

## GLOBAL WELL-POSEDNESS AND ASYMPTOTIC BEHAVIOR OF SOLUTIONS TO A REACTION-CONVECTION-DIFFUSION CHOLERA EPIDEMIC MODEL

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**ABSTRACT.** In this paper, we study the initial boundary value problem of a reaction-convection-diffusion epidemic model for cholera dynamics, which was developed in [38], named susceptible-infected-recovered-susceptible-bacteria (SIRS-B) epidemic PDE model. First, a local well-posedness result relying on the theory of cooperative dynamics systems is obtained. Via *a priori* estimates making use of the special structure of the system and continuation of local theory argument, we show that in fact this problem is globally well-posed. Secondly, we analyze the local asymptotic stability of the solutions based on the basic reproduction number associated with this model.

**1. Introduction.** Cholera is an infectious disease caused by the bacterium *Vibrio cholerae*. It can be transmitted through indirect environment-to-person contact (i.e., via ingesting food or water contaminated by cholera) or direct person-to-person contact. This bacterium produces an enterotoxin that can quickly lead to a watery diarrhea and severe dehydration, and it can kill infected persons within hours if left untreated. Although simple treatments like oral rehydration salts or intravenous fluids are extremely effective, globally cholera cases have increased steadily since 2005 [40] and this disease is still present in Africa, Southeast Asia, Haiti and central Mexico. Recent severe cholera outbreaks took place in South Sudan (2014) [41], Haiti (2010-2012) [1], Zimbabwe (2008-2009) [19], Angola (2006) [29], South Africa (2000-2001) [23], which have caused a large number of reported cases. For example, as far as the Haiti cholera outbreak is concerned, there were 734,134 reported cases and 8,896 deaths as of February 28, 2015. These cholera outbreaks with increasing frequency and severity have highlighted inadequacy of our knowledge and practical controls of cholera epidemics.

Mathematical modeling of cholera plays an important role toward designing effective strategies for the prevention and control of the disease; representative work can be found, for example, in [1, 2, 4, 5, 6, 13, 17, 21, 27, 28, 30, 31, 32, 36]. The influence of the movement of both humans [8] and water [26] on the spatial spread of cholera have been investigated in [4, 10, 24, 28, 37, 38]. Particularly,

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Bertuzzo et al. [4, 28] proposed simple partial differential equation (PDE) models to study cholera spatial epidemic spreading along a theoretical river as an extension of Codeço's ordinary differential equation (ODE) framework [6], where only indirect (or, environment-to-human) transmission route was considered. Wang et al. [37, 38] developed generalized susceptible-infected-recovered-susceptible-bacteria (SIRS-B) epidemic PDE models that account for the spatial movement of the pathogen and human hosts while incorporating general incidence functions and intrinsic bacterial dynamics.

However, there is no work, as far as we are aware of, that has been devoted to well-posedness and asymptotic behavior of the solutions of these developed PDE models. To fill in this gap, we consider the generalized diffusion-convection-reaction cholera epidemic model introduced in [38], which we refer to as SIRS-B epidemic PDE model. In this work, we study global well-posedness and asymptotic behavior of the solutions of this PDE model. Our analytical result shows local threshold-type dynamics based on the basic reproduction number  $\mathcal{R}_0$ .

The rest of the paper is organized as follows. The main results for the well-posedness and asymptotic behavior of the solutions associated with the SIRS-B epidemic PDE model are summarized in the next section. Notations, definitions and preliminaries are provided in Section 3. Proof of the main results are presented in Sections 4-6. Finally, concluding remark and some discussion are made in Section 7.

**2. Statement of main results.** We study the following SIRS-B epidemic PDE model for cholera dynamics with  $x \in [0, 1], t \geq 0$ :

$$\frac{\partial S}{\partial t} = D_1 \frac{\partial^2 S}{\partial x^2} + b - Sf_1(I) - Sf_2(B) - dS + \sigma R, \quad (1a)$$

$$\frac{\partial I}{\partial t} = D_2 \frac{\partial^2 I}{\partial x^2} + Sf_1(I) + Sf_2(B) - I(d + \gamma), \quad (1b)$$

$$\frac{\partial R}{\partial t} = D_3 \frac{\partial^2 R}{\partial x^2} + \gamma I - R(d + \sigma), \quad (1c)$$

$$\frac{\partial B}{\partial t} = D_4 \frac{\partial^2 B}{\partial x^2} - U \frac{\partial B}{\partial x} + \xi I + h(B) - \delta B, \quad (1d)$$

(cf. [38]) subjected to the following initial and Neumann and Robin boundary conditions respectively:

$$S(x, 0) = \phi_1(x) \geq 0, \quad (2a)$$

$$I(x, 0) = \phi_2(x) \geq 0, \quad (2b)$$

$$R(x, 0) = \phi_3(x) \geq 0, \quad (2c)$$

$$B(x, 0) = \phi_4(x) \geq 0, \quad (2d)$$

where each  $\phi_i (i = 1, 2, 3, 4)$  is assumed to be continuous in space  $x$ , and

$$\frac{\partial S}{\partial x}(x, t)|_{x=0,1} = 0, \quad (3a)$$

$$\frac{\partial I}{\partial x}(x, t)|_{x=0,1} = 0, \quad (3b)$$

$$\frac{\partial R}{\partial x}(x, t)|_{x=0,1} = 0, \quad (3c)$$

$$D_4 \frac{\partial B}{\partial x}(x, t) - UB(x, t)|_{x=0} = \frac{\partial B}{\partial x}(x, t)|_{x=1} = 0. \quad (4a)$$

The functions are denoted as follows:

1.  $S$ , the number of susceptible hosts,
2.  $I$ , the number of infectious hosts,
3.  $R$ , the number of recovered hosts,
4.  $B$ , the concentration of the bacteria (vibrios) in the contaminated water.

The parameters are as follows:

1.  $d$  the natural death rate of human hosts,
2.  $\gamma$ , the recovery rate of infectious individuals,
3.  $b$ , the influx of susceptible host,
4.  $\sigma$ , the rate at which recovered individuals lose immunity,
5.  $\delta$ , the natural death rate of bacteria,
6.  $\xi$ , the shedding rate of bacteria by infectious human hosts,
7.  $D_i, i = 1, 2, 3, 4$ , the diffusion coefficients,
8.  $U$ , bacterial convection coefficient.

We assume all of these parameters to be positive. The functions  $f_1, f_2, h$  represent the direct, indirect transmission rates, intrinsic growth of bacteria, respectively and satisfy the following conditions:  $\forall I, B \geq 0$ ,

$$(H1) \quad f_1(0) = 0, f_1'(I) > 0, f_1''(I) \leq 0,$$

$$(H2) \quad f_2(0) = 0, f_2'(B) > 0, f_2''(B) \leq 0,$$

$$(H3) \quad h(0) = 0, h''(B) \leq 0$$

(cf. [37, 38]). Biologically (H1) and (H2) imply that the disease transmission rates are monotonically increasing, but subject to saturation effects. Similarly (H3) indicates that the growth rate of bacteria is also subject to saturation effects.

For instance, a typical example takes the following form

$$f_1(I) = \beta_1 I, \quad (5a)$$

$$f_2(B) = \beta_2 \frac{B}{B + K}, \quad (5b)$$

$$h(B) = gB \left(1 - \frac{B}{K_B}\right), \quad (5c)$$

where

$$\beta_1, \beta_2, g, K, K_B > 0, \quad (6)$$

and  $\beta_1, \beta_2$  represent direct and indirect transmission parameters and  $K$  the maximal capacity of free-living pathogen in the environment. Hereafter let us write  $\partial_t, \partial_x, \partial_{xx}^2$  for  $\frac{\partial}{\partial t}, \frac{\partial}{\partial x}, \frac{\partial^2}{\partial x^2}$ , respectively.

The generalized SIRS-B epidemic PDE model was introduced in [37] as an extension from the SIRS-B ODE model by including diffusive terms to capture the movement of human hosts and bacteria in a heterogeneous environment and convection term to depict the drift for vibrio's transport. In this paper, our mathematical analysis will be focused on the SIRS-B epidemic PDE model.

