A GENERAL MULTIPATCH CHOLERA MODEL IN PERIODIC ENVIRONMENTS

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Abstract. This paper is devoted to a general multipatch cholera epidemic model to investigate disease dynamics in a periodic environment. The basic reproduction number $R_0$ is introduced and a threshold type of result is established in terms of $R_0$. Specifically, we show that when $R_0 < 1$, the disease-free steady state is globally attractive if either immigration of hosts is homogeneous or immunity loss of human hosts can be neglected; when $R_0 > 1$, the disease is uniformly persistent and our system admits at least one positive periodic solution. Numerical simulations are carried out to illustrate the impact of asymptotic infections and population dispersal on the spread of cholera. Our result indicates that (a) neglecting asymptotic infections may underestimate the risk of infection; (b) travel can help the disease to become persistent (resp. eradicated) in the network, even though the disease dies out (resp. persists) in each isolated patch.

1. Introduction. Cholera is an ancient intestinal disease for humans. The causative agent of the disease, *Vibrio cholerae*, is a water-borne bacterium that is a natural inhabitant of brackish aquatic environments. The colonization and multiplication of *Vibrio cholerae* O1 or O139 within the human small intestine can lead to an acute diarrhoeal infection, which can spread rapidly in populations with limited access to clean water and sanitation resources, especially in areas where the public health infrastructure is underdeveloped. The disease can be transmitted to humans through indirect contact with the contaminated aquatic environment (e.g., ingesting contaminated water or food), or indirect contact with infected individuals (e.g., hugging, shaking hands and eating food prepared by infected individuals) [15, 23].

The dynamics of cholera involve multiple interactions among the human host, the...
pathogen, and the environment [25]. Even though cholera has been an object of intense study for over a hundred years, it remains a major public health burden across the globe. The disease has resulted in a number of outbreaks spanning the continents of Africa, America, and Asia, including the recent devastating outbreaks in Zimbabwe (2008-2009), Haiti (2010-2012), as well as the one in Yemen (2016-2020), which is the largest documented cholera outbreak in history, with more than 1.3 million reported cases and over 2,800 deaths [4, 39].

In order to better understand the transmission dynamics of cholera, a large body of deterministic mathematical models have been proposed and analyzed (e.g., [1, 5, 6, 7, 8, 9, 13, 14, 15, 23, 25, 27, 31, 41, 40, 36] and the references therein). Most of these models are built upon relatively simple autonomous ordinary differential equation (ODE) systems, where detailed stability and bifurcation analysis are allowed. Although useful results have been obtained, such models should be considered as unrealistic. This is because spatial and temporal heterogeneities (involving distinctions in ecological and geographical environments, population characteristics, and socioeconomic structures) cause variations in the disease contact rates, human activity levels, bacterial dispersal and degradation, etc., which in turn strongly affect cholera dynamics. First, the need for two infectious classes was emphasized by making a distinction between asymptomatic (mild/inapparent) and symptomatic (severe) infections in infected individuals [11, 20, 24]. Secondly, cholera is a seasonal disease in many endemic places and infection peaks often occur annually in the rainy or monsoon season [34]. Several studies have been devoted to seasonal variation in cholera dynamics [9, 12, 11, 22, 27]. For instance, Codeço [9] conducted simple numerical simulation to study cholera dynamics in three scenarios with time-periodic parameters. Eisenberg et al. [12] published an ODE model with the inclusion of a time-dependent parameter to account for rainfall in Haiti. Posny and Wang [27] developed and analyzed a general ODE system of cholera epidemics that incorporates seasonality. Thirdly, the disease threshold dynamics are highly heterogeneous and the underlying transmission pattern varied widely among different regions [16, 23]. Efforts have already been made to study the spatial dynamics of cholera transmission. ODE models based on patch/network structures were investigated in [13, 28, 33]. Models based on partial differential equations (PDEs) were also proposed and analyzed to study spatial dynamics of cholera (e.g., [3, 7, 35, 36, 38] and the references therein). For example, Wang et al. [38] utilized a reaction-convection-diffusion system to study the spatial-temporal dynamics of cholera transmission, which incorporates seasonality and spatial heterogeneity into the model. Although there are no rigorous derivations, models like [38] are expected to correspond to the limiting case of infinitely many patches, each with infinitely large population.

The goal of this work is to investigate the epidemic dynamics of cholera in non-homogeneous environments using a multipatch model. Motivated by [11, 13, 24, 27], we propose a general cholera model to study disease dynamics in a periodic environment of $n$ patches, where the disease can spread from one patch to the other due to human hosts moving between regions and the pathogen (i.e., the bacterium $Vibrio cholerae$) moving along water in a hydrological landscape (e.g., a river network). This model makes a distinction between asymptomatic and symptomatic infections in infected hosts, uses time-periodic parameters to describe the seasonality of the disease transmission, and incorporates the spatial movement of the hosts and
pathogens in a heterogeneous environment with \( n \) patches. Our focus is to investigate the impact of asymptotic infections and population dispersal on the spread of cholera in non-homogeneous environments. Our model takes the form:

\[
\begin{align*}
\frac{dS_i}{dt} &= \Lambda_i - S_i f_i(t, I_{A_i}, I_{S_i}, B_i) + \sigma_i R_i - \mu_i S_i + \sum_{j=1}^{n}\left(D_{ij}^S S_j - D_{ij}^S S_i\right), \\
\frac{dI_{A_i}}{dt} &= p_i S_i f_i(t, I_{A_i}, I_{S_i}, B_i) - (\mu_{A_i} + \gamma_{A_i}) I_{A_i} + \sum_{j=1}^{n}\left(D_{ij}^{A_i} I_{A_j} - D_{ij}^{A_i} I_{A_i}\right), \\
\frac{dI_{S_i}}{dt} &= (1 - p_i)S_i f_i(t, I_{A_i}, I_{S_i}, B_i) - (\mu_{S_i} + \gamma_{S_i}) I_{S_i} + \sum_{j=1}^{n}\left(D_{ij}^{S_i} I_{S_j} - D_{ij}^{S_i} I_{S_i}\right), \\
\frac{dB_i}{dt} &= h_i(t, I_{A_i}, I_{S_i}, B_i) + \sum_{j=1}^{n}\left(D_{ij}^{B_i} B_j - D_{ij}^{B_i} B_i\right), \\
S_i(0) &\geq 0, \quad I_{A_i}(0) \geq 0, \quad I_{S_i}(0) \geq 0, \quad R_i(0) \geq 0, \quad B_i(0) \geq 0, \quad i = 1, 2, \cdots, n, 
\end{align*}
\]  

(1)

where

\[
\mu_i \leq \mu_{A_i} \leq \mu_{S_i}, \quad i = 1, 2, \cdots, n. 
\]  

(2)

Here \( S_i(t), I_{A_i}(t), I_{S_i}(t) \), and \( R_i(t) \) denote the number of susceptible, infected in asymptomatic and symptomatic class, and recovered humans, respectively, and \( B_i(t) \) is the concentration of bacteria in the environment in patch \( i \) at time \( t \). In this paper, we refer infected human individuals with asymptomatic (resp. symptomatic) infections to as non-infectious infected (resp. infectious) hosts. We assume

| Definition | 
|---|---|
| \( \Lambda_i \) | Recruitment rate of susceptible humans into patch \( i \) |
| \( \sigma_i \) | Immunity waning rate in path \( i \) |
| \( \mu_i \) | Natural death rate oh hosts in path \( i \) |
| \( p_i \) | Proportion of infections being asymptomatic in path \( i \), \( 0 \leq p_i \leq 1 \) |
| \( \mu_{A_i} \) | Death rate of asymptomatic infected hosts in path \( i \) |
| \( \gamma_{A_i} \) | Recovery rate from asymptomatic infection in path \( i \) |
| \( \mu_{S_i} \) | Death rate of symptomatic infected hosts in path \( i \) |
| \( \gamma_{S_i} \) | Recovery rate from symptomatic infection in path \( i \) |
| \( D_{ij}^u \) | Immigration rate of population \( u \) from path \( i \) to patch \( j \), with \( u = S, I_A, I_S, R, B \) and \( i \neq j \) |

that \( D_{ij}^S \geq 0, D_{ij}^A = 0, \) and \( D^u = (D_{ij}^u) \) is irreducible for \( u = S, I_A, I_S, R, B \), and the rest of parameters are all positive. The matrix \( D^u \) represents the spatial movement of population \( u \) between patches, \( u = S, I_A, I_S, R, B \). The general incidence function \( f_i(t, I_{A_i}, I_{S_i}, B_i) \) describes the transmission rate caused by direct and indirect transmission pathways. The function \( h_i(t, I_{A_i}, I_{S_i}, B_i) \) captures the rate of change of the bacterial concentration in the environment. We assume that the functions \( f_i(t, x_1, x_2, x_3) \) and \( h_i(t, x_1, x_2, x_3) \) are \( \tau \)-periodic in time. Moreover, for all \( t \in \mathbb{R}, x_1, x_2, x_3 \geq 0 \), the functions \( f_i \) and \( h_i \) \((i = 1, 2, \cdots, n)\) satisfy the following assumptions:

