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Global Analysis of a Spatiotemporal Cellular Model for the Transmission of Hepatitis C Virus With Hattaf-Yousfi Functional Response

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Abstract. This paper carries out a mathematical analysis of the global dynamics of a partial differential equation viral infection cellular model. We study the dynamics of a hepatitis C virus (HCV) model, under therapy, that considers both absorption phenomenon and diffusion of virions, infected and uninfected hepatocytes in the liver. Firstly, we prove the boundedness of the potential solutions, global existence, uniqueness, and positivity of the obtained initial value and boundary problem solution. Then, the dynamical behaviour of the model is entirely determined by a threshold parameter called the basic reproduction number denoted $\mathcal{R}_0$. We show that the uninfected spatially homogeneous equilibrium of the model is globally asymptotically stable if $\mathcal{R}_0 \leq 1$ by using the direct Lyapunov method. The latter means that the HCV infection is cleared, and the disease dies out. Also, the global asymptotical properties stability of the infected spatially homogeneous equilibrium of the model are studied via a skilful construction of a suitable Lyapunov functional. It means that the HCV infection persists in the host, and the infection becomes chronic. Finally, numerical simulations are performed to support the obtained theoretical results.

1. Introduction

The dynamics of viruses, in particular the dynamics of the hepatitis C virus, remains a very active field of research in the world of sciences. Moreover, the 2020 Nobel Prize in Medicine was awarded to three researchers, namely the British Michael Hougton and the Americans Harvey Alter and Charles Rice. They were awarded this Nobel Prize for their very advanced research work on the hepatitis C virus. According to World Health Organization(WHO) [41], 71 million persons were living with chronic hepatitis C virus (HCV) infection worldwide and 399 000 persons had

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died from cirrhosis or hepatocellular carcinoma following a survey done in 2015. Aside from the burden of HCV infection secondary to liver-related sequelae, HCV causes an additional burden through comorbidities among persons with HCV infection, including depression, diabetes mellitus and chronic renal disease. In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy for 2016-2021 on viral hepatitis (HBV and HCV infection), which proposes to eliminate viral hepatitis as a public health threat by 2030. Elimination is defined as a 90% reduction in new chronic infections and a 65% reduction in mortality compared with the 2015 baseline. Mathematicians cannot stay aside from this disastrous situation decried by WHO. In view of the vital importance of the liver and the aforementioned facts, any contribution to a better understanding of HCV infection process and strategy to eradicate this infection is of great interest. Mathematical models have been developed to help understand and control the dynamics of HCV within an infected host such as in [6, 7, 14, 35]. The dynamics of viral infections such as the Ebola virus disease(EVD), the human immunodeficiency virus (HIV) infection, the hepatitis B virus (HBV) infection, the hepatitis C virus (HCV) infection and, new corona virus infection have been modeled mathematically in a host. One of the earliest temporal models was the within-host basic viral infection model proposed in [31] to study HIV infection, and later adopted to HBV [8, 32]. Particularly, numerous mathematical models describing the temporal dynamics of HCV have been initially proposed by Neumann and al [30] using the classical viral infection cellular model, and later have been extended in [6, 10, 14, 35]. Motivated by what has been done in [8, 30, 32], Chong and al. [7] formulated the basic HCV temporal intra-host model with therapy as a system of three differential equations :

$$\begin{cases} \dfrac{dH(t)}{dt} = \lambda - dH(t) - (1-\eta)\beta H(t)V(t), \\ \dfrac{dI(t)}{dt} = (1-\eta)\beta H(t)V(t) - \alpha I(t), \\ \dfrac{dV(t)}{dt} = (1-\varepsilon)kI(t) - \mu V(t), \end{cases} \tag{1.1}$$

where the equations relate the dynamics relationship between, H as the uninfected target cells (hepatocytes), I as the infected cells and V as the viral load (amount of viruses present in the liver). In the system (1.1) the key assumption is that hepatocytes and viruses are well mixed, and neglects the mobility of hepatocytes C viruses, the infected and uninfected target cells. To study the influences of spatial structures of virus dynamics, Wang and Wang in [39] assuming that the motion of virus follows Fickian diffusion, that is to say, the population flux of virus is proportional to the concentration gradient and the proportionality constant is taken to be negative [13]. Moreover, in model (1.1), the rate of infection is assumed to be bilinear in the virus V and uninfected hepatocytes T. It is shown in [29] that this bilinear rate of infection could be unrealistic. However, the actual incidence rate is probably not linear over the entire range of T and V. Thus is reasonable to assume that the infection rate is given by a more general one, known as the Hattaf-Yousfi functional response [18] of the form $\frac{\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}$ where $\alpha_0 > 0$, $\alpha_1 \geq 0$, $\alpha_2 \geq 0$, $\alpha_3 \geq 0$ are constants. The function $\frac{\beta H}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}$ satisfies the hypotheses (H_1), (H_2) and (H_3) of general incidence rate presented in [16, 19–21]. The Hattaf-Yousfi type of functional response was introduced by Hattaf and al. [18]. This functional response generalizes many functional responses and it was used in [34] to describe the dynamics of labour market. Thus, when $\alpha_0 = 1$, the Hattaf-Yousfi functional response is reduced to the specific functional response used by Hattaf and al in [17]. Furthermore, if $\alpha_3 = \alpha_1\alpha_2$ and $\alpha_0 = 1$, the Hattaf-Yousfi functional response is reduced to Crowley-Martin functional response [9] and was used in [43]. When $\alpha_3 = 0$ et $\alpha_0 = 1$ the Hattaf-Yousfi functional response is simplified to Beddington-DeAngelis functional response [5, 11], and was used in [25, 26, 38, 42]. When $\alpha_1 > 0$, $\alpha_2 = \alpha_3 = 0$ and $\alpha_0 = 1$, the Hattaf-Yousfi functional response is reduced to Holling type II functional response [28]. And when $\alpha_1 = \alpha_3 = 0$, $\alpha_2 > 0$ and $\alpha_0 = 1$ it expresses a saturation response [36]. Moreover, when $\alpha_1 = \alpha_2 = \alpha_3 = 0$, and $\alpha_0 = 1$ the Hattaf-Yousfi functional response is reduced to the mass action principle(or Holling type I functional response). Also ordinary differential system (1.1) don't take into consideration the cure of infected hepatocytes. In this work, motivated by the breaches observed in the analysis and the formulation of system (1.1), we construct and analyze a partial differential equation (PDE)-cellular model system for HCV infection, which derives from system (1.1) by incorporating the space, Hattaf-Yousfi incidence rate, absorption effect and spontaneous cure. It is worth mentioning that in [7] the authors used mass-action kinetics for viral infection, neglected the cure rate, ignored the absorption effect and the diffusion of free virions, susceptible cells and infected cells. Thus the obtained model is an extension of the one in the first part of the work done by Chong et al. [7].

The work is organized as follows. In section 2, we model the phenomenon described through a reaction-diffusion equations which leads to a initial value and boundary problem. Section 3 is devoted to the study of the existence and uniqueness of the global solution of our initial and boundary value problem, and of the properties of this solution, namely positivity and boundedness. Section 4 deals with the stability and the analysis of spatially homogeneous equilibria and numerical simulations in section 5. We conclude our work and provide a discussion in section 6.

2. Formulation of the PDE-cellular model

Let $\Omega \subset \mathbb{R}^3$ be a bounded connected domain representing the liver. Let $t \geq 0$ be a given time and $x = (x_1, x_2, x_3) \in \Omega$. Denote respectively by $H(x, t)$, $I(x, t)$ and $V(x, t)$ the concentrations of healthy hepatocytes, HCV infected hepatocytes, and free HCV virions at time t and location x. The dynamics of HCV infection intra-host is the result of the dynamics of each compartment H, I, and V, and the various interactions between them. We now describe the evolution of each compartment.

2.1. **Fluctuation of healthy hepatocytes.** Let ν be an elementary volume in Ω. The variation of the quantity of healthy hepatocytes in ν is described under the following assumptions. Healthy hepatocytes are produced at constant rate λ from the bone narrow and die at rate dH. Virions infect the healthy hepatocytes at the rate $\frac{\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}$, where β is the rate of transmission of the infection and α_j, $j=0,1,2,3$ are positive constants. This generalized incidence function replaces the mass-action function which has been shown to cause unrealistic conditions for successful chronic HCV infection. ρI is the cure rate of infected hepatocytes either by noncytolytic mechanism or immunity or treatment. In addition, the therapeutic effect of treatment in this model involved the reduction of new infections, which is described in a fraction as $(1-\eta)$. The spatial motion of healthy hepatocytes follows the Fickian diffusion law. Thus, the variation of healthy hepatocytes is expressed by the following equation:

$$\frac{\partial H}{\partial t}=D_1\Delta H(x,t)+\lambda-dH(x,t)-\frac{(1-\eta)\beta H(x,t)V(x,t)}{\alpha_0+\alpha_1 H(x,t)+\alpha_2 V(x,t)+\alpha_3 H(x,t)V(x,t)}+\rho I(x,t),$$

where D_1 represents the Healthy hepatocytes diffusion coefficient and

$$\Delta=\frac{\partial^2}{\partial x_1^2}+\frac{\partial^2}{\partial x_2^2}+\frac{\partial^2}{\partial x_3^2}$$

is the usual Laplacian operator in three-dimensional space.

2.2. **Fluctuation of HCV infected cells.** The HCV infected cells die at rate α per day so that $\frac{1}{\alpha}$ is the life-expectancy of HCV infected hepatocytes. Healthy hepatocytes become infected at the rate $\frac{\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}$. The spatial motion of HCV infected cells follows the Fickian diffusion law. Thus, the variation of infected hepatocytes is expressed by the following equation

$$\frac{\partial I}{\partial t}=D_2\Delta I(x,t)+\frac{(1-\eta)\beta H(x,t)V(x,t)}{\alpha_0+\alpha_1 H(x,t)+\alpha_2 V(x,t)+\alpha_3 H(x,t)V(x,t)}-(\alpha+\rho)I(x,t),$$

where D_2 represents the HCV infected cells diffusion coefficient.

2.3. **Fluctuation of free HCV virions.** The infected hepatocytes produce virus at rate kI, and virus is cleared at the rate μV. Also, the population of virions decreases due to the infection at the rate $\frac{u(1-\eta)\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}$ due to absorption effect, where $u\in\{0,1\}$. The spatial motion of virions follows the Fickian diffusion law. In addition, the therapeutic effect of treatment in this model involved blocking virions production (referred to as drug effectiveness) which, is described in fraction $(1-\varepsilon)$. Thus, the variation of free virions is expressed by the following equation:

$$\frac{\partial V}{\partial t}=D_3\Delta V(x,t)+(1-\varepsilon)kI(x,t)-\mu V(x,t)-u\frac{(1-\eta)\beta H(x,t)V(x,t)}{\alpha_0+\alpha_1 H(x,t)+\alpha_2 V(x,t)+\alpha_3 H(x,t)V(x,t)},$$

where D_3 represents the free HCV virions diffusion coefficient.

2.4. **The initial boundary value problem associated to PDE-cellular model.** In this section, we use the previous equations describing variables variations to set up a complete PDE system modelling biological dynamics for HCV infection. Let $T>0$ be a fixed time and define

$$\Omega_T=\Omega\times(0,T).$$

Therefore, in Ω_T the full system of PDE governing the HCV infection becomes :

$$\begin{cases} \dfrac{\partial H}{\partial t} = D_1 \Delta H(x,t) + \lambda - dH - \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} + \rho I, \\ \dfrac{\partial I}{\partial t} = D_2 \Delta I(x,t) + \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} - (\alpha+\rho) I, \\ \dfrac{\partial V}{\partial t} = D_3 \Delta V + (1-\varepsilon) kI - \mu V - \dfrac{u(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV}. \end{cases} \tag{2.1}$$

We use the Neumann homogeneous boundary conditions:

$$\frac{\partial H}{\partial \eta} = \frac{\partial I}{\partial \eta} = \frac{\partial V}{\partial \eta} = 0 \text{ on } \partial\Omega \times [0,T], \tag{2.2}$$

where $\frac{\partial}{\partial \eta}$ denotes the outward normal derivative on $\partial\Omega$. The initial conditions are the following :

$$H(x,0) = H_0, \quad I(x,0) = I_0, \quad V(x,0) = V_0, \quad x \in \Omega. \tag{2.3}$$

The boundary conditions in (2.2) imply that the Healthy hepatocytes, the HCV infected cells and free HCV virions do not move across the boundary $\partial\Omega$. For an epidemiological significance, we assume that the initial conditions are positive and Hölder continuous, and satisfy $\frac{\partial H_0}{\partial \eta} = \frac{\partial I_0}{\partial \eta} = \frac{\partial V_0}{\partial \eta} = 0$ on $\partial\Omega$. We then obtain the following initial boundary value problem, denoted IBVP associated to the previous PDE-cellular model:

$$\begin{cases} \dfrac{\partial H}{\partial t} = D_1 \Delta H + \lambda - dH - \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} + \rho I \text{ in } \Omega_T, \\ \dfrac{\partial I}{\partial t} = D_2 \Delta I + \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} - (\alpha+\rho) I \text{ in } \Omega_T, \\ \dfrac{\partial V}{\partial t} = D_3 \Delta V + (1-\varepsilon) kI - \mu V - \dfrac{u(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} \text{ in } \Omega_T, \\ \dfrac{\partial H}{\partial \eta} = \dfrac{\partial I}{\partial \eta} = \dfrac{\partial V}{\partial \eta} = 0 \text{ on } \partial\Omega \times [0,T], \\ H(x,0) = H_0, \; I(x,0) = I_0, \; V(x,0) = V_0, \quad x \in \Omega, \end{cases} \tag{2.4}$$

on which our study will focus on.

3. Qualitative and quantitative analysis and some properties of the solutions for IBVP (2.4)

In this section, we provide a thorough study of the dynamics of IBVP (2.4) which yields various outcomes. Precisely, we prove existence, uniqueness, positivity and boundedness of solutions for IBVP (2.4). This is done by combining variational method and semigroups techniques to some useful functional analysis arguments.

3.1. Local existence and uniqueness of solutions for the IBVP (2.4).

Set

$$F(H,I,V) = (F_1(H,I,V), F_2(H,I,V), F_3(H,I,V))^T \tag{3.1}$$

where

$$F_1(H,I,V) = \lambda - dH - \frac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} + \rho I,$$

$$F_2(H,I,V) = \frac{(1-\eta)\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV} - (\alpha+\rho)I,$$

and

$$F_3(H,I,V) = (1-\varepsilon)kI - \mu V - u\frac{(1-\eta)\beta HV}{\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV}.$$

We have the following result which guarantees that the right-hand side, without diffusion, of the PDE-model system (2.4) is Lipschitz.

