PROCEEDINGS OF THE
AMERICAN MATHEMATICAL SOCIETY
https://doi.org/10.1090/proc/14868

FAST DIFFUSION INHIBITS DISEASE OUTBREAKS

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(Communicated by Wenxian Shen)

Abstract. We show that the basic reproduction number of an SIS patch model with standard incidence is either strictly decreasing and strictly convex with respect to the diffusion coefficient of infected subpopulation if the patch reproduction numbers of at least two patches in isolation are distinct or constant otherwise. Biologically, it means that fast diffusion of infected people reduces the risk of infection. This completely solves and generalizes a conjecture by Allen et al. [SIAM J. Appl. Math., 67 (2007) pp. 1283–1309]. Furthermore, a substantially improved and reachable lower bound on the multipatch reproduction number, a generalized monotone result on the spectral bound of the Jacobian matrix of the model system at the disease-free equilibrium, and the limit of the endemic equilibrium as the diffusion coefficient goes to infinity are obtained. The approach and results can be applied to a class of epidemic patch models where only one class of infected compartments migrate between patches and one transmission route is involved.

1. Introduction

In 2007, Allen and her collaborators proposed the following SIS epidemic patch model:

$$\begin{aligned}\frac{dS_i}{dt} &= d_S \sum_{j\in\Omega} L_{ij}S_j - \beta_i \frac{S_iI_i}{S_i+I_i} + \gamma_i I_i,\ i\in\Omega,\\ \frac{dI_i}{dt} &= d_I \sum_{j\in\Omega} L_{ij}I_j + \beta_i \frac{S_iI_i}{S_i+I_i} - \gamma_i I_i,\ i\in\Omega,\end{aligned}\tag{1.1}$$

where $\Omega=\{1,2,\dots,n\}$ and $n\geq 2$ is the number of patches. The variables $S_i(t)$ and $I_i(t)$ represent the number of susceptible and infected individuals in patch i at time t, respectively. The parameters β_i and γ_i are positive transmission coefficient and recovery rate in patch i, respectively; d_S and d_I are positive diffusion coefficients for the susceptible and infected subpopulations, respectively; L_{ij} is a nonnegative constant that denotes the degree of movement from patch j to patch i for $i\neq j$ and $-L_{ii}=\sum_{j=1,j\neq i}^{n} L_{ji}$ is the degree of movement from patch i to all other patches.

Received by the editors July 29, 2019, and, in revised form, September 7, 2019, and September 11, 2019.

2010 *Mathematics Subject Classification.* Primary 91D25, 34D20, 92D30, 34D05, 15B48, 15A42.

Key words and phrases. Patch model, basic reproduction number, monotonicity, diffusion coefficient, spectral bound, essentially nonnegative matrix.

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This study was partially supported by NSFC (11601336, 11571097), Program for Professor of Special Appointment (Eastern Scholar) at Shanghai Institutions of Higher Learning (TP2015050), and Shanghai Gaofeng Project for University Academic Development Program.

The following three assumptions on the initial condition, the connectivity matrix $L = (L_{ij})$, and the patch reproduction number $\mathcal{R}_0^{(i)} = \beta_i/\gamma_i$ are made:

- (A1) $S_i(0) \geq 0$ and $I_i(0) \geq 0$ for $i \in \Omega$, and $\sum_{i\in\Omega} I_i(0) > 0$;
- (A2) L is essentially nonnegative (or called quasi-positive), irreducible, and symmetric;
- (A3) $H^- = \{i \in \Omega : \mathcal{R}_0^{(i)} < 1\}$ and $H^+ = \{i \in \Omega : \mathcal{R}_0^{(i)} > 1\}$ are nonempty and $H^- \cup H^+ = \Omega$.

It follows from Theorem 6.4.16 in Berman and Plemmons [7] that L has rank $n-1$ and hence the system of linear equations

$$\sum_{j\in\Omega} L_{ij}S_j = 0,\ i = 1, \ldots, n \text{ and } \sum_{i\in\Omega} S_i = \sum_{i\in\Omega}(S_i(0) + I_i(0))$$

has a unique positive solution, denoted by $\boldsymbol{S}^0$. Then the model (1.1) admits a unique disease-free equilibrium (DFE) $E_0 = (\boldsymbol{S}^0, \mathbf{0})$. Linearizing the model system (1.1) at the DFE gives the new infection and transition matrices

$$F = \operatorname{diag}\{\beta_1, \ldots, \beta_n\} \text{ and } V = D - d_I L = \operatorname{diag}\{\gamma_1, \ldots, \gamma_n\} - d_I L,$$

where $D = \operatorname{diag}\{\gamma_1, \ldots, \gamma_n\}$. Following the recipe of van den Driessche and Watmough [31], the basic reproduction number for model (1.1) is defined as the spectral radius of the next generation matrix (Diekmann et al. [12]) FV^{-1}, i.e.,

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

Allen et al. [1] showed that the DFE is globally asymptotically stable if $\mathcal{R}_0 < 1$ and there exists a unique endemic equilibrium if $\mathcal{R}_0 > 1$ and (A2) is satisfied. Under assumptions (A1)–(A3), two main theorems linked spatial heterogeneity, habitat connectivity, and movement rate to disease dynamics are presented. Three open problems are left in their discussion. The first one is to conjecture that the basic reproduction number $\mathcal{R}_0$ is a monotone decreasing function of d_I. Biologically speaking, an increase in the diffusion of infected subpopulation can lower the potential for disease transmission. The two-patch case can be easily verified by direct calculation. Nevertheless, when three or more patches are concerned, the expression of V^{-1} is complicated so that a direct proof of the monotonicity is intractable. Recently, Gao [15] gave an affirmative answer to the conjecture by using the Perron–Frobenius theorem. The proof strongly relies on the symmetry of connectivity matrix L. The main purpose of the present paper is to extend the conjecture to asymmetric L and to seek its applications.

