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On the Behavior of Numerical Solutions with Natural of Stability and Controllability of Viral Dynamical Models

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Abstract

The system of differential equationsfor simple mathematical models of Human Immune-deficiency Virus (HIV)for the model which components are plasma densities of uninfectedCD4+T helper cells, infectedCD4+Thelper cells and free virus (HIV-1) will be study within the nature of equilibrium points and discuss stability for each of them. After that we study controllability using therapy that uses constant drug dosage of reverse transcription inhibitor (RTI) and protease inhibitor (PI) to help HIV– infected patient to achieve long term non-progressor (LTNP) status. . Also, observability and output controllability will apply on this model where in general the state controllability is neither necessary nor sufficient for controlling the output. The analytical treatments are complemented with the numerical solution of the system.

Keywords:*HIV;Viral population growth;HIV Math. Model.*

1 Introduction

The Human Immune-deficiency Virus (HIV) which causes Acquired Immune Deficiency Syndrome (AIDS) destroys the immune system by infecting CD4+T helper cells which are play an important role in immune system. CD4+T helper cells assist in immune responses for strange bodies (assist in phagocytosis). When the CD4+T helper cells count reaches $200\ \mathrm{mm}^{-3}$or below in an HIV infected patient, the patient is having AIDS and will likely die from any infection. Moreover, a monotherapy is likely to fail because HIV can easily develop resistance to monotherapies. To avoid this problem, Highly Active Anti-Retroviral Therapy (HAART) is widely used to treat HIV-infected patients. HAART, which is known as a 'cocktail,' is effective in the prolonged reduction of the viral load. HAART uses a combination of two types of drugs. These drugs can be classified as Reverse Transcriptase Inhibitors (RTIs), which block the reverse transcription of HIV from RNA to DNA, and Protease Inhibitors (PIs), which inhibit the production of new composition components of HIV (such as enzymes) by cutting protein chains. Although prolonged treatment is needed because the viral load rebounds after cease HAART, the long-term use HAART is not recommended due to its serious side effects [5]. Therefore, a therapy that enables an HIV-infected patient to become a Long-Term Non-Progressor (LTNP) is needed. An LTNP is a patient who has been infected with HIV but does not progress to the status of AIDS for at least seven years by sustained immune responses without medication.

There has been much interest recently in mathematical models of viral population dynamics in host cells [12], with most attention focused on HIV [14]. The aim of such modeling is not only to understand the nature of various diseases and their time courses, but also to develop efficient regimes for drug treatments, including the highly successful combination therapies ([2]; [13]; [15]; [22]). Stochastic models have also proven to be useful, especially in determining probabilities of detection of the virus ([9]; [17]; [7]; [20]).

These processes have been translated into a basic model for viral population growth, consisting of three differential equations which govern the evolution of the numbers or densities of uninfected host cells, infected cells and virus particles. The elementary properties of such systems of equations are well understood in constituting a special case and their numerical solution proceed routinely with software such as Mat lab and Mathematica, because the infected cells are those of the immune system itself, dynamical models for HIV-1 usually consist of systems of differential equations which range from the simple two-component models [1], to three-component [6]and four-component models ([11]; [10]) and possibly as many as ten components[4]. The basic components consist of the densities (in units, for example, of numbers per cubic mm of plasma) of uninfected (activated) CD4+T cells, infected such cells and HIV-1 virions.

In a previous communication [18],they are investigated the nature of equilibrium points in two, three or four components models and included certain drug treatments in the four-component case. The solutions of such systems of differential equations exhibit similar overall behavior. For example, the three

model has just two equilibrium points. One of them at a zero level of infection and is either an asymptotically stable node or a saddle point. The other equilibrium point is at nonnegative values of infection and uninfected CD4+ T-cells; with standard parameter values is an asymptotically stable spiral point. Phase portraits of such studied were given in [18], where they complemented an analytical approach with numerical examples to ascertain general classes of behaviors of solutions.

The two-component model is also particularly investigated in [19] by addressing the question of the occurrence of solutions with periodic behavior, corresponding to a continually recurring disease process. Such investigations have previously been carried out for classical competition models of the Lotka–Volterra type [21]. They report that the obtained results may also apply qualitatively to the three or four components models where the analysis is algebraically more complicated.