Proposition 3.1. *Let $T \in \mathbb{R}_+^*$ and $(H,I,V) \in (C_B^0(\Omega\times[0,T]))^3$, where $C_B^0(\Omega\times[0,T])$ is the space of bounded and continuous functions on $\Omega\times[0,T]$. We suppose that F in (3.1) is defined on $L^2(\Omega\times(0,T))$. Then F_1, F_2 and F_3 are uniformly Lipschitz continuous on $L^2(\Omega\times(0,T))$ with respect to H, I and V.*

Proof. Let $T \in \mathbb{R}_+^*$ and $(H_1,I_1,V_1),(H_2,I_2,V_2) \in (C_B^0(\Omega\times[0,T]))^3$. First, by direct computation, we have :

$$\|F_1(H_1,I_1,V_1)-F_1(H_2,I_2,V_2)\|_2 \le K_1^1\|H_1-H_2\|_2 + K_2^1\|I_1-I_2\|_2 + K_3^1\|V_1-V_2\|_2, \tag{3.2}$$

with

$$K_1^1 = d+(1-\eta)\beta\left(\frac{1}{\alpha_2}+\frac{V_m}{\alpha_0}\right), \quad K_2^1=\rho, \quad K_3^1 = (1-\eta)\beta\left(\frac{1}{\alpha_1}+\frac{H_m}{\alpha_0}\right), \tag{3.3}$$

with H_m and V_m given below.
Then

$$\|F_2(H_1,I_1,V_1)-F_2(H_2,I_2,V_2)\|_2 \le K_1^2\|H_1-H_2\|_2 + K_2^2\|I_1-I_2\|_2 + K_3^2\|V_1-V_2\|_2, \tag{3.4}$$

with

$$K_1^2 = (1-\eta)\beta\left(\frac{1}{\alpha_2}+\frac{V_m}{\alpha_0}\right), \quad K_2^2=(\alpha+\rho) \ \text{ and } \ K_3^2 = (1-\eta)\beta\left(\frac{1}{\alpha_1}+\frac{H_m}{\alpha_0}\right). \tag{3.5}$$

Finally

$$\|F_3(H_1,I_1,V_1)-F_3(H_2,I_2,V_2)\|_2 \le K_1^3\|H_1-H_2\|_2 + K_2^3\|I_1-I_2\|_2 + K_3^3\|V_1-V_2\|_2, \tag{3.6}$$

with

$$K_1^3 = u(1-\eta)\beta\left(\frac{1}{\alpha_2}+\frac{V_m}{\alpha_0}\right), \quad K_2^3=k(1-\varepsilon), \ \text{ and } \ K_3^3 = \mu+u(1-\eta)\beta\left(\frac{1}{\alpha_1}+\frac{H_m}{\alpha_0}\right). \tag{3.7}$$

This completes the proof of Proposition 3.1. □

Now, consider the following IBVP

$$\begin{cases} \partial_t H - D_1\Delta H = f(t,H,I,V) & \text{in} \quad \Omega\times(0,T) \\ \partial_t I - D_2\Delta I = g(t,H,I,V) & \text{in} \quad \Omega\times(0,T) \\ \partial_t V - D_3\Delta V = h(t,H,I,V) & \text{in} \quad \Omega\times(0,T) \\ \frac{\partial H}{\partial\eta}=0;\ \frac{\partial I}{\partial\eta}=0;\ \frac{\partial V}{\partial\eta}=0 & \text{on} \quad \partial\Omega\times[0,T] \\ H=H_0, I=I_0, V=V_0 & \text{on} \quad \Omega\times\{t=0\}. \end{cases} \tag{3.8}$$

In what follows, we will need the following definition and results.

Definition 3.1. (Sectorial operator, [22]) Let A be a linear operator in a Banach space X and suppose A is closed and densely defined. If there exist real numbers a, $\omega \in (0, \pi)$, $M \geq 1$ such that

$$\rho(A) \supset \Sigma = \{\lambda_0 \in \mathbb{C} \ : \ \omega \leq arg(\lambda_0 - a) \leq \pi, \lambda_0 \neq 0\} \tag{3.9}$$

and

$$\|R_{\lambda_0}(A)\| \leq \frac{M}{|\lambda_0 - a|} \ \text{ for all } \ \lambda_0 \in \Sigma, \tag{3.10}$$

then we say that A is sectorial.

Remark 3.1. The Neumann realization of the Laplacian $A = -\Delta$, with domain

$$D(A) = \left\{\omega \in H^2(\Omega) : \frac{\partial \omega}{\partial \eta} = 0\right\}$$

is a sectorial operator in $L^2(\Omega)$. But since $C_0^\infty(\Omega) \subset D(A)$, it is densely defined in $L^2(\Omega)$. For $\beta \geq 0$ large enough, we define the fractional powers of the Helmholtz operator, $\mathcal{H}^\odot = -\Delta + \beta I$, with domain $D(\mathcal{H}^\odot)$ equipped with graph norm $\| \, . \, \|_{D(\mathcal{H}^\odot)} = \| \, . \, \|_2 + \|\mathcal{H}^\odot . \|_2$.

We have the following general results.

Lemma 3.2. *[1] Let $1 \leq p < \infty$. Then $D(\mathcal{H}^\odot) \subset C_0^\infty(\Omega)$ with continuous injection for $\beta > \frac{n}{2p}$.*

Lemma 3.3. *[22] $D(\mathcal{H}^\beta) \subset C_B^0(\Omega)$ with continuous injection for $\beta > \frac{n}{4}$.*

Theorem 3.4. *[22] If A is sectorial, then $-A$ is the infinitesimal generator of an analytic semigroup, $G(t)$.*
If $R_{\lambda_0} > a, \ a \in \mathbb{R}$ whenever $\lambda_0 \in \sigma$, then for any $t > 0$,

$$\|G(t)\| \leq Ce^{-at} \ , \quad \|AG(t)\| \leq \frac{C}{t} e^{-at}$$

and

$$\frac{d}{dt} G(t) = -AG(t) \ , \quad t > 0.$$

Corollary 3.5. *Let G be the analytic semigroup generated by $-A$. The following properties hold for the semigroup G and the fractional powers of the Helmholtz operator $\mathcal{H}^\beta$:*

1) *$G(t) : L^2(\Omega) \to D(\mathcal{H}^\odot)$ for all $t > 0$,*
2) *$\|G(t)\omega\|_{\mathcal{H}^\odot} \leq C_{\beta,2} t^{-\beta} \|\omega\|_2$ for all $t > 0$, $\omega \in L^2$,*
3) *$G(t)\mathcal{H}^\odot \omega = \mathcal{H}^\odot G(t)\omega$ for all $t > 0$, $\omega \in D(\mathcal{H}^\odot)$.*

Remark 3.2. The following basic hypotheses are assumed to hold :

- **(H1):** $D_1 > 0, \ D_2 > 0$ and $D_3 > 0$,
- **(H2):** $H_0 \geq 0$, $I_0 \geq 0$ and $V_0 \geq 0$ are continuous on $\overline{\Omega}$, $H_0, I_0, V_0 \in C_B^0(\Omega)$,
- **(H3):** f, g and h are continuously differentiable functions from $\overline{\mathbb{R}}_+^4$ into $\mathbb{R}$ with $f(t, 0, s, z) \geq 0$, $g(t, r, 0, z) \geq 0$ and $h(t, r, s, 0) \geq 0$ for all $t, \ r, \ s, \ z \geq 0$.

For $x \in \Omega$, $t \geq 0$, H, I, $V \in (C_B^0(\Omega))^3$, define $\mathcal{F}, \mathcal{G}$ and $\mathcal{Q}$ on $\mathbb{R}_+ \times (C_B^0(\Omega))^3$ by :

$$[\mathcal{F}(t, H, I, V)](x) = f(t, H(x), I(x), V(x)),\ [\mathcal{G}(t, H, I, V)](x) = g(t, H(x), I(x), V(x)),$$
$$[\mathcal{Q}(t, H, I, V)](x) = h(t, H(x), I(x), V(x)).$$

In addition, we let G_1, G_2 and G_3 be the analytical semigroup generated by $A_1 = D_1 \times \Delta$, $A_2 = D_2 \times \Delta$ and $A_3 = D_3 \times \Delta$ respectively.

In the sequel, we will need the following results.

Lemma 3.6. *[22] If H, I and V are continuous from $[0, T]$ to $L^2(\Omega)$, then the integrals :*

$$I_1(t) = \int_0^t G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))d\tau,\ I_2(t) = \int_0^t G_2(t-\tau)\mathcal{G}(\tau, H(\tau), I(\tau), V(\tau))d\tau,$$
$$I_3(t) = \int_0^t G_3(t-\tau)\mathcal{Q}(\tau, H(\tau), I(\tau), V(\tau))d\tau,$$

exist and $I_1(t)$, $I_2(t)$ and $I_3(t)$ are continues on $[0, T[$ with $I_1(t) \in D(A_1)$, $I_2(t) \in D(A_2)$, $I_3(t) \in D(A_3)$ and $I_1(t) \to 0^+$ in L^2 as $t \to 0^+$, $I_2(t) \to 0^+$ in L^2 as $t \to 0^+$ and $I_3(t) \to 0^+$ in L^2 as $t \to 0^+$.

Lemma 3.7. *If the IBVP (3.8) has a classical solution, then H, I and V satisfy the following equalities :*

$$H(t) = G_1(t)H_0 + \int_0^t G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))d\tau, \quad (3.11)$$
$$I(t) = G_2(t)I_0 + \int_0^t G_2(t-\tau)\mathcal{G}(\tau, H(\tau), I(\tau), V(\tau))d\tau, \quad (3.12)$$
$$V(t) = G_3(t)V_0 + \int_0^t G_3(t-\tau)\mathcal{Q}(\tau, H(\tau), I(\tau), V(\tau))d\tau. \quad (3.13)$$

Proof. Consider the L^2-valued functions $\theta_j(\tau) = G_j(t-\tau)\omega_j(\tau)$, $j = 1, 2, 3$ with $\omega_1 = H$, $\omega_2 = I$ and $\omega_3 = V$. Then θ_j is differentiable since G_j is analytic and ω_j is differentiable. Then by Theorem 3.4, we have

$$\begin{aligned}
\frac{d\theta_1}{d\tau} &= \frac{d}{d\tau}\Big[G_1(t-\tau)\Big]H(\tau) + G_1(t-\tau)H'(\tau),\\
&= -D_1 \times \Delta\big(G_1(t-\tau)\big)H(\tau) + G_1(t-\tau)\big[D_1 \times \Delta H(\tau) + \mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))\big],\\
&= -D_1 \times \Delta\big(G_1(t-\tau)\big)H(\tau) + D_1 \times G_1(t-\tau) \times \Delta H(\tau) + G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau)),
\end{aligned}$$

According to corollary 3.5 with $\beta = 0$, we have

$$D_1 \times G_1(t-\tau)\Delta H(\tau) = D_1 \times \Delta G_1(t-\tau)H(\tau).$$

Therefore

$$\begin{aligned}
\frac{d\theta_1}{d\tau} &= -D_1 \times \Delta G_1(t-\tau)H(\tau) + D_1 \times \Delta G_1(t-\tau)H(\tau) + G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau)),\\
&= G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau)). \quad (3.14)
\end{aligned}$$

In the similar way, we also have :

$$\begin{aligned}
\frac{d\theta_2}{d\tau} &= \frac{d}{d\tau}\Big[G_2(t-\tau)\Big]I(\tau) + G_2(t-\tau)I^{'}(\tau),\\
&= -D_2 \times \Delta\big(G_2(t-\tau)\big)I(\tau) + D_2 \times G_2(t-\tau) \times \Delta I(\tau) + G_2(t-\tau)\mathcal{G}(\tau, H(\tau), I(\tau), V(\tau)),\\
&= G_2(t-\tau)\mathcal{G}(\tau, H(\tau), I(\tau), V(\tau)). \qquad (3.15)
\end{aligned}$$

$$\begin{aligned}
\frac{d\theta_3}{d\tau} &= \frac{d}{d\tau}\Big[G_3(t-\tau)\Big]V(\tau) + G_3(t-\tau)V^{'}(\tau),\\
&= -D \times \Delta G_3(t-\tau)V(\tau) + D \times G_3(t-\tau)\Delta V(\tau) + G_3(t-\tau)\mathcal{Q}(\tau, H(\tau), I(\tau), V(\tau)),\\
&= G_3(t-\tau)\mathcal{Q}(\tau, H(\tau), I(\tau), V(\tau)). \qquad (3.16)
\end{aligned}$$

Integrating equations (3.14), (3.15) and (3.16) with respect to time, we obtain equations (3.11), (3.12) and (3.13) respectively. □

Remark 3.3. Since in this work, $n = 3$, we take $p = 2$ so that $\beta > \frac{3}{4}$ and therefore the domain $D(\mathcal{H}^{\odot})$ is continuously embedded in $C_0^{\infty}(\Omega)$ by Lemma 3.2. Now, let H, I and V be continuous functions from $[0, T]$ to $D(\mathcal{H}^{\odot}) \hookrightarrow C_B^0(\Omega)$ satisfying (3.11), (3.12) and (3.13) respectively. We can then claim that H, I and V verify system (3.8). The continuity of H, I and V implies continuity of $t \mapsto \mathcal{F}(t, H(t), I(t), V(t))$, $t \mapsto \mathcal{G}(t, H(t), I(t), V(t))$ and $t \mapsto \mathcal{Q}(t, H(t), I(t), V(t))$.

One can then conclude that, the linear Cauchy problem

$$\begin{cases}
\partial_t y_1 - D_1\Delta y_1 = \mathcal{F}(t, H(t), I(t), V(t)),\\
\partial_t y_2 - D_2\Delta y_2 = \mathcal{G}(t, H(t), I(t), V(t)),\\
\partial_t y_3 - D\Delta y_3 = \mathcal{Q}(t, H(t), I(t), V(t)),\\
y_1(0) = H_0, y_2(0) = I_0, y_3(0) = V_0,
\end{cases}$$

has a unique solution, with y_1, y_2 and y_3 given by (3.11), (3.12) and (3.13) respectively.

Following [2], [4], [3], [22], [24], we have the following main result for the local existence of (2.4), based on L^2-theory.

Proposition 3.8. *If hypotheses (H1), (H2) and (H3) are satisfied, then the initial value and boundary problem (3.8) admits a unique solution* $(H, I, V) \in (C_B^0(]0, T], D(\mathcal{H}^{\beta})))^3$, *with* $H(0) = H_0 \in C_B^0(\Omega)$, $I(0) = I_0 \in C_B^0(\Omega)$ *and* $V(0) = V_0 \in C_B^0(\Omega)$.

The proof of this proposition is given in "Appendix A ".

