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NETWORK-LEVEL REPRODUCTION NUMBER AND EXTINCTION THRESHOLD FOR VECTOR-BORNE DISEASES

Ling Xue and Caterina Scoglio

Kansas State Epicenter
Department of Electrical & Computer Engineering
Kansas State University
Manhattan, KS 66506, USA

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Abstract. The basic reproduction number of deterministic models is an essential quantity to predict whether an epidemic will spread or not. Thresholds for disease extinction contribute crucial knowledge of disease control, elimination, and mitigation of infectious diseases. Relationships between basic reproduction numbers of two deterministic network-based ordinary differential equation vector-host models, and extinction thresholds of corresponding stochastic continuous-time Markov chain models are derived under some assumptions. Numerical simulation results for malaria and Rift Valley fever transmission on heterogeneous networks are in agreement with analytical results without any assumptions, reinforcing that the relationships may always exist and proposing a mathematical problem for proving existence of the relationships in general. Moreover, numerical simulations show that the basic reproduction number does not monotonically increase or decrease with the extinction threshold. Consistent trends of extinction probability observed through numerical simulations provide novel insights into mitigation strategies to increase the disease extinction probability. Research findings may improve understandings of thresholds for disease persistence in order to control vector-borne diseases.

1. **Introduction.** Vector-borne diseases greatly impact health of humans and animals and are among the leading causes of worldwide death every year [12]. These diseases may cause significant economic losses in regard to animal trade, agriculture, health care, and tourism. From economy and humanity point of view, there is a need for prevention and control of vector-borne diseases. A dynamic model of vector-borne diseases may be used to learn many characteristics of an outbreak such as the probability of an outbreak, the size of outbreak, duration time of the outbreak, or the probability for the epidemic to die out [6] to improve understanding of disease transmission and persistence. Efficient mitigation strategies deduced from model results may stop an outbreak at early stages by reducing spreading parameters [6].

Globalization of trade and travel is one key factor driving the emergence of vector-borne diseases; heterogeneous structure also plays an important role in infectious disease dynamics [16]. Modeling the spatial spread of vector-borne diseases is a challenging task [3], but one possible approach is to consider a meta-population

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as a directed graph, or a network, with each node representing a subpopulation in a location, and links placed between two locations if possibility of transmission exists, such as movement or proximity [5]. Network models are widely used in epidemiology to understand the spread of infectious diseases through connected populations [22, 34].

The basic reproduction number, R_0, defined as the number of secondary cases produced by an infected individual in a naive population [10], is an important threshold on epidemiology, as well as type reproduction number [27], target reproduction [29], and threshold index for epidemicity [14]. The basic reproduction number is an important metric, predicting whether a disease will spread or die out in deterministic population and communicable disease theory [2]. If $R_0 > 1$, one infectious individual generally produces more than one infection, leading to the spread of an epidemic; whereas, on average, if $R_0 < 1$, one infectious individual generates less than one infection, and the epidemic may die out [10]. The same trajectory can always be observed with deterministic models given the same initial conditions [17]. If it is possible for an epidemic to reoccur, a real world epidemic does not allow observations of the same infection happening to the same person at the same time [17]. Moreover, deterministic models have the disadvantage that the number of infected individuals may go to less than one [19].

In comparison, Markov chain models are more realistic in the sense of only taking integer values instead of continuously varying quantities [19] and taking into account chances by approximating or mimicking random or probabilistic factors. The last infectious individual may recover before the infection is transmitted to other susceptible individuals so that the disease may become extinct [19]. Consequently, an infection introduced to a completely susceptible population may not invade the system even if $R_0 > 1$ [19]. Threshold for the extinction of an infectious disease to occur and probability of disease extinction are of our interests. Bienaymé-Galton-Watson branching processes are widely used to study disease extinction involving multi-type infections.

Lloyd [19] reviewed theory of branching processes and computed extinction probability using branching processes for Ross malaria model [28] taking into account stochasticity and heterogeneity. Pénisson [23] presented several statistical tools to study extinction of populations composed of different types of individuals, and their behaviors before extinction and in the case of a very late extinction. Allen and Lahodny Jr [1] computed basic reproduction numbers for deterministic models, and *extinction thresholds*, denoted by E_0 here, for corresponding continuous-time Markov chain (CTMC) models using continuous-time branching process, and derived relationships between the two thresholds. A CTMC model is a stochastic counterpart of a ordinary differential equation (ODE) model [1].

According to current knowledge, very little work has been done on deriving relationships between basic reproduction numbers for network-based deterministic models and extinction thresholds for corresponding stochastic CTMC models. Lahodny Jr and Allen [18] estimated probability of disease extinction for a Susceptible-Infected-Susceptible (SIS) multipatch model and illustrated some differences between thresholds for deterministic models and stochastic models numerically. Allen and van den Driessche [2] established connections between extinction thresholds for continuous-time models and discrete-time models and proved that $R_0 \leq 1$ if and only if $E_0 \leq 1$ for network-based models under the assumption that the expectation

matrix for computing E_0 is symmetric, which is not required in our approach. Although probability of disease extinction is defined as the probability for the number of infections to become zero when time goes to infinity, various numerical approximations for many types of models within finite time showed agreement with predicted extinction probability using branching processes [1, 2, 18].

Objectives of our research are to relate the extinction threshold, E_0, in a stochastic setting and the basic reproduction number, R_0, in a deterministic setting for vector-host meta-population models, as well as gain understanding as to how to increase extinction probability.

The contribution of our work is summarized as follows:

1. Relationships between extinction thresholds and basic reproduction numbers are derived for network-based vector-host models under some assumptions.
2. Numerical simulations show that the relationships still exist after removing above assumptions.
3. Consistent trends of extinction probability varying with disease parameters are observed through extensive numerical simulations.
4. The relationship between varying disease parameters and potential mitigation strategies is biologically interpreted.

This paper is organized as follows. Section 2 reviews the next generation matrix approach for computing R_0 and the branching process for deriving E_0. Section 3 calculates R_0 for a deterministic vector-host model in which transmission dynamics of vectors are described by a Susceptible-Infected (SI) model and transmission dynamics of hosts are described by an SIS model. We relate E_0 of corresponding CTMC model and R_0 analytically. In Section 4, an analogue of results in Section 3 is obtained for a model in which transmission dynamics of vectors are described by a Susceptible-Exposed-Infected (SEI) model and transmission dynamics of hosts are described by a Susceptible-Exposed-Infected-Recovered (SEIR) model. The homogeneous models presented [1] are generlized to network models by taking into account local transmission and trans-location transmission due to proximity. In Section 5, the relationships derived in Sections 3 and 4 are numerically shown to exist without any assumptions for simplified malaria and Rift Valley fever meta-population models. The sensitivity test determined key parameters in predicting uncertainty of extinction probability. Relationships between varying parameters and extinction probabilities are explored through extensive simulations for homogeneous populations and a two-node network. Section 6 provides a summary and discussion of mathematical derivations and simulation results.

2. **Preliminary.**

The next generation matrix approach used to compute R_0 for compartmental models is reviewed here, followed by a review of the multitype branching process approximation used to derive E_0 for corresponding CTMC models.

2.1. **Computation of R_0 using the next generation matrix approach.**

The next generation matrix approach is frequently used to compute R_0. In this section, we briefly review this approach. For more details, we refer to [9, Chapter 5], [33]. For simplicity, let $x = (x_1, \cdots, x_m)^T$, where each x_i stands for compartments that are only related to infected and asymptomatically infected individuals. The original nonlinear system of ODEs including these compartments can be written as

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \mathscr{F} - \mathscr{V}, \tag{1}$$

where $\mathscr{F} = (\mathscr{F}_i)$ and $\mathscr{V} = (\mathscr{V}_i)$ represent new infections and transfer between compartments, respectively. Moreover, $\mathscr{F}_i$ represents the rate at which new infections appear in compartment i, and $\mathscr{V}_i = \mathscr{V}_i^- - \mathscr{V}_i^+$, where $\mathscr{V}_i^-$ (resp. $\mathscr{V}_i^+$) represents the rate at which individuals transfer from (resp. into) compartment i. The Jacobian matrices F representing transmission, and V representing transition are defined as:

$$F = [\frac{\mathscr{F}_i(x^0)}{\partial x_j}], \quad V = [\frac{\partial \mathscr{V}_i(x^0)}{\partial x_j}], \tag{2}$$

where x^0 denotes disease free equilibrium (DFE). Matrix F is nonnegative and V is a nonsingular M-matrix. Recall that an $n \times n$ matrix A is called an M-matrix if it can be be expressed in the form $A = sI - B$, such that matrix B is non-negative, and $s \geq \rho(B)$, the spectral radius of B.

Matrix FV^{-1} is called the next generation matrix. The (i, k) entry of FV^{-1} indicates the expected number of new infections in compartment i produced by the infected individual originally introduced into compartment k, where $i, k = 1, \cdots, m$.

The *basic reproduction number*, R_0, is defined as the spectral radius of FV^{-1}, denoted by $\rho(FV^{-1})$.

2.2. **Deriving E_0 using branching process approximation.** Calculating the probability of disease extinction is one of the most interesting applications of branching process. The branching process may lead to disease extinction or persistence. We are interested in conditions under which a disease may become extinct and the probability for this event to occur. We review the approach of using branching process to compute extinction threshold and extinction probability for multi-type infections.

