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# Center manifold analysis and Hopf bifurcation of within-host virus model

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**Abstract** A mathematical model of a within-host viral infection is presented. A local stability analysis of the model is conducted in two ways. At first, the basic reproduction number of the system is calculated. It is shown that when the reproduction number falls below unity, the disease free equilibrium (DFE) is globally asymptotically stable, and when it exceeds unity, the DFE is unstable and there exists a unique infectious equilibrium which may or may not be stable. In the case of instability, there exists an asymptotically stable periodic solution. Secondly, an analysis of local center manifold shows that when $\mathfrak{R}_0 = 1$, a transcritical bifurcation occurs where upon increasing $\mathfrak{R}_0$ greater than one the DFE loses stability and a locally asymptotically positive infection equilibrium appears.

**Keywords.** Within-host virus model, Local and global stability, Center manifold, Reproduction number, Hopf Bifurcation.

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## 1. Introduction

The classical mathematical model of within-host virus infection [10],[8]:

$$\begin{cases} \dot{T}(t) &= f(T) - kVT, \\ \dot{T}^*(t) &= kVT - \beta T^*, \\ \dot{V}(t) &= N\beta T^* - \gamma V(-kVT), \end{cases} \tag{1.1}$$

is developed [11] to the following model:

$$\begin{cases} \dot{T}(t) &= f(T) - k_1VT - k_2TT^*, \\ \dot{T}^*(t) &= k_1VT + k_2TT^* - \beta T^*, \\ \dot{V}(t) &= N\beta T^* - \gamma V - k_3VT - k_4VT^*. \end{cases} \tag{1.2}$$

In the above model it is assumed that $f : \mathbb{R}_+ \to \mathbb{R}$ is a smooth function and satisfies the following condition:

$$\begin{aligned} &\exists T_0 \quad \texttt{s.t.} \quad f(T)(T - T_0) < 0, \forall T \neq T_0 \\ &\qquad \texttt{and} \quad f'(T) < 0, \quad \forall T \in [0, T_0], \end{aligned} \tag{1.3}$$

and it is proved that:
If $\mathfrak{R}_o < 1$, then, $E_0$, the only equilibrium of the system (1.2) is globally asymptotically stable; if $\mathfrak{R}_o > 1$, $E_0$, $\bar{E}$ are the only two equilibria of (1.2) and $E_0$ is unstable and $\bar{E}$ is locally asymptotically stable, and in the case $k_3 = 0$, it is proved that infectious equilibria is globally asymptotically stable, which $\mathfrak{R}_o$ is the reproduction number of the related system.
A similar study has been done in [3] for within-host viral infection with age-since-infection structured for infected cells and it has been again supposed that the homeostatically regulated growth rate of the uninfected cell population is given by the smooth function $f : \mathbb{R}_+ \to \mathbb{R}$, which is assumed to satisfy the following:

$$\begin{aligned} &\exists T_0 \quad \texttt{s.t.} \quad f(T)(T - T_0) < 0, \forall T \neq T_0 \\ &\qquad \texttt{and} \quad f'(T) < 0, \quad \forall T \neq T_0. \end{aligned} \tag{1.4}$$

Moreover to prove the global stability of the infection equilibrium it is imposed the following "sector" condition, first introduced in [5]:

$$(f(T) - f(\bar{T}))(1 - \frac{\bar{T}}{T}) \leq 0. \tag{1.5}$$

Yang et al. [17] studied the model in [3], with $f(T) = s - dT$, which satisfies in conditions (1.4) and (1.5), and Bedington-DeAngelies infection function. In the later study, the globally asymptotically stability of the infection equilibrium has been proved.
The question arises here is that how the dynamical behavior changes if the $f(t)$ is not satisfied at the above conditions. In this study, in section 2 we analyze the within-host virus model, system (2.1), which incorporates the reinfection of infected cells and

supposes that cells are produced naturally by logistic function.
After that, we first find the equilibrium points of the system (2.1) and then we study the stability or instability of them by defining suitable basic reproduction number. In section 3, we consider the center manifold of the system (2.1) for the basic reproduction number sufficiently near unity. Then, at section 4, we give some numerical results. Finally, we will have some remarks in section 5.

