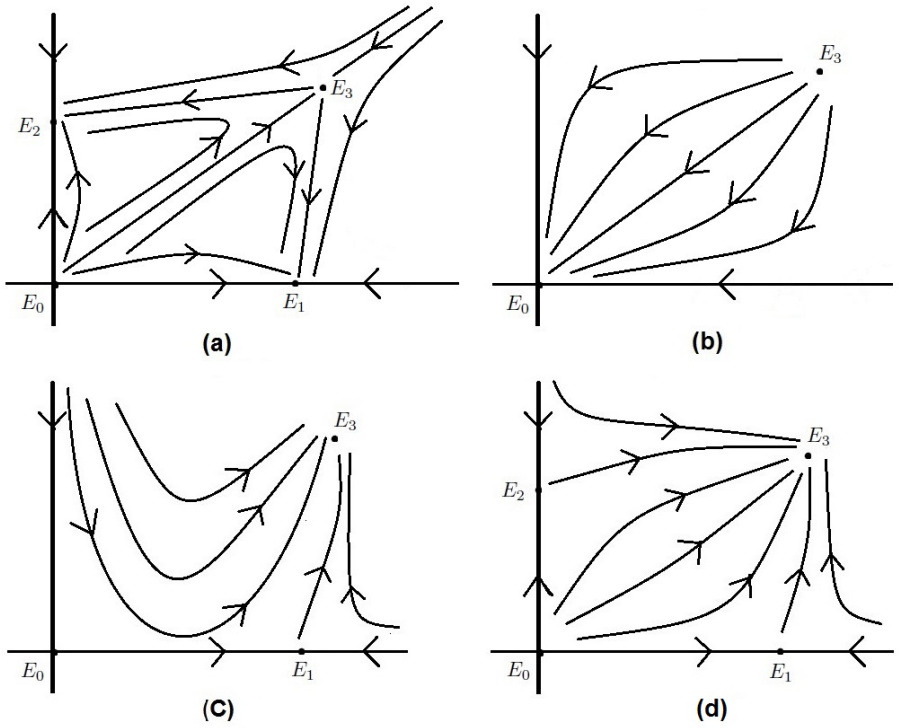

FIGURE 2. phase space for solutions. (a): E_3 is a saddle point, so E_1 and E_2 are stable points and E_0 is source. (b): E_3 is source; hence, E_0 is a stable point, and E_1 and E_2 do not exist. (c): E_3 is a stable point, and E_2 does not exist; thus, E_0 and E_1 are saddle points. (d): E_3 is a stable point, and E_2 exists; therefore, E_0 is source, and E_1 and E_2 are saddle points.

Now we turn to the global stability of E_3.

Theorem 6.3. *suppose all equilibrium points exist and E_1 and E_2 are saddle point, then E_3 is globally stable.*

Proof. We suppose all equilibrium points exist. Existence of E_1 and E_2 means E_0 is source. If E_1 and E_2 are saddle points it means $\beta k + r - s > 0$. Also, one solution path of E_0 approaches to them on coordinate axes. Other solutions that keep out them must approach to a periodic solution or an equilibrium point with assistance of $Poincaré - Bendixson$ theorem. Furthermore, this case is correct for other solutions which do not occur on coordinate axes and keep out of E_0. However, we saw that E_3 did not Hopf bifurcation; hence, it

did not have any periodic solution. As a result, these solutions approach to E_3; then, E_3 is globally stable. □

Hence, we attain conditions for global stability of E_3, and it is the best situation for therapy. Because as we said before, this equilibrium point happens in the natural phenomena. As a result, parameters which happen in this situation cause to control tumor.

7. Numerical Simulation

In this section, we carry out some numerical simulations to confirm some of above results. We suppose that parameters are arbitrary and fixed at the following values:

$$r = 0.2, \quad d = 0.01, \quad \beta = 0.1, \quad s = 1, \quad a = 2, \quad k = 70. \tag{7.1}$$

In this case $E_3 = (11.9194, 1.51613)$ and system (2.1) is:

$$\begin{aligned} \dot{x} &= 0.2x(t)(1 - \frac{x(t) + y(t)}{70}) - 0.01x(t) - 0.1x(t)y(t), \\ \dot{y} &= 0.1x(t)y(t) + y(t)(1 - \frac{x(t) + y(t)}{70}) - 2y(t). \end{aligned} \tag{7.2}$$

We see that $\beta k + r - s = 6.2$ and $A := ds - ar = -0.39$; hence, E_3 is asymptotically stable (see Figures 3 and 4). In this case eigenvalues for E_0 are $\lambda_1 = 0.19$ and $\lambda_2 = -1$; moreover, eigenvalues for $E_1 = (66.5, 0)$ are $\lambda_1 = -0.19$ and $\lambda_2 = 4.7$. As a result, E_0 and E_1 are saddle points. However, E_2 does not exist.