We refer to [1, 23] for the rest of this section. Let $\overrightarrow{I}(t) = (I_1(t), \cdots, I_n(t))^T : t \in (0, \infty)$ be a set of discrete-valued vector random variables. Assume that individuals of type i produce individuals of type j and that the number of infected individuals produced by type i are independent of the number of infected individuals produced by other individuals of type i or type j for $i, j = 1, \cdots, n, i \neq j$. Additionally, individuals of type i have identical probability generating function (pgf). Let $\{I_{ji}\}_{j=1}^n$ be offspring random variables for type i, where I_{ji} is the number of infected individuals of type j produced by individuals of type i. The probability that one individual of type i produces i_j infected individuals of type j is given as

$$P_i(i_1, \cdots, i_n) = \text{Prob}\{I_{1i} = i_1, \cdots, I_{ni} = i_n\}.$$

The offspring pgf array $(g_1, \cdots, g_n) : [0, 1]^n \to [0, 1]^n$, is defined as

$$g_i(w_1, \cdots, w_n) = \sum_{i_n=0}^{\infty} \cdots \sum_{i_1=0}^{\infty} P_i(i_1, \cdots, i_n) w_1^{i_1} \cdots w_n^{i_n}. \tag{3}$$

Note that a trivial fixed point of $(g_1, \cdots, g_n)$ always exists at $\mathbf{1} = (1, \cdots, 1)$.

We denote by $M = [m_{ij}]_{n \times n}$ the expectation matrix of offspring distribution which is nonnegative, where $m_{ij} := \frac{\partial g_i}{\partial w_j}|_{w=\mathbf{1}} < \infty$ represents the expected number of new infected individuals of type j produced by an individual of type i, where $w = (w_1, \cdots, w_n)$.

The *extinction threshold*, E_0, is defined as the spectral radius of the expectation matrix, denoted by $\rho(M)$.

Recall that (B_0) and (B_1) assumptions in [23] are as follows:

(B_0) g_i is not simple. Here, a function is called simple if it is linear with no constant term.

(B_1) Matrix M is irreducible.

If $E_0 > 1$, under assumptions (B_0) and (B_1), the pgf has at most one fixed point in $(0,1)^n$, denoted by $w^* = (w_1^*, \cdots, w_n^*)$, if extinction array w^* in $(0,1)^n$ exists. In the following, extinction array only refers to $w^* \in (0,1)^n$. If $I_j(0) = i_j$, then disease extinction probability, denoted by P_E, is

$$P_E = \lim_{t\to\infty} \text{Prob}\{\overrightarrow{I}(t) = 0\} = w_1^{*i_1} \cdots w_n^{*i_n} < 1. \tag{4}$$

If $E_0 \leq 1$, then

$$P_E = \lim_{t\to\infty} \text{Prob}\{\overrightarrow{I}(t) = 0\} = 1.$$

3. **SI vector model and SIS host metapopulation model.** In this section, a deterministic vector-host model in which disease transmission dynamics of vectors are described by an SI model, while transmission dynamics of hosts are described by an SIS model. This model is an extension of the vector-host model in [1] to a meta-population model. The basic reproduction number and extinction threshold for corresponding CTMC model are analytically related.

3.1. **The basic reproduction number.** The model for vectors consists of compartment G representing susceptible vectors, and compartment J representing infected vectors. Disease dynamics of hosts are modeled by an SIS model.

$$\begin{aligned}
\frac{\mathrm{d}G_i}{\mathrm{d}t} &= \eta_i - \beta_i G_i I_i/N_i - \sum_{j=1,j\neq i}^{n} \omega_{ji} G_i I_j/N_j - \mu_i G_i \\
\frac{\mathrm{d}J_i}{\mathrm{d}t} &= \beta_i G_i I_i/N_i + \sum_{j=1,j\neq i}^{n} \omega_{ji} G_i I_j/N_j - \mu_i J_i \\
\frac{\mathrm{d}S_i}{\mathrm{d}t} &= \psi_i + \gamma_i I_i - \alpha_i S_i J_i/N_i - \sum_{j=1,j\neq i}^{n} \sigma_{ji} S_i J_j/N_i - d_i S_i \\
\frac{\mathrm{d}I_i}{\mathrm{d}t} &= \alpha_i S_i J_i/N_i + \sum_{j=1,j\neq i}^{n} \sigma_{ji} S_i J_j/N_i - \gamma_i I_i - d_i I_i
\end{aligned} \tag{5}$$

The recruitment rate of vectors (resp. hosts) in node i is η_i (resp. ψ_i) for all $i = 1, \cdots, n$. The total number of hosts in node i is denoted by N_i. The rate of new infections in vectors in node i produced by local hosts and hosts in other nodes are $\beta_i G_i I_i/N_i$ and $\sum_{j=1,j\neq i}^{n} \omega_{ji} G_i I_j/N_j$, respectively. The death rate of susceptible and infected vectors in node i are μG_i and μJ_i, respectively. The rate of host infection in node i produced by local vectors and vectors in other nodes are $\alpha_i S_i J_i/N_i$ and $\sum_{j=1,j\neq i}^{n} \sigma_{ji} S_i J_j/N_i$, respectively. Death rates of susceptible and infected hosts in node i are $d_i S_i$ and $d_i I_i$, respectively. The rate of recovery for hosts in node i is $\gamma_i I_i$.

Since J_i and I_i, $i = 1, \cdots n$ are compartments related only to infected and asymptomatically infected, system of ODEs (5) can be rewritten as

$$\frac{d}{dt}\begin{bmatrix} J_1 & \cdots & J_n & I_1 & \cdots & I_n \end{bmatrix}^T = \mathscr{F} - \mathscr{V},$$

where $\mathscr{F}$ and $\mathscr{V}$ represent new infections and transfer between compartments as (1), respectively. A unique solution at DFE, represented by $(G_i^0, 0, N_i^0, 0)$ exists,

where $G_i^0 = \frac{\eta_i}{\mu_i}$ and $N_i^0 = \frac{\psi_i}{d_i}$. The Jacobian matrices F and V defined in (2) for this model are

$$F = \begin{bmatrix} 0 & \mathcal{A} \\ \mathcal{B} & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \Lambda_1 & 0 \\ 0 & \Lambda_2 \end{bmatrix},$$

where

$$\mathcal{A} = \begin{bmatrix} \hat{\beta}_1 & \hat{\omega}_{21} & \cdots & \hat{\omega}_{n1} \\ \hat{\omega}_{12} & \hat{\beta}_2 & \cdots & \hat{\omega}_{n2} \\ \cdots & \cdots & \ddots & \cdots \\ \hat{\omega}_{1n} & \hat{\omega}_{2n} & \cdots & \hat{\beta}_n \end{bmatrix}, \quad \mathcal{B} = \begin{bmatrix} \alpha_1 & \sigma_{21} & \cdots & \sigma_{n1} \\ \sigma_{12} & \alpha_2 & \cdots & \sigma_{n2} \\ \cdots & \cdots & \ddots & \cdots \\ \sigma_{1n} & \alpha_2 & \cdots & \alpha_n \end{bmatrix}, \tag{6}$$

$$\Lambda_1 = \operatorname{diag}(\mu_1, \cdots, \mu_n), \quad \Lambda_2 = \operatorname{diag}(d_1 + \gamma_1, \cdots, d_n + \gamma_n). \tag{7}$$

Here

$$\hat{\beta}_i = \frac{\beta_i G_i^0}{N_i^0} \quad \text{and} \quad \hat{\omega}_{ij} = \frac{\omega_{ij} G_j^0}{N_i^0}.$$

The notation $\operatorname{diag}(\mu_1, \mu_2, \cdots, \mu_n)$ represents the diagonal matrix with diagonal entries $\mu_1, \cdots, \mu_n$. To calculate R_0, we first prove the following lemma.

Lemma 3.1. *Let A_1, A_2 be square matrices of the same size and $A = \begin{bmatrix} 0 & A_1 \\ A_2 & 0 \end{bmatrix}$, then $\rho(A) = \sqrt{\rho(A_2 A_1)}$.*

Proof. For any $\lambda \neq 0$,

$$|\lambda I - A| = \begin{vmatrix} \lambda I & -A_1 \\ -A_2 & \lambda I \end{vmatrix} = \begin{vmatrix} \lambda I & -A_1 \\ 0 & \lambda I - \frac{A_2 A_1}{\lambda} \end{vmatrix} = |\lambda^2 I - A_2 A_1|. \tag{8}$$

Therefore, $\rho(A) = \sqrt{\rho(A_2 A_1)}$ if $\rho(A_2 A_1) \neq 0$.

If $\rho(A_2 A_1) = 0$, we assume that $\rho(A) \neq 0$. Then there exists a $\lambda' \neq 0$ such that $|\lambda' I - A| = 0$. By (8), $|\lambda'^2 I - A_2 A_1| = 0$ for a nonzero λ', contradicting the assumption that $\rho(A_2 A_1) = 0$. Therefore, $\rho(A) = \sqrt{\rho(A_2 A_1)}$. □

A direct calculation gives $FV^{-1} = \begin{bmatrix} 0 & \mathcal{A}\Lambda_2^{-1} \\ \mathcal{B}\Lambda_1^{-1} & 0 \end{bmatrix}$. By Lemma 3.1, we have the following proposition:

Proposition 1. *The basic reproduction number of the model (5) is*

$$R_0 = \sqrt{\rho(\mathcal{B}\Lambda_1^{-1}\mathcal{A}\Lambda_2^{-1})}. \tag{9}$$

3.2. **The threshold for extinction probability.** In this section, we compute E_0 for corresponding CTMC of model (5). See Table 1 for state transitions and rates.