In this paper we represent full mathematical analysis of three-component model by general discussion the equilibrium and stability of this model; moreover we discuss controllability by adding drugs for this model. Finally we compare the numerical solutions using simulation results for parameters.

2 The Mathematical Model of HIV

Let $x(t)$ denoted plasma densities of uninfected CD4+T helper cells at timet, $y(t)$ represented densities of infected CD4+T helper cells and $v(t)$ is densities of free virus as shown in the following figure.

The differential equations which describe the mathematical model can be constructed as follow:

$$\begin{aligned} \frac{dx(t)}{dt} &= s - \mu x(t) - \beta x(t)v(t) \\ \frac{dy(t)}{dt} &= \beta x(t)v(t) - \alpha y(t) \\ \frac{dv(t)}{dt} &= cy(t) - \gamma v(t) \end{aligned} \qquad (1)$$

Where s is the rate of production of CD4+T cells,$\mu$is the rate of theirdeath,β is the rate of infection of CD4+T cells by virus,α is the rate of disappearance of infected cells,c is the rate of production of virus by infected cells and γ is the rate death of virus particles.

3 The Stability for HIV Model

The studying of the above system for the patient requires the knowledge ofthe stability about its equilibrium points. The equilibrium points for HIV model can be obtained by solving equations

$$\frac{dx}{dt} = \frac{dy}{dt} = \frac{dv}{dt} = 0 \qquad (2)$$

Then the equilibrium points are:

$$P_1 = \left(\frac{s}{\mu}\ ,0\ ,0\ \right) and P_2 = \left(\frac{\alpha}{k}\ ,\frac{sk-\alpha\mu}{\alpha k}\ ,\frac{sk-\alpha\mu}{\alpha\beta}\right) \qquad (3)$$

where$k = \frac{\beta c}{\gamma}$

We use the Jacobian matrix method[16] to discuss the stability of the HIV system then the Jacobianmatrix is

$$J_e = \begin{pmatrix} -\mu-\beta v_e & 0 & -\beta x_e \\ \beta v_e & -\alpha & \beta x_e \\ 0 & c & -\gamma \end{pmatrix} \qquad (4)$$

Which take the following form at the first equilibrium point(P_1)in(3)

$$J_1 = \begin{pmatrix} -\mu & 0 & \frac{-\beta s}{\mu} \\ 0 & -\alpha & \frac{\beta s}{\mu} \\ 0 & c & -\gamma \end{pmatrix} \qquad (5)$$

Then the eigen values ofJ_1 are

$$\lambda_1 = -\mu\ , \qquad \lambda_2 = \frac{-(\alpha+\gamma)}{2} + \sqrt{\left(\frac{\alpha+\gamma}{2}\right)^2 + \frac{c\beta s}{\mu} - \alpha\gamma} and \lambda_3$$

$$= \frac{-(\alpha+\gamma)}{2} - \sqrt{\left(\frac{\alpha+\gamma}{2}\right)^2 + \frac{c\beta s}{\mu} - \alpha\gamma} \qquad (6)$$

The real model require that the values of $s\ ,\mu\ ,\beta\ ,\alpha\ ,and\gamma$ are usually greater than zero,$c > \gamma$with respect to$v(t)$,$\beta > \alpha$with respect to$y(t)$,$s > \mu$with respect to$x(t)$, according the natural of them, then we can deduce$\frac{c\beta s}{\mu} - \alpha\gamma > 0$.

i.e

$$\lambda_1 = -\mu < 0\ \ ,\ \ \lambda_2 = \frac{-(\alpha+\gamma)}{2} + \sqrt{\left(\frac{\alpha+\gamma}{2}\right)^2 + \frac{c\beta s}{\mu} - \alpha\gamma} > 0 \quad and$$

$$\lambda_3 = \frac{-(\alpha+\gamma)}{2} - \sqrt{\left(\frac{\alpha+\gamma}{2}\right)^2 + \frac{c\beta s}{\mu} - \alpha\gamma} < 0 \qquad (7)$$

