

PAPER

Global dynamics of a degenerate reaction-diffusion cholera model with phage-bacteria interaction in a heterogeneous environment

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Abstract

To investigate multiple effects of the interaction between *V. cholerae* and phage on cholera transmission, we propose a degenerate reaction-diffusion model with different dispersal rates, which incorporates a short-lived hyperinfectious (HI vibrios) state of *V. cholerae* and lower-infectious (LI vibrios) state of *V. cholerae*. Our main purpose is to investigate the existence and stability analysis of multi-class boundary steady states, which is much more complicated and challenging than the case when the boundary steady state is unique. In a spatially heterogeneous case, the basic reproduction number $\mathcal{R}_0$ is defined as the spectral radius of the sum of two linear operators associated with HI vibrios infection and LI vibrios infection. If $\mathcal{R}_0 \leq 1$, the disease-free steady state is globally asymptotically stable. If $\mathcal{R}_0 > 1$, the uniform persistence of phage-free model, as well as the existence of the phage-free steady state, are established. In a spatially homogeneous case, when $\mathcal{R}_0 > 1$, the global asymptotic stability of phage-free steady state and the uniform persistence of the phage-present model are discussed under some additional conditions. The mathematical approach here has wide applications in degenerate Partial Differential Equations.

1 Introduction

Cholera, a waterborne disease caused by *V. cholerae*, can be found in diverse aquatic environments, such as the ocean, estuaries, rivers, and lakes [11, 33, 59]. It is characterised by severe vomiting and diarrhoea, and if not promptly treated, the disease can lead to severe dehydration and death [7, 16, 22]. This is attributed to the ability of *V. cholerae* to produce cholera toxin, which stimulates water and electrolyte secretion by intestinal endothelial cells [27]. The primary symptoms of cholera include diarrhoea, dehydration, abdominal cramps, a drop in blood pressure and kidney failure [5]. Besides, the dynamics of cholera epidemics involve a complex web of interactions between human hosts, pathogens and environments [51]. The disease is primarily transmitted to humans by ingesting water or food contaminated with toxigenic forms of *V. cholerae* O1 and O139 from the environment [8, 14, 21]. Cholera outbreaks frequently arise in regions lacking access to antibiotics and adequate public health infrastructure, especially in developing countries with limited healthcare resources, such as the Indian subcontinent, parts of Asia, Africa and Latin America. Cholera remains a persistent health challenge [23, 35].

Research on mathematical models of cholera can be traced back to 1973, when Capasso and Paveri-Fontana [6] introduced an ordinary differential equation (ODE) model to study the spread of cholera in the Mediterranean region. The model described compartments for *V. cholerae* and infected individuals, investigating the transmission of cholera in the European Mediterranean region. Joh et al.

first proposed an iSIR model describing indirectly transmitted infectious diseases with immunological threshold [20], with a follow up work [25] studying a seasonal forcing iSIR model with a smoothing immunological threshold. Tien and Earn [43] proposed a waterborne disease model incorporating both direct transmission and indirect transmission with bilinear incidence. Wu and Zou [58] examined a diffusive host-pathogen model that incorporates distinct dispersal rates for susceptible and infected hosts. They analysed the asymptotic profiles of the positive steady state as the dispersal rate of the susceptible or infected hosts tends to zero. The findings indicate that the infected hosts concentrate at certain points, which can be characterised as the pathogen's most favoured sites when the mobility of the infected host is limited. Wang et al. [52] proposed a new reaction-convection-diffusion model to investigate the spatiotemporal dynamics of cholera transmission. The model incorporates time-periodic parameters to describe the seasonality of the disease transmission and bacterial growth rates. Wang and Wang [45] proposed a reaction-diffusion cholera model incorporating the different dispersal rates of the susceptible and infected hosts in the absence of diffusion term for the cholera equation.

Recent laboratory findings in [3, 14] suggested that the *V. cholerae* induces a short-lived, hyperinfectious (HI) state through the gastrointestinal tract and decays into a lower infectiousness (LI) state within hours [14, 30]. Moreover, the infectivity of freshly shed *V. cholerae* greatly out-competes bacteria grown in vitro, exhibiting infectivity levels up to 700 times higher [31, 51]. HI vibrios, being closer to human hosts than environmental vibrios, are more likely to come into contact with human susceptible individuals [14]. To investigate hyperinfectious state of *V. cholerae* is crucial and also holds substantial practical significance. Furthermore, incorporating these hyperinfectious states and lower infectiousness states of *V. cholerae* into cholera disease models may lead to a better understanding of the observed cholera epidemic patterns.

Research on hyperinfectivity of *V. cholerae* has received increasing attention in recent years. Hartley et al. [14] incorporated hyperinfectivity vibrios into the mathematical model. The results suggest that for minimising the epidemic spread of cholera, intervention measures should focus on minimising the transmission risk of short-lived, highly infectious cholera vibrios. Shuai et al. [39] investigated cholera dynamics with both hyperinfectivity and temporary immunity. Wang and Wang [51] introduced a novel modelling framework to investigate the impact of bacterial hyperinfectivity on cholera epidemics in a spatially heterogeneous environment. Specifically, this model categorised *V. cholerae* into HI vibrios compartment and LI vibrios compartment. Wang and Wu [46] extended the work in [45] by incorporating bacterial hyperinfectivity and saturation mechanism for indirect transmission pathway. Wang et al. [49] developed a reaction-advection-diffusion model with a general boundary conditions, considering HI and LI vibrio strains, convection factors, and human behaviour change, to establish the threshold-type results of cholera transmission in spatial-temporal heterogeneous environment (see also [53]). Wang et al. [48] formulated a generalised cholera model incorporating nonlocal time delays to investigate the effects of bacterial hyperinfectivity on cholera outbreaks and to derive the detailed classifications of global dynamics in a spatially heterogeneous environment.

Phages, viruses that specifically infect and destroy bacteria, have been characterised as bacterial parasites, with each phage type exhibiting a distinct ability to replicate within specific strains of host bacteria [55]. The interaction mechanism between bacteriophages and bacteria begins when a lytic phage inserts its genetic material into a bacterial cell, where it proliferates, leading to cell lysis and the release of new phages into the environment [4]. This process can significantly impact the severity of cholera outbreaks. For example, the investigation of the cholera epidemic in Dhaka, Bangladesh, indicates that lytic bacteriophages may mitigate epidemic severity by eliminating bacteria in both reservoirs and infected individuals [10, 19].

Phages (viruses of bacteria) play a pivotal role in shaping both the evolution and dynamics of bacterial species, especially for *V. cholerae* [19, 23, 30, 32]. Kong et al. [23] proposed an ODE model incorporating a Holling II response function to depict the interaction between *V. cholerae* and bacteriophages. Misra et al. [29] investigated a reaction-diffusion system for the biological control of cholera epidemics. They focused on temporal evolution of cholera within a region and explored its control using lytic bacteriophage in aquatic reservoirs. Botelho et al. [4] proposed an ODE model with the bacteria-phage

interaction of Holling type I. This model includes human populations (SIRS), bacteria population (B) and phage population (p) to represent these interactions. In their study, they derived threshold parameters to characterise the stability of equilibria. The findings suggest that the reservoir environment might contribute to the periodicity of cholera outbreaks. Hu et al. [18] proposed a cholera model comprising coupled reaction-diffusion equations and ODEs to discuss the effects of spatial heterogeneity, horizontal transmission, environmental viruses and phages on the spread of *V. cholerae*.

The aim of the paper is to investigate multiple effects of the interaction between *V. cholerae* and phage on cholera transmission, thereby improving our understanding of the transmission mechanism of cholera diseases and proposing targeted disease control measures. Generally speaking, it is very challenging to discuss the threshold-type results in the case of multi-class steady states. Fortunately, in this paper, we derive the existence and stability analysis of multi-class steady states for some special cases.

The remainder of the paper is organised as follows. In Section 2, we propose a degenerate reaction-diffusion model with different dispersal rates, which incorporates short-lived hyperinfectious (HI vibrios) state of *V. cholerae* and lower-infectious (LI vibrios) state of *V. cholerae* simultaneously in a heterogeneous environment. In Section 3, we present the main results of this paper, including the well-posedness, dynamics of the disease-free steady state, dynamics of the phage-free steady state and dynamics of the phage-present steady state. In Section 4, we give the proofs of the main results. A brief discussion of this paper is given in Section 5.

2 Mathematical model

Building upon the model presented by Jensen et al. [19], which integrates cholera epidemiology with bacterial and bacteriophage population dynamics, we examine the interaction between HI vibrios and LI vibrios with bacteriophages, as well as the intrinsic growth rate of *V. cholerae*, and divide the infected human hosts into two parts, one consists of human hosts infected only with *V. cholerae*, denoted as I_1 , while the other consists of human hosts that are simultaneously infected with *V. cholerae* and bacteriophages, indicating the parasitism of bacteriophages within the host cells (bacteria), denoted as I_2 . Based on the above considerations, we propose a degenerate reaction-diffusion cholera model:

$$\left\{ \begin{array}{l} \frac{\partial S}{\partial t} = d_s \Delta S + \Lambda(x) - \alpha_1(x)f_1(B_1)S - \alpha_2(x)f_2(B_2)S - \mu(x)S, \\ \frac{\partial I_1}{\partial t} = d_l \Delta I_1 + \alpha_1(x) \left(1 - \frac{P}{L+P}\right) f_1(B_1)S + \alpha_2(x) \left(1 - \frac{P}{L+P}\right) f_2(B_2)S - \mu(x)I_1, \\ \frac{\partial I_2}{\partial t} = d_l \Delta I_2 + \alpha_1(x) \frac{P}{L+P} f_1(B_1)S + \alpha_2(x) \frac{P}{L+P} f_2(B_2)S - \mu(x)I_2, \\ \frac{\partial B_1}{\partial t} = h_1(x, B_1) + \eta(x)(I_1 + I_2) - b_1(x)B_1P - \delta_1(x)B_1, \\ \frac{\partial B_2}{\partial t} = h_2(x, B_2) + \delta_1(x)B_1 - b_2(x)B_2P - \delta_2(x)B_2, \\ \frac{\partial P}{\partial t} = \alpha(x)\eta(x)I_2 + \chi_1(x)b_1(x)B_1P + \chi_2(x)b_2(x)B_2P - m(x)P. \end{array} \right. \quad (2.1)$$

The population density of susceptible individuals at location x and time t is denoted by $S(x, t)$. The population densities of phage-negative and phage-positive infected individuals at location x and time t are denoted by $I_1(x, t)$, $I_2(x, t)$, respectively. Let $I(x, t) = I_1(x, t) + I_2(x, t)$, where $I(x, t)$ denotes all human hosts infected with *V. cholerae*. The concentrations of HI and LI vibrios in the water environment at location x and time t are denoted by $B_1(x, t)$, $B_2(x, t)$, respectively. The concentration of phage in the water environment at location x and time t is denoted by $P(x, t)$. The recruitment rate of susceptible human hosts is represented by $\Lambda(x)$. The parameters $\alpha_1(x)$ and $\alpha_2(x)$ can be interpreted as the rates of

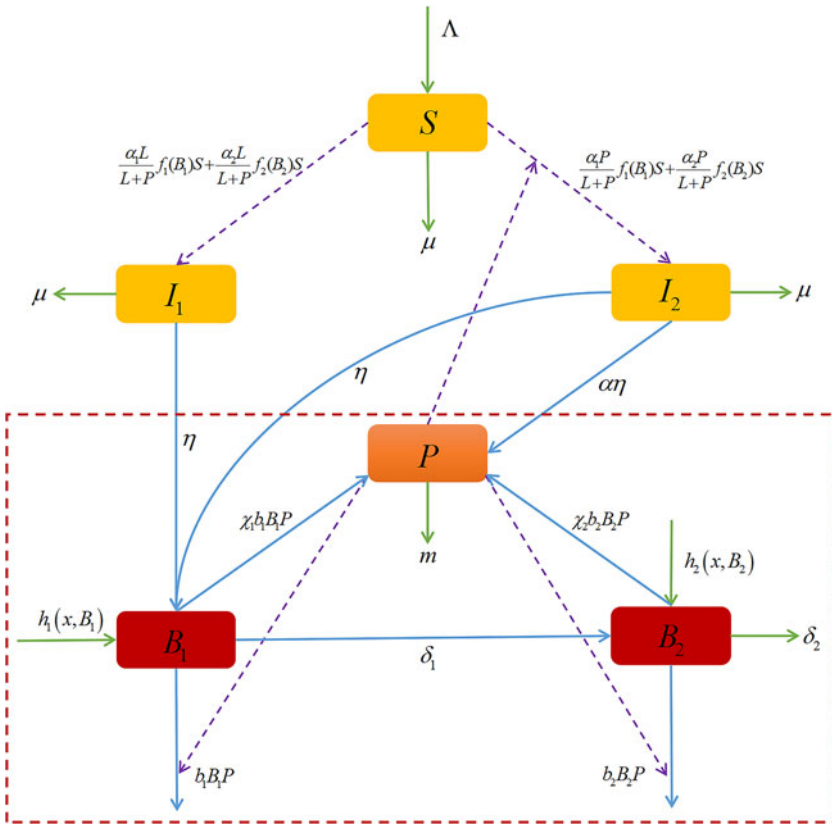


Figure 1. Schematic diagram of model (2.1). The green solid line represents the recruitment and mortality rates of human hosts and *V. cholerae*, and the blue solid line denotes the direct development of cholera. The purple dashed line represents the infection process and the interaction between phages and *V. cholerae*.

HI and LI vibrios consumption. $L(x)$ represents the half-saturation concentration of phage. For simplicity, we consider only natural deaths by $\mu(x)$ and disregard deaths caused by the disease. The functions $h_1(x, B_1)$ and $h_2(x, B_2)$ are the intrinsic growth rates of HI and LI vibrios, respectively. The rate of bacterial shedding is represented by $\eta(x)$, while $\delta_1(x)$, $\delta_2(x)$ denote the natural death rate of HI and LI vibrios, respectively. Phage interacts with both HI and LI vibrios, resulting in bacterial death rates of $b_1(x)$ and $b_2(x)$, respectively. Meanwhile, the phage has a gain from two vibrios' deaths represented by $\chi_1(x)$ and $\chi_2(x)$. The mean phage shed rate is denoted as $\alpha(x)$, and $m(x)$ represents the phage decay rate. The cholera transmission process is shown in Figure 1. In model (2.1), we choose

$$f_i(B_i) = \frac{B_i}{B_i + H_i(x)}, \quad i = 1, 2, \quad x \in \Omega,$$

where $H_i(x)$ denotes the half-saturation concentration of bacteria. d_s, d_i represent the dispersal rates of susceptible and infected human hosts, respectively. Here, we assume that the dispersal rate d_i for both phage-negative and phage-positive infections are equal. We also consider an isolated habitat Ω , which is characterised by the homogeneous Neumann boundary condition.

$$\frac{\partial S}{\partial \nu} = \frac{\partial I_1}{\partial \nu} = \frac{\partial I_2}{\partial \nu} = 0, \quad x \in \partial\Omega, \quad t > 0, \quad (2.2)$$

and the initial conditions are

$$S(x, 0) = S^0(x), I_1(x, 0) = I_1^0(x), I_2(x, 0) = I_2^0(x), B_1(x, 0) = B_1^0(x), B_2(x, 0) = B_2^0(x), P(x, 0) = P^0(x), \quad (2.3)$$

for $x \in \bar{\Omega}$, and where $S^0(x), I_1^0(x), I_2^0(x), B_1^0(x), B_2^0(x), P^0(x)$ are nonnegative continuous functions. Furthermore, if spatial heterogeneity is not considered, model (2.1) degenerates to the homogeneous model:

$$\left\{ \begin{array}{l} \frac{\partial S}{\partial t} = d_s \Delta S + \Lambda - \alpha_1 f_1(B_1)S - \alpha_2 f_2(B_2)S - \mu S, \quad x \in \Omega, t > 0, \\ \frac{\partial I_1}{\partial t} = d_I \Delta I_1 + \alpha_1 \left(1 - \frac{P}{L+P}\right) f_1(B_1)S + \alpha_2 \left(1 - \frac{P}{L+P}\right) f_2(B_2)S - \mu I_1, \quad x \in \Omega, t > 0, \\ \frac{\partial I_2}{\partial t} = d_I \Delta I_2 + \alpha_1 \frac{P}{L+P} f_1(B_1)S + \alpha_2 \frac{P}{L+P} f_2(B_2)S - \mu I_2, \quad x \in \Omega, t > 0, \\ \frac{\partial B_1}{\partial t} = h_1(B_1) + \eta(I_1 + I_2) - b_1 B_1 P - \delta_1 B_1, \quad x \in \Omega, t > 0, \\ \frac{\partial B_2}{\partial t} = h_2(B_2) + \delta_1 B_1 - b_2 B_2 P - \delta_2 B_2, \quad x \in \Omega, t > 0, \\ \frac{\partial P}{\partial t} = \alpha \eta I_2 + \chi_1 b_1 B_1 P + \chi_2 b_2 B_2 P - mP, \quad x \in \Omega, t > 0. \end{array} \right. \quad (2.4)$$

In the following, we make some basic assumptions:

- (H₁) d_s, d_I are positive C^1 -function on $\bar{\Omega}$;
- (H₂) $(I_1^0, I_2^0, B_1^0, B_2^0, P^0) \not\equiv 0$ on $\bar{\Omega}$;
- (H₃) $h_i(x, v), h_2(x, v) \in C^{0,1}(\bar{\Omega} \times \mathbb{R}_+)$ are nonnegative and strictly concave down in relation to the second variable, and $h_i(x, v) = 0, i = 1, 2$, if and only if $v = 0$, then

$$\lim_{v \rightarrow \infty} \frac{h_i(x, v)}{v} < \delta_i(x), \quad i = 1, 2, \quad x \in \Omega. \quad (2.5)$$

For the assumption (H₃), we also refer to [4, 51], these general incidence functions are set to be

$$h_i(x, B_i) = \theta(x) B_i \left(1 - \frac{B_i}{H_{B_i}(x)}\right), \quad i = 1, 2, \quad x \in \Omega,$$

where $\theta(x)$ is the intrinsic growth rate of bacteria, and $H_{B_i}(x)$ denotes the maximum capacity of the bacteria.