3.2. **Boundedness of the solutions for IBVP (2.4).**

Proposition 3.9. *Let* $(H, I, V) \in \left(C^0\left(\overline{\Omega} \times [0, T)\right) \cap C_B^{2,1}(\Omega \times [0, T))\right)^3$
be the solution of (2.4) with bounded initial conditions i.e. $0 < H_0(x) < H_m$, $0 < I_0(x) < H_m$,

$0 < V_0(x) < V_m$ for all $x \in \overline{\Omega}$, and satisfying the boundary condition $\frac{\partial H_0}{\partial \eta} = 0$, $\frac{\partial I_0}{\partial \eta} = 0$, $\frac{\partial V_0}{\partial \eta} = 0$ on $\partial\Omega$. Then,

$$\forall (x,t) \in \overline{\Omega} \times [0,T], \quad H(x,t) \leq H_m, \quad I(x,t) \leq H_m \ \ \textit{and} \ \ V(x,t) \leq V_m$$

with

$$H_m = \max\left\{\frac{\lambda}{\delta_2}, \max_{x\in\bar{\Omega}}\{H(x,0)+I(x,0)\}\right\} \ \ \textit{and} \ \ V_m = \max\left\{\frac{(1-\varepsilon)kH_m}{\mu}, \max_{x\in\bar{\Omega}} V_0(x)\right\}.$$

Proof. Consider the function S defined for all $(x,t) \in \overline{\Omega} \times [0,T]$ by

$$S(x,t) = H(x,t) + I(x,t).$$

Adding the first two equations in (2.4), yields

$$\frac{\partial S(x,t)}{\partial t} - D_1 \Delta H(x,t) - D_2 \Delta I(x,t) = \lambda - dH(x,t) - \alpha I(x,t).$$

It follows that

$$\frac{\partial S(x,t)}{\partial t} - \max\{D_1, D_2\}\Delta\left(H(x,t)+I(x,t)\right) \ \ \leq \ \ \lambda - \min\{d,\alpha\}\left(H(x,t)+I(x,t)\right),$$

we have

$$\begin{cases} \frac{\partial S(x,t)}{\partial t} - \delta_1 \Delta S(x,t) \leq \lambda - \delta_2 S(x,t), \quad x \in \Omega, \quad t \in [0,T] \\ \\ \frac{\partial S(x,t)}{\partial \eta} = 0, \quad x \in \partial\Omega, \quad t \in [0,T] \\ S(x,0) = \max\limits_{x\in\bar{\Omega}} S_0(x), \end{cases} \tag{3.17}$$

where $S_0(x) = \{H(x,0)+I(x,0)\}$, $\delta_1 = \max\{D_1, D_2\}$ et $\delta_2 = \min\{d, \alpha\}$. By using the standard parabolic comparison of the scalar parabolic equations [33], one has

$$S(x,t) \leq \bar{S}(t),$$

where $\bar{S}(t) = \frac{\lambda}{\delta_2}\left(1 - e^{-\delta_2 t}\right) + \max\limits_{x\in\bar{\Omega}} S_0(x) e^{-\delta_2 t}$ is the solution of the problem

$$\begin{cases} \frac{d\bar{S}(t)}{dt} = \lambda - \delta_2 \bar{S}(t), \\ \\ \bar{S}(0) = \max\limits_{x\in\bar{\Omega}} S_0(x), \end{cases} \tag{3.18}$$

which dominates system (3.17). The general solution of (3.18) is on the form $\bar{S}(t) = k(t)e^{-\delta_2 t}$. By Lagrange's method, we have $k(t) = \frac{\lambda}{\delta_2} e^{\delta_2 t} + c$, $c \in \mathbb{R}$. Hence

$$\bar{S}(t) = \left(\frac{\lambda}{\delta_2} e^{\delta_2 t} + c\right) e^{-\delta_2 t}.$$

Initial condition yields $c = \max\limits_{x\in\bar{\Omega}} S_0(x) - \frac{\lambda}{\delta_2}$.

Therefore

$$\bar{S}(t) = \frac{\lambda}{\delta_2}\left(1 - e^{-\delta_2 t}\right) + \max_{x\in\bar{\Omega}} S_0(x) e^{-\delta_2 t}.$$

Then, it follows that :

$$\begin{aligned}
S(x,t) &\leq \bar{S}(t) \\
&\leq \frac{\lambda}{\delta_2}\left(1-e^{-\delta_2 t}\right)+\max_{x\in\bar{\Omega}} S_0(x)e^{-\delta_2 t} \\
&\leq \max\left\{\frac{\lambda}{\delta_2},\max_{x\in\bar{\Omega}} S_0(x)\right\}\left(1-e^{-\delta_2 t}\right)+\max\left\{\frac{\lambda}{\delta_2},\max_{x\in\bar{\Omega}} S_0(x)\right\}e^{-\delta_2 t} \\
&\leq \max\left\{\frac{\lambda}{\delta_2},\max_{x\in\bar{\Omega}} S_0(x)\right\}.
\end{aligned}$$

Thus,

$$S(x,t)\leq \max\left\{\frac{\lambda}{\delta_2},\max_{x\in\bar{\Omega}}\{H(x,0)+I(x,0)\}\right\}.$$

Therefore

$$S(x,t)\leq H_m=\max\left\{\frac{\lambda}{\delta_2},\max_{x\in\bar{\Omega}}\{H(x,0)+I(x,0)\}\right\},\forall (x,t)\in\Omega\times[0,T_{max}),$$

where T_{max} is the maximal time of existence of the solution of system (2.4), this implies that S is bounded.

Hence H and I are bounded since S is bounded. This prove that H and I are bounded.

Now, to show that V is bounded, from the third equation of IBVP (2.4), we have

$$\begin{aligned}
&\frac{\partial V(x,t)}{\partial t}-D_3\Delta V(x,t)\leq (1-\varepsilon)kI(x,t)-\mu V(x,t),\quad x\in\Omega,\quad t\in[0,T] \\
&\frac{\partial V(x,t)}{\partial \eta}=0,\quad x\in\partial\Omega,\quad t\in[0,T] \\
&V(x,0)=\max_{x\in\bar{\Omega}} V_0(x).
\end{aligned}$$

It follows from the previous system, inequality

$$\begin{cases}
\frac{\partial V(x,t)}{\partial t}-D\Delta V(x,t)\leq (1-\varepsilon)kH_m-\mu V(x,t) \\
\\
\frac{\partial V(x,t)}{\partial \eta}=0 \\
V(x,0)=\max_{x\in\bar{\Omega}} V_0(x),
\end{cases} \tag{3.19}$$

By using the standard parabolic comparison of the scalar parabolic equations [33], one has

$$V(x,t)\leq \overline{V}(t),$$

where $\overline{V}(t)=\frac{(1-\varepsilon)kH_m}{\mu}(1-e^{-\mu t})+\max_{x\in\bar{\Omega}} V_0(x)e^{-\mu t}$ is the solution of the problem

$$\begin{cases}
\frac{d\overline{V}(t)}{dt}=(1-\varepsilon)kH_m-\mu\overline{V}(t), \\
\\
\overline{V}(0)=\max_{x\in\overline{\Omega}} V_0(x),
\end{cases} \tag{3.20}$$

which dominates system (3.19). Indeed, the general solution of (3.20) is on the form $\overline{V}(t) = c(t)e^{-\mu t}$. By the Lagrange's method, we have $c(t) = \frac{(1-\varepsilon)kH_m}{\mu}(e^{\mu t}-1)+c_0$, $c_0 \in \mathbb{R}$.
thus,

$$\overline{V}(t) = \Big[\frac{(1-\varepsilon)kH_m}{\mu}(e^{\mu t}-1)+c_0\Big]e^{-\mu t}.$$

Initial condition yields $\max_{x\in\bar{\Omega}} V_0(x) = \overline{V}(0) = c_0$. It follows from that

$$\overline{V}(t) = \frac{(1-\varepsilon)kH_m}{\mu}(1-e^{-\mu t}) + \max_{x\in\bar{\Omega}} V_0(x)e^{-\mu t}.$$

Therefore

$$\begin{array}{rcl} V(x,t) & \leq & \overline{V}(t) \\ & \leq & \max\left\{\dfrac{(1-\varepsilon)kH_m}{\mu}, \max\limits_{x\in\bar{\Omega}} V_0(x)\right\}(1-e^{-\mu t}) + \max\left\{\dfrac{(1-\varepsilon)kH_m}{\mu}, \max\limits_{x\in\bar{\Omega}} V_0(x)\right\}e^{-\mu t} \\ & \leq & \max\left\{\dfrac{(1-\varepsilon)kH_m}{\mu}, \max\limits_{x\in\bar{\Omega}} V_0(x)\right\}. \end{array}$$

Since

$$V(x,t) \leq \overline{V}(t) \leq \max\left\{\frac{(1-\varepsilon)kH_m}{\mu}, \max_{x\in\bar{\Omega}} V_0(x)\right\}, \quad \forall (x,t) \in \overline{\Omega}\times[0,T_{max});$$

where T_{max} is the maximal time of existence of the solution of system (2.4), this implies that V is bounded.
Thus $H(x,t), I(x,t)$ and $V(x,t)$ are bounded on $\overline{\Omega}\times[0,T_{max})$. Therefore, it follows from the standard theory of semi-linear parabolic system in [23] that $T_{max} = +\infty$. This completes the proof of proposition 3.9. □

3.3. **Global existence, uniqueness and positivity for the IBVP (2.4).** We recast the IBVP (2.4) as follows:

$$\begin{cases} \dfrac{\partial w}{\partial t} - \overline{D}\Delta w + q(w)w = f(w) \quad \text{in } \Omega\times[0,T), \\ \dfrac{\partial w_1}{\partial \eta} = 0, \ \dfrac{\partial w_2}{\partial \eta} = 0, \ \dfrac{\partial w_3}{\partial \eta} = 0 \quad \text{on } \partial\Omega\times[0,T), \\ w(x,0) = w_0(x) \quad \text{in } \Omega, \end{cases} \tag{3.21}$$

where $w = (w_1, w_2, w_3)^T = (H, I, V)^T$, $\overline{D} = diag(D_1, D_2, D_3)$, $q(w) = diag\left(q_1(w), q_2(w), q_3(w)\right)$, $f(w) = \big(f_1(w), f_2(w), f_3(w)\big)^T$, with

$$q_1(w) = d + \frac{(1-\eta)\beta w_3}{\alpha_0 + \alpha_1 w_1 + \alpha_2 w_3 + \alpha_3 w_1 w_3}, \quad q_2(w) = (\alpha + \rho),$$

$$q_3(w) = \mu + \frac{u(1-\eta)\beta w_1}{\alpha_0 + \alpha_1 w_1 + \alpha_2 w_3 + \alpha_3 w_1 w_3}, \quad f_1(w) = \lambda + \rho w_2,$$

$$f_2(w) = \frac{(1-\eta)\beta w_1 w_3}{\alpha_0 + \alpha_1 w_1 + \alpha_2 w_3 + \alpha_3 w_1 w_3}, \quad f_3(w) = (1-\varepsilon)k w_2.$$

Note that $D_1, D_2, D_3 > 0$. Denote $\mathcal{H} = L^2(\Omega)$ and $E = H^1(\Omega)$ and define as in [12] the Hilbert space

$$W(0, T, E, E') = \left\{ u \in L^2\left((0, T), E\right) : \ \frac{\partial u}{\partial t} \in L^2\left((0, T), E'\right) \right\},$$

endowed with the norm

$$\|u\|_W^2 = \|u\|^2_{L^2((0,T),E)} + \left\|\frac{\partial u}{\partial t}\right\|^2_{L^2((0,T),E')}$$

and the following hypothesis for initial conditions:

$$w_{01} \in L^\infty(\Omega), w_{02}, w_{03} \in \mathcal{H} \text{ and } w_{0i} \geq 0 \text{ for } i \in \{1, 2, 3\}. \tag{3.22}$$

Here, we apply Theorem 2.7 of [12]. So, one approaches the solution by a sequence of solutions of linear equations. For $n = 0$, w^0 denotes the solution of

$$\begin{cases} \frac{\partial w^0}{\partial t} - \overline{D}\Delta w^0 = 0 & \text{in} \quad \Omega \times (0, T), \\ w^0(0) = w_0 & \text{in} \quad \Omega, \\ \frac{\partial w_i^0}{\partial \eta} = 0. & \text{on} \quad \partial\Omega \end{cases} \tag{3.23}$$

This equation admits a strong solution and $w^0 \geq 0$.

By induction, $w^n = ((w_1^n, w_1^n, w_1^n))$ denotes the solution of

$$\begin{cases} \frac{\partial w^n}{\partial t} - \overline{D}\Delta w^n + q(w^{n-1})w^n = f(w^{n-1}) & \text{in} \quad \Omega \times (0, T), \\ w^n(0) = w_0 & \text{in} \quad \Omega, \\ \frac{\partial w^n}{\partial \eta} = 0. & \text{on} \quad \partial\Omega. \end{cases} \tag{3.24}$$

Since (3.24) is a linear equation, $q_i(w^{n-1})$ and $f_i(w^{n-1})$ can replace a_0 and $f(t)$ of Corollary 2.10 in [12]. Suppose that there exists a unique nonnegative solution w_i^{n-1}. Assuming by induction that $w_i^j \geq 0$ for $0 \leq j \leq n-1$ and that by Proposition 3.9 w_i^j is bounded for $0 \leq j \leq n-1$, one has

$$0 \leq \frac{u(1-\eta)\beta w_1^{n-1}}{\alpha_0 + \alpha_1 w_1^{n-1} + \alpha_2 w_3^{n-1} + \alpha_3 w_1^{n-1} w_3^{n-1}} \leq u(1-\eta)\beta \tag{3.25}$$

which implies that

$$\mu \leq q_3(w^{n-1}) \leq \mu + u(1-\eta)\beta. \tag{3.26}$$

Since w_i^j are bounded , we have

$$d \leq q_1(w^{n-1}) \leq d + (1-\eta)\beta.$$

In addition, q_2 is a constant.

It then follows that $q_1(w^{n-1})$, $q_2(w^{n-1})$, $q_3(w^{n-1}) \in L^\infty(\Omega \times (0,T))$. We also have $f(w^{n-1}) \geq 0$ and $f(w^{n-1}) \in L^2((0,T),E')$. Then, by Corollary 2.10 of [12], there exists a unique solution $w^n \in W(0,T,E,E')$ with $w^n \geq 0$. Since $f_1(w) = \lambda + \rho w_2$, $f_2(w) = \frac{(1-\eta)\beta w_1 w_3}{\alpha_0+\alpha_1 w_1+\alpha_2 w_3+\alpha_3 w_1 w_3} \leq (1-\eta)\beta w_3$ and $f_3(w) = (1-\varepsilon)kw_2$, then $f_1(w^{n-1}) = \lambda + \rho w_2^{n-1}$, $f_2(w^{n-1}) \leq (1-\eta)\beta w_3^{n-1}$ and $f_3(w^{n-1}) = (1-\varepsilon)kw_2^{n-1}$ remain bounded in $L^2(]0,T[,E)$. We deduce that w_2^n and w_3^n remain bounded in $C^0([0,T],\mathcal{H})$ and $L^2((0,T),E)$.

