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# Partial Differential Equations of A Virus Dynamical Model

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## Abstract

In this work, we investiguate a reaction-diffusion model with homogeneous Neumann boundary conditions of virus transmission. The model that we study in work is a generalization of the model developed by Zhang, et al.; in other words, we are trying to understand the influence of diffusion on virus dynamics. We prove global existence, uniqueness, positivity and boundness of the solution using a variational theory and some other useful tools from functional analysis. From the characteristic equation, we derive the local stability of the equilibriums. Moreover, the global asymptotical properties of the free-virus equilibrium and the endemic equilibruims of the model are studied by constructsing of a suitable Lyapunov functions. Finally, numerical simulations are performed to support the theoretical results obtained. Our numerical results indicate that the introduction of the diffusion in the model does not suppressthe dynamics of the virus, one obtains globally the configurations that in the absence of thediffusion. However, the mathematical analysis becomes more complicated.

## Keywords

Cell-to-cell transmission, Stability, Reaction-diffusion virus, Model

## 1. Introduction

Viral diseases have been known for millennia. Already under the Babylonians, it was known that rabies is transmitted by the bite of the rabid dog. Smallpox, a disease causing high mortality, has accompanied humans foralong time and has been found on mummies in Egypt.

In 1884, the development of the Chamberland Candles [1], which eliminated bacteria from a solution, represented the first step in the discoveryof viruses. Adolf Mayer (1843-1942) described in detail a disease of tobacco plants which he called tobacco mosaic. He realizes that the disease isinfectious because it can be transmitted by what he believes to be bacteria.

The tobacco mosaic virus (TMV/VMT) will remain an importantmodel in all fundamental virus studies. In 1935, Wendell Stanley succeeded in crystallizing the tobacco mosaic virus (TMV/VMT), which allowed its chemicalanalysis and the following year Bawden and Pirie described astructure combining proteins and ribonucleic acid. The first human virus,the agent of yellow fever, was identified in 1901 by Walter Reed, James Carroll and Jesse Lazear. Another example is the Ebola virus, which causes Ebola hemorrhagic fever with a mortality rate from 50% to 90%.

Currently, new viruses continue to be discovered, such as the hepatitis C virus in 1989, the Nipah virus in 1999 (respiratory infection in pigs andencephalitis in humans), Metapneumovirus in 2001, the SARS virus (severeacute respiratory syndrome) in 2003.

There exists in the literature, several mathematical models using ordinary differential equations (ODEs), delay

differential equations (DDEs) and partial differential equations (PDEs), have been developed to help understand the dynamics the mechanisms and dynamics of within-host viralinfections (see [2, 3, 4, 5, 6]).

There have been many advances in the understanding of infections ofcells by viruses, one can quote on this subject the work of Spouge and al forthe transmission of virus to cell to cell via virological synapses ( cf [10]). In Zhang et al. [11], they have developed the following model of viral transmissionbased on ODE with two different types of infection and a cure rate:

$$(1)\begin{cases}\dfrac{\partial H}{\partial t} = \Lambda - dH - (\beta I + \alpha V)H + \rho\, I \\ \dfrac{\partial I}{\partial t} = (\beta I + \alpha V)H - (a + \rho)\, I \\ \dfrac{\partial V}{\partial t} = kI - uV\end{cases}$$

where $H$; $I$ and $V$ represent the concentrations of uninfected cells,infected cells, and free virus respectively. $\pi$ is the regeneration rate of uninfected cells, $d$; $a$ and $u$ are the death rates of three kinds of cellsrepresentsthe curate, $kI$ is the rate at which infected cells produce free viruses. $(\beta I + \alpha V)H$ represents the total infection rate of host cells, which is divided into two parts $\beta IH$ and $\alpha VH$. The former represents the part whereinfected cells infect host cells by direct contact, and the lattermeans that host cells are infected by the free virus. Using a Lyapunov functions, the authors have establihed the local andglobal stability of the points of equilibrium.