It should be pointed out that since multiple effects of the interaction between *V. cholerae* and phages on cholera transmission, the complexity of model (2.1)–(2.3) leads to several mathematical difficulties:

- (i) We prove the global asymptotic stability of the disease-free steady state for the critical case when $\mathcal{R}_0 = 1$ for the high-dimensional system, which is instituted by six equations.
- (ii) Generally speaking, it is very challenging to discuss the threshold-type results in the case of multi-class steady states. Fortunately, in this paper, we derive the existence and stability analysis of multi-class steady states for some special cases. We show the existence of phage-free steady state in a heterogeneous environment. An appropriate Lyapunov function is constructed to discuss the global stability of the phage-free steady state in a homogeneous environment.

3 Main results

In this section, we state the main results of this paper, whose proofs are given in Section 4.

3.1 Well-posedness of the model

Define $H = C(\bar{\Omega}, \mathbb{R}^6)$, which is assigned the following supremum norm:

$$\|\varphi\|_H := \max \left\{ \sup_{x \in \Omega} |\varphi_1(x)|, \sup_{x \in \Omega} |\varphi_2(x)|, \sup_{x \in \Omega} |\varphi_3(x)|, \sup_{x \in \Omega} |\varphi_4(x)|, \sup_{x \in \Omega} |\varphi_5(x)|, \sup_{x \in \Omega} |\varphi_6(x)| \right\},$$

with $\varphi = (\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5, \varphi_6) \in H$. Define $H^+ = C(\bar{\Omega}, \mathbb{R}_+^6)$ as the positive cone of H . Let $L_p(\Omega)$ be the Banach space of function y whose p -th power of absolute value is integrable on Ω for $1 \leq p \leq \infty$ with

$$\begin{cases} \|y\|_p = \left(\int_{\Omega} |y|^p \right)^{\frac{1}{p}}, & 1 \leq p < \infty, \\ \|y\|_{\infty} = \text{ess sup } |y(x)|, & p = \infty. \end{cases}$$

Define

$$z^m = \max_{x \in \Omega} z(x), \quad z_m = \min_{x \in \Omega} z(x),$$

where $z(x) \in C(\bar{\Omega}, \mathbb{R})$. Define $\mathbb{B}_i: D(\mathbb{B}_i) \rightarrow C(\bar{\Omega}, \mathbb{R})$ as the linear operator with

$$\mathbb{B}_1\phi := d_s \Delta \phi(x), \quad \mathbb{B}_2\phi := d_l \Delta \phi(x),$$

where $D(\mathbb{B}_i) := \{\phi \in \cap_{y \geq 1} W^{2,y}(\Omega): \frac{\partial \phi}{\partial \nu} = 0 \text{ on } \partial\Omega \text{ and } \mathbb{B}_i\phi \in C(\bar{\Omega}, \mathbb{R})\}$. By [56], we know that the operator $\mathbb{B}_i$ is the infinitesimal generator of the strongly continuous semigroup $\{e^{t\mathbb{B}_i}\}_{t \geq 0}$, $i = 1, 2$. The operator $\mathcal{B}: H \rightarrow H$ defined by

$$\mathcal{B}\varphi(x) := \begin{pmatrix} \mathbb{B}_1\varphi_1(x) \\ \mathbb{B}_2\varphi_2(x) \\ \mathbb{B}_2\varphi_3(x) \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad \varphi = (\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5, \varphi_6) \in D(\mathbb{B}_1) \times D(\mathbb{B}_2) \times D(\mathbb{B}_2) \times [C(\bar{\Omega}, \mathbb{R})]^3 \subset H \quad (3.1)$$

is also the infinitesimal generator of the strongly continuous semigroup $\{e^{t\mathcal{B}}\}_{t \geq 0}$ in H . Moreover, we define the nonlinear operator $\mathcal{L}: H \rightarrow H$ as

$$\mathcal{L}(\varphi)(x) := \begin{pmatrix} \Lambda(x) - \alpha_1(x)f_1(\varphi_4)\varphi_1 - \alpha_2(x)f_2(\varphi_5)\varphi_1 - \mu(x)\varphi_1 \\ \frac{\alpha_1(x)f_1(\varphi_4)L\varphi_1}{L + \varphi_6} + \frac{\alpha_2(x)f_2(\varphi_5)L\varphi_1}{L + \varphi_6} - \mu(x)\varphi_2 \\ \frac{\alpha_1(x)f_1(\varphi_4)\varphi_6\varphi_1}{L + \varphi_6} + \frac{\alpha_2(x)f_2(\varphi_5)\varphi_6\varphi_1}{L + \varphi_6} - \mu(x)\varphi_3 \\ h_1(x, \varphi_4) + \eta(x)(\varphi_2 + \varphi_3) - b_1(x)\varphi_4\varphi_6 - \delta_1(x)\varphi_4 \\ h_2(x, \varphi_5) + \delta_1(x)\varphi_4 - b_2(x)\varphi_5\varphi_6 - \delta_2(x)\varphi_5 \\ \alpha(x)\eta(x)\varphi_3 + \chi_1(x)b_1(x)\varphi_4\varphi_6 + \chi_2(x)b_2(x)\varphi_5\varphi_6 - m(x)\varphi_6 \end{pmatrix}. \quad (3.2)$$

Thus, model (2.1) can be expressed as

$$\frac{d}{dt} c(\cdot, t; c^0) = \mathcal{B}c(\cdot, t; c^0) + \mathcal{L}(c(\cdot, t; c^0)), \quad c(\cdot, 0; c^0) = c^0. \quad (3.3)$$

Theorem 3.1. *For any $c^0(x) = (S^0(x), I_1^0(x), I_2^0(x), B_1^0(x), B_2^0(x), P^0(x)) \in H^+$, model (2.1)–(2.3) admits a unique global nonnegative classical solution defined on $\bar{\Omega} \times [0, \infty)$. Moreover, model (2.1)–(2.3) has a connected global attractor in H^+ .*

3.2 Dynamics of the disease-free steady state

A steady state of model (2.1)–(2.3) is a solution of the following model

$$\begin{cases} d_S \Delta S + \Lambda(x) - \alpha_1(x)f_1(B_1)S - \alpha_2(x)f_2(B_2)S - \mu(x)S = 0, & x \in \Omega, \\ d_I \Delta I_1 + \alpha_1(x)\frac{L}{L+P}f_1(B_1)S + \alpha_2(x)\frac{L}{L+P}f_2(B_2)S - \mu(x)I_1 = 0, & x \in \Omega, \\ d_I \Delta I_2 + \alpha_1(x)\frac{P}{L+P}f_1(B_1)S + \alpha_2(x)\frac{P}{L+P}f_2(B_2)S - \mu(x)I_2 = 0, & x \in \Omega, \\ h_1(x, B_1) + \eta(x)(I_1 + I_2) - b_1(x)B_1P - \delta_1(x)B_1 = 0, & x \in \Omega, \\ h_2(x, B_2) + \delta_1(x)B_1 - b_2(x)B_2P - \delta_2(x)B_2 = 0, & x \in \Omega, \\ \alpha(x)\eta(x)I_2 + \chi_1(x)b_1(x)B_1P + \chi_2(x)b_2(x)B_2P - m(x)P = 0, & x \in \Omega, \end{cases} \quad (3.4)$$

for $t > 0$. Model (2.1)–(2.3) admits a unique disease-free steady state $F_0 = (S^*(x), 0, 0, 0, 0, 0)$, where $S^*(x)$ is the unique positive solution of

$$\begin{cases} d_S \Delta S + \Lambda(x) - \mu(x)S = 0, & x \in \Omega, \\ \frac{\partial S}{\partial \nu} = 0, & x \in \partial\Omega. \end{cases} \quad (3.5)$$

Define

$$\hat{h}_i(x) = \frac{\partial h_i(x, 0)}{\partial B_i}, \quad i = 1, 2, \quad x \in \Omega.$$

Linearising model (2.1)–(2.3) at F_0 and adding the equations for $I_1(x, t)$ and $I_2(x, t)$, we obtain

$$\begin{cases} \frac{\partial I}{\partial t} = d_I \Delta I + \frac{\alpha_1(x)S^*B_1}{H_1} + \frac{\alpha_2(x)S^*B_2}{H_2} - \mu(x)I, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_1}{\partial t} = \hat{h}_1(x)B_1 + \eta(x)I - \delta_1(x)B_1, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_2}{\partial t} = \hat{h}_2(x)B_2 + \delta_1(x)B_1 - \delta_2(x)B_2, & x \in \Omega, \quad t > 0, \\ \frac{\partial I}{\partial \nu} = 0, & x \in \partial\Omega, \quad t > 0. \end{cases} \quad (3.6)$$

Let $J(t)$ be the solution semiflow associated with model (3.6), where $J(t)\varphi = (I(\cdot, t, \varphi), B_1(\cdot, t, \varphi), B_2(\cdot, t, \varphi))$ for $\varphi \in C(\bar{\Omega}, \mathbb{R}^3)$. Since model (3.6) is cooperative, $J(t)$ is a C_0 -semigroup with generator

$$\mathcal{A} = \begin{pmatrix} d_I \Delta - \mu & \frac{\alpha_1 S^*}{H_1} & \frac{\alpha_2 S^*}{H_2} \\ \eta & \hat{h}_1 - \delta_1 & 0 \\ 0 & \delta_1 & \hat{h}_2 - \delta_2 \end{pmatrix} = \begin{pmatrix} d_I \Delta - \mu & 0 & 0 \\ \eta & \hat{h}_1 - \delta_1 & 0 \\ 0 & \delta_1 & \hat{h}_2 - \delta_2 \end{pmatrix} + \begin{pmatrix} 0 & \frac{\alpha_1 S^*}{H_1} & \frac{\alpha_2 S^*}{H_2} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} =: V + F.$$

To ensure the well-definedness of $\mathcal{A}$, we impose the following assumption on $\hat{h}_i(x)$ for the remainder of this paper:

$$\hat{h}_i(x) < \delta_i(x), \quad \forall x \in \Omega, \quad i = 1, 2. \quad (3.7)$$

Following [42, 50], the basic reproduction number $\mathcal{R}_0$ of model (2.1)–(2.3) is defined as the spectral radius of $-FV^{-1}$, which is denoted by $r(-FV^{-1})$, namely

$$\mathcal{R}_0 := r(-FV^{-1}).$$

From the similar results in [42, 50], we can assert the following statement.

Lemma 3.2. $\mathcal{R}_0 - 1$ has the same sign as $s(\mathcal{A})$, where $s(\mathcal{A})$ denotes the spectrum bound of $\mathcal{A}$ with $s(\mathcal{A}) = \sup\{\operatorname{Re}\lambda, \lambda \in \sigma(\mathcal{A})\}$.

To derive an equivalent formula for the basic reproduction number $\mathcal{R}_0$, similar to the proof in [38, 47], we introduce the following result involving the next generation operators D_H and D_L for HI vibrios and LI vibrios infections, respectively.

Lemma 3.3. *Let*

$$F = \begin{pmatrix} 0 & F_{11} & F_{12} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

be a positive operator, and

$$V = \begin{pmatrix} d_I \Delta - V_{11} & 0 & 0 \\ V_{21} & -V_{22} & 0 \\ 0 & V_{32} & -V_{33} \end{pmatrix}$$

be a resolvent-positive operator with $s(V) < 0$, where $s(V)$ denotes the spectral bound of V , then we obtain

$$r(-FV^{-1}) = r(D_H + D_L),$$

where $D_H = F_{11}V_{22}^{-1}V_{21}(V_{11} - d_I\Delta)^{-1}$ and $D_L = F_{12}V_{33}^{-1}V_{32}V_{22}^{-1}V_{21}(V_{11} - d_I\Delta)^{-1}$.

In addition, based on Lemma 3.3, we can derive a specific form for $\mathcal{R}_0$ as follows:

$$\mathcal{R}_0 = r(D_H + D_L),$$

where

$$D_H = \frac{\alpha_1(x)\Lambda(x)\eta(x)(\mu(x) - d_I\Delta)^{-1}}{\mu(x)H_1(\delta_1(x) - \hat{h}_1(x))}$$

is the next generation operator for HI vibrios transmission to human hosts, and

$$D_L = \frac{\alpha_2(x)\Lambda(x)\delta_1(x)\eta(x)(\mu(x) - d_I\Delta)^{-1}}{\mu(x)H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))}$$

is the next generation operator for LI vibrios transmission to human hosts.

If considering exclusively the infection of human hosts by HI vibrios, the basic reproduction number $\mathcal{R}_0^H$ can be represented as

$$\begin{aligned} \mathcal{R}_0^H &= r(D_H) \\ &= r\left(\frac{\alpha_1(x)\Lambda(x)\eta(x)(\mu(x) - d_I\Delta)^{-1}}{\mu(x)H_1(\delta_1(x) - \hat{h}_1(x))}\right) \\ &= \sup_{\varphi \in H^1(\Omega), \varphi \neq 0} \frac{\int_{\Omega} \alpha_1(x)\Lambda(x)\eta(x)\varphi^2 / \mu(x)H_1(\delta_1(x) - \hat{h}_1(x))dx}{\int_{\Omega} d_I|\nabla\varphi|^2 + \mu(x)\varphi^2 dx}. \end{aligned}$$

On the other hand, if considering exclusively the infection of human hosts by LI vibrios, the basic reproduction number $\mathcal{R}_0^L$ can be represented as

$$\begin{aligned} \mathcal{R}_0^L &= r(D_L) \\ &= r\left(\frac{\alpha_2(x)\Lambda(x)\delta_1(x)\eta(x)(\mu(x) - d_I\Delta)^{-1}}{\mu(x)H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))}\right) \\ &= \sup_{\varphi \in H^1(\Omega), \varphi \neq 0} \frac{\int_{\Omega} \alpha_2(x)\Lambda(x)\delta_1(x)\eta(x)\varphi^2 / \mu(x)H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))dx}{\int_{\Omega} d_I|\nabla\varphi|^2 + \mu(x)\varphi^2 dx}. \end{aligned}$$

By [2, Theorem 2] and the expressions of $\mathcal{R}_0^H$ and $\mathcal{R}_0^L$, we immediately get Theorems 3.4 and 3.5.

Theorem 3.4. *The following statements are valid:*

(i) $\mathcal{R}_0^H$ is decreasing in d_I with

$$\lim_{d_I \rightarrow 0} \mathcal{R}_0^H = \max \left\{ \frac{\alpha_1 \Lambda \eta}{\mu^2 H_1(\delta_1 - \hat{h}_1)} : x \in \bar{\Omega} \right\}$$

and

$$\lim_{d_I \rightarrow \infty} \mathcal{R}_0^H = \frac{\int_{\Omega} \alpha_1 \Lambda \eta / \mu H_1(\delta_1 - \hat{h}_1) dx}{\int_{\Omega} \mu dx}.$$

(ii) If Ω is a favourable environment for HI vibrios in the sense that

$$\int_{\Omega} \frac{\alpha_1 \Lambda \eta}{\mu H_1(\delta_1 - \hat{h}_1)} dx > \int_{\Omega} \mu dx,$$

then $\mathcal{R}_0^H > 1$ for all $d_I > 0$.

(iii) If Ω is a non-favourable environment for HI vibrios in the sense that

$$\int_{\Omega} \frac{\alpha_1 \Lambda \eta}{\mu H_1(\delta_1 - \hat{h}_1)} dx < \int_{\Omega} \mu dx,$$

Meanwhile, there is a favourable site x within the domain in the sense that $\alpha_1(x)\Lambda(x)\eta(x) > \mu^2(x)H_1(\delta_1(x) - \hat{h}_1(x))$, then there exists $\bar{d}_I$ such that $\mathcal{R}_0^H > 1$ when $d_I < \bar{d}_I$, and $\mathcal{R}_0^H < 1$ when $d_I > \bar{d}_I$.

Theorem 3.5. *The following statements are valid:*

(i) $\mathcal{R}_0^L$ is decreasing in d_I with

$$\lim_{d_I \rightarrow 0} \mathcal{R}_0^L = \max \left\{ \frac{\alpha_2 \Lambda \delta_1 \eta}{\mu^2 H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} : x \in \bar{\Omega} \right\}$$

and

$$\lim_{d_I \rightarrow \infty} \mathcal{R}_0^L = \frac{\int_{\Omega} \alpha_2 \Lambda \delta_1 \eta / \mu H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2) dx}{\int_{\Omega} \mu dx}.$$

(ii) If Ω is a favourable environment for LI vibrios in the sense that

$$\int_{\Omega} \frac{\alpha_2 \Lambda \delta_1 \eta}{\mu H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} dx > \int_{\Omega} \mu dx,$$

then $\mathcal{R}_0^L > 1$ for all $d_I > 0$.

(iii) If Ω is a non-favourable environment for LI vibrios in the sense that

$$\int_{\Omega} \frac{\alpha_2 \Lambda \delta_1 \eta}{\mu H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} dx < \int_{\Omega} \mu dx,$$

Meanwhile, there is a favourable site x within the domain in the sense that $\alpha_2(x)\Lambda(x)\delta_1(x)\eta(x) > \mu^2(x)H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))$, then there exists $\hat{d}_I$ such that $\mathcal{R}_0^L > 1$ when $d_I < \hat{d}_I$, and $\mathcal{R}_0^L < 1$ when $d_I > \hat{d}_I$.