The remainder of this paper is organized as follows. In Section 2, based on some profound results on the spectral theory of nonnegative matrices, the basic reproduction number $\mathcal{R}_0$ is shown to be strictly decreasing and strictly convex in d_I even if the connectivity matrix L is asymmetric. Section 3 is devoted to the application of the monotonicity of $\mathcal{R}_0$ to estimate $\mathcal{R}_0$ and the spectral bound of $F - V$. A brief discussion is given at the end.

2. MONOTONICITY OF $\mathcal{R}_0$

Throughout this paper, unless otherwise indicated, we assume that:

- (B1) L is an essentially nonnegative and irreducible matrix with zero column sums;

(B2) at least two patch reproduction numbers are different, i.e., there exist $i \neq j$ such that $\mathcal{R}_0^{(i)} \neq \mathcal{R}_0^{(j)}$ (otherwise, by Proposition 2.2 in Gao and Ruan [16], the multipatch reproduction number $\mathcal{R}_0$ is constant irrespective of L and d_I).

Now we provide a simpler proof for the conjecture of Allen et al. [1] than that of Gao [15]. The single and double prime symbols denote the first and second derivatives with respect to d_I, respectively.

Theorem 2.1. *For model* (1.1)*, if the connectivity matrix* L *is symmetric, then the basic reproduction number* $\mathcal{R}_0$ *is strictly decreasing in* $d_I \in [0,\infty)$ *and* $\mathcal{R}_0'(d_I) < 0$ *for* $d_I \in (0,\infty)$.

Proof. The fact $\mathcal{R}_0 = \rho(FV^{-1}) = \rho(V^{-1}F)$ implies that there exists a column vector $\boldsymbol{v} := \boldsymbol{v}(d_I) = (v_1, \ldots, v_n)^T \gg \boldsymbol{0}$ such that $V^{-1}F\boldsymbol{v} = \mathcal{R}_0\boldsymbol{v}$, or equivalently,

$$\left(\frac{1}{\mathcal{R}_0}F - V\right)\boldsymbol{v} = \left(\frac{1}{\mathcal{R}_0}F - D + d_I L\right)\boldsymbol{v} = \boldsymbol{0}. \tag{2.1}$$

Differentiating both sides of (2.1) with respect to d_I gives

$$\left(-\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F + L\right)\boldsymbol{v} + \left(\frac{1}{\mathcal{R}_0}F - D + d_I L\right)\boldsymbol{v}' = \boldsymbol{0}. \tag{2.2}$$

Multiplying (2.1) by $(\boldsymbol{v}')^T$ and (2.2) by $\boldsymbol{v}^T$, and subtracting the two resulting equations yield

$$\boldsymbol{v}^T\left(-\frac{\mathcal{R}_0'}{\mathcal{R}_0^2}F + L\right)\boldsymbol{v} = 0$$

due to the symmetry of $\frac{1}{\mathcal{R}_0}F - D + d_I L$. We thus have

$$\mathcal{R}_0' = \frac{\boldsymbol{v}^T L\boldsymbol{v}}{\boldsymbol{v}^T F\boldsymbol{v}}\mathcal{R}_0^2.$$

It follows from the symmetry of L that

$$\begin{aligned}\boldsymbol{v}^T L\boldsymbol{v} &= \sum_{i=1}^n\sum_{j=1}^n L_{ij}v_iv_j = \sum_{i=1}^n\sum_{j\neq i} L_{ij}v_iv_j + \sum_{i=1}^n L_{ii}v_i^2\\ &= \sum_{i=1}^n\sum_{j\neq i} L_{ij}v_iv_j - \sum_{i=1}^n\sum_{j\neq i} L_{ji}v_i^2 = \sum_{i=1}^n\sum_{j\neq i} L_{ij}v_i(v_j - v_i)\\ &= \sum_{i=1}^n\sum_{j\neq i} L_{ij}v_j(v_i - v_j) = -\frac{1}{2}\sum_{i=1}^n\sum_{j\neq i} L_{ij}(v_i - v_j)^2 \leq 0.\end{aligned}$$

Similar to the proof of Lemma 3.4 in Allen et al. [1], we can use the irreducibility of L to prove by contradiction that $\boldsymbol{v}^T L\boldsymbol{v} < 0$. In particular, if $v_1 = \cdots = v_n$, then (2.1) implies that $\mathcal{R}_0^{(i)} = \mathcal{R}_0$ for $1 \leq i \leq n$, a contradiction. Hence $\mathcal{R}_0'(d_I) < 0$ for $d_I \in (0,\infty)$. □

Before stating the general result on the strict monotonicity of $\mathcal{R}_0$ with respect to d_I in case of asymmetric L, we introduce a lemma on the spectral bound of a class of essentially nonnegative matrices.

Lemma 2.2 (Theorem 1 in Altenberg [4], Theorem 1.1 in Altenberg [5], and Theorem 5.2 in Karlin [21])**.** *Let P be an irreducible stochastic matrix* (*i.e., nonnegative and each column summing to one*)*, and let D be a positive diagonal matrix that is not a scalar multiple of identity matrix $\mathbb{I}_n$ of order $n \geq 2$. Put*

$$M(\alpha) = (1-\alpha)\mathbb{I}_n + \alpha P.$$

Then for $\alpha > 0$, the spectral bound $s(M(\alpha)D)$ has the following properties:

(a) $\frac{d}{d\alpha} s(M(\alpha)D) < 0$. *Thus $s(M(\alpha)D)$ decreases strictly as α increases.*

(b) *$s(M(\alpha)D)$ is strictly convex in α. Thus $\frac{d^2}{d\alpha^2} s(M(\alpha)D) \geq 0$.*

Proof. By the implicit function theorem, $s(M(\alpha)D)$, the spectral bound of the essentially nonnegative matrix $M(\alpha)D$, is twice differentiable with respect to $\alpha \in (0,\infty)$. Part (a) comes from the proof of Theorem 2 of Altenberg [3], which uses the results of Friedland and Karlin [13], Friedland [14], and Karlin [21].