(A1) \( f_i(t, 0, 0, 0) = h_i(t, 0, 0, 0) = 0 \);  
(A2) \( f_i(t, x_1, x_2, x_3) \geq 0 \);  
(A3) \( f_i(t, 0, x_3) > 0 \) if \( x_3 > 0 \); \( h_i(t, x_1, x_2, 0) > 0 \) if \( x_1 > 0 \) or \( x_2 > 0 \);
simplicity, we drop the subscript 1 and the system takes the form:

$$\begin{align*}
2. \text{Single-patch model.} \text{Consider the single-patch case of our model (1). For} \text{simplicity, we drop the subscript 1 and the system takes the form:} \\
\frac{dS}{dt} &= \Lambda - Sf(t, I_A, I_S, B) + \sigma R - \mu S, \\
\frac{dI_A}{dt} &= pSf(t, I_A, I_S, B) - (\mu_A + \gamma_A)I_A, \\
\frac{dI_S}{dt} &= (1 - p)Sf(t, I_A, I_S, B) - (\mu_S + \gamma_S)I_S, \\
\frac{dR}{dt} &= \gamma_A I_A + \gamma_S I_S - (\mu + \sigma)R, \\
\frac{dB}{dt} &= h(t, I_A, I_S, B), \\
S(0) &\geq 0, \quad I_A(0) \geq 0, \quad I_S(0) \geq 0, \quad R(0) \geq 0, \quad B(0) \geq 0.
\end{align*}$$

Note that if \(p = 0\) (resp. \(p = 1\)), then the dynamics of system (4) can be reduced to a lower-dimensional system \((S, I_S, R, B)\) (resp. \((S, I_A, R, B)\)) and the mathematical arguments will be similar to those in this section, and we omit the details. In this paper, we only focus on the investigation in the case where \(0 < p < 1\).

We first show that \(\mathbb{R}_+^5\) is positively invariant for (4). For any \((S^0, I_A^0, I_S^0, R^0, B^0) \in \mathbb{R}_+^5\), it follows from [29, Theorem 5.2.1] that system (4) has a unique local nonnegative solution

\[(S(t), I_A(t), I_S(t), R(t), B(t)) \in \mathbb{R}_+^5\]

through the initial value

\[(S(0), I_A(0), I_S(0), R(0), B(0)) = (S^0, I_A^0, I_S^0, R^0, B^0).\]
The following system will play an important role in our subsequent discussions:

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \mu S, \\
S(0) &\geq 0.
\end{align*}
\]  

**Lemma 2.1.** System (5) admits a unique positive steady state \( S^* := \frac{\Lambda}{\mu} \) which is globally attractive in \( \mathbb{R} \), that is, for any \( S(0) \in \mathbb{R} \), we have

\[
\lim_{t \to \infty} S(t) = S^*.
\]

Let

\[
N(t) = S(t) + I_A(t) + I_S(t) + R(t)
\]

represent the total population of human. Then it follows from (4) and the facts \( \mu \leq \mu_A \) and \( \mu \leq \mu_S \) that

\[
\frac{dN(t)}{dt} \leq \Lambda - \mu N(t).
\]

From the comparison arguments and Lemma 2.1, we see that \( N(t) \) is ultimately bounded. By the positivity of solutions of (4), and (6), it follows that \( S(t), I_A(t), I_S(t), \) and \( R(t) \) are ultimately bounded. From the fifth equations of (4), we see that \( B(t) \) is also ultimately bounded. Thus, the solutions of system (4) exist globally on the interval \([0, \infty)\).

Therefore, we have the following result:

**Lemma 2.2.** \( \mathbb{R}_+^5 \) is positively invariant for (4) and system (4) admits a unique bounded solution with the initial value in \( \mathbb{R}_+^5 \). Further, (4) admits a connected global attractor on \( \mathbb{R}_+^5 \) which attracts all positive orbits in \( \mathbb{R}_+^5 \).

### 2.1. Basic reproduction number of system (4)

In order to find the disease-free steady state, we first substitute \( I_A(t) = I_S(t) = B(t) = 0 \) into system (4), and it follows that \( R \) satisfies

\[
\begin{align*}
\frac{dR}{dt} &= -(\mu + \sigma)R, \\
R(0) &\geq 0.
\end{align*}
\]

It is easy to see that

\[
\lim_{t \to \infty} R(t) = 0.
\]

This implies that \( S(t) \) in system (4) is asymptotic to system (5). By the theory of asymptotically periodic semiflows (see, e.g., [43] or [44, section 3.2]) and Lemma 2.1, it follows that

\[
\lim_{t \to \infty} S(t) = S^*.
\]

Thus, the disease-free steady state takes the following form

\[
E_0 = (S, I_A, I_S, R, B) = (S^*, 0, 0, 0, 0).
\]

Before proceeding, we introduce some notations for simplicity.

\[
\begin{align*}
\beta_A(t) &= \frac{\partial f(t, 0, 0, 0)}{\partial I_A}, & \beta_S(t) &= \frac{\partial f(t, 0, 0, 0)}{\partial I_S}, & \beta_B(t) &= \frac{\partial f(t, 0, 0, 0)}{\partial B}, \\
\xi_A(t) &= \frac{\partial h(t, 0, 0, 0)}{\partial I_A}, & \xi_S(t) &= \frac{\partial h(t, 0, 0, 0)}{\partial I_S}, & \delta(t) &= -\frac{\partial h(t, 0, 0, 0)}{\partial B}.
\end{align*}
\]

By (A4), all the functions defined in (9) are positive.

Linearizing the system (4) at the disease-free steady state \( E_0 \), we then get the following linear system
\[ \begin{align*}
\frac{dI_A}{dt} &= pS^* [\beta_A(t)I_A + \beta_S(t)I_S + \beta_B(t)B] - (\mu_A + \gamma_A)I_A, \\
\frac{dI_S}{dt} &= (1-p)S^* [\beta_A(t)I_A + \beta_S(t)I_S + \beta_B(t)B] - (\mu_S + \gamma_S)I_S, \\
\frac{dB}{dt} &= \xi_A(t)I_A + \xi_S(t)I_S - \delta(t)B.
\end{align*} \]  

From (A4), it follows that system (10) is cooperative (see, e.g., [29]) and irreducible (see a simple test on page 256 of [30]). From system (10), we define

\[ \mathbb{F}(t) = \begin{pmatrix} pS^*\beta_A(t) & pS^*\beta_S(t) & pS^*\beta_B(t) \\ (1-p)S^*\beta_A(t) & (1-p)S^*\beta_S(t) & (1-p)S^*\beta_B(t) \\ 0 & 0 & 0 \end{pmatrix}, \]  

and

\[ \mathbb{V}(t) = \begin{pmatrix} \mu_A + \gamma_A & 0 & 0 \\ 0 & \mu_S + \gamma_S & 0 \\ -\xi_A(t) & -\xi_S(t) & \delta(t) \end{pmatrix}. \]  

Suppose \( \Phi_{\mathbb{V}L}(t) \) is the monodromy matrix of the linear \( \tau \)-periodic differential system \( \frac{d\xi(t)}{dt} = \mathbb{V}(t)\xi, \) and \( r(\Phi_{\mathbb{V}L}(\tau)) \) is the spectral radius of \( \Phi_{\mathbb{V}L}(\tau) \). Assume \( Y(t, s), \ t \geq s, \) is the evolution operator of the linear \( \tau \)-periodic system

\[ \frac{dy(t)}{dt} = -\mathbb{V}(t)y, \]  

that is, for each \( s \in \mathbb{R}, \) the \( 3 \times 3 \) matrix \( Y(t, s) \) satisfies

\[ \frac{d}{dt} Y(t, s) = -\mathbb{V}(t)Y(t, s), \ \forall \ t \geq s, \ Y(s, s) = I, \]

where \( I \) is the \( 3 \times 3 \) matrix. Thus, the fundamental solution matrix \( \Phi_{-\mathbb{V}L}(t) \) of (13) is equal to \( Y(t, 0), \ t \geq 0. \)

We assume that \( \phi(s), \tau \)-periodic in \( s, \) is the initial distribution of infectious individuals. Then \( \mathbb{F}(s)\phi(s) \) is the rate of new infections produced by the infected individuals who were introduced at time \( s. \) Given \( t \geq s, \) then \( Y(t, s)\mathbb{F}(s)\phi(s) \) gives the distribution of those infected individuals who were newly infected at time \( s \) and remain in the infected compartments at time \( t. \) It follows that

\[ \psi(t) := \int_{-\infty}^{t} Y(t, s)\mathbb{F}(s)\phi(s)ds = \int_{0}^{\infty} Y(t, t - a)\mathbb{F}(t - a)\phi(t - a)da \]

is the distribution of accumulative new infections at time \( t \) produced by all those infected individuals \( \phi(s) \) introduced at time previous to \( t. \)

Let \( C_{\tau} \) be the ordered Banach space of all \( \tau \)-periodic functions from \( \mathbb{R} \) to \( \mathbb{R}^3, \) which is equipped with the maximum norm \( \| \cdot \| \) and the positive cone \( C^+_\tau := \{ \phi \in C_{\tau} : \phi(t) \geq 0, \ \forall \ t \in \mathbb{R} \}. \) Then we define a linear operator \( L : C_{\tau} \rightarrow C_{\tau} \) by

\[ (L\phi)(t) = \int_{0}^{\infty} Y(t, t - a)\mathbb{F}(t - a)\phi(t - a)da, \ \forall \ t \in \mathbb{R}, \ \phi \in C_{\tau}. \]  

Then we call \( L \) the next infection operator [37], and define the basic reproduction number as \( \mathcal{R}_0 := r(L), \) the spectral radius of \( L. \)

In the case where (4) is autonomous, the time-dependent functions defined in (9) all become constant, \( S^* = \Lambda/\mu, \) and

\[ \mathcal{R}_0^A = \frac{p\Lambda (\beta_A \delta + \beta_B \xi_A)}{\mu \delta (\mu_A + \gamma_A)} + \frac{(1-p)\Lambda (\beta_S \delta + \beta_B \xi_S)}{\mu \delta (\mu_S + \gamma_S)} := \mathcal{R}_{0A} + \mathcal{R}_{0S}. \]
The quantities $R_{0A}$ and $R_{0S}$ measure the contribution of $I_A$ and $I_S$, respectively, to the overall infection risk.