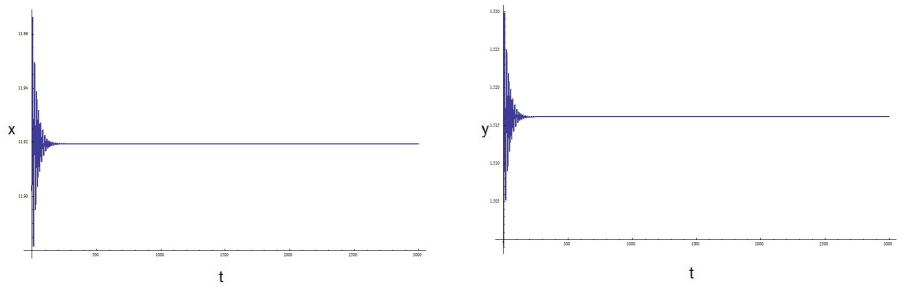

Figure 3. $x(t)$ and $y(t)$ are attracted to components of E_3 with parameters given in (7.1).

Now, if we suppose that parameters are arbitrary and fixed at the following values:

$$r = 0.2, \quad d = 0.1, \quad \beta = 0.1, \quad s = 1.001, \quad a = 1, \quad k = 29. \tag{7.3}$$

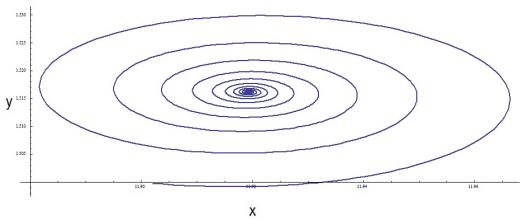

FIGURE 4. The equilibrium E_3 of system (7.2) is asymptotically stable with parameters given in (7.1).

In this case $E_3 = (0.462125, 0.905669)$ and system (2.1) is:

$$\begin{aligned} \dot{x} &= 0.2x(t)(1 - \frac{x(t) + y(t)}{29}) - 0.1x(t) - 0.1x(t)y(t), \\ \dot{y} &= 0.1x(t)y(t) + 1.001y(t)(1 - \frac{x(t) + y(t)}{29}) - y(t). \end{aligned} \tag{7.4}$$

We see that $\beta k + r - s = 2.099$ and $A = ds - ar = -0.099$; hence, E_3 is asymptotically stable. In this case eigenvalues for E_0 are $\lambda_1 = 0.1$ and $\lambda_2 = 0.001$. Eigenvalues for $E_1 = (14.5, 0)$ are $\lambda_1 = -0.1$ and $\lambda_2 = 0.9505$. Furthermore, eigenvalues for $E_2 = (0, 0.028971)$ are $\lambda_1 = -0.001$ and $\lambda_2 = 0.0969031$. As a result, E_1 and E_2 are saddle points, and E_0 is source. Hence, we have conditions in theorem (6.3), so E_3 is globally stable. It will be seen in Figures 5 and 6. Another parameters, that we assume, are for stability of E_0. If we assume

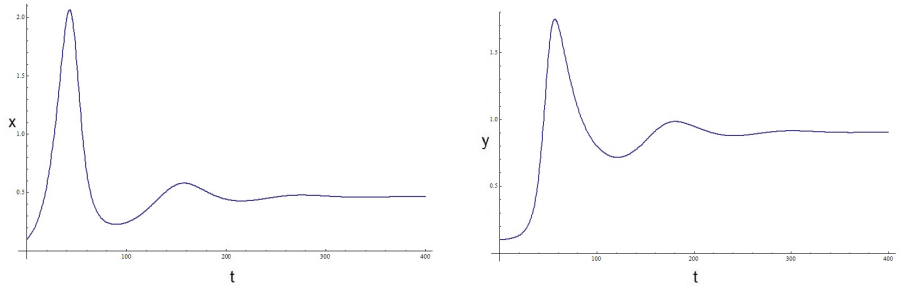

FIGURE 5. $x(t)$ and $y(t)$ are attracted to components of E_3 with parameters given in (7.3).

that parameters are arbitrary and fixed at the following values:

$$r = 0.1, \quad d = 1, \quad \beta = 5, \quad s = 2, \quad a = 3, \quad k = 5. \tag{7.5}$$