In the basic mathematical model proposed by Zhang et al. [11], as well as in the other models which resulted fromthis work (cf [12]), thespatial mobility of cells and viruses is ignored. Taking spatial movementinto account inmany biological phenomena is no longer to be justifed, asevidenced by the work of Funk et al. [13] on the study of virus-immunespatial dynamics, reaction-diffusion models of the hepatitis B (see [14]). Motivated by the work of Zhang et al., we introduce diffusion into their model and analyze the impact ofspatial mobility on equilibrium states. More precisely, we are interested in the following model:

$$(2)\begin{cases}\dfrac{\partial H}{\partial t} = \Lambda - dH - (\beta I + \alpha V)H + \rho\, I \\ \dfrac{\partial I}{\partial t} = (\beta I + \alpha V)H - (a + \rho)\, I \\ \dfrac{\partial V}{\partial t} = d_V\, \Delta V + kI - uV\end{cases}$$

with homogeneous Neumann boundary conditions

$$(3)\ \frac{\partial V}{\partial \eta} = 0 \ \text{ on } \ \Omega \text{ x } (0, \ \infty)$$

and initial conditions

$$(4)\quad H(x,0) = H_0, \qquad I(x,0) = I_0, \qquad V(x,0) = V_0 \ \ x \in \Omega\,.$$

Here $\Omega$ is a bounded domain in $\mathbb{R}^n$ with smooth boundary $\partial\Omega$, $\frac{\partial V}{\partial \eta}$ is the normal derivative of $V$ on $\partial\Omega$.

The rest of paper is organized as follows. The next section deals with theglobal existence, positivity, and boundedness of solutions of problem (2)-(4). In Section 3, we discuss the stability analysis of equilibria. In Section 4, we present the numerical simulation to illustrate our result.

## 2. Global existence, positivity, and boundedness of solution

This section is devoted to the study of the global existence, positivity, and boundedness of solutions of problem 2-4. We state the following result.

***Theorem 1***. *For any given initial data* $\Phi = (H_0, I_0, V_0)^T$ *satisfying condition* $(4)$*; there exists a unique solution of system* $(2)$ *defined on* $[0, +\infty)$ *and this solution remains nonnegative and bounded for all* $t \geq 0$.

**Proof.** We define the Banach space $X = (C(\overline{\Omega}))^3$; problem can be written abstractly in the space $X$ as follow:

$$(5)\quad \begin{cases} u'(t) = Au(t) + F\big(u(t)\big), \quad t > 0, \\ u(0) = u_0 \in C(\Omega) \end{cases}$$

where $u = (H,\ I,\ V)^T$, $u_0 = (H_0, I_0,\ V_0)^T$ and $Au = (0,\ 0,\ d_V \Delta u)^T$ and

$$F(u(t)) = \begin{pmatrix} \Lambda - dH - (\beta I + \alpha V)H + \rho I \\ (\beta I + \alpha V)H - (a + \rho) I \\ kI - uV \end{pmatrix}$$

Since $F$ is locally Lipschitz in $X$, thus there exists a unique local solution of the system (2) on the interval $[0,\ T_{max})$; where $T_{max}$ denotes the maximal existence time for solution of the system (2) (see [15]).

We have $H(x,t) \geq 0,\ I(x,t) \geq 0,\ V(x,t) \geq 0$, since $\mathbf{0} = (0,0,0)$ represents a lower-solution of the model (5).

In order to prove the boundedness of solutions, let us set $W = H + I$. This implies

$$(6)\quad \begin{aligned} \frac{\partial W}{\partial t} &= \Lambda - dH - \rho I - (a + \rho)I \\ &= \Lambda - dH - aI \\ &= \Lambda - \gamma_1 W \end{aligned}$$

where $\gamma_1 = \min(d, a)$. Hence

$$W(x,t) \leq max\left\{\frac{\Lambda}{\gamma_1},\ max_{x \in \overline{\Omega}}(H_0(x) + I_0(x))\right\}$$

This implies that $H$ and $I$ are bounded. Furthermore, from the boundness for $I$ and the system (2); it follows that $V$ satisfies the following system

$$(7)\quad \begin{aligned} \frac{\partial V}{\partial t} - d_V \Delta V &\leq k\gamma_2 - uV \quad in\ \Omega * [0,\ T_{max}) \\ \frac{\partial V}{\partial \eta} &= 0 \quad in\ \partial\Omega * [0,\ T_{max}) \\ V(x,0) &= V_0(x) \quad on\ \Omega \end{aligned}$$

where $\gamma_2 = max\left\{\frac{\Lambda}{\gamma_1},\ max_{x \in \overline{\Omega}}(H_0(x) + I_0(x))\right\}$.

Using the comparison principle [16], we deduce that $V \leq \tilde{V}$; where $\tilde{V}(t) = V_0(x)e^{-ut} + \frac{k\gamma_2}{u}(1 - e^{-ut})$ is the solution fo the following ODE

$$\begin{aligned} \tfrac{\partial \tilde{V}}{\partial t} &= k\gamma_2 - u\tilde{V} \quad on \quad [0, T_{max}) \\ \tilde{V}(0) &= ||V_0||_\infty = max_{x \in \overline{\Omega}}(V_0(x)). \end{aligned}$$

Since $\tilde{V} \leq max\left\{\frac{k\gamma_2}{u},\ ||V_0||_\infty\right\}$ for all $t \in (0,\ \infty)$; we have that

$$(8)\quad V(x,t) \leq max\left\{\frac{k\gamma_2}{u},\ ||V_0||_\infty\right\} \text{ for all } (x,t) \in \overline{\Omega}\ X\ [0,\ T_{max}).$$

Using [17], Theorem 2, to establish the $L^\infty$ uniform boundedness of $V$, it is sufficient to show the $L^1$ uniform boundedness.

