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# A Stability analysis for a mathematical model for the determination of optimum drug for chemotherapy of HIV

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***Abstract***

***We propose a system of ordinary differential equations modeling the interaction of HIV virus and the immune system of the human body. We propose an optimal amount of medicine for the chemotherapy for patients with human immunodeficiency virus (HIV) and we show that the endemic equilibrium is asymptotically stable.***

**Keywords:** Optimal control, HIV – infection dynamics, AVK method, therapy therapeutic period, asymptotically stable.

## 1.0 Introduction

Many scientists have examined various chemotherapies for patients with human immunodeficiency virus (HIV) to determine the optimal scheme for treatment. The challenge of the disease, Acquired Immune Deficiency Syndrone (AIDS) is that the CD4+T cells that HIV infects are the very ones that are necessary to ward off invasion [1]. The HIV is fused into the host CD4+T cell and since HIV is a retrovirus, the RNA of the virus is converted into DNA inside the CD4+T cell. Thus the DNA of the virus is duplicated and the new virus particles bud from the CD+T cell [1, 2].

At the beginning of the 80's when AIDS became epidemic, many attempts were for controlling the disease by biologists, mathematicians and medical doctors. When medical practioners began research on drugs for preventing the disease with new therapeutical strategies mathematicians developed mathematical models that were used in the experiments [3,4]. One important use of the mathematical models is for finding the optimal drug for the control of the disease. An ordinary system of differential equations which describes the interaction of HIV in the immune system is utilized, and the optimal control of the system of equations is explored. Dynamic programming and various techniques were used in finding ways of maximizing the number of uninfected CD4+T cells and minimizing the negative effects of the chemotherapy. Such techniques include the so called AVK method that was developed by engineer A.V Kamyad.

In this paper we propose a new optimality technique and we further show that the endemic equilibrium is asymptotically stable.

## 2. Mathematical Model

We modify the model in [3] to obtain

$$\frac{dx}{dt} = \frac{s}{1+V} - \mu_1 X - k_1 VX + rX\left(1 - \frac{X+Y+Z}{N\max}\right) \tag{1}$$

$$\frac{dY}{dt} = k_1 VX - \mu_2 Y - k_2 Y \tag{2}$$

$$\frac{dZ}{dt} = k_2 Y - \mu_3 Z + k_3 VY \tag{3}$$

$$\frac{dV}{dt} = (1-u)\, L\mu_3 Z - k_1 VX - \mu_4 V - k_3 VY, \tag{4}$$

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where $\mu_1, \mu_2, \mu_3, \mu_4$ with negative signs indicate the rate of natural death of uninfected CD4+T cells, latently infected CD4+T cells, actively infected CD4+T cells and free virus. $k_1, k_2$ and $k_3$ are rate CD4+T cells become infected by virus, rate latently infected cells covert to actively infected cells and rate at which free virus converts latently infected cells to actively infected cells. In previous models in literature $k_3 = 0$ and it suffices to take $k_3 = 0$, $k_3 \neq 0$ follows.
The initial conditions are

$$X(0) = X_0,\ Y(0) = Y_0,\ Z(0) = Z_0,\ V(0) = V_0 \qquad (5)$$

## 3.0 Optimal Control

In most medicine therapies, the therapeutic period is less than 2 years. To keep the healthy cells high and keep the side effects of the medicine therapy low the following target function is normally used to maximize the dynamics [5]:

$$J(u) = \int_{tstart}^{tfinal} \left( X(t) - \frac{1}{2} B u(t)^2 \right) dt, \quad (B > 0), \qquad (6)$$

where for most of HIV chemotherapy drugs $t_{final} - t_{start} < 2$ years. The integrand X indicates one wants to maximize the number of uninfected CD4+T cells and minimize the side effects of the chemotherapy, B>0 represents a desired weight on the benefit and cost [3]. If u(t) = 1 represents maximal use of chemotherapy, then the maximal cost is represented by $u^2$. The goal is to characterize the optimal control u* satisfying [1]

$$J(u) \leq J(u^*)$$
$$0 \leq u \leq 1$$

**Theorem 1**

There exists an optimal control u* that maximizes the objective function J(u)

**Theorem 2**

$0 < u^* < 1$

**Theorem 3**

Let the endemic equilibrium be $(X^*, Y^*, Z^*, V^*),\ 0 < X^* \leq X_0$

Then the endemic equilibrium is asymptotically stable.