The offsrping pgf for J_i, given $J_i(0) = 1$, $I_i(0) = 0$, where $i = 1, \cdots, n$, is

$$g_i = \frac{\alpha_i w_i u_i + \sum_{j=1, j\neq i}^n \sigma_{ij} w_i u_j + \mu_i}{\alpha_i + \sum_{j=1, j\neq i}^n \sigma_{ij} + \mu_i};$$

and the offsrping pgf for I_i, given $I_i(0) = 1$, $J_i(0) = 0$, where $i = 1, \cdots, n$, is

$$g_{i+n} = \frac{\hat{\beta}_i u_i w_i + \sum_{j=1, j\neq i}^n \hat{\omega}_{ij} u_i w_j + d_i + \gamma_i}{\hat{\beta}_i + \sum_{j=1, j\neq i}^n \hat{\omega}_{ij} + d_i + \gamma_i}.$$

Hence, the pgfs are

$$g_i(w_1, \cdots, w_n, u_1, \cdots, u_n)$$

Description	State transition $a \to b$	Rate $P(a,b)$
Host birth	$(S,I,G,J) \to (S+1,I,G,J)$	ψ
Death of S	$(S,I,G,J) \to (S-1,I,G,J)$	dS
Host local infection	$(S,I,G,J) \to (S-1,I+1,G,J)$	$\alpha SJ/N$
Host infection by J_j	$(S,I,G,J) \to (S-1,I+1,G,J)$	$\sigma_{ji}S_iJ_j/N_i$
Host recovery	$(S,I,G,J) \to (S+1,I-1,G,J)$	γI
Death of I	$(S,I,G,J) \to (S,I-1,G,J)$	dI
Vector birth	$(S,I,G,J) \to (S,I,G+1,J)$	η
Death of G	$(S,I,G,J) \to (S,I,G-1,J)$	μG
Vector local infection	$(S,I,G,J) \to (S,I,G-1,J+1)$	$\beta GI/N$
Vector infection by I_j	$(S,I,G,J) \to (S,I,G-1,J+1)$	$\omega_{ji}G_iI_j/N_j$
Death of J	$(S,I,G,J) \to (S,I,G,J-1)$	μJ

TABLE 1. State transitions and rates for corresponding continuous-time Markov chain for deterministic model (5) omitting node index i.

$$= \begin{cases} \frac{\alpha_i w_i u_i + \sum_{j=1,j\neq i}^{n} \sigma_{ij} w_i u_j + \mu_i}{\alpha_i + \sum_{j=1,j\neq i}^{n} \sigma_{ij} + \mu_i}, & \text{if } 1 \le i \le n, \\ \frac{\hat{\beta}_k u_k w_k + \sum_{j=1,j\neq k}^{n} \hat{\omega}_{kj} u_k w_j + d_k + \gamma_k}{\hat{\beta}_k + \sum_{j=1,j\neq k}^{n} \hat{\omega}_{kj} + d_k + \gamma_k}, & \text{if } n+1 \le i \le 2n, \end{cases}$$

where $j = 1, \cdots, n$, the index $k = i - n$ for $n+1 \le i \le 2n$.

The expectation matrix M is:

$$M = \begin{bmatrix} \Lambda_3\Lambda_4 & \mathcal{A}\Lambda_5 \\ \mathcal{B}\Lambda_4 & \Lambda_6\Lambda_5 \end{bmatrix}, \tag{10}$$

where $\mathcal{A}, \mathcal{B}$ are the same as those in (6), and

$$\Lambda_3 = \operatorname{diag}(\alpha_1 + \sum_{i\neq 1}\sigma_{1i}, \cdots, \alpha_n + \sum_{i\neq n}\sigma_{ni}), \quad \Lambda_4 = \operatorname{diag}(\frac{1}{C_1}, \cdots, \frac{1}{C_n}),$$

$$\Lambda_6 = \operatorname{diag}(\hat{\beta}_1 + \sum_{i\neq 1}\hat{\omega}_{1i}, \cdots, \hat{\beta}_n + \sum_{i\neq n}\hat{\omega}_{ni}), \quad \Lambda_5 = \operatorname{diag}(\frac{1}{D_1}, \cdots, \frac{1}{D_n}),$$

$$C_i = \alpha_i + \sum_{j\neq i}\sigma_{ij} + \mu_i, \quad D_i = \hat{\beta}_i + \sum_{j\neq i}\hat{\omega}_{ij} + d_i + \gamma_i, \quad \text{for } i = 1, \cdots, n.$$

Note that if both $\mathcal{A}$ and $\mathcal{B}$ are positive matrices, then the assumptions (B_0) and (B_1) in [23] hold for this model.

Lemma 3.2. *Let A_1, A_2 be nonnegative square matrices with the same size such that $\rho(A_2A_1)$ is an eigenvalue of A_2A_1 and Λ, Λ' be nonnegative diagonal matrices such that $0 \le k_1 I \le \begin{bmatrix} \Lambda & 0 \\ 0 & \Lambda' \end{bmatrix} \le k_2 I$ for some real numbers k_1, k_2. Then the spectral radius of $B = \begin{bmatrix} \Lambda & A_1 \\ A_2 & \Lambda' \end{bmatrix}$ satisfies that*

$$\sqrt{\rho(A_2A_1)} + k_1 \le \rho(B) \le \sqrt{\rho(A_2A_1)} + k_2.$$

Proof. Since $0 \le \begin{bmatrix} k_1 I & A_1 \\ A_2 & k_1 I \end{bmatrix} \le B \le \begin{bmatrix} k_2 I & A_1 \\ A_2 & k_2 I \end{bmatrix}$, by Theorem 4 in [35],

$$\rho(\begin{bmatrix} k_1 I & A_1 \\ A_2 & k_1 I \end{bmatrix}) \le \rho(B) \le \rho(\begin{bmatrix} k_2 I & A_1 \\ A_2 & k_2 I \end{bmatrix}). \tag{11}$$

By hypothesis and (8), $\rho(\begin{bmatrix} 0 & A_1 \\ A_2 & 0 \end{bmatrix})$ is an eigenvalue of $\begin{bmatrix} 0 & A_1 \\ A_2 & 0 \end{bmatrix}$. Following Lemma 3.1 and the fact that $|\lambda' + k| < \lambda + k$ for any $k > 0$ if $|\lambda'| < \lambda$,

$$\rho(\begin{bmatrix} k_1 I & A_1 \\ A_2 & k_1 I \end{bmatrix}) = \rho(\begin{bmatrix} 0 & A_1 \\ A_2 & 0 \end{bmatrix}) + k_1 = \sqrt{\rho(A_2 A_1)} + k_1.$$

Similarly, $\rho(\begin{bmatrix} k_2 I & A_1 \\ A_2 & k_2 I \end{bmatrix}) = \sqrt{\rho(A_2 A_1)} + k_2$. Lemma follows (11). □

Remark 1. If both A_1 and A_2 are positive matrices, then $\rho(A_2 A_1)$ is an eigenvalue of $A_2 A_1$ by Perron-Frobenius theorem.

By Lemma 3.2, we have the following proposition:

Proposition 2. *The extinction threshold of model (5) satisfies that*

$$\min_{1\le i\le n}\left(\frac{\alpha_i + \sum_{j=1,j\neq i}^n \sigma_{ij}}{C_i}, \frac{\hat\beta_i + \sum_{j=1,j\neq i}^n \hat\omega_{ij}}{D_i}\right) + \sqrt{\rho(\mathcal{B}\Lambda_4\mathcal{A}\Lambda_5)} \le E_0$$
$$\le \max_{1\le i\le n}\left(\frac{\alpha_i + \sum_{j=1,j\neq i}^n \sigma_{ij}}{C_i}, \frac{\hat\beta_i + \sum_{j=1,j\neq i}^n \hat\omega_{ij}}{D_i}\right) + \sqrt{\rho(\mathcal{B}\Lambda_4\mathcal{A}\Lambda_5)}.$$

3.3. **The relationship between R_0 and E_0.** To obtain a theoretical relationship between R_0 in (9) and E_0, we assume that

$$\frac{\mu_i}{C_i} = k_1 \quad \text{and} \quad \frac{d_i + \gamma_i}{D_i} = k_2, \quad \forall\ i = 1, \cdots, n \tag{12}$$

for constant numbers $k_1, k_2 \in [0, 1]$ throughout this section. The assumption can be interpreted biologically as: the probability of natural death is identical for vectors from each node, and the probability of natural death is identical for hosts from each node. The assumption shall be removed for numerical simulations in the next section.

