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Impacts of Seasonal and Spatial Variations on the Transmission of Typhoid Fever

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Abstract: Typhoid fever is a disease caused by the bacteria Salmonella Typhi through the ingestion of contaminated food or water, and it is still serious in developing countries. The infection routes include both human-to-human transmission and environment-to-human transmission. It was observed that higher incidence of typhoid fever occur during the rainy season and people living near water bodies may have a higher rate of typhoid infection. On the other hand, asymptomatically infected individuals also play a central role in the transmission of typhoid since they are not experiencing any symptoms but they are able to shed S. Typhi into the environment for years. Thus, a well-described model of the Typhoid transmission should include the asymptomatical compartment and the factors of spatial homogeneity and seasonality. This motivates us to develop a periodic two-patch system to investigate the spatial and seasonal effects on the transmission of Typhoid fever, in which the bacteria in the environment is included, and the population of human is divided into five classes, namely, susceptible individuals, infected individuals, carrier individuals, individuals under treatment and recovered individuals. We first introduce the basic reproduction number for the model, then we show that the extinction/persistence of Typhoid can be determined by $\mathcal{R}_0$. Our numerical results indicate that an outbreak of Typhoid fever in a two-patch environment could be eliminated if migration between patches is prohibited. Finally, we also numerically observe that the infection risks of Typhoid may be underestimated if seasonal effects are ignored.

Keywords: Typhoid Fever, Spatial Homogeneity, Seasonal Effects, Basic Reproduction Number, Threshold Dynamics

1. Introduction

Typhoid fever is an infection caused by the bacteria Salmonella Typhi (S. Typhi), which is usually spread by ingesting contaminated food/water. According to the World Health Organization, typhoid is still endemic in several developing countries. The infection routes of Typhoid include both direct (i.e.human-to-human) transmission and indirect (i.e. environment-to-human) transmission, which is associated with the ingestion of contaminated food/water. It is worth pointing out that asymptomatically infected individuals also play an important role in the transmission of typhoid since they are not experiencing any symptoms but they are able to shed S. Typhi into the environment for many years, thereby sustaining transmission [15, 16]. Those observations motivate the authors in [16] developed a system of ordinary differential equations to model the spread of typhoid, where the factors of limited treatment resources on the spread of typhoid was further included.

Our aim of this paper is to incorporate spatial and temporal effects into the model proposed in [16]. During the rainy season, a large increase of flooding may occur by the rainfall and the water resources is contaminated by the excreta with pathogenic bacteria, resulting in a higher incidence of typhoid fever [12, 13]. It was evident that the supply of clean and safe drinking water plays an important role in controlling typhoid infection, and people living near water bodies (e.g. rivers) may have a higher rate of typhoid infection [4]. Thus, the effect of spatial homogeneity should be included. To develop spatially explicit models, there are two common approaches. The first one is a continuum approach using an advection-dispersion-reaction system to describe the transport and interaction of population in a (bounded) habitat. Here we adopt the second approach, namely, we can divide the habitat into several areas, and the population gradient between areas is simply described by the migration of population. To make mathematical analysis more tractable, we will focus on the case that the habitat is divided into two areas, which is also referred to as "two-patch model". On the other hand, it is confirmed that temperature changes have significant impacts on the enteric diseases [9, 10], and the increase in rainfall and temperature lead to more typhoid fever cases in the study area [4]. Thus, it is natural to further explore the seasonal variations in temperature and rainfall on the transmission of typhoid. Based on those aforementioned facts, we shall propose and analyze a time-periodic system in a two-patch environment which is modified from the one in [16].

The population of human at time t in path i is divided into five classes: susceptible individuals ($S_i(t)$), infected individuals ($I_i(t)$), carrier individuals ($C_i(t)$), individuals under treatment ($Q_i(t)$) and recovered individuals ($R_i(t)$). Besides, $B_i(t)$ stands for the density of bacteria in the environment in patch i at time t. Then the extended version of the model in [16] takes the following form:

$$\begin{cases} \frac{dS_1}{dt} = \Lambda_1 - \frac{\beta_{C_1}(t)(I_1+\eta_1 C_1)S_1}{S_1+I_1+C_1+Q_1+R_1} - \frac{\beta_{B_1}(t)B_1S_1}{B_1+K_{B_1}} - \mu_1 S_1 + \rho_1 R_1 - m_{12}^S S_1 + m_{21}^S S_2, \\ \frac{dI_1}{dt} = \frac{\beta_{C_1}(t)(I_1+\eta_1 C_1)S_1}{S_1+I_1+C_1+Q_1+R_1} + \frac{\beta_{B_1}(t)B_1S_1}{B_1+K_{B_1}} - (\mu_1+\sigma_1+\delta_{I_1}+\epsilon_{I_1})I_1 - \theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2, \\ \frac{dC_1}{dt} = \sigma_1 I_1 - (\mu_1+\delta_{C_1}+\epsilon_{C_1})C_1 - m_{12}^C C_1 + m_{21}^C C_2, \\ \frac{dQ_1}{dt} = \theta_1 I_1 - (\mu_1+\gamma_1+\delta_{Q_1})Q_1, \\ \frac{dR_1}{dt} = \gamma_1 Q_1 + \epsilon_{I_1} I_1 + \epsilon_{C_1} C_1 - (\mu_1+\rho_1)R_1 - m_{12}^R R_1 + m_{21}^R R_2, \\ \frac{dB_1}{dt} = g_1 B_1 + \alpha_{I_1}(t) I_1 + \alpha_{C_1}(t) C_1 - \mu_{B_1} B_1 - m_{12}^B B_1 + m_{21}^B B_2, \\ \frac{dS_2}{dt} = \Lambda_2 - \frac{\beta_{C_2}(t)(I_2+\eta_2 C_2)S_2}{S_2+I_2+C_2+Q_2+R_2} - \frac{\beta_{B_2}(t)B_2S_2}{B_2+K_{B_2}} - \mu_2 S_2 + \rho_2 R_2 + m_{12}^S S_1 - m_{21}^S S_2, \\ \frac{dI_2}{dt} = \frac{\beta_{C_2}(t)(I_2+\eta_2 C_2)S_2}{S_2+I_2+C_2+Q_2+R_2} + \frac{\beta_{B_2}(t)B_2S_2}{B_2+K_{B_2}} - (\mu_2+\sigma_2+\delta_{I_2}+\epsilon_{I_2})I_2 - \theta_2 I_2 + m_{12}^I I_1 - m_{21}^I I_2, \\ \frac{dC_2}{dt} = \sigma_2 I_2 - (\mu_2+\delta_{C_2}+\epsilon_{C_2})C_2 + m_{12}^C C_1 - m_{21}^C C_2, \\ \frac{dQ_2}{dt} = \theta_2 I_2 - (\mu_2+\gamma_2+\delta_{Q_2})Q_2, \\ \frac{dR_2}{dt} = \gamma_2 Q_2 + \epsilon_{I_2} I_2 + \epsilon_{C_2} C_2 - (\mu_2+\rho_2)R_2 + m_{12}^R R_1 - m_{21}^R R_2, \\ \frac{dB_2}{dt} = g_2 B_2 + \alpha_{I_2}(t) I_2 + \alpha_{C_2}(t) C_2 - \mu_{B_2} B_2 + m_{12}^B B_1 - m_{21}^B B_2, \\ S_i(0) \geq 0,\ I_i(0) \geq 0,\ C_i(0) \geq 0,\ Q_i(0) \geq 0,\ R_i(0) \geq 0,\ B_i(0) \geq 0,\ i = 1, 2. \end{cases} \tag{1}$$

The constant Λ_i represents the recruitment of susceptible population, and μ_i represents the natural death rate for the general population in the environment of patch i. Susceptible people are infected either through human-to-human transmission at the rate $\frac{\beta_{C_i}(t)(I_i+\eta_i C_i)S_i}{S_i+I_i+C_i+Q_i+R_i}$ or through the environmental bacteria from contaminated drinking water/food at the rate $\frac{\beta_{B_i}(t)B_iS_i}{B_i+K_{B_i}}$. The parameter $\beta_{C_i}(t)$ is the so-called typhoid transmission rate for susceptible individuals and infected/carrier individuals, and η_i is used to measure the relative infectiousness of carriers C_i compared to infected individuals I_i. We will assume $0 < \eta_i < 1$ when the carriers C_i have less infectious ability than infected individuals I_i. Otherwise, we will assume that $\eta_i \geq 1$. The parameter $\beta_{B_i}(t)$ is the per capita contact rate between susceptible individuals and the contaminated environment, and K_{B_i} is the saturation constant. Infected individuals progress to the carrier class at the rate σ_i; the naturally recovery rate for infected (resp. carrier) individuals is denoted by ϵ_{I_i} (resp. ϵ_{C_i}); the mortality rate due to disease for infected (resp. carrier) individuals is denoted by δ_{I_i} (resp. δ_{C_i}); the parameter $\alpha_{I_i}(t)$ (resp. $\alpha_{C_i}(t)$) represents the shedding rate of bacteria by infected (resp. carrier) individuals. The recruitment into treatment class is denoted by $\theta_i I_i$. The mortality rate due to illness in patients under treatment is δ_{Q_i}, and its recovery rate is γ_i. The recovered individuals will only be temporarily immune to typhoid, leading to the individual being susceptible again at the rate ρ_i. The generation rate of bacteria is expressed in terms of $g_i B_i$, where g_i is a constant; the production rates of bacteria from infected persons and carriers are denoted by $\alpha_{I_i}(t)$ and $\alpha_{C_i}(t)$, respectively. We further assume that the bacteria in the environment becomes non-infectious at a rate μ_{B_i}. Here, for $w = S, I, C, R, B$, m_{21}^w represents the immigration rate of population w from patch 2 to patch 1, while m_{12}^w represents the immigration rate of population w from patch 1 to patch 2. We also point out that the class Q_i, $i = 1, 2$, represents the typhoid patients who are detected and quarantined symptomatic and chronic enteric carriers. Thus, Q_i, $i = 1, 2$ is supposed to be on treatment, and those terms $-m_{12}^Q Q_1 + m_{21}^Q Q_2$ and $m_{12}^Q Q_1 - m_{21}^Q Q_2$ are ignored in system (1), due to the fact that the population Q_i cannot move in the environment. This makes our mathematical analysis more difficult and challenging.

