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Stability Analysis for Fractional Differential Equations and Their Applications in the Models of HIV-1 Infection

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Abstract: In the paper, stability for fractional order differential equations is studied. Then the result obtained is applied to analyse the stability of equilibrium for the model of HIV.

Keywords: Stability, Fractional differential equation, Model of HIV, Equilibrium.

1 Introduction

As is known to all that the conventional calculus has been well studied and its applications can be found in many fields such as incompressible viscous flows [shan, shu and lu(2008)], the material failure evolution [chen, gan and chen(2008)], acoustic waveguide modeling [lu and zhu(2007)], atomic-scale modeling [nishidate and nikishkov(2008)] and so on. Referring to fractional calculus, it is not familiar to most people. In fact, fractional calculus is three centuries as old as the conventional calculus. But the investigation of the theory of fractional differential equations has only been started quite recently [Caputo(1967); Kilbas, Srivastava and Trujillo(2006)]. Meanwhile, the applications of fractional differential equations to physics, biology and engineering are a recent focus of interest [Kilbas, Srivastava and Trujillo(2006); Hilfer(2001)]. Many systems are known to display fractional order dynamics, such as viscoelastic systems [Bagley(1983); Koeller(1984)], electrode-electrolyte polarization [Ichise, Nagayanagi and Kojima(1971)] and complex adaptive systems in biology [Ahmed, Elgazzar and Hegazi(2008)].

More recently, there are some investigators to study the qualitative properties and numerical solutions of fractional-order biological models [Ahmed, El-Sayed and El-Saka(2007); Ahmed and Elgazzar(2007); Ahmed, El-Sayed and El-Saka(2004)]. In [Ahmed, El-Sayed and El-Saka(2007)], the fractional-order predator-prey model

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and the fractional-order rabies model are investigated; the existence and uniqueness of solutions are proved; the stability of equilibrium points are studied; numerical solutions of these models are given. In [Ahmed and Elgazzar(2007)], a fractional order model for nonlocal epidemics is given. Stability of fractional order equations is studied. The results are expected to be relevant to foot-and-mouth disease, SARS and avian flu. In [Ahmed, El-Sayed and El-Saka(2004)], some Routh-Hurwitz stability conditions are generalized to the fractional order case. The results agree with those obtained numerically for Lorenz, Rössler, Chua and Chen fractional order equations.

We know that there are different approaches of modeling various biological systems, e.g. ordinary differential equations, difference equations, partial differential equations and coupled map lattice. In these papers mentioned above, fractional order equations (FOD) are used. The main reason is that FOD are naturally related to systems with memory which exists in most biological systems. Also they are closely related to fractals which are abundant in biological systems.

We know that the Human Immunodeficiency Virus type I (HIV-1) causes AIDS (Acquired Immune Deficiency Syndrome). The major target of HIV-1 infection is a class of lymphocytes or white blood cells known as $CD4^+$ T-cells which are the most abundant white blood cells of the immune system. It is thought that HIV-1, although attacking many different cells, wreaks the most havoc on the $CD4^+$ T-cells by causing their destruction and decline and decreasing the body's ability to fight infection.

Since the early 1980s there has been a tremendous effort made in the mathematical modeling of HIV-1. Many mathematical models were derived in order to describe the dynamics of HIV-1 infection in the bloodstream where the cell-free-viral spread is the predominant route of viral spread [De Leenheer and Smith(2003); Perelson, Kirschner and De Boer(1993); Perelson(1989)]. In [Kouche and Ainseba(2007)], Kouche et al proposed a model of cell-to-cell spread of HIV-1 infection in tissue culture, i.e.,

$$\begin{cases} \frac{dx(t)}{dt} = rx(t)\left(1 - \frac{x(t)+y(t)+\int_{-\infty}^{t} \frac{f(t-s)x(s)y(s)}{C+x(s)}ds}{K}\right) - \alpha\frac{x(t)y(t)}{C+x(t)} \\ \frac{dy(t)}{dt} = \beta \int_{-\infty}^{t} \frac{f(t-s)x(s)y(s)}{C+x(s)}ds - \delta y(t), \end{cases} \tag{1}$$

where $x(t)$ and $y(t)$ denote the concentrations of healthy and infected cells at time t respectively, r is the effective reproductive rate of healthy cells, K is the effective carrying capacity of the system, δ is the death rate of infected cells, α is the maximum rate of infection, β is such that $\frac{\beta}{\alpha}$ represents the fraction of cells surviving

the incubation period, and C denote the half saturation constant of the proliferation process. By taking as a delay kernel $f(s)$ the Gamma distribution function of order 0 called weak kernel

$$f(s) = \mu e^{-\mu s}, \;\; s \geq 0,$$

and putting

$$z(t) = \int_{-\infty}^{t} \mu e^{-\mu(t-s)} \frac{x(s)y(s)}{C+x(s)} ds,$$

they obtained the following system of three ordinary differential equations

$$\begin{cases} \frac{dx(t)}{dt} = rx(t)\left(1 - \frac{x(t)+y(t)+z(t)}{K}\right) - \alpha \frac{x(t)y(t)}{C+x(t)} \\ \frac{dy(t)}{dt} = \beta z(t) - \delta y(t) \\ \frac{dy(t)}{dt} = \mu \frac{x(t)y(t)}{C+x(t)} - \mu z(t) \end{cases} \tag{2}$$

