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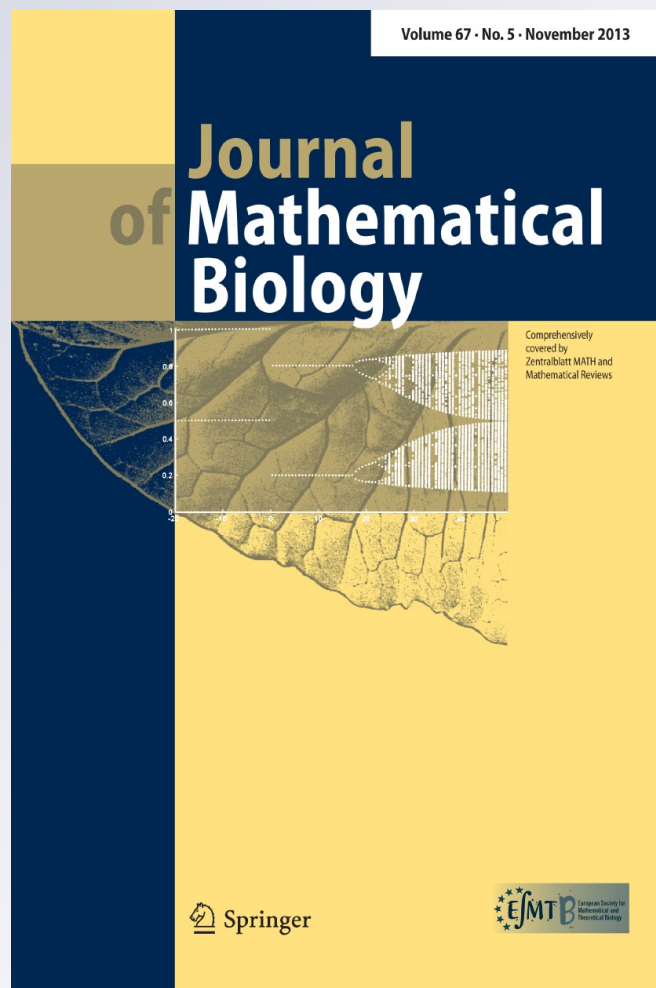**Abstract**   A new quantity called the target reproduction number is defined to measure control strategies for infectious diseases with multiple host types such as waterborne, vector-borne and zoonotic diseases. The target reproduction number includes as a special case and extends the type reproduction number to allow disease control targeting contacts between types. Relationships among the basic, type and target reproduction numbers are established. Examples of infectious disease models from the literature are given to illustrate the use of the target reproduction number.

1 Introduction

The basic reproduction number $\mathcal{R}_0$ is a well-known threshold quantity in mathematical epidemiology determining whether an infectious disease dies out after introduction

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into a fully susceptible population of hosts (Anderson and May 1991; Diekmann and Heesterbeek 2000). In a heterogeneous population where the individuals can be subdivided into n epidemiologically different infected host types, it is a standard approach to regard growth or decline of the infected population in terms of a generation process, letting the $n \times n$ next-generation matrix $K = (k_{ij})$ represent the transmission and spread of the infection from one generation to the next (Diekmann and Heesterbeek 2000). The entry k_{ij} of K is defined as the expected number of new cases that an infected individual of type j causes among the susceptible individuals of type i, in a fully susceptible population. Then $\mathcal{R}_0$ is the spectral radius of K (Diekmann and Heesterbeek 2000; Diekmann et al. 2010; van den Driessche and Watmough 2002.

If a prevention, intervention or (more generally) control strategy, such as vaccination, social distancing, treatment, is aimed at all host individuals, regardless of their epidemiological type, then the value of $\mathcal{R}_0$ is also a measure of the strength of the control needed to prevent outbreaks from occurring in a given population (Anderson and May 1991; Diekmann and Heesterbeek 2000). If a control strategy is aimed at particular host types only, such as vector control, culling of wildlife reservoir hosts, vaccination of domestic animals in a system with wildlife reservoirs, then the so-called type reproduction number $\mathcal{T}$ takes over the role of $\mathcal{R}_0$ in that its value has a direct relation with control effort needed (Roberts and Heesterbeek 2003; Heesterbeek and Roberts 2007). This quantity measures the strength of control needed when targeting a subset of the types of host available for a given infectious disease agent. In most cases, a strategy that reduces the susceptibility for infection of individuals of host type 1, say, influences all entries of the next-generation matrix that represent potentially infectious contacts between an infected of any type j and a susceptible of type 1. In other words, this strategy influences all entries of K in its first row. A strategy that influences infectivity of infected individuals of type 1, influences all entries in the first column of K, i.e., the entries describing all infections caused by infected individuals of type 1.

While control targeted at specific types of individuals already covers a wider range of possible interventions in a heterogeneous host population, compared to those evaluated in terms of the value of $\mathcal{R}_0$ only, there are situations where measures are targeted at still smaller subsets of individuals. Specifically, control can be targeted not at types per se, but rather at interactions between types. Such measures would not necessarily influence susceptibility or infectivity of individuals of affected types, but could target contacts between two or more specific types. For example, think of strategies that decrease the possibilities for transmission of Nipah virus among pigs, while not influencing contacts among bats and humans; see, for example, Pulliam et al. (2012) and references therein. Or think of preventing contact with a contaminated environment for children in cholera outbreaks. Such control strategies are not affecting entire columns or rows of K, but rather specific entries of K.

For such strategies, the same general idea can be used as for the type reproduction number, which is based on a transformation of the next-generation matrix K by projection matrices that regulate the restriction to the types affected by the targeted control. By extending this idea, individual entries or sets of such entries can be singled out for control. Here we show how this can be achieved. We call the resulting quantity the *target* reproduction number, to distinguish its restriction to specific interactions

between types, rather than all interactions involving a given type of host. The type reproduction number, in its single and multiple-type form (Roberts and Heesterbeek 2003; Heesterbeek and Roberts 2007), is then naturally a special case of this quantity. Because the fundamental principle is the same, we retain the basic letter $\mathcal{T}$ to denote both quantities.

We first define the target reproduction number and show that similar relations hold as for the type reproduction number. We present an interpretation for the target reproduction number which is also similar, but add to that by putting this interpretation in the terminology of weighted graphs, an interpretation that could lead to interesting new insight. Finally, examples with models from the literature appropriate for cholera, bluetongue, Nipah virus, bovine tuberculosis in possums, a sexually transmitted infection with a core group, and diseases spread in a spatially heterogeneous population are given to illustrate the use of the target reproduction number.