Theorem 3.3. *Under the assumption (12),*

(1) If $R_0 \le \frac{1-k_2}{1-\sqrt{k_1 k_2}} \le 1$ or $E_0 \le \frac{1-k_2}{1-\sqrt{k_1 k_2}} \le 1$, then $R_0 \le E_0$;

(2) If $R_0 \ge \frac{1-k_1}{1-\sqrt{k_1 k_2}} \ge 1$ or $E_0 \ge \frac{1-k_1}{1-\sqrt{k_1 k_2}} \ge 1$, then $R_0 \ge E_0$.

Proof. Under the assumption (12), $\Lambda_1\Lambda_4 = k_1 I$, $\Lambda_3\Lambda_4 = (1-k_1)I$, $\Lambda_2\Lambda_5 = k_2 I$ and $\Lambda_6\Lambda_5 = (1-k_2)I$, where I is the identity matrix. Therefore, M in (10) can be rewritten as follows,

$$M = \begin{bmatrix} 0 & k_2\mathcal{A}\Lambda_2^{-1} \\ k_1\mathcal{B}\Lambda_1^{-1} & 0 \end{bmatrix} + \begin{bmatrix} (1-k_1)I & 0 \\ 0 & (1-k_2)I \end{bmatrix}.$$

Without loss of generality, we assume that $k_1 < k_2$. By Lemma 3.2 and (9),

$$R_0\sqrt{k_1 k_2} + 1 - k_2 \le E_0 \le R_0\sqrt{k_1 k_2} + 1 - k_1. \tag{13}$$

Following (13),

$$R_0(1-\sqrt{k_1 k_2}) - (1-k_1) \le R_0 - E_0 \le R_0(1-\sqrt{k_1 k_2}) - (1-k_2),$$
$$\tfrac{1}{\sqrt{k_1 k_2}}(E_0(1-\sqrt{k_1 k_2}) - 1 + k_1) \le R_0 - E_0 \le \tfrac{1}{\sqrt{k_1 k_2}}(E_0(1-\sqrt{k_1 k_2}) - 1 + k_2).$$

Theorem follows the above two inequalities. □

Corollary 1. *If the further assumption is made that $k_1 = k_2$ in addition to assumption (12), then $R_0 \le 1$ if and only if $E_0 \le 1$. Moreover, $|R_0 - 1| \ge |E_0 - 1|$.*

Proof. By Theorem 3.3 (1), if $R_0 \leq 1$, then $R_0 \leq E_0$. Assuming that $E_0 > 1$, by Theorem 3.3 (2), $R_0 \geq E_0$, which is a contradiction. Conversely, if $E_0 \leq 1$, then $R_0 \leq 1$ following a similar argument. Hence, $R_0 \leq 1$ if and only if $E_0 \leq 1$. The proof for $|R_0 - 1| \geq |E_0 - 1|$ directly follows Theorem 3.3. □

4. **SEI vector model and SEIR host metapopulation model.** A deterministic model in which vectors are divided into compartments S, E, and I, and hosts are classified into compartments S, E, I, and R is presented. The basic reproduction number for this model and the extinction threshold for corresponding CTMC model are connected.

4.1. **The basic reproduction number.** The following model extends the model in Section 3.1 by adding compartment Z for exposed vectors, and compartment E for exposed hosts. Other terms have identical meanings as corresponding terms in model (5). The rate at which exposed vectors and exposed hosts in node i transfer to infected compartments are $\varphi_i Z_i$ and $\varepsilon_i E_i$, respectively.

$$\begin{aligned}
\frac{\mathrm{d}G_i}{\mathrm{d}t} &= \eta_i - \beta_i G_i I_i/N_i - \sum_{j=1, j\neq i}^{n} \omega_{ji} G_i I_j/N_j - \mu_i G_i \\
\frac{\mathrm{d}Z_i}{\mathrm{d}t} &= \beta_i G_i I_i/N_i + \sum_{j=1, j\neq i}^{n} \omega_{ji} G_i I_j/N_j - \varphi_i Z_i - \mu_i Z_i \\
\frac{\mathrm{d}J_i}{\mathrm{d}t} &= \varphi_i Z_i - \mu_i J_i \\
\frac{\mathrm{d}S_i}{\mathrm{d}t} &= \psi_i - \alpha_i S_i J_i/N_i - \sum_{j=1, j\neq i}^{n} \sigma_{ji} S_i J_j/N_i - d_i S_i \\
\frac{\mathrm{d}E_i}{\mathrm{d}t} &= \alpha_i S_i J_i/N_i + \sum_{j=1, j\neq i}^{n} \sigma_{ji} S_i J_j/N_i - \varepsilon_i E_i - d_i E_i \\
\frac{\mathrm{d}I_i}{\mathrm{d}t} &= \varepsilon_i E_i - \gamma_i I_i - d_i I_i \\
\frac{\mathrm{d}R_i}{\mathrm{d}t} &= \gamma_i I_i - d_i R_i
\end{aligned} \tag{14}$$

Compartments related to infected and asymptomatically infected are Z_i, E_i, J_i and I_i, $i = 1, \cdots, n$. The unique solution at DFE is $(G_i^0, 0, 0, N_i^0, 0, 0, 0)$, where G_i^0 and N_i^0 are the same as those in Section 3.1. The above system of ODEs including these compartments can be rewritten as follows:

$$\frac{d}{dt}\begin{bmatrix} Z_1 & \cdots & Z_n & E_1 \cdots & E_n & J_1 & \cdots & J_n & I_1 & \cdots & I_n \end{bmatrix}^T = \mathscr{F} - \mathscr{V}.$$

where $\mathscr{F}$ and $\mathscr{V}$ represent new infections and transfer between compartments as (1), respectively. The Jacobian matrices F and V at DFE are

$$F = \begin{bmatrix} 0 & 0 & 0 & \mathcal{A} \\ 0 & 0 & \mathcal{B} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \Lambda_7 & 0 & 0 & 0 \\ 0 & \Lambda_8 & 0 & 0 \\ -\Lambda_9 & 0 & \Lambda_1 & 0 \\ 0 & -\Lambda_{10} & 0 & \Lambda_2 \end{bmatrix},$$

where Λ_1 and Λ_2 are given in (7); matrices $\mathcal{A}$ and $\mathcal{B}$ are in Equation (6); and

$$\Lambda_7 = \mathrm{diag}(\varphi_1 + \mu_1, \cdots, \varphi_n + \mu_n), \quad \Lambda_8 = \mathrm{diag}(\varepsilon_1 + d_1, \cdots, \varepsilon_n + d_n),$$

Description	State transition $a \to b$	Rate $P(a,b)$
Host birth	$(S,E,I,R,G,Z,J) \to (S+1,E,I,R,G,Z,J)$	ψ
Death of S	$(S,E,I,R,G,Z,J) \to (S-1,E,I,R,G,Z,J)$	dS
Death of E	$(S,E,I,R,G,Z,J) \to (S,E-1,I,R,G,Z,J)$	dE
Death of I	$(S,E,I,R,G,Z,J) \to (S,E,I-1,R,G,Z,J)$	dI
Death of R	$(S,E,I,R,G,Z,J) \to (S,E,I,R-1,G,Z,J)$	dR
Host local infection	$(S,E,I,R,G,Z,J) \to (S-1,E+1,I,R,G,Z,J)$	$\alpha SJ/N$
Host infection by J_j	$(S,E,I,R,G,Z,J) \to (S-1,E+1,I,R,G,Z,J)$	$\sigma_{ji}SJ_j/N$
Host recovery	$(S,E,I,R,G,Z,J) \to (S,E,I-1,R+1,G,Z,J)$	γI
Host Latent to infectious	$(S,E,I,R,G,Z,J) \to (S,E-1,I+1,R,G,Z,J)$	εE
Vector birth	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G+1,Z,J)$	η
Death of G	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G-1,Z,J)$	μG
Death of Z	$(S,E,I,R,G,Z,J) \to S,E,I,R,G,Z-1,J)$	μZ
Death of J	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G,Z,J-1)$	μJ
Vector local infection	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G-1,Z+1,J)$	$\beta GI/N$
Vector infection by I_j	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G-1,Z+1,J)$	$\omega_{ji}GI_j/N_j$
Vector Latent to infectious	$(S,E,I,R,G,Z,J) \to (S,E,I,R,G,Z-1,J+1)$	φZ

TABLE 2. State transitions and rates for corresponding continuous-time Markov chain for deterministic model (14) omitting node index i.

$$\Lambda_9 = \mathrm{diag}(\varphi_1, \cdots, \varphi_n), \quad \Lambda_{10} = \mathrm{diag}(\varepsilon_1, \cdots, \varepsilon_n).$$

By a direct calculation,

$$FV^{-1} = \begin{bmatrix} 0 & \mathcal{A}\Lambda_2^{-1}\Lambda_{10}\Lambda_8^{-1} & 0 & \mathcal{A}\Lambda_2^{-1} \\ \mathcal{B}\Lambda_1^{-1}\Lambda_9\Lambda_7^{-1} & 0 & \mathcal{B}\Lambda_1^{-1} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

Following Lemma 3.1,

Proposition 3. *The basic reproduction number of the model (14) is*

$$R_0 = \sqrt{\rho(\mathcal{B}\Lambda_1^{-1}\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_2^{-1}\Lambda_{10}\Lambda_8^{-1})}. \tag{15}$$

4.2. **The threshold for extinction probability.** State transitions and rates for corresponding CTMC of model (14) are listed in Table 2.