To our knowledge, no works are contributed to the analysis for a model of fractional-order differential equations of HIV-1. Because of this, in this paper, we investigate the following fractional-order differential system

$$\begin{cases} D^q x(t) = rx(t)\left(1 - \frac{x(t)+y(t)+z(t)}{K}\right) - \alpha \frac{x(t)y(t)}{C+x(t)}, \\ D^q y(t) = \beta z(t) - \delta y(t), \\ D^q z(t) = \mu \frac{x(t)y(t)}{C+x(t)} - \mu z(t), \end{cases} \tag{3}$$

and study local asymptotical stability of its equilibrium points.

This paper is organized as follows. In section 2, we present some necessary definitions and notations. In section 3, fractional order differential systems are studied, and asymptotic stability conditions for equilibrium points are given. In section 4, by utilizing the given result, we analyze the stability of a fractional order model of HIV-1. Simulations and some remarks are given in section 5.

2 Preliminaries

Fractional derivatives are generalizations for derivative of integer order. There are several forms of definitions of fractional integral and derivative, such as, Riemann-Liouville fractional integral and fractional derivative, Marchaud fractional integral and derivative, Caputo's integral and derivative, Grünwald-Letnikov fractional

derivative, and so on. It should be pointed out that applied problems require definitions of fractional derivatives allowing the utilization of physically interpretable initial conditions. In fact, Caputo's fractional derivative exactly satisfies these demands. The Caputo fractional derivative was introduced [Caputo(1967); Kilbas, Srivastava and Trujillo(2006)] to alleviate some of the difficulties associated with Riemann-Liouville approach to fractional differential equations when applied to the solution of physical problems. Therefore, in this article, we deal with the systems of fractional-order differential equations involving Caputo's derivative.

For completeness, here we first present the definitions and some fundamental facts on Caputo's derivative of fractional order.

Let $[a,b]$ be a finite interval on the real line R.

Definition 1 *For any $q \in \mathbb{C}$, $\Re(q) \geq 0$, Caputo fractional derivative of order q of $f(t)$ can be defined as*

$$ {}^{C}D^{q}_{a^+} f(t) = \frac{1}{\Gamma(n-q)} \int_a^t \frac{f^{(n)}(s)}{(t-s)^{q+1-n}} ds, $$

where

$$ n = q \ \ for \ \ q \in \mathbb{N}_0; \ \ otherwise \ \ n = [\Re(q)] + 1. $$

In particular, when $0 < \Re(q) < 1$, we have

$$ {}^{C}D^{q}_{a^+} f(t) = \frac{1}{\Gamma(1-q)} \int_a^t \frac{f'(s)}{(t-s)^{q}} ds. $$

As is well known, in the fractional differential equations, the initial conditions are specified in terms of fractional derivatives of the unknown function in the Riemann-Liouville approach. But, in the Caputo approach, the initial conditions could be specified in terms of integer derivatives with known physical interpretations. This means that the Caputo formulation is more popular in applications of physical interest. In fact, the following assertion, which yields the Laplace transform of the Caputo fractional derivative ${}^{C}D^{q}_{0^+} f(t)$, is true.

Lemma 1 [Kilbas, Srivastava and Trujillo(2006)] *Let $q > 0$, $n-1 < q \leq n$ $(n \in N)$ be such that $y(t) \in C^n(R^+)$, $y^{(n)}(t) \in L_1(0,b)$ for any $b > 0$, the estimate*

$$ |y^{(n)}(t)| \leq Be^{q_0 t} \quad (t > b > 0) $$

holds for $y^{(n)}(t)$, the Laplace transforms $\mathscr{L}[y(t)]$ and $\mathscr{L}[D^n y(t)]$ exist, and

$$ \lim_{x \to +\infty} (D^k y)(t) = 0, \ \ k = 0, 1, \cdots, n-1. $$

Then the following relation holds:

$$\mathscr{L}\Big[{}^{C}D^{q}_{0^+}y(t)\Big] = s^q\mathscr{L}[y(t)] - \sum_{k=0}^{n-1} s^{q-k-1}D^k y(0).$$

In particular, if $0 < q \leq 1$, then

$$\mathscr{L}\Big[{}^{C}D^{q}_{0^+}y(t)\Big] = s^q\mathscr{L}[y(t)] - s^{q-1}y(0).$$

Because of so, in the sense of Caputo's fractional derivative, we could consider the following initial value problem

$$\begin{cases} {}^{C}D^{q}_{0^+}y(t) = f(x,y), \\ y(0) = y_0,\ y'(0) = y_1, \cdots, y^{(n-1)}(0) = y_{n-1}. \end{cases}$$

For the sake of simplicity, in this paper we denote the Caputo's fractional derivative of order q by D^q.