2 Target reproduction number

The definition of the target reproduction number is completely analogous to that of the type reproduction number in Roberts and Heesterbeek (2003), Heesterbeek and Roberts (2007), and basically adds more specific projection matrices to single out more specific targets for control. Assume that several entries of the $n \times n$ next-generation matrix K are targeted. Let S be the set of all targeted entries, denoted by $S = \{(i_1, j_1), \ldots, (i_m, j_m)\}$. Define two index sets $S_1 = \{i_1, \ldots, i_m\}$ and $S_2 = \{j_1, \ldots, j_m\}$, representing the first and second indices of targeted entries in S. Then the *target reproduction number* $\mathcal{T}_S$ with respect to the target set S is defined as

$$\mathcal{T}_S = \rho(E_{S_1} P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1} E_{S_1}), \tag{2.1}$$

provided the spectral radius $\rho(K - P_{S_1} K P_{S_2}) < 1$, where I is the $n \times n$ identity matrix, E_{S_1} is an $n \times n$ matrix with entry $e_{kk} = 1$ if $k \in S_1$ and $e_{rs} = 0$ for all other entries, and P_{S_1}, P_{S_2} are $n \times n$ projection matrices on set S_1, S_2, respectively (e.g., for projection matrix $P_{S_1} = (p_{ij})$, $p_{kk} = 1$ if $k \in S_1$ and $p_{rs} = 0$ for all other entries). If $\rho(K - P_{S_1} K P_{S_2}) > 1$, then $\mathcal{T}_S$ is not defined since the disease cannot be eradicated by targeting only S. Notice that $E_{S_1} = P_{S_1}$ and $E_{S_1} P_{S_1} = P_{S_1}$, which implies that all indices of nonzero rows and columns of matrix $E_{S_1} P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1} E_{S_1}$ are included in S_1. It follows that $\mathcal{T}_S = \rho(P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1})$, since E_{S_1} can be dropped as the rows and columns not in S_1 do not contribute to the spectral radius.

When only one entry of K is targeted (i.e., $S = \{(i, j)\}$), a more meaningful notation $\mathcal{T}_{ij}$ is used to denote the target reproduction number $\mathcal{T}_S$. It follows that

$$\mathcal{T}_{ij} = e_i^T P_i K P_j (I - K + P_i K P_j)^{-1} e_i, \tag{2.2}$$

provided the spectral radius $\rho(K - P_i K P_j) < 1$. Here e_i is the i-th unit vector in $\mathbb{R}^n$, and P_i, P_j are projection matrices. If all the entries in a certain row of K are targeted, i.e., $S = \{(i, 1), (i, 2), \ldots, (i, n)\}$, then $S_1 = \{i\}$ and $S_2 = \{1, 2, \ldots, n\}$. Thus the target reproduction number $\mathcal{T}_S$ in (2.1) becomes the type reproduction number (Roberts and Heesterbeek 2003; Heesterbeek and Roberts 2007)

$$\mathcal{T}_i = e_i^T P_i K (I - K + P_i K)^{-1} e_i. \tag{2.3}$$

Similarly, the type reproduction numbers with respect to several targeted rows of K can also be obtained from (2.1) with an appropriate target set containing all entries in these rows. In particular, if all entries in K are targeted (i.e., $S = \{(i, j) \mid 1 \leq i, j \leq n\}$), then $\mathcal{T}_S = \mathcal{R}_0$.

The following result establishes the relation between $\mathcal{R}_0$ and $\mathcal{T}_S$ with a general target set S.

Theorem 2.1 *Suppose that K is irreducible and $\rho(K - P_{S_1} K P_{S_2}) < 1$. Then, $\mathcal{T}_S < 1$ if and only if $\mathcal{R}_0 < 1$; and $\mathcal{T}_S = 1$ if and only if $\mathcal{R}_0 = 1$.*

The target reproduction number can be used to measure the effort required to control infectious diseases. Biologically, if a proportion more than $1 - 1/\mathcal{T}_S$ of the entries in S can be reduced, then the disease can be eradicated.

Theorem 2.2 *Suppose that K is irreducible and $\rho(K - P_{S_1} K P_{S_2}) < 1$. Let K_c be a controlled next-generation matrix formed by replacing entry k_{ij} in K by $k_{ij}/\mathcal{T}_S$ whenever $(i, j) \in S$. Then $\rho(K_c) = 1$.*

The proofs of Theorems 2.1 and 2.2 are provided in the Appendix.

3 Interpretations for target reproduction number

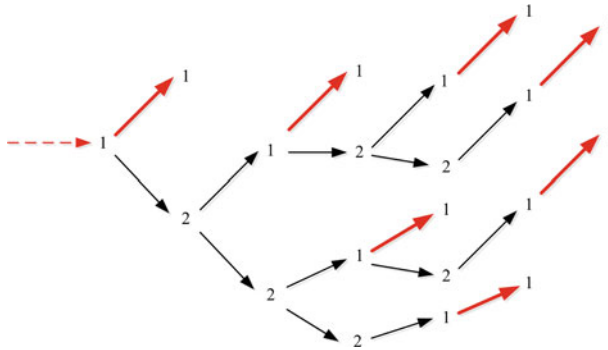### 3.1 Interpretation in terms of tree diagram

In order to understand the biological meaning of target reproduction numbers, a 2×2 next-generation matrix $K = \begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix}$ is considered. By targeting one entry, it follows from (2.2) that

$$\mathcal{T}_{11} = \frac{k_{11}(1 - k_{22})}{1 - k_{22} - k_{12}k_{21}} \qquad \text{provided} \quad k_{22} + k_{12}k_{21} < 1,$$

$$\mathcal{T}_{12} = \mathcal{T}_{21} = \frac{k_{12}k_{21}}{(1 - k_{11})(1 - k_{22})} \qquad \text{provided} \quad k_{11} < 1, \ k_{22} < 1,$$

and

$$\mathcal{T}_{22} = \frac{k_{22}(1 - k_{11})}{1 - k_{11} - k_{12}k_{21}} \qquad \text{provided} \quad k_{11} + k_{12}k_{21} < 1.$$

Notice that $\mathcal{T}_{12} = \mathcal{T}_{21}$, which means that the same effort is required to eradicate the disease when targeting at the $(1, 2)$ or $(2, 1)$ entry in K. For heterosexually transmitted infections or vector-host diseases, $k_{11} = k_{22} = 0$, so $\mathcal{T}_{12} = k_{12}k_{21} = \mathcal{R}_0^2$.