The offspring pgf for Z_i, given $Z_i = 1, E_i = J_i = I_i = 0$, where $i = 1, \cdots n$ is

$$g_i = \frac{\varphi_i u_i + \mu_i}{\varphi_i + \mu_i};$$

and the offspring pgf for E_i, given $E_i = 1, Z_i = J_i = I_i = 0$, is

$$g_{i+n} = \frac{\varepsilon_i u_{i+n} + d_i}{\varepsilon_i + d_i};$$

and the offspring pgf for J_i, given $J_i = 1, Z_i = J_i = I_i = 0$, is

$$g_{i+2n} = \frac{\alpha_i u_i w_{i+n} + \sum_{j=1,\neq i}^{n} \sigma_{ij} u_i w_{j+n} + \mu_i}{\alpha_i + \sum_{j=1,\neq i}^{n} \sigma_{ij} + \mu_i};$$

and the offspring pgf for I_i, given $E_i = 1, Z_i = J_i = I_i = 0$, is

$$g_{i+3n} = \frac{\hat{\beta}_i u_{i+n} w_i + \sum_{j=1,j\neq i}^{n} \hat{\omega}_{ij} u_{i+n} w_j + d_i + \gamma_i}{\hat{\beta}_i + \sum_{j=1,j\neq i}^{n} \hat{\omega}_{ij} + d_i + \gamma_i}.$$

Hence, the pgfs are:

$$g_i(w_1, \cdots, w_{2n}, u_1, \cdots, u_{2n}) = \begin{cases} \frac{\varphi_i u_i + \mu_i}{\varphi_i + \mu_i}, & \text{if } 1 \le i \le n, \\ \frac{\varepsilon_k u_i + d_k}{\varepsilon_k + d_k}, & \text{if } n+1 \le i \le 2n, \\ \frac{\alpha_p u_p w_{p+n} + \sum_{j=1,\neq p}^{n} \sigma_{pj} u_p w_{j+n} + \mu_p}{\alpha_p + \sum_{j=1,\neq p}^{n} \sigma_{pj} + \mu_p}, & \text{if } 2n+1 \le i \le 3n, \\ \frac{\hat{\beta}_q u_{q+n} w_q + \sum_{j=1,j\neq q}^{n} \hat{\omega}_{qj} u_{q+n} w_j + d_q + \gamma_q}{\hat{\beta}_q + \sum_{j=1,j\neq q}^{n} \hat{\omega}_{qj} + d_q + \gamma_q}, & \text{if } 3n+1 \le i \le 4n, \end{cases}$$

where the indexes $k = i - n$ for $n+1 \le i \le 2n$, $p = i - 2n$ for $2n+1 \le i \le 3n$, and $q = i - 3n$ for $3n+1 \le i \le 4n$.

The expectation matrix M is:

$$M = \begin{bmatrix} 0 & 0 & 0 & \mathcal{A}\Lambda_5 \\ 0 & 0 & \mathcal{B}\Lambda_4 & 0 \\ \Lambda_9\Lambda_7^{-1} & 0 & I - \Lambda_1\Lambda_4 & 0 \\ 0 & \Lambda_{10}\Lambda_8^{-1} & 0 & I - \Lambda_2\Lambda_5 \end{bmatrix}.$$

Similarly, the assumptions (B_0) and (B_1) in [23] hold for this model if both $\mathcal{A}$ and $\mathcal{B}$ are positive matrices. By Lemma 3.2, as well as Remark 1, we have the following proposition:

Proposition 4. *The extinction threshold of the model (14) satisfies that*

$$\sqrt[4]{\rho(\Lambda_{10}\Lambda_8^{-1}\mathcal{B}\Lambda_4\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_5)} \le E_0 \le \sqrt[4]{\rho(\Lambda_{10}\Lambda_8^{-1}\mathcal{B}\Lambda_4\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_5)} + \max_{1\le i\le n}\left(\frac{\alpha_i + \sum_{j\neq i}\sigma_{ij}}{C_i}, \frac{\hat{\beta}_i + \sum_{j\neq i}\hat{\omega}_{ij}}{D_i}\right).$$

4.3. **The relationship between R_0 and E_0.** In this section, we assume that (12) holds and $k_1 < k_2$. Under the assumption (12), we shall give a relationship between R_0 and E_0.

Lemma 4.1. *Let A_1, A_2 be square matrices with the same size and $B = \begin{bmatrix} 0 & A_1 \\ A_2 & kI \end{bmatrix}$ with $k \ge 0$. If $\rho(A_2A_1)$ is an eigenvalue of A_2A_1, then*

$$\rho(B) = \frac{1}{2}(k + \sqrt{k^2 + 4\rho(A_2A_1)}).$$

Proof. If $k = 0$, lemma is reduced to Lemma 3.1. We now assume that $k > 0$. For any $\lambda \neq 0$, we have

$$\begin{aligned} |\lambda I - B| &= \begin{vmatrix} \lambda I & -A_1 \\ -A_2 & (\lambda - k)I \end{vmatrix} = \begin{vmatrix} \lambda I & -A_1 \\ 0 & (\lambda - k)I - \frac{A_2A_1}{\lambda} \end{vmatrix} \\ &= |(\lambda^2 - k\lambda)I - A_2A_1|. \end{aligned} \tag{16}$$

If $\lambda = 0$, then $\lambda - k \neq 0$. By similar calculation as we did in (16), we still have $|\lambda I - B| = |(\lambda^2 - k\lambda)I - A_2A_1|$. From this identity, $\lambda^2 - k\lambda$ is an eigenvalue of A_2A_1 if λ is an eigenvalue of B, i.e., given an eigenvalue μ of A_2A_1, the root of the equation $\lambda^2 - k\lambda = \mu$ is an eigenvalue of B. Therefore,

$$\begin{aligned}\rho(B) &= \max\{|\lambda| \mid \lambda^2 - k\lambda = \mu \text{ for some eigenvalue } \mu \text{ of } A_2A_1\}\\ &= \max\{\frac{1}{2}|k \pm \sqrt{k^2+4\mu}| \text{ for some eigenvalue } \mu \text{ of } A_2A_1\}.\end{aligned}$$

Since $\rho(A_2A_1)$ is one of eigenvalues of A_2A_1, $\frac{1}{2}(k+\sqrt{k^2+4\rho(A_2A_1)})$ is an eigenvalue of B. By the following inequality

$$|k \pm \sqrt{k^2+4\mu}| \leq k + \sqrt{|k^2+4\mu|} \leq k + \sqrt{k^2+4|\mu|} \leq k + \sqrt{k^2+4\rho(A_2A_1)},$$

we have $\rho(B) = \frac{1}{2}(k + \sqrt{k^2+4\rho(A_2A_1)})$. □

By using Lemma 4.1, we have the following theorem.

Theorem 4.2. *Under assumption (12),*

(1) If $\sqrt{R_0} \leq \frac{1-k_2}{2(1-\sqrt[4]{k_1k_2})} \leq 1$ *or* $E_0 \leq \frac{1-k_2}{2(1-\sqrt[4]{k_1k_2})} \leq 1$, *then* $\sqrt{R_0} \leq E_0$;

(2) If $\sqrt{R_0} \geq \frac{1-k_1}{1-\sqrt[4]{k_1k_2}} \geq 1$ *or* $E_0 \geq \frac{1-k_1}{1-\sqrt[4]{k_1k_2}} \geq 1$, *then* $\sqrt{R_0} \geq E_0$.

Proof. Under assumption (12), we have

$$\begin{bmatrix} 0 & A_1 \\ A_2 & (1-k_2)I \end{bmatrix} \leq M \leq \begin{bmatrix} 0 & A_1 \\ A_2 & (1-k_1)I \end{bmatrix},$$

where $A_1 = \begin{bmatrix} 0 & \mathcal{A}\Lambda_5 \\ \mathcal{B}\Lambda_4 & 0 \end{bmatrix}$ and $A_2 = \begin{bmatrix} \Lambda_9\Lambda_7^{-1} & 0 \\ 0 & \Lambda_{10}\Lambda_8^{-1} \end{bmatrix}$. By Theorem 4 in [35] and Lemma 4.1, we have

$$\frac{1-k_2+\sqrt{(1-k_2)^2+4\rho(A_2A_1)}}{2} \leq E_0 \leq \frac{1-k_1+\sqrt{(1-k_1)^2+4\rho(A_2A_1)}}{2}. \tag{17}$$

By Lemma 3.1, (15) and the fact that $\rho(AB) = \rho(BA)$ for any square matrices A and B, we have

$$\begin{aligned}\rho(A_2A_1) &= \sqrt{\rho(\Lambda_{10}\Lambda_8^{-1}\mathcal{B}\Lambda_4\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_5)} = \sqrt{\rho(\mathcal{B}\Lambda_4\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_5\Lambda_{10}\Lambda_8^{-1})}\\ &= \sqrt{k_1k_2\rho(\mathcal{B}\Lambda_1^{-1}\Lambda_9\Lambda_7^{-1}\mathcal{A}\Lambda_2^{-1}\Lambda_{10}\Lambda_8^{-1})} = \sqrt{k_1k_2}R_0.\end{aligned}$$

By (17), we have

$$\sqrt{R_0}\sqrt[4]{k_1k_2} + \tfrac{1-k_2}{2} \leq E_0 \leq \sqrt{R_0}\sqrt[4]{k_1k_2} + 1 - k_1.$$

Hence,

$$\begin{aligned}&\sqrt{R_0}(1-\sqrt[4]{k_1k_2}) - (1-k_1) \leq \sqrt{R_0} - E_0 \leq \sqrt{R_0}(1-\sqrt[4]{k_1k_2}) - \tfrac{1-k_2}{2},\\ &\tfrac{1}{\sqrt[4]{k_1k_2}}(E_0(1-\sqrt[4]{k_1k_2}) - 1 + k_1) \leq \sqrt{R_0} - E_0 \leq \tfrac{1}{\sqrt[4]{k_1k_2}}(E_0(1-\sqrt[4]{k_1k_2}) - \tfrac{1-k_2}{2}).\end{aligned}$$

Theorem follows from these two inequalities. □

Unlike Corollary 1, we can not obtain a similar result directly from Theorem 4.2. Fortunately, we still have a similar result.

