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A graph-theoretic method for the basic reproduction number in continuous time epidemiological models

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Abstract In epidemiological models of infectious diseases the basic reproduction number $\mathcal{R}_0$ is used as a threshold parameter to determine the threshold between disease extinction and outbreak. A graph-theoretic form of Gaussian elimination using digraph reduction is derived and an algorithm given for calculating the basic reproduction number in continuous time epidemiological models. Examples illustrate how this method can be applied to compartmental models of infectious diseases modelled by a system of ordinary differential equations. We also show with these examples how lower bounds for $\mathcal{R}_0$ can be obtained from the digraphs in the reduction process.

Mathematics Subject Classification (2000) 92D30 · 05C50

1 Introduction

In epidemiological models of infectious diseases, the basic reproduction number, $\mathcal{R}_0$, defined as the number of new infections that occur after one initial infective is introduced into a susceptible population [1], is used as a threshold parameter to determine the condition for disease outbreaks; see, for example, [7,16,22]. This

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quantity is considered essential in the study of population dynamics of infectious diseases [14,15,23]. Using the precise definition of $\mathcal{R}_0$ given in [10,11], we derive a graph-theoretic method, analogous to a method developed in [3] for discrete systems, to compute $\mathcal{R}_0$ for continuous time epidemiological models.

In general, for standard epidemiological models, an infection dies out if $\mathcal{R}_0 < 1$; whereas an infection invades a susceptible population if $\mathcal{R}_0 > 1$ [16]. For both discrete and continuous time models, $\mathcal{R}_0$ can be calculated as the spectral radius of the next generation matrix [11,19]. This calculation involves several matrix operations that can be computationally complicated as the number of compartments in the model increases. The graph-theoretic method we present here allows for calculating $\mathcal{R}_0$ more easily for some complex continuous time epidemiological models.

We begin in Sect. 2 by giving a determinantal formula for $\mathcal{R}_0$. Then, in Sect. 3, we describe the graph reduction procedure for this formula, and use this in Sect. 4 to give an algorithm to calculate $\mathcal{R}_0$. In Sect. 5, we show with examples how the method is applied to calculate $\mathcal{R}_0$ for ordinary differential equation (ODE) epidemiological models. We conclude in Sect. 6 with a discussion.

2 Basic reproduction number

We first give a formula for determining the basic reproduction number for an ODE disease transmission model. This is in the same spirit as a formula for the net reproductive rate for stage structured population models as given in [3,19]. We use the notation as in [11] for an ODE disease transmission model, which is assumed to have a disease free equilibrium (DFE) in which all infected variables are zero, and the model without disease is assumed to be stable.

Consider the ODE system for the infected variables linearized about the DFE, and write the coefficient matrix as $\mathbf{F} - \mathbf{V}$ assumed to be irreducible, where $\mathbf{F}$ contains new infection terms and $\mathbf{V}$ contains the terms representing transfer between compartments. From [11], $\mathbf{F}$ is (entrywise) non-negative, non-zero, and $\mathbf{V}$ is a non-singular M-matrix. Thus, the next generation matrix $\mathbf{FV}^{-1}$ is non-negative and non-zero. The basic reproduction number $\mathcal{R}_0$ is defined as $\mathcal{R}_0 = \rho(\mathbf{FV}^{-1})$, where ρ denotes the spectral radius. The DFE is locally asymptotically stable if $\mathcal{R}_0 < 1$, but unstable if $\mathcal{R}_0 > 1$ [10,11]. The following result is used for our graph-theoretic method to compute $\mathcal{R}_0$.

Theorem 1 *Let* $\mathbf{F}$ *be a non-zero non-negative matrix and* $\mathbf{V}$ *be a non-singular* M*-matrix such that* $\mathbf{F} - \mathbf{V}$ *is irreducible. Then* $\mathcal{R}_0 = \rho(\mathbf{FV}^{-1}) > 0$ *and* $\mathcal{R}_0$ *is the reciprocal of the smallest positive root* x *of the polynomial equation* $\det(\mathbf{F}x - \mathbf{V}) = 0$.