3 Stability conditions for fractional order differential equations

In this section, we study the stability for fractional differential equations.
Consider the system

$$D^q x(t) = f_1(x,y), \quad D^q y(t) = f_2(x,y), \quad q \in [0,1). \tag{4}$$

with the initial values

$$x(0) = x_0, \ \ y(0) = y_0, \tag{5}$$

where the fractional derivative in (4) is in the sense of Caputo fractional derivative.
In order to evaluate the equilibrium points, set

$$D^q x(t) = 0, \ \ D^q y(t) = 0 \Rightarrow f_1(x,y) = 0, \ \ f_2(x,y) = 0,$$

from which we can obtain the equilibrium solutions $x_{eq}, \ \ y_{eq}$.
To evaluate the asymptotic stability, let

$$x(t) = x_{eq} + \delta_1(t), \ \ y(t) = y_{eq} + \delta_2(t),$$

then

$$D^q\big(x_{eq} + \delta_1(t)\big) = f_1\big(x_{eq} + \delta_1(t), y_{eq} + \delta_2(t)\big),$$

$$D^q\big(y_{eq}+\delta_2(t)\big)=f_2\big(x_{eq}+\delta_1(t),y_{eq}+\delta_2(t)\big),$$

from which we can get

$$D^q\delta_1(t)=f_1\big(x_{eq}+\delta_1(t),y_{eq}+\delta_2(t)\big),$$

$$D^q\delta_2(t)=f_2\big(x_{eq}+\delta_1(t),y_{eq}+\delta_2(t)\big).$$

Note that, for $i=1,2$,

$$f_i\Big(x_{eq}+\delta_1(t),y_{eq}+\delta_2(t)\Big)\simeq f_i\big(x_{eq},y_{eq}\big)+\frac{\partial f_i}{\partial x}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_1(t)+\frac{\partial f_i}{\partial y}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_2(t)+\cdots,$$

where $f_i\Big(x_{eq},y_{eq}\Big)=0$. Thus we have

$$D^q\delta_1(t)\simeq\frac{\partial f_1}{\partial x}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_1+\frac{\partial f_1}{\partial y}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_2,$$

$$D^q\delta_2(t)\simeq\frac{\partial f_2}{\partial x}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_1+\frac{\partial f_2}{\partial y}\Big|_{\left(x_{eq},y_{eq}\right)}\delta_2.$$

Furthermore we obtain the following system

$$D^q\overrightarrow{\delta}=C\overrightarrow{\delta},\tag{6}$$

with the initial values

$$\delta_1(0)=x(0)-x_{eq},\quad \delta_2(0)=y(0)-y_{eq},\tag{7}$$

where

$$\overrightarrow{\delta}=\begin{bmatrix}\delta_1\\ \delta_2\end{bmatrix},\quad C=\begin{bmatrix}c_{11}&c_{12}\\ c_{21}&c_{22}\end{bmatrix},$$

and

$$c_{i1}=\frac{\partial f_i}{\partial x}\Big|_{\left(x_{eq},y_{eq}\right)},\quad c_{i2}=\frac{\partial f_i}{\partial y}\Big|_{\left(x_{eq},y_{eq}\right)},\quad i=1,2.$$

Let λ_1 and λ_2 are the eigenvalues of C and B is the matrix of eigenvectors of C. We have

$$B^{-1}CB=\Lambda,$$

where Λ is a diagonal matrix of C given by

$$\Lambda = \begin{bmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{bmatrix}.$$

Then

$$CB = B\Lambda, \quad C = B\Lambda B^{-1},$$

which leads to

$$D^q \overrightarrow{\delta} = \left(B\Lambda B^{-1}\right) \overrightarrow{\delta},$$

$$D^q\left(B^{-1} \overrightarrow{\delta}\right) = \Lambda\left(B^{-1} \overrightarrow{\delta}\right),$$

thus

$$D^q \overrightarrow{\beta} = \Lambda \overrightarrow{\beta}, \quad \overrightarrow{\beta} = B^{-1} \overrightarrow{\delta}, \tag{8}$$

where

$$\overrightarrow{\beta} = \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix},$$

i.e.