Consequently the system is unstable at this point.
At the second equilibrium pointP_2,$J_e$takes the form

$$J_2 = \begin{pmatrix} -\frac{sk}{\alpha} & 0 & \frac{-\alpha\gamma}{c} \\ \frac{sk}{\alpha} - \mu & -\alpha & \frac{\alpha\gamma}{c} \\ 0 & c & -\gamma \end{pmatrix} \qquad (8)$$

The characteristic equation ofJ_2 at this point is

$$\lambda^3 + \left(\frac{sk}{\alpha} + \alpha + \gamma\right)\lambda^2 + \frac{sk}{\alpha}(\alpha + \gamma)\lambda + \alpha sk - \alpha\gamma\mu = 0 \qquad (9)$$

We will studythe stability by using the method of **Hurwitz**[8], where the eigen values cannot be obtained as similar as the above case.

Then we defined that $a_3 = 1$, $a_2 = \frac{sk}{\alpha} + \alpha + \gamma$, $a_1 = \frac{sk}{\alpha}(\alpha + \gamma)$ and $a_0 = \gamma sk - \alpha\gamma\mu$, and from (9)Hurwitz matrix **H**becomes

$$\boldsymbol{H} = \begin{pmatrix} \frac{sk}{\alpha} + \alpha + \gamma & 1 & 0 \\ \gamma sk - \alpha\gamma\mu & \frac{sk}{\alpha}(\alpha + \gamma) & \frac{sk}{\alpha} + \alpha + \gamma \\ 0 & 0 & \gamma sk - \alpha\gamma\mu \end{pmatrix} \qquad (10)$$

Depending on the natural values of the various parameters as mentioned above then

$$\Delta_1 = \frac{sk}{\alpha} + \alpha + \gamma > 0 ,$$

$$\Delta_2 = \begin{vmatrix} \frac{sk}{\alpha} + \alpha + \gamma & 1 \\ \gamma sk - \alpha\gamma\mu & \frac{sk}{\alpha} + (\alpha + \gamma) \end{vmatrix} = \left(\frac{SK}{\alpha} + \alpha + \gamma\right)\frac{SK}{\alpha}(\alpha + \gamma) - \gamma sk + \alpha\gamma\mu$$

$$= \left(\frac{SK}{\alpha}\right)^2 (\alpha + \gamma) + sk\alpha + \gamma\frac{sk}{\alpha}(\alpha + \gamma) + \alpha\gamma\mu > 0 ,$$

$$\text{and}\Delta_3 = \begin{vmatrix} \frac{sk}{\alpha} + \alpha + \gamma & 1 & 0 \\ \gamma sk - \alpha\gamma\mu & \frac{sk}{\alpha}(\alpha + \gamma) & \frac{sk}{\alpha} + \alpha + \gamma \\ 0 & 0 & \gamma sk - \alpha\gamma\mu \end{vmatrix} = (\gamma sk - \alpha\gamma\mu)\Delta_2$$

$$> \quad 0 \qquad (11)$$

Then the system is asymptotically stable by **Hurwitz** analysis

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4 Controllability due to Drugs

The controllability study of such system required, we must insert input U(drugs) in the previous model. General, there are two kinds of drugs , the first is Revere Transcription Inhibitor RTI with drug efficacy U_R which block the revere transcription of HIV from RNA to DNA,then the model becomes

$$\frac{dx(t)}{dt} = s - \mu x(t) - (1 - U_R)\beta x(t)v(t)$$

$$\frac{dy(t)}{dt} = (1 - U_R)\beta x(t)v(t) - \alpha y(t) \qquad (12)$$

$$\frac{dv(t)}{dt} = cy(t) - \gamma v(t)$$

Which can be written in the linearized form[5]

$$X` = AX + BU \qquad (13)$$

such that the state evolution matrix is $A = \begin{pmatrix} -\mu - \beta v_0 & 0 & -\beta x_0 \\ \beta v_0 & -\alpha & \beta x_0 \\ 0 & c & -\gamma \end{pmatrix}$,

the control gain matrix is$B = \begin{pmatrix} \beta v_0 x_0 \\ -\beta v_0 x_0 \\ 0 \end{pmatrix}$ and input $U = U_R$