We further have the following result:

**Lemma 2.3.** [37, Theorem 2.2] The following statements hold.

(i) $R_A^0 = 1$ if and only if $r(\Phi(\cdot) - \psi(\cdot)(\tau)) = 1$;
(ii) $R_A^0 > 1$ if and only if $r(\Phi(\cdot) - \psi(\cdot)(\tau)) > 1$;
(iii) $R_A^0 < 1$ if and only if $r(\Phi(\cdot) - \psi(\cdot)(\tau)) < 1$.

Thus, the disease-free steady state $E_0(t)$ is locally asymptotically stable if $R_A^0 < 1$, and unstable if $R_A^0 > 1$.

### 2.2. Threshold dynamics

Here we review some basic results related to a monodromy matrix that is needed for our subsequent discussions. Let $A(t)$ be a continuous, cooperative, irreducible, and $\tau$-periodic $k \times k$ matrix function. Suppose $\Phi_{A(t)}(t)$ is the monodromy matrix of the linear ordinary differential system

$$
\frac{dx(t)}{dt} = A(t)x,
$$

and $r(\Phi_{A(t)}(\tau))$ is the spectral radius of $\Phi_{A(t)}(\tau)$. From [2, Lemma 2] (see also [17, Theorem 1.1]), it follows that $\Phi_{A(t)}(t)$ is a matrix with all entries positive for each $t > 0$. By the Perron-Frobenius theorem, $r(\Phi_{A(t)}(\tau))$ is the principal eigenvalue of $\Phi_{A(t)}(\tau)$ in the sense that it is simple and admits a positive eigenvector. We further have the following results:

**Lemma 2.4.** ([42, Lemma 2.1]) Let $\lambda = \frac{1}{\tau} \ln r(\Phi_{A(t)}(\tau))$. Then there exists a positive, $\tau$-periodic function $v(t)$ such that $e^{\lambda t}v(t)$ is a solution of (16).

Let $X = \mathbb{R}^5_+$. Suppose $P : X \to X$ is the Poincaré map associated with system (4), that is,

$$
P(x^0) = u(\tau, x^0), \quad \forall \ x^0 := (S^0, I_A^0, I_S^0, R^0, B^0) \in X,
$$

where $u(t, x^0)$ is the unique solution of system (4) with $u(0, x^0) = x^0$. It is easy to see that

$$
P^n(x^0) = u(n\tau, x^0), \quad \forall \ n \geq 0.
$$

Let

$$
X_0 := \{(S, I_A, I_S, R, B) \in X : (I_A, I_S, B) \neq (0, 0, 0)\},
$$

and

$$
\partial X_0 := X \setminus X_0 = \{(S, I_A, I_S, R, B) \in X : I_A = I_S = B = 0\}.
$$

**Lemma 2.5.** Assume that $(S(t), I_A(t), I_S(t), R(t), B(t))$ is a solution of the system (4) with initial value $(S^0, I_A^0, I_S^0, R^0, B^0) \in X_0$. Then $(S(t), I_A(t), I_S(t), R(t), B(t)) \gg 0$, $\forall \ t > 0$.

**Proof.** Given an initial value $(S^0, I_A^0, I_S^0, R^0, B^0) \in X_0$. In view of the first equation of system (4), it follows that

$$
S(t) = e^{-\int_0^t b(s_1)ds_1} \left[ \int_0^t e^{\int_0^s b(s_1)ds_1} a(s_2)ds_2 + S^0 \right],
$$

where

$$
a(t) := \Lambda + \sigma R(t) \geq \Lambda > 0,
$$

and

$$
b(t) := f(t, I_A, I_S, B) + \mu.
$$
Thus, $S(t) > 0$, $\forall t > 0$. Observing that $f(t, 0, 0, 0) = 0$ and 
\[
\frac{df(t, \theta I_A, \theta I_S, \theta B)}{d\theta} = \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_A)} I_A + \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_S)} I_S + \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta B)} B.
\]
Integrating both sides from $\theta = 0$ to $\theta = 1$ and using (A4), we can rewrite $f(t, I_A, I_S, B)$ as follows
\[
f(t, I_A, I_S, B) = a_1(t) I_A + a_2(t) I_S + a_3(t) B,
\]
where
\[
\begin{align*}
a_1(t) &= \int_0^1 \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_A)} d\theta > 0, \\
a_2(t) &= \int_0^1 \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_S)} d\theta > 0, \\
a_3(t) &= \int_0^1 \frac{\partial f(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta B)} d\theta > 0.
\end{align*}
\]
(20)

Similarly, we can rewrite $h(t, I_A, I_S, B)$ as follows
\[
h(t, I_A, I_S, B) = b_1(t) I_A + b_2(t) I_S + b_3(t) B,
\]
where
\[
\begin{align*}
b_1(t) &= \int_0^1 \frac{\partial h(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_A)} d\theta > 0, \\
b_2(t) &= \int_0^1 \frac{\partial h(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta I_S)} d\theta > 0, \\
b_3(t) &= \int_0^1 \frac{\partial h(t, \theta I_A, \theta I_S, \theta B)}{\partial (\theta B)} d\theta < 0.
\end{align*}
\]
(21)

By [29, Theorem 4.1.1] as generalized to nonautonomous systems, the irreducibility of the cooperative matrix
\[
\begin{pmatrix}
pS(t)a_1(t) - (\mu + \gamma_A) & pS(t)a_2(t) & pS(t)a_3(t) \\
(1-p)S(t)a_1(t) & (1-p)S(t)a_2(t) - (\mu S + \gamma_S) & (1-p)pS(t)a_3(t) \\
b_1(t) & b_2(t) & b_3(t)
\end{pmatrix}
\]
(22)

implies that
\[
(I_A(t), I_S(t), B(t))^T \succ 0, \quad \forall t > 0.
\]
(23)
In view of the fourth equation of system (4) and (23), we can further show that $R(t) > 0$, $\forall t > 0$. We complete the proof.

\[\square\]

Remark 2.1. In the proof of Lemma 2.5, we see that the assumption (A4) can be weakened since we only need the matrix given in (22) is cooperative and irreducible.

Lemma 2.6. Let $\mathcal{R}_f^* > 1$. Then there exists $\sigma_0 > 0$ such that for any $(S^0, r^0_A, r^0_S, R^0, B^0) \in \mathcal{X}_0$ with
\[
\| (S^0, r^0_A, r^0_S, R^0, B^0) - \mathcal{E}_0 \| \leq \sigma_0,
\]
we have
\[
\limsup_{n \to \infty} \| (S^n(S^0, r^0_A, r^0_S, R^0, B^0) - \mathcal{E}_0) \| \geq \sigma_0.
\]

Proof. Since $\mathcal{R}_f^* > 1$, Lemma 2.3 implies that $r(\Phi_{\mathcal{E}_0}(\cdot) - \mathcal{V}(\cdot)(\tau)) > 1$. Thus, we may choose $\rho_0 > 0$ small enough such that $0 < \rho_0 < \rho^*$ and $r(\Phi_{\mathcal{E}_0}(\cdot) - \mathcal{V}(\cdot) + \mathcal{H}_{\rho_0}(\cdot)) > 1$, where
\[
\mathcal{H}_{\rho_0}(t) = \begin{pmatrix}
\mathbb{H}_{11}(t) & \mathbb{H}_{12}(t) & \mathbb{H}_{13}(t) \\
\mathbb{H}_{21}(t) & \mathbb{H}_{22}(t) & \mathbb{H}_{23}(t) \\
\mathbb{H}_{31}(t) & \mathbb{H}_{32}(t) & \mathbb{H}_{33}(t)
\end{pmatrix}
\]
with the following entries

\[
\begin{align*}
H_{11}(t) &= p(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial t^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial t \partial I} \right| \right], \\
H_{12}(t) &= p(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial t^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial t \partial B} \right| \right], \\
H_{13}(t) &= p(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial B^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial t \partial B} \right| \right], \\
H_{21}(t) &= (1 - p)(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial I_A^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial I_A \partial I} \right| \right], \\
H_{22}(t) &= (1 - p)(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial I_A^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial I_A \partial B} \right| \right], \\
H_{23}(t) &= (1 - p)(S^*(t) - \rho_0)\rho_0\left[\frac{1}{2} \frac{\partial^2 f(t,0,0,0)}{\partial B^2} - \left| \frac{\partial^2 f(t,0,0,0)}{\partial I_A \partial B} \right| \right], \\
H_{31}(t) &= \rho_0\left[\frac{1}{2} \frac{\partial^2 h(t,0,0,0)}{\partial I_A^2} - \left| \frac{\partial^2 h(t,0,0,0)}{\partial I_A \partial I} \right| \right], \\
H_{32}(t) &= \rho_0\left[\frac{1}{2} \frac{\partial^2 h(t,0,0,0)}{\partial I_A^2} - \left| \frac{\partial^2 h(t,0,0,0)}{\partial I_A \partial B} \right| \right], \\
H_{33}(t) &= \rho_0\left[\frac{1}{2} \frac{\partial^2 h(t,0,0,0)}{\partial B^2} - \left| \frac{\partial^2 h(t,0,0,0)}{\partial I_A \partial B} \right| \right].
\end{align*}
\]

By the continuity of the solutions with respect to the initial values, there exists a $\sigma_0 > 0$ such that for all $(S^0, I^0_A, I^0_B, R^0, B^0) \in \mathbb{K}_0$ with

$$
\|(S^0, I^0_A, I^0_B, R^0, B^0) - \mathcal{E}_0\| \leq \sigma_0,
$$

there holds $\|u(t, (S^0, I^0_A, I^0_B, R^0, B^0)) - u(t, \mathcal{E}_0)\| < \rho_0, \forall t \in [0, \tau]$.