In the whole paper, we always assume that $\beta_{C_i}(t)$, $\beta_{B_i}(t)$, $\alpha_{I_i}(t)$, and $\alpha_{C_i}(t)$ are ω-periodic functions, for $i = 1, 2$, and

$$\mu_{B_i} - g_i > 0, \ \forall\, i = 1, 2, \tag{2}$$

which coincides with the parameters given in the table on page 664 of [16]. The organization of the rest of this paper is as follows. The well-posedness of our proposed model and the basic reproduction number, $\mathcal{R}_0$, are discussed in the next section. In Section 3, we show that the global dynamics of our proposed model can be determined in terms of the basic reproduction number, $\mathcal{R}_0$. Numerical simulations and biological interpretations are presented in Section 4 and Section 5, respectively.

2. The Reproduction Number

We first consider the following system

$$\begin{cases} \frac{dS_1}{dt} = \Lambda_1 - (\mu_1 + m_{12}^S)S_1 + m_{21}^S S_2, \\ \frac{dS_2}{dt} = \Lambda_2 + m_{12}^S S_1 - (\mu_2 + m_{21}^S)S_2, \\ S_i(0) \geq 0, \ i = 1, 2. \end{cases} \tag{3}$$

Let

$$(S_1^*, S_2^*) = (\frac{\Lambda_1(\mu_2 + m_{21}^S) + \Lambda_2 m_{21}^S}{\mu_1\mu_2 + \mu_1 m_{21}^S + \mu_2 m_{12}^S}, \frac{\Lambda_2(\mu_1 + m_{12}^S) + \Lambda_1 m_{12}^S}{\mu_1\mu_2 + \mu_1 m_{21}^S + \mu_2 m_{12}^S}). \tag{4}$$

Then we can verify that system (3) is a cooperative system (see, e.g., [19]) and (S_1^*, S_2^*) is the only positive steady state. Thus, we have the following result concerning with the global stability of (S_1^*, S_2^*) (see, e.g., [8]).

Lemma 2.1. The positive steady state (S_1^*, S_2^*) is globally attractive in $\mathbb{R}_+^2$ for system (3). That is, we have

$$\lim_{t\to\infty}(S_1(t), S_2(t)) = (S_1^*, S_2^*), \ \forall\, (S_1(0), S_2(0)) \in \mathbb{R}_+^2.$$

We further have the following result:

Lemma 2.2. System (1) has a unique and bounded solution with the initial value in $\mathbb{R}_+^{12}$, which is positively invariant. Moreover, system (1) has a connected global attractor on $\mathbb{R}_+^{12}$ in the sense that it attracts all positive orbits in $\mathbb{R}_+^{12}$.

Proof We show that system (1) admits a unique noncontinuable solution and the solutions to (1) remain non-negative if they are non-negative initially. In view of [19, Theorem 5.2.1], we can show that for any $x^0 \in \mathbb{R}_+^{12}$, system (1) has a unique local solution $u(t, x^0) \in \mathbb{R}_+^{12}$ with $u(0, x^0) = x^0$. This shows the positive invariance of $\mathbb{R}_+^{12}$ for system (1). Next, we show that the solutions $u(t, x^0)$ for system (1) are eventually bounded. For this end, we let

$$\begin{cases} N_1(t) = S_1(t) + I_1(t) + C_1(t) + Q_1(t) + R_1(t) \\ N_2(t) = S_2(t) + I_2(t) + C_2(t) + Q_2(t) + R_2(t). \end{cases} \tag{5}$$

Then we substitute $N(t) = N_1(t) + N_2(t)$ into system (1), and it follows that

$$\frac{dN}{dt} = \Lambda_1 + \Lambda_2 - \mu_1 N_1 - \mu_2 N_2 - \delta_{I_1} I_1 - \delta_{C_1} C_1 - \delta_{Q_1} Q_1 - \delta_{I_2} I_2 - \delta_{C_2} C_2 - \delta_{Q_2} Q_2.$$

By the positivity of solutions, we see that

$$\frac{dN}{dt} \leq \Lambda_1 + \Lambda_2 - \underline{\mu} N_1 - \underline{\mu} N_2 = \Lambda_1 + \Lambda_2 - \underline{\mu} N.$$

where $\underline{\mu} = \min\{\mu_1, \mu_2\}$. Thus, $\limsup_{t\to\infty} N(t) \leq \frac{\Lambda_1 + \Lambda_2}{\underline{\mu}}$. This means that $N(t)$ is ultimately bounded. Since solutions of (1) are nonnegative, it follows from (5) that
$S_i(t)$, $I_i(t)$, $C_i(t)$, $Q_i(t)$, and $R_i(t)$ are ultimately bounded, for $i = 1, 2$. Then there exists a $\tau_0 > 0$ and $\chi_i > 0$ such that

$$\alpha_{I_i}(t) I_i(t) + \alpha_{C_i}(t) C_i(t) \leq \chi_i, \ \forall\, t \geq \tau_0, \ i = 1, 2.$$

This inequality together with the sixth and twelfth equations of (1) imply that

$$\begin{cases} \frac{dB_1}{dt} \leq \chi_1 - (\mu_{B_1} - g_1 + m_{12}^B)B_1 + m_{21}^B B_2, \ \forall\, t \geq \tau_0, \\ \frac{dB_2}{dt} \leq \chi_2 + m_{12}^B B_1 - (\mu_{B_2} - g_2 + m_{21}^B)B_2, \ \forall\, t \geq \tau_0. \end{cases}$$

In view of the assumption (2), we see that

$$\mu_{01} := \mu_{B_1} - g_1 > 0 \text{ and } \mu_{02} := \mu_{B_2} - g_2 > 0.$$

By Lemma 2.1 and the comparison principle, it follows that

$$\limsup_{t\to\infty}(B_1(t), B_2(t)) \leq (\frac{\chi_1(\mu_{02} + m_{21}^B) + \chi_2 m_{21}^B}{\mu_{01}\mu_{02} + \mu_{01} m_{21}^B + \mu_{02} m_{12}^B}, \frac{\chi_2(\mu_{01} + m_{12}^B) + \chi_1 m_{12}^B}{\mu_{01}\mu_{02} + \mu_{01} m_{21}^B + \mu_{02} m_{12}^B}),$$

which reveals that $B_1(t)$ and $B_2(t)$ are also eventually bounded. Therefore, we have established the global existence for the solutions of system (1), and the rest of the result follows [7, Theorem 3.4.8].

The disease-free state of system (1), E_0, takes the following form

$$E_0 = (S_1^*, 0, 0, 0, 0, 0, S_2^*, 0, 0, 0, 0, 0), \tag{6}$$

where (S_1^*, S_2^*) is given in (4). We linearize system (1) at the disease-free state E_0 and we arrive at the following linear system

$$\begin{cases} \frac{dI_1}{dt} = [\beta_{C_1}(t) - (\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1} + \theta_1)]I_1 + \eta_1\beta_{C_1}(t)C_1 + S_1^*\frac{\beta_{B_1}(t)}{K_{B_1}}B_1 - m_{12}^I I_1 + m_{21}^I I_2, \\ \frac{dC_1}{dt} = \sigma_1 I_1 - (\mu_1 + \delta_{C_1} + \epsilon_{C_1})C_1 - m_{12}^C C_1 + m_{21}^C C_2, \\ \frac{dB_1}{dt} = g_1 B_1 + \alpha_{I_1}(t)I_1 + \alpha_{C_1}(t)C_1 - \mu_{B_1}B_1 - m_{12}^B B_1 + m_{21}^B B_2, \\ \frac{dI_2}{dt} = [\beta_{C_2}(t) - (\mu_2 + \sigma_2 + \delta_{I_2} + \epsilon_{I_2} + \theta_2)]I_2 + \eta_2\beta_{C_2}(t)C_2 + S_2^*\frac{\beta_{B_2}(t)}{K_{B_2}}B_2 + m_{12}^I I_1 - m_{21}^I I_2, \\ \frac{dC_2}{dt} = \sigma_2 I_2 - (\mu_2 + \delta_{C_2} + \epsilon_{C_2})C_2 + m_{12}^C C_1 - m_{21}^C C_2, \\ \frac{dB_2}{dt} = g_2 B_2 + \alpha_{I_2}(t)I_2 + \alpha_{C_2}(t)C_2 - \mu_{B_2}B_2 + m_{12}^B B_1 - m_{21}^B B_2. \end{cases} \tag{7}$$

Note that system (7) is cooperative (see, e.g., [19]) and irreducible (see a simple test on page 256 of [20]). From system (7), we define

$$\mathbb{F}(t) = \begin{pmatrix} \beta_{C_1}(t) & \eta_1\beta_{C_1}(t) & S_1^*\frac{\beta_{B_1}(t)}{K_{B_1}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_{C_2}(t) & \eta_2\beta_{C_2}(t) & S_2^*\frac{\beta_{B_2}(t)}{K_{B_2}} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{8}$$

and

$$\mathbb{V}(t) = \begin{pmatrix} \mathbb{V}_{11} + m_{12}^I & 0 & 0 & -m_{21}^I & 0 & 0 \\ -\sigma_1 & \mathbb{V}_{22} + m_{12}^C & 0 & 0 & -m_{21}^C & 0 \\ -\alpha_{I_1}(t) & -\alpha_{C_1}(t) & \mathbb{V}_{33} + m_{12}^B & 0 & 0 & -m_{21}^B \\ -m_{12}^I & 0 & 0 & \mathbb{V}_{44} + m_{21}^I & 0 & 0 \\ 0 & -m_{12}^C & 0 & -\sigma_2 & \mathbb{V}_{55} + m_{21}^C & 0 \\ 0 & 0 & -m_{12}^B & -\alpha_{I_2}(t) & -\alpha_{C_2}(t) & \mathbb{V}_{66} + m_{21}^B \end{pmatrix} \tag{9}$$

where $\mathbb{V}_{11} = \mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1} + \theta_1$, $\mathbb{V}_{22} = \mu_1 + \delta_{C_1} + \epsilon_{C_1}$, $\mathbb{V}_{33} = \mu_{B_1} - g_1$, $\mathbb{V}_{44} = \mu_2 + \sigma_2 + \delta_{I_2} + \epsilon_{I_2} + \theta_2$, $\mathbb{V}_{55} = \mu_2 + \delta_{C_2} + \epsilon_{C_2}$, and $\mathbb{V}_{66} = \mu_{B_2} - g_2$.

