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EFFECTS OF ASYMPTOMATIC INFECTIONS ON THE SPATIAL SPREAD OF INFECTIOUS DISEASES*

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Abstract. Asymptomatic infection and transmission are common for quite a few directly or indirectly transmitted diseases such as COVID-19, cholera, and Zika fever. In this paper, we propose a susceptible-infective-asymptomatic-recovered patch model to address the influence of asymptomatic infections on the spatial spread of infectious diseases. The multipatch basic reproduction number $\mathcal{R}_0$ of the model is defined and shown to be a threshold quantity for disease eradication and persistence. Namely, the disease disappears if $\mathcal{R}_0 \leq 1$ whereas it spreads otherwise. The monotonicity of $\mathcal{R}_0$ with respect to the dispersal rates of the symptomatic and asymptomatic populations is investigated. In particular, for the two-patch case, $\mathcal{R}_0$ is either strictly decreasing or strictly increasing or constant in terms of dispersal rates. However, nonmonotonic dependence can occur with movement between three or more patches. The asymptotic profiles of the endemic equilibrium (when it exists) as one or all dispersal rates approach zero or infinity are studied. Interestingly, an increase in infectious dispersal may decrease $\mathcal{R}_0$ but increase the number of nonsusceptible individuals. Analytical and numerical results confirm that ignoring asymptomatic carriers not only significantly underestimates the infection risk but also impairs the efficacy of travel restrictions.

Key words. asymptomatic infection, patch model, basic reproduction number, monotonicity, endemic equilibrium, COVID-19

AMS subject classifications. 92D30, 91D25, 34C60, 34D05, 15A42

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1. Introduction.

An asymptomatic case is an individual who tests positive but experiences no symptoms throughout the course of infection. Asymptomatic infection is very common for many infectious diseases including coronavirus disease 2019 (COVID-19), Ebola virus disease, influenza, hand-foot-mouth disease, cholera, chlamydia, human papillomavirus infection, Zika fever, dengue fever, yellow fever, and malaria. For example, a review of 16 cohort studies estimated that 40%∼45% of COVID-19 infections are asymptomatic [36]. Another recent meta-analysis based on 13 studies involving 21,708 people found that the percentage of asymptomatic COVID-19 cases is approximately 17% [6]. The ratio of asymptomatic to symptomatic infections for cholera ranges from 3 to 100 [28]. About one in five people infected with Zika virus displays symptoms [13]. The proportion of symptomatic patients and

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severity are typically correlated to age and gender. Asymptomatic infectives are hard to detect and may, depending on the specific disease, transmit the infection to others, acting as silent spreaders. Some studies show that asymptomatic and symptomatic COVID-19 persons have similar initial viral loads [8]. However, asymptomatic carriers are likely to have a shorter duration of viral shedding or infectiousness which may confer a relatively short period of immunity. Since asymptomatic patients probably do not seek treatment, they may require a longer time to recover from infections for some diseases. On the other hand, symptomless people may have more contacts with others through normal daily activities, so a significant proportion of new infections could be attributed to asymptomatic transmission.

Understanding the role of asymptomatic infections in disease transmission is crucial to public health. A large number of mathematical models with asymptomatic infections have been developed and analyzed [10]. Based on SIS and SIR epidemic models, Kemper [26, 27] studied the contribution of asymptomatic infections to disease spread. Cooke [11] generalized the model of Kemper [26] by choosing different recovery rates for infectives with and without symptoms and general contact rates. Busenberg and van den Driessche [5] proposed an SIAS (I=infective, A=asymptomatic) endemic model incorporating vital dynamics, vertical transmission, transition between groups A and I, and different proportions of susceptibles infected by groups A and I being symptomatic. Hyman, Li, and Stanley [24] constructed a general model with differential infectivity for the transmission of HIV where the infected population is subdivided into multiple subgroups according to infectivity. Models with asymptomatic infections have been extensively used to depict specific diseases such as COVID-19 [21, 42, 47], Middle East respiratory syndrome [46], influenza [3, 23], hand-foot-mouth disease [44], cholera [28, 35], Zika fever [18], dengue fever [22], yellow fever [48], and malaria [39]. For more details, the reader can refer to a survey article by Chisholm et al. [10].

Global travel and tourism accelerate the spread of infectious diseases and constitute a major challenge for infection prevention and control. The COVID-19 epidemic, which was first reported in Wuhan, China, in December 2019, was declared a pandemic in March 2020. There are plenty of studies on modeling and analyzing the impact of human movement on the spatio-temporal spread of infectious diseases (see Allen et al. [1], Arino [2], Castillo-Chavez, Bichara, and Morin [7], Gao [14], Gao and Ruan [19], Li and Shuai [29], Song, Lou, and Xiao [41], and the references therein). Entry and exit screening can hardly detect asymptomatic travelers who are more likely to spread the infectious agent from one area to another due to their uninterrupted mobility. We are interested in exploring the joint effect of asymptomatic infection and population dispersal. Existing related models are from quantitative research for COVID-19 using Lagrangian and Eulerian approaches by Gatto et al. [21] and Wang et al. [45], respectively, and for Zika using a Lagrangian approach by Moreno et al. [34], and global stability analysis for waterborne diseases using a Lagrangian approach by Rebaza [37].

In the next section, we propose an SIAR patch model to address asymptomatic infection and spatial heterogeneity. In section 3, the threshold dynamics of the model in terms of the basic reproduction number are obtained and the dependence and independence of the basic reproduction number on dispersal rates are analyzed in detail. We also study the asymptotic profiles of the endemic equilibrium for small or large dispersal rates. In section 4, we numerically investigate the effects of asymptomatic infection on disease persistence and prevalence. A brief discussion of main results and future work is given in section 5.

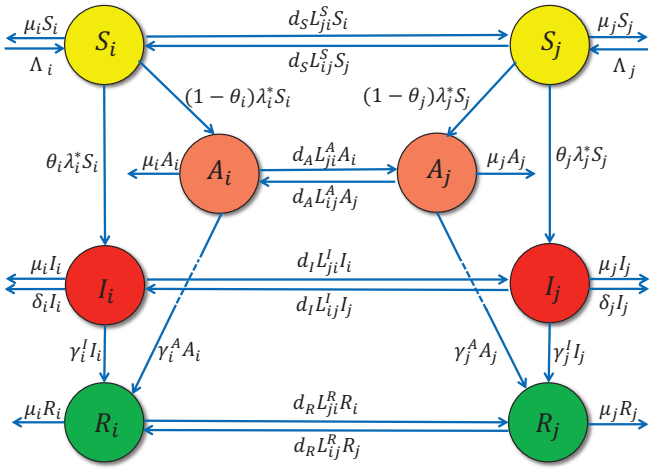


FIG. 1. *Flow diagram of the disease spread between patch i and patch j with $\lambda_k^* = \beta_k(I_k + \tau_k A_k)/N_k$ representing the force of infection of patch $k = i, j$.*

2. Model formulation. We consider a discrete space consisting of $n \geq 2$ patches connected by human movement. The total population N_i in patch $i \in \Omega = \{1, \ldots, n\}$ is divided into classes consisting of susceptible, symptomatic, asymptomatic, and recovered individuals, denoted by S_i, I_i, A_i, and R_i, respectively. The disease spread between patch i and patch j for $i \neq j$ is sketched in Figure 1. Based on the flowchart, an SIAR patch model is given as follows:

$$
\begin{aligned}
\frac{dS_i}{dt} &= d_S \sum_{j\in\Omega} L_{ij}^S S_j + \Lambda_i - \beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - \mu_i S_i, \ i \in \Omega,\\
\frac{dI_i}{dt} &= d_I \sum_{j\in\Omega} L_{ij}^I I_j + \theta_i \beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - (\mu_i + \gamma_i^I + \delta_i) I_i, \ i \in \Omega,\\
\frac{dA_i}{dt} &= d_A \sum_{j\in\Omega} L_{ij}^A A_j + (1-\theta_i)\beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - (\mu_i + \gamma_i^A) A_i, \ i \in \Omega,\\
\frac{dR_i}{dt} &= d_R \sum_{j\in\Omega} L_{ij}^R R_j + \gamma_i^I I_i + \gamma_i^A A_i - \mu_i R_i, \ i \in \Omega.
\end{aligned}
\tag{2.1}
$$

In patch i, Λ_i is the recruitment rate, β_i is the transmission coefficient between symptomatic and susceptible individuals, τ_i is the relative infectiousness of asymptomatic individuals compared to symptomatic individuals, $\theta_i \in (0, 1)$ is the proportion of new infections that are symptomatic, γ_i^I and γ_i^A are the recovery rates of symptomatic and asymptomatic persons, respectively, and μ_i and δ_i are the natural and disease-induced mortality rates, respectively. It is natural to assume that only symptomatic infections may cause death. The dispersal rate and connectivity matrix of the susceptible, symptomatic, asymptomatic, and recovered people are $d_\natural$ and $L^\natural = (L_{ij}^\natural)$ with $\natural$ denoting S, I, A, and R, respectively. Here $L_{ij}^\natural$ represents the degree of incoming movement from patch j to patch i for $j \neq i$ and $-L_{ii}^\natural = \sum_{j\neq i} L_{ji}$ is the degree of outgoing movement from patch i to all other patches. Note that our model ignores the transition possibility between asymptomatic and symptomatic states [10].

The connectivity matrices $L^\natural$ with $\natural \in \{S, I, A, R\}$ are assumed to be essentially nonnegative and irreducible with zero column sums, i.e., $L^\natural$ are irreducible Laplacian matrices. Unless otherwise indicated, all parameters except the disease-caused death rate and these involved in the connectivity matrices are assumed to be positive throughout this paper. The incidence term $\frac{I_i+\tau_i A_i}{N_i}S_i$ is defined to be zero when S_i or $I_i + \tau_i A_i$ equals zero, so system (2.1) is Lipschitz continuous in the nonnegative orthant. Thus, we can easily show that the model is well-posed and dissipative.

THEOREM 2.1. *For model* (2.1) *with nonnegative initial conditions, there is a unique solution satisfying* $S_i(t) > 0$, $I_i(t) \geq 0$, $A_i(t) \geq 0$, *and* $R_i(t) \geq 0$ *for all time* $t > 0$. *Moreover, the total population over all patches* $N(t) := \sum_{i\in\Omega} N_i(t)$ *is in the interval* $[\min\{N(0), \Lambda/\mu_u\}, \max\{N(0), \Lambda/\mu_l\}]$ *with* $\Lambda = \sum_{i\in\Omega}\Lambda_i$, $\mu_l = \min_{i\in\Omega}\mu_i$, *and* $\mu_u = \max_{i\in\Omega}(\mu_i + \delta_i)$.

It is worth noting that the single patch case of model (2.1) is related to an HIV model with differential infectivity proposed by Hyman, Li, and Stanley [24] and the disease dynamics are completely determined by the basic reproduction number in the case of no disease-caused deaths [31].

3. Main results. In this section, we first derive the basic reproduction number of model (2.1) and use it to establish threshold dynamics. Then we study the relation between the basic reproduction number and dispersal rates under different circumstances. After that, we seek conditions under which the basic reproduction number is independent of dispersal or dispersal rates. Finally, the asymptotic behavior of the endemic equilibrium is considered as one or all dispersal rates tend to zero or infinity.

3.1. Threshold dynamics. Clearly, model (2.1) has a unique disease-free equilibrium $E_0 = (\boldsymbol{S}^0, \mathbf{0}, \mathbf{0}, \mathbf{0})$, where $\boldsymbol{S}^0$ is the unique positive solution to

$$\Lambda_i - \mu_i S_i + d_S \sum_{j\in\Omega} L^S_{ij} S_j = 0,\ i \in \Omega.$$

The incidence and transition matrices are respectively

$$F = \begin{pmatrix} F_{11} & F_{12} \\ F_{21} & F_{22} \end{pmatrix} \text{ and } V = \begin{pmatrix} V_{11} & 0 \\ 0 & V_{22} \end{pmatrix},$$

where

$$\begin{aligned}
&F_{11} = \operatorname{diag}(\theta_1\beta_1, \ldots, \theta_n\beta_n),\ F_{12} = \operatorname{diag}(\theta_1\tau_1\beta_1, \ldots, \theta_n\tau_n\beta_n),\\
&F_{21} = \operatorname{diag}((1-\theta_1)\beta_1, \ldots, (1-\theta_n)\beta_n),\\
&F_{22} = \operatorname{diag}((1-\theta_1)\tau_1\beta_1, \ldots, (1-\theta_n)\tau_n\beta_n),\\
&V_{11} = D_I - d_I L^I,\ D_I = \operatorname{diag}(\mu_1 + \gamma_1^I + \delta_1, \ldots, \mu_n + \gamma_n^I + \delta_n),\\
&V_{22} = D_A - d_A L^A,\ D_A = \operatorname{diag}(\mu_1 + \gamma_1^A, \ldots, \mu_n + \gamma_n^A).
\end{aligned}$$

Using the next generation matrix method [12, 43], the basic reproduction number of model (2.1) is defined as $\mathcal{R}_0 = \rho(FV^{-1})$, where ρ denotes the spectral radius. Let $\mathbb{I}_n$ be the identity matrix of order n. Since $F_{12} = F_{11}F_{21}^{-1}F_{22}$, it follows from row and column operations of the determinant that

$$\begin{aligned}
|\lambda\mathbb{I}_{2n} - FV^{-1}| &= \begin{vmatrix} \lambda\mathbb{I}_n - F_{11}V_{11}^{-1} & -F_{12}V_{22}^{-1} \\ -F_{21}V_{11}^{-1} & \lambda\mathbb{I}_n - F_{22}V_{22}^{-1} \end{vmatrix} = \begin{vmatrix} \lambda\mathbb{I}_n & -\lambda F_{11}F_{21}^{-1} \\ -F_{21}V_{11}^{-1} & \lambda\mathbb{I}_n - F_{22}V_{22}^{-1} \end{vmatrix}\\
&= \begin{vmatrix} \lambda\mathbb{I}_n & 0 \\ -F_{21}V_{11}^{-1} & \lambda\mathbb{I}_n - F_{22}V_{22}^{-1} - F_{11}V_{11}^{-1} \end{vmatrix} = \lambda^n \left|\lambda\mathbb{I}_n - F_{22}V_{22}^{-1} - F_{11}V_{11}^{-1}\right|.
\end{aligned}$$

Thus, by taking $\mathcal{R}_0 = \rho(V^{-1}F)$ and a similar calculation using $F_{21} = F_{22}F_{12}^{-1}F_{11}$,

$$\mathcal{R}_0 = \rho(FV^{-1}) = \rho\left(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1}\right) = \rho(V^{-1}F) = \rho\left(V_{11}^{-1}F_{11} + V_{22}^{-1}F_{22}\right).$$

So the basic reproduction number of patch i in isolation is $\mathcal{R}_0^{(i)} = \mathcal{R}_{0I}^{(i)} + \mathcal{R}_{0A}^{(i)}$, where

$$\mathcal{R}_{0I}^{(i)} = \frac{\theta_i\beta_i}{\mu_i + \gamma_i^I + \delta_i} \quad \text{and} \quad \mathcal{R}_{0A}^{(i)} = \frac{(1-\theta_i)\tau_i\beta_i}{\mu_i + \gamma_i^A}$$

are the numbers of secondary cases generated by symptomatic and asymptomatic transmissions of an infected person, respectively. Clearly, the disease-free equilibrium E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ but unstable if $\mathcal{R}_0 > 1$ [43].