General, a system with state vector (13)of three dimensions is controllable if the controllability matrix

$$C = (B, AB, A^2B) \qquad (14)$$

has column rank 3 (i.e. three linearly independents).
In our case(14) can be reduced to

$$\begin{pmatrix} 1 & -(\mu + \beta v_0) & \mu^{2+}\beta^2 {v_0}^2 + 2\mu\beta v_0 + c\beta x_0 \\ 0 & \alpha - \mu & \mu^2 + \mu\beta v_0 - \alpha\beta v_0 - \alpha^2 \\ 0 & 0 & (\mu - \alpha)(\mu - \gamma) \end{pmatrix}$$

Then, the following cases are obtained:

1- If $\mu \neq \alpha and \mu \neq \gamma$which means the death rate of uninfected cells not equal the death rate of infected cells and the death rate of uninfected cells not equal the death rate of free virus, this matrix reduces to$\begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$ with rank = 3 and the system is controllable.

2- If $\mu = \alpha or \mu = \gamma$which means the death rate of uninfected cells equal the death rate of infected cells or the death rate of uninfected cells equal the death rate of free virus the system is uncontrollable because

at$\mu = \alpha and \mu \neq \gamma$the matrix reduces to $\begin{pmatrix} 1 & 0 & -\gamma\mu - \beta\gamma v_0 + c\beta x_0 \\ 0 & 1 & -\gamma - \mu - \beta v_0 \\ 0 & 0 & 0 \end{pmatrix}$with rank = 2,

at$\mu = \gamma and \mu \neq \alpha$ the matrix reduces to$\begin{pmatrix} 1 & 0 & -\alpha\mu - \alpha\beta v_0 + c\beta x_0 \\ 0 & 1 & -\alpha - \mu - \beta v_0 \\ 0 & 0 & 0 \end{pmatrix}$with rank = 2 ,

finally$\mu = \gamma and \mu = \alpha$ the matrix reduces to

$$\begin{pmatrix} 1 & 0 & -\mu^2 - \beta\mu v_0 + c\beta x_0 \\ 0 & 1 & -2\mu - \beta v_0 \\ 0 & 0 & 0 \end{pmatrix}$$ with rank = 2.

WhileU_R is still exist, we add the second type of drugs, namely protease inhibitor PI with drug efficacy U_P which inhibits the production of new composition ofHIVby cutting protein chains then the system converted to

$$\frac{dx(t)}{dt} = s - \mu x(t) - (1 - U_R)\beta x(t)v(t)$$

$$\frac{dy(t)}{dt} = (1 - U_R)\beta x(t)v(t) - \alpha y(t) \qquad (15)$$

$$\frac{dv(t)}{dt} = (1 - U_P)cy(t) - \gamma v(t)$$

Which can be written in the linearized form of equation (13)such that,

the state evolution matrix is$A = \begin{pmatrix} -\mu - \beta v_0 & 0 & -\beta x_0 \\ \beta v_0 & -\alpha & \beta x_0 \\ 0 & c & -\gamma \end{pmatrix}$,

thecontrol gain matrix is$B = \begin{pmatrix} \beta x_0 v_0 & 0 \\ -\beta x_0 v_0 & 0 \\ 0 & -cy_0 \end{pmatrix}$, and input$U = \begin{pmatrix} U_R \\ U_P \end{pmatrix}$.

Then controllability matrix (14) can be reduced to

$$\begin{pmatrix} \beta x_0 v_0 & 0 & -\beta x_0 v_0(\mu + \beta v_0)\beta c x_0 y_0 & \beta x_0 v_0[\mu^2 + \beta^2 {v_0}^2 + 2\mu\beta v_0 + c\beta x_0] & -\beta c x_0 y_0(\mu + \gamma + \beta v_0) \\ 0 & -cy_0 & -\beta c x_0 v_0 & \gamma c y_0 & \beta x_0 v_0[c\beta v_0 + c(\alpha + \gamma)] & -cy_0(c\beta x_0 + \gamma^2) \\ 0 & 0 & \beta x_0 v_0(\alpha - \mu) & 0 & \beta x_0 v_0[(\mu - \alpha)(\mu + \alpha + \beta v_0)] & \beta c x_0 y_0(\alpha - \mu) \end{pmatrix}$$