Part (b) comes from the proof of Karlin's Theorem 5.2 by Altenberg [4]. For the convenience of readers, let us outline the argument. Note that

$$M(\alpha)D = (\alpha(P-\mathbb{I}_n) + \mathbb{I}_n)D = \alpha(P-\mathbb{I}_n)D + \beta D = \alpha A + \beta D,$$

where $A := (P-\mathbb{I}_n)D$ is an essentially nonnegative matrix and $\beta = 1$. Now let β vary in the interval $[0,+\infty)$. By Theorem 4.1 of Friedland [14] (which strengthens the work of Cohen [8]), the spectral bound $s(\alpha A + \beta D)$ is strictly convex in D and hence in β as well. Then by Lemma 1 on dual convexity in Altenberg [4], we have that $s(\alpha A + \beta D)$ is strictly convex in α, which also implies that $s(\alpha A + \beta D)$ is strictly decreasing in α. $\square$

Next we remove the restriction on the symmetry of the connectivity matrix L. The basic reproduction number $\mathcal{R}_0$ for model (1.1) is found to be not only strictly decreasing but also strictly convex in $d_I \in [0,\infty)$.

Theorem 2.3. *For model* (1.1)*, the basic reproduction number $\mathcal{R}_0$ is strictly decreasing and strictly convex in $d_I \in [0,\infty)$. Moreover, $\mathcal{R}_0'(d_I) < 0$ and $\mathcal{R}_0''(d_I) > 0$ for $d_I \in (0,\infty)$.*

Proof. Denote $\tilde{D} = DF^{-1}$, $\tilde{L} = LF^{-1}$, and $\tilde{V} = \tilde{D} - d_I\tilde{L}$. By the Perron–Frobenius theorem [19], there is a real vector $\boldsymbol{v} \gg 0$ such that

$$FV^{-1}\boldsymbol{v} = (DF^{-1} - d_I LF^{-1})^{-1}\boldsymbol{v} = \tilde{V}^{-1}\boldsymbol{v} = \mathcal{R}_0\boldsymbol{v},$$

which implies that

$$\frac{1}{\mathcal{R}_0}\boldsymbol{v} = \tilde{V}\boldsymbol{v},$$

or equivalently,

$$(k\mathbb{I}_n - \tilde{V})\boldsymbol{v} = \left(k - \frac{1}{\mathcal{R}_0}\right)\boldsymbol{v} \quad \text{for } k \in \mathbb{R}.$$

Clearly, the square matrix

$$k\mathbb{I}_n - \tilde{V} = (k\mathbb{I}_n - \tilde{D}) + d_I\tilde{L} = (k\mathbb{I}_n - DF^{-1}) + d_I LF^{-1}$$

is nonnegative and irreducible for sufficiently large k. Thus

$$\rho(d_I) := \rho(k\mathbb{I}_n - \tilde{D} + d_I\tilde{L}) = k - \frac{1}{\mathcal{R}_0(d_I)},$$

or equivalently,

$$\mathcal{R}_0(d_I) = \frac{1}{k - \rho(d_I)}.$$

Therefore, the first and second derivatives of $\mathcal{R}_0$ with respect to d_I are, respectively,

$$\mathcal{R}_0'(d_I) = \frac{\rho'(d_I)}{(k - \rho(d_I))^2} \tag{2.3}$$

and

$$\mathcal{R}_0''(d_I) = \frac{(k - \rho(d_I))\rho''(d_I) + 2(\rho'(d_I))^2}{(k - \rho(d_I))^3}. \tag{2.4}$$

Choose k large enough so that all the diagonal entries of

$$\hat{D} := k\mathbb{I}_n - \tilde{D}$$

are positive and the matrix

$$\hat{P} := \mathbb{I}_n + \tilde{L}\hat{D}^{-1}$$

is irreducible and stochastic. Note that $\hat{D}$ is not a scalar multiple of the identity matrix $\mathbb{I}_n$ due to assumption (B2). By Lemma 2.2, letting $\hat{M}(d_I) = (1-d_I)\mathbb{I}_n + d_I\hat{P}$, the spectral radius

$$\rho(d_I) = \rho(k\mathbb{I}_n - \tilde{D} + d_I\tilde{L}) = \rho(\hat{D} + d_I(\hat{P} - \mathbb{I}_n)\hat{D}) = s((\mathbb{I}_n + d_I(\hat{P} - \mathbb{I}_n))\hat{D}) = s(\hat{M}(d_I)\hat{D})$$

satisfies $\rho'(d_I) < 0$ and $\rho''(d_I) \geq 0$. It follows from (2.3) and (2.4) that $\mathcal{R}_0'(d_I) < 0$ and $\mathcal{R}_0''(d_I) > 0$. Therefore, the strict monotonicity and strict convexity of $\mathcal{R}_0(d_I)$ follow. $\square$

Biologically, fast diffusion of the infected subpopulation decreases the disease transmission potential. The negativity of $\mathcal{R}_0'(d_I)$ and the positivity of $\mathcal{R}_0''(d_I)$ mean that $\mathcal{R}_0$ is monotone decreasing but has a positive acceleration. So the impact of increasing infected human diffusion on reducing the infection risk keeps shrinking. In particular, the fastest declining speed for $\mathcal{R}_0$ is achieved at $d_I = 0$. Suppose that $\mathcal{R}_0^{(1)} \leq \mathcal{R}_0^{(2)} \leq \cdots \leq \mathcal{R}_0^{(n-1)} < \mathcal{R}_0^{(n)}$; then

$$\mathcal{R}_0'(0) = \lim_{d_I \to 0} \mathcal{R}_0'(d_I) = \frac{\beta_n}{\gamma_n^2} L_{nn} < 0. \tag{2.5}$$