$$\begin{cases} D^q \beta_1 = \lambda_1 \beta_1, \\ D^q \beta_2 = \lambda_2 \beta_2. \end{cases} \tag{9}$$

The solutions of Eqs. (9) are given by

$$\beta_1(t) = \sum_{n=0}^{\infty} \frac{(\lambda_1)^n t^{n\alpha}}{\Gamma(n\alpha+1)} \beta_1(0) = E_\alpha(\lambda_1 t^\alpha)\beta_1(0), \tag{10}$$

$$\beta_2(t) = \sum_{n=0}^{\infty} \frac{(\lambda_2)^n t^{n\alpha}}{\Gamma(n\alpha+1)} \beta_2(0) = E_\alpha(\lambda_2 t^\alpha)\beta_2(0), \tag{11}$$

where the function $E_q(\cdot)$ is the classical Mittag-Leffler function [Ahmed and El-gazzar(2007)], defined by

$$E_q(z) := \sum_{n=0}^{\infty} \frac{z^k}{\Gamma(nq+1)}, \quad z \in \mathbb{C}; \ \Re(q) > 0.$$

By using the result of Matignon [Matignon(1996)], we know that, if

$$|arg(\lambda_1)| > \frac{q\pi}{2}, \quad |arg(\lambda_2)| > \frac{q\pi}{2},$$

then $\beta_1(t)$, $\beta_2(t)$ are decreasing and then $\delta_1(t)$, $\delta_2(t)$ are decreasing.

So the equilibrium point $\left(x_{eq}, y_{eq}\right)$ is locally asymptotically stable if all the eigenvalues of the Jacobian matrix

$$A = \begin{bmatrix} \partial f/\partial x & \partial f/\partial y \\ \partial g/\partial x & \partial g/\partial y \end{bmatrix}$$

evaluated at equilibrium point satisfies the following condition:

$$|arg(\lambda)| > \frac{q\pi}{2}. \tag{12}$$

4 Stability of fractional order models of HIV-1 infection

In this section, by using the result obtained in section 3, we investigate the stability of fractional order model of HIV-1 infection, i.e., the system (3).

In order to find the equilibria of system (3), we put

$$\begin{cases} rx\left(1-\frac{x+y+z}{K}\right)-\alpha\frac{xy}{C+x}=0, \\ \beta z-\delta y=0, \\ \mu\frac{xy}{C+x}-\mu z=0. \end{cases} \tag{13}$$

It is not difficult to see the algebraic system (13) has three equilibria: the trivial equilibrium $E_0=(0,0,0)$, the healthy equilibrium $E_1=(K,0,0)$, and in case that the basic reproduction number $R_0=\frac{1}{\delta}\left(\frac{\beta K}{C+K}\right)>1$, there is a third positive equimibria $E^*=\left(x^*,y^*,z^*\right)$ called infected equilibrium, where

$$x^*=\frac{\delta C}{\beta-\delta},\quad y^*=\frac{\beta C(r\delta C-rK\beta-rK\delta)}{(\beta-\delta)(\beta rC+rC\delta+\alpha K\beta-K\alpha\delta)},$$

$$z^*=\frac{\delta C(r\delta C-rK\beta-rK\delta)}{(\beta-\delta)(\beta rC+rC\delta+\alpha K\beta-K\alpha\delta)}.$$

At any point $M(x,y,z)$, the Jacobian matrix of system (3) is given by

$$J(M)=\begin{pmatrix} r-\frac{2rx+ry+rz}{K}-\frac{\alpha Cy}{(C+x)^2} & -r\frac{x}{K}-\frac{\alpha x}{C+x} & -r\frac{x}{K} \\ 0 & -\delta & \beta \\ \frac{\mu Cy}{(C+x)^2} & \mu\frac{x}{C+x} & -\mu \end{pmatrix}.$$

Theorem 1 *Assume that $R_0 < 1$. Then $E_1 = (K,0,0)$ is locally asymptotically stable.*

Proof. At healthy equilibrium $E_1 = (K,0,0)$, the characteristic polynomial has the form

$$P(\lambda) = |\lambda I - J(E_1)| = \begin{vmatrix} \lambda + r & r + \frac{\alpha K}{C+K} & r \\ 0 & \lambda + \delta & -\beta \\ 0 & -\mu \frac{K}{C+K} & \lambda + \mu \end{vmatrix}$$
$$= \lambda^3 + (\lambda + \mu + \delta)\lambda^2 + [r\mu + r\delta + \mu\delta(1 - R_0)]\lambda + r\delta\mu(1 - R_0).$$