In case all infections are symptomatic, i.e., $\theta_i = 1$ for all $i \in \Omega$, the SIAR patch model (2.1) is reduced to an SIR patch model (see, e.g., McCormack and Allen [33])

$$\begin{aligned}
\frac{dS_i}{dt} &= d_S \sum_{j\in\Omega} L_{ij}^S S_j + \Lambda_i - \beta_i \frac{I_i}{N_i} S_i - \mu_i S_i,\ i \in \Omega,\\
\frac{dI_i}{dt} &= d_I \sum_{j\in\Omega} L_{ij}^I I_j + \beta_i \frac{I_i}{N_i} S_i - (\mu_i + \gamma_i^I + \delta_i) I_i,\ i \in \Omega,\\
\frac{dR_i}{dt} &= d_R \sum_{j\in\Omega} L_{ij}^R R_j + \gamma_i^I I_i - \mu_i R_i,\ i \in \Omega.
\end{aligned} \tag{3.1}$$

Following the analysis on the SIS patch model with standard incidence (Allen et al. [1], Gao [14], and Gao and Dong [16]), we have the following monotonic result on the basic reproduction number of model (3.1).

THEOREM 3.1. *For model* (3.1)*, the reproduction number* $\mathcal{R}_0(d_I) = \rho(F_{11}V_{11}^{-1})$ *and the spectral bound* $s(d_I) := s(F_{11}-V_{11}) = s(F_{11}-D_I+d_IL^I)$ *are strictly decreasing and strictly convex in* $d_I \in [0,\infty)$ *if* $\mathcal{R}_0^{(i)} = \beta_i/(\mu_i+\gamma_i^I+\delta_i)$ *and* $\beta_i-\mu_i-\gamma_i^I-\delta_i$ *are respectively nonconstant in* $i \in \Omega$*, and constant otherwise, where* $F_{11} = \operatorname{diag}(\beta_1,\dots,\beta_n)$*,* $D_I = \operatorname{diag}(\mu_1+\gamma_1^I+\delta_1,\dots,\mu_n+\gamma_n^I+\delta_n)$*, and* L^I *is an irreducible and essentially nonnegative matrix with zero column sums. Moreover,*

$$\min_{i\in\Omega}\mathcal{R}_0^{(i)} < \mathcal{R}_0(\infty) = \sum_{i\in\Omega}\beta_i L_{ii}^{I*}\Big/\sum_{i\in\Omega}(\mu_i+\gamma_i^I+\delta_i)L_{ii}^{I*} < \mathcal{R}_0(d_I) < \mathcal{R}_0(0) = \max_{i\in\Omega}\mathcal{R}_0^{(i)}$$

holds for any $d_I > 0$ *if* $\mathcal{R}_0^{(i)}$ *is nonconstant in* $i \in \Omega$*. Here* $\mathcal{R}_0(\infty)$ *is the limit of* $\mathcal{R}_0(d_I)$ *as* $d_I \to \infty$ *and* L_{ii}^{I*} *is the* (i,i) *cofactor of* L^I*.*

Before presenting an estimate on the basic reproduction number of model (2.1), we introduce a lemma on the spectral radius of a positive linear combination of a class of next generation matrices. Let $\mathbf{1} = (1,\dots,1)^{\mathrm{T}}$. We denote both zero row and column vectors by $\mathbf{0}$ and the reader can distinguish them from the context.

LEMMA 3.2. *Let* p *be a positive integer. For* $i = 1,\dots,p$*, let* $D_i = \operatorname{diag}(\gamma_{i1},\dots,\gamma_{in})$ *be a positive diagonal matrix and* L_i *be an essentially nonnegative and irreducible matrix with zero column sums. Then*

$$\rho\left(\sum_{i=1}^{p} m_i D_i (D_i - d_i L_i)^{-1}\right) = \sum_{i=1}^{p} m_i,$$

provided that $m_i \ge 0$ *and* $d_i \ge 0$ *for* $1 \le i \le p$*.*

Proof. Denote $V_i = D_i - d_iL_i$. It follows from $\mathbf{1}^{\mathrm{T}}L_i = \mathbf{0}$ that $\mathbf{1}^{\mathrm{T}}V_i = \mathbf{1}^{\mathrm{T}}D_i$, or equivalently, $\mathbf{1}^{\mathrm{T}}D_iV_i^{-1} = \mathbf{1}^{\mathrm{T}}$, for $i = 1,\dots,p$. Hence,

$$\mathbf{1}^{\mathrm{T}} \sum_{i=1}^{p} m_i D_i V_i^{-1} = \sum_{i=1}^{p} m_i \left(\mathbf{1}^{\mathrm{T}} D_i V_i^{-1}\right) = \sum_{i=1}^{p} m_i \mathbf{1}^{\mathrm{T}}.$$

The proof is completed by using the Perron–Frobenius theorem [4]. ∎

Note that the basic reproduction number $\mathcal{R}_0$ for model (2.1) depends on the movement of symptomatic and asymptomatic individuals but not on the movement of susceptible or recovered individuals. Moreover, it is bounded from above and below by the patch reproduction numbers of symptomatic and asymptomatic populations.

THEOREM 3.3. *For model* (2.1)*, the basic reproduction number* $\mathcal{R}_0$ *satisfies*

$$\min_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \min_{i\in\Omega} \mathcal{R}_{0A}^{(i)} \le \mathcal{R}_0 \le \max_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \max_{i\in\Omega} \mathcal{R}_{0A}^{(i)},$$

and the asymptotic profiles of $\mathcal{R}_0$ *with respect to small and large dispersal rates are*

$$\lim_{\substack{d_I\to 0+\\ d_A\to 0+}} \mathcal{R}_0(d_I, d_A) = \max_{i\in\Omega} \mathcal{R}_0^{(i)} \text{ and } \lim_{\substack{d_I\to \infty\\ d_A\to \infty}} \mathcal{R}_0(d_I, d_A) = \mathcal{R}_{0I}(\infty) + \mathcal{R}_{0A}(\infty),$$

respectively, where

$$\mathcal{R}_{0I}(\infty) := \lim_{d_I\to\infty} \mathcal{R}_{0I}(d_I) = \frac{\sum_{i\in\Omega} \theta_i \beta_i L_{ii}^{I*}}{\sum_{i\in\Omega} (\mu_i + \gamma_i^I + \delta_i) L_{ii}^{I*}},$$
$$\mathcal{R}_{0A}(\infty) := \lim_{d_A\to\infty} \mathcal{R}_{0A}(d_A) = \frac{\sum_{i\in\Omega} (1-\theta_i) \tau_i \beta_i L_{ii}^{A*}}{\sum_{i\in\Omega} (\mu_i + \gamma_i^A) L_{ii}^{A*}},$$

and $\mathcal{R}_{0I}(d_I) = \rho(F_{11}V_{11}^{-1})$*, and* $\mathcal{R}_{0A}(d_A) = \rho(F_{22}V_{22}^{-1})$ *with* $L_{ii}^{\natural *}$ *denoting the* (i,i) *cofactor of* $L^{\natural}$ *for* $i \in \Omega$ *and* $\natural \in \{I, A\}$*. Furthermore, the inequality*

$$\min_{i\in\Omega} \mathcal{R}_0^{(i)} \le \mathcal{R}_0 \le \max_{i\in\Omega} \mathcal{R}_0^{(i)}$$

holds if $\theta_i = \theta, \tau_i = \tau$ *and* $\gamma_i^I + \delta_i = \gamma_i^A$ *for* $i \in \Omega$*.*

Proof. Denote $\underline{m}_I = \min_{i\in\Omega} \mathcal{R}_{0I}^{(i)}$, $\underline{m}_A = \min_{i\in\Omega} \mathcal{R}_{0A}^{(i)}$, $\bar{m}_I = \max_{i\in\Omega} \mathcal{R}_{0I}^{(i)}$, and $\bar{m}_A = \max_{i\in\Omega} \mathcal{R}_{0A}^{(i)}$. Since V_{ii} is either an irreducible nonsingular M-matrix or a positive diagonal matrix (if $d_I = 0$ or d_A=0), its inverse exists and is a positive matrix or a positive diagonal matrix (if $d_I = 0$ or $d_A = 0$), $i = 1, 2$. Then

$$\underline{m}_I D_I \le F_{11} \le \bar{m}_I D_I \text{ and } \underline{m}_A D_A \le F_{22} \le \bar{m}_A D_A,$$

which imply that

$$\underline{m}_I D_I V_{11}^{-1} \le F_{11} V_{11}^{-1} \le \bar{m}_I D_I V_{11}^{-1} \text{ and } \underline{m}_A D_A V_{22}^{-1} \le F_{22} V_{22}^{-1} \le \bar{m}_A D_A V_{22}^{-1}$$

and hence

$$\underline{m}_I D_I V_{11}^{-1} + \underline{m}_A D_A V_{22}^{-1} \le F_{11} V_{11}^{-1} + F_{22} V_{22}^{-1} \le \bar{m}_I D_I V_{11}^{-1} + \bar{m}_A D_A V_{22}^{-1}.$$

Therefore,

$$\rho\left(\underline{m}_I D_I V_{11}^{-1} + \underline{m}_A D_A V_{22}^{-1}\right) \le \rho\left(F_{11} V_{11}^{-1} + F_{22} V_{22}^{-1}\right) \le \rho\left(\bar{m}_I D_I V_{11}^{-1} + \bar{m}_A D_A V_{22}^{-1}\right).$$

It follows from Lemma 3.2 that

$$\rho(\underline{m}_I D_I V_{11}^{-1} + \underline{m}_A D_A V_{22}^{-1}) = \underline{m}_I + \underline{m}_A \quad \text{and} \quad \rho(\bar{m}_I D_I V_{11}^{-1} + \bar{m}_A D_A V_{22}^{-1}) = \bar{m}_I + \bar{m}_A,$$

thus completing the proof of the general estimate on $\mathcal{R}_0 = \rho(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1})$.

The limit of $\mathcal{R}_0$ as $d_I \to 0+$ and $d_A \to 0+$ is obtained by the continuity of $\mathcal{R}_0$ in $d_I \geq 0$ and $d_A \geq 0$. By using Lemma 3.2 in Gao and Dong [16], we have

$$\lim_{d_I\to\infty} V_{11}^{-1} = \frac{1}{\sum_{i\in\Omega}(\mu_i + \gamma_i^I + \delta_i)L_{ii}^{I*}} L^{I*} \text{ and } \lim_{d_A\to\infty} V_{22}^{-1} = \frac{1}{\sum_{i\in\Omega}(\mu_i + \gamma_i^A)L_{ii}^{A*}} L^{A*},$$

where $L^{\natural *} = (L_{ij}^{\natural *})^{\mathrm{T}}$ is the adjoint matrix of $L^{\natural}$ for $\natural \in \{I, A\}$. Thus, it follows from

$$\mathbf{1}^{\mathrm{T}} \left(F_{11} \lim_{d_I\to\infty} V_{11}^{-1} + F_{22} \lim_{d_A\to\infty} V_{22}^{-1} \right) = \mathcal{R}_{0I}(\infty)\mathbf{1}^{\mathrm{T}} + \mathcal{R}_{0A}(\infty)\mathbf{1}^{\mathrm{T}}$$

and the Perron–Frobenius theorem that

$$\begin{aligned} \lim_{\substack{d_I\to\infty \\ d_A\to\infty}} \mathcal{R}_0(d_I, d_A) &= \lim_{\substack{d_I\to\infty \\ d_A\to\infty}} \rho\left(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1}\right) \\ &= \rho\left(F_{11} \lim_{d_I\to\infty} V_{11}^{-1} + F_{22} \lim_{d_A\to\infty} V_{22}^{-1} \right) = \mathcal{R}_{0I}(\infty) + \mathcal{R}_{0A}(\infty). \end{aligned}$$

If, in addition, $\theta_i = \theta, \tau_i = \tau$ and $\gamma_i^I + \delta_i = \gamma_i^A$ for $i \in \Omega$, then

$$\begin{aligned} \max_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \max_{i\in\Omega} \mathcal{R}_{0A}^{(i)} &= \max_{i\in\Omega} \theta \frac{\beta_i}{\mu_i + \gamma_i^A} + \max_{i\in\Omega} (1-\theta)\tau \frac{\beta_i}{\mu_i + \gamma_i^A} \\ &= (\theta + (1-\theta)\tau) \max_{i\in\Omega} \frac{\beta_i}{\mu_i + \gamma_i^A} = \max_{i\in\Omega} (\theta + (1-\theta)\tau) \frac{\beta_i}{\mu_i + \gamma_i^A} = \max_{i\in\Omega} \mathcal{R}_0^{(i)}. \end{aligned}$$

A similar argument establishes the result $\min_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \min_{i\in\Omega} \mathcal{R}_{0A}^{(i)} = \min_{i\in\Omega} \mathcal{R}_0^{(i)}$. □

Moreover, any value between the lower and upper bounds of $\mathcal{R}_0$ in Theorem 3.3 is reachable under an appropriate dispersal strategy.

COROLLARY 3.4. *For model* (2.1)*, given any number*

$$r \in (\underline{r}, \bar{r}) := \left(\min_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \min_{i\in\Omega} \mathcal{R}_{0A}^{(i)}, \max_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \max_{i\in\Omega} \mathcal{R}_{0A}^{(i)} \right),$$

there exist some dispersal rates d_I and d_A and connectivity matrices L^I and L^A such that the corresponding basic reproduction number $\mathcal{R}_0(d_I, d_A, L^I, L^A) = r$.