Proof From the assumptions, $\mathbf{FV}^{-1}$ is a non-zero non-negative matrix, and by [19, Proposition 4.1] and Perron–Frobenius theory the principal submatrix corresponding to the non-zero rows of $\mathbf{F}$ is irreducible. Thus $\lambda = \rho(\mathbf{FV}^{-1}) > 0$ is the largest positive root of the polynomial equation $\det(\lambda\mathbf{I} - \mathbf{FV}^{-1}) = 0$. Since $\mathbf{V}$ is non-singular and $\lambda > 0$, the polynomial equation is equivalent to $\det(\mathbf{F}\lambda^{-1} - \mathbf{V}) = 0$ (where $\mathbf{V} - \mathbf{F}\lambda^{-1}$ is a singular M-matrix) and λ^{-1} is the smallest positive root. From the definition of $\mathcal{R}_0 = \rho(\mathbf{FV}^{-1})$, the result follows. □

To use the above theorem in digraph reduction (Sect. 3) and in computing $\mathcal{R}_0$ (Sect. 4), we need to consider Gaussian elimination using row reductions. Let **A** be an irreducible $n \times n$ singular M-matrix. Then each proper principal submatrix is a nonsingular M-matrix [2, Theorem 4.16], and, in particular, each main diagonal entry of **A** is positive. Performing Gaussian elimination successively reducing the jth column ($j = 1, \ldots, n-1$) to have the (j, j) entry equal to 1 and (i, j) entry equal to zero for $i > j$. At each step every diagonal entry is positive, whereas at the final reduction step, the (n, n) entry is zero since **A** is singular [24, Lemma 4]. With $\lambda = \rho(\mathbf{F}\mathbf{V}^{-1})$, letting $-\mathbf{A} = \mathbf{F}\lambda^{-1} - \mathbf{V}$ the negative of an irreducible M-matrix, the above discussion shows that no zero divisor results in the Gaussian elimination on $\mathbf{F}\lambda^{-1} - \mathbf{V}$, and that at each step, other than the last, every diagonal entry is negative. Note that by permutation similarity, it does not matter in which order the columns are chosen. Since the equation $\det(\mathbf{F}\lambda^{-1} - \mathbf{V}) = 0$ gives the same polynomial in λ as $\det(\mathbf{E}(\mathbf{F}\lambda^{-1} - \mathbf{V})) = 0$ where **E** is a product of elementary matrices, the above Gaussian elimination results in a polynomial equation that gives $\mathcal{R}_0$ as in Theorem 1. Such row operations correspond to reductions in the digraph associated with $\mathbf{F}\lambda^{-1} - \mathbf{V}$, which we now describe.

To a real $n \times n$ matrix $\mathbf{A} = (a_{ij})$, there corresponds a labelled directed graph (digraph) $D(\mathbf{A})$ with nodes $1, 2, \ldots, n$ and a directed edge (arc) $j \to i$ if and only if $a_{ij} \neq 0$ for $i, j = 1, 2, \ldots, n$. The weight of this arc is a_{ij}, and $D(\mathbf{A})$ has a loop at node i of weight a_{ii} if $a_{ii} \neq 0$. Note that **A** completely describes $D(\mathbf{A})$ and conversely. The correspondence of a digraph with the coefficient matrix of a system of equations has been pioneered in the engineering literature by [8,21]; see [6, chapter 3] for a detailed description and further references. For a given **A** the digraph $D(\mathbf{A})$ described above is the *Coates digraph* of **A**. Note that, given $D(\mathbf{A})$, matrix **A** is the transpose of that often used as the weighted adjacency matrix; see, e.g., [13]

Our digraph reduction rules on the Coates digraph of **A** are now stated. They are similar of those given in [6]; see also [3,5,21], and are elementary Gaussian elimination steps. A node with weight -1 is called a *trivial node*.

3 Reduction on digraph associated with $\mathbf{F}\lambda^{-1} - \mathbf{V}$

Rule 1 (Creating a trivial node) *To reduce the loop* $-a_{ii} < 0$ *to* -1 *at node* i*, every arc entering* i *has weight divided by* a_{ii} (Fig. 1a).

Note that there may be a loop at j in Fig. 1a, and that after reduction node i has a loop with weight -1. This operation is equivalent to dividing row i of $\det(\mathbf{F}\lambda^{-1} - \mathbf{V})$ by $a_{ii} > 0$, which multiplies the value of the determinant by $1/a_{ii}$.

Rule 2 (Elimination of arcs through a trivial node) *For a trivial node* i *on a path* $j \to i \to k$*, the two arcs are replaced by* $j \to k$ *with weight equal to the product of weights on arc* $j \to i$ *and* $i \to k$*. Weights on multiple arcs* $j \to k$ *are added. If there are no more paths through the trivial node* i*, then it can be disregarded. See Fig.* 1b*, in which node* i *is not shown in the third digraph.*

In this case if j is equal to k, then weights are added to the loop. This operation is equivalent to the elementary Gaussian elimination that adds a_{ki} times row i to row k, thus reducing the (k, i) entry to 0. This operations leaves the determinant unchanged.