To state our results clearly, let us denote the solution

$$u = (u_1, u_2, u_3, u_4) \triangleq (S, I, R, B) \in \mathbb{R}^4, \quad \phi \triangleq (\phi_1, \phi_2, \phi_3, \phi_4). \quad (7)$$

We also denote the Lebesgue spaces  $L^p$  with their norms by  $\|\cdot\|_{L^p}$ ,  $p \in [1, \infty]$ , the Sobolev spaces  $H^s$  with their norms by  $\|\cdot\|_{H^s}$ ,  $s \in \mathbb{Z}_+$ , e.g.

$$\|f\|_{L^p([0,1])} \triangleq \begin{cases} \left(\int_0^1 |f(x)|^p dx\right)^{\frac{1}{p}} & \text{if } p \in [1, \infty), \\ \text{esssup}_{x \in [0,1]} |f(x)| & \text{if } p = \infty, \end{cases}$$

$$\|f\|_{H^s([0,1])} \triangleq \|f\|_{L^2([0,1])} + \sum_{1 \leq k \leq s, k \in \mathbb{Z}_+} \|D_x^k f\|_{L^2([0,1])}.$$

Finally, we denote

$$X \triangleq C([0, 1], \mathbb{R}^4) = \prod_{i=1}^4 X_i, \quad X_i \triangleq C([0, 1], \mathbb{R}), \tag{8}$$

the space of  $\mathbb{R}^4$ -valued functions continuous in  $x \in [0, 1]$  with the usual sup norm

$$\|u\|_{C([0,1])} \triangleq \|S\|_{C([0,1])} + \|I\|_{C([0,1])} + \|R\|_{C([0,1])} + \|B\|_{C([0,1])}. \tag{9}$$

We define analogously

$$X^+ \triangleq C([0, 1], \mathbb{R}_+^4) = \prod_{i=1}^4 X_i^+, \quad X_i^+ \triangleq \{f \in C([0, T], \mathbb{R}) : f \geq 0\}. \tag{10}$$

We now state our results:

**Theorem 2.1.** *Under the hypothesis of (H1)-(H3),  $\forall \phi \in X^+$  the system (1a)-(1d) subjected to (2a)-(2d) and (3a)-(4a) admits a unique mild solution on the interval of existence  $[0, \sigma)$  where  $\sigma = \sigma(\phi)$ . The solution  $(S, I, R, B)(t)$  remains nonnegative for all  $t \in [0, \sigma)$ . Moreover, if  $\sigma < \infty$ , then the sup norm of the solution becomes unbounded as  $t$  approaches  $\sigma$  from below.*

Via *a priori* estimates and continuation of local theory, we can extend this result to global in time in case where  $D_1 = D_2 = D_3 = D$ . We note that this constraint of the common diffusion coefficient is in fact found elsewhere as well (see e.g. (1.5) in [14]). For clarity, we shall consider the case of (5a), (5b), (5c) in its proof, although our proof could be modified for various cases.

The major obstacle to such *a priori* estimates for the SIRS-B epidemic PDE model (1a)-(1d) is that in contrast to other PDEs, (e.g. see fluid mechanics in [11]), the solution to (1a)-(1d) does not possess any obvious conserved quantity such as the  $L^2$ -norm bound, while being non-linear. This implies that for fixed a time  $T > 0$  a priori, no energy estimates with Gronwall’s inequality type argument can establish a bound up to time  $T$ . We overcome this difficulty by taking advantage of the structure of the system (1a)-(1d) by defining  $V \triangleq S + I + R$  in order to cancel the nonlinear terms (see (17a)-(17c)) and carefully raising the regularity of estimates making use of diffusive terms, in particular to control the advection term (see (24)).

Let us also recall the notion of a semiflow on  $Y$ , typically a subset of some Banach space, by  $\Phi : Y \times \mathbb{R}^+ \mapsto Y$  that satisfies

1.  $\Phi_0 = id_Y$ ,
2.  $\Phi_t \circ \Phi_s = \Phi_{t+s}$  for  $t, s \geq 0$

(cf. [33]). Furthermore, let us denote

$$X_\Lambda \triangleq \{\psi \in X : \psi(x) \in \mathbb{R}_+^4, x \in [0, 1]\}.$$

We now state our global well-posedness result.

**Theorem 2.2.** *If  $D_1 = D_2 = D_3$  and  $f_1, f_2$  and  $h$  satisfy (5a), (5b) and (5c), then  $\forall \phi \in X^+ \cap (H^1([0, 1]))^4$ , the system (1a)-(1d) subjected to (2a)-(2d) and (3a)-(4a) admits a unique nonnegative mild solution on the interval of existence  $[0, T]$  for any  $T > 0$  such that*

$$\sup_{t \in [0, T]} \|u(t)\|_{H^1([0, 1])} + \int_0^T \|u\|_{H^2([0, 1])}^2 d\tau < \infty.$$

Therefore,  $\Phi_t(\phi) = u(t, \phi)$  is a semiflow on  $X_{\mathbb{R}_+^4}$ .

An important disease threshold is the basic reproduction number  $\mathcal{R}_0$ , which measures the expected number of secondary infections caused by one infectious individual during its infectious period in an otherwise susceptible population (cf. [9]). This important concept was originally proposed and is well-known for ODE epidemics models and has been extended to reaction-diffusion and reaction-convection-diffusion epidemic systems with homogeneous Neumann boundary conditions in recent development due to Thieme [35], Wang and Zhao [39], and Hsu et al. [14].

The authors in [37] particularly verified global dynamics of cholera epidemic using a SIRS-B epidemic ODE model; that is, when  $\mathcal{R}_0^{ODE}$ , the basic reproduction number associated with this ODE model, satisfies  $\mathcal{R}_0^{ODE} \leq 1$ , this ODE model only has the disease-free equilibrium (DFE) which is globally asymptotically stable; whereas if  $\mathcal{R}_0^{ODE} > 1$ , then this ODE model has two equilibriums, namely the DFE which is unstable and endemic equilibrium which is globally asymptotically stable (see Theorem 2.1 [37]). We establish local stability results concerning the SIRS-B epidemic PDE model (1a)-(1d) in the following theorem. For simplicity, we denote  $\mathcal{R}_0$  to be the basic reproduction number associated with the SIRS-B epidemic PDE model.

**Theorem 2.3.** *Suppose that the hypothesis of Theorem 2.2 holds.*

1. *If  $\mathcal{R}_0 < 1$ , then the DFE,  $(N^*, 0, 0, 0)$ , is locally asymptotically stable for (1a)-(1d).*
2. *If  $\mathcal{R}_0 > 1$ , then there exists  $\epsilon_0 > 0$  such that any positive solution of (1a)-(1d) satisfies*

$$\limsup_{t \rightarrow \infty} \|(S(t, \cdot), I(t, \cdot), R(t, \cdot), B(t, \cdot)) - (N^*, 0, 0, 0)\|_{C([0, 1])} \geq \epsilon_0.$$

**Remark 1.** 1. Concerning Theorems 2.1 and 2.2, in fact we prove more according to Theorem 7.3.1, Corollary 7.3.2 [33]. Indeed, in addition to the statements of Theorems 2.1 and 2.2, the following properties hold:

- (a)  $S, I, R$  and  $B$  are continuously differentiable in time on  $(0, \sigma)$ , the solution satisfies (12),
- (b) it is in fact a classical solution of (1a)-(1d),
- (c) if  $Y \subset X_{\mathbb{R}_+^4}$  is closed and bounded,  $t_0 > 0$  and  $\cup_{t \in [0, t_0]} \Phi_t(Y)$  is bounded, then  $\Phi_{t_0}(Y)$  has compact closure in  $X_{\mathbb{R}_+^4}$ .

We chose to state Theorems 2.1 and 2.2 for simplicity.

2. To the best of our knowledge, despite the intensive study on these types of models as initial boundary value problems, the global well-posedness result seems to be new. It is also a non-trivial problem for (1a)-(1d) as a non-linear PDE model. Moreover, the structure of the system (1a)-(1d) that allows us to cancel the nonlinear terms as we did is in fact common in relevant models (see e.g. [12, 15, 16]). Hence, we believe that our method may be extended to various other models.

**3. Preliminaries.** Let us denote a constant that depends on  $a, b$  by  $c(a, b)$  and write  $A \lesssim_{a,b} B, A \approx_{a,b} B$  to imply that there exists some constant  $c(a, b)$  such that  $A \leq c(a, b)B, A = c(a, b)B$  respectively.