Proposition 5. *If a further assumption is made that* $k_1 = k_2$ *besides assumption (12), then* $R_0 \leq 1$ *if and only if* $E_0 \leq 1$. *Furthermore, if* $R_0 > 1$, *then* $\sqrt{R_0 - 1} \geq E_0 - 1 \geq 0$.

Parameter	Description	Range	Dimension	Source
α	Contact rate: mosquitoes to humans	$0.010 - 0.27$	1/day	[8]
β	Contact rate: humans to mosquitoes	$0.072 - 0.64$	1/day	[8]
μ	Per capita death rate for mosquitoes	$0.020 - 0.27$	1/day	[8]
d	Per capita death rate for humans	$0.000027 - 0.00014$	1/day	[8]
γ	Per capita recovery rate for humans	$0.0014 - 0.0017$	1/day	[8]
η	Mosquito recruitment rate	$1 - 5$	1/day	Assume
ψ	Human recruitment rate	$1 - 60$	1/day	Assume

TABLE 3. Parameters of the malaria metapopulation model.

Proof. If $k_1 = k_2 = k$, by (17), we have $E_0 = \frac{1-k+\sqrt{(1-k)^2+4kR_0}}{2}$.

If $R_0 < 1$, we have

$$E_0 < \frac{1-k+\sqrt{(1-k)^2+4k}}{2} = \frac{1-k+\sqrt{(1+k)^2}}{2} = 1.$$

Similarly, if $R_0 \geq 1$, then $E_0 \geq 1$. This proves the first part.

For the second part, if $R_0 > 1$, we have

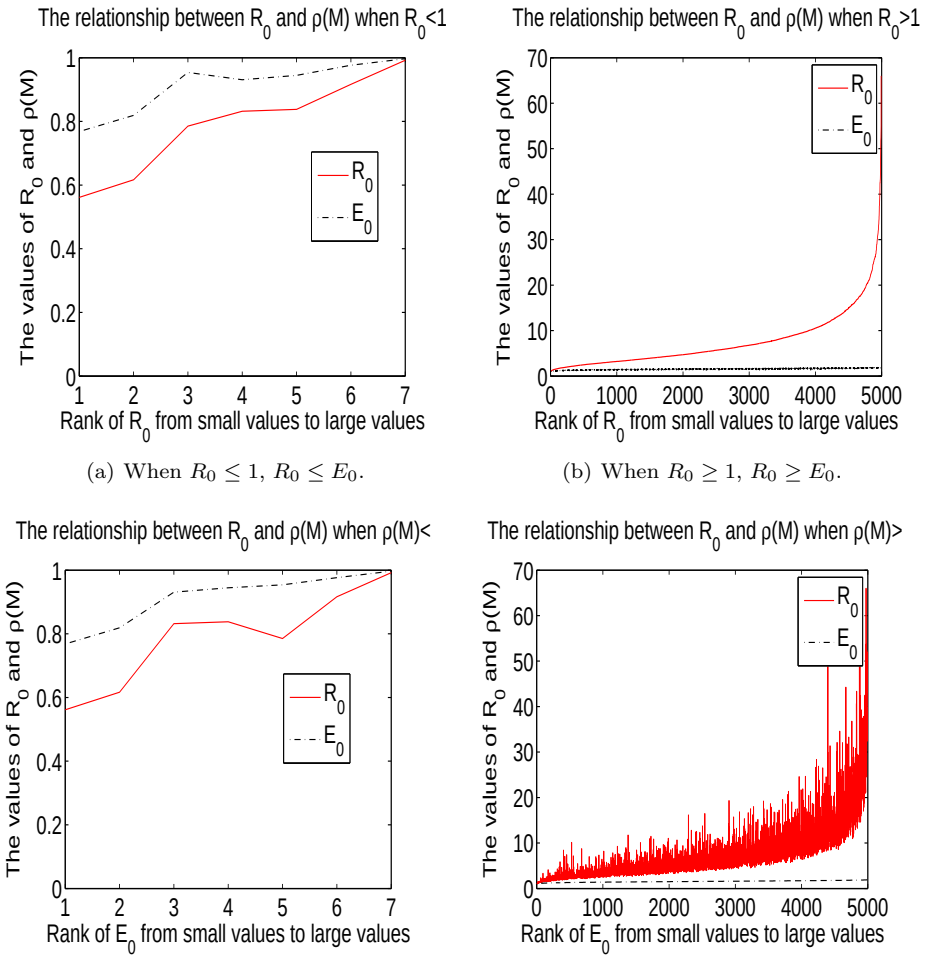
$$E_0 - 1 = \frac{-(1+k)+\sqrt{(1+k)^2+4k(R_0-1)}}{2} \leq \sqrt{k(R_0-1)} \leq \sqrt{R_0-1}.$$

This finishes the proof. □

5. **Numerical results.** We show numerically general relations between R_0 and E_0 for two models on heterogeneous networks with different weights between different links. Trends of parameters varying with extinction array are summarized.

5.1. **Numerical results on relations between R_0 and E_0.** Model (5) is applied to study thresholds for malaria transmission through numerical simulations. Five thousand realizations with parameters uniformly distributed within ranges listed in Table 3 on a four-node network give rise to R_0 ranging from 0.7668 to 63.8111 and E_0 from 0.8965 to 1.9140. The ranges of R_0 and E_0 vary with the number of nodes of a network and the assumed ranges of vector (host) recruitment rates with ranges of other parameters fixed. The values of R_0 are sorted from small to large values in Figure 1(a) and 1(b), and E_0 are ranked from small values to large values in Figure 1(c) and 1(d). The largest value of E_0 is 0.9980 when all values of R_0 are smaller than 1 and $R_0 \leq E_0$, as shown in Figure 1(a). The smallest value of E_0 is 1.003 when all values of R_0 are greater than 1 and $R_0 \geq E_0$, as shown in Figure 1(b). The largest value of R_0 is 0.9947 when all values of E_0 are smaller than 1, as shown in Figure 1(c). The smallest value of R_0 is 1.006 when all values of E_0 are greater than 1, as shown in Figure 1(d). The value of E_0 is not monotonically increasing with the increase of R_0, as shown Figure 1(a) and 1(b). Similarly, R_0 fluctuates as E_0 increases, as shown in Figure 1(c) and 1(d).

Model (14) is applied to numerical examine the relationship between R_0 and E_0 for Rift Valley fever. See Table 4 for descriptions and ranges of parameters. Five



(a) When $R_0 \leq 1$, $R_0 \leq E_0$.

(b) When $R_0 \geq 1$, $R_0 \geq E_0$.

(c) When $E_0 \leq 1$, $R_0 \leq E_0$.

(d) When $E_0 \geq 1$, $R_0 \geq E_0$.

FIGURE 1. Relationships between R_0 and E_0 for malaria model.

thousand realizations produce R_0 ranging between 0.2289 and 54.5086 and E_0 from 0.6757 to 1.9763. The values of R_0 are ordered from small to large magnitudes in Figure 2(a) and 2(b), and the values of E_0 are ordered from small to large values in Figure 2(c) and 2(d). The largest value of E_0 is 1 when all values of R_0 are smaller than 1, and $\sqrt{R_0} \leq E_0$, as shown in Figure 2(a). The smallest value of E_0 is 1.005 when all values of R_0 are greater than 1, and $\sqrt{R_0} \geq E_0$, as shown in Figure 2(b). The largest value of R_0 is 0.9998 when all values of E_0 are smaller than 1, and $\sqrt{R_0} \geq E_0$, as shown in Figure 2(c). The smallest value of R_0 is 1.008 when all values of E_0 are greater than 1, and $\sqrt{R_0} \geq E_0$, as shown in Figure 2(d). When R_0 increases, E_0 does not always increase, as shown in Figure 2(a) and 2(b). Similarly, R_0 fluctuates as E_0 increases, as shown in Figure 2(c) and 2(d).