Proof. By the continuity of $\mathcal{R}_0$ in dispersal rates and connectivity matrices, it suffices to show that $\mathcal{R}_0$ can approach $\underline{r}$ and $\bar{r}$ from above and below, respectively. We now prove the upper bound case. Suppose that $i_\natural$ satisfies $\mathcal{R}_{0\natural}^{(i_\natural)} = \max_{i\in\Omega} \mathcal{R}_{0\natural}^{(i)}$ for $\natural \in \{I, A\}$. Let $\boldsymbol{e}_{i_\natural}$ be the unit column vector having one in the $i_\natural$th component and zero elsewhere for $\natural \in \{I, A\}$. We can choose a sequence of positive column vectors $\{\boldsymbol{\alpha}_k^\natural\}$ converging to $\boldsymbol{e}_{i_\natural}$ such that

$$\left| \frac{\mathbf{1}^{\mathrm{T}} F_{11} \boldsymbol{\alpha}_k^I}{\mathbf{1}^{\mathrm{T}} D_I \boldsymbol{\alpha}_k^I} - \mathcal{R}_{0I}^{(i_I)} \right| < \frac{1}{k} \quad \text{and} \quad \left| \frac{\mathbf{1}^{\mathrm{T}} F_{22} \boldsymbol{\alpha}_k^A}{\mathbf{1}^{\mathrm{T}} D_A \boldsymbol{\alpha}_k^A} - \mathcal{R}_{0A}^{(i_A)} \right| < \frac{1}{k} \text{ for } k \in \mathbb{N}.$$

According to Remark 2 in Gao, van den Driessche, and Cosner [20], for any given positive vector $\boldsymbol{\alpha}$, there is a connectivity matrix L having $\boldsymbol{\alpha}$ as its right eigenvector

corresponding to the zero eigenvalue. Thus, there exist L_k^I and L_k^A associated with $\boldsymbol{\alpha}_k^I$ and $\boldsymbol{\alpha}_k^A$, respectively, satisfying $\mathcal{R}_{0I}(\infty, L_k^I) = \frac{\mathbf{1}^{\mathrm{T}} F_{11} \boldsymbol{\alpha}_k^I}{\mathbf{1}^{\mathrm{T}} D_I \boldsymbol{\alpha}_k^I}$ and $\mathcal{R}_{0A}(\infty, L_k^A) = \frac{\mathbf{1}^{\mathrm{T}} F_{22} \boldsymbol{\alpha}_k^A}{\mathbf{1}^{\mathrm{T}} D_A \boldsymbol{\alpha}_k^A}$ and hence

$$\left|\mathcal{R}_{0\natural}(\infty, L_k^\natural) - \mathcal{R}_{0\natural}^{(i_\natural)}\right| < \frac{1}{k} \quad \text{for } k \in \mathbb{N} \text{ and } \natural \in \{I, A\}. \tag{3.2}$$

Here $\mathcal{R}_{0\natural}(\infty, L_k^\natural)$ is the limit of $\mathcal{R}_{0\natural}(d_\natural)$ with connectivity matrix $L_k^\natural$ as $d_\natural \to \infty$.

Using Theorem 3.3, there exist two positive sequences $\{d_{Ik}\}$ and $\{d_{Ak}\}$ such that

$$\left|\mathcal{R}_0\left(d_{Ik}, d_{Ak}, L_k^I, L_k^A\right) - \mathcal{R}_{0I}\left(\infty, L_k^I\right) - \mathcal{R}_{0A}\left(\infty, L_k^A\right)\right| < \frac{1}{k} \quad \text{for } k \in \mathbb{N}, \tag{3.3}$$

where $\mathcal{R}_0(d_{Ik}, d_{Ak}, L_k^I, L_k^A)$ denotes $\mathcal{R}_0(d_{Ik}, d_{Ak})$ with connectivity matrices L_k^I and L_k^A. A combination of (3.2) and (3.3) gives

$$\begin{aligned}
&\left|\mathcal{R}_0(d_{Ik}, d_{Ak}, L_k^I, L_k^A) - \left(\mathcal{R}_{0I}^{(i_I)} + \mathcal{R}_{0A}^{(i_A)}\right)\right| \\
\le &\left|\mathcal{R}_0(d_{Ik}, d_{Ak}, L_k^I, L_k^A) - \left(\mathcal{R}_{0I}\left(\infty, L_k^I\right) + \mathcal{R}_{0A}\left(\infty, L_k^A\right)\right)\right| \\
&+ \left|\mathcal{R}_{0I}\left(\infty, L_k^I\right) - \mathcal{R}_{0I}^{(i_I)}\right| + \left|\mathcal{R}_{0A}\left(\infty, L_k^A\right) - \mathcal{R}_{0A}^{(i_A)}\right| < \frac{3}{k}, \ k \in \mathbb{N},
\end{aligned}$$

which implies that $\mathcal{R}_0(d_{Ik}, d_{Ak}, L_k^I, L_k^A) \to \bar{r} = \mathcal{R}_{0I}^{(i_I)} + \mathcal{R}_{0A}^{(i_A)}$ as $k \to \infty$. The lower bound case can be shown similarly. ∎

By using a Lyapunov function and persistence theory, the basic reproduction number $\mathcal{R}_0$ is shown to be a threshold between disease extinction and persistence.

THEOREM 3.5. *For model* (2.1)*, if* $\mathcal{R}_0 \le 1$*, then the disease-free equilibrium* E_0 *is globally asymptotically stable; if* $\mathcal{R}_0 > 1$*, then the disease is uniformly persistent and there exists at least one endemic equilibrium.*

Proof. The proof follows the method of Theorem 2.2 in Shuai and van den Driessche [40]. Let $\boldsymbol{x} = (I_1, \ldots, I_n, A_1, \ldots, A_n)^{\mathrm{T}}$ and $\boldsymbol{y} = (S_1, \ldots, S_n, R_1, \ldots R_n)^{\mathrm{T}}$. Then,

$$\boldsymbol{x}' = (F - V)\boldsymbol{x} - \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{y}),$$

where the prime denotes the first derivative and $\boldsymbol{f} = (f_1^I, \ldots, f_n^I, f_1^A, \ldots, f_n^A)^{\mathrm{T}}$ with

$$\begin{aligned}
f_i^I(\boldsymbol{x}, \boldsymbol{y}) &= \theta_i \beta_i (I_i + \tau_i A_i)\left(1 - \frac{S_i}{N_i}\right), \ i \in \Omega, \\
f_i^A(\boldsymbol{x}, \boldsymbol{y}) &= (1 - \theta_i)\beta_i (I_i + \tau_i A_i)\left(1 - \frac{S_i}{N_i}\right), \ i \in \Omega.
\end{aligned}$$

Since $S_i/N_i \le 1$, it follows that $\boldsymbol{f}(\boldsymbol{x}, \boldsymbol{y}) \ge \mathbf{0}$. Let $\boldsymbol{\omega}^{\mathrm{T}}$ be the left eigenvector of $V^{-1}F$ associated with $\mathcal{R}_0 = \rho(V^{-1}F)$, i.e., $\boldsymbol{\omega}^{\mathrm{T}} V^{-1} F = \mathcal{R}_0 \boldsymbol{\omega}^{\mathrm{T}}$.

Since $V^{-1}F$ is irreducible and positive, $\boldsymbol{\omega}^{\mathrm{T}}$ is positive. Consider a Lyapunov function $Q(\boldsymbol{x}) = \boldsymbol{\omega}^{\mathrm{T}} V^{-1} \boldsymbol{x}$. The derivative of $Q(\boldsymbol{x})$ along a solution of (2.1) is

$$\begin{aligned}
Q'(\boldsymbol{x}) &= \boldsymbol{\omega}^{\mathrm{T}} V^{-1} \boldsymbol{x}' = \boldsymbol{\omega}^{\mathrm{T}} V^{-1}(F - V)\boldsymbol{x} - \boldsymbol{\omega}^{\mathrm{T}} V^{-1} \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{y}) \\
&= (\mathcal{R}_0 - 1)\, \boldsymbol{\omega}^{\mathrm{T}} \boldsymbol{x} - \boldsymbol{\omega}^{\mathrm{T}} V^{-1} \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{y}).
\end{aligned}$$

The second term is nonpositive. Thus, if $\mathcal{R}_0 < 1$, then the only invariant set where $Q' = 0$ is the singleton $\{E_0\}$ due to the irreducibility of L^I and L^A. If $\mathcal{R}_0 = 1$, then $Q' = 0$ implies $\boldsymbol{x} = \mathbf{0}$. We can proceed as before. Thus, by LaSalle's invariance principle, E_0 is globally asymptotically stable if $\mathcal{R}_0 \le 1$.

If $\mathcal{R}_0 > 1$, then E_0 is unstable and the system is uniformly persistent and as in [40] there exists at least one endemic equilibrium. ∎

3.2. Dependence of $\mathcal{R}_0$ on dispersal rates. Since the long-term disease dynamics of model (2.1) are entirely governed by the basic reproduction number $\mathcal{R}_0$, it is desirable to eradicate a disease by reducing $\mathcal{R}_0$ to less than unity. A natural question is how $\mathcal{R}_0$ varies with model parameters, especially the dispersal rates. Recently, there has been increasing interest in this topic [1, 9, 14, 16, 19, 41]. In what follows, we give three conditions under which $\mathcal{R}_0$ is a monotone decreasing function of the dispersal rate of the symptomatic population. Biologically speaking, these conditions mean that in each patch the same proportion of new infected individuals are symptomatic, and the asymptomatic individuals have the same relative infectiousness. By similar reasoning, similar conclusions can be given for the basic reproduction number with respect to the dispersal rate of the asymptomatic population. These monotone results can be used to improve the estimate of $\mathcal{R}_0$ [16].

THEOREM 3.6. *Suppose $\theta_i = \theta$ and $\tau_i = \tau$ for all $i \in \Omega$, and L^I and L^A are symmetric. Then the basic reproduction number $\mathcal{R}_0(d_I)$ of model (2.1) is constant in terms of d_I if $D_I\mathbf{1}$ is a right eigenvector of $F_{11}D_I^{-1}+F_{22}V_{22}^{-1} = \theta BD_I^{-1}+(1-\theta)\tau BV_{22}^{-1}$ associated with eigenvalue $\mathcal{R}_0(0) = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})$, i.e.,*

$$\left(F_{11}D_I^{-1} + F_{22}V_{22}^{-1}\right) D_I\mathbf{1} = \mathcal{R}_0(0)D_I\mathbf{1}$$

and strictly decreasing otherwise, where $B = \operatorname{diag}(\beta_1, \ldots, \beta_n)$. If, in addition, $\gamma_i^I + \delta_i = \gamma_i^A$ for all $i \in \Omega$, then $\mathcal{R}_0$ is constant in terms of d_I if $\mathcal{R}_0^{(1)} = \cdots = \mathcal{R}_0^{(n)}$ and strictly decreasing otherwise.

Proof. Since $\mathcal{R}_0 = \rho(FV^{-1}) = \rho(V^{-1}F)$ and $V^{-1}F$ is a nonnegative and irreducible matrix whenever $d_I > 0$ or $d_A > 0$, there exists a positive right eigenvector $\boldsymbol{v} = \left(\begin{smallmatrix}\boldsymbol{v}_I\\ \boldsymbol{v}_A\end{smallmatrix}\right)$ such that

$$V^{-1}F\boldsymbol{v} = \mathcal{R}_0\boldsymbol{v} \Longleftrightarrow \left(\frac{1}{\mathcal{R}_0}F - V\right)\boldsymbol{v} = \mathbf{0}.$$

More explicitly, we have

$$\left(\frac{1}{\mathcal{R}_0}F_{11} - V_{11}\right)\boldsymbol{v}_I + \frac{1}{\mathcal{R}_0}F_{12}\boldsymbol{v}_A = \mathbf{0}, \tag{3.4a}$$

$$\frac{1}{\mathcal{R}_0}F_{21}\boldsymbol{v}_I + \left(\frac{1}{\mathcal{R}_0}F_{22} - V_{22}\right)\boldsymbol{v}_A = \mathbf{0}. \tag{3.4b}$$

Differentiating both sides of the two equations in (3.4) with respect to d_I gives

$$\left(-\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F_{11} + L^I\right)\boldsymbol{v}_I + \left(\frac{1}{\mathcal{R}_0}F_{11} - V_{11}\right)\boldsymbol{v}_I' - \frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F_{12}\boldsymbol{v}_A + \frac{1}{\mathcal{R}_0}F_{12}\boldsymbol{v}_A' = \mathbf{0}, \tag{3.5a}$$

$$-\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F_{21}\boldsymbol{v}_I + \frac{1}{\mathcal{R}_0}F_{21}\boldsymbol{v}_I' - \frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F_{22}\boldsymbol{v}_A + \left(\frac{1}{\mathcal{R}_0}F_{22} - V_{22}\right)\boldsymbol{v}_A' = \mathbf{0}. \tag{3.5b}$$

It follows from $(\boldsymbol{v}_I')^{\mathrm{T}}\times(3.4\mathrm{a}) - (\boldsymbol{v}_I)^{\mathrm{T}}\times(3.5\mathrm{a})$ and $(\boldsymbol{v}_A')^{\mathrm{T}}\times(3.4\mathrm{b}) - (\boldsymbol{v}_A)^{\mathrm{T}}\times(3.5\mathrm{b})$ and the symmetry of L^I and L^A that

$$\begin{aligned}
&\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}(\boldsymbol{v}_I)^{\mathrm{T}}(F_{11}\boldsymbol{v}_I + F_{12}\boldsymbol{v}_A) = (\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I + \frac{1}{\mathcal{R}_0}\left((\boldsymbol{v}_I)^{\mathrm{T}}F_{12}\boldsymbol{v}_A' - (\boldsymbol{v}_I')^{\mathrm{T}}F_{12}\boldsymbol{v}_A\right),\\
&\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}(\boldsymbol{v}_A)^{\mathrm{T}}(F_{21}\boldsymbol{v}_I + F_{22}\boldsymbol{v}_A) = \frac{1}{\mathcal{R}_0}\left((\boldsymbol{v}_A)^{\mathrm{T}}F_{21}\boldsymbol{v}_I' - (\boldsymbol{v}_A')^{\mathrm{T}}F_{21}\boldsymbol{v}_I\right).
\end{aligned} \tag{3.6}$$

The assumptions $\theta_i = \theta$ and $\tau_i = \tau$ for all $i \in \Omega$ lead to

$$F_{11} = \theta B,\ F_{12} = \theta\tau B,\ F_{21} = (1-\theta)B,\ F_{22} = (1-\theta)\tau B. \tag{3.7}$$