Indeed, let $A(d_I) = k\mathbb{I}_n - \tilde{D} + d_I\tilde{L}$; when $d_I = 0$, the right and left eigenvectors corresponding to the largest eigenvalue $k - 1/\mathcal{R}_0(0)$ of matrix $A(0) = k\mathbb{I}_n - \tilde{D}$ are, respectively,

$$\boldsymbol{x}(0) := (0, \ldots, 0, 1)^T \quad \text{and} \quad \boldsymbol{y}^T(0) := (0, \ldots, 0, 1).$$

By our assumption, the largest eigenvalue is not repeated; then $\rho(0) = k - 1/\mathcal{R}_0^{(n)}$ and

$$\left.\frac{d\rho}{dd_I}\right|_{d_I=0} = \boldsymbol{y}^T(0) \left.\frac{dA(d_I)}{dd_I}\right|_{d_I=0} \boldsymbol{x}(0) = \boldsymbol{y}^T(0)\tilde{L}\boldsymbol{x}(0) = \frac{L_{nn}}{\beta_n}.$$

Substituting the above results into (2.3) gives (2.5).

3. Applications

We will demonstrate some simple applications of the approach and results obtained in the previous section to the SIS epidemic patch model (1.1).

3.1. Asymptotic behavior of $\mathcal{R}_0$ and $s(F-V)$.

Lemma 3.1. *Let* $L = (L_{ij})$ *be an* $n \times n$ *matrix with zero column sums and let* $L^* = (L^*_{ij})^T$ *be the adjoint matrix of* L *with* L^*_{ij} *representing the* (i,j) *cofactor of* L*. Then*

(a) $L^*_{ij} = L^*_{jj}$ *for* $1 \le i,j \le n$*. In particular, if* L *is symmetric, then* $L^*_{ij} = L^*_{11}$ *for* $1 \le i,j \le n$*.*

(b) $(L^*_{11}, \ldots, L^*_{nn})^T$ *is either zero or a right eigenvector of* L *associated with the zero eigenvalue. In addition, if* L *is essentially nonnegative and irreducible, then the vector* $(-1)^{n-1}(L^*_{11}, \ldots, L^*_{nn})^T$ *is strictly positive.*

Proof. (a) For any $i \ne j$ and $1 \le i,j \le n$, we have

$$L^*_{ij} - L^*_{jj} = \begin{vmatrix} L_{11} & \cdots & L_{1j-1} & 0 & L_{1j+1} & \cdots & L_{1n} \\ \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ L_{i-11} & \cdots & L_{i-1j-1} & 0 & L_{i-1j+1} & \cdots & L_{i-1n} \\ L_{i1} & \cdots & L_{ij-1} & 1 & L_{ij+1} & \cdots & L_{in} \\ L_{i+11} & \cdots & L_{i+1j-1} & 0 & L_{i+1j+1} & \cdots & L_{i+1n} \\ \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ L_{j-11} & \cdots & L_{j-1j-1} & 0 & L_{j-1j+1} & \cdots & L_{j-1n} \\ L_{j1} & \cdots & L_{jj-1} & -1 & L_{jj+1} & \cdots & L_{jn} \\ L_{j+11} & \cdots & L_{j+1j-1} & 0 & L_{j+1j+1} & \cdots & L_{j+1n} \\ \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ L_{n1} & \cdots & L_{nj-1} & 0 & L_{nj+1} & \cdots & L_{nn} \end{vmatrix} = 0$$

due to the zero column sums of the associated matrix. If L is symmetric, so is L^*. Hence $L^*_{ij} = L^*_{1j} = L^*_{j1} = L^*_{11}$ for $1 \le i,j \le n$.

(b) It follows from $LL^* = (\det L)\mathbb{I}_n = 0_{n\times n}$ that the (i,j) entry of LL^* satisfies

$$\sum_{k\in\Omega} L_{ik}L^*_{jk} = \sum_{k\in\Omega} L_{ik}L^*_{kk} = 0 \Rightarrow L(L^*_{11}, \ldots, L^*_{nn})^T = \mathbf{0}.$$

If in addition, L is essentially nonnegative and irreducible, then $L_{kk} < 0$ for $k = 1, \ldots, n$ and L^*_{ii} is the determinant of a diagonally dominant matrix, denoted by $\tilde{L}_{ii}$.

(i) If $\tilde{L}_{ii}$ is irreducible, by Corollary 6.2.27 in Horn and Johnson [19], every eigenvalue of matrix $-\tilde{L}_{ii}$ has positive real part and hence $(-1)^{n-1}L^*_{ii} = (-1)^{n-1}\det\tilde{L}_{ii} = \det(-\tilde{L}_{ii}) > 0$.

(ii) If $\tilde{L}_{ii}$ is reducible, then $\tilde{L}_{ii}$ is similar via a permutation to a block upper triangular matrix where each diagonal block is either a single negative entry or an irreducibly diagonally dominant submatrix. The result is obtained by again applying Corollary 6.2.27 in Horn and Johnson [19] to each diagonal block. □

Lemma 3.2. *Let* $D = \operatorname{diag}\{\gamma_1, \ldots, \gamma_n\}$ *be a positive diagonal matrix and let* L *be an essentially nonnegative and irreducible matrix with zero column sums. As* $d_I \to \infty$*, the inverse of* $V = D - d_I L$ *converges to a strictly positive rank-one matrix*

$$V^{-1}_\infty := \lim_{d_I\to\infty} V^{-1} = \frac{1}{\sum\limits_{i\in\Omega} \gamma_i L^*_{ii}} L^*,$$

where $L^* = (L^*_{ij})^T$ *is the adjoint matrix of* L*.*

Proof. Since V is a strictly diagonally dominant and irreducible M-matrix, the inverse of V exists and it is positive. Obviously,

$$V^{-1} = \frac{1}{\det V} V^*,$$

where $V^* = (V_{ij}^*)^T$ is the adjoint matrix of V with V_{ij}^* representing the (i,j) cofactor of V. The determinant of V can be written as