## 2. Basic reproduction number Analysis

Consider the following within-host virus model.

$$\begin{cases} \dot{T}(t) &= s + rT(1 - \frac{T}{\tilde{T}}) - kVT, \\ \dot{T}^*(t) &= kVT - \beta T^*, \\ \dot{V}(t) &= N\beta T^* - \gamma V - kVT - \delta VT^*, \end{cases} \tag{2.1}$$

where $T(t)$ is the number of susceptible cells, $T^*(t)$ is the number of infected cells and $V$ is the number of virus population. Also, $s$ represents the rate at which new $T$ cells are created from the sources within the body, such as thymus and $r = p - d$ and $\frac{r}{\tilde{T}} = \frac{p}{T_{max}}$, which $d$ is the death rate of $T$ cells and $p$ is the maximum proliferation rate and $T_{max}$ is the $T$ cell population density at which proliferation shouts off. Moreover, $k$ is the infection rate constant and $\beta$ is the $T^*$ cells death rate. Further, $N$ represents the total number of free virus particles released by each productively infected cell over its lifespan, and $\gamma$ is the clearence rate of viruses particles. Finally, $\delta$ represents the reinfection rate of $T^*$ by free viruses. $s, p, T_{max}, k, \beta, N, \gamma$ and $\delta$ are all positive constants.
System (2.1) always has unique disease free equilibrium $E_0 = (T_0, 0, 0)$, where

$$T_0 = \frac{\tilde{T}}{2} + \sqrt{\left(\frac{\tilde{T}}{2}\right)^2 + \frac{s\tilde{T}}{r}} \geq \tilde{T}, \tag{2.2}$$

with equality as $s = 0$.

**Proposition 2.1.** *Any solution,* $\big(T(t), T^*(t), V(t)\big)$ *of* (2.1) *with nonnegative initial condition will be nonnegative for all* $t > 0$*; moreover,* $T^*(0) + V(0) > 0$*, then the solution will be positive.*

*Proof.* It is easy to see that $T(t)$ is positive. If not, then we let $t_1 > 0$ be the first time such that $T(t_1) = 0$. By the first equation of the system (2.1), we have $\dot{T}(t_1) = s > 0$. That means, $T(t) < 0$ for $t \in (t_1 - \epsilon, t_1)$, where $\epsilon$ is arbitrarily small positive constant. This leads to a contradiction. Now, let $T^*(0) + V(0) > 0$ and $t_1 > 0$ be the first time such that $T^*(t_1) = 0$ or $V(t_1) = 0$. Without loss of generality let $T^*(t_1) = 0$. Then by the second equation of (2.1), we have $\dot{T}^*(t_1) = kT(t_1)V(t_1) > 0$, which again as before this leads to a contradiction. Similarly, the case $T^*(t_1) > 0$ or $V(t_1) = 0$ leads to a contradiction by third equation of (2.1). And the last case, $T^*(t_1) = 0$ and

$V(t_1) = 0$ are equivalent to $V(t) = T^*(t) = 0, \forall t \geq 0$ which contradict with initial condition. □

**Proposition 2.2.** *For any solution* $\Big(T(t), T^*(t), V(t)\Big)$ *of* (2.1)*, we have that:*

$$\limsup T(t)_{t\to\infty} \leq T_0 = \frac{\tilde{T}}{2} + \sqrt{\left(\frac{\tilde{T}}{2}\right)^2 + \frac{s\tilde{T}}{r}}.$$

*Proof.* Consider the following one dimensional system:

$$\dot{T}_1(t) = s + rT_1(1 - \frac{T_1}{\tilde{T}}).$$

$T_0$ is the only positive stable equilibrium point of it.

1 if $T_1(t_0) < T_0$, the right hand side of the above equation is positive, therefore $T_1(t_0)$ is increasing in positive direction.
2 if $T_1(t_0) > T_0$, the right hand side of the above equation is negative, therefore $T_1(t_0)$ is decreasing in positive direction.
Therefore: $\limsup_{t\to\infty} T_1(t) = T_0$.

Now from the non-negativity of the solutions of (2.1), we have the following inequality:

$$\dot{T}(t) \leq \dot{T}_1(t) \Rightarrow \limsup_{t\to\infty} T(t) \leq \limsup_{t\to\infty} T_1(t) = T_0$$

□

**Proposition 2.3.** *Solutions to* (2.1) *remain bounded in forward time.*

*Proof.* From proposition (2.2), $T(t)$ is bounded. It can be verified that $s+rT(1-\frac{T}{\tilde{T}}) \leq A - BT$ is true, where $A = \frac{T_0 r}{\tilde{T}}(2T_0 - \tilde{T})$ and $B = \frac{r}{\tilde{T}}(T_0 - \tilde{T})$. Now, from the first and second equations of (2.1), we have the following:

$$\frac{d(T + T^*)}{dt} \leq A - \alpha(T + T^*),$$

where, $\alpha = \min\{B, \beta\}$. Therefore, $\limsup_{t\to\infty}(T + T^*) \leq \frac{A}{\alpha}$. This proves the boundedness of $T$ and $T^*$. Let $C$ be a bound for $T^*$, then from the third equation of (2.1), we have $\frac{dV}{dt} \leq NC - \gamma V$ and $\limsup_{t\to\infty} V \leq \frac{NC}{\gamma}$. □