Then, the following cases are obtained:

1- If $\mu \neq \alpha and \mu \neq \gamma$which means the death rate of uninfected cells not equal the death rate of infected cells, this matrix reduces to

$$\begin{pmatrix} 1 & 0 & 0 & \frac{cy_0}{v_0} & -\alpha\mu - \alpha\beta v_0 + c\beta x_0 & -\frac{c\gamma y_0}{v_0} \\ 0 & 1 & 0 & -\gamma & \frac{-\beta\gamma v_0 x_0 + \beta\mu v_0 x_0}{y_0} & \gamma^2 \\ 0 & 0 & 1 & 0 & -\alpha - \mu - \beta v_0 & \frac{cy_0}{v_0} \end{pmatrix}$$ with rank = 3

and the system is controllable .

2- If $\mu = \alpha and \mu \neq \gamma$ which means the death rate of uninfected cells equal the death rate of infected cells, this matrix reduces to

$$\begin{pmatrix} 1 & 0 & -\mu-\beta v_0 & \frac{cy_0}{v_0} & \mu^2+2\beta\mu v_0+\beta^2 v_0^2+c\beta x_0 & -\frac{c(\gamma+\mu+\beta v_0)y_0}{v_0} \\ 0 & 1 & \frac{\beta v_0 x_0}{y_0} & -\gamma & \frac{-\beta\gamma v_0 x_0-\beta\mu v_0 x_0-\beta^2 v_0^2 x_0}{y_0} & \gamma^2+c\beta x_0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

with rank = 2and the system is uncontrollable .

5 Observability and Output Controllability

The concept of observability is useful in solving the problem of reconstructing immeasurable state variables from measurable variables in the minimum possible length of time. Consequently it becomes necessary in order to construct the control signals.

Such that complete state controllability in neither necessary nor sufficient for controlling the output of the system.

Then, the previous (13) with suitable system output equations, that refer to observable items in the previous input controllability model (the model of Revere Transcription Inhibitor RTI input with drug efficacy $\boldsymbol{U_R}$ which block the revere transcription of HIV from RNA to DNA and output of $y_1(t)$and $y_2(t)$ for uninfected cells and free virus respectively), becomes

$$\begin{aligned} y_1(t) &= x(t) \\ y_2(t) &= v(t) \end{aligned} \qquad (16)$$

added to system (12) .

The linearized form [5] ofthe new system $(12), (16)$ is

$$\dot{X} = AX + BU \qquad (17)$$
$$Y = CX \qquad (18)$$

such that the state evolution matrix is $A = \begin{pmatrix} -\mu-\beta v_0 & 0 & -\beta x_0 \\ \beta v_0 & -\alpha & \beta x_0 \\ 0 & c & -\gamma \end{pmatrix}$,

the control gain matrix is $B = \begin{pmatrix} \beta v_0 x_0 \\ -\beta v_0 x_0 \\ 0 \end{pmatrix}$, input $U = U_R$

and output matrix is $C = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix}$

General, a system with state vector (17) and output vector (18) is observable if the observability matrix

$$V = (C, CA, CA^2)^T \qquad (19)$$

has rank 4 (i.e. four linearly independents) [3].
In our case

$$V = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ -\mu - \beta v_0 & 0 & -\beta x_0 \\ 0 & c & -\gamma \\ (-\mu - \beta v_0)^2 & -c\beta x_0 & \beta\gamma x_0 - \beta(-\mu - \beta v_0)x_0 \\ c\beta v_0 & -c\alpha - c\gamma & \gamma^2 + c\beta x_0 \end{pmatrix} \qquad (20)$$

which has rank = 3 and the system is observable, **i.e.** the behavior of $x(t) = y_1$ and $v(t) = y_2$ can be observed during a period of treatment.
While, to control the output rather than the state of the system, a linearized of $(12), (16)$ with state vector (17) and output vector (18) is output controllable if the output controllability matrix

$$OC = (CB, CAB, CA^2B) \qquad (21)$$

has rank 2 (i.e. two linearly independents) [3], which can be written in the form

$$\begin{pmatrix} \beta v_0 x_0 & \beta v_0(-\mu - \beta v_0)x_0 & \beta v_0(-\mu - \beta v_0)^2 x_0 + c\beta^2 v_0 x_0^2 \\ 0 & -c\beta v_0 x_0 & -\beta(-c\alpha - c\gamma)v_0 x_0 + c\beta^2 v_0^2 x_0 \end{pmatrix} \qquad (22)$$