Assume $Y(t,s),\ t \geq s$, is the evolution operator of the linear ω-periodic system

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

and I stands for the identity matrix with size 6. Then, for each $s \in \mathbb{R}$, the 6×6 matrix $Y(t,s)$ satisfies

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

Assume that C_ω represents the ordered Banach space of all ω-periodic functions from $\mathbb{R}$ to $\mathbb{R}^6$, which is equipped with the maximum norm $\|\cdot\|$. The associated positive cone C_ω^+ is defined by $C_\omega^+ := \{\phi \in C_\omega : \phi(t) \geq 0,\ \forall\ t \in \mathbb{R}\}$. Suppose that $\phi(s)$, ω-periodic in s, is the initial distribution of infectious individuals. Then the next infection operator $\mathbb{L} : C_\omega \to C_\omega$ is defined by ([3, 5, 22])

$$(\mathbb{L}\phi)(t) = \int_0^\infty Y(t, t-a)\mathbb{F}(t-a)\phi(t-a)da,\ \forall\, t \in \mathbb{R},\ \phi \in C_\omega.$$

Then the basic reproduction number is given by $\mathcal{R}_0 := r(\mathbb{L})$, the spectral radius of $\mathbb{L}$.

Wang and Zhao [22] further provide an idea to numerically calculate $\mathcal{R}_0$. For a parameter $\lambda \in (0,\infty)$, we assume that $\mathcal{W}(t,s,\lambda)$, $t \geq s$, $s \in \mathbb{R}$ is the evolution operator of the linear ω-periodic system on $\mathbb{R}^6$,

$$\frac{dw}{dt} = \left(-\mathbb{V}(t) + \frac{\mathbb{F}(t)}{\lambda}\right) w, \;\; t \in \mathbb{R}.$$

By [22, Theorem 2.1] , we have the following results.

Lemma 2.3. Assume that $\rho(\mathcal{W}(\omega,0,\lambda))$ stands for the spectral radius of $\mathcal{W}(\omega,0,\lambda)$. Then

1. If the algebraic equation $\rho(\mathcal{W}(\omega,0,\lambda)) = 1$ admits a positive solution λ_0, then λ_0 is an eigenvalue of the operator $\mathbb{L}$, and hence $\mathcal{R}_0 > 0$.
2. $\lambda = \mathcal{R}_0$ will be the unique solution of $\rho(\mathcal{W}(\omega,0,\lambda)) = 1$ if $\mathcal{R}_0 > 0$.
3. $\mathcal{R}_0 = 0$ if and only if $\rho(\mathcal{W}(\omega,0,\lambda)) < 1$ for all $\lambda > 0$.

Suppose $\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(t)$ is the monodromy matrix of the linear ω-periodic differential system $\frac{dz(t)}{dt} = (\mathbb{F}(t) - \mathbb{V}(t))z$, and $r(\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(\omega))$ is the spectral radius of $\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(\omega)$. By [22, Theorem 2.2], we further have the following result:

Lemma 2.4. $\mathcal{R}_0 - 1$ and $r(\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(\omega)) - 1$ have the same sign. That is, the state E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.

3. Global Dynamics

We first consider the linear ordinary differential system

$$\frac{dx(t)}{dt} = \mathbf{A}(t)x, \tag{10}$$

where $\mathbf{A}(t)$ is a continuous, cooperative, irreducible, and ω-periodic $k \times k$ matrix function. Assume that $\Phi_{\mathbf{A}(\cdot)}(t)$ is the monodromy matrix of (10) and $r(\Phi_{\mathbf{A}(\cdot)}(\omega))$ is the spectral radius of $\Phi_{\mathbf{A}(\cdot)}(\omega)$. In view of [1, Lemma 2] (see also [6, Theorem 1.1]) and the Perron-Frobenius theorem [19], we see that $r(\Phi_{\mathbf{A}(\cdot)}(\omega))$ is the principal eigenvalue of $\Phi_{\mathbf{A}(\cdot)}(\omega)$.

We further have the following results:

Lemma 3.1. ([23, Lemma 2.1]) Let $\lambda = \frac{1}{\omega}\ln r(\Phi_{\mathbf{A}(\cdot)}(\omega))$. Then there exists a positive, ω-periodic function $v(t)$ such that $e^{\lambda t}v(t)$ is a solution of (10).

For further discussions, we need the following property.

Lemma 3.2. Assume that

$$(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t))$$

is a solution of the system (1) with initial value

$$(S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{R}_+^{12},$$

and

$$(I_1^0, C_1^0, B_1^0, I_2^0, C_2^0, B_2^0) \neq (0,0,0,0,0,0). \tag{11}$$

Then

$$(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t)) \gg 0, \; \forall\, t > 0.$$

Proof In view of the first equation in system (1), it follows that

$$S_1(t) = e^{-\int_0^t b(s_1)ds_1}\left[\int_0^t e^{\int_0^{s_2} b(s_1)ds_1} a(s_2)ds_2 + S_1^0\right],$$

where

$$a(t) := \Lambda_1 + \rho_1 R_1 + m_{21}^S S_2 \geq \Lambda_1 > 0,$$

and

$$b(t) := \frac{\beta_{C_1}(t)(I_1(t) + \eta_1 C_1(t))}{(S_1 + I_1 + C_1 + Q_1 + R_1)(t)} + \frac{\beta_{B_1}(t)B_1(t)}{B_1(t) + K_{B_1}} + \mu_1 + m_{12}^S.$$

Thus, $S_1(t) > 0$, $\forall\, t > 0$. Same arguments show that $S_2(t) > 0$, $\forall\, t > 0$.

Let

$$\mathbb{J}(t) = \begin{pmatrix} \mathbb{J}_{11}(t) & \mathbb{J}_{12}(t) & \mathbb{J}_{13}(t) & m_{21}^I & 0 & 0 \\ \sigma_1 & \mathbb{J}_{22}(t) & 0 & 0 & m_{21}^C & 0 \\ \alpha_{I_1}(t) & \alpha_{C_1}(t) & \mathbb{J}_{33}(t) & 0 & 0 & m_{21}^B \\ m_{12}^I & 0 & 0 & \mathbb{J}_{44}(t) & \mathbb{J}_{45}(t) & \mathbb{J}_{46}(t) \\ 0 & m_{12}^C & 0 & \sigma_2 & \mathbb{J}_{55}(t) & 0 \\ 0 & 0 & m_{12}^B & \alpha_{I_2}(t) & \alpha_{C_2}(t) & \mathbb{J}_{66}(t) \end{pmatrix},$$

where

$$\begin{cases} \mathbb{J}_{11}(t) = \frac{\beta_{C_1}(t)S_1(t)}{(S_1+I_1+C_1+Q_1+R_1)(t)} - (\mu_1+\sigma_1+\delta_{I_1}+\epsilon_{I_1}) - \theta_1 - m_{12}^I, \\ \mathbb{J}_{12}(t) = \frac{\eta_1\beta_{C_1}(t)S_1(t)}{(S_1+I_1+C_1+Q_1+R_1)(t)}, \ \mathbb{J}_{13}(t) = \frac{\beta_{B_1}(t)S_1(t)}{B_1(t)+K_{B_1}}, \\ \mathbb{J}_{22}(t) = -(\mu_1+\delta_{C_1}+\epsilon_{C_1}) - m_{12}^C, \ \mathbb{J}_{33}(t) = g_1 - \mu_{B_1} - m_{12}^B, \\ \mathbb{J}_{44}(t) = \frac{\beta_{C_2}(t)S_2(t)}{(S_2+I_2+C_2+Q_2+R_2)(t)} - (\mu_2+\sigma_2+\delta_{I_2}+\epsilon_{I_2}) - \theta_2 - m_{21}^I, \\ \mathbb{J}_{45}(t) = \frac{\eta_2\beta_{C_2}(t)S_2(t)}{(S_2+I_2+C_2+Q_2+R_2)(t)}, \ \mathbb{J}_{46}(t) = \frac{\beta_{B_2}(t)S_2(t)}{B_2(t)+K_{B_2}}, \\ \mathbb{J}_{55}(t) = -(\mu_2+\delta_{C_2}+\epsilon_{C_2}) - m_{21}^C, \ \mathbb{J}_{66}(t) = g_2 - \mu_{B_2} - m_{21}^B. \end{cases}$$

Then the matrix $\mathbb{J}(t)$ is cooperative (see, e.g., [19]) and irreducible (see a simple test on page 256 of [20]), where we have used the fact that $S_i(t) > 0, \ \forall \, t > 0, \, i = 1, 2$. By (11) and the irreducibility of the cooperative matrix $\mathbb{J}(t)$, we can use a generalized version of [19, Theorem 4.1.1] to show that

$$(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t))^T \gg 0, \ \forall \, t > 0. \tag{12}$$

In view of the equations of Q_1, Q_2, R_1 and R_2 in system (1), together with (12), we can further show that $Q_i(t) > 0, \ R_i(t) > 0, \ \forall \, t > 0, \ i = 1, 2$. We complete the proof.

Let $\mathbb{X} = \mathbb{R}_+^{12}$. Define a family of maps $\{\Psi(t)\}_{t\geq 0}$ from $\mathbb{X}$ to $\mathbb{X}$ by

$$\Psi(t)x^0 = u(t, x^0), \ \forall \, x^0 = (S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X},$$

where $u(t, x^0)$ is the unique solution of system (1) with $u(0, x^0) = x^0$ (see Lemma 2.2 and the proof therein). Suppose $P : \mathbb{X} \to \mathbb{X}$ is the Poincaré map associated with system (1), that is,

$$P(x^0) = u(\omega, x^0), \ \forall \, x^0 \in \mathbb{X}.$$

Note that $P^n(x^0) = u(n\omega, x^0), \ \forall \, n \geq 0$.