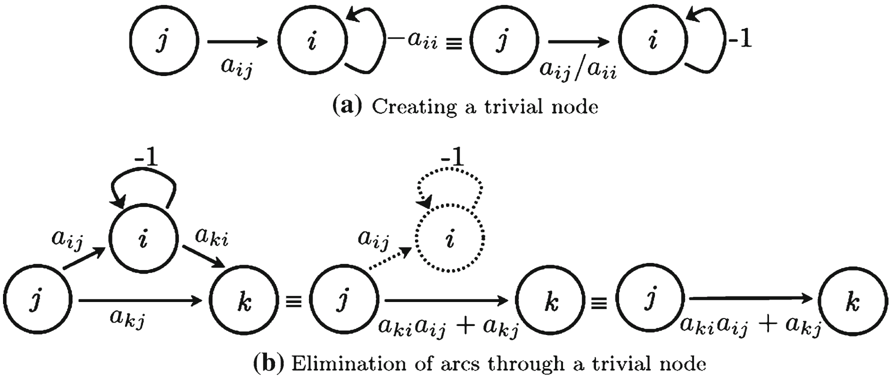


Fig. 1 Digraph reduction rules

4 Algorithm to compute $\mathcal{R}_0$ from the digraph associated with $\mathbf{F}\lambda^{-1} - \mathbf{V}$

Using Theorem 1 and the two digraph reduction rules, we now give a symbolic computation method to calculate $\mathcal{R}_0$. For a connected dynamical system, consider the matrix $\mathbf{F}\lambda^{-1} - \mathbf{V}$. If this matrix is irreducible, then draw the associated digraph with arc $j \to i$ if and only if the (i, j) entry of the matrix is nonzero. If $j = i$ and the (i, i) entry is -1, then i is called a trivial node.

1. In the digraph choose a node i with a loop.
2. Use Rule 1 to make node i trivial.
3. Recalculate all paths going through node i using Rule 2. Node i can then be disregarded.
4. Continue steps 1, 2, 3 until only one node remains.
5. Set the weight of this loop to zero giving an equation for λ. Then by Theorem 1, $\mathcal{R}_0$ is the reciprocal of the smallest positive root of this equation.

Note that in implementation nodes other than i can also be made trivial at step 2, but node i must be trivial before step 3 is performed. This algorithm is equivalent to symbolic Gaussian elimination on $\det(\mathbf{F}\lambda^{-1} - \mathbf{V}) = 0$. If the digraph is not strongly connected, then the algorithm can be applied to each strongly connected component.

5 Examples

5.1 Vector–host model

As an simple illustrative example, consider the vector–host model presented in [11]. The equations for a coupled SIS (host) and SI (vector) model are given by

$$\frac{dI}{dt} = \beta_s SV - (b + \gamma)I, \tag{1}$$

$$\frac{dV}{dt} = \beta_m MI - cV, \tag{2}$$

$$\frac{dS}{dt} = b - bS + \gamma I - \beta_s SV, \tag{3}$$

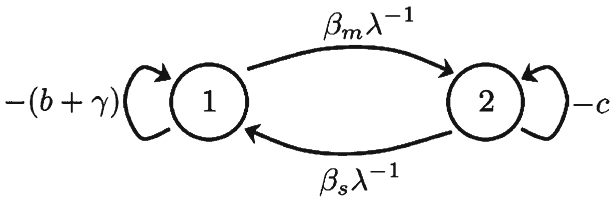
$$\frac{dM}{dt} = c - cM - \beta_m MI, \tag{4}$$

where the compartments correspond to proportions of infective host (I), infective vector (V), susceptible host (S), and susceptible vector (M). For the host, $b > 0$ is the birth and death rate constant, γ is the recovery rate constant; for the vector, $c > 0$ is the birth and death rate constant. Cross infections have disease transmission coefficients β_s, β_m. The disease free equilibrium is $(0, 0, 1, 1)^T$, and

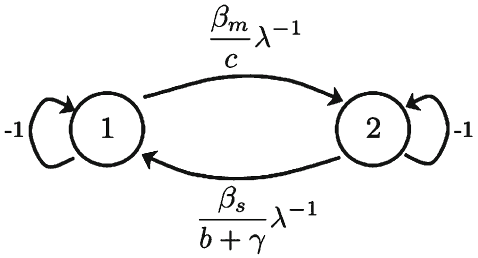
$$\mathbf{F} = \begin{pmatrix} 0 & \beta_s \\ \beta_m & 0 \end{pmatrix}, \quad \mathbf{V} = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix}, \tag{5}$$

with $\mathbf{V}$ non-singular. Figure 2 with nodes 1,2 representing I,V, respectively, shows the digraph representation of matrix $\mathbf{F}\lambda^{-1} - \mathbf{V}$ and the detailed digraph reduction procedure to obtain $\mathcal{R}_0$. Following the algorithm presented in Sect. 4, Fig. 2b is obtained from Fig. 2a after choosing both node 1 and node 2 and applying Rule 1. Then apply Rule 2, yielding the digraph shown in Fig. 2c, in which node 1 is not shown. Finally, applying the last step of the algorithm and solving the quadratic equation gives

