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A general theory for target reproduction numbers with applications to ecology and epidemiology

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Abstract
A general framework for threshold parameters in population dynamics is developed using the concept of target reproduction numbers. This framework identifies reproduction numbers and other threshold parameters in the literature in terms of their roles in population control. The framework is applied to the analysis of single and multiple control strategies in ecology and epidemiology, and this provides new biological insights.

Keywords Basic reproduction number · Net reproductive value · Leslie matrix · Lefkovitch matrix · Disease model · Control

1 Introduction

Some of the most central quantities in theoretical biology are threshold parameters determining population persistence or disease invasibility, thereby providing biological insights regarding population protection and disease control. Reproduction

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numbers are threshold parameters that have been widely used in population dynamics, especially for applications in ecology and epidemiology. However, due to the complexity of biological problems and multiplicities of their mathematical representations, there are often several different choices for threshold parameters, leading to varied reproduction numbers (Bani-Yaghoub et al. 2012; Cushing and Diekmann 2016). This has stimulated much discussion (Cushing and Diekmann 2016; Heffernan et al. 2005; Keeling and Grenfell 2000; Li et al. 2011; Roberts 2007; van den Driessche 2017), and has even led to many analog names (e.g., reproductive rates, reproduction ratios and net reproductive values) coexisting in the literature. The purpose of this paper is to identify these reproduction numbers based on their roles on population control, identifying how they serve as threshold parameters for population dynamics. The tool used is an extended version of target reproduction numbers, which was first introduced by Shuai et al. (2013) as a generalization of type reproduction numbers (Heesterbeek and Roberts 2007; Roberts and Heesterbeek 2003). It will be shown that many reproduction numbers and related threshold parameters are indeed target reproduction numbers corresponding to specific population control strategies.

In epidemiology, the *basic reproduction number* (the average number of secondary infections caused by a typical infectious individual introduced into a completely susceptible host population; $\mathcal{R}_0 > 0$) often serves as a sharp threshold parameter determining whether or not the infectious disease dies out by $\mathcal{R}_0 < 1$ or > 1, respectively. The next-generation matrix method (Diekmann et al. 2013; van den Driessche and Watmough 2002), in which biological terms are classified as either disease transmission or transfer, leads to a next-generation matrix K. This has become a standard tool for deriving the basic reproduction number, which is defined as the spectral radius of the next-generation matrix (i.e., $\mathcal{R}_0 = \rho(K)$), for many infectious disease models. The basic reproduction number can be used to determine the herd immunity fraction $1 - \frac{1}{\mathcal{R}_0}$, which is the fraction of the host population needed to become immune (e.g., via vaccine) in order to control the disease (Anderson and May 1991). However, if the vaccine is only applied to a certain group (group i) of the host population, then the *type reproduction number* $\mathcal{T}_i$ determines the vaccine coverage needed for group i in order to control the disease among all groups, and the required fraction of vaccine coverage in group i is $1 - \frac{1}{\mathcal{T}_i}$; see Heesterbeek and Roberts (2007), Roberts and Heesterbeek (2003). Recently, a generalization of type reproduction numbers namely *target reproduction numbers* $\mathcal{T}_C$ has been introduced for measuring strategies that control only certain infection and/or transition terms during the disease transmission process (Shuai et al. 2013). Specifically, the next generation matrix is decomposed into two parts: target matrix C of terms subject to change and residual matrix $K - C$ of terms not subject to change. Then the controlled reproduction matrix $\frac{1}{\mathcal{T}_C}C + (K - C) = K - (1 - \frac{1}{\mathcal{T}_C})C$ has the spectral radius 1 at the threshold value. That is, the required change for terms in C is measured by the fraction $1 - \frac{1}{\mathcal{T}_C}$, as established later in Theorem 1.

In ecology, the population growth rate ($\lambda > 0$) and the *net reproductive value* (the lifetime reproductive output of an individual; $R_0 > 0$) are often derived in matrix population models to determine whether the population persists or goes to extinction (Caswell 2001). Let P denote a nonnegative irreducible population projection matrix in the model (e.g., a Lefkovitch matrix or a Leslie matrix), where $P = T + F$ can be decomposed into two parts according to their ecological meaning: transition matrix

T and fertility matrix F. Then the population growth rate determines the effort to be used to scale both transition and fertility matrices in order to reach the threshold value of one (crossing from extinction to persistence or from persistence to extinction). Specifically, the controlled population growth rate corresponding to the controlled population projection matrix $\frac{1}{\lambda}T + \frac{1}{\lambda}F$ is one. In contrast, the net reproductive value R_0 determines the effort needed to scale only fertility and the resulting projection matrix $T + \frac{1}{R_0}F$ has growth rate one (Cushing and Zhou 1994; Li and Schneider 2002). It will be shown later (Lemma 1) that the net reproductive value R_0 is a target reproduction number corresponding to fertility control, while the population growth rate λ is a target reproduction number corresponding to both fertility and transition control.

The connection between these threshold parameters in ecology and epidemiology has been well-recognized from both aspects, and these parameters have also been widely used in population and disease control. Nevertheless, a general mathematical framework is still missing to unify these parameters. The consequence is that researchers often need to define, derive, and study these threshold parameters anew for different classes of problems in ecology and/or epidemiology. In this paper, we provide such a general framework on threshold parameters using target reproduction numbers. First, we extend the definition of the target reproduction number to a general setting so that it unifies the above threshold parameters. Although the definition of the target reproduction number is purely algebraic, a graph interpretation is presented to provide biological meaning. We develop both algebraic and graphic approaches to compute target reproduction numbers, and demonstrate their use for one or multiple control strategies. Applications are illustrated using both ecological and epidemiological models taken from the literature.

2 Target reproduction number

2.1 A general algebraic theory

Let $A = [a_{ij}] = B + C$ be a nonnegative irreducible $n \times n$ matrix, where the nonnegative *target matrix* $C = [c_{ij}]$ consists of all targeted entries, and the nonnegative *residual matrix* $B = [b_{ij}]$ consists of all entries not targeted. Note that each a_{ij} may be divided into two parts, one part b_{ij} unchanged, and one part c_{ij} subject to change, either a decrease or increase; that is, $a_{ij} = b_{ij} + c_{ij}$, $1 \le i, j \le n$. For controllability, matrix B is required to have $\rho(B) < 1$, where ρ denotes the spectral radius.

Definition 1 Let A, B, C be nonnegative $n \times n$ matrices such that $A = B + C$ is irreducible, $C \neq 0$, and $\rho(B) < 1$. Then the *target reproduction number* $\mathcal{T}_C > 0$ is defined as

$$\mathcal{T}_C = \rho(C(I - B)^{-1}), \tag{2.1}$$

where I is the $n \times n$ identity matrix.

The target reproduction number $\mathcal{T}_C$ defined above extends the one in Shuai et al. (2013), in which each entry of A is either targeted or not targeted (i.e., each entry is not

divided into two parts). If $\mathbf{S}$ is the set of (whole) entries of A that are targeted, then the target matrix C and residual matrix B are chosen as follows: if $(i, j) \in \mathbf{S}$, then $c_{ij} = a_{ij}$ and $b_{ij} = 0$; whereas if $(i, j) \notin \mathbf{S}$, then $c_{ij} = 0$ and $b_{ij} = a_{ij}$. In this situation, the target reproduction number $\mathcal{T}_C$ in (2.1) becomes the target reproduction number in Shuai et al. (2013). Furthermore, when the target matrix C consists of only one or several rows (or columns) of entries of A, the target reproduction number becomes the type reproduction number, previously defined by Heesterbeek and Roberts (2007), Roberts and Heesterbeek (2003).

The target reproduction number $\mathcal{T}_C$ also works for situations where parts of entires of A are targeted. For example, let $A = \begin{bmatrix} b_{11}+c_{11} & b_{12} \\ b_{21} & 0 \end{bmatrix}$ with target matrix $C = \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix}$ and residual matrix $B = \begin{bmatrix} b_{11} & b_{12} \\ b_{21} & 0 \end{bmatrix}$. Then, by Definition 1, the target reproduction number $\mathcal{T}_C = \rho(C(I-B)^{-1}) = \frac{c_{11}}{1-b_{11}-b_{12}b_{21}}$, provided that $1 - b_{11} - b_{12}b_{21} > 0$ equivalently $\rho(B) < 1$.