5.2. **Trends of extinction array with varying parameters.** Consistent trends of w^* are observed by numerical simulations for homogeneous populations and a

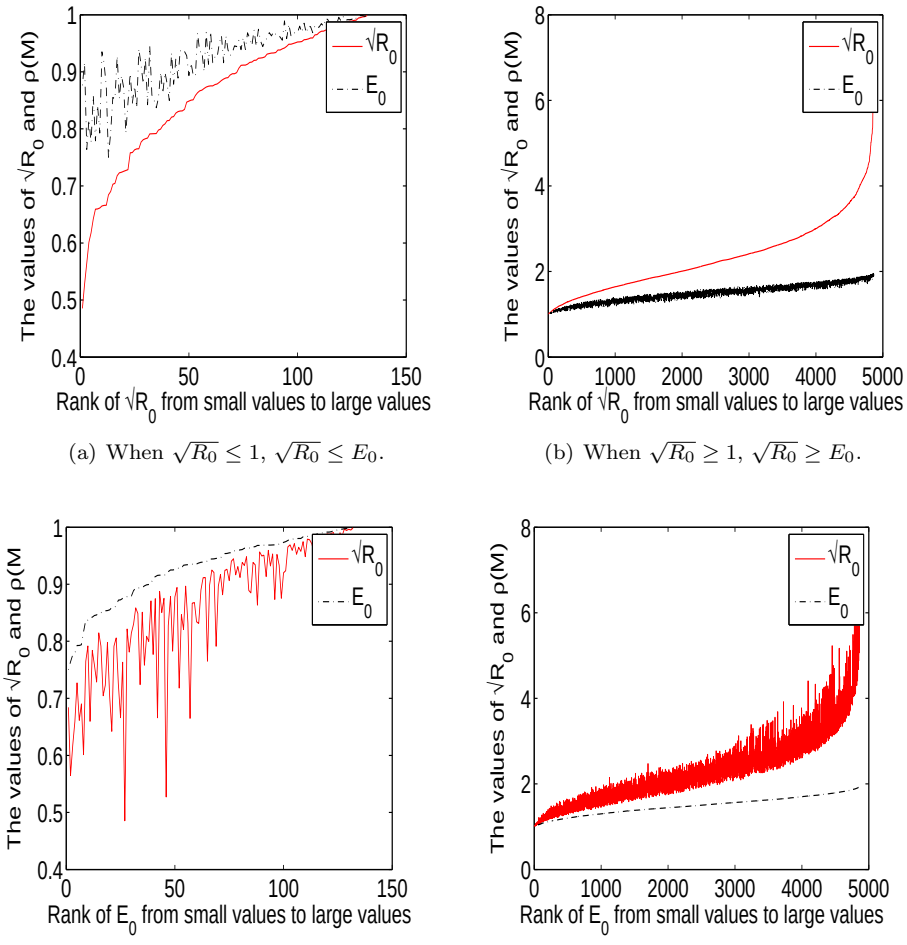
Parameter	Description	Range	Dimension	Source
α	Contact rate: mosquito to livestock	$0.0021 - 0.2762$	1/day	[7, 13, 15, 20, 25, 31, 32]
β	Contact rate: livestock to mosquitoes	$0 - 0.32$	1/day	[7, 13, 15, 20, 25, 30]
$1/\mu$	Longevity of mosquitoes	$3 - 60$	1/day	[4, 21, 25]
$1/d$	Longevity of livestock	$360 - 3600$	1/day	[26]
$1/\gamma$	Recover rate in livestock	$2 - 5$	1/day	[11]
$1/\varphi$	Incubation period in mosquitoes	$4 - 8$	days	[31]
$1/\epsilon$	Incubation period in livestock	$2 - 6$	days	[24]
η	Mosquito recruitment rate	$1 - 500$	1/day	Assume
ψ	Livestock recruitment rate	$1 - 10$	1/day	Assume

TABLE 4. Parameters of the Rift Valley fever metapopulation model.

two-node network for Model (14). Table 5 lists three different values for each parameter and corresponding extinction array for homogeneous populations as an example. Table 6 shows trends of extinction array by varying one parameter at a time, keeping other parameters fixed and $E_0 > 1$ for homogeneous populations and a two-node network. If at least one entry of extinction array increases and others remain constant, then we say that the array increases. The extinction array w^* decreases with the increase of contact rates from local vectors and vectors in other nodes to local hosts, contact rates from local hosts and hosts in other nodes to local vectors, death rates of hosts, recruitment rates of vectors, and incubation rates of vectors and hosts, whereas, w^* increases with the increase of vector death rates, host recovery rates, and host recruitment rates.

6. **Discussions.** The basic reproduction number, R_0, for deterministic vector-host models and thresholds for extinction probabilities, E_0 for corresponding CTMC models are analytically and numerically connected. For model (5), our analysis show that $R_0 \leq 1$, if and only if $E_0 \leq 1$, and $|R_0 - 1| \geq |E_0 - 1|$ under certain assumptions. Numerical simulations for a malaria model on heterogeneous networks with different number of nodes show that Corollary 1 holds without any assumptions. For model (14), analytical results show that $R_0 < 1$ if and only if $E_0 < 1$, and $\sqrt{R_0 - 1} \geq E_0 - 1 \geq 0$ by the same assumption in (12). Extensive numerical simulation results for a Rift Valley fever model on networks with various number of nodes show that Proposition 5 holds without any assumptions.

Conjecture 1. *Theorems 3.3, 4.2, Corollary 1, and Proposition 5 hold without assumption (12), i.e., $R_0 \leq 1$ if and only if $E_0 \leq 1$ for both models (5) and (14), besides, $|R_0 - 1| \geq |E_0 - 1|$ for model (5), and $|\sqrt{R_0 - 1}| \geq |E_0 - 1|$ for model (14) without assumption (12).*



(a) When $\sqrt{R_0} \leq 1$, $\sqrt{R_0} \leq E_0$.

(b) When $\sqrt{R_0} \geq 1$, $\sqrt{R_0} \geq E_0$.

(c) When $E_0 \leq 1$, $\sqrt{R_0} \leq E_0$.

(d) When $E_0 \geq 1$, $\sqrt{R_0} \geq E_0$.

FIGURE 2. Relationships between R_0 and E_0 for Rift Valley fever model.

The first part, $R_0 \leq 1$ if and only if $E_0 \leq 1$ was proven by Allen and van den Driessche under the assumption (16) in [2], i.e., $(F-V)^T = W(M-I)$, where F and V are Jacobian matrices defined in (2), M is a mean matrix of offspring distribution defined in Section 2.2, I is the identity matrix, and W is a positive diagonal matrix with each entry w_i representing the rate parameter at which lifespan of group i are exponentially distributed for $i = 1, \cdots n$ [23]. This assumption holds for model (5) and model (14) if M is symmetric.

Consistent trends in the extinction array w^* while changing one parameter through numerical simulations is helpful in deducing trends of extinction probability and possible interventions for vector-borne diseases. According to Equation (4), the probability of disease extinction is monotonically increasing (decreasing) with the increase (decrease) of the extinction array when the initial number of infection is fixed. The following biological interpretations of disease extinction or persistence are in terms of fixed initial number of infections. If contact rates from vectors to hosts

Changing parameter	$(w_1^*, w_2^*, u_1^*, u_2^*)$
$\alpha = 0.0601$	$(0.9965, 0.9978, 0.9961, 0.9978)$
$\alpha = 0.0766$	$(0.8648, 0.9212, 0.8467, 0.9212)$
$\alpha = 0.0781$	$(0.8546, 0.9158, 0.8352, 0.9158)$
$\beta = 0.0639$	$(0.9158, 0.9824, 0.9046, 0.9824)$
$\beta = 0.1026$	$(0.6623, 0.8967, 0.6173, 0.8966)$
$\beta = 0.1426$	$(0.5448, 0.8224, 0.4841, 0.8223)$
$\mu = 1/60$	$(0.1955, 0.4961, 0.1419, 0.4956)$
$\mu = 1/59$	$(0.1996, 0.5016, 0.1453, 0.5110)$
$\mu = 1/56$	$(0.2127, 0.5188, 0.1565, 0.5182)$
$d = 1/3477$	$(0.4621, 0.7398, 0.3904, 0.7395)$
$d = 1/3370$	$(0.4554, 0.7312, 0.3828, 0.7310)$
$d = 1/3311$	$(0.4518, 0.7265, 0.3787, 0.7262)$
$\gamma = 1/5$	$(0.4247, 0.6877, 0.3480, 0.6874)$
$\gamma = 1/4$	$(0.4698, 0.7491, 0.3992, 0.7488)$
$\gamma = 1/3$	$(0.5451, 0.8226, 0.4845, 0.8224)$
$\epsilon = 1/6$	$(0.4700, 0.7493, 0.3994, 0.7489)$
$\epsilon = 1/4$	$(0.4698, 0.7491, 0.3992, 0.7488)$
$\epsilon = 1/2$	$(0.4697, 0.7489, 0.3990, 0.7488)$
$\varphi = 1/8$	$(0.5494, 0.7784, 0.4293, 0.7782)$
$\varphi = 1/7$	$(0.5312, 0.7715, 0.4218, 0.7712)$
$\varphi = 1/6$	$(0.5119, 0.7643, 0.4142, 0.7641)$
$\eta = 19$	$(0.5412, 0.8195, 0.4801, 0.8193)$
$\eta = 76$	$(0.5264, 0.8069, 0.4632, 0.8066)$
$\eta = 482$	$(0.2907, 0.3169, 0.1961, 0.3162)$
$\psi = 1$	$(0.4698, 0.7491, 0.3992, 0.7488)$
$\psi = 2$	$(0.6859, 0.9123, 0.6553, 0.9122)$
$\psi = 3$	$(0.9219, 0.9838, 0.9115, 0.9838)$

TABLE 5. The extinction array changes with one parameter within the range at a time for homogeneous populations, while keeping other parameters fixed and $E_0 > 1$ for model (14). Fixed parameters are: $\alpha = 0.2$, $\beta = 0.19$, $\mu = 1/30$, $d = 1/3600$, $\gamma = 1/4$, $\epsilon = 1/2$, $\varphi = 1/4$, $\eta = 100$, $\psi = 1$ in this example. Same trends are obtained with various sets of fixed parameters.