Since $\frac{\partial V}{\partial \eta} = 0$ and

$$\frac{\partial (H + I + V)}{\partial t} - \Delta(d_V V) \leq \Lambda + k\gamma_2 - \gamma_3(H + I + V),$$

where $\gamma_3 = min\{\gamma_1, \gamma_2\}$, we get

$$(9)\quad \frac{\partial}{\partial t}\left(\int (H + I + V)dx\right) \leq meas(\Omega)(\pi + k\gamma_2) - \gamma_3\left(\int (H + I + V)dx\right).$$

Hence

$$(10) \qquad \int (\mathrm{H} + \mathrm{I} + \mathrm{V})\mathrm{dx} \leq \mathrm{meas}(\Omega)\left(\max\left\{\frac{\Lambda + \mathrm{k}\gamma_2}{\gamma_3},\ ||\mathrm{H}_0 + \mathrm{I}_0 + \mathrm{V}_0||_\infty\right\}\right)$$

which implies that

$$(10) \qquad Sup_{t\geq 0}\left(\int V(x,t)dx\right) \leq K \coloneqq meas(\Omega)\left(max\left\{\frac{\Lambda + k\gamma_2}{\gamma_3},\ ||H_0 + I_0 + V_0||_\infty\right\}\right)$$

Using [17, Theorem 3.1], we deduce that there exists a positive constant $K^*$ that depends on $K$ and on $||H_0 + I_0 + V0||\infty$ such that

$$(11) \qquad Sup_{t\geq 0}||V(.,t)||_\infty \leq K^*.$$

From the above, we have proved that $H$, $I$ and $V$ are bounded on $\overline{\Omega}\, X\, [0\ , T_{max}\,)$. Therefore, it follows from the standard theory for semilinear parabolic systems (see [18]) that $T_{max} = +\infty$. This completes the proof of the theorem.

## 3. Qualitative analysis of the spacial model

The basis reproduction number [19, 20] of the model (2); is given by

$$(12) \qquad R_0 = \frac{\Lambda(\alpha k + \beta u)}{du(a+\rho)}$$

It is not hard to show that the system (2); is always a disease-free equilibrium of the form $E_0 = (h_0\ ,\ 0,\ \ 0)$, where $h_0 = \frac{\Lambda}{\mathrm{d}}$. Further, if $R_0 > 1$; the system (2); has a unique endemic equilibrium $E^* = (H^*,\ I^*,\ V^*)$ where

$$(13) \qquad H^* = \frac{\Lambda}{dR_0}$$

$$(14) \quad I^* = \frac{\Lambda}{a}\left(1 - \frac{1}{R_0}\right)$$

$$(15) \quad V^* = \frac{k}{u}I^*.$$

The objective of this section is to discuss the local and global stability of the equilibria.

### 3.1 Local stability of the equilibria

We now discuss the stability of the corresponding steady states of the model. Let us assume that $0 < \lambda_1 < \lambda_2 < \cdots < \lambda_n$ be the eigenvalues of the operator $-\Delta$on $\Omega$ with the homogeneous Neumann boundary conditions and $\mathrm{E}(\lambda_i)$ be the eigenfunction space corresponding to $\lambda_i$ in $C^1(\Omega)$. Let $\{\psi_{ij} : j = 1, 2 \ldots, dim\mathrm{E}(\lambda_i)\}$ represent an orthonormal basis of $\mathrm{E}(\lambda_i)$, $\mathbb{X}_{ij} = \{\phi\psi_{ij} :\ \phi\ \epsilon\ \mathbb{R}^3\}$ and $\mathbb{X} = (C(\Omega)^1)^3$, then

$$\mathbb{X} = \bigoplus_{i=1}^{\infty} \mathbb{X}_i \quad and \quad \mathbb{X}_i = \bigoplus_{j=1}^{dimE(\lambda_i)} \mathbb{X}_{ij}.$$