Let

$$A_C(\tau) = B + \frac{1}{\tau}C \tag{2.2}$$

denote the *controlled matrix* corresponding to the target matrix C with certain population control effort $\tau > 0$, thus every entry c_{ij} of C becomes c_{ij}/τ. Since A is irreducible, the monotone property of the spectral radius of $A_C(\tau)$ holds (Berman and Plemmons 1979, p. 27), and thus $\rho(A_C(\tau))$ is monotone decreasing as τ increases. The following result, which extends an earlier result by Shuai et al. (2013, Theorem 2.2), describes the effort that is needed such that the controlled matrix has spectral radius 1.

Theorem 1 *Let A, B, C be nonnegative $n \times n$ matrices such that $A = B + C$ is irreducible, $C \neq 0$, and $\rho(B) < 1$. Then $\rho(A_C(\tau)) = 1$ if and only if $\tau = \mathcal{T}_C$.*

Proof It follows from $\rho(B) < 1$ that $C(I-B)^{-1}$ is a nonnegative matrix. Let $x^T \geq 0$ be a nonnegative left eigenvector of $C(I-B)^{-1}$ associated with the Perron eigenvalue $\mathcal{T}_C = \rho(C(I-B)^{-1})$, i.e., $x^T C(I-B)^{-1} = \mathcal{T}_C x^T$. Hence $x^T C = \mathcal{T}_C x^T (I-B) = \mathcal{T}_C x^T - \mathcal{T}_C x^T B$, which implies that $x^T(B + \frac{1}{\mathcal{T}_C}C) = x^T$. This is, the nonnegative irreducible matrix $B + \frac{1}{\mathcal{T}_C}C$ has a nonnegative left-eigenvector x^T corresponding to the eigenvalue 1. By Perron-Frobenius Theory (see, e.g., Berman and Plemmons (1979, Theorem 1.4) or Li and Schneider (2002, Theorem 2.1)), the spectral radius of $B + \frac{1}{\mathcal{T}_C}C$ is the unique eigenvalue with a nonnegative eigenvector, and thus $\rho(A_C(\mathcal{T}_C)) = \rho(B + \frac{1}{\mathcal{T}_C}C) = 1$. By the monotone property of the spectral radius of $A_C(\tau)$ (Berman and Plemmons 1979, p. 27), $\rho(A_C(\tau)) = 1$ if and only if $\tau = \mathcal{T}_C$. □

The following result shows that $\mathcal{T}_C$ and $\rho(A)$ always stay on the same side of the value 1; see Shuai et al. (2013, Theorem 2.1) for an earlier result on the target reproduction number, and also earlier results on the net reproductive rate by Cushing and Zhou (1994), Li and Schneider (2002). As $\rho(A)$ often provides a sharp threshold for population dynamics, the various target reproduction numbers $\mathcal{T}_C$ thus also serve as sharp threshold parameters and some of them may have explicit and simpler expressions than $\rho(A)$. Using the notation of Berman and Plemmons (1979) for matrices

$X = [x_{ij}]$ and $Y = [y_{ij}]$, the inequality $X < Y$ means $x_{ij} \leq y_{ij}$ for all i, j and $X \neq Y$.

Theorem 2 *Let A, B, C be nonnegative $n \times n$ matrices such that $A = B + C$ is irreducible, $C \neq 0$, and $\rho(B) < 1$. Then the following statement holds:*

(1) $\rho(A) > 1 \Longleftrightarrow \mathcal{T}_C > 1$;
(2) $\rho(A) = 1 \Longleftrightarrow \mathcal{T}_C = 1$;
(3) $\rho(A) < 1 \Longleftrightarrow \mathcal{T}_C < 1$.

Proof Since A is irreducible, $A_C(\mathcal{T}_C) = B + \frac{1}{\mathcal{T}_C}C$ is also irreducible. If $\mathcal{T}_C > 1$, then $A_C(\mathcal{T}_C) < A = B + C$ and thus $\rho(A_C(\mathcal{T}_C)) < \rho(A)$ (see, e.g., Berman and Plemmons (1979, p. 27)). By Theorem 1, $\rho(A_C(\mathcal{T}_C)) = 1$. Therefore, $\rho(A) > 1$. Similarly, if $\mathcal{T}_C < 1$, then $A_C(\mathcal{T}_C) > A$ and $1 = \rho(A_C(\mathcal{T}_C)) > \rho(A)$. □

The relation between two target reproduction numbers of the same matrix A is described in the following result, which extends an earlier result by Shuai et al. (2013, Theorem 4.3). Biologically, less effort is required when targeting more entries.

Theorem 3 *Let A, B, C, B', C' be nonnegative $n \times n$ matrices such that $A = B + C = B' + C'$ is irreducible, $C \neq 0$, $C' \neq 0$, $\rho(B) < 1$ and $\rho(B') < 1$. If $C > C'$, then one of the following statements holds:*

(1) $1 < \mathcal{T}_C < \mathcal{T}_{C'}$;
(2) $\mathcal{T}_C = \mathcal{T}_{C'} = 1$;
(3) $\mathcal{T}_{C'} < \mathcal{T}_C < 1$.

Proof If $\mathcal{T}_C > 1$, then, by Theorem 2, $\rho(A) > 1$ and $\mathcal{T}_{C'} > 1$. In the following, we prove $\mathcal{T}_{C'} > \mathcal{T}_C$. Assume, on the contrary, that $\mathcal{T}_C \geq \mathcal{T}_{C'}$. Then

$$\begin{aligned} A_C(\mathcal{T}_C) &= B + \frac{1}{\mathcal{T}_C}C \\ &= B' + \frac{1}{\mathcal{T}_{C'}}C' + B - B' + \frac{1}{\mathcal{T}_C}C - \frac{1}{\mathcal{T}_{C'}}C' \\ &\leq A_{C'}(\mathcal{T}_{C'}) + B - B' + \frac{1}{\mathcal{T}_{C'}}(C - C') \\ &< A_{C'}(\mathcal{T}_{C'}) + B - B' + C - C' \\ &= A_{C'}(\mathcal{T}_{C'}). \end{aligned}$$

Since both $A_C(\mathcal{T}_C)$ and $A_{C'}(\mathcal{T}_{C'})$ are irreducible, $\rho(A_C(\mathcal{T}_C)) < \rho(A_{C'}(\mathcal{T}_{C'}))$. However, by Theorem 1, $\rho(A_C(\mathcal{T}_C)) = \rho(A_{C'}(\mathcal{T}_{C'})) = 1$, which is a contradiction. Therefore, $1 < \mathcal{T}_C < \mathcal{T}_{C'}$. The case with $\mathcal{T}_C < 1$ can be proved by reversing all inequalities above. □

2.2 Graph theoretic interpretation

The previous section uses matrix-theoretic results for target reproduction numbers. Alternatively, graph-theoretic results can be obtained to provide a powerful tool for

computing target reproduction numbers explicitly in terms of cycle-unions of the related digraph. Let $\mathcal{D} = \mathcal{D}(A) = \mathcal{D}(B, C)$ be the *weighted multi-digraph* associated with the residual matrix B and target matrix C; that is, $\mathcal{D}$ consists of vertices labelled by $1, 2, \ldots, n$, and two arcs ji from vertex j to vertex i (of weights b_{ij} and c_{ij}) if and only if $b_{ij} > 0$ and $c_{ij} > 0$, one arc ji (of weight given by the nonzero value) if and only if one of b_{ij} and c_{ij} is nonzero, and no arc if both of them are zero. An arc corresponding to an entry in C is called a *target arc*. A *cycle-union* $\mathcal{U}$ of $\mathcal{D}$ is a subdigraph such that each component of $\mathcal{U}$ is a cycle of length ≥ 1; that is, a cycle-union is a union of vertex-disjoint cycles of $\mathcal{D}$. Let $c(\mathcal{U})$ denote the number of cycles in such a subdigraph. The weight $w(\mathcal{U})$ of a cycle-union $\mathcal{U}$ is the product of weights of arcs in $\mathcal{U}$. The empty digraph (consisting of no vertex and no arc) is regarded as a trivial cycle-union with weight 1. See Moon et al. (2014) or West (1996) for additional and detailed graph-theoretic definitions.

The following result provides an alternative way to compute the target reproduction number $\mathcal{T}_C$.

Theorem 4 *Let A, B, C be nonnegative $n \times n$ matrices such that $A = B + C$ is irreducible, $C \neq 0$, and $\rho(B) < 1$. Then $\tau = \mathcal{T}_C$ satisfies the following characteristic equation*

$$\alpha_r \tau^{-r} + \alpha_{r-1} \tau^{-(r-1)} + \cdots + \alpha_1 \tau^{-1} + \alpha_0 = 0. \tag{2.3}$$

Here r is the rank of the target matrix C and for $1 \leq i \leq r$,

$$\alpha_i = \sum_{\mathcal{U}^i} (-1)^{c(\mathcal{U}^i)} w(\mathcal{U}^i), \tag{2.4}$$

where the sum is over all cycle-unions $\mathcal{U}^i$ of $\mathcal{D}$ that contain i target arcs of C.