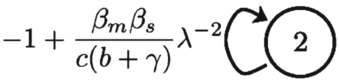
$$\mathcal{R}_0 = \sqrt{\frac{\beta_m \beta_s}{c(b+\gamma)}}. \tag{6}$$



(a) Digraph of $\mathbf{F}\lambda^{-1} - \mathbf{V}$



(b) Creation of trivial nodes using Rule 1



(c) Using Rule 2

Fig. 2 Graph reduction procedure applied to the vector–host model

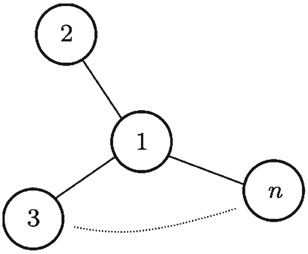


Fig. 3 Star topology for travelling

The square root here indicates a geometric mean, and this basic reproduction number gives a threshold for the vector-host model with the DFE linearly stable if $\mathcal{R}_0 < 1$ but unstable if $\mathcal{R}_0 > 1$.

5.2 Star topology model

Consider an epidemiological model with n spatial patches in which susceptible (S), exposed (E) , and recovered (R) people can travel going through a central hub. Infective people (I) are too sick to travel. The topology of this system is a star with a center patch and $n-1$ patches around it as shown in Fig. 3. This star topology is suggested for models of communities at nodes 2, 3, …, n that use a common hospital or school at the center node 1. In [12] this topology (called spider) is used to describe the spread of tuberculosis in possums moving between patches. The dynamics at the center (node 1 in Fig. 3) is given by

$$\frac{dS_1}{dt} = -\beta_1 S_1 I_1 + A_1 - d_1 S_1 + w_1 R_1 + \sum_{j=2}^{n} m_{1j} S_j - \sum_{j=2}^{n} m_{j1} S_1, \tag{7}$$

$$\frac{dE_1}{dt} = \beta_1 S_1 I_1 - (d_1 + \alpha_1) E_1 + \sum_{j=2}^{n} m_{1j} E_j - \sum_{j=2}^{n} m_{j1} E_1, \tag{8}$$

$$\frac{dI_1}{dt} = \alpha_1 E_1 - (d_1 + \varepsilon_1 + \gamma_1) I_1, \tag{9}$$

$$\frac{dR_1}{dt} = \gamma_1 I_1 - (d_1 + w_1) R_1 + \sum_{j=2}^{n} m_{1j} R_j - \sum_{j=2}^{n} m_{j1} R_1. \tag{10}$$

Similarly for the patches $j = 2, \ldots, n$

$$\frac{dS_j}{dt} = -\beta_j S_j I_j + A_j - d_j S_j + w_j R_j + m_{j1} S_1 - m_{1j} S_j, \tag{11}$$

$$\frac{dE_j}{dt} = \beta_j S_j I_j - (d_j + \alpha_j) E_j + m_{j1} E_1 - m_{1j} E_j, \tag{12}$$

$$\frac{dI_j}{dt} = \alpha_j E_j - (d_j + \varepsilon_j + \gamma_j) I_j, \tag{13}$$

$$\frac{dR_j}{dt} = \gamma_j I_j - (d_j + w_j) R_j + m_{j1} R_1 - m_{1j} R_j. \tag{14}$$

For patch $k = 1, 2, \ldots, n$, $A_k > 0$ is the constant input into the susceptible compartment, $d_k > 0$ is the natural death rate constant, ε_k is the disease induced death rate constant, α_k^{-1} is the mean latency period, γ_k^{-1} is the mean infective period, w_k^{-1} is the mean period of temporary immunity, and β_k is the disease transmission coefficient assuming mass action incidence. In addition, $m_{j1}, m_{1j} > 0$ are the rates of travel from patch 1 to patch j, patch j to patch 1, respectively, and are assumed the same for susceptible, exposed and recovered individuals. Here the variables S_k, E_k, I_k, R_k denote the number of individuals in each compartment.