Remark 3.6. For model (2.4), there exists a disease-free steady state $\tilde{F}_0 = (S^*, 0, 0, 0, 0, 0)$, where $S^* = \frac{\Lambda}{\mu}$. By a simple computation, the basic reproduction number of model (2.4) is

$$\tilde{\mathcal{R}}_0 = \frac{\alpha_1 \Lambda \eta}{\mu^2 H_1(\delta_1 - \hat{h}_1)} + \frac{\alpha_2 \Lambda \eta \delta_1}{\mu^2 H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)}.$$

The extinction of the disease for model (2.1)–(2.3) in terms of $\mathcal{R}_0$ can be expressed as follows:

Theorem 3.7. *The following two statements are valid:*

- (i) *If $\mathcal{R}_0 < 1$, the disease-free steady state F_0 of model (2.1)–(2.3) is globally asymptotically stable;*
- (ii) *If $\mathcal{R}_0 = 1$, the disease-free steady state F_0 of model (2.1)–(2.3) is globally asymptotically stable.*

3.3 Dynamics of the phage-free steady state

In this subsection, we discuss the case that phages and phage-positive infected individuals are absent in model (2.1), and analyse the dynamics of the model under this case.

Theorem 3.8. *If $\mathcal{R}_0 > 1$, model (2.1) has at least one phage-free steady state $F_1 = (S^a(x), I_1^a(x), 0, B_1^a(x), B_2^a(x), 0)$.*

Remark 3.9. *Although we establish the existence of phage-free steady state for model (2.1), the problems of uniqueness and local/global stability are still unresolved. However, if the heterogeneous space degenerates to a homogeneous one, that is, model (2.1) degenerates to model (2.4), we can determine the uniqueness and stability of F_1 .*

For model (2.4), if $\tilde{\mathcal{R}}_0 > 1$, there exists a phage-free steady state $\tilde{F}_1 = (\tilde{S}^a, \tilde{I}_1^a, 0, \tilde{B}_1^a, \tilde{B}_2^a, 0)$, where

$$\tilde{S}^a = \frac{\Lambda - \mu \tilde{I}_1^a}{\mu} > 0, \quad \tilde{B}_1^a = \frac{\eta \tilde{I}_1^a}{(\delta_1 - \hat{h}_1)} > 0, \quad \tilde{B}_2^a = \frac{\delta_1 \eta \tilde{I}_1^a}{(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} > 0,$$

and $\tilde{I}_1^a$ is the positive root of $f(I_1) = \tilde{A}I_1^2 + \tilde{B}I_1 + \tilde{C}$, where

$$\tilde{A} = -\frac{\delta_1 \eta^2 (\alpha_1 + \alpha_2 + \mu)}{(\delta_1 - \hat{h}_1)^2 (\delta_2 - \hat{h}_2)}, \quad \tilde{B} = \left(\frac{\Lambda \delta_1 \eta^2 (\alpha_1 + \alpha_2)}{\mu (\delta_1 - \hat{h}_1)^2 (\delta_2 - \hat{h}_2)} - \frac{\eta H_2 (\alpha_1 + \mu)}{(\delta_1 - \hat{h}_1)} - \frac{\delta_1 \eta H_1 (\alpha_2 + \mu)}{(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} \right),$$

$$\tilde{C} = \left(\frac{\Lambda \alpha_1 \eta H_2}{\mu (\delta_1 - \hat{h}_1)} + \frac{\Lambda \alpha_2 \delta_1 \eta H_1}{\mu (\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} - \mu H_1 H_2 \right) = \mu H_1 H_2 (\tilde{\mathcal{R}}_0 - 1).$$

If $\tilde{\mathcal{R}}_0 > 1$, we find that $f(0) = \tilde{C} > 0$. Additionally, since $\tilde{A} < 0$, it follows that $f(I_1) = 0$ has two real roots: one positive and one negative. Hence, model (2.4) has a unique phage-free positive steady state $\tilde{F}_1 = (\tilde{S}^a, \tilde{I}_1^a, 0, \tilde{B}_1^a, \tilde{B}_2^a, 0)$ for $\tilde{\mathcal{R}}_0 > 1$. Assume that $b_2 = 0$, the following theorem presents a result regarding the global stability of the phage-free steady state $\tilde{F}_1$.

Theorem 3.10. *If $\tilde{\mathcal{R}}_0 > 1$, $\tilde{B}_1^a \leq \tilde{B}_1^b$ and $l_1 \leq \frac{\mu X_1}{\alpha \eta}$ hold, then the phage-free steady state $\tilde{F}_1$ of model (2.4) is globally asymptotically stable.*

3.4 Dynamics of phage-present steady state

In this section, the existence and uniform persistence of phage-present steady state of model (2.1) are difficult to obtain due to the spatial heterogeneity and other mathematical difficulties. Therefore, we focus on proving the existence and uniform persistence of the phage-present steady state for its homogeneous case. Assuming $\alpha = b_2 = 0$ and $I = I_1 + I_2$ in this subsection. From model (2.4), we assume that there

exists the phage-present positive steady state $\tilde{F}_2 = (\tilde{S}^b, \tilde{I}^b, \tilde{B}_1^b, \tilde{B}_2^b, \tilde{P}^b)$. We have

$$\begin{cases} \Lambda - \alpha_1 f_1(\tilde{B}_1^b) \tilde{S}^b - \alpha_2 f_2(\tilde{B}_2^b) \tilde{S}^b - \mu \tilde{S}^b = 0, \\ \alpha_1 f_1(\tilde{B}_1^b) \tilde{S}^b + \alpha_2 f_2(\tilde{B}_2^b) \tilde{S}^b - \mu \tilde{I}^b = 0, \\ h_1(\tilde{B}_1^b) + \eta \tilde{I}^b - b_1 \tilde{B}_1^b \tilde{P}^b - \delta_1 \tilde{B}_1^b = 0, \\ h_2(\tilde{B}_2^b) + \delta_1 \tilde{B}_1^b - \delta_2 \tilde{B}_2^b = 0, \\ \chi_1 b_1 \tilde{B}_1^b \tilde{P}^b - m \tilde{P}^b = 0. \end{cases} \quad (3.8)$$

One gets

$$\tilde{S}^b = \frac{\Lambda}{\frac{\alpha_1 m}{m + H_1 \chi_1 b_1} + \frac{\alpha_2 (h_2 \chi_1 b_1 + \delta_1 m)}{h_2 \chi_1 b_1 + \delta_1 m + H_2 \delta_2 \chi_1 b_1} + \mu}, \quad \tilde{I}^b = \frac{\Lambda - \mu \tilde{S}^b}{\mu} > 0,$$

$$\tilde{B}_1^b = \frac{m}{\chi_1 b_1}, \quad \tilde{B}_2^b = \frac{(h_2 \chi_1 b_1 + \delta_1 m)}{\delta_2 \chi_1 b_1}, \quad \tilde{P}^b = \frac{\chi_1 h_1 b_1 + \chi_1 \eta b_1 \tilde{I}^b - \delta_1 m}{m b_1}.$$

We define the phage invasion reproduction number as

$$\tilde{\mathcal{R}}_0^b = \frac{\chi_1 h_1 b_1 + \chi_1 \eta b_1 \tilde{I}^b}{\delta_1 m}.$$

If $\tilde{\mathcal{R}}_0^b > 1$, then $\tilde{P}^b > 0$. Consequently, model (2.4) has a unique phage-present positive steady state $\tilde{F}_2 = (\tilde{S}^b, \tilde{I}^b, \tilde{B}_1^b, \tilde{B}_2^b, \tilde{P}^b)$. The following theorem demonstrates the uniform persistence of the disease for model (2.4) when $\tilde{\mathcal{R}}_0 > 1$.

Theorem 3.11. *If $\tilde{\mathcal{R}}_0 > 1$, and $\tilde{B}_1^a > \tilde{B}_1^b$ hold, there exists a $\tilde{\vartheta} > 0$ such that for the initial condition $c^0(\cdot) = (S^0, I_1^0, I_2^0, B_1^0, B_2^0, P^0)(\cdot) \in H^+$ with $I_1^0(x) \not\equiv 0$ or $I_2^0(x) \not\equiv 0$ or $B_1^0(x) \not\equiv 0$ or $B_2^0(x) \not\equiv 0$ or $P^0(x) \not\equiv 0$, the solution $\tilde{c}(x, t; c^0) = (S(x, t), I_1(x, t), I_2(x, t), B_1(x, t), B_2(x, t), P(x, t))$ of model (2.4) satisfies $\lim_{t \rightarrow \infty} \inf \tilde{c}(x, t; c^0) \geq \tilde{\vartheta}$ uniformly for $x \in \bar{\Omega}$.*

4 Proofs

4.1 Proof of Theorem 3.1

In this section, we present a series of lemmas to prove Theorem 3.1. The first lemma is just a consequence of applying the general results in [28].

Lemma 4.1. *Let $\mathcal{B}$ and $\mathcal{L}$ be defined by (3.1)–(3.2). For any $c^0 \in D(\mathcal{B}) \subset H^+$, there exists a $T_M > 0$ satisfying that model (3.3) admits a unique nonnegative solution*

$$c(\cdot, t; c^0) = e^{t\mathcal{B}} c^0 + \int_0^t e^{(t-s)\mathcal{B}} \mathcal{L}(c(\cdot, s; c^0)) ds, \quad t \in [0, T_M),$$

where $T_M \leq +\infty$, then we have $\lim_{t \rightarrow T_M} \|c(\cdot, t; c^0)\| = \infty$ if $T_M = \infty$.

Lemma 4.2. *For any $c^0(x) = (S^0(x), I_1^0(x), I_2^0(x), B_1^0(x), B_2^0(x), P^0(x)) \in H^+$, model (2.1)–(2.3) admits a unique nonnegative global solution defined on $\bar{\Omega} \times [0, \infty)$.*

Proof. Let $c(x, t) = (S, I_1, I_2, B_1, B_2, P)$ be a solution associated with $c^0(x) = (S^0(x), I_1^0(x), I_2^0(x), B_1^0(x), B_2^0(x), P^0(x))$. The first equation of model (2.1) implies that $\partial S / \partial t \leq d_s \Delta S + \Lambda(x) - \mu(x)S$.

By [24, Lemma 1], we derive

$$\begin{cases} \frac{\partial \bar{S}}{\partial t} = d_s \Delta \bar{S} + \Lambda(x) - \mu(x) \bar{S}, & x \in \Omega, \quad t > 0, \\ \frac{\partial \bar{S}}{\partial \nu} = 0, & x \in \partial\Omega, \quad t > 0, \end{cases} \quad (4.1)$$

has a unique positive steady state $S^*(x)$, which is globally asymptotically stable. According to the comparison principle, we have

$$\limsup_{t \rightarrow \infty} S(x, t) \leq \limsup_{t \rightarrow \infty} \bar{S}(x, t) = S^*(x). \quad (4.2)$$

Thus, there exists a $Q_1 > 0$ satisfying

$$\|S(x, t)\| \leq Q_1, \quad t \geq 0. \quad (4.3)$$

Let $\{J_2(t)\}_{t \geq 0}$ be the semigroup generated by the operator $d_l \Delta - \mu(\cdot)$, then from the second equation of model (2.1), we have

$$I_1(x, t) = J_2(t)I_1^0(x) + \int_0^t J_2(t-s) \left(\frac{\alpha_1(x)LB_1(x, s)S(x, s)}{(L + P(x, s))(B_1(x, s) + H_1)} + \frac{\alpha_2(x)LB_2(x, s)S(x, s)}{(L + P(x, s))(B_2(x, s) + H_2)} \right) ds,$$

from (4.3), we derive

$$\begin{aligned} \|I_1(x, t)\| &\leq e^{-\lambda_1 t} \|I_1^0\| + Q_1 \alpha_1^m \int_0^t e^{-\lambda_1(t-s)} \left(\frac{\|L\| \|B_1(x, s)\|}{(\|L\| + \|P(x, s)\|)(\|B_1(x, s)\| + \|H_1\|)} \right) ds \\ &\quad + Q_1 \alpha_2^m \int_0^t e^{-\lambda_1(t-s)} \left(\frac{\|L\| \|B_2(x, s)\|}{(\|L\| + \|P(x, s)\|)(\|B_2(x, s)\| + \|H_2\|)} \right) ds \\ &\leq e^{-\lambda_1 t} \|I_1^0\| + 2Q_1 \hat{\alpha}^m \int_0^t e^{-\lambda_1(t-s)} ds \\ &\leq \|I_1^0\| + 2Q_1 \hat{\alpha}^m \frac{1}{\lambda_1}, \quad t \geq 0, \end{aligned} \quad (4.4)$$

where $\hat{\alpha}^m = \max_{x \in \bar{\Omega}} \{\alpha_1^m(x), \alpha_2^m(x)\}$, and $\lambda_1 > 0$ is the principal eigenvalue of $-d_l \Delta + \mu(\cdot)$. Similarly, from the third equation of model (2.1), we have

$$I_2(x, t) = J_2(t)I_2^0(x) + \int_0^t J_2(t-s) \left(\frac{\alpha_1(x)P(x, s)B_1(x, s)S(x, s)}{(L + P(x, s))(B_1(x, s) + H_1)} + \frac{\alpha_2(x)P(x, s)B_2(x, s)S(x, s)}{(L + P(x, s))(B_2(x, s) + H_2)} \right) ds,$$

one gets

$$\begin{aligned} \|I_2(x, t)\| &\leq e^{-\lambda_1 t} \|I_2^0\| + Q_1 \alpha_1^m \int_0^t e^{-\lambda_1(t-s)} \left(\frac{\|P(x, s)\| \|B_1(x, s)\|}{(\|L\| + \|P(x, s)\|)(\|B_1(x, s)\| + \|H_1\|)} \right) ds \\ &\quad + Q_1 \alpha_2^m \int_0^t e^{-\lambda_1(t-s)} \left(\frac{\|P(x, s)\| \|B_2(x, s)\|}{(\|L\| + \|P(x, s)\|)(\|B_2(x, s)\| + \|H_2\|)} \right) ds \\ &\leq e^{-\lambda_1 t} \|I_2^0\| + 2Q_1 \hat{\alpha}^m \int_0^t e^{-\lambda_1(t-s)} ds \\ &\leq \|I_2^0\| + 2Q_1 \hat{\alpha}^m \frac{1}{\lambda_1}, \quad t \geq 0. \end{aligned} \quad (4.5)$$

By [37, proof of Theorem 2.3] and assumption (H_3) , for $v \geq 0$, there exist C_0 and C_1 satisfying $h_1(x, v) - \delta_1 v \leq C_0 - C_1 v$, we derive

$$h_1(x, \hat{B}_1(x, t)) - \delta_1 \hat{B}_1(x, t) \leq C_0 - C_1 \hat{B}_1(x, t), \quad x \in \Omega, \quad t > 0, \quad (4.6)$$

in which $\hat{B}_1(x, t)$ satisfies

$$\begin{cases} \frac{\partial \hat{B}_1(x, t)}{\partial t} = \eta(x)(I_1(x, t) + I_2(x, t)) + C_0 - C_1 \hat{B}_1(x, t), & x \in \Omega, t > 0, \\ \frac{\partial \hat{B}_1(x, t)}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \\ \hat{B}_1(x, 0) = B_1(x, 0) = B_1^0(x), & x \in \Omega. \end{cases} \quad (4.7)$$

For the first equation of model (4.7), applying the Gronwall's inequality yields

$$\hat{B}_1(x, t) = e^{-C_1 t} B_1^0(x) + \int_0^t e^{-C_1(t-s)} (C_0 + \eta(x)(I_1(x, s) + I_2(x, s))) ds,$$

based on (4.4)–(4.5), there exist $Q_2 > 0$ and $Q_3 > 0$ satisfying $\|I_1(x, t)\| \leq Q_2$ and $\|I_2(x, t)\| \leq Q_3$, along with the comparison principle, we derive

$$\begin{aligned} \|B_1(x, t)\| &\leq \|\hat{B}_1(x, t)\| \leq e^{-C_1 t} \|B_1^0\| + \int_0^t e^{-C_1(t-s)} C_0 ds + \int_0^t e^{-C_1(t-s)} \eta(x) (\|I_1(x, s)\| + \|I_2(x, s)\|) ds \\ &\leq \|B_1^0\| + \frac{C_0}{C_1} + \eta^m(Q_2 + Q_3) \int_0^t e^{-C_1(t-s)} ds \\ &\leq \|B_1^0\| + \frac{1}{C_1} (C_0 + \eta^m(Q_2 + Q_3)), \quad t \geq 0. \end{aligned} \quad (4.8)$$

Similarly, there exist $C_2 > 0$ and $C_3 > 0$ satisfying $h_2(x, \nu) - \delta_2 \nu \leq C_2 - C_3 \nu$, we derive

$$h_2(x, \hat{B}_2(x, t)) - \delta_2 \hat{B}_2(x, t) \leq C_2 - C_3 \hat{B}_2(x, t), \quad x \in \Omega, t > 0, \quad (4.9)$$

in which $\hat{B}_2(x, t)$ satisfies

$$\begin{cases} \frac{\partial \hat{B}_2(x, t)}{\partial t} = \delta_1(x) B_1(x, t) + C_2 - C_3 \hat{B}_2(x, t), & x \in \Omega, t > 0, \\ \frac{\partial \hat{B}_2(x, t)}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \\ \hat{B}_2(x, 0) = B_2(x, 0) = B_2^0(x), & x \in \Omega. \end{cases} \quad (4.10)$$

For the first equation of model (4.10), applying the Gronwall's inequality again yields

$$\hat{B}_2(x, t) = e^{-C_3 t} B_2^0(x) + \int_0^t e^{-C_3(t-s)} (C_2 + \delta_1(x) B_1(x, s)) ds,$$

based on (4.8), there is a $Q_4 > 0$ satisfying $\|B_1(x, t)\| \leq Q_4$, along with the comparison principle, we derive

$$\begin{aligned} \|B_2(x, t)\| &\leq \|\hat{B}_2(x, t)\| \leq e^{-C_3 t} \|B_2^0\| + \int_0^t e^{-C_3(t-s)} C_2 ds + \int_0^t e^{-C_3(t-s)} \delta_1(x) \|B_1(x, s)\| ds \\ &\leq \|B_2^0\| + \frac{C_2}{C_3} + \delta_1^m Q_4 \int_0^t e^{-C_3(t-s)} ds \\ &\leq \|B_2^0\| + \frac{1}{C_3} (C_2 + \delta_1^m Q_4), \quad t \geq 0. \end{aligned} \quad (4.11)$$