Proof By Theorem 1, τ is equal to $\mathcal{T}_C$ when 1 is an eigenvalue of the controlled matrix $A_C(\tau) = B + \frac{1}{\tau} C$. That is, $\det(I - B - \frac{1}{\tau} C) = 0$. Applying a determinant expansion formula in Moon et al. (2014, Proposition 2.2) yields

$$\sum_{\mathcal{U}} (-1)^{c(\mathcal{U})} w(\mathcal{U}) = 0, \tag{2.5}$$

where the sum is over all cycle-unions $\mathcal{U}$ of the weighted multi-digraph $\mathcal{D}_C$ associated with matrices B and $\frac{1}{\tau} C$. Note that $\mathcal{D}_C$ has the same vertex and arcs sets as those of $\mathcal{D}$ but different weights; specifically, the weight of each target arc in $\mathcal{D}_C$ equals $\frac{1}{\tau}$ of the weight of the target arc in $\mathcal{D}$. Thus the weight of each cycle-union $\mathcal{U}$ of $\mathcal{D}_C$ in (2.5) contains the factor τ^{-1} the same number of times as the number of target arcs in $\mathcal{U}$. Since $\mathcal{U}$ is the union of vertex-disjoint cycles of $\mathcal{D}_C$, $\mathcal{U}$ contains at most r target arcs, where r is the rank of the target matrix C. Rewriting (2.5) according to the power of τ^{-1} gives (2.3) with the coefficient α_i of the term τ^{-i} equal to the sum of weights of all cycle-unions that contain i target arcs. □

Graph reduction rules by de-Camino-Beck and Lewis (2007, 2008) have previously been used to derive the characteristic equation (2.3). Our new result Theorem 4 shows

that the coefficients in the characteristic equation can be interpreted as cycle-unions of the graph/network. Thus the characteristic equation can be derived by computing all cycle-unions in the network. For a complex network, the graph reduction rules (de-Camino-Beck and Lewis 2007, 2008) can be applied to reduce the network before applying Theorem 4.

If the rank of the target matrix C is 1, then Theorem 4 gives an explicit expression for the target reproduction number in terms of cycle-unions as derived in the following result. Earlier results of this type have previously been established by Rueffler and Metz (2013), Rueffler et al. (2013) for the net reproductive value R_0, which is a target reproduction number corresponding to fertility control as shown later in Lemma 1.

Theorem 5 *Let A, B, C be nonnegative $n \times n$ matrices such that $A = B + C$ is irreducible, $C \neq 0$, and $\rho(B) < 1$. If the rank of the target matrix C is 1, then*

$$\mathcal{T}_C = \frac{\sum_{\mathcal{U}} (-1)^{1+c(\mathcal{U})} w(\mathcal{U})}{\sum_{\mathcal{V}} (-1)^{c(\mathcal{V})} w(\mathcal{V})}, \tag{2.6}$$

where the sums are over all cycle-unions $\mathcal{U}$ and cycle-unions $\mathcal{V}$ of $\mathcal{D}(B, C)$ that do and do not contain a target arc in C, respectively.

Proof Since the rank of C is 1, $r = 1$ and the characteristic equation (2.3) with (2.4) gives

$$\alpha_1 \mathcal{T}_C^{-1} + \alpha_0 = 0 \tag{2.7}$$

with

$$\alpha_0 = \sum_{\mathcal{V}} (-1)^{c(\mathcal{V})} w(\mathcal{V}) \quad \text{and} \quad \alpha_1 = \sum_{\mathcal{U}} (-1)^{c(\mathcal{U})} w(\mathcal{U}),$$

where cycle-unions $\mathcal{U}$ and $\mathcal{V}$ are given as above. Solving $\mathcal{T}_C$ from (2.7) gives (2.6). □

If $c_{ij} = a_{ij}$ for some i and $1 \leq j \leq n$ and $c_{ij} = 0$ otherwise, then $\mathcal{T}_C$ becomes the type reproduction number $\mathcal{T}_i$ targeting all entries in row (or column) i of A (Heesterbeek and Roberts 2007; Roberts and Heesterbeek 2003). If $c_{ij} = a_{ij}$ for some i, j and $c_{ij} = 0$ otherwise, then $\mathcal{T}_C$ becomes the target reproduction number $\mathcal{T}_{ij}$ targeting only one entry (i, j) of A (Moon et al. 2014; Shuai et al. 2013). The following results follow directly from Theorem 5, and have previously been established by Moon et al. (2014, Theorems 4.1 and 5.3) by using generating functions for walks in a digraph.

Corollary 1 *Let A be a nonnegative $n \times n$ irreducible matrix, and $\mathcal{T}_i$ and $\mathcal{T}_{ij}$ be well defined for some i, j. Then*

$$\mathcal{T}_i = \frac{\sum_{\mathcal{U}_i} (-1)^{1+c(\mathcal{U}_i)} w(\mathcal{U}_i)}{\sum_{\mathcal{V}_i} (-1)^{c(\mathcal{V}_i)} w(\mathcal{V}_i)}, \tag{2.8}$$

where the sums are over all cycle-unions $\mathcal{U}_i$ and cycle-unions $\mathcal{V}_i$ of $\mathcal{D}(A)$ that do and do not contain a vertex in row (or column) i, respectively; and

$$\mathcal{T}_{ij} = \frac{\sum_{\mathcal{U}_{ij}} (-1)^{1+c(\mathcal{U}_{ij})} w(\mathcal{U}_{ij})}{\sum_{\mathcal{V}_{ij}} (-1)^{c(\mathcal{V}_{ij})} w(\mathcal{V}_{ij})}, \tag{2.9}$$

where the sums are over all cycle-unions $\mathcal{U}_{ij}$ and cycle-unions $\mathcal{V}_{ij}$ of $\mathcal{D}(A)$ that do and do not contain arc ji of weight a_{ij}, respectively.

An illustration of these results is given for a perennial weed, scentless chamomile, in Sect. 3.4.

A characteristic equation such as (2.3) can be extended to the case where multiple control strategies are applied for matrix A. For example, let $\mathbf{S}$ be the target set with effort τ and $\mathbf{U}$ be the target set with effort σ. Let $\tilde{A} = [\tilde{a}_{ij}]$ be the controlled matrix after these two control efforts, then

$$\tilde{a}_{ij} = \begin{cases} a_{ij} & \text{if } (i,j) \notin \mathbf{S} \cup \mathbf{U}, \\ \frac{1}{\tau} a_{ij} & \text{if } (i,j) \in \mathbf{S}, (i,j) \notin \mathbf{U}, \\ \frac{1}{\sigma} a_{ij} & \text{if } (i,j) \in \mathbf{U}, (i,j) \notin \mathbf{S}, \\ \frac{1}{\tau\sigma} a_{ij} & \text{if } (i,j) \in \mathbf{S} \cap \mathbf{U}. \end{cases}$$

Then using an argument similar to that in the proof of Theorem 4, the characteristic equation such that $\rho(\tilde{A}) = 1$ is

$$\sum_{i=0}^{r} \sum_{j=0}^{s} \alpha_{ij} \tau^{-i} \sigma^{-j} = 0, \tag{2.10}$$

where r, s are the ranks of the target matrices corresponding to $\mathbf{S}$ and $\mathbf{U}$, and

$$\alpha_{ij} = \sum_{\mathcal{U}^{ij}} (-1)^{c(\mathcal{U}^{ij})} w(\mathcal{U}^{ij}).$$

Here the sum is over all cycle-unions $\mathcal{U}^{ij}$ that contain i target arcs in $\mathbf{S}$ and j target arcs in $\mathbf{U}$. The characteristic equation (2.10) can be used to derive minimum cost population control strategies; see Sects. 3.4 and 4.2 for applications in ecology and epidemiology, respectively.