Now, we deduce that the sequence $(w_i^n)_{n\geq 0}$ (one can extract a subsequence $(w_i^m)_{m\geq 0}$) converges weakly to w_i in $L^2((0,T),E)$ and weakly star in $L^\infty((0,T),\mathcal{H})$ to w_i. Applying Proposition 2.11 in [12], it holds that for all n,

$$w_i^n(t) \quad = \quad G_i(t)w_{0i} + \int_0^t G_i(t-s)g_i^n(s)ds, \tag{3.27}$$

where $G_i(t)$ is the semigroup generated by the unbounded operator $A_i = -D_iA_{\mathcal{H}}$, and

$$g_i^n(s) = -q_i(w^{n-1}(s))w_i^n(s) + f_i(w^{n-1}(s)). \tag{3.28}$$

Then, $g_i^n \in L^2((0,T),E)$. Since the sequence $(w_i^n)_{n\geq 0}$ is bounded in $C^0([0,T],\mathcal{H})$, the sequence $(g_i^n)_{n\geq 0}$ is bounded in $C^0([0,T],\mathcal{H})$. Now, consider the operator $\mathcal{G}_i$ from $C^0((0,T),\mathcal{H})$ into $C^0((0,T),\mathcal{H})$ defined by

$$\mathcal{G}_i(f) = \int_0^t G_i(t-s)f(s)ds. \tag{3.29}$$

Let us prove that $\mathcal{G}_i$ is a compact operator. Considering the triple $(L^2(\Omega), H^1(\Omega), a)$ with

$$a(w,v) = \sum_{j=1}^{3} \int_\Omega \frac{\partial w}{\partial x_j}\frac{\partial v}{\partial x_j}dx, \tag{3.30}$$

where Ω is regular and bounded. As in [12], the unbounded variational operator $A_{\mathcal{H}}$ associated to a is a positive symmetric operator with compact resolvent $R_\lambda(A_{\mathcal{H}})$. It admits a sequence $(\lambda_k)_k$ of positive eigenvalues with $\lim_{k\to+\infty} \lambda_k = +\infty$ and a Hilbert basis $(e_k)_k$ of $\mathcal{H}$ consisting of eigenvectors of $A_{\mathcal{H}}$. If $(G(t))_{t>0}$ is the semigroup generated by $-A_{\mathcal{H}}$, then for all $w_0 \in \mathcal{H}$,

$$G(t)w_0 = \sum_{k=0}^{+\infty} e^{-t\lambda_k}(w_0,e_k)e_k. \tag{3.31}$$

This proves that the operator is compact for all $t > 0$ since

$$\lim_{k\to+\infty} e^{-t\lambda_k} = 0.$$

We have the same formula for $G_i(t)$, and it suffices to replace λ_k by $D_i\lambda_k$. Setting

$$G_N(t)w = \sum_{k=0}^{N} e^{-t\lambda_k}(w, e_k)e_k, \tag{3.32}$$

one sees that $G_N(t)$ is an operator with finite rank which converges to $G(t)$. The following Theorem is relevant in the sequel.

Theorem 3.10. *[12] Let $t \mapsto G(t)$ be an application from $[0, +\infty)$ into $\mathcal{L}(\mathcal{H})$.*
One assumes that there exists a sequence of operators $(G_N(t))_{N\geq 0}$ on $\mathcal{H}$ verifying the following properties:

1) *for all N and all $t > 0$, $G_N(t)$ has finite rank independent of t,*
2) *$t \mapsto G_N(t)$ is continuous from $[0, +\infty)$ into $\mathcal{L}(\mathcal{H})$ for all N,*
3) *for $N \to +\infty$, $G_N(t)$ converges to $G(t)$ in $L^1(]0, T[, \mathcal{L}(\mathcal{H}))$ for all $T > 0$.*

Then the operator $\mathcal{G}$ is compact from $C^0([0, T], \mathcal{H})$ to $C^0([0, T], \mathcal{H})$ for all $T > 0$.

We are now in the position to prove the global existence, uniqueness and positivity of the solution to the IBVP (2.4).

Theorem 3.11. *If the initial condition satisfies (3.22), then the IBVP (3.21) admits a unique non-negative solution $w \in (W(0, T, E, E'))^3$.*

The proof of Theorem 3.11 is contained in "appendix B ".

Remark 3.4. It is worth noting that positivity of the solution may be proved by applying the maximum principle. Moreover, from the above results and the boundedness of the solution, one has observed that the solution of IBVP (2.4) enters the region:

$$\Sigma = \left\{(H, I, V) \in \Omega^3 \times \mathbb{R}^3_+ :\ 0 < H(x, t) \leq H_m, 0 < I(x, t) \leq H_m, 0 < V(x, t) \leq V_m\right\},$$

where

$$H_m = \max\left\{\frac{\lambda}{\delta_2}, \max_{x\in\overline{\Omega}}\{H(x, 0) + I(x, 0)\}\right\} \text{ et } V_m = \max\left\{\frac{(1-\varepsilon)kH_m}{\mu}, \max_{x\in\overline{\Omega}} V(x, 0)\right\}.$$

Hence the region Σ, of biological interest, is positively-invariant under the flow induced by IBVP (2.4).

4. Stability analysis of the spatially homogeneous equilibria

4.1. **HCV-spatial homogeneous uninfected equilibrium E_0.** The spatial homogeneous uninfected equilibrium of the PDE-model system (2.4) arises when there is no virus within a host i.e., V=0. Easy calculations shows that the HCV-spatial homogeneous uninfected equilibrium for PDE-model system (2.4) is given by

$$E_0 = (\Lambda, 0, 0)$$

where

$$\Lambda = \frac{\lambda}{d}.$$

4.2. **Basic reproduction number $\mathcal{R}_0$.** In order to define the Basic reproduction number $\mathcal{R}_0$ for system (2.4), we first observe that system (2.4) has a spatially homogeneous uninfected equilibrium E_0. It should be noted that one of the main tools in epidemic models is the basic reproduction number $\mathcal{R}_0$ which is an important threshold parameter to discuss the dynamic behaviour of the epidemic model. It quantifies the infection risk. It measures the expected average number of new infected hepatocytes generated by a single virion in a completely healthy hepatocyte. It should be also noted that, while a huge number of works deals with the threshold dynamics for ODE-models, very few studies are devoted to PDE-models. This is eventually due to the fact that the concept of basic reproduction number has just recently been extended to PDE-models such as reaction-diffusion and reaction-convection-diffusion epidemic models with mixed boundary conditions [37, 40]. The definition of $\mathcal{R}_0$ in this work follows the approach developed in [40].

In order to find the basic reproduction number $\mathcal{R}_0$ for the system (2.4), we obtain the following linear system at E_0 for the infected classes:

$$\begin{cases} \dfrac{\partial I}{\partial t} = D_2 \Delta I - (\alpha+\rho) I + \dfrac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} V \ \text{ in } \ \Omega_T, \\ \dfrac{\partial V}{\partial t} = D_3 \Delta V + (1-\varepsilon) k I - \mu V - \dfrac{u(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} V \ \text{ in } \ \Omega_T, \\ \dfrac{\partial I}{\partial \eta} = \dfrac{\partial V}{\partial \eta} = 0 \ \text{ on } \ \partial\Omega \times [0, T]. \end{cases} \tag{4.1}$$

Substituting $I(x,t) = e^{\lambda t}\psi_2(x)$ and $V(x,t) = e^{\lambda t}\psi_3(x)$ in (4.1), we obtain the following cooperative eigenvalue problem:

$$\begin{cases} \lambda\psi_2(x) = D_2\Delta\psi_2(x) - (\alpha+\rho)\psi_2(x) + \dfrac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\psi_3(x) \ \text{ in } \ \Omega, \\ \lambda\psi_3(x) = D_3\Delta\psi_3(x) + (1-\varepsilon)k\psi_2(x) - \mu\psi_3(x) - \dfrac{u(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\psi_3(x) \ \text{ in } \ \Omega, \\ \dfrac{\partial\psi_2(x)}{\partial\eta} = \dfrac{\partial\psi_3(x)}{\partial\eta} = 0 \ \text{ on } \ \partial\Omega. \end{cases} \tag{4.2}$$

As in [40], let T: $C(\bar{\Omega}, \mathbb{R}^2) \to C(\bar{\Omega}, \mathbb{R}^2)$ be the solution semigroup of the following reaction-diffusion system:

$$\begin{cases} \dfrac{\partial I}{\partial t} = D_2 \Delta I - (\alpha + \rho) I \text{ in } \Omega_T, \\ \dfrac{\partial V}{\partial t} = D_3 \Delta V + (1-\varepsilon) k I - \mu V - \dfrac{u(1-\eta)\beta\Lambda}{\alpha_0 + \alpha_1 \Lambda} V \text{ in } \Omega_T, \\ I(x,0) = \psi_2(x), \; V(x,0) = \psi_3(x), \text{ in } \Omega_T \\ \dfrac{\partial I}{\partial \eta} = \dfrac{\partial V}{\partial \eta} = 0 \text{ on } \partial\Omega. \end{cases} \tag{4.3}$$

Thus, with initial infection $\Psi(x) = (\psi_2, \psi_3)$ the distribution of those infections members becomes $T(t)\Psi(x)$ as time evolves. Therefore, the distribution of total new infections is

$$\int_0^\infty F(x) T(t) \Psi(x) dt,$$

then, we define

$$L(\phi)(x) := \int_0^\infty F(x) T(t) \Psi(x) dt = F(x) \int_0^\infty T(t) \Psi(x) dt.$$

L is a positive and continuous operator which maps the initial infection distribution to the distribution of the total infective members produced during the infection period. Applying the idea of next generation operators [40], we define the spectral radius of L as the basic reproduction number

$$\mathcal{R}_0 := \rho(L).$$

The matrices F and V defined as

$$F(x) = \begin{pmatrix} 0 & \frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} \\ 0 & 0 \end{pmatrix}, \quad V(x) = \begin{pmatrix} \alpha+\rho & 0 \\ -(1-\varepsilon)k & \left[\mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right] \end{pmatrix}.$$

Then

$$FV^{-1} = \frac{\alpha_0 + \alpha_1\Lambda}{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right]} \begin{pmatrix} \frac{(1-\eta)(1-\varepsilon)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda} & \frac{(\alpha+\rho)(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} \\ 0 & 0 \end{pmatrix}.$$

By [40] (theorem 3.4), one has

$$\mathcal{R}_0 = \frac{(1-\eta)(1-\varepsilon)k\beta\Lambda}{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right]}. \tag{4.4}$$

4.3. **Existence and uniqueness of HCV-spatial homogeneous infected equilibrium E^*.** In this section, we address the existence and uniqueness of infected spatial homogeneous equilibrium (2.4). The latter denoted as $E^* = (H^*, I^*, V^*)$ with $H^* \neq 0$, $I^* \neq 0$ et $V^* \neq 0$ satisfying the following algebraic system :

$$\begin{cases} \lambda - dH^* - (1-\eta)L(H^*, I^*, V^*)V^* + \rho I^* = & 0, \\ (1-\eta)L(H^*, I^*, V^*)V^* - (\alpha+\rho)I^* = & 0, \\ (1-\varepsilon)kI^* - \mu V^* - u(1-\eta)L(H^*, I^*, V^*)V^* = & 0, \end{cases} \tag{4.5}$$

where

$$L(H, I, V) = \frac{\beta H}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV}.$$

Adding the first and second equation of (4.5), we have

$$\lambda - dH^* - \alpha I^* = 0$$

which yields

$$I^* = \frac{\lambda - dH^*}{\alpha}. \tag{4.6}$$

As far as, using the second and third equation of (4.5), one has

$$-u(\alpha+\rho)I^* + (1-\varepsilon)kI^* - \mu V^* = 0,$$

i.e.,

$$V^* = \frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu} I^*,$$

hence

$$V^* = \frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu} \frac{\lambda - dH^*}{\alpha} \tag{4.7}$$

according to (4.6). The substitution of (4.7) in (4.5) yields :

$$(1-\eta)L\left(H^*, \frac{\lambda - dH^*}{\alpha}, \frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu} \frac{\lambda - dH^*}{\alpha}\right) \frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu} I^* - (\alpha+\rho)I^* = 0.$$

Thus, we have

$$(1-\eta)\Big((1-\varepsilon)k - u(\alpha+\rho)\Big) L\left(H^*, \frac{\lambda - dH^*}{\alpha}, \frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu} \frac{\lambda - dH^*}{\alpha}\right) = (\alpha+\rho)\mu$$

since $I^* \neq 0$. Furthermore, $I^* \geq 0$, gives $\frac{\lambda - dH^*}{\alpha} \geq 0$. Thus $H^* \leq \frac{\lambda}{d}$. Hence there is not a biological equilibrium when $H^* > \frac{\lambda}{d}$.