Since $R_0 < 1$, all the coefficients of $P(\lambda)$ are positive, and the inequality

$$(\lambda + \mu + \delta)[r\mu + r\delta + \mu\delta(1 - R_0)] > r\delta\mu(1 - R_0)$$

holds. Thus by Routh-Hurwitz Theorem, we know that all roots of $P(\lambda)$ have negative real parts. This means that the condition (12) is satisfied and $E_1 = (K,0,0)$ is locally asymptotically stable. ■

The Jacobian matrix $J(E^*)$ of (3) at $E^* = \left(x^*, y^*, z^*\right)$ is given by

$$J(E^*) = \begin{pmatrix} -a & -b & -r\frac{x^*}{K} \\ 0 & -\delta & \beta \\ \frac{\mu C y^*}{(C+x^*)^2} & \mu\frac{\delta}{\beta} & -\mu \end{pmatrix},$$

where $a = -r + \frac{r}{K}y^* + 2\frac{r}{K}x^* + \frac{r}{K}z^* + \frac{\alpha C y^*}{(C+x^*)^2}$ and $b = r\frac{x^*}{K} + \alpha\frac{\delta}{\beta}$. In order to proceed further, we make the following assumption on the parameters of system (3)

$$r - 2r\frac{x^*}{K} - r\frac{y^*}{K} - \frac{r}{K}z^* - \frac{\alpha C y^*}{(C+x^*)^2} < 0, \tag{14}$$

and denote by D and Δ, the following expressions:

$$D = 2a\delta + a^2 + ar\frac{x^*}{K}\frac{Cy^*}{(C+x^*)^2} - b\frac{C\beta y^*}{(C+x^*)^2},$$

$$\Delta = D^2 - 4(a^2\delta + a\delta^2)\left(r\frac{x^*}{K}\frac{Cy^*}{(C+x^*)^2} + a\right).$$

Theorem 2 *Assume that $R_0 > 1$ and (14) holds.*
1) If either $\Delta < 0$ or $\Delta = 0$ and $D > 0$, then E^* is locally asymptotically stable for all $\mu > 0$;
2) If $\Delta = 0$ and $D < 0$, then there exists $\mu_0 > 0$, such that E^* is locally asymptotically stable for $\mu > 0$ and $\mu \neq \mu_0$;

3) If $\Delta > 0$, we have the following two cases:

(i) $D > 0$, then E^* is locally asymptotically stable for all $\mu > 0$;

(ii) $D < 0$, then there exist $0 < \mu_1 < \mu_2$, such that E^* is locally asymptotically stable for $\mu < \mu_1$ or $\mu > \mu_2$.

Proof. At the infected equilibrium $E^* = \left(x^*, y^*, z^*\right)$, the characteristic polynomial has the form

$$\begin{aligned} P(\lambda) = |\lambda I - J(E^*)| &= \begin{vmatrix} \lambda + a & b & r\frac{x^*}{K} \\ 0 & \lambda + \delta & -\beta \\ -\frac{\mu C y^*}{(C+x^*)^2} & -\mu\frac{\delta}{\beta} & \lambda + \mu \end{vmatrix} \\ &= \lambda^3 + (a+\mu+\delta)\lambda^2 + \Big(a\mu + a\delta + \frac{rx^*}{K}\frac{\mu C y^*}{(C+x^*)^2}\Big)\lambda \\ &\quad + \delta\frac{rx^*}{K}\frac{\mu C y^*}{(C+x^*)^2} + b\frac{\mu\beta C y^*}{(C+x^*)^2}. \end{aligned} \tag{15}$$

Since (14) holds, then $a > 0$ and all the coefficients of $P(\lambda)$ are positive. Applying Routh-Hurwitz Theorem to (15), we know that $E^* = \left(x^*, y^*, z^*\right)$ is locally asymptoticqlly stable if

$$\begin{aligned} A(\mu) = (a+\delta+\mu)\Big(a\delta + a\mu + \frac{rx^*}{K}\frac{\mu C y^*}{(C+x^*)^2}\Big) - b\frac{\mu\beta C y^*}{(C+x^*)^2} \\ - \delta\frac{rx^*}{K}\frac{\mu C y^*}{(C+x^*)^2} > 0. \end{aligned} \tag{16}$$

We rewrite (16) into the following form

$$A(\mu) = \Big(r\frac{x^*}{K}\frac{Cy^*}{(C+x^*)^2} + a\Big)\mu^2 + D\mu + a\delta^2 + a^2\delta,$$

for which the discriminant is Δ. Then we have the following conclusion:

If $\Delta < 0$ or $\Delta = 0$ and $D > 0$, then $A(\mu)$ have no real root or one negative real root. In this case $A(\mu) > 0$ and E^* is locally asymptotically stable for all $\mu > 0$.