Fig. 1 The tree diagram for $\mathcal{T}_{11}$

To give an interpretation of target reproduction numbers, rewrite $\mathcal{T}_{11}$ as follows

$$
\begin{aligned}
\mathcal{T}_{11} &= k_{11} \frac{1}{1 - \frac{k_{12}k_{21}}{1-k_{22}}} \\
&= k_{11}[1 + k_{12}k_{21}(1 + k_{22} + k_{22}^2 + \cdots) + k_{12}^2 k_{21}^2 (1 + k_{22} + k_{22}^2 + \cdots)^2 + \cdots] \\
&= k_{11} + k_{21}k_{12}k_{11} + k_{21}k_{22}k_{12}k_{11} + k_{21}k_{22}^2 k_{12}k_{11} + (k_{21}k_{12})^2 k_{11} \\
&\quad + 2k_{21}k_{22}k_{12}k_{21}k_{12}k_{11} + \cdots
\end{aligned}
$$

in which each term corresponds to one path of the tree diagram starting with type 1 and ending with an arc from type 1 to type 1 (no intermediate arc from type 1 to type 1), see Fig. 1. Here k_{ij} corresponds to the arc from type j to type i; biologically, it represents the infection passed from host type j to host type i. Similarly, rewrite $\mathcal{T}_{12}$ as follows

$$
\begin{aligned}
\mathcal{T}_{12} &= k_{12}k_{21} \frac{1}{(1-k_{11})(1-k_{22})} \\
&= k_{12}k_{21}(1+k_{11}+k_{11}^2+\cdots)(1+k_{22}+k_{22}^2+\cdots) \\
&= k_{21}k_{12}+k_{11}k_{21}k_{12}+k_{21}k_{22}k_{12}+k_{11}^2 k_{21}k_{12}+k_{11}k_{21}k_{22}k_{12}+k_{21}k_{22}^2 k_{12}+\cdots
\end{aligned}
$$

where each term corresponds to one path of the tree diagram starting with type 1 ending with an arc from type 2 to type 1 (no intermediate arc from type 2 to type 1), see Fig. 2. In general, the terms in $\mathcal{T}_{ij}$ correspond to paths that start with type i and end with an arc from type j to type i (no intermediate arc from type j to type i) in the tree diagram.

For the 2×2 next-generation matrix K as above, choose the target set as $S = \{(1, 1), (1, 2)\}$, and thus $S_1 = \{1\}$ and $S_2 = \{1, 2\}$. By definition, $E_{S_1} = P_{S_1} = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$, and $P_{S_2} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$. Algebraic calculations using (2.1) give $\mathcal{T}_S = \rho(E_{S_1} P_{S_1} K P_{S_2} (I -$
$K + P_{S_1} K P_{S_2})^{-1} E_{S_1}) = \rho\left(\begin{bmatrix} k_{11} + \frac{k_{12}k_{21}}{1-k_{22}} & 0 \\ 0 & 0 \end{bmatrix}\right) = k_{11} + \frac{k_{12}k_{21}}{1-k_{22}}$ provided $k_{22} < 1$,
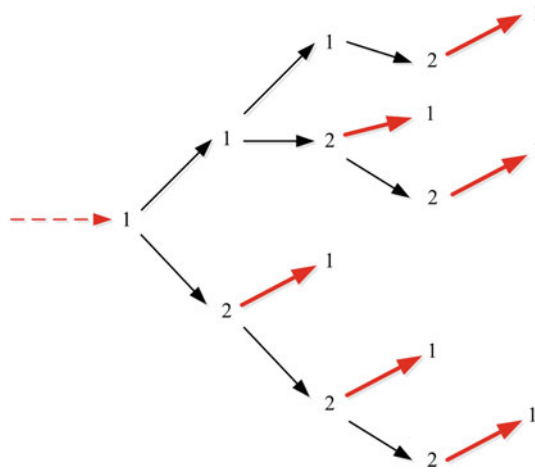
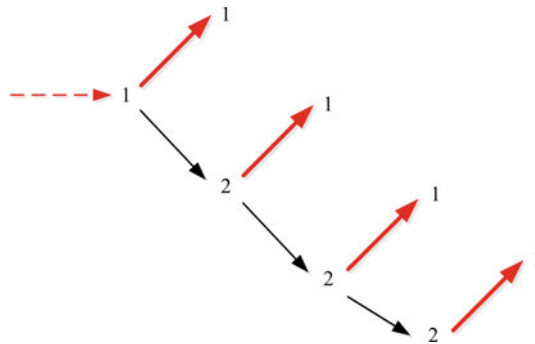**Fig. 2** The tree diagram for $\mathcal{T}_{12}$

Fig. 3 The tree diagram for $\mathcal{T}_S$ with $S = \{(1, 1), (1, 2)\}$

which agrees with the type reproduction number defined in Roberts and Heesterbeek (2003), Heesterbeek and Roberts (2007). Notice that each term on the right hand side of

$$\mathcal{T}_S = k_{11} + k_{12}k_{21}(1 + k_{22} + k_{22}^2 + \cdots)$$

corresponds to one path of the tree diagram shown in Fig. 3.

Let $U = \{(1, 1), (2, 1)\}$, $V = \{(1, 1), (2, 2)\}$, and $W = \{(1, 2), (2, 1)\}$. Then

$$\mathcal{T}_U = \rho\left(\begin{bmatrix} k_{11} & \frac{k_{11}k_{12}}{1-k_{22}} \\ k_{21} & \frac{k_{12}k_{21}}{1-k_{22}} \end{bmatrix}\right) = k_{11} + \frac{k_{12}k_{21}}{1 - k_{22}} = \mathcal{T}_S$$

provided $k_{22} < 1$; this suggests that there are some relations between $\mathcal{T}_S$ and $\mathcal{T}_U$ (see Theorem 4.2 for more details). Also,

$$\mathcal{T}_V = \rho\left(\begin{bmatrix} \frac{k_{11}}{1-k_{12}k_{21}} & \frac{k_{11}k_{12}}{1-k_{12}k_{21}} \\ \frac{k_{21}k_{22}}{1-k_{12}k_{21}} & \frac{k_{22}}{1-k_{12}k_{21}} \end{bmatrix}\right) = \frac{k_{11} + k_{22} + \sqrt{(k_{11} - k_{22})^2 + k_{11}k_{12}k_{21}k_{22}}}{2(1 - k_{12}k_{21})}$$

provided $k_{12}k_{21} < 1$; and

$$\mathcal{T}_W = \rho\left(\begin{bmatrix} 0 & \frac{k_{12}}{1-k_{22}} \\ \frac{k_{21}}{1-k_{11}} & 0 \end{bmatrix}\right) = \sqrt{\frac{k_{12}k_{21}}{(1-k_{11})(1-k_{22})}}$$

provided $k_{11} < 1$ and $k_{22} < 1$. Note that each matrix entry (i, j) can be expanded in terms of walks from j to i that contain exactly one arc (not repeated) corresponding to entries in the target set.