The Jacobian matrix of (2.1) at $E_0$ is as follows:

$$J(E_0) = \begin{bmatrix} r - \frac{2rT_0}{\tilde{T}} & 0 & -kT_0 \\ 0 & -\beta & kT_0 \\ 0 & N\beta & -\gamma - kT_0 \end{bmatrix}. \tag{2.3}$$

The basic reproduction number, $\mathfrak{R}_o$, is "the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual"

[1], [6]. The basic reproduction number can not be determined from the structure of the mathematical model alone, but depend on the definition of the infected and uninfected compartments. A more general basic reproduction number is defined as the number of new infections produced by a typical infective individual in a population at a DFE [14]. Following the definitions in [14], the basic reproduction number is defined as follows:

$$\rho(FV^{-1}),$$

where $\rho(A)$ denotes the spectral radius of a matrix $A$. Now, let $T^*$, $V$ be the infected and $T$ be the uninfected compartments of the system (2.1). Then,

$$F = \begin{bmatrix} 0 & kT_0 \\ N\beta & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} \beta & 0 \\ 0 & \gamma + kT_0 \end{bmatrix}, \qquad \mathfrak{R}_0 = \sqrt{\frac{NkT_0}{\gamma + kT_0}}. \tag{2.4}$$

For convenience in computation, whitout loss of generality we may drop the square root of reproduction number.

**Lemma 2.4.** (i) $\mathfrak{R}_0 > 1$, *then* $N > 1$.

(ii) $s > 0$, $\mathfrak{R}_0 > 1$ *is equivalent to* $\dfrac{(N-1)k\tilde{T}s}{(T_0 - \tilde{T})r\gamma} > 1$.

*Proof.* (i) $\mathfrak{R}_0 > 1 \Rightarrow (N-1)kT_0 > \gamma > 0 \Rightarrow N > 1$.

(ii) Let $s > 0$.

$$\mathfrak{R}_0 > 1 \Leftrightarrow \frac{(N-1)kT_0}{\gamma} > 1$$

$$\Leftrightarrow \frac{(N-1)k\tilde{T}s}{(T_0 - \tilde{T})r\gamma} > 1,$$

where the later inequality follows from (2.2). □

One of the eigenvalue of $J(E_0)$ is given by $\lambda_1 = r(1 - \dfrac{2T_0}{\tilde{T}}) < 0$ and the remaining two are:

$$\lambda_2 = \frac{-(\beta + \gamma + kT_0) - \sqrt{(\beta + \gamma + kT_0)^2 - 4\beta\left((\gamma + kT_0) - NkT_0\right)}}{2}, \tag{2.5}$$

and

$$\lambda_3 = \frac{-(\beta + \gamma + kT_0) + \sqrt{(\beta + \gamma + kT_0)^2 - 4\beta\left((\gamma + kT_0) - NkT_0\right)}}{2}. \tag{2.6}$$

**Theorem 2.5.** *When* $\mathfrak{R}_0 < 1$, *then* $E_0$ *is locally asymptotically stable and if* $\mathfrak{R}_0 > 1$, $E_0$ *is unstable.*

*Proof.* $\mathfrak{R}_0 < 1 \Rightarrow 0 < (\gamma + kT_0) - NkT_0 \Rightarrow \mathbf{Re}(\lambda_2) < 0$ and $\mathbf{Re}(\lambda_3) < 0$, so $E_0$ is locally asymptotically stable. On the contrary, if $\mathfrak{R}_0 > 1$ then $\lambda_3 > 0$ and $E_0$ is unstable. □

**Theorem 2.6.** *When* $\mathfrak{R}_0 < 1$, *then the infection free equilibrium,* $E_0$, *is globally asymptotically stable.*

*Proof.* We show that $E_0$ attracts nonnegative solutions of (2.1). From the proposition (2.2), we have $T(t) \leq T_0$. It follows that for any given $\epsilon$, there exists some $t_o$ such that $\limsup_{t\to\infty} T(t) \leq T_0 + \epsilon, t_0 \leq t$.
We now Define a Lyapunov function as follows:

$$L\Big((T, T^*, V)\Big) = NT^* + V.$$

Since $\mathfrak{R}_0 = \dfrac{NkT_0}{\gamma + kT_0} < 1$, we can select $\epsilon$ small enough such that $(N-1)k(T_0+\epsilon)-\gamma \leq 0$. By calculating the time derivative along the solution of system (2.1), we have:

1 If $N \leq 1$,

$$\frac{dL}{dt} = \Big[(N-1)kT - \gamma - \gamma T^*\Big]V \leq 0,$$

with the equality if and only if $V = 0$.