First, we denote the following operators  $F_i : [0, 1] \times \mathbb{R}^4 \mapsto \mathbb{R}^4, (i = 1, 2, 3, 4)$ :

$$F_1(x, u(x, t)) \triangleq b - Sf_1(I) - Sf_2(B) - dS + \sigma R, \tag{11a}$$

$$F_2(x, u(x, t)) \triangleq Sf_1(I) + Sf_2(B) - I(d + \gamma), \tag{11b}$$

$$F_3(x, u(x, t)) \triangleq \gamma I - R(d + \sigma), \tag{11c}$$

$$F_4(x, u(x, t)) \triangleq \xi I + h(B) - \delta B. \tag{11d}$$

Let  $A_i^0, i = 1, 2, 3$  denote the differential operator,

$$A_i^0 u_i \triangleq D_i \partial_{xx}^2 u_i, \\ A_4^0 u_4 \triangleq D_4 \partial_{xx}^2 u_4 - U \partial_x u_4,$$

defined on its domain

$$D(A_i^0) \triangleq \{u_i \in C^2((0, 1)) \cap C^1([0, 1]) : A_i^0 u_i \in C([0, 1]), \partial_x u_i|_{x=0,1} = 0\}, \\ D(A_4^0) \triangleq \{u_4 \in C^2((0, 1)) \cap C^1([0, 1]) : \\ A_4^0 u_4 \in C([0, 1]), D_4 \partial_x u_4 - U u_4|_{x=0} = \partial_x u_4|_{x=1} = 0\}.$$

Furthermore, we let  $A_i, (i = 1, 2, 3, 4)$  be the closure of  $A_i^0$  so that  $A_i$  on  $X_i$  generates an analytic semigroup of bounded linear operators  $T_i(t)$  for  $t \geq 0$  such that

$$u_i(x, t) = (T_i(t)\phi_i)(x)$$

satisfies

$$\partial_t u_i(t) = A_i u_i(t), \quad u_i(0) = \phi_i \in D(A_i)$$

where

$$D(A_i) \triangleq \left\{ \psi \in X_i : \lim_{t \rightarrow 0^+} \frac{(T_i(t) - I)\psi}{t} = A_i \psi \text{ exists} \right\};$$

i.e., for  $i = 1, 2, 3,$

$$\begin{cases} \partial_t u_i(x, t) = D_i \partial_{xx}^2 u_i(x, t), & t > 0, x \in (0, 1), \\ \partial_x u_i|_{x=0,1} = 0, & u_i(x, 0) = \phi_i(x), \end{cases}$$

and

$$\begin{cases} \partial_t u_4(x, t) = D_4 \partial_{xx}^2 u_4(x, t) - U \partial_x u_4(x, t), & t > 0, x \in (0, 1), \\ D_4 \partial_x u_4 - U u_4|_{x=0} = \partial_x u_4|_{x=1} = 0, & u_4(x, 0) = \phi_4(x) \end{cases}$$

(cf. [20, 25]). Let  $T(t) : X \mapsto X$  be defined by

$$T(t) \triangleq \prod_{i=1}^4 T_i(t)$$

so that it is a semigroup of operators on  $X$  generated by

$$A \triangleq \prod_{i=1}^4 A_i \text{ with domain } D(A) \triangleq \prod_{i=1}^4 D(A_i)$$

and now

$$u(x, t) = \begin{pmatrix} u_1(x, t) \\ u_2(x, t) \\ u_3(x, t) \\ u_4(x, t) \end{pmatrix} = \begin{pmatrix} T_1(t)\phi_1(x) \\ T_2(t)\phi_2(x) \\ T_3(t)\phi_3(x) \\ T_4(t)\phi_4(x) \end{pmatrix} = (T(t)\phi)(x)$$

solves

$$\begin{cases} \partial_t u = D\partial_{xx}^2 u - E\partial_x u, & t > 0, x \in (0, 1), \\ D\partial_x u|_{x=0} - Eu|_{x=0} = 0, & \partial_x u|_{x=1} = 0, \quad u(x, 0) = \phi(x), \end{cases}$$

where

$$D \triangleq \begin{pmatrix} D_1 & 0 & 0 & 0 \\ 0 & D_2 & 0 & 0 \\ 0 & 0 & D_3 & 0 \\ 0 & 0 & 0 & D_4 \end{pmatrix}, \quad E \triangleq \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & U \end{pmatrix}.$$

Hence, with

$$F \triangleq \begin{pmatrix} F_1 \\ F_2 \\ F_3 \\ F_4 \end{pmatrix},$$

the system (1a)-(1d) may be reformulated as

$$\partial_t u = D\partial_{xx}^2 u - E\partial_x u + F(x, u(x, t)) \quad (12)$$

for which its mild solution can be obtained for any  $\phi \in X$  if it is continuous and satisfies

$$u(t) = T(t)\phi + \int_0^t T(t-s)F(x, u(x, s))ds.$$

Next, we state some important definitions with an ordered Banach space  $X$  with a closed convex cone  $X_+$  that is normal and generating, excluding the case  $X = \{0\}$ :

**Definition 3.1.** For a closed linear operator  $\Theta : D(\Theta) \mapsto X$ ,  $\lambda \in \mathbb{C}$  is a resolvent value of  $\Theta$  if  $\lambda I - \Theta$  has a bounded inverse operator that is defined on all of  $X$ . The set of resolvent values of  $\Theta$  is called the resolvent set of  $\Theta$  and is denoted by  $\rho(\Theta)$ . The set  $\mathbb{C} \setminus \rho(\Theta) \triangleq \sigma(\Theta)$  is called the spectrum of  $\Theta$ . A closed operator  $\Theta$  in  $X$  is called resolvent-positive if the resolvent set of  $\Theta$ ,  $\rho(\Theta)$  contains a ray  $(\eta, \infty)$  and  $(\lambda I - \Theta)^{-1}$  is a positive operator  $\forall \lambda > \eta$ .

**Definition 3.2.** A linear operator  $\Phi : Y \mapsto X$ , defined on a linear subspace  $Y$  of  $X$ , is called positive if  $\Phi x \in X_+ \forall x \in Y \cap X_+$  and  $\Phi$  is not the zero operator. If  $\Psi$  is a resolvent-positive operator and  $\Phi : D(\Psi) \mapsto X$  is a positive linear operator, then  $\Theta = \Psi + \Phi$  is called a positive perturbation of  $\Psi$ .

We recall that an  $n \times n$  matrix  $M = (M_{ij})$  is irreducible if  $\forall I \subsetneq N = \{1, \dots, n\}$ ,  $\exists i \in I$  and  $j \in J = N \setminus I$  such that  $M_{ij} \neq 0$  where  $I \neq \emptyset$ . We also recall the spectral radius  $r(\Theta)$  of a square matrix  $\Theta$  is defined by

$$r(\Theta) \triangleq \sup\{|\lambda| : \lambda \in \sigma(\Theta)\}$$

where  $\sigma(\Theta)$  is the spectrum of  $\Theta$  and its spectral bound

$$s(\Theta) \triangleq \sup\{Re\lambda : \lambda \in \sigma(\Theta)\}.$$

Finally, we recall that for  $S = \{S(t); t \geq 0\}$ , a  $C_0$ -semigroup, the exponential growth bound of  $S$  is defined as

$$w(S) \triangleq \inf\{m \in \mathbb{R} : \exists M \geq 1 : \forall t \geq 0, \|S(t)\| \leq Me^{mt}\}.$$

Next, let us recall as lemmas, some important results on which our proof will heavily rely. First, we summarize Theorem 7.3.1 and Corollary 7.3.2 of [33]:

**Lemma 3.3.** (cf. Theorem 7.3.1, Corollary 7.3.2 [33]) Suppose that  $F : [0, 1] \times \mathbb{R}_+^4 \mapsto \mathbb{R}^4$  has the property that

$$F_i(x, u) \geq 0 \text{ whenever } x \in [0, 1], u \in \mathbb{R}_+^4 \text{ and } u_i = 0.$$

Then  $\forall \phi \in X_{\mathbb{R}_+^4}$ ,

$$\begin{cases} \partial_t u_i(x, t) = D_i \partial_{xx}^2 u_i(x, t) + F_i(x, u(x, t)), & t > 0, x \in (0, 1), \\ \alpha_i(x) u_i(x, t) + \delta_i \partial_x u_i(x, t) = 0, & t > 0, x = 0, 1, \\ u_i(x, 0) = \phi_i(x), & x \in (0, 1), \end{cases}$$

has a unique noncontinuable mild solution  $u(t) = u(t, \phi) \in X_{\mathbb{R}_+^4}$  defined on  $[0, \sigma)$  where  $\sigma = \sigma(\phi) \leq \infty$ . Moreover, if  $\sigma < \infty$ , then  $|u(t)| \rightarrow \infty$  as  $t \rightarrow \sigma$  from below.