Considering the last equation of model (2.1), we have

$$P(x, t) = e^{\int_0^t (\chi_1(x) b_1(x) B_1(x, s) + \chi_2(x) b_2(x) B_2(x, s) - m(x)) ds} P^0(x) + \int_0^t \alpha(x) \eta(x) I_2(x, s) ds, \quad x \in \Omega.$$

Based on (4.11), there is a $Q_5 > 0$ satisfying $\|B_2(x, t)\| \leq Q_5$, then

$$\begin{aligned} \|P(x, t)\| &\leq e^{\int_0^t \chi^m b^m (\|B_1(x, s)\| + \|B_2(x, s)\|) ds} \|P^0\| + \alpha^m \eta^m \int_0^t \|I_2(x, s)\| ds \\ &\leq e^{\chi^m b^m (Q_4 + Q_5)t} \|P^0\| + \alpha^m \eta^m Q_3, \quad t \geq 0, \end{aligned} \quad (4.12)$$

where

$$\chi^m = \max_{x \in \bar{\Omega}} \{\chi_1(x), \chi_2(x)\}, \quad b^m = \max_{x \in \bar{\Omega}} \{b_1(x), b_2(x)\}.$$

By (4.3)–(4.5), (4.8), (4.11)–(4.12) and Lemma 4.1, the solution $c(x, t) = (S, I_1, I_2, B_1, B_2, P)$ exists globally. $\square$

Lemma 4.3. *There exists a constant $\hat{M}_\infty > 0$ independent of $c^0 = (S^0(x), I_1^0(x), I_2^0(x), B_1^0(x), B_2^0(x), P^0(x)) \in H^+$ satisfying*

$$\limsup_{t \rightarrow \infty} (S(x, t) + I_1(x, t) + I_2(x, t) + B_1(x, t) + B_2(x, t) + P(x, t)) \leq \hat{M}_\infty.$$

Proof. From the first equation of model (2.1), we derive

$$\frac{\partial S(x, t)}{\partial t} \leq d_S \Delta S + \Lambda^m - \mu_m S(x, t).$$

By the comparison principle, there exists $T_1 > 0$ such that for all $t \geq T_1$ and $x \in \bar{\Omega}$,

$$S(x, t) \leq M_1, \quad \text{where } M_1 = \frac{\Lambda^m}{\mu_m} + 1. \quad (4.13)$$

The second equation $I_1(x, t)$ of model (2.1) yields

$$\frac{\partial I_1(x, t)}{\partial t} \leq d_I \Delta I_1 + (\alpha_1^m + \alpha_2^m) M_1 - \mu_m I_1(x, t).$$

Applying the comparison principle, there exists $T_2 > T_1$ such that for all $t \geq T_2$ and $x \in \bar{\Omega}$,

$$I_1(x, t) \leq M_2, \quad \text{where } M_2 = \frac{(\alpha_1^m + \alpha_2^m) M_1}{\mu_m} + 1. \quad (4.14)$$

Similarly, one gets

$$I_2(x, t) \leq M_2, \quad x \in \bar{\Omega}, \quad t \geq T_2. \quad (4.15)$$

From the fourth equation of models (2.1) and (4.6), we derive

$$\frac{\partial B_1(x, t)}{\partial t} \leq 2\eta^m M_2 + C_0 - C_1 B_1(x, t).$$

By the comparison principle, there exists $T_3 > T_2$ such that for all $t \geq T_3$ and $x \in \bar{\Omega}$,

$$B_1(x, t) \leq M_3 \quad \text{where } M_3 = \frac{2\eta^m M_2 + C_0}{C_1} + 1. \quad (4.16)$$

Similarly, for equation $B_2(x, t)$ of models (2.1) and (4.9), one gets

$$\frac{\partial B_2(x, t)}{\partial t} \leq \delta_1^m M_3 + C_2 - C_3 B_2(x, t).$$

The comparison principle yields $T_4 > T_3$ such that for all $t \geq T_4$ and $x \in \bar{\Omega}$,

$$B_2(x, t) \leq M_4, \quad \text{where } M_4 = \frac{\delta_1^m M_3 + C_2}{C_3} + 1. \quad (4.17)$$

Let $\bar{N}(x, t) = \chi_1(x) B_1(x, t) + \chi_2(x) B_2(x, t) + P(x, t)$, we obtain

$$\frac{\partial \bar{N}(x, t)}{\partial t} \leq \chi_1^m h_1^m + \chi_2^m h_2^m + (\alpha^m + 2\chi_1^m) \eta^m M_2 + \delta_1^m \chi_2^m M_3 - \delta_m (\chi_1(x) B_1(x, t) + \chi_2(x) B_2(x, t) + P(x, t)),$$

where $\delta_m = \min_{x \in \bar{\Omega}} \{\delta_1(x), \delta_2(x), m(x)\}$, $h_i^m = \max_{x \in \bar{\Omega}} h_i(x, B_i)$, $i = 1, 2$. By the comparison principle, there exists a $T_5 > T_4$ such that for all $t \geq T_5$ and $x \in \bar{\Omega}$,

$$P(x, t) \leq M_5, \text{ where } M_5 = \frac{\chi_1^m h_1^m + \chi_2^m h_2^m + (\alpha^m + 2\chi_1^m)\eta^m M_2 + \delta_1^m \chi_2^m M_3}{\delta_m} + 1. \quad (4.18)$$

Let $\hat{M}_\infty = M_2 + \sum_{i=1}^5 M_i$. Then by (4.13)–(4.18), for all $t \geq T_5$, the solution satisfies

$$\limsup_{t \rightarrow \infty} (S(x, t) + I_1(x, t) + I_2(x, t) + B_1(x, t) + B_2(x, t) + P(x, t)) \leq \hat{M}_\infty.$$

This establishes Lemma 4.3. $\square$

Define $\hat{J}(t) : H^+ \rightarrow H^+$ as the semiflow generated by model (2.1)–(2.3), namely $\hat{J}(t)c^0 = c(x, t)$ for $t > 0$. We observe that the last three equations in model (2.1)–(2.3) lack diffusion terms; the solution semiflow $\hat{J}(t)$ loses its compactness. We introduce the Kuratowski measure of noncompactness, denoted as $\kappa(\cdot)$,

$$\kappa = \inf\{R : \mathcal{P} \text{ has a finite cover of diameter } < R\}.$$

Denote

$$K(I_1, I_2, B_1, B_2, P) = \begin{pmatrix} h_1(x, B_1) + \eta(x)(I_1 + I_2) - b_1(x)B_1P - \delta_1(x)B_1 \\ h_2(x, B_2) + \delta_1(x)B_1 - b_2(x)B_2P - \delta_2(x)B_2 \\ \alpha(x)\eta(x)I_2 + \chi_1(x)b_1(x)B_1P + \chi_2(x)b_2(x)B_2P - m(x)P \end{pmatrix}$$

as the vector field associated with the last three equations of model (2.1). The Jacobian of K with (B_1, B_2, P) is defined as

$$K_{13} = \frac{\partial K(I_1, I_2, B_1, B_2, P)}{\partial (B_1, B_2, P)} = \begin{pmatrix} \frac{\partial h_1}{\partial B_1} - b_1P - \delta_1 & 0 & -b_1B_1 \\ \delta_1 & \frac{\partial h_2}{\partial B_2} - b_2P - \delta_2 & -b_2B_2 \\ \chi_1b_1P & \chi_2b_2P & \chi_1b_1B_1 + \chi_2b_2B_2 - m \end{pmatrix}.$$

Lemma 4.4. $\hat{J}(t)$ is asymptotically smooth and κ -contracting if there exists a $r^* > 0$ satisfying

$$u^T K_{13} u \leq -r^* u^T u, \quad \forall u \in \mathbb{R}^3, \quad x \in \bar{\Omega}, \quad c \in \Gamma_Z. \quad (4.19)$$

Proof. By using similar proof in [36, Lemma 23.1(2)], we can derive that $\hat{J}(t)$ is asymptotically compact on any closed bounded set $\mathcal{P}$ for $\hat{J}(t)\mathcal{P} \subset \mathcal{P}$. Thus, the omega limit $\omega(\mathcal{P})$ is nonempty, invariant and compact, and attracts $\mathcal{P}$. This proves the asymptotic smoothness of $\hat{J}(t)$. By [26, Lemma 2.1(b)], we have

$$\kappa(\hat{J}(t)\mathcal{P}) \leq \kappa(\omega(\mathcal{P})) + \bar{d}(\hat{J}(t), \omega(\mathcal{P})) = \bar{d}(\hat{J}(t)\mathcal{P}, \omega(\mathcal{P})),$$

where $\bar{d}(\hat{J}(t)\mathcal{P}, \omega(\mathcal{P}))$ denotes the distance from $\hat{J}(t)\mathcal{P}$ to $\omega(\mathcal{P})$, which tends to zero as $t \rightarrow +\infty$. Consequently, $\hat{J}(t)$ is κ -contracting. $\square$

Remark 4.5. A sufficient condition for (4.19) is that

$$\frac{\partial h_1}{\partial B_1} < 2b_1\hat{M}_1, \quad \frac{\partial h_2}{\partial B_2} + \delta_1 < 2b_1\hat{M}_1 + \delta_2, \quad 2\chi^m b^m \hat{M}_1 < m.$$

Proof of Theorem 3.1 The global existence and uniqueness of solution of model (2.1)–(2.3) can be obtained from Lemmas 4.1–4.2. In view of Lemma 4.3, $\hat{J}(t)$ is point dissipative. According to Lemma 4.4, $\hat{J}(t)$ is asymptotically smooth. Thus, by [13, Theorem 2.1], model (2.1)–(2.3) has a connected global attractor in H^+ . $\square$

4.2 Proof of Lemma 3.3

Let $\psi = Fw$ and $w = -V^{-1}\varphi$. Then,

$$\varphi_1 = (V_{11} - d_l \Delta)w_1, \quad \varphi_2 = V_{22}w_2 - V_{21}w_1, \quad \varphi_3 = V_{33}w_3 - V_{32}w_2,$$

we can easily derive

$$w_1 = (V_{11} - d_l \Delta)^{-1}\varphi_1,$$

$$w_2 = V_{22}^{-1}(\varphi_2 + V_{21}(V_{11} - d_l \Delta)^{-1}\varphi_1),$$

$$w_3 = V_{33}^{-1}(\varphi_3 + V_{32}V_{22}^{-1}(\varphi_2 + V_{21}(V_{11} - d_l \Delta)^{-1}\varphi_1)).$$

By a straightforward calculation, we get

$$\begin{aligned} \psi_1 &= F_{12}V_{33}^{-1}(\varphi_3 + V_{32}V_{22}^{-1}(\varphi_2 + V_{21}(V_{11} - d_l \Delta)^{-1}\varphi_1)) + F_{11}V_{22}^{-1}(\varphi_2 + V_{21}(V_{11} - d_l \Delta)^{-1}\varphi_1), \\ \psi_2 &= 0, \quad \psi_3 = 0, \end{aligned}$$

and

$$-FV^{-1} \begin{pmatrix} \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = \begin{pmatrix} D_1\varphi_1 + D_2\varphi_2 + D_3\varphi_3 \\ 0 \\ 0 \end{pmatrix},$$

where

$$D_1 = F_{11}V_{22}^{-1}V_{21}(V_{11} - d_l \Delta)^{-1} + F_{12}V_{33}^{-1}V_{32}V_{22}^{-1}V_{21}(V_{11} - d_l \Delta)^{-1},$$

$$D_2 = F_{11}V_{22}^{-1} + F_{12}V_{33}^{-1}V_{32}V_{22}^{-1},$$

$$D_3 = F_{12}V_{33}^{-1}.$$

It follows by iteration that

$$(-FV^{-1})^n \begin{pmatrix} \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = \begin{pmatrix} D_1^n\varphi_1 + D_1^{n-1}D_2\varphi_2 + D_1^{n-1}D_3\varphi_3 \\ 0 \\ 0 \end{pmatrix}.$$

Then, we have

$$\|D_1^n\| \leq \|(-FV^{-1})^n\| \leq \|D_1^{n-1}\|(\|D_1\| + \|D_2\| + \|D_3\|).$$

By applying the Gelfand's formula and the squeeze theorem, we obtain $r(-FV^{-1}) = r(D_H + D_L)$. This establishes Lemma 3.3.

4.3 Proof of Theorem 3.7

Before proving Theorem 3.7, we first give some preliminaries.

Lemma 4.6. Define λ^0 as the principal eigenvalue of the eigenvalue problem

$$\begin{cases} d_l \Delta \varphi - \mu(x)\varphi + \left(\frac{\alpha_1(x)S^*\eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x)S^*\eta(x)\delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \varphi = \lambda \varphi, & x \in \Omega, \\ \frac{\partial \varphi}{\partial \nu} = 0, & x \in \partial\Omega. \end{cases} \quad (4.20)$$

Then $\mathcal{R}_0 - 1$ and $s(\mathcal{A})$ have the same sign as λ^0 .

Proof. It is well-known that there exists a least eigenvalue λ^0 associated with the eigenvalue problem (4.20), its corresponding eigenfunction $\bar{\varphi}$ can be chosen to be positive on Ω , that is,

$$\begin{cases} d_l \Delta \bar{\varphi} - \mu(x) \bar{\varphi} + \left(\frac{\alpha_1(x) S^* \eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x) S^* \eta(x) \delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \bar{\varphi} = \lambda^0 \bar{\varphi}, & x \in \Omega, \\ \frac{\partial \bar{\varphi}}{\partial \nu} = 0, & x \in \partial \Omega. \end{cases} \quad (4.21)$$

Next, we consider the following eigenvalue problem

$$\begin{cases} d_l \Delta \varphi - \mu(x) \varphi + \left(\frac{\alpha_1(x) S^* \eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x) S^* \eta(x) \delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \frac{1}{\mathcal{R}_0} \varphi = 0, & x \in \Omega, \\ \frac{\partial \varphi}{\partial \nu} = 0, & x \in \partial \Omega. \end{cases} \quad (4.22)$$

By multiplying (4.21) with φ and (4.22) with $\bar{\varphi}$, and performing integration by parts on Ω , subtracting the resulting equation, we get

$$\left(1 - \frac{1}{\mathcal{R}_0} \right) \int_{\Omega} \left(\frac{\alpha_1(x) S^* \eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x) S^* \eta(x) \delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \bar{\varphi} \varphi dx = \lambda^0 \int_{\Omega} \bar{\varphi} \varphi dx.$$

Apparently,

$$\int_{\Omega} \left(\frac{\alpha_1(x) S^* \eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x) S^* \eta(x) \delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \bar{\varphi} \varphi dx$$

and $\int_{\Omega} \bar{\varphi} \varphi dx$ are both positive, it implies that $\left(1 - \frac{1}{\mathcal{R}_0} \right)$ and λ^0 have the same sign, namely $\mathcal{R}_0$ and λ^0 have the same sign. This establishes Lemma 4.6. $\square$

Let $I(x, t) = e^{\lambda t} \phi_2$, $B_1(x, t) = e^{\lambda t} \phi_3$, $B_2(x, t) = e^{\lambda t} \phi_4$ in model (3.6), then

$$\begin{cases} \lambda \phi_2 = d_l \Delta \phi_2 + \frac{\alpha_1(x) S^*}{H_1} \phi_3 + \frac{\alpha_2(x) S^*}{H_2} \phi_4 - \mu(x) \phi_2, & x \in \Omega, \\ \lambda \phi_3 = \eta(x) \phi_2 + \hat{h}_1(x) \phi_3 - \delta_1(x) \phi_3, & x \in \Omega, \\ \lambda \phi_4 = \delta_1(x) \phi_3 + \hat{h}_2(x) \phi_4 - \delta_2(x) \phi_4, & x \in \Omega, \\ \frac{\partial \phi_2}{\partial \nu} = 0, & x \in \partial \Omega. \end{cases} \quad (4.23)$$

Lemma 4.7. If $\mathcal{R}_0 \geq 1$, then $s(\mathcal{A})$ is the principal eigenvalue of problem (4.23) with respect to a strongly positive eigenfunction.