Let us consider the function ψ defined on $\left[0, \frac{\lambda}{d}\right]$ by :

$$\psi(x) \quad = \quad (1-\eta)\gamma L\left(x, \frac{\lambda - dx}{\alpha}, \frac{\gamma(\lambda - dx)}{\mu\alpha}\right) - (\alpha+\rho)\mu,$$

where

$$\gamma = (1-\varepsilon)k - u(\alpha+\rho).$$

We have

$$\psi(0) = -(\alpha+\rho)\mu < 0$$

and

$$\begin{aligned}
\psi\left(\frac{\lambda}{d}\right) &= (1-\eta)\gamma L\left(\frac{\lambda}{d},0,0\right) - (\alpha+\rho)\mu, \\
&= (1-\eta)\left[(1-\varepsilon)k - u(\alpha+\rho)\right]\frac{\beta\Lambda}{\alpha_0+\alpha_1\Lambda} - (\alpha+\rho)\mu, \\
&= \frac{(1-\eta)(1-\varepsilon)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda} - \frac{u(1-\eta)(\alpha+\rho)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} - (\alpha+\rho)\mu, \\
&= \frac{1}{\alpha_0+\alpha_1\Lambda}\left[(1-\eta)(1-\varepsilon)k\beta\Lambda - \mu(\alpha+\rho)(\alpha_0+\alpha_1\Lambda) - u(1-\eta)(\alpha+\rho)\beta\Lambda\right], \\
&= \frac{1}{\alpha_0+\alpha_1\Lambda}\Big[(1-\eta)(1-\varepsilon)k\beta\Lambda - (\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right]\Big], \\
&= \frac{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right]}{\alpha_0+\alpha_1\Lambda}(\mathcal{R}_0 - 1),
\end{aligned}$$

It follows that

$$\psi\left(\frac{\lambda}{d}\right) = \frac{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right]}{\alpha_0+\alpha_1\Lambda}(\mathcal{R}_0 - 1) > 0 \text{ if and only if } \mathcal{R}_0 > 1.$$

Moreover, letting $y = \dfrac{\lambda - d.x}{\alpha}$ and $z = \dfrac{\gamma(\lambda - d.x)}{\mu\alpha}$, we have

$$\begin{aligned}
\psi^{'}(x) &= (1-\eta)\gamma.\frac{d}{dx}\Big[L\left(x, \frac{\lambda-dx}{\alpha}, \frac{\gamma(\lambda-dx)}{\mu\alpha}\right) - (\alpha+\rho)\mu\Big], \\
&= (1-\eta)\gamma\left(\frac{\partial L}{\partial x} - \frac{d}{\alpha}\frac{\partial L}{\partial y} - \frac{\gamma d}{\mu\alpha}\frac{\partial L}{\partial z}\right), \\
&= (1-\eta)\gamma\left(\frac{\partial L}{\partial x} - \frac{d}{\alpha}\frac{\partial L}{\partial x}\frac{\partial x}{\partial y} - \frac{\gamma d}{\mu\alpha}\frac{\partial L}{\partial x}\frac{\partial x}{\partial z}\right), \\
&= (1-\eta)\gamma\left(\frac{\partial L}{\partial x} - \frac{d}{\alpha}\frac{\partial L}{\partial x}\left(-\frac{\alpha}{d}\right) - \frac{\gamma d}{\mu\alpha}\frac{\partial L}{\partial x}\left(-\frac{\mu\alpha}{\gamma d}\right)\right), \\
&= 3(1-\eta)\gamma\frac{\partial L}{\partial x}, \\
&= 3(1-\eta)\gamma\frac{\beta\alpha_0 + \beta\alpha_2 V}{(\alpha_0 + (\alpha_1+\alpha_3 V)x + \alpha_2 V)^2} > 0 \quad \text{if} \quad \gamma > 0.
\end{aligned}$$

Therefore, if $\mathcal{R}_0 > 1$ there exists a unique spatially homogeneous infected equilibrium $E^* = (H^*, I^*, V^*)$ with $H^* \in \left(0, \frac{\lambda}{d}\right)$, $I^* > 0$ and $V^* > 0$.

The previous investigations can be summarized in the following theorem :

Theorem 4.1. *1) If $\mathcal{R}_0 \leq 1$, then the PDE-system (2.4) admits a unique spatially homogeneous uninfected equilibrium $E_0 = \left(\frac{\lambda}{d}, 0, 0\right)$.*
2) If $\mathcal{R}_0 > 1$ and $\gamma > 0$, then the PDE system (2.4) admits a unique spatially homogeneous infected equilibrium $E^* = (H^*, I^*, V^*)$ with $H^* \in \left(0, \frac{\lambda}{d}\right)$, $I^* > 0$ and $V^* > 0$.

Remark 4.1. Due to the spatial dependence of the state variables, spatially-inhomogeneous steady states can exist.

Indeed, any spatially-inhomogeneous equilibrium point $E = (H, I, V)$ of the model (2.4) subject to the homogeneous Neumann boundary condition must solve the following system.

$$\begin{cases} D_1\Delta H + \lambda - dH - \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} + \rho I = 0, \\ D_2\Delta I + \dfrac{(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} - (\alpha+\rho)I = 0, \\ D_3\Delta V + (1-\varepsilon)kI - \mu V - \dfrac{u(1-\eta)\beta HV}{\alpha_0 + \alpha_1 H + \alpha_2 V + \alpha_3 HV} = 0, \\ \dfrac{\partial H}{\partial \eta} = \dfrac{\partial I}{\partial \eta} = \dfrac{\partial V}{\partial \eta} = 0. \end{cases} \tag{4.8}$$

Investigation of the local stability of such spatially-inhomogeneous equilibria will be the concern of a forthcoming paper via an in-depth analysis of the above system.

4.4. **Local stability of HCV-uninfected equilibrium.** The objective of this section is to discuss the local stability of the spatially homogeneous uninfected equilibrium for the PDE system (2.4). We address local stability by analysing the characteristic equation.

Theorem 4.2. *The spatially homogeneous uninfected equilibrium E_0 of PDE-model system (2.4) is locally asymptotically stable if $\mathcal{R}_0 \le 1$ and it is unstable if $\mathcal{R}_0 > 1$.*

Proof. Let $\{\mu_l, \varphi_l\}$ be an eigenpair of the Laplace operator $-\Delta$ on Ω with the homogeneous Neumann boundary condition where $0 = \mu_1 < \mu_2 < \mu_3 < \cdots$. Let E_{μ_l} be the eigenspace corresponding to μ_l in $C^1(\Omega)$ and $\{\varphi_{lj}, j = 1, 2, \cdots, \dim E_{\mu_l}\}$ be an orthogonal basis of E_{μ_l}. Let $\mathbb{X} = (C^1(\Omega))^3$ and $\mathbb{X}_{lj} = \{\varphi_{lj} c, \ / \ c \in \mathbb{R}^3\}$.
Consider the following direct sum

$$\mathbb{X} = \bigoplus_{l=1}^{\infty} \mathbb{X}_l \ \text{ with } \ \mathbb{X}_l = \bigoplus_{j=1}^{dimE_{\mu_l}} \mathbb{X}_{lj},$$

where $\mathbb{X}_{lj}$ is the eigenspace corresponding to μ_l. Linearizing (2.4) at the spatially homogeneous uninfected equilibrium E_0 we obtain the following linearized system :

$$\begin{cases} \dfrac{\partial w_1}{\partial t} = D_1\Delta w_1 - dw_1 + \rho w_2 - \dfrac{(1-\eta)\beta\Lambda}{\alpha_0 + \alpha_1\Lambda} w_3, \\ \dfrac{\partial w_2}{\partial t} = D_2\Delta w_2 - (\alpha+\rho)w_2 + \dfrac{(1-\eta)\beta\Lambda}{\alpha_0 + \alpha_1\Lambda} w_3, \\ \dfrac{\partial w_3}{\partial t} = D_3\Delta w_3 + (1-\varepsilon)kw_2 - \Big[\mu + u\dfrac{(1-\eta)\beta\Lambda}{\alpha_0 + \alpha_1\Lambda}\Big] w_3, \end{cases} \tag{4.9}$$

where $W = (w_1, w_2, w_3)^T = (H, I, V)^T$.

From the previous system (4.9), we obtain

$$W_t = \mathcal{L}W = \overline{D}\Delta W + \mathcal{K}(E_0)W$$

where

$$\mathcal{K}(E_0)W = \begin{pmatrix} -dw_1 + \rho w_2 - \frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} w_3 \\ -(\alpha+\rho)w_2 + \frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} w_3 \\ (1-\varepsilon)kw_2 - \left(\mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) w_3 \end{pmatrix}. \tag{4.10}$$

For each $l \geq 1$, $\mathbb{X}_l$ is invariant under the operator $\mathcal{L}$, and $\tilde{\lambda}$ is an eigenvalue of $\mathcal{L}$ if and only if it is an eigenvalue of the matrix $-\mu_l\overline{D} + \mathcal{K}(E_0)$ for some $l \geq 1$, in which case, there is an eigenvector in $\mathbb{X}_l$. So, one has

$$det\left(-\mu_l\overline{D} + \mathcal{K}(E_0) - \tilde{\lambda}Id\right) = \begin{vmatrix} -\left(\mu_l D_1 + d + \tilde{\lambda}\right) & \rho & -\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} \\ 0 & -\left(\mu_l D_2 + (\alpha+\rho) + \tilde{\lambda}\right) & \frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} \\ 0 & (1-\varepsilon)k & -\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) - \tilde{\lambda} \end{vmatrix}$$

The characteristic equation of $-\mu_l\overline{D} + \mathcal{K}(E_0)$ is

$$-\left(\mu_l D_1 + d + \tilde{\lambda}\right)\left[\left[\mu_l D_2 + (\alpha+\rho) + \tilde{\lambda}\right]\left[\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) + \tilde{\lambda}\right] - \frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right] = 0, \tag{4.11}$$

from (4.11), we get

$$\tilde{\lambda}_0 = -\mu_l D_1 - d < 0,$$

and another characteristic eigenvalues are the roots of the following equation :

$$\tilde{\lambda}^2 + B\tilde{\lambda} + (\mu_l D_2 + \alpha + \rho)\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) - \frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda} = 0, \tag{4.12}$$

where

$$B = \left[\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) + \mu_l D_2 + (\alpha+\rho)\right].$$

Let

$$C = (\mu_l D_2 + \alpha + \rho)\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) - \frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda}.$$

One has,

$$\begin{aligned} C &= \mu_l D_2\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) + (\alpha+\rho)\mu_l D_3 + (\alpha+\rho)\left(\mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) \\ &- \frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{\alpha_0+\alpha_1\Lambda}, \\ &= \mu_l D_2\left(\mu_l D_3 + \mu + u\frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda}\right) + (\alpha+\rho)\mu_l D_3 \\ &+ \frac{1}{\alpha_0+\alpha_1\Lambda}\Big[(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda) + u(1-\eta)\beta\Lambda\right] - (1-\varepsilon)(1-\eta)k\beta\Lambda\Big], \end{aligned}$$

$$
\begin{aligned}
&= \mu_l D_2 \left(\mu_l D_3 + \mu + u \frac{(1-\eta)\beta\Lambda}{\alpha_0+\alpha_1\Lambda} \right) + (\alpha+\rho)\mu_l D_3 \\
&+ \frac{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda)+u(1-\eta)\beta\Lambda\right]}{\alpha_0+\alpha_1\Lambda}(1-\mathcal{R}_0).
\end{aligned}
$$

Since $B > 0$, if $\mathcal{R}_0 \leq 1$ then C is also positive. Hence by virtue of the Routh-Hurwitz criterion, equation (4.12) does not admit solution with positive real part. Thus none characteristic eigenvalue have positive real part. Therefore if $\mathcal{R}_0 \leq 1$, the spatially homogeneous uninfected equilibrium $E_0 = \left(\frac{\lambda}{d}, 0, 0\right)$ of (2.4) is locally asymptotically stable.

Otherwise if $\mathcal{R}_0 > 1$, then for $l = 1$, (in this case $\mu_1 = 0$) one has,

$$
C = \frac{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda)+u(1-\eta)\beta\Lambda\right]}{\alpha_0+\alpha_1\Lambda}(1-\mathcal{R}_0) < 0.
$$

Hence there is a complex root of equation (4.12) with positive real part in the spectrum of $\mathcal{K}$ according to Routh-Hurwitz criterion. Therefore the uninfected equilibrium $E_0 = \left(\frac{\lambda}{d}, 0, 0\right)$ of (2.4) is unstable. This completes the proof of Theorem 4.2. □

4.5. **Global stability of HCV-Uninfected equilibrium.** The objective of this section is to discuss the global stability of the spatially homogeneous uninfected equilibrium for the PDE system (2.4). We address global stability by using the construction of Lyapunov functional method. This Lyapunov functional is obtained from those of differential equations by applying the method presented in [15]. For this purpose, we start by letting

$$
\tau_0 = \frac{(1-\varepsilon)k(1-\eta)\beta\Lambda}{\mu\alpha_0(\alpha+\rho)}.
$$

Then, it is easy to see that

$$
\frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{(\alpha+\rho)\left[\mu(\alpha_0+\alpha_1\Lambda)+u(1-\eta)\beta\Lambda\right]} \leq \frac{(1-\varepsilon)k(1-\eta)\beta\Lambda}{\mu\alpha_0(\alpha+\rho)},
$$

i.e.,

$$
\mathcal{R}_0 \leq \tau_0.
$$

We state the following result on global stability at E_0 as follows :

Theorem 4.3. *The spatially homogeneous uninfected equilibrium E_0 of PDE-model system (2.4) is globally asymptotically stable in the positively-invariant region Σ if $\tau_0 < 1$.*

Proof. Let us consider the following function

$$
G_1(t) = \frac{(1-\varepsilon)k}{\alpha+\rho} I(t) + V(t).
$$

Then, the differentiation of G_1 with respect to t gives

$$
\frac{dG_1}{dt} = \left(\frac{(1-\varepsilon)k - u(\alpha+\rho)}{\mu(\alpha+\rho)(\alpha_0+\alpha_1 H+\alpha_2 V+\alpha_3 HV)}(1-\eta)\beta H - 1 \right) \mu V.
$$

Since $H \leq \frac{\lambda}{d} = \Lambda$ in the positively-invariant region Σ, one has

$$\begin{aligned}
\frac{dG_1}{dt} &\leq \left[\frac{\big[(1-\varepsilon)k - u(\alpha+\rho)\big](1-\eta)\beta\Lambda}{\mu\alpha_0(\alpha+\rho)} - 1\right]\mu V,\\
&\leq \left[\frac{(1-\varepsilon)(1-\eta)k\beta\Lambda}{\mu\alpha_0(\alpha+\rho)} - 1\right]\mu V,\\
&\leq (\tau_0 - 1)\mu V.
\end{aligned}$$

Now, we define the Lyapunov function as follows

$$L_1 = \int_\Omega G_1 dx.$$

The computation of the time derivative of L_1 along the positive solutions of the PDE-model system (2.4) yields

$$\begin{aligned}
\frac{dL_1}{dt} &= \frac{d}{dt}\Big[\int_\Omega G_1 dx\Big],\\
&= \int_\Omega \frac{dG_1}{dt} dx,\\
&\leq \int_\Omega \Big[(\tau_0 - 1)\mu V\Big] dx.
\end{aligned}$$

It is clear that the condition $\tau_0 \leq 1$ gives $\frac{dL_1}{dt} \leq 0$ for all H, I, V > 0. We note that the solutions of system (2.4) are limited by Υ, the greatest invariant subset of E=$\Big\{(H, I, V) \in \Sigma | \frac{dL_1}{dt} = 0\Big\}$. We realize that $\frac{dL_1}{dt} = 0$ if and only if V $= 0$ and I $= 0$. Each element of Υ satisfies V $= 0$ and consequently I=0. By Lyapunov-LaSalle invariance principle [27], E_0 is globally asymptotically stable if $\tau_0 < 1$. So, we obtain a sufficient condition $\mathcal{R}_0 \leq \tau_0$ which ensures that the HCV spatially homogeneous equilibrium E_0 of PDE-model system (2.4) is globally asymptotically stable if $\tau_0 < 1$. This completes the proof of theorem 4.3. □

4.6. **Local stability of HCV spatially homogeneous infected equilibrium.** Let us study the local stability of the unique infected spatially homogeneous equilibrium E^* of our PDE-model system. Consider the Laplace operator $-\Delta$ and let $0 = \mu_1 < \mu_2 < \mu_3 < \cdots$ be its eigenvalues on Ω with the homogeneous Neumann boundary condition, and E_{μ_l} be the eigenspace corresponding to μ_l in $C^1(\Omega)$. Let also $\mathbb{X} = (C^1(\Omega))^3$, $\{\varphi_{lj}, j = 1, 2, \cdots, dimE_{\mu_l}\}$ be an orthogonal basis of E_{μ_l} and $\mathbb{X}_{lj} = \{\varphi_{lj} c \ / \ c \in \mathbb{R}^3\}$.

