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A mathematical model and simulation of HIV infection of $CD4^+$T cells with past and current history

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Abstract

We studied the behaviour of the $CD4^+$T cells using series solution method. We observed that when r, the rate at which T cells multiply through mitosis is sufficiently large, there is an increase in the growth of healthy $CD4^+$T cells. This showed that the healthy $CD4^+$T cells may never die out completely. The series solutions give the relationship between healthy and the infected $CD4^+$T cells over time. The results obtained showed that r plays a crucial role in the growth or decline of healthy $CD4^+$T cells.

Keywords: Kronecker product, braid group, Burau representation, irreducible.

1.0 Introduction

Acquire Immune deficiency Syndrome (AIDS) is a group of various illness that characterize a disease resulting from damage to the immune system caused by infection with human immunodeficiency virus (HIV). AIDS is caused by HIV. It enters a host by attacking a protein on its outer envelope to $CD4^+$T cells, a protein present on the surface of several types of immune system cells. Helper T cells ($CD4^+$ T cells) appear to be the main target of the virus. HIV decrease helper T cells and over mechanisms of cell death appear to be operative after infection of a $CD4^+$T cells with HIV (Field time causes a dramatic decrease in their numbers. When the helper T cells population is depressed, the ability to resist infection is severely impaired. This makes AIDS patient to be more susceptible to cancer and other opportunistic infections [1]. To the infected fellow, there is a gradual loss of immune cells called $CD4^+$T lymphocytes and immune function.

HIV is a deadly disease and so there is a need to control the spread of the disease. Many researchers studied the models of the spread of the disease. Among the researchers are mathematicians, medical scientists and biologists.

Tullis [2] presented mathematical model of the effect of affinity hemodialysis on the T-cell deplexion leading to AIDS. Kimbir [3] studied a two-sex model for HIV/AIDS transmission dynamic in a polygamous female dominant population. It was observed that a disease- free equilibrium state exists which is locally and asymptotically stable (LAS) if the parameter $R_0 < 1$. The author concluded that it is possible to eradicate HIV/AIDS in polygamous growing population. Garba and Gumel [4] used a deterministic model for assessing the impact of counseling, use of condom and treatment strategies on the transmission dynamics of HIV/AIDS in Nigeria. The results shows that whenever the associated reproduction number $R_0 < 1$, the disease free equilibrium is globally asymptotically stable (GAS).

Oluyo et al. [5] discussed mathematical analysis of the global dynamics of a model of HIV infection of CD_4^+ T-cells using Rene Descartes theory of solutions, it was shown that if the so called basic reproduction $R_0 < 1$, the infection will eventually die out but if $R_0>1$ then the infection will lead to full blow AIDS. Oluyo and Ayeni [6] discussed a mathematical model of virus neutralizing antibody response. It was shown that the spread of the disease can be controlled if the critical parameter $R = \dfrac{\delta \mathrm{B}^*}{\mu_0} < 1,$ where $\delta \mathrm{B}^*$ is the scale initial value of B cells and μ is the death rate of the virus.

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Wang and Li [7] discussed mathematical analysis of the global dynamics of the model for HIV infection of CD_4^+ T cells. Global dynamics of the model is rigorously established. In their model they showed that if the basic reproduction number $R_0 < 1$, the HIV infection is cleared from the T-cell population; If $R_0 > 1$, the HIV infection persists.

The result is similar to Oluyo [8] using contact tracing as a method of controlling the spread of HIV/AIDS and observed that contact tracing could be used to control the spread of the virus.

In this present work, we modified the work done by Wang and Li [7] by incorporating a memory term $(1+\beta V)$. The new term gives information about the past and current states of the disease.