If $\Delta = 0$ and $D < 0$, then $A(\mu)$ have one positive real root μ_0. Thus $A(\mu) > 0$ for all $\mu > 0$ and $\mu \neq \mu_0$. E^* is then locally asymptotically stable for all $\mu > 0$ and $\mu \neq \mu_0$.

Now assuming that $\Delta > 0$. Then if $D > 0$, $A(\mu)$ have two negative real roots, so $A(\mu) > 0$. In this case the infected equilibrium E^* is locally asymptotically stable. In the case $D < 0$, $A(\mu)$ have two positive real roots $0 < \mu_1 < \mu_2$ such that $A(\mu) > 0$ for $\mu \in (0, \mu_1) \cup (\mu_2, +\infty)$. Thus we have that E^* is locally asymptotically stable for $\mu \in (0, \mu_1) \cup (\mu_2, +\infty)$. ■

5 Simulations

In this section, we give some numerical simulations of model (3) to illustrate our results on stability, the values of the parameters are given in **Table** 1, more details can be found in [Kouche and Ainseba(2007)].

Table 1: Parameters and values of models (3)

Parameters	Values
r healthy cell reproductive rate	0.65/day
K carrying capacity of the system	2×10^6/ml
δ death rate of infected cells	0.3/day
x_0 initial concentration of healthy cells	5×10^5/ml
y_0 initial concentration of infected cells	5×10^2/ml
C the half saturation constant of the proliferation process	3.7×10^6/ml
α the maximum rate of infection	11/day

Suppose that 7.7% of infected cells survive incubation which corresponds to a value of $\beta = 0.847$. Then, $R_0 = 0.9906 < 1$, the condition of Theorem 1 is satisfied. Numerical simulations (see **Figure** 1) show that the healthy cells predominate. In this case, E_1 is asymptotically stable. However, we note that in reality it is unlikely that so few cells would survive latency.

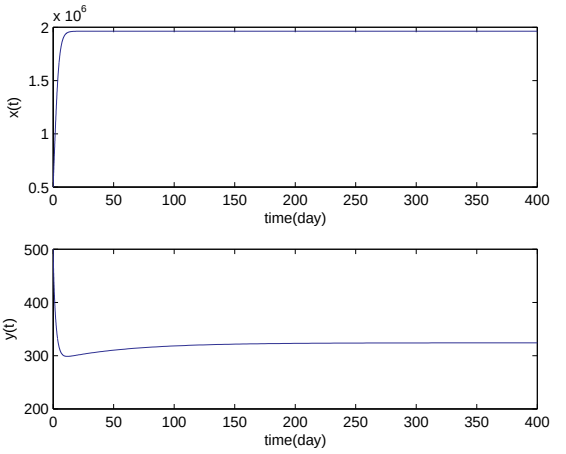

Figure 1: $q = 0.9$, 7.7% of infected cells survive incubation

Suppose that 30% of infected cells survive incubation which corresponds to a value

of $\beta = 3.3$. Then, $R_0 = 3.8596 > 1$, $a = 0.0815$, $D = -0.0937 < 0$, $\Delta = 0.0051 > 0$. The condition 3(ii) of Theorem 2 is then satisfied. Two positive real roots μ_1 and μ_2 are: $\mu_1 = 0.111$, $\mu_2 = 0.9712$. According to Theorem 2, we know if $\mu \in (0,\mu_1) \cup (\mu_2, +\infty)$, the infected equilibrium $E^* = (3.7 \times 10^5, 1.8 \times 10^5, 1.6 \times 10^4)$ is locally asymptotically stable. Then, we take $\mu = 1/day$ which is a realistic value since the incubation period is around 1 day (see [Spouge, Shrager and Dimitrov(1996)]). Numerical simulations give the graphics in **Figure** 2. In this case, healthy cells and infected cells co-exist. This would correspond to the case where, in models representing cell-free viral spread, we have an endemically infected steady state. This means that infection is present but it does not grow out of bound, and levels of healthy cells do not crash to zero. In the (x,y)-plane, trajectories spiral toward the equilibrium (see **Figure** 3).