3.2 Interpretation in terms of walks in digraph

Although the interpretations of target reproduction numbers in terms of tree diagrams shown for the case $n = 2$ hold for general cases as well, an alternative and equivalent interpretation in terms of walks on digraph can work better for larger dimensions. Let $\mathcal{G}$ be the *weighted digraph* associated with the $n \times n$ next-generation matrix K; that is, an arc $j \to i$ from vertex j to vertex i in $\mathcal{G}$ exists iff $k_{ij} > 0$ and its weight is equal to k_{ij}. A (directed) *walk* $i \to \cdots \to j$ from vertex i to vertex j in $\mathcal{G}$ is a subgraph of $\mathcal{G}$ consisting of $m + 1$ vertices $i = i_1, i_2, \ldots, i_m, i_{m+1} = j$ and a sequence of m arcs $i = i_1 \to i_2, i_2 \to i_3, \ldots, i_{m-1} \to i_m, i_m \to i_{m+1} = j$; the *length* of this walk is defined as m and the *weight* of the walk is equal to the product $k_{i_2,i_1}k_{i_3,i_2}\cdots k_{i_m,i_{m-1}}k_{i_{m+1},i_m}$. The walk $i \to \cdots \to j$ is *closed* if $i = j$. For our purpose, the empty graph (consisting of no vertices or arcs) is considered as a trivial walk from an arbitrary vertex to another arbitrary vertex (these two vertices could be the same, thus the empty graph is also a closed walk); the length of the trivial walk is 0 and the weight is defined as 1. Let A be a set of arcs in $\mathcal{G}$, then the subgraph $\mathcal{G}\backslash A$ is formed from the digraph $\mathcal{G}$ after deleting all arcs in A. We refer the reader to Harary (1972), West (1996) for detailed discussions on digraphs and walks.

By (2.2), $\mathcal{T}_{ij}$ is equal to the (i, i) entry of matrix $P_i K P_j (I - K + P_i K P_j)^{-1}$, and thus is equal to the product of k_{ij} and the (j, i) entry of the matrix $(I - K + P_i K P_j)^{-1} = I + (K - P_i K P_j) + (K - P_i K P_j)^2 + \cdots$, provided that $\rho(K - P_i K P_j) < 1$. Notice that the (j, i) entry of $I + (K - P_i K P_j) + (K - P_i K P_j)^2 + \cdots$ is the sum of weights of all walks (of any length) from vertex i to vertex j in digraph $\mathcal{G}\backslash A$, where $A = \{j \to i\}$ corresponds to the targeted entry (i, j). Therefore, $\mathcal{T}_{ij}$ is the sum of weights of all closed walks (of any length) in $\mathcal{G}$ that contain arc $j \to i$ exactly once. Note that Fig. 1 (Fig. 2) gives all paths corresponding to closed walks in the digraph that contain arc $1 \to 1$ (arc $2 \to 1$, respectively) exactly once.

For a target set S containing more than one element, if $S_1 = \{i\}$ contains only one element, then the rank of matrix $E_{S_1} P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1} E_{S_1}$ is equal to 1. For this case, each term in $\mathcal{T}_S$ can be interpreted as a path of the tree diagram that starts with type i and ends with an arc from type j to type i if $(i, j) \in S$ (with no intermediate arc from type j to type i nor including other arcs corresponding to entries in S); see, for example, Fig. 3. Alternatively, $\mathcal{T}_S$ is the sum of weights of all closed walks in the weighted digraph $\mathcal{G}$ associated with K that contain arc $j \to i$ exactly once if $(i, j) \in S$ but no other arcs corresponding to entries in S.

In general, if $S_1 = \{i_1, i_2, \ldots, i_m\}$ contains m elements, then the matrix $E_{S_1} P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1} E_{S_1}$ contains a nonzero $m \times m$ block, with all zeros outside the block. This nonzero block has both row and column indices given by $i_1, i_2, \ldots, i_m$. Thus, the target reproduction number $\mathcal{T}_S$ is the spectral radius of this nonzero block, i.e., an $m \times m$ matrix, in which the (i_s, i_t) entry is the sum of weights of all walks from vertex i_t to vertex i_s in $\mathcal{G}$ that contain exactly one arc (not repeated) corresponding to entries in S.

4 Relationships among reproduction numbers

In this section we study the relationships among target reproduction numbers, type reproduction numbers and the basic reproduction number.

A (directed) *cycle* $\mathcal{C}$ is a nontrivial closed walk with all vertices distinct (except the first and last). A weighted digraph $\mathcal{G}$ is said to be *weight balanced* (e.g., see Li and Shuai 2010; Kolotilina 1993) if for any given cycle $\mathcal{C}$ in $\mathcal{G}$, the weight of $\mathcal{C}$ is equal to the weight of the reverse of $\mathcal{C}$, constructed by reversing the direction of all arcs in $\mathcal{C}$. If $K = K^T$, then the associated digraph $\mathcal{G}$ is weight balanced. If a weighted digraph contains only cycles of lengths 1 or 2, then it is weight balanced.

Suppose that the weighted digraph $\mathcal{G}$ associated with a next-generation matrix K is weight balanced. Then the weight of any given closed walk in $\mathcal{G}$ is the same as the weight of the reverse of the closed walk. Hence, each term (i.e., the weight of a closed walk containing arc $j \to i$ exactly once) in $\mathcal{T}_{ij}$ corresponds and is equal to one term in $\mathcal{T}_{ji}$ by reversing the direction of all arcs in the closed walk. Therefore, the following result holds and establishes the relationships between $\mathcal{T}_{ij}$ and $\mathcal{T}_{ji}$.

Theorem 4.1 *Suppose that K is irreducible and that the weighted digraph $\mathcal{G}$ associated with K is weight balanced. Then $\mathcal{T}_{ij} = \mathcal{T}_{ji}$, whenever it is well defined.*

If the weight balance condition in Theorem 4.1 fails, then in general, $\mathcal{T}_{ij} \neq \mathcal{T}_{ji}$ (see Sect. 5.3 for an example).

Let $S^T = \{(j, i) \mid \forall (i, j) \in S\}$ be the transpose of a target set S. The following result establishes the relationship between $\mathcal{T}_S$ and $\mathcal{T}_{S^T}$, generalizing Theorem 4.1 from targeting only one entry to a set of entries. The proof is given in the Appendix.

Theorem 4.2 *Suppose that K is irreducible and that the weighted digraph $\mathcal{G}$ associated with K is weight balanced. Then $\mathcal{T}_S = \mathcal{T}_{S^T}$, whenever it is well defined.*

Given two target sets, S and U, we say that the control strategy U is *stronger* than the control strategy S if $S \subset U$. The following result (the proof is given in the Appendix) shows that less effort is required to control diseases when a stronger control strategy is applied.