**Endemic Equilibrium**

Let $\frac{dx}{dt} = \frac{dY}{dt} = \frac{dZ}{dt} = \frac{dV}{dt} = 0$

Then

$$\frac{S}{1+V_x} - \mu_1 X_* - k_1 V_* X_* + r X_* \left( 1 - \frac{X_* + Y_* + Z_*}{N\max} \right) = 0 \qquad (7)$$

$$k_1 V_* X_* - \mu_2 Y_* - k_2 Y_* = 0 \qquad (8)$$

$$k_2 Y_* - \mu_3 Z_* = 0 \qquad (9)$$

$$(1-u) L \mu_3 Z_* - k_1 V_* X_* - \mu_4 V_* = 0 \qquad (10)$$

**Solving, we obtain**

$$V_* = c Z_*,\ Y_* = a Z_*,\ X_* = \frac{a}{bc}, \qquad (11)$$

where $a = \frac{\mu_3}{k_2},\ b = \frac{k_1}{\mu_2 + k_2}$

$$c = \frac{(1-u)\left(L\mu_3 - \frac{k_1}{b}a\right)}{\mu_4}$$

**Proof of Theorem 2**

Clearly u>0 by definition. If u = 1, then c is less than zero. Thus the equilibrium point is negative. This establishes the theorem.

**Proof of Theorem 1**

Let $X_* = X_0$. Then $X_*$ is maximum and $X_* = \frac{a}{bc}$ for a fixed $a = \frac{\mu_3}{K_2}$, $b = \frac{k_2}{\mu_2 + k_2}$

Then $c = \frac{a}{bX_*}$. Then

$$(1-u)\, L\mu_3 - \frac{k_1 a}{b} = \frac{a}{bX_*}$$

$$1-u = \left(\frac{a}{bx_*} + \frac{k_1 a}{b}\right) \Big/ L\,\mu_3$$

This establishes theorem 1.

**Proof of Theorem 3**

Let $x = X - X_*, y = Y - Y_*, z = Z - Z_*$

$v = V - V_*$

Then

$$\begin{pmatrix} \frac{dx}{dt} \\ \frac{dy}{dt} \\ \frac{dz}{dt} \\ \frac{dv}{dt} \end{pmatrix} = \begin{pmatrix} a_1 & \frac{-rX_*}{N\max} & \frac{-rX_*}{N\max} & -b \\ k_1 V_* & -(\mu_2 + k_2) & 0 & k_1 X_* \\ 0 & k_2 & -\mu_3 & 0 \\ 0 & (1-u)L\,\mu_3 & -(k_1 X_* + \mu_4) & \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ v \end{pmatrix} \quad + non - linear\ terms$$

**(Using the data [1])**

$\mu_1 = 0.02,\ \mu_2 = 0.03,\ \ u = 0.25$

$\mu_3 = 0.24,\ \mu_4 = 7,\ k_1 = 0.000024$

$k_2 = 0.003,\ r = 0.03,\ N\max = 1500\ and\ \ s = 10.$

Then the eigenvalues are:

$\lambda_1 = -0.03650934816$

$\lambda_2 = -6.978440435$

$\lambda_3 = -0.001625 + 0.013794i$

$\lambda_4 = -0.001625 - 0.013794i$

This shows that $(X_*, Y_*\ Z_*, V_*)$ is asymptotically stable. This completes the proof.

## 5.0 Conclusion

We have shown that optimizing chemotherapy must involve the objective functional J(u). The minimal negative effect u is a function of the initial value $X_0$.

## References

[1]. K. R. Fister, S. Lenhart and J. Scott McNally (1998): Optimizing Chemotherapy in an HIV model, Electronic Journal of Differential Equations, No. 32, pp 1 - 12

[2]. K.P. Badakhshan and A.V. Kamyad (2007): Numerical solution of nonlinear optimal control problems using non-linear programming, Applied mathematics and computation V0l. 187, pp 1511 – 1519.

[3]. H.G. Zadeh, H.C. Nejad, R. Jahani, H.R. Nahad and M.M. Abadi (2011a) Optimal control of HIV infection dynamics, Australian Journal of Basic and Applied Sciences, Vol. 509, pp 1051 – 1059.

[4]. H.G. Zadeh, H.C. Nejad, M.M. Abadi and H.M. Sani, (2011b) A new fast optimal control for HIV – infection dynamics based on AVK method and fuzzy estimator, American Journal of Scientific Research Vol. 32, pp 11 – 16.

[5]. A.E. Labarre, JR (1961): Elementary Mathematical Analysis, Addison – Wesley Publishing Company, INC., P 120.