We therefore can rewrite (3.6) in an explicit form as follows:

$$\theta\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}(\boldsymbol{v}_I)^{\mathrm{T}}B(\boldsymbol{v}_I+\tau\boldsymbol{v}_A) = (\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I + \frac{\theta\tau}{\mathcal{R}_0}\left((\boldsymbol{v}_I)^{\mathrm{T}}B\boldsymbol{v}_A' - (\boldsymbol{v}_I')^{\mathrm{T}}B\boldsymbol{v}_A\right), \tag{3.8a}$$

$$(1-\theta)\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}(\boldsymbol{v}_A)^{\mathrm{T}}B(\boldsymbol{v}_I+\tau\boldsymbol{v}_A) = \frac{1-\theta}{\mathcal{R}_0}\left((\boldsymbol{v}_A)^{\mathrm{T}}B\boldsymbol{v}_I' - (\boldsymbol{v}_A')^{\mathrm{T}}B\boldsymbol{v}_I\right). \tag{3.8b}$$

Directly calculating $(1-\theta)\times$(3.8a)$+\theta\tau\times$(3.8b) yields

$$(1-\theta)\theta\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}(\boldsymbol{v}_I+\tau\boldsymbol{v}_A)^{\mathrm{T}}B(\boldsymbol{v}_I+\tau\boldsymbol{v}_A) = (1-\theta)(\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I,$$

and hence

$$\mathcal{R}_0'(d_I) = \frac{\mathcal{R}_0^2}{\theta}\cdot\frac{(\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I}{(\boldsymbol{v}_I+\tau\boldsymbol{v}_A)^{\mathrm{T}}B(\boldsymbol{v}_I+\tau\boldsymbol{v}_A)}.$$

Thus $\mathcal{R}_0'$ is nonpositive since B is a positive diagonal matrix and L^I is the negative of a symmetric singular M-matrix (i.e., negative semidefinite). Furthermore, if we denote $\boldsymbol{v}_I = (v_1^I,\dots,v_n^I)^{\mathrm{T}}$, then

$$(\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I = -\frac{1}{2}\sum_{i,j\in\Omega}L_{ij}^I\left(v_i^I - v_j^I\right)^2 \le 0.$$

Solving $\boldsymbol{v}_A$ from (3.4a) gives

$$\boldsymbol{v}_A = -F_{12}^{-1}(F_{11}-\mathcal{R}_0V_{11})\boldsymbol{v}_I, \tag{3.9}$$

and substituting it into (3.4b) yields

$$\frac{1}{\mathcal{R}_0}F_{21}\boldsymbol{v}_I = \left(\frac{1}{\mathcal{R}_0}F_{22}F_{12}^{-1}F_{11} - F_{22}F_{12}^{-1}V_{11} - V_{22}F_{12}^{-1}F_{11} + \mathcal{R}_0V_{22}F_{12}^{-1}V_{11}\right)\boldsymbol{v}_I.$$

By noting $F_{21} = F_{22}F_{12}^{-1}F_{11}$, the above equality can be simplified to

$$\mathcal{R}_0V_{22}F_{12}^{-1}V_{11}\boldsymbol{v}_I = (F_{22}F_{12}^{-1}V_{11} + V_{22}F_{12}^{-1}F_{11})\boldsymbol{v}_I,$$

which is equivalent to

$$\mathcal{R}_0V_{11}\boldsymbol{v}_I = (F_{11}V_{11}^{-1} + F_{12}V_{22}^{-1}F_{22}F_{12}^{-1})V_{11}\boldsymbol{v}_I. \tag{3.10}$$

Suppose there exists some $\hat{d}_I \ge 0$ such that $\mathcal{R}_0'(\hat{d}_I) = 0$. It suffices to show that $\mathcal{R}_0(d_I) \equiv \mathcal{R}_0(\hat{d}_I)$ for any $d_I \in [0,\infty)$. Following the proof of Lemma 3.4 in Allen et al. [1], the irreducibility of L^I and $(\boldsymbol{v}_I)^{\mathrm{T}}L^I\boldsymbol{v}_I = 0$ imply that $\boldsymbol{v}_I = k\mathbf{1}$ for some $k > 0$ as $d_I = \hat{d}_I$. It follows from $V_{11}\mathbf{1} = D_I\mathbf{1}$ and (3.7) that (3.10) becomes

$$\begin{aligned}\mathcal{R}_0(\hat{d}_I)D_I\mathbf{1} &= F_{11}\mathbf{1} + F_{22}V_{22}^{-1}D_I\mathbf{1}\\ &= F_{11}\left(D_I - d_IL^I\right)^{-1}\left(D_I - d_IL^I\right)\mathbf{1} + F_{22}V_{22}^{-1}D_I\mathbf{1}\\ &= \left(F_{11}\left(D_I - d_IL^I\right)^{-1} + F_{22}V_{22}^{-1}\right)D_I\mathbf{1}\end{aligned}$$

for any $d_I \ge 0$. By the Perron–Frobenius theorem, we have

$$\mathcal{R}_0(\hat{d}_I) = \rho\left(F_{11}\left(D_I - d_I L^I\right)^{-1} + F_{22}V_{22}^{-1}\right) = \mathcal{R}_0(d_I)\ \forall d_I \geq 0.$$

In addition, if $\gamma_i^I + \delta_i = \gamma_i^A$ for $i \in \Omega$, then

$$V_{22}\mathbf{1} = D_A\mathbf{1} = D_I\mathbf{1} \Rightarrow V_{22}^{-1}D_I\mathbf{1} = \mathbf{1}$$

and hence

$$\mathcal{R}_0(\hat{d}_I)D_I\mathbf{1} = F_{11}\mathbf{1} + F_{22}V_{22}^{-1}D_I\mathbf{1} = (F_{11} + F_{22})\mathbf{1},$$

which implies that $\mathcal{R}_0^{(1)} = \cdots = \mathcal{R}_0^{(n)} = \mathcal{R}_0(\hat{d}_I)$. ∎

Under the same assumptions as in Theorem 3.6, we can use a similar approach to conclude that the initial exponential growth rate of model (2.1), i.e., $s(F-V)$, the spectral bound of the Jacobian matrix of model (2.1) at the disease-free equilibrium E_0, is monotone decreasing with respect to d_I and d_A. In fact, the matrix $F-V+k\mathbb{I}_{2n}$ is nonnegative and irreducible for large enough $k > 0$ so that $\rho(F - V + k\mathbb{I}_{2n}) = s(F-V+k\mathbb{I}_{2n}) = s(F-V)+k$ holds and the associated eigenvector is strictly positive. This is a generalization of the results on the SIS or SIR patch model (Lemma 3.4 in Allen et al. [1] and Corollary 3.5 in Gao and Dong [16]).

PROPOSITION 3.7. *Suppose $\theta_i = \theta$ and $\tau_i = \tau$ for all $i \in \Omega$, and L^I and L^A are symmetric. Then the spectral bound of the Jacobian matrix of system (2.1) at the disease-free equilibrium, $s(d_I) := s(F-V) = s(F-\mathrm{diag}(D_I - d_I L^I, V_{22}))$, is constant in terms of d_I if $\begin{pmatrix}\mathbf{1}\\ F_{12}^{-1}(s(0)\mathbb{I}_n - F_{11} + D_I)\mathbf{1}\end{pmatrix}$ is a right eigenvector of $F - \mathrm{diag}(D_I, V_{22})$ associated to eigenvalue $s(0) = s(F-\mathrm{diag}(D_I, V_{22}))$ and strictly decreasing otherwise.*

For some diseases, it may be that $d_S = d_A = d_R$ and $L^S = L^I = L^A = L^R$, or approximate equalities hold. In case where L^I and L^A are equal and diagonally similar to a symmetric matrix, the reproduction number is still monotone decreasing in dispersal rates. The proof of the following is in the supplementary material (SM1).

PROPOSITION 3.8. *Assume that* (i) *$\theta_i = \theta$ and $\tau_i = \tau$ for $i \in \Omega$;* (ii) *the connectivity matrices L^I and L^A are equal (i.e., $L^I = L^A := L$);* (iii) *there is a positive diagonal matrix C such that CLC^{-1} is symmetric. Let $\boldsymbol{\alpha}_0$ be a positive right eigenvector of L corresponding to eigenvalue zero. Then the basic reproduction number $\mathcal{R}_0(d_I)$ of model (2.1) is constant in terms of d_I if $D_I\boldsymbol{\alpha}_0$ is a right eigenvector of $F_{11}D_I^{-1} + F_{22}V_{22}^{-1} = \theta BD_I^{-1} + (1-\theta)\tau BV_{22}^{-1}$ associated to eigenvalue $\mathcal{R}_0(0) = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})$, i.e.,*

$$\left(F_{11}D_I^{-1} + F_{22}V_{22}^{-1}\right)D_I\boldsymbol{\alpha}_0 = \mathcal{R}_0(0)D_I\boldsymbol{\alpha}_0$$

and strictly decreasing otherwise, where $B = \mathrm{diag}(\beta_1, \ldots, \beta_n)$. If, in addition, $\gamma_i^I + \delta_i = \gamma_i^A$ for all $i \in \Omega$, then $\mathcal{R}_0$ is constant in terms of d_I if $\mathcal{R}_0^{(1)} = \cdots = \mathcal{R}_0^{(n)}$ and strictly decreasing otherwise.

Remark 3.9. The necessary and sufficient condition for a connectivity matrix L to meet assumption (iii) in Proposition 3.8 is that it is symmetrizable. A square matrix M is called symmetrizable if DM is symmetric for some positive diagonal matrix $D = \mathrm{diag}(d_1, \ldots, d_n)$. In matrix theory, a matrix $M = (m_{ij})_{n\times n}$ is symmetrizable if and only if $m_{ij} = m_{ji} = 0$ or $m_{ij}m_{ji} > 0$ for all $1 \leq i, j \leq n$, and $m_{i_1i_2}m_{i_2i_3}\cdots m_{i_ki_1} = m_{i_2i_1}m_{i_3i_2}\cdots m_{i_1i_k}$ for all $k \geq 3$ and $i_1, i_2, \ldots, i_k \in \{1, \ldots, n\}$ (see Maybee [32]). Denote $D^{\frac{1}{2}} = \mathrm{diag}(\sqrt{d_1}, \ldots, \sqrt{d_n})$ and $D^{-\frac{1}{2}} = \mathrm{diag}(1/\sqrt{d_1}, \ldots, 1/\sqrt{d_n})$. If M is symmetrizable, then

$$DM = (DM)^{\mathrm{T}} = M^{\mathrm{T}}D^{\mathrm{T}} = M^{\mathrm{T}}D \Leftrightarrow D^{-\frac{1}{2}}DMD^{-\frac{1}{2}} = D^{-\frac{1}{2}}M^{\mathrm{T}}DD^{-\frac{1}{2}}$$
$$\Leftrightarrow D^{\frac{1}{2}}MD^{-\frac{1}{2}} = D^{-\frac{1}{2}}M^{\mathrm{T}}D^{\frac{1}{2}} = \left(D^{\frac{1}{2}}MD^{-\frac{1}{2}}\right)^{\mathrm{T}},$$

that is, $D^{\frac{1}{2}}MD^{-\frac{1}{2}}$ is symmetric. A special case is that if a connectivity matrix $L = (L_{ij})_{n\times n}$ has no cycles of length ≥ 3, that is, L has only loops $L_{ii} < 0$ and cycles of length 2 from products $L_{ij}L_{ji} > 0$ $(i \neq j)$, then it is symmetrizable and hence satisfies assumption (iii) (see Lemma 12.3.1 in Johnson and Saiago [25]). In particular, this holds for the two-patch case.

When symptomatic or asymptomatic individuals do not move between patches, the monotonic result on $\mathcal{R}_0$ holds with no restrictions on model parameters.

THEOREM 3.10. *For model* (2.1)*, if* $d_I = 0$ *(or* $d_A = 0$*), then the basic reproduction number* $\mathcal{R}_0$ *is strictly decreasing with respect to* d_A *(or* d_I*) whenever* $\mathcal{R}_0^{(i)}$ *is nonconstant in* $i \in \Omega$*, and constant otherwise.*

Proof. We only consider the case of $d_A = 0$ while the case of $d_I = 0$ can be shown similarly. Notice that $F_{11}V_{11}^{-1} = (V_{11}F_{11}^{-1})^{-1} = (D_IF_{11}^{-1} - d_IL^IF_{11}^{-1})^{-1}$, without loss of generality, we assume that $F_{11} = \mathbb{I}_n$. Otherwise, we can define $\tilde{D}_I = D_IF_{11}^{-1}$, $\tilde{L}^I = L^IF_{11}^{-1}$ and $\tilde{V}_{11} = V_{11}F_{11}^{-1}$, and replace D_I, L^I, and V_{11} by $\tilde{D}_I$, $\tilde{L}^I$, and $\tilde{V}_{11}$ in the following argument, respectively. For convenience, let

$$D_I = \mathrm{diag}(c_1, \ldots, c_n) \quad \text{and} \quad F_{22}V_{22}^{-1} = W = \mathrm{diag}(w_1, \ldots, w_n).$$

Since $F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1} = V_{11}^{-1} + W$ is a positive matrix, by the Perron–Frobenius theorem, there exists a positive eigenvector $\boldsymbol{u} \gg \mathbf{0}$ such that

$$(V_{11}^{-1} + W)\boldsymbol{u} = \mathcal{R}_0(d_I)\boldsymbol{u}.$$

Clearly, $\mathcal{R}_0(d_I) > \max_{i\in\Omega} w_i$. Let $\boldsymbol{v} := (\mathcal{R}_0(d_I)\mathbb{I}_n - W)\boldsymbol{u} = V_{11}^{-1}\boldsymbol{u}$, which implies that $\boldsymbol{u} = V_{11}\boldsymbol{v} = (D_I - d_IL^I)\boldsymbol{v}$. Notice that V_{11} is irreducible; we then have $\boldsymbol{v} \gg \mathbf{0}$. An easy computation yields that

$$(d_IL^I - D_I + (\mathcal{R}_0(d_I)\mathbb{I}_n - W)^{-1})\boldsymbol{v} = (d_IL^I - D_I)\boldsymbol{v} + \boldsymbol{u} = \mathbf{0}.$$