2 If $N > 1$, but small enough such that $\mathfrak{R}_0 = \dfrac{NkT_0}{\gamma + kT_0} < 1$, we can select $\epsilon$ small enough such that $(N-1)k(T_0+\epsilon) - \gamma \leq 0$. In this case:

$$\frac{dL}{dt} = \Big[(N-1)kT - \gamma\Big]V - \gamma T^* V \leq \Big[(N-1)k(T_0+\epsilon) - \gamma\Big]V \leq 0,$$

and $dL/dt = 0$ if and only if $V = 0$. The largest compact invariant set in $[(T, T^*, V), dL/dt = 0]$ is the singlton $\{E_0\}$. Therefore, by the Lasalle-Lyapunov theorem [16], every nonnegative solution of (2.1) approaches $E_0$ as $t \to \infty$. □

FIGURE 1. A numerical solution of system (2.1) tends to the infection free equilibrium, $E_0$, as time tends to infinity, where parameters value are $[s, p, d, T_{\max}, k, \beta, N, \gamma, \delta] = [50, 0.009, 0.008, 6000, 0.0000005, 0.8, 5000, 3, 0.00001]$. In this case $T_0 = 6246.8$, $\mathfrak{R}_0 = 0.6245$. (A) Time series of $T$, $T^*$ and $V$. (B) An orbit in the $TT^*V$ space.

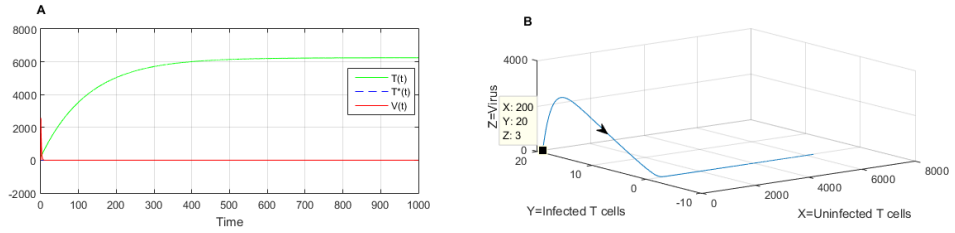


FIGURE 2. A numerical solution of system (2.1) tends to the infection equilibrium $\bar{E}$, as time tends to infinity, where parameters value are $[s, p, d, T_{\max}, k, \beta, N, \gamma, \delta] = [50, 0.0001, 0.008, 6000, 0.0000005, 0.8, 2000, 10, 0.00001]$. In this case $T_0 = 6116.5$, $\Re_0 = 5.0919$, $\bar{E} = 1.0e+04 \times [0.1200, 0.0061, 8.1698]$. (A) Time series of $T$, $T^*$ and $V$. (B) An orbit in the $TT^*V$ space.

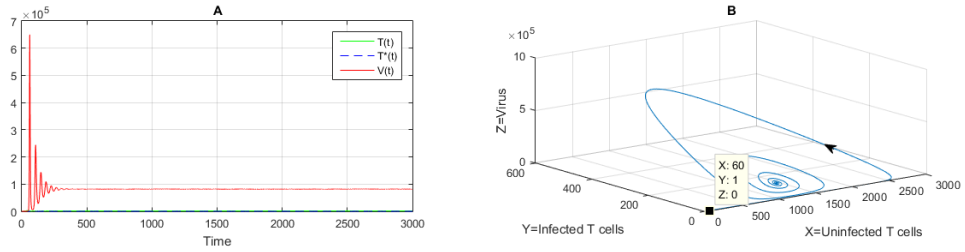
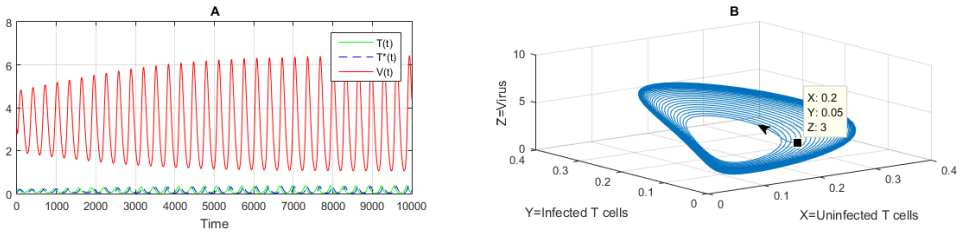



FIGURE 3. A numerical solution of system (2.1) tends to the limit cycle, as time tends to infinity, and $\bar{E}$ is unstable, where parameters value are $[s, p, d, T_{\max}, k, \beta, N, \gamma, \delta] = [0.00001, 0.03290, 0.00005, 4.6208225, 0.01, 0.0351, 37.0370, 0.03, 0.1]$. In this case $T_0 = 4.6141$, $\Re_0 = 22.4442$, $\bar{E} = [0.1116, 0.1022, 3.2145]$. (A) Time series of $T$, $T^*$ and $V$. (B) An orbit in the $TT^*V$ space.