2. Model Formulation

Our modified model is:

$$\left.\begin{aligned} \frac{dT}{dt} &= s-\alpha T-\frac{rTT^*}{T_{\max}}-\frac{kVT}{1+\beta V}+\gamma T^*, && T(0)=T_0 \\ \frac{dT^*}{dt} &= \frac{kVT}{1+\beta V}-\beta T^*-\gamma T^*, && T^*(0)=T_0^* \\ \frac{dV}{dt} &= N\beta T^*-\gamma V, && V(0)=V_0 \end{aligned}\right\} \qquad (2.1)$$

The term $1+\beta V$ is an additional to Wang and Li model of 2006 [7] and it accounts for the history of the disease.

Here, as in Odebiyi [9],

T = Concentration of the susceptible $CD4^+$Tcells

T^* = Concentration of the infected $CD4^+$Tcells by the HIV viruses

$T_{\max}$ = Maximum level of $CD4^+$Tcells concentration in the body

V = Free HIV viruses particles in the blood

α = natural turn-over rates of uninfected T cells

β = natural turn-over rates of infected T cells

γ = natural turn-over rates of virus particles

N = number of virus particles CD4+ infected cells produce during its life time

r = rate at which T cells multiply through mitosis

s = Constant production rate at which the body produces $CD4^+$T cells from precursor in the bone marrow and thymus

KVT = describe the incidence of the HIV infection of healthy $CD4^+$T cells where k>0 is the infection rate.

3. Method of Solution

3.1 Stabilility Analysis

We have to distinguish between two types of equilibrium of (2.1). The steady states of the system (2.1) satisfy the following algebraic system:

$$\left.\begin{aligned} s-\alpha T-\frac{rTT^*}{T_{\max}}-\frac{KVT}{1+\beta V}+\gamma T^* &= 0 \\ \frac{KVT}{1+\beta V}-\beta T^*-\gamma T^* &= 0 \\ N\beta T^*-\gamma V &= 0 \end{aligned}\right\} \qquad (3.1)$$

when $V=0,\ T^*=0$, we have the disease free equilibrium

$$p_1=(\bar{T},0,0)=\left(\frac{s}{\alpha},0,0\right)$$

and the endemic equilibrium i.e the infected equilibrium

$$p_2=(\tilde{T},\tilde{T}^*,\tilde{V})=(\phi,\ \phi_1,\ \phi_2),$$

where

$$\sigma=\frac{r}{T_{\max}},\ p=\frac{N\beta}{\gamma},\ \phi=\frac{\theta\pm\sqrt{\theta^2+4\varphi}}{2kp\sigma},\ \theta=(\beta+\gamma)(\sigma-\alpha p\beta)-kp\beta,\ \varphi=\beta(\beta+\gamma)(sp+1)$$

$$\phi_1=\frac{s-\alpha\phi}{\sigma\phi+\beta},\ \phi_2=\frac{p(s-\alpha\phi)}{\sigma\phi+\beta}$$

The Jacobian of (2.1) is

$$Df(T,T^*,V)=\begin{pmatrix}-\alpha-\frac{rT^*}{T_{\max}}-\frac{KV}{1+\beta V} & -\frac{rT}{T_{\max}}+\gamma & -\frac{KT}{(1+\beta V)^2}\\ \frac{KV}{1+\beta V} & -(\beta+\gamma) & \frac{KT}{(1+\beta V)^2}\\ 0 & N\beta & -\gamma\end{pmatrix} \tag{3.2}$$

The linearization of (2.1) at p_1 is

$$Df\left(\frac{s}{\alpha},0,0\right)=\begin{pmatrix}-\alpha & \tau & -\tau_1\\ 0 & -\tau_2 & \tau_1\\ 0 & N\beta & -\gamma\end{pmatrix}, \tag{3.3}$$

where

$$\tau=-\frac{rs}{\alpha T_{\max}}+\gamma,\ \tau_1=\frac{Ks}{\alpha},\ \tau_2=(\beta+\gamma)$$

with eigenvalues

$$\lambda_1=-\alpha,\qquad \lambda_2=\frac{-(\gamma+\tau_2)+\sqrt{(\gamma+\tau_2)^2-4(\gamma\tau_2-N\beta\tau_1)}}{2},$$
$$\lambda_3=\frac{-(\gamma+\tau_2)-\sqrt{(\gamma+\tau_2)^2-4(\gamma\tau_2-N\beta\tau_1)}}{2} \tag{3.4}$$

By definition, all the parameters are non-negative.