3 Applications to ecology

3.1 Net reproductive value as a target reproduction number

A discrete-time matrix model (Caswell 2001) for an age or stage structured population is defined as

$$x_{t+1} = P x_t, \tag{3.1}$$

where x_t is a vector of ages/stages at time t and P is a nonnegative irreducible matrix, customarily called a *population projection matrix*, which describes transitions from one age/stage to another one (Caswell 2001). The spectral radius $\lambda = \rho(P)$ is called the (geometric) *population growth rate*, which determines whether the population grows or goes to extinction, depending on whether $\lambda > 1$ or $\lambda < 1$. (Note that λ is not strictly a rate as it is dimensionless.) The projection matrix P can be decomposed, based on biological interpretations, as $P = T + F$, where $T \geq 0$ contains the survivorship transitions and $F \geq 0$ contains the fecundities. Hence, T and F are called the *transition matrix* and the *fecundity matrix* (or *fertility matrix*), respectively. The *net reproductive value* R_0 is defined as the spectral radius of the next generation matrix $F(I - T)^{-1}$, that is,

$$R_0 = \rho(F(I - T)^{-1}); \tag{3.2}$$

see Allen and van den Driessche (2008), Cushing and Zhou (1994), Li and Schneider (2002). The following result shows that R_0 is the target reproduction number that corresponds to the population control strategy targeting all fecundities in the projection matrix.

Lemma 1 *Suppose that $\rho(T) < 1$. Then the net reproductive value R_0 is the target reproduction number $\mathcal{T}_C$ as in (2.1) for $A = P$ corresponding to the target matrix $C = F$.*

Proof Let $A = P = B + C$, $B = T$, and $C = F$ in Definition 1. The the target reproduction number $\mathcal{T}_C$ as in (2.1) becomes $\mathcal{T}_C = \rho(F(I - T)^{-1}) = R_0$ by (3.2). □

An illustration of this result is given for a Lefkovitch model for salmonid conservation in Sect. 3.3.1.

By identifying $\lambda = \rho(P) = \mathcal{T}_P$ and $R_0 = \mathcal{T}_F$ with $P \geq F$, the next result follows directly from Theorem 3. This result previously appeared in Li and Schneider (2002, Theorem 3.1) and Cushing and Zhou (1994, Theorem 3 and Corollary 7).

Lemma 2 *Suppose that $\rho(T) < 1$ and $T \neq 0$. Then one of the following holds:*

(1) $1 < \lambda < R_0$;
(2) $\lambda = R_0 = 1$;
(3) $R_0 < \lambda < 1$.

We remark that if $T = 0$, then the growth rate and the net reproductive value are equal, i.e., $\lambda = R_0$.

In the remaining part of this ecological section, we demonstrate the applications of target reproduction numbers with common types of projection matricies P in the literature.

3.2 Application to *n*-stage Lefkovitch matrix model

Consider the following Lefkovitch matrix

$$P = \begin{pmatrix} s_1 + b_1 & b_2 & b_3 & \cdots & b_{n-2} & b_{n-1} & b_n \\ t_1 & s_2 & & & & & \\ & t_2 & s_3 & & & & \\ & & \ddots & \ddots & & & \\ & & & & s_{n-2} & & \\ & & & & t_{n-2} & s_{n-1} & \\ & & & & & t_{n-1} & s_n \end{pmatrix}, \tag{3.3}$$

where $s_i \geq 0$ describes the probability of staying, $t_i > 0$ describes the probability of transition, and $b_i \geq 0$ with $b_n > 0$ describes the fertility (Caswell 2001). According to Lemma 1, the net reproductive value R_0 is the target reproduction number $\mathcal{T}_C$ with the fertility matrix being the target matrix C, that is,

$$C = \begin{pmatrix} b_1 & b_2 & \cdots & b_{n-1} & b_n \\ & & & & \\ & & \mathbf{0} & & \\ & & & & \end{pmatrix}.$$

Notice that the target matrix C contains only part of the $(1, 1)$ entry of P, demonstrating the extension of target reproduction numbers as described in Sect. 2. Since C has rank 1, Theorem 5 can be used to derive the following explicit expression

$$R_0 = \frac{b_1(1-s_2)\cdots(1-s_n) + t_1 b_2(1-s_3)\cdots(1-s_n) + \cdots + t_1\cdots t_{n-1}b_n}{(1-s_1)\cdots(1-s_n)},$$

i.e.,

$$R_0 = \frac{b_1}{1-s_1} + \frac{t_1 b_2}{(1-s_1)(1-s_2)} + \cdots + \frac{t_1\cdots t_{n-1}b_n}{(1-s_1)\cdots(1-s_n)}. \tag{3.4}$$

To assess the impact of control we consider the case in which the following steps happen in each time interval in the order stated

- production of b_i offsprings per survivor;
- survival with probability p_i;
- proportion q_i stays in the same class while proportion $1 - q_i$ moves to the next class.

In terms of these quantities, $s_i = p_i q_i$ and $t_i = p_i(1 - q_i)$.

When $q_i = 0$ for all i, $s_i = 0, t_i = p_i$ and P in (3.3) becomes a Leslie matrix (Caswell 2001). As a consequence, the net reproductive value (3.4) becomes $R_0 = \sum_{i=1}^{n} b_i \prod_{j=1}^{i-1} p_j$, with the convention that $\prod_{j=1}^{0} p_j = 1$. This agrees with previous results on Leslie matrices; see, for example, Caswell (2001).

3.3 Application to 4-stage Lefkovitch matrix model, with a case study on protecting salmonids

In this section we consider the Lefkovitch matrix in the form of (3.3) with 4 stages (i.e., $n = 4$) and discuss various population control strategies. That is,

$$P = \begin{pmatrix} s_1 + b_1 & b_2 & b_3 & b_4 \\ t_1 & s_2 & 0 & 0 \\ 0 & t_2 & s_3 & 0 \\ 0 & 0 & t_3 & s_4 \end{pmatrix}, \tag{3.5}$$

with $s_i = p_1 q_i$ and $t_i = p_i(1 - q_i)$.

3.3.1 The target matrix C has only nonzero entries of b_i for $1 \le i \le 4$, i.e., control of offspring production. By Lemma 1, the target reproduction number $\mathcal{T}_C$ is the same as R_0 as given in (3.4) with $n = 4$. That is, the controlled projection matrix $P_C = \begin{pmatrix} s_1 + \frac{b_1}{R_0} & \frac{b_2}{R_0} & \frac{b_3}{R_0} & \frac{b_4}{R_0} \\ t_1 & s_2 & 0 & 0 \\ 0 & t_2 & s_3 & 0 \\ 0 & 0 & t_3 & s_4 \end{pmatrix}$ has spectral radius 1.

3.3.2 The target matrix C has only nonzero entries of s_1 and t_1, i.e., control of survival probability p_1 in stage 1. The corresponding target reproduction number takes the form

$$\mathcal{T}_C = \frac{s_1}{m_1} + \frac{t_1 b_2}{m_1(1 - s_2)} + \frac{t_1 t_2 b_3}{m_1(1 - s_2)(1 - s_3)} + \frac{t_1 t_2 t_3 b_4}{m_1(1 - s_2)(1 - s_3)(1 - s_4)},$$

with $m_1 = 1 - b_1$.

3.3.3 The target matrix C has only nonzero entry s_4, i.e., control of survival probability at the last stage. The target reproduction number is

$$\mathcal{T}_C = \mathcal{T}_{44} = \frac{s_4 z}{z - t_1 t_2 t_3 b_4}$$

with $z = (1 - s_1 - b_1)(1 - s_2)(1 - s_3) - t_1 b_2 (1 - s_3) - t_1 t_2 b_3$ encoding all cycle-unions that do not contain the last stage.

3.3.4 An immediate application of the Lefkovitch matrix (3.5) is to the salmonid model proposed by Huang and Lewis (2015, Appendix C), in which $s_1 = s_2 = 0$ and $b_1 = b_2 = b_3 = 0$. That is, the projection matrix for protecting salmonids takes the following form

$$P = \begin{pmatrix} 0 & 0 & 0 & b_4 \\ t_1 & 0 & 0 & 0 \\ 0 & t_2 & s_3 & 0 \\ 0 & 0 & t_3 & s_4 \end{pmatrix}. \tag{3.6}$$

First the net reproductive value R_0 is the target reproduction number $\mathcal{T}_1$ (targeting all entries in the first row or the first column). Since the first row and the first column both contain only one non-zero entry, it follows from Theorem 5 that $R_0 = \mathcal{T}_1 = \mathcal{T}_{21} = \mathcal{T}_{14}$. Biologically, in order to protect endangered salmonids (i.e., $R_0 < 1$), either the average number of fertilized eggs produced per adult, b_4, could be increased by $b_4(1/R_0 - 1)$, i.e., the average number of fertilized eggs produced per adult becomes b_4/R_0 (actually this leads to a controlled reproductive value $R_c = 1$, thus a little bit more increase is needed), or the proportion of eggs that hatch to fry stage each year, t_1, could be increased to t_1/R_0.