Since $d_k, A_k > 0$, there exist a DFE $(\bar{S}_k, 0, 0, 0)$ with $\bar{S}_k = A_k/d_k > 0$, $k = 1, \ldots, n$. Linearizing around the DFE and taking E_k, I_k variables gives the coefficient matrix $\mathbf{F} - \mathbf{V}$ where $\mathbf{F}$ is a block diagonal matrix that can be written using the direct sum symbol $\oplus$ as

$$\mathbf{F} = \begin{pmatrix} 0 & \beta_1 \bar{S}_1 \\ 0 & 0 \end{pmatrix} \oplus \begin{pmatrix} 0 & \beta_2 \bar{S}_2 \\ 0 & 0 \end{pmatrix} \oplus \cdots \oplus \begin{pmatrix} 0 & \beta_n \bar{S}_n \\ 0 & 0 \end{pmatrix}, \tag{15}$$

and

$$\mathbf{V} = \begin{pmatrix} \mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} & \ldots & \mathbf{V}_{1n} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & 0 & \ldots & 0 \\ \vdots & 0 & 0 & \ddots & \vdots \\ \mathbf{V}_{n1} & 0 & \ldots & 0 & \mathbf{V}_{nn} \end{pmatrix}, \tag{16}$$

where $\mathbf{V}_{k\ell}$ is a 2×2 block with

$$\mathbf{V}_{11} = \begin{pmatrix} d_1 + \alpha_1 + \sum_{j=2}^{n} m_{j1} & 0 \\ \alpha_1 & d_1 + \varepsilon_1 + \gamma_1 \end{pmatrix}, \tag{17}$$

$$\mathbf{V}_{jj} = \begin{pmatrix} d_j + \alpha_j + m_{1j} & 0 \\ \alpha_j & d_j + \varepsilon_j + \gamma_j \end{pmatrix}, \tag{18}$$

$$\mathbf{V}_{j1} = \begin{pmatrix} -m_{j1} & 0 \\ 0 & 0 \end{pmatrix}, \quad \mathbf{V}_{1j} = \begin{pmatrix} -m_{1j} & 0 \\ 0 & 0 \end{pmatrix}, \tag{19}$$

for $j = 2, \ldots, n$.

The digraph of $\mathbf{F}\lambda^{-1} - \mathbf{V}$ is shown in Fig. 4, here node $2i - 1$ represents E_i and node $2i$ represents I_i. Using the algorithm presented in Sect. 4, Fig. 5a shows the digraph reduction procedure using Rules 1 and 2 so that nodes distance two from the center node can be disregarded. Such nodes are not shown in the figures. Figure 5b shows the procedure to make nodes $3, 5, \ldots, 2n - 1$ trivial, and Fig. 5c shows the use of Rule 2 so that these nodes can be disregarded. Finally, Fig. 5d shows Rules 1 and 2 applied, leaving node 1 as the one remaining node. The final step of the algorithm gives the following equation, which can in general be written as a polynomial of degree n for λ (since the denominator in the last term is nonzero):

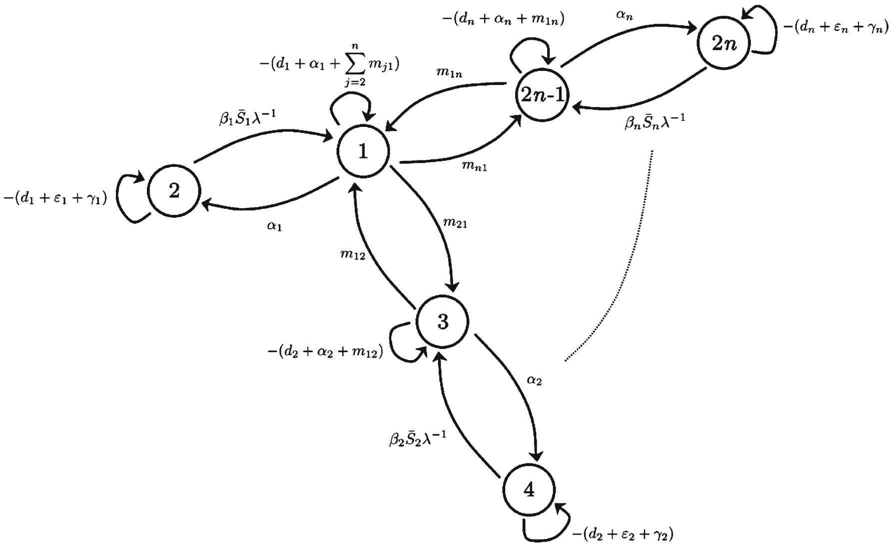


Fig. 4 Digraph for $\mathbf{F}\lambda^{-1} - \mathbf{V}$ from (15)–(19)

$$0 = \frac{\alpha_1\beta_1\bar{S}_1}{(d_1+\varepsilon_1+\gamma_1)\lambda} - \left(d_1+\alpha_1+\sum_{j=2}^{n} m_{j1}\right) + \sum_{j=2}^{n}\left[\frac{m_{1j}m_{j1}}{(d_j+\alpha_j+m_{1j}) - \frac{\alpha_j\beta_j\bar{S}_j}{(d_j+\varepsilon_j+\gamma_j)\lambda}}\right]. \tag{20}$$

Then $\mathcal{R}_0$ can be found as the reciprocal of the smallest positive root of this polynomial equation. Note that the systematic digraph reduction is easy to implement for this topology, and avoids calculation of the inverse of the $2n \times 2n$ matrix $\mathbf{V}$ needed to calculate $\mathcal{R}_0 = \rho(\mathbf{F}\mathbf{V}^{-1})$. No additional arcs in the digraph are created (i.e. there is no fill-in, see, e.g., [9]) during the symbolic Gaussian elimination steps in the order described above.