The output controllability matrix (22) is generally has rank = 2 which means that the system is output controllable.
i.e.the control system for one drug in case 1. is also output control indeed in case 2. the system is output control while the system is complete state uncontrollable.
The discussion of output controllability for two drugs model is easy to apply as above.

6 Numerical Results

Using atypical parameters $s = 0.272$, $\mu = 0.00136$, $\beta = 0.027$, $\alpha = 0.003$, $c = 50$ and $\gamma = 2$given in [3]hence the equilibrium points$(3)$are:

$$P_1 = (200\,, 0\,, 0)\ ,$$
$$P_2 = (\,0.004444444444449319, 90.66465185185184, 2266.6162962962962)$$

The eigen values of(6) or (7)corresponding to$P_1$are{-17.4635,15.4605,-0.00136}, which is exactly unstable as mentioned above.
The eigen values corresponding to $P_2$are{-61.2001,-1.9999,-0.00300008}which it is easily deduced in this case and its asymptotically stable. On other hand, using

P_2 and the method of **Hurwitz** we find that $\Delta_1 = 63.203, \Delta_2 = 7747.28, \Delta_3 = 2844.74$ which satisfy (14) and confirm the system is asymptotically stable.
Near unstable first equilibrium point P_1 in (3) assuming at $(200\ ,0\ ,1)$ the controllability matrix (14) is $\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ -5.4 & 0.162 & -1458.0046208879999 \\ 0 & -270 & 548.1 \end{pmatrix}$

with rank = 3, observability matrix (20) is

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ -0.02836 & 0 & -5.4 \\ 0 & 50 & -2 \\ 0.0008042896 & -270 & 10.953144 \\ 1.35 & -100.15 & 274 \end{pmatrix}$$ with rank = 3

and output controllability matrix (22) is

$$\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ 0. & -270. & 548.1 \end{pmatrix}$$ with rank = 2

hence the system is controllable , observable and output controllable.
while for $\alpha = 0.00136 = \mu$ and all other parameters as above the controllability matrix (14) takes form $\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ -5.4 & 0.153144 & -1458.00434316384 \\ 0 & -270. & 547.6572 \end{pmatrix}$
with rank = 2,

observability matrix (20) is $\begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ -0.02836 & 0 & -5.4 \\ 0 & 50 & -2 \\ 0.0008042896 & -270 & 10.953144 \\ 1.35 & -100.068 & 274 \end{pmatrix}$
with rank = 3
and output controllability matrix (22) is

$$\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ 0. & -270. & 547.6572 \end{pmatrix}$$ with rank = 2

and for $\gamma = 0.00136 = \mu$ and all other parameters as first case the controllability matrix (14) takes form $\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ -5.4 & 0.162 & -1458.0046208879999 \\ 0 & -270. & 8.467200000000002 \end{pmatrix}$

with rank = 2, observability matrix (20) is

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ -0.02836 & 0 & -5.4 \\ 0 & 50 & -0.00136 \\ 0.0008042896 & -270 & 0.160488 \\ 1.35 & -0.218 & 270.0000018496 \end{pmatrix}$$ with rank = 3

and output controllability matrix (22) is

$$\begin{pmatrix} 5.4 & -0.153144 & 1458.00434316384 \\ 0. & -270. & 8.467200000000002 \end{pmatrix}$$ with rank = 2

hence the system is observable and output controllable as first case but not complete state controllable.

The numerical solutions of the original ordinary differential equations model through 400 days at the first equilibrium point $P_1 = (200\,,0\,,0)$ and the second equilibrium point
$P_2 = (0.004444444444449319,\ 90.66465185185184,2266.6162962962962)$ is represented in figure 1, and figure 2respectively it's clear that there is no change in the behavior of uninfected and infected cells and free virus through that time (the steady state equilibrium cases).