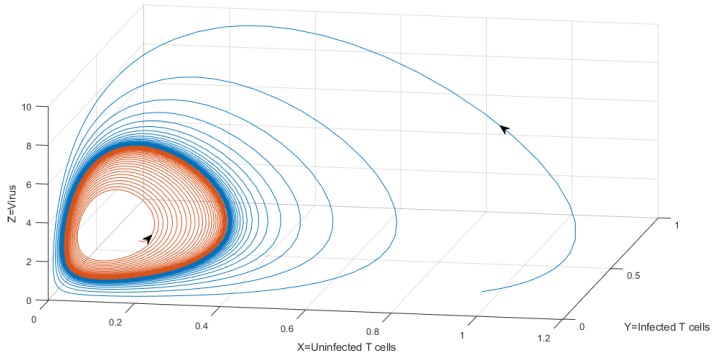

## 3. CENTER MANIFOLD ANALYSIS AT THE CRITICAL CASE $\Re_0 = 1$

Let $\mu$ be a bifurcation parameter and $x_0$ is a DFE for all value of $\mu$ such that $\Re_0 < 1$ for $\mu < 0$ and $\Re_0 > 1$ for $\mu > 0$. Consider,

$$\dot{x} = f(x, \mu), \tag{3.1}$$

where $f$ is satisfied the conditions $(A_1) - (A_5)$ in [14] and [2] are continuously differentiable at least twice in both $x$ and $\mu$. The results of center manifold theory [16] and [[14],Theorem 4] show that if the zero eigenvalue of $D_x f(x, \mu)$ be simple, then there exists $\delta > 0$ such that:

FIGURE 4. Numerical solutions of system (2.1) with different initial points, tends to the stable limit cycle, as time tends to infinity, and $\bar{E}$ is unstable, where parameters value are the same as Figure 3.




(i) if $a < 0$, then there are locally asymptotically stable endemic equilibria near $x_0$ for $0 < \mu < \delta$.

(ii) if $a > 0$, then there are unstable endemic equilibria near $x_0$ for $-\delta < \mu < 0$,

where,

$$a = \frac{v}{2} D_{xx} f(x_0, 0) w^2 = \frac{1}{2} \sum_{i,j,k=1}^{n} v_i w_j w_k \frac{\partial^2 f_i}{\partial x_j \partial x_k}(x_0, 0), \tag{3.2}$$

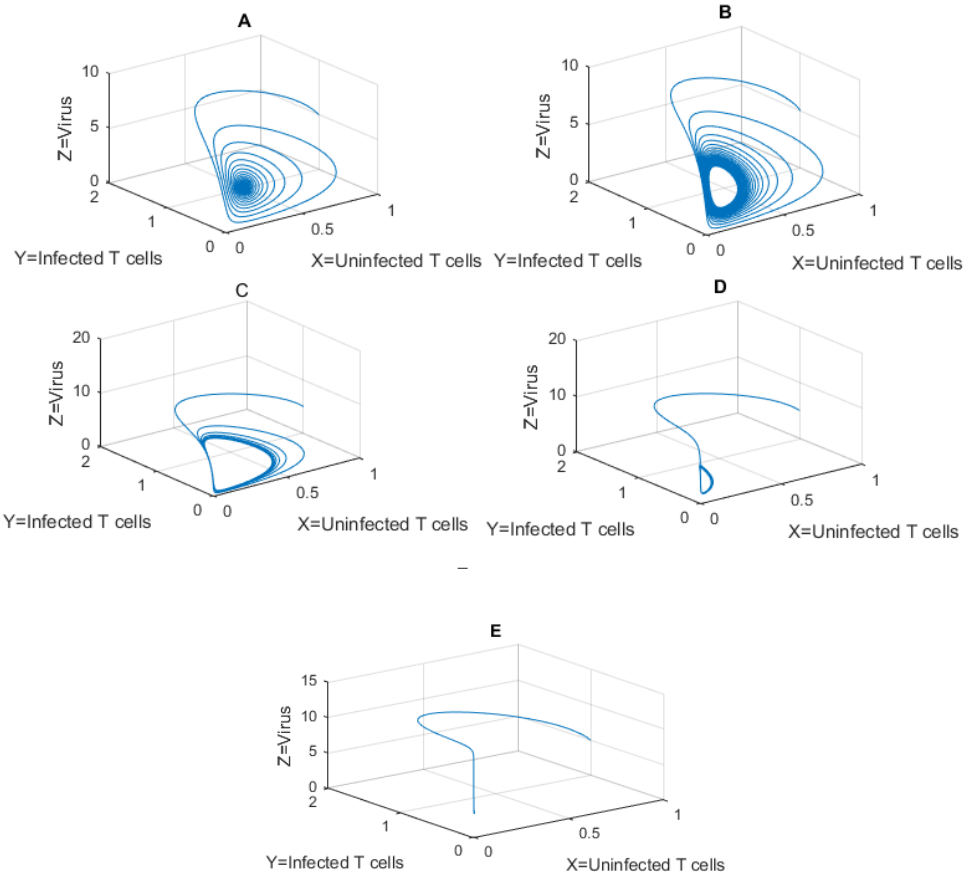
that, $v$ and $w$ are the left and right nullvectors of $D_x f(x_0, 0)$ respectively that $vw = 1$. It should be noted that if $a$ is negative, then a branch of super-threshold endemic equilibria exists, and the bifurcation is supercritical. If $a > 0$, then there are unstable sub-threshold endemic equilibria, and the bifurcation is subcritical. In the Lemma 3 [14] it is proved that:

