Mathematical Biology

Habitat fragmentation promotes malaria persistence

Daozhou Gao[1] (ORCID) **· P. van den Driessche[2] · Chris Cosner[3]** (ORCID)

Abstract

Based on a Ross–Macdonald type model with a number of identical patches, we study the role of the movement of humans and/or mosquitoes on the persistence of malaria and many other vector-borne diseases. By using a theorem on line-sum symmetric matrices, we establish an eigenvalue inequality on the product of a class of nonnegative matrices and then apply it to prove that the basic reproduction number of the multipatch model is always greater than or equal to that of the single patch model. Biologically, this means that habitat fragmentation or patchiness promotes disease outbreaks and intensifies disease persistence. The risk of infection is minimized when the distribution of mosquitoes is proportional to that of humans. Numerical examples for the two-patch submodel are given to investigate how the multipatch reproduction number varies with human and/or mosquito movement. The reproduction number can surpass any given value whenever an appropriate travel pattern is chosen. Fast human and/or mosquito movement decreases the infection risk, but may increase the total number of infected humans.

Keywords Vector-borne disease · Basic reproduction number · Human movement · Disease persistence · Line-sum symmetric matrix · Habitat fragmentation

✉ Chris Cosner
 gcc@math.miami.edu

 Daozhou Gao
 dzgao@shnu.edu.cn

 P. van den Driessche
 pvdd@uvic.math.ca

[1] Mathematics and Science College, Shanghai Normal University, Shanghai 200234, China

[2] Department of Mathematics and Statistics, University of Victoria, Victoria, BC V8W 2Y2, Canada

[3] Department of Mathematics, University of Miami, Coral Gables, FL 33146, USA

1 Introduction

Vector-borne diseases are illness caused by pathogens, which are transmitted to humans or animals by the bites of infected vectors such as mosquitoes (e.g., malaria, dengue fever, Rift Valley fever, and Zika virus disease), ticks (e.g., Lyme disease and babesiosis), aquatic snails (e.g., schistosomiasis), fleas (e.g., plague), bugs (e.g., Chagas disease), and sandflies (e.g., onchocerciasis). They are responsible for over 17% of the estimated global burden of all infectious diseases (World Health Organization 2017). For example, malaria alone caused an estimated 219 million cases and approximately 435,000 deaths worldwide in 2017, though the mortality rates have reduced by about 60% since 2000 (World Health Organization 2018). Rift Valley fever results in significant economic costs through human morbidity and loss of livestock. The 2015-16 Zika virus outbreak caused up to one million suspected cases and thousands of confirmed microcephaly cases in Brazil (Pan American Health Organization 2017).

Mathematical modeling and analysis of vector-borne diseases, with a long history of development and application, have attracted considerable attention among governmental agencies and institutional researchers (Mandal et al. 2011; Reiner et al. 2013). The original mathematical model for malaria transmission was proposed by Ross (1911) and later extended by Macdonald (1957) in the 1950s. In this seminal work, the malaria transmission cycle is depicted in Fig. 1.

Both humans and mosquitoes are either susceptible or infectious and their respective total population sizes, H and V, are constant. The rates of change of the number of infectious humans and infectious mosquitoes, $h(t)$ and $v(t)$, are described by a system of two ordinary differential equations as follows:
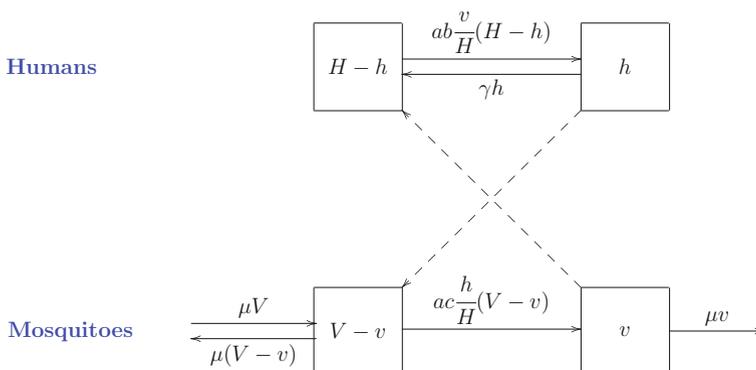

Fig. 1 Flowchart of the Ross–Macdonald model for malaria. The variables and parameters are defined in the text

$$\frac{dh}{dt} = ab\frac{v}{H}(H - h) - \gamma h,$$
$$\frac{dv}{dt} = ac\frac{h}{H}(V - v) - \mu v,$$

(1)

where $H - h$ and $V - v$ are respectively the number of susceptible humans and susceptible mosquitoes, a is the rate of biting on humans by a single mosquito, γ is the rate at which infectious humans recover, μ is the birth rate and the mortality rate of mosquitoes, b and c are the transmission probabilities from an infectious mosquito to a susceptible human and from an infectious human to a susceptible mosquito per bite, respectively. The reader may refer to the paper by Smith and McKenzie (2004) for a detailed derivation and some results on the model.

Obviously the origin is the disease-free equilibrium of the so called Ross–Macdonald model (1). We can use the next generation matrix method (Diekmann et al. 1990; van den Driessche and Watmough 2002) to define a basic reproduction number for the average number of secondary infections produced by a typical infectious individual (human or mosquito) during the entire infectious period provided that everyone else of both populations is susceptible. The disease will disappear if the reproduction number is less than or equal to unity and will eventually stabilize at an endemic equilibrium if the reproduction number is greater than one. The Ross–Macdonald model reflects the essential feature of the malaria transmission process, namely, the transmission from infected mosquitoes to susceptible humans and from infected humans to susceptible mosquitoes. The model and its threshold quantity play a critical role in the World Health Organization's Global Malaria Eradication Programme (1955–1969) (Smith et al. 2012). It is now widely accepted as a solid framework for the study of the transmission dynamics of malaria and many other mosquito-borne or vector-borne diseases like West Nile virus (Bowman et al. 2005; Chen et al. 2016), dengue fever (Abdelrazec et al. 2016; Feng and Velasco-Hernández 1997), yellow fever (Codeço et al. 2007), and Zika (Gao et al. 2016; Kucharski et al. 2016). Interestingly, Ross received a Nobel Prize in Physiology or Medicine for his discovery of the life cycle of the malarial parasite in 1902, but he considered his epidemiological mathematics as his greatest contribution.

Since the Ross–Macdonald model is the earliest and simplest malaria model, it inevitably has some major limitations due to failure to take many ecological and epidemiological factors into account. Over the last few decades, a large number of studies on mathematical models of malaria have been done by adding factors such as superinfection, age structure (children are more susceptible than adults), acquired immunity and vital dynamics in humans, extrinsic incubation period of malaria parasites in mosquitoes (10 days or longer), environmental factors (temperature, humidity and rain are important for the survival of mosquitoes and the development of parasites), treatment and drug resistance, a hypothetical vaccine to the model (Mandal et al. 2011; Reiner et al. 2013; Smith et al. 2012). Among these extensions, a few efforts have been made to incorporate spatial heterogeneity in discrete or continuous space (Arino et al. 2012; Auger et al. 2008; Bai et al. 2018; Cosner et al. 2009; Gao and Ruan 2012; Lou and Zhao 2011). Both observation data and theoretical research suggest that human movement may strengthen the spread and persistence of malaria

around the world (Cosner et al. 2009; Gao and Ruan 2012; Khuu et al. 2017). We refer the readers to two review articles by Cosner (2015) and Gao and Ruan (2014).

In this paper, we will study the effect of human and/or mosquito movement on the persistence of malaria in a fragmented environment with identical patches, i.e., there is no epidemiological or demographic difference among patches in case they are isolated. Such a tough restriction enables us to exclusively focus on the movement itself with no interference from spatial heterogeneities. In the next section, we present a generalized Ross–Macdonald model where population dispersal among identical patches is considered and we summarize the global stability result on it. Section 3 is devoted to the main results and their proofs for comparing the basic reproduction numbers of the single patch model and the multipatch model. Some numerical examples are given in Sect. 4. Finally we discuss the biological meaning of our results, their relevance to other studies, and future research questions.

2 Model Formulation

We begin by formulating a simple multipatch malaria model where the model of each patch in isolation is exactly the same as the Ross–Macdonald model (1) and humans and mosquitoes move between n identical patches. In patch i, let $H_i(t)$ and $V_i(t)$ be the total human and mosquito populations at time t, respectively; $h_i(t)$ and $v_i(t)$ be the numbers of infectious humans and infectious mosquitoes at time t, respectively. Then the multipatch Ross–Macdonald model takes the form

$$
\begin{aligned}
\frac{dH_i}{dt} &= \sum_{j=1}^{n} c_{ij} H_j, \ 1 \le i \le n, \\
\frac{dV_i}{dt} &= \sum_{j=1}^{n} d_{ij} V_j, \ 1 \le i \le n, \\
\frac{dh_i}{dt} &= ab \frac{v_i}{H_i}(H_i - h_i) - \gamma h_i + \sum_{j=1}^{n} c_{ij} h_j, \ 1 \le i \le n, \\
\frac{dv_i}{dt} &= ac \frac{h_i}{H_i}(V_i - v_i) - \mu v_i + \sum_{j=1}^{n} d_{ij} v_j, \ 1 \le i \le n,
\end{aligned}
\tag{2}
$$

with nonnegative initial conditions

$$(H_1(0), \ldots, H_n(0), V_1(0), \ldots, V_n(0), h_1(0), \ldots, h_n(0), v_1(0), \ldots, v_n(0))$$

satisfying $\sum_{i=1}^{n} H_i(0) = H > 0$ and $\sum_{i=1}^{n} V_i(0) = V > 0$.

The parameters $c_{ij} \ge 0$ and $d_{ij} \ge 0$ are the movement rate of humans and mosquitoes from patch j to patch i for $i \ne j$, respectively; $-c_{ii} = \sum_{j=1, j \ne i}^{n} c_{ji}$ and $-d_{ii} = \sum_{j=1, j \ne i}^{n} d_{ji}$ are the emigration rates of humans and mosquitoes in patch i, respectively. Thus the human and mosquito travel rate matrices $C = (c_{ij})_{n \times n}$ and $D = (d_{ij})_{n \times n}$ are Laplacian matrices. Unless otherwise indicated, we assume throughout this paper that C and D are irreducible such that n patches cannot be separated into two disconnected parts. A square matrix is called quasi-positive, Metzler or essentially nonnegative if all its off-diagonal entries are nonnegative. The assumptions

on the signs of c_{ij} and d_{ij} for $i \neq j$ mean that matrices C and D are quasi-positive, and the assumptions on c_{ii} and d_{ii} mean that C and D have zero column sums. The following lemma is part of Corollary 4.3.2 in Smith (1995) and Theorem 6.2.7 in Berman and Plemmons (1979). It guarantees the existence and uniqueness of positive equilibrium for the human and mosquito movement models and the validity of the definition of the multipatch basic reproduction number.

