

Mathematical Modelling of HIV Diseases Using Numerical Solution

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Abstract – Human Immunodeficiency Virus (HIV) is a retrovirus that causes Acquired Immunodeficiency Syndrome (AIDS) which is characterized by the progressive failure of the human immune system. AIDS is a major public health, sociological and economic concern and a cause of deaths in many parts of India.

HIV primarily infects a class of white blood cells called CD4+T cells and this selective depletion of CD4+T cells which plays a central role in immune regulation serves as a clinical indicator for measuring the progression of HIV infection. Numerical simulation of the model is implemented to investigate the sensitivity of certain key parameters on the spread of the disease. The current paper highlights the mathematical modeling of HIV diseases using numerical solution.

Keywords: HIV, Numerical, Disease

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INTRODUCTION

Diseases can be transmitted many ways, some of which can be classified as either horizontal or vertical. In the case of HIV/AIDS, horizontal transmission can result from direct physical contact between an infected individual and a susceptible individual.

Vertical transmission, on the other hand, can result from direct transfer of a disease from an infected mother to an unborn or newborn offspring. Diseases that can be transmitted vertically include chugs, dengue fever, hepatitis B and HIV/AIDS just to name a few. Vertical transmission of HIV/AIDS can occur during pregnancy, delivery or breastfeeding and is influenced by many factors, including maternal viral load and the type of delivery.

About 20% of the children infected with HIV develop AIDS in the first year of their lives, and most of them die by the age of 4 years. The others, up to 80% of infected children, develop symptoms of HIV/AIDS at school entry age (7-9 years) or even during adolescence.

HIV/AIDS transmission in Africa is primarily through heterosexual sex and vertical transmission (mother-to-child). Forty percent of all HIV/AIDS cases result from mother to child transmission.

Fractional differential equations arise in many engineering and scientific disciplines as the mathematical modeling of systems and processes in various fields, such as physics, mechanics, chemical

technology, population dynamics, biotechnology, and economics. As one of the important topics in the research differential equations, the boundary value problem has attained a great deal of attention.

Many mathematicians and researchers in the field of application are trying to model fractional order differential equations. In biology, the researchers found that biological membranes with fractional order have the nature of electronic conductivity, so it can be classified as a model of the fractional order. Because of the memory property of fractional calculus, we introduce the fractional calculus into HIV model. Both in mathematics and biology, fractional calculus will correspond with objective reality more than ODE. It is particularly important for us to study fractional HIV model.

Furthermore, delay plays an important role in the process of spreading infectious diseases; it can be used to simulate the incubation period of infectious diseases, the period of patients infected with disease, period of patients' immune to disease, and so on.

Human immunodeficiency virus infection destroys the body immune system, increases the risk of certain pathologies, damages body organs such as the brain, kidney, and heart, and causes death. Unfortunately, this infectious disease currently has no cure; however, there are effective retroviral drugs for improving the patients' health conditions

but excessive use of these drugs is not without harmful side effects.

MATHEMATICAL MODELLING OF HIV DISEASES USING NUMERICAL SOLUTION

Mathematical models have played an important role in understanding the dynamics of this infectious disease. One of such models for the HIV infection of CD4+T cells is given by the following system of differential equations.

$$\begin{aligned} \frac{dT}{dt} &= s - \alpha T + rT \left(1 - \frac{T+I}{T_{max}}\right) - kVT \\ \frac{dI}{dt} &= kVT - \beta I \\ \frac{dV}{dt} &= N\beta I - \gamma V \end{aligned} \tag{1}$$

The merit of the Differential Transform method (DTM) is that the method does not require discretization or perturbation and is easy to implement, while also greatly reducing the size of computational work to be done. However, the DTM does not give a satisfactory approximation for a large time where the convergence region of semi-analytic methods are said to be narrow. Since the DTM solutions blow out after a short time a multi-staging technique known as the Multistage Differential Transform Method (MDTM) is proposed.