**Claim.**

$$
\limsup_{n \to \infty} \|P^n(S^0, I^0_A, I^0_B, R^0, B^0), \mathcal{E}_0\| \geq \sigma_0.
$$

Assume, by contradiction, that the above claim does not hold. Then we have

$$
\limsup_{n \to \infty} \|P^n(S^0, I^0_A, I^0_B, R^0, B^0), \mathcal{E}_0\| < \sigma_0,
$$

for some $(S^0, I^0_A, I^0_B, R^0, B^0)) \in \mathbb{K}_0$. Without loss of generality, we assume that

$$
\|P^n(S^0, I^0_A, I^0_B, R^0, B^0), \mathcal{E}_0\| < \sigma_0, \forall n \geq 0.
$$

It follows that

$$
\|u(t, P^n(S^0, I^0_A, I^0_B, R^0, B^0)) - u(t, \mathcal{E}_0)\| < \rho_0, \forall t \in [0, \tau], n \geq 0.
$$

For any $t \geq 0$, let $t = m\tau + t'$, where $t' \in [0, \tau)$, and $m$ is the largest integer less than or equal to $\frac{t}{\tau}$. Therefore, we have

$$
\|u(t, (S^0, I^0_A, I^0_B, R^0, B^0)) - u(t, \mathcal{E}_0)\| = \|u(t', P^m(S^0, I^0_A, I^0_B, R^0, B^0)) - u(t', \mathcal{E}_0)\| < \rho_0.
$$

(24)

Note that

$$(S(t), I_A(t), I_S(t), R(t), B(t)) = u(t, (S^0, I^0_A, I^0_B, R^0, B^0))$$

and $u(t, \mathcal{E}_0) = \mathcal{E}_0, \forall t \geq 0$. It then follows from (24) that for all $t \geq 0$, we have

$$S(t) > S^* - \rho_0 > 0, 0 < I_A(t) < \rho_0, 0 < I_S(t) < \rho_0, 0 < B(t) < \rho_0.$$

From the equations of $I_A$ in (4), it follows that

$$
\frac{dI_A}{dt} \geq p(S^* - \rho_0)f(t, I_A, I_S, B) - (\mu + \gamma_A)I_A.
$$
Using (A1), (A5), (A6) and (A7), we have
\[ f(t, I_A, I_S, B) \geq \beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B \]
\[ + \frac{1}{2} \rho_0 \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A^2} I_A + \frac{1}{2} \rho_0 \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S^2} I_S + \frac{1}{2} \rho_0 \frac{\partial^2 f(t, 0, 0, 0)}{\partial B^2} B \]
\[ + \rho_0 \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial I_S} \right| I_A - \rho_0 \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial B} \right| \]
\[ B - \rho_0 \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S \partial B} \right| I_S. \]
Then
\[ \frac{dI_A}{dt} \geq p(S^* - \rho_0) \left[ \beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B \right] - (\mu + \gamma_A) I_A \]
\[ + p(S^* - \rho_0) \rho_0 \left[ \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A^2} I_A + \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S^2} I_S + \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial B^2} B \right] \]
\[ - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial I_S} \right| I_A - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial B} \right| \]
\[ I_S - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S \partial B} \right| B \].

Similarly, we also have
\[ \frac{dI_S}{dt} \geq (1 - p)(S^* - \rho_0) \left[ \beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B \right] - (\mu_S + \gamma_S) I_S \]
\[ + (1 - p)(S^* - \rho_0) \rho_0 \left[ \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A^2} I_A + \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S^2} I_S + \frac{1}{2} \frac{\partial^2 f(t, 0, 0, 0)}{\partial B^2} B \right] \]
\[ - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial I_S} \right| I_A - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_A \partial B} \right| \]
\[ I_S - \left| \frac{\partial^2 f(t, 0, 0, 0)}{\partial I_S \partial B} \right| B \].

And
\[ \frac{dB}{dt} \geq [\xi_A(t) I_A + \xi_S(t) I_S - \delta(t) B] \]
\[ + \rho_0 \left[ \frac{1}{2} \frac{\partial^2 h(t, 0, 0, 0)}{\partial I_A^2} I_A + \frac{1}{2} \frac{\partial^2 h(t, 0, 0, 0)}{\partial I_S^2} I_S + \frac{1}{2} \frac{\partial^2 h(t, 0, 0, 0)}{\partial B^2} B \right] \]
\[ - \left| \frac{\partial^2 h(t, 0, 0, 0)}{\partial I_A \partial I_S} \right| I_A - \left| \frac{\partial^2 h(t, 0, 0, 0)}{\partial I_A \partial B} \right| \]
\[ I_S - \left| \frac{\partial^2 h(t, 0, 0, 0)}{\partial I_S \partial B} \right| B \].

Since \((S^0, I^0_A, I^0_S, R^0, B^0) \in X_0\), it follows from Lemma 2.5 that
\[ (I_A(t), I_S(t), B(t)) \gg 0, \quad \forall \ t > 0. \]

Thus, we may fix a \( \tilde{t}_0 > 0 \) such that \((I_A(\tilde{t}_0), I_S(\tilde{t}_0), B(\tilde{t}_0)) \gg 0\).

By Lemma 2.4, it follows that there exists a positive, \( \tau \)-periodic function \( J(t) \) and \( \tilde{\lambda} = \frac{1}{\tau} \ln \tau \left( \Phi(t) - \Psi(t) + H_\rho(t) \right) \) such that \( \tilde{J}(t) := d_{\tilde{\lambda}}(t - \tilde{t}_0) J(t) \) is a solution of
\[ \frac{dx(t)}{dt} = (\Psi(t) - \Psi(t) + H_\rho(t)) x(t), \]
where \( \tilde{d} \) satisfies \( \tilde{J}(\tilde{t}_0) := \tilde{d} J(\tilde{t}_0) \leq (I_A(\tilde{t}_0), I_S(\tilde{t}_0), B(\tilde{t}_0)) \). The standard comparison theorem (see, e.g., [30, Theorem B.1]) implies that
\[ (I_A(t), I_S(t), B(t)) \geq \tilde{J}(t), \quad \forall \ t \geq \tilde{t}_0. \]

In particular, there exists \( n_1 \) such that
\[ (I_A(n\tau), I_S(n\tau), B(n\tau)) \geq \tilde{J}(n\tau), \quad \forall \ n \geq n_1. \]
Since \( \tilde{n} > 0 \), it follows that \( \tilde{J}(n\tau) \to \infty \) as \( n \to \infty \). Thus, \((I_A(n\tau), I_S(n\tau), B(n\tau)) \to \infty \) as \( n \to \infty \). This contradiction completes the proof. \( \square \)
Theorem 2.1. The following statements hold.