Let $\overline{E} = (\overline{H}\ ,\ \overline{I},\ \overline{V})$ be an arbitrary steady state of the system (2). We define the following perturbation about $\overline{E}$:

$$(16) \qquad U_1(x,t) = H(x,t) - \overline{H}\ ,\ \ U_2(x,t) = I(x,t) - \overline{I}\ \ and\ U_3(x,t) = V(x,t) - \overline{V}$$

Linearizing the system (2); at $\overline{\boldsymbol{E}}$; we obtain

$$(17) \qquad \frac{\partial U}{\partial t} = D\Delta U + J * U(x,t)$$

where

$$J = \begin{pmatrix} -d - (\beta\ \overline{I} + \alpha\,\overline{V}) & \rho - \beta\ \overline{H} & \alpha\,\overline{H} \\ (\beta\ \overline{I} + \alpha\ \overline{V}) & \beta\ \overline{H} - (a+\rho) & \alpha\,\overline{H} \\ 0 & k & -u \end{pmatrix}$$

is the Jacobian matrix of (16); without diffusion ( i.e. $d_v$) at $\overline{E}$ and $D = diag(0,\ 0,\ d_v)$ and $U = (U_1\ , U_2\ , U_3)^T$.

We define the operator $\boldsymbol{L}$ by

$$LU = D\Delta U + J * U(x,t)$$

$\mathbb{x}_i$ is invariant under the operator $L$ for all $i \geq 1$. Further, $\eta$ is an eigenvalue of $\boldsymbol{L}$ if and only if it is a root of the equation

$$det(-\lambda_i D + J - I_3) = 0 \tag{18}$$

for some $i \geq 1$ and in this case, there exists an eigenvector in $\gamma_i$ i:

We have

$$-\lambda_i D + J - \eta I_3 = \begin{pmatrix} -d - (\beta\ \overline{I} + \alpha\ \overline{V}) - \eta & \rho - \beta\ \overline{H} & \alpha\ \overline{H} \\ (\beta\ \overline{I} + \alpha\ \overline{V}) & \beta\ \overline{H} - (a+\rho) - \eta & \alpha\ \overline{H} \\ 0 & k & -\boldsymbol{\lambda_i} d_V - u - \eta \end{pmatrix}$$

At the boundary equilibrium $E_0 = (h_0\ ,\ 0,\ 0)$; it is easy to see that $\eta_1 = -u - \boldsymbol{\lambda_i} d_V$ is one root of (18); and the other two roots $\eta_2,\ \eta_3$ satisfy

$$\begin{aligned} \eta_2 + \eta_3 &= -(a + \rho + u + \boldsymbol{\lambda_i} d_V - h_0) \\ &= \left(\frac{\alpha k}{u R_0} + \beta h_0 \left(\frac{1}{R_0} - 1\right) + u + \boldsymbol{\lambda_i} d_V\right) \end{aligned} \tag{19}$$

$$\begin{aligned} \eta_2 \eta_3 &= (a + \rho - \beta h_0)(u + \lambda_i d_V) - \mathrm{a}k h_0 \\ &\geq (a + \rho)(u + \lambda_i d_V)(1 - R_0) \end{aligned} \tag{20}$$

Then, when $R_0 < 1$, $\eta_2 + \eta_3 < 0$ and $\boldsymbol{\eta_2 \eta_3} > 0$ all the root of (18); at $E_0$ have negative real parts then $E_0$ is locally asymptotically stable. For $R_0 > 0$; we take $\boldsymbol{\lambda_i} = \boldsymbol{\lambda_0} = 0$ to obtain $\boldsymbol{\eta_2 \eta_3} < 0$. Which implies that (18) has a positive eigenvalue and $E_0$ is unstable.

Evaluating (18) at $E^*$ and using [11], we obtain

$$A\eta^3 + B\eta^2 + C\eta + D = 0, \tag{21}$$

where

$$A = (u + \lambda_i d_V) H^*$$

$$B = \rho \Lambda I^* + (u + \lambda_i d_V)^2 H^* + \alpha k H^*$$

$$C = \alpha \Lambda H^* + \alpha u^2 + \alpha \rho k H^* I^* + \rho (u + \lambda_i d_V)^2 I^* - u a \rho (u + \lambda_i d_V) I^* - \rho^2 (u + \lambda_i d_V) I^* + a\beta (u + \lambda_i d_V) I^* H^* + u \rho \beta I^* H^*,$$

$$\mathrm{D} = a\alpha k (u + \lambda_i d_V) I^* H^* + a\beta (u + \lambda_i d_V)^2 H^* I^* + \rho\beta (u + \lambda_i d_V)^2 H^* I^* - a\rho (u + \lambda_i d_V)^2 I^* - \rho^2 (u + \lambda_i d_V)^2 I^* + \rho\alpha k (u + \lambda_i d_V) H^*.$$