Proof. Let

$$T_{\lambda} = d_l \Delta + \frac{\alpha_1(x) S^* \eta(x)}{\lambda + H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x) S^* \eta(x) \delta_1(x)}{\lambda + H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} - \mu(x)$$

be a family of linear operators on $C(\bar{\Omega})$. Notice that $s(T_{\lambda})$ is decreasing and continuously dependent on λ , where λ denotes the principal eigenvalue of $T_{\lambda} c = \lambda c$. As a result, it has the following variational characterisation:

$$s(T_{\lambda}) = \sup_{\varphi \in H^1(\Omega), \varphi \neq 0} \left\{ \frac{\int_{\Omega} \left(\frac{\alpha_1 S^* \eta}{\lambda + H_1(\delta_1 - \hat{h}_1)} + \frac{\alpha_2 S^* \eta \delta_1}{\lambda + H_2(\delta_1 - \hat{h}_1)(\delta_2 - \hat{h}_2)} \right) \varphi^2 - d_l |\nabla \varphi|^2 - \mu \varphi^2 dx}{\int_{\Omega} \varphi^2 dx} \right\}.$$

Clearly, we have $s(T_{\lambda}) < 0$ if λ is large enough. From $\mathcal{R}_0 \geq 1$ and Lemma 4.6, the following equation holds $s(T_0) = \lambda^0 \geq 0$. Therefore, we deduce that there exists a unique $\bar{\lambda}$ satisfying $s(T_{\bar{\lambda}}) = \bar{\lambda}$. Let $\bar{\phi} > 0$ be an eigenvector with respect to $s(T_{\bar{\lambda}})$, we get $T_{\bar{\lambda}} \bar{\phi} = \bar{\lambda} \bar{\phi}$. Similar to the results in [50, Theorem 2.3], we have $\bar{\lambda} = s(\mathcal{A})$. This establishes Lemma 4.7. $\square$

Proof of Theorem 3.7 (i) The locally asymptotically stability of F_0 for model (2.1)–(2.3) follows from [50, Theorem 3.1]. Next, we only need to establish the global attractivity of F_0 . Initially, we set $\varepsilon_0 > 0$. From (4.2), we deduce that there exists a $t_1 > 0$ such that $0 \leq S(\cdot, t) \leq S^*(x) + \varepsilon_0$ for all $t > t_1$, and from the comparison principle for cooperative models, we get $(I(x, t), B_1(x, t), B_2(x, t)) \leq (\bar{I}(x, t), \bar{B}_1(x, t), \bar{B}_2(x, t))$, where $(\bar{I}(x, t), \bar{B}_1(x, t), \bar{B}_2(x, t))$ is the solution of the following model

$$\begin{cases} \frac{\partial \bar{I}}{\partial t} = d_I \Delta \bar{I} + \frac{\alpha_1(x)(S^* + \varepsilon_0)}{H_1} \bar{B}_1 + \frac{\alpha_2(x)(S^* + \varepsilon_0)}{H_2} \bar{B}_2 - \mu(x) \bar{I}, & x \in \Omega, \quad t > t_1, \\ \frac{\partial \bar{B}_1}{\partial t} = \eta(x) \bar{I} + \hat{h}_1(x) \bar{B}_1 - \delta_1(x) \bar{B}_1, & x \in \Omega, \quad t > t_1, \\ \frac{\partial \bar{B}_2}{\partial t} = \delta_1(x) \bar{B}_1 + \hat{h}_2(x) \bar{B}_2 - \delta_2(x) \bar{B}_2, & x \in \Omega, \quad t > t_1, \\ \frac{\partial \bar{I}}{\partial \nu} = 0, & x \in \partial \Omega, \quad t > t_1, \\ \bar{I}(x, t_1) = I(x, t_1), \quad \bar{B}_1(x, t_1) = B_1(x, t_1), \quad \bar{B}_2(x, t_1) = B_2(x, t_1), & x \in \Omega. \end{cases} \quad (4.24)$$

Let $J_{\varepsilon_0}(t)$ be the linear semigroup of model (4.24) with respect to C_{ε_0} , where C_{ε_0} is defined as the following generator

$$C_{\varepsilon_0} = \begin{pmatrix} d_I \Delta - \mu & \frac{\alpha_1(S^* + \varepsilon_0)}{H_1} & \frac{\alpha_2(S^* + \varepsilon_0)}{H_2} \\ \eta & \hat{h}_1 - \delta_1 & 0 \\ 0 & \delta_1 & \hat{h}_2 - \delta_2 \end{pmatrix}.$$

Next, we prove that $\|J_{\varepsilon_0}(t)\| \leq Ne^{\gamma_{\varepsilon_0} t}$ for some $N > 0$, where $\gamma_{\varepsilon_0} := \lim_{t \rightarrow \infty} \frac{\ln \|J_{\varepsilon_0}(t)\|}{t}$ is the exponential growth bound of $J_{\varepsilon_0}(t)$. Note that

$$\gamma_{\varepsilon_0} = \max\{s(C_{\varepsilon_0}), \gamma_{\text{ess}}(J_{\varepsilon_0}(t))\},$$

where $\gamma_{\text{ess}}(J_{\varepsilon_0}(t)) := \lim_{t \rightarrow \infty} \frac{n(J_{\varepsilon_0}(t))}{t}$, and $n(\cdot)$ represents the measure of non-compactness. Similar to the arguments in [58, Lemma 3.5], there exists a $\delta_* > 0$ such that $\gamma_{\text{ess}}(J_{\varepsilon_0}) \leq -\delta_*$. Then we can choose ε_0 small enough such that $\gamma_{\varepsilon_0} < 0$. To see this, γ_{ε_0} has the same sign as $s(C_{\varepsilon_0})$. Moreover, $s(C_{\varepsilon_0})$ has the same sign as λ_{ε_0} , in which λ_{ε_0} represents the principal eigenvalue of the eigenvalue problem

$$\begin{cases} d_I \Delta \varphi - \mu(x) \varphi + \left(\frac{\alpha_1(x)(S^* + \varepsilon_0)\eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x)(S^* + \varepsilon_0)\eta(x)\delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \varphi = \lambda \varphi, & x \in \Omega, \\ \frac{\partial \varphi}{\partial \nu} = 0, & x \in \partial \Omega. \end{cases} \quad (4.25)$$

According to Lemma 4.6, $\mathcal{R}_0 < 1$ and the continuous dependence of $\lambda_{\varepsilon_0}^0$ on ε_0 , it can be inferred that $\lambda_{\varepsilon_0}^0 < 0$ if ε_0 is small enough. Then we get $\gamma_{\varepsilon_0} < 0$. It implies that $(\bar{I}(x, t), \bar{B}_1(x, t), \bar{B}_2(x, t)) \rightarrow (0, 0, 0)$ as $t \rightarrow \infty$ uniformly for $x \in \bar{\Omega}$. Clearly, we derive $(I(x, t), B_1(x, t), B_2(x, t)) \rightarrow (0, 0, 0)$ as $t \rightarrow \infty$ uniformly for $x \in \bar{\Omega}$. Then, we have $(I_1(x, t), I_2(x, t), B_1(x, t), B_2(x, t)) \rightarrow (0, 0, 0, 0)$ as $t \rightarrow \infty$ uniformly for $x \in \bar{\Omega}$. Furthermore, it follows from model (4.2) that $S(x, t) \rightarrow S^*(x)$ as $t \rightarrow \infty$ uniformly for $x \in \bar{\Omega}$. This establishes Theorem 3.7 (i). $\square$

Proof of Theorem 3.7 (ii) First, we prove the local stability of F_0 . For any given $\varepsilon > 0$, we assume that $\vartheta > 0$ and initial conditions $c^0 = (S^0, I_1^0, I_2^0, B_1^0, B_2^0, P^0)$ with $\|c^0 - F_0\| \leq \vartheta$. Let

$$v_1(x, t) = \frac{S(x, t)}{S^*(x)} - 1, \quad a(t) = \max_{x \in \bar{\Omega}} \{v_1(x, t), 0\}. \quad (4.26)$$

From model (3.5), we have $d_S \Delta S^* + \Lambda - \mu S^* = 0$, and by the first equation of model (2.1), we derive

$$\frac{\partial v_1}{\partial t} - d_S \Delta v_1 - 2d_S \frac{\nabla S^* \cdot \nabla v_1}{S^*} + \frac{\Lambda}{S^*} v_1 = -\frac{\alpha_1 B_1 S}{S^*(B_1 + H_1)} - \frac{\alpha_2 B_2 S}{S^*(B_2 + H_2)}.$$

Define $\hat{J}_1(t)$ as the positive semigroup generated by the following operator

$$d_S \Delta + 2d_S \frac{\nabla S^* \cdot \nabla}{S^*} - \frac{\Lambda}{S^*}.$$

By [57, Proposition 2.3], there exists a $z_1 > 0$ satisfying $\|\hat{J}_1(t)\| \leq \bar{M} e^{-z_1 t}$ for some $\bar{M} > 0$. We derive

$$v_1(\cdot, t) = \hat{J}_1(t)v_{10} - \int_0^t \hat{J}_1(t-s) \left(\frac{\alpha_1 B_1(\cdot, s)S(\cdot, s)}{S^*(B_1(\cdot, s) + H_1)} + \frac{\alpha_2 B_2(\cdot, s)S(\cdot, s)}{S^*(B_2(\cdot, s) + H_2)} \right) ds,$$

where $v_{10} = \frac{S^0}{S^*} - 1$. In view of the positivity of $\hat{J}_1(t)$, one gets

$$\begin{aligned} a(t) &= \max_{x \in \bar{\Omega}} \{v_1(x, t), 0\} = \max_{x \in \bar{\Omega}} \left\{ \hat{J}_1(t)v_{10} - \int_0^t \hat{J}_1(t-s) \left(\frac{\alpha_1 B_1(\cdot, s)S(\cdot, s)}{S^*(B_1(\cdot, s) + H_1)} + \frac{\alpha_2 B_2(\cdot, s)S(\cdot, s)}{S^*(B_2(\cdot, s) + H_2)} \right) ds, 0 \right\} \\ &\leq \max_{x \in \bar{\Omega}} \{\hat{J}_1(t)v_{10}, 0\} \leq \|\hat{J}_1(t)v_{10}\| \\ &\leq \bar{M} e^{-z_1 t} \left\| \frac{S^0}{S^*} - 1 \right\| \\ &\leq \frac{\vartheta \bar{M} e^{-z_1 t}}{S_m^*}, \end{aligned} \quad (4.27)$$

where $S_m^* = \min_{x \in \bar{\Omega}} S^*(x)$. From $\mathcal{B}_0 = 1$ and [58, Lemma 3.6], we obtain $\|J(t)\| \leq \bar{M}$ for $t \geq 0$ and $\bar{M} > 0$. Recall that $a(t) \leq \vartheta \bar{M} e^{-z_1 t} / S_m^*$, we derive

$$\begin{aligned} \begin{pmatrix} I(\cdot, t) \\ B_1(\cdot, t) \\ B_2(\cdot, t) \end{pmatrix} &\leq J(t) \begin{pmatrix} I^0 \\ B_1^0 \\ B_2^0 \end{pmatrix} + \int_0^t J(t-s) \begin{pmatrix} \left(\frac{\alpha_1 B_1(\cdot, s)S^*}{H_1} + \frac{\alpha_2 B_2(\cdot, s)S^*}{H_2} \right) \left(\frac{S(\cdot, s)}{S^*} - 1 \right) \\ 0 \\ 0 \end{pmatrix} ds \\ &\leq \bar{M} \vartheta + \int_0^t J(t-s) \hat{\alpha}^m S^* (B_1(\cdot, s) + B_2(\cdot, s)) \left(\frac{S(\cdot, s)}{S^*} - 1 \right) ds, \end{aligned}$$

where $I^0 = I_1^0 + I_2^0$. Thus,

$$\begin{aligned} \max\{\|I(x, t)\|, \|B_1(x, t)\|, \|B_2(x, t)\|\} &\leq \bar{M} \vartheta + \bar{M} \|\hat{\alpha}^m\| \|S^*\| \int_0^t a(s) (\|B_1(\cdot, s)\| + \|B_2(\cdot, s)\|) ds \\ &\leq \bar{M} \vartheta + \tilde{M}_1 \vartheta \int_0^t e^{-z_1 s} (\|B_1(\cdot, s)\| + \|B_2(\cdot, s)\|) ds, \end{aligned} \quad (4.28)$$

where $\tilde{M}_1 = \bar{M}^2 \|\hat{\alpha}^m\| \|S^*\| / S_m^*$. This yields that

$$\|B_1(\cdot, t)\| + \|B_2(\cdot, t)\| \leq 2\bar{M} \vartheta + 2\tilde{M}_1 \vartheta \int_0^t e^{-z_1 s} (\|B_1(\cdot, s)\| + \|B_2(\cdot, s)\|) ds.$$

Utilising Gronwall's inequality, we derive

$$\begin{aligned} \|B_1(\cdot, t)\| + \|B_2(\cdot, t)\| &\leq 2\bar{M} \vartheta e^{\int_0^t 2\tilde{M}_1 \vartheta e^{-z_1 s} ds} \\ &\leq 2\bar{M} \vartheta e^{2\tilde{M}_1 \vartheta / z_1}. \end{aligned} \quad (4.29)$$

Moreover, we can also derive

$$\begin{aligned}\|I(\cdot, t)\| &\leq \bar{M}\vartheta + \tilde{M}_1\vartheta \int_0^t e^{-z_1 s} (\|B_1(\cdot, s)\| + \|B_2(\cdot, s)\|) ds \\ &\leq \bar{M}\vartheta + 2\tilde{M}_1\bar{M}\vartheta^2 e^{2\tilde{M}_1\vartheta/z_1} \int_0^t e^{-z_1 s} ds \\ &\leq \bar{M}\vartheta \left(1 + 2\tilde{M}_1\vartheta e^{2\tilde{M}_1\vartheta/z_1}/z_1\right).\end{aligned}\quad (4.30)$$

The last equation in model (2.1) yields

$$\frac{\partial P}{\partial t} \leq \alpha^m \eta^m \bar{M}\vartheta \left(1 + 2\tilde{M}_1\vartheta e^{2\tilde{M}_1\vartheta/z_1}/z_1\right) + \chi^m b^m 2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} P - mP.$$

Let $\tilde{M}_2 = \alpha^m \eta^m \bar{M}\vartheta (1 + 2\tilde{M}_1\vartheta e^{2\tilde{M}_1\vartheta/z_1}/z_1)$, $\tilde{M}_3 = \chi^m b^m 2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1}$, we have

$$\|P(x, t)\| \leq e^{-mt} \|P^0\| + \int_0^t e^{-m(t-s)} (\tilde{M}_2 + \tilde{M}_3 \|P(\cdot, s)\|) ds.$$

Applying Gronwall's inequality, we obtain

$$\begin{aligned}\|P(x, t)\| &\leq (\vartheta e^{-mt} + \tilde{M}_2) e^{\int_0^t \tilde{M}_3 e^{-m(t-s)} ds} \\ &\leq (\vartheta e^{-mt} + \tilde{M}_2) e^{\tilde{M}_3 t}.\end{aligned}\quad (4.31)$$

By the first equation of models (2.1) and (4.28), we get

$$\frac{\partial S}{\partial t} - d_s \Delta S > \Lambda(x) - \mu(x)S - (2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} \hat{\alpha}^m)S.$$

Let $\hat{S}$ be the solution of the following model

$$\begin{cases} \frac{\partial \hat{S}}{\partial t} = d_s \Delta \hat{S} + \Lambda(x) - \mu(x)\hat{S} - (2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} \hat{\alpha}^m)\hat{S}, & x \in \Omega, \quad t > 0, \\ \frac{\partial \hat{S}}{\partial \nu} = 0, & x \in \partial\Omega, \quad t > 0, \\ \hat{S}(x, 0) = S^0, & x \in \Omega. \end{cases}\quad (4.32)$$

The comparison principle yields that $S(x, t) \geq \hat{S}(x, t)$ for $x \in \bar{\Omega}$ and $t \geq 0$. Define S_ϑ^* as the positive steady state of model (4.32) and $\hat{v} = \hat{S} - S_\vartheta^*$, $\hat{v}(x, t)$ satisfies

$$\begin{cases} \frac{\partial \hat{v}}{\partial t} = d_s \Delta \hat{v} - (\mu(x) + 2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} \hat{\alpha}^m)\hat{v}, & x \in \Omega, \quad t > 0, \\ \frac{\partial \hat{v}}{\partial \nu} = 0, & x \in \partial\Omega, \quad t > 0, \\ \hat{v}(x, 0) = S^0 - S_\vartheta^*, & x \in \Omega. \end{cases}\quad (4.33)$$

Define $J_1(t)$ as the semigroup generated by $d_s \Delta - \mu$, then we have $\|J_1(t)\| \leq \bar{M}e^{-\mu_m t}$, where $\bar{M} > 0$ and large enough. From model (4.33), we derive

$$\hat{v}(\cdot, t) = J_1(t)(S^0 - S_\vartheta^*) - \int_0^t J_1(t-s) 2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} \hat{\alpha}^m \hat{v}(\cdot, s) ds.$$

Then

$$\|\hat{v}(\cdot, t)\| \leq \bar{M}\|S^0 - S_\vartheta^*\| e^{-\mu_m t} + \int_0^t \bar{M}e^{-\mu_m(t-s)} 2\bar{M}\vartheta e^{2\tilde{M}_1\vartheta/z_1} \|\hat{\alpha}^m\| \|\hat{v}(\cdot, s)\| ds.$$

Applying the Gronwall's inequality again yields

$$\|\hat{S}(\cdot, t) - S_\vartheta^*\| = \|\hat{v}(\cdot, t)\| \leq \bar{M}\|S^0 - S_\vartheta^*\| e^{(\bar{M}_4 - \mu_m)t}, \quad (4.34)$$

where $\bar{M}_4 = 2\bar{M}^2 \vartheta e^{2\tilde{M}_1\vartheta/z_1} \|\hat{\alpha}^m\|$. □

Choosing $\vartheta > 0$ small enough such that $\tilde{M}_4 < \mu_m/2$, (4.34) yields that

$$\|\hat{S}(\cdot, t) - S_\vartheta^*\| \leq \bar{M}\|S^0 - S_\vartheta^*\|e^{-\mu_m t/2}. \quad (4.35)$$

Inequality (4.35) implies that

$$\begin{aligned} S(\cdot, t) - S^* &\geq \hat{S}(\cdot, t) - S^* \\ &= \hat{S}(\cdot, t) - S_\vartheta^* + S_\vartheta^* - S^* \\ &\geq -\bar{M}\|S^0 - S_\vartheta^*\|e^{-\mu_m t/2} + S_\vartheta^* - S^* \\ &\geq -\bar{M}(\|S^0 - S^*\| + \|S^* - S_\vartheta^*\|) - \|S_\vartheta^* - S^*\| \\ &\geq -\bar{M}\vartheta - (\bar{M} + 1)\|S_\vartheta^* - S^*\|. \end{aligned} \quad (4.36)$$

Since $a(t) \leq \vartheta \bar{M}e^{-z_1 t}/S_m^* \leq \vartheta \bar{M}/S_m^*$, we have

$$S(\cdot, t) - S^* = S^* \left(\frac{S(x, t)}{S^*} - 1 \right) \leq \|S^*\|a(t) \leq \vartheta \bar{M}\|S^*\|/S_m^*. \quad (4.37)$$

From (4.36)–(4.37), we have

$$\|S(\cdot, t) - S^*\| \leq \max \{ \bar{M}\vartheta + (\bar{M} + 1)\|S_\vartheta^* - S^*\|, \vartheta \bar{M}\|S^*\|/S_m^* \}. \quad (4.38)$$

Thus, from (4.28)–(4.31), (4.38) and $\lim_{\vartheta \rightarrow 0} S_\vartheta^* = S^*$, we choose $\vartheta > 0$ small enough satisfying for $t > 0$,

$$\|S(x, t) - S^*\|, \|I_1(\cdot, t)\|, \|I_2(\cdot, t)\|, \|B_1(\cdot, t)\|, \|B_2(\cdot, t)\|, \|P(\cdot, t)\| \leq \varepsilon.$$

This proves the local stability of $F_0 = (S^*, 0, 0, 0, 0, 0)$. Then we need to discuss the global attractivity of F_0 . Theorem 3.1 implies that $\hat{J}(t)$ has a connected global attractor $\mathcal{D}$. From Lemma 4.7, the eigenvalue problem (4.23) has a positive eigenvector (ϕ_2, ϕ_3, ϕ_4) with $s(\mathcal{A}) = 0$. Let

$$\partial Y_1 = \{(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{B}_1, \hat{B}_2, \hat{P}) \in H^+ : \hat{I}_1 = \hat{I}_2 = \hat{B}_1 = \hat{B}_2 = \hat{P} = 0\}.$$

We present the following two claims.