Theorem 4.3 *Suppose that K is irreducible. Assume that $S \subset U$, and that both $\mathcal{T}_S$ and $\mathcal{T}_U$ are well defined. Then, either $1 < \mathcal{T}_U < \mathcal{T}_S$, or $\mathcal{T}_S = \mathcal{T}_U = 1$, or $\mathcal{T}_S < \mathcal{T}_U < 1$.*

Let Ω be the target set including all entries of K, that is, $\Omega = \{(i, j) \mid i, j = 1, 2, \ldots, n\}$. Then $\mathcal{T}_\Omega = \mathcal{R}_0$. The following result, which is a special case of Theorem 4.3 by setting $U = \Omega$, establishes the relationships between the basic reproduction number and target/type reproduction number.

Theorem 4.4 *Suppose that K is irreducible and $S \subset \Omega$. Let $\mathcal{T}_S$ be the target/type reproduction number with respect to the target set S. Then, either $1 < \mathcal{R}_0 < \mathcal{T}_S$, or $\mathcal{T}_S = \mathcal{R}_0 = 1$, or $\mathcal{T}_S < \mathcal{R}_0 < 1$.*

Theorem 4.4 provides a complete answer to the relationships among reproduction numbers, generalizing and extending the earlier result for the case that K has order 2 in Allen and Lahodny (2012, Section 3.1). The result of Theorem 4.4 also establishes the relationships between reproduction numbers that were observed numerically in Chow et al. (2011) for a multigroup disease model with group-targeted vaccination strategies.

One final comment on the relationship between the target and the type reproduction number is relevant. Calculating the target reproduction number from K might be rephrased as calculating a type reproduction number for a larger matrix related to K by expanding the number of types or states-at-infection (Diekmann et al. 2010) that define K and its dimension. We do not explore this further here.

5 Applications

In this section we consider possible applications of target reproduction numbers in controlling infectious diseases.

5.1 Waterborne disease

Waterborne diseases such as cholera and salmonellosis can be transmitted directly by person-to-person contact or indirectly via contaminated water. A waterborne disease model has recently been proposed in Bani-Yaghoub et al. (2011) that incorporates the free-living pathogen growing in the water. The next-generation matrix for the model can be written as follows:

$$K = \begin{bmatrix} \dfrac{\beta S_0}{d} & \dfrac{\lambda S_0}{\delta} \\[2mm] \dfrac{\xi}{d} & \dfrac{b}{\delta} \end{bmatrix},$$

where β and λ are coefficients for direct and indirect transmissions, respectively, S_0 is the number of susceptible individuals without presentation of the infection, d and δ represent the removal rates of infectious individuals and the pathogen, respectively, ξ represents the pathogen shedding rate of infectious individuals, and b represents the growth rate of the pathogen in the environment. Therefore, the $(1, 1)$ entry represents the direct transmission, the $(1, 2)$ entry represents the indirect transmission, the $(2, 1)$ entry describes that infectious individuals shed the pathogen into the water, and the $(2, 2)$ entry represents the pathogen growth in the water. Different disease control strategies are discussed below.

Vaccination   Assume that the public health department decides to vaccinate the host population. Then the target set is $S = \{(1, 1), (1, 2)\}$, and the target reproduction number with respect to S (i.e., the type reproduction number targeting the host type 1) from (2.1) is $\mathcal{T}_S = \mathcal{T}_1 = \frac{\beta S_0}{d} + \frac{\lambda \xi S_0}{d(\delta-b)}$ provided $b < \delta$.

Human sanitation There are several major control mechanisms recommended by the WHO. One is hygienic disposal of human faeces, and thus the target set is $S = \{(2, 1)\}$. Another control mechanism is providing an adequate supply of safe drinking water and good food hygiene/cooking, thus the target set is $S = \{(1, 2)\}$. Using the formula derived in Sect. 3.1, the target reproduction number for each mechanism is $\mathcal{T}_{12} = \mathcal{T}_{21} = \frac{\lambda \xi S_0}{(d - \beta S_0)(\delta - b)}$ provided $\beta S_0 < d$ and $b < \delta$.

Isolation Isolation can be used to reduce the direct person-to-person transmission. The target set is $S = \{(1, 1)\}$, and the target reproduction number is $\mathcal{T}_{11} = \frac{\beta S_0 (\delta - b)}{d\delta - bd - \lambda \xi S_0}$ provided $bd + \lambda \xi S_0 < d\delta$.

Pathogen sanitation Suppose that the growth rate of the pathogen in the water can be reduced by sanitation. Then the target set is $S = \{(2, 2)\}$ and the corresponding target reproduction number is $\mathcal{T}_{22} = \frac{b(d - \beta S_0)}{d\delta - \beta \delta S_0 - \lambda \xi S_0}$ provided $\beta \delta S_0 + \lambda \xi S_0 < d\delta$.

5.2 Bluetongue disease

Bluetongue is a viral disease of ruminants such as cattle and sheep and is transmitted by midges. A bluetongue model has been recently proposed in Gourley et al. (2011) that includes midges as vectors, and cattle and sheep as hosts. The next-generation matrix for the ODE bluetongue model (Gourley et al. 2011, Section 4.2) has the form

$$K = \begin{bmatrix} 0 & k_{12} & k_{13} \\ k_{21} & 0 & 0 \\ k_{31} & 0 & 0 \end{bmatrix},$$

in which k_{12} and k_{13} represent the transmission from sheep and cattle to midges, respectively, while k_{21} and k_{31} represent the transmission from midges to sheep and cattle. If the transmission between sheep and midges can be reduced or cut off by intervention strategies such as isolation, vaccination or treatment, then the target set is $S = \{(1, 2), (2, 1)\}$. Calculations using (2.1) show that $\mathcal{T}_S = \sqrt{\frac{k_{12}k_{21}}{1 - k_{13}k_{31}}}$ provided $k_{13}k_{31} < 1$. If only one-way transmission can be reduced (i.e., k_{12} or k_{21}), then the target reproduction number becomes $\mathcal{T}_{12} = \mathcal{T}_{21} = \frac{k_{12}k_{21}}{1 - k_{13}k_{31}}$ provided $k_{13}k_{31} < 1$, which agrees with the type reproduction number $\mathcal{T}_2$ in Gourley et al. (2011). Similarly, $\mathcal{T}_{13} = \mathcal{T}_{31} = \frac{k_{13}k_{31}}{1 - k_{12}k_{21}}$ provided $k_{12}k_{21} < 1$, agreeing with $\mathcal{T}_3$ in Gourley et al. (2011). Notice that the weighted digraph associated with K is weight balanced, thus $\mathcal{T}_{ij} = \mathcal{T}_{ji}$, by Theorem 4.1.