$$\det V = a_n d_I^n + a_{n-1} d_I^{n-1} + \cdots + a_1 d_I + a_0,$$

where $a_n = (-1)^n \det L = 0$ and $a_{n-1} = \sum_{i\in\Omega} \gamma_i (-1)^{n-1} L_{ii}^* = (-1)^{n-1} \sum_{i\in\Omega} \gamma_i L_{ii}^* > 0$. The positivity of a_{n-1} comes from Lemma 3.1(b). Meanwhile, the (i,j) cofactor of V can be written as

$$V_{ij}^* = b_{n-1} d_I^{n-1} + \cdots + b_1 d_I + b_0 > 0,$$

where $b_{n-1} = (-1)^{n-1} L_{ij}^* = (-1)^{n-1} L_{jj}^* > 0$. Thus, the (j,i) entry of V_∞^{-1} is

$$\lim_{d_I\to\infty} \frac{V_{ij}^*}{\det V} = \lim_{d_I\to\infty} \frac{b_{n-1} d_I^{n-1} + \cdots + b_1 d_I + b_0}{a_{n-1} d_I^{n-1} + \cdots + a_1 d_I + a_0} = \frac{b_{n-1}}{a_{n-1}} = L_{ij}^* \Bigg/ \sum_{i\in\Omega} \gamma_i L_{ii}^* .$$

The proof is complete. ☐

Next, we improve some known results on the bounds of the basic reproduction number and the spectral bound of the Jacobian matrix associated with model (1.1).

Theorem 3.3. *For model* (1.1) *with* $d_I \in (0,\infty)$*, the basic reproduction number* $\mathcal{R}_0$ *satisfies*

$$\begin{aligned}\min_{i\in\Omega} \mathcal{R}_0^{(i)} < \mathcal{R}_0(\infty) = \sum_{i\in\Omega} \beta_i L_{ii}^* \Bigg/ \sum_{i\in\Omega} \gamma_i L_{ii}^* \\ < \mathcal{R}_0(d_I) = \rho(FV^{-1}) < \mathcal{R}_0(0) = \max_{i\in\Omega} \mathcal{R}_0^{(i)},\end{aligned}$$

where $\mathcal{R}_0^{(i)} = \beta_i/\gamma_i$ *and* $L^* = (L_{ij}^*)^T$ *is the adjoint matrix of* L.

Proof. The result that the multipatch reproduction number $\mathcal{R}_0$ is between the minimum and maximum patch reproduction numbers was proved by Gao and Ruan [16]. Indeed, this can be established by multiplying both sides of (2.1) by $\mathbf{1} = \{1,\ldots,1\}$, i.e.,

$$\mathbf{1}(FD^{-1} - \mathcal{R}_0 \mathbb{I}_n) D\boldsymbol{v} = 0,$$

where $FD^{-1} - \mathcal{R}_0\mathbb{I}_n = \operatorname{diag}\{\mathcal{R}_0^{(1)} - \mathcal{R}_0, \ldots, \mathcal{R}_0^{(n)} - \mathcal{R}_0\}$ and $D\boldsymbol{v} \gg \mathbf{0}$.

Next it suffices to consider

$$\begin{aligned}\mathcal{R}_0(\infty) := \lim_{d_I\to\infty} \mathcal{R}_0(d_I) = \lim_{d_I\to\infty} \rho(FV^{-1}) &= \rho\Big(\lim_{d_I\to\infty}(FV^{-1})\Big) \\ &= \rho\Big(F \lim_{d_I\to\infty} V^{-1}\Big) = \rho(FV_\infty^{-1}).\end{aligned}$$

The positive matrix FV_∞^{-1} satisfies

$$\mathbf{1}FV_\infty^{-1} = (\beta_1,\ldots,\beta_n)V_\infty^{-1} = \frac{1}{\sum\limits_{i\in\Omega} \gamma_i L_{ii}^*} (\beta_1,\ldots,\beta_n) L^* = \frac{\sum\limits_{i\in\Omega} \beta_i L_{ii}^*}{\sum\limits_{i\in\Omega} \gamma_i L_{ii}^*} \mathbf{1}.$$

The proof is complete via the Perron–Frobenius theorem and the strict monotonicity of $\mathcal{R}_0$ with respect to d_I. ☐

The distribution of infected individuals among patches as $d_I \to \infty$ is proportional to the positive eigenvector $(-1)^{n-1}(L_{11}^*, \dots, L_{nn}^*)^T$ of the connectivity matrix L. The larger lower bound of $\mathcal{R}_0(d_I)$ is actually the ratio of the average transmission rate $\sum_\beta := (-1)^{n-1}\sum_{i\in\Omega}\beta_i L_{ii}^*$ to the average recovery rate $\sum_\gamma := (-1)^{n-1}\sum_{i\in\Omega}\gamma_i L_{ii}^*$. Similar to Allen et al. [1], we call a patchy environment Ω a *low-risk domain* if

$$\sum\nolimits_\beta < \sum\nolimits_\gamma,$$

but a *high-risk domain* if

$$\sum\nolimits_\beta \geq \sum\nolimits_\gamma.$$

Using Theorems 2.3 and 3.3, we can easily obtain a generalization of Theorem 1 in Allen et al. [1] as follows.

Corollary 3.4. *For model* (1.1), *suppose that* $\mathcal{R}_0(0) = \max_{i\in\Omega}\mathcal{R}_0^{(i)} > 1$. *The following hold:*

(a) *In a low-risk domain, there exists a unique threshold value* $d_I^* \in (0,\infty)$ *determined by the polynomial equation* $\det(F-V) = \det(F-D+d_IL) = 0$ *such that* $\mathcal{R}_0 > 1$ *for* $d_I < d_I^*$ *and* $\mathcal{R}_0 < 1$ *for* $d_I > d_I^*$.

(b) *In a high-risk domain, we have* $\mathcal{R}_0 > 1$ *for all* $d_I \geq 0$.

With respect to the spectral bound of $F - V$, the following is a generalization of Lemma 3.4 in Allen et al. [1].