Since the second row contains only one non-zero entry, $\mathcal{T}_2 = \mathcal{T}_{21} = \mathcal{T}_{32} = R_0$. For example, to control the proportion of fry that survive to the juvenile stage each year, t_2 could be increased to t_2/R_0. Similarly, other target reproduction numbers can be calculated to measure the change of s_3, t_3 or s_4 needed in order to protect the endangered population. The increase of s_4 could be achieved by reducing the harvest for adult salmonids, thus $\mathcal{T}_{44} = s_4(1 - s_3)/((1 - s_3) - t_1t_2t_3b_4)$ guides the needed amount of harvest reduction.

3.4 Application to controlling scentless chamomile

Scentless chamomile (*Matricaria perforata*) is an invasive weed in north America, found in agricultural farmland and disturbed habitats. It is a perennial with three stages: seed bank (in the ground, 1), rosettes (2), and flowering plants (3). Biological transitions can be represented either by weights in a life-cycle graph or by entries in a projection matrix. In a given year, seeds in the seed bank will remain in the seed bank with probability a_{11}. They will germinate from the seed bank into a rosette with probability a_{21}, and germinate into a flower with probability a_{31}. They will die with probability $1 - a_{11} - a_{21} - a_{31}$. Rosettes will transform into flowers with probability a_{32}, and die with probability $1 - a_{32}$. The flowers contribute to all fecundities as follows. In a single year, flowers will produce a_{13} seed bank seeds per flower, will produce a_{23} rosettes per flower, and will produce a_{33} new flowers per flower. Then the original flower will die. Full details of the life cycle dynamics can be found in de-Camino-Beck and Lewis (2007).

The resulting projection matrix for the growth of scentless chamomile (de-Camino-Beck and Lewis 2007, 2008) is

$$A = \begin{bmatrix} a_{11} & 0 & a_{13} \\ a_{21} & 0 & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix}. \tag{3.7}$$

The corresponding weighted digraph $\mathcal{D}(A)$ is given in Fig. 1. There are multiple biological control measures for scentless chamomile. Generally, they can target either

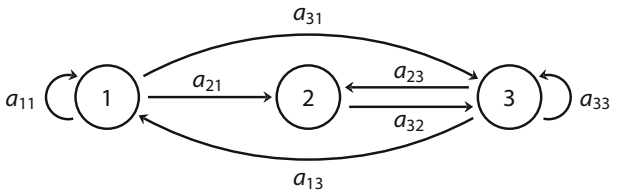

Fig. 1 Digraph $\mathcal{D}(A)$ for scentless chamomile, as given by matrix (3.7). For a full biological explanation of the weights, see the text

the seed production (e.g., seed weevils) or the plant growth (e.g., gall midges) (Hinz and McClay 2000). Controls affecting seed production will reduce a_{13}, a_{23} and a_{33}. Controls affecting plant growth will reduce a_{21}, a_{31} and a_{32}. They may also have a smaller affect on a_{33}, but we do not consider this. For completeness we also consider the possibility that level of seeds in the seed bank can be controlled by removal of soil infested with seeds, thereby reducing a_{11}. However, in practice, this is not a typical method for control.

In what follows we first consider the three different strategies in isolation, and then consider a mixed strategy.

3.4.1 Control of offspring reproduction We consider the case where the target matrix C has only nonzero entries $c_{i3} = a_{i3}$ for $1 \le i \le 3$, so that the target matrix is the fecundity matrix (de-Camino-Beck and Lewis 2007, 2008). Since this matrix has rank 1, by Corollary 1,

$$\mathcal{T}_3 = \frac{a_{33} + a_{13}a_{31} + a_{23}a_{32} + a_{13}a_{32}a_{21} - a_{11}a_{33} - a_{11}a_{23}a_{32}}{1 - a_{11}}, \tag{3.8}$$

provided $a_{11} < 1$. In the denominator, 1 is the weight of an empty digraph while a_{11} is the weight of the cycle-union consisting of a loop (i.e., cycle of length 1) at vertex 1. In the numerator of $\mathcal{T}_3$, the first four terms are the weights of four cycle-unions that consist of only one cycle and contain exactly one target entry, while the last two terms are the weights of two cycle-unions that each consist of two cycles and contain exactly one target entry (see Fig. 1). The target reproduction number $\mathcal{T}_3$ agrees with the expression of the basic reproductive ratio R_0 in de-Camino-Beck and Lewis (2007) derived by graph reduction rules, agreeing with Lemma 1.

3.4.2 Control of survival probability at the first stage We next consider the case where the target matrix C has only one nonzero entry $c_{11} = a_{11}$, i.e., control of the survival probability of seeds. By Corollary 1, the target reproduction number is

$$\mathcal{T}_{11} = \frac{a_{11}(1 - a_{33} - a_{23}a_{32})}{1 - a_{33} - a_{13}a_{31} - a_{23}a_{32} - a_{13}a_{32}a_{21}}, \tag{3.9}$$

provided that the denominator is positive. Biologically this positivity means that the growth of scentless chamomile can be controlled by only targeting the survival probability of seeds. Note that all terms in (3.9) are the weights of cycle-unions in $\mathcal{D}(A)$,

and all terms in (3.8) also appear in (3.9) but are relocated based on whether the term contains a target entry.

3.4.3 Control of survival probability at the last stage In the last single strategy, the target matrix C has only nonzero entries $c_{21} = a_{21}$, $c_{31} = a_{31}$, and $c_{32} = a_{32}$, i.e., control of the growth terms. From (2.1), the target reproduction number $\mathcal{T}_C = \rho(C(I - A + C)^{-1})$. Since matrix C has rank 2, it follows that, provided $a_{11} < 1$, $a_{33} < 1$,

$$\mathcal{T}_C = \rho\left(\begin{bmatrix} 0 & qa_{13}a_{21} \\ a_{32} & qa_{13}a_{31} + qa_{23}a_{32}(1 - a_{11}) \end{bmatrix}\right), \tag{3.10}$$

with $q = 1/((1 - a_{11})(1 - a_{33}))$. Alternatively, an explicit equation involving $\mathcal{T}_C$ can be derived as follows. Let $\tilde{A} = \begin{bmatrix} a_{11} & 0 & a_{13} \\ a_{21}/\sigma & 0 & a_{23} \\ a_{31}/\sigma & a_{32}/\sigma & a_{33} \end{bmatrix}$ be the controlled matrix. By Theorem 1, the target reproduction number $\mathcal{T}_C$ is the value of σ such that $\rho(\tilde{A}) = 1$. By Theorem 2 and applying formula (3.8) to matrix $\tilde{A}$, it follows that $\rho(\tilde{A}) = 1$ if and only if

$$\mathcal{T}_3(\tilde{A}) = \frac{a_{33} + a_{13}a_{31}\sigma^{-1} + a_{23}a_{32}\sigma^{-1} + a_{13}a_{32}a_{21}\sigma^{-2} - a_{11}a_{33} - a_{11}a_{23}a_{32}\sigma^{-1}}{1 - a_{11}} = 1.$$

Solving this gives a quadratic equation in σ^{-1}, namely,

$$a_{13}a_{21}a_{32}(\sigma^{-1})^2 + (a_{13}a_{31} + a_{23}a_{32} - a_{11}a_{23}a_{32})\sigma^{-1} + (-1 + a_{11} + a_{33} - a_{11}a_{33}) = 0. \tag{3.11}$$

When multiplied by σ^2, this agrees with the characteristic equation of the matrix in (3.10). As shown in Theorem 4, the terms in (3.11) have graphical interpretations: the coefficient of the quadratic term corresponds to the weight of the cycle (or cycle-union in general) that contains two target entries, the coefficient of the linear terms corresponds to the weights of cycle-unions that contain one target entry, and the constant term corresponds to the weights of cycle-unions that do not contain any target entry (including the empty digraph of weight 1).

The cycles and cycle-unions used to calculate the target reproduction numbers can be interpreted biologically in terms of the organism's life cycle. For example, in (3.11), the term containing two target entries, $a_{13}a_{21}a_{32}$, starts with flowers, goes to the seed bank (a_{13}), then to rosettes (a_{21}), then back to flowers (a_{32}). The terms containing one target entry and a single cycle are as follows: flowers-seed bank-flowers ($a_{13}a_{31}$) and flowers-rosettes-flowers ($a_{23}a_{32}$). The term containing one target entry and the union of two cycles is flowers-rosettes-flowers ($a_{23}a_{32}$) multiplied by seed bank-seed bank (a_{11}). The terms containing no target entries are as follows: the empty digraph (-1), seed bank-seed bank (a_{11}), flowers-flowers (a_{33}), and the product of the latter two representing the union of the two cycles.

