# MODELLING HIV INFECTION OF CD4+ T CELLS USING FRACTIONAL ORDER DERIVATIVES

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## ABSTRACT

In this paper, the stability of the time dependent differential equation for HIV infection of CD4+ T cell model was studied using the fractional order derivatives. It is discovered that the eigenvalues showed that the system was unstable with three different equilibrium points using Matlab 7.5.0.342 R2007b version.

## 1. INTRODUCTION

Weli *et.al.* (2014) studied the time dependent ordinary differential equation model on HIV infection of CD4+ T cells of a patient. The following three differential equations describe the model.

$$\frac{dT}{dt} = s - dT + \alpha T \left( 1 - \frac{T}{T_{max}} \right) - \beta TV$$

$$\frac{dI}{dt} = \beta TV - \delta I \qquad\qquad (1.1)$$

$$\frac{dV}{dt} = \rho I - cV$$

$T(t)$ is the number of target cells, $I(t)$ is the number of infected cells, $V(t)$ is the viral load of the virions and the R is positive constant. $\alpha$ is the maximum proliferation rate of the target cell, $\beta$ is the infection rate constant, $\delta$ is the death rate of cells infected, $\rho$ is the reproductive rate of infected cells, $s$ is the rate at which the new $T$ cells are created from source within the body, $c$ is clearance rate constant of virions, $d$ is the death rate of $T(t)$ cells of CD4+ T cells and $T_{max}$ is the T population density at which proliferation shuts off. $\left( 1 - \frac{T}{T_{max}} \right)$ describes the logistic growth of the healthy CD4+T cells.

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## 2. LITERATURE REVIEW

In this section, we shall review some existing literature done by some researchers.

Arafa *et.al.* (2016) studied the stability of equilibrium points of a model of HIV infection of CD4+ T using Mittag-Leffler method. The results showed that the fractional ordinary differential equations has more advantages than classical integer-order modeling.

Arafa *et.al.* (2013) studied the nonlinear differential equation system such as Lorenz system of fractional order. They used generalized Mittag-Leffler to solve the approximate and analytical solutions of the system. The result showed that the fractional order differential equation spread at a faster rate than the classical differential equation.

Arafa *et.al.* (2012) studied the effect of changing the average number of viral particles with distinct sets of initial condition. They used the Generalized Euler Method. The result showed the numerical solution of the HIV primary infection.

Goreno and Mainardi (2000) reviewed a variety of fractional evolution processes. They used fractional order whose solutions turned out to be related to Mittag-Leffler-type.

Hegazi *et.al* (2011) studied the synchronization of chaotic and hyperchaotic systems using fractional order. The result showed the effect of the method used on the synchronized systems.

Matignon (1996) studied the internal and external stabilities for finite-dimensional linear fractional differential systems. He used a fractional differential system in polynomial representation to establish the stabilities of the roots of some polynomial which lie outside the closed angular sector.

Merdan (2007) studied HIV infection model of CD4+ T cells using homotype perturbation method. His result showed the reliability and simplicity of the method.

Merdan *et.al* (2011) studied HIV infection model of CD4+ T cells using Variational Iteration Method. Their results showed the reliability and simplicity of the method.

Rida and Arafa (2011) studied a linear fractional differential equations using the Mittag-Leffler function method. They results showed that method was efficient.

## 3. FRACTIONAL ORDER DERIVATIVES

Now, following the Arafa *et.al.* (2016), we introduce the fractional order derivative of HIV infection of CD $4^+$ T cells:

$$D^{\eta_1}(T) = s - dT + \alpha T\left(1 - \frac{T}{T_{max}}\right) - \beta TV$$

$$D^{\eta_2}(I) = \beta TV - \delta I \tag{3.1}$$

$$D^{\eta_3}(V) = \rho I - cV$$

Where $\eta_1, \eta_2, \eta_3 > 0$ with initial conditions $T(0) = 0.1$, $I(0) = 0$, $V(0) = 0.1$.


## 4. EQUILIBRIUM POINTS

We suppose that:

$$T(t) = x_1(t)$$

$$I(t) = x_2(t) \tag{4.1}$$

$$V(t) = x_3(t)$$

Thus for the equilibrium point, set $D^{\eta} x_i(t) = 0$ for $i = 1,2,3,...$

Hence, (1.1) becomes:

$$s - dx_1 + \alpha x_1\left(1 - \frac{x_1}{T_{max}}\right) - \beta x_1 x_3 = 0 \tag{4.2}$$

$$\beta x_1 x_3 - \delta x_2 = 0 \tag{4.3}$$

$$\rho x_2 - c x_3 = 0 \tag{4.4}$$

Solving (4.2), (4.3) and (4.4) to have that if $x_3 = 0 \Rightarrow x_2 = 0$.