Corollary 3.5. *The spectral bound of the Jacobian matrix of model system* (1.1) *at the disease-free equilibrium,* $\lambda^* := s(F-V)$, *satisfies*

(a) λ^* *is strictly decreasing and strictly convex in* $d_I \in [0,\infty)$.

(b) $\lambda^* \to \max_{i\in\Omega}(\beta_i - \gamma_i)$ *as* $d_I \to 0$.

(c) $\lambda^* \to \sum_{i\in\Omega}(\beta_i-\gamma_i)L_{ii}^* / \sum_{i\in\Omega}L_{ii}^*$ *as* $d_I \to \infty$.

(d) *In a low-risk domain, if* $\mathcal{R}_0(0) = \max_{i\in\Omega}\mathcal{R}_0^{(i)} > 1$, *then there exists a unique* $d_I^* \in (0,\infty)$ *determined by the polynomial equation* $\det(F-V) = \det(F-D+d_IL) = 0$ *such that* $\lambda^* > 0$ *for* $d_I < d_I^*$ *and* $\lambda^* < 0$ *for* $d_I > d_I^*$.

(e) *In a high-risk domain, we have* $\lambda^* > 0$ *for all* $d_I \geq 0$.

Proof. Note that (b) is obvious, while (d) and (e) follow immediately from (a) and (c). Let us show the remaining two parts.

(a) Choose k large enough so that all the diagonal entries of $\hat{D} := k\mathbb{I}_n + F - D$ are positive and that $\hat{P} := \mathbb{I}_n + L\hat{D}^{-1}$ is an irreducible stochastic matrix. Recall that $V = D - d_IL$. For any $d_I \geq 0$, applying Lemma 2.2 to the nonnegative and irreducible matrix

$$k\mathbb{I}_n + F - V = (k\mathbb{I}_n + F - D) + d_IL = \hat{D} + d_I(\hat{P} - \mathbb{I}_n)\hat{D} = \Big((1-d_I)\mathbb{I}_n + d_I\hat{P}\Big)\hat{D}$$

gives that

$$\rho(d_I) := \rho(k\mathbb{I}_n + F - V) = s(k\mathbb{I}_n + F - V) = k + s(F-V)$$

is strictly decreasing in d_I. It follows that λ^* strictly decreases as d_I increases.

(c) For sufficiently large k, there exists a real column vector $\boldsymbol{x} := \boldsymbol{x}(d_I) \gg 0$ satisfying $x_1 + \cdots + x_n = 1$ such that

$$(k\mathbb{I}_n + F - V)\boldsymbol{x} = ((k\mathbb{I}_n + F - D) + d_IL)\boldsymbol{x} = \rho(d_I)\boldsymbol{x} = (k + s(F-V))\boldsymbol{x},$$

or equivalently,

$$(((p-k)\mathbb{I}_n - F + D) - d_I L)\boldsymbol{x} = (p-k-s(F-V))\boldsymbol{x}, \forall\, p \in \mathbb{R}.$$

Denote $\tilde{V} = ((p-k)\mathbb{I}_n - F + D) - d_I L$. For sufficiently large p such that $(p-k)\mathbb{I}_n - F + D$ is a positive diagonal matrix, then

$$\tilde{V}^{-1}\boldsymbol{x} = \frac{1}{p-k-s(F-V)}\boldsymbol{x}. \tag{3.1}$$

The boundedness of $\boldsymbol{x}$ guarantees that we can pick up a sequence $\{d_l\}$ satisfying $0 < d_1 < \cdots < d_l < \cdots$ and $\lim_{l\to\infty} d_l = \infty$ such that $\boldsymbol{x}(\infty) := \lim_{l\to\infty} \boldsymbol{x}(d_l)$ exists. By taking $l \to \infty$, the equation (3.1) gives

$$\tilde{V}_\infty^{-1}\boldsymbol{x}(\infty) = \frac{1}{p-k-s_\infty}\boldsymbol{x}(\infty),$$

which implies $s_\infty := \lim_{l\to\infty} s(F-V) = \lim_{l\to\infty} s(F-D+d_l L)$ exists. It follows that

$$\mathbf{1}\tilde{V}_\infty^{-1}\boldsymbol{x}(\infty) = \frac{1}{p-k-s_\infty}\mathbf{1}\boldsymbol{x}(\infty),$$

that is,

$$\frac{\sum\limits_{i\in\Omega} L^*_{ii}}{\sum\limits_{i\in\Omega}(p-k-\beta_i+\gamma_i)L^*_{ii}} \sum_{i\in\Omega} x_i(\infty) = \frac{1}{p-k-s_\infty}\sum_{i\in\Omega} x_i(\infty).$$

The proof is complete by solving s_∞. □

3.2. **Limiting endemic equilibrium.** When $\mathcal{R}_0 > 1$, the model (1.1) has at least one endemic equilibrium, denoted by

$$E^* := (\boldsymbol{S}^*, \boldsymbol{I}^*) = (S_1^*, \dots, S_n^*, I_1^*, \dots, I_n^*),$$

which is a positive solution to

$$d_S \sum_{j\in\Omega} L_{ij}S_j^* - \beta_i \frac{S_i^* I_i^*}{S_i^* + I_i^*} + \gamma_i I_i^* = 0,\ i \in \Omega, \tag{3.2a}$$

$$d_I \sum_{j\in\Omega} L_{ij}I_j^* + \beta_i \frac{S_i^* I_i^*}{S_i^* + I_i^*} - \gamma_i I_i^* = 0,\ i \in \Omega. \tag{3.2b}$$

Previously, Allen et al. [1] and Li and Peng [23] studied the asymptotic behavior of the endemic equilibrium as $d_S \to 0$ and $d_I \to 0$, respectively. We will study the case of $d_I \to \infty$. Allen et al. [2] and Peng [25] considered similar problems for an SIS reaction-diffusion model.