By the Perron–Frobenius theorem, the essential nonnegativity and irreducibility of $d_IL^I - D_I + (\mathcal{R}_0(d_I)\mathbb{I}_n - W)^{-1}$ mean that

$$s(d_IL^I - D_I + (\mathcal{R}_0(d_I)\mathbb{I}_n - W)^{-1}) = 0.$$

Define $\chi(d_I, \lambda) = s(d_IL^I - D_I + (\lambda\mathbb{I}_n - W)^{-1})$ for $d_I > 0$ and $\lambda > \max_{i\in\Omega} w_i$. In particular, $\chi(d_I, \mathcal{R}_0(d_I)) = 0$ for any $d_I > 0$. Again by the Perron–Frobenius theorem (see, e.g., Corollary 2.1.5 in Berman and Plemmons [4]), $\chi(d_I, \lambda)$ is strictly decreasing in $\lambda > \max_{i\in\Omega} w_i$. By Corollary 3.5 in Gao and Dong [16], $\chi(d_I, \lambda)$ is strictly decreasing in $d_I > 0$ if and only if $-D_I + (\lambda\mathbb{I}_n - W)^{-1}$ is not a scalar multiple of $\mathbb{I}_n$. Therefore, given a pair of $\tilde{d}_I$ and d_I satisfying $\tilde{d}_I > d_I > 0$, we have

$$\chi(\tilde{d}_I, \mathcal{R}_0(d_I)) \leq \chi(d_I, \mathcal{R}_0(d_I)) = 0 = \chi(\tilde{d}_I, \mathcal{R}_0(\tilde{d}_I)),$$

which implies that $\mathcal{R}_0(d_I) \geq \mathcal{R}_0(\tilde{d}_I)$. The equality $\mathcal{R}_0(d_I) = \mathcal{R}_0(\tilde{d}_I)$ holds if and only if $\chi(\tilde{d}_I, \mathcal{R}_0(d_I)) = \chi(d_I, \mathcal{R}_0(d_I))$, and hence if and only if

$$-D_I + (\mathcal{R}_0(d_I)\mathbb{I}_n - W)^{-1} = k\mathbb{I}_n,$$

for some constant $k \in \mathbb{R}$. Thus, $\chi(d_I, \mathcal{R}_0(d_I)) = s(d_IL^I + k\mathbb{I}_n) = k + s(d_IL^I) = k = 0$. We conclude that $-c_i + (\mathcal{R}_0(d_I) - w_i)^{-1} = 0$ for all $i \in \Omega$, i.e., $\mathcal{R}_0(d_I) = \mathcal{R}_0^{(i)} = 1/c_i + w_i$ is constant in $i \in \Omega$. ∎

When only two patches are concerned, we show below that the basic reproduction number $\mathcal{R}_0$ is either strictly decreasing or strictly increasing or constant with respect to d_I and d_A depending on parameter values (see section 4 for numerical examples). Nevertheless, following Theorem 3.1, the reproduction number of the corresponding SIR patch model (3.1) is either strictly decreasing or constant in dispersal rate of the infected population. This means that the presence of asymptomatic infections can alter the relation between $\mathcal{R}_0$ and d_I. It is worth mentioning that Gao and Ruan [19] analyzed the dependence of the basic reproduction number on the dispersal rate and dispersal asymmetry for a two-patch malaria model.

PROPOSITION 3.11. *For model* (2.1) *with* $n = 2$*, if all parameters are positive, then the derivative of* $\mathcal{R}_0$ *with respect to* d_I *or* d_A *has sign-preserving property, i.e.,*

$$\operatorname{sgn}\left(\frac{d\mathcal{R}_0}{dd_I}\right) = \operatorname{sgn}\left(\left.\frac{d\mathcal{R}_0}{dd_I}\right|_{d_I=0+}\right) \quad \textit{and} \quad \operatorname{sgn}\left(\frac{d\mathcal{R}_0}{dd_A}\right) = \operatorname{sgn}\left(\left.\frac{d\mathcal{R}_0}{dd_A}\right|_{d_A=0+}\right)$$

for $d_I > 0$ *and* $d_A > 0$.

Proof. We prove the case of d_I, and a similar argument holds for d_A. Note that

$$F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1} = \left(V_{11}F_{11}^{-1}\right)^{-1} + F_{22}V_{22}^{-1} = \left(D_I F_{11}^{-1} - d_I L^I F_{11}^{-1}\right)^{-1} + F_{22}V_{22}^{-1}.$$

Here $D_I F_{11}^{-1}$ is a positive diagonal matrix, $L^I F_{11}^{-1}$ is an essentially nonnegative and irreducible matrix with zero column sums, and $F_{22}V_{22}^{-1}$ is a positive matrix with positive determinant. Thus, it suffices to consider the case of $F_{11} = \mathbb{I}_2$, i.e.,

$$\mathcal{R}_0(d_I) = \rho\left(\left(D_I - d_I L^I\right)^{-1} + F_{22}V_{22}^{-1}\right),$$

where

$$D_I = \begin{pmatrix} \gamma_1 & 0 \\ 0 & \gamma_2 \end{pmatrix},\ L^I = \begin{pmatrix} -L_{21} & L_{12} \\ L_{21} & -L_{12} \end{pmatrix},\ \text{and}\ \ F_{22}V_{22}^{-1} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$$

satisfy γ_1, γ_2, L_{12}, L_{21}, a_{11}, a_{12}, a_{21}, $a_{22} > 0$, and $a_{11}a_{22} > a_{12}a_{21}$. A direct calculation yields

$$\mathcal{R}_0(d_I) = \frac{\phi + \sqrt{\psi}}{2\Delta},$$

where

$$\begin{aligned} \Delta &= (L_{12}\gamma_1 + L_{21}\gamma_2)d_I + \gamma_1\gamma_2, \\ \phi &= (a_{11} + a_{22})\Delta + (L_{12} + L_{21})d_I + \gamma_1 + \gamma_2, \\ \psi &= \phi^2 - 4\Delta(1 + a_{11}\gamma_1 + a_{22}\gamma_2 + (a_{11}a_{22} - a_{12}a_{21})\Delta \\ &\quad + ((a_{11} - a_{12})L_{21} + (a_{22} - a_{21})L_{12})d_I) > 0. \end{aligned}$$

Thus, we have

$$\frac{d\mathcal{R}_0}{dd_I} = \frac{2\sqrt{\psi}(\phi'\Delta - \phi\Delta') + (\psi'\Delta - 2\psi\Delta')}{4\Delta^2\sqrt{\psi}}, \tag{3.11}$$

where the prime represents the derivative with respect to d_I.

Since $\phi'\Delta - \phi\Delta' = -L_{12}\gamma_1^2 - L_{21}\gamma_2^2 < 0$, the derivative $\mathcal{R}_0'(d_I) = 0$ if and only if

$$\psi'\Delta - 2\psi\Delta' > 0, \tag{3.12a}$$

$$(\psi'\Delta - 2\psi\Delta')^2 = 4\psi(\phi'\Delta - \phi\Delta')^2. \tag{3.12b}$$

It is straightforward to obtain

$$(\psi'\Delta - 2\psi\Delta')^2 - 4\psi(\phi'\Delta - \phi\Delta')^2 = -16\Delta^2 g_1 g_2,$$

where

$$g_1 = (a_{11}L_{12}\gamma_1 + a_{12}L_{21}\gamma_2 + L_{12})L_{21}\gamma_2 - (a_{22}L_{21}\gamma_2 + a_{21}L_{12}\gamma_1 + L_{21})L_{12}\gamma_1,$$
$$g_2 = (a_{11}\gamma_1 + a_{21}\gamma_2 + 1)\gamma_2 - (a_{22}\gamma_2 + a_{12}\gamma_1 + 1)\gamma_1.$$

So, (3.12b) holds if and only if $g_1 = 0$ or $g_2 = 0$. Next we show that (3.12b) implies (3.12a). Solving a_{11} from $g_1 = 0$ and substituting it into the left side of (3.12a) give

$$\psi'\Delta - 2\psi\Delta' = \frac{2\left(L_{12}\gamma_1^2 + L_{21}\gamma_2^2\right)}{L_{12}L_{21}\gamma_1\gamma_2}\left(\left(a_{12}L_{21}^2\gamma_2^2 + a_{21}L_{12}^2\gamma_1^2\right)\Delta + \left(L_{12}\gamma_1^2 + L_{21}\gamma_2^2\right)L_{12}L_{21}d_I\right) > 0.$$

Similarly, solving a_{11} from $g_2 = 0$ and substituting it into the left side of (3.12a) give

$$\psi'\Delta - 2\psi\Delta' = \frac{2\left(L_{12}\gamma_1^2 + L_{21}\gamma_2^2\right)}{\gamma_1\gamma_2}\left(\left(a_{12}\gamma_1^2 + a_{21}\gamma_2^2\right)\Delta + \left(L_{12}\gamma_1^2 + L_{21}\gamma_2^2\right)d_I\right) > 0.$$

Therefore, $\mathcal{R}_0'(d_I) = 0$ if and only if either $g_1 = 0$ or $g_2 = 0$ holds. Note that both g_1 and g_2 are independent of d_I. Thus, if $\mathcal{R}_0'(d_I^0) = 0$ for some $d_I^0 \geq 0$, then $\mathcal{R}_0'(d_I) \equiv 0$ for all $d_I \in [0, \infty)$, i.e., $\mathcal{R}_0(d_I) \equiv$ const. ∎

Remark 3.12. Based on the above proof, for the two-patch case, we can obtain an explicit condition to determine the sign of the right derivative of $\mathcal{R}_0$ with respect to d_I at zero and use it to decide the monotonicity of $\mathcal{R}_0(d_I)$. In particular, using the notation in the proof, $\mathcal{R}_0(d_I)$ is constant if and only if one of the following holds:

$$\frac{1}{\gamma_1} + a_{11} + a_{21}\frac{\gamma_2}{\gamma_1} = \frac{1}{\gamma_2} + a_{22} + a_{12}\frac{\gamma_1}{\gamma_2},$$
$$\frac{1}{\gamma_1} + a_{11} + a_{12}\frac{L_{21}\gamma_2}{L_{12}\gamma_1} = \frac{1}{\gamma_2} + a_{22} + a_{21}\frac{L_{12}\gamma_1}{L_{21}\gamma_2},$$

where the left- and right-hand sides of the equalities are related to $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$, respectively. A tedious calculation shows that each equality with respect to d_A has at most one positive root and hence there exist at most two positive d_{A1} and d_{A2} such that $\mathcal{R}_0(d_I)$ is constant in $d_I \geq 0$ as $d_A = d_{A1}$ or d_{A2} whenever $\mathcal{R}_0(d_I, d_A) \not\equiv$ const.

3.3. Independence of $\mathcal{R}_0$ on dispersal rates. The aforementioned analysis indicates that the relation between the reproduction number and population dispersal could be very complicated when there are no or weak restrictions on model parameters. An interesting question is to determine under what conditions $\mathcal{R}_0$ is independent of dispersal and dispersal rates, respectively, which means that $\mathcal{R}_0(d_I, d_A, L^I, L^A)$ is constant for any dispersal rates d_I and d_A and any connectivity matrices L^I and L^A, and $\mathcal{R}_0(d_I, d_A)$ is constant for any dispersal rates d_I and d_A, respectively. The present analysis can play a key role in completely classifying the model parameter space on the monotonicity of $\mathcal{R}_0$ with respect to dispersal rates.

PROPOSITION 3.13. *For model* (2.1)*, the following statements on* $\mathcal{R}_0$ *hold:*

(a) $\mathcal{R}_0$ *is independent of dispersal if and only if both* $\mathcal{R}_{0I}^{(i)}$ *and* $\mathcal{R}_{0A}^{(i)}$ *are constant in* $i \in \Omega$.

(b) $\mathcal{R}_0$ *is independent of dispersal rates* d_I *and* d_A *if and only if* $\mathcal{R}_0^{(i)}$ *is constant in* $i \in \Omega$ *and* $s((D_A F_{22}^{-1} F_{11} D_I^{-1} - d_A L^A F_{22}^{-1})^{-1} - D_I F_{11}^{-1} F_{22} D_A^{-1} + d_I L^I F_{11}^{-1}) = 0$ *for any* $d_I \geq 0$ *and* $d_A \geq 0$.

(c) $\mathcal{R}_0$ *is independent of dispersal rates* d_I *and* d_A *if* $\mathcal{R}_0^{(i)}$ *is constant in* $i \in \Omega$ *and* $D_I \boldsymbol{\alpha}^I = k D_A \boldsymbol{\alpha}^A$ *for some* $k > 0$*, where* $\boldsymbol{\alpha}^\natural$ *is a right positive eigenvector with eigenvalue zero of matrix* $L^\natural$ *for* $\natural \in \{I, A\}$*, but not conversely.*

(d) $\mathcal{R}_0$ *is independent of dispersal rates* d_I *and* d_A *if* $\mathcal{R}_0$ *is independent of dispersal, but not conversely.*

Proof. Denote $\tilde{D}_I = D_I F_{11}^{-1}$, $\tilde{L}^I = L^I F_{11}^{-1}$, $\tilde{V}_{11} = V_{11} F_{11}^{-1} = \tilde{D}^I - d_I \tilde{L}^I$, $\tilde{D}_A = D_A F_{22}^{-1}$, $\tilde{L}^A = L^A F_{22}^{-1}$, and $\tilde{V}_{22} = V_{22} F_{22}^{-1} = \tilde{D}^A - d_A \tilde{L}^A$.

(a) If $\mathcal{R}_{0I}^{(i)} = \mathcal{R}_{0I}^{(1)}$ and $\mathcal{R}_{0A}^{(i)} = \mathcal{R}_{0A}^{(1)}$ for $i \in \Omega$, then it follows from Lemma 3.2 and

$$\begin{aligned} F_{11} V_{11}^{-1} + F_{22} V_{22}^{-1} &= F_{11} D_I^{-1} D_I V_{11}^{-1} + F_{22} D_A^{-1} D_A V_{22}^{-1} \\ &= \mathcal{R}_{0I}^{(1)} D_I \left(D_I - d_I L^I\right)^{-1} + \mathcal{R}_{0A}^{(1)} D_A (D_A - d_A L^A)^{-1} \end{aligned}$$

that $\mathcal{R}_0 = \rho(F_{11} V_{11}^{-1} + F_{22} V_{22}^{-1}) = \mathcal{R}_{0I}^{(1)} + \mathcal{R}_{0A}^{(1)} = \mathcal{R}_0^{(1)}$ for any d_I, d_A, L^I and L^A.

On the contrary, suppose $\mathcal{R}_0$ is independent of dispersal. Then, by Corollary 3.4,

$$\min_{i \in \Omega} \mathcal{R}_{0I}^{(i)} + \min_{i \in \Omega} \mathcal{R}_{0A}^{(i)} = \max_{i \in \Omega} \mathcal{R}_{0I}^{(i)} + \max_{i \in \Omega} \mathcal{R}_{0A}^{(i)},$$

which implies that $\max_i \mathcal{R}_{0I}^{(i)} = \min_i \mathcal{R}_{0I}^{(i)}$, and $\max_i \mathcal{R}_{0A}^{(i)} = \min_i \mathcal{R}_{0A}^{(i)}$. So both $\mathcal{R}_{0I}^{(i)}$ and $\mathcal{R}_{0A}^{(i)}$ are constant in $i \in \Omega$.