We have, $A,\ B > 0$ and noticing that$H^*(u\beta\ + \alpha k) = u(a + \rho)$ we deduce that

$$C = \gamma \alpha k H^* + \gamma u^2 + \rho u^2 I^* + u a \beta I^* H^* > 0$$

$$D = a\alpha u k I^* H^* + a\beta u^2 I^* H^* > 0$$

and

$$\mathrm{BC} - \mathrm{AD} = \left(\gamma u + \rho u I^* + \alpha k H^{*2}\right).(\alpha \Lambda k H^* + u\alpha\beta I^* H^* + \Lambda u^2 + \rho u^2 H^*)$$

$$+ u^4 H^* (\Lambda + \rho I^*) + \alpha k u^2 H^{*2} (\Lambda - a I^*) > 0$$

where $R_0 > 1$ and $H^* = \Lambda / a(1 - 1/R_0)$ are used.

Then, by the Routh-Hurwitz Criterion [21], we know that all the roots of (18) at $E^*$ always have negative real parts. Thus, the epidemic equilibrium $E^*$ is locally asymptotically stable for $R_0 > 1$. The characterization of the local stability of virus-free equilibrium $E_0$and endemic equilibrium are given by the following result.

***Theorem 2***. *For model (2); we have the following conclusion:*

*I.* $E_0$ *is locally stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

*II.* $E^*$ *is locally stable if* $R_0 > 1$.

### 3.2 Global stability of the two equilibria

Our aim in step is establish the global stability of virus-free equilibrium and endemic equilibrium for the for reaction diffusion equations $(2)-(4)$. Inspired by the work of Zhang et al., we construct the Lyapunov functions which allow us under certain conditions to have the global stability of the equilibruim points.

***Theorem 3***.

*If $R_0 < 1$; the virus-free equilibrium $E_0$ is globally asymptotically stable.*

**Proof.** In the case where the mobility of viruses is not taken into account, in the works of Zhang et al., the authors used the following Lyapunovfunctional for the study of the global stability $E_0$.

$$L_1(H,I,V) = H - h_0 - H_0 ln\left(\frac{H}{h_0}\right) + \frac{\rho}{2(d+a)h_0}(H - h_0 + I)^2 + I + pV$$

with $p > 0$ is a constant to be determined.

We introduce the following Lyapunov function

$$K_1(H,I,V) = \int L_1\big(H(x,t), I(x,t), V(x,t)\big)dx.$$

Differentiating $K_1$ with respect to $t$ along the solutions of the model $(2)-(4)$; we obtain

$$(22)\quad \frac{dK_1}{dt} = -\left(\frac{h_0}{H} + \frac{\rho}{Hh_0} + \frac{d\rho}{(d+a)h_0}\right)(H - H_0)^2 + k\left(p - \frac{a+\rho+\beta h_0}{k}\right)I + \left(\frac{\alpha h_0}{u} - p\right)uv + \mathrm{p}d_V\int \Delta V dx$$

Combining the divergence theorem and homogeneous Neumann boundary conditions$(4)$; we have $\int \Delta V dx = 0$ and since $R_0 < 1$; we have $(\alpha u + \beta k) < u(a+\rho)$; then taking $p > 0$ such that $\frac{\beta h_0}{u} < p < \frac{(a+\rho-\alpha h_0)}{k}$. It follows that $\frac{dK_1}{dt} < 0$. Consequently, $E_0$ is globally asymptotically stable.

***Theorem 4***.

*If $1 < R_0 \leq 1 + \delta$; the epidemic equilibrium $E^*$ is globally asymptotically stable, where*

$$\delta = \frac{\left(\beta\pi + (a-\rho)d + \sqrt{(\beta\pi + (a-\rho)d)^2 + 4a\rho d^2}\right)}{2\rho d}.$$

**Proof.**

Assuming that $R_0 > 1$; we define a Lyapunov functional for the system $(2)-(4)$; at $E^*$ as follows

$$K_2(H,I,V) = \int L_2\big(H(x,t), I(x,t), V(x,t)\big)dx$$

where

$$\begin{aligned} L_2(H,I,V) = H - H^* - H^* ln\left(\frac{H}{H^*}\right) + \left(I - I^* - I^* ln\left(\frac{I}{I^*}\right)\right) \\ + \frac{\alpha H^* V^*}{kI^*}\left(V - V^* - V^* ln\left(\frac{V}{V^*}\right)\right) \\ + \frac{\rho}{2(d+a)}(H - H^* + I - I^*)^2 \end{aligned}$$