Table 1: Differential Transform Table

FUNCTIONAL FORM	TRANSFORMED FORM
$u(x, t)$	$U_k(x) = \frac{1}{k!} \left[\frac{\partial^k u(x, t)}{\partial t^k} \right]_{t=0}$
$u(x, t) \pm v(x, t)$	$U_k(x) \pm V_k(x)$
$\alpha u(x, t)$	$\alpha U_k(x)$ (α is a constant)
$x^m t^n$	$x^m \delta(k - n)$
$x^m t^n u(x, t)$	$x^m U(k - n)$
$u(x, t) v(x, t)$	$\sum_{r=0}^k U_r(x) V_{k-r}(x)$
$\frac{\partial^r}{\partial t^r} u(x, t)$	$\frac{(k+r)!}{k!} U_{k+r}(x)$
$\frac{\partial}{\partial x} u(x, t)$	$\frac{\partial}{\partial x} U_k(x)$
Nonlinear Function $N(u(x, t)) = F(u(x, t))$	$N_k = \frac{1}{k!} \left[\frac{\partial^k}{\partial t^k} F(U_0) \right]_{t=0}$

Local stability of the disease free equilibrium of the model was established by the next generation

method. The results show that the disease free equilibrium is locally stable at threshold parameter less than unity and unstable at threshold parameter greater than unity. Globally, the disease free equilibrium is not stable due existence of forward bifurcation at threshold parameter equal to unity. However, it is shown that using treatment measures (ARVs) and control of the rate of vertical transmission have the effect of reducing the transmission of the disease significantly.

The basic fact reflected by the specific mathematical model with time delay is that the change of trajectory about time not only depends on the moment itself but also is affected by some certain conditions before, even the reflection of some certain factors before. This kind of circumstance is abundant in the objective world.

$$\begin{aligned} D^\theta T(t) &= s - \mu_r T(t) + rT(t) \left(1 - \frac{T(t)+I(t)}{T_{max}}\right) \\ &\quad - k_1 T(t) V(t), \end{aligned} \tag{2}$$

$$D^\theta I(t) = k_1 T(t - \tau) V(t - \tau) - \mu_i I(t),$$

$$D^\theta V(t) = N\mu_i I(t) - k_1 T(t) V(t) - \mu_v V(t),$$

with the initial conditions:

$$T(\theta) = T_0, \quad I(0) = 0, \quad V(\theta) = V_0, \quad \theta \in [-\tau, 0]. \tag{3}$$

Motivated by the works mentioned above, we will consider this model where the T-cell proliferation does play an important role in HIV infection under antiretroviral therapy; a more appropriate method is given to ensure that both equilibria are asymptotically stable.

We calculate the basic reproduction number, the IFE, two IPEs and, and so on under certain conditions and judge the stability of the equilibrium. In addition, we describe the dynamic behaviors of the fractional HIV model by using the Adams-type predictor-corrector method algorithm.

At last, we extend the model to incorporate the term which we consider the loss of virion and a bilinear term during attacking the target cells. In this paper, we establish mathematical model as follows:

$$\begin{aligned} D^\theta T(t) &= s - \mu_1 T(t) + \frac{rT(t)V_i(t)}{C+V_i(t)} \\ &\quad - k(1-n_n)T(t-\tau)V_i(t-\tau), \end{aligned} \tag{4}$$

$$D^\theta I(t) = k(1-n_n)T(t-\tau)V_i(t-\tau) - \mu_2 I(t),$$

$$D^\theta V(t) = (1-n_p)N\mu_2 I(t) - \mu_3 V_i(t),$$

with the initial conditions:

$$T(\theta) = T_0, \quad I(0) = 0, \quad V(\theta) = V_0, \quad \theta \in [-\tau, 0], \tag{5}$$

