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On a diffusive bacteriophage dynamical model for bacterial infections

Hyacinthe M. Ndongmo Teytsa[*,‡,§], Berge Tsanou[*,†,‡,§,‖],
Jean Lubuma[†] and Samuel Bowong[‡,§,¶]

[*]*Department of Mathematics and Computer Science*
University of Dschang, P.O. Box 67, Dschang, Cameroon

[†]*Department of Mathematics and Applied Mathematics*
University of Pretoria, Pretoria 0002, South Africa

[‡]*IRD UMI 209 UMMISCO*
University of Yaounde I, P.O. Box 337, Yaounde, Cameroon

[§]*LIRIMA-EPITAG Team Project*
University of Yaounde I, P.O. Box 812, Yaounde, Cameroon

[¶]*Department of Mathematics and Computer Science*
University of Douala, P.O. Box 24157, Douala, Cameroon
[‖]*bergetsanou@gmail.com*

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Bacteriophages or phages are viruses that infect bacteria and are increasingly used to control bacterial infections. We develop a reaction–diffusion model coupling the interactive dynamic of phages and bacteria with an epidemiological bacterial-borne disease model. For the submodel without phage absorption, the basic reproduction number $\mathcal{R}_0$ is computed. The disease-free equilibrium (DFE) is shown to be globally asymptotically stable whenever $\mathcal{R}_0$ is less than one, while a unique globally asymptotically endemic equilibrium is proven whenever $\mathcal{R}_0$ exceeds one. In the presence of phage absorption, the above stated classical condition based on $\mathcal{R}_0$, as the average number of secondary human infections produced by susceptible/lysogen bacteria during their entire lifespan, is no longer sufficient to guarantee the global stability of the DFE. We thus derive an additional threshold $\mathcal{N}_0$, which is the average offspring number of lysogen bacteria produced by one infected human during the phage–bacteria interactions, and prove that the DFE is globally asymptotically stable whenever both $\mathcal{R}_0$ and $\mathcal{N}_0$ are under unity, and infections persist uniformly whenever $\mathcal{R}_0$ is greater than one. Finally, the discrete counterpart of the continuous partial differential equation model is derived by constructing a nonstandard finite difference scheme which is dynamically consistent. This consistency is shown by constructing suitable discrete Lyapunov functionals thanks to which the global stability results for the continuous model are replicated. This scheme is implemented in

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[‖]Corresponding author.

MatLab platform and used to assess the impact of spatial distribution of phages, on the dynamic of bacterial infections.

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1. Introduction

Bacteriophages are among the most common and diverse viruses in the biosphere that are found wherever bacteria exist. When they infect the bacteria, some of these viruses exhibit two life cycles, namely, the so-called lytic and lysogenic cycles. While within the lytic life cycle, bacteria cells infected by phages are broken (i.e. lysed) and destroyed after immediate replication of the virions, the lysogenic life cycle does not result in immediate lysing of the host cells. Hence, the name "temperate phages" for the phages undergoing the lysogenic cycle. As the lysogenic cycle allows the host cell to continue to survive and reproduce, the virus called prophage in this case is replicated in all cell's offsprings. Sometime, the most worrying fact of interaction between phages and bacteria is that during phage infection, the resulted prophage may provide benefits to host bacterium by adding new functions of the bacterial genome. For instance, the conversion of harmless strains *Vibrio cholerae* by bacteriophages may cause virulent cholera epidemics [3, 4]. In this regard, mathematical modeling in biology/ecology can be a useful tool to gain more insight into the phage–bacteria interactions and their impacts on the spread of bacterial-borne diseases.

The spread of bacterial-borne diseases such as cholera is affected by various spatial heterogeneity factors including position, water resource, movement of human beings. The dispersal of phages and bacteria is also used as central role that affects the spatial spreading of diseases. Several mathematical studies have contributed to the understanding of the spatial dynamics of bacterial infections [9, 22, 23, 25, 28, 29]. While a large number of the works focused on the diffusion of humans and bacteria, little effort has been devoted to the impact of spatial distribution of phages and the influence of phage–bacteria infection on the spread of bacterial infections.

In this work, we contribute to fill this gap. We propose a system of reaction–diffusion partial differential equations (PDEs) that model the interactive dynamics of phages and bacteria and their influence on bacterial-borne disease, by considering the phage absorption and the diffusion of phages and humans. In doing so, we have extended our ordinary differential equation models [15, 16] on phage–bacteria interactions. We explicitly compute the basic reproduction number $\mathcal{R}_0$ of the reaction–diffusion model using the method described in [24].

In order to put more emphasis on the impact of phage absorption and phage–bacteria interactions on the model dynamics, we proceed in two steps. First, we study the model without phage absorption by setting the rate of phage infection to zero. For this submodel, suitable Lyapunov functionals are constructed to establish the global stability of the spatially homogeneous steady solutions. It is precisely shown that the disease-free equilibrium (DFE), E_0, is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$, whereas there exists a unique globally asymptotically stable endemic equilibrium, E^*, if $\mathcal{R}_0 > 1$. Second, we consider the full system with positive phage absorption rate. We prove that the condition $\mathcal{R}_0 \leq 1$ is no longer sufficient to eliminate the disease. We derive an additional threshold $\mathcal{N}_0$, construct suitable Lyapunov functionals and show that the DFE is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$ and $\mathcal{N}_0 \leq 1$. Moreover, it is proven that, whenever $\mathcal{R}_0 > 1$, all the subpopulations are uniformly persistent.

Since the continuous model cannot be solved by analytical techniques, we develop a nonstandard finite difference (NSFD) scheme by carefully using Mickens's rules [11, 12]. Our NSFD scheme is shown to be dynamically consistent with the continuous system in the sense that it preserves the positivity, boundedness of the solutions of the continuous model, as well as the global stability of the equilibria.

The rest of this paper is organized as follows. Section 2 is devoted to the model derivation. The well-posedness and the computation of the basic reproduction number are derived in Sec. 3. Theoretical analysis of models is done in Sec. 4. Section 5 deals with the mathematical analysis of the discretized system and numerical simulations, a conclusion completes the paper in Sec. 6.

2. Model Description

We propose a multi-host reaction–diffusion model, which couples the interactive dynamics of bacteria and phages with an epidemiological bacterial-borne disease in humans. The proposed model is specific in that phages and bacteria interact in a predator–prey relationship in such a manner that the phage absorption potential by bacteria is explicitly taken into account.

2.1. *An interactive/ecological model of phages and bacteria with diffusion*

When constructing the model, for simplicity, we assume that when phages, with density $P \equiv P(x,t)$ at location x and time t, infect the bacterium population, the density of the latter splits into two classes, namely, susceptible or uninfected bacteria (not yet infected by phage), $B \equiv B(x,t)$, and infected bacteria $J \equiv J(x,t)$. Susceptible bacteria are free-living agents capable of self-multiplication in the environment at the constant rate r. Following [27], we look at the environment as a transition of the disease (i.e. the pathogen growth rate is always less than its decay rate μ_b). We recall that in the interactive dynamics of populations, a functional response refers to the change in the density of prey attack per predator in unit time. For populations interacting in the predator–prey relationship, Holling functions of type I, II and III are commonly used as functional responses [18]. Given the distinction we make in our model between the phage attack rate and the decay rate due to attachment, it is appropriate, as suggested by Smith in [20], to consider in this case a more general functional response of the form

$$h(B,P) = \varepsilon B f(P), \tag{2.1}$$

where ε is the phage absorption rate, and the function f, the phage attack rate, is defined by

$$f(P) = \frac{P}{F_m(cP)}. \tag{2.2}$$

In (2.2), $c = \varepsilon/e$ and $1/e$ represent the injection time and the time between binding of phage to host bacteria and subsequent injection of genetic material into host, respectively. The integer m denotes the number of binding sites for phage per host (bacterium) and

$$F_m(P) = 1 + \sum_{l=1}^{m} \prod_{i=1}^{l} \left(\frac{P}{i+P}\right). \tag{2.3}$$

We refer the interested reader to [20] for more details on the justifications and construction of the functional response h. Note that in practice, the loss of phages may be significant during phage–bacteria interactions. For example, if we assume that a phage does not detect the status (uninfected or infected) of the host cell to which it binds, then one should not ignore the loss phages due to wasted attacks on already infected hosts [20]. We take into account the fact that a host cell has a multiplicity of potential phage binding sites on its surface, more than one of which may be simultaneously bounded by phage. Thus, the rate of phages loss due to attachment can be described by the expression

$$-\varepsilon(B+J)P. \tag{2.4}$$

Moreover, μ_p denotes the natural phage decay rate. We assume that the spatial displacement of bacteria and phages is modeled by the diffusion operator $D_b\Delta$, where D_b is the diffusion coefficient of bacteria and phages and Δ is the Laplace operator. As explained earlier, the lysogenic life cycle allows the infected bacterial host cell to continue to survive and reproduce, while at the same time the infecting phage is reproduced in all of the cell's offsprings. Therefore, we need to incorporate the bacterial cell multiplication, the size of which is denoted by ϕ. In the course of this division, some environmental conditions (the effect of UV radiations, the presence of certain chemicals) can lead to the release of prophage causing proliferation of new phages. This mechanism from which lysogen bacteria switch from a the lysogenic life cycle to the lytic life cycle is called the prophage induction and we denote by γ the rate at which such induction occurs. Putting all together, the interactive reaction–diffusion dynamics of phages and bacteria is given by the following system:

$$\begin{cases} \dfrac{\partial B(x,t)}{\partial t} = rB - \mu_b B - \varepsilon B f(P) + D_b \Delta B, & x \in \Omega, \ t > 0, \\ \dfrac{\partial J(x,t)}{\partial t} = \phi \varepsilon B f(P) - (\mu_b + \gamma) J + D_b \Delta J, & x \in \Omega, \ t > 0, \\ \dfrac{\partial P(x,t)}{\partial t} = \theta \gamma J - \varepsilon (B + J) P - \mu_p P + D_b \Delta P, & x \in \Omega, \ t > 0. \end{cases} \tag{2.5}$$

2.2. *A bacteria-borne epidemiological model with bacteria–phages interactions*

We denote by $\Omega \subset \mathbb{R}^n, n \in \mathbb{N}$, the spatial habitat where the human population lives and uses the water from nearby aquatic reservoirs. We shall focus our model on cholera. However, the model can be readily applied to all bacterial- and water-borne diseases that threaten humans beings living in surrounding water sources contaminated by bacterial pathogens able to interact with specific phages.

Cholera is an infectious disease which causes watery diarrhea, and can lead to dehydration and even death if untreated. It is caused by eating food or drinking water contaminated with a bacterium called *V. cholerae*. The two ecological serogroups (*V. cholerae* O1 and *V. cholerae* O139) have the ability to colonize the hosts small intestine. *Vibrio cholerae* can survive in some aquatic environment for more than three months up to two years living in association with zooplankton, phytoplankton and the aquatic organism such as bacteriophages [30].

Let $S(x,t)$ and $I(x,t)$ be the density of susceptible and infected humans at location x and time t, respectively. The total human population at time $t \geq 0$ at location x is then $N(x,t) = S(x,t) + I(x,t)$. All new born humans are recruited in the susceptible class at the constant rate Λ. Human individuals die naturally at rate μ_h, and by disease-induced death at rate d. They recover at rate δ. The susceptible human population acquires an infection by indirect infection (contact with environment). Vibriophages (phages that infect *V. cholerae*) can convert their bacterial host from nonpathogenic strain to pathogenic strain through a process called phage conversion, by providing the host with phage-encoded virulence genes. For instance, toxigenic *V. cholerae* isolates carry the ctxAB genes encoded by lysogenic phage.

On the one hand, the ingestion of infected bacteria causes disease at rate $\beta\alpha J$, where β is the ingestion/consumption rate of bacteria from the environment. The constant rate α is the probability that the consumption of infected bacteria leads to human infection. On the other hand, when the susceptible bacteria are ingested from the environment and reach the small intestine within the human body, complex biological interactions, chemical reactions and genetic transduction take place that lead to human cholera [26]. The ingestion of susceptible bacteria can cause infection at rate $\beta\rho B$, where ρ is the probability that the consumption of susceptible bacteria by temperate phage in the small intestine will lead to the disease in humans. The overall force infection is then given by the following Holling type II functional response:

$$\lambda(B,J) = \beta \frac{\alpha J + \rho B}{\alpha J + \rho B + H}, \tag{2.6}$$

where H is the half-saturation bacteria density. Infected humans contribute to the infection of the environment by shedding susceptible and infected bacteria through feces or vomiting. Therefore, the shedding rate of susceptible bacteria (B) and infected bacteria (J) are ω and η, respectively. We assume that D is the diffusion coefficient of susceptible (S) and infected (I) humans. Based on the above description and assumptions, the following reaction–diffusion model for bacterial infections is given:

$$\begin{cases} \dfrac{\partial S(x,t)}{\partial t} = \Lambda - \lambda(B,J)S - \mu_h S + \delta I + D\Delta S, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I(x,t)}{\partial t} = \lambda(B,J)S - (\mu_h + d + \delta)I + D\Delta I, & x \in \Omega,\ t > 0, \\ \dfrac{\partial B(x,t)}{\partial t} = \omega I + rB - \mu_b B - \varepsilon B f(P) + D_b \Delta B, & x \in \Omega,\ t > 0, \\ \dfrac{\partial J(x,t)}{\partial t} = \eta I + \phi\varepsilon B f(P) - (\mu_b + \gamma)J + D_b \Delta J, & x \in \Omega,\ t > 0, \\ \dfrac{\partial P(x,t)}{\partial t} = \theta\gamma J - \varepsilon(B+J)P - \mu_p P + D_b \Delta P, & x \in \Omega,\ t > 0. \end{cases} \tag{2.7}$$

The system is appended with the following initial conditions through functions of the space variable x assumed to continuous:

$$S(x,0) = s(x), \quad I(x,0) = i(x), \quad B(x,0) = b(x), \quad J(x,0) = j(x), \quad P(x,0) = p(x),$$

Finally, we consider the Neumann boundary conditions

$$\frac{\partial S}{\partial z} = \frac{\partial I}{\partial z} = \frac{\partial B}{\partial z} = \frac{\partial J}{\partial z} = \frac{\partial P}{\partial z} = 0, \quad x \in \partial\Omega,\ t > 0,$$

where $\partial/\partial z$ denotes the differentiation along the outward normal z to the boundary, $\partial\Omega$, of the domain Ω assumed to be smooth. These conditions show that across the boundary, no external input and output is imposed from outside on these populations. This is not a severe limitation in the sense that the displacement of populations can be controlled during an epidemic situation, and that bacteria and phages can be assumed to live and evolve in water pond.

3. Basic Properties of the Full Model

In this section, we derive the global well-posedness and the threshold dynamics of model (2.7). We therefore assume that $\Omega \subset \mathbb{R}^n$ is a bounded open set with smooth enough boundary $\partial\Omega$.

We adopt the following notations: $u(x,t) = (S(x,t), I(x,t), B(x,t), J(x,t), P(x;t))$; the initial condition is $u(x,0) = (s(x), i(x), b(x), j(x), p(x))$, $X = \mathcal{C}(\overline{\Omega}, \mathbb{R}^5)$ is the Banach space of continuous vector-valued functions from $\overline{\Omega}$ into $\mathbb{R}^n$, equipped with the usual supremum norm $||\ .\ ||_X$; $X^+ = C(\overline{\Omega}, \mathbb{R}^5_+)$ so that (X, X^+) is a strongly ordered space. We further assume that

$$\gamma_1(t), \gamma_2(t), \gamma_3(t), \gamma_4(t), \gamma_5(t) : \mathcal{C}(\overline{\Omega}, \mathbb{R}) \to \mathcal{C}(\overline{\Omega}, \mathbb{R}),$$

are the $\mathcal{C}_0$-semigroups with infinitesimal generators the operators $D\Delta S - \mu_h$, $D\Delta I - (\mu_h + d + \delta)$, $D_b\Delta B - (\mu_b - r)$, $D_b\Delta J - (\mu_b + \gamma)$ and $D_b\Delta P - \mu_p$, respectively, subject to Neumann boundary conditions [17]. Clearly, $\forall\, \varphi \in \mathcal{C}(\overline{\Omega}, \mathbb{R})$, we have

$$\begin{aligned}
\gamma_1(t)\varphi(x) &= e^{-\mu_h t}\int_\Omega \Phi(x,t,s)\varphi(s)ds, \quad \gamma_2(t)\varphi(x) = e^{-(\mu_h+d+\delta)t} \\
&\quad \times \int_\Omega \Phi(x,t,s)\varphi(s)ds, \\
\gamma_3(t)\varphi(x) &= e^{-(\mu_b - r)t}\int_\Omega \Psi(x,t,s)\varphi(s)ds, \quad \gamma_4(t)\varphi(x) = e^{-(\mu_b+\gamma)t} \\
&\quad \times \int_\Omega \Psi(x,t,s)\varphi(s)ds, \\
\gamma_5(t)\varphi(x) &= e^{-\mu_P t}\int_\Omega \Psi(x,t,s)\varphi(s)ds, t > 0,
\end{aligned}$$

where Φ and Ψ are Green functions associated with the operators $D\Delta$ and $D_b\Delta$ subject to Neumann boundary condition, respectively. Thanks to [8, Corollary 4], $\Gamma(t) = (\gamma_1(t), \gamma_2(t), \gamma_3(t), \gamma_4(t), \gamma_5(t)) : \mathcal{C}(\overline{\Omega}, \mathbb{R}^5) \to \mathcal{C}(\overline{\Omega}, \mathbb{R}^5)$ is a compact and strongly positive semigroup.