Let

$$\mathbb{X}_0 = \left\{(S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X} : I_i^0 > 0, C_i^0 > 0, B_i^0 > 0, i = 1, 2\right\}$$

and

$$\begin{aligned} \partial\mathbb{X}_0 := \mathbb{X}\backslash\mathbb{X}_0 = \big\{&(S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X} : I_1^0 = 0 \\ &\text{or } I_2^0 = 0 \text{ or } C_1^0 = 0 \text{ or } \ C_2^0 = 0 \text{ or } B_1^0 = 0 \text{ or } \ B_2^0 = 0\big\}. \end{aligned}$$

Lemma 3.3. Let $\mathcal{R}_0 > 1$. Then there exists a $\varsigma_0 > 0$ such that for any $x^0 \in \mathbb{X}_0$ with $\|x^0 - E_0\| \leq \varsigma_0$, we have

$$\limsup_{n\to\infty} d(P^n(x^0), E_0) \geq \varsigma_0.$$

Proof Assume $\mathcal{R}_0 > 1$. Then $r(\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(\omega)) > 1$ (see Lemma 2.4). Thus, we find a small $\xi_0 > 0$ such that $r(\Phi_{\mathbb{F}_{\xi_0}(\cdot)-\mathbb{V}(\cdot)}(\omega)) > 1$, where $\mathbb{F}_{\xi_0}(t) =$

$$\begin{pmatrix} \frac{\beta_{C_1}(t)(S_1^*-\xi_0)}{S_1^*+5\xi_0} & \frac{\eta_1\beta_{C_1}(t)(S_1^*-\xi_0)}{S_1^*+5\xi_0} & \frac{\beta_{B_1}(t)(S_1^*-\xi_0)}{\xi_0+K_{B_1}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\beta_{C_2}(t)(S_2^*-\xi_0)}{S_2^*+5\xi_0} & \frac{\eta_2\beta_{C_2}(t)(S_2^*-\xi_0)}{S_2^*+5\xi_0} & \frac{\beta_{B_2}(t)(S_2^*-\xi_0)}{\xi_0+K_{B_2}} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Since solutions are continuous with respect to the initial values, we can find a $\varsigma_0 > 0$ such that for any $x^0 \in \mathbb{X}_0$ with $\|x^0 - E_0\| \leq \varsigma_0$, there holds

$$\|u(t, x^0) - u(t, E_0)\| < \xi_0, \ \forall \, t \in [0, \omega],$$

Claim. For all $x^0 \in \mathbb{X}_0$ with $\|x^0 - E_0\| \leq \varsigma_0$, there holds

$$\limsup_{n\to\infty} d(P^n(x^0), E_0) \geq \varsigma_0.$$

Suppose that the above claim is not true. Then we have

$$\limsup_{n\to\infty} d(P^n(x^0), E_0) < \varsigma_0,$$

for some $x^0 \in \mathbb{X}_0$ with $\|x^0 - E_0\| \leq \varsigma_0$. Without loss of generality, we assume that

$$d(P^n(x^0), E_0) < \varsigma_0,\ \forall\, n \geq 0.$$

It follows that

$$\|u(t, P^n(x^0)) - u(t, E_0)\| < \xi_0,\ \forall\, t \in [0, \omega],\ n \geq 0.$$

Given any $t \geq 0$, we rewrite $t = m\omega + t'$, where $t' \in [0, \omega)$, and m is the largest integer less than or equal to $\frac{t}{\omega}$. Therefore, it follows that

$$\|u(t, x^0) - u(t, E_0)\| = \|u(t', P^m(x^0)) - u(t', E_0)\| < \xi_0 \tag{13}$$

Note that

$$(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t)) = u(t, x^0)$$

and $u(t, E_0) = E_0, \forall\, t \geq 0$. From (13), for all $t \geq 0$, we have

$$S_i^* + \xi_0 > S_i(t) > S_i^* - \xi_0 > 0,\ 0 < I_i(t), C_i(t), Q_i(t), R_i(t), B_i(t) < \xi_0,\ i = 1, 2.$$

From the equation of I_1 in (1), we see that

$$\begin{aligned}
\frac{dI_1}{dt} &= \frac{\beta_{C_1}(t)(I_1 + \eta_1 C_1)S_1}{S_1 + I_1 + C_1 + Q_1 + R_1} + \frac{\beta_{B_1}(t)B_1 S_1}{B_1 + K_{B_1}} - (\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1})I_1 - \theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2 \\
&\geq \frac{\beta_{C_1}(t)(I_1 + \eta_1 C_1)(S_1^* - \xi_0)}{S_1^* + 5\xi_0} + \frac{\beta_{B_1}(t)B_1(S_1^* - \xi_0)}{\xi_0 + K_{B_1}} - (\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1})I_1 - \theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2 \\
&= \frac{\beta_{C_1}(t)(S_1^* - \xi_0)}{S_1^* + 5\xi_0} I_1 + \frac{\eta_1 \beta_{C_1}(t)(S_1^* - \xi_0)}{S_1^* + 5\xi_0} C_1 + \frac{\beta_{B_1}(t)(S_1^* - \xi_0)}{\xi_0 + K_{B_1}} B_1 - (\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1})I_1 \\
&\quad -\theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2,\ t \geq 0.
\end{aligned}$$

From the equation of I_2 in (1), we can use the same arguments to show that

$$\begin{aligned}
\frac{dI_2}{dt} \geq\ & \frac{\beta_{C_2}(t)(S_2^* - \xi_0)}{S_2^* + 5\xi_0} I_2 + \frac{\eta_2 \beta_{C_2}(t)(S_2^* - \xi_0)}{S_2^* + 5\xi_0} C_2 + \frac{\beta_{B_2}(t)(S_2^* - \xi_0)}{\xi_0 + K_{B_2}} B_2 \\
& -(\mu_2 + \sigma_2 + \delta_{I_2} + \epsilon_{I_2})I_2 - \theta_2 I_2 + m_{12}^I I_1 - m_{21}^I I_2,\ t \geq 0.
\end{aligned}$$

Then, for $t \geq 0$, we further have the following inequalities

$$\begin{cases}
\frac{dI_1}{dt} \geq \frac{\beta_{C_1}(t)(S_1^* - \xi_0)}{S_1^* + 5\xi_0} I_1 + \frac{\eta_1 \beta_{C_1}(t)(S_1^* - \xi_0)}{S_1^* + 5\xi_0} C_1 + \frac{\beta_{B_1}(t)(S_1^* - \xi_0)}{\xi_0 + K_{B_1}} B_1 \\
\qquad -(\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1})I_1 - \theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2, \\
\frac{dC_1}{dt} = \sigma_1 I_1 - (\mu_1 + \delta_{C_1} + \epsilon_{C_1})C_1 - m_{12}^C C_1 + m_{21}^C C_2, \\
\frac{dB_1}{dt} = g_1 B_1 + \alpha_{I_1}(t) I_1 + \alpha_{C_1}(t) C_1 - \mu_{B_1} B_1 - m_{12}^B B_1 + m_{21}^B B_2, \\
\frac{dI_2}{dt} \geq \frac{\beta_{C_2}(t)(S_2^* - \xi_0)}{S_2^* + 5\xi_0} I_2 + \frac{\eta_2 \beta_{C_2}(t)(S_2^* - \xi_0)}{S_2^* + 5\xi_0} C_2 + \frac{\beta_{B_2}(t)(S_2^* - \xi_0)}{\xi_0 + K_{B_2}} B_2 \\
\qquad -(\mu_2 + \sigma_2 + \delta_{I_2} + \epsilon_{I_2})I_2 - \theta_2 I_2 + m_{12}^I I_1 - m_{21}^I I_2, \\
\frac{dC_2}{dt} = \sigma_2 I_2 - (\mu_2 + \delta_{C_2} + \epsilon_{C_2})C_2 + m_{12}^C C_1 - m_{21}^C C_2, \\
\frac{dB_2}{dt} = g_2 B_2 + \alpha_{I_2}(t) I_2 + \alpha_{C_2}(t) C_2 - \mu_{B_2} B_2 + m_{12}^B B_1 - m_{21}^B B_2.
\end{cases} \tag{14}$$

In view of the fact $x^0 \in \mathbb{X}_0$ and Lemma 3.2, it follows that

$$(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t))^T \gg 0,\ \forall\, t > 0.$$

Thus, we find a fixed $\tilde{t}_0 > 0$ such that

$$(I_1(\tilde{t}_0), C_1(\tilde{t}_0), B_1(\tilde{t}_0), I_2(\tilde{t}_0), C_2(\tilde{t}_0), B_2(\tilde{t}_0)) \gg 0.$$

In view of Lemma 3.1, we may find a positive, ω-periodic function $J(t)$ and $\tilde{J}(t) := \tilde{d}e^{\tilde{\lambda}(t-\tilde{t}_0)}J(t)$ is a solution of

$$\frac{dx(t)}{dt} = (\mathbb{F}_{\xi_0}(t) - \mathbb{V}(t))\, x(t).$$

Here $\tilde{\lambda} := \frac{1}{\omega}\ln\left[r(\Phi_{\mathbb{F}_{\xi_0}(\cdot)-\mathbb{V}(\cdot)}(\omega))\right]$ and $\tilde{d}$ is small enough such that

$$\tilde{J}(\tilde{t}_0) = \tilde{d}J(\tilde{t}_0) \le (I_1(\tilde{t}_0), C_1(\tilde{t}_0), B_1(\tilde{t}_0), I_2(\tilde{t}_0), C_2(\tilde{t}_0), B_2(\tilde{t}_0)).$$

The comparison argument (see, e.g., [20, Theorem B.1]) and the inequalities (14) establish that

$$(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t))^T \ge \tilde{J}(t),\ \forall\, t \ge \tilde{t}_0.$$

In particular, there exists n_1 such that

$$(I_1(n\omega), C_1(n\omega), B_1(n\omega), I_2(n\omega), C_2(n\omega), B_2(n\omega))^T \ge \tilde{J}(n\omega),\ \forall\, n \ge n_1.$$

Since $\tilde{\lambda} > 0$, it follows that $\tilde{J}(n\omega) \to \infty$ as $n \to \infty$. Thus,

$$(I_1(n\omega), C_1(n\omega), B_1(n\omega), I_2(n\omega), C_2(n\omega), B_2(n\omega))^T \to \infty$$

as $n \to \infty$. This contradiction completes the proof.

Next, we show that $\mathcal{R}_0$ is an important index for disease persistence.

Theorem 3.1. The statements are valid.