1. If $\gamma\tau_2>N\beta\tau_1$ and $(\gamma+\tau_2)^2-4(\gamma\tau_2-N\beta\tau_1)>0$ the eigenvalues are real, unequal and negative. Hence, the critical point $\left(\frac{s}{\alpha},0,\ 0\right)$ is an asymptotically stable improper node of the system.
2. If $(\gamma+\tau_2)^2-4(\gamma\tau_2-N\beta\tau_1)=0$ the eigenvalues are negative. Hence, the critical point $\left(\frac{s}{\alpha},0,\ 0\right)$ is globally asymptotically stable.
3. If $\gamma\tau_2>N\beta\tau_1$ and $(\gamma+\tau_2)^2-4(\gamma\tau_2-N\beta\tau_1)<0$ we have one negative root and two complex root whose real part are equal and negative. Hence, the critical point $\left(\frac{s}{\alpha},0,\ 0\right)$ is globally asymptotically stable.

The linearization of (2.1) at p_2 is

$$Df(\phi,\phi_1,\phi_2)=\begin{pmatrix}-\sigma_1 & \sigma_2 & -\sigma_3\\ \sigma_4 & -\tau_2 & \sigma_3\\ 0 & N\beta & -\gamma\end{pmatrix}, \tag{3.5}$$

where

$$\sigma_1 = \alpha + \frac{r\phi_1}{T_{\max}} + \frac{K\phi_2}{1+\beta\phi_2},\ \sigma_2 = -\frac{r\phi}{T_{\max}} + \gamma,\ \sigma_3 = \frac{K\phi}{(1+\beta\phi_2)^2},\ \sigma_4 = \frac{K\phi_2}{1+\beta\phi_2},\ \tau_2 = (\beta+\gamma)$$

Thus

$$|A - \lambda I| = 0$$

Implies

$$z(\lambda) = \lambda^3 + (\sigma_1 + \tau_2 + \gamma)\lambda^2 + (\sigma_1\tau_2 + (\sigma_1 + \tau_2)\gamma - \sigma_3 N\beta - \sigma_2\sigma_4)\lambda + ((\sigma_1\tau_2 - \sigma_2\sigma_4)\gamma + (\sigma_4 - \sigma_1)\sigma_3 N\beta) = 0 \quad (3.6)$$

It has been shown by Ayeni et al. [10] that (3.6) has three negative roots or one negative root and two complex roots. Hence, the critical point $(\phi,\ \phi_1,\ \phi_2)$ is globally asymptotically stable.

3.5 Analytical Solution

We first reduce the system (2.1) to origin by let

$$\left.\begin{aligned} x &= T - \phi \\ y &= T - \phi_1 \\ z &= V - \phi_2 \end{aligned}\right\}, \quad (3.7)$$

where $\phi,_1 \phi_2, \phi_3$ is the infected equilibrium.

and we obtain (neglecting non linear terms)

$$\left.\begin{aligned} \frac{dx}{dt} &= -\sigma_1 x + \sigma_2 y - \sigma_3 z \\ \frac{dy}{dt} &= \sigma_4 x - \tau_2 y + \sigma_3 z \\ \frac{dz}{dt} &= N\beta y - \gamma z \end{aligned}\right\}, \quad (3.8)$$

where

$\sigma_1, \sigma_2, \sigma_3, \sigma_4$ and τ_2 are as defined in (3.5)

Then we consider power series in the form

$$y_i = y_0 + a_i t + a_2 t^2 + ... + a_n t^n, \quad (3.9)$$

where

$a_1, a_2, ..., a_n,$ are all constant terms.