**Remark 2.** Lemma 3.3 remains valid even if the Laplacian is replaced by a general second order differential operator (see pg. 121 [33]). In relevance we also refer readers to Theorem 1.1 of [22] for similar general well-posedness result.

We state more useful lemmas:

**Lemma 3.4.** (Theorem 3.12 [35]) Let  $A$  be the generator of a  $C_0$ -semigroup  $S$  on an ordered Banach space  $X$  with a normal and generating cone  $X_+$ . Then  $A$  is resolvent-positive if and only if  $S$  is a positive semigroup; i.e.  $S(t)X_+ \subset X_+ \forall t \geq 0$ .

**Remark 3.** One standard characterization of generators of positive semigroups is the matrix semigroups:  $T(t) \triangleq e^{tA}$  where  $A = (a_{ij})_{n \times n}, a_{ij} \geq 0 \forall i \neq j$  (e.g. pg. 298 [3]).

We recall that a Banach space is called an abstract  $M$ -space if it is a linear lattice, and  $x, y \geq 0$  implies

$$\|x \vee y\| = \max(\|x\|, \|y\|)$$

(cf. [18]).

**Lemma 3.5.** (Theorem 3.14 [35]) Let  $A$  be the infinitesimal generator of a positive  $C_0$ -semigroup  $S$  on an ordered Banach space  $X$ . Then  $s(A) = w(S)$  if  $X$  is an abstract  $M$  space.

**Remark 4.** An example of  $M$ -space is the space  $C(\Omega)$  of all bounded continuous real valued functions on Hausdorff space  $\Omega$  with the sup norm (see [18]).

**Lemma 3.6.** (Theorem 3.5 [35]) Let  $\Psi$  be a resolvent-positive operator in  $X, s(\Psi) < 0$  and  $\Theta = \Phi + \Psi$  be a positive perturbation of  $\Psi$ . If  $\Theta$  is resolvent-positive, then  $s(\Theta)$  has the same sign as  $r(-\Phi\Psi^{-1}) - 1$ .

**Lemma 3.7.** (Theorem 2.1 [7]) Let  $T(\cdot)$  be a nonlinear semigroup on  $X$  and let  $x_0$  be an equilibrium. Suppose that  $T(\cdot)$  is Frechet-differentiable at  $x_0$  with  $U(t) = T'(t, [x_0])$  and the zero solution is exponentially asymptotically stable with respect to this linearized semigroup  $U(\cdot)$ . Then  $x_0$  is exponentially asymptotically stable with respect to  $T(\cdot)$ .

**4. Proof of Theorem 2.1.** By (2a)-(2d) and hypothesis,  $\phi \in X_{\mathbb{R}_+^4}$ . Now we check when  $u \in \mathbb{R}_+^4, u_1 = 0$ , by (11a) and (7)

$$F_1(x, u) = 0 + b + \sigma R \geq 0. \tag{13}$$



When  $u \in \mathbb{R}_+^4, u_2 = 0$ , by (11b), (7), (H1) and (H2),

$$F_2(x, u) = 0 + S f_2(B) \geq 0. \quad (14)$$

When  $u \in \mathbb{R}_+^4, u_3 = 0$ , by (11c) and (7),

$$F_3(x, u) = 0 + \gamma I \geq 0. \quad (15)$$

When  $u \in \mathbb{R}_+^4, u_4 = 0$ , by (11d), (7) and (H3),

$$F_4(x, u) = 0 + \xi I \geq 0. \quad (16)$$

Hence, the proof of Theorem 2.1 is complete by Lemma 3.3 and Remark 2 due to (13)-(16).  $\square$

**5. Proof of Theorem 2.2.** In this section, we extend the local unique solution constructed in Theorem 2.1 to global in time via a priori estimates and continuation of local theory. By hypothesis we may let  $D = D_1 = D_2 = D_3$ . By Theorem 2.1, we know there exists a unique solution  $u$  on  $[0, \sigma)$ . Let us fix  $\delta \in (0, \sigma)$  arbitrary. Restarting at the time  $\tilde{\delta} \in (0, \delta)$ , we know there exists a unique solution  $\tilde{u}$  on  $[\tilde{\delta}, \sigma^*)$ . By uniqueness,  $\tilde{u} = u$  on  $[\tilde{\delta}, \sigma^*)$ . If  $\sigma^* > \sigma$ , then we have extended the local solution beyond  $\sigma$  already. Suppose  $\sigma^* \leq \sigma$ . Then necessarily according to the blow up criterion of Theorem 2.1,

$$\limsup_{t \nearrow \sigma^*} \sup_{x \in [0, 1]} |u(x, t)| = \infty.$$

We show that  $\forall t < \sigma^*$ , we have the uniform bound of

$$\sup_{x \in [0, 1]} |u(x, t)| \leq c,$$

which contradicts the definition of  $\sigma^*$ . We remark that due to the uniqueness of the solution on  $[0, \sigma^*)$ ,  $\sigma^* \leq \sigma$ , by local theory,  $u$  is nonnegative; i.e.  $S, I, R, B \geq 0$ . For brevity, when no confusion arises, we write  $L^p$  to imply  $L^p([0, 1])$  below for  $p \in [1, \infty]$ . We prove two propositions for which we emphasize again that they hold for the general case, for instance when  $f_1, f_2$  and  $h$  have at most a linear growth; we chose to describe the proof in the case where (5a)-(5c) is satisfied for clarity.

**Proposition 1.** *If  $u = (S, I, R, B)$  solves (1a)-(1d) subjected to (2a)-(2d) and (3a)-(4a) in  $[0, \sigma^*)$  under the hypothesis of Theorem 2.2, then  $\forall p \in [2, \infty)$ ,*

$$\sup_{t \in [0, \sigma^*)} \|u(t)\|_{L^p([0, 1])} \lesssim_{u_0, \sigma^*, p} 1.$$

*Proof.* From (1a)-(1c), (3a)-(3c), by letting

$$V \triangleq S + I + R,$$

we see that we have,

$$\partial_t V - D \partial_{xx}^2 V = -dV + b, \quad (17a)$$

$$\partial_x V|_{x=0, 1} = 0, \quad (17b)$$

$$V(x, 0) = V_0(x), \quad (17c)$$

where  $V_0(x) = \phi_1(x) + \phi_2(x) + \phi_3(x)$ . We fix  $p \in [2, \infty)$ , multiply (17a) by  $|V|^{p-2}V$  and integrate over  $[0, 1]$  to obtain

$$\frac{1}{p} \partial_t \|V\|_{L^p}^p - D \int_0^1 (\partial_{xx}^2 V) |V|^{p-2} V dx = -d \int_0^1 |V|^p dx + b \int_0^1 |V|^{p-2} V dx. \quad (18)$$

We compute the diffusive term as

$$\begin{aligned}
 -D \int_0^1 (\partial_{xx}^2 V) |V|^{p-2} V dx &= -D \int_0^1 \partial_x ((\partial_x V) |V|^{p-2} V) - \partial_x V \partial_x (|V|^{p-2} V) dx \\
 &= D(p-1) \int_0^1 \partial_x V |V|^{p-2} \partial_x V dx \\
 &= D(p-1) \int_0^1 \left| \partial_x V |V|^{\frac{p-2}{2}} \right|^2 dx \geq 0
 \end{aligned} \tag{19}$$

by (17b). Therefore, taking into account of (19) into (18) and using Hölder's inequality of  $\frac{1}{p} + \frac{p-1}{p} = 1$ , we obtain

$$\begin{aligned}
 \frac{1}{p} \partial_t \|V\|_{L^p}^p &\leq -d \int_0^1 |V|^p dx + b \int_0^1 |V|^{p-2} V dx \\
 &\leq b \|V\|_{L^{p-1}}^{p-1} \leq b \|V\|_{L^p}^{p-1}.
 \end{aligned} \tag{20}$$

We write

$$\frac{1}{p} \partial_t \|V\|_{L^p}^p = \|V\|_{L^p}^{p-1} \partial_t \|V\|_{L^p}.$$