DISCUSSION

This study presents a mathematical model with two control variables, where the uninfected CD4+T cells follow the logistic growth function and the incidence term is saturated with free virions. We use the efficacy of drug therapies to block the infection of new cells and prevent the production of new free

virions. Our aim is to apply optimal control approach to maximize the concentration of uninfected CD4⁺T cells in the body by using minimum drug therapies. We establish the existence of an optimal control pair and use Pontryagin's principle to characterize the optimal levels of the two controls. The resulting optimality system is solved numerically to obtain the optimal control pair. Finally, we discuss the numerical simulation results which confirm the effectiveness of the model.

$$\frac{\partial v}{\partial y} = 0, \quad \dots\dots(06)$$

$$v_0 \frac{\partial u'}{\partial t} = v \frac{\partial^2 u'}{\partial y^2} - \left(\frac{\sigma B_0^2}{\rho} + \frac{v}{k} \right) u' + g\beta(T' - T_0) + g\beta'(C' - C_0), \quad \dots\dots(07)$$

$$v_0 \frac{\partial T'}{\partial t} = \frac{k_0}{\rho C_p} \frac{\partial}{\partial y} \left[1 + \alpha(T' - T_0) \frac{\partial T'}{\partial y} \right] - \frac{1}{\rho C_p} \frac{\partial q_r}{\partial y}, \quad \dots\dots (08)$$

$$v_0 \frac{\partial C'}{\partial t} = D \frac{\partial^2 C'}{\partial y^2} - R'(C' - C_0), \quad \dots\dots (09)$$

$$|a_k| \leq \frac{1}{2\pi} \oint_C \frac{|f(z)|}{|z|^{k+1}} |dz| \leq \frac{1}{2\pi} \oint_C \frac{M}{r^{k+1}} |dz| = \frac{M}{2\pi r^{k+1}} \oint_C |dz| = \frac{M}{2\pi r^{k+1}} 2\pi r = \frac{M}{r^k}, \quad \dots\dots(10)$$

Acquired immunodeficiency syndrome (AIDS) is caused by a virus known as human immunodeficiency virus (HIV). Since HIV emerged in 1981, several studies, including mathematical modeling, have been devoted to understand the transmission of the infection. HIV models can be classified into two categories: population-level models and within-host models.

One of the major havoc wrought by the HIV is the destruction of CD4⁺T cells which play a significant role in the regulation of the body immune system. HIV causes a decline in the number of functional CD4⁺T cells thereby reducing the competency of the body defense mechanism to fight cell infections. Several mathematical models have been formulated to study the interactions between HIV and CD4⁺T cells.

Although HIV is not yet curable, there are antiretroviral drugs that help in boosting the immune system against cell infections. These antiretroviral drugs are categorized into two groups which are reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs). RTIs disrupt the conversion of RNA of the virus to DNA so that new HIV infection of cells is prevented. On the other hand, PIs hinder the production of the virus particles by the actively infected CD4⁺T cells.

Although there is presently no known cure for HIV/AIDS, there are now available antiretroviral HIV drugs which block infection of new cells and reduce viral load in the body and so HIV positive individual can now enjoy relatively good health and increased life expectancy. Early diagnosis with immediate

commencement of the use of approved antiretroviral drugs before CD4⁺T cells levels fall below 350 cells/mm³, regardless of whether a person is showing signs of HIV or not, is highly advantageous. Most HIV/AIDS victims will have to take two or more drugs for the rest of their lives; however, antiretroviral HIV drugs also have side effects like any other drugs. In order to avoid or reduce these side effects, a rightful dose of an appropriate combination of these drugs is very essential. Therefore, it is important on the part of HIV positive individual to follow the antiretroviral treatment regimen.

CONCLUSION

Governments especially in developing countries should be more responsive in providing improved health system and antiretroviral drugs for their teeming populations suffering and dying unnecessarily because they could not afford the drugs. Educational awareness programmes are still very much needed to prevent and contain the spread and for the proper management of the disease.

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