Let the solution of the system (3.8) be

$$\left.\begin{aligned} x(t) &= x_0 + a_1 t + a_2 t^2 + ... + a_n t^n \\ y(t) &= y_0 + b_1 t + b_2 t^2 + ... + b_n t^n \\ z(t) &= z_0 + c_1 t + c_2 t^2 + ... + c_n t^n \end{aligned}\right\} \quad (3.10)$$

where (x_0, y_0, z_0) is the infected equilibrium.

Let

$$\left.\begin{aligned} x_1(t) &= x_0 + a_1 t \\ y_1(t) &= y_0 + b_1 t \\ z_1(t) &= z_0 + c_1 t \end{aligned}\right\} \quad (3.11)$$

Then

$$\left.\begin{aligned} x_1^{\,1} &= a_1 \\ y_1^{\,1} &= b_1 \\ z_1^{1} &= c_1 \end{aligned}\right\} \tag{3.12}$$

Substituting (3.11) and (3.12) into (3.8) and neglecting higher order terms of t, we have

$$\left.\begin{aligned} a_1 &= -\sigma_1 x_0 + \sigma_2 y_0 - \sigma_3 z_0 \\ b_1 &= \sigma_4 x_0 - \tau_2 y_0 + \sigma_3 z_0 \\ c_1 &= N\beta y_0 - \gamma z_0 \end{aligned}\right\} \tag{3.13}$$

and (3.11) can be written as

$$\left.\begin{aligned} x_1(t) &= x_0 + (-\sigma_1 x_0 + \sigma_2 y_0 - \sigma_3 z_0)t \\ y_1(t) &= y_0 + (\sigma_4 x_0 - \tau_2 y_0 + \sigma_3 z_0)t \\ z_1(t) &= z_0 + (N\beta y_0 - \gamma z_0)t \end{aligned}\right\} \tag{3.14}$$

Let

$$\left.\begin{aligned} x_2(t) &= x_0 + a_1 t + a_2 t^2 \\ y_2(t) &= y_0 + b_1 t + b_2 t^2 \\ z_2(t) &= z_0 + c_1 t + c_2 t^2 \end{aligned}\right\} \tag{3.15}$$

and differentiating gives

$$\left.\begin{aligned} x_2^{\,1}(t) &= a_1 + 2a_2 t \\ y_2^{\,1}(t) &= b_1 + 2b_2 t^2 \\ z_2^{1}(t) &= c_1 + 2c_2 t^2 \end{aligned}\right\} \tag{3.16}$$

Substituting (3.15) and (3.16) into (3.8), neglecting higher order terms and equating coefficient of t, we obtain

$$\left.\begin{aligned} a_2 &= \frac{1}{2}(-\sigma_1 a_1 + \sigma_2 b_1 - \sigma_3 c_1) \\ b_2 &= \frac{1}{2}(\sigma_4 a_1 - \tau_2 b_1 + \sigma_3 c_1) \\ z_2(t) &= \frac{1}{2}(N\beta b_1 - \gamma c_1) \end{aligned}\right\} \tag{3.17}$$

Then we obtain the solution of (3.8) as

$$x(t) = x_0 + (-\sigma_1 x_0 + \sigma_2 y_0 - \sigma_3 z_0)t + \frac{1}{2}(-\sigma_1 a_1 + -\sigma_2 b_1 - \sigma_3 c_1)t^2 \tag{3.18}$$

$$y(t) = y_0 + (\sigma_4 x_0 - \tau_2 y_0 + \sigma_3 z_0)t + \frac{1}{2}(\sigma_4 a_1 - \tau_2 b_1 + \sigma_3 c_1)t^2 \tag{3.19}$$

$$z_1(t) = z_0 + (N\beta y_0 - \gamma z_0)t + \frac{1}{2}(N\beta b_1 - \gamma c_1)t^2 \tag{3.20}$$

4. Results and Discussion

We have obtained the equilibrium states of a mathematical model of HIV/AIDS and conducted a linear stability analysis. We have shown that when r increases and very large, $CD4^+T$ cells change from concave to convex; concave here implies that $CD4^+T$ cells will be zero after some time while convex curve implies that they will never be zero.