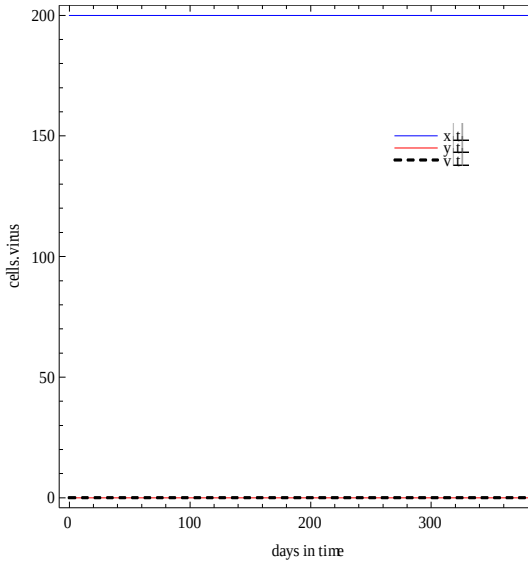

Fig.1

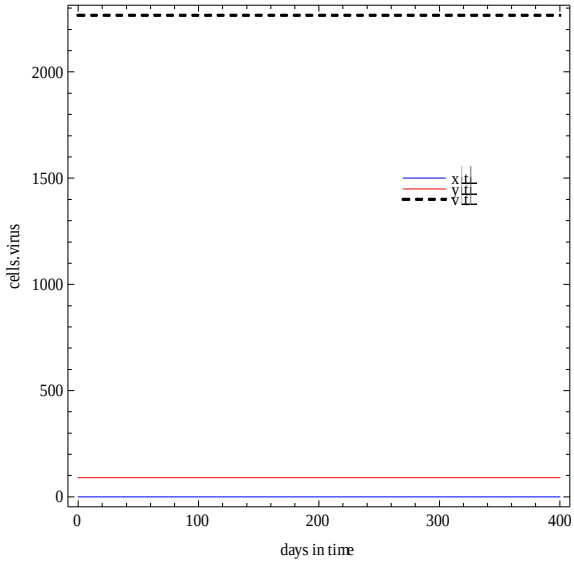

Fig.2

To consider the behavior of the numerical solutions of the same model at near the first equilibrium point P_1, we choose the initial point at $x = 200$, $y = 0$ and $v = 1$ which represents an early virus patient .

Figure 3 shows that the uninfected cells x(t) which begin at 200 and decay to zero through 12 hours, the infected cells y(t) growth to 200 at the same time such that the number of virus v(t) is increases rapidly to reach at 5000 in three days without any drugs.

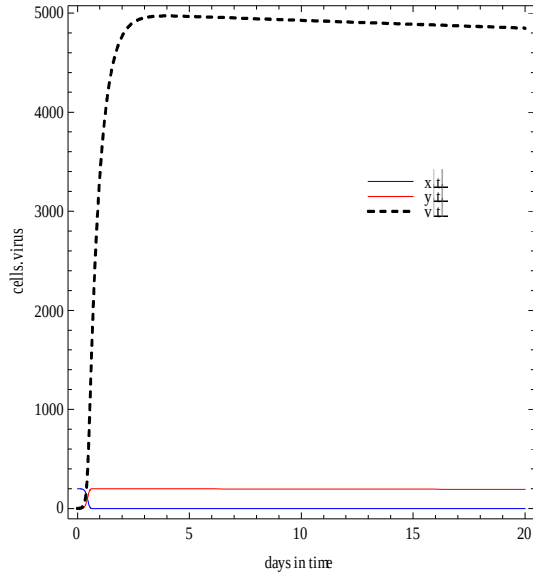

Fig.3

Figure 4 represent the same patient by using one kind of medication RTI with drug efficacy$U_R = 0.98$, where the number of virus growth to the same maximum number through 10 days and decays when the time increases, while the uninfected and infected cells have the previous behavior without changing in time which is longer than the case without drugs.