3.4.4 Now we consider the minimum cost population control strategies for the scentless chamomile matrix A in (3.7) with the combination of control strategies in 3.4.1 and

3.4.3 above, i.e., control of fecundity and growth. In order to determine the minimum cost control effort, consider the controlled matrix $\tilde{A} = \begin{bmatrix} a_{11} & 0 & a_{13}/\tau \\ a_{21}/\sigma & 0 & a_{23}/\tau \\ a_{31}/\sigma & a_{32}/\sigma & a_{33}/\tau \end{bmatrix}$ with $\tau > 1$ and $\sigma > 1$, and set $\rho(\tilde{A}) = 1$, which is equivalent to setting $\mathcal{T}_3(\tilde{A}) = 1$ by Theorem 2. It follows from (3.8), since $a_{11} < 1$, that

$$\frac{\tau^{-1}(a_{33} + a_{13}a_{31}\sigma^{-1} + a_{23}a_{32}\sigma^{-1} + a_{13}a_{32}a_{21}\sigma^{-2} - a_{11}a_{33} - a_{11}a_{23}a_{32}\sigma^{-1})}{1 - a_{11}} = 1,$$

thus

$$\tau = \frac{a_{13}a_{32}a_{21}}{1 - a_{11}}\sigma^{-2} + \Big(a_{23}a_{32} + \frac{a_{13}a_{31}}{1 - a_{11}}\Big)\sigma^{-1} + a_{33}, \tag{3.12}$$

namely,

$$\begin{aligned} &a_{13}a_{32}a_{21}\tau^{-1}\sigma^{-2} + \Big(a_{13}a_{31} + a_{23}a_{32} - a_{11}a_{23}a_{32}\Big)\tau^{-1}\sigma^{-1} \\ &\quad + (a_{33} - a_{11}a_{33})\tau^{-1} - 1 + a_{11} = 0. \end{aligned} \tag{3.13}$$

Suppose the costs per unit of effort for control strategies with respect to strategies 3.4.1 and 3.4.3 are d_1 and d_2, respectively. We assume, for illustration, that $\tau - 1$ and $\sigma - 1$ measure the efforts needed for the control matrix $\tilde{A}$, and the corresponding total cost function is defined as $D = d_1(\tau - 1) + d_2(\sigma - 1)$. Using (3.12), it follows

$$D(\sigma) = d_2(\sigma - 1) + d_1\frac{a_{13}a_{32}a_{21}}{1 - a_{11}}\sigma^{-2} + d_1\Big(a_{23}a_{32} + \frac{a_{13}a_{31}}{1 - a_{11}}\Big)\sigma^{-1} + d_1(a_{33} - 1). \tag{3.14}$$

It can be verified that the minimum cost $D^* = D(\sigma^*)$ is achieved when $\sigma = \sigma^*$ where σ^* is a critical point of $D(\sigma)$. In particular, σ^* is the unique positive root of

$$D'(\sigma) = d_2 - 2d_1\frac{a_{13}a_{32}a_{21}}{1 - a_{11}}\sigma^{-3} - d_1\Big(a_{23}a_{32} + \frac{a_{13}a_{31}}{1 - a_{11}}\Big)\sigma^{-2} = 0,$$

or equivalently

$$(\sigma^*)^3 - \frac{d_1}{d_2}\Big(a_{23}a_{32} + \frac{a_{13}a_{31}}{1 - a_{11}}\Big)\sigma^* - 2\frac{d_1a_{13}a_{32}a_{21}}{d_2(1 - a_{11})} = 0.$$

Figure 2 illustrates the cost minimization process graphically. It is possible to control the populations when values of σ and τ fall above the solid curve. The straight line shows the cost curve for various different costs. The minimum cost, and resulting values $\sigma = \sigma^*$ and $\tau = \tau^*$ occur when the cost curve is tangent to the control curve.

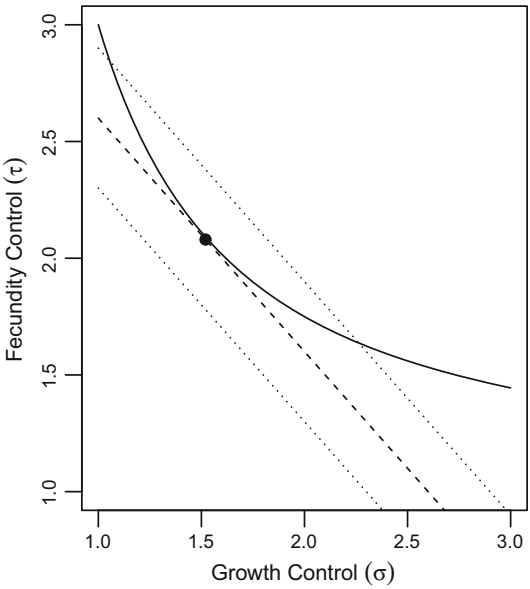

Fig. 2 Demonstration of the calculation of minimum cost control for the scentless chamomile system studied in Sect. *3.4.4*. The solid curve describes the relationship between fecundity control (τ) and growth control (σ) given by Eq. (3.12). Control is achieved for all points (σ, τ) lying above this curve. The dashed line shows the total cost function which achieves minimum cost. This is achieved at the value (σ^*, τ^*) given by the dot. The lower dotted line shows that control cannot be achieved for a lower than minimum cost, and the higher dotted line shows that when costs are higher a range of fecundity and growth values are available for successful control. For illustrative purposes, the coefficients for each power of σ in (3.12) were taken equal to 1 and d_2/d_1 was taken equal to 1. The dashed curve shows a total cost of $D = 1.6\, d_1$ and the upper and lower dotted curves show $D = 1.9\, d_1$ and $D = 1.3\, d_1$, respectively. These values yield $(\sigma^*, \tau^*) = (1.52, 2.08)$

4 Applications to epidemiology

4.1 Basic reproduction numbers as target reproduction numbers

Consider an ordinary differential equation compartmental model for infectious diseases. Let J be the Jacobian matrix, representing the linearization of the dynamics of the populations in the disease compartments at the disease-free state. Following the next generation matrix method (Diekmann et al. 2010, 2013; van den Driessche and Watmough 2002), consider a decomposition of J as $J = F - V$, where F and V represent the *transmission matrix* and *transfer matrix*, respectively. In particular, the inverse of V exists, and both F and V^{-1} are nonnegative. Then the *basic reproduction number* $\mathcal{R}_0$ is defined as the spectral radius of the *next generation matrix* FV^{-1}, that is, $\mathcal{R}_0 = \rho(FV^{-1})$. It sometimes happens that several terms in the disease models might have arguable biological interpretations or customarily be treated in a certain way for mathematical simplicity, resulting in a different decomposition of $J = \tilde{F} - \tilde{V}$, another next generation matrix $\tilde{F}\tilde{V}^{-1}$, and another basic reproduction number $\tilde{\mathcal{R}}_0 = \rho(\tilde{F}\tilde{V}^{-1})$. Since both next generation matrices FV^{-1} and $\tilde{F}\tilde{V}^{-1}$ cor-

respond to the same stability problem of matrix J, it follows that $\mathcal{R}_0$ and $\tilde{\mathcal{R}}_0$ always stay on the same side of the threshold value 1; see, for example, Knipl (2016, Proposition 2.1). Set $A = FV^{-1}$, and thus $\mathcal{R}_0 = \rho(A)$. Then the following result shows that $\tilde{\mathcal{R}}_0$ is actually a certain target reproduction number for matrix A, which extends and provides biological insights to earlier results by Bani-Yaghoub et al. (2012, Section 3.2) and Saad-Roy et al. (2015, Theorem 1).