The graphs of healthy $CD4^+T$ cells x(t), infected cells y(t) and the virus z(t) are presented in Figures 1-7. Figure 1 displays the graph of healthy $CD4^+T$ cells x(t) against t for value of r =0.05. Figure 2 displays the graph of healthy $CD4^+T$ cells x(t) against t for value of r =10. From Figures 1-2 it is seen that $CD4^+T$ cells increases and later decreases with time(t). Figure 3 displays graph of healthy $CD4^+T$ cells x(t) against t for value of r =1000 and it is observed that $CD4^+T$ cells decreases and later increases with time (t). Figure 4 displays the graph of healthy $CD4^+T$ cells x(t) against t for different values of r. From Figure 4 it is seen that for r =0.05 and 10, $CD4^+T$ cells curve took a concave form while for r =1000 it took a convex form. Figure 5 displays the graph of healthy $CD4^+T$ cells x(t) and the infected cells y(t) against time for r =0.05. Figure 6 displays the graph of healthy $CD4^+T$ cells x(t), the infected cells y(t) and the virus z(t) against time(t) for r =0.05. Figure 7 displays the graph of healthy $CD4^+T$ cells x(t), the infected cells y(t) and the virus z(t) against time for r =1000.

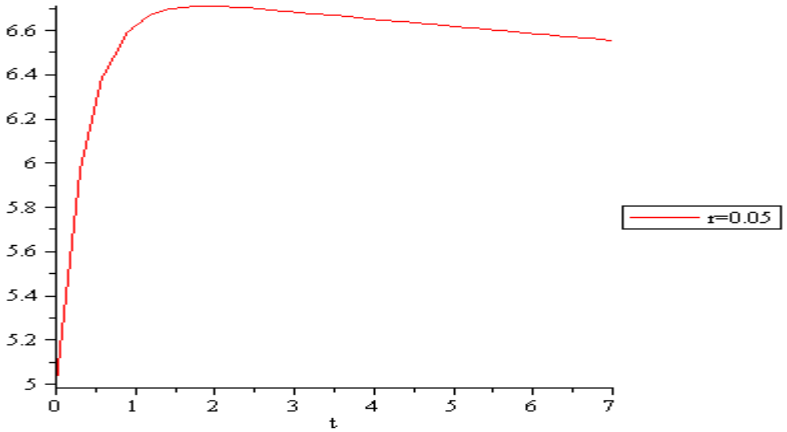

Figure 1: Graph of healthy CD4+T cells (x(t)) against time (t) for r=0.05 and $\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

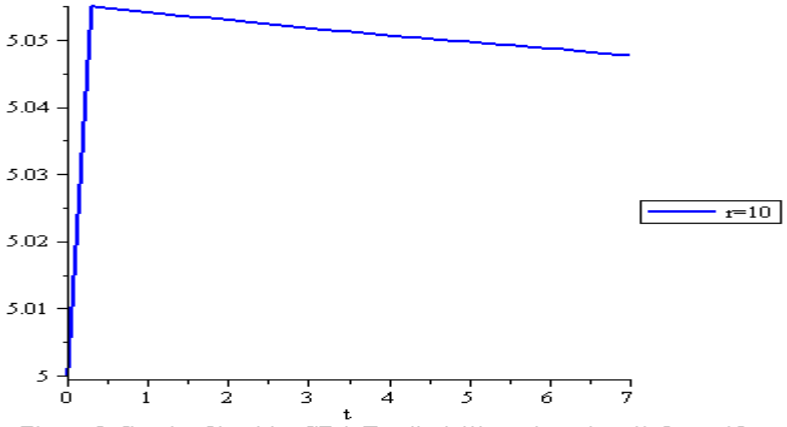

Figure 2: Graph of healthy CD4+T cells (x(t)) against time (t) for r=10 and $\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