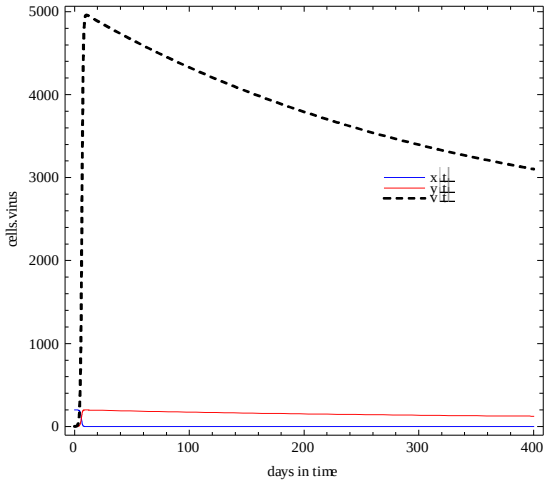

Fig.4

The case of the patient will be improved when one using two kinds of medication RTI with drug efficacyU_R and PI with drug efficacy $U_P$as shown in figure 5, figure 6 and figure 7 by increasing the values of U_R and U_P respectively. The observation time is increasing to reach 200 days in figure 7 with maximum number of virus less than 100 and the number of infected cells not reached to 200.

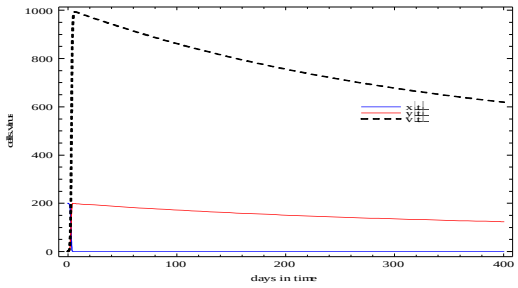

Fig.5represents ofx(t), y(t) and v(t) count with$U_R = 0.8$ and$U_P = 0.8$

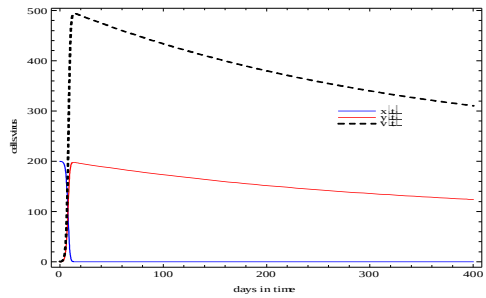

Fig.6represents of x(t), y(t) and v(t) count with $U_R = 0.9$ and$U_P = 0.9$

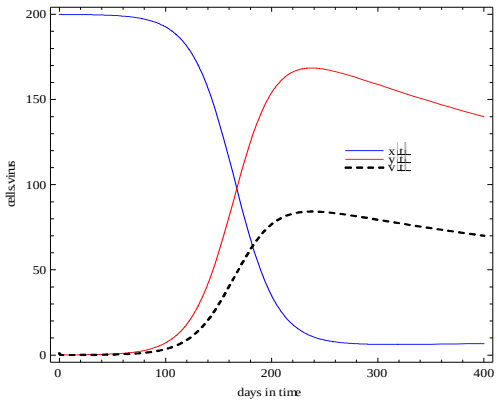

Fig.7represents of $x(t), y(t)$ and $v(t)$ count with $U_R = 0.98$ and$U_P = 0.98$

The behavior of uninfected and infected cells and free virus through time changes according to the efficacy of drugs which shows the concept of controllability.

The study of patient near the second equilibrium point P_2 is not interested where the patient may be dead, according to the controllability conceptwhich has no real meaning with this case.

7 Conclusions

The three-component HIV model which includes uninfected CD4+T helper cells, infected cells and virions is generally investigated such that P_1 is an unstable saddle point and P_2 is either and a node or spiral point if $\alpha\gamma < \frac{c\beta s}{\mu}$ otherwise, P_2 is at unphysical values and P_1 is an asymptotically stable node or spiral point. The control theory concept of controllability, observability and output controllability of non-linear system is applied to this model; we have illustrated the effects of two treatments of drugs (reverse transcription inhibitor and protease inhibitor) could be eliminated the virus within the numerical solution of the model. Finally, all computations are performed by mathematica programs.

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