$$a = \frac{1}{2} \sum_{i=1}^{n} v_i \left( \sum_{j,k=1}^{m} w_j w_k \frac{\partial^2 f_i}{\partial x_j \partial x_k} + 2 \sum_{j=1}^{m} \sum_{k=m+1}^{n} w_j w_l \frac{\partial^2 f_i}{\partial x_j \partial x_l} \right) \Bigg|_{(x_0,0)}, \tag{3.3}$$

where $1, \ldots, m$ corresponds to the infected compartments.

It can be easily verified that the system (2.1) satisfies at the condition $(A_1) - (A_5)$ in [14]. Also, from (2.5) and (2.6), the zero eigenvalue of Jacobian matrix at $E_0$ is simple when $\mathfrak{R}_0 = 1$. So, the result of theorem 4 [14] can be applied. By applying the relation (3.3) to the system (2.1) at the $E_0$ with supposition that $T^*$ and $V$ are infected compartments, consider:

FIGURE 5. Different patterns of system (2.1) behavior. In this figures, except $\gamma$ the rest parameters are the same as Figure 3, and in all cases $T_0 = 4.6141$. (A) $\gamma = 0.05$, $\Re_0 = 17.7752$, eigenvalues $\bar{E} = -0.1038 + 0.0000i, -0.0006 - 0.0233i, -0.0006 + 0.0233i$, (B) $\gamma = .035$, $\Re_0 = 21.0612$, eigenvalues $\bar{E} = -0.0844 + 0.0000i, 0.0001 - 0.0217i, 0.0001 + 0.0217i$, (C) $\gamma = 0.015$, $\Re_0 = 27.9506$, eigenvalues $\bar{E} = -0.0582 + 0.0000i, 0.0009 - 0.0172i, 0.0009 + 0.0172i$, (D) $\gamma = 0.005$, $\Re_0 = 33.4159$, eigenvalues $\bar{E} = -0.0439 + 0.0000i, 0.0006 - 0.0116i, 0.0006 + 0.0116i$, (E) $\gamma = 0.001$, $\Re_0 = 36.2513$ eigenvalues $\bar{E} = -0.0372 + 0.0000i, -0.0010 - 0.0058i, -0.0010 + 0.0058i$.



$$w = \frac{1}{\sqrt{\left(\frac{k\tilde{T}T_0}{r\tilde{T}-2rT_0}\right)^2+\left(\frac{kT_0}{\beta}\right)^2+1}}\begin{bmatrix}\frac{k\tilde{T}T_0}{r\tilde{T}-2rT_0}\\ \frac{kT_0}{\beta}\\ 1\end{bmatrix},$$

$$v = \frac{1}{\sqrt{N^2+1}}\begin{bmatrix}0\\ N\\ 1\end{bmatrix},$$

as right and left nullvectors to the Jacobian matrix at $E_0$. Then

$$\begin{aligned}
a &= v_1w_3w_1\frac{\partial^2 f_1}{\partial V\partial T}+v_2w_3w_1\frac{\partial^2 f_2}{\partial V\partial T}+v_3w_3w_2\frac{\partial^2 f_3}{\partial V\partial T^*}+v_3w_3w_1\frac{\partial^2 f_3}{\partial V\partial T}\\
&= v_1w_3w_1(-k)+v_2w_3w_1(k)+v_3w_3w_2(-\delta)+v_3w_3w_1(-k)\\
&= w_3\Big(v_2w_1k-v_3w_2\delta-v_3w_1k\Big)\\
&= w_3v_3\Big(Nw_1k-w_2\delta-w_1k\Big)\\
&= w_3w_1v_3\Big(Nk+r\delta\frac{2\frac{T_0}{\tilde{T}}-1}{\beta}-k\Big).
\end{aligned}$$