In the special case that there is no disease transmission in patches $2, \ldots, n$ (i.e. $\beta_j = 0$ for $j = 2, \ldots, n$), Eq. (20) gives $\mathcal{R}_0$ explicitly as

$$\mathcal{R}_0 = \frac{\alpha_1\beta_1\bar{S}_1}{(d_1+\varepsilon_1+\gamma_1)\left[d_1+\alpha_1+\sum_{j=2}^{n} m_{j1} - \sum_{j=2}^{n}\frac{m_{1j}m_{j1}}{(d_j+\alpha_j+m_{1j})}\right]}, \tag{21}$$

showing how travel into and out of the patch with disease influences $\mathcal{R}_0$. This expression is an approximation in the case of a star topology with center node (e.g. hospital, school) having much greater disease transmission than the other nodes. Equations (20) and (21) can be used to determine the sensitivity of $\mathcal{R}_0$ to changes in parameter values, as well as to calculate $\mathcal{R}_0$ from parameter estimates obtained from data.

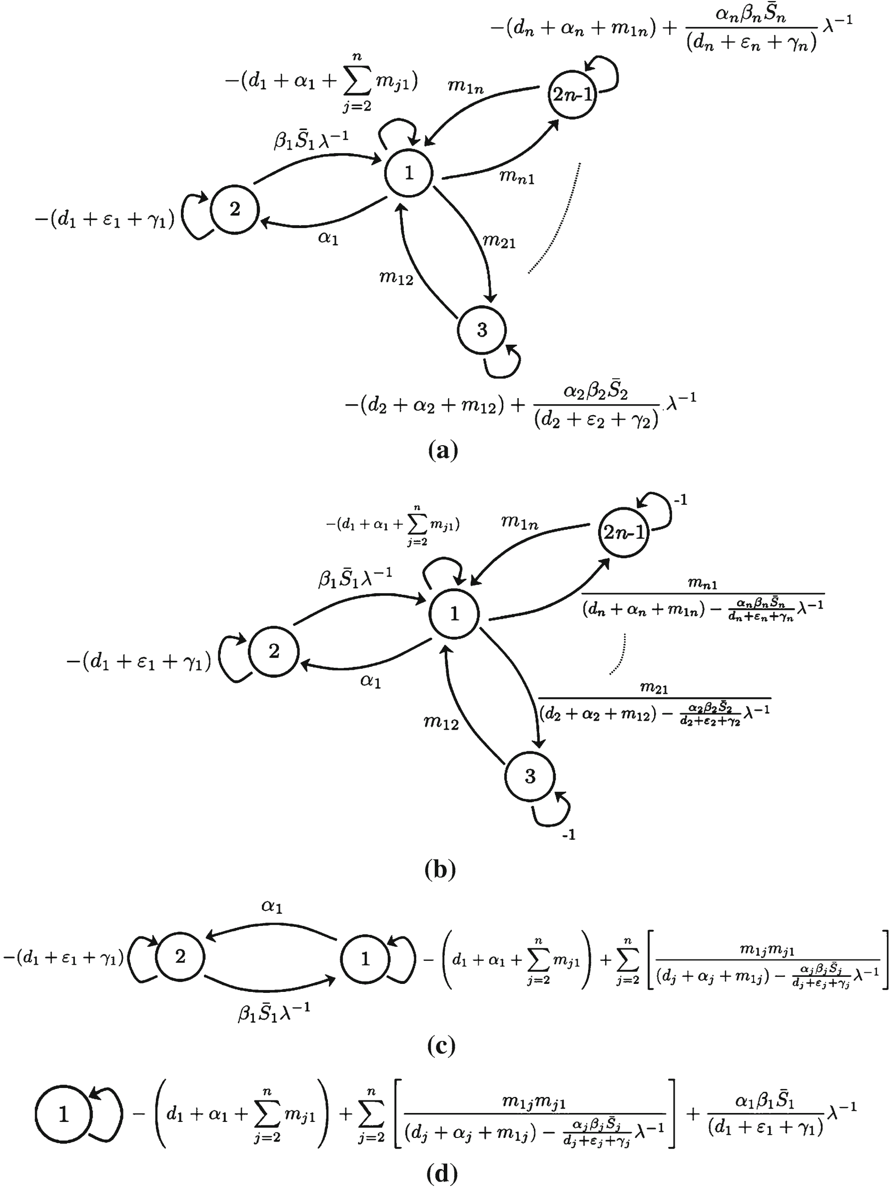


Fig. 5 Digraph reduction procedure for Fig. 4

5.3 West Nile virus model

In this example we use a model for West Nile virus (WNv) derived in [25], and later simplified in [17]; see also [18]. The ODE equations for exposed and infective female mosquitoes (E_V and I_V), and infective birds (I_R) from [18, Sect. 3.1] are