Lemma 1 *Let $C = (c_{ij})_{n \times n}$ be an irreducible quasi-positive matrix satisfying $\sum_{i=1}^{n} c_{ij} = 0$ for $j = 1, \ldots, n$ and $\mathscr{C} = (\delta_{ij} \gamma_i)_{n \times n} - C$ with $\gamma_i > 0$ for $i = 1, \ldots, n$. Here δ_{ij} is the Kronecker delta, i.e., 1 when $i = j$ and 0 otherwise. Then C has a simple positive right eigenvector corresponding to the eigenvalue zero; $\mathscr{C}^{-1}$ exists and is positive.*

The equations for the total human and mosquito populations in model (2) are decoupled from the remaining equations. It follows from Lemma 1 that the model (2) has a unique disease-free equilibrium

$$E_0 = (H_1^*, \ldots, H_n^*, V_1^*, \ldots, V_n^*, 0, \ldots, 0, 0, \ldots, 0),$$

where $(H_1^*, \ldots, H_n^*)$ and $(V_1^*, \ldots, V_n^*)$ are the unique positive solutions to

$$\sum_{j=1}^{n} c_{ij} H_j = 0, \; i = 1, \ldots, n, \; \sum_{i=1}^{n} H_i = \sum_{i=1}^{n} H_i(0) = H,$$

and

$$\sum_{j=1}^{n} d_{ij} V_j = 0, \; i = 1, \ldots, n, \; \sum_{i=1}^{n} V_i = \sum_{i=1}^{n} V_i(0) = V,$$

respectively; see Lemma 1 in Cosner et al. (2009). It is worth noting that $(H_1^*, \ldots, H_n^*)^T$ and $(V_1^*, \ldots, V_n^*)^T$ are respectively the positive right eigenvectors of C and D corresponding to the zero eigenvalue. Indeed, they are respectively a positive multiple of the positive vectors

$$(-1)^{n-1}(C_{11}, \ldots, C_{nn})^T \text{ and } (-1)^{n-1}(D_{11}, \ldots, D_{nn})^T,$$

normalized by the total human and mosquito population sizes, where C_{ii} and D_{ii} denote the (i, i) cofactor of C and D, respectively (Gao and Dong 2019). Explicit expressions for C_{ii} and D_{ii} can be obtained through Kirchhoff's Matrix Tree Theorem (see Moon 1970).

Using the next generation matrix method (Diekmann et al. 1990; van den Driessche and Watmough 2002), the new infection and disease transition matrices of the model (2) are respectively

$$F = \begin{pmatrix} 0 & \mathscr{A} \\ \mathscr{B} & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} \mathscr{C} & 0 \\ 0 & \mathscr{D} \end{pmatrix},$$

where $\mathscr{A} = abI_n$, $\mathscr{B} = ac(\delta_{ij} V_i^*/H_i^*)_{n \times n}$, $\mathscr{C} = \gamma I_n - C$, and $\mathscr{D} = \mu I_n - D$. The $n \times n$ identity matrix is denoted by I_n. It follows from Proposition 2.1 in Iggidr et al. (2016) that the next generation matrix

$$FV^{-1} = \begin{pmatrix} 0 & \mathscr{A}\mathscr{D}^{-1} \\ \mathscr{B}\mathscr{C}^{-1} & 0 \end{pmatrix}$$

is irreducible if and only if $\mathscr{A}\mathscr{D}^{-1}\mathscr{B}\mathscr{C}^{-1}$ and $\mathscr{B}\mathscr{C}^{-1}\mathscr{A}\mathscr{D}^{-1}$ are irreducible. By Lemma 1, the irreducibilities of C and D imply that both $\mathscr{C}^{-1}$ and $\mathscr{D}^{-1}$ exist and are positive. Thus, $\mathscr{A}\mathscr{D}^{-1}\mathscr{B}\mathscr{C}^{-1}$ and $\mathscr{B}\mathscr{C}^{-1}\mathscr{A}\mathscr{D}^{-1}$ are positive and irreducible. The basic reproduction number of the n-patch model (2) is

$$\mathcal{R}_0(n) = \rho(FV^{-1}) = \rho \begin{pmatrix} 0 & \mathscr{A}\mathscr{D}^{-1} \\ \mathscr{B}\mathscr{C}^{-1} & 0 \end{pmatrix} = \sqrt{\rho(\mathscr{A}\mathscr{D}^{-1}\mathscr{B}\mathscr{C}^{-1})}, \qquad (3)$$

where ρ is the spectral radius of a square matrix. In particular, if $n = 1$ then the basic reproduction number of the single patch model (1) is

$$\mathcal{R}_0(1) = \sqrt{\frac{a^2 bcV}{\gamma \mu H}}. \qquad (4)$$

By the theory of monotone dynamical systems (Smith 1995), it is shown that the disease dynamics of system (2) are completely determined by its basic reproduction number even if the model parameters a, b, c, γ and μ are location-dependent.

Theorem 1 (Cosner et al. 2009) *For system (2), if $\mathcal{R}_0(n) \leq 1$ then the disease-free equilibrium, E_0, is globally stable among nonnegative solutions; if $\mathcal{R}_0(n) > 1$ then there is a unique positive equilibrium which is globally stable among positive solutions.*

In order to eradicate malaria, it follows that we need to reduce $\mathcal{R}_0(n)$ to be less than one by implementing suitable control measures such as vector control and insecticide-treated bednets that increase or decrease certain parameter values. Obviously, $\mathcal{R}_0(n)$ is monotone increasing in terms of a, b and c, and monotone decreasing with respect to γ and μ. The classification of the relationship between $\mathcal{R}_0(n)$ and travel rate c_{ij} or d_{ij} is a challenging question. We will investigate the effect of population dispersal or patchiness on disease persistence by comparing the basic reproduction numbers of the single patch model (1) and the n-patch model (2), i.e., $\mathcal{R}_0(1)$ versus $\mathcal{R}_0(n)$.

For model (2) with two identical patches connected by human movement, Gao and Ruan (2014) explicitly solved $\mathcal{R}_0(2)$ and showed that $\mathcal{R}_0(2) \geq \mathcal{R}_0(1)$. This implies that human movement always facilitates malaria transmission in an environment with two identical patches. However, solving $\mathcal{R}_0(n)$ or the spectral radius of the $n \times n$ matrix $\mathscr{A}\mathscr{D}^{-1}\mathscr{B}\mathscr{C}^{-1}$ becomes extremely difficult or even impossible when three or more identical patches are concerned. In what follows, we show that the inequality $\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$ still holds for the multipatch Ross–Macdonald model with an arbitrary number of patches connected by movement of humans, mosquitoes or both.

3 Main results

Before stating the main results and their proofs, we prove a lemma and establish a general result on the spectral radius of a class of nonnegative matrices.

A square matrix $A = (a_{ij})_{n \times n}$ is called *line-sum-symmetric* if for every $1 \leq i \leq n$, the sum of the entries in the ith row of A equals the sum of the entries in the ith column of A, i.e., $\sum_{j=1}^{n} a_{ij} = \sum_{j=1}^{n} a_{ji}$ for $1 \leq i \leq n$. The following result will be used to prove the second lemma below.

Lemma 2 (Eaves et al. 1985) *Let $A = (a_{ij})_{n \times n}$ be an $n \times n$ nonnegative matrix. Then A is line-sum-symmetric if and only if*

$$\sum_{i,j=1}^{n} a_{ij} \frac{x_i}{x_j} \geq \sum_{i,j=1}^{n} a_{ij}$$

for all $x_i > 0$ and $1 \leq i \leq n$. Moreover, if A is irreducible and line-sum-symmetric, equality holds if and only if all the coordinates of $\mathbf{x} = (x_1, \ldots, x_n)$ coincide, i.e., $x_i = x_j$ for any $1 \leq i, j \leq n$.

Lemma 3 *Let $A = (a_{ij})_{n \times n}$ be an irreducible quasi-positive matrix satisfying $\sum_{i=1}^{n} a_{ij} = 0$ for $j = 1, \ldots, n$; $(w_1, \ldots, w_n)^T$ be a right positive eigenvector of A corresponding to the eigenvalue zero; $\bar{w} = \frac{1}{n} \sum_{i=1}^{n} w_i$, the average of $w_1, \ldots, w_n$; $M = \mathrm{diag}\{w_1, \ldots, w_n\}$ and $N = r I_n - A$ with $r > 0$. Assume that $\mathbf{x} = (x_1, \ldots, x_n)^T$ and $\mathbf{y} = (y_1, \ldots, y_n)^T$ are two positive vectors, and λ is a positive constant. The following statements are valid:*

(1) *if $M^{-1} N^{-1} \mathbf{x} = \lambda \mathbf{y}$ then $\lambda \geq \frac{1}{nr\bar{w}} \sum_{i=1}^{n} \frac{x_i}{y_i}$ with equality if and only if*

$$y_1 = \cdots = y_n \quad \text{and} \quad \frac{x_1}{y_1} \frac{1}{w_1} = \cdots = \frac{x_n}{y_n} \frac{1}{w_n} = r\lambda; \tag{5}$$

(2) *if $M N^{-1} \mathbf{x} = \lambda \mathbf{y}$ then $\lambda \geq \frac{1}{nr\bar{w}} \sum_{i=1}^{n} \frac{x_i}{y_i} w_i^2$ with equality if and only if*

$$\frac{y_1}{w_1^2} = \cdots = \frac{y_n}{w_n^2} \quad \text{and} \quad \frac{x_1}{y_1} w_1 = \cdots = \frac{x_n}{y_n} w_n = r\lambda; \tag{6}$$

(3) *if $N^{-1} M^{-1} \mathbf{x} = \lambda \mathbf{y}$ then $\lambda \geq \frac{1}{nr\bar{w}} \sum_{i=1}^{n} \frac{x_i}{y_i}$ with equality if and only if*

$$\frac{y_1}{w_1} = \cdots = \frac{y_n}{w_n} \quad \text{and} \quad \frac{x_1}{y_1} \frac{1}{w_1} = \cdots = \frac{x_n}{y_n} \frac{1}{w_n} = r\lambda; \tag{7}$$

(4) *if* $N^{-1}Mx = \lambda y$ *then* $\lambda \geq \dfrac{1}{nr\bar{w}} \sum\limits_{i=1}^{n} \dfrac{x_i}{y_i} w_i^2$ *with equality if and only if*

$$\frac{y_1}{w_1} = \cdots = \frac{y_n}{w_n} \quad and \quad \frac{x_1}{y_1} w_1 = \cdots = \frac{x_n}{y_n} w_n = r\lambda. \tag{8}$$

Proof The first equation $M^{-1}N^{-1}x = \lambda y$ is equivalent to $-\frac{1}{\lambda}x = -NMy$, or explicitly,

$$-\frac{1}{\lambda}\begin{pmatrix} x_1 \\ \vdots \\ x_n \end{pmatrix} = \left[-r\begin{pmatrix} w_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & w_n \end{pmatrix} + \begin{pmatrix} a_{11}w_1 & \cdots & a_{1n}w_n \\ \vdots & \ddots & \vdots \\ a_{n1}w_1 & \cdots & a_{nn}w_n \end{pmatrix} \right] \begin{pmatrix} y_1 \\ \vdots \\ y_n \end{pmatrix}. \tag{9}$$