From (2.2), $w_1<0$, and from $\mathfrak{R}_0=1$ and that $r$ and $\tilde{T}$ have the same sign, we have:

$$(N-1)k+\frac{r\delta}{\beta}\Big(2\frac{T_0}{\tilde{T}}-1\Big)=\frac{\gamma}{T_0}+\frac{r\delta}{\beta}\Big(2\frac{T_0}{\tilde{T}}-1\Big)>0. \tag{3.4}$$

Therefore $a<0$. Hence, by the theorem 4 [14], the DFE is locally asymptotically stable if $\mathfrak{R}_0$ is slightly less than one (i.e., $\mu<0$), and if $\mathfrak{R}_0$ is slightly greater than one then the DFE is unstable and there is a locally asymptotically stable positive equilibrium near the DFE. In this case, a branch of super-threshold endemic equilibria exists, and the bifurcation is super-critical. This case is often referred to forward bifurcation. Backward bifurcation has been studied for HIV model [7], [15], SIS model [2] and for tuberculosis [4], but in our model from the above analysis backward bifurcation does not occur.

Now Let $\mathfrak{R}_0>1$, and $\bar{E}=(\bar{T},\bar{T}^*,\bar{V})$ be the infectious equilibrium. From (2.1) we have:

$$\begin{cases}
s+r\bar{T}(1-\frac{\bar{T}}{\tilde{T}})-k\bar{V}\bar{T}=0,\\
k\bar{V}\bar{T}-\beta\bar{T}^*=0,\\
N\beta\bar{T}^*-\gamma\bar{V}-k\bar{V}\bar{T}-\delta\bar{V}\bar{T}^*=0.
\end{cases}$$

Using the second equation to third equation we have the following system:

$$\begin{cases} s + r\bar{T}(1 - \frac{\bar{T}}{\tilde{T}}) = k\bar{V}\bar{T}, \\ \bar{T}^* = \frac{k\bar{V}\bar{T}}{\beta}, \\ N\beta\Big(\frac{k\bar{V}\bar{T}}{\beta}\Big) - \gamma\bar{V} - k\bar{V}\bar{T} - \delta\bar{V}\Big(\frac{k\bar{V}\bar{T}}{\beta}\Big) = 0. \end{cases} \tag{3.5}$$

Simplifying the third equation and using the first equation into the third equation, the next follows:

$$\begin{aligned} & Nk\bar{T} - \gamma - k\bar{T} - \delta\Big(\frac{k\bar{V}\bar{T}}{\beta}\Big) = 0, \\ & \Rightarrow Nk\bar{T} - \gamma - k\bar{T} - \frac{\delta}{\beta}\Big(s + r\bar{T}(1 - \frac{\bar{T}}{\tilde{T}})\Big) = 0, \\ & \Rightarrow \Big( - \gamma\beta - \delta s\Big) + \Big((N-1)k\beta - \delta r\Big)\bar{T} + \frac{\delta r}{\tilde{T}}\bar{T}^2 = 0. \end{aligned}$$

The only positive root of the later quadratic equation is as follows:

$$\begin{aligned} \bar{T} &= \frac{(1-N)k\beta\tilde{T} + \delta r\tilde{T} + \tilde{T}\sqrt{\Delta}}{2\delta r}, \\ \Delta &= \Big((1-N)k\beta + \delta r\Big)^2 + 4\Big(\gamma\beta + \delta s\Big)(\frac{\delta r}{\tilde{T}}), \end{aligned} \tag{3.6}$$

and corresponding $\bar{T}^*$ and $\bar{V}$ are calculated from the first and second equations of (3.5).

Now let study local stability of the $\bar{E}$. The Jacobian matrix of system (2.1) at $\bar{E}$ is as follows:

$$J(\bar{E}) = \begin{bmatrix} r - \frac{2r\bar{T}}{\tilde{T}} - k\bar{V} & 0 & -k\bar{T} \\ k\bar{V} & -\beta & k\bar{T} \\ -k\bar{V} & N\beta - \delta\bar{V} & -\gamma - k\bar{T} - \delta\bar{T}^* \end{bmatrix}. \tag{3.7}$$

Now we obtain the characteristic equation of linearized system of (2.1) at $\bar{E}$:

$$A_{\bar{E}}(\lambda) = \lambda^3 + \alpha_1\lambda^2 + \alpha_2\lambda + \alpha_3,$$

where,

$$\alpha_1 = (\frac{r\bar{T}}{\tilde{T}} + \frac{s}{\bar{T}}) + (\beta + \gamma + k\bar{T} + \delta\bar{T}^*) > 0,$$
$$\alpha_2 = (\frac{r\bar{T}}{\tilde{T}} + \frac{s}{\bar{T}})(\beta + \gamma + k\bar{T} + \delta\bar{T}^*) + \delta k\bar{T}\bar{V} - N\beta k\bar{T}\bar{V}$$
$$+ (\beta\gamma + k\beta\bar{T} + \delta k\bar{T}\bar{V}) - k^2\bar{T}\bar{V},$$
$$\alpha_3 = (\frac{r\bar{T}}{\tilde{T}} + \frac{s}{\bar{T}})\Big[\delta k\bar{T}\bar{V} - N\beta k\bar{T}\bar{V} + \beta(\gamma + k\bar{T} + \delta\bar{T}^*)\Big]$$
$$+ k\beta\bar{V}\bar{T}\Big((N-1)k - \frac{\delta k\bar{V}}{\beta}\Big).$$