Differentiating $K_2$ with respect to $t$ along the solutions of the model $(2)-(4)$; we obtain

$$\begin{aligned} \frac{\partial K_2}{\partial t} &= H - H^* - H^* ln\left(\frac{H}{H^*}\right) + \left(I - I^* - I^* ln\left(\frac{I}{I^*}\right)\right) \\ (23)\qquad &= \left(H - H^* - H^* ln\left(\frac{H}{H^*}\right)\right)\frac{\alpha H^* V^*}{kI^*} \\ &= \frac{\rho}{2(d+a)}(H - H^* + I - I^*)^2. \end{aligned}$$

Differentiating $K_2$ with respect to $t$ along the solutions of the model $(2)-(4)$; we get

$$\frac{\partial K_2}{\partial t} = \int \Big\{ \Lambda - dH - (\beta I + \alpha V)H + \rho I - \frac{H}{H^*}(\pi - dH - (\beta I + \alpha V)H + \rho I) + (\beta I + \alpha V)H$$
$$(24) \quad - (a+\rho)I - \frac{I}{I^*}\big((\beta I + \alpha V)H + (a+\rho)I\big) + \frac{\alpha H^* V^*}{I^*}\left( d_V \Delta V + kI - uv + \frac{V^*}{V}(d_V \Delta V + kI - uv) \right)$$
$$+ \frac{\rho}{2(d+a)}(H - H^* + I - I^*).(\pi - dH + \rho I \ - (a+\rho)I) \Big\}\, dx$$

Then, by the same method using in the proof of Theorem 2 of in the paper of Zhang et al., we deduce that

$$\frac{\partial K_2}{\partial t} = \int \left\{ \left( dH^* - \beta I^* H^* - \rho I^* + \frac{d\rho H}{a+\rho} + \rho I \right) + \frac{(H-H^*)^2}{HH^*} - \frac{a\rho}{(d+a)H^*}(I - I^*)^2 \right.$$
$$(25) \qquad \left. - \alpha H^* V^* \left( 3 - \frac{H^*}{H} + \frac{I^* V H}{H^* V^* I} - \frac{V^* I}{V I^*} \right) \right\} dx$$
$$+ \frac{\alpha d_V H^* V^*}{kI^*} \left( \int \Delta V dx - V^* \int \frac{\Delta V}{V} dx \right)$$

Note that $\int \Delta V dx = 0$ and $\int \frac{\Delta V}{V} dx = \int \frac{|\Delta V|^2}{V^2} dx$. Therefore, we have

$$\frac{\partial K_2}{\partial t} = \int \left\{ \left( dH^* - \beta I^* H^* - \rho I^* + \frac{d\rho H}{a+\rho} + \rho I \right) + \frac{(H-H^*)^2}{HH^*} - \frac{a\rho}{(d+a)H^*}(I - I^*)^2 \right.$$
$$(26) \qquad \left. - \alpha H^* V^* \left( 3 - \frac{H^*}{H} + \frac{I^* V H}{H^* V^* I} - \frac{V^* I}{V I^*} \right) \right\} dx$$
$$- \frac{\alpha d_V H^* V^{*2}}{kI^*} \left( \int \frac{|\Delta V|^2}{V^2} dx \right)$$

Since the arithmetic mean is greater than or equal to the geometric mean, it follows that

$$(27) \qquad 3 - \frac{H^*}{H} + \frac{I^* V H}{H^* V^* I} - \frac{V^* I}{V I^*} \ \leq 0.$$

Consequently if $R_0 > 1$ and$dH^* - \beta I^* H^* - \rho I^* > 0$ then $\frac{\partial K_2}{\partial t} \leq 0$. Moreover, $\frac{\partial K_2}{\partial t} = 0$ if and only $H = H^*$, $I = I^*$ and $V = V^*$. Therefore, under above conditions if $M = \{E^*\}$ represents the largest compact invariant set in $\left\{ (H, I, V) : \ \frac{\partial K_2}{\partial t} = 0 \right\}$ and by the LaSalle's invariance principle [22] we deduce that $E^*$ is globally asymptotically stable whenever $R_0 > 1$as the steady state $E^*$ exists whenever $R_0 > 1$.

Let remarks that the condition $dH^* - \beta I^* H^* - \rho I^* \geq 0$ is equivalent to

$$(28) \qquad 1 < R_0 \ \leq 1 + \frac{\left( \beta\pi + \ (a-\rho)d + \sqrt{(\beta\pi + \ (a-\rho)d)^2 + 4a\rho d^2} \right)}{2\rho d} = 1 + \delta$$

## 4. Numerical simulation

In this section, we carry out some numerical simulations to illustrate the theoretical results obtained in the previous sections. For this purpose, we consider three sets of parameters values corresponding to the cases $R_0 > 1$. For the sake of simplicity of numerical simulations, we take one-dimensional spatial domain $\Omega = [0, \ 50]$ and the values of the diffusion coefficient as $d_V = 10$.