Theorem 6 *Suppose that $J = F - V = \tilde{F} - \tilde{V}$, the inverse of V and $\tilde{V}$ both exist, and F, $\tilde{F}$, V^{-1}, $\tilde{V}^{-1}$ are nonnegative. If $F - \tilde{F} > 0$ and $\rho((F - \tilde{F})V^{-1}) < 1$, then $\tilde{\mathcal{R}}_0 = \rho(\tilde{F}\tilde{V}^{-1})$ is the target reproduction number $\mathcal{T}_C$ as in (2.1) for $A = FV^{-1}$ corresponding to the target matrix $C = \tilde{F}V^{-1}$.*

Proof Since $A = FV^{-1}$ and $C = \tilde{F}V^{-1}$, it follows that $B = A - C = (F - \tilde{F})V^{-1}$. Notice that $F - \tilde{F} = V - \tilde{V}$, and thus $B = (V - \tilde{V})V^{-1} = I - \tilde{V}V^{-1}$. Hence, the target reproduction number (2.1) becomes $\mathcal{T}_C = \rho(C(I - B)^{-1}) = \rho(\tilde{F}V^{-1}V\tilde{V}^{-1}) = \rho(\tilde{F}\tilde{V}^{-1}) = \tilde{\mathcal{R}}_0$. □

Biologically, the basic reproduction number $\mathcal{R}_0 = \rho(FV^{-1})$ can be regarded as the target reproduction number for $A = FV^{-1}$ corresponding to the target matrix $C = A = FV^{-1}$, i.e., targeting all entries in A.

Theorem 7 *Let F, $\tilde{F}$, V, $\tilde{V}$ satisfy assumptions in Theorem 6, and $F > \tilde{F}$. Set $\mathcal{R}_0 = \rho(FV^{-1})$ and $\tilde{\mathcal{R}}_0 = \rho(\tilde{F}\tilde{V}^{-1})$. Then one of the following holds:*

(1) $1 < \mathcal{R}_0 < \tilde{\mathcal{R}}_0$;
(2) $\mathcal{R}_0 = \tilde{\mathcal{R}}_0 = 1$;
(3) $\tilde{\mathcal{R}}_0 < \mathcal{R}_0 < 1$.

Proof By Theorem 6, $\tilde{\mathcal{R}}_0 = \mathcal{T}_C$, where $\mathcal{T}_C$ is defined as in (2.1) with $A = FV^{-1}$ and $C = \tilde{F}V^{-1}$. On the other hand, $\mathcal{R}_0 = \mathcal{T}_{C'}$ with $C' = A$. Since $F > \tilde{F}$, it follows that $C' > C$, and thus the relations between $\mathcal{R}_0 = \mathcal{T}_{C'}$ and $\tilde{\mathcal{R}}_0 = \mathcal{T}_C$ follow from Theorem 3. □

4.2 Application to heterogeneous infectious disease control

Heterogeneity exists and plays an important role in infectious disease transmission. Mathematical models have been employed to understand the disease dynamics and to evaluate the disease intervention and control strategies. For example, the multi-group type of models (which also are called Lagrangian models (Cosner et al. 2009)) have been used to investigate the effect of the core group in sexually transmitted infections (Lajmanovich and Yorke 1976), and to model the spatial spread of infectious diseases (Lloyd and May 1996). It turns out that the basic reproduction number $\mathcal{R}_0$, defined as the spectral radius of the next generation matrix (Diekmann et al. 2013; van den Driessche and Watmough 2002), generally determines whether the disease dies out from all groups or persists at an endemic level in each group (Guo et al. 2006; Lajmanovich and Yorke 1976; Lloyd and May 1996). Hence, in order to eradicate the disease from all groups, various disease intervention and control strategies need to reduce the value of the (controlled) reproduction number below 1; see, for example,

Chow et al. (2011), Heesterbeek and Roberts (2007), Roberts and Heesterbeek (2003). In this section, we evaluate group-targeted vaccination strategies (Chow et al. 2011) by incorporating the vaccine cost into target reproduction numbers.

An n-group infectious disease model applicable for viral diseases such as measles or influenza leads to an $n \times n$ next generation matrix $A = [\frac{\beta_{ij} N_i}{d+\gamma}]$, where d is the birth and death rate, γ is the recovery rate (thus $1/\gamma$ is the mean infectious period), β_{ij} is the mass action transmission coefficient from infectious individuals in group j to susceptible individuals in group i, and N_i is the constant total population in group i. To simplify our exposition, we consider a 2-group model and take

$$A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}, \tag{4.1}$$

where a_{ii} represents the within-group transmission in group i ($i = 1, 2$), while a_{ij} represents the between-group transmission in group i due to infectious individuals in group j ($j \neq i$). Suppose that a vaccine can be employed to target host individuals in group i with a cost per unit effort d_i; that is, it costs $d_i p_i$ to effectively vaccinate a fraction p_i ($0 < p_i \leq 1$) of the host individuals in group i. In reality, d_i might depend on the population size of group i, the type of vaccine applied, and the cost covering the utility and human resource. The within-group and between-group transmission after the vaccine effort applied in group i become a_{ii}/τ_i and a_{ij}/τ_i with $\tau_i = 1/(1-p_i) \geq 1$. This removal of a vaccinated proportion, p_i, from a population of size N_i reduces the population size to $(1 - p_i)N_i$. With target sets $S_{\tau_i} = \{(i, j) | j = 1, 2\}$ for $i = 1, 2$, with effort τ_i, the controlled next generation matrix is

$$\tilde{A} = \begin{bmatrix} a_{11}/\tau_1 & a_{12}/\tau_1 \\ a_{21}/\tau_2 & a_{22}/\tau_2 \end{bmatrix}. \tag{4.2}$$

Then the type reproduction numbers $\mathcal{T}_1, \mathcal{T}_2$ can be calculated using Corollary 1 and assuming $a_{11} < 1, a_{22} < 1$:

$$\mathcal{T}_1 = \frac{a_{11} + a_{12}a_{21} - a_{11}a_{22}}{1 - a_{22}} = a_{11} + \frac{a_{12}a_{21}}{1 - a_{22}}, \tag{4.3}$$

and

$$\mathcal{T}_2 = a_{22} + \frac{a_{12}a_{21}}{1 - a_{11}}. \tag{4.4}$$

Applying (4.3) for matrix $\tilde{A}$ in (4.2) gives

$$\tilde{\mathcal{T}}_1 = a_{11}\tau_1^{-1} + \frac{a_{12}a_{21}\tau_1^{-1}\tau_2^{-1}}{1 - a_{22}\tau_2^{-1}}. \tag{4.5}$$

From Theorem 2, $\rho(\tilde{A}) = 1$ iff $\tilde{\mathcal{T}}_1 = 1$, and since $\tau_i = 1/(1 - p_i)$ it follows that

$$1 = a_{11}(1 - p_1) + \frac{a_{12}a_{21}(1 - p_1)(1 - p_2)}{1 - a_{22}(1 - p_2)}. \tag{4.6}$$

Let $D = D(p_1, p_2)$ denote the cost function with vaccination among two groups that effectively vaccinates fractions p_i of the group populations. Then, by assumption,

$$D = d_1 p_1 + d_2 p_2, \qquad 0 \le p_1, p_2 \le 1. \tag{4.7}$$

The minimum cost group-targeted vaccination strategies can be investigated by minimizing the cost function D in (4.7) subject to the constraint (4.6).

Theorem 8 *Suppose that $\mathcal{R}_0 = \rho(A) > 1$, $a_{11} < 1$, and $a_{22} < 1$. Let $\mathcal{T}_1, \mathcal{T}_2$ be as defined in (4.3)–(4.4). Then the cost function $D(p_1, p_2)$ in (4.7) subject to (4.6) achieves the minimum $D^* = D(p_1^*, p_2^*)$ where p_1^* and p_2^* satisfy the following conditions.*

(1) *If $a_{11}a_{22} < a_{12}a_{21}$, then either $p_1^* = 0$ or $p_2^* = 0$.*

(1a) *If, in addition, $\dfrac{d_2}{d_1} > \bar{r} := \dfrac{1 - \frac{1}{\mathcal{T}_1}}{1 - \frac{1}{\mathcal{T}_2}}$, then $p_1^* = 1 - \dfrac{1}{\mathcal{T}_1}$ and $p_2^* = 0$.*

(1b) *If, in addition, $\dfrac{d_2}{d_1} < \bar{r}$, then $p_1^* = 0$ and $p_2^* = 1 - \dfrac{1}{\mathcal{T}_2}$.*

(2) *If $a_{11}a_{22} > a_{12}a_{21}$, then p_1^* and p_2^* depend on the following constants*

$$\bar{p}_1 = 1 - \frac{a_{22} - \sqrt{\frac{d_2}{d_1} a_{12}a_{21}}}{a_{11}a_{22} - a_{12}a_{21}} \quad \text{and} \quad \bar{p}_2 = 1 - \frac{a_{11} - \sqrt{\frac{d_1}{d_2} a_{12}a_{21}}}{a_{11}a_{22} - a_{12}a_{21}}. \tag{4.8}$$

(2a) *If*

$$r_* := \frac{(a_{22} + a_{12}a_{21} - a_{11}a_{22})^2}{a_{12}a_{21}} < \frac{d_2}{d_1} < r^* := \frac{a_{12}a_{21}}{(a_{11} + a_{12}a_{21} - a_{11}a_{22})^2},$$

then $0 < p_1^* = \bar{p}_1 < 1 - \dfrac{1}{\mathcal{T}_1}$ and $0 < p_2^* = \bar{p}_2 < 1 - \dfrac{1}{\mathcal{T}_2}$.