It is not easy to find rigorously local stability condition of $\bar{E}$. By Center manifold analysis in section 3, we showed that when $\mathfrak{R}_0 > 1$ is sufficiently close to 1, the infection equilibrium is asymptoticaly stable. By Routh-Horwitz criterion,

$$\alpha_1 > 0, \alpha_2 > 0, \alpha_3 > 0, \text{and } \alpha_1\alpha_2 - \alpha_3 > 0, \tag{3.8}$$

if and only if the infectious equilibrium is asymptoticaly stable [12].

The next theorem states necessary and sufficient condition for finding Hopf critical point without finding the eigenvalues and its proof can be found in [18].

**Theorem 3.1.** *For $x \in \mathcal{R}^n, \mu \in \mathbb{R}$, and $f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n$, assume that the general nonlinear ordinary differential system*

$$\dot{x} = f(x, \mu)$$

*has a locally asymptotically stable equilibrium. The necessray and sufficient condition for finding Hopf bifurcation to occur from the equilibrium is*

$$\Delta_{n-1} = 0,$$

*with $\alpha_n$ and $\Delta_i > 0$, where $1 \le i \le n-2$. For $x \in \mathbb{R}^3$ it is equivalent to $\Delta_1 = \alpha_1 > 0$, and $\Delta_2 = \alpha_1\alpha_2 - \alpha_3 = 0$, where $\alpha_1, \alpha_2$ and $\alpha_3$ are defined above.*

## 4. Numerical results

In this section, we implement numerical simulations to testify the theoretical results in previous sections. The parameter values for some infectious models in literatures are listed in Table 1. In order to check our computation in this paper, we choose arbitrary values for some parameters in some cases. In Figure 1, $\mathfrak{R}_0 < 1$, and DFE is globally asymptotically stable. When $\mathfrak{R}_0 > 1$, there exists an infectious equilibrium which is locally asymptotically stable, Figure 2, if and only if (3.8) is satisfied, otherwise it is unstable and there exists an asymptotically stable limit cycle, Figures 3 and 4. Figure (5) shows that when $1 < \mathfrak{R}_0$, is small enough or large enough, the infectious equilibrium is locally asymptotically stable.

TABLE 1. Parameter definition and values from literatures.

| Parameter | Value | Description | Reference |
|---|---|---|---|
| $s$ | 50 cells ml day$^{-1}$ | Recruiment rate of uninfected cells | [13] |
| $p$ | Varied | Maximum proliferation rate | See text |
| $d$ | 0.008 day$^{-1}$ | Death rate of uninfected cells | [13] |
| $Tmax$ | Varied | Density of $T$ cell at which proliferation shouts off | See text |
| $k$ | $5 \times 10^{-7}$ ml virion day$^{-1}$ | Infection rate of target cells by virus | [13] |
| $\beta$ | 0.8 day$^{-1}$ | Death rate of infected cells | [19] |
| N | Varied | Burst size of virus | See text |
| $\gamma$ | 3 day$^{-1}$ | Clearance rate of free virus | [9] |
| $\delta$ | Varied | Reinfection rate of infected cells | See text |

## 5. Concluding remarks

In this paper, a class of viral infection model with logistic function as production rate of uninfected cells, also introducing reinfection of infected cells are considered. Then, a detailed analysis on the local asymptotic stability of the equilibria of the viral infection model is carried out. It is shown that, if $\mathfrak{R}_0 < 1$, then there exits unique infection free equilibrium which is globally asymptotically stable, and when $\mathfrak{R}_0 = 1$, it is critical point. In this case also, by center manifold analysis we have shown that infection free equilibrium is asymptotically stable. While $\mathfrak{R}_0 > 1$, different patterns of system behavior are observed. In this case, there are two equilibria, the DFE which is unstable and the infectious equilibrium. When $\mathfrak{R}_0$ crossing unity, a transcritical bifurcation is occurred. The DFE become unstable and the infectious equilibria engenders. When $\mathfrak{R}_0$ is sufficiently close to unity, the later equilibria is stable and by increasing $\mathfrak{R}_0$, a forward Hopf bifurcation may occurs. In this case, by increasing more in $\mathfrak{R}_0$, a backward hopf bifurcation occures and infectious equilibria become stable. In this case, infectious equilibrium become unstable and a stable limit cycle engenders.

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