From [19, Corollary 7.3.2], it is obvious that for all $x_0 \in X^+$, the system (2.7) admits a unique mild solution $u(x,t)$ defined on the interval $[0,\tau)$, with $\tau = \tau(x_0)$, which is nonnegative for all $t \in [0,\tau)$.

The following result establishes the global well-posedness result for (2.7).

Theorem 3.1. *For any $\varphi \in X^+$, system* (2.7) *admits a unique solution $u(t,x,\varphi)$ defined on $[0,\infty) \times \overline{\Omega}$, and every solution semiflow $\varphi_t : X^+ \to X^+$ is bounded.*

Proof. Following the tangent condition for parabolic equations [19], solutions corresponding to nonnegative initial conditions are nonnegative. Adding the first and the second equations of (2.7) yields

$$\begin{aligned}
\frac{\partial S(x,t) + \partial I(x,t)}{\partial t} &= D\Delta(S(x,t) + I(x,t)) + \Lambda - (\mu_h + d)I(x,t) - \mu_h S(x,t) \\
&\le D\Delta(S(x,t) + I(x,t)) + \Lambda - \mu_h(S(x,t) + I(x,t)).
\end{aligned}$$

By the comparison principle for parabolic equations [7], $S(x,t)$ and $I(x,t)$ are uniformly bounded.

Multiplying the third equation by θ, and add it to the fourth and proceed as above, we have

$$\begin{aligned}\frac{\partial\left(\phi B(x,t)+J(x,t)\right)}{\partial t} &= (\phi\omega+\eta)I(x,t)+D_b\Delta(\phi B(x,t)+J(x,t))\\ &\quad-(\mu_b-r)\phi B(x,t)-(\mu_b+\gamma)J(x,t)\\ &\le(\phi\omega+\eta)I(x,t)+D_b\Delta(\phi B(x,t)+J(x,t))\\ &\quad-(\mu_b-r)(\phi B(x,t)+J(x,t)).\end{aligned}$$

Next, using the boundedness of $I(x,t)$, and once more the comparison principle for parabolic equations we obtain also that $B(x,t)$, $J(x,t)$ are uniformly bounded. From the last equation of system (2.7), we proceed similarly to show that $P(x,t)$ is uniformly bounded. Consequently, the solution $Z(.,t,\varphi)$ of system (2.7) exists globally on $[0,\infty)$.

Moreover, the comparison principle yields

$$\limsup_{t\to+\infty}(S(x,t)+I(x,t))\le\frac{\Lambda}{\mu_h},\quad \text{uniformly},\quad \forall\, x\in\overline{\Omega}.$$

Thus, for sufficiently $\chi>0$, there exists t_0 such that $\forall t>t_0$

$$S(.,t)\le\frac{\Lambda}{\mu_h}(1+\chi)\quad\text{and}\quad I(.,t)\le\frac{\Lambda}{\mu_h}(1+\chi),\quad\forall\, t>t_0.$$

Hence, $S(x,t)$ and $I(x,t)$ are ultimately bounded. Similarly, there exists $t_1>t_0$ such that $\forall t>t_1$

$$\begin{aligned}&\phi B(.,t)+I(.,t)\le\frac{(\omega\phi+\eta)\Lambda}{\mu_h(\mu_b-r)}(1+\chi)\quad\text{and}\\ &\qquad P(.,t)\le\frac{\theta\gamma(\phi\omega+\eta)\Lambda}{\mu_h(\mu_b-r)\mu_P}(1+\chi),\quad\forall\, t>t_1,\quad t_1>t_0.\end{aligned}$$

Thus, the positive orbits of a bounded subset of X^+ are bounded and this achieved the proof.

Now we compute for model (2.7) the basic reproduction number, $\mathcal{R}_0$, defined as the average number of secondary human infections produced by susceptible or lysogen bacteria in their entire lifespan. This threshold quantity will serve to study the asymptotic behavior of the system. The DFE of model (2.7) is $E_0=(S_0,0,0,0,0)$ with $S_0=\Lambda/\mu_h$. We compute the basic reproduction number using the technique presented in [24]. To achieve this, let us consider the following subsystem that reduced to infected compartments:

$$
\begin{cases}
\dfrac{\partial I}{\partial t} = \lambda(B,J)S - (\mu_h + d + \delta)I + D\Delta I, & x \in \Omega,\ \ t > 0,\\[2mm]
\dfrac{\partial B}{\partial t} = \omega I + rB - \mu_b B - \varepsilon B f(P) + D_b \Delta B, & x \in \Omega,\ \ t > 0,\\[2mm]
\dfrac{\partial J}{\partial t} = \eta I + \phi\varepsilon B f(P) - (\mu_b + \gamma)J + D_b \Delta J, & x \in \Omega,\ \ t > 0,\\[2mm]
\dfrac{\partial P(x,t)}{\partial t} = \theta\gamma J - \varepsilon(B+J)P - \mu_p P + D_b \Delta P, & x \in \Omega,\ \ t > 0\\[2mm]
\dfrac{\partial I}{\partial z} = \dfrac{\partial B}{\partial z} = \dfrac{\partial P}{\partial z} = \dfrac{\partial J}{\partial z} = 0, & x \in \partial\Omega,\ \ t > 0,\\[2mm]
I(x,0) = i(x), B(x,0) = b(x), J(x,0) = j(x), P(x,0) = p(x), & x \in \Omega.
\end{cases}
\tag{3.1}
$$

Let $\varsigma(t)$ be the solution semigroup of (3.1), and $X_0(x) = (i(x), b(x), j(x), p(x))^T$ the initial distribution of the subpopulations. The distribution of new infection at time t is given by $\varsigma(t)X_0(x)$. Define

$$
F(x) \equiv F = \begin{pmatrix} 0 & \beta\rho S_0/H & \beta\alpha S_0/H & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},
$$

and

$$
V(x) \equiv V = \begin{pmatrix} (\mu_h + d + \delta) & 0 & 0 & 0 \\ -\omega & (\mu_b - r) & 0 & 0 \\ -\eta & 0 & (\mu_b + \gamma) & 0 \\ 0 & 0 & -\theta\gamma & \mu_p \end{pmatrix},
$$

representing the matrices of appearance of new infections and transitions, respectively. Since (2.7) is a reaction–diffusion epidemic model with spatially homogeneous parameters and appended with the Neumann boundary condition, with diffusion coefficients not depending on the space variable, it follows from [24, Theorem 3.5] that the basic reproduction number is given by

$$
\mathcal{R}_0 = r(FV^{-1}), \tag{3.2}
$$

the explicit expression of which is

$$
\mathcal{R}_0 = \frac{\beta\omega\rho S_0}{H(\mu_b - r)(\mu_h + d + \delta)} + \frac{\beta\eta\alpha S_0}{H(\mu_b + \gamma)(\mu_h + d + \delta)}. \tag{3.3}
$$

□

4. Asymptotic Analysis of the Model

We now focus on the asymptotic behavior of the solutions of (2.7). We point out that our main goal is to study the impact of phage–bacteria interactions on the diffusive dynamic of an epidemiological bacteria-borne disease. We proceed in two steps. First, we neglect the phage absorption rate by setting $\varepsilon = 0$. The dynamic of resulted model is completely driven by the threshold $\mathcal{R}_0$. Second, we prove for the full model that $\mathcal{R}_0$ may not be sufficient for the disease elimination.

4.1. *The submodel without phage absorption*

Pointing out that the interactions between phages and bacteria interactions can also take place in the small intestine of the infected humans, we assume that even when $\varepsilon = 0$, the presence of infected bacteria can be justified by their shedding [15, 26] in the environment by infected humans. The resulted subsystem is the following:

$$\begin{cases} \dfrac{\partial S(x,t)}{\partial t} = \Lambda - \lambda(B,J)S - \mu_h S + \delta I + D\Delta S, \quad x \in \Omega,\ t > 0, \\ \dfrac{\partial I(x,t)}{\partial t} = \lambda(B,J)S - (\mu_h + d + \delta)I + D\Delta I, \quad x \in \Omega,\ t > 0, \\ \dfrac{\partial B(x,t)}{\partial t} = \omega I + rB - \mu_b B + D_b \Delta B, \quad x \in \Omega,\ t > 0, \\ \dfrac{\partial J(x,t)}{\partial t} = \eta I - (\mu_b + \gamma)J + D_b \Delta J, \quad x \in \Omega,\ t > 0, \\ \dfrac{\partial P(x,t)}{\partial t} = \theta\gamma J - \mu_p P + D_b \Delta P, \quad x \in \Omega,\ t > 0 \\ S(x,0) = s(x), \quad I(x,0) = i(x), \quad B(x,0) = b(x), \\ J(x,0) = j(x), \quad P(x,0) = p(x), \\ \dfrac{\partial S}{\partial z} = \dfrac{\partial I}{\partial z} = \dfrac{\partial B}{\partial z} = \dfrac{\partial J}{\partial z} = \dfrac{\partial P}{\partial z} = 0, \quad x \in \Omega,\ t > 0. \end{cases} \tag{4.1}$$

Note that the DFE of (4.1) is the same as that of the full model and is given by $E_0 = (S_0, 0, 0, 0, 0)$. The following theorem gives the global stability of E_0 of the model (4.1).

Theorem 4.1. *If $\mathcal{R}_0 \leq 1$, the DFE is globally asymptotically stable in Ω.*

Proof. The global stability of the constant steady-state solution E_0 of the reaction–diffusion system (4.1) subject to Neumann boundary conditions is based on the construction of a Lyapunov functional for the involved PDEs and the application of LaSalle Invariance Principle. Inspired by [6, 23, 25, 29], we choose the following

Lyapunov functional candidate:

$$\mathcal{L}(x,t) = \int_\Omega \mathcal{L}_0(x,t)dx, \tag{4.2}$$

with

$$\begin{aligned}\mathcal{L}_0(x,t) = S(x,t) - S_0 - S_0 \ln\left(\frac{S(x,t)}{S_0}\right) + I(x,t) \\ + \frac{\beta\rho S_0}{H(\mu_b - r)} B(x,t) + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)} J(x,t).\end{aligned} \tag{4.3}$$

Dropping the argument (x,t) for notational simplicity, we have

$$\begin{aligned}\frac{\partial \mathcal{L}_0}{\partial t} &= \left(1 - \frac{S_0}{S}\right)\frac{\partial S}{\partial t} + \frac{\partial I}{\partial t} + \frac{\beta\rho S_0}{H(\mu_b - r)}\frac{\partial B}{\partial t} + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}\frac{\partial J}{\partial t} \\ &= \left(1 - \frac{S_0}{S}\right)(D\Delta S + \Lambda - \lambda(B,J)S - \mu_h S + \delta I) + (D\Delta J + \lambda(B,J)S \\ &\quad - (\mu_h + d + \delta)I) + \frac{\beta\rho S_0}{H(\mu_b - r)}(D_b\Delta B + \omega I - (\mu_b - r)B) + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)} \\ &\quad \times (D_b \Delta J + \eta I - (\mu_b+\gamma)J) \\ &= -\frac{\mu_h}{S}(S_0 - S)^2 + D\left(1 - \frac{S_0}{S}\right)\Delta S + \lambda(B,J)S + \frac{S - S_0}{S}\delta I \\ &\quad - (\mu_h + d + \delta)I + D\Delta I + \frac{\beta\omega\rho S_0}{H(\mu_b - r)}I - \frac{\beta\rho S_0}{H}B \\ &\quad + \frac{\beta\rho S_0}{H(\mu_b - r)}B_b\Delta B + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)}I - \frac{\beta\alpha S_0}{H}J + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}D_b\Delta J.\end{aligned}$$

Using, $\lambda(B,J)S_0 \leq \beta\alpha(S_0/H)J + \beta(\rho S_0/H)B$, some simple algebraic manipulations lead us to

$$\begin{aligned}\frac{\partial \mathcal{L}_0}{\partial t} &\leq -\frac{\mu_h}{S}(S_0 - S)^2 + D\left(1 - \frac{S_0}{S}\right)\Delta S + I\left(\frac{\beta\omega\rho S_0}{H(\mu_b - r)} + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)}\right. \\ &\quad \left. - (\mu_h + d + \delta)\right) + D\Delta I + \frac{\beta\rho S_0}{H(\mu_b - r)}D_b\Delta B + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}D_b\Delta J \\ &\leq -\frac{\mu_h}{S}(S_0 - S)^2 + D\left(1 - \frac{S_0}{S}\right)\Delta S + I(\mu_h + d + \delta)(\mathcal{R}_0 - 1) + D\Delta I \\ &\quad + \frac{\beta\rho S_0}{H(\mu_b - r)}D_b\Delta B + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}D_b\Delta J.\end{aligned}$$

Moreover, using the boundary conditions, it is straightforward that

$$\int_\Omega \Delta S dx = \int_\Omega \Delta I dx = \int_\Omega \Delta_b B dx = \int_\Omega \Delta_b J dx = 0, \quad \int_\Omega \frac{\Delta S}{S} dx = \int_\Omega \frac{|\Delta S|^2}{S^2} dx \geq 0.$$

Putting all together, we have

$$\frac{d\mathcal{L}(x,t)}{dt} = \int_\Omega \frac{\partial \mathcal{L}_0(x,t)}{\partial t} dx \leq \int_\Omega \left(-\frac{\mu_h}{S}(S_0 - S)^2 + I(\mu_h + d + \delta)(\mathcal{R}_0 - 1) \right) dx \leq 0.$$

Finally, it is easy to prove that the largest invariant set contained in Ω such that $d\mathcal{L}(x,t)/dt = 0$ is $\{E_0\}$. Therefore, the application of LaSalle's Invariance Principle shows that the DFE is globally asymptotically stable in Ω. □

Theorem 4.2. *The following statements hold whenever* $\mathcal{R}_0 > 1$:

(i) *The system* (4.1) *has a unique endemic equilibrium* E^*.
(ii) *The unique endemic equilibrium of* (4.1) *is globally asymptotically stable in* Ω *for* $\delta = 0$.