(i) If $R_0^* < 1$, then the disease-free state $E_0$ is globally attractive for system (4) in the sense that

$$
\lim_{t \to \infty} (S(t), I_A(t), I_S(t), R(t), B(t)) = E_0;
$$

(ii) If $R_0^* > 1$, then there exists an $\eta > 0$ such that for any solution

$$(S(t), I_A(t), I_S(t), R(t), B(t))$$

with initial value $(S_0^0, I_A^0, I_S^0, R^0, B^0) \in \mathcal{X}_0$ satisfies

$$\liminf_{t \to \infty} I_A(t) \geq \eta, \quad \liminf_{t \to \infty} I_S(t) \geq \eta, \quad \liminf_{t \to \infty} B(t) \geq \eta.$$

Further, system (4) admits at least one positive $\tau$-periodic solution

$$(\tilde{S}(t), \tilde{I}_A(t), \tilde{I}_S(t), \tilde{R}(t), \tilde{B}(t)).$$

Proof. Part (i). We first consider the case where $R_0^* < 1$. From Lemma 2.3, it follows that $r(\Phi_{E_0^0}(\tau)) < 1$. Now we choose $\xi_0 > 0$ sufficiently small such that $r(\Phi_{E_0^0}(\tau)) < 1$, where $\Phi_{E_0}(t)$ =

$$
\begin{pmatrix}
p(S^* + \xi_0)\beta_A(t) & p(S^* + \xi_0)\beta_S(t) & p(S^* + \xi_0)\beta_B(t) \\
(1-p)(S^* + \xi_0)\beta_A(t) & (1-p)(S^* + \xi_0)\beta_S(t) & (1-p)(S^* + \xi_0)\beta_B(t)
\end{pmatrix}.
$$

If $(S(t), I_A(t), I_S(t), R(t), B(t))$ is a nonnegative solution of system (4) in $\mathcal{X}$, then it follows from (6), (7), Lemma 2.1, together with the comparison arguments that there is a $t_0 > 0$ such that for any $t \geq t_0$, we have

$$S(t) \leq S^* + \xi_0.$$

By Lemma 2.4, it follows that there exists a positive, $\tau$-periodic function $v(t)$ and

$$\lambda = \frac{1}{\tau} \ln \left[ r(\Phi_{E_0^0}(\tau)) \right]$$

such that $\tilde{v}(t) := d e^{\lambda t} v(t)$ is a solution of

$$\frac{dx(t)}{dt} = (\Phi_{E_0}(t) - \mathcal{V}(t)) x(t),$$

where $\tilde{d}$ satisfies $\tilde{v}(t_0) := \tilde{d}v(t_0) \geq (I_A(t_0), I_S(t_0), B(t_0))$.

On the other hand, it follows from assumption (A5) that

$$f(t, I_A, I_S, B) \leq \beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B,$$

and

$$h(t, I_A, I_S, B) \leq \xi_A(t) I_A + \xi_S(t) I_S - \delta(t) B.$$

Then it follows from the equations of $I_A, I_S$ and $B$ in (4) that

$$\frac{dI_A}{dt} \leq p(S^* + \xi_0) [\beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B] - (\mu + \gamma_A) I_A, \ t \geq t_0,$$

$$\frac{dI_S}{dt} \leq (1-p)(S^* + \xi_0) [\beta_A(t) I_A + \beta_S(t) I_S + \beta_B(t) B] - (\mu_S + \gamma_S) I_S, \ t \geq t_0,$$

and

$$\frac{dB}{dt} \leq \xi_A(t) I_A + \xi_S(t) I_S - \delta(t) B, \ t \geq t_0.$$

The standard comparison theorem (see, e.g., [30, Theorem B.1]) implies that

$$(I_A(t), I_S(t), B(t)) \leq \tilde{v}(t), \ \forall \ t \geq t_0.$$
Since $\lambda < 0$, it follows that $\bar{v}(t) \to 0$ as $t \to \infty$. Thus, $(I_A(t), I_S(t), B(t)) \to 0$ as $t \to \infty$. Thus, $R(t)$ is asymptotic to system (8), and hence, $\lim_{t \to \infty} R(t) = 0$, where we have used the theory of asymptotically periodic semiflows (see, e.g., [43] or [44, section 3.2]). This implies that $S(t)$ in system (4) is asymptotic to system (5). By the theory of asymptotically periodic semiflows (see, e.g., [43] or [44, section 3.2]) and Lemma 2.1, it follows that $\lim_{t \to \infty} S(t) = S^*$. We complete the proof of Part (i).

Part (ii). We next consider the case where $\mathbb{R}_0^p > 1$. From Lemma 2.2, it follows that the discrete-time system $\{P^n\}_{n \geq 0}$ admits a global attractor in $\mathbb{X}$. Now we prove that $\{P^n\}_{n \geq 0}$ is uniformly persistent with respect to $(\mathbb{X}_0, \partial \mathbb{X}_0)$. By Lemma 2.5, it follows that $\mathbb{X}_0$ and $\partial \mathbb{X}_0$ are positively invariant under the solution flow of (4). Clearly, $\mathbb{X}_0 \cup \partial \mathbb{X}_0 = \mathbb{X}$, $\mathbb{X}_0 \cap \partial \mathbb{X}_0 = \emptyset$, and $\partial \mathbb{X}_0$ is relatively closed in $\mathbb{X}$. Let

$$
M_0 = \{(S^0, I_A^0, I_S^0, R^0, B^0) \in \partial \mathbb{X}_0 : P^n(S^0, I_A^0, I_S^0, R^0, B^0) \in \partial \mathbb{X}_0, \forall n \geq 0\}.
$$

It is easy to show that

$$
M_0 := \{(S^0, I_A^0, I_S^0, R^0, B^0) \in \mathbb{X} : I_A^0 = I_S^0 = R^0 = B^0 = 0\}. \quad \text{(26)}
$$

Actually, it suffices to prove that for any $(S^0, I_A^0, I_S^0, R^0, B^0) \in M_0$ and for any $m \geq 0$, we have $I_A(m\tau) = I_S(m\tau) = B(m\tau) = 0$. If it is not true, then there exists $m_1 \geq 0$ such that $(S^0, I_A^0, I_S^0, R^0, B^0) \in M_0$ and

$$
(I_A(m_1\tau), I_S(m_1\tau), B(m_1\tau)) \not= (0, 0, 0).
$$

Then the irreducibility of the cooperative matrix (22) implies that

$$
(I_A(m\tau), I_S(m\tau), B(m\tau))^T \gg (0, 0, 0), \forall m > m_1.
$$

This contradicts the definition of $M_0$, and hence, (26) is true.

It is clear that there is a unique fixed point of $P$ in $M_0$, which is $\mathbb{E}_0 = (S^*, 0, 0, 0, 0)$. If

$$(S(t), I_A(t), I_S(t), R(t), B(t))$$

is a nonnegative solution of system (4) initiating from $M_0$, it is not hard to see that $(S(t), I_A(t), I_S(t), R(t), B(t))$ approaches $\mathbb{E}_0$ as $t$ approaches $\infty$, that is, every orbit of $P$ in $M_0$ approaches to $\{\mathbb{E}_0\}$. In view of Lemma 2.6, we see that $\{\mathbb{E}_0\}$ is an isolated invariant set in $\mathbb{X}$ and $W^s(\mathbb{E}_0) \cap \mathbb{X}_0 = \emptyset$, where $W^s(\mathbb{E}_0)$ is the stable set of $\mathbb{E}_0$, and $\{\mathbb{E}_0\}$ is acyclic in $M_0$. By [44, Theorem 1.3.1], it follows that $\{P^n\}_{n \geq 0}$ is uniformly persistent with respect to $(\mathbb{X}_0, \partial \mathbb{X}_0)$.

By [44, Theorem 3.1.1], the solutions of system (4) are uniformly persistent with respect to $(\mathbb{X}_0, \partial \mathbb{X}_0)$, that is, there exists an $\eta > 0$ such that for any solution

$$(S(t), I_A(t), I_S(t), R(t), B(t))$$

with initial value $(S^0, I_A^0, I_S^0, R^0, B^0) \in \mathbb{X}_0$ satisfies

$$\lim_{t \to \infty} I_A(t) \geq \eta, \lim_{t \to \infty} I_S(t) \geq \eta, \lim_{t \to \infty} B(t) \geq \eta.$$

Furthermore, [44, Theorem 1.3.6] implies that $P$ has a fixed point

$$(\hat{S}(0), \hat{I}_A(0), \hat{I}_S(0), \hat{R}(0), \hat{B}(0)) \in \mathbb{X}_0,$$

and hence, $\hat{I}_A(0) > 0$, $\hat{I}_S(0) > 0$, $\hat{B}(0) > 0$. By the similar arguments to those in Lemma 2.5, we can further show that

$$(\hat{S}(t), \hat{I}_A(t), \hat{I}_S(t), \hat{R}(t), \hat{B}(t)) \gg 0.$$

We complete the proof of Part (ii). \qed
3. **Multipatch model.** This section is devoted to the study of the dynamics of (1) with the case where \(0 < p_i < 1, \ i = 1, \ldots, n\). We first consider the following system

\[
\begin{align*}
\frac{dS_i}{dt} &= \Lambda_i - \mu_i S_i + \sum_{j=1}^{n} (D_{ij}^S S_j - D_{ij}^S S_i), \\
S_i(0) &\geq 0, \ 1 \leq i \leq n.
\end{align*}
\]  

(27)

The following result is related to the dynamics of system (27):

**Lemma 3.1.** System (27) admits a unique positive equilibrium \(S^* := (S_1^*, S_2^*, \ldots, S_n^*)\) which is globally attractive in \(\mathbb{R}^n\), that is, for any \((S_1(0), \ldots, S_n(0)) \in \mathbb{R}^n\), we have

\[
\lim_{t \to \infty} (S_1(t), S_2(t), \ldots, S_n(t)) = \hat{S}^*.
\]  

(28)

**Proof.** It is easy to see that system (27) is cooperative and strongly subhomogeneous (see, e.g., [44, Section 2.3]). By [44, Theorem 2.3.2], we see that there exists a unique positive equilibrium \((S_1^*, S_2^*, \ldots, S_n^*)\) such that (28) holds. \(\square\)

**Remark 3.1.** For the case where \(n = 1, 2\), we further have the following explicit formula for \((S_1^*, S_2^*)\):

\[
(S_1^*, S_2^*) = \left(\frac{\Lambda_1 (\mu_2 + D_{12}^S) + \Lambda_2 D_{21}^S}{\mu_1 \mu_2 + \mu_1 D_{12}^S + \mu_2 D_{12}^S}, \frac{\Lambda_2 (\mu_1 + D_{12}^S) + \Lambda_1 D_{21}^S}{\mu_1 \mu_2 + \mu_1 D_{12}^S + \mu_2 D_{12}^S}\right).
\]  

(29)

**Lemma 3.2.** \(\mathbb{R}_+^{5n}\) is positively invariant for (1) and system (1) admits a unique bounded solution with the initial value in \(\mathbb{R}_+^{5n}\). Further, (1) admits a connected global attractor on \(\mathbb{R}_+^{5n}\) which attracts all positive orbits in \(\mathbb{R}_+^{5n}\).