Increasing parameter	$(w_1^*, \cdots, w_n^*, u_1^*, \cdots, u_n^*)$
α_i, β_i, d_i, ε_i, φ_i, η_i, σ_{ij}, ω_{ij} $(i, j = 1, \cdots, n, i \neq j)$	decreases
μ_i, γ_i, ψ_i $(i = 1, \cdots, n)$	increases

TABLE 6. Summary of trends for extinction array changing with one parameter at a time, while keeping other parameters fixed and $E_0 > 1$ for model (14) for homogeneous populations and a two-node network throughout various simulations.

(α, σ), or those from hosts to vectors (β, ω) increase, the probability for the disease to persist is higher. If death rates of hosts (d) increase, the number of vectors is relatively dominant. Consequently, the disease is more likely to persist. Similarly, growing vector recruitment rates (η) increase probability for disease persistence. The higher incubation rates in vectors (φ) or in hosts (ϵ) lead to faster vector or

host infections, such that the disease is prone to persist. On the contrary, increasing death rates of vectors (μ) may reduce rates of host infection, and, ultimately, may increase the likelihood of disease extinction. Increasing recovery rates of hosts (γ) may reduce the number of infections, such that probability of disease extinction increases. Increasing recruitment rate of hosts (ψ) may reduce vector infection rates and increase probability of disease extinction.

The findings show that extinction probability of vector-borne diseases may increase by properly controlling vector and host population size, and promptly detecting and applying treatment for hosts. Analytical and numerical results shed light on deriving relationships between R_0 and E_0, as well as connections between varying parameters and increasing extinction probabilities for many other vector-borne diseases transmitted among heterogeneous works. In summary, the resulting mathematical derivations and numerical simulations facilitate understanding thresholds for the spread of vector-borne diseases, as well as provide novel insights into disease prevention, mitigation and control strategies.

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REFERENCES

[1] L. J. Allen and G. E. Lahodny Jr, Extinction thresholds in deterministic and stochastic epidemic models, *Journal of Biological Dynamics*, **6** (2012), 590–611.

[2] L. J. Allen and P. van den Driessche, Relations between deterministic and stochastic thresholds for disease extinction in continuous- and discrete-time infectious disease models, *Mathematical Biolosciences*, **243** (2013), 99–108.

[3] J. Arino and P. van den Driessche, The basic reproduction number in a multi-city compartmental epidemic model, *Lecture Notes in Control and Information Sciences*, **294** (2003), 135–142.

[4] M. Bates, The natural history of mosquitoes, *American Journal of Public Health*, **39** (1949), p1592.

[5] D. Bisanzio, L. Bertolotti, L. Tomassone, G. Amore, C. Ragagli, A. Mannelli, M. Giacobini and P. Provero, Modeling the spread of vector-borne diseases on bipartite networks, *PloS ONE*, **5** (2010), e13796.

[6] T. Britton and D. Lindenstrand, Epidemic modelling: Aspects where stochasticity matters, *Mathematical Biosciences*, **222** (2009), 109–116.

[7] D. V. Canyon, J. L. K. Hii and R. Muller, The frequency of host biting and its effect on oviposition and survival in Aedes aegypti (Diptera: Culicidae), *Bulletin of Entomological Research*, **89** (1999), 35–39.

[8] N. Chitnis, J. M. Hyman and J. M. Cushing, Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model, *Bulletin of Mathematical Biology*, **70** (2008), 1272–1296.

[9] O. Diekmann and J. A. P. Heesterbeek, *Mathematical Epidemiology of Infectious Diseases*, Wiley, Chichester, 2000.

[10] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations, *Journal of Mathematical Biology*, **28** (1990), 365–382.

[11] B. J. Erasmus and J. A. W. Coetzer, The symptomatology and pathology of Rift Valley fever in domestic animals, *Contributions to Epidemiology and Biostatistics*, **3** (1981), 77–82.

[12] N. G. Gratz, Emerging and resurging vector-borne diseases, *Annual Review of Entomology*, **44** (1999), 51–75.

[13] R. O. Hayes, C. H. Tempelis, A. D. Hess and W. C. Reeves, Mosquito host preference studies in Hale County, Texas, *American Journal of Tropical Medicine and Hygiene*, **22** (1973), 270–277.

[14] G. R. Hosack, P. A. Rossignol and P. V. den Driessche, The control of vector-borne disease epidemics, *Journal of Theoretical Biology*, **255** (2008), 16–25.

[15] C. J. Jones and J. E. Lloyd, Mosquitos feeding on sheep in southeastern Wyoming, *Journal of the American Mosquito Control Association*, **1** (1985), 530–532.

[16] R. Kao, Networks and models with heterogeneous population structure in epidemiology, in *Network Science* (eds. E. Estrada, M. Fox, D. Higham and G. Oppo), Springer, (2010), 51–84.

[17] M. J. Keeling and P. Rohani, *Modeling Infectious Diseases in Humans and Animals*, Princeton University Press, 2008.

[18] G. E. Lahodny Jr and L. J. Allen, Probability of a disease outbreak in stochastic multipatch epidemic models, *Bulletin of Mathematical Biology*, **75** (2013), 1157–1180.

[19] A. L. Lloyd, J. Zhang and A. M. Root, Stochasticity and heterogeneity in host-vector models, *Journal of the Royal Society Interface*, **4** (2007), 851–863.

[20] L. A. Magnarelli, Host feeding patterns of Connecticut mosquitos (Diptera: Culicidae), *American Journal of Tropical Medicine and Hygiene*, **26** (1977), 547–552.

[21] C. G. Moore, R. G. McLean, C. J. Mitchell, R. S. Nasci, T. F. Tsai, C. H. Caslisher, A. A. Marfin, P. S. Moorse and D. J. Gubler, *Guidelines for Arbovirus Surveillance Programs in the United States*, Centers for Disease Control and Prevention, 1993.

[22] F. Natale, A. Giovannini, L. Savini, D. Palma, L. Possenti, G. Fiore and P. Calistri, Network analysis of Italian cattle trade patterns and evaluation of risks for potential disease spread, *Preventive Veterinary Medicine*, **92** (2009), 341–350.

[23] S. Pénisson, *Conditional Limit Theorems for Multitype Branching Processes and Illustration in Epidemiological Risk Analysis*, PhD thesis, Institut für Mathematik der Unversität Potsdam, Germany, 2010.

[24] C. J. Peters and K. J. Linthicum, Rift Valley fever, in *Handbook of Zoonoses* (ed. G. Beran), 2^{nd} edition, Section B: Viral, CRC Press, Inc., Boca Raton, Fl, (1994), 125–138.

[25] H. D. Pratt and C. G. Moore, *Vector-borne Disease Control: Mosquitoes of Public Health Importance and Their Control*, U.S. Department of Health and Human Services, Atlanta, GA, 1993.

[26] O. M. Radostits, *Herd Healthy: Food Animal Production Medicine*, Saunders, 2001.

[27] M. G. Roberts and J. A. P. Heesterbeek, A new method for estimating the effort required to control an infectious disease, *Proceedings of the Royal Society B: Biological Sciences*, **270** (2003), 1359–1364.

[28] R. Ross, Some quantitative studies in epidemiology, *Nature*, **87** (1911), 466–467.

[29] Z. Shuai, J. A. P. Heesterbeek and P. van den Driessche, Extending the type reproduction number to infectious disease control targeting contacts between types, *Journal of mathematical biology*, **67** (2013), 1067–1082.

[30] M. J. Turell and C. L. Bailey, Transmission studies in mosquitoes (Diptera: Culicidae) with disseminated Rift Valley fever virus infections, *Journal of Medical Entomology*, **24** (1987), 11–18.

[31] M. J. Turell, C. L. Bailey and J. R. Beaman, Vector competence of a Houston, Texas strain of Aedes Albopictus for Rift Valley fever virus, *Journal of the American Mosquito Control Association*, **4** (1988), 94–96.

[32] M. J. Turell, M. E. Faran, M. Cornet and C. L. Bailey, Vector competence of senegalese Aedes fowleri (Diptera: Culicidae) for Rift Valley fever virus, *Journal of Medical Entomology*, **25** (1988), 262–266.

[33] P. van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Mathematical biosciences*, **180** (2002), 29–48.

[34] M. C. Vernon and M. J. Keeling, Representing the UK's cattle herd as static and dynamic networks, *Proceedings of the Royal Society B: Biological Sciences*, **276** (2009), 469–476.

[35] L. Xue and C. Scoglio, The network level reproduction number for infectious diseases with both vertical and horizontal transmission, *Mathematical Biosciences*, **243** (2013), 67–80.

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E-mail address: lxue@ksu.edu
E-mail address: caterina@k-state.edu