Proof. (i) Let $E^* = (S^*, I^*, B^*, J^*, P^*)$ be any endemic equilibrium of the model (4.1). Then

$$\begin{cases} \lambda^* = \beta \dfrac{(\alpha J^* + \rho B^*)}{\alpha J^* + \rho B^* + H}, \\ \Lambda - \lambda^* S^* - \mu_h S^* + \delta I^* = 0, \\ \lambda^* S^* - (\mu_h + d + \delta) I^* = 0, \\ \omega I^* - (\mu_b - r) B^* = 0, \\ \eta I^* - (\mu_b + \gamma) J^* = 0, \\ \theta \gamma J^* - \mu_p P^* = 0. \end{cases} \tag{4.4}$$

From the third equation of (4.4)

$$I^* = \frac{\lambda^* S^*}{\mu_h + d + \delta}. \tag{4.5}$$

Plugging (4.5) in the second equation of (4.4) yields

$$S^* = \frac{\Lambda(\mu_h + d + \delta)}{\lambda^*(\mu_h + d) + \mu_h(\mu_h + d + \delta)}. \tag{4.6}$$

Inserting (4.5) into (4.4) yields

$$I^* = \frac{\Lambda \lambda^*}{\lambda^*(\mu_h + d) + \mu_h(\mu_h + d + \delta)}. \tag{4.7}$$

From the fourth equation of (4.4)

$$B^* = \frac{\omega I^*}{\mu_b - r},$$

and using (4.7) yields

$$B^* = \frac{\omega\Lambda\lambda^*}{(\mu_b - r)(\lambda^*(\mu_h + d) + \mu_h(\mu_h + d + \delta))}. \tag{4.8}$$

By the same way, from the fifth equation of (4.4)

$$J^* = \frac{\eta\Lambda\lambda^*}{(\mu_b + \gamma)(\lambda^*(\mu_h + d) + \mu_h(\mu_h + d + \delta))}. \tag{4.9}$$

Now using the explicit expression of λ^*, one has the following:

$$\lambda^* = \frac{[\beta\rho\omega(\mu_b + \gamma) + \beta\eta\alpha(\mu_b - r)]\Lambda\lambda^*}{(\mu_b + \gamma)(\mu_b - r)(\lambda^*(\mu_h + d) + \mu_h(\mu_h + d + \delta))}.$$

Since we are interested in the positive values of λ^*, some algebraic computations give

$$\lambda^* = \frac{H\mu_h(\mu_h + d + \delta)(\mu_b + \gamma)(\mu_b - r)(\mathcal{R}_0 - 1)}{\Lambda[\alpha\eta(\mu_b - r) + \rho\omega(\mu_b + \gamma)] + H(\mu_b + \gamma)(\mu_b - r)(\mu_h + d)}. \tag{4.10}$$

Plugging λ^* in the expressions of S^*, I^*, B^* J^* and P^* and setting

$$K_1 = H\mu_h(\mu_b - r)(\mu_b + \gamma)(\mu_h + d)(\mathcal{R}_0 - 1) + \frac{\mu_h}{\Lambda}K_2,$$

with

$$K_2 = \Lambda[\Lambda(\alpha\eta(\mu_b - r) + \rho\omega(\mu_b + \gamma)) + H(\mu_b + \gamma)(\mu_b - r)(\mu_h + d)],$$

takes us to

$$\begin{cases} S^* = \dfrac{K_2}{K_1}, \quad I^* = \Lambda H(\mu_b - r)(\mu_b + \gamma)\mu_h(\mu_h + d + \delta)\dfrac{(\mathcal{R}_0 - 1)}{K_1}, \\ B^* = \Lambda H(\mu_b + \gamma)\mu_h(\mu_h + d + \delta)\dfrac{(\mathcal{R}_0 - 1)}{K_1}, \\ J^* = \Lambda H(\mu_b - r)\mu_h(\mu_h + d + \delta)\dfrac{(\mathcal{R}_0 - 1)}{K_1}, \\ P^* = \theta\gamma\Lambda H(\mu_b - r)\mu_h(\mu_h + d + \delta)\dfrac{(\mathcal{R}_0 - 1)}{\mu_p K_1}. \end{cases} \tag{4.11}$$

One can remark that one has for $\mathcal{R}_0 = 1$, $S^* = S_0$, $I^* = 0$, $B^* = 0$, $J^* = 0$, $P^* = 0$, so that we recover the DFE.

(ii) For the global stability of the endemic equilibrium E^*, let's choose the following Lyapunov functional candidate:

$$\mathcal{U}(x,t) = \int_\Omega \mathcal{L}_0^*(x,t)dx, \tag{4.12}$$

with

$$\begin{aligned}\mathcal{L}_0^*(x,t) &= S(x,t) - S^* - S^*\ln\left(\frac{S(x,t)}{S^*}\right) + I(x,t) - I^* - I^*\ln\left(\frac{I(x,t)}{I^*}\right)\\ &\quad + \frac{\beta\rho B^* S^*}{(\rho B^* + \alpha J^* + H)\omega I^*}\left(B(x,t) - B^* - B^*\ln\left(\frac{B(x,t)}{B^*}\right)\right)\\ &\quad + \frac{\beta\alpha J^* S^*}{(\rho B^* + \alpha J^* + H)\eta I^*}\left(J(x,t) - J^* - J^*\ln\left(\frac{J(x,t)}{J^*}\right)\right).\end{aligned}$$

$$\begin{aligned}\frac{\partial\mathcal{L}_0^*}{\partial t} &= \left(1 - \frac{S^*}{S}\right)\frac{\partial S}{\partial t} + \left(1 - \frac{I^*}{I}\right)\frac{\partial I}{\partial t} + \frac{\beta\rho B^* S^*}{(\rho B^* + \alpha J^* + H)\omega I^*}\left(1 - \frac{B^*}{B}\right)\frac{\partial B}{\partial t}\\ &\quad + \frac{\beta\alpha J^* S^*}{(\rho B^* + \alpha J^* + H)\eta I^*}\left(1 - \frac{J^*}{J}\right)\frac{\partial J}{\partial t}\\ &= \left(1 - \frac{S^*}{S}\right)(\Lambda - \lambda S - \mu_h S + D\Delta S) + \left(1 - \frac{I^*}{I}\right)(\lambda S - (\mu_h + d)I + D\Delta I)\\ &\quad + \frac{\beta\rho B^* S^*}{(\rho B^* + \alpha J^* + H)\omega I^*}\left(1 - \frac{B^*}{B}\right)(\omega I - (\mu_b - r)B + D_b\Delta B)\\ &\quad + \frac{\beta\alpha J^* S^*}{(\rho B^* + \alpha J^* + H)\eta I^*}\left(1 - \frac{J^*}{J}\right)(\eta I - (\mu_b + \gamma)J + D_b\Delta J).\end{aligned}$$

At the endemic equilibrium E^*, one has

$$(\mu_h + d) = \lambda^* S^*, \quad (\mu_b - r) = \omega I^*/B^*, \quad (\mu_b + \gamma) = \eta I^*/J^*.$$

Thus

$$\begin{aligned}\frac{\partial\mathcal{L}_0^*}{\partial t} &= \left(1 - \frac{S^*}{S}\right)(\Lambda - \lambda S - \mu_h S + D\Delta S) + \left(1 - \frac{I^*}{I}\right)\left(\lambda S - \frac{\lambda^* S^*}{I^*}I + D\Delta I\right)\\ &\quad + \frac{\beta\rho B^* S^*}{(\rho B^* + \alpha J^* + H)\omega I^*}\left(1 - \frac{B^*}{B}\right)\left(\omega I - \frac{\omega I^*}{B^*}B + D_b\Delta B\right)\\ &\quad + \frac{\beta\alpha J^* S^*}{(\rho B^* + \alpha J^* + H)\eta I^*}\left(1 - \frac{J^*}{J}\right)\left(\eta I - \frac{\eta I^*}{J^*}J + D_b\Delta J\right).\end{aligned}$$

Expanding and grouping like terms of this last expression give

$$\begin{aligned}\frac{\partial\mathcal{L}_0^*}{\partial t} &= -\frac{\mu_h}{S}(S - S^*)^2 + \lambda_1(B^*, J^*)S^*\\ &\quad \times\left(3 - \frac{S^*}{S} + \frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)} - \frac{\lambda_1(B,J)SI^*}{\lambda_1(B^*,J^*)S^*I} - \frac{B^*I}{BI^*} - \frac{B}{B^*}\right) + \lambda_2(J^*, B^*)S^*\\ &\quad \times\left(3 - \frac{S^*}{S} + \frac{\lambda_2(J,B)}{\lambda_2(J^*,B^*)} - \frac{\lambda_2(J,B)SI^*}{\lambda_2(J^*,B^*)S^*I} - \frac{J^*I}{JI^*} - \frac{J}{J^*}\right) + D\left(1 - \frac{S^*}{S}\right)\Delta S\end{aligned}$$

$$+ D\left(1-\frac{I^*}{I}\right)\Delta I + D_b\frac{\lambda_1(B^*,J^*)S^*}{\omega I^*}\left(1-\frac{B^*}{B}\right)\Delta B$$
$$+ D_b\frac{\lambda_2(J^*,B^*)S^*}{\eta I^*}\left(1-\frac{J^*}{J}\right)\Delta J,$$

wherein $\lambda_1(B,J) = \beta\rho B/(\rho B+\alpha J+H)$, $\lambda_2(J,B) = \beta\alpha J/(\rho B+\alpha J+H)$ are increasing functions of B and J, respectively. For more investigations, let's set

$$h(x) = x-1-\ln x, \quad x>0, \quad h(x)\geq 0, \forall x>0.$$

Therefore, the derivative of $\mathcal{U}$ along the solutions of system (2.7), can be bounded above as follows:

$$\begin{aligned}\frac{d\mathcal{U}}{dt} &= \int_\Omega \frac{\partial \mathcal{L}_0^*}{\partial t}dx \leq -\frac{\mu_h}{S}(S-S^*)^2 - \lambda_1(B^*,J^*)S^*\left(h\left(\frac{S^*}{S}\right)\right.\\ &\quad + h\left(\frac{\lambda_1(B,J)SI^*}{\lambda_1(B^*,J^*)S^*I}\right) + h\left(\frac{B^*I}{BI^*}\right) + h\left(\frac{B}{B^*}\right) - h\left(\left.\frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)}\right)\right)\\ &\quad - \lambda_2(J^*,B^*)S^*\left(h\left(\frac{S^*}{S}\right) + h\left(\frac{\lambda_2(J,B)SI^*}{\lambda_2(J^*,B^*)S^*I}\right)\right.\\ &\quad + h\left(\frac{J^*I}{JI^*}\right) + h\left(\frac{J}{J^*}\right) - h\left(\left.\frac{\lambda_2(J,B)}{\lambda_2(J^*,B^*)}\right)\right).\end{aligned}$$

Furthermore, since $\lambda_1(B,J)$ is an increasing function of B, we have

$$\begin{aligned}h\left(\frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)}\right) - h\left(\frac{B}{B^*}\right) &= \frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)} - \frac{B}{B^*} + \ln\left(\frac{B\lambda_1(B,J)}{B^*\lambda_1(B^*,J^*)}\right)\\ &\leq \frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)} - \frac{B}{B^*} + \frac{B\lambda_1(B,J)}{B^*\lambda_1(B^*,J^*)} - 1\\ &= \left(\frac{\lambda_1(B,J)}{\lambda_1(B^*,J^*)} - \frac{B}{B^*}\right)\left(1-\frac{\lambda_1(B^*)}{\lambda_1(B)}\right)\\ &= \frac{\lambda_1(B,J)(B^*-B)\left(\lambda_1(B,J)-\lambda_1(B^*,J^*)\right)}{\lambda_1^2(B^*)B^*}\\ &\quad - \frac{B\left(\lambda_1(B,J)-\lambda_1(B^*,J^*)\right)^2}{\lambda_1^2(B^*,J^*)B^*}\\ &\leq 0.\end{aligned}$$

Similarly, remembering that $\lambda_2(J,B)$ is an increasing function of J, we obtain

$$h\left(\frac{\lambda_2(J,B)}{\lambda_2(J^*,B^*)}\right) - h\left(\frac{J}{J^*}\right) \leq 0.$$

Up to now, we proven that $d\mathcal{U}/dt \leq 0$. Moreover, the largest invariant set contained in Ω such that $d\mathcal{U}/dt = 0$ is $\{E^*\}$, and the application of LaSalle's Invariance Principle proves that the E^* of the PDE (4.1) is globally asymptotically stable in Ω.

4.2. *The full model with positive absorption rate*

4.2.1. *Stability of DFE*

In the presence of phage absorption ($\varepsilon > 0$) the DFE is preserved. Its local stability is given by the following proposition.

Proposition 4.3. *Whenever* $\mathcal{R}_0 < 1$, *the DFE of the PDE* (2.7) *is locally asymptotically stable.*

Proof. Let $0 = \mu_0 < \mu_1 < \mu_i < \mu_{i+1}, i = 1, 2, \ldots$, be the eigenvalues of $-\Delta$ on Ω with homogeneous Neumann boundary condition, $E(\mu_i)$ the space of eigenfunctions corresponding to μ_i and $\{\varphi_{ij} : j = 1, 2, \ldots, \dim(E(\mu_i))\}$ an orthogonal basis of $E(\mu_i))$. Then $\mathbb{X} = (\mathcal{C}^1(\overline{\Omega}))^5$ can be decomposed as

$$\mathbb{X} = \bigoplus_{i=1}^{\infty} \mathbb{X}_i, \quad \mathbb{X}_{ij} = \bigoplus_{i=1}^{\dim E(\mu_i)} \mathbb{X}_{ij},$$

where $\mathbb{X}_{ij} = \{c\varphi_{ij} : c \in (\mathbb{R})^3\}$.

Linearizing the system at E_0 gives $\partial Z(x,t)/\partial t = \mathrm{diag}(D, D, D_b, D_b)\Delta Z(x,t) + J(E_0)Z(x,t)$, where $Z(x,t) = (S(x,t), I(x,t), B(x,t), J(x,t), P(x,t))$, and

$$J(E_0) = \begin{pmatrix} -\mu_h & \delta & -\beta\rho S_0/H & -\beta\alpha S_0/H & 0 \\ 0 & -(\mu_h + d + \delta) & \beta\rho S_0/H & \beta\alpha S_0/H & 0 \\ 0 & \omega & -(\mu_b - r) & 0 & 0 \\ 0 & \eta & 0 & -(\mu_b + \gamma) & 0 \\ 0 & 0 & 0 & \theta\gamma & -\mu_P \end{pmatrix}.$$

The characteristic polynomial at E_0 is $(x + \mu_h + \mu_i D)(x + \mu_p + \mu_i D_b)P(x)$ with

$$\begin{aligned} P(x) = {} & (x + \mu_h + d + \delta + \mu_i D)(x + \mu_b - r + \mu_i D_b)(x + \mu_b + \gamma + \mu_i D_b) \\ & - \frac{\beta\rho\omega S_0}{H}(x + \mu_b + \gamma + \mu_i D_b) - \frac{\beta\alpha\eta S_0}{H}(x + \mu_b - r + \mu_i D_b). \end{aligned}$$

The expansion of $P(x)$ yields $P(x) = x^3 + a_2x^2 + a_1x + a_0$, where

$$\begin{cases} a_2 = (\mu_h + d + \delta + \mu_i D + \mu_b - r + \mu_i D_b + \mu_b + \gamma + \mu_i D_b), \\ a_1 = (\mu_h + d + \delta + \mu_i D)(\mu_b - r + \mu_i D_b) \\ \qquad + (\mu_h + d + \delta + \mu_i D)(\mu_b + \gamma + \mu_i D_b) \\ \qquad + (\mu_b + \gamma + \mu_i D_b)(\mu_b - r + \mu_i D_b) - \beta\omega\rho S_0/H - \beta\alpha\eta S_0/H, \\ a_0 = (\mu_h + d + \delta + \mu_i D)(\mu_b - r + \mu_i D_b)(\mu_b + \gamma + \mu_i D_b)(1 - R), \end{cases} \tag{4.13}$$

with

$$\begin{aligned} R &= \frac{\beta\rho\omega S_0}{H(\mu_h + d + \delta + \mu_i D)(\mu_b - r + \mu_i D_b)} \\ &\quad + \frac{\beta\alpha\eta S_0}{H(\mu_h + d + \delta + \mu_i D)(\mu_b + \gamma + \mu_i D_b)} \\ &\le \mathcal{R}_0. \end{aligned}$$