Theorem 3.6. *For model* (1.1)*, assume* $\mathcal{R}_0(\infty) := \lim_{d_I\to\infty} \mathcal{R}_0(d_I) = \rho(FV_\infty^{-1}) > 1$ (*i.e., a high-risk domain*)*. Then the endemic equilibrium of model* (1.1) *satisfies*

$$E^* \to m(\hat{S}_1, \dots, \hat{S}_n, |L^*_{11}|, \dots, |L^*_{nn}|) \gg \mathbf{0} \quad \text{as} \quad d_I \to \infty,$$

where $(\hat{S}_1, \dots, \hat{S}_n)$ *is the unique positive solution to*

$$d_S \sum_{j\in\Omega} L_{ij}\hat{S}_j - \beta_i \frac{|L^*_{ii}|}{\hat{S}_i + |L^*_{ii}|}\hat{S}_i + \gamma_i |L^*_{ii}| = 0,\ i \in \Omega,$$

and

$$m = \frac{\sum_{i\in\Omega}(S_i(0) + I_i(0))}{\sum_{i\in\Omega}(\hat{S}_i + |L^*_{ii}|)}.$$

Proof. It is clear that each entry of the endemic equilibrium E^* is bounded for any $d_I > 0$. So, we have (up to a sequence of d_I)

$$E^* \to \tilde{E} := (\tilde{\boldsymbol{S}}, \tilde{\boldsymbol{I}}) = (\tilde{S}_1, \ldots, \tilde{S}_n, \tilde{I}_1, \ldots, \tilde{I}_n) \geq \mathbf{0} \quad \text{as } d_I \to \infty.$$

Following equation (3.2b) and the irreducibility of L, we know either $\tilde{\boldsymbol{I}} = \mathbf{0}$ or $\tilde{\boldsymbol{I}} \gg \mathbf{0}$.

Suppose $\tilde{\boldsymbol{I}} = \mathbf{0}$; then the equation (3.2a) indicates that $\tilde{\boldsymbol{S}} = \boldsymbol{S}^0$ and hence $E^* \to \tilde{E} = E_0$ as $d_I \to \infty$. It follows from $\mathcal{R}_0(\infty) = \lim_{d_I \to \infty} \mathcal{R}_0(d_I) > 1$ and Corollary 3.5 that $\lambda^*(\infty) = \lim_{d_I \to \infty} \lambda^*(d_I) > 0$. By choosing $\varepsilon \in (0, \lambda^*(\infty))$, there is a $\tilde{d}_I > 0$ so that

$$\beta_i(1 - S_i^*/(S_i^* + I_i^*)) < \varepsilon, \ i \in \Omega$$

for $d_I > \tilde{d}_I$. Denote $F^* = \operatorname{diag}\{\beta_1 S_1^*/(S_1^* + I_1^*), \ldots, \beta_n S_n^*/(S_n^* + I_n^*)\}$. The equation (3.2b) can be rewritten in a matrix form

$$(F^* - V)(\boldsymbol{I}^*)^T = \mathbf{0},$$

which implies

$$s(F^* - V) = 0.$$

On the other hand, for $d_I > \tilde{d}_I$, it follows from

$$F^* - V > \operatorname{diag}\{\beta_1 - \varepsilon, \ldots, \beta_n - \varepsilon\} - V = F - V - \varepsilon \mathbb{I}_n$$

that

$$s(F^* - V) > s(F - V) - \varepsilon = \lambda^*(d_I) - \varepsilon \ \geq \ \lambda^*(\infty) - \varepsilon > 0,$$

which results in a contradiction. This means that $\tilde{\boldsymbol{I}} \gg \mathbf{0}$.

The boundedness of

$$\beta_i \frac{\tilde{I}_i}{\tilde{S}_i + \tilde{I}_i} \tilde{S}_i - \gamma_i \tilde{I}_i, \ i \in \Omega,$$

implies

$$\sum_{j \in \Omega} L_{ij} \tilde{I}_j = 0, \ i \in \Omega.$$

Hence, the limiting endemic equilibrium $\tilde{E}$ is a solution of the system of $2n+1$ equations

$$d_S \sum_{j \in \Omega} L_{ij} \tilde{S}_j - \beta_i \frac{\tilde{I}_i}{\tilde{S}_i + \tilde{I}_i} \tilde{S}_i + \gamma_i \tilde{I}_i = 0, \ i \in \Omega, \tag{3.3a}$$

$$\sum_{j \in \Omega} L_{ij} \tilde{I}_j = 0, \ i \in \Omega, \tag{3.3b}$$

$$\sum_{i \in \Omega} (\tilde{S}_i + \tilde{I}_i) = \sum_{i \in \Omega} (S_i(0) + I_i(0)). \tag{3.3c}$$

By Lemma 3.1, solving (3.3b) gives

$$(\tilde{I}_1, \ldots, \tilde{I}_n) = m(-1)^{n-1}(L_{11}^*, \ldots, L_{nn}^*) = m(|L_{11}^*|, \ldots, |L_{nn}^*|), \ m > 0,$$

and substituting it into (3.3a) and (3.3c) yields

$$d_S \sum_{j \in \Omega} L_{ij} \tilde{S}_j - \beta_i \frac{m|L_{ii}^*|}{\tilde{S}_i + m|L_{ii}^*|} \tilde{S}_i + \gamma_i m |L_{ii}^*| = 0, \ i \in \Omega, \tag{3.4}$$

and

$$m = \frac{\sum_{i\in\Omega}(S_i(0)+I_i(0)) - \sum_{i\in\Omega}\tilde{S}_i}{\sum_{i\in\Omega}|L^*_{ii}|},$$

respectively. Denote $\hat{S}_i = \tilde{S}_i/m$ for $i \in \Omega$. The equation (3.4) can be rewritten as

$$d_S \sum_{j\in\Omega} L_{ij}\hat{S}_j - \beta_i \frac{|L^*_{ii}|}{\hat{S}_i + |L^*_{ii}|}\hat{S}_i + \gamma_i |L^*_{ii}| = 0, \; i \in \Omega. \tag{3.5}$$