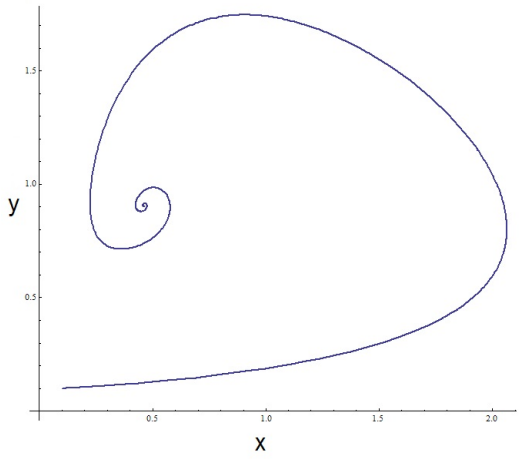

FIGURE 6. The equilibrium E_3 of system (7.4) is asymptotically stable with parameters given in (7.3).

In this case system (2.1) is:

$$\begin{aligned} \dot{x} &= 0.1x\,(t)(1-\frac{x\,(t)+y\,(t)}{5})-x\,(t)-5x\,(t)y\,(t), \\ \dot{y} &= 5x\,(t)y\,(t)+2y\,(t)(1-\frac{x\,(t)+y\,(t)}{5})-3y\,(t). \end{aligned} \tag{7.6}$$

We see that eigenvalues for E_0 are $\lambda_1 = -0.9$ and $\lambda_2 = -1$. Therefore, E_0 is a stable point. On the other hand, E_1, E_2 and E_3 do not exist. Hence, we have conditions in theorem (6.1), so E_0 is globally stable. It will be seen in Figures 7 and 8.

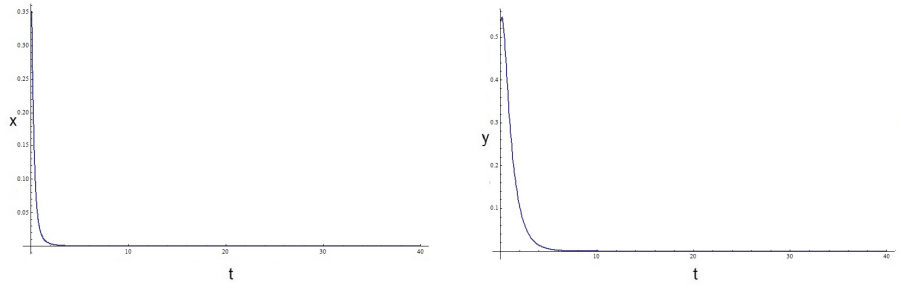

FIGURE 7. $x(t)$ and $y(t)$ are attracted to components of E_0 with parameters given in (7.5).

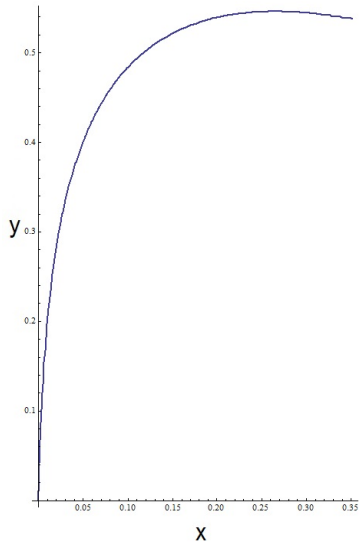

FIGURE 8. The equilibrium E_0 of system (7.6) is asymptotically stable with parameters given in (7.5).

8. Conclusion

In this paper, we consider a virus therapy for cancer and analyze stability of four equilibrium points of this system. Furthermore, we investigated global stability for E_0 and E_3 because these points are important in biology. As we saw, equilibrium E_1 exists and may be stable. Stability of E_1 is not useful because it means that uninfected tumor cells exist then therapy fails. In addition, equilibrium E_2 implies that all tumor cells were infected but the virus could not destroy cells and finally tumor cells remained with infection. In two cases volume of tumor can be reduced to a lower size.

We note that E_3 is the most interesting equilibrium point from the biological point of view since its existence means that both of the uninfected and infected tumor cells exist and its stability means that the tumor growth is controlled in a way that it can not reach to the carrying capacity k. Especially when solutions are attracted to E_3 we hope to have comparative treatment. Hence, if we provide conditions for parameters in theorem 6.3 it means that with this therapy we could control size of tumor, that is $x + y$, which not to be greater but tumor exists and does not completely destroy. In addition, if we provide conditions for parameters in theorem 6.1 then therapy is effective.

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