(2b) *If $\dfrac{d_2}{d_1} > r^*$, then $p_1^* = 1 - \dfrac{1}{\mathcal{T}_1}$ and $p_2^* = 0$.*

(2c) *If $\dfrac{d_2}{d_1} < r_*$, then $p_1^* = 0$ and $p_2^* = 1 - \dfrac{1}{\mathcal{T}_2}$.*

Proof It follows from (4.6) that

$$p_1 = p_1(p_2) = 1 - \frac{1 - a_{22}(1 - p_2)}{a_{11} + (1 - p_2)(a_{12}a_{21} - a_{11}a_{22})}.$$

Thus

$$p_1' = \frac{-a_{12}a_{21}}{(a_{11} + (1 - p_2)(a_{12}a_{21} - a_{11}a_{22}))^2} < 0,$$
$$p_1'' = \frac{2a_{12}a_{21}(a_{11}a_{22} - a_{12}a_{21})}{(a_{11} + (1 - p_2)(a_{12}a_{21} - a_{11}a_{22}))^3},$$

and the sign of p_1'' agrees with the sign of $a_{11}a_{22} - a_{12}a_{21}$.

When $a_{11}a_{22} < a_{12}a_{21}$, $p_1 = p_1(p_2)$ is a continuous curve in the p_1-p_2 plane connecting $(1 - \frac{1}{\mathcal{T}_1}, 0)$ and $(0, 1 - \frac{1}{\mathcal{T}_2})$, which is decreasing and concave down as $p_1'' < 0$. The cost function $D = d_1 p_1 + d_2 p_2$ corresponds to a series of straight lines with different values D. The minimum value of D is obtained when one of the straight lines cross one of the boundary points $(0, 1 - \frac{1}{\mathcal{T}_2})$ or $(1 - \frac{1}{\mathcal{T}_1}, 0)$.

When $a_{11}a_{22} > a_{12}a_{21}$, the curve $p_1 = p_1(p_2)$ is decreasing and concave up. The minimum value of D might be obtained when the straight line is tangent to the curve $p_1 = p_1(p_2)$ at the interception point $(\bar{p}_1, \bar{p}_2)$, where $\bar{p}_1$ and $\bar{p}_2$ are given as in (4.8). It can be verified that if the assumption in (2a) is satisfied, both $\bar{p}_i$ are in the biologically reasonable range between 0 and $1 - \frac{1}{\mathcal{T}_i}$. Otherwise, the minimum value of D is obtained when the straight line crosses the boundary point $(1 - \frac{1}{\mathcal{T}_1}, 0)$ or $(0, 1 - \frac{1}{\mathcal{T}_2})$; this is the case (2b) or (2c). □

Note that $r_* = r^* = \bar{r}$ if and only if $a_{11}a_{22} = a_{12}a_{21}$ (i.e., A and $\tilde{A}$ are singular matrices) provided $\mathcal{R}_0 > 1$. Biologically, if between-group transmission is larger than within-group transmission in a two-group disease model, then the one-group vaccination strategy is better than the two-group vaccination strategy. On the other hand, if within-group transmission is larger than between-group transmission (e.g., for infectious diseases that spread in several geographic regions), then the two-group vaccination strategy might be more cost-effective (especially when the cost per unit effort d_i in each group is relatively comparable). For the latter situation, when the cost per unit ratio d_2/d_1 increases, (4.8) shows that it is better to increase vaccine coverage in group 1, as $\bar{p}_1$ increases . We now illustrate these statements with specific examples.

Example 1 Let $A = [a_{ij}] = \begin{bmatrix} 0.5 & 0.6 \\ 0.6 & 0.5 \end{bmatrix}$, then $\mathcal{T}_1 = \mathcal{T}_2 = a_{11} + \frac{a_{12}a_{21}}{1-a_{22}} = 1.22$. In this example, both within-group transmissions and between-group transmissions are equal, with the latter being larger. By Theorem 2, $\mathcal{R}_0 = \rho(A) > 1$. Note that $a_{11} < 1, a_{22} < 1$ and $a_{11}a_{22} = 0.25 < a_{12}a_{21} = 0.36$; all assumptions in Theorem 8(1) are satisfied. By Theorem 8, a better vaccination strategy is to target the group with lower cost per unit effort as $\bar{r} = \frac{1-\frac{1}{\mathcal{T}_1}}{1-\frac{1}{\mathcal{T}_2}} = 1$, and more than $p_1 = 1 - 1/\mathcal{T}_1$ of the host population in this group needs to be effectively vaccinated in order to eradicate the disease from both groups.

Example 2 Let $A = [a_{ij}] = \begin{bmatrix} 0.6 & 0.5 \\ 0.5 & 0.6 \end{bmatrix}$, then $\mathcal{T}_1 = \mathcal{T}_2 \approx 1.11$ and $\mathcal{R}_0 = \rho(A) > 1$. In this case, within-group transmissions are larger. Since $a_{11}a_{22} = 0.36 > a_{12}a_{21} = 0.25$, by Theorem 8(2), $r_* = 0.9604$, $r^* = 1.0412$ and the minimum cost vaccination strategy is determined by the cost per unit ratio in two groups. Specifically, if $r_* < d_2/d_1 < r^*$, then it is better to vaccinate both groups with more than $\bar{p}_i$ of the host population in each group i to require immunity from vaccine. If $d_2/d_1 > r^*$, then it is better to vaccinate group 1 such that more than $1 - 1/\mathcal{T}_1$ of the group population is effectively vaccinated. If $d_2/d_1 < r_*$, then the better vaccination strategy is to target group 2 such that more than $1 - 1/\mathcal{T}_2$ of the population in group 2 requires immunity from vaccine.

Example 3 The results developed above can also be applied to diseases with no between-group transmission such as a vector-borne disease (e.g., malaria) or a heterosexually transmitted diseases (e.g., gonorrhea). Let $A = [a_{ij}] = \begin{bmatrix} 0 & a_{12} \\ a_{21} & 0 \end{bmatrix}$ be the next generation matrix for simple disease models in which transmission happens due to host-vector contact for vector-borne diseases or due to heterosexual contact for sexually transmitted infections (STIs). By Theorem 8 (1), it is better to target either the vector population or the host population for vector-borne diseases and target either the female or male group for STIs, depending on the cost of corresponding one-group target strategies. For example, in order to eradicate malaria, the mosquito population or the susceptible human population needs to be reduced below a certain threshold. According to Theorem 8, it is better to apply all available resources to target only one population, either mosquito control or human protection (e.g., bed nets, vaccination), depending on the relative costs involved. However, our underlying model is very simple, and since control or vaccination costs are expected to be variable (e.g., rising when nearing a high vaccination rate), it may be more effective to target both hosts. This could be the subject of further research using more realistic and complicated infectious disease models.

5 Concluding remarks

We have developed a general mathematical framework, based on newly extended target reproduction numbers, which unifies threshold parameters in theoretical biology. The extended target reproduction numbers include the classical net reproductive value used in ecology, and the basic and type reproduction numbers used in epidemiology. These parameters delineate conditions under which a population or disease persists or goes extinct. Specifically, knowledge of these target reproduction numbers aids in measuring the change of certain parameter values in order to protect endangered species (e.g., salmonids, see Sect. 3.3), and to determine vaccination strategies for disease control (e.g., a two group infectious disease model, see Examples 1 and 2 in Sect. 4.2).

Our results on target reproduction numbers are developed algebraically, but graph theoretic interpretations using cycle-unions in the digraph underlying the dynamics are also given. This approach leads to a characteristic equation that is useful for deriving minimum cost population mixed control strategies in terms of the cost of each individual control strategy (see Sect. 3.4.4 and Fig. 2 for control of scentless chamomile, and Sect. 4.2 for disease control by vaccination). The general framework developed can be applied to Leslie matrices, with extensions to Lefkovitch matrices for stage structured populations, as well as to multigroup disease transmission models. Using parameter values and cost functions estimated from data, the results can be applied to give practical suggestions for minimum cost control strategies to control or preserve populations and to eradicate infectious diseases.

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