Clearly, $a_0 \geq (\mu_h + d + \delta + \mu_i D)(\mu_b - r + \mu_i D_b)(\mu_b + \gamma + \mu_i D_b)(1 - \mathcal{R}_0) \geq 0$. Moreover

$$\begin{aligned} a_1 a_2 - a_0 &= a_0 + (\mu_h + d + \delta + \mu_i D)^2 (\mu_b - r + \mu_i D_b) \\ &\quad \times \left(1 - \frac{\beta\rho\omega S_0}{(\mu_h + d + \delta + \mu_i D)(\mu_b - r + \mu_i D_b)}\right) \\ &\quad + (\mu_h + d + \delta + \mu_i D)^2 (\mu_b + \gamma + \mu_i D_b) \\ &\quad \times \left(1 - \frac{\beta\alpha\eta S_0}{(\mu_h + d + \delta\mu_i D)(\mu_b + \gamma + \mu_i D_b)}\right) \\ &\quad + (\mu_h + d + \delta + \mu_i D)[(\mu_b - r + \mu_i D_b)^2 + (\mu_b + \gamma + \mu_i D_b)^2 \\ &\quad + (\mu_b + \gamma + \mu_i D_b)(\mu_b - r + \mu_i D_b)] + (\mu_b + \gamma + \mu_i D_b)^2 (\mu_b - r + \mu_i D_b) \\ &\geq a_0 + (\mu_h + d + \delta + \mu_i D)^2 \left[(\mu_b - r + \mu_i D) + (\mu_b + \gamma + \mu_i D_b)\right](1 - R) \\ &\quad + (\mu_h + d + \delta + \mu_i D)[(\mu_b - r + \mu_i D_b)^2 + (\mu_b + \gamma + \mu_i D_b)^2 \\ &\quad + (\mu_b + \gamma + \mu_i D_b)(\mu_b - r + \mu_i)] + (\mu_b + \gamma + \mu_i D_b)^2 (\mu_b - r + \mu_i D_b) \\ &\geq a_0 + (\mu_h + d + \delta + \mu_i D)^2 \left[(\mu_b - r + \mu_i D) + (\mu_b + \gamma + \mu_i D_b)\right](1 - \mathcal{R}_0) \\ &\quad + (\mu_h + d + \delta + \mu_i D)[(\mu_b - r + \mu_i D_b)^2 + (\mu_b + \gamma + \mu_i D_b)^2 \\ &\quad + (\mu_b + \gamma + \mu_i D_b)(\mu_b - r + \mu_i)] \\ &\quad + (\mu_b + \gamma + \mu_i D_b)^2 (\mu_b - r + \mu_i D_b) > 0. \end{aligned}$$

Hence, the DFE of system (2.7) is locally asymptotically stable. □

We now focus on the global asymptotic stability (GAS) of DFE which is needed for the possible elimination of the disease. We point out that our model couples and epidemiological model with an ecological model, and one should notice that the corresponding reproduction number $\mathcal{R}_0$ does not depend on the parameters describing the phage–bacteria interactions. Moreover, one should mention that under the influence of those interactions, the density of susceptible bacteria decreases. while that of the infected bacteria increases. Consequently, for the possible control of the epidemic, another threshold is needed. The existence of the latter threshold denoted by $\mathcal{N}_0$, is actually expected because the infected human individuals contribute to the growth of bacteria. The threshold quantity $\mathcal{N}_0$ should actually be the average offspring number of lysogen bacteria produced, by one infected human during the phage–bacteria interactions [16].

$$\mathcal{N}_0 = \frac{\beta\alpha\phi\omega S_0}{H(\mu_b+\gamma)(\mu_h+d+\delta)} + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)(\mu_h+d+\delta)}. \tag{4.14}$$

The global stability the DFE is then summarized in the following theorem.

Theorem 4.4. *The DFE is globally asymptotically stable whenever* $\max\{\mathcal{R}_0, \mathcal{N}_0\} \leq 1$.

Proof. The proof of this theorem is done in two steps.

Step 1: $\max\{\mathcal{R}_0, \mathcal{N}_0\} = \mathcal{R}_0$.

We choose the following Lyapunov functional candidate:

$$\begin{aligned}\mathcal{V} = \int_\Omega \mathcal{L}_1 dx \quad \text{with} \quad \mathcal{L}_1 &= S - S_0 - S_0 \ln\left(\frac{S}{S_0}\right)\\ &+ I + \frac{\beta\rho S_0}{H(\mu_b - r)}B + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}J, \end{aligned}\tag{4.15}$$

$$\begin{aligned}\frac{\partial \mathcal{L}_1}{\partial t} &= \left(1 - \frac{S_0}{S}\right)\frac{\partial S}{\partial t} + \frac{\partial I}{\partial t} + \frac{\beta\rho S_0}{H(\mu_b - r)}\frac{\partial B}{\partial t} + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}\frac{\partial J}{\partial t}\\
&= \left(1 - \frac{S_0}{S}\right)(D\Delta S + \Lambda - \lambda(B,J)S - \mu_h S + \delta I) + (D\Delta J + \lambda(B,J)S\\
&\quad - (\mu_h + d + \delta)I) + \frac{\beta\rho S_0}{H(\mu_b - r)}(D_b\Delta B + \omega I - (\mu_b - r)B - \varepsilon B f(P))\\
&\quad + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}(D_b\Delta J + \eta I + \phi\varepsilon B f(P) - (\mu_b+\gamma)J)\\
&= -\frac{\mu_h}{S}(S_0 - S)^2 + D\left(1 - \frac{S_0}{S}\right)\Delta S + \lambda(B,J)S + \frac{S - S_0}{S}\delta I\\
&\quad - (\mu_h + d + \delta)I + D\Delta I + \frac{\beta\omega\rho S_0}{H(\mu_b - r)}I - \frac{\beta\rho S_0}{H}B - \frac{\beta\rho S_0}{H(\mu_b - r)}\varepsilon B f(P)\\
&\quad + \frac{\beta\rho S_0}{H(\mu_b - r)}B_b\Delta B + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)}I + \frac{\beta\phi\alpha S_0}{H(\mu_b+\gamma)}\varepsilon B f(P)\\
&\quad - \frac{\beta\alpha S_0}{H}J + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}D_b\Delta J.\end{aligned}$$

Clearly, $\lambda(B,J)S_0 \leq \beta\alpha(S_0/H)J + \beta(\rho S_0/H)B$. After grouping like terms, one has

$$\begin{aligned}\frac{\partial \mathcal{L}_1}{\partial t} \leq{}& -\frac{\mu_h}{S}(S_0 - S)^2 + D\left(1 - \frac{S_0}{S}\right)\Delta S\\
&+ I\left(\frac{\beta\omega\rho S_0}{H(\mu_b - r)} + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)} - (\mu_h + d + \delta)\right) + \varepsilon B f(P)\end{aligned}$$

$$\times \left(\frac{\beta\phi\alpha S_0}{H(\mu_b+\gamma)} - \frac{\beta\rho S_0}{H(\mu_b-r)} \right) + D\Delta I + \frac{\beta\rho S_0}{H(\mu_b-r)} D_b \Delta B + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)} D_b \Delta J.$$

Remark that

$$\left(\frac{\beta\phi\alpha S_0}{H(\mu_b+\gamma)} - \frac{\beta\rho S_0}{H(\mu_b-r)} \right) = \frac{(\mu_h+d+\delta)}{\omega}(\mathcal{N}_0 - \mathcal{R}_0),$$

that is

$$\begin{aligned} \frac{\partial \mathcal{L}_1}{\partial t} &= -\frac{\mu_h}{S}(S_0-S)^2 + D\left(1-\frac{S_0}{S}\right)\Delta S + I(\mu_h+d+\delta)(\mathcal{R}_0-1) \\ &\quad + \frac{(\mu_h+d+\delta)}{\omega}\varepsilon B f(P)(\mathcal{N}_0-\mathcal{R}_0) + D\Delta I + \frac{\beta\rho S_0}{H(\mu_b-r)}D_b\Delta B \\ &\quad + \frac{\beta\alpha S_0}{H(\mu_b+\gamma)}D_b\Delta J, \end{aligned}$$

this implies that

$$\begin{aligned} \frac{d\mathcal{V}}{dt} = \int_\Omega \frac{\partial \mathcal{L}_1}{\partial t}dx &\le -\frac{\mu_h}{S}(S_0-S)^2 + I(\mu_h+d+\delta)(\mathcal{R}_0-1) \\ &\quad + \frac{(\mu_h+d+\delta)}{\omega}\varepsilon B f(P)(\mathcal{N}_0-\mathcal{R}_0) \le 0. \end{aligned}$$

Step 2: $\max\{\mathcal{R}_0, \mathcal{N}_0\} = \mathcal{N}_0$**.**

We choose the following Lyapunov functional in this case:

$$\begin{aligned} \mathcal{W} &= \int_\Omega \mathcal{L}_2 dx \quad \text{with } \mathcal{L}_2 = S - S_0 - S_0\ln\left(\frac{S}{S_0}\right) + I + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}B \\ &\quad + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}J, \\ \frac{\partial \mathcal{L}_2}{\partial t} &= \left(1-\frac{S_0}{S}\right)\frac{\partial S}{\partial t} + \frac{\partial I}{\partial t} + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}\frac{\partial B}{\partial t} + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}\frac{\partial J}{\partial t} \\ &= \left(1-\frac{S_0}{S}\right)(D\Delta S + \Lambda - \lambda(B,J)S - \mu_h S + \delta I) + (D\Delta J + \lambda(B,J)S \\ &\quad - (\mu_h+d+\delta)I) + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}(D_b\Delta B + \omega I - (\mu_b-r)B - \varepsilon B f(P)) \\ &\quad + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}(D_b\Delta J + \eta I + \phi\varepsilon B f(P) - (\mu_b+\gamma)J). \end{aligned} \tag{4.16}$$

Using again the inequalities $\lambda(B,J)S_0 \leq \beta\alpha(S_0/H)J + \beta(\rho S_0/H)B$ and grouping like terms, $\partial\mathcal{L}_2/\partial t$ becomes

$$\begin{aligned}
\frac{\partial\mathcal{L}_2}{\partial t} &\leq -\frac{\mu_h}{S}(S_0-S)^2 + D\left(1-\frac{S_0}{S}\right)\Delta S + J\frac{1}{\phi\omega+\eta} \\
&\quad \times\left(\frac{\beta\alpha S_0\phi\omega}{H} + \frac{\beta\alpha S_0\eta}{H} - (\mu_b+\gamma)(\mu_h+d+\delta)\right) \\
&\quad + D\Delta I + B\frac{1}{\phi\omega+\eta}\left(\frac{\beta\rho S_0\phi\omega}{H} + \frac{\beta\eta\alpha S_0}{H} - \phi(\mu_b-r)(\mu_h+d+\delta)\right) \\
&\quad + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta B + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta J \\
&= J\frac{(\mu_b+\gamma)(\mu_h+d+\delta)}{\phi\omega+\eta} \\
&\quad \times\left(\frac{\beta\alpha S_0\phi\omega}{H(\mu_b+\gamma)(\mu_h+d+\delta)} + \frac{\beta\alpha S_0\eta}{H(\mu_b+\gamma)(\mu_h+d+\delta)} - 1\right) \\
&\quad + B\frac{\phi(\mu_b-r)(\mu_h+d+\delta)}{\phi\omega+\eta} \\
&\quad \times\left(\frac{\beta\rho S_0\omega}{H(\mu_b-r)(\mu_h+d+\delta)} + \frac{\beta\eta\alpha S_0}{H\phi(\mu_b-r)(\mu_h+d+\delta)} - 1\right) \\
&\quad + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta B + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta J \\
&\quad + D\Delta I + D\left(1-\frac{S_0}{S}\right)\Delta S - \frac{\mu_h}{S}(S_0-S)^2.
\end{aligned}$$

Knowing that $\mathcal{R}_0 \leq \mathcal{N}_0$ implies that $1/\phi(\mu_b-r) \leq 1/(\mu_b+\gamma)$, we have

$$\begin{aligned}
\frac{\partial\mathcal{L}_2}{\partial t} &\leq J\frac{(\mu_b+\gamma)(\mu_h+d+\delta)}{\phi\omega+\eta} \\
&\quad \times\left(\frac{\beta\alpha S_0\phi\omega}{H(\mu_b+\gamma)(\mu_h+d+\delta)} + \frac{\beta\alpha S_0\eta}{H(\mu_b+\gamma)(\mu_h+d+\delta)} - 1\right) \\
&\quad + B\frac{\phi(\mu_b-r)(\mu_h+d+\delta)}{\phi\omega+\eta} \\
&\quad \times\left(\frac{\beta\rho S_0\omega}{H(\mu_b-r)(\mu_h+d+\delta)} + \frac{\beta\eta\alpha S_0}{H(\mu_b+\gamma)(\mu_h+d+\delta)} - 1\right) \\
&\quad + \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta B + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta J
\end{aligned}$$

$$
\begin{aligned}
&+ D\Delta I + D\left(1-\frac{S_0}{S}\right)\Delta S - \frac{\mu_h}{S}(S_0-S)^2\\
&= -\frac{\mu_h}{S}(S_0-S)^2 + J\frac{(\mu_b+\gamma)(\mu_h+d+\delta)}{\phi\omega+\eta}(\mathcal{N}_0-1)\\
&+ B\frac{\phi(\mu_b-r)(\mu_h+d+\delta)}{\phi\omega+\eta}(\mathcal{R}_0-1)\\
&+ \frac{\phi(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta B + \frac{(\mu_h+d+\delta)}{\omega\phi+\eta}D_b\Delta J\\
&+ D\Delta I + D\left(1-\frac{S_0}{S}\right)\Delta S.
\end{aligned}
$$

Then

$$
\begin{aligned}
\frac{d\mathcal{W}}{dt} &\le -\frac{\mu_h}{S}(S_0-S)^2 + J\frac{(\mu_b+\gamma)(\mu_h+d+\delta)}{\phi\omega+\eta}(\mathcal{N}_0-1)\\
&\quad + B\frac{\phi(\mu_b-r)(\mu_h+d+\delta)}{\phi\omega+\eta}(\mathcal{R}_0-1) \le 0.
\end{aligned} \tag{4.17}
$$

Thus, from step 1 and step 2 above, it can be easily shown that the largest invariant set contained in Ω such that $d\mathcal{W}/dt = 0$ is $\{E_0\}$, and the application of LaSalle's Invariance Principle proves that the DFE is globally asymptotically stable in Ω.

□

Due to the complexity of model (2.7), the existence and global stability of the endemic equilibrium have not been investigated for $\varepsilon > 0$. Alternatively, in what follows, we prove the uniform persistence of the full model in this case.

4.2.2. *Uniform persistence of system* (2.7)

Let's consider the following linear system obtained by linearizing model (2.7) around the DFE:

$$
\begin{cases}
\dfrac{\partial I(x,t)}{\partial t} = \dfrac{\beta\rho\omega S_0}{H}B + \dfrac{\beta\alpha\eta S_0}{H}J\\
\qquad\qquad - (\mu_h+d+\delta)I + D\Delta I, & x\in\Omega,\ t>0,\\
\dfrac{\partial B(x,t)}{\partial t} = \omega I - (\mu_b - r)B + D_b\Delta B, & x\in\Omega,\ t>0,\\
\dfrac{\partial J(x,t)}{\partial t} = \eta I - (\mu_b+\gamma)J + D_b\Delta J, & x\in\Omega,\ t>0,\\
\dfrac{\partial I}{\partial z} = \dfrac{\partial B}{\partial z} = \dfrac{\partial J}{\partial z} = 0, & x\in\partial\Omega,\ t>0.
\end{cases} \tag{4.18}
$$

Assuming that (4.18) has a solution of the form $I(x,t) = e^{\nu t}\gamma_2(x)$, $B(x,t) = e^{\nu t}\gamma_3(x)$ and $J(x,t) = e^{\nu t}\gamma_4(x)$, leads us to the following eigenvalue problem:

$$\begin{cases} \nu\gamma_2(x) = \dfrac{\beta\rho\omega S_0}{H}\gamma_3(x) + \dfrac{\beta\alpha\eta S_0}{H}\gamma_4(x) \\ \qquad\qquad - (\mu_h + d + \delta)\gamma_2(x) + D\Delta\gamma_2(x), & x \in \Omega, \\ \nu\gamma_3(x) = \omega\gamma_2(x) - (\mu_b - r)\gamma_3(x) + D_b\Delta\gamma_3(x), & x \in \Omega, \\ \nu\gamma_4(x) = \eta\gamma_2(x) - (\mu_b + \gamma)\gamma_4(x) + D_b\Delta\gamma_4(x), & x \in \Omega, \\ \dfrac{\partial\gamma_2}{\partial z} = \dfrac{\partial\gamma_3}{\partial z} = \dfrac{\partial\gamma_4}{\partial z} = 0, & x \in \partial\Omega. \end{cases} \tag{4.19}$$

The proofs of the following lemmas can be readily adapted from their analogs in [24].

Lemma 4.5. *The problem* (4.19) *has a principal eigenvalue* ν_0 *with a positive eigenfunction and* ν_0 *has the same sign as* $\mathcal{R}_0 - 1$.