Dividing by  $\|V\|_{L^p}^{p-1}$  in (20) and integrating over  $[0, t]$ ,  $t < \sigma^*$  lead to

$$\|V(t)\|_{L^p} \leq \|V_0\|_{L^p} + bt$$

and hence taking sup over  $t \in [0, \sigma^*)$  on the right hand side and then on the left hand side give

$$\sup_{t \in [0, \sigma^*)} \|V(t)\|_{L^p} \leq \|V_0\|_{L^p} + b\sigma^* \lesssim_{V_0, \sigma^*} 1.$$

This implies

$$\sup_{t \in [0, \sigma^*)} (\|S\|_{L^p} + \|I\|_{L^p} + \|R\|_{L^p})(t) \lesssim_{V_0, \sigma^*, p} 1. \tag{21}$$

Next, similarly multiplying (1d) by  $|B|^{p-2}B$  and integrating over  $[0, 1]$  yield

$$\begin{aligned}
 &\frac{1}{p} \partial_t \|B\|_{L^p}^p - D_4 \int_0^1 (\partial_{xx}^2 B) |B|^{p-2} B dx \\
 &= -U \int_0^1 (\partial_x B) |B|^{p-2} B dx - \delta \int_0^1 |B|^p dx + \xi \int_0^1 I |B|^{p-2} B dx \\
 &\quad + g \int_0^1 |B|^p dx - \frac{g}{K_B} \int_0^1 |B|^p B dx.
 \end{aligned} \tag{22}$$

In contrast to the previous case, we will need the diffusive term to handle the advection term. Taking into account of the boundary value of  $B$  which differs from  $S, I, R$ , we find that

$$\begin{aligned}
 &-D_4 \int_0^1 (\partial_{xx}^2 B) |B|^{p-2} B dx \\
 &= -D_4 \int_0^1 \partial_x ((\partial_x B) |B|^{p-2} B) - (\partial_x B) \partial_x (|B|^{p-2} B) dx \\
 &= -D_4 (\partial_x B(1, t) |B(1, t)|^{p-2} B(1, t) - \partial_x B(0, t) |B(0, t)|^{p-2} B(0, t))
 \end{aligned}$$

$$\begin{aligned}
& + D_4(p-1) \int_0^1 |B|^{p-2} (\partial_x B) (\partial_x B) dx \\
& = U |B|^p(0, t) + D_4(p-1) \int_0^1 \left| |\partial_x B| |B|^{\frac{p-2}{2}} \right|^2 dx
\end{aligned}$$

and therefore,

$$D_4(p-1) \int_0^1 \left| |\partial_x B| |B|^{\frac{p-2}{2}} \right|^2 dx \leq -D_4 \int_0^1 (\partial_{xx}^2 B) |B|^{p-2} B dx. \quad (23)$$

We compute the advection term:

$$\begin{aligned}
& -U \int_0^1 (\partial_x B) |B|^{p-2} B dx \\
& \leq U \int_0^1 |\partial_x B| |B|^{\frac{p-2}{2}} |B|^{\frac{p}{2}} dx \\
& = U \int_0^1 \frac{\sqrt{2D_4(p-1)}}{\sqrt{2D_4(p-1)}} |\partial_x B| |B|^{\frac{p-2}{2}} |B|^{\frac{p}{2}} dx \\
& \leq D_4(p-1) \int_0^1 \left| |\partial_x B| |B|^{\frac{p-2}{2}} \right|^2 dx + \frac{U^2}{4D_4(p-1)} \int_0^1 |B|^p dx,
\end{aligned} \quad (24)$$

where the last inequality follows from Young's inequality of  $ab \leq \frac{a^2}{2} + \frac{b^2}{2}$ . Next,

$$-\delta \int_0^1 |B|^p dx + \xi \int_0^1 I |B|^{p-2} B dx \leq \xi \|I\|_{L^p} \|B\|_{L^p}^{p-1} \quad (25)$$

by Hölder's inequality of  $\frac{1}{p} + \frac{p-1}{p} = 1$ . Finally, because  $B \geq 0$  on  $[0, \sigma^*)$ ,

$$-\frac{g}{K_B} \int_0^1 |B|^p B dx = -\frac{g}{K_B} \|B\|_{L^{p+1}}^{p+1} \leq 0 \quad (26)$$

as  $g$ , and  $K_B > 0$  by (6). Thus, absorbing the diffusive term from (24) into (23), taking (25) and (26) into (22), we obtain

$$\frac{1}{p} \partial_t \|B\|_{L^p}^p \leq \left( \frac{U^2}{4D_4(p-1)} + g \right) \|B\|_{L^p}^p + \xi \|I\|_{L^p} \|B\|_{L^p}^{p-1}.$$

Writing  $\frac{1}{p} \partial_t \|B\|_{L^p}^p = \|B\|_{L^p}^{p-1} \partial_t \|B\|_{L^p}$ , we obtain after dividing by  $\|B\|_{L^p}^{p-1}$ ,

$$\partial_t \|B\|_{L^p} \leq \left( \frac{U^2}{4D_4(p-1)} + g \right) \|B\|_{L^p} + \xi \|I\|_{L^p}.$$

Therefore, using (21) Gronwall's inequality type argument gives

$$\|B(t)\|_{L^p} \lesssim_{V_0, \sigma^*, p} \|B_0\|_{L^p} e^t + \int_0^t e^{t-\tau} d\tau \lesssim_{V_0, B_0, \sigma^*, p} 1.$$

This completes the proof of Proposition 1.  $\square$

**Proposition 2.** *If  $u = (S, I, R, B)$  solves (1a)-(1d) subjected to (2a)-(2d) and (3a)-(4a) in  $[0, \sigma^*)$  under the hypothesis of Theorem 2.2, then*

$$\sup_{t \in [0, \sigma^*]} \|\partial_x u(t)\|_{L^2([0,1])} + \int_0^{\sigma^*} \|\partial_{xx}^2 u\|_{L^2}^2 d\tau \lesssim_{u_0, \sigma^*} 1.$$

*Proof.* We multiply (1a) by  $-\partial_{xx}^2 S$  and integrate over space  $[0, 1]$  to obtain

$$\begin{aligned} & \frac{1}{2} \partial_t \|\partial_x S\|_{L^2}^2 + D \|\partial_{xx}^2 S\|_{L^2}^2 \\ &= \int_0^1 [dS + S\beta_1 I + S\beta_2 \left(\frac{B}{K+B}\right) - b - \sigma R] \partial_{xx}^2 S dx \end{aligned} \tag{27}$$

where we used that

$$\begin{aligned} & \int_0^1 (\partial_t S)(-\partial_{xx}^2 S) dx \\ &= - \left[ \partial_t S(1, t) \partial_x S(1, t) - \partial_t S(0, t) \partial_x S(0, t) - \int_0^1 \frac{1}{2} \partial_t (\partial_x S)^2 dx \right] \\ &= \frac{1}{2} \partial_t \|\partial_x S\|_{L^2}^2 \end{aligned} \tag{28}$$

due to (3a). Now we bound

$$\begin{aligned} & \int_0^1 [dS + S\beta_1 I + S\beta_2 \left(\frac{B}{K+B}\right) + b + \sigma R] \partial_{xx}^2 S dx \\ & \leq (d\|S\|_{L^2} + \beta_1 \|S\|_{L^4} \|I\|_{L^4} + \beta_2 \|S\|_{L^2} + \sigma \|R\|_{L^2}) \|\partial_{xx}^2 S\|_{L^2} + b \|\partial_{xx}^2 S\|_{L^1} \\ & \lesssim_{u_0, \sigma^*} \|\partial_{xx}^2 S\|_{L^2} \\ & \leq \frac{D}{2} \|\partial_{xx}^2 S\|_{L^2}^2 + c \end{aligned} \tag{29}$$

by Hölder’s inequalities, Proposition 1 and Young’s inequality. Applying the estimate in (29) to (27) and absorbing the diffusive term gives

$$\partial_t \|\partial_x S\|_{L^2}^2 + D \|\partial_{xx}^2 S\|_{L^2}^2 \lesssim_{u_0, \sigma^*} 1. \tag{30}$$

Likewise, we can show that

$$\partial_t \|\partial_x I\|_{L^2}^2 + D \|\partial_{xx}^2 I\|_{L^2}^2 \lesssim_{u_0, \sigma^*} 1 \tag{31}$$

and

$$\partial_t \|\partial_x R\|_{L^2}^2 + D \|\partial_{xx}^2 R\|_{L^2}^2 \lesssim_{u_0, \sigma^*} 1. \tag{32}$$