1. If $\mathcal{R}_0 < 1$ and $\rho_1 = \rho_2 = 0$, then the disease-free state E_0 is globally attractive for system (1) in the sense that

$$\lim_{t\to\infty}(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t)) = E_0;$$

2. If $\mathcal{R}_0 > 1$, there exists an $\zeta > 0$ such that for any solution

$$(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t))$$

with initial value $x^0 := (S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X}$ and

$$I_1^0 \ne 0 \text{ or } I_2^0 \ne 0 \text{ or } C_1^0 \ne 0 \text{ or } C_2^0 \ne 0 \text{ or } B_1^0 \ne 0 \text{ or } B_2^0 \ne 0, \tag{15}$$

we have

$$\liminf_{t\to\infty} I_i(t) \ge \zeta,\ \liminf_{t\to\infty} C_i(t) \ge \zeta,\ \liminf_{t\to\infty} B_i(t) \ge \zeta,\ i = 1, 2. \tag{16}$$

Moreover, system (1) has at least one positive ω-periodic solution

$$(\hat{S}_1(t), \hat{I}_1(t), \hat{C}_1(t), \hat{Q}_1(t), \hat{R}_1(t), \hat{B}_1(t), \hat{S}_2(t), \hat{I}_2(t), \hat{C}_2(t), \hat{Q}_2(t), \hat{R}_2(t), \hat{B}_2(t)).$$

Proof Part (i). We first consider the case where $\mathcal{R}_0 < 1$ with $\rho_1 = \rho_2 = 0$. Thus, $r(\Phi_{\mathbb{F}(\cdot)-\mathbb{V}(\cdot)}(\omega)) < 1$ (see Lemma 2.4). Now we take $\xi_1 > 0$ sufficiently small such that $r(\Phi_{\mathbb{F}_{\xi_1}(\cdot)-\mathbb{V}(\cdot)}(\omega)) < 1$. Here

$$\mathbb{F}_{\xi_1}(t) = \begin{pmatrix} \beta_{C_1}(t) & \eta_1\beta_{C_1}(t) & (S_1^* + \xi_1)\frac{\beta_{B_1}(t)}{K_{B_1}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_{C_2}(t) & \eta_2\beta_{C_2}(t) & (S_2^* + \xi_1)\frac{\beta_{B_2}(t)}{K_{B_2}} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

From the positivity of solutions and the assumption $\rho_1 = \rho_2 = 0$, it follows from the first and seventh equations of (1) that

$$\begin{cases} \frac{dS_1}{dt} \le \Lambda_1 - \mu_1 S_1 - m_{12}^S S_1 + m_{21}^S S_2, \\ \frac{dS_2}{dt} \le \Lambda_2 - \mu_2 S_2 + m_{12}^S S_1 - m_{21}^S S_2. \end{cases} \tag{17}$$

In view of (17), (3), Lemma 2.1, together with the comparison arguments that there is a $t_1 > 0$ such that

$$S_i(t) \le S_i^* + \xi_1,\ \forall\, t \ge t_1,\ i = 1, 2.$$

Then we have the following inequalities

$$\begin{cases} \frac{dI_1}{dt} \le \beta_{C_1}(t)(I_1 + \eta_1 C_1) + \frac{\beta_{B_1}(t)(S_1^*+\xi_1)}{K_{B_1}} B_1 \\ \qquad -(\mu_1 + \sigma_1 + \delta_{I_1} + \epsilon_{I_1}) I_1 - \theta_1 I_1 - m_{12}^I I_1 + m_{21}^I I_2,\ \forall\, t \ge t_1, \\ \frac{dC_1}{dt} = \sigma_1 I_1 - (\mu_1 + \delta_{C_1} + \epsilon_{C_1}) C_1 - m_{12}^C C_1 + m_{21}^C C_2,\ \forall\, t \ge t_1, \\ \frac{dB_1}{dt} = g_1 B_1 + \alpha_{I_1}(t) I_1 + \alpha_{C_1}(t) C_1 - \mu_{B_1} B_1 - m_{12}^B B_1 + m_{21}^B B_2,\ \forall\, t \ge t_1, \\ \frac{dI_2}{dt} \le \beta_{C_2}(t)(I_2 + \eta_2 C_2) + \frac{\beta_{B_2}(t)(S_2^*+\xi_1)}{K_{B_2}} B_2 \\ \qquad -(\mu_2 + \sigma_2 + \delta_{I_2} + \epsilon_{I_2}) I_2 - \theta_2 I_2 + m_{12}^I I_1 - m_{21}^I I_2,\ \forall\, t \ge t_1, \\ \frac{dC_2}{dt} = \sigma_2 I_2 - (\mu_2 + \delta_{C_2} + \epsilon_{C_2}) C_2 + m_{12}^C C_1 - m_{21}^C C_2,\ \forall\, t \ge t_1, \\ \frac{dB_2}{dt} = g_2 B_2 + \alpha_{I_2}(t) I_2 + \alpha_{C_2}(t) C_2 - \mu_{B_2} B_2 + m_{12}^B B_1 - m_{21}^B B_2,\ \forall\, t \ge t_1. \end{cases} \tag{18}$$

By Lemma 3.1, we can find a positive, ω-periodic function $v(t)$ and $\bar{v}(t) := \bar{d} e^{\lambda_1 (t-t_1)} v(t)$ is a solution of

$$\frac{dx(t)}{dt} = (\mathbb{F}_{\xi_1}(t) - \mathbb{V}(t))\, x(t),$$

where $\lambda_1 := \frac{1}{\omega} \ln \left[r(\Phi_{\mathbb{F}_{\xi_1}(\cdot) - \mathbb{V}(\cdot)}(\omega)) \right]$ and $\bar{d} > 0$ is large enough such that

$$\bar{v}(t_1) = \bar{d} v(t_1) \ge (I_1(t_1), C_1(t_1), B_1(t_1), I_2(t_1), C_2(t_1), B_2(t_1)).$$

Then (18) and the comparison argument (see, e.g., [20, Theorem B.1]) imply that

$$(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t)) \le \bar{v}(t),\ \forall\, t \ge t_1.$$

With $\lambda_1 < 0$, we see that $\bar{v}(t) \to 0$ as $t \to \infty$. Therefore,

$$(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t)) \to 0 \text{ as } t \to \infty.$$

Then $Q_i(t)$, $i = 1, 2$, in (1) is asymptotic to the following system

$$\frac{dQ_i}{dt} = -(\mu_i + \gamma_i + \delta_{Q_i}) Q_i.$$

Thus, $\lim_{t\to\infty} Q_i(t) = 0,\ i = 1, 2$. Here we used the theory of asymptotically periodic semiflows (see, e.g., [24] and [25, section 3.2]). Similarly, $(R_1(t), R_2(t))$ in (1) is asymptotic to the following system

$$\begin{cases} \frac{dR_1}{dt} = -(\mu_1 + \rho_1) R_1 - m_{12}^R R_1 + m_{21}^R R_2, \\ \frac{dR_2}{dt} = -(\mu_2 + \rho_2) R_2 + m_{12}^R R_1 - m_{21}^R R_2, \end{cases} \tag{19}$$

and hence, $\lim_{t\to\infty}(R_1(t), R_2(t)) = (0, 0)$. Thus, $(S_1(t), S_2(t))$ in system (1) is asymptotic to system (3). By Lemma 2.1, we see that $\lim_{t\to\infty}(S_1(t), S_2(t)) = (S_1^*, S_2^*)$. This proves Part (i).

Part (ii). Assume that $\mathcal{R}_0 > 1$. In view of Lemma 2.2, we see that the discrete-time system $\{P^n\}_{n\ge 0}$ admits a global attractor in $\mathbb{X}$. Now we are ready to show that $\{P^n\}_{n\ge0}$ is uniformly persistent with respect to $(\mathbb{X}_0, \partial\mathbb{X}_0)$. By Lemma 3.2, it follows that $\mathbb{X}_0$ is positively invariant under the solution flow of (1). Clearly, $\mathbb{X}_0$ is open in $\mathbb{X}$, $\mathbb{X}_0 \cup \partial\mathbb{X}_0 = \mathbb{X}$, and $\mathbb{X}_0 \cap \partial\mathbb{X}_0 = \emptyset$.

Let

$$M_\partial = \{x^0 \in \partial\mathbb{X}_0 : P^n(x^0) \in \partial\mathbb{X}_0,\ \forall\, n \in \mathbb{N}\},$$

and $\varpi(x^0)$ be the omega limit set of the orbit $\Gamma^+ = \{P^n(x^0) : \forall n \in \mathbb{N}\}$. Recall that E_0 represents the disease-free state of system (1), which is given in (6). Then $P(E_0) = E_0$.

Inspired by the work [21], we set

$$\mathbb{M}_0 = \{(S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X} : I_i^0 = C_i^0 = B_i^0 = 0, i = 1, 2\}.$$

Claim 1. $\mathbb{M}_0 = M_\partial$.

For any $x^0 := (S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{M}_0$, we have $I_i^0 = C_i^0 = B_i^0 = 0,\ \forall\, i = 1, 2$. This implies that $I_i(t, x^0) = C_i(t, x^0) = B_i(t, x^0) = 0,\ \forall\, i = 1, 2,\ \forall\, t \ge 0$. Hence, $I_i(n\omega, x^0) = C_i(n\omega, x^0) = B_i(n\omega, x^0) = 0,\ \forall\, i = 1, 2,\ \forall\, n \in \mathbb{N}$. Thus, it is easy to see that $x^0 \in \partial\mathbb{X}_0$ and $P^n(x^0) \in \partial\mathbb{X}_0,\ \forall\, n \in \mathbb{N}$. This means that $x^0 \in M_\partial$. Therefore, $\mathbb{M}_0 \subseteq M_\partial$. On the other hand, for any $x^0 :=$

$(S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in M_\partial$, we must have

$$I_i^0 = C_i^0 = B_i^0 = 0,\ \forall\, i = 1,2. \tag{20}$$

Otherwise,

$$(I_1^0, C_1^0, B_1^0, I_2^0, C_2^0, B_2^0) \neq (0,0,0,0,0,0),$$

which together with Lemma 3.2 implies that

$$(I_1(n\omega), C_1(n\omega), B_1(n\omega), I_2(n\omega), C_2(n\omega), B_2(n\omega))^T \gg (0,0,0,0,0,0),\ \forall\, n > 0.$$

The definition of M_∂ contradicts the above inequality, and hence, (20) holds. Thus, $x^0 \in \mathbb{M}_0$, and hence, $M_\partial \subseteq \mathbb{M}_0$. Therefore, Claim 1 is true.

Claim 2. E_0 is globally stable in M_∂.