Lemma 4.6. *Let* $Z(.,t,\varphi)$ *be a solution of the model* (2.7) *with initial condition* $Z(.,t,\varphi) = \varphi \in \mathbb{X}^+$, *one has*

(i) $\forall\,\varphi \in \mathbb{X}^+$, *we have* $S(x,t,\varphi) > 0$, $\forall\, x \in \overline{\Omega}$, $t > 0$ *and there is a constant* τ *such that*

$$\liminf_{t\to\infty} \geq \tau, \quad \textit{uniformly for } x \in \overline{\Omega},$$

(ii) *if there exists* $t_1 > 0$ *such that* $I(.,t,\varphi) \neq 0$ *or* $B(.,t,\varphi) \neq 0$ *or* $J(.,t,\varphi) \neq 0$, *then* $I(x,t,\varphi) > 0$, $B(x,t,\varphi) > 0$ *and* $J(x,t,\varphi) > 0$, $x \in \overline{\Omega}$, $t > t_1$.

The following theorem allows us to use $\mathcal{R}_0$ as a threshold index for disease persistence.

Theorem 4.7. *Whenever* $\mathcal{R}_0 > 1$, *there exists* $\zeta > 0$ *such that for all* $\varphi \in \mathbb{X}^+$, *with* $\varphi_2 \neq 0$ *or* $\varphi_3 \neq 0$, *or* $\varphi_4 \neq 0$, *one has*

$$\liminf_{t\to\infty} S(x,t,\varphi) \geq \zeta, \quad \liminf_{t\to\infty} I(x,t,\varphi) \geq \zeta, \quad \liminf_{t\to\infty} B(x,t,\varphi) \geq \zeta,$$
$$\liminf_{t\to\infty} J(x,t,\varphi) \geq \zeta, \quad \liminf_{t\to\infty} P(x,t,\varphi) \geq \zeta,$$

uniformly for $x \in \overline{\Omega}$, *where* $Z(x,t,\varphi)$ *is a solution of the system* (2.7) *with initial condition* $Z(.,0,\varphi) = \varphi \in \mathbb{X}^+$.

Proof. If $\mathcal{R}_0 > 1$, then $\nu_0 > 0$. For any $\pi \in (0, \pi^*)$, π^* sufficiently small, let $\nu_0(\pi)$ the principal eigenvalue of the following eigenvalue problem:

$$\begin{cases} \nu\gamma_2(x) = \dfrac{\beta\rho\omega(S_0-\pi)}{H}\gamma_3(x) + \dfrac{\beta\alpha\eta(S_0-\pi)}{H}\gamma_4(x) - (\mu_h+d+\delta)\gamma_2(x) \\ \qquad + D\Delta\gamma_2(x), & x \in \Omega, \\ \nu\gamma_3(x) = \omega\gamma_2(x) - (\mu_b - r)\gamma_3(x) + D_b\Delta\gamma_3(x), & x \in \Omega, \\ \nu\gamma_4(x) = \eta\gamma_2(x) - (\mu_b + \gamma)\gamma_4(x) + D_b\Delta\gamma_4(x), & x \in \Omega, \\ \dfrac{\partial\gamma_2}{\partial z} = \dfrac{\partial\gamma_3}{\partial z} = \dfrac{\partial\gamma_4}{\partial z} = 0, & x \in \partial\Omega. \end{cases}$$

One has, $\lim_{\pi\to 0}\nu(\pi) = \nu_0$, one can fix $\pi_0 \in (0, \pi^*)$ such that $\nu(\pi) > 0$. Let

$$\mathbb{W} = \{\varphi \in \mathbb{X}^+ : \varphi_3 \neq 0, \varphi_4 \neq 0, \varphi_4 \neq 0\},$$

and

$$\partial\mathbb{W} = \{\varphi \in \mathbb{X}^+ : \varphi_2 \equiv 0, \varphi_3 \equiv 0, \varphi_4 \equiv 0\}.$$

$\mathbb{W}$ is a positive invariant set for the solution semiflow $\phi(t)$. Define

$$\mathbb{M}_\partial = \{\varphi \in \partial\mathbb{W} : \phi(t)\varphi \in \partial\mathbb{W}, t \geq 0\}.$$

Let $\omega(\varphi)$ be the omega set of the orbit of $\phi(t)$ through $\varphi \in \mathbb{X}^+$. For a $\phi \in \mathbb{M}_\partial$, we have $\phi(t)\varphi \in \partial\mathbb{W}$, $\forall t > 0$. Thus, $I(., t, \varphi) \equiv 0$, $B(., t, \varphi) \equiv 0$ and $J(., t, \varphi) \equiv 0$ $\forall t > 0$. From the first equation of (2.7), one has

$$\begin{cases} \dfrac{\partial S(x,t)}{\partial t} = \Lambda - \mu_h S + D\Delta S, \;\; x \in \Omega, \;\; t > 0, \\ \dfrac{\partial S}{\partial z} = 0, \;\; x \in \partial\Omega, \;\; t > 0. \end{cases}$$

Using the theory of asymptotically semiflow [21], $\lim_{t\to\infty} S(., t, \varphi) = S_0$ uniformly for $x \in \overline{\Omega}$, and $\omega(\varphi) = E_0$, $\varphi \in \mathbb{M}_\partial$.

Now we show that

$$\limsup_{t\to+\infty} ||\phi(t)\varphi - E_0|| \geq \pi_0.$$

Suppose by contradiction that $\limsup_{t\to+\infty}||\phi(t)\varphi_0 - E_0|| \leq \pi_0$, $\varphi_0 \in \mathbb{W}$. Then there exists $t^* > 0$ such that

$$S_0 - \pi_0 < S(x,t,\varphi_0) < S_0 + \pi_0, \quad I(x,t,\varphi_0) < \pi_0, \quad B(x,t,\varphi_0) < \pi_0,$$
$$J(x,t,\varphi_0) < \pi_0, t \geq t^*.$$

We know that $I(x,t,\varphi_0)$, $B(x,t,\varphi_0)$ and $J(x,t,\varphi_0)$ satisfy

$$\begin{cases} \dfrac{\partial I(x,t)}{\partial t} \geq \dfrac{\beta\rho\omega(S_0-\pi_0)}{H}B + \dfrac{\beta\alpha\eta(S_0-\pi_0)}{H}J \\ \qquad\qquad - (\mu_h+d+\delta)I + D\Delta I, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial B(x,t)}{\partial t} \geq \omega I - (\mu_b - r)B + D_b\Delta B, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial J(x,t)}{\partial t} \geq \eta I - (\mu_b+\gamma)J + D_b\Delta J, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial I}{\partial z} = \dfrac{\partial B}{\partial z} = \dfrac{\partial J}{\partial z} = 0, & x\in\partial\Omega. \end{cases}$$

Let $\psi_{\nu_0(\pi_0)} = (\psi_{2_{\nu_0(\pi_0)}}, \psi_{3_{\nu_0(\pi_0)}}, \psi_{4_{\nu_0(\pi_0)}})$ be the positive eigenfunction associated with $\nu_0(\pi_0)$. Thus, the following linear system:

$$\begin{cases} \dfrac{\partial u_1(x,t)}{\partial t} = \dfrac{\beta\rho\omega(S_0-\pi_0)}{H}u_2 + \dfrac{\beta\alpha\eta(S_0-\pi_0)}{H}u_3 \\ \qquad\qquad - (\mu_h+d+\delta)u_1 + D\Delta u_1, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial u_2(x,t)}{\partial t} = \omega u_1 - (\mu_b - r)u_2 + D_b\Delta u_2, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial u_3(x,t)}{\partial t} = \eta u_1 - (\mu_b+\gamma)u_3 + D_b\Delta u_3, & x\in\Omega,\ t>t^*, \\ \dfrac{\partial u_1}{\partial z} = \dfrac{\partial u_2}{\partial z} = \dfrac{\partial u_3}{\partial z} = 0, & x\in\partial\Omega, \end{cases}$$

has a solution $u(x,t) = \exp^{\nu_0(\pi_0)t}\psi_{\lambda_0(\pi_0)}(x)$, since $I(x,t,\varphi_0)>0$, $B(x,t,\varphi_0)>0$, $J(x,t,\varphi_0)>0$, $x\in\overline{\Omega}$ and $t>0$; there exists $\sigma>0$ such that

$$(I(x,t,\varphi_0), B(x,t,\varphi_0), J(x,t,\varphi_0)) \geq \sigma\exp^{\nu_0(\pi_0)t}\psi_{\lambda_0(\pi_0)}(x), \quad x\in\overline{\Omega},\ t>0.$$

Since $\lambda_0(\pi_0)>0$ then

$$\lim_{t\to\infty}(I(x,t,\varphi_0), B(x,t,\varphi_0), J(x,t,\varphi_0)) = \infty.$$

This is a contradiction since the variables I, B, J are bounded.

Next, define the continuous function $q:\mathbb{X}^+\to[0,\infty)$ by

$$q(\varphi) = \min\left\{\min_{x\in\overline{\Omega}}\varphi_3(x), \min_{x\in\overline{\Omega}}\varphi_4(x)\right\}, \quad \forall\,\varphi\in\mathbb{X}^+.$$

We have $q^{-1}(0,\infty)\subseteq\mathbb{W}$ and q is a generalized distance function for the semiflow $\phi(t):\mathbb{X}^+\to\mathbb{X}^+$. Any forward orbit of $\phi(t)$ in $\mathbb{M}_\partial$ converges to E_0. The above claims imply that E_0 is isolated in $\mathbb{X}^+$ and $\mathbb{W}^s\cap\mathbb{W}=\emptyset$, where $\mathbb{W}^s$ is the stable set of E_0. It is clear that there is no cycle in $\mathbb{M}_\partial$ from E_0 to E_0. We conclude that there exists $\zeta>0$ such that

$$\min_{\psi\in\omega(\varphi)} q(\psi) > \zeta, \quad \forall\,\varphi\in\mathbb{W}.$$

Choose ζ small enough such that $\liminf_{t\to+\infty} S(.,t,\varphi) \geq \zeta$ uniformly for $x \in \overline{\Omega}$. We proceed by the same way to show that $\liminf_{t\to+\infty} P(.,t,\varphi) \geq \zeta$ uniformly for $x \in \overline{\Omega}$ and this achieves the proof.

5. NSFD Scheme and Numerical Simulations

5.1. *NSFD of models* (2.7)

Already, in the deterministic space-independent model investigated in [15, 16], the system of ordinary differential equations could not completely be solved by analytic techniques. With now the addition of more realism through the incorporation of diffusive terms in space, the complete analytical solution of the resulting system of reaction–diffusion PDEs becomes more challenging. Consequently, numerical simulations are of fundamental importance in gaining some useful insight on the solution of the continuous differential equation model. We consider Mickens' NSFD method, which has shown great potential in producing schemes that are dynamically consistent with the continuous model [10–13]. We assume that the spatial domain in the bounded interval $\Omega = [a, b]$ and we discretize the region $[a, b] \times [0, \infty)$ through the mesh points (x_n, t_k), $n = 0, \ldots, M$, $k \in \mathbb{N}$, where $x_n = a + n\Delta x$ and $t_k = k\Delta t$, $\Delta x = (b - a)/M$ and Δt being the space and time step sizes, respectively, for a given integer $M > 0$. Following Mickens' rules, we propose the NSFD scheme below that generate the sequence $(S_n^k, I_n^k, B_n^k, J_n^k, P_n^k)$ of approximate solution $(S(x,t), I(x,t), B(x,t), J(x,t), P(x,t))$ at the point $(x,t) = (x_n, t_k)$ for the model (5.1) in which we assume throughout this section that the cholera immunity is livelong, i.e. $\delta = 0$.

$$\begin{cases} \dfrac{S_n^{k+1} - S_n^k}{\Delta t} = \Lambda - \lambda(B_n^k, J_n^k)S_n^{k+1} - \mu_h S_n^{k+1} + D\dfrac{S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}}{(\Delta x)^2}, \\ \dfrac{I_n^{k+1} - I_n^k}{\Delta t} = \lambda(B_n^k, J_n^k)S_n^{k+1} - (\mu_h + d)I_n^{k+1} + D\dfrac{I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}}{(\Delta x)^2}, \\ \dfrac{B_n^{k+1} - B_n^k}{\Delta t} = \omega I_n^{k+1} + rB_n^{k+1} - \mu_b B_n^{k+1} - \varepsilon B_n^{k+1} f(P_n^k) \\ \qquad\qquad + D_b\dfrac{B_{n+1}^{k+1} - 2B_n^{k+1} + B_{n-1}^{k+1}}{(\Delta x)^2}, \\ \dfrac{J_n^{k+1} - J_n^k}{\Delta t} = \eta I_n^{k+1} + \phi\varepsilon B_n^{k+1} f(P_n^k) - (\mu_b + \gamma)J_n^{k+1} \\ \qquad\qquad + D_b\dfrac{J_{n+1}^{k+1} - 2J_n^{k+1} + J_{n-1}^{k+1}}{(\Delta x)^2}, \\ \dfrac{P_n^{k+1} - P_n^k}{\Delta t} = \theta\gamma J_n^{k+1} - \varepsilon(B_n^{k+1} + J_n^{k+1})P_n^k - \mu_p P_n^{k+1} \\ \qquad\qquad + D_b\dfrac{P_{n+1}^{k+1} - 2P_n^{k+1} + P_{n-1}^{k+1}}{(\Delta x)^2}. \end{cases} \tag{5.1}$$

In (5.1), the discrete force of infection is given by

$$\lambda(B_n^k, J_n^k) = \beta \frac{\alpha J_n^k + \rho B_n^k}{\alpha J_n^k + \rho B_n^k + H}. \tag{5.2}$$

The discrete model is completed by the initial conditions

$$S_n^0 = s(x_n), \quad I_n^0 = i(x_n), \quad B_n^0 = b(x_n), \quad J_n^0 = j(x_n), \quad P_n^0 = p(x_n), \tag{5.3}$$

as well as extra grid points $x_{-1} := a - \Delta x$ and $x_{M+1} = b + \Delta x$, at which boundary conditions of the continuous model lead to the following:

$$S_{-1}^k = S_0^k, \quad S_{M+1}^k = S_M^k, \quad I_{-1}^k = I_0^k, \quad I_{M+1}^k = I_M^k, \tag{5.4}$$

$$J_{-1}^k = J_0^k, \quad J_{M+1}^k = J_M^k, \quad P_{-1}^k = P_0^k, \quad P_{M+1}^k = P_M^k. \tag{5.5}$$

Note that system (5.1) is indeed a NSFD scheme as *per* the formal definition in [1] (see also [5]): the nonlinear terms

$$\lambda(B, J)S, \quad Bf(P) \quad \text{and} \quad (B + J)P,$$

are approximated in a nonlocal way, that is, by functions of several points of the mesh.

Before going forward with the qualitative analysis of the NSFD scheme (5.1), we state upfront that this scheme has first-order accuracy in Δt and second-order accuracy in Δx. To show this, we compute $T(\Delta x, \Delta t)$, the local truncation error of the NSFD scheme (5.1) defined as the amount by which the solution (S, I, B, J, P) of the continuous model (2.7) fails to satisfy the discrete model when $(S_n^k, I_n^k, B_n^k, J_n^k, P_n^k)$ is replaced with $(S(x_n, t_k), I(x_n, t_k), B(x_n, t_k), J(x_n, t_k), P(x_n, t_k))$. For instance, in the interior of $(a, b) \times (0, \infty)$, the component $T^S(\Delta x, \Delta t)$ of $T(\Delta x, \Delta t)$ for the finite difference equation of the susceptible-dependent variable is given by

$$\begin{aligned} T^S(\Delta x, \Delta t) = {} & \frac{S(x_n, t_{k+1}) - S(x_n, t_k)}{\Delta t} - \Lambda + [\lambda(B(x_n, t_k), J(x_n, t_k)) + \mu_h] S \\ & \times (x_n, t_{k+1}) - D \frac{S(x_{n+1}, t_{k+1}) - 2S(x_n, t_{k+1}) + S(x_{n-1}, t_{k+1})}{(\Delta x)^2}. \end{aligned}$$

Assuming that the solution $S(x, t)$ is sufficiently differentiable and has bounded partial derivatives, performing Taylor expansion of $S(x, t)$ about the point (x_n, t_k) and using the fact that the function (S, B, J) satisfies the first equation in (2.7) at the point (x_n, t_k), we obtain (see, for instance, [14] for details of these Taylor expansions applied to the θ-method for parabolic equations, with $\theta = 1$)

$$T^S(\Delta x, \Delta t) = O[\Delta t + (\Delta x)^2].$$

Other components T^I, T^B, T^J and T^P of the local truncation error are dealt with in a similar manner. We now investigate the dynamics that the NSFD scheme inherits from the continuous model. □

Theorem 5.1. *The NSFD scheme* (5.1)–(5.5) *is dynamically consistent with respect to the positive and boundedness properties of the solution of the continuous model* (2.7), *irrespective of the sizes of the step sizes* $\Delta t > 0$ *and* $\Delta x > 0$.