$$\frac{dE_V}{dt} = \alpha_V \beta_R \frac{I_R}{N_R}(N_V - E_V - I_V) - (\kappa_V + d_V)E_V, \tag{22}$$

$$\frac{dI_V}{dt} = \kappa_V E_V - d_V I_V, \tag{23}$$

$$\frac{dI_R}{dt} = \alpha_R \beta_R I_V \frac{N_R - I_R}{N_R} - (\delta_R + \gamma_R)I_R. \tag{24}$$

Here the parameters are defined as follows [18]: d_V is the mosquito death rate constant, κ_V^{-1} is the average mosquito latent time, δ_R is the bird disease-induced death rate constant, β_R is the biting rate of mosquitoes on birds, γ_R^{-1} is the average bird infective time, and α_V, α_R are the WNv transmission probabilities per bite to mosquitoes, birds, respectively. The mosquito and bird populations are N_V and N_R (assumed constant), and the cross-infection disease transmission is modeled by mass action incidence normalized by N_R.

The digraph reduction procedure on the digraph of $\mathbf{F}\lambda^{-1} - \mathbf{V}$ for this system at the DFE with $S_V = N_V$, $S_R = N_R$ is detailed in Fig. 6 in which nodes that can be disregarded are not shown. Note that there is a fill-in as the arc from I_R to I_V is not present in Fig. 6a but has positive weight in Fig. 6c. Application of the last step in the algorithm, yields the basic reproduction number

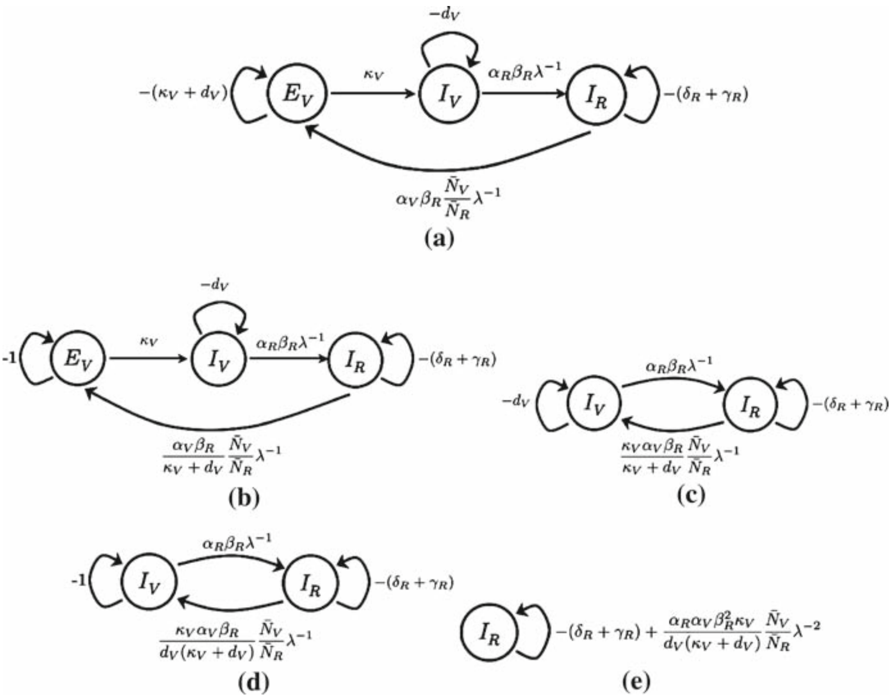


Fig. 6 WNv digraph reduction procedure

$$\mathcal{R}_0 = \sqrt{\frac{\alpha_V \alpha_R \beta_R^2 \kappa_V N_V}{d_V(\kappa_V + d_V)(\delta_R + \gamma_R) N_R}}. \tag{25}$$