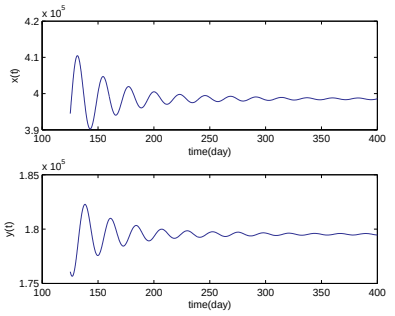

Figure 2: $q = 0.9$, $\mu = 1$, 30% of infected cells survive incubation

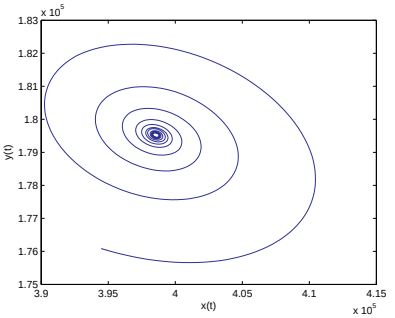

Figure 3: $q = 0.9$, $\mu = 1$, (x,y)-plane

If we take $\mu = 0.5/day$, then the components $x(t)$ and $y(t)$ oscillate with increasing time (see **Figure** 4). In the (x,y)-plane, trajectories are approaching the periodic solution as the time increases (see **Figure** 5). Thus we can say that E^* is unstable.

Suppose that 80% of infected cells survive incubation which corresponds to a value of $\beta = 8.8$. Then, $R_0 = 10.2924 > 1$, $a = 0.0251$, $D = -0.1678 < 0$, $\Delta = 0.0279 > 0$. The condition 3(ii) of Theorem 2 is then satisfied. Two positive real roots μ_1 and μ_2 are: $\mu_1 = 0.0146$, $\mu_2 = 6.1303$. According to Theorem 2, we know if $\mu \in (0,\mu_1) \cup (\mu_2, +\infty)$, the infected equilibrium $E^* = (1.3 \times 10^5, 1.97 \times 10^5, 6.7 \times 10^3)$ is locally asymptotically stable. Then, we take $\mu = 7/day$, numerical simulations are showed in **Figure** 6. In the (x,y)-plane, trajectories spiral toward the equilibrium (see **Figure** 7).

If we take $\mu = 1/day$ which is a realistic value, then the components $x(t)$ and $y(t)$ oscillate with increasing time (see **Figure** 8). And compared with **Figure** 4, the oscillations are more frequent(i.e., the periods are shorter) and the amplitudes are

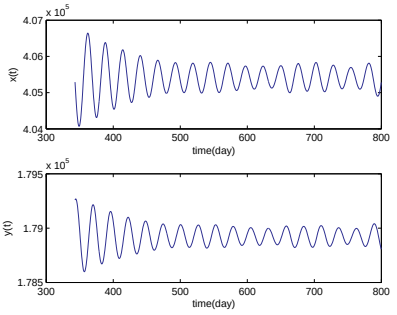

Figure 4: $q = 0.9$, $\mu = 0.5$, 30% of infected cells survive incubation

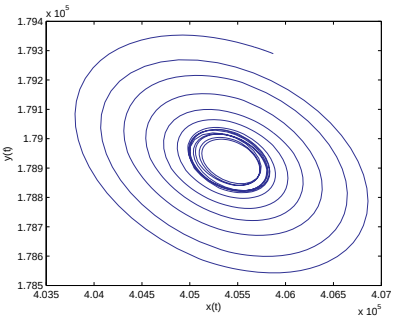

Figure 5: $q = 0.9$, $\mu = 0.5$, (x,y)-plane

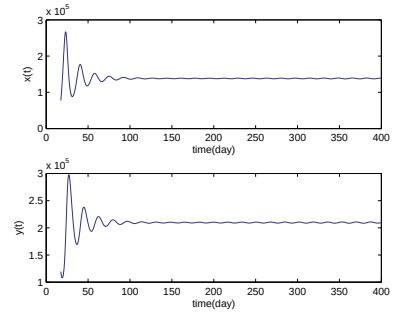

Figure 6: $q = 0.9$, $\mu = 7$, 80% of infected cells survive incubation

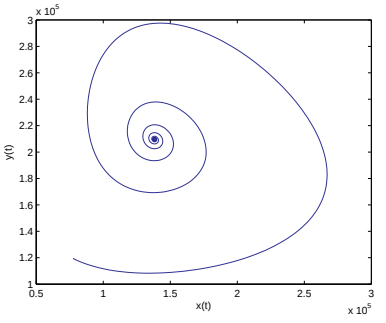

Figure 7: $q = 0.9$, $\mu = 7$, (x,y)-plane

smaller. In the (x,y)-plane, trajectories are approaching the periodic solution as the time increases (see **Figure** 9), so we can say that E^* is unstable. Besides, we conclude that increasing the value of β will decrease the periods and the amplitudes of the periods solutions.

Remark 1. In the simulations above, the fractional-order $q = 0.9$ is close to the integer-order 1. The results obtained from the fractional model of HIV-1 are very similar to those of the ODE model. But we have to point out that in ODE model, if not more than 7.7% of infected cells survive the incubation period, infected cells are cleared and the infection dies out as the time increase. However, in our model, from **Figure** 1, we see that infected cells can not be all cleared, though the number is very smaller compared with that of the healthy cells. Furthermore, if the infected equilibrium E^* is unstable, the amplitudes in ODE model are more larger than those in our model.