Since both the row sums and column sums of $AM = (a_{ij}w_j)_{n \times n}$ are zero, adding kI_n with k sufficiently large to that matrix gives a nonnegative irreducible and line-sum-symmetric matrix. The ith row of (9) can then be written as

$$-\frac{1}{\lambda}x_i + ky_i = -rw_i y_i + \sum_{j=1}^{n}(a_{ij}w_j + \delta_{ij}k)y_j$$

or

$$-\frac{1}{\lambda}\frac{x_i}{y_i} + k + rw_i = \sum_{j=1}^{n}(a_{ij}w_j + \delta_{ij}k)\frac{y_j}{y_i}, \tag{10}$$

for $i = 1, \ldots, n$. It follows from Lemma 2 that summing (10) over i gives

$$-\frac{1}{\lambda}\sum_{i=1}^{n}\frac{x_i}{y_i} + nk + r\sum_{i=1}^{n}w_i = \sum_{i,j=1}^{n}(a_{ij}w_j + \delta_{ij}k)\frac{y_j}{y_i}$$

$$\geq \sum_{i,j=1}^{n}(a_{ij}w_j + \delta_{ij}k) = \sum_{i,j=1}^{n}a_{ij}w_j + \sum_{i,j=1}^{n}\delta_{ij}k = nk.$$

So

$$\lambda \geq \frac{1}{nr\bar{w}}\sum_{i=1}^{n}\frac{x_i}{y_i}$$

with equality if and only if $y_1 = \cdots = y_n$. But then (10) gives

$$-\frac{1}{\lambda}\frac{x_i}{y_i} + k + rw_i = \sum_{j=1}^{n}(a_{ij}w_j + \delta_{ij}k) = k,$$

which is impossible unless

$$\frac{x_1}{y_1}\frac{1}{w_1} = \cdots = \frac{x_n}{y_n}\frac{1}{w_n} = r\lambda. \tag{11}$$

On the other hand, (11) implies that

$$\frac{1}{nr\bar{w}}\sum_{i=1}^n \frac{x_i}{y_i} = \frac{1}{nr\bar{w}}\sum_{i=1}^n (r\lambda w_i) = \frac{r\lambda}{nr\bar{w}}\sum_{i=1}^n w_i = \frac{r\lambda}{nr\bar{w}}n\bar{w} = \lambda,$$

proving the equality case and completing the proof of part (1).

The three equations

$$MN^{-1}x = \lambda y, \ N^{-1}M^{-1}x = \lambda y, \text{ and } N^{-1}Mx = \lambda y$$

can be rewritten respectively as

$$M^{-1}N^{-1}\tilde{x} = \lambda\tilde{y}, \ M^{-1}N^{-1}\hat{x} = \lambda\hat{y}, \text{ and } M^{-1}N^{-1}\check{x} = \lambda\check{y},$$

where

$$\tilde{x} = x, \ \tilde{y} = M^{-2}y, \ \hat{x} = M^{-1}x, \ \hat{y} = M^{-1}y, \ \check{x} = Mx, \text{ and } \check{y} = M^{-1}y.$$

Using these, parts (2)–(4) can be deduced from part (1). □

Theorem 2 *For $k = 1, \ldots, p$, let $A_k = (a_{ijk})_{n\times n}$ be an irreducible quasi-positive matrix satisfying $\sum_{i=1}^n a_{ijk} = 0$ for $j = 1, \ldots, n$; $(w_{1k}, \ldots, w_{nk})^T$ be a right positive eigenvector of A_k corresponding to the eigenvalue zero; $\bar{w}_k = \frac{1}{n}\sum_{i=1}^n w_{ik}$, the average of $w_{1k}, \ldots, w_{nk}$; $M_k = \text{diag}\{w_{1k}, \ldots, w_{nk}\}$ and $N_k = r_k I_n - A_k$ with $r_k > 0$; $W_k = M_k^{-1}N_k^{-1}$ or $N_k^{-1}M_k^{-1}$. Then*

$$\rho\left(\prod_{k=1}^p W_k\right) \geq \prod_{k=1}^p \frac{1}{r_k\bar{w}_k}$$

with equality if and only if $w_{1k} = \cdots = w_{nk}$ for $k = 1, \ldots, p$, or equivalently, $\sum_{j=1}^n a_{ijk} = 0$ for $i = 1, \ldots, n$ and $k = 1, \ldots, p$.

Additionally, if $\tilde{W}_1 = M_1 N_1^{-1}$ or $N_1^{-1}M_1$, and $W_2 = M_2^{-1}N_2^{-1}$ or $N_2^{-1}M_2^{-1}$, then we have

$$\rho(\tilde{W}_1 W_2) = \rho(W_2\tilde{W}_1) \geq \frac{\bar{w}_1}{r_1 r_2\bar{w}_2}$$

with equality if and only if

(i) *$w_{11}/w_{12} = \cdots = w_{n1}/w_{n2}$, or equivalently, the right positive eigenvectors associated with the eigenvalue zero of A_1 and A_2 are proportional, provided that $\tilde{W}_1 = M_1 N_1^{-1}$ and $W_2 = N_2^{-1}M_2^{-1}$, or $\tilde{W}_1 = N_1^{-1}M_1$ and $W_2 = M_2^{-1}N_2^{-1}$;*

(ii) $w_{1k} = \cdots = w_{nk}$ for $k = 1, 2$, or equivalently, $\sum_{j=1}^{n} a_{ijk} = 0$ for $i = 1, \ldots, n$ and $k = 1, 2$, provided that $\tilde{W}_1 = M_1 N_1^{-1}$ and $W_2 = M_2^{-1} N_2^{-1}$, or $\tilde{W}_1 = N_1^{-1} M_1$ and $W_2 = N_2^{-1} M_2^{-1}$.

Proof Since $(w_{1k}, \ldots, w_{nk})^T$ and N_k^{-1} are positive by Lemma 1, it follows that W_k is positive and the $pn \times pn$ matrix

$$W = \begin{pmatrix} 0 & W_1 & 0 & 0 & \cdots & 0 \\ 0 & 0 & W_2 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & W_{p-1} \\ W_p & 0 & 0 & 0 & \cdots & 0 \end{pmatrix}$$

is nonnegative and irreducible (Iggidr et al. 2016). By the Perron–Frobenius theorem (Horn and Johnson 2013), the spectral radius of matrix W is a simple eigenvalue of matrix W associated with a positive eigenvector $\boldsymbol{v} = (\boldsymbol{v}_1^T, \ldots, \boldsymbol{v}_p^T)^T$ with $\boldsymbol{v}_k = (v_{1k}, \ldots, v_{nk})^T$ for $k = 1, \ldots, p$. That is,

$$W\boldsymbol{v} = \lambda \boldsymbol{v} \quad \text{and} \quad \lambda \equiv \rho(W),$$

or explicitly,

$$W_k \boldsymbol{v}_{k+1} = \lambda \boldsymbol{v}_k, \text{ for } k = 1, \ldots, p, \text{ where } \boldsymbol{v}_{p+1} = \boldsymbol{v}_1. \tag{12}$$

Thus

$$\left(\prod_{k=1}^{p} W_k \right) \boldsymbol{v}_1 = \left(\prod_{k=1}^{p} W_k \right) \boldsymbol{v}_{p+1} = \lambda^p \boldsymbol{v}_1 \quad \text{and} \quad \rho \left(\prod_{k=1}^{p} W_k \right) = \lambda^p.$$

Since by assumption $W_k = M_k^{-1} N_k^{-1}$ or $N_k^{-1} M_k^{-1}$, it follows from part (1) or (3) of Lemma 3 that (12) implies

$$\lambda \geq \frac{1}{n r_k \bar{w}_k} \sum_{i=1}^{n} \frac{v_{i(k+1)}}{v_{ik}}$$

with equality if and only if

$$v_{1k} = \cdots = v_{nk} \quad \text{or} \quad \frac{v_{1k}}{w_{1k}} = \cdots = \frac{v_{nk}}{w_{nk}}, \tag{13}$$

and

$$\frac{v_{1(k+1)}}{v_{1k}} \frac{1}{w_{1k}} = \cdots = \frac{v_{n(k+1)}}{v_{nk}} \frac{1}{w_{nk}} = r_k \lambda, \tag{14}$$

for $k = 1, \ldots, p$. Therefore, by a generalized Hölder inequality (Evans [1998]),

$$
\begin{aligned}
\lambda^p &\geq \prod_{k=1}^{p} \left(\frac{1}{nr_k\bar{w}_k} \sum_{i=1}^{n} \frac{v_{i(k+1)}}{v_{ik}} \right) = \left(\prod_{k=1}^{p} \frac{1}{nr_k\bar{w}_k} \right) \prod_{k=1}^{p} \left(\sum_{i=1}^{n} \frac{v_{i(k+1)}}{v_{ik}} \right) \\
&\geq \left(\prod_{k=1}^{p} \frac{1}{nr_k\bar{w}_k} \right) \left(\sum_{i=1}^{n} \left(\frac{v_{i2}}{v_{i1}} \times \cdots \times \frac{v_{i(k+1)}}{v_{ik}} \times \cdots \times \frac{v_{ip}}{v_{i(p-1)}} \times \frac{v_{i1}}{v_{ip}} \right)^{1/p} \right)^p \\
&= \left(\prod_{k=1}^{p} \frac{1}{nr_k\bar{w}_k} \right) \left(\sum_{i=1}^{n} (1)^{1/p} \right)^p = \left(\prod_{k=1}^{p} \frac{1}{nr_k\bar{w}_k} \right) n^p = \prod_{k=1}^{p} \frac{1}{r_k\bar{w}_k},
\end{aligned}
$$

proving the inequality statement of the theorem. The second inequality above is an equality if and only if there exist positive constants $m_1, \ldots, m_p$ such that

$$
m_1 \frac{v_{i2}}{v_{i1}} = \cdots = m_k \frac{v_{i(k+1)}}{v_{ik}} = \cdots = m_{p-1} \frac{v_{ip}}{v_{i(p-1)}} = m_p \frac{v_{i1}}{v_{ip}}, \tag{15}
$$

for $i = 1, \ldots, n$.