Claim 1. For any $c^0 = (S^0, I_1^0, I_2^0, B_1^0, B_2^0, P^0) \in \mathcal{D}$, the omega limit set $\omega(c^0) \subset \partial Y_1$.

In view of (4.2), we have $S^0 \leq S^*$. If $I_1^0 = I_2^0 = B_1^0 = B_2^0 = P^0 = 0$, the claim easily follows from the fact that ∂Y_1 is invariant for $\hat{J}(t)$. Hence, we assume that either $I_1^0 \neq 0$ or $I_2^0 \neq 0$ or $B_1^0 \neq 0$ or $B_2^0 \neq 0$ or $P^0 \neq 0$. From the results in Theorem 3.1, we easily know that $c(x, t, c^0) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. $S(x, t)$ satisfies

$$\begin{cases} \frac{\partial S}{\partial t} < d_S \Delta S + \Lambda(x) - \mu(x)S, & x \in \Omega, t > 0, \\ \frac{\partial S}{\partial \nu} = 0, & x \in \partial \Omega, t > 0, \\ S(x, 0) \leq S^*(x), & x \in \Omega. \end{cases}$$

Applying the comparison principle, we have $S(x, t) < S^*(x)$ for $x \in \bar{\Omega}$ and $t > 0$. Motivated by [9], we assume

$$u(t; c^0) = \inf \{ \tilde{u} \in \mathbb{R} : I(\cdot, t) \leq \tilde{u}\phi_2 \text{ and } B_1(\cdot, t) \leq \tilde{u}\phi_3 \text{ and } B_2(\cdot, t) \leq \tilde{u}\phi_4 \},$$

and $u(t; c^0) > 0$ holds for all $t > 0$, we also know that $u(t; c^0)$ is strictly decreasing. Then we choose a $t_2 > 0$ satisfying $\tilde{I}(\cdot, t) = u(t_2; c^0)\phi_2$, $\tilde{B}_1(\cdot, t) = u(t_2; c^0)\phi_3$, $\tilde{B}_2(\cdot, t) = u(t_2; c^0)\phi_4$ for $t \geq t_2$. Note that $S(x, t) < S^*$, we have

$$\left\{ \begin{array}{l} \frac{\partial \tilde{I}}{\partial t} > d_I \Delta \tilde{I} + \frac{\alpha_1(x)(S^* - \vartheta) \tilde{B}_1}{H_1 + \vartheta} + \frac{\alpha_2(x)(S^* - \vartheta) \tilde{B}_2}{H_2 + \vartheta} - \mu(x) \tilde{I}, \quad x \in \Omega, \quad t > t_2, \\ \frac{\partial \tilde{B}_1}{\partial t} = \eta(x) \tilde{I} + \frac{\partial h_1(x, \vartheta)}{\partial B_1} \tilde{B}_1 - b_1(x) \vartheta \tilde{B}_1 - \delta_1(x) \tilde{B}_1, \quad x \in \Omega, \quad t > t_2, \\ \frac{\partial \tilde{B}_2}{\partial t} = \delta_1(x) \tilde{B}_1 + \frac{\partial h_2(x, \vartheta)}{\partial B_2} \tilde{B}_2 - b_2(x) \vartheta \tilde{B}_2 - \delta_2(x) \tilde{B}_2, \quad x \in \Omega, \quad t > t_2, \\ \frac{\partial \tilde{I}}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t > t_2, \\ \tilde{I}(x, t_2) \geq I(x, t_2), \quad \tilde{B}_1(x, t_2) \geq B_1(x, t_2), \quad \tilde{B}_2(x, t_2) \geq B_2(x, t_2), \quad x \in \Omega. \end{array} \right. \quad (4.39)$$

Applying the comparison principle, we have $(\tilde{I}(x, t), \tilde{B}_1(x, t), \tilde{B}_2(x, t)) \geq (I(x, t), B_1(x, t), B_2(x, t))$ for $x \in \bar{\Omega}$ and $t \geq t_2$. From model (4.39) and the strong comparison principle, we have $u(t_2; c^0)\phi_2 = \tilde{I}(x, t) > I(x, t)$, $u(t_2; c^0)\phi_3 = \tilde{B}_1(x, t) > B_1(x, t)$, $u(t_2; c^0)\phi_4 = \tilde{B}_2(x, t) > B_2(x, t)$ for $x \in \bar{\Omega}$ and $t > t_2$. Due to $t_2 > 0$ is arbitrary, $u(t; c^0)$ is strictly decreasing function. Define $u_* = \lim_{t \rightarrow \infty} u(t; c^0)$, which implies $u_* = 0$, and define $\mathbb{T} = (\mathbb{T}_1, \mathbb{T}_2, \mathbb{T}_3, \mathbb{T}_4, \mathbb{T}_5, \mathbb{T}_6) \in \omega(c^0)$. Then there exists a sequence $\{t_k\}$ with $t_k \rightarrow \infty$ satisfying $\hat{J}(t_k)c^0 \rightarrow \mathbb{T}$. We easily obtain $u(t, \mathbb{T}) = u_*$ for $t \geq 0$. In view of $\lim_{t_k \rightarrow \infty} \hat{J}(t + t_k)c^0 = \hat{J}(t) \lim_{t_k \rightarrow \infty} \hat{J}(t_k)c^0 = \hat{J}(t)\mathbb{T}$. If $\mathbb{T}_2 \neq 0$ or $\mathbb{T}_3 \neq 0$ or $\mathbb{T}_4 \neq 0$ or $\mathbb{T}_5 \neq 0$ or $\mathbb{T}_6 \neq 0$, it follows from [58, Theorem 3.12] that $u(t; \mathbb{T})$ is strictly decreasing. This leads to a contradiction. Hence, we have $\mathbb{T}_2 = \mathbb{T}_3 = \mathbb{T}_4 = \mathbb{T}_5 = \mathbb{T}_6 = 0$. By the theory of asymptotically autonomous semiflows in [41], it follows that

$$\lim_{t \rightarrow \infty} \|(S(x, t), I_1(x, t), I_2(x, t), B_1(x, t), B_2(x, t), P(x, t)) - (S^*, 0, 0, 0, 0, 0)\| = 0.$$

Claim 2. $\mathcal{D} = \{F_0\}$.

Since $\{F_0\}$ is globally attractive in ∂Y_1 , $\{F_0\}$ is the unique invariant subset of model (2.1)–(2.3) in ∂Y_1 . In view of the fact that the omega limit set $\omega(c^0)$ is compact invariant and $\omega(c^0) \subset \partial Y_1$, for any $c^0 \in \mathcal{D}$, we get $\omega(c^0) = \{F_0\}$. Since the global attractor $\mathcal{D}$ is compact invariant in H^+ , F_0 is stable, and according to [58, Lemma 3.11], one gets $\mathcal{D} = \{F_0\}$. Combining the global attractivity and local stability, we immediately obtain the globally asymptotical stability of F_0 , completing the proof of Theorem 3.7 (ii).

4.4 Proof of Theorem 3.8

If $\mathcal{R}_0 > 1$, model (2.1) has a phage-free steady state $F_1 = (S^a(x), I_1^a(x), 0, B_1^a(x), B_2^a(x), 0)$. Let $I_2(x, t) = P(x, t) = 0$ in model (2.1), we have

$$\left\{ \begin{array}{l} \frac{\partial S}{\partial t} = d_S \Delta S + \Lambda(x) - \alpha_1(x)f_1(B_1)S - \alpha_2(x)f_2(B_2)S - \mu(x)S, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial I_1}{\partial t} = d_I \Delta I_1 + \alpha_1(x)f_1(B_1)S + \alpha_2(x)f_2(B_2)S - \mu(x)I_1, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial B_1}{\partial t} = h_1(x, B_1) + \eta(x)I_1 - \delta_1(x)B_1, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial B_2}{\partial t} = h_2(x, B_2) + \delta_1(x)B_1 - \delta_2(x)B_2, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial S}{\partial \nu} = \frac{\partial I_1}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t > 0, \\ S(x, 0) = S^0(x), \quad I_1(x, 0) = I_1^0(x), \quad B_1(x, 0) = B_1^0(x), \quad B_2(x, 0) = B_2^0(x), \quad x \in \Omega. \end{array} \right. \quad (4.40)$$

By applying a similar proof as in Theorem 3.1, for model (4.40), we have the following corollary:

Corollary 4.8. Let $\mathbb{E} = C(\bar{\Omega}, \mathbb{R}^4)$ be the Banach space and its positive cone is denoted by $\mathbb{E}^+$.

- (i) For any $c^0(x) = (S^0(x), I_1^0(x), B_1^0(x), B_2^0(x)) \in \mathbb{E}^+$, model (4.40) admits a unique global nonnegative classical solution $\bar{c}(\cdot, t; c^0)$ defined on $\Omega \times [0, \infty)$.
- (ii) Let $\tilde{J}_1(t): \mathbb{E}^+ \rightarrow \mathbb{E}^+$ be the semiflow generated by model (4.40), namely $\tilde{J}_1(t)c^0 = \bar{c}(x, t)$ for $t > 0$. Moreover, $\tilde{J}_1(t)$ is point dissipative.
- (iii) The semiflow $\tilde{J}_1(t)$ of model (4.40) has a connected global attractor in $\mathbb{E}^+$.

Note that model (4.40) has a disease-free steady state $\bar{F}_0 = (S^*(x), 0, 0, 0)$. Linearising model (4.40) at $\bar{F}_0$ yields

$$\begin{cases} \frac{\partial I_1}{\partial t} = d_I \Delta I_1 + \frac{\alpha_1(x) S^* B_1}{H_1} + \frac{\alpha_2(x) S^* B_2}{H_2} - \mu(x) I_1, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_1}{\partial t} = \hat{h}_1(x) B_1 + \eta(x) I_1 - \delta_1(x) B_1, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_2}{\partial t} = \hat{h}_2(x) B_2 + \delta_1(x) B_1 - \delta_2(x) B_2, & x \in \Omega, \quad t > 0, \\ \frac{\partial I_1}{\partial \nu} = 0, & x \in \partial \Omega, \quad t > 0. \end{cases} \quad (4.41)$$

We continue the discussion on the threshold dynamics of model (4.40). The following theorem presents the uniform persistence and the existence of phage-free steady state for model (4.40) when $\mathcal{R}_0 > 1$.

Theorem 4.9. If $\mathcal{R}_0 > 1$, there exists $\bar{\vartheta} > 0$ such that for any $c^0(\cdot) = (S^0, I_1^0, B_1^0, B_2^0)(\cdot) \in \mathbb{E}^+$ with $I_1^0(x) \not\equiv 0$ or $B_1^0(x) \not\equiv 0$ or $B_2^0(x) \not\equiv 0$, the solution $\bar{c}(x, t; c^0) = (S(x, t), I_1(x, t), B_1(x, t), B_2(x, t))$ of model (4.40) satisfies $\lim_{t \rightarrow \infty} \inf \bar{c}(x, t) \geq \bar{\vartheta}$ uniformly for $x \in \bar{\Omega}$. Moreover, model (4.40) has at least one positive steady state.

Before proving Theorem 4.9, we first give some preliminaries. We define

$$\mathbb{E}_0 = \{\varphi \in \mathbb{E}^+ : \varphi_1(\cdot) > 0, \varphi_2(\cdot) \not\equiv 0, \varphi_3(\cdot) \not\equiv 0, \varphi_4(\cdot) \not\equiv 0\},$$

and

$$\partial \mathbb{E}_0 := \mathbb{E}^+ \setminus \mathbb{E}_0 = \{\varphi \in \mathbb{E}^+ : \varphi_2(\cdot) \equiv 0 \text{ or } \varphi_3(\cdot) \equiv 0 \text{ or } \varphi_4(\cdot) \equiv 0\}.$$

Define

$$F_\partial := \{\varphi \in \partial \mathbb{E}_0 : \tilde{J}_1(t)\varphi \in \partial \mathbb{E}_0\},$$

for $t \geq 0$, and $\omega(\varphi)$ be the omega limit set of the orbit $G^+ := \{\tilde{J}_1(t)\varphi : t \geq 0\}$.

Claim 1. $\mathbb{E}_0$ is positively invariant regarding $\tilde{J}_1(t)$, namely $\tilde{J}_1(t)\mathbb{E}_0 \subseteq \mathbb{E}_0$ for all $t \geq 0$.

Let $c^0 \in \mathbb{E}_0$, which implies $I_1^0 \not\equiv 0$ and $B_1^0 \not\equiv 0$ and $B_2^0 \not\equiv 0$. We derive that $\partial I_1 / \partial t \geq d_I \Delta I_1 - \mu(x) I_1$ from model (4.40). Thus, I_1 is an upper solution of the problem

$$\begin{cases} \frac{\partial I_1^*(x, t)}{\partial t} = d_I \Delta I_1^* - \mu(x) I_1^*(x, t), & x \in \Omega, \quad t > 0, \\ \frac{\partial I_1^*(x, t)}{\partial \nu} = 0, & x \in \partial \Omega, \quad t > 0, \\ I_1^*(\cdot, 0) = I_1(\cdot, 0) = I_1^0(\cdot), & x \in \Omega. \end{cases}$$

It follows from the maximum principle and $I_1^0 \not\equiv 0$ that $I_1^*(x, t) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. It holds that $I_1(x, t) \geq I_1^*(x, t) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. Assume that there exist $\tilde{t} > 0$ and $\tilde{x} \in \bar{\Omega}$ such that $B_1(\tilde{x}, \tilde{t}) = 0$,

and from the third equation of model (4.40), along with $(\mathbf{H}_3)$, we derive

$$0 = \frac{\partial B_1(\tilde{x}, \tilde{t})}{\partial t} = \eta(\tilde{x})I_1(\tilde{x}, \tilde{t}).$$

It implies that $\eta(\tilde{x})I_1(\tilde{x}, \tilde{t}) = 0$, which leads to a contradiction. Hence, we get $B_1(x, t) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. From the fourth equation of model (4.40), one gets

$$\frac{\partial B_2}{\partial t} \geq h_2(x, B_2) + \delta_1(x)B_1 - \delta_2(x)B_2, \quad x \in \Omega, \quad t > 0.$$

Similar to [17, Lemma 2.1] and [44, Proposition 3.1], by strong maximum principle [34, Theorem 4] and Hopf boundary theorem [34, Theorem 3], we derive $B_2(x, t) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. Then $\tilde{J}_1(t)c^0 \in \mathbb{E}_0$.