We first show that $\varpi(x^0) = E_0,\ \forall\, x^0 \in M_\partial$. Given $x^0 \in M_\partial = \mathbb{M}_0$, we see that $I_i(t, x^0) = C_i(t, x^0) = B_i(t, x^0) = 0,\ i = 1, 2,\ t \geq 0$. Then, for $t \geq 0$, $(S_1(t), Q_1(t), R_1(t), S_2(t), Q_2(t), R_2(t))$ satisfies

$$\begin{cases} \frac{dS_1}{dt} = \Lambda_1 - \mu_1 S_1 + \rho_1 R_1 - m_{12}^S S_1 + m_{21}^S S_2, \\ \frac{dQ_1}{dt} = -(\mu_1 + \gamma_1 + \delta_{Q_1}) Q_1, \\ \frac{dR_1}{dt} = \gamma_1 Q_1 - (\mu_1 + \rho_1) R_1 - m_{12}^R R_1 + m_{21}^R R_2, \\ \frac{dS_2}{dt} = \Lambda_2 - \mu_2 S_2 + \rho_2 R_2 + m_{12}^S S_1 - m_{21}^S S_2, \\ \frac{dQ_2}{dt} = -(\mu_2 + \gamma_2 + \delta_{Q_2}) Q_2, \\ \frac{dR_2}{dt} = \gamma_2 Q_2 - (\mu_2 + \rho_2) R_2 + m_{12}^R R_1 - m_{21}^R R_2. \end{cases} \tag{21}$$

In view of system (21), we see that $\lim_{t\to\infty} Q_i(t) = 0,\ i = 1, 2$. Then $(R_1(t), R_2(t))$ in (1) is asymptotic to system (19), and hence, $\lim_{t\to\infty}(R_1(t), R_2(t)) = (0, 0)$. Thus, $(S_1(t), S_2(t))$ in system (1) is asymptotic to system (3). By Lemma 2.1, it follows that $\lim_{t\to\infty}(S_1(t), S_2(t)) = (S_1^*, S_2^*)$. Thus, we have shown that $\varpi(x^0) = E_0$. In view of above claims and Lemma 3.3, we see that $\{E_0\}$ is an isolated invariant set in $\mathbb{X}$ and $W^s(E_0) \cap \mathbb{X}_0 = \emptyset$, where $W^s(E_0)$ is the stable set of E_0, and $\{E_0\}$ is acyclic in M_∂. In view of [25, Theorem 1.3.1], we see that $\{P^n\}_{n\geq 0}$ is uniformly persistent with respect to $(\mathbb{X}_0, \partial\mathbb{X}_0)$ in the sense that there exists $\tilde{\zeta} > 0$ such that

$$\liminf_{n\to\infty} \mathrm{d}(P^n(x^0), \partial\mathbb{X}_0) \geq \tilde{\zeta},\ \forall x^0 \in \mathbb{X}_0,$$

where d is the norm-induced distance in $\mathbb{R}^{12}$. By [14, Theorem 3.7], we know that P has a global attractor A_0 in $\mathbb{X}_0$. Since $A_0 = PA_0$, we have that $I_i^0 > 0,\ C_i^0 > 0,\ B_i^0 > 0,\ i = 1, 2$, for all

$$x^0 := (S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in A_0.$$

Let $B_0 := \bigcup_{t\in[0,\omega]} \Psi(t)A_0$. Then $B_0 \subset \mathbb{X}_0$ and $\lim_{t\to\infty} \mathrm{d}(\Psi(t)\phi, B_0) = 0, \forall x^0 \in \mathbb{X}_0$. Then there exists an $\zeta > 0$ such that for any solution

$$(S_1(t), I_1(t), C_1(t), Q_1(t), R_1(t), B_1(t), S_2(t), I_2(t), C_2(t), Q_2(t), R_2(t), B_2(t))$$

with initial value $x^0 \in \mathbb{X}_0$ satisfies

$$\liminf_{t\to\infty} I_i(t) \geq \zeta,\ \liminf_{t\to\infty} C_i(t) \geq \zeta,\ \liminf_{t\to\infty} B_i(t) \geq \zeta,\ i = 1, 2.$$

Furthermore, [25, Theorem 1.3.6] implies that P has a fixed point

$$\hat{x} = (\hat{S}_1(0), \hat{I}_1(0), \hat{C}_1(0), \hat{Q}_1(0), \hat{R}_1(0), \hat{B}_1(0), \hat{S}_2(0), \hat{I}_2(0), \hat{C}_2(0), \hat{Q}_2(0), \hat{R}_2(0), \hat{B}_2(0))$$

in $\mathbb{X}_0$, and hence, $\hat{I}_i(0) > 0,\ \hat{C}_i(0) > 0,\ \hat{B}_i(0) > 0, i = 1, 2$.

Clearly, $u(t, \hat{x}) = (\hat{S}_1, \hat{I}_1, \hat{C}_1, \hat{Q}_1, \hat{R}_1, \hat{B}_1, \hat{S}_2, \hat{I}_2, \hat{C}_2, \hat{Q}_2, \hat{R}_2, \hat{B}_2)(t)$ is an ω-periodic solution of (1). We can further show that

$$(\hat{S}_1(t), \hat{I}_1(t), \hat{C}_1(t), \hat{Q}_1(t), \hat{R}_1(t), \hat{B}_1(t), \hat{S}_2(t), \hat{I}_2(t), \hat{C}_2(t), \hat{Q}_2(t), \hat{R}_2(t), \hat{B}_2(t)) \gg 0,$$

due to the similar arguments to those in Lemma 3.2.

The rest of the mathematical arguments were motivated by the work [21]. For any $x^0 := (S_1^0, I_1^0, C_1^0, Q_1^0, R_1^0, B_1^0, S_2^0, I_2^0, C_2^0, Q_2^0, R_2^0, B_2^0) \in \mathbb{X}$ with the property in (15), it is easy to see that $x^0 \notin \mathbb{M}_0$. We claim that there exists an integer $n_0 = n_0(x^0) \geq 0$ such that $P^{n_0}(x^0) \in \mathbb{X}_0$. Otherwise, $P^n(x^0) \in \partial\mathbb{X}_0$, for all $n \geq 0$, which implies that $x^0 \in M_\partial = \mathbb{M}_0$, and it is a contradiction. Since

$$\Psi(t)x^0 = \Psi(t - n_0\omega)(\Psi(n_0\omega)x^0) = \Psi(t - n_0\omega)(P^{n_0}(x^0)),$$

we see that (16) is also valid. The proof of Part (ii) is finished.

4. Numerical Simulations

This section is devoted to the numerical investigation of seasonal and spatial influences on the dynamics of system (1). Except the migration rates, the parameters used in our numerical simulations were given in Table 1. In order to study the spatial influence on system (1), we first put $m_{21}^w = m_{12}^w = 0$, $w = S, I, C, R, B$, into system (1), and we obtain the following model in a single patch i:

$$\begin{cases} \frac{dS_i}{dt} = \Lambda_i - \frac{\beta_{C_i}(t)(I_i+\eta_i C_i)S_i}{S_i+I_i+C_i+Q_i+R_i} - \frac{\beta_{B_i}(t)B_iS_i}{B_i+K_{B_i}} - \mu_i S_i + \rho_i R_i, \\ \frac{dI_i}{dt} = \frac{\beta_{C_i}(t)(I_i+\eta_i C_i)S_i}{S_i+I_i+C_i+Q_i+R_i} + \frac{\beta_{B_i}(t)B_iS_i}{B_i+K_{B_i}} - (\mu_i + \sigma_i + \delta_{I_i} + \epsilon_{I_i})I_i - \theta_i I_i, \\ \frac{dC_i}{dt} = \sigma_i I_i - (\mu_i + \delta_{C_i} + \epsilon_{C_i})C_i, \\ \frac{dQ_i}{dt} = \theta_i I_i - (\mu_i + \gamma_i + \delta_{Q_i})Q_i, \\ \frac{dR_i}{dt} = \gamma_i Q_i + \epsilon_{I_i} I_i + \epsilon_{C_i} C_i - (\mu_i + \rho_i)R_i, \\ \frac{dB_i}{dt} = g_i B_i + \alpha_{I_i}(t) I_i + \alpha_{C_i}(t) C_i - \mu_{B_i} B_i, \\ S_i(0) \geq 0,\ I_i(0) \geq 0,\ C_i(0) \geq 0,\ Q_i(0) \geq 0,\ R_i(0) \geq 0,\ B_i(0) \geq 0, \end{cases} \tag{22}$$

where either $i = 1$ or $i = 2$. Next, we define the basic reproduction number, $\mathcal{R}_0^{(i)}$, for system (22). Let

$$\mathbf{F}^{(i)}(t) = \begin{pmatrix} \beta_{C_i}(t) & \eta_i\beta_{C_i}(t) & S_i^* \frac{\beta_{B_i}(t)}{K_{B_i}} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$\mathbf{V}^{(i)}(t) = \begin{pmatrix} \mathbf{V}_{11}^{(i)} & 0 & 0 \\ -\sigma_i & \mathbf{V}_{22}^{(i)} & 0 \\ -\alpha_{I_i}(t) & -\alpha_{C_i}(t) & \mathbf{V}_{33}^{(i)} \end{pmatrix},$$

where $\mathbf{V}_{11}^{(i)} = \mu_i + \sigma_i + \delta_{I_i} + \epsilon_{I_i} + \theta_i$, $\mathbf{V}_{22}^{(i)} = \mu_i + \delta_{C_i} + \epsilon_{C_i}$, and $\mathbf{V}_{33}^{(i)} = \mu_{B_i} - g_i$. By the same ideas in Lemma 2.3 (see also [22, Theorem 2.1]), we let $\mathcal{W}^{(i)}(t, s, \lambda)$, $t \geq s$, $s \in \mathbb{R}$ be the evolution operator of the linear ω-periodic system on $\mathbb{R}^3$,

$$\frac{dw}{dt} = \left(-\mathbf{V}^{(i)}(t) + \frac{\mathbf{F}^{(i)}(t)}{\lambda}\right)w,\ \ t \in \mathbb{R},$$

with parameter $\lambda \in (0, \infty)$. Then $\lambda = \mathcal{R}_0^{(i)}$ is the unique solution of

$$\rho(\mathcal{W}^{(i)}(\omega, 0, \lambda)) = 1, \tag{23}$$

where $\rho(\mathcal{W}^{(i)}(\omega, 0, \lambda))$ is the spectral radius of $\mathcal{W}^{(i)}(\omega, 0, \lambda)$. Use the property (23) and the parameters in Table 1, we can numerically observe that $\mathcal{R}_0^{(1)} < 1$ and $\mathcal{R}_0^{(2)} < 1$ whenever $0 \leq d_1, d_2 \leq 1$ (see Figure 1). This reveals that the disease cannot spread in a single patch with parameters in Table 1 and $0 \leq d_1, d_2 \leq 1$.