Suppose that $\lambda^p = \prod_{k=1}^{p} \frac{1}{r_k\bar{w}_k}$. Then (13)–(15) hold. We claim that

$$
v_{1k} = \cdots = v_{nk}, \text{ for } k = 1, \ldots, p
$$

and hence it follows from (14) that $w_{1k} = \cdots = w_{nk} = \bar{w}_k$ for $k = 1, \ldots, p$, which means that $\mathbf{1} = (1, \ldots, 1)^T$ is a right eigenvector of A_k associated with the eigenvalue zero. In fact, assume from (13) that

$$
\frac{v_{1k_0}}{w_{1k_0}} = \cdots = \frac{v_{nk_0}}{w_{nk_0}} \tag{16}
$$

for some $k_0 \in \{1, \ldots, p\}$, then (15) gives

$$
\frac{v_{i(k_0+1)}}{v_{ik_0}} = \frac{m_{k_0-1}}{m_{k_0}} \frac{v_{ik_0}}{v_{i(k_0-1)}}, \quad i = 1, \ldots, n, \text{ with } m_0 = m_p \text{ and } \mathbf{v}_0 = \mathbf{v}_p
$$

implying from (14) that

$$
\frac{m_{k_0-1}}{m_{k_0}} \frac{v_{1k_0}}{v_{1(k_0-1)}} \frac{1}{w_{1k_0}} = \cdots = \frac{m_{k_0-1}}{m_{k_0}} \frac{v_{nk_0}}{v_{n(k_0-1)}} \frac{1}{w_{nk_0}}
$$

and hence by (16), $v_{1(k_0-1)} = \cdots = v_{n(k_0-1)}$. The proof is complete if $v_{1k}/w_{1k} = \cdots = v_{nk}/w_{nk}$ holds for all k. Otherwise, without loss of generality, suppose that $v_{11} = \cdots = v_{n1}$ and $p \geq 3$. If $v_{13} = \cdots = v_{n3}$, then by (15),

$$
m_1 \frac{v_{i2}}{v_{i1}} = m_2 \frac{v_{i3}}{v_{i2}}, \quad i = 1, \ldots, n
$$

implies that $v_{12} = \cdots = v_{n2}$; else by (13), $v_{13}/w_{13} = \cdots = v_{n3}/w_{n3}$ and by (16), this also implies that $v_{12} = \cdots = v_{n2}$. The case $p = 2$ can be similarly proved.

On the other hand, if $\sum_{j=1}^{n} a_{ijk} = 0$ for $i = 1, \ldots, n$ and $k = 1, \ldots, p$, then $\mathbf{1}$ is a right eigenvector of matrices A_k and N_k corresponding to the eigenvalues zero and r_k, respectively, and $M_k = \bar{w}_k I_n$. Thus,

$$
\left(\prod_{k=1}^{p} W_k \right) \mathbf{1} = \left(\prod_{k=1}^{p} \left(\frac{1}{\bar{w}_k} N_k^{-1} \right) \right) \mathbf{1} = \left(\prod_{k=1}^{p} \frac{1}{\bar{w}_k} \right) \left(\prod_{k=1}^{p} N_k^{-1} \right) \mathbf{1}
$$

$$
= \left(\prod_{k=1}^{p} \frac{1}{\bar{w}_k} \right) \left(\prod_{k=1}^{p-1} N_k^{-1} \right) (N_p^{-1} \mathbf{1}) = \left(\prod_{k=1}^{p} \frac{1}{\bar{w}_k} \right) \left(\prod_{k=1}^{p-1} N_k^{-1} \right) \left(\frac{1}{r_p} \mathbf{1} \right)
$$

$$
= \cdots = \left(\prod_{k=1}^{p} \frac{1}{\bar{w}_k} \right) \left(\prod_{k=2}^{p} \frac{1}{r_k} \right) \left(\frac{1}{r_1} \mathbf{1} \right) = \left(\prod_{k=1}^{p} \frac{1}{r_k \bar{w}_k} \right) \mathbf{1},
$$

which means that $\rho(\prod_{k=1}^{p} W_k) = \prod_{k=1}^{p} \frac{1}{r_k \bar{w}_k}$, completing the equality statement.

Now consider the case $p = 2$. If $\tilde{W}_1 = M_1 N_1^{-1}$ or $N_1^{-1} M_1$, and $W_2 = M_2^{-1} N_2^{-1}$ or $N_2^{-1} M_2^{-1}$, then using the same approach as above and Lemma 3,

$$
\lambda \geq \frac{1}{n r_1 \bar{w}_1} \sum_{i=1}^{n} \left(\frac{v_{i2}}{v_{i1}} \right) (w_{i1})^2 \quad \text{and} \quad \lambda \geq \frac{1}{n r_2 \bar{w}_2} \sum_{i=1}^{n} \frac{v_{i1}}{v_{i2}},
$$

which imply that

$$
\lambda^2 \geq \left(\frac{1}{n r_1 \bar{w}_1} \sum_{i=1}^{n} \left(\frac{v_{i2}}{v_{i1}} \right) (w_{i1})^2 \right) \left(\frac{1}{n r_2 \bar{w}_2} \sum_{i=1}^{n} \frac{v_{i1}}{v_{i2}} \right)
$$

$$
= \frac{1}{n^2 r_1 r_2 \bar{w}_1 \bar{w}_2} \left(\sum_{i=1}^{n} \left(\frac{v_{i2}}{v_{i1}} w_{i1}^2 \right) \right) \left(\sum_{i=1}^{n} \frac{v_{i1}}{v_{i2}} \right)
$$

$$
\geq \frac{1}{n^2 r_1 r_2 \bar{w}_1 \bar{w}_2} \left(\sum_{i=1}^{n} \left(\sqrt{\frac{v_{i2}}{v_{i1}} w_{i1}^2} \sqrt{\frac{v_{i1}}{v_{i2}}} \right) \right)^2
$$

$$
= \frac{1}{n^2 r_1 r_2 \bar{w}_1 \bar{w}_2} \left(\sum_{i=1}^{n} w_{i1} \right)^2 = \frac{1}{n^2 r_1 r_2 \bar{w}_1 \bar{w}_2} (n \bar{w}_1)^2 = \frac{\bar{w}_1}{r_1 r_2 \bar{w}_2}
$$

by the Cauchy–Schwarz inequality. The equality conditions are proved in the following two cases.

If $\lambda^2 = \frac{\bar{w}_1}{r_1 r_2 \bar{w}_2}$ then the multiplication of the second conditions in (5)–(8) gives

$$
\frac{w_{11}}{w_{12}} = \cdots = \frac{w_{n1}}{w_{n2}} = r_1 r_2 \lambda^2 = \frac{\bar{w}_1}{\bar{w}_2} \Leftrightarrow M_1 M_2^{-1} = \frac{\bar{w}_1}{\bar{w}_2} I_n. \tag{17}
$$

(i) Let $\tilde{W}_1 = M_1 N_1^{-1}$ and $W_2 = N_2^{-1} M_2^{-1}$, or $\tilde{W}_1 = N_1^{-1} M_1$ and $W_2 = M_2^{-1} N_2^{-1}$. Suppose that $w_{i1}/w_{i2} = \bar{w}_1/\bar{w}_2$ for $i = 1, \ldots, n$. Then $\boldsymbol{w}_1 = (w_{11}, \ldots, w_{n1})$ is a right eigenvector of matrices A_1, A_2, N_1 and N_2, associated with the eigenvalues zero, zero, r_1, and r_2, respectively. It follows from $N_1^{-1} N_2^{-1} \boldsymbol{w}_1 = \frac{1}{r_1 r_2} \boldsymbol{w}_1$ and (17) that $\lambda^2 \equiv \rho(\tilde{W}_1 W_2) = \frac{\bar{w}_1}{r_1 r_2 \bar{w}_2}$.

(ii) Let $\tilde{W}_1 = M_1 N_1^{-1}$ and $W_2 = M_2^{-1} N_2^{-1}$. Then the equality $\lambda^2 = \frac{\bar{w}_1}{r_1 r_2 \bar{w}_2}$ implies

$$\frac{v_{11}}{w_{11}^2} = \cdots = \frac{v_{n1}}{w_{n1}^2} \text{ and } \frac{v_{12}}{v_{11}} w_{11} = \cdots = \frac{v_{n2}}{v_{n1}} w_{n1} = r_1 \lambda, \qquad (18a)$$

$$v_{12} = \cdots = v_{n2} \text{ and } \frac{v_{11}}{v_{12}} \frac{1}{w_{12}} = \cdots = \frac{v_{n1}}{v_{n2}} \frac{1}{w_{n2}} = r_2 \lambda, \qquad (18b)$$

$$m_1 \frac{v_{i2}}{v_{i1}} w_{i1}^2 = m_2 \frac{v_{i1}}{v_{i2}} \Leftrightarrow \frac{v_{i1}}{v_{i2}} \frac{1}{w_{i1}} = \sqrt{\frac{m_1}{m_2}}, \ i = 1, \ldots, n. \qquad (18c)$$

The first equations in (18a) and (18b) give

$$\frac{v_{11}}{v_{12}} \frac{1}{w_{11}^2} = \cdots = \frac{v_{n1}}{v_{n2}} \frac{1}{w_{n1}^2},$$

which implies $w_{11} = \cdots = w_{n1}$ by (18c) and therefore by the second equations in (18a) and (18b), $w_{12} = \cdots = w_{n2}$.
Let $\tilde{W}_1 = N_1^{-1} M_1$ and $W_2 = N_2^{-1} M_2^{-1}$. Then by (17),

$$\begin{aligned}
\bar{w}_1/(r_1 r_2 \bar{w}_2) = \lambda^2 &\equiv \rho(\tilde{W}_1 W_2) = \rho(N_1^{-1} M_1 N_2^{-1} M_2^{-1}) \\
&= \rho(M_1 N_2^{-1} M_2^{-1} N_1^{-1}) = (\bar{w}_1/\bar{w}_2)^2 \rho(M_2 N_2^{-1} M_1^{-1} N_1^{-1})
\end{aligned}$$

implies that $\rho(M_2 N_2^{-1} M_1^{-1} N_1^{-1}) = \bar{w}_2/(r_1 r_2 \bar{w}_1)$. This case can then proceed as above.
On the other hand, suppose that $w_{ik} = \bar{w}_k$ for $i = 1, \ldots, n$ and $k = 1, 2$; it follows from $N_1^{-1} N_2^{-1} \mathbf{1} = \frac{1}{r_1 r_2} \mathbf{1}$ that $\lambda^2 \equiv \rho(\tilde{W}_1 W_2) = \frac{\bar{w}_1}{r_1 r_2 \bar{w}_2}$.

$\square$

Now let us return to the multipatch Ross–Macdonald model (2) in an environment with n identical patches formulated in Sect. 2, using the notation and definition of $\mathcal{R}_0(n)$ and $\mathcal{R}_0(1)$ given there in (3) and (4).

Theorem 3 *Consider model (2) with n identical patches connected by human and mosquito movement, i.e., $C = (c_{ij})_{n \times n}$ and $D = (d_{ij})_{n \times n}$ are irreducible. Then the basic reproduction number $\mathcal{R}_0(n)$ for the n-patch model (2) can be estimated against the basic reproduction number $\mathcal{R}_0(1)$ for the single patch model (1) according to*

$$\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$$

with equality if and only if the mosquito to human ratio in each patch remains the same under movement, i.e., $V_i^*/H_i^* = V/H$ for $i = 1, \ldots, n$, or equivalently, human

and mosquito movement rate matrices C and D have the same eigenspace associated with the eigenvalue zero.

Proof With the irreducibilities of travel rate matrices C and D, we have

$$\mathcal{R}_0^2(n) = a^2bc \cdot \rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}),$$

where $\mathcal{B}_1 = (\delta_{ij}V_i^*)_{n \times n}$, $\mathcal{B}_2 = (\delta_{ij}H_i^*)_{n \times n}$, $\mathcal{C} = \gamma I_n - C$, and $\mathcal{D} = \mu I_n - D$.