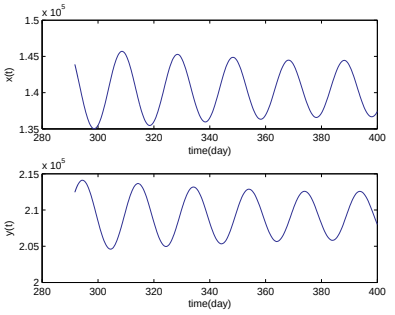

Figure 8: $q = 0.9$, $\mu = 1$, 80% of infected cells survive incubation

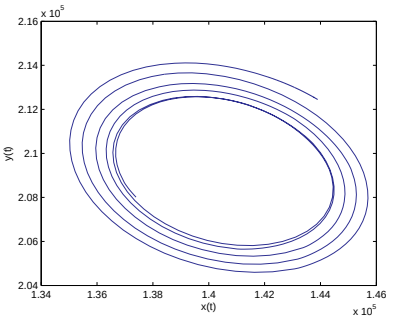

Figure 9: $q = 0.9$, $\mu = 1$, (x,y)-plane

Remark 2. In section 3, we have pointed out that if all the eigenvalues of the Jacobian matrix satisfy the condition $|arg(\lambda)| > \frac{q\pi}{2}$, then the equilibrium point is locally asymptotically stable. So in the case of 80% that infected cells survive incubation, $q = 0.9$, $\mu_1 = 0.0146$, $\mu_2 = 6.1303$, if we take $\mu = 5 \in (\mu_1, \mu_2)$, the infected equilibrium E^* is also locally asymptotically stable (see **Figure** 10 and **Figure** 11). Moreover, we can calculate that $|arg(\lambda_1)| = 3.1416$ and $|arg(\lambda_{2,3})| = 1.5643$. They are all larger than $\frac{q\pi}{2} = 0.9 * \pi/2 = 1.4137$. Here, the bifurcations are not μ_1 and μ_2, while in the ODE model they are the bifurcations.

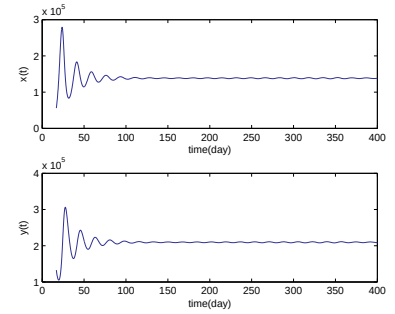

Figure 10: $q = 0.9$, $\mu = 5$, 80% of infected cells survive incubation

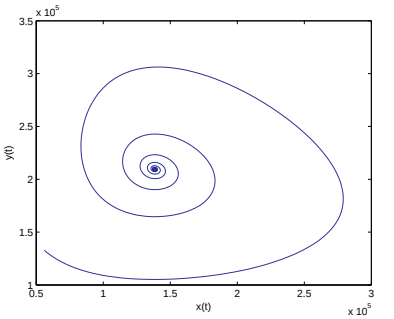

Figure 11: $q = 0.9$, $\mu = 5$, (x,y)-plane

Remark 3. In the simulations above, we take the fractional-order $q = 0.9$ which is close to the integer-order 1. If we take the order $q = 0.5$, the simulations are showed in the following figures. The results are very different from those of the fractional-order $q = 0.9$. Furthermore, we can find that if $q < 0.9$ which is far way from the integer-order 1, simulations are all very different. Why do such differences happen

and what the fractional-order serves in the HIV-1 model? We will discuss these questions in our later studies.

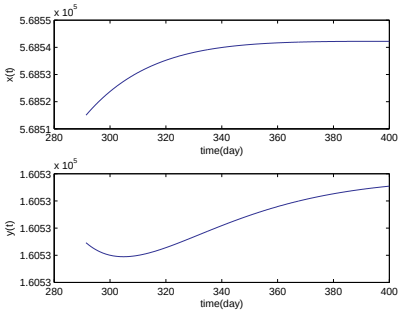

Figure 12: $q = 0.5$, $\mu = 1$, 30% of infected cells survive incubation

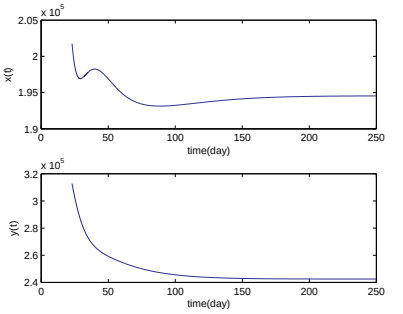

Figure 13: $q = 0.5$, $\mu = 1$, 80% of infected cells survive incubation

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