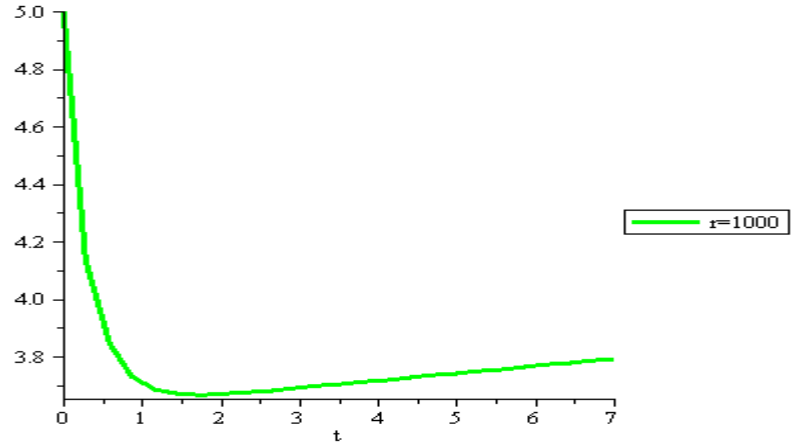

Figure 3: Graph of healthy CD4+T cells (x(t)) against time (t) for r=1000 and $\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

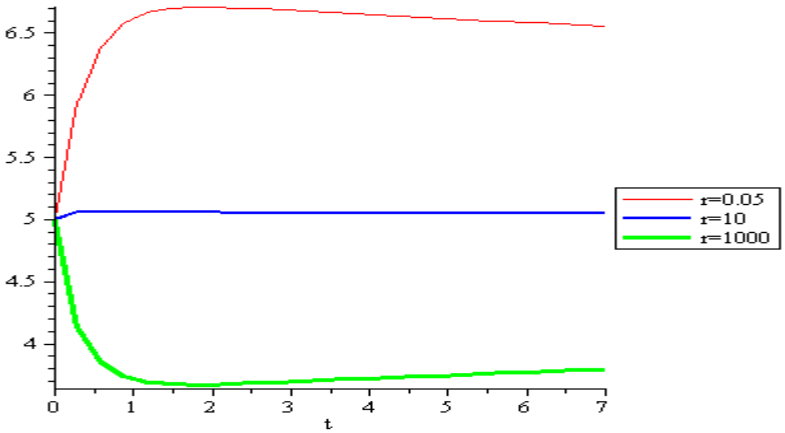

Figure 4: Graph of healthy CD4+T cells (x(t)) against time (t) for different values of r and
$\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

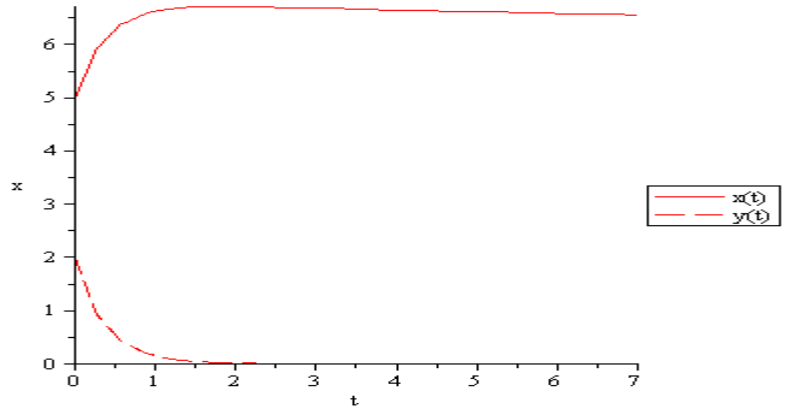

Figure 5: Graph of healthy CD4+T cells (x(t)) and infected cells (y(t)) against time (t) for r=0.05 and
$\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