In the first test (Figures 1-3), we choose the following data set of system (3) $\Lambda = 15$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$. Using these values, ones get $R_0 = 1.125$ and $\delta = 0.3583$ and we have $1 < R_0 < 1 + \delta$. In this case, system (3) has a epidemic equilibrium $E^*$ which is globally asymptotically stable (see Figures 1-3).

In Figures 4-6, we choose $\Lambda = 20$ and do not change the other parameter values. By calculation, we have $R_0$ which satisfy Theorem 4; then the disease-free equilibrium is still present and the system (2) has a unique endemic equilibrium $E^*$. Therefore, by Theorem 4 $E^*$ is globally asymptotically stable. Numerical simulation illustrates our result (see Figures 4-6).

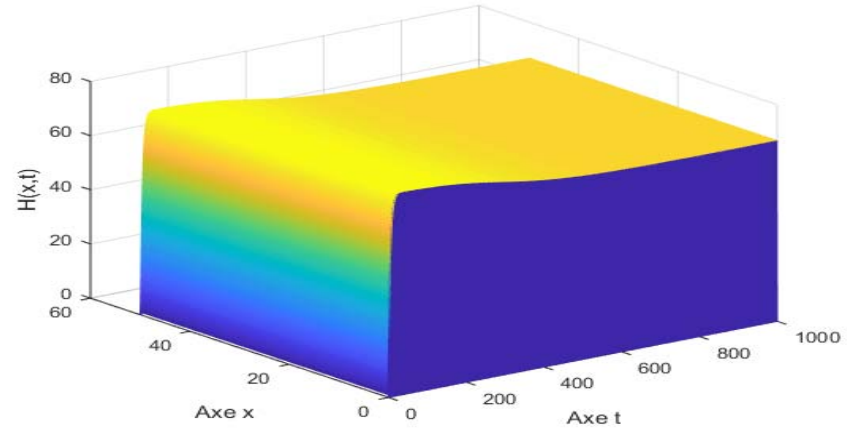


**Figure 1. Concentrations of uninfected cells $\Lambda = 15$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

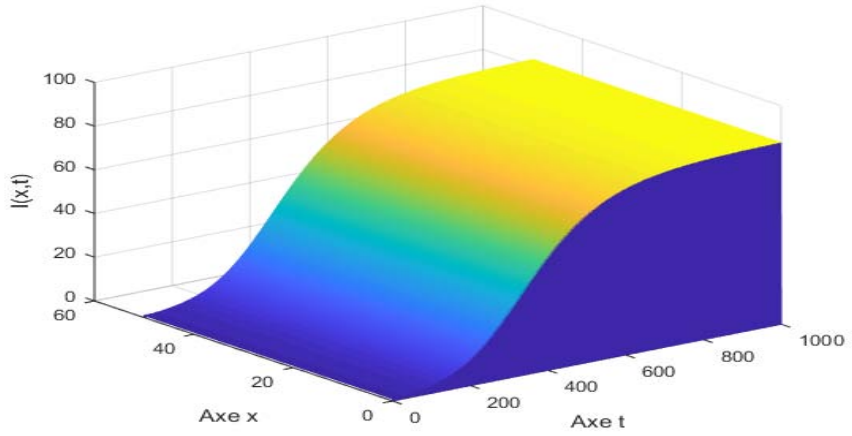