For completeness we leave the details of the derivation of (31) and (32) in the Appendix while we elaborate on the estimate on (1d) due to its difference. We multiply (1d) by  $-\partial_{xx}^2 B$ , integrate in space over  $[0, 1]$  to obtain

$$\begin{aligned} & \frac{1}{2} \partial_t \left( \frac{U}{D_4} |B(0, t)|^2 + \|\partial_x B\|_{L^2}^2 \right) + D_4 \|\partial_{xx}^2 B\|_{L^2}^2 \\ &= \int_0^1 [U \partial_x B + B\delta - \xi I - gB \left(1 - \frac{B}{K_B}\right)] \partial_{xx}^2 B dx \end{aligned} \tag{33}$$

where we made use of

$$\begin{aligned} & \int_0^1 (\partial_t B)(-\partial_{xx}^2 B) dx \\ &= - \left[ \partial_t B(1, t) \partial_x B(1, t) - \partial_t B(0, t) \partial_x B(0, t) - \frac{1}{2} \int_0^1 \partial_t |\partial_x B|^2 dx \right] \\ &= - \left[ \partial_t B(1, t) 0 - \partial_t B(0, t) \frac{U}{D_4} B(0, t) - \frac{1}{2} \int_0^1 \partial_t |\partial_x B|^2 dx \right] \\ &= \frac{1}{2} \partial_t \left( \frac{U}{D_4} |B(0, t)|^2 + \|\partial_x B\|_{L^2}^2 \right) \end{aligned}$$

due to (4a). Now we bound

$$\begin{aligned} & \int_0^1 \left[ U \partial_x B + B \delta - \xi I - gB \left( 1 - \frac{B}{K_B} \right) \right] \partial_{xx}^2 B dx \\ & \leq [U \|\partial_x B\|_{L^2} + \|B\|_{L^2} \delta + \xi \|I\|_{L^2} + g \left( \|B\|_{L^2} + \frac{\|B\|_{L^4}^2}{K_B} \right)] \|\partial_{xx}^2 B\|_{L^2} \\ & \leq \frac{D_4}{2} \|\partial_{xx}^2 B\|_{L^2}^2 + c(1 + \|\partial_x B\|_{L^2}^2) \end{aligned} \quad (34)$$

by Hölder's inequalities, Proposition 1 and Young's inequalities. Thus, applying the estimate in (34) to (33) and absorbing the diffusive term lead to

$$\partial_t \left( \frac{U}{D_4} |B(0, t)|^2 + \|\partial_x B\|_{L^2}^2 \right) + D_4 \|\partial_{xx}^2 B\|_{L^2}^2 \lesssim 1 + \|\partial_x B\|_{L^2}^2. \quad (35)$$

Summing (30), (31), (32) and (35) lead to

$$\begin{aligned} & \partial_t \left( \|\partial_x S\|_{L^2}^2 + \|\partial_x I\|_{L^2}^2 + \|\partial_x R\|_{L^2}^2 + \frac{U}{D_4} |B(0, t)|^2 + \|\partial_x B\|_{L^2}^2 \right) \\ & \quad + \min\{D, D_4\} \|\partial_{xx}^2 u\|_{L^2}^2 \lesssim_{u_0, \sigma^*} (1 + \|\partial_x B\|_{L^2}^2). \end{aligned} \quad (36)$$

This implies

$$\partial_t \ln \left( e + \|\partial_x S\|_{L^2}^2 + \|\partial_x I\|_{L^2}^2 + \|\partial_x R\|_{L^2}^2 + \frac{U}{D_4} |B(0, t)|^2 + \|\partial_x B\|_{L^2}^2 \right) \lesssim_{u_0, \sigma^*} 1$$

and hence integrating in time gives

$$\sup_{t \in [0, \sigma^*]} \|\partial_x u(t)\|_{L^2} \lesssim_{u_0, \sigma^*} 1.$$

Integrating (36) in time  $[0, \sigma^*]$  and using this uniform bound completes the proof of Proposition 2.  $\square$

We may now complete the proof of Theorem 2.2. By Sobolev embedding (e.g. [11] Theorem II 3.2, Theorem II 3.4),

$$\sup_{t \in [0, \sigma^*]} \|u\|_{C([0, 1])} \leq c \|u\|_{H^1([0, 1])} \leq c$$

due to Propositions 1 and 2. This completes the proof of the first statement of Theorem 2.2.

The second statement of Theorem 2.2 is an immediate consequence of the first statement and Theorem 7.3.1 (d) of [33]. This completes the proof of Theorem 2.2.  $\square$

**6. Proof of Theorem 2.3.** The proof of this section is partially inspired by the work in [39].

**6.1. Proof of Theorem 2.3 (1).** We denote the DFE by  $(S, I, R, B) = (N^*, 0, 0, 0)$ , where  $N^* \geq 0$ . We linearize (1a)-(1d) about the DFE to obtain

$$\begin{cases} \partial_t S = D_1 \partial_{xx}^2 S - N^* \left( \beta_1 I + \frac{\beta_2}{K} B \right) - dS + \sigma R, \\ \partial_t I = D_2 \partial_{xx}^2 I + N^* \beta_1 I + N^* \frac{\beta_2}{K} B - I(d + \gamma), \\ \partial_t R = D_3 \partial_{xx}^2 R + \gamma I - R(d + \sigma), \\ \partial_t B = D_4 \partial_{xx}^2 B - U \partial_x B + \xi I + gB - \delta B. \end{cases}$$

We formally denote the right hand side as

$$\tilde{\Theta}(S, I, R, B) \triangleq \begin{pmatrix} D_1 \partial_{xx}^2 S - N^*(\beta_1 I + \frac{\beta_2}{K} B) - dS + \sigma R \\ D_2 \partial_{xx}^2 I + N^* \beta_1 I + N^* \frac{\beta_2}{K} B - I(d + \gamma) \\ D_3 \partial_{xx}^2 R + \gamma I - R(d + \sigma) \\ D_4 \partial_{xx}^2 B - U \partial_x B + \xi I + gB - \delta B \end{pmatrix}.$$

We write

$$\begin{aligned} & \Theta \begin{pmatrix} I \\ B \end{pmatrix} \\ & \triangleq \begin{pmatrix} D_2 \partial_{xx}^2 I + N^* \beta_1 I + N^* \frac{\beta_2}{K} B - I(d + \gamma) \\ D_4 \partial_{xx}^2 B - U \partial_x B + \xi I + gB - \delta B \end{pmatrix} \\ & = \begin{pmatrix} D_2 \partial_{xx}^2 + (-d - \gamma) + N^* \beta_1 & N^* \frac{\beta_2}{K} \\ \xi & D_4 \partial_{xx}^2 - U \partial_x - \delta + g \end{pmatrix} \begin{pmatrix} I \\ B \end{pmatrix} \\ & = \left( \begin{pmatrix} D_2 \partial_{xx}^2 - d - \gamma & 0 \\ 0 & D_4 \partial_{xx}^2 - U \partial_x - \delta \end{pmatrix} + \begin{pmatrix} N^* \beta_1 & N^* \frac{\beta_2}{K} \\ \xi & g \end{pmatrix} \right) \begin{pmatrix} I \\ B \end{pmatrix} \\ & \triangleq (\Psi + \Phi) \begin{pmatrix} I \\ B \end{pmatrix}. \end{aligned}$$

We see that if there exists any nonnegative eigenvalue  $\lambda$  of  $\tilde{\Theta}$ , then it must be an eigenvalue of  $\Theta$ . Now for any

$$\phi = \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} \in C([0, 1], \mathbb{R}_+^2),$$

$$\Phi \phi = \begin{pmatrix} N^* \beta_1 \phi_1 + N^* \frac{\beta_2}{K} \phi_2 \\ \xi \phi_1 + g \phi_2 \end{pmatrix} \in C([0, 1], \mathbb{R}_+^2).$$

Therefore,  $\Phi$  is a positive linear operator. It is clear that because  $\Theta$  and  $\Psi$  are both generators of positive  $C_0$ -semigroups by Remark 3, by Lemma 3.4, they are resolvent-positive.