Take $\tilde{W}_1 = N_1^{-1}M_1$ and $W_2 = M_2^{-1}N_2^{-1}$ where $M_1 = \mathcal{B}_1$, $N_1 = \mathcal{D}$, $M_2 = \mathcal{B}_2$ and $N_2 = \mathcal{C}$. Then by Theorem 2 for $p = 2$,

$$\mathcal{R}_0^2(n) = a^2bc \cdot \rho(\tilde{W}_1 W_2) \geq a^2bc \cdot \frac{V/n}{\gamma\mu H/n} = \frac{a^2bcV}{\gamma\mu H} = \mathcal{R}_0^2(1).$$

The equality case is immediately proved by using the second case of (i) in Theorem 2. □

Remark 1 The equalities $H_i^* = H/n$ and $V_i^* = V/n$ for $1 \leq i \leq n$ hold if and only if the human and mosquito travel rate matrices C and D are line-sum symmetric. A square matrix is line-sum symmetric if it is symmetric, but not vice versa. Thus $\mathcal{R}_0(n) = \mathcal{R}_0(1)$ whenever both C and D are symmetric.

In what follows, we show that the estimation $\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$ remains valid when only humans or mosquitoes move between patches.

Corollary 1 *For model (2), the following statements are valid:*

(1) *If the n identical patches are connected by human movement (i.e., $C = (c_{ij})_{n \times n}$ is irreducible and $D = (d_{ij})_{n \times n} = 0_{n \times n}$) and mosquitoes are initially present in all patches (i.e., $V_i(0) > 0$ for $i = 1, \ldots, n$), then*

$$\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$$

with equality if and only if $(V_1(0), \ldots, V_n(0))^T$ is a right positive eigenvector of C associated with the zero eigenvalue.

(2) *If the n identical patches are connected by mosquito movement (i.e., $C = (c_{ij})_{n \times n} = 0_{n \times n}$ and $D = (d_{ij})_{n \times n}$ is irreducible) and humans are initially present in all patches (i.e., $H_i(0) > 0$ for $i = 1, \ldots, n$), then*

$$\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$$

with equality if and only if $(H_1(0), \ldots, H_n(0))^T$ is a right positive eigenvector of D associated with the zero eigenvalue.

Proof Suppose only humans move. It follows $\mathcal{D} = \mu I_n$, $\mathcal{B}_1 = (\delta_{ij}V_i(0))_{n \times n}$ and $\mathcal{B}_2 = (\delta_{ij}H_i^*)_{n \times n}$ and hence

$$\mathcal{R}_0^2(n) = \rho(\mathcal{A}\mathcal{D}^{-1}\mathcal{B}\mathcal{C}^{-1}) = a^2bc/\mu \cdot \rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}).$$

By the Perron–Frobenius theorem, the positive matrix $\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}$ has a positive right eigenvector, denoted by $\boldsymbol{w}$, corresponding to the spectral radius $\rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1})$, i.e.,

$$\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}\boldsymbol{w} = \rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1})\boldsymbol{w} \Leftrightarrow \mathcal{B}_2^{-1}\mathcal{C}^{-1}\boldsymbol{w} = \rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1})\mathcal{B}_1^{-1}\boldsymbol{w}.$$

Using the first part of Lemma 3, we have

$$\rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}) \geq \frac{1}{\gamma \sum_{i=1}^n H_i^*} \sum_{i=1}^n \frac{w_i}{w_i/V_i(0)} = \frac{V}{\gamma H}$$

with equality if and only if

$$\frac{w_1}{V_1(0)} = \cdots = \frac{w_n}{V_n(0)} \quad \text{and} \quad \frac{V_1(0)}{H_1^*} = \cdots = \frac{V_n(0)}{H_n^*} = \gamma\rho(\mathcal{B}_1\mathcal{B}_2^{-1}\mathcal{C}^{-1}).$$

Now suppose only mosquitoes move. If follows $\mathcal{C} = \gamma I_n$, $\mathcal{B}_1 = (\delta_{ij}V_i^*)_{n\times n}$ and $\mathcal{B}_2 = (\delta_{ij}H_i(0))_{n\times n}$ and hence

$$\mathcal{R}_0^2(n) = \rho(\mathcal{A}\mathcal{D}^{-1}\mathcal{B}\mathcal{C}^{-1}) = a^2bc/\gamma \cdot \rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}).$$

Again by the Perron–Frobenius theorem, the positive matrix $\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}$ has a positive right eigenvector, denoted by $\boldsymbol{w}$, corresponding to the spectral radius $\rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1})$, i.e.,

$$\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}\boldsymbol{w} = \mathcal{D}^{-1}\mathcal{B}_1(\mathcal{B}_2^{-1}\boldsymbol{w}) = \rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1})\boldsymbol{w}.$$

Applying the fourth part of Lemma 3 and the Cauchy–Schwarz inequality, we obtain

$$\rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}) \geq \frac{1}{\mu \sum_{i=1}^n V_i^*} \sum_{i=1}^n \frac{w_i/H_i(0)}{w_i}(V_i^*)^2 \geq \frac{\sum_{i=1}^n V_i^*}{\mu \sum_{i=1}^n H_i(0)} = \frac{V}{\mu H}$$

with equality if and only if

$$\frac{w_1}{V_1^*} = \cdots = \frac{w_n}{V_n^*} \quad \text{and} \quad \frac{w_1/H_1(0)}{w_1}V_1^* = \cdots = \frac{w_n/H_n(0)}{w_n}V_n^* = \mu\rho(\mathcal{D}^{-1}\mathcal{B}_1\mathcal{B}_2^{-1}).$$

The proofs for the estimation $\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$ and the condition for equality are complete. $\qquad\square$

Remark 2 The lower bound of $\mathcal{R}_0(n)$ is always achievable. In fact, given a positive vector $\boldsymbol{x} = (x_1, \ldots, x_n)^T$, there exist some travel rate matrices, e.g.,

$$-\sum_{i=1}^{n} x_i I_n + \begin{pmatrix} x_1 & x_1 & \cdots & x_1 \\ x_2 & x_2 & \cdots & x_2 \\ \vdots & \vdots & \ddots & \vdots \\ x_n & x_n & \cdots & x_n \end{pmatrix} \text{ and } \begin{pmatrix} -x_1^{-1} & x_2^{-1} & 0 & \cdots & 0 \\ 0 & -x_2^{-1} & x_3^{-1} & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ x_1^{-1} & 0 & 0 & \cdots & -x_n^{-1} \end{pmatrix},$$

having x as its right eigenvector corresponding to the eigenvalue zero.

It follows from Theorem 3 and Corollary 1 that habitat fragmentation, e.g., a large area of habitat split into some patches, may intensify malaria persistence and promote disease outbreaks. The assumption that humans and mosquitoes are homogeneously mixed or evenly distributed could underestimate the basic reproduction number. In other words, the habitat connectivity of isolated identical patches with the same initial number of humans and mosquitoes tends to increase the risk of infection. It is worth pointing out that Dye and Hasibeder (1986) and Hasibeder and Dye (1988) established similar results based on a spatial malaria model using a Lagrangian approach (mimicking commuting behavior) instead of an Eulerian approach (mimicking migration) (Bichara and Castillo-Chavez 2016; Cosner et al. 2009).

The inequality $\mathcal{R}_0(n) \geq \mathcal{R}_0(1)$ may fail when the incidence rates are not standard, or some patches are host free (Auger et al. 2008), or the travel rates of the susceptible and the infectious humans are not the same (see "Appendix"), or the model structure is more complicated, or a directly transmitted disease is considered. More specifically, Gao and Ruan (2012) proposed a multipatch malaria model with SEIRS structure for humans and SEI structure for mosquitoes and presented a numerical example where human movement leads to disease extinction in all identical patches, even though the disease persists in each isolated patch. For an SIS patch model with standard incidence, Gao and Ruan (2011) proved that the multipatch basic reproduction number is between the maximum and minimum of the basic reproduction numbers of all patches in isolation. Thus, the single patch and multipatch basic reproduction numbers for the SIS model are equal when all patches are identical.

Remark 3 Consider a malaria model with n identical patches similar to (2), but with bilinear incidence $\alpha(H_i - h_i)v_i$ and $\beta(V_i - v_i)h_i$ (see e.g., Gao et al. 2013) instead of normalized incidence $ab(H_i - h_i)v_i/H_i$ and $ac(V_i - v_i)h_i/H_i$, respectively. The basic reproduction numbers of this new multipatch model and the corresponding single patch model are respectively

$$\tilde{\mathcal{R}}_0(n) = \sqrt{\rho(\tilde{\mathscr{A}}\tilde{\mathscr{D}}^{-1}\tilde{\mathscr{B}}\tilde{\mathscr{C}}^{-1})} \text{ and } \tilde{\mathcal{R}}_0(1) = \sqrt{\alpha\beta V H/(\gamma\mu)},$$

where $\tilde{\mathscr{A}} = (\delta_{ij}\alpha H_i^*)_{n\times n}$, $\tilde{\mathscr{B}} = (\delta_{ij}\beta V_i^*)_{n\times n}$, $\tilde{\mathscr{C}} = \gamma I_n - C$, and $\tilde{\mathscr{D}} = \mu I_n - D$. For an example with two patches, setting $\alpha = \beta = \gamma = \mu = H = V = 1$, $c_{12} = d_{21} = 1$ and $c_{21} = d_{12} = 2$, it follows that $\tilde{\mathcal{R}}_0(2) = 0.2073 < \tilde{\mathcal{R}}_0(1) = 1$.

Remark 4 Consider model (2) with 2 identical patches connected by human movement and the second patch is vector free (i.e., $V_1^* = V$ and $V_2^* = 0$, all vectors are confined in the first patch), then

$$\mathcal{R}_0^2(2) = \frac{a^2 bc V}{\gamma \mu H} \frac{(c_{12} + c_{21})(\gamma + c_{12})}{c_{12}(\gamma + c_{12} + c_{21})} > \mathcal{R}_0^2(1) = \frac{a^2 bc V}{\gamma \mu H}.$$

However, if 2 identical patches are connected by mosquito movement and the second patch is host free (i.e., $H_1^* = H$ and $H_2^* = 0$), then

$$\mathcal{R}_0^2(2) = \frac{a^2 bc V}{\gamma \mu H} \frac{d_{12}(\mu + d_{12})}{(d_{12} + d_{21})(\mu + d_{12} + d_{21})} < \mathcal{R}_0^2(1) = \frac{a^2 bc V}{\gamma \mu H}.$$

Thus, the impact of habitat fragmentation on disease spread becomes complicated when hosts and/or vectors are not present in some patches.

So far, we have established a lower bound for the basic reproduction number of model (2). An upper bound that depends on the maximal ratio of mosquitoes to humans in each patch can be obtained as follows.