**Figure 2. Concentrations of infected cells $\Lambda = 15$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

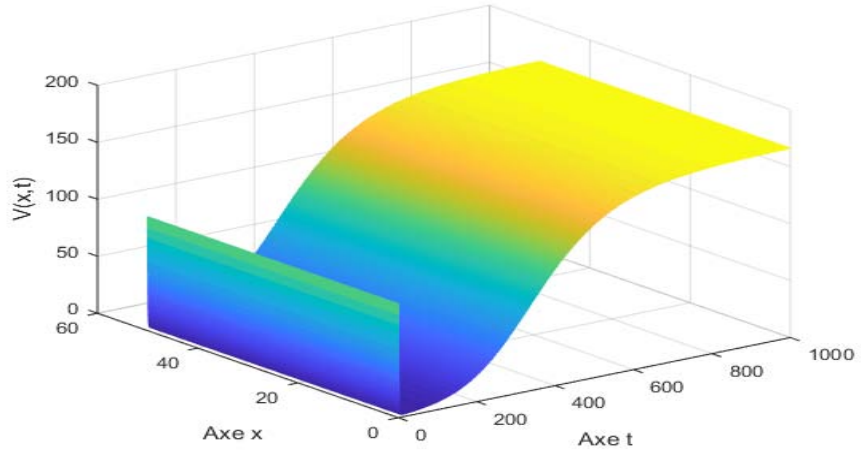


**Figure 3. Concentrations of and free virus for $\Lambda = 15$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

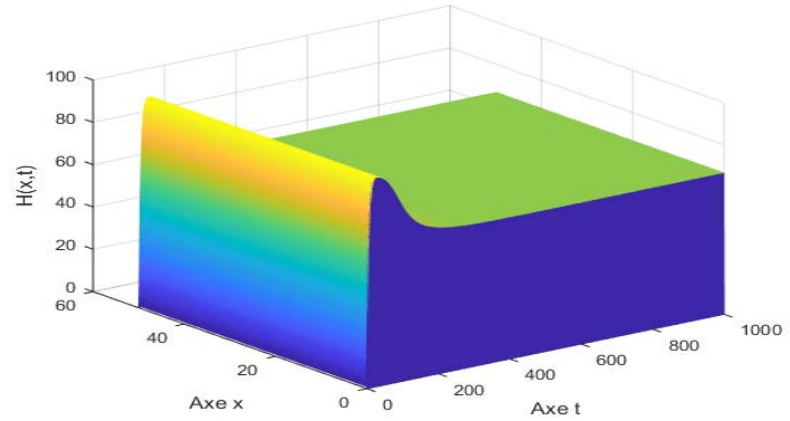


**Figure 4. Concentrations of uninfected cells $\Lambda = 20$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

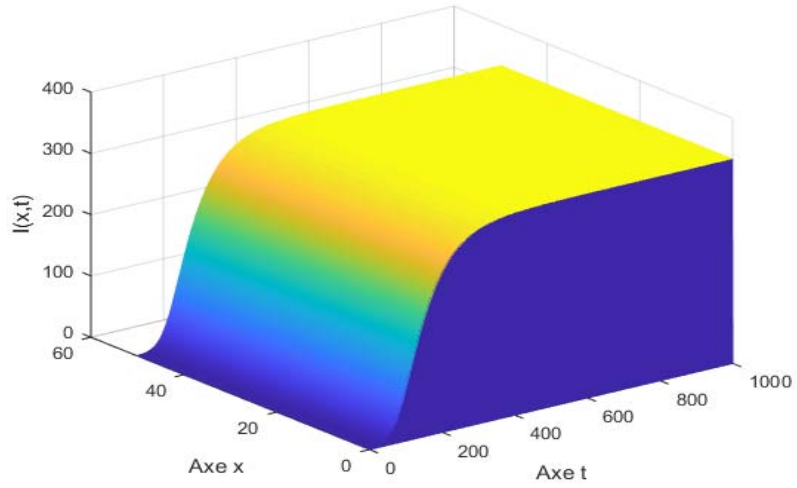


**Figure 5. Concentrations of infected cells $\Lambda = 20$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

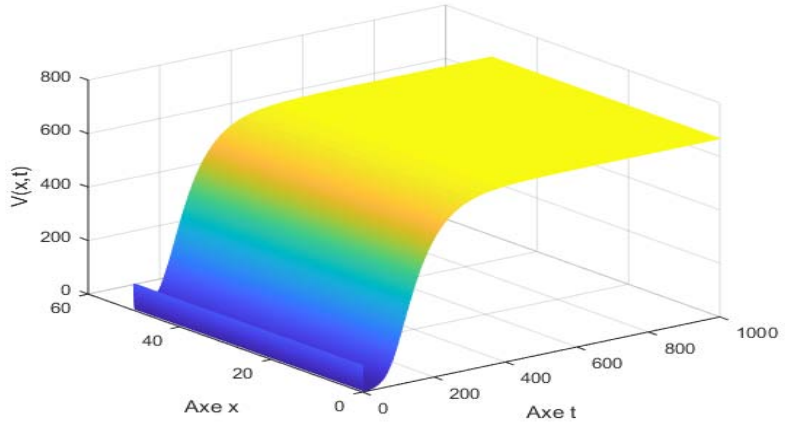


**Figure 6. Concentrations of and free virus for $\Lambda = 20$, $d = 0.2$, $\beta = 0.008$, $\alpha = 0.005$, $\rho = 0.1$, $a = 0.02$, $k = 2$ and $u = 1$.**

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