**Proof.** For any initial value

\[
v^0 := (\hat{S}^0, \hat{I}_A^0, \hat{I}_S^0, \hat{R}^0, \hat{B}^0) \in \mathbb{R}_+^{5n},
\]  

(30)

it follows from [29, Theorem 5.2.1] that system (1) admits a unique nonnegative solution

\[
v(t, v^0) := (\hat{S}(t), \hat{I}_A(t), \hat{I}_S(t), \hat{R}(t), \hat{B}(t)) \in \mathbb{R}_+^{5n}.
\]  

(31)

Next, we show that solutions of system (1) are eventually bounded. Let

\[
W(t) = \sum_{i=1}^{n} \left(S_i(t) + I_{A_i}(t) + I_{S_i}(t) + R_i(t)\right).
\]  

(32)

In view of system (1), it follows from the assumption (2) that \(W(t)\) satisfies

\[
\frac{dW}{dt} \leq \sum_{i=1}^{n} A_i - \min_{1 \leq i \leq n} \{\mu_i\} W.
\]  

(33)

Then

\[
\limsup_{t \to \infty} W(t) \leq \frac{\sum_{i=1}^{n} A_i}{\min_{1 \leq i \leq n} \{\mu_i\}}.
\]  

(34)

This implies that \(W(t)\) is ultimately bounded. By the positivity of solutions of (1), and (32), it follows that \(S_i(t), I_{A_i}(t), I_{S_i}(t),\) and \(R_i(t)\) are ultimately bounded, \(i = 1, \ldots, n\). Combing those facts and the assumption (A5), it follows that there exist \(t_0 > 0, \ A_{B_j} > 0,\) and \(\mu_{B_j} > 0\) such that

\[
h_j(t, I_{A_j}, I_{S_j}, B_j) \leq A_{B_j} - \mu_{B_j} B_j, \ \forall \ t \geq t_0, \ j = 1, \ldots, n.
\]
From the above inequalities and the fifth equations of (1), we see that \( (B_i(t), \ldots, B_n(t)) \) satisfies
\[
\begin{align*}
\frac{dB_i}{dt} &\leq \Lambda B_i - \mu B_i + \sum_{j=1}^{n} (D_{ji}^B B_j - D_{ij}^B B_i), \quad \forall \ t \geq t_0, \\
B_i(0) &\geq 0, \ i = 1, 2, \ldots, n,
\end{align*}
\]
(35)

By similar arguments in Lemma 3.1 and the Comparison Principle (see, e.g., [29]), we see that
\[
\lim \sup_{t \to \infty} (B_1(t), B_2(t), \ldots, B_n(t)) \leq (B_1^*, B_2^*, \ldots, B_n^*),
\]
where \((B_1^*, B_2^*, \ldots, B_n^*)\) is the unique positive equilibrium of the system
\[
\begin{align*}
\frac{dB_i}{dt} &\leq \Lambda B_i - \mu B_i + \sum_{j=1}^{n} (D_{ji}^B B_j - D_{ij}^B B_i), \quad \forall \ t \geq 0, \\
B_i(0) &\geq 0, \ i = 1, 2, \ldots, n.
\end{align*}
\]
Thus, \((B_1(t), \ldots, B_n(t))\) is also ultimately bounded. Therefore, the solutions of system (1) exist globally on the interval \([0, \infty)\).

In order to determine the disease-free steady state of system (1), we put \(I_{A_i} = I_{S_i} = B_i = 0, \ 1 \leq i \leq n, \) in (1), and we obtain the following subsystem
\[
\begin{align*}
\frac{dS_i}{dt} &= \Lambda_i + \sigma_i R_i - \mu_i S_i + \sum_{j=1}^{n} (D_{ji}^SS_j - D_{ij}^SS_i), \\
\frac{dR_i}{dt} &= -\mu_i S_i + \sum_{j=1}^{n} (D_{ji}^R R_j - D_{ij}^R R_i), \\
S_i(0) &\geq 0, \ R_i(0) \geq 0, \ 1 \leq i \leq n.
\end{align*}
\]
(36)
It is easy to see that the second subsystem in (36) is cooperative and it admits a unique equilibrium \((R_1, R_2, \ldots, R_n) = (0, 0, \ldots, 0)\). Then it follows from the theory in [18] that
\[
\lim_{t \to \infty} (R_1(t), R_2(t), \ldots, R_n(t)) = \hat{0} := (0, 0, \ldots, 0).
\]
Thus, \((S_1(t), S_2(t), \ldots, S_n(t))\) in (36) is asymptotic to the system (27). Thus, the disease-free steady state of system (1) takes the form \(E_0 = (\hat{S}^*, \hat{0}, \hat{0}, \hat{0})^T\), where \(\hat{S}^* = (S_1^*, S_2^*, \ldots, S_n^*)\) and \(\hat{0}\) is the all zeros row vector of dimension \(n\).

Linearizing the system (1) at the disease-free steady state \(E_0 = (\hat{S}^*, \hat{0}, \hat{0}, \hat{0})^T\) yields the following linear system
\[
\begin{align*}
\frac{dI_{A_i}}{dt} &= p_i S_i^* \left[ \beta_{A_i}(t) I_{A_i} + \beta_{S_i}(t) I_{S_i} + \beta_B(t) B_i \right], \\
\frac{dI_{S_i}}{dt} &= (1 - p_i) S_i^* \left[ \beta_{A_i}(t) I_{A_i} + \beta_{S_i}(t) I_{S_i} + \beta_B(t) B_i \right], \\
\frac{dB_i}{dt} &= \xi_{A_i}(t) I_{A_i} + \xi_{S_i}(t) I_{S_i} - \delta_i(t) B_i + \sum_{j=1}^{n} (D_{ji}^B B_j - D_{ij}^B B_i),
\end{align*}
\]
(37)
where
\[
\begin{align*}
\beta_{A_i}(t) &= \frac{\partial f_I(t, 0, 0, 0)}{\partial I_{A_i}}, \quad \beta_{S_i}(t) = \frac{\partial f_I(t, 0, 0, 0)}{\partial I_{S_i}}, \quad \beta_B(t) = \frac{\partial f_I(t, 0, 0, 0)}{\partial B_i}, \\
\xi_{A_i}(t) &= \frac{\partial h_I(t, 0, 0, 0)}{\partial I_{A_i}}, \quad \xi_{S_i}(t) = \frac{\partial h_I(t, 0, 0, 0)}{\partial I_{S_i}}, \quad \delta_i(t) = -\frac{\partial h_I(t, 0, 0, 0)}{\partial B_i},
\end{align*}
\]
(38)
for \(1 \leq i \leq n\).
Before proceeding to define matrices for new infection and transmission, we need to introduce some notations. Let $I_n$ be the $n \times n$ identity matrix, and $0_n$ be the $n \times n$ matrix with all zero entries. Define

\[ V_w = \text{diag}(\mu_w, \gamma_w), w = A, S, \quad V_B(t) = \text{diag}(\delta_i(t)), \]

\[ \xi_w(t) = \text{diag}(\xi_w(t)), w = A, S, \]

\[ L_w = \text{diag}(\sum_{j \neq i} D_{ij}^{w}) - D^{w}, w = A, S, \quad L_B = \text{diag}(\sum_{j \neq i} D_{ij}^{B}) - D^{B}, \]

\[ \Gamma_p = \text{diag}(p_1, p_2, \cdots, p_n), \]

\[ \zeta_p = \begin{pmatrix} \Gamma_p & 0_n & 0_n \\ 0_n & I_n - \Gamma_p & 0_n \\ 0_n & 0_n & I_n \end{pmatrix}. \]

From system (37), we assume that

\[ \psi(t) = \zeta_p \begin{pmatrix} F_A(t) & F_S(t) & F_B(t) \\ F_A(t) & F_S(t) & F_B(t) \\ 0_n & 0_n & 0_n \end{pmatrix}, \tag{39} \]

and

\[ \Psi(t) = \begin{pmatrix} V_A + L_A & 0_n & 0_n \\ 0_n & V_S + L_S & 0_n \\ -\xi_A(t) & -\xi_S(t) & V_B(t) + L_B \end{pmatrix}. \tag{40} \]

Suppose $\Psi_{\tau}(t)$ is the monodromy matrix of the linear $\tau$-periodic differential system $\frac{d\phi(t)}{dt} = \psi(t)\phi$, and $r(\Psi_{\tau}(\tau))$ is the spectral radius of $\Psi_{\tau}(\tau)$. Assume $\Phi(t, s), t \geq s$, is the evolution operator of the linear $\tau$-periodic system

\[ \frac{dy(t)}{dt} = -\psi(t)y, \tag{41} \]

that is, for each $s \in \mathbb{R}$, the $3n \times 3n$ matrix $Y(t, s)$ satisfies

\[ \frac{d}{dt} Y(t, s) = -\psi(t)Y(t, s) \quad \forall \ t \geq s, \quad Y(s, s) = I_{3n}, \]

where $I_{3n}$ is the $3n \times 3n$ matrix. Thus, the fundamental solution matrix $\Psi_{-\tau}(t)$ of (41) is equal to $Y(t, 0), \ t \geq 0$.