Proposition 1 *Consider model* (2) *with n identical patches connected by human and mosquito movement, i.e., $C = (c_{ij})_{n \times n}$ and $D = (d_{ij})_{n \times n}$ are irreducible. Then*

$$\frac{a^2 bc}{\gamma \mu} \min_{1 \leq i \leq n} \frac{V_i^*}{H_i^*} \leq \mathcal{R}_0^2(1) \leq \mathcal{R}_0^2(n) \leq \frac{a^2 bc}{\gamma \mu} \max_{1 \leq i \leq n} \frac{V_i^*}{H_i^*}.$$

Proof Similar to the proof of Theorem 3.1 in Gao (2019), without loss of generality, assume that $V_1^*/H_1^* \leq \cdots \leq V_n^*/H_n^*$. Then

$$\frac{V_1^*}{H_1^*} I_n \leq \mathscr{B}_1 \mathscr{B}_2^{-1} \leq \frac{V_n^*}{H_n^*} I_n$$

$$\Leftrightarrow \frac{V_1^*}{H_1^*} \mathscr{C}^{-1} \mathscr{D}^{-1} \leq \mathscr{B}_1 \mathscr{B}_2^{-1} \mathscr{C}^{-1} \mathscr{D}^{-1} \leq \frac{V_n^*}{H_n^*} \mathscr{C}^{-1} \mathscr{D}^{-1}$$

$$\Rightarrow \rho\left(\frac{V_1^*}{H_1^*} \mathscr{C}^{-1} \mathscr{D}^{-1}\right) = \frac{V_1^*}{\gamma \mu H_1^*} \leq \rho(\mathscr{B}_1 \mathscr{B}_2^{-1} \mathscr{C}^{-1} \mathscr{D}^{-1})$$

$$\leq \rho\left(\frac{V_n^*}{H_n^*} \mathscr{C}^{-1} \mathscr{D}^{-1}\right) = \frac{V_n^*}{\gamma \mu H_n^*},$$

due to the fact that $\rho(\mathscr{C}^{-1} \mathscr{D}^{-1}) = 1/(\gamma \mu)$. □

To what extent would human and/or mosquito movement increase the multipatch basic reproduction number? In particular, does there exist an upper bound of $\mathcal{R}_0(n)$ that is independent of travel rate matrices C and D? We will consider this point in the next section.

4 Numerical examples

In this section, we perform some numerical simulations for the model (2) with two identical patches to explore how human and/or mosquito movement affects the basic

reproduction number $\mathcal{R}_0(2)$ and disease prevalence. For illustration, the choice of parameter values does not strictly follow the epidemiology and ecology of malaria.

Example 1 Bound of the reproduction number. To see whether the multipatch reproduction number has a uniform bound from above for any travel pattern, we consider a two-patch case where all parameters are set to one except human and mosquito movement rates. Then

$$\mathcal{R}_0(2) = \sqrt{\rho(\mathscr{B}_1\mathscr{B}_2^{-1}\mathscr{C}^{-1}\mathscr{D}^{-1})} \text{ and } \mathcal{R}_0(1) = 1,$$

where $\mathscr{B}_1 = (\delta_{ij} V_i^*)_{2\times 2}, \mathscr{B}_2 = (\delta_{ij} H_i^*)_{2\times 2}, \mathscr{C} = I_2 - (c_{ij})_{2\times 2}, \mathscr{D} = I_2 - (d_{ij})_{2\times 2}$ and

$$H_1^* = \frac{c_{12}}{c_{12} + c_{21}}, \ H_2^* = \frac{c_{21}}{c_{12} + c_{21}}, \ V_1^* = \frac{d_{12}}{d_{12} + d_{21}}, \ V_2^* = \frac{d_{21}}{d_{12} + d_{21}}.$$

Case 1 We choose the travel rates as follows: $c_{12} = 1, c_{21} = \phi, d_{12} = 1$ and $d_{21} = \psi$ with $(\phi, \psi) \in \text{Int}\mathbb{R}_+^2$. Denote $\Gamma = \psi(1 + \psi) + \phi(4 + 3\psi + \psi^2)$. The basic reproduction number of model (2) is

$$\mathcal{R}_0(2) = \sqrt{\frac{(1 + \phi)(\Gamma + \sqrt{\Gamma^2 - 4\phi(2 + \phi)\psi(2 + \psi)})}{2\phi(2 + \phi)(1 + \psi)(2 + \psi)}} \geq 1$$

with equality if and only if $\phi = \psi$. Denote $\Gamma_\infty = 4 + 3\psi + \psi^2$. Direct calculations yield

$$\lim_{\phi \to 0+} \mathcal{R}_0(2) = +\infty \text{ and } \lim_{\phi \to +\infty} \mathcal{R}_0(2) = \sqrt{\frac{\Gamma_\infty + \sqrt{\Gamma_\infty^2 - 4\psi(2 + \psi)}}{2(1 + \psi)(2 + \psi)}},$$

and

$$\lim_{\psi \to 0+} \mathcal{R}_0(2) = \sqrt{\frac{2 + 2\phi}{2 + \phi}} \text{ and } \lim_{\psi \to +\infty} \mathcal{R}_0(2) = \frac{1 + \phi}{\sqrt{\phi(2 + \phi)}}.$$

Case 2 We choose the travel rates as follows: $c_{12} = 1, c_{21} = \phi, d_{12} = \psi$ and $d_{21} = 1$ with $(\phi, \psi) \in \text{Int}\mathbb{R}_+^2$. Denote $\Lambda = 1 + \phi(1 + \psi)^2$. The basic reproduction number of model (2) now becomes

$$\mathcal{R}_0(2) = \sqrt{\frac{(1 + \phi)(\Lambda + \sqrt{\Lambda^2 - \phi(2 + \phi)\psi(2 + \psi)})}{\phi(2 + \phi)(1 + \psi)(2 + \psi)}} \geq 1$$

with equality if and only if $\phi\psi = 1$. Again direct calculations yield

$$\lim_{\phi \to 0+} \mathcal{R}_0(2) = +\infty \text{ and } \lim_{\phi \to +\infty} \mathcal{R}_0(2) = \sqrt{\frac{(1 + \psi)^2 + \sqrt{(1 + \psi)^4 - \psi(2 + \psi)}}{(1 + \psi)(2 + \psi)}},$$
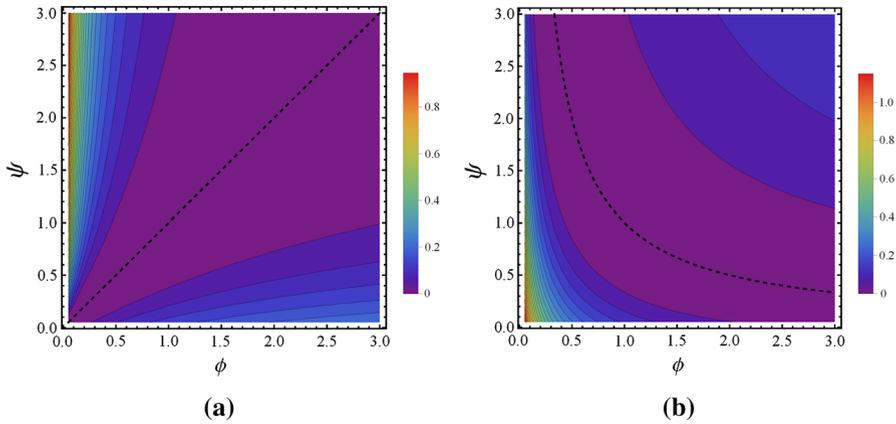
Fig. 2 The contour plot of the logarithm of the basic reproduction number, $\ln(\mathcal{R}_0(2))$, with respect to ϕ and ψ for Case 1 and Case 2. The black dashed curve is the contour of $\ln(\mathcal{R}_0(2)) = 0$

and

$$\lim_{\psi \to 0+} \mathcal{R}_0(2) = \frac{1 + \phi}{\sqrt{\phi(2 + \phi)}} \quad \text{and} \quad \lim_{\psi \to +\infty} \mathcal{R}_0(2) = \sqrt{\frac{2 + 2\phi}{2 + \phi}}.$$

The changes of $\mathcal{R}_0(2)$ versus relative travel rates ϕ and ψ for Case 1 and Case 2 are plotted in Fig. 2. It is initially decreasing and then increasing in both ϕ and ψ. Both analytical and numerical analyses show that $\mathcal{R}_0(2)$ can surpass any given positive number under appropriate human and mosquito movements such that the maximum of $\mathcal{R}_0(2)$ does not exist. Interestingly, although the limiting processes $\phi \to 0+$ and $\phi \to +\infty$ both result in the number of humans approaching $H = 1$ in one patch and zero in the other patch, the limits are completely different even if the movement rate matrix for mosquitoes is symmetric ($\psi = 1$) or there is no mosquito movement.

Example 2 Higher diffusion rates. By changing the travel rate matrices C and D to $d_H C$ and $d_V D$, respectively, we consider the relation between the basic reproduction number $\mathcal{R}_0(2)$ and the diffusion coefficients of humans and mosquitoes, d_H and d_V. The travel related parameters are set as $c_{12} = 0.01$, $c_{21} = 0.05$, $d_{12} = 0.01$, $d_{21} = 0.02$, other parameters are fixed at one. Clearly, the ratios of mosquitoes to humans in patches 1 and 2 at the disease-free equilibrium are respectively 2 and 0.8 which are independent of the diffusion coefficients. The dependence of $\mathcal{R}_0(2)$ on d_H and d_V is illustrated in Fig. 3. Both numerical and analytical approaches demonstrate that $\mathcal{R}_0(2)$ is monotone decreasing in both d_H and d_V if $\mathcal{R}_0(2) \not\equiv \mathcal{R}_0(1)$. Namely, faster diffusion leads to lower risk of infection when only two identical patches are considered. Further, this result remains valid for an environment with an arbitrary number of identical or nonidentical patches connected by either human or mosquito movement (Gao 2019; Gao and Dong 2019). In addition, the limits of $\mathcal{R}_0(2)$ as d_H and d_V go to zero and infinity are respectively
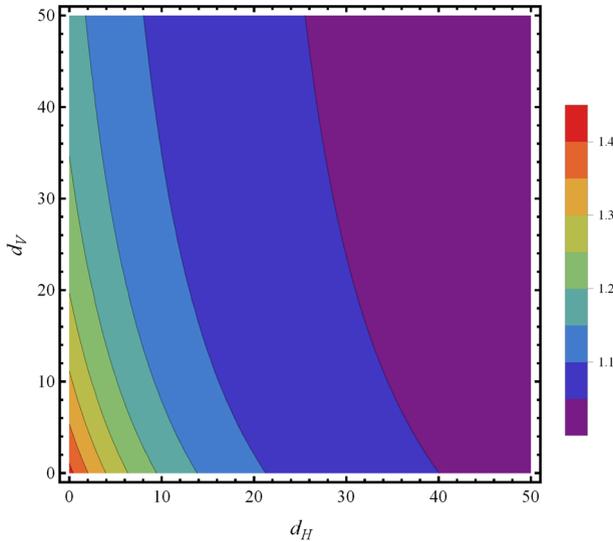
Fig. 3 The contour plot of the basic reproduction number $\mathcal{R}_0(2)$ in terms of d_H and d_V

$$\lim_{\substack{d_H \to 0+ \\ d_V \to 0+}} \mathcal{R}_0(2) = \max_{1 \leq i \leq 2} \sqrt{\frac{a^2 bc V_i^*}{\gamma \mu H_i^*}} \quad \text{and} \quad \lim_{d_H \to \infty} \mathcal{R}_0(2) = \mathcal{R}_0(1)$$

and

$$\lim_{d_V \to \infty} \mathcal{R}_0(2) = \mathcal{R}_0(1) \sqrt{1 + \frac{\gamma(c_{12}d_{21} - c_{21}d_{12})^2}{c_{12}c_{21}(d_{12} + d_{21})^2(\gamma + (c_{12} + c_{21})d_H)}} \geq \mathcal{R}_0(1),$$

which again suggest that the effects of human and mosquito movements on malaria spread are different.