(b) Suppose $\mathcal{R}_0$ is independent of dispersal rates. Then, in particular, $\mathcal{R}_0(d_I, 0)$ is constant for any $d_I \geq 0$. So, $\mathcal{R}_0^{(i)}$ is constant in $i \in \Omega$, i.e., $\tilde{D}_I^{-1} + \tilde{D}_A^{-1} = \mathcal{R}_0 \mathbb{I}_n$, by using Theorem 3.10. There exists a right positive vector $\boldsymbol{v}$ such that

$$\begin{aligned} \left(F_{11} V_{11}^{-1} + F_{22} V_{22}^{-1}\right) \boldsymbol{v} = \left(\tilde{V}_{11}^{-1} + \tilde{V}_{22}^{-1}\right) \boldsymbol{v} &= \mathcal{R}_0 \boldsymbol{v} \\ \Leftrightarrow \left(\tilde{V}_{22} \tilde{V}_{11}^{-1} + \mathbb{I}_n\right) \boldsymbol{v} &= \mathcal{R}_0 \tilde{V}_{22} \boldsymbol{v} \\ \Leftrightarrow \left(\tilde{V}_{22} + \tilde{V}_{11}\right) \tilde{V}_{11}^{-1} \boldsymbol{v} &= \mathcal{R}_0 \tilde{V}_{22} \tilde{V}_{11} \tilde{V}_{11}^{-1} \boldsymbol{v} \\ \Leftrightarrow \left(\tilde{V}_{22} + \tilde{V}_{11}\right) \boldsymbol{w} &= \mathcal{R}_0 \tilde{V}_{22} \tilde{V}_{11} \boldsymbol{w}, \end{aligned}$$

where $\boldsymbol{w} = \tilde{V}_{11}^{-1} \boldsymbol{v} \gg \mathbf{0}$. This is equivalent to

$$\begin{aligned} \boldsymbol{w} &= (\mathcal{R}_0 \tilde{V}_{22} - \mathbb{I}_n)(\mathcal{R}_0 \tilde{V}_{11} - \mathbb{I}_n) \boldsymbol{w} \\ &= (\mathcal{R}_0 \tilde{D}_A - \mathbb{I}_n - d_A \tilde{L}^A)(\mathcal{R}_0 \tilde{D}_I - \mathbb{I}_n - d_I \tilde{L}^I) \boldsymbol{w} \\ &= (\tilde{D}_A \tilde{D}_I^{-1} - d_A \tilde{L}^A)(\tilde{D}_I \tilde{D}_A^{-1} - d_I \tilde{L}^I) \boldsymbol{w} \\ \Leftrightarrow &\left((\tilde{D}_A \tilde{D}_I^{-1} - d_A \tilde{L}^A)^{-1} - \tilde{D}_I \tilde{D}_A^{-1} + d_I \tilde{L}^I\right) \boldsymbol{w} = 0, \end{aligned}$$

where the third equality is based on $\tilde{D}_I^{-1} + \tilde{D}_A^{-1} = \mathcal{R}_0 \mathbb{I}_n$. Note that the matrix $\tilde{M} = (\tilde{D}_A \tilde{D}_I^{-1} - d_A \tilde{L}^A)^{-1} - \tilde{D}_I \tilde{D}_A^{-1} + d_I \tilde{L}^I$ is essentially nonnegative and irreducible. By the Perron–Frobenius theorem, $s(\tilde{M}) = 0$ for any $d_I \geq 0$ and $d_A \geq 0$.

Sufficiency can be shown by reversing the argument for the necessity. The only point we need to address is that if $\boldsymbol{w} \gg \mathbf{0}$, then $\boldsymbol{v} = \tilde{V}_{11}\boldsymbol{w} \gg \mathbf{0}$. In fact,

$$(\tilde{V}_{22} + \tilde{V}_{11})\boldsymbol{w} = \mathcal{R}_0\tilde{V}_{22}\tilde{V}_{11}\boldsymbol{w} \Leftrightarrow \boldsymbol{w} = \left(\mathcal{R}_0\mathbb{I}_n - \tilde{V}_{22}^{-1}\right)\tilde{V}_{11}\boldsymbol{w}.$$

It follows from

$$\mathbf{1}^{\mathrm{T}}\tilde{D}_A\left(\tilde{D}_A^{-1} - \left(\tilde{D}_A - d_A\tilde{L}^A\right)^{-1}\right) = \mathbf{0} \Rightarrow s\left(\tilde{D}_A^{-1} - \left(\tilde{D}_A - d_A\tilde{L}^A\right)^{-1}\right) = 0$$

that

$$\mathcal{R}_0\mathbb{I}_n - \tilde{V}_{22}^{-1} = \tilde{D}_I^{-1} + \tilde{D}_A^{-1} - \left(\tilde{D}_A - d_A\tilde{L}^A\right)^{-1}$$

is an irreducible nonsingular M-matrix such that $(\mathcal{R}_0\mathbb{I}_n - \tilde{V}_{22}^{-1})^{-1}$ exists and is positive (see, e.g., Theorem 6.2.7 in Berman and Plemmons [4]). So $\boldsymbol{v} = \tilde{V}_{11}\boldsymbol{w} = (\mathcal{R}_0\mathbb{I}_n - \tilde{V}_{22}^{-1})^{-1}\boldsymbol{w} \gg \mathbf{0}$.

(c) Suppose $\mathcal{R}_0^{(i)}$ is constant in $i \in \Omega$ and $D_I\boldsymbol{\alpha}^I = kD_A\boldsymbol{\alpha}^A$ for some $k > 0$, or equivalently, $\tilde{D}_I^{-1} + \tilde{D}_A^{-1} = \mathcal{R}_0\mathbb{I}_n$ and $\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I = k\tilde{D}_A\tilde{\boldsymbol{\alpha}}^A$ with $\tilde{\boldsymbol{\alpha}}^I = F_{11}\boldsymbol{\alpha}^I$ and $\tilde{\boldsymbol{\alpha}}^A = F_{22}\boldsymbol{\alpha}^A$ for $k > 0$. Note $\tilde{L}^I\tilde{\boldsymbol{\alpha}}^I = L^I\boldsymbol{\alpha}^I = \mathbf{0}$ and $\tilde{L}^A\tilde{\boldsymbol{\alpha}}^A = L^A\boldsymbol{\alpha}^A = \mathbf{0}$. Then

$$\begin{aligned}\left(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1}\right)\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I &= \left(\left(\tilde{D}_I - d_I\tilde{L}^I\right)^{-1} + \left(\tilde{D}_A - d_A\tilde{L}^A\right)^{-1}\right)\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I \\ &= \left(\tilde{D}_I - d_I\tilde{L}^I\right)^{-1}\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I + k\left(\tilde{D}_A - d_A\tilde{L}^A\right)^{-1}\tilde{D}_A\tilde{\boldsymbol{\alpha}}^A = \tilde{\boldsymbol{\alpha}}^I + k\tilde{\boldsymbol{\alpha}}^A \\ &= \tilde{\boldsymbol{\alpha}}^I + k\cdot\frac{1}{k}\tilde{D}_A^{-1}\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I = \left(\mathbb{I}_n + \tilde{D}_A^{-1}\tilde{D}_I\right)\tilde{\boldsymbol{\alpha}}^I = \mathcal{R}_0\tilde{D}_I\tilde{\boldsymbol{\alpha}}^I.\end{aligned}$$

Thus, $\mathcal{R}_0 = \rho(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1})$ is unaffected by the selection of d_I and d_A.

On the other hand, suppose $\mathcal{R}_0$ is independent of dispersal rates. Clearly, $D_I\boldsymbol{\alpha}^I = kD_A\boldsymbol{\alpha}^A$ can fail if both $\mathcal{R}_{0I}^{(i)}$ and $\mathcal{R}_{0A}^{(i)}$ are constant in $i \in \Omega$, i.e., $D_IF_{11}^{-1}$ and $D_AF_{22}^{-1}$ are scalar multiple of the identity matrix $\mathbb{I}_n$ by (a). Moreover, the equality may still fail even if $\mathcal{R}_{0I}^{(i)}$ and $\mathcal{R}_{0A}^{(i)}$ are nonconstant. Consider, for instance, $F_{11} = F_{22} = \mathbb{I}_3$, $D_I = \mathrm{diag}(1, \frac{3}{2}, 1)$, $D_A = \mathrm{diag}(1, \frac{3}{4}, 1)$, and

$$L^I = \begin{pmatrix} -\frac{3}{2} & 2 & 1 \\ 1 & -3 & 1 \\ \frac{1}{2} & 1 & -2 \end{pmatrix} \quad \text{and} \quad L^A = \begin{pmatrix} -2 & 1 & 1 \\ 1 & -\frac{3}{2} & 1 \\ 1 & \frac{1}{2} & -2 \end{pmatrix}.$$

Then a straightforward calculation yields

$$\mathcal{R}_0(d_I, d_A) = \rho\left(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1}\right) = \rho\left(\left(D_I - d_IL^I\right)^{-1} + \left(D_A - d_AL^A\right)^{-1}\right) \equiv 2$$

and the associated left eigenvector

$$(2(d_I + 2d_A + 9d_Id_A), 3(d_I + d_A + 6d_Id_A), 2(d_I + 2d_A + 9d_Id_A)).$$

However, $D_I\boldsymbol{\alpha}^I = (2, \frac{3}{2}, 1)^{\mathrm{T}} \neq kD_A\boldsymbol{\alpha}^A = k(5, \frac{9}{2}, 4)^{\mathrm{T}}$ for any $k > 0$ where $\boldsymbol{\alpha}^I = (2, 1, 1)^{\mathrm{T}}$ and $\boldsymbol{\alpha}^A = (5, 6, 4)^{\mathrm{T}}$.

(d) It leaves only one thing to argue, that is, the independence of $\mathcal{R}_0$ on dispersal rates does not imply the independence of $\mathcal{R}_0$ on dispersal. Consider, for example,

$$F_{11} = \begin{pmatrix} 1 & 0 \\ 0 & 2 \end{pmatrix},\ F_{22} = \begin{pmatrix} 2 & 0 \\ 0 & 1 \end{pmatrix},\ D_I = D_A = \mathbb{I}_2, \quad \text{and} \quad L^I = L^A = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix},$$

then $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 3$ and $D_I\boldsymbol{\alpha}^I = D_A\boldsymbol{\alpha}^A$ with $\boldsymbol{\alpha}^I = \boldsymbol{\alpha}^A = \binom{1}{1}$. According to case (c), $\mathcal{R}_0$ is independent of dispersal rates. However, it follows from $\mathcal{R}_{0I}^{(1)} = 1 \neq \mathcal{R}_{0I}^{(2)} = 2$ and case (a) that $\mathcal{R}_0$ is not independent of dispersal. ∎

Remark 3.14. For the SIR patch model (3.1), by Theorem 3.1, it is simple to verify that $\mathcal{R}_0$ is independent of the dispersal rate if and only if $\mathcal{R}_0$ is independent of dispersal. Thus, the independence of the basic reproduction number on dispersal gives one more difference between SIR and SIAR patch models.

3.4. Asymptotic profiles of the endemic equilibrium. In this subsection, we focus on the asymptotic properties of the endemic equilibrium of model (2.1) for slow or fast dispersal. When $\mathcal{R}_0 > 1$, by Theorem 3.5, there always exists at least one endemic equilibrium, denoted by

$$E^* = (S_1^*, \dots, S_n^*, I_1^*, \dots, I_n^*, A_1^*, \dots, A_n^*, R_1^*, \dots, R_n^*),$$

which is a positive solution to

$$d_S \sum_{j\in\Omega} L_{ij}^S S_j^* + \Lambda_i - \beta_i \frac{I_i^* + \tau_i A_i^*}{N_i^*} S_i^* - \mu_i S_i^* = 0,\ i \in \Omega, \tag{3.13a}$$

$$d_I \sum_{j\in\Omega} L_{ij}^I I_j^* + \theta_i\beta_i \frac{I_i^* + \tau_i A_i^*}{N_i^*} S_i^* - (\mu_i + \gamma_i^I + \delta_i) I_i^* = 0,\ i \in \Omega, \tag{3.13b}$$

$$d_A \sum_{j\in\Omega} L_{ij}^A A_j^* + (1-\theta_i)\beta_i \frac{I_i^* + \tau_i A_i^*}{N_i^*} S_i^* - (\mu_i + \gamma_i^A) A_i^* = 0,\ i \in \Omega, \tag{3.13c}$$

$$d_R \sum_{j\in\Omega} L_{ij}^R R_j^* + \gamma_i^I I_i^* + \gamma_i^A A_i^* - \mu_i R_i^* = 0,\ i \in \Omega, \tag{3.13d}$$

with $N_i^* = S_i^* + I_i^* + A_i^* + R_i^*$. In general, the basic reproduction number $\mathcal{R}_0$ determines the disease dynamics, but cannot characterize the endemic level. We first study the asymptotic profile of the endemic equilibrium E^* as $d_I \to 0+$, i.e., the symptomatic people have very limited mobility. The proof is provided in the supplementary material (SM2).

THEOREM 3.15. *Assume* $\lim_{d_I\to 0+} \mathcal{R}_0(d_I) = \mathcal{R}_0(0) = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1}) > 1$. *Then the endemic equilibrium of model* (2.1) *satisfies (up to a sequence of* $d_I \to 0+$*)*

$$(S_i^*, I_i^*, A_i^*, R_i^*) \to (\tilde{S}_i, \tilde{I}_i, \tilde{A}_i, \tilde{R}_i),\ i \in \Omega, \quad \textit{as}\ \ d_I \to 0+,$$

where $(\tilde{S}_i, \tilde{I}_i, \tilde{A}_i, \tilde{R}_i) \gg \mathbf{0}$ *for all* $i \in \Omega$.

Similar to Theorem 3.15, if $\lim_{d_A\to 0+} \mathcal{R}_0(d_A) = \rho(F_{11}V_{11}^{-1} + F_{22}D_A^{-1}) > 1$, then for fixed $d_I > 0$ the endemic equilibrium E^* approaches a positive limiting endemic equilibrium as $d_A \to 0+$ or $d_\natural \to 0+$ for all $\natural \in \{S, A, R\}$ (up to a sequence). Consequently, the asymptotic profile of the endemic equilibrium of model (2.1) as $d_\natural \to 0+$ is different from that of the SIS patch model without vital dynamics in which the endemic equilibrium converges to a limiting disease-free equilibrium as $d_S \to 0+$ if at least one patch reproduction number is less than one [1, 9].