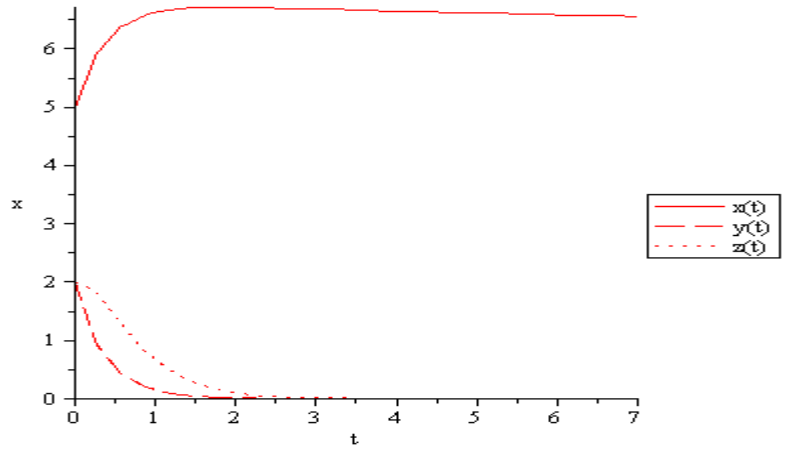

Figure 6: Graph of healthy CD4+T cells (x(t)), infected cells (y(t)) and virus (z(t)) against time (t) for r=0.05 and
$\alpha = 0.02,\ \beta = 0.,\ \gamma = 2.4,\ T_{max} = 1500,\ k = 0.0027,\ s = 0.1,\ N = 10$

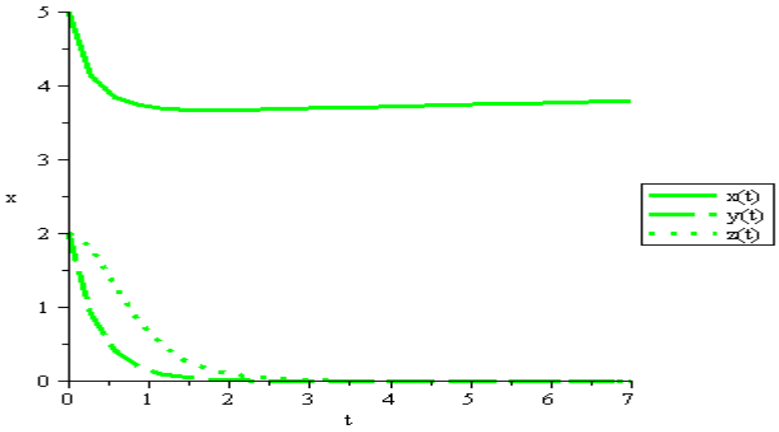

Figure 7: Graph of healthy CD4+T cells (x(t)), infected cells (y(t)) and virus (z(t)) against time (t) for r=1000 and
$\alpha = 0.02$, $\beta = 0.$, $\gamma = 2.4$, $T_{max} = 1500$, $k = 0.0027$, $s = 0.1$, $N = 10$

5.0 Conclusion

In this reseach work, we established the equilibrium states of a mathematical model of HIV/AIDS. The results shows that it is asymptotically stable under some conditions. We can conclude that the population pattern of the $CD4^+T$ cells can therefore be controlled. Also it is worth pointing out that r plays a very crucial role in the growth and decline of healthy $CD4^+T$ cells. Moreso, we observed from our graphs that as r is sufficiently large, $CD4^+T$ cells move from a concave graph to a convex graph such that an infected patient remains only HIV positive. $CD4^+T$ cells will never be zero.

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