Then,

$$\mathbb{X} = \bigoplus_{l=1}^{\infty} \mathbb{X}_l \ \text{ with } \ \mathbb{X}_l = \bigoplus_{j=1}^{dimE_{\mu_l}} \mathbb{X}_{lj}.$$

Now, let set $w_1 = H$, $w_2 = I$, $w_3 = V$. Further we use the vector notation $W = (w_1, w_2, w_3)^T = (H, I, V)^T$. Then the linearization of the PDE system at E^* is of the form

$$W_t = \mathcal{L}W = \overline{D}\Delta W + \mathcal{K}(E^*)W,$$

where

$$\mathcal{K}(E^*)W = \begin{pmatrix} -(d+A)\,w_1 + \rho w_2 - Bw_3 \\ Aw_1 - (\alpha+\rho)w_2 + Bw_3 \\ -uAw_1 + (1-\varepsilon)kw_2 - (\mu+uB)\,w_3 \end{pmatrix}, \tag{4.13}$$

with

$$A = \frac{(1-\eta)(\alpha_0+\alpha_2 V^*)\beta V^*}{(\alpha_0+\alpha_1 H^*+\alpha_2 V^*+\alpha_3 H^* V^*)^2}$$

and

$$B = \frac{(1-\eta)(\alpha_0+\alpha_1 H^*)\beta H^*}{(\alpha_0+\alpha_1 H^*+\alpha_2 V^*+\alpha_3 H^* V^*)^2}.$$

For each $l \geq 1$, $\mathbb{X}_l$ is invariant under the operator $\mathcal{L}$, and $\tilde{\lambda}$ is an eigenvalue $\mathcal{L}$ if and only if it is an eigenvalue of the matrix $-\mu_l\overline{D} + \mathcal{K}(E^*)$ for some $l \geq 1$, in which case, there is an eigenvector in $\mathbb{X}_l$. Therefore we get:

$$det\Big(-\mu_l\overline{D} + \mathcal{K}(E^*) - \tilde{\lambda} Id \Big) = \begin{vmatrix} -(\mu_l D_1 + d + A) - \tilde{\lambda} & \rho & -B \\ A & -(\mu_l D_2 + \alpha + \rho) - \tilde{\lambda} & B \\ -uA & (1-\varepsilon)k & -(\mu_l D_3 + \mu + uB) - \tilde{\lambda} \end{vmatrix}.$$

The characteristic equation of $-\mu_l\overline{D} + \mathcal{K}(E^*)$ is on the form

$$\tilde{\lambda}^3 + a_2\tilde{\lambda}^2 + a_1\tilde{\lambda} + a_0 = 0 \tag{4.14}$$

where

$$a_2 = (\mu_l D_1 + d + A + \mu_l D_2 + \alpha + \rho + \mu_l D_3 + \mu + uB) > 0,$$

$$a_1 = (\mu_l D_1 + d + A)(\mu_l D_2 + \alpha + \rho + \mu_l D_3 + \mu + uB) + (\mu_l D_2 + \alpha + \rho)(\mu_l D_3 + \mu + uB) - (1-\varepsilon)kB,$$

$$a_0 = (\mu_l D_1 + d + A)(\mu_l D_2 + \alpha + \rho)(\mu_l D_3 + \mu + uB) - (\mu_l D_1 + d + A)(1-\varepsilon)kB.$$

If $a_1 > 0$ and $a_1 a_2 > a_0$ from the above investigations, it then follows from Routh-Hurwitz criterion that all roots of (4.14) have negative real parts and therefore we have the following result.

Theorem 4.4. *If $a_1 > 0$ and $a_1 a_2 > a_0$, then the spatially homogeneous infected equilibrium $E^* = (H^*, I^*, V^*)$ of the PDE-model system (2.4) is locally asymptotically stable when it exists.*

4.7. **Global stability of HCV-spatially homogeneous infected equilibrium.** The objective of this section is to discuss the global stability of the spatially homogeneous infected equilibrium E^* for the PDE system (2.4). We address global stability by using the method of construction of Lyapunov functionals. These Lyapunov functional is obtained from those for differential equations by applying the method of Hattaf and Yousfi presented in [15]. We address this study with certain assumptions namely : $u = 0$ (i.e., there is no absorption effect), $\alpha_0 = 1$ et $\alpha_3 = \alpha_1\alpha_2$. Thus we have the following results.

Theorem 4.5. *The spatially homogeneous infected equilibrium E^* of PDE-model system (2.4) is globally asymptotically stable when it exists.*

Proof. We first define the function

$$
\begin{aligned}
G_2(H,I,V) &= H - H^* - \int_{H^*}^{H} \frac{(\alpha+\rho)I^*}{\frac{(1-\eta)\beta\tau V^*}{(1+\alpha_1\tau)(1+\alpha_2 V^*)}} d\tau + I - I^* - I^* \ln(\frac{I}{I^*}) \\
&+ \frac{\alpha+\rho}{(1-\varepsilon)k}(\alpha_0+\alpha_2 V^*)\left(V - V^* - \int_{V^*}^{V} \frac{(\alpha+\rho)I^*}{\frac{(1-\eta)\beta\tau H^*}{(1+\alpha_1 H^*)(1+\alpha_2\tau)}} d\tau\right).
\end{aligned}
$$

Then, the computation of the derivative of G_2 with respect to t yields :

$$
\begin{aligned}
\frac{dG_2}{dt} =& \left[\lambda - dH - \alpha I - \frac{(\alpha+\rho)\mu}{(1-\varepsilon)k}V\right] \\
&- (\alpha+\rho)I^* \frac{(1+\alpha_1 H)(1+\alpha_2 V^*)}{(1-\eta)\beta H V^*}\left[\lambda - dH - \frac{(1-\eta)\beta HV}{(1+\alpha_1 H)(1+\alpha_2 V)} + \rho I\right] \\
&- \frac{I^*}{I}\left[\frac{(1-\eta)\beta HV}{(1+\alpha_1 H)(1+\alpha_2 V)} - (\alpha+\rho)I\right] - \frac{\alpha+\rho}{(1-\varepsilon)k}\frac{V^*}{V}\left[(1-\varepsilon)kI - \mu V\right].
\end{aligned}
$$

Since

$$
\frac{(1-\eta)\beta H^* V^*}{(1+\alpha_1 H^*)(1+\alpha_2 V^*)} = (\alpha+\rho)I^*,
$$

$$
\lambda = dH^* + \alpha I^*,
$$

and

$$
\frac{(\alpha+\rho)\mu}{(1-\varepsilon)k} = \frac{(\alpha+\rho)I^*}{V^*},
$$

we have

$$
\begin{aligned}
\frac{dG_2}{dt} &= \left[dH^* + \alpha I^* - dH - \alpha I - (\alpha+\rho)I^*\frac{V}{V^*}\right] \\
&\quad -(\alpha+\rho)I^* \frac{(1+\alpha_1 H)(1+\alpha_2 V^*)}{(1-\eta)\beta H V^*}\left[dH^* + \alpha I^* - dH - \frac{(1-\eta)\beta HV}{(1+\alpha_1 H)(1+\alpha_2 V)} + \rho I\right] \\
&\quad -\frac{I^*}{I}\left[\frac{(1-\eta)\frac{(1+\alpha_1 H^*)(1+\alpha_2 V^*)(\alpha+\rho)I^*}{(1-\eta)H^* V^*}HV}{(1+\alpha_1 H)(1+\alpha_2 V)} - (\alpha+\rho)I\right] - (\alpha+\rho)I\frac{V^*}{V} + \frac{(\alpha+\rho)\mu}{(1-\varepsilon)k}V^*,
\end{aligned}
$$

$$
\begin{aligned}
=& \left[dH^* + (\alpha+\rho)I^* - \rho I^* - dH - \alpha I - (\alpha+\rho)I^*\frac{V}{V^*}\right] \\
&- \Big[\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}dH^* + \frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\alpha I^* - \frac{1+\alpha_1 H}{1+\alpha_1 H^*}dH^* - \frac{V}{V^*}\frac{1+\alpha_2 V^*}{1+\alpha_2 V}(\alpha+\rho)I^* \\
&+ \frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\rho I\Big] \\
&+ (\alpha+\rho)I^*\left[1 - \frac{HI^*V(1+\alpha_1 H^*)(1+\alpha_2 V^*)}{H^* I V^*(1+\alpha_1 H)(1+\alpha_2 V)}\right] + (\alpha+\rho)I^*\left(1 - \frac{I}{I^*}\frac{V^*}{V}\right),
\end{aligned}
$$

$$
\begin{aligned}
=& dH^*\left[1-\frac{H}{H^*}-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}+\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\right]\\
&+(\alpha+\rho)I^*\left[1-\frac{HI^*V(1+\alpha_1 H^*)(1+\alpha_2 V^*)}{H^*IV^*(1+\alpha_1 H)(1+\alpha_2 V)}+\frac{V}{V^*}\frac{1+\alpha_2 V^*}{1+\alpha_2 V}\right]\\
&+(\alpha+\rho)I^*\left(2-\frac{V}{V^*}-\frac{I}{I^*}\frac{V^*}{V}\right)-\alpha I^*\left(\frac{\rho}{\alpha}+\frac{I}{I^*}\right)-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\alpha I^*-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\rho I,
\end{aligned}
$$

$$
\begin{aligned}
=& -\frac{d(H-H^*)^2}{H(1+\alpha_1 H^*)}+(\alpha+\rho)I^*\left[-1-\frac{V}{V^*}+\frac{V}{V^*}\frac{1+\alpha_2 V^*}{1+\alpha_2 V}+\frac{1+\alpha_2 V}{1+\alpha_2 V^*}\right]\\
&+(\alpha+\rho)I^*\left[4-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}-\frac{HI^*V(1+\alpha_1 H^*)(1+\alpha_2 V^*)}{H^*IV^*(1+\alpha_1 H)(1+\alpha_2 V)}-\frac{I}{I^*}\frac{V^*}{V}-\frac{1+\alpha_2 V}{1+\alpha_2 V^*}\right]\\
&-\alpha I^*\left(\frac{\rho}{\alpha}+\frac{I}{I^*}\right)-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\alpha I^*-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}\rho I+(\alpha+\rho)I^*\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}.
\end{aligned}
$$

Therefore

$$
\begin{aligned}
\frac{dG_2}{dt}=& -\frac{d(H-H^*)^2}{H(1+\alpha_1 H^*)}-\frac{\alpha_2(\alpha+\rho)I^*(V-V^*)^2}{V^*(1+\alpha_2 V^*)(1+\alpha_2 V)}-\alpha I^*\left(\frac{\rho}{\alpha}+\frac{I}{I^*}\right)\\
&+(\alpha+\rho)I^*\left[4-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}-\frac{HI^*V(1+\alpha_1 H^*)(1+\alpha_2 V^*)}{H^*IV^*(1+\alpha_1 H)(1+\alpha_2 V)}-\frac{I}{I^*}\frac{V^*}{V}-\frac{1+\alpha_2 V}{1+\alpha_2 V^*}\right].
\end{aligned}
$$

We have :

$$
(\alpha+\rho)I^*\left[4-\frac{H^*}{H}\frac{1+\alpha_1 H}{1+\alpha_1 H^*}-\frac{HI^*V(1+\alpha_1 H^*)(1+\alpha_2 V^*)}{H^*IV^*(1+\alpha_1 H)(1+\alpha_2 V)}-\frac{I}{I^*}\frac{V^*}{V}-\frac{1+\alpha_2 V}{1+\alpha_2 V^*}\right]\leq 0
$$

since the left side of the latter inequality is the difference between the geometric mean and the arithmetic mean. That is $\frac{dG_2}{dt}\leq 0$. Otherwise $\frac{dG_2}{dt}=0$ if and only if $H=H^*$, $I=I^*$ et $V=V^*$. Thus G_2 is a Lyapunov functional of the differential equation associated to the PDE-model system (2.4). Therefore using Lyapunov-LaSalle invariance principle [27] combined to the method presented in [15], the functional defined by

$$L_2(t)=\int_{\Omega}G_2(t)dx$$

is a Lyapunov functional of the PDE-model system (2.4) at the spatially homogeneous infected equilibrium E^*. Therefore E^* is globally asymptotically stable. This completes the proof of Theorem 4.5. □

5. Numerical simulations

In this section, we present the numerical simulations to illustrate our theoretical results. To simplify, we consider IBVP (2.4) with $\Omega=(1)$ under Neumann boundary condition

$$\frac{\partial H}{\partial \nu}=0,\ \frac{\partial I}{\partial \nu}=0,\ \frac{\partial V}{\partial \nu}=0\quad t>0,\quad x=1 \tag{5.1}$$

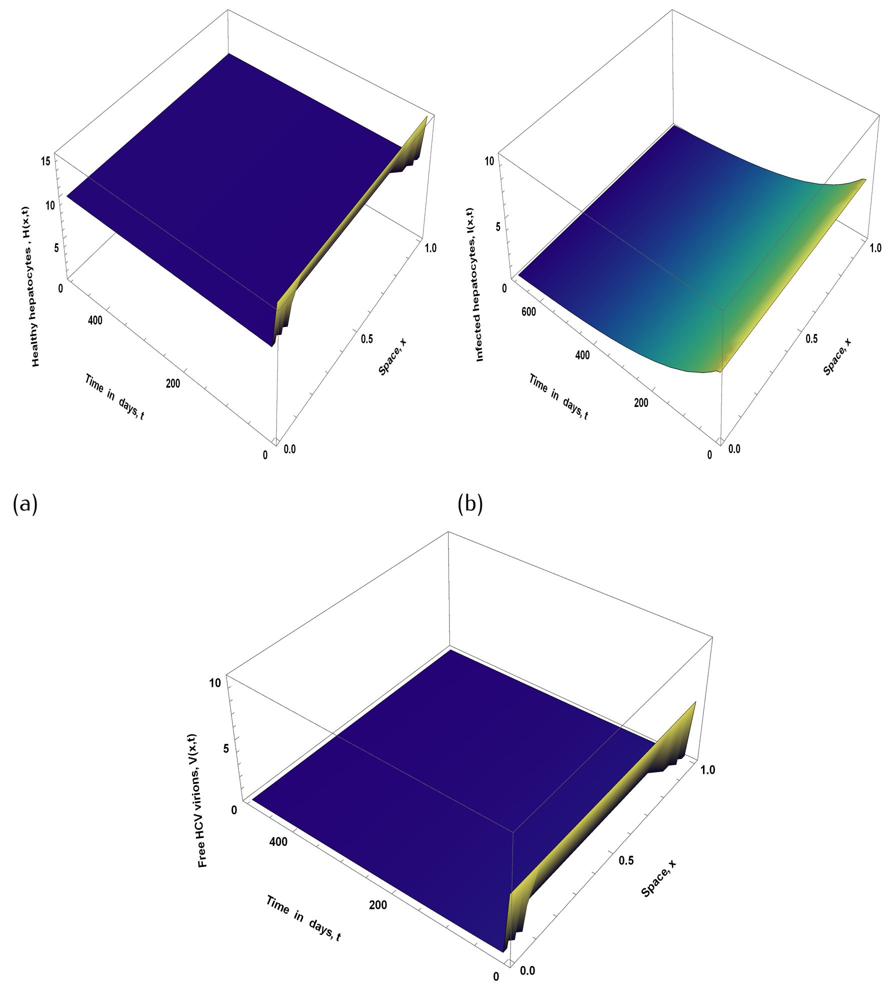
and, following initial conditions

$$H(x,0)=5,\quad I(x,0)=5,\quad V(x,0)=5, \tag{5.2}$$

and

$$H(x,0) = 15, \quad I(x,0) = 5, \quad V(x,0) = 5. \tag{5.3}$$

Now we choose the numerical values of the parameters for the PDE-cellular model system (2.4) as follows: $\lambda = 50$; $d = 5$; $\rho = 0,01$; $\alpha = 0,05$; $D_1 = D_2 = D_3 = 0,1$; $\eta = 0,00004$; $\alpha_3 = 0,03$; $\varepsilon = 0,5$; $\alpha_2 = 0,02$; $k = 2$; $\alpha_1 = 0,1$; $\mu = 20$; $\alpha_0 = 1$; $\beta = 0,24$ et $u = 1$. By calculation we have $\mathcal{R}_0 = 0.943361$. In this case, PDE-cellular model system (2.4) has a spatially homogeneous equilibrium $E_0 = (10,0,0)$. Hence by Theorem 4.3 E_0 is globally asymptotically stable. Numerical simulation illustrates our result (see FIGURE 1). Otherwise we choose the numerical values of