Remark 3.16. As $d_\natural \to 0+$ for all $\natural \in \{S, I, A, R\}$, if $\mathcal{R}_0^{(i)} > 1$, then the population of patch i at the endemic equilibrium E^* approaches the globally asymptotically stable endemic equilibrium of patch i in isolation, denoted by $(S_i^*(0), I_i^*(0), A_i^*(0), R_i^*(0))$, which can be solved explicitly [31]. This gives the respective prevalences of symptomatic and asymptomatic infections in the ith isolated patch

$$\frac{I_i^*(0)}{N_i^*(0)} = \frac{\theta_i\mu_i}{\mu_i+\gamma_i^I+(1-\theta)\delta_i}\left(1-\frac{1}{\mathcal{R}_0^{(i)}}\right),$$
$$\frac{A_i^*(0)}{N_i^*(0)} = \frac{\mu_i+\gamma_i^I+\delta_i}{\mu_i+\gamma_i^I+(1-\theta)\delta_i}(1-\theta_i)\frac{\mu_i}{\mu_i+\gamma_i^A}\left(1-\frac{1}{\mathcal{R}_0^{(i)}}\right).$$

Furthermore, the ratio of nonsusceptible population to total population in patch i is

$$\frac{I_i^*(0)+A_i^*(0)+R_i^*(0)}{N_i^*(0)} = 1-\frac{S_i^*(0)}{N_i^*(0)} = 1-\frac{1}{\mathcal{R}_0^{(i)}},$$

which is the same as the disease prevalence of an SIAS or SIS model. So, for a single patch, the higher the infection risk (measured by $\mathcal{R}_0^{(i)}$), the larger the nonsusceptible ratio. In particular, if $\delta_i = 0$, then the endemic equilibrium of patch i in isolation is

$$\left(\frac{\Lambda_i}{\mu_i}\cdot\frac{1}{\mathcal{R}_0^{(i)}}, I_i^*(0), \frac{1-\theta_i}{\theta_i}\cdot\frac{\mu_i+\gamma_i^I}{\mu_i+\gamma_i^A}I_i^*(0), \left(\frac{\gamma_i^I}{\mu_i}+\frac{1-\theta_i}{\theta_i}\cdot\frac{\mu_i+\gamma_i^I}{\mu_i+\gamma_i^A}\cdot\frac{\gamma_i^A}{\mu_i}\right)I_i^*(0)\right)$$

with $I_i^*(0) = \theta_i\frac{\Lambda_i}{\mu_i+\gamma_i^I}\big(1-1/\mathcal{R}_0^{(i)}\big)$.

When infection does not affect host mobility, the endemic equilibrium E^* converges as the uniform dispersal rate goes to infinity. The following result and Remark 3.16 make it possible to compare the effect of small and large dispersal on local and global infection size [15, 17].

PROPOSITION 3.17. *For model* (2.1)*, if* $\delta_i = 0$ *for* $i \in \Omega$*,* $d_\natural = d$ *and* $L^\natural = L$ *for* $\natural \in \{S, I, A, R\}$*, and* $\lim_{d\to\infty}\mathcal{R}_0(d) > 1$*, then the endemic equilibrium satisfies*

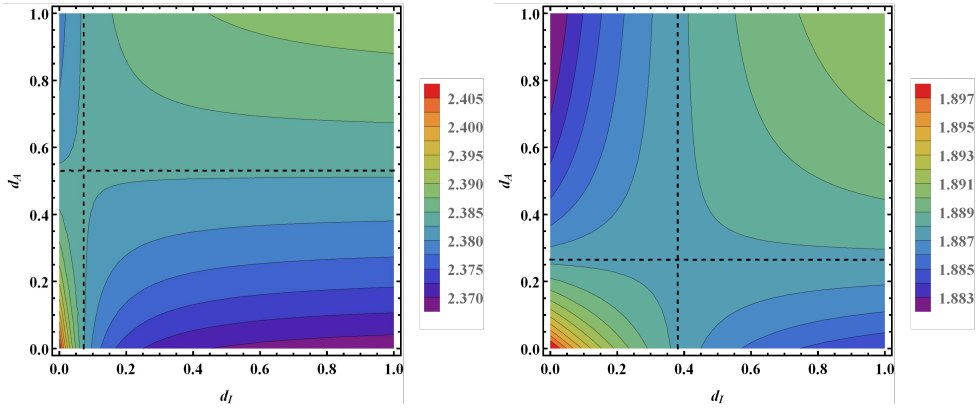
$$E^*(d) \to E^*(\infty) := (m^S\boldsymbol{\alpha}, m^I\boldsymbol{\alpha}, m^A\boldsymbol{\alpha}, m^R\boldsymbol{\alpha}) \quad as \quad d\to\infty,$$

where $\boldsymbol{\alpha} = (\alpha_1,\dots,\alpha_n) \gg \mathbf{0}$ *with* $\sum_{i\in\Omega}\alpha_i = 1$ *is the right eigenvector of* L *associated with the zero eigenvalue and* $m^\natural > 0$ *for* $\natural \in \{S, I, A, R\}$ *can be determined explicitly in terms of model parameters. If, in addition,* $\theta_i = \theta$ *or* $\tau_i = \tau$ *for all* $i \in \Omega$*, then the overall nonsusceptible ratio at* $E^*(\infty)$ *is* $1 - 1/\mathcal{R}_0(\infty,\infty)$*.*

The proof of Proposition 3.17 appears in the supplementary material (SM3). The nonsusceptible ratio agrees with that of the SIS patch model studied by Gao [15] and Gao and Lou [17]. The above result remains true when the dispersal rates are distinct but all go to infinity.

4. Numerical simulations. To further illustrate the effects of dispersal and asymptomatic infection on disease persistence and prevalence in a heterogeneous environment, we present some simulations related to the epidemiology of COVID-19. The selected parameter values with day as the default time unit mainly come from Byambasuren et al. [6], Gatto et al. [21], Oran and Topol [36], and the references therein. For convenience, we denote $\tilde{\gamma}_i^I = \mu_i + \gamma_i^I + \delta_i$ and $\tilde{\gamma}_i^A = \mu_i + \gamma_i^A$ for $i \in \Omega$.

Example 4.1 (infection risk versus dispersal rates). By Theorem 3.6, Proposition 3.8, and Theorem 3.10, an increase in dispersal rate of the infected populations, d_I or d_A, has a high possibility to decrease the basic reproduction number $\mathcal{R}_0$ and hence reduces the risk of infection. However, $\mathcal{R}_0$ can be increasing or nonmonotone in d_I or d_A when the underlying conditions of these results fail. For model (2.1) with two patches, by choosing two parameter sets, we make two contour plots of $\mathcal{R}_0$ versus



(a) (b)

FIG. 2. *The contour plots of the basic reproduction number $\mathcal{R}_0$ versus dispersal rates d_I and d_A under parameter settings* (a) $\beta_1 = 0.77, \beta_2 = 0.35, \tilde{\gamma}_1^I = 0.24, \tilde{\gamma}_2^I = 0.13, \tilde{\gamma}_1^A = 0.18, \tilde{\gamma}_2^A = 0.21, \theta_1 = \theta_2 = 0.66, \tau_1 = 0.20, \tau_2 = 0.92$, $L_{12}^I = L_{21}^I = 0.08$ *and* $L^A = L^I$; *and* (b) $\beta_1 = 0.59, \beta_2 = 0.44, \tilde{\gamma}_1^I = 0.25, \tilde{\gamma}_2^I = 0.22, \tilde{\gamma}_1^A = 0.24, \tilde{\gamma}_2^A = 0.11, \theta_1 = \theta_2 = 0.72, \tau_1 = \tau_2 = 0.29$, $L_{12}^I = 0.06, L_{21}^I = 0.01$, *and* $L_{12}^A = L_{21}^A = 0.10$.

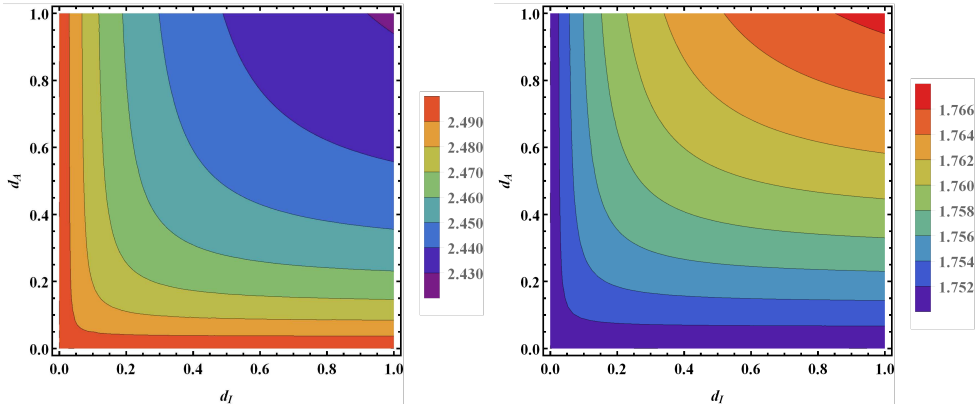
d_I and d_A in Figure 2. In both scenarios, $\mathcal{R}_0$ is decreasing for small dispersal rates but increasing for large dispersal rates. The horizontal and vertical dashed lines given by Remark 3.12 are the contours where $\mathcal{R}_0$ is constant with respect to d_I and d_A, respectively. Note that the independence of $\mathcal{R}_0$ on d_I does not imply the independence of $\mathcal{R}_0$ on d_A and vice versa. It follows from Theorem 3.6 and Proposition 3.8 that the nondecreasing dependences in Figure 2 are due to the difference in asymptomatic infectivity and the connectivity matrices, respectively.

When three or more patches are concerned, nonmonotonic dependence of $\mathcal{R}_0$ on dispersal rates can occur. Assume a three-patch environment with parameter values at

$$\begin{aligned}&\beta_1 = 0.39,\ \beta_2 = 0.35,\ \beta_3 = 0.33,\ \tilde{\gamma}_1^I = 0.12,\ \tilde{\gamma}_2^I = 0.27,\ \tilde{\gamma}_3^I = 0.11,\\ &\tilde{\gamma}_1^A = 0.29,\ \tilde{\gamma}_2^A = 0.11,\ \tilde{\gamma}_3^A = 0.19,\ \theta = 0.75,\ \tau = 0.4,\ L^I = L^A = L,\\ &L_{12} = 0.1,\ L_{13} = 0.004,\ L_{21} = 0.05,\ L_{23} = 0.06,\ L_{31} = 0.05,\ L_{32} = 0.02.\end{aligned}$$

Thus, $\mathcal{R}_0(0.2, 0) = 2.3015 > \mathcal{R}_0(0.2, 0.6) = 2.2994 < \mathcal{R}_0(0.2, 4) = 2.3009$ implies that $\mathcal{R}_0(d_I, d_A)$ is not monotone in terms of d_A as $d_I = 0.2$. This also suggests that the conclusion of Proposition 3.8 may fail if the matrix L is not symmetrizable.

Under special situations, the basic reproduction number $\mathcal{R}_0$ can be simultaneously decreasing or increasing in both dispersal rates which implies that $\mathcal{R}_0(d_I, d_A) < \mathcal{R}_0(0, 0)$ or $\mathcal{R}_0(d_I, d_A) > \mathcal{R}_0(0, 0)$ for any $d_I > 0$ and $d_A > 0$. In Figure 3(a), the patch reproduction numbers are $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = \mathcal{R}_0(0, 0) = \frac{5}{2}$ with $\mathcal{R}_{0I}^{(1)} = 2, \mathcal{R}_{0A}^{(1)} = \frac{1}{2}$, $\mathcal{R}_{0I}^{(2)} = \frac{3}{2}$, and $\mathcal{R}_{0A}^{(2)} = 1$, and symmetric dispersal (L^I and L^A are symmetric) always reduces the infection risk. In Figure 3(b), we have $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = \mathcal{R}_0(0, 0) = \frac{7}{4}$ with $\mathcal{R}_{0I}^{(1)} = \frac{3}{4}, \mathcal{R}_{0A}^{(1)} = 1$, $\mathcal{R}_{0I}^{(2)} = 1$, and $\mathcal{R}_{0A}^{(2)} = \frac{3}{4}$, and asymmetric dispersal of symptomatic cases strengthens disease persistence. These mean the failure of the upper and lower bounds of $\mathcal{R}_0$ in terms of the maximum and minimum of $\{\mathcal{R}_0^{(i)}\}_{i\in\Omega}$, differing from the SIR patch model (3.1).



(a) (b)

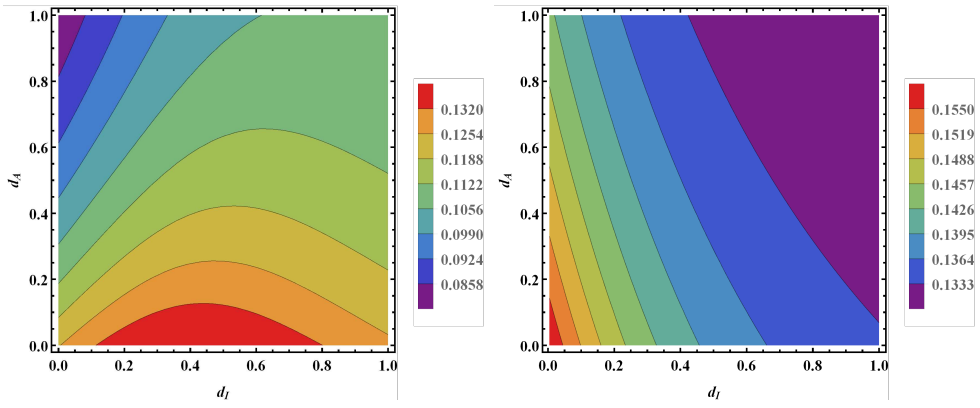
FIG. 3. *The contour plots of the basic reproduction number $\mathcal{R}_0$ versus dispersal rates d_I and d_A under parameter settings* (a) $\beta_1 = \beta_2 = \frac{1}{2}, \tilde{\gamma}_1^I = \frac{1}{6}, \tilde{\gamma}_2^I = \frac{2}{9}, \tilde{\gamma}_1^A = \frac{1}{6}, \tilde{\gamma}_2^A = \frac{1}{12}, \theta_1 = \theta_2 = \frac{2}{3}, \tau_1 = \tau_2 = \frac{1}{2}$, $L_{12}^I = L_{21}^I = \frac{1}{10}$ *and* $L^A = L^I$*; and* (b) $\beta_1 = \beta_2 = \frac{1}{2}, \tilde{\gamma}_1^I = \frac{1}{3}, \tilde{\gamma}_2^I = \frac{1}{4}, \tilde{\gamma}_1^A = \frac{1}{4}, \tilde{\gamma}_2^A = \frac{1}{3}, \theta_1 = \theta_2 = \frac{1}{2}, \tau_1 = \tau_2 = 1$, $L_{12}^I = L_{12}^A = L_{21}^A = \frac{1}{30}$, *and* $L_{21}^I = \frac{1}{5}$.