Claim 2. *If $\mathcal{R}_0 > 1$, there exists $\bar{\delta} > 0$ such that the semiflow $\tilde{J}_1(t)$ of model (4.40) satisfies $\lim_{t \rightarrow \infty} \sup \|\tilde{J}_1(t)\varphi - \bar{F}_0\| \geq \bar{\delta}$ for all $\varphi \in \mathbb{E}_0$.*

By way of contradiction, assuming that there exists a $\varphi_0 \in \mathbb{E}_0$ satisfying

$$\lim_{t \rightarrow +\infty} \|\tilde{J}_1(t)\varphi_0 - (S^*(x), 0, 0, 0)\| < \bar{\delta}.$$

Thus, there exists $t^* > 0$ satisfying $S(x, t, \varphi_0) \geq S^*(x) - \bar{\delta}$, $\forall t \geq t^*$. Therefore, $(I_1(x, t, \varphi_0), B_1(x, t, \varphi_0), B_2(x, t, \varphi_0))$ is an upper solution of the following linear model

$$\begin{cases} \frac{\partial \tilde{I}_1}{\partial t} = d_I \Delta \tilde{I}_1 + \frac{\alpha_1(x)(S^* - \bar{\delta})\tilde{B}_1}{H_1 + \bar{\delta}} + \frac{\alpha_2(x)(S^* - \bar{\delta})\tilde{B}_2}{H_2 + \bar{\delta}} - \mu(x)\tilde{I}_1, & x \in \Omega, \quad t \geq t^*, \\ \frac{\partial \tilde{B}_1}{\partial t} = \eta(x)\tilde{I}_1 + \frac{\partial h_1(x, \bar{\delta})}{\partial B_1}\tilde{B}_1 - b_1(x)\bar{\delta}\tilde{B}_1 - \delta_1(x)\tilde{B}_1, & x \in \Omega, \quad t \geq t^*, \\ \frac{\partial \tilde{B}_2}{\partial t} = \delta_1(x)\tilde{B}_1 + \frac{\partial h_2(x, \bar{\delta})}{\partial B_2}\tilde{B}_2 - b_2(x)\bar{\delta}\tilde{B}_2 - \delta_2(x)\tilde{B}_2, & x \in \Omega, \quad t \geq t^*, \\ \frac{\partial \tilde{I}_1}{\partial \nu} = 0, & x \in \partial\Omega, \quad t \geq t^*, \\ \tilde{I}_1(x, t^*) = \varphi_2 \leq I_1(\cdot, t^*), \quad \tilde{B}_1(x, t^*) = \varphi_3 \leq B_1(\cdot, t^*), \quad \tilde{B}_2(x, t^*) = \varphi_4 \leq B_2(\cdot, t^*). \end{cases} \quad (4.42)$$

Denote $\lambda_{\bar{\delta}}^0$ as the principal eigenvalue of the following eigenvalue problem

$$\begin{cases} d_I \Delta \varphi - \mu(x)\varphi + \left(\frac{\alpha_1(x)(S^* - \bar{\delta})\eta(x)}{H_1(\delta_1(x) - \hat{h}_1(x))} + \frac{\alpha_2(x)(S^* - \bar{\delta})\eta(x)\delta_1(x)}{H_2(\delta_1(x) - \hat{h}_1(x))(\delta_2(x) - \hat{h}_2(x))} \right) \varphi = \lambda \varphi, & x \in \Omega, \\ \frac{\partial \varphi}{\partial \nu} = 0, & x \in \partial\Omega. \end{cases} \quad (4.43)$$

Then $\lambda_{\bar{\delta}}^0$ is continuous in $\bar{\delta}$. The following eigenvalue problem

$$\begin{cases} \lambda \varphi_2 = d_I \Delta \varphi_2 + \frac{\alpha_1(x)(S^* - \bar{\delta})}{H_1}\varphi_3 + \frac{\alpha_2(x)(S^* - \bar{\delta})}{H_2}\varphi_4 - \mu(x)\varphi_2, & x \in \Omega, \\ \lambda \varphi_3 = \eta(x)\varphi_2 + \hat{h}_1(x)\varphi_3 - \delta_1(x)\varphi_3, & x \in \Omega, \\ \lambda \varphi_4 = \delta_1(x)\varphi_3 + \hat{h}_2(x)\varphi_4 - \delta_2(x)\varphi_4, & x \in \Omega, \\ \frac{\partial \varphi_2}{\partial \nu} = 0, & x \in \partial\Omega, \end{cases} \quad (4.44)$$

has a principal eigenvalue $\tilde{\lambda}_{\bar{\delta}}^0$ with respect to positive eigenvector $(\varphi_2^{\bar{\delta}}(x), \varphi_3^{\bar{\delta}}(x), \varphi_4^{\bar{\delta}}(x))$. We can choose a small enough $\rho_1 > 0$ such that

$$(I_1(\cdot, t^*; \varphi_0), B_1(\cdot, t^*; \varphi_0), B_2(\cdot, t^*; \varphi_0)) \geq \rho_1 (\varphi_2^{\bar{\delta}}(x), \varphi_3^{\bar{\delta}}(x), \varphi_4^{\bar{\delta}}(x)).$$

Then the linear model (4.42) with initial conditions $(\tilde{I}_1(x, t^*), \tilde{B}_1(x, t^*), \tilde{B}_2(x, t^*)) = \rho_1 (\varphi_2^{\tilde{\delta}}(x), \varphi_3^{\tilde{\delta}}(x), \varphi_4^{\tilde{\delta}}(x))$ has a unique solution

$$(\tilde{I}_1(x, t^*; \varphi_0), \tilde{B}_1(x, t^*; \varphi_0), \tilde{B}_2(x, t^*; \varphi_0)) = \rho_1 e^{\tilde{\lambda}_0^{\tilde{\delta}}(t-t^*)} (\varphi_2^{\tilde{\delta}}(x), \varphi_3^{\tilde{\delta}}(x), \varphi_4^{\tilde{\delta}}(x)).$$

By the comparison principle of quasimonotone model, we have

$$(I_1(x, t^*; \varphi_0), B_1(x, t^*; \varphi_0), B_2(x, t^*; \varphi_0)) \geq (\tilde{I}_1(x, t^*; \varphi_0), \tilde{B}_1(x, t^*; \varphi_0), \tilde{B}_2(x, t^*; \varphi_0)),$$

on $\bar{\Omega} \times [t^*, \infty)$, which implies that $\lim_{t \rightarrow \infty} \|(I_1(\cdot, t; \varphi_0), B_1(\cdot, t; \varphi_0), B_2(\cdot, t; \varphi_0))\| = \infty$, which contradicts the boundedness of $(I_1(\cdot, t), B_1(\cdot, t), B_2(\cdot, t))$ by Corollary 4.8. This establishes Claim 2.

Proof of Theorem 4.9 First, we prove that $\omega(\varphi) = \{\bar{F}_0\}$, $\varphi \in F_{\bar{\theta}}$. For any $\varphi \in F_{\bar{\theta}}$, we have $\tilde{J}_1(t)\varphi \in F_{\bar{\theta}}$, $t \geq 0$. Then, $I_1(\cdot, t) \equiv 0$ or $B_1(\cdot, t) \equiv 0$ or $B_2(\cdot, t) \equiv 0$ for $t \geq 0$. In the case that $I_1(\cdot, t) \equiv 0$, we can derive that $B_1(\cdot, t) \equiv 0$ and $B_2(\cdot, t) \equiv 0$ from the second equation of model (4.40). Therefore, $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$. In the case that $B_1(\cdot, t) \equiv 0$, we can derive that $I_1(\cdot, t) \equiv 0$ from the third equation of model (4.40), then $B_2(\cdot, t) \equiv 0$ and $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$. In the case that $B_2(\cdot, t) \equiv 0$, we can derive that $B_1(\cdot, t) \equiv 0$ from the fourth equation of model (4.40), then $I_1(\cdot, t) \equiv 0$ and $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$. This shows $\omega(\varphi) = \{\bar{F}_0\}$. $\square$

Define a continuous function

$$\tau(\varphi) = \min \left\{ \min_{x \in \bar{\Omega}} \varphi_2(x), \min_{x \in \bar{\Omega}} \varphi_3(x), \min_{x \in \bar{\Omega}} \varphi_4(x) \right\}, \quad \varphi \in \mathbb{E}^+.$$

Apparently, $\tau^{-1}(0, \infty) \subseteq \mathbb{E}_0$. The function τ is a generalised distance function for the semiflow $\tilde{J}_1(t)$. In view of Claim 1 and Claim 2, we know that the singleton $\{\bar{F}_0\}$ is an isolated invariant set for $\tilde{J}_1(t)$ in $\mathbb{E}^+$, then $W^s(\{\bar{F}_0\}) \cap \mathbb{E}_0 = \emptyset$, where $W^s(\{\bar{F}_0\})$ represents the stable subset of $\{\bar{F}_0\}$. Besides, no subset of $\{\bar{F}_0\}$ forms a cycle in $\partial \mathbb{E}_0$. By [40, Theorem 3], there exists a $\vartheta_1 > 0$ satisfying $\lim_{t \rightarrow \infty} \inf \tau(\tilde{J}_1(t)\varphi) \geq \vartheta_1$, $\forall \varphi \in \mathbb{E}_0$. Moreover, from Corollary 4.8, there exists $\tilde{t}_1 > 0$ satisfying that $B_1(\cdot, t) \leq \hat{M}_\infty$, $B_2(\cdot, t) \leq \hat{M}_\infty$ for $x \in \Omega$ and $t \geq \tilde{t}_1$. Then, we get

$$\frac{\partial S}{\partial t} \geq d_s \Delta S + \Lambda_m - ((\alpha_1 + \alpha_2)\hat{M}_\infty + \mu^m)S, \quad x \in \Omega, \quad t > \tilde{t}_1.$$

Thus, we have $\lim_{t \rightarrow \infty} \inf S(x, t; \varphi) > \vartheta_2 := \Lambda_m / ((\alpha_1 + \alpha_2)\hat{M}_\infty + \mu^m)$. Let $\bar{\vartheta} = \min\{\vartheta_1, \vartheta_2\}$. This establishes the uniform persistence. It follows from [26, Theorem 4.7] that model (4.40) admits at least one steady state in $\mathbb{E}_0$, which is positive. This establishes Theorem 4.9.

Based on above theorem and [60, Theorem 1.3.6]. This establishes Theorem 3.8.

4.5 Proof of Theorem 3.10

We choose the Lyapunov function

$$\begin{aligned} L_1(t) = & \int_{\Omega} \tilde{S}^a Y \left(\frac{S}{\tilde{S}^a} \right) dx + \int_{\Omega} \tilde{I}_1^a Y \left(\frac{I_1}{\tilde{I}_1^a} \right) dx + \int_{\Omega} I_2 dx + l_1 \int_{\Omega} \tilde{B}_1^a Y \left(\frac{B_1}{\tilde{B}_1^a} \right) dx \\ & + l_2 \int_{\Omega} \tilde{B}_2^a Y \left(\frac{B_2}{\tilde{B}_2^a} \right) dx + l_3 \int_{\Omega} P dx, \end{aligned}$$

where the constants $l_1 > 0, l_2 > 0, l_3 > 0$ are to be determined, and $Y(x) = x - 1 - \ln x (x > 0)$. By calculating the derivative of $L_1(t)$, one gets

$$\begin{aligned} \frac{dL_1(t)}{dt} = & \int_{\Omega} \left(1 - \frac{\tilde{S}^a}{S} \right) \left(d_s \Delta S + \Lambda - \frac{\alpha_1 B_1 S}{B_1 + H_1} - \frac{\alpha_2 B_2 S}{B_2 + H_2} - \mu S \right) dx \\ & + \int_{\Omega} \left(1 - \frac{\tilde{I}_1^a}{I_1} \right) \left(d_I \Delta I_1 + \frac{\alpha_1 L B_1 S}{(L + P)(B_1 + H_1)} + \frac{\alpha_2 L B_2 S}{(L + P)(B_2 + H_2)} - \mu I_1 \right) dx \end{aligned}$$

$$\begin{aligned}
 & + \int_{\Omega} \left(d_l \Delta I_2 + \frac{\alpha_1 P B_1 S}{(L+P)(B_1+H_1)} + \frac{\alpha_2 P B_2 S}{(L+P)(B_2+H_2)} - \mu I_2 \right) dx \\
 & + l_1 \int_{\Omega} \left(1 - \frac{\tilde{B}_1^a}{B_1} \right) (h_1(B_1) + \eta(I_1 + I_2) - b_1 B_1 P - \delta_1 B_1) dx \\
 & + l_2 \int_{\Omega} \left(1 - \frac{\tilde{B}_2^a}{B_2} \right) (h_2(B_2) + \delta_1 B_1 - \delta_2 B_2) dx \\
 & + l_3 \int_{\Omega} (\alpha \eta I_2 + \chi_1 b_1 B_1 P - mP) dx.
 \end{aligned}$$

Since $\tilde{F}_1 = (\tilde{S}^a, \tilde{I}_1^a, 0, \tilde{B}_1^a, \tilde{B}_2^a, 0)$ is the phage-free steady state of model (2.4), we derive

$$\begin{aligned}
 \frac{dL_1(t)}{dt} & \leq -d_s \int_{\Omega} \tilde{S}^a \frac{|\nabla S|^2}{S^2} dx - d_l \int_{\Omega} \tilde{I}_1^a \frac{|\nabla I_1|^2}{I_1^2} dx + d_l \int_{\Omega} \Delta I_2 dx - \int_{\Omega} \mu S \left(1 - \frac{\tilde{S}^a}{S} \right)^2 dx \\
 & + \int_{\Omega} (l_3 \alpha \eta - \mu) I_2 dx + \int_{\Omega} l_1 \eta \tilde{I}_1^a \left(1 - \frac{B_1}{\tilde{B}_1^a} + \frac{I_1}{\tilde{I}_1^a} - \frac{I_1 \tilde{B}_1^a}{\tilde{I}_1^a B_1} \right) dx + \int_{\Omega} l_2 \delta_1 \tilde{B}_1^a \left(1 - \frac{B_2}{\tilde{B}_2^a} + \frac{B_1}{\tilde{B}_1^a} - \frac{B_1 \tilde{B}_2^a}{\tilde{B}_1^a B_2} \right) dx \\
 & + \int_{\Omega} l_1 (B_1 - \tilde{B}_1^a) \left(\frac{h_1(B_1)}{B_1} - \frac{h_1(\tilde{B}_1^a)}{\tilde{B}_1^a} \right) dx + \int_{\Omega} l_2 (B_2 - \tilde{B}_2^a) \left(\frac{h_2(B_2)}{B_2} - \frac{h_2(\tilde{B}_2^a)}{\tilde{B}_2^a} \right) dx \\
 & + \int_{\Omega} \frac{\alpha_1 \tilde{S}^a \tilde{B}_1^a}{H_1 + \tilde{B}_1^a} \left[2 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} + \frac{B_1/(H_1 + B_1)}{\tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} - \frac{\tilde{S} \tilde{I}_1^a B_1/(H_1 + B_1)}{\tilde{S}^a \tilde{I}_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} \right] dx \\
 & + \int_{\Omega} \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{H_2 + \tilde{B}_2^a} \left[2 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} + \frac{B_2/(H_2 + B_2)}{\tilde{B}_2^a/(H_2 + \tilde{B}_2^a)} - \frac{\tilde{S} \tilde{I}_1^a B_2/(H_2 + B_2)}{\tilde{S}^a \tilde{I}_1 \tilde{B}_2^a/(H_2 + \tilde{B}_2^a)} \right] dx \\
 & + \int_{\Omega} \left[b_1 \tilde{B}_1^a P \left(-\frac{l_1 B_1}{\tilde{B}_1^a} + l_1 + \frac{l_3 \chi_1 B_1}{\tilde{B}_1^a} \right) - l_3 m P \right] dx.
 \end{aligned}$$

After a simple calculation, we have

$$\begin{aligned}
 1 - \frac{B_1}{\tilde{B}_1^a} + \frac{I_1}{\tilde{I}_1^a} - \frac{I_1 \tilde{B}_1^a}{\tilde{I}_1^a B_1} & \leq \left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right) - \left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right), \\
 1 - \frac{B_2}{\tilde{B}_2^a} + \frac{B_1}{\tilde{B}_1^a} - \frac{B_1 \tilde{B}_2^a}{\tilde{B}_1^a B_2} & \leq \left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) - \left(\frac{B_2}{\tilde{B}_2^a} - \ln \frac{B_2}{\tilde{B}_2^a} \right).
 \end{aligned}$$

By (H_3) , one gets

$$(B_1 - \tilde{B}_1^a) \left(\frac{h_1(B_1)}{B_1} - \frac{h_1(\tilde{B}_1^a)}{\tilde{B}_1^a} \right) \leq 0, \quad (B_2 - \tilde{B}_2^a) \left(\frac{h_2(B_2)}{B_2} - \frac{h_2(\tilde{B}_2^a)}{\tilde{B}_2^a} \right) \leq 0.$$

Since $1 - x \leq -\ln x$ for $x > 0$, we have

$$\begin{aligned}
 & 2 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} + \frac{B_1/(H_1 + B_1)}{\tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} - \frac{\tilde{S} \tilde{I}_1^a B_1/(H_1 + B_1)}{\tilde{S}^a \tilde{I}_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} \\
 & = \left(2 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} - \frac{\tilde{S} \tilde{I}_1^a B_1/(H_1 + B_1)}{\tilde{S}^a \tilde{I}_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} + 1 - \frac{B_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)}{\tilde{B}_1^a B_1/(H_1 + B_1)} + \frac{B_1}{\tilde{B}_1^a} \right) - \frac{H_1 (B_1 - \tilde{B}_1^a)^2}{\tilde{B}_1^a (H_1 + \tilde{B}_1^a) (H_1 + B_1)} \\
 & \leq 3 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} - \frac{\tilde{S} \tilde{I}_1^a B_1/(H_1 + B_1)}{\tilde{S}^a \tilde{I}_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)} - \frac{B_1 \tilde{B}_1^a/(H_1 + \tilde{B}_1^a)}{\tilde{B}_1^a B_1/(H_1 + B_1)} + \frac{B_1}{\tilde{B}_1^a}
 \end{aligned}$$

$$\begin{aligned}
&= \left(\frac{B_1}{\tilde{B}_1^a} - \frac{I_1}{\tilde{I}_1^a} \right) + \left(1 - \frac{\tilde{S}^a}{S} \right) + \left(1 - \frac{\tilde{S}^a B_1 / (H_1 + B_1)}{\tilde{S}^a I_1 \tilde{B}_1^a / (H_1 + \tilde{B}_1^a)} \right) + \left(1 - \frac{B_1 \tilde{B}_1^a / (H_1 + \tilde{B}_1^a)}{\tilde{B}_1^a B_1 / (H_1 + B_1)} \right) \\
&\leq \left(\frac{B_1}{\tilde{B}_1^a} - \frac{I_1}{\tilde{I}_1^a} \right) - \ln \frac{\tilde{S}^a}{S} - \ln \frac{\tilde{S}^a B_1 / (H_1 + B_1)}{\tilde{S}^a I_1 \tilde{B}_1^a / (H_1 + \tilde{B}_1^a)} - \ln \frac{B_1 \tilde{B}_1^a / (H_1 + \tilde{B}_1^a)}{\tilde{B}_1^a B_1 / (H_1 + B_1)} \\
&= \left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) - \left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right).
\end{aligned}$$

Similarly, we also have

$$2 - \frac{\tilde{S}^a}{S} - \frac{I_1}{\tilde{I}_1^a} + \frac{B_2 / (H_2 + B_2)}{\tilde{B}_2^a / (H_2 + \tilde{B}_2^a)} - \frac{\tilde{S}^a B_2 / (H_2 + B_2)}{\tilde{S}^a I_1 \tilde{B}_2^a / (H_2 + \tilde{B}_2^a)} \leq \left(\frac{B_2}{\tilde{B}_2^a} - \ln \frac{B_2}{\tilde{B}_2^a} \right) - \left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right).$$