Table 1. *Parameter values (except migration rates) used in our numerical simulations, where the values of d_1 and d_2 will be given.*

Parameters	Mean value	References
$\beta_{C_1}(t)$	$0.3 \times [d_1 \times cos(2\pi t/365) + 1.01]$	Assumed
$\beta_{C_2}(t)$	$0.4 \times [d_2 \times cos(2\pi t/365) + 1.01]$	Assumed
$\eta_1,\ \eta_2$	1.2	[15]
$\beta_{B_1}(t)$	$3 \times 10^{-6} \times [d_1 \times \cos(2\pi t/365) + 1.01]$	Assumed
$\beta_{B_2}(t)$	$1 \times 10^{-6} \times [d_2 \times \cos(2\pi t/365) + 1.01]$	Assumed
$K_{B_1},\ K_{B_2}$	0.62	[16]
$\theta_1,\ \theta_2$	0.2827	[11]
$\delta_{I_1},\ \delta_{I_2}$	0.06	[15]
$\delta_{C_1},\ \delta_{C_2}$	0.004	[15]
$\delta_{Q_1},\ \delta_{Q_2}$	0.0033	[15]
$\sigma_1,\ \sigma_2$	0.04	[2]
$\epsilon_{I_1},\ \epsilon_{I_2}$	0.1	[15]
$\epsilon_{C_1},\ \epsilon_{C_2}$	0.001	[16]
$\alpha_{I_1}(t)$	$10 \times [d_1 \times cos(2\pi t/365) + 1.01]$	Assumed
$\alpha_{I_2}(t)$	$10 \times [d_2 \times cos(2\pi t/365) + 1.01]$	Assumed
$\alpha_{C_1}(t)$	$5 \times [d_1 \times cos(2\pi t/365) + 1.01]$	Assumed
$\alpha_{C_2}(t)$	$5 \times [d_2 \times cos(2\pi t/365) + 1.01]$	Assumed
$\mu_{B_1},\ \mu_{B_2}$	0.0345	[17]
$\gamma_1,\ \gamma_2$	0.002485	[11]
μ_1	0.136	Assumed
μ_2	0.281	Assumed
Λ_1	$\mu_1 \times 0.7$	Assumed
Λ_2	$\mu_2 \times 1$	Assumed
$\rho_1,\ \rho_2$	0.0013	[18]
$g_1,\ g_2$	0.014	[17]

Next, we numerically investigate the influence of migration on the transmission of typhoid. We will show that typhoid can become epidemic if we incorporate suitable migration rates between patch 1 and patch 2 with parameters in Table 1 into system (1) whenever d_1 and d_2 are close to 1. That is, we observe that typhoid can become epidemic with suitable migration rates between patch 1 and patch 2, although it cannot be epidemic in each isolated single patch (without migration). More precisely, the immigration rates are chosen as follows:

$$\begin{aligned} m_{12}^S &= 1,\ m_{21}^S = 30, \\ m_{12}^I &= 1,\ m_{21}^I = 20, \\ m_{12}^C &= 1,\ m_{21}^C = 15, \\ m_{12}^R &= 1,\ m_{21}^R = 10, \\ m_{12}^B &= 1,\ m_{21}^B = 50, \end{aligned} \tag{24}$$

where the migration rates from patch 2 to patch 1 are much bigger than those from patch 1 to patch 2. We first assume the parameters in system (1) take those in Table 1 and (24), then the basic reproduction number $\mathcal{R}_0$ of system (1) can be numerically computed by the ideas in Lemma 2.3, and an interesting phenomenon occurs that $\mathcal{R}_0 > 1$ when d_1, d_2 are close to 1 (see Figure 2); nevertheless, $\mathcal{R}_0^{(i)} < 1,\ i = 1, 2$ (see Figure 1). This indicates that migration between patches does play a central role in the transmission of typhoid. Finally, we also numerically show the extinction of the isolated single patch system (22) with $i = 1, 2$, respectively, but persistence of the two-patch system (1) occurs after the migration rates are included. The parameters we used are in Table 1 and (24). Putting $d_1 = 0.96$ (resp. $d_2 = 0.95$), and the extinction of system (22) with $i = 1$ (resp. $i = 2$) is illustrated in Figure 3 (resp. Figure 4). After we put $d_1 = 0.96$ and $d_2 = 0.95$ and the immigration rates are chosen in (24), persistence of system (1) occurs (see Figure 5).

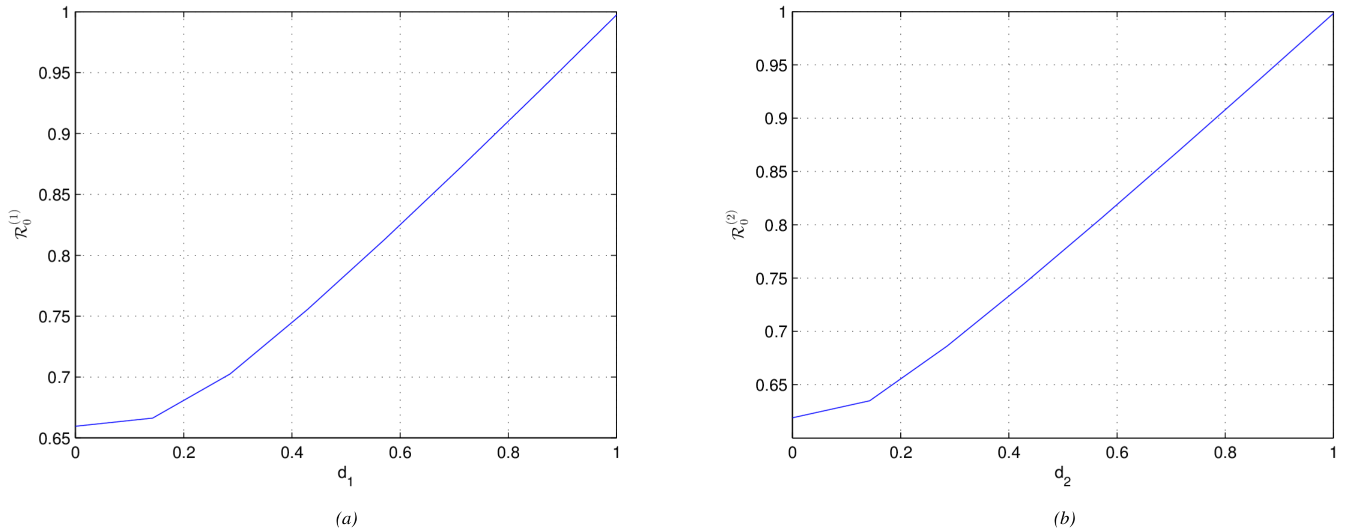

Figure 1. *The basic reproduction number, $\mathcal{R}_0^{(i)}$, in each single patch. (a) $\mathcal{R}_0^{(1)}$ for patch 1 (system (22) with $i = 1$) with respect to the parameter $d_1 \in [0, 1]$; (b) $\mathcal{R}_0^{(2)}$ for patch 2 (system (22) with $i = 2$) with respect to the parameter $d_2 \in [0, 1]$. All parameters we used are in Table 1 and we observe that $\mathcal{R}_0^{(i)} < 1$ when $d_1,\ d_2 \in [0, 1]$, $i = 1, 2$.*

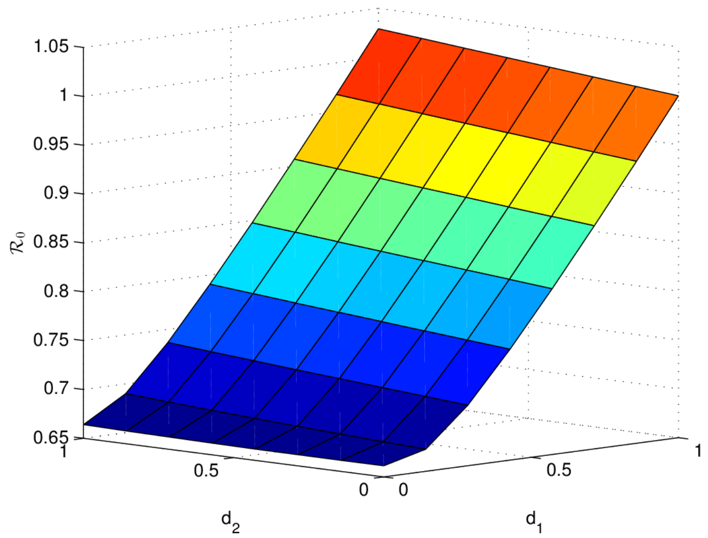

Figure 2. *$\mathcal{R}_0$ of system (1) with respect to the parameters $d_1,\ d_2 \in [0, 1]$. All parameters we used are in Table 1 and (24).*

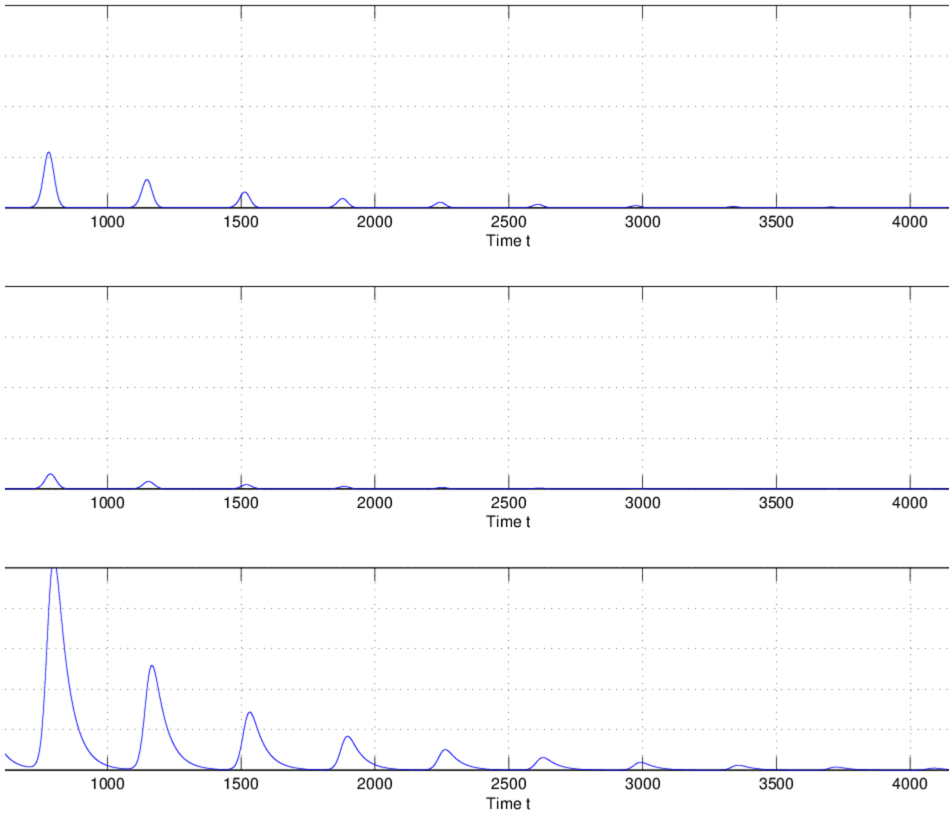

Figure 3. *Extinction occurs for the single patch system* (22) *with* $i = 1$ *and* $d_1 = 0.96$*, where the used parameters are in Table 1 and only the dynamics of* $(I_1(t), C_1(t), B_1(t))$ *are shown.*