And $x_1 = \dfrac{\alpha T_{max} - dT_{max} \pm \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}$ (4.5)

Then,

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{\alpha T_{max} - dT_{max} + \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}, 0, 0\right) \tag{4.5a}$$

and,

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{\alpha T_{max} - dT_{max} - \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}, 0, 0\right) \tag{4.5b}$$

are equilibrium points.


Next suppose $x_2 \neq 0$ and $x_3 \neq 0$, then another equilibrium point is

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{c\delta}{\rho\beta}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha^2 c^2 \delta^2}{\beta\delta\rho T_{max}}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha c^2 \delta^2}{\beta c\delta T_{max}}\right) \tag{4.6}$$

## 5.      NUMERICAL STABILITY OF THE SYSTEM

With the given parameter values:

$\alpha = 6.8day^{-1}, \beta = 0.0002mm^{-3}, \delta = 0.5day^{-1}, \rho = 1000mm^{3}day^{-1},$
$s = (5day^{-1})(mm^{-3}), c = 10day^{-1}, d = 0.01day^{-1}, T_{max} = 1300mm^{3}day^{-1}.$

So, from (4.5a): $x_1^{eq} = 1.2988e + 003$.

Next, to form the Jacobian matrix, let $F(x_1,x_2,x_3)$, $G(x_1,x_2,x_3)$ and $H(x_1,x_2,x_3)$ be three continuous and differentiable functions such that:

$$F(x_1,x_2,x_3) = s - dx_1 + \alpha x_1\left(1 - \frac{x_1}{T_{max}}\right) - \beta x_1 x_3 \tag{5.1}$$

$$G(x_1,x_2,x_3) = \beta x_1 x_3 - \delta x_2 \tag{5.2}$$

$$H(x_1,x_2,x_3) = \rho x_2 - cx_3 \tag{5.3}$$

So that the Jacobian matrix becomes:

$$A = \begin{pmatrix} -6.7977 & 0 & -0.2598 \\ 0 & -0.500 & 0.2598 \\ 0 & 1000 & -10 \end{pmatrix}$$

Its eigenvalues are $\lambda_1 = -6.7977 < 0$, $\lambda_2 = 11.5536 > 0$, $\lambda_3 = -22.0536 < 0$.

Hence, the equilibrium point

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{\alpha T_{max} - dT_{max} + \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}, 0, 0\right) \text{ is unstable.}$$

Next, for: $\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{\alpha T_{max} - dT_{max} - \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}, 0, 0\right)$

Then the Jacobian matrix becomes:

$$A = \begin{pmatrix} 6.7977 & 0 & 1.4719e-004 \\ 0 & -0.5000 & -1.4719e-004 \\ 0 & 1000 & -10 \end{pmatrix}$$

Its eigenvalues are $\lambda_1 = 6.7977 > 0$, $\lambda_2 = -0.5155 < 0$, $\lambda_3 = -9.9845 < 0$.

Hence, the equilibrium point

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{\alpha T_{max} - dT_{max} - \sqrt{d^2 T_{max}^2 - 2d\alpha T_{max}^2 + \alpha^2 T_{max}^2 + 4\alpha s T_{max}}}{2\alpha}, 0, 0\right) \text{ is unstable.}$$

Next for the point:

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{c\delta}{\rho\beta}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha^2 c^2 \delta^2}{\beta\delta\rho T_{max}}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha c^2 \delta^2}{\beta c\delta T_{max}}\right)$$

The Jacobian matrix becomes:

$$A = \begin{pmatrix} 6.4588 & 0 & -0.0050 \\ 0.0696 & -0.5000 & 0.0050 \\ 0 & 1000 & -10 \end{pmatrix}$$

Its eigenvalues are $\lambda_1 = 6.4556 > 0$, $\lambda_2 = 0.0051 > 0$, $\lambda_3 = -10.5020 < 0$.

Hence, the equilibrium point

$$\left(x_1^{eq}, x_2^{eq}, x_3^{eq}\right) = \left(\frac{c\delta}{\rho\beta}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha^2 c^2 \delta^2}{\beta\delta\rho T_{max}}, \frac{s\rho\beta T_{max} - dc\delta T_{max} + \alpha c\delta T_{max} - \alpha c^2 \delta^2}{\beta\delta\rho T_{max}}\right)$$

is unstable.

## 6. CONCLUSION

It was studied in this work that the given HIV infection of CD4$^+$ T cells model was unstable with the help of eigenvalues given the values of the parameters $\alpha, \beta, \delta, \rho, s, c, d, T_{max}$.

For a unique equilibrium point, the system gave at least a positive eigenvalue. There is a need for varying the data parameters or looking for the second order fractional derivatives of the discussed model.

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