We now show that  $s(\Psi) < 0$ , partially following the argument in [33]. Let us first consider the following system:

$$\begin{cases} \partial_t B = D_4 \partial_{xx}^2 B - U \partial_x B, \\ D_4 \partial_x B(x, t) - UB(x, t)|_{x=0} = \partial_x B(x, t)|_{x=1} = 0. \end{cases} \tag{37}$$

Substituting  $B = e^{\lambda t} \phi(x)$  gives

$$\lambda \phi(x) = D_4 \phi'' - U \phi'; \tag{38}$$

hence, we see that the asymptotic behavior of solutions to (37) is determined by those of the eigenvalue problem of (38) with its corresponding boundary value from (37). By Theorem 7.6.1 [33], it has a real principal eigenvalue  $\lambda_0$  and a corresponding eigenvector  $w_0(x) > 0$  for all  $x \in [0, 1]$ . Moreover, there are countably many eigenvalues  $\lambda_n, n \geq 0$  which are all real that may be ordered as

$$\dots < \lambda_{n+1} < \lambda_n < \dots < \lambda_1 < \lambda_0.$$

We define

$$Q(w) \triangleq D_4 \partial_{xx}^2 w - U \partial_x w,$$

and compute

$$\begin{aligned}
 & \lambda_0 \int_0^1 |w_0(x)|^2 dx \\
 &= \int_0^1 (Qw_0)(x)w_0(x) dx \\
 &= \int_0^1 (D_4 \partial_{xx}^2 w_0 - U \partial_x w_0) w_0 dx \\
 &= D_4 [\partial_x w_0(1)w_0(1) - \partial_x w_0(0)w_0(0)] - D_4 \int_0^1 |\partial_x w_0|^2 dx - \frac{U}{2} [w_0^2(1) - w_0^2(0)] \\
 &= -\frac{U}{2} [w_0^2(1) + w_0^2(0)] - D_4 \int_0^1 |\partial_x w_0|^2 dx < 0
 \end{aligned}$$

because  $w_0(x) > 0$  for all  $x \in [0, 1]$ . This implies  $\lambda_0 < 0$ . Thus, it has a principal eigenvalue  $\lambda_0 < 0$  with an associated eigenvector  $w_0 > 0$ .

Now for any eigenvalue of  $\Psi$ , it is also an eigenvalue of

$$\partial_t B = (D_4 \partial_{xx}^2 - U \partial_x - \delta)B.$$

Since this may be seen as a sum of a second differentiation operator  $D_4 \partial_{xx}^2 - U \partial_x$  and a scalar constant operator  $M(x) \triangleq -\delta$ ,  $M(x)$  which again trivially satisfies  $M_{ij} \geq 0 \forall i \neq j$  and is irreducible, by Theorem 7.6.1 [33] there exists a real principal eigenvalue  $\lambda^*$  and an associated eigenvector  $\psi^* > 0$  such that

$$\lambda^* \psi^*(x) = D_4 \psi^{*''}(x) - U \psi^{*'}(x) - \delta \psi^*(x) \quad (39)$$

or

$$(\lambda^* + \delta) \psi^*(x) = D_4 \psi^{*''}(x) - U \psi^{*'}(x).$$

Comparing this eigenvalue problem with (38) which has eigenvalues  $\lambda_n, n \geq 0$ , we see that the eigenvalues of (39) are given by  $\lambda_n - \delta$ . In particular,  $\lambda^* < 0$  because  $\lambda_0 < 0, \delta > 0$ . Therefore,  $s(\Psi) < 0$ .

We now conclude the proof. By Lemma 3.6, the hypothesis that

$$\mathcal{R}_0 - 1 \triangleq r(-\Phi \Psi^{-1}) - 1 < 0$$

implies  $s(\Theta) < 0$  and hence  $s(\tilde{\Theta}) < 0$ . By Lemma 3.5 and Remark 4, if  $Q$  is the infinitesimal generator of  $\tilde{\Theta}$ , then  $w(Q) = s(\tilde{\Theta}) < 0$ . Now the local asymptotic stability follows from Lemma 3.7.  $\square$

**6.2. Proof of Theorem 2.3 (2).** As in the proof of Theorem 2.3 (1) we consider

$$\begin{cases} \partial_t I = D_2 \partial_{xx}^2 I - [(d + \gamma) - N^* \beta_1] I + N^* \frac{\beta_2}{K} B, \\ \partial_t B = D_4 \partial_{xx}^2 B - U \partial_x B + B(-\delta) + \xi I + gB, \end{cases}$$

so that its corresponding eigenvalue problem may be written as

$$\begin{cases} \lambda I = D_2 \partial_{xx}^2 I - [(d + \gamma) - N^* \beta_1] I + N^* \frac{\beta_2}{K} B, \\ \lambda B = D_4 \partial_{xx}^2 B - U \partial_x B + B(-\delta + g) + \xi I. \end{cases} \quad (40)$$

We may write this as

$$\begin{pmatrix} D_2 \partial_{xx}^2 I \\ D_4 \partial_{xx}^2 B - U \partial_x B \end{pmatrix} + \begin{pmatrix} -[(d + \gamma) - N^* \beta_1] & N^* \frac{\beta_2}{K} \\ \xi & -\delta + g \end{pmatrix} \begin{pmatrix} I \\ B \end{pmatrix}.$$

Now we can denote matrix

$$M(x) \triangleq \begin{pmatrix} -[(d + \gamma) - N^*\beta_1] & N^*\frac{\beta_2}{K} \\ \xi & -\delta + g \end{pmatrix}$$

which satisfies  $M_{ij} \geq 0 \forall i \neq j$  as  $\xi > 0$ . Moreover, it is clear that  $M$  is an irreducible matrix. Thus, by Theorem 7.6.1 [33], there exists a real principal eigenvalue  $\lambda^*$  and its corresponding positive eigenfunction  $\phi^*(x) \gg 0$ . We note that the Theorem 7.6.1 [33] is applicable with a general second differentiation operator and mixed boundary conditions such as in the case of  $I, B$  (see pg. 120, 121 [33]).

Now by hypothesis,  $\mathcal{R}_0 > 1$  so that  $\mathcal{R}_0 - 1 > 0$  and hence  $r(-\Phi\Psi^{-1}) - 1 > 0$ . From the proof of Theorem 2.3 (1), we know that this implies  $s(\Theta) > 0$ . It is clear from the form of  $\Theta$ , as  $N^*\frac{\beta_2}{K} \geq 0, \xi > 0$ , by Lemma 3.4, Remark 3, it is resolvent-positive and hence by Theorem 3.2 [35],  $s(\Theta) \in \sigma(\Theta)$ . Since  $\lambda^*$  is real, we have then  $\lambda^* > 0$ .

To reach a contradiction, suppose  $\forall \epsilon_0 > 0$ , there exists a positive solution  $(S, I, R, B)$  such that

$$\limsup_{t \rightarrow \infty} \|(S, I, R, B)(t) - (N^*, 0, 0, 0)\|_{C([0,1])} < \epsilon_0;$$

i.e. in particular

$$\limsup_{t \rightarrow \infty} \|I\|_{C([0,1])} < \epsilon_0, \quad \limsup_{t \rightarrow \infty} \|B\|_{C([0,1])} < \epsilon_0. \tag{41}$$

We consider the eigenvalue problem of

$$\begin{cases} \lambda I = D_2 \partial_{xx}^2 I + ((N^* - \epsilon_0)\beta_1 - (d + \gamma)) I + (N^* - \epsilon_0) \left(\frac{\beta_2}{\epsilon_0 + K}\right) B, \\ \lambda B = D_4 \partial_{xx}^2 B - U \partial_x B + gB \left(1 - \frac{\epsilon_0}{K_B}\right) - \delta B + \xi I. \end{cases} \tag{42}$$