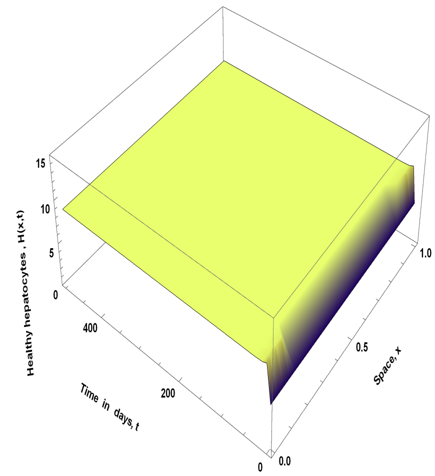


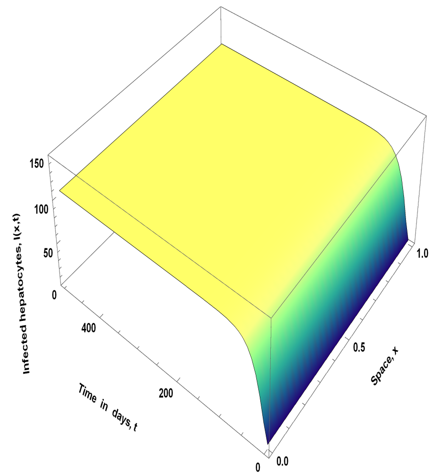
(a) (b) (c)

FIGURE 1. Simulations of IBVP (2.4) under Neumann boundary conditions (5.1) and initial condition (5.2)

the parameters for the PDE-cellular model system (2.4) as follows : $\lambda = 50$; $d = 5$; $\rho = 0,01$; $\alpha = 0,05$; $D_1 = D_2 = D_3 = 0,1$; $\eta = 0,00004$; $\varepsilon = 0,5$; $\alpha_0 = 1$; $\alpha_1 = 0,1$; $\alpha_2 = 0,02$; $\alpha_3 = 0,03$; $k = 2$; $\mu = 2$; $\beta = 0,24$ et $u = 1$. By calculation we have $\mathcal{R}_0 = 6.25009$. In this case, PDE-cellular model system (2.4) has a spatially homogeneous equilibrium $E^* = (5;500;235)$.

Hence by Theorem 4.5 E^* is globally asymptotically stable. Numerical simulation illustrates our result (see FIGURE 2).





(a) (b) (c)

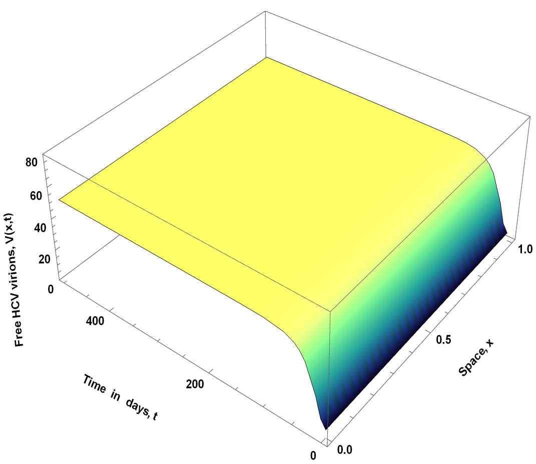


FIGURE 2. Simulations of IBVP (2.4) under Neumann boundary conditions (5.1) and initial condition (5.3)

6. Conclusion

In this work, we addressed the dynamics of a reaction diffusion HCV intra-host infection model with the Hattaf-Yousfi incidence rate, which is a generalized non-linear incidence rate. The object of this work was to make a mathematical analysis of a cellular model of HCV infection which assumes that virions diffuse into the liver, which uses the Hattaf-Yousfi functional response generalizing most of the functional responses that exist. Our model also takes into account the absorption effect which is much neglected in the literature. We first showed that the initial value and boundary problem (2.4) admits a unique global solution in time. And secondly, we have shown that this unique solution is positive and uniformly bounded. Then, we determined the expression of basic reproduction number $\mathcal{R}_0$ which is the parameter from which we studied the dynamics of our model at equilibria whose existence and uniqueness of these have been previously proven. More precisely, we have shown that, if $\mathcal{R}_0 < 1$, the unique uninfected equilibrium point is locally and globally asymptotically stable. This means that, under this condition,infection disappears. Otherwise, the uninfected equilibrium point is unstable; and in this case the infection persists in the host. It has also been shown under the hypothesis $\mathcal{R}_0 > 1$, that the infected equilibrium point is locally and globally asymptotically stable. This edifying work ended with numerical simulations, carried out on the Mathematica software, which confirmed our theoretical results. In order to get as close as possible to complex reality of biological phenomena, we envisage in the future, the mathematical analysis of models taking into account cell proliferation, the delays and more generalization of the incident rate function.

Appendix A. Proof of Proposition 3.8

The proof is established by using Banach's Fixed Point Theorem.
Choose β such that $\frac{3}{4} < \beta < 1$, then the injection $\mathcal{I} : D(\mathcal{H}^{\beta}) \to C_B^0$ is continuous by Lemma 3.3.
For $r_0 > 0$ and $T > 0$, the following closed ball is considered :

$$B_{r_0}(H_0, I_0, V_0) = \left\{(H, I, V) \in (C_B^0((0, T], D(\mathcal{H}^{\beta})))^3 : \|H - H_0\|_{\beta}, \|I - I_0\|_{\beta}, \|V - V_0\|_{\beta} \leq r_0\right\}. \tag{A.1}$$

By Proposition 3.1, we have the local Lipschitz properties:

$$\begin{aligned}
\|\mathcal{F}(t, H_1, I_1, V_1) - \mathcal{F}(t, H_2, I_2, V_2)\|_2 &\leq K_1^1\|H_1 - H_2\|_{D(\mathcal{H}^{\beta})} + K_2^1\|I_1 - I_2\|_{D(\mathcal{H}^{\beta})} + K_3^1\|V_1 - V_2\|_{D(\mathcal{H}^{\beta})},\\
\|\mathcal{G}(t, H_1, I_1, V_1) - \mathcal{G}(t, H_2, I_2, V_2)\|_2 &\leq K_1^2\|H_1 - H_2\|_{D(\mathcal{H}^{\beta})} + K_2^2\|I_1 - I_2\|_{D(\mathcal{H}^{\beta})} + K_3^2\|V_1 - V_2\|_{D(\mathcal{H}^{\beta})},\\
\|\mathcal{Q}(t, H_1, I_1, V_1) - \mathcal{Q}(t, H_2, I_2, V_2)\|_2 &\leq K_1^3\|H_1 - H_2\|_{D(\mathcal{H}^{\beta})} + K_2^3\|I_1 - I_2\|_{D(\mathcal{H}^{\beta})} + K_3^3\|V_1 - V_2\|_{D(\mathcal{H}^{\beta})},
\end{aligned} \tag{A.2}$$

for $t \in [0, T]$, $(H_1, I_1, V_1), (H_2, I_2, V_2) \in B_{r_0}(H_0, I_0, V_0)$ and Lipschitz-constants $K_j^i > 0$, $i, j = 1, 2, 3$. In addition $(y_1, y_2, y_3) \in B_{r_0}(H_0, I_0, V_0)$, define $P : [0, T] \to L^2(\Omega)$, $Q : [0, T] \to L^2(\Omega)$ and $R : [0, T] \to L^2(\Omega)$ as follows

$$\begin{aligned}
Py_1(t) &= G_1(t)H_0 + \int_0^t G_1(t - \tau)\mathcal{F}(t, y_1(\tau), y_2(\tau), y_3(\tau))d\tau,\\
Qy_2(t) &= G_2(t)I_0 + \int_0^t G_2(t - \tau)\mathcal{G}(t, y_1(\tau), y_2(\tau), y_3(\tau))d\tau,\\
Ry_3(t) &= G_3(t)V_0 + \int_0^t G_3(t - \tau)\mathcal{Q}(t, y_1(\tau), y_2(\tau), y_3(\tau))d\tau.
\end{aligned}$$

Finally, set $M_1 = \sup\limits_{t\in[0,T]} \|\mathcal{F}(t, y_1(0), y_2(0), y_3(0))\|_2$, $M_2 = \sup\limits_{t\in[0,T]} \|\mathcal{G}(t, y_1(0), y_2(0), y_3(0))\|_2$, $M_3 = \sup\limits_{t\in[0,T]} \|\mathcal{Q}(t, y_1(0), y_2(0), y_3(0))\|_2$ and choose T so that:

$$\|G_1(h)H_0 - H_0\|_{\beta}, \|G_2(h)I_0 - I_0\|_{\beta}, \|G_3(h)V_0 - V_0\|_{\beta} \leq \frac{3r_0}{4}, \quad 0 \leq h \leq T, \tag{A.3}$$

$$C^i_{\beta,2}(M_i + r_0K^i_1 + r_0K^i_2 + r_0K^i_3)\int_0^T s^{-\beta}ds \le \frac{r_0}{4}, \quad i = 1, 2, 3, \tag{A.4}$$

where $C^i_{\beta,2}$ is the constant in property 2) of Corollary 3.5 for operator A (A is zero for $i = 1, 2$). Note that such T exists since $G_1(h)$, $G_2(h)$ and $G_3(h)$ converge to Id as h tends to 0^+ by definition of an analytic semigroup and

$$\int_0^T s^{-\beta}ds = \frac{1}{1-\beta}h^{1-\beta} \to 0, \quad h \to 0^+ \;\; for \;\; \beta < 1.$$

Then the proof will continue according to the following two points :

(a): it is shown that (P,Q,R) maps $B_{r_0}(H_0, I_0, V_0)$ into itself,

(b): it is shown that (P,Q,R) is a strict contraction on $B_{r_0}(H_0, I_0, V_0)$, allowing the use of Banach's Fixed Point Theorem to get the existence of a unique fixed point in $B_{r_0}(H_0, I_0, V_0)$.

Let $(H, I, V) \in B_{r_0}(H_0, I_0, V_0)$. Then, using (A.3) and property 2) of Corollary 3.5, we have :

$$\begin{aligned}
\|PH(t) - H_0\|_{D(\mathcal{H}^\beta)} &= \left\|G_1(t)H_0 - H_0 + \int_0^t G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))d\tau\right\|_{D(\mathcal{H}^\beta)},\\
&\le \|G_1(t)H_0 - H_0\|_{D(\mathcal{H}^\beta)} + \int_0^t \|G_1(t-\tau)\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))\|_{D(\mathcal{H}^\beta)}d\tau,\\
&\le \frac{3r_0}{4} + \int_0^t C^1_{\beta,2}(t-s)^{-\beta}\left\|\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau))\right\|_2 d\tau,\\
&\le \frac{3r_0}{4} + \int_0^t C^1_{\beta,2}(t-s)^{-\beta}\Big\|\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau)) - \mathcal{F}(\tau, H_0, I_0, V_0)\\
&\quad + \mathcal{F}(\tau, H_0, I_0, V_0)\Big\|_2 d\tau,\\
&\le \frac{3r_0}{4} + \int_0^t C^1_{\beta,2}(t-s)^{-\beta}\Big(\left\|\mathcal{F}(\tau, H(\tau), I(\tau), V(\tau)) - \mathcal{F}(\tau, H_0, I_0, V_0)\right\|_2\\
&\quad + \left\|\mathcal{F}(\tau, H_0, I_0, V_0)\right\|_2\Big)d\tau,
\end{aligned}$$

$$\begin{aligned}
\|PH(t) - H_0\|_{D(\mathcal{H}^\beta)} &\le \frac{3r_0}{4} + \int_0^t C^1_{\beta,2}(t-s)^{-\beta}\Big(K^1_1r_0 + K^1_2r_0 + K^1_3r_0 + M_1\Big)d\tau,\\
&\le \frac{3r_0}{4} + C^1_{\beta,2}\left(K^1_1r_0 + K^1_2r_0 + K^1_3r_0 + M_1\right)\int_0^t (t-s)^{-\beta}d\tau,\\
&\le \frac{3r_0}{4} + 0,\\
&\le r_0 \;\text{ for }\; 0 \le t \le T,
\end{aligned}$$

and similarly

$$\|QI(t) - I_0\|_{D(\mathcal{H}^\beta)} \le r_0 \;\text{ and }\; < \|RV(t) - V_0\|_{D(\mathcal{H}^\beta)} \le r_0.$$

Showing that (P, Q, R) maps $B_{r_0}(H_0, I_0, V_0)$ into itself. Furthermore, from property 1) in Corollary 3.5 and Lemma 3.6 we compute:

$$\|PH(t+h) - PH(t)\|_{D(\mathcal{H}^\beta)}$$

$$
\begin{aligned}
&= \Big\|G_1(t+h)H_0 - G_1(t)H_0 + \int_0^{t+h} G_1(t+h-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau \\
&\quad - \int_0^t G_1(t-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau\Big\|_{D(\mathcal{H}^\beta)}, \\
&= \Big\|G_1(t)G_1(h)H_0 - G_1(t)H_0 + \int_0^t G_1(h)G_1(t-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau \\
&\quad + \int_t^{t+h} G_1(h)G_1(t-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau \\
&\quad - \int_0^t G_1(t-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau\Big\|_{D(\mathcal{H}^\beta)}, \\
&= \Big\|G_1(t)(G_1(h)-Id)H_0 + \int_0^t (G_1(h)-Id)G_1(t-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau \\
&\quad + \int_t^{t+h} G_1(t+h-\tau)\mathcal{F}(\tau,H(\tau),I(\tau),V(\tau))d\tau\Big\|_{D(\mathcal{H}^\beta)}.
\end{aligned}
$$

The strong continuity of the semigroup and Lemma 3.6 yields

$$\|PH(t+h) - PH(t)\|_{D(\mathcal{H}^\beta)} \to 0 \text{ as } h \to 0^+.$$

Therefore P is continuous from [0,T] into $D(\mathcal{H}^\beta)$.