Proof. The first finite difference equation in (5.1) corresponds to a system of $M+1$ algebraic equations for the unknown vector $S^{k+1} = (S_0^{k+1}, \ldots, S_M^{k+1})^T$

$$A^k S^{k+1} = S^k + \Delta t(\Lambda, \ldots, \Lambda)^T, \tag{5.6}$$

where the entries of the tridiagonal matrix

$$A^k = \begin{pmatrix} a_0^k & a & 0 & \cdots & 0 & 0 & 0 \\ a & a_1^k & a & \cdots & 0 & 0 & 0 \\ 0 & a & a_2^k & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & a_{M-2}^k & a & 0 \\ 0 & 0 & 0 & \cdots & a & a_{M-1}^k & a \\ 0 & 0 & 0 & \cdots & 0 & a & a_M^k \end{pmatrix},$$

are given by

$$\begin{aligned} a &= -D\Delta t/(\Delta x)^2, \\ a_0^k &= 1 + D\Delta t/(\Delta x)^2 + \Delta t(\lambda(B_0^k, J_0^k) + \mu_h), \\ a_i^k &= 1 + 2D\Delta t/(\Delta x)^2 + \Delta t(\lambda(B_i^k, J_i^k) + \mu_h), \quad \text{for } i = 1, \ldots, M-1, \\ a_M^k &= 1 + D\Delta t/(\Delta x)^2 + \Delta t(\lambda(B_M^k, J_M^k) + \mu_h). \end{aligned}$$

Hence, A^k is a strictly diagonally dominant matrix which, in view of the decomposition $A^k = D - B$ where $D = \text{diag}(A^k) \geq 0$ and $B \geq 0$, is a nonsingular M-matrix (see [2]). Thus, $(A^k)^{-1} \geq 0$ and $S^{k+1} = (A^k)^{-1}(S^k + \Delta t(\Lambda, \ldots, \Lambda)^T) \geq 0$ whenever $S^k \geq 0$. Similarly, $I_n^{k+1} \geq 0$, $B_n^{k+1} \geq 0$, $J_n^{k+1} \geq 0$ and $P_n^{k+1} \geq 0$ because each corresponding finite difference equation in (5.1) is a system of $M+1$ algebraic equations of the form (5.6) whose involved matrix is strictly diagonally dominant, with positive diagonal and nonpositive off-diagonal, thus making it a nonsingular M-matrix, as sketched below. For the second equation of (5.1)

$$AI^{k+1} = I^k + \Delta t T^{k+1},$$

where

$$T^{k+1} = (\lambda(B_0^k, J_0^k)S_0^{k+1}, \lambda(B_1^k, J_1^k)S_1^{k+1}, \dots, \lambda(B_M^k, J_M^k)S_M^{k+1})^T,$$

$$A = \begin{pmatrix} a_1 & a_2 & 0 & \cdots & 0 & 0 & 0 \\ a_2 & a_3 & a_2 & \cdots & 0 & 0 & 0 \\ 0 & a_2 & a_3 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & a_3 & a_2 & 0 \\ 0 & 0 & 0 & \cdots & a_2 & a_3 & a_2 \\ 0 & 0 & 0 & \cdots & 0 & a_2 & a_1 \end{pmatrix},$$

and

$$a_1 = 1 + D\Delta t/(\Delta x)^2 + \Delta t(\mu_h + d), \quad a_2 = -D\Delta t/(\Delta x)^2,$$
$$a_3 = 1 + 2D\Delta t/(\Delta x)^2 + \Delta t(\mu_h + d).$$

For the third equation of (5.1)

$$C^k B^{k+1} = B^k + \omega \Delta t I^{k+1},$$

where

$$C^k = \begin{pmatrix} c_0^k & c & 0 & \cdots & 0 & 0 & 0 \\ c & c_1^k & c & \cdots & 0 & 0 & 0 \\ 0 & c & c_2^k & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & c_{M-2}^k & c & 0 \\ 0 & 0 & 0 & \cdots & c & c_{M-1}^k & c \\ 0 & 0 & 0 & \cdots & 0 & c & c_M^k \end{pmatrix},$$

$$c = -D_b\Delta t/(\Delta x)^2,$$
$$c_0^k = 1 + D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon f(P_0^k) + \mu_b - r),$$
$$c_i^k = 1 + 2D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon f(P_i^k) + \mu_b - r), \quad \text{for } i = 1, \dots, M-1,$$
$$c_M^k = 1 + D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon f(P_M^k) + \mu_b - r).$$

For the fourth equation of (5.1)

$$KJ^{k+1} = J^k + \Delta t(\eta I^{k+1} + L^{k+1}),$$

where

$$L^{k+1} = (\phi\varepsilon B_0^{k+1} f(P_0^k), \phi\varepsilon B_1^{k+1} f(P_1^k), \ldots, \phi\varepsilon B_M^{k+1} f(P_M^k))^T,$$

$$K = \begin{pmatrix} d_1 & d_2 & 0 & \cdots & 0 & 0 & 0 \\ d_2 & d_3 & d_2 & \cdots & 0 & 0 & 0 \\ 0 & d_2 & d_3 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & d_3 & d_2 & 0 \\ 0 & 0 & 0 & \cdots & d_2 & d_3 & d_2 \\ 0 & 0 & 0 & \cdots & 0 & d_2 & d_1 \end{pmatrix},$$

$$d_1 = 1 + D_b\Delta t/(\Delta x)^2 + \Delta t(\mu_b + \gamma), \quad d_2 = -D_b\Delta t/(\Delta x)^2,$$

$$d_3 = 1 + 2D_b\Delta t/(\Delta x)^2 + \Delta t(\mu_b + \gamma).$$

For the fifth equation of (5.1)

$$E^k P^{k+1} = P^k + \theta\gamma J^{k+1},$$

where

$$E^k = \begin{pmatrix} e_0^k & e & 0 & \cdots & 0 & 0 & 0 \\ e & e_1^k & e & \cdots & 0 & 0 & 0 \\ 0 & e & e_2^k & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & e_{M-2}^k & e & 0 \\ 0 & 0 & 0 & \cdots & e & e_{M-1}^k & e \\ 0 & 0 & 0 & \cdots & 0 & e & e_M^k \end{pmatrix},$$

$$e = -D_b\Delta t/(\Delta x)^2,$$

$$e_0^k = 1 + D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon(B_0^k + J_0^k) + \mu_p),$$

$$c_i^k = 1 + 2D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon(B_i^k + J_i^k) + \mu_p), \quad \text{for } i = 1, \ldots, M-1,$$

$$e_M^k = 1 + D_b\Delta t/(\Delta x)^2 + \Delta t(\varepsilon(B_M^k + J_M^k) + \mu_p).$$

Regarding the boundedness of the solutions of (5.1), this is a straightforward consequence of the discrete Gronwall inequality. Indeed, setting

$$N^k = \sum_{n=0}^{M} (S_n^k + I_n^k), \tag{5.7}$$

adding the first two equations of (5.1) and using the boundary conditions (5.4) and (5.5) implies

$$N^{k+1} \leq \frac{\Lambda(M+1)\Delta t}{1+\mu_h \Delta t} + \frac{N^k}{1+\mu_h \Delta t},$$

from which it follows by the discrete Gronwall inequality that

$$N^k \leq \frac{\Lambda(M+1)}{\mu_h}\left(1 - \frac{1}{(1+\mu_h \Delta t)^k}\right) + \frac{N^0}{(1+\mu_h \Delta t)^k}. \tag{5.8}$$

Thus

$$N^k \leq \frac{\Lambda}{\mu_h}(M+1) \quad \text{if } N^0 \leq \frac{\Lambda}{\mu_h}(M+1).$$

Next, setting

$$D^k = \sum_{n=0}^{M} (\phi B_n^k + J_n^k),$$

and using the third and the fourth equations of (5.1) in which $\sum_{n=0}^{M} I_n^{k+1} \leq \frac{\Lambda}{\mu_h}(M+1)$, we obtain

$$D^{k+1} \leq \frac{(\phi\omega + \eta)\Lambda(M+1)\Delta t}{1+\mu\Delta t} + \frac{D^k}{1+\mu\Delta t},$$

where $\mu = \min(\phi(\mu_b - r), (\mu_b + \gamma))$. Therefore, Gronwall discrete inequality yields

$$D^k \leq \frac{(\phi\omega + \eta)\Lambda(M+1)}{\mu\mu_h}\left(1 - \frac{1}{(1+\mu\Delta t)^k}\right) + \frac{D^0}{(1+\mu\Delta t)^k}. \tag{5.9}$$

Hence

$$D^k \leq \frac{(\phi\omega + \eta)\Lambda(M+1)}{\mu\mu_h} \quad \text{if } D^0 \leq \frac{(\phi\omega + \eta)\Lambda(M+1)}{\mu\mu_h}.$$

By setting $P^k = \sum_{n=0}^{M} P_n^{k+1}$, it follows in a similar manner from the fifth equation of (5.1) that

$$P^k \leq \frac{\theta\gamma(\phi\omega + \eta)\Lambda(M+1)}{\mu_p \mu\mu_h}\left(1 - \frac{1}{(1+\mu_p \Delta t)^k}\right) + \frac{P^0}{(1+\mu_p \Delta t)^k}, \tag{5.10}$$

so that

$$P^k \leq \frac{\theta\gamma(\phi\omega + \eta)\Lambda(M+1)}{\mu_p \mu\mu_h} \quad \text{if } P^0 \leq \frac{\theta\gamma(\phi\omega + \eta)\Lambda(M+1)}{\mu_p \mu\mu_h}.$$

Finally, if $N^0 > \frac{\Lambda}{\mu_h}(M+1)$ or $D^0 > \frac{(\phi\omega+\eta)\Lambda(M+1)}{\mu\mu_h}$ or $P^0 > \frac{\theta\gamma(\phi\omega+\eta)\Lambda(M+1)}{\mu_p\mu\mu_h}$, it follows from (5.8), (5.9) and (5.10) that

$$\limsup_{k\to+\infty} N^k \leq \frac{\Lambda}{\mu_h}(M+1), \ \limsup_{k\to+\infty} D^k \leq \frac{(\phi\omega + \eta)\Lambda(M+1)}{\mu\mu_h} \quad \text{and}$$

$$\limsup_{k\to+\infty} P^k \leq \frac{\theta\gamma(\phi\omega + \eta)\Lambda(M+1)}{\mu_p \mu\mu_h}.$$

Thus, the solutions of the system (5.1) with nonnegative initial conditions such that

$$N^0 \leq \frac{\Lambda}{\mu_h}(M+1),\ D^0 \leq \frac{(\phi\omega+\eta)\Lambda(M+1)}{\mu\mu_h} \text{ and } P^0 \leq \frac{\theta\gamma(\phi\omega+\eta)\Lambda(M+1)}{\mu_p\mu\mu_h},$$

are nonnegative and remain in this region, which is attractive.

Another important feature of the continuous model that the NSFD scheme preserves is the disease-free fixed point and the endemic fixed point, which are exactly its disease-free and the endemic equilibrium points. Their global stability is given in the next result. □

Theorem 5.2. *For the system* (5.1)–(5.5) *with* $\Delta t > 0$ *and* $\Delta x > 0$

(i) *the disease-free fixed point is globally stable whenever* $\max\{\mathcal{R}_0, \mathcal{N}_0\} \leq 1$.
(ii) *the endemic fixed point is globally stable if* $\mathcal{R}_0 > 1$ *and* $\varepsilon = 0$.

Proof. (i) We propose the discrete Lyapunov functional candidate that reads as follows:

$$\mathcal{L}^k = \sum_{n=0}^{M} \frac{1}{\Delta t}\left\{S_n^k - S_0 - S_0 \ln\left(\frac{S_n^k}{S_0}\right) + I_n^k + b(1+c\Delta t)B_n^k + d(1+e\Delta t)J_n^k\right\}, \tag{5.11}$$

where b, c, d, e are positive constant to be determined shortly.

$$\begin{aligned}
\mathcal{L}^{k+1} - \mathcal{L}^k \leq{}& \sum_{n=0}^{M} \frac{1}{\Delta t}\Bigg\{\left(1 - \frac{S_0}{S_n^{k+1}}\right)(S_n^{k+1} - S_n^k) + (I_n^{k+1} - I_n^k) \\
&+ b(1+c\Delta t)(B_n^{k+1} - B_n^k)\Bigg\} + \sum_{n=0}^{M} \frac{1}{\Delta t} d(1+e\Delta t)\left(J_n^{k+1} - J_n^k\right) \\
={}& \sum_{n=0}^{M} \frac{1}{\Delta t}\Bigg\{\left(1 - \frac{S_0}{S_n^{k+1}}\right)\Bigg(\Lambda - \lambda(B_n^k, J_n^k)S_n^{k+1} - \mu_h S_n^{k+1} \\
&+ D\frac{S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}}{(\Delta x)^2}\Bigg)\Bigg\} + \sum_{n=0}^{M} \frac{1}{\Delta t} \\
&\times\left\{\lambda\left(B_n^k, J_n^k\right) S_n^{k+1} - (\mu_h + d)I_n^{k+1} + D\frac{I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}}{(\Delta x)^2}\right\} \\
&+ \sum_{n=0}^{M} \frac{1}{\Delta t} b(1+c\Delta t)\Bigg\{\omega I_n^{k+1} + rB_n^{k+1} - \mu_b B_n^{k+1} - \varepsilon B_n^{k+1} f(P_n^k) \\
&+ D_b\frac{B_{n+1}^{k+1} - 2B_n^{k+1} + B_{n-1}^{k+1}}{(\Delta x)^2}\Bigg\} + \sum_{n=0}^{M} \frac{1}{\Delta t} d(1+e\Delta t)
\end{aligned}$$

$$\times\left\{\eta I_n^{k+1} + \phi\varepsilon B_n^{k+1} f(P_n^k) - (\mu_b+\gamma) J_n^{k+1} + D_b \frac{J_{n+1}^{k+1} - 2J_n^{k+1} + J_{n-1}^{k+1}}{(\Delta x)^2}\right\}.$$

Using the inequality $\lambda(B_n^k, J_n^k) \leq (\beta\rho/H)B_n^k + (\beta\alpha/H)J_n^k$ and grouping like terms, one has

$$\begin{aligned}\mathcal{L}^{k+1} - \mathcal{L}^k = \sum_{n=0}^{M} &\left\{ -\frac{\mu_h}{S_n^{k+1}}(S_n^{k+1} - S_0)^2 + \frac{\beta\rho S_0}{H} B_n^k + \frac{\beta\alpha S_0}{H} J_n^k \right.\\ &\left. + I_n^{k+1}(b\omega + d\eta - (\mu_h + d)) \right\} + \Pi^k\\ &+ \sum_{n=0}^{M} \{\varepsilon B_n^{k+1} f(P_n^k)(d\phi - b) - b(\mu_b - r)B_n^{k+1} - d(\mu_b+\gamma)J_n^{k+1}\\ &+ bc(B_n^{k+1} - B_n^k)\} + \sum_{n=0}^{M}\{ed(J_n^{k+1} - J_n^k)\}\end{aligned}$$

with

$$\begin{aligned}\Pi^k &= \sum_{n=0}^{M} \frac{1}{(\Delta x)^2}\left\{ D(S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}) + S_0 D\left(2 - \frac{S_{n+1}^{k+1}}{S_n^{k+1}} + \frac{S_{n-1}^{k+1}}{S_n^{k+1}}\right)\right.\\ &\quad \left. + D(I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1})\right\} + \sum_{n=0}^{M}\frac{1}{(\Delta x)^2}\\ &\quad \times\{D_b(B_{n+1}^{k+1} - 2B_n^{k+1} + B_{n-1}^{k+1}) + D_b(J_{n+1}^{k+1} - 2J_n^{k+1} + J_{n-1}^{k+1})\}\\ &\leq \sum_{n=0}^{M}\frac{1}{(\Delta x)^2}\{D(S_{M+1}^{k+1} - S_M^{k+1} + S_{-1}^{k+1} - S_0^{k+1})\\ &\quad + D(I_{M+1}^{k+1} - I_M^{k+1} + I_{-1}^{k+1} - I_0^{k+1})\} + \sum_{n=0}^{M}\frac{1}{(\Delta x)^2}\\ &\quad \times\{D_b(B_{M+1}^{k+1} - B_M^{k+1} + B_{-1}^{k+1} - B_0^{k+1})\\ &\quad + D_b(J_{M+1}^{k+1} - J_M^{k+1} + J_{-1}^{k+1} - J_0^{k+1})\}\\ &= 0.\end{aligned}$$