Let $l_1 = \left(\frac{\alpha_1 \tilde{S}^a \tilde{B}_1^a}{\eta \tilde{I}_1^a (H_1 + \tilde{B}_1^a)} + \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{\eta \tilde{I}_1^a (H_2 + \tilde{B}_2^a)} \right)$, $l_2 = \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{\delta_1 \tilde{B}_1^a (H_2 + \tilde{B}_2^a)}$, $l_3 = \frac{l_1}{\chi_1}$, we derive

$$\begin{aligned}
\frac{dL_1(t)}{dt} &\leq -d_s \int_{\Omega} \tilde{S}^a \frac{|\nabla S|^2}{S^2} dx - d_i \int_{\Omega} \tilde{I}_1^a \frac{|\nabla I_1|^2}{I_1^2} dx - \int_{\Omega} \mu S \left(1 - \frac{\tilde{S}^a}{S} \right)^2 dx + \int_{\Omega} (l_3 \alpha \eta - \mu) I_2 dx \\
&+ \int_{\Omega} \frac{\alpha_1 \tilde{S}^a \tilde{B}_1^a}{H_1 + \tilde{B}_1^a} \left[\left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right) - \left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) \right] dx + \int_{\Omega} \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{H_2 + \tilde{B}_2^a} \left[\left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right) - \left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) \right] dx \\
&+ \int_{\Omega} \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{H_2 + \tilde{B}_2^a} \left[\left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) - \left(\frac{B_2}{\tilde{B}_2^a} - \ln \frac{B_2}{\tilde{B}_2^a} \right) \right] dx + \int_{\Omega} \frac{\alpha_1 \tilde{S}^a \tilde{B}_1^a}{H_1 + \tilde{B}_1^a} \left[\left(\frac{B_1}{\tilde{B}_1^a} - \ln \frac{B_1}{\tilde{B}_1^a} \right) - \left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right) \right] dx \\
&+ \int_{\Omega} \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{H_2 + \tilde{B}_2^a} \left[\left(\frac{B_2}{\tilde{B}_2^a} - \ln \frac{B_2}{\tilde{B}_2^a} \right) - \left(\frac{I_1}{\tilde{I}_1^a} - \ln \frac{I_1}{\tilde{I}_1^a} \right) \right] dx + \int_{\Omega} l_1 P \left(b_1 \tilde{B}_1^a - \frac{m}{\chi_1} \right) dx \\
&\leq - \int_{\Omega} \mu S \left(1 - \frac{\tilde{S}^a}{S} \right)^2 dx + \int_{\Omega} (l_3 \alpha \eta - \mu) I_2 dx + \int_{\Omega} l_1 P \left(b_1 \tilde{B}_1^a - \frac{m}{\chi_1} \right) dx.
\end{aligned}$$

Hence, based on $l_1 \leq \mu \chi_1 / \alpha \eta$ and $\tilde{B}_1^a \leq m / \chi_1 b_1 = \tilde{B}_1^b$, we have $dL_1(t)/dt \leq 0$. Moreover, $dL_1(t)/dt = 0$ if and only if $S = \tilde{S}^a$, $I_1 = \tilde{I}_1^a$, $I_2 = 0$, $B_1 = \tilde{B}_1^a$, $B_2 = \tilde{B}_2^a$, $P = 0$. The largest invariant set of $\{(S, I_1, I_2, B_1, B_2, P) | \frac{dL_1(t)}{dt} = 0\}$ is the singleton $\{\tilde{F}_1\}$. Then, from LaSalle invariant principle [12, 15], $\tilde{F}_1$ is globally asymptotically stable.

4.6 Proof of Theorem 3.11

Before proving Theorem 3.11, we first give some preliminaries.

We define

$$\mathbb{H}_0 = \{\varphi \in H^+ : \varphi_1(\cdot) > 0, \varphi_2(\cdot) \neq 0, \varphi_3(\cdot) \neq 0, \varphi_4(\cdot) \neq 0, \varphi_5(\cdot) \neq 0, \varphi_6(\cdot) \neq 0\},$$

and

$$\partial \mathbb{H}_0 := H^+ \setminus \mathbb{H}_0 = \{\varphi \in H^+ : \varphi_2(\cdot) \equiv 0 \text{ or } \varphi_3(\cdot) \equiv 0 \text{ or } \varphi_4(\cdot) \equiv 0 \text{ or } \varphi_5(\cdot) \equiv 0 \text{ or } \varphi_6(\cdot) \equiv 0\}.$$

Define $\tilde{F}_\partial := \{\varphi \in \partial \mathbb{H}_0 : \tilde{J}_1(t)\varphi \in \partial \mathbb{H}_0\}$, for $t \geq 0$, and $\tilde{\omega}(\varphi)$ be the omega limit set of the orbit $\tilde{G}^+ := \{\tilde{J}_1(t)\varphi : t \geq 0\}$. Similar to the proof of Theorem 4.9, $\mathbb{H}_0$ is the positive invariant set for solution semiflow $\tilde{J}_1(t)$ of model (2.4), and we have the following claim.

Claim 1. If $\tilde{\mathcal{R}}_0 > 1$, there exists $\tilde{\delta} > 0$ such that the semiflow $\tilde{J}_1(t)$ of model (2.4) satisfies $\lim_{t \rightarrow \infty} \sup \|\tilde{J}_1(t)\varphi - \tilde{F}_0\| \geq \tilde{\delta}$ for all $\varphi \in \mathbb{H}_0$.

Claim 2. If $\tilde{\mathcal{R}}_0 > 1$, and $\tilde{B}_1^a > \tilde{B}_1^b$ holds, there exists $\hat{\delta} > 0$ such that the semiflow $\bar{J}_1(t)$ of model (2.4) satisfies $\lim_{t \rightarrow \infty} \sup \|\bar{J}_1(t)\varphi - \tilde{F}_1\| \geq \hat{\delta}$ for all $\varphi \in \mathbb{H}_0$.

Based on $\tilde{B}_1^a > \tilde{B}_1^b$, we can choose a sufficiently small $\hat{\delta} > 0$ such that

$$\chi_1 b_1(\tilde{B}_1^a - \hat{\delta}) - m > \chi_1 b_1 \tilde{B}_1^b - m = 0. \quad (4.45)$$

By way of contradiction, assuming that there exists a $\varphi_0 \in \mathbb{H}_0$ satisfying $\limsup_{t \rightarrow \infty} \|\bar{J}_1(t)\varphi_0 - \tilde{F}_1\| < \hat{\delta}$. This implies that there exists a $\tilde{t}_2 > 0$ satisfying $\tilde{B}_1^a - \hat{\delta} < B_1(x, t; \varphi_0)$. Hence, we have

$$\frac{\partial P}{\partial t} \geq \chi_1 b_1(\tilde{B}_1^a - \hat{\delta})P - mP, \quad x \in \Omega, \quad t > \tilde{t}_2.$$

Since $\varphi_0 \in \mathbb{H}_0$, and the results mentioned above, it follows that $P(x, t) > 0$ for $x \in \bar{\Omega}$ and $t > 0$. This implies that there is a constant $p_1 > 0$ such that $P(x, t; \varphi_0) \geq p_1 P^0(x)$. By applying the standard comparison principle, one gets

$$P(x, t) \geq p_1 P^0(x) e^{(\chi_1 b_1(\tilde{B}_1^a - \hat{\delta}) - m)(t - \tilde{t}_2)}, \quad x \in \Omega, \quad t > \tilde{t}_2.$$

From (4.45), we obtain $\lim_{t \rightarrow \infty} P(x, t) = \infty$, which contradicts the boundedness of $P(x, t)$. This establishes Claim 2.

Proof of Theorem 3.11 First, we prove that $\tilde{\omega}(\varphi) = \{\tilde{F}_0\} \cup \{\tilde{F}_1\}$, $\varphi \in \tilde{F}_\partial$. For any $\varphi \in \tilde{F}_\partial$, we have $\bar{J}_1(t)\varphi \in \tilde{F}_\partial$, $t \geq 0$. Thus, $I_1(\cdot, t) \equiv 0$ or $I_2(\cdot, t) \equiv 0$ or $B_1(\cdot, t) \equiv 0$ or $B_2(\cdot, t) \equiv 0$ or $P(\cdot, t) \equiv 0$ for $t \geq 0$. In the case that $I_1(\cdot, t) \equiv 0$, we can derive that $B_1(\cdot, t) \equiv 0$, $B_2(\cdot, t) \equiv 0$ from the second equation of model (2.4). Then we have $I_2(\cdot, t) \equiv 0$ from the fourth equation of model (2.4). Besides, we obtain $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$, then from the sixth equation of model (2.4), one gets $\lim_{t \rightarrow \infty} P(\cdot, t) = 0$. This shows $\tilde{\omega}(\varphi) = \{\tilde{F}_0\}$. In the case that $B_1(\cdot, t) \equiv 0$, we can derive that $I_1(\cdot, t) \equiv 0$, $I_2(\cdot, t) \equiv 0$. Similarly, we also have $B_2(\cdot, t) \equiv 0$, $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$ and $\lim_{t \rightarrow \infty} P(\cdot, t) = 0$. This shows $\tilde{\omega}(\varphi) = \{\tilde{F}_0\}$. In the case that $B_2(\cdot, t) \equiv 0$, we can derive that $B_1(\cdot, t) \equiv 0$ from the fifth equation of model (2.4). Then we have $I_1(\cdot, t) \equiv 0$, $I_2(\cdot, t) \equiv 0$ and $S(\cdot, t) \rightarrow S^*(x)$ uniformly for $x \in \bar{\Omega}$ and $\lim_{t \rightarrow \infty} P(\cdot, t) = 0$. This also shows $\tilde{\omega}(\varphi) = \{\tilde{F}_0\}$. In the case that $P(\cdot, t) \equiv 0$, it implies that $I_2(\cdot, t) \equiv 0$. Conversely, if $I_2(\cdot, t) \equiv 0$, then we also have $P(\cdot, t) \equiv 0$. Thus, model (2.4) becomes

$$\begin{cases} \frac{\partial S}{\partial t} = d_S \Delta S + \Lambda - \alpha_1 f_1(B_1)S - \alpha_2 f_2(B_2)S - \mu S, & x \in \Omega, \quad t > 0, \\ \frac{\partial I_1}{\partial t} = d_I \Delta I_1 + \alpha_1 f_1(B_1)S + \alpha_2 f_2(B_2)S - \mu I_1, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_1}{\partial t} = h_1(B_1) + \eta I_1 - \delta_1 B_1, & x \in \Omega, \quad t > 0, \\ \frac{\partial B_2}{\partial t} = h_2(B_2) + \delta_1 B_1 - \delta_2 B_2, & x \in \Omega, \quad t > 0, \\ \frac{\partial S}{\partial v} = \frac{\partial I_1}{\partial v} = 0, & x \in \partial\Omega, \quad t > 0, \\ S(x, 0) = S^0(x), \quad I_1(x, 0) = I_1^0(x), \quad B_1(x, 0) = B_1^0(x), \quad B_2(x, 0) = B_2^0(x), & x \in \Omega. \end{cases} \quad (4.46)$$

If $\tilde{\mathcal{R}}_0 > 1$, model (4.46) has a positive steady state $\tilde{F}_1 = (\tilde{S}^a, \tilde{I}_1^a, \tilde{B}_1^a, \tilde{B}_2^a)$. We choose the Lyapunov function

$$\begin{aligned} L_2(t) = & \int_{\Omega} \tilde{S}^a Y \left(\frac{S}{\tilde{S}^a} \right) dx + \int_{\Omega} \tilde{I}_1^a Y \left(\frac{I_1}{\tilde{I}_1^a} \right) dx + \left(\frac{\alpha_1 \tilde{S}^a \tilde{B}_1^a}{\eta \tilde{I}_1^a (H_1 + \tilde{B}_1^a)} + \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{\eta \tilde{I}_1^a (H_2 + \tilde{B}_2^a)} \right) \int_{\Omega} \tilde{B}_1^a Y \left(\frac{B_1}{\tilde{B}_1^a} \right) dx \\ & + \frac{\alpha_2 \tilde{S}^a \tilde{B}_2^a}{\delta_1 \tilde{B}_1^a (H_2 + \tilde{B}_2^a)} \int_{\Omega} \tilde{B}_2^a Y \left(\frac{B_2}{\tilde{B}_2^a} \right) dx. \end{aligned}$$

By applying the similar proof in Theorem 3.10, we have

$$\frac{dL_2(t)}{dt} \leq -d_s \int_{\Omega} \tilde{S}^a \frac{|\nabla S|^2}{S^2} dx - d_i \int_{\Omega} \tilde{I}_1^a \frac{|\nabla I_1|^2}{I_1^2} dx - \int_{\Omega} \mu S \left(1 - \frac{\tilde{S}^a}{S}\right)^2 dx.$$

Apparently, we can obtain $dL_2(t)/dt \leq 0$. Moreover, $dL_2(t)/dt = 0$ if and only if $S = \tilde{S}^a$, $I_1 = \tilde{I}_1^a$, $B_1 = \tilde{B}_1^a$, $B_2 = \tilde{B}_2^a$. The largest invariant set of $\{(S, I_1, B_1, B_2) | \frac{dL_2(t)}{dt} = 0\}$ is the singleton $\{\tilde{F}_1\}$. Then, from LaSalle invariant principle [12], $\tilde{F}_1$ is globally asymptotically stable. Hence, we have $\lim_{t \rightarrow \infty} (S(x, t), I_1(x, t), B_1(x, t), B_2(x, t)) = (\tilde{S}^a, \tilde{I}_1^a, \tilde{B}_1^a, \tilde{B}_2^a)$. This also shows $\tilde{\omega}(\varphi) = \{\tilde{F}_1\}$. We conclude that $\tilde{\omega}(\varphi) = \{\tilde{F}_0\} \cup \{\tilde{F}_1\}$ for any $\varphi \in \tilde{F}_a$. Define a continuous function

$$\tilde{\tau}(\varphi) = \min \left\{ \min_{x \in \Omega} \varphi_2(x), \min_{x \in \Omega} \varphi_3(x), \min_{x \in \Omega} \varphi_4(x), \min_{x \in \Omega} \varphi_5(x), \min_{x \in \Omega} \varphi_6(x) \right\}, \quad \varphi \in H^+.$$

Apparently, $\tilde{\tau}^{-1}(0, \infty) \subseteq \mathbb{H}_0$. The function $\tilde{\tau}$ is a generalised distance function for the semiflow $\tilde{J}_1(t)$. By the above discussions, we know that the singleton $\tilde{\omega}(\varphi) = \{\tilde{F}_0\} \cup \{\tilde{F}_1\}$ is an isolated invariant set for $\tilde{J}_1(t)$ in H^+ , then $W^s(\{\tilde{F}_0\}) \cap \mathbb{H}_0 = \emptyset$, $W^s(\{\tilde{F}_1\}) \cap \mathbb{H}_0 = \emptyset$, where $W^s(\{\tilde{F}_0\})$ and $W^s(\{\tilde{F}_1\})$ represent the stable subset of $\{\tilde{F}_0\}$ and $\{\tilde{F}_1\}$, respectively. Besides, no subset of $\{\tilde{F}_0\} \cup \{\tilde{F}_1\}$ forms a cycle in $\partial \mathbb{H}_0$. By [40, Theorem 3], there exists a $\tilde{\vartheta}_1 > 0$ satisfying $\lim_{t \rightarrow +\infty} \inf \tilde{\tau}(\tilde{J}_1(t)\varphi) \geq \tilde{\vartheta}_1$, $\forall \varphi \in \mathbb{H}_0$. Recall that ϑ_2 in proof of Theorem 4.9. Let $\tilde{\vartheta} = \min\{\tilde{\vartheta}_1, \vartheta_2\}$. The proof is complete. $\square$

5 Concluding remarks

Cholera is a waterborne infectious disease that can easily lead to large-scale outbreaks in areas with poor sanitation, causing persistent distress and threats. Consequently, researchers actively seek methods and measures to control cholera outbreaks. Jensen et al. discovered that under biologically plausible conditions, bacteriophages can mitigate cholera epidemics [19]. This is attributed to the cholera-specific lytic bacteriophages potentially reducing cholera prevalence by eliminating bacteria present in reservoirs and infected human hosts. Additionally, recent research findings in [14] indicated that *V. cholerae* exhibits a hyperinfectious state upon entering the gastrointestinal tract, diminishing to a lower-infectious state within hours. The different infectivity states of cholera vibrio influence the transmission dynamics of cholera outbreaks differently.

This paper incorporated the interaction between bacteriophages and HI vibrios and LI vibrios, as well as the intrinsic growth rate of *V. cholerae*, and proposed a degenerate reaction-diffusion cholera model. We divided the infected human hosts into two parts for study: one part consists of human hosts infected only with *V. cholerae*, denoted as I_1 , while the other part consists of human hosts that are simultaneously infected with *V. cholerae* and bacteriophages, indicating the parasitism of bacteriophages within the host cells (bacteria), denoted as I_2 . We also introduce the interaction between HI vibrios and LI vibrios and bacteriophages in this process.

In this work, we originally established the existence and uniform boundedness of the solution, and then derived the well-posedness of the solutions. In a spatially heterogeneous case, the basic reproduction number $\mathcal{R}_0$ is defined as the spectral radius of the sum of two linear operators associated with HI vibrios infection and LI vibrios infection. Generally speaking, it is very challenging to discuss the threshold-type results in the case of multi-class steady states. Fortunately, in this paper, we derived the existence and stability analysis of multi-class steady states for some special cases. We showed the existence of phage-free steady state in a heterogeneous environment. An appropriate Lyapunov function was constructed to discuss the global stability of the phage-free steady state in a homogeneous environment.

In considering the constraints established by our mathematical model, which mandates that disease transmission occurs through the consumption of bacteria rather than through human-to-human contact, there is potential for future research to explore the incorporation of direct interpersonal transmission pathways to enhance this approach. Furthermore, the examination of global stability of the phage-free steady state in a homogeneous environment requires two additional conditions. Future studies could seek

to investigate the global stability of the phage-free steady state independently of additional conditions. The global stability of the phage-present steady state of model (2.4) also poses some challenges [54]. Moreover, the existence and uniform persistence of the phage-present steady state of model (2.1) are difficult to obtain due to the spatial heterogeneity and other mathematical difficulties. The situation in a heterogeneous environment presents several interesting open problems. We consider these challenges for further investigation.

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