5.3 Waterborne disease in two human groups

Consider that a certain waterborne disease such as cholera spreads among two human groups (group I and II) who share the same water source. The next-generation matrix has the following form

$$K = \begin{bmatrix} k_{11} & k_{12} & k_{13} \\ k_{21} & k_{22} & k_{23} \\ k_{31} & k_{32} & 0 \end{bmatrix},$$

where k_{11}, k_{22} represent the within-group (direct) transmission, k_{12}, k_{21} represent the inter-group (direct) transmission, k_{13}, k_{23} represent the indirect transmission via the contaminated water, and k_{31}, k_{32} represent the shedding from infectious individuals in group I and group II, respectively. Assume that the pathogen cannot survive in the environment without the presence of infection.

Provision of clean water in one group Suppose that clean water is provided in group I. The target set is $S = \{(1, 3)\}$. Then the target reproduction number is

$$\mathcal{T}_{13} = \frac{k_{13}(k_{31} + k_{32}k_{21} - k_{31}k_{22})}{1 - k_{11} - k_{22} - k_{12}k_{21} - k_{23}k_{32} - k_{12}k_{23}k_{31} + k_{11}k_{22} + k_{11}k_{23}k_{32}},$$

provided that $k_{11} < 1$, $k_{22} < 1$ and $k_{11} + k_{22} + k_{12}k_{21} + k_{23}k_{32} + k_{12}k_{23}k_{31} < 1 + k_{11}k_{22} + k_{11}k_{23}k_{32}$.

Provision of clean water in both groups Clean water is assumed to be provided in both groups, then the target set is now $S = \{(1, 3), (2, 3)\}$. The target reproduction number with respect to S is

$$\mathcal{T}_S = \frac{k_{13}(k_{31} + k_{32}k_{21} - k_{31}k_{22}) + k_{23}(k_{32} + k_{31}k_{12} - k_{32}k_{11})}{1 - k_{11} - k_{22} - k_{12}k_{21} + k_{11}k_{22}},$$

provided that $k_{11} < 1$, $k_{22} < 1$ and $k_{11} + k_{22} + k_{12}k_{21} < 1 + k_{11}k_{22}$.

Sanitation in one group Suppose that the control mechanisms like hygienic disposal of human faeces are used in group I. The target set is $S = \{(3, 1)\}$. Then the target reproduction number is

$$\mathcal{T}_{31} = \frac{k_{31}(k_{13} + k_{12}k_{23} - k_{13}k_{22})}{1 - k_{11} - k_{22} - k_{12}k_{21} - k_{23}k_{32} - k_{13}k_{32}k_{21} + k_{11}k_{22} + k_{11}k_{23}k_{32}},$$

provided $k_{11} < 1$, $k_{22} < 1$ and $k_{11} + k_{22} + k_{12}k_{21} + k_{23}k_{32} + k_{13}k_{32}k_{21} < 1 + k_{11}k_{22} + k_{11}k_{23}k_{32}$. Notice that $\mathcal{T}_{31} = \mathcal{T}_{13}$ if $k_{12}k_{23}k_{31} = k_{21}k_{32}k_{13}$, i.e., the digraph associated with K is weight balanced.

Sanitation in both groups If hygienic disposal of human faeces is used in both groups, then the target set becomes $S = \{(3, 1), (3, 2)\}$. The target reproduction number with respect to S is

$$\mathcal{T}_S = \frac{k_{31}(k_{13} + k_{12}k_{23} - k_{13}k_{22}) + k_{32}(k_{23} + k_{21}k_{13} - k_{23}k_{11})}{1 - k_{11} - k_{22} - k_{12}k_{21} + k_{11}k_{22}},$$

provided $k_{11} < 1$, $k_{22} < 1$ and $k_{11} + k_{22} + k_{12}k_{21} < 1 + k_{11}k_{22}$.

Education campaign Disease education and awareness campaigns can help in preventing and controlling infectious diseases. For example, proper hand-washing can significantly reduce the direct person-to-person transmission of cholera and other waterborne diseases (Farmer et al. 2011). In this case, the target set is $S = \{(1, 1), (1, 2), (2, 1), (2, 2)\}$. The target reproduction number with respect to S is

$$\mathcal{T}_S = \frac{1}{1 - k_{13}k_{31} - k_{23}k_{32}} \rho \left(\begin{bmatrix} k_{11} + k_{12}k_{23}k_{31} - k_{11}k_{23}k_{32} & k_{12} + k_{11}k_{13}k_{32} - k_{13}k_{31}k_{12} \\ k_{21} + k_{22}k_{23}k_{31} - k_{23}k_{32}k_{21} & k_{22} + k_{21}k_{13}k_{32} - k_{22}k_{13}k_{31} \end{bmatrix} \right),$$

provided $k_{13}k_{31} + k_{23}k_{32} < 1$, where ρ denotes the spectral radius.

5.4 Spatially heterogeneous disease model

A multi-group model is proposed in Lloyd and May (1996, Eqs. 6–8) to understand the effect of spatially heterogeneity on the persistence and dynamics of childhood diseases. The next-generation matrix for the model in Lloyd and May (1996) with three groups (i.e., groups I, II and III) has the form

$$
K = \begin{bmatrix} k_{11} & k_{12} & k_{13} \\ k_{21} & k_{22} & k_{23} \\ k_{31} & k_{32} & k_{33} \end{bmatrix}.
$$

Each diagonal entry represents the within-group transmission while off-diagonal entries represent the inter-group transmission due to social contacts among groups such as travel.

Travel restriction in one group If the travel restriction policy is used in group I, reducing the human travel in and out of group I, then the target set is $S = \{(1, 2), (1, 3), (2, 1), (3, 1)\}$. The target reproduction number with respect to S is

$$
\mathcal{T}_S = \sqrt{\frac{k_{12}k_{21} + k_{13}k_{31} + k_{12}k_{23}k_{31} + k_{13}k_{32}k_{21} - k_{22}k_{13}k_{31} - k_{33}k_{12}k_{21}}{(1 - k_{11})(1 - k_{22} - k_{33} - k_{23}k_{32} + k_{22}k_{33})}},
$$

provided that $k_{11} < 1$, $k_{22} < 1$, $k_{33} < 1$ and $k_{22} + k_{33} + k_{23}k_{32} < 1 + k_{22}k_{33}$.