We assume that $\varphi(s), s$ is the initial distribution of infectious individuals. Then $\Phi(s)\varphi(s)$ is the rate of new infections produced by the infected individuals who were introduced at time $s$. Given $t \geq s$, then $Y(t, s)\Phi(s)\varphi(s)$ gives the distribution of those infected individuals who were newly infected at time $s$ and remain in the infected compartments at time $t$. It follows that

\[ \int_{-\infty}^{t} Y(t, s)\Phi(s)\varphi(s)ds = \int_{0}^{\infty} Y(t, t-a)\Phi(t-a)\varphi(t-a)da \]

is the distribution of accumulative new infections at time $t$ produced by all those infected individuals $\varphi(s)$ introduced at time previous to $t$.

Let $C_{\tau}$ be the ordered Banach space of all $\tau$-periodic functions from $\mathbb{R}$ to $\mathbb{R}^{3n}$, which is equipped with the maximum norm $\| \cdot \|$ and the positive cone $C_{\tau}^+ := \{ \varphi \in C_{\tau} : \varphi(t) \geq 0, \forall \ t \in \mathbb{R} \}$. Then we define a linear operator $L : C_{\tau} \to C_{\tau}$ by

\[ (L \varphi)(t) = \int_{0}^{\infty} Y(t, t-a)\Phi(t-a)\varphi(t-a)da, \quad \forall \ t \in \mathbb{R}, \ \varphi \in C_{\tau}. \tag{42} \]

Then we call $L$ the next infection operator [37], and define the basic reproduction number as $R_0 := r(L)$, the spectral radius of $L$.

We further have the following result:
Lemma 3.3. [37, Theorem 2.2] The following statements hold.

(i) $R_0 = 1$ if and only if $r(\Psi_{F(\cdot)}(\cdot)(\cdot)) = 1$;
(ii) $R_0 > 1$ if and only if $r(\Psi_{F(\cdot)}(\cdot)(\cdot)) > 1$;
(iii) $R_0 < 1$ if and only if $r(\Psi_{F(\cdot)}(\cdot)(\cdot)) < 1$.

Thus, the disease-free steady state $E_0$ is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.

In order to discuss the extinction of system (1), we impose the following assumptions:

$$\sigma_i = 0, \quad 1 \leq i \leq n,$$

and

$$D_{ij}^u = D_{ij}, \quad u = S, I_A, I_S, R, \quad 1 \leq i \neq j \leq n. \tag{44}$$

Recall that in the proof of Lemma 3.2, we show that for any initial value $v^0 := (\hat{S}^0, \hat{I}_A^0, \hat{I}_S^0, \hat{R}^0, \hat{B}^0) \in \mathbb{R}^5_+$, system (1) admits a unique nonnegative solution

$$v(t, v^0) := (\hat{S}(t), \hat{I}_A(t), \hat{I}_S(t), \hat{R}(t), \hat{B}(t)) \in \mathbb{R}^5_+. \tag{43}$$

Theorem 3.1. The following statements hold.

(i) Assume that either (43) or (44) holds. If $R_0 < 1$, then the disease-free state $E_0$ is globally attractive for system (1) in the sense that

$$\lim_{t \to \infty} v(t, v^0) = E_0; \tag{45}$$

(ii) If $R_0 > 1$, then there exists an $\eta > 0$ such that for any initial value $v^0 \in \mathbb{R}^5_+$ with $(\hat{P}_A^0, \hat{P}_S^0, \hat{B}^0) \neq (0, 0, 0)$, $i = 1, 2, \cdots, n$, the solution $v(t, v^0)$ satisfies

$$\liminf_{t \to \infty} I_A(t) \geq \eta, \quad \liminf_{t \to \infty} I_S(t) \geq \eta, \quad \liminf_{t \to \infty} B_i(t) \geq \eta, \quad i = 1, 2, \cdots, n$$

Further, system (1) admits at least one positive $\tau$-periodic solution

$$(\hat{S}(t), \hat{I}_A(t), \hat{I}_S(t), \hat{R}(t), \hat{B}(t)). \tag{46}$$

Proof. Part (i). We first consider the case where $R_0 < 1$. From Lemma 3.3, it follows that $r(\Psi_{F(\cdot)}(\cdot)(\cdot)) < 1$. Now we choose $\xi_0 > 0$ sufficiently small such that $r(\Psi_{F_{\xi_0}}(\cdot)(\cdot)(\cdot)) < 1$, where $F_{\xi_0}$ is the matrix in (39) with replacing $S_i^*$ by $S_i^* + \xi_0, i = 1, \cdots, n$.

Case 1. (43) holds. From the first equation of system (1) and (43), it follows that

$$\begin{cases} \frac{dS_i}{dt} \leq \Lambda_i - \mu_i S_i + \sum_{j=1}^n (D_{ji}^S S_j - D_{ij}^S S_i), \quad t \geq 0, \\
S_i(0) \geq 0, \quad i = 1, 2, \cdots, n. \tag{47} \end{cases}$$

By Lemma 3.1 and comparison principle, we see that

$$\limsup_{t \to \infty}(S_1(t), S_2(t), \ldots, S_n(t)) \leq (S_1^*, S_2^*, \ldots, S_n^*). \tag{48}$$

Case 2. (44) holds. Let

$$N_i(t) = S_i(t) + I_A_i(t) + I_S_i(t) + R_i(t), \quad i = 1, 2, \ldots, n. \tag{49}$$

In view of (1), (2) and (44), we see that $(N_1(t), N_2(t), \ldots, N_n(t))$ satisfies

$$\begin{cases} \frac{dN_i}{dt} \leq \Lambda_i - \mu_i N_i + \sum_{j=1}^n (D_{ji}^S N_j - D_{ij}^S N_i), \quad t \geq 0, \\
N_i(0) \geq 0, \quad i = 1, 2, \cdots, n. \tag{50} \end{cases}$$
By Lemma 3.1 and comparison principle, we see that
\[
\limsup_{t \to \infty} (N_1(t), N_2(t), \ldots, N_n(t)) \leq (S_1^*, S_2^*, \ldots, S_n^*).
\]
This implies that
\[
\limsup_{t \to \infty} (S_1(t), S_2(t), \ldots, S_n(t)) \leq (S_1^*, S_2^*, \ldots, S_n^*).
\]
From the discussions of either Case 1 or Case 2, we can find a \( t_0 > 0 \) such that
\[
S_1(t) \leq S_1^* + \xi_0, \quad S_2(t) \leq S_2^* + \xi_0, \quad \ldots, \quad S_n(t) \leq S_n^* + \xi_0, \quad \forall \ t \geq t_0.
\]
Then the rest of the arguments are similar to those in the proof of Theorem 2.1 (i), and we omit the details.

Part (ii). For the case where \( R_0 > 1 \), we can use the similar arguments in Lemma 2.6 and Theorem 2.1 (ii) to establish the results in part (ii), and we skip the detailed arguments.

4. Numerical results. In this section, we conduct numerical simulations to study the impact of asymptomatic infections and the population dispersal on the disease threshold dynamics. We have paid special attention to the basic reproduction number, \( R_0 \), as the means to characterize the disease threshold. All numerical results presented below are carried out using the 2-patch model. The base parameter values in the isolated patch model are taken from [23, 24]. More specifically, \( \tau = 365 \) day, \( \Lambda_i = 5.4435 \) person/day, \( \mu_i = \mu_A = (43.5 \text{ year})^{-1} \), \( \gamma_A_i = 0.15 \text{ day}^{-1} \), \( \mu_S_i = 1.7016 \times 10^3 \text{ day}^{-1} \gamma_S_i = 2.4245 \times 10^{-4} \text{ day}^{-1} \), \( \sigma_i = (3 \text{ year})^{-1} \), for \( i = 1, 2 \).

\[
f_i(t, I_{A_i}, I_{S_i}, B_i) = \beta_{H, i}(1 + \theta \cos(2\pi t / \tau)) S_i(0.5 I_{A_i} + I_{S_i}) + \beta_{E, i}(1 + \theta \cos(2\pi t / \tau)) \frac{S_i B_i}{B_i + K},
\]

\[
h_i(t, I_{A_i}, I_{S_i}, B_i) = \xi_{A,i}(1 + \theta \cos(2\pi t / \tau)) I_{A_i} + \xi_{S,i}(1 + \theta \cos(2\pi t / \tau)) I_{S_i} - \delta_i B_i,
\]
where the base value of direct and indirect transmission rates are \( \beta_{H,i} = 1.1 \times 10^{-4} \) person\(^{-1}\) week\(^{-1}\) and \( \beta_{E,i} = 0.075 \) week\(^{-1}\), respectively, bacterial shedding rate due to \( I_{A_i} \) is \( \xi_{A,i} = 0.5 \) cell ml\(^{-1}\) week\(^{-1}\) and bacterial shedding rate due to \( I_{S_i} \) is \( \xi_{S,i} = 50 \) cells ml\(^{-1}\) week\(^{-1}\), the death rate of bacteria \( \delta_i = 0.033 \) day\(^{-1} \) (\( i = 1, 2 \)), and the relative strength of the seasonal effect \( \theta = 0.5 \) and the bacterial half satiation rate \( K = 10^6 \) cells ml\(^{-1}\).