A similar Calculation shows that Q and R have the same properties and item (a) is proved.

Presently let us show that (P,Q,R) is a strict contraction on $B_{r_0}(H_0,I_0,V_0)$.

Let $(y_1,y_2,y_3),\ (z_1,z_2,z_3) \in B_{r_0}(H_0,I_0,V_0)$. Then

$$
\begin{aligned}
&\|Py_1(t) - Pz_1(t)\|_{D(\mathcal{H}^\beta)} \\
= &\ \Big\|\int_0^t G_1(t-\tau)\Big(\mathcal{F}(\tau,y_1(\tau),y_2(\tau),y_3(\tau)) - \mathcal{F}(\tau,z_1(\tau),z_2(\tau),z_3(\tau))\Big)d\tau\Big\|_{D(\mathcal{H}^\beta)}, \\
\le &\ \int_0^t \Big\|G_1(t-\tau)\Big(\mathcal{F}(\tau,y_1(\tau),y_2(\tau),y_3(\tau)) - \mathcal{F}(\tau,z_1(\tau),z_2(\tau),z_3(\tau))\Big)\Big\|_{D(\mathcal{H}^\beta)} d\tau, \\
\le &\ \int_0^t C^1_{\beta,2}(t-\tau)^{-\beta}\Big\|\mathcal{F}(\tau,y_1(\tau),y_2(\tau),y_3(\tau)) - \mathcal{F}(\tau,z_1(\tau),z_2(\tau),z_3(\tau))\Big\|_2 d\tau, \\
\le &\ \int_0^t C^1_{\beta,2}(t-\tau)^{-\beta}\Big(K^1_1\|y_1-z_1\|_{D(\mathcal{H}^\beta)} + K^1_2\|y_2-z_2\|_{D(\mathcal{H}^\beta)} + K^1_3\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\Big)d\tau, \\
\le &\ C^1_{\beta,2}\Big(K^1_1 \sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)} + K^1_2 \sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)} \\
+ &\ K^1_3 \sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\Big)\int_0^t (t-\tau)^{-\beta}d\tau.
\end{aligned}
$$

That is :

$$\|Py_1(t) - Pz_1(t)\|_{D(\mathcal{H}^\beta)}$$

$$
\begin{aligned}
&\leq C^1_{\beta,2}\left(K^1_1+K^1_2+K^1_3+\frac{M_1}{r_0}\right)\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}\right.\\
&\quad\left.+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right)\int_0^t(t-\tau)^{-\beta}d\tau,\\
&\leq \left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right)\\
&\quad\times C^1_{\beta,2}\left(K^1_1+K^1_2+K^1_3+\frac{M_1}{r_0}\right)\int_0^t s^{-\beta}ds,\\
&\leq \left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right)\\
&\quad\times\frac{1}{r_0}C^1_{\beta,2}\left(r_0K^1_1+r_0K^1_2+r_0K^1_3+M_1\right)\int_0^T s^{-\beta}ds,\\
&\leq \left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right)\frac{1}{r_0}\times\frac{r_0}{4},\\
&\leq \frac{1}{4}\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right),
\end{aligned}
$$

for every $t\in[0,T]$. Hence

$$
\sup_{t\in[0,T]}\|Py_1(t)-Pz_1(t)\|_{D(\mathcal{H}^\beta)} \leq \frac{1}{4}\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right).
$$

Similarly

$$
\sup_{t\in[0,T]}\|Qy_1(t)-Qz_1(t)\|_{D(\mathcal{H}^\beta)} \leq \frac{1}{4}\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right)
$$

and

$$
\sup_{t\in[0,T]}\|Ry_1(t)-Rz_1(t)\|_{D(\mathcal{H}^\beta)} \leq \frac{1}{4}\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right).
$$

Thus

$$
\begin{aligned}
&\sup_{t\in[0,T]}\|(P,Q,R)(y_1(t),y_2(t),y_3(t))-(P,Q,R)(z_1(t),z_2(t),z_3(t))\|_{D(\mathcal{H}^\beta)^3}\\
&\leq \sup_{\tau\in[0,t]}\left(\|Py_1-Pz_1\|_{D(\mathcal{H}^\beta)}+\|Qy_2-Qz_2\|_{D(\mathcal{H}^\beta)}+\|Ry_3-Rz_3\|_{D(\mathcal{H}^\beta)}\right),\\
&\leq \sup_{\tau\in[0,t]}\|Py_1-Pz_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|Qy_2-Qz_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|Ry_3-Rz_3\|_{D(\mathcal{H}^\beta)},\\
&\leq \frac{3}{4}\left(\sup_{\tau\in[0,t]}\|y_1-z_1\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_2-z_2\|_{D(\mathcal{H}^\beta)}+\sup_{\tau\in[0,t]}\|y_3-z_3\|_{D(\mathcal{H}^\beta)}\right),\\
&\leq \frac{3}{4}\sup_{t\in[0,T]}\|(y_1(t),y_2(t),y_3(t))-(z_1(t),z_2(t),z_3(t))\|_{D(\mathcal{H}^\beta)^3}.
\end{aligned}
$$

Hence (P,Q,R) is a strict contraction on $B_{r_0}(H_0,I_0,V_0)$ and this proves Part b). According to Banach's Fixed Point Theorem, (P,Q,R) has a unique fixed point in $B_{r_0}(H_0,I_0,V_0)$. This is the solution of (2.4) on [0,T] with initial value $(H(0),I(0),V(0))=(H_0,I_0,V_0)$ in $(D(\mathcal{H}^\beta))^3$. This completes the proof of Proposition 3.8.

Appendix B. Proof of Theorem 3.11

We first prove the existence and positivity of the solution. From Theorem 3.10, there exist a sequence (w_i^m) and a function w_i such that

$$w_i^m \to w_i \ \text{ in } \ C^0([0,T],\mathcal{H}),$$

with $w_i \geq 0$ and $w_i(0) = w_{0i}$.
We check that

$$q_i(w^{m-1}) \to q_i(w) \ \text{ and } \ q_i(w^{m-1})w_i^m \to q_i(w)w_i \ \text{ in } \ C^0([0,T],\mathcal{H}).$$

We also have

$$f_i(w^{m-1}) \to f_i(w) \ \text{ in } \ C^0([0,T],\mathcal{H})\bigcap L^2((0,T),E').$$

But, w_i^m is solution of

$$\Big\langle \frac{\partial w_i^m}{\partial t}, v_i\Big\rangle + \Big\langle A_i w_i^m, v_i\Big\rangle + \big(q_i(w^{m-1})w_i^m, v_i\big) = \Big\langle f_i(w^{m-1}), v_i\Big\rangle, \quad \forall v_i \in E. \tag{B.1}$$

We take $\phi \in \mathcal{D}((0,T))$, such that $\phi v_i \in L^2((0,T),E)$,

$$\int_0^T \Big\langle \frac{\partial w_i^m}{\partial t}, \phi v_i\Big\rangle dt + \int_0^T \Big\langle A_i w_i^m, \phi v_i\Big\rangle dt + \int_0^T \big(q_i(w^{m-1})w_i^m, \phi v_i\big)\, dt = \int_0^T \Big\langle f_i(w^{m-1}), \phi v_i\Big\rangle dt. \tag{B.2}$$

The second term in the left side and the right side of the equality (B.2) converges due to the weak convergence in $L^2((0,T),E')$. The third term in the left-hand side of (B.2) also converges, due to the convergence in $C([0,T],\mathcal{H})$. We deduce that $\frac{\partial w_i^m}{\partial t}$ converges weakly in $L^2((0,T),E')$.

But we have

$$w_i^m \to w_i \ \text{ in } \ C^0([0,T],\mathcal{H}).$$

Then

$$\frac{\partial w_i^m}{\partial t} \to \frac{\partial w_i}{\partial t} \ \text{ in } \ \mathcal{D}'((0,T),\mathcal{H})$$

Therefore, we obtain

$$\frac{\partial w_i^m}{\partial t} \to \frac{\partial w_i}{\partial t} \ \text{ weakly in } \ L^2((0,T),E'),$$

and

$$\int_0^T \Big\langle \frac{\partial w_i}{\partial t}, \phi v_i\Big\rangle dt + \int_0^T \Big\langle A_i w_i, \phi v_i\Big\rangle dt + \int_0^T \Big(q_i(w)w_i, \phi v_i\Big)_{\mathcal{H}} dt = \int_0^T \Big\langle f_i(w), \phi v_i\Big\rangle dt. \tag{B.3}$$

This being true for all ϕ, one has

$$\Big\langle \frac{\partial w_i}{\partial t}, v_i\Big\rangle + \Big\langle A_i w_i, v_i\Big\rangle + \Big(q_i(w)w_i, v_i\Big)_{\mathcal{H}} = \Big\langle f_i(w), v_i\Big\rangle, \quad \forall v_i \in E.$$

That is to say,

$$\frac{d}{dt}(w_i, v_i)_{\mathcal{H}} + a(w_i, v_i) + \Big(q_i(w)w_i, v_i\Big)_{\mathcal{H}} = \Big\langle f_i(w), v_i\Big\rangle, \ \forall v_i \in E, \tag{B.4}$$

$$\frac{\partial w_i}{\partial t} = f_i(w) - A_i w_i - q_i(w)w_i \ \text{ in } \ L^2((0,T),E'). \tag{B.5}$$

According to (3.27) and (3.28) we have

$$w_i^m(t) \;=\; G_i(t)w_{0i} + \int_0^t G_i(t-s)(-q_i(w^{m-1})w_i^m + f_i(w^{m-1}))(s)ds, \tag{B.6}$$

and in addition, as $q_i(w^{m-1})w_i^m$ and $f_i(w^{m-1})$ converge in $C^0([0,T],\mathcal{H})$ and the operator $\mathcal{G}_i$, defined by the relation (3.29), is compact, using the limit in (B.6) one has,

$$w_i(t) \;=\; G_i(t)w_{0i} + \int_0^t G_i(t-s)(-q_i(w)w_i + f_i(w))(s)ds. \tag{B.7}$$

It remains to prove uniqueness.

Let v be another solution of IBVP (3.21). Then

$$v_i \in W(0,T,E,E') \Rightarrow v_i \in C^0([0,T],\mathcal{H}) \text{ and } v_i \geq 0.$$

Consequently we obtain

$$q_i(v)v_i + f_i(v) \in L^2((0,T),E').$$

Thus, by Proposition 2.11 of [12], one has

$$v_i(t) \;=\; G_i(t)w_{0i} + \int_0^t G_i(t-s)(-q_i(v)v_i + f_i(v))(s)ds.$$

Subtracting, we have

$$w_i(t) - v_i(t) = \int_0^t G_i(t-s)\Big(-(q_i(w)w_i - q_i(v)v_i) + (f_i(w) - f_i(v))\Big)(s)ds, \tag{B.8}$$

with

$$\begin{aligned} q_i(w)w_i - q_i(v)v_i \;&=\; q_i(w)w_i - q_i(w)v_i + q_i(w)v_i - q_i(v)v_i, \\ &=\; q_i(w)(w_i - v_i) + (q_i(w) - q_i(v))v_i. \end{aligned}$$

Since w_i is positive, one has

$$\left\| \frac{w_j}{\alpha_0 + \alpha_1 w_k + \alpha_2 w_j + \alpha_3 w_k w_j} \right\| \leq \frac{1}{K}\|w_j\|_\infty$$

where

$$\|w_j\|_\infty = \|w_j\|_{L^\infty((0,T),\mathcal{H})}.$$

If we define

$$\|w\|_\infty = \sum_{j=1}^{3} \|w_j\|_\infty,$$

there is $M_1 > 0$ such that

$$\|q(w)\|_\infty \leq M_1\|w_j\|_\infty.$$

So, for $r = 1, 2, 3$, the numerator of $q_r(w) - q_r(v)$ is the sum of terms of the form $(w_k - v_k)v_j$ or $(w_j - v_j)w_k$, and we can find $M_2 > 0$ such that

$$\left|q_r(w) - q_r(v)\right|_{\mathcal{H}}(s) \leq M_2\Big(\sum_{j=1}^{3} |w_j(s) - v_j(s)|_{\mathcal{H}}\Big).$$

Also we can find $M_3 > 0$ such that

$$\left|f_r(w) - f_r(v)\right|_{\mathcal{H}}(s) \leq M_3\Big(\sum_{j=1}^{3} |w_j(s) - v_j(s)|_{\mathcal{H}}\Big).$$

Summing up $|w_j(s) - v_j(s)|_{\mathcal{H}}$ and noting that $\|G_j(t-s)\| \leq N_j e^{\theta_j T}$ with $N_j,\ \theta_j > 0$, we can find $M > 0$ such that

$$\sum_{j=1}^{3} |w_j(s) - v_j(s)|_{\mathcal{H}} \leq M\|w - v\|_{\infty}.$$

Replacing in (B.8), we obtain

$$\sum_{j=1}^{3} |w_j(s) - v_j(s)|_{\mathcal{H}} \leq M^2\|w - v\|_{\infty} \int_0^t s ds = M^2\frac{t^2}{2}\|w - v\|_{\infty}.$$

By induction, we have

$$\sum_{j=1}^{3} |w_j(s) - v_j(s)|_{\mathcal{H}} \leq \frac{M^n}{n!}T^n\|w - v\|_{\infty},$$

with

$$\lim_{n\to+\infty} \frac{M^n}{n!}T^n\|w - v\|_{\infty} = 0.$$

Therefore $w = v$. This ends the proof of Theorem 3.11.

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Conflict of Interests

The authors declare that they have no conflict of interests regarding the publication of this paper.

Authors' Contribution

A. Nangue provided the subject, wrote the introduction, the conclusion, checked the proofs and verified the calculation. He also managed the wellposedness of the initial and boundary value problem. B. Nde Tchiffo conceived the study and computed equilibria and their global stabilities. The two authors together undertook the numerical simulations on Mathematica. All the authors read and approved the final manuscript.

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