Global travel restriction Assume that the travel restriction policy is used in all groups, then the target set becomes $S = \{(1, 2), (1, 3), (2, 1), (2, 3), (3, 1), (3, 2)\}$. The target reproduction number with respect to S has the form

$$
\mathcal{T}_S = \rho \left(\begin{bmatrix} 0 & \frac{k_{12}}{1-k_{22}} & \frac{k_{13}}{1-k_{33}} \\ \frac{k_{21}}{1-k_{11}} & 0 & \frac{k_{23}}{1-k_{33}} \\ \frac{k_{31}}{1-k_{11}} & \frac{k_{32}}{1-k_{22}} & 0 \end{bmatrix} \right),
$$

provided that $k_{11} < 1$, $k_{22} < 1$ and $k_{33} < 1$.

5.5 Core group disease model

In the studies of sexually transmitted infections, a core group is a group in the population with higher sexual activity than other groups. Epidemic models with such a core group have been recently revisited in Edwards et al. (2010), and the next-generation matrix for the model with one core group and one non-core group has the following form

$$K = \begin{bmatrix} 0 & k_{12} & 0 & k_{14} \\ k_{21} & 0 & k_{23} & 0 \\ 0 & k_{32} & 0 & k_{34} \\ k_{41} & 0 & k_{43} & 0 \end{bmatrix}.$$

Here k_{12} and k_{21} represent the heterosexual transmission between male and female within the core group, k_{34} and k_{43} represent the transmission within the non-core group, and other k_{ij}'s represent the cross infection between the two groups.

Target within core group transmission The target set is $S = \{(1, 2), (2, 1)\}$. Then the target reproduction number is

$$\mathcal{T}_S = \frac{\rho\left(\begin{bmatrix} k_{12}k_{23}k_{34}k_{41} & k_{12}(1 - k_{14}k_{41} - k_{34}k_{43}) \\ k_{21}(1 - k_{23}k_{32} - k_{34}k_{43}) & k_{14}k_{21}k_{32}k_{43} \end{bmatrix}\right)}{1 - k_{14}k_{41} - k_{23}k_{32} - k_{34}k_{43} + k_{14}k_{41}k_{23}k_{32}},$$

provided $k_{14}k_{41} + k_{34}k_{43} < 1$, $k_{23}k_{32} + k_{34}k_{43} < 1$ and $k_{14}k_{41} + k_{23}k_{32} + k_{34}k_{43} - k_{14}k_{41}k_{23}k_{32} < 1$.

Target the core group: male only Let $S = \{(1, 2), (1, 4)\}$ be the target set. The corresponding target reproduction number is

$$\mathcal{T}_S = \frac{k_{12}(k_{21} + k_{23}k_{34}k_{41} - k_{21}k_{34}k_{43}) + k_{14}(k_{41} + k_{43}k_{32}k_{21} - k_{41}k_{23}k_{32})}{1 - k_{23}k_{32} - k_{34}k_{43}},$$

provided $k_{23}k_{32} + k_{34}k_{43} < 1$. Notice that this agrees with the type reproduction number defined in (17) in Edwards et al. (2010).

Target the core group: both male and female The target reproduction number with respect to the target set $S = \{(1, 2), (1, 4), (2, 1), (2, 3)\}$ is

$$\mathcal{T}_S = \frac{1}{1 - k_{34}k_{43}}\rho\left(\begin{bmatrix} k_{14}k_{41} & k_{12} + k_{14}k_{43}k_{32} - k_{12}k_{34}k_{43} \\ k_{21} + k_{23}k_{34}k_{41} - k_{21}k_{34}k_{43} & k_{23}k_{32} \end{bmatrix}\right),$$

provided $k_{34}k_{43} < 1$, agreeing with (18) in Edwards et al. (2010).

5.6 Infection among multiple populations/species

Consider the example of metapopulation infection dynamics in (Roberts and Heesterbeek 2003, Section 4) describing the spread of bovine tuberculosis in the adult/juvenile brush-tailed possum population in multiple habitat patches. The next-generation matrix for the model with two patches is

$$K = \begin{bmatrix} k_{11} & k_{12} & k_{13} & 0 \\ k_{21} & k_{22} & k_{23} & 0 \\ k_{31} & 0 & k_{33} & k_{34} \\ k_{41} & 0 & k_{43} & k_{44} \end{bmatrix}.$$

Host type 1 (the first row of K) represents juveniles in patch 1, host type 2 represents adults in patch 1, host type 3 represents juveniles in patch 2, and host type 4 represents adults in patch 2. Notice that adult possum do not migrate to other patches. Suppose that disease control strategies are used in patch 1 to reduce the disease spread among adults in patch 1 (i.e., decrease k_{22}). The target reproduction number with respect to set $\{(2, 2)\}$ is

$$\mathcal{T}_{22} = k_{22}\{(1 - k_{11})[k_{34}k_{43} - (1 - k_{33})(1 - k_{44})] + k_{13}(k_{31} - k_{31}k_{44} + k_{34}k_{41})\}/$$
$$\{(1 - k_{44})[(1 - k_{33})(k_{12}k_{21} + k_{11} - 1) + k_{31}(k_{13} + k_{12}k_{23})]$$
$$+ k_{34}k_{43}(1 - k_{11} - k_{12}k_{21}) + k_{34}k_{41}(k_{13} + k_{12}k_{23})\},$$

provided $k_{33} < 1$, $k_{44} < 1$, $k_{11} + k_{12}k_{21} + \frac{k_{31}(1-k_{44})(k_{13}+k_{12}k_{23})+k_{34}k_{41}(k_{13}+k_{12}k_{23})}{1-k_{33}-k_{44}-k_{34}k_{43}+k_{33}k_{44}} < 1$ and $k_{33} + k_{44} + k_{34}k_{43} < 1 + k_{33}k_{44}$.

For Nipah virus (Pulliam et al. 2012), the rows 1–4 of K can represent humans, pigs, fruit and bats, respectively, with $k_{31} = k_{33} = k_{41} = k_{43} = 0$. To eliminate the virus by targeting the disease transmission among pigs, the above expression for $\mathcal{T}_{22}$ shows that it is necessary to first reduce both k_{44} and $k_{11} + k_{12}k_{21}$ below one.