4.1. Asymptomatic infections. Recall that \( p_1, p_2 \in [0, 1] \) represent the fraction of infected human individuals in the asymptomatic state in patch 1 and 2, respectively. To study the impact of asymptomatic infections on the dynamics of the disease, we compute the basic reproduction number \( R_0 \) of our 2-patch model as a function of \( p_1 \) and \( p_2 \) when all the parameter values of the two isolated patches are identical except \( p_1 \) and \( p_2 \). The result is displayed in Figure 1. It shows that if the population dispersal (of human hosts and pathogens) is symmetric (i.e., \( D_{12}^q = D_{21}^q \) for \( q = S, I_A, I_S, R, B \)), then (a) \( R_0 \) is a symmetric function in terms of \( p_1 \) and \( p_2 \); that is, \( R_0(p_1, p_2) = R_0(p_2, p_1) \) for all \( p_1, p_2 \in [0, 1] \); (b) for a fixed \( p_i \), \( R_0 \) increases as \( p_j \) increases, where \( 1 \leq i \neq j \leq 2 \), which indicates that neglecting asymptomatic infections (i.e., \( p_i = 0 \)) may underestimate the risk of the infection; (c) when \( p_1 \neq p_2 \), we assume that \( p_m < p_M \) for \( 1 \leq m \neq M \leq 2 \).

In this case, numerical result shows that \( R_0^{(m)} \leq R_0 \leq R_0^{(M)} \), where \( R_0^{(i)} \) is the patch reproduction number of patch \( i \) (i.e., the basic reproduction number of the
isolated patch $i$). This indicates that the population dispersal tends to balance the risk of the infection.

4.2. **Population dispersal.** When the population dispersal is not symmetric (e.g., $D_{12}^q = 10 D_{21}^q$ for $q = S, I_A, I_S, R, B$), Figure 2 shows that $R_0$ remains to be monotonically increasing as a function of $p_1$ and $p_2$ but the symmetric property is lost;
i.e., \( R_0(p_1, p_2) \neq R_0(p_2, p_1) \) for all \( 0 \leq p_1, p_2 \leq 1 \) and the network reproduction number \( R_0 \) is bounded below by the minimum of the patch reproduction number \( R_0^{(m)} \) and bounded above by the maximum of the patch reproduction number \( R_0^{(M)} \); i.e., \( R_0^{(m)} \leq R_0 \leq R_0^{(M)} \). In addition, we observe that, when the population dispersal from patch 1 to patch 2 is much larger than that from patch 2 to patch 1, the infection risk is greatly reduced in patch 1 as \( p \) slightly elevated in patch 2 as \( p \) is sufficiently close to zero and slightly elevated in patch 2 as \( p \) is sufficiently close to zero.

In what follows, we present three more examples to illustrates the effect of population dispersal on the disease dynamics. Here the base value of dispersal rates are \( D_{12}^S = 1, D_{12}^I = 0.05, D_{12}^B = 0.1, D_{12}^M = 1, \) and \( D_{21}^u = 5D_{12}^u \), for \( u = S, I_A, I_S, R, B \). \( \beta_{H,1} = 5.5 \times 10^{-5} \) person\(^{-1}\) week\(^{-1}\), \( \mu_S = 18.2531 \) day\(^{-1}\) and the rest of parameter values are set as the base values. The movement/immigration matrix of population \( u \) is \( D^u = \begin{pmatrix} 0 & D_{21}^u r_u \\ D_{21}^u r_u & 0 \end{pmatrix} \), for \( u = S, I_A, I_S, B \). We compare the spatial movement of humans (in different classes) and pathogen in the geographical spread of cholera by varying \( r_u \), for \( u = S, I_A, I_S, B \).

In Example 1, the isolated patch reproduction numbers are \( R_0^{(1)} = 0.8641 < 1 \) and \( R_0^{(1)} = 1.1600 > 1 \) (where \( p_1 = 0.70 \) and \( p_2 = 0.85 \)). The result associated with these four different strategies (i.e., controlling the travel of population \( u \), for \( u = S, I_A, I_S, B \)) is displayed in Figure 3. It shows that (a) controlling the spatial movement of susceptible hosts may reduce the infection risk below the unity when \( r_S \) is extremely low, and it tends to enlarge the infection risk as \( r_S \) is further elevated; (b) increasing the dispersal rate of susceptible and infected hosts, and bacteria may bring down the infection risk, but controlling the travel of susceptible individuals in general has an opposite effect on the infection risk as compared to controlling the dispersal of infected hosts and bacteria; (c) in order to eradicate the disease, the most efficient strategy among these four control strategies is to promote the travel of infected human hosts in symptomatic class, as increasing \( r_{I_S} \) appears to be the only strategy among these four that can efficiently reduce \( R_0 \) from above one to below one. A possible biological interpretation is that higher values of \( r_{I_S} \) tend to smooth out the spatial distribution of infectious hosts and reduce the overall infection risk.

In Example 2, both isolated patch reproduction numbers are below the unity, specifically, \( R_0^{(1)} = 0.9592 < 1 \) and \( R_0^{(1)} = 0.9604 < 1 \) (where \( p_1 = 0.5 \) and \( p_2 = 0.7 \)). Figure 4 shows that increasing population dispersal of infectious human hosts by increasing \( r_{I_S} \) could decrease the basic reproduction number from above one to below one, which indicates that faster immigration of infectious hosts could reduce the infection risk. However, \( R_0 > 1 \) iff \( 0 \leq r_{I_S} < 38.1 \) in this example. This shows that even if the basic reproduction number of each isolated patch is below the unity, the basic reproduction number of the multipatch model could be above the unity provided that \( r_{I_S} \) is low enough. Biologically this demonstrates the possibility that although each isolated patch has a low prevalence of the disease, open travel of infectious individuals could increase the infection risk and the disease could persist if the immigration of infectious hosts is not too fast. Furthermore, if the value of \( r_{I_S} \) is kept elevated, \( R_0 \) can decrease from above one to below one.

In Example 3, both isolated patch reproduction numbers are above the unity with \( R_0^{(1)} = 1.1454 > 1 \) and \( R_0^{(1)} = 1.0935 > 1 \) (where \( p_1 = 0.1 \) and \( p_2 = 0.8 \)). Similar to Examples 1-2, \( R_0 \) is a decreasing function of \( r_{I_S} \). Additionally, Figure 5
Figure 3. The basic reproduction number $R_0$ as a function of $r_u$ of model (1) with $R_0^{(1)} = 0.8641$ and $R_0^{(2)} = 1.1600$, where $u = S, I_A, I_S, B$.

shows that although each isolated patch has a high prevalence of the disease (i.e., $\min_i \{R_0^{(i)}\} > 1$), the infection could be eradicated in the patch model provided that the dispersal of infectious hosts is fast enough (i.e., $R_0 < 1$ iff $r_{IS} > 27.5$ in this case).
5. Discussion. This paper proposes a general multipatch model to study cholera epidemics in a periodic environment. The model incorporates seasonality into a general formulation for the force of infection (i.e., the disease incidence), asymptotic infections, spatial movements of hosts and pathogens, with the aim to capture the interaction among climatic, geographical, ecological, and biological factors in the evolution of cholera epidemics. Using the theory developed in [37], we have derived the basic reproduction number $R_0$ for our model. Applying the theory of monotone dynamical systems and the persistence theory [44], we show that $R_0$ serves a threshold parameter for uniform persistence and global extinction of the disease. More specifically, if $R_0 < 1$, the disease-free steady state is globally attractive and the disease dies out; if $R_0 > 1$, the disease is uniformly persistent and our system exhibits seasonal fluctuation.
It is worthy mentioning that our periodic multipatch modeling framework can incorporate a wide range of epidemiologically relevant factors, including biological (e.g., intrinsic bacterial growth and death), environmental (e.g., host shedding and pathogen dispersal), geographical (e.g., locational difference in ecology and demographics), climatic (e.g., seasonal fluctuation), and physical (e.g., human and bacterial dispersal). On the other hand, our model allows us to consider multiple transmission pathways for cholera that includes both direct (human-to-human) and indirect (environment-to-human) routes. These make it possible to study the complex interaction among many simultaneous and coupled processes that contribute to the whole picture of cholera transmission dynamics. Additionally, our numerical investigations for the 2-patch model indicate that (a) neglecting asymptotic infections may underestimate the risk of infection; (b) travel can help the disease to become persistent (resp. eradicated) in the network, even though the disease dies out (resp. persists) in each isolated patch.

As the number of patches goes to infinity, it would be very interesting to rigorously analyze the relationship of disease dynamics of cholera between our multipatch model and the corresponding partial differential equation model. In addition, hosts usually require a large number of *Vibrio cholerae* (10^3 ∼ 10^5 cells) to become infected [21, 10]. The impact of immunological threshold [19, 26] on the dynamics of cholera will provide an interesting topic in future research.

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