Example 4.2 (underestimate the infection risk). In the case where only symptomatic infections are counted, the single patch and multipatch basic reproduction numbers of model (2.1) are $\mathcal{R}_{0I}^{(i)}$ and $\mathcal{R}_{0I} = \rho(F_{11}V_{11}^{-1})$, respectively. Clearly, $\mathcal{R}_{0I}^{(i)} < \mathcal{R}_0^{(i)} = \mathcal{R}_{0I}^{(i)} + \mathcal{R}_{0A}^{(i)}$ and $\mathcal{R}_{0I} < \mathcal{R}_0 = \rho(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1})$. Biologically speaking, ignoring asymptomatic infection will locally and globally underestimate the infection risk. Further, the extent of underestimation is significantly affected by population dispersal. For example, a two-patch environment with parameter setting

$$\beta_1 = 0.42,\ \beta_2 = 0.32,\ \tilde{\gamma}_1^I = 0.16,\ \tilde{\gamma}_2^I = 0.18,\ \tilde{\gamma}_1^A = 0.14,\ \tilde{\gamma}_2^A = 0.17,$$
$$\theta_1 = \theta_2 = 0.8,\ \tau_1 = 0.5,\ \tau_2 = 0.36,\ L_{12}^I = 0.02,\ L_{21}^I = 0.1,\ L^A = L^I$$

gives $\mathcal{R}_{0I}^{(1)} = 2.1, \mathcal{R}_{0I}^{(2)} = 1.42, \mathcal{R}_0^{(1)} = 2.4$, and $\mathcal{R}_0^{(2)} = 1.56$. So the percentages of underestimation of the basic reproduction number for patches 1 and 2 are $\mathcal{U}^{(1)} := 1 - \mathcal{R}_{0I}^{(1)}/\mathcal{R}_0^{(1)} = 12.5\%$ and $\mathcal{U}^{(2)} := 1 - \mathcal{R}_{0I}^{(2)}/\mathcal{R}_0^{(2)} = 8.7\%$, respectively. When the two patches are connected, the relative underestimation of the multipatch basic reproduction number, $\mathcal{U}(d_I, d_A) := 1 - \mathcal{R}_{0I}(d_I)/\mathcal{R}_0(d_I, d_A)$, is plotted in Figure 4(a). In this scenario, an increase in the dispersal rate of symptomatic cases initially increases and then decreases relative underestimation while increasing the dispersal rate of asymptomatic cases decreases relative underestimation. Note that $\mathcal{U}$ is not necessarily between the maximum and minimum of $\{\mathcal{U}^{(1)}, \mathcal{U}^{(2)}\}$.

Using the same parameter set as Figure 4(a) except that $\tilde{\gamma}_1^I = 0.21, \tilde{\gamma}_2^I = 0.16, \tau_2 = 0.5$, $L_{12}^I = 0.01$, and $L_{21}^I = 0.02$, then $\mathcal{R}_{0I}^{(1)} = \mathcal{R}_{0I}^{(2)} = 1.6, \mathcal{R}_0^{(1)} = 1.9$, and $\mathcal{R}_0^{(2)} = 1.79$. It follows from Theorem 3.1 and $\mathcal{R}_{0I}^{(1)} = \mathcal{R}_{0I}^{(2)}$ that $\mathcal{R}_{0I}(d_I)$ is constant. By Proposition 3.8, we know $\mathcal{R}_0(d_I, d_A)$ is strictly decreasing in d_I and d_A. So is the relative underestimation $\mathcal{U}$ as illustrated in Figure 4(b). According to Proposition 3.13(d), it is possible that $\mathcal{R}_0(d_I, d_A)$ is constant but $\mathcal{R}_{0I}(d_I)$ is decreasing, so $\mathcal{U}$ is increasing in d_I. These suggest that the dependence of the level of underestimation on dispersal rates can be complicated. To further quantify the level of underestimation, we use the Latin hypercube sampling method to randomly gener-



(a) (b)

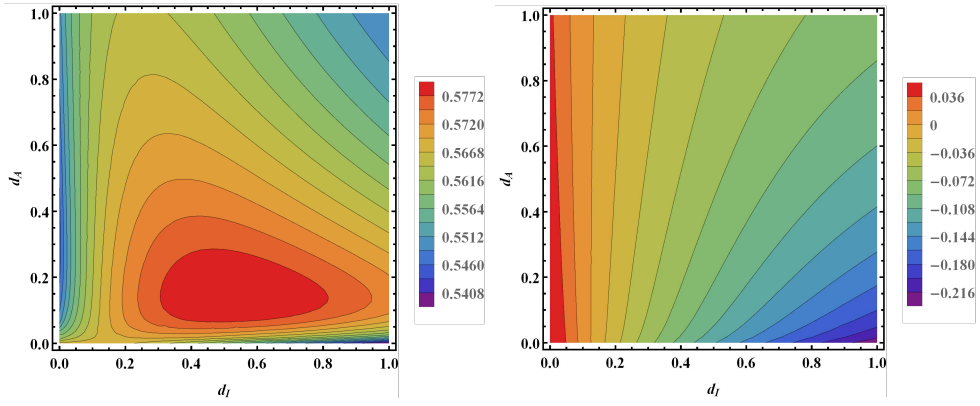
FIG. 4. *The contour plots of the relative underestimation of the multipatch basic reproduction number,* $\mathcal{U}(d_I, d_A) = 1 - \mathcal{R}_{0I}(d_I)/\mathcal{R}_0(d_I, d_A)$*, under two different scenarios. See text in Example* 4.2 *for parameter values.*

ate 10^5 parameter sets with biological reasonable parameter ranges and restrictions: $\beta_i \in [0.2, 0.6], \tilde{\gamma}_i^I, \tilde{\gamma}_i^A \in [0.1, 0.3], \theta_i \in [0.4, 0.9], \tau_i \in [0.2, 1], d_I, d_A \in (0, 1]$, and $d_I \le d_A$, $L_{12}^I, L_{21}^I \in (0, 0.1]$, and $L^A = L^I$ for $i = 1, 2$. The average percentage of underestimation of $\mathcal{R}_0$ is 23.7% with the maximum value approximately 77%.

Example 4.3 (nonsusceptible ratio versus dispersal rates). The basic reproduction number of model (2.1) determines whether an infectious disease can spread in a population. By Remark 3.16, it also determines what proportion of the population will be infected at the globally stable endemic equilibrium in the single patch case. However, the reproduction number may be unable to play such a role in the multipatch case [15, 17]. For illustrative purpose only, we consider a two-patch environment with parameter setting $\beta_1 = 0.4, \beta_2 = 0.54, \gamma_1^I = 0.15, \gamma_2^I = 0.24, \gamma_1^A = 0.17, \gamma_2^A = 0.19, \theta_i = 0.9, \tau_i = 0.4$, $\Lambda_1 = 50, \Lambda_2 = 21$, $\mu_i = 0.004$, and $\delta_i = 0$ for $i = 1, 2$. Then $\mathcal{R}_0^{(1)} = 2.43$ and $\mathcal{R}_0^{(2)} = 2.10$ and hence the nonsusceptible ratios of patches 1 and 2 in isolation are $1 - 1/\mathcal{R}_0^{(1)} = 0.59$ and $1 - 1/\mathcal{R}_0^{(2)} = 0.52$, respectively. When the two patches are connected by human movement with $L_{12}^I = 0.012, L_{21}^I = 0.06, L^S = L^A = L^R = L^I$, and $d_S = d_A = d_R$, the ratio of nonsusceptible population over both patches and the difference of nonsusceptible ratios of patches 1 and 2 at the endemic equilibrium, i.e.,

$$\frac{\sum_{i=1}^2 (I_i^* + A_i^* + R_i^*)}{\sum_{i=1}^2 N_i^*} = 1 - \frac{S_1^* + S_2^*}{N_1^* + N_2^*} \text{ and } \frac{I_1^* + A_1^* + R_1^*}{N_1^*} - \frac{I_2^* + A_2^* + R_2^*}{N_2^*} = \frac{S_2^*}{N_2^*} - \frac{S_1^*}{N_1^*}$$

are plotted in Figure 5. The overall nonsusceptible ratio can nonmonotonically vary with respect to d_I and d_A even if they are proportional and the high risk patch (where the patch reproduction number is larger) may no longer have high nonsusceptible ratio. For example, $1 - S_1^*/N_1^* = 0.49 < 1 - 1/\mathcal{R}_0^{(2)} < 1 - 1/\mathcal{R}_0^{(1)} < 1 - S_2^*/N_2^* = 0.61$ at $(d_I, d_A) = (0.8, 0.2)$. However, by Proposition 3.8, $\mathcal{R}_0$ is strictly decreasing in terms of dispersal rates for the scenario. This means that travel restriction may reduce the infection risk but increase the nonsusceptible population size, leading to a counterintuitive relation between infection risk and nonsusceptible ratio in measuring the effectiveness of interventions.



(a) (b)

FIG. 5. *The contour plots of* (a) *the nonsusceptible ratio over two patches and* (b) *the difference of the nonsusceptible ratios of patches* 1 *and* 2 *at the endemic equilibrium. See text in Example* 4.3 *for parameter values.*

5. Discussion. Asymptomatic infections occur commonly for a few widespread infectious diseases such as COVID-19, influenza, and Zika fever. Their role in disease transmission and herd immunity has attracted considerable attention in recent years. In this paper, we introduced a metapopulation model for disease spread across a number of spatial patches where the population is split into susceptible, symptomatically infected, asymptomatically infected, and recovered individuals in every patch. We computed the basic reproduction number $\mathcal{R}_0$ of the model and obtained its threshold property. That is, the disease-free equilibrium is globally asymptotically stable if $\mathcal{R}_0 \leq 1$ and the disease is uniformly persistent if $\mathcal{R}_0 > 1$. It is shown that under certain biologically meaningful conditions (Theorem 3.6, Proposition 3.8, and Theorem 3.10) the reproduction number is monotone decreasing in terms of the dispersal rates of symptomatic and asymptomatic persons. For the two-patch case, $\mathcal{R}_0$ either strictly increases, strictly decreases, or remains unchanged with respect to dispersal rates. Some necessary and sufficient conditions for $\mathcal{R}_0$ to be independent of dispersal rates and dispersal were given. When $\mathcal{R}_0 > 1$, we studied the asymptotic profiles of the endemic equilibrium as one or all dispersal rates approach zero or infinity.

Additionally, three numerical examples were presented to further study the influence of asymptomatic carriers and their dispersal on the spread of infectious agents. The first example confirmed the theoretical results on the dependence of $\mathcal{R}_0$ versus dispersal rates. The difference in the transmissibility or dispersal pattern of the asymptomatic class relative to the symptomatic class can cause nondecreasing dependence. Nonmonotonic dependence can happen when people move between three or more patches. In the second example, we showed that ignoring asymptomatic infections not only locally but also globally underestimates the transmission potential. The overall relative level of underestimation significantly varies with dispersal rates and may not be in the range of the relative underestimations of isolated patches. The last example investigated the relation between the total nonsusceptible population and human movement. There is a potential inconsistent feedback to fast dispersal between the basic reproduction number and the number of nonsusceptible individuals.

Besides underestimating the infection risk, there are some other critical differences between the SIAR patch model (2.1) and the SIR patch model (3.1). First, the basic

reproduction number of model (3.1) is either strictly decreasing or constant in the dispersal rate of the infected population, whereas that of model (2.1) is either strictly decreasing, or strictly increasing, or constant in terms of dispersal rates for the two-patch case and can be nonmonotonic for the case of three or more patches. In reality, the proportion and relative infectivity of asymptomatic infections are probably spatially heterogeneous due to factors like age structure, awareness program, and contact tracing. Meanwhile, the connectivity matrix may not be symmetric or symmetrizable. Thus, the possibility of increasing the infection risk via fast dispersal is not negligible. Second, the basic reproduction number of model (3.1) is between the maximum and minimum of the set of patch reproduction numbers, but this is generally not true for model (2.1). Thus, it is possible that the disease dies out or persists in a strongly connected patchy environment even if it is persistent or extinct in each isolated patch as asymptomatic infections occur. Third, the independences of the reproduction number of model (3.1) on dispersal rate and dispersal are equivalent, whereas they are not for model (2.1). In addition, the dependence of the local or global nonsusceptible ratio on dispersal rates for model (3.1) is more complicated than that for an SIS patch model and the weak order-preserving property correlating patch reproduction number with local nonsusceptible ratio may fail [15, 17]. So the presence and movement of asymptomatic patients must be considered in predicting the transmission potential and designing travel policy. The control strategies toward SARS may not work for COVID-19 due to the difference in asymptomatic or presymptomatic transmission.

The current study generalizes some findings on SIS and SIR patch models to the SIAR patch model [1, 15, 16, 29]. It is applicable to patch models with SIA, SIAS, or SIARS structure in each patch since their reproduction numbers take the same form [10]. The main results throughout this paper can be extended to a differential infectivity SIR patch model where the infected population is divided into multiple infectious subgroups [24] (see supplementary material (SM4)). In particular, when only two patches are concerned, the proof of Proposition 3.11 is still valid and hence the basic reproduction number is either strictly increasing or strictly decreasing or constant in the dispersal rate of any given infectious subgroup. There are a variety of directions deserving further investigation. The dependence of the basic reproduction number of model (3.1) with respect to dispersal rates is generally unclear in the case of three or more patches. It is interesting to characterize the independence of the reproduction number on dispersal rates in an easy-to-verify way. We would like to know how the total number of symptomatic and/or asymptomatic infections and its distribution change with dispersal [15, 17]. What is the effect of the travel of susceptible and recovered individuals for disease control? The uniqueness and global stability of the endemic equilibrium are unknown even under strict conditions of no disease-induced mortality and the same dispersal rate and connectivity matrix for all disease states. A partial answer may be achievable by constructing a suitable Lyapunov function with a graph-theoretic approach [29]. The model presented here can be generalized to include a latent period and temporary immunity [38, 41], progression and regression between asymptomatic and symptomatic stages [5, 10], travel restriction and border screening [30], multiple transmission modes [18, 44], seasonal variation in contacts and survivability of pathogens [44], quarantine and isolation [42], and vaccination [48].

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