$\mathcal{L}^{k+1} - \mathcal{L}^k$ becomes

$$\begin{aligned}
\mathcal{L}^{k+1} - \mathcal{L}^k \leq \sum_{n=0}^{M} \Bigg\{ & -\frac{\mu_h}{S_n^{k+1}}(S_n^{k+1} - S_0)^2 + \frac{\beta\rho S_0}{H} B_n^k + \frac{\beta\alpha S_0}{H} J_n^k \\
& + I_n^{k+1}(b\omega + d\eta - (\mu_h + d)) \Bigg\} + \sum_{n=0}^{M} \Bigg\{ \varepsilon B_n^{k+1} f(P_n^k)(d\phi - b) \\
& - b(\mu_b - r) B_n^{k+1} - d(\mu_b + \gamma) J_n^{k+1} + bc(B_n^{k+1} - B_n^k) \Bigg\} \\
& + \sum_{n=0}^{M} \{ ed(J_n^{k+1} - J_n^k) \} \\
= \sum_{n=0}^{M} \Bigg\{ & -\frac{\mu_h}{S_n^{k+1}}(S_n^{k+1} - S_0)^2 + I_n^{k+1}(b\omega + d\eta - (\mu_h + d)) \\
& + \varepsilon B_n^{k+1} f(P_n^k)(d\phi - b) \Bigg\} + \sum_{n=0}^{M} \Bigg\{ B_n^k \left(\frac{\beta\rho S_0}{H} - bc \right) + J_n^k \left(\frac{\beta\alpha S_0}{H} - ed \right) \\
& + B_n^{k+1}(bc - b(\mu_b - r)) \Bigg\} + \sum_{n=0}^{M} \{ J_n^{k+1}(ed - b(\mu_b + \gamma)) \}.
\end{aligned}$$

For the case $\max\{\mathcal{R}_0, \mathcal{N}_0\} = \mathcal{R}_0$, let's choose b, c, d, e as follows:

$$b = \beta\rho S_0/H(\mu_b - r), \quad c = (\mu_b - r), \quad d = \beta\alpha S_0/H(\mu_b + \gamma), \quad e = (\mu_b + \gamma).$$

Then

$$\begin{aligned}
\mathcal{L}^{k+1} - \mathcal{L}^k \leq \sum_{n=0}^{M} \Bigg\{ & -\frac{\mu_h}{S_n^{k+1}}(S_n^{k+1} - S_0)^2 + (\mu_h + d) I_n^{k+1}(\mathcal{R}_0 - 1) \\
& + \frac{\mu_h + d + \delta}{\omega} \varepsilon B_n^{k+1} f(P_n^k)(\mathcal{N}_0 - \mathcal{R}_0) \Bigg\}.
\end{aligned} \tag{5.12}$$

For the case $\max\{\mathcal{R}_0, \mathcal{N}_0\} = \mathcal{N}_0$, we choose $b = \phi(\mu_h + d)/(\phi\omega + \eta)$, $c = (\mu_b - r)$, $d = (\mu_h + d)/(\phi\omega + \eta)$, $e = (\mu_b + \gamma)$

$$\mathcal{L}^{k+1} - \mathcal{L}^k \leq \sum_{n=0}^{M} \left\{ -\frac{\mu_h}{S_n^{k+1}} \left(S_n^{k+1} - S_0 \right)^2 + J_n^{k+1} \frac{(\mu_b + \gamma)(\mu_h + d)}{\phi\omega + \eta} (\mathcal{N}_0 - 1) \right\} \tag{5.13}$$

$$+ \sum_{n=0}^{M} \left\{ B_n^{k+1} \frac{\phi(\mu_b - r)(\mu_h + d)}{\phi\omega + \eta} (\mathcal{R}_0 - 1) \right\}. \tag{5.14}$$

Using (5.12) and (5.13) proves that $\mathcal{L}^{k+1} - \mathcal{L}^k \leq 0$. Hence, the sequence $\{\mathcal{L}^k\}$ is decreasing and bounded. Thus there exists, a positive function $\widetilde{\mathcal{L}}$ such that

$$\lim_{t\to+\infty} \mathcal{L}^k = \widetilde{\mathcal{L}}.$$

Thus

$$\lim_{k\to+\infty} S_n^k = S_0, \quad \lim_{k\to+\infty} I_n^k = 0, \quad \lim_{k\to+\infty} B_n^k = 0, \quad \lim_{k\to+\infty} J_n^k = 0, \quad \lim_{k\to+\infty} P_n^k = 0.$$

(ii) For the global stability, we use the following discrete Lyapunov functional candidate:

$$\begin{aligned}
\mathcal{L}^k &= \sum_{n=0}^{M} \frac{1}{\Delta t}\left\{ S_n^k - S^* - S^*\ln\left(\frac{S_n^k}{S^*}\right) + I_n^k - I^* - I^*\ln\left(\frac{I_n^k}{I^*}\right)\right\} \\
&\quad + \sum_{n=0}^{M} \frac{1}{\Delta t}\left\{ \frac{\beta\alpha B^* S^*}{(\rho B^* + \alpha J^* + H)\omega I^*}(1 + (\mu_b - r)\Delta t)\left(B_n^k - B^* - B^*\ln\left(\frac{B_n^k}{B^*}\right)\right)\right\} \\
&\quad + \sum_{n=0}^{M} \frac{1}{\Delta t}\left\{ \frac{\beta\alpha J^* S^*}{(\rho B^* + \alpha J^* + H)\eta I^*}(1 + (\mu_b + \gamma)\Delta t)\left(J_n^k - J^* - J^*\ln\left(\frac{J_n^k}{J^*}\right)\right)\right\}.
\end{aligned}$$

Some direct computations yield

$$\begin{aligned}
\mathcal{L}^{k+1} - \mathcal{L}^k \leq \sum_{n=0}^{M} \Bigg\{ &\left(1 - \frac{S^*}{S^{k+1}}\right)(\mu_h S^* - \mu_h S_n^{k+1}) + \left(1 - \frac{S^*}{S^{k+1}}\right) \\
&\times (\lambda(B^*, J^*)S^* - \lambda(B_n^k, J_n^k)S_n^{k+1})\Bigg\} \\
&+ \sum_{n=0}^{M}\Bigg\{ \left(1 - \frac{I^*}{I_n^{k+1}}\right)\lambda\left(B_n^k, J_n^k\right)S_n^{k+1} - \left(1 - \frac{I^*}{I_n^{k+1}}\right) \\
&\times \frac{\lambda(B^*, J^*)S^*}{I^*} I_n^{k+1}\Bigg\} + \sum_{n=0}^{M}\left(1 - \frac{B^*}{B_n^{k+1}}\right)\frac{\beta\rho B^* S^* I_n^{k+1}}{(\rho B^* + \alpha J^* + H)I^*} \\
&+ \sum_{n=0}^{M}\Bigg\{ -\left(1 - \frac{B^*}{B_n^{k+1}}\right)\frac{\beta\rho B^* S^* I_n^{k+1}}{(\rho B^* + \alpha J^* + H)}\frac{B_n^{k+1}}{B^*} \\
&+ \left(1 - \frac{J^*}{J_n^{k+1}}\right)\frac{\beta\alpha J^* I_n^{k+1}}{(\rho B^* + \alpha J^* + H)I^*}\Bigg\} \\
&+ \sum_{n=0}^{M}\left\{ -\left(1 - \frac{J^*}{J_n^{k+1}}\right)\frac{\beta\rho B^*}{(\rho B^* + \alpha J^* + H)}\frac{J_n^{k+1}}{J^*}\right\}
\end{aligned}$$

$$
\begin{aligned}
&+\sum_{n=0}^{M}\left\{\frac{\beta\alpha J^*}{(\rho B^*+\alpha J^*+H)}\left(\frac{J_n^{k+1}}{J^*}-\frac{J_n^k}{J^*}-\ln\left(\frac{J_n^k}{J_n^{k+1}}\right)\right)\right\}\\
&+\sum_{n=0}^{M}\left\{\frac{\beta\alpha J^* I_n^{k+1}}{(\rho B^*+\alpha J^*+H)}\left(\frac{B_n^{k+1}}{B^*}-\frac{B_n^k}{B^*}-\ln\left(\frac{B_n^k}{B_n^{k+1}}\right)\right)\right\}.
\end{aligned}
$$

Recall the following functions:

$$\lambda_1(B)=\frac{\beta\rho B}{\rho B+\alpha J+H},\quad \lambda_2(J)=\frac{\beta\alpha J}{\rho B+\alpha J+H},$$

and define the function

$$h(x)=x-1-\ln x.$$

Then one has

$$
\begin{aligned}
\mathcal{L}^{k+1}-\mathcal{L}^k \le{}& \sum_{n=0}^{M}\left\{-\frac{\mu_h}{S_n^{k+1}}\left(S_n^{k+1}-S^*\right)^2\right\}\\
&-\sum_{n=0}^{M}\left\{\frac{\beta\rho B^*}{(\rho B^*+\alpha J^*+H)}\left(h\left(\frac{S^*}{S_n^{k+1}}\right)+h\left(\frac{\lambda_1\left(B_n^k\right)S_n^{k+1}I^*}{\lambda_1(B^*)S^*I_n^{k+1}}\right)\right.\right.\\
&\left.\left.+h\left(\frac{B^*I_n^{k+1}}{B_n^{k+1}I^*}\right)\right)\right\}+\sum_{n=0}^{M}\left(h\left(\frac{B_n^{k+1}}{B^*}\right)-h\left(\frac{\lambda_1\left(B_n^k\right)}{\lambda_1(B^*)}\right)\right)\\
&-\sum_{n=0}^{M}\left\{\frac{\beta\alpha J^*}{(\rho B^*+\alpha J^*+H)}\left(h\left(\frac{S^*}{S_n^{k+1}}\right)+h\left(\frac{\lambda_2\left(J_n^k\right)S_n^{k+1}I^*}{\lambda_2\left(J^*\right)S^*I_n^{k+1}}\right)\right.\right.\\
&\left.\left.+h\left(\frac{J^*I_n^{k+1}}{J_n^{k+1}I^*}\right)\right)\right\}+\sum_{n=0}^{M}\left(h\left(\frac{J_n^{k+1}}{J^*}\right)-h\left(\frac{\lambda_2\left(J_n^k\right)}{\lambda_2(J^*)}\right)\right)\\
\le{}& 0.
\end{aligned}
$$

Thus, $\{\mathcal{L}^k\}$ is a nonincreasing sequence, there exists, $\overline{\mathcal{L}}$ such that

$$\lim_{k\to}\mathcal{L}^k=\overline{\mathcal{L}}.$$

and

$$
\begin{aligned}
&\lim_{k\to+\infty}S_n^k=S^*,\quad \lim_{k\to+\infty}I_n^k=I^*,\quad \lim_{k\to+\infty}B_n^k=B^*,\quad \lim_{k\to+\infty}J_n^k=J^*,\\
&\lim_{k\to+\infty}P_n^k=P^*.
\end{aligned}
$$

□

5.2. *Numerical illustration of theoretical results*

Here, we simulate the model to support our theoretical results and assess the role the diffusion on the spatiotemporal evolution of the bacterial infections. We choose $m=3$. This last choice is not a strong limitation because $F_m(P)$ depends rather weakly on m and $F_3(P)$ is a good approximation of $F_{100}(P)$ on $0<m<5$ [20].

Just for illustration purposes, we assume that the spatial domain is the segment $\Omega = [0, 100]$ and choose the space step size $\Delta x = 0.75$, and the time step size $\Delta t = 0.5$. To numerically illustrate the stability of equilibria of PDE model (2.7), we select three sets of model's parameters as follows.

(i) We take $\varepsilon = 0.71$, and other parameters such that $\mathcal{R}_0 = 0.1097 < 1$ and $\mathcal{N}_0 = 0.1049 < 1$. This is used to support numerically Theorem 4.4 about the GAS of the DFE $E_0 = (5000, 0, 0, 0, 0)$ as displayed in Fig. 1.

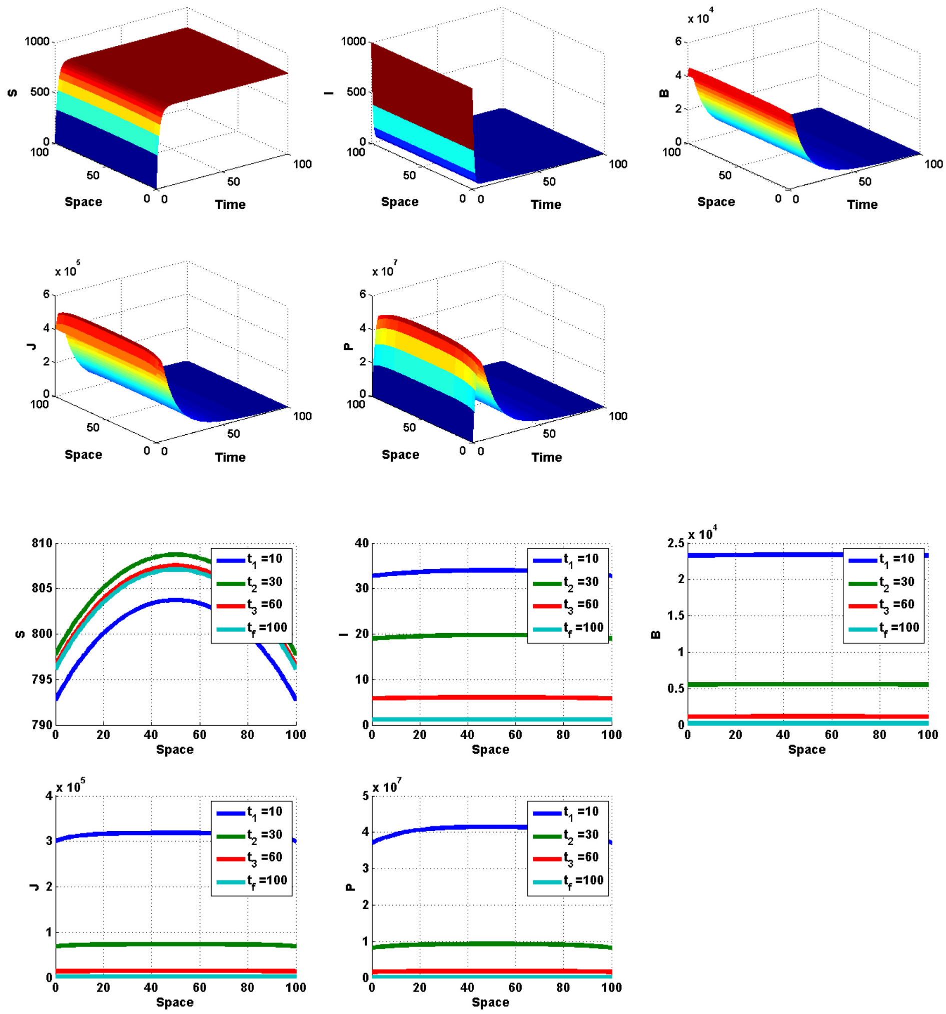

Fig. 1. Global stability of the DFE of the model with absorption rate $\varepsilon = 0.71 > 0$ and snapshots of the solution at different instants when the solution diffuses in the space: Initial conditions $(s(x), i(x), b(x), j(x), p(x)) = (100, 1000, 4 \times 10^4, 4 \times 10^5, 10^6)$, $\mathcal{R}_0 = 0.1097 < 1$ and $\mathcal{N}_0 = 0.1049 < 1$.

(ii) For $\varepsilon = 0$, we choose a set of parameters such that $\mathcal{R}_0 = 2.16 > 1$. This case numerically illustrates Theorem 4.2, that is the equilibrium $E^* = (5000, 4000, 4\times10^4, 6.5\times10^5, 6\times10^8)$ is globally asymptotically stable as shown in Fig. 2.