For the same parameter setting, however, Fig. 4a indicates that the model (2) with diffusion may constantly incur a larger number of infected humans than that without diffusion ($d_H \to 0+$ and $d_V \to 0+$). The disease prevalence in humans over two patches could be monotone or nonmonotone in d_H and d_V. There are inconsistent consequences between the risk of infection and the disease prevalence as the diffusion coefficients d_H and d_V vary. When we change the travel rates to $c_{12} = 0.01$, $c_{21} = 0.009$, $d_{12} = 0.01$ and $d_{21} = 0.04$, there is a dashed curve passing through the origin as shown in Fig. 4b above which diffusion causes more infections and below which diffusion causes less infections.

5 Discussion

It is well known that population dispersal can intensify or weaken disease spread like diffusion-driven population persistence or extinction in population ecology. Wang
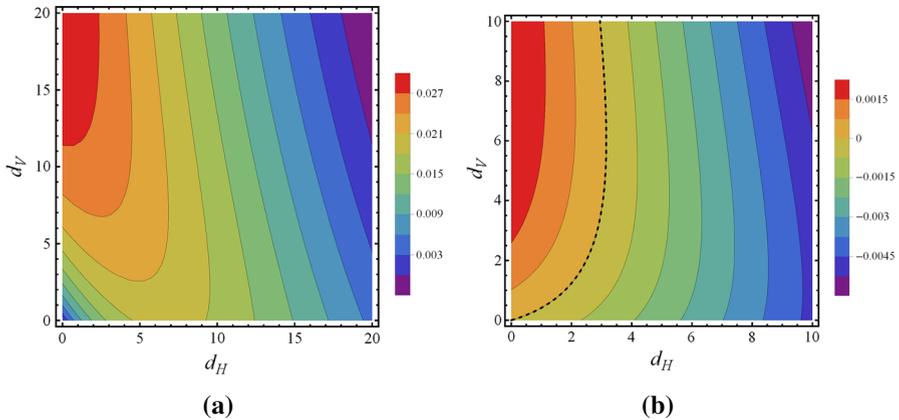
(a)   **(b)**

Fig. 4 The contour plot of the difference of the overall disease prevalence in humans with and without diffusion in terms of d_H and d_V under two travel patterns

and Zhao (2004) considered an SIS multipatch model with bilinear incidence and gave two numerical examples: one showed that suitable dispersal rates lead to either disease spread or disease extinction in both patches when a low transmission patch and a high transmission patch are concerned, the other found that population dispersal can result in the spread of disease in both patches even though the disease cannot spread in each isolated patch. Jin and Wang (2005) further studied the model and showed that population dispersal may result in disease extinction even though it cannot be eradicated in each isolated patch. Wang and Mulone (2003) proposed a two-patch SIS model with standard incidence and showed that the disease remains extinct/persistent in both patches when population dispersal occurs if it disappears/spreads in each isolated patch. Gao and Ruan (2011) drew the same conclusion for an n-patch SIS model incorporating the impact of media coverage. Based on an SIS model with two patches, Salmani and van den Driessche (2006) found that small and large travel rates could aid disease persistence whereas intermediate rates stabilize the disease-free equilibrium. Gao and Ruan (2012) considered a complicated multipatch malaria model and numerically showed that human movement can help malaria become extinct or persistent in two identical patches, even though the disease persists or dies out in each isolated patch. Hsieh et al. (2007) proposed an SEIRP patch model and performed numerical simulations under various travel policies.

In this paper, we considered a Ross–Macdonald type model with n identical patches to address the impact of human and/or mosquito movement on malaria persistence. We first proved a generalized eigenvalue inequality and used it to estimate the spectral radius of the product of a class of nonnegative matrices. Then we showed that the basic reproduction number of the multipatch Ross–Macdonald model is no less than that of the single patch model. Biologically speaking, habitat fragmentation strengthens the persistence of the disease. Ignorance of spatial structure could substantially underestimate the basic reproduction number such that more efforts are required to achieve disease elimination or eradication. A similar result associated with the Lagrangian approach was previously obtained by Dye and Hasibeder (1986) and Hasibeder and

Dye ([1988](#)). The findings are in accordance with a recent study on pathogen dynamics by White et al. ([2018](#)) using an individual-based model integrated with movement ecology approaches. The multipatch basic reproduction number equals that of the single patch model if and only if all connected patches have the same ratio of mosquitoes to humans at the disease-free equilibrium. The human population acts as a blood source for mosquitoes. In other words, once the distribution of humans is determined, the basic reproduction number is minimized when the movement of the mosquito population follows a strategy for which the resulting distribution of mosquitoes is proportional to that of humans. A similar result holds if the distribution of the mosquito population is fixed. This diffusion strategy is somewhat linked to the concept of the ideal free distribution (IFD) in ecology, which states that the distribution of organisms should match the distribution of resources (Cantrell et al. [2012a](#); Fretwell and Lucas [1969](#)). Malaria persistence is minimized when the distribution of mosquitoes obeys IFD. However, in reality, mosquitoes are unevenly distributed due to their limited mobility. For example, an urban area with dense human population has less mosquitoes while a rural area with sparse human population has more mosquitoes. To reduce the disease persistence, a control strategy that makes the geographic distribution of hosts and vectors nearly uniform may be desirable.

Moreover, we numerically and analytically showed that the basic reproduction number goes to infinity when one of the two human movement rates tends to zero and the remaining one is fixed. The fact was observed by Auger et al. ([2008](#)) in case only hosts migrate between patches. There is some inconsistency between the reproduction number and the overall disease prevalence in response to increasing diffusion. That is, fast host and/or vector diffusion decreases the disease transmission potential, but may increase the number of infected humans. Dye and Hasibeder ([1986](#)) studied the single patch case and they showed that the reproduction number is increasing in the human population size H, but the number of infected hosts is initially increasing then decreasing in H. The main conclusion that the multipatch basic reproduction number is greater than or equal to the single patch reproduction number is generally invalid if part of the model assumptions are not satisfied. Some mathematical results like Lemma [3](#) and Theorem [2](#) are applicable to the proof of similar arguments for multipatch epidemic models with different model structures or transmission modes.

Finally, we remark that current work can be extended in at least three possible ways. The first is to study the malaria model in a temporal varying environment driven by periodic human migration and seasonal changes in mosquito population and behavior. The global dynamics for such a periodic multipatch malaria model established by Gao et al. ([2014](#)) are a good first step. The second is to extend the multipatch ODE model to the nonlocal model with integral kernel $k(x, y)$ and diffusion-advection model with diffusion rate $d(x)$ and advection $\boldsymbol{p}(x)$ (Cosner [2015](#)) where, for example, the movement term $\sum_{j=1}^{n} c_{ij} H_j(t)$ is replaced by

$$\int_{\Omega} k(x, y) H(y, t) dy - \left(\int_{\Omega} k(y, x) dy \right) H(x, t)$$

and

$$\nabla \cdot [d(x) \nabla H - H \boldsymbol{p}(x)],$$

respectively. Here Ω is a bounded subset of $\mathbb{R}^N$, and $x, y \in \Omega$. The continuous version of Lemma 2 in terms of integrals to nonlocal diffusion established by Cantrell et al. (2012b) should be helpful in comparing the reproduction numbers of the model with and without diffusion. The impact of the distribution of humans on malaria risk in a continuous space was partially observed by Lou and Zhao (2011). The third is to consider similar questions for epidemic models with different structures (e.g., SEIR for humans and SEI for mosquitoes) or different transmission modes (e.g., water-borne diseases and sexually transmitted diseases). We leave these challenging problems for future investigation.

Appendix: Unequal travel rates

Let S_i, I_i, X_i, and Y_i be the numbers of susceptible and infectious humans, susceptible and infectious mosquitoes, respectively. Denote the total human and mosquito populations in the ith patch by $H_i = S_i + I_i$ and $V_i = X_i + Y_i$, respectively. Assuming unequal travel rates for susceptible and infectious humans, the model equations are

$$
\begin{aligned}
\frac{dS_i}{dt} &= -ab\frac{Y_i}{H_i}S_i + \gamma I_i + \sum_{j=1}^{n} \tilde{c}_{ij} S_j, \ 1 \le i \le n, \\
\frac{dX_i}{dt} &= -ac\frac{I_i}{H_i}X_i + \mu Y_i + \sum_{j=1}^{n} d_{ij} X_j, \ 1 \le i \le n, \\
\frac{dI_i}{dt} &= ab\frac{Y_i}{H_i}S_i - \gamma I_i + \sum_{j=1}^{n} c_{ij} I_j, \ 1 \le i \le n, \\
\frac{dY_i}{dt} &= ac\frac{I_i}{H_i}X_i - \mu Y_i + \sum_{j=1}^{n} d_{ij} Y_j, \ 1 \le i \le n.
\end{aligned}
\tag{A}
$$

We assume that the travel rate matrices $\tilde{C} = (\tilde{c}_{ij})_{n \times n}$, $C = (c_{ij})_{n \times n}$, and $D = (d_{ij})_{n \times n}$ are irreducible. For any given nonnegative initial condition, the model (A) has a unique disease-free equilibrium

$$
E_0 = (H_1^*, \ldots, H_n^*, V_1^*, \ldots, V_n^*, 0, \ldots, 0, 0, \ldots, 0),
$$

where $(H_1^*, \ldots, H_n^*)$ and $(V_1^*, \ldots, V_n^*)$ are respectively the unique positive solution to

$$
\sum_{j=1}^{n} \tilde{c}_{ij} H_j = 0, \ i = 1, \ldots, n, \ \ \sum_{i=1}^{n} H_i = \sum_{i=1}^{n} H_i(0) = H > 0,
$$

and

$$\sum_{j=1}^{n} d_{ij} V_j = 0, \ i = 1, \ldots, n, \ \sum_{i=1}^{n} V_i = \sum_{i=1}^{n} V_i(0) = V > 0.$$

Following the next generation matrix method (Diekmann et al. 1990; van den Driessche and Watmough 2002), we define the basic reproduction number of the model (A) as

$$\hat{\mathcal{R}}_0(n) = \sqrt{\rho(\hat{\mathscr{A}} \hat{\mathscr{D}}^{-1} \hat{\mathscr{B}} \hat{\mathscr{C}}^{-1})},$$

where $\hat{\mathscr{A}} = ab I_n$, $\hat{\mathscr{B}} = ac(\delta_{ij} V_i^*/H_i^*)_{n \times n}$, $\hat{\mathscr{C}} = \gamma I_n - C$, and $\hat{\mathscr{D}} = \mu I_n - D$. In particular, the basic reproduction number of a single patch model is

$$\hat{\mathcal{R}}_0(1) = \sqrt{\frac{a^2 bcV}{\gamma \mu H}}.$$

Claim: consider n identical patches connected by human movement (i.e., $\tilde{C}$ and C are irreducible, and $D = 0_{n \times n}$) and mosquitoes are initially evenly distributed (i.e., $V_1(0) = \cdots = V_n(0) = V/n$), then th inequality $\hat{\mathcal{R}}_0(n) \geq \hat{\mathcal{R}}_0(1)$ may fail.