6 Appendix

Proof of Theorem 2.1 Observe that $I - (K - P_{S_1}KP_{S_2})$ is a nonsingular M-matrix since $K - P_{S_1}KP_{S_2}$ is nonnegative with spectral radius less than 1. For definition and properties of M-matrices, see Berman and Plemmons (1979). It follows that $M := P_{S_1}KP_{S_2}(I - K + P_{S_1}KP_{S_2})^{-1}$ is nonnegative, and $(I - M)P_{S_1}KP_{S_2} = M(I - K)$. Since S_1 includes all indices of rows where M has nonzero entries, it follows that $\rho(M) = \rho(E_{S_1}ME_{S_1}) = \mathcal{T}_S$. Let w be a positive eigenvector of the nonnegative irreducible matrix K with respect to $\rho(K) = \mathcal{R}_0$. Then

$$(I - M)P_{S_1}KP_{S_2}w = M(I - K)w = (1 - \mathcal{R}_0)Mw. \qquad (6.1)$$

Notice that all indices of nonzero rows of M are included in S_1. Also notice that $P_{S_1}KP_{S_2}w$ is a vector in $\mathbb{R}^n$ with positive entries only in each position $j \in S_1$. If $\mathcal{R}_0 = \rho(K) < 1$, then $(1 - \mathcal{R}_0)Mw > 0$, thus (6.1) gives $MP_{S_1}KP_{S_2}w < P_{S_1}KP_{S_2}w$. By applying a result of Collatz to the rows whose indices are included in S_1 (see, for example, Horn and Johnson 1985, Corollary 8.1.29), $\mathcal{T}_S = \rho(M) < 1$. If $\mathcal{T}_S < 1$, then $\mathcal{R}_0 < 1$ from (6.1). Similarly, it can be shown that $\mathcal{R}_0 = 1$ iff $\mathcal{T}_S = 1$, and $\mathcal{R}_0 > 1$ iff $\mathcal{T}_S > 1$. □

Proof of Theorem 2.2 Since each targeted entry of K appears only in the term $P_{S_1}KP_{S_2}$ in (2.1), $\mathcal{T}_S$ depends linearly on the targeted entry. Let $\mathcal{T}_S^c$ be the target

reproduction number corresponding to K_c, thus $\mathcal{T}_S^c = \mathcal{T}_S/\mathcal{T}_S = 1$, which implies $\rho(K_c) = 1$, by Theorem 2.1. □

Proof of Theorem 4.2 Consider the next-generation matrix K^T, the transpose of K, and let $\hat{\mathcal{T}}_S$ be the corresponding target reproduction number with respect to the target S (i.e., K in (2.1) is replaced by K^T). Let $\hat{K}_c$ be the controlled next-generation matrix corresponding to K^T and target set S, defined as in Theorem 2.2; that is, the (i, j) entry k_{ji} in K^T is replaced by $k_{ji}/\hat{\mathcal{T}}_S$ if $(i, j) \in S$. Similarly, let $K_{\hat{c}}$ be the controlled next-generation matrix corresponding to K and target set S^T; that is, the (j, i) entry k_{ji} in K is replaced by $k_{ji}/\mathcal{T}_{S^T}$ if $(i, j) \in S$. Notice that if $\mathcal{T}_{S^T} = \hat{\mathcal{T}}_S$, then $\hat{K}_c = (K_{\hat{c}})^T$ and $\rho(\hat{K}_c) = \rho(K_{\hat{c}})$. Now suppose that $\mathcal{T}_{S^T} \neq \hat{\mathcal{T}}_S$, then either $k_{ji}/\hat{\mathcal{T}}_S > k_{ji}/\mathcal{T}_{S^T}$ for all $(i, j) \in S$, or $k_{ji}/\hat{\mathcal{T}}_S < k_{ji}/\mathcal{T}_{S^T}$ for all $(i, j) \in S$. By the monotone property of the spectral radius of nonnegative irreducible matrices (e.g., see Berman and Plemmons 1979, p. 27), $\rho(K_{\hat{c}}) \neq \rho(\hat{K}_c)$, contradicting $\rho(K_{\hat{c}}) = \rho(\hat{K}_c) = 1$ required by Theorem 2.2. Hence, $\mathcal{T}_{S^T} = \hat{\mathcal{T}}_S$.

On the other hand, since K is irreducible and the associated weighted digraph $\mathcal{G}$ is weight balanced, there exists a nonsingular $n \times n$ diagonal matrix D such that $M = DKD^{-1}$ is symmetric; see, for example, Corollary 1 in Kolotilina (1993). It follows that $DKD^{-1} = M = M^T = (DKD^{-1})^T = D^{-1}K^T D$, and thus $K^T = D^2 K (D^{-1})^2$. Hence

$$
\begin{aligned}
\hat{\mathcal{T}}_S &= \rho(P_{S_1} K^T P_{S_2} (I - K^T + P_{S_1} K^T P_{S_2})^{-1}) \\
&= \rho(P_{S_1} D^2 K (D^{-1})^2 P_{S_2} (I - D^2 K (D^{-1})^2 + P_{S_1} D^2 K (D^{-1})^2 P_{S_2})^{-1}) \\
&= \rho(D^2 P_{S_1} K (D^{-1})^2 P_{S_2} D^2 (I - K + P_{S_1} K P_{S_2})^{-1} (D^{-1})^2) \\
&= \rho(D^2 P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1} (D^2)^{-1}) \\
&= \rho(P_{S_1} K P_{S_2} (I - K + P_{S_1} K P_{S_2})^{-1}) \\
&= \mathcal{T}_S.
\end{aligned}
$$

Therefore, $\mathcal{T}_S = \mathcal{T}_{S^T}$. □

Proof of Theorem 4.3 It follows from Theorem 2.1 that $\mathcal{T}_S = \mathcal{T}_U = 1$ if and only if $\mathcal{R}_0 = 1$, and that $\mathcal{T}_S > 1$ and $\mathcal{T}_U > 1$ if $\mathcal{R}_0 > 1$. The relation between $\mathcal{T}_S$ and $\mathcal{T}_U$ for $\mathcal{R}_0 > 1$ is proved by contradiction. Suppose that $\mathcal{T}_U > \mathcal{T}_S$. Let K_{c_S} and K_{c_U} be the controlled next-generation matrices defined as in Theorem 2.2, that is, the entry k_{ij} in the next-generation matrix K is replaced by $k_{ij}/\mathcal{T}_S$ (or $k_{ij}/\mathcal{T}_U$) if $(i, j) \in S$ (or $(i, j) \in U$). Since $\mathcal{T}_U > \mathcal{T}_S > 1$ and $S \subset U$, it follows that $K_{c_S} > K_{c_U}$. Hence, by the monotone property of the spectral radius of nonnegative irreducible matrices (e.g., see Berman and Plemmons 1979, p. 27), $\rho(K_{c_S}) > \rho(K_{c_U})$, contradicting $\rho(K_{c_S}) = \rho(K_{c_U}) = 1$ required by Theorem 2.2. Therefore, $\mathcal{T}_S > \mathcal{T}_U > 1$ if $\mathcal{R}_0 > 1$. A similar argument can be used to show that $\mathcal{T}_S < \mathcal{T}_U < 1$ if $\mathcal{R}_0 < 1$. □

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