Consider the following auxiliary system:

$$\frac{d\hat{S}_i}{dt} = d_S \sum_{j\in\Omega} L_{ij}\hat{S}_j - \beta_i \frac{|L^*_{ii}|}{\hat{S}_i + |L^*_{ii}|}\hat{S}_i + \gamma_i |L^*_{ii}|, \; i \in \Omega, \tag{3.6}$$

which is dissipative, cooperative, and irreducible in $\mathbb{R}^n_+$. Let $\hat{\boldsymbol{f}}$ denote the vector field described by (3.6). Following $\hat{\boldsymbol{f}}(\mathbf{0}) \gg \mathbf{0}$ and Theorem 3.2.1 in Smith [28], the solution starting at the origin converges to a positive equilibrium $\omega(\mathbf{0})$. It is easy to check that every positive equilibrium of system (3.6) is locally asymptotically stable by computing the corresponding Jacobian matrix. By the theory of connecting orbits [18], the system (3.6) cannot have more than one positive equilibrium. Furthermore, Theorem C in Jiang [20] implies that the unique positive equilibrium $\omega(\mathbf{0})$ is globally asymptotically stable in $\mathbb{R}^n_+$.

Once the equation (3.5) is solved, we can then obtain

$$\tilde{S}_i = m\hat{S}_i \quad \text{and} \quad \tilde{I}_i = m|L^*_{ii}|, \; i \in \Omega,$$

where

$$m = \frac{\sum_{i\in\Omega}(S_i(0)+I_i(0))}{\sum_{i\in\Omega}(\hat{S}_i + |L^*_{ii}|)}.$$

The existence of a unique positive solution to (3.5) implies the convergence of the endemic equilibrium E^* as $d_I \to \infty$. □

An easy way to calculate $\sum_{i\in\Omega}\beta_i L^*_{ii}$, $\sum_{i\in\Omega}\gamma_i L^*_{ii}$, and $\sum_{i\in\Omega} L^*_{ii}$ is through the Laplace expansion

$$\begin{vmatrix} x_1 & x_2 & \cdots & x_n \\ L_{21} & L_{22} & \cdots & L_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ L_{n1} & L_{n2} & \cdots & L_{nn} \end{vmatrix} = \sum_{i\in\Omega} x_i L^*_{ii},$$

by setting $x_i = \beta_i, \gamma_i$ and 1 for $i \in \Omega$, respectively. The above-mentioned analysis can be adopted to some other epidemic patch models in studying the monotonicity, convexity, and asymptotic properties of the basic reproduction number and the spectral bound which serve as threshold quantities between disease persistence and extinction [6, 16, 24, 30].

4. DISCUSSION

It is clear that for SIS epidemic reaction-diffusion models the basic reproduction number is a monotone decreasing function of the diffusion coefficient for the infected population (e.g., Allen et al. [2], Deng and Wu [11], Li et al. [22]). However, the dependence of $\mathcal{R}_0$ on d_I for SIS epidemic patch models was generally unknown [1, 15]. In this paper, by applying some recent advances in the spectral theory of linear operators [3, 4], we show that $\mathcal{R}_0$ for the SIS epidemic patch model remains strictly decreasing in d_I regardless of the symmetry of the connectivity matrix. Moreover, the first and second derivatives of $\mathcal{R}_0$ with respect to d_I are strictly negative and strictly positive for all $d_I > 0$, respectively. Based on the approach and results, an improved and reachable lower bound of $\mathcal{R}_0$, a generalized monotone result on the spectral bound of $F - V$, and the limiting endemic equilibrium as $d_I \to \infty$ are obtained.

The present work is applicable to epidemic patch models in which exactly one class of infected compartments migrate between patches and one transmission route is involved. In other words, the next generation matrix can be written in the form of $FV^{-1} = F(D - d_I L)^{-1}$ where F and D are positive diagonal matrices and L is an essentially nonnegative and irreducible matrix with zero column sums. For example, it works for an SIS patch model with bilinear incidence [32], the SIS patch model with media effect in Gao and Ruan [16], SIR or SIRS patch model [24], SEIRS patch model in the absence of diffusion for infectious subpopulation [27], the multipatch cholera model studied by Tien et al. [30], and a Ross-Macdonald-type malaria model with human movement analyzed by Auger et al. [6], Cosner et al. [9], and Gao et al. [17]. These suggest that diffusion can help accelerate the elimination of infectious diseases. Additionally, it can be used to study population persistencce in a patchy environment (e.g., the single-species multipatch logistic model).

The asymmetric movement in patch models can be viewed as advection-diffusion in reaction-diffusion models, so it is not surprising that the basic reproduction number of the SIS model of reaction-diffusion-advection-type considered by Cui and Lou [10] is also monotone decreasing in the diffusion coefficient for the infected population d_I if the advection rate is proportional to d_I. It is worth mentioning that based on a cholera model Tien et al. [30] derived the limit of $\mathcal{R}_0(d_I)$ as $d_I \to \infty$ and found that the difference of $\mathcal{R}_0(d_I)$ and its limit is an infinitesimal of the same order as $1/d_I$ through a Laurent series expansion. The strict monotonicity of $\mathcal{R}_0$ with respect to d_I may fail when the SIS patch model (1.1) is extended to a multigroup-multipatch model (Example 4.3 in Gao [15]), an SEIRS reaction-diffusion model [29], an SIS reaction-diffusion periodic model (Theorem 2.5e in Peng and Zhao [26]), a periodic patch model (it is easy to find a counterexample by using the constructive method in Peng and Zhao [26]), or a reaction-diffusion model with advection (Theorem 1.4 in Cui and Lou [10]). Generally speaking, the influence of diffusion on disease persistence is strongly affected by model structures and model formulations and further investigations are required.

Acknowledgments

We sincerely thank Drs. Lee Altenberg, Jifa Jiang, Yuan Lou, and Gilbert Strang for their valuable discussions and comments. We are also grateful to the editor and the referee for their time and help.

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