Again, we may write the right hand side as

$$\begin{pmatrix} D_2 \partial_{xx}^2 I \\ D_4 \partial_{xx}^2 B - U \partial_x B \end{pmatrix} + M^{\epsilon_0}(x) \begin{pmatrix} I \\ B \end{pmatrix}$$

with

$$M^{\epsilon_0}(x) \triangleq \begin{pmatrix} (N^* - \epsilon_0)\beta_1 - (d + \gamma) & (N^* - \epsilon_0) \left(\frac{\beta_2}{\epsilon_0 + K}\right) \\ \xi & g \left(1 - \frac{\epsilon_0}{K_B}\right) - \delta \end{pmatrix}$$

so that  $M^{\epsilon_0}_{ij} \geq 0 \forall i \neq j$  and it is also irreducible. Thus, by Theorem 7.6.1 [33], it has its own principal eigenvalue  $\lambda_{\epsilon_0}^*$  and its corresponding positive eigenvector such that  $\phi_{\epsilon_0}^*(x) \gg 0$ . Since (42) approaches (40) as  $\epsilon_0 \rightarrow 0^+$ , and hence we have  $\lim_{\epsilon_0 \rightarrow 0} \lambda_{\epsilon_0}^* = \lambda^* > 0$ ; therefore, fixing  $\epsilon_0$  small enough, we have  $\lambda_{\epsilon_0}^* > 0$ . Thus, for  $t_0 > 0$  large enough, we see that

$$\begin{cases} \partial_t I \geq D_2 \partial_{xx}^2 I + ((N^* - \epsilon_0)\beta_1 - (d + \gamma)) I + (N^* - \epsilon_0) \left(\frac{\beta_2}{\epsilon_0 + K}\right) B, \\ \partial_t B \geq D_4 \partial_{xx}^2 B - U \partial_x B + gB \left(1 - \frac{\epsilon_0}{K_B}\right) - \delta B + \xi I, \end{cases}$$

holds  $\forall t \geq t_0$ . Since  $(I(t_0), B(t_0)) \gg 0$  in  $C([0, 1], \mathbb{R}^2)$  due to Theorem 2.1 and hypothesis, we can find  $\eta \in (0, 1)$  sufficiently small so that for  $\phi_{\epsilon_0}^*(x) \gg 0$ ,

$$(I(t_0), B(t_0)) \geq \eta \phi_{\epsilon_0}^*.$$

Since  $\lambda_{\epsilon_0}^*$  is the principal eigenvalue with eigenfunctions

$$\phi_{\epsilon_0}^* \triangleq \begin{pmatrix} \phi_{\epsilon_0,1}^* \\ \phi_{\epsilon_0,2}^* \end{pmatrix},$$



we have

$$\begin{pmatrix} D_2 \partial_{xx}^2 \phi_{\epsilon_0,1}^* + ((N^* - \epsilon_0)\beta_1 - (d + \gamma)) \phi_{\epsilon_0,1}^* + (N^* - \epsilon_0) \left( \frac{\beta_2 \phi_{\epsilon_0,2}^*}{\epsilon_0 + K} \right) \\ D_4 \partial_{xx}^2 \phi_{\epsilon_0,2}^* - U \partial_x \phi_{\epsilon_0,2}^* + g \phi_{\epsilon_0,2}^* \left( 1 - \frac{\epsilon_0}{K_B} \right) - \delta \phi_{\epsilon_0,2}^* + \xi \phi_{\epsilon_0,1}^* \end{pmatrix} = \lambda_{\epsilon_0}^* \phi_{\epsilon_0}^*;$$

thus, we see that

$$\begin{cases} \partial_t I = D_2 \partial_{xx}^2 I + ((N^* - \epsilon_0)\beta_1 - (d + \gamma)) I + (N^* - \epsilon_0) \left( \frac{\beta_2}{\epsilon_0 + K} \right) B, \\ \partial_t B = D_4 \partial_{xx}^2 B - U \partial_x B + g B \left( 1 - \frac{\epsilon_0}{K_B} \right) - \delta B + \xi I, \end{cases}$$

has a solution of  $\phi_{\epsilon_0}^*(x)e^{\lambda_{\epsilon_0}^*(t-t_0)}$ . Hence,  $\eta \phi_{\epsilon_0}^*(x)e^{\lambda_{\epsilon_0}^*(t-t_0)}$  is a solution due to the linearity of the system. Therefore, by standard comparison principle argument or specifically application of Theorem 7.3.4 [33] which is applicable because

$$F^- \triangleq \begin{pmatrix} F_1^- \\ F_2^- \end{pmatrix} \triangleq \begin{pmatrix} ((N^* - \epsilon_0)\beta_1 - (d + \gamma)) I + (N^* - \epsilon_0) \left( \frac{\beta_2}{\epsilon_0 + K} \right) B \\ g B \left( 1 - \frac{\epsilon_0}{K_B} \right) - \delta B + \xi I \end{pmatrix}$$

and

$$F \triangleq \begin{pmatrix} F_1 \\ F_2 \end{pmatrix} \triangleq \begin{pmatrix} -[(d + \gamma) - N^*\beta_1]I + N^* \frac{\beta_2}{K} B \\ B(-\delta + g) + \xi I \end{pmatrix}$$

are both cooperative as

$$\frac{\partial F_1^-}{\partial B} = \frac{(N^* - \epsilon_0)\beta_2}{\epsilon_0 + K} \geq 0, \quad \frac{\partial F_1}{\partial B} = \frac{N^*\beta_2}{K} \geq 0, \quad \frac{\partial F_2^-}{\partial I} = \frac{\partial F_2}{\partial I} = \xi \geq 0$$

(see pg. 129 [33]), we see that

$$(I(t, x), B(t, x)) \geq \eta e^{\lambda_{\epsilon_0}^*(t-t_0)} \phi_{\epsilon_0}^*(x) \rightarrow \infty \quad (t \rightarrow \infty).$$

This contradicts (41). □

**7. Discussion.** In this work, we rigorously verify that the SIRS-B epidemic PDE model is globally well-posed, and we establish disease threshold dynamics in terms of the basic reproduction number  $\mathcal{R}_0$  associated with this model. Our result shows that if  $\mathcal{R}_0 < 1$ , the DFE is asymptotically stable; whereas if  $\mathcal{R}_0 > 1$ , the DFE is unstable and the disease will persist; that is,  $\mathcal{R}_0$  is a threshold parameter for local stability of the DFE.

The analysis presented here is intended to inform the dynamics of cholera spatial spread along a theoretical fluvial system. The techniques developed here can be applicable to a broader spectrum of emerging infectious diseases. We would like to point out that there are a number of interesting questions at this point, that would make for interesting future investigations. First, our proof of global well-posedness relies on homogeneous diffusion of human hosts. Practically, infected persons may not be as active as the susceptible and recovered people in terms of their spatial diffusion; i.e.,  $D_2$  might be much smaller than  $D_1$  and  $D_4$ . Secondly, global dynamics of cholera spatial epidemics are still unknown. A more challenging problem is to study the global dynamics and cholera spreading speeds when the spatial domain is a 2D region, and spatial and temporal heterogeneity are considered (for example, heterogeneity due to seasonal effect, disease surveillance and human regulation etc).

**Appendix.** In this Appendix, we derive (31) and (32) for completeness. We multiply (1b) by  $-\partial_{xx}^2 I$  and integrate over  $[0, 1]$  in space to obtain

$$\begin{aligned} & \frac{1}{2} \partial_t \|\partial_x I\|_{L^2}^2 + D \|\partial_{xx}^2 I\|_{L^2}^2 \\ &= \int_0^1 \left[ I(d + \gamma) - S\beta_1 I - S\beta_2 \left( \frac{B}{K + B} \right) \right] \partial_{xx}^2 I dx \end{aligned} \quad (43)$$

where we used a similar computation to (28) due to (3b). Now we estimate

$$\begin{aligned} & \int_0^1 [I(d + \gamma) - S\beta_1 I - S\beta_2 \left( \frac{B}{K + B} \right)] \partial_{xx}^2 I dx \\ & \leq [\|I\|_{L^2}(d + \gamma) + \|S\|_{L^4} \beta_1 \|I\|_{L^4} + \|S\|_{L^2} \beta_2] \|\partial_{xx}^2 I\|_{L^2} \\ & \leq \frac{D}{2} \|\partial_{xx}^2 I\|_{L^2}^2 + c \end{aligned} \quad (44)$$

by Hölder's inequalities, Proposition 1 and Young's inequalities. Applying the estimate of (44) in (43) and absorbing the diffusive term lead to (31). Similarly, we compute

$$\begin{aligned} \frac{1}{2} \partial_t \|\partial_x R\|_{L^2}^2 + D \|\partial_{xx}^2 R\|_{L^2}^2 &= \int_0^1 [R(d + \sigma) - \gamma I] \partial_{xx}^2 R dx \\ &\leq (\|R\|_{L^2}(d + \sigma) + \gamma \|I\|_{L^2}) \|\partial_{xx}^2 R\|_{L^2} \\ &\leq \frac{D}{2} \|\partial_{xx}^2 R\|_{L^2}^2 + c. \end{aligned}$$

Absorbing the diffusive term leads to (32).

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