(iii) To support the uniform persistence, we take $\varepsilon = 0.71$, and select other parameters such that $\mathcal{R}_0 = 5.027 > 1$, the uniform persistence is illustrated in Fig. 3.

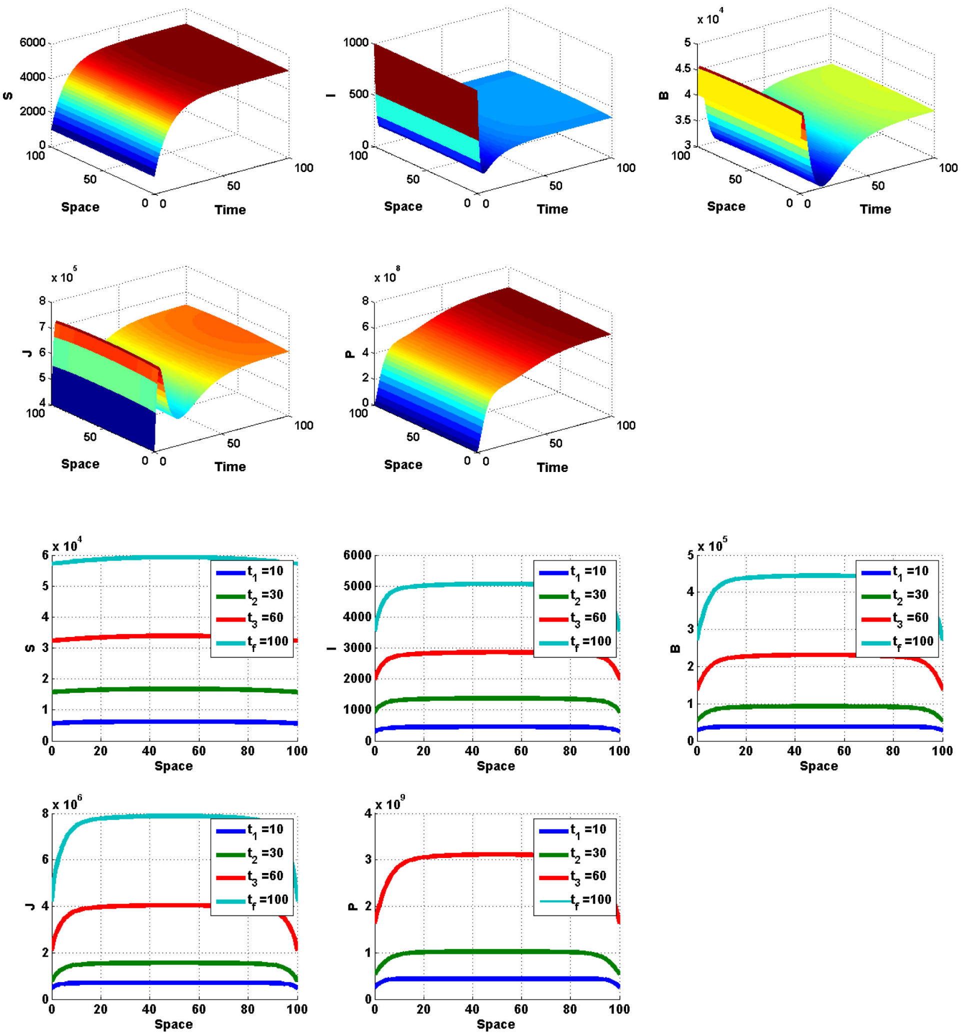

Fig. 2. Global stability of the endemic equilibrium E^* of the model without absorption rate ($\varepsilon = 0$), and snapshots of the solution at different instants when the solution diffuses in the space: Initial conditions $(s(x), i(x), b(x), j(x), p(x)) = (10^3, 10^3, 4\times10^4, 4\times10^5, 10^8)$, $\mathcal{R}_0 = 2.16 > 1$.

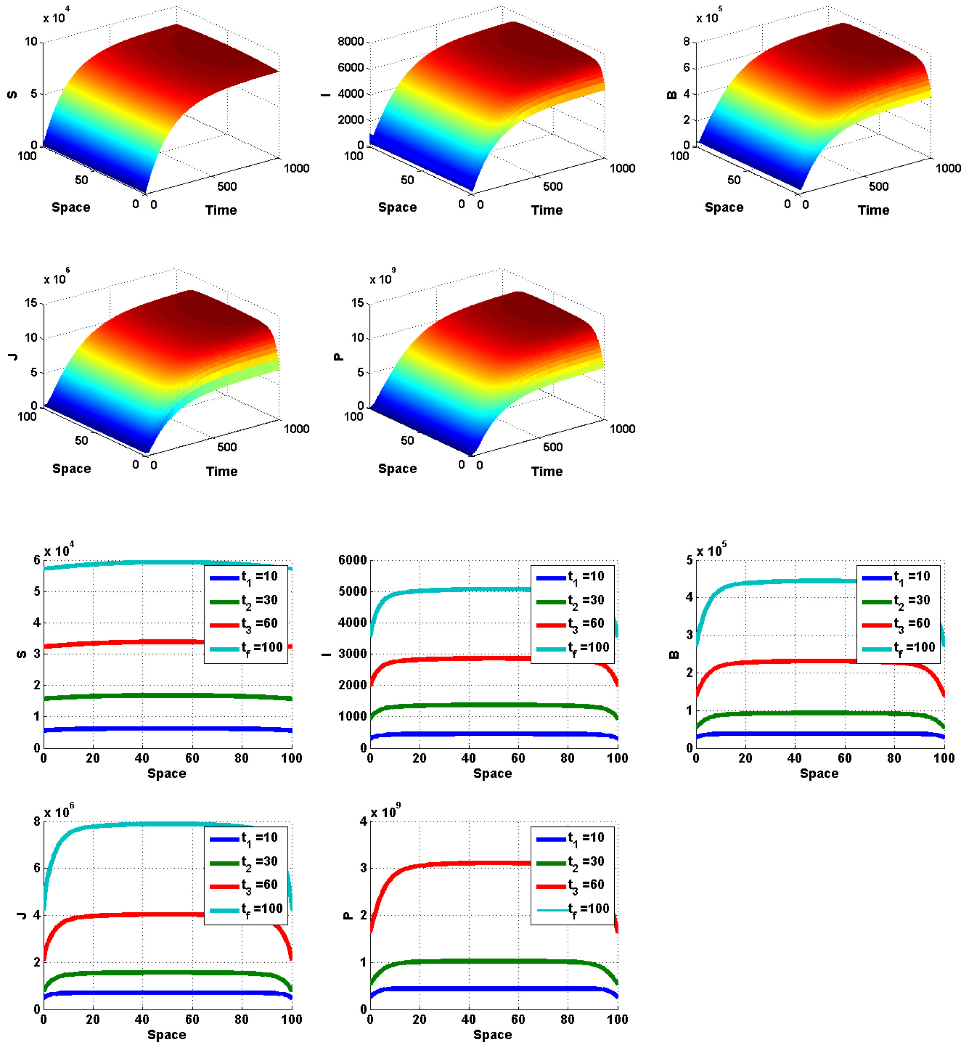

Fig. 3. Uniform persistence of the full model, $\varepsilon = 0.71$, and snapshots of the solution at different instants when the solution diffuses in the space: Initial conditions $(s(x), i(x), b(x), j(x), p(x)) = (10^4, 4 \times 10^2, 0.5 \times 10^4, 4 \times 10^5, 10^9)$. The parameters are chosen such that $\mathcal{R}_0 = 5.027 > 1$.

5.3. *Impacts of spatial distribution of phages, bacteria and humans*

To carry out the influence of the diffusion on the system, we fix the values of the coefficients D and D_b. In Figs. 1 and 4–6, the time evolution of solutions is illustrated for different values of the diffusion coefficients for humans, phages and bacteria (assuming that phages and bacteria diffuse similarly).

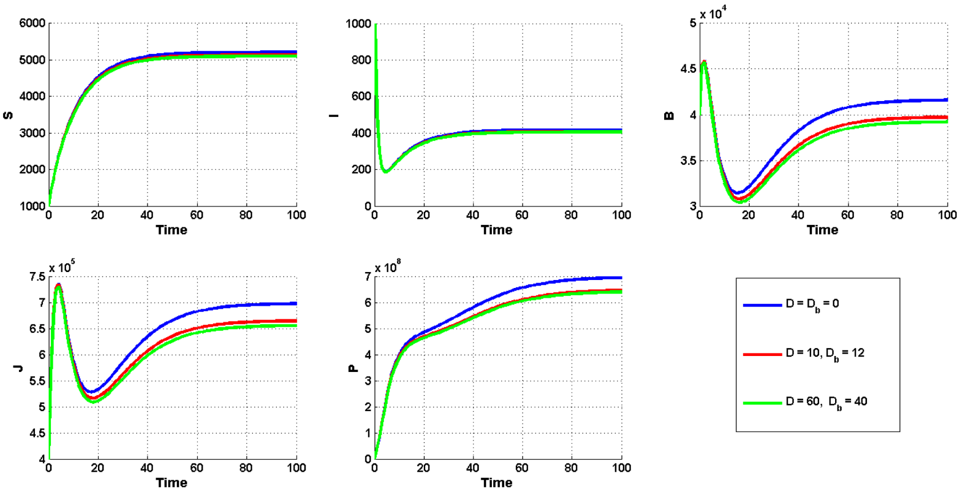

Fig. 4. Time evolution of the solutions with increasing values of D, D_b showing the spatially homogeneous convergence of the system to its endemic equilibrium E^* ($\mathcal{R}_0 = 2.16 > 1$).

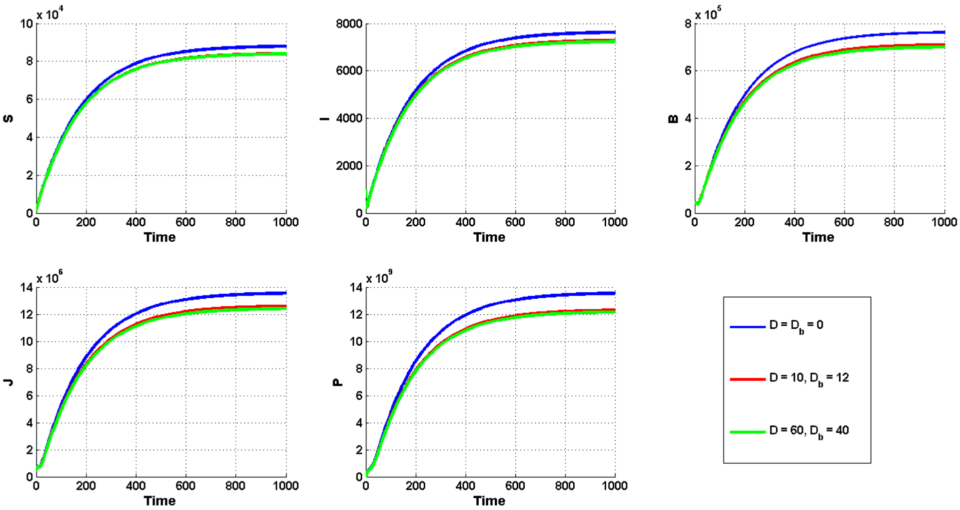

Fig. 5. Time evolution of the solutions with set values of D, D_b showing the spatially homogeneous persistence of the model ($\mathcal{R}_0 = 5.027 > 1$).

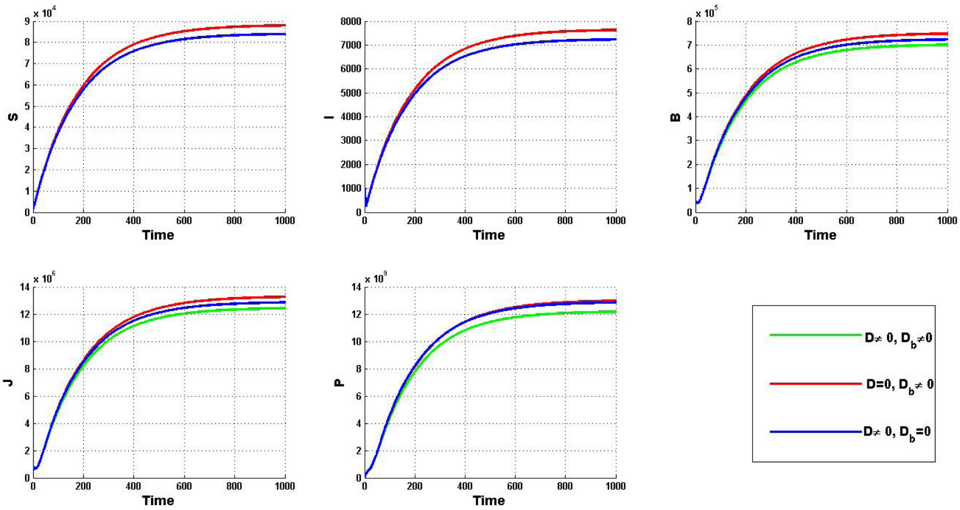

Fig. 6. Time evolution of the solutions showing the impact of spatial distribution of phages, bacteria and humans.

6. Conclusion and Perspectives

In this work, we have modeled and analyzed the impact of spatial evolution of phages and bacteria on a continuous reaction–diffusion bacteria-borne disease model. Precisely, we have developed a continuous model and its discrete NSFD counterpart.

(I) We've first proposed a reaction–diffusion model to assess the impact of spatial aspect of phage–bacteria infection on the indirectly transmitted bacterial infections. The introduction of the diffusion coefficients is motivated by the human host movement, phage–bacteria movement in the environment, the dispersal of phages and bacteria, the water resource and position. We explicitly computed the basic reproduction number $\mathcal{R}_0$ and use it as the threshold stability of the existent equilibria. We split the system into two subsystem:

(i) We first analyze the model without phage absorption. On the one hand, using the techniques by Lyapunov and LaSalle, we have shown that the DFE is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$. On the other hand, we proved that there exists a unique globally asymptotically stable endemic equilibrium E^* whenever $\mathcal{R}_0 > 1$.

(ii) Second, we have considered the full model (with positive phage absorption rate). The threshold $\mathcal{R}_0$ have been used as the threshold index of this model. Indeed, whenever $\mathcal{R}_0 \leq 1$ the DFE is locally asymptotically stable, and is unstable for $\mathcal{R}_0 > 1$ and the system is shown to be uniformly persistent. Here, the condition $\mathcal{R}_0 \leq 1$ is not sufficient to achieve the possible elimination of disease (i.e. the GAS of the DFE is no longer achieved under the sole condition of $\mathcal{R}_0 \leq 1$). However, we derive another threshold $\mathcal{N}_0$, and proved using the Lyapunov–LaSalle's techniques that the DFE is GAS if $\mathcal{R}_0 \leq 1$ and $\mathcal{N}_0 \leq 1$.

(II) After proposing a NSFD scheme, we've derived the discrete counterpart of the continuous model. The results show that the discretized scheme preserves the main properties of solutions for the original continuous model, including positivity, ultimate boundedness, equilibria and their global stability.

(III) The discrete model was further used to illustrate all the theoretical results of the continuous model with regard to GAS and uniform persistence.

(IV) In order to support theoretical results, discrete model has been simulated. From a set of diffusion rate, we illustrated the impact of diffusion on the asymptotic behavior of the bacterial infections dynamic's. Figures 4–6, specially illustrate the spatial convergence to constant equilibria. Indeed, increasing values of diffusion parameter's reduces significantly the range of equilibria.

Taking into account the spatial movement of phages and bacteria, our reaction–diffusion epidemic model predicts that the classical requirement consisting to bring the basic reproduction number under unity is not sufficient to control bacterial infections. This has been shown by deriving a second threshold needed for the global stability of the constant equilibrium DFE. From the epidemiological point of view, both thresholds should be dropped under unity in order to eliminate the disease.

The work done so far in this paper is far from being complete. It offers many possibilities for further investigations which include the following:

(1) The proof of the global stability of the endemic equilibrium for any model whenever $\mathcal{R}_0 > 1$ and $\delta > 0$.
(2) An in-depth study of the full model with positive phage attack rate ($\varepsilon > 0$) though very difficult an era of exciting mathematical problem to tackle in the near future.
(3) Analyze of the model with space-dependent diffusion coefficients and/or disease transmission parameters.
(4) The existence of traveling waves solutions is also one of the hot topics we are still investigating.
(5) The incorporation of periodic time-dependent model parameters due to the seasonality of outbreaks.

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