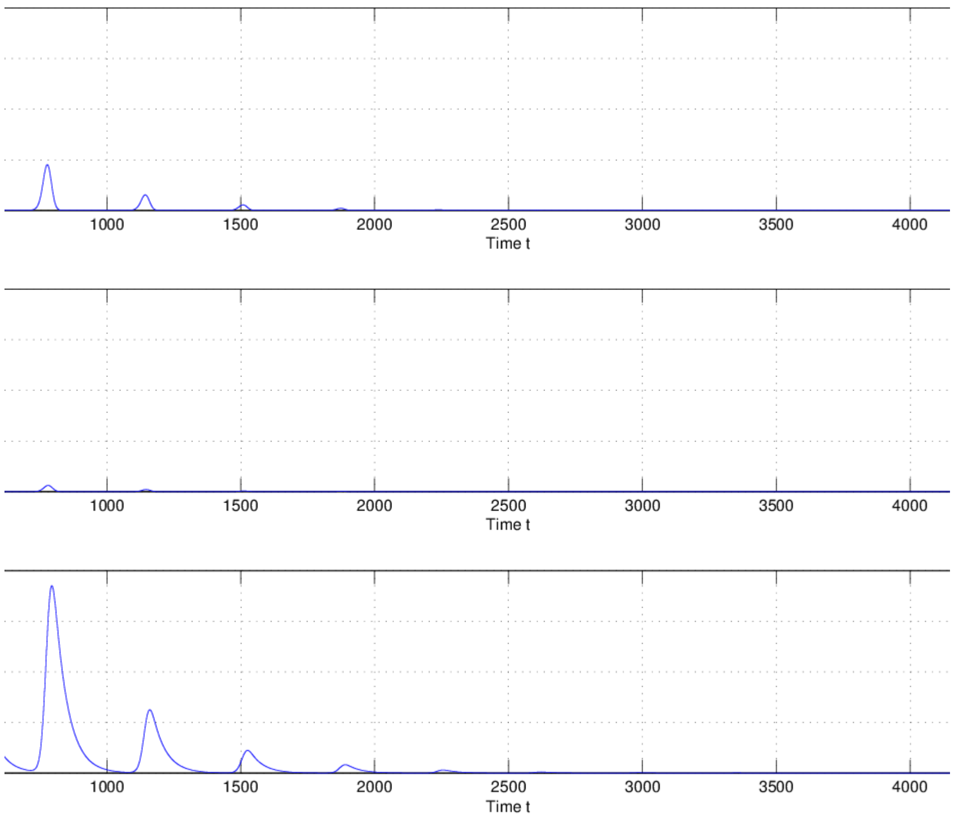

Figure 4. *Extinction occurs for the single patch system* (22) *with* $i = 2$ *and* $d_2 = 0.95$*, where the used parameters are in Table 1 and only the dynamics of* $(I_2(t), C_2(t), B_2(t))$ *are shown.*

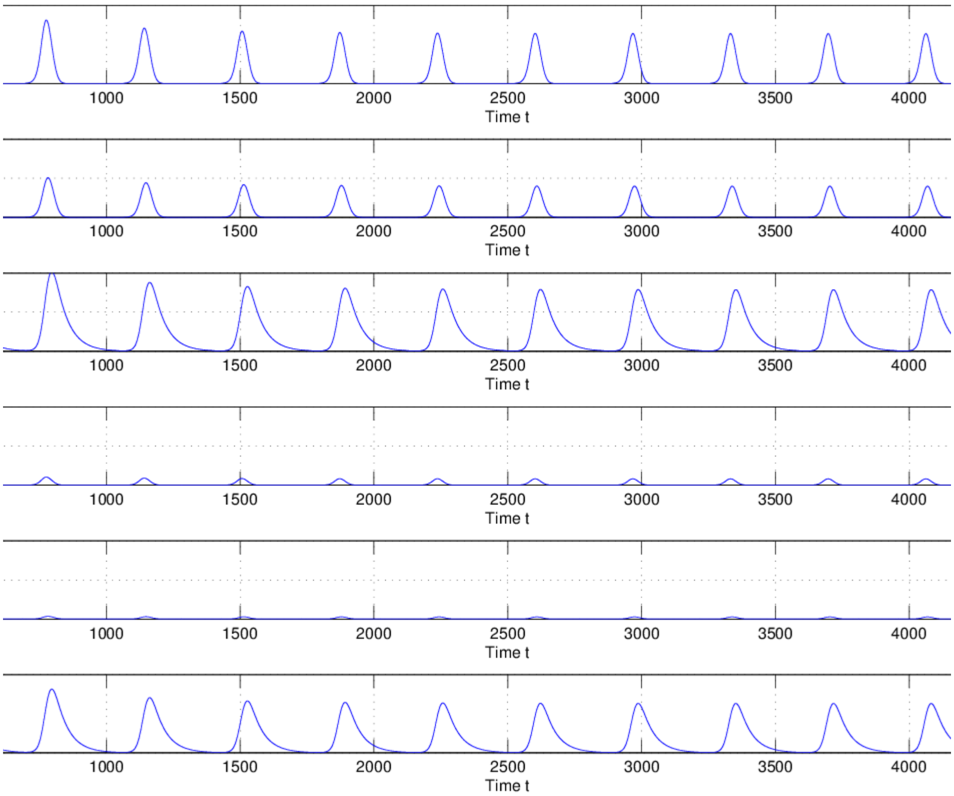

Figure 5. Persistence occurs for the two-patch system (1) *with* $d_1 = 0.96$ *and* $d_2 = 0.95$*, where the used parameters are in Table 1 and* (24)*, and only the dynamics of* $(I_1(t), C_1(t), B_1(t), I_2(t), C_2(t), B_2(t))$ *are shown.*

5. Conclusion

Typhoid can be a serious problem in several developing countries, and the infection of typhoid is through both direct (i.e. human-to-human) transmission and indirect (i.e. environment-to-human) transmission, which is associated with the ingestion of contaminated food or water. Asymptomatically infected individuals are not experiencing any symptoms but they can shed S. Typhi into the environment for years, thereby sustaining transmission [15, 16]. A higher incidence of typhoid fever [12, 13] is usually observed during the rainy season since a large increase of flooding may occur by the rainfall and the water resources is contaminated by the excreta with pathogenic bacteria. It is also reported that people living near water bodies may have a higher rate of typhoid infection [4]. Thus, this study constructed and analyzed a system that incorporates seasonal effects into a two-patch model describing the transmission of Typhoid fever in a seasonally and spatially variable environment, in which the bacteria in the environment was included and the population of human is divided into five classes, namely, susceptible individuals, infected individuals, carrier individuals, individuals under treatment and recovered individuals.

The well-posedness of model (1) (see Lemma 2.2) is first established, and the associated reproduction number, $\mathcal{R}_0$ is also provided. Since the population Q_i, $i = 1, 2$, in system (1) is supposed to be on treatment and it cannot move in the environment, leading to that those terms $-m_{12}^Q Q_1 + m_{21}^Q Q_2$ and $m_{12}^Q Q_1 - m_{21}^Q Q_2$ must be ignored. This makes mathematical analysis more difficult and we can prove the extinction of Typhoid fever only when $\mathcal{R}_0 < 1$ and the additional condition $\rho_i = 0$, $i = 1, 2$, is imposed, where ρ_i represents the immunity waning rate in patch i (see Theorem 3.1 (i)). When $\mathcal{R}_0 > 1$, the Typhoid fever can persist in the environment if one of the initial values of infected individuals (I_i^0), carrier individuals (C_i^0) and bacteria (B_i^0) is non-zero, for some patch i (see Theorem 3.1 (ii)).

The numerical results in Section 4 further indicate that migration rates between patches may reverse the outcome of the persistence of Typhoid fever. The used parameters of system (1) takes the form in Table 1 with $d_1 = 0.96$ and $d_2 = 0.95$. When migration rates are further chosen as those in (24), it is observed that Typhoid fever persists (see Figure 5), however, typhoid may become extinct when migration rates are changed into zeros (see Figure 3 and Figure 4). Thus, our simulation confirms that spatial effects do play an important role in the transmission of Typhoid fever.

Finally, the influences of seasonal factors on the transmission of typhoid are also performed numerically. For this purpose, the used parameters of system (1) takes the form in Table 1 with $d_1, d_2 \in [0, 1]$, then the dependence of $\mathcal{R}_0$ on $d_1, d_2 \in [0, 1]$ is illustrated in Figure 2. The basic reproduction number, $[\mathcal{R}_0]$, of the time-averaged autonomous system corresponding to (1) is also calculated. For a continuous periodic function $g(t)$ with the period ω, we define its average as $[g] := \frac{1}{\omega}\int_0^\omega g(t)dt$. In view of Table 1, it is not hard to see that $\omega = 365$, $[\beta_{C_1}] = 0.3 \times 1.01$, $[\beta_{C_2}] = 0.4 \times 1.01$, $[\beta_{B_1}] = 3 \times 10^{-6} \times 1.01$, $[\beta_{B_2}] = 1 \times 10^{-6} \times 1.01$, $[\alpha_{I_1}] = 10 \times 1.01$, $[\alpha_{I_2}] = 10 \times 1.01$, $[\alpha_{C_1}] = 5 \times 1.01$, and $[\alpha_{C_2}] = 5 \times 1.01$. Assume that $[\mathbb{F}]$ and $[\mathbb{V}]$ take the forms in (8) and (9), respectively, in which $\beta_{C_i}(t)$, $\beta_{B_i}(t)$, $\alpha_{I_i}(t)$ and $\alpha_{C_i}(t)$ are replaced by $[\beta_{C_i}]$, $[\beta_{B_i}]$, $[\alpha_{I_i}]$ and $[\alpha_{C_i}]$, respectively, $i = 1, 2$. Then $[\mathcal{R}_0]$ equals the spectral radius of $[\mathbb{F}][\mathbb{V}]^{-1}$, that is, $[\mathcal{R}_0] = \rho([\mathbb{F}][\mathbb{V}]^{-1}) = 0.6612$, which is independent of the choices of $d_1,\ d_2 \in [0, 1]$. Comparing $[\mathcal{R}_0] = 0.6612$ with $\mathcal{R}_0$ in Figure 2, it follows that one may underestimate the infection risks if the seasonal effects are ignored.

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