Under the above assumptions we actually have

$$\hat{\mathcal{R}}_0(n) = \sqrt{a^2 bcV/(n\mu)} \cdot \sqrt{\rho(MN^{-1})}$$

with $M = \text{diag}\{1/H_1^*, \ldots, 1/H_n^*\}$ and $N = \gamma I_n - C$. Thus,

$$\hat{\mathcal{R}}_0(n) \geq \hat{\mathcal{R}}_0(1) \Leftrightarrow \rho(MN^{-1}) \geq n/(\gamma H).$$

In particular, the above inequality for the two-patch case holds if and only if

$$e_1 \equiv (\tilde{c}_{12} - \tilde{c}_{21})(\tilde{c}_{12}\gamma - \tilde{c}_{21}\gamma + 2\tilde{c}_{12}c_{21} - 2\tilde{c}_{21}c_{12}) > 0$$

or

$$e_2 \equiv \tilde{c}_{12} c_{21}(\tilde{c}_{12} - 3\tilde{c}_{21}) + \tilde{c}_{21} c_{12}(\tilde{c}_{21} - 3\tilde{c}_{12}) + \gamma(\tilde{c}_{12} - \tilde{c}_{21})^2 > 0.$$

However, even if a realistic restriction $\tilde{c}_{ij} \geq c_{ij}$ for $i \neq j$ is introduced, $\gamma = 0.25$, $\tilde{c}_{12} = 0.5 > c_{12} = 0.125$ and $\tilde{c}_{21} = 1 > c_{21} = 0.5$ giving $e_1 = -0.0625$ and $e_2 = -0.625$, a counterexample.

Nevertheless, consider model (A) with $D = 0_{n \times n}$ and $C = d_I \tilde{C}$ with $d_I \in (0, 1)$ denoting the relative diffusion rate of infectious humans to susceptible humans, then $\hat{\mathcal{R}}_0(n) \geq \hat{\mathcal{R}}_0(1)$ still holds. Moreover, $\hat{\mathcal{R}}_0(n)$ is strictly decreasing and strictly convex in d_I if $\hat{\mathcal{R}}_0(n) \not\equiv \hat{\mathcal{R}}_0(1)$, i.e., $(V_1(0), \ldots, V_n(0) \gg 0$ is not a right eigenvector of $\tilde{C}$ associated with the eigenvalue zero (Gao and Dong 2019). Therefore, the assumption

that susceptible and infectious individuals have identical travel rates can underestimate the risk of infection.

References

Abdelrazec A, Bélair J, Shan C, Zhu H (2016) Modeling the spread and control of dengue with limited public health resources. Math Biosci 271:136–145

Arino J, Ducrot A, Zongo P (2012) A metapopulation model for malaria with transmission-blocking partial immunity in hosts. J Math Biol 64(3):423–448

Auger P, Kouokam E, Sallet G, Tchuente M, Tsanou B (2008) The Ross–Macdonald model in a patchy environment. Math Biosci 216(2):123–131

Bai Z, Peng R, Zhao XQ (2018) A reaction–diffusion malaria model with seasonality and incubation period. J Math Biol 77(1):201–228

Berman A, Plemmons RJ (1979) Nonnegative matrices in the mathematical sciences. Academic Press, New York

Bichara D, Castillo-Chavez C (2016) Vector-borne diseases models with residence times-a Lagrangian perspective. Math Biosci 281:128–138

Bowman C, Gumel AB, van den Driessche P, Wu J, Zhu H (2005) A mathematical model for assessing control strategies against West Nile virus. Bull Math Biol 67(5):1107–1133

Cantrell RS, Cosner C, Lou Y (2012a) Evolutionary stability of ideal free dispersal strategies in patchy environments. J Math Biol 65(5):943–965

Cantrell RS, Cosner C, Lou Y, Ryan D (2012b) Evolutionary stability of ideal free dispersal strategies: a nonlocal dispersal model. Can Appl Math Q 20(1):15–38

Chen J, Huang J, Beier JC, Cantrell RS, Cosner C, Fuller DO, Zhang G, Ruan S (2016) Modeling and control of local outbreaks of West Nile virus in the United States. Discrete Contin Dyn Syst B 21(8):2423–2449

Codeço CT, Luz PM, Coelho F, Galvani AP, Struchiner C (2007) Vaccinating in disease-free regions: a vaccine model with application to yellow fever. J R Soc Interface 4(17):1119–1125

Cosner C (2015) Models for the effects of host movement in vector-borne disease systems. Math Biosci 270:192–197

Cosner C, Beier JC, Cantrell RS, Impoinvil D, Kapitanski L, Potts MD, Troyo A, Ruan S (2009) The effects of human movement on the persistence of vector-borne diseases. J Theor Biol 258(4):550–560

Diekmann O, Heesterbeek JAP, Metz JAJ (1990) On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. J Math Biol 28(4):365–382

Dye C, Hasibeder G (1986) Population dynamics of mosquito-borne disease: effects of flies which bite some people more frequently than others. Trans R Soc Trop Med Hyg 80:69–77

Eaves BC, Hoffman AJ, Rothblum UG, Schneider H (1985) Line-sum-symmetric scalings of square nonnegative matrices. Math Program Stud 25:124–141

Evans LC (1998) Partial differential equations. American Mathematical Society, Providence

Feng Z, Velasco-Hernández JX (1997) Competitive exclusion in a vector-host model for the dengue fever. J Math Biol 35(5):523–544

Fretwell SD, Lucas HL (1969) On territorial behavior and other factors influencing habitat distribution in birds. I. Theoretical development. Acta Biotheor 19(1):16–36

Gao D (2019) Travel frequency and infectious diseases. SIAM J Appl Math 79(4):1581–1606

Gao D, Dong CP (2019) Fast diffusion inhibits disease outbreaks. Preprint https://arxiv.org/abs/1907.12229

Gao D, Cosner C, Cantrell RS, Beier JC, Ruan S (2013) Modeling the spatial spread of Rift Valley fever in Egypt. Bull Math Biol 75(3):523–542

Gao D, Lou Y, Ruan S (2014) A periodic Ross–Macdonald model in a patchy environment. Discrete Contin Dyn Syst B 19(10):3133–3145

Gao D, Lou Y, He D, Porco TC, Kuang Y, Chowell G, Ruan S (2016) Prevention and control of Zika as a mosquito-borne and sexually transmitted disease: a mathematical modeling analysis. Sci Rep 6:28070

Gao D, Ruan S (2011) An SIS patch model with variable transmission coefficients. Math Biosci 232(2):110–115

Gao D, Ruan S (2012) A multipatch malaria model with logistic growth populations. SIAM J Appl Math 72(3):819–841

Gao D, Ruan S (2014) Malaria models with spatial effects. In: Chen D, Moulin B, Wu J (eds) Analyzing and modeling spatial and temporal dynamics of infectious diseases. Wiley, Hoboken, pp 109–136

Hasibeder G, Dye C (1988) Population dynamics of mosquito-borne disease: persistence in a completely heterogeneous environment. Theor Popul Biol 33(1):31–53

Horn RA, Johnson CR (2013) Matrix analysis, 2nd edn. Cambridge University Press, New York

Hsieh YH, van den Driessche P, Wang L (2007) Impact of travel between patches for spatial spread of disease. Bull Math Biol 69(4):1355–1375

Iggidr A, Gauthier S, Souza MO (2016) On the dynamics of a class of multi-group models for vector-borne diseases. J Math Anal Appl 441(2):723–743

Jin Y, Wang W (2005) The effect of population dispersal on the spread of a disease. J Math Anal Appl 308(1):343–364

Khuu D, Eberhard ML, Bristow BN, Javanbakht M, Ash LR, Shafir SC, Sorvillo FJ (2017) Malaria-related hospitalizations in the United States, 2000–2014. Am J Trop Med Hyg 97(1):213–221

Kucharski AJ, Funk S, Eggo RM, Mallet HP, Edmunds WJ, Nilles EJ (2016) Transmission dynamics of Zika virus in island populations: a modelling analysis of the 2013–14 French Polynesia outbreak. PLoS Negl Trop Dis 10(5):e0004726

Lou Y, Zhao XQ (2011) A reaction–diffusion malaria model with incubation period in the vector population. J Math Biol 62(4):543–568

Macdonald G (1957) The epidemiology and control of malaria. Oxford University Press, London

Mandal S, Sarkar RR, Sinha S (2011) Mathematical models of malaria—a review. Malar J 10:202

Moon JW (1970) Counting labelled tress. Canadian Mathematical Congress, Montreal

Pan American Health Organization (2017) Zika - epidemiological report Brazil. https://www.paho.org/hq/dmdocuments/2017/2017-phe-zika-situation-report-bra.pdf Accessed 6 Dec 2018

Reiner RC Jr, Perkins TA, Barker CM et al (2013) A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970–2010. J R Soc Interface 10(81):20120921

Ross R (1911) The prevention of malaria, 2nd edn. John Murray, London

Salmani M, van den Driessche P (2006) A model for disease transmission in a patchy environment. Discrete Contin Dyn Syst B 6(1):185–202

Smith HL (1995) Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems. American Mathematical Society, Providence

Smith DL, McKenzie FE (2004) Statics and dynamics of malaria infection in Anopheles mosquitoes. Malar J 3:13

Smith DL, Battle KE, Hay SI, Barker CM, Scott TW, McKenzie FE (2012) Ross, Macdonald, and a theory for the dynamics and control of mosquito-transmitted pathogens. PLoS Pathog 8(4):e1002588

van den Driessche P, Watmough J (2002) Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math Biosci 180(2):29–48

Wang W, Mulone G (2003) Threshold of disease transmission in a patch environment. J Math Anal Appl 285(1):321–335

Wang W, Zhao XQ (2004) An epidemic model in a patchy environment. Math Biosci 190(1):97–112

White LA, Forester JD, Craft ME (2018) Disease outbreak thresholds emerge from interactions between movement behavior, landscape structure, and epidemiology. Proc Natl Acad Sci USA 115(28):7374–7379

World Health Organization (2017) Vector-borne diseases. https://www.who.int/en/news-room/fact-sheets/detail/vector-borne-diseases. Accessed 6 Dec 2018

World Health Organization (2018) World malaria report 2018. http://www.who.int/malaria/publications/world-malaria-report-2018/en. Accessed 6 Dec 2018