Now, consider the system in which birds can travel between neighboring patches. As an example, consider a network of three patches. The digraph of $\mathbf{F}\lambda^{-1} - \mathbf{V}$ for this system is shown in Fig. 7. Each patch in the digraph in Fig. 7a is as shown in Fig. 6 with migration of infective birds included. The biting rate $\beta_{Ri}, i = 1, 2, 3$, is the only parameter that varies between patches. Different biting rates could occur in patches with different vegetation density. Dense vegetation may provide wind cover and increase the ability of a mosquito to land on a bird and therefore increase the biting rate. Travel of infective birds from patch i to j is at rate m_{ji} with $m_{12}, m_{21}, m_{23}, m_{32}$ the only positive rates. Reducing each patch to one node at I_{Ri} (as in Fig. 6c in which nodes that are disregarded are not shown) gives Fig. 7b with

$$a_{ii} = \delta_R + \gamma_R + \sum_{j=1}^{3} m_{ji} - \frac{\alpha_R \alpha_V \beta_{Ri}^2 \kappa_V}{d_V(\kappa_V + \alpha_V)} \frac{N_V}{N_R} \lambda^{-2} > 0. \tag{26}$$

Further reduction to node I_{R1} leads to Fig. 7c, in which the last step of the algorithm gives

$$0 = -a_{11} + \frac{m_{21} m_{12}}{a_{22} - \frac{m_{32} m_{23}}{a_{33}}}, \tag{27}$$

or equivalently,

$$-a_{11} a_{22} a_{33} + m_{21} m_{12} a_{33} + m_{32} m_{23} a_{11} = 0, \tag{28}$$

which is a cubic polynomial in λ^2. The reciprocal of the smallest positive root gives a formula for $\mathcal{R}_0$.

This reduction procedure can be extended to any number of patches between which birds travel. An alternative patchy model for the spread of WNv is considered in [20].

6 Discussion

Using a digraph reduction procedure, we give a new method for calculating $\mathcal{R}_0$ for continuous time epidemiological models. This method applies to compartmental models that possess a DFE. The method is equivalent to symbolic Gaussian elimination. Since the digraph reduction method avoids the direct calculation of a matrix inverse or determinants, this method can be practical for large systems and is a good alternative to the direct method. Consider for example the vector–host model presented in Sect. 5.1. Because there are only two compartments, the traditional method might be more direct. However, a quick inspection of Fig. 2 might also reveal the solution without having to explicitly apply the graph reduction rules. For more complicated systems, like the one presented in Sect. 5.2, the graph-theoretic method might be simpler to apply since the matrix $\mathbf{F}\lambda^{-1} - \mathbf{V}$ has sparse structure.

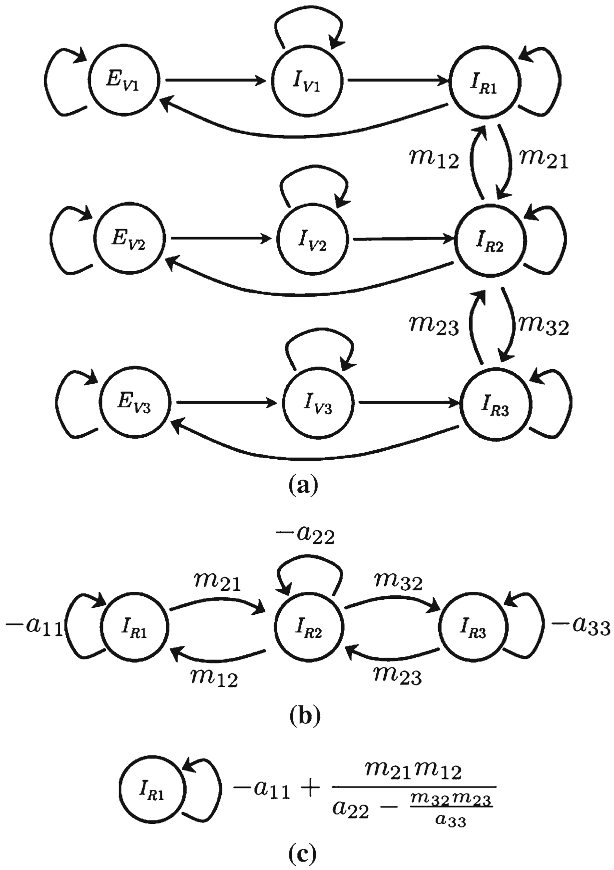


Fig. 7 Patch WNv reduction procedure

Each digraph in the reduction process corresponds to a model that is equivalent to the original model as far as $\mathcal{R}_0$ is concerned. Since at any intermediate step in the digraph reduction (with more than one node remaining), a loop at a vertex is negative, any node with a loop with new infections (λ terms in the loop) gives lower bounds on $\mathcal{R}_0$.

For example, in the star topology model (Sect. 5.2), Fig. 5a for node 3 gives

$$\mathcal{R}_0 > \frac{\alpha_2\beta_2\bar{S}_2}{(d_2+\varepsilon_2+\gamma_2)(d_2+\alpha_2+m_{12})}. \tag{29}$$

The numerator $\alpha_2\beta_2\bar{S}_2$ relates to the flow between nodes 3 and 4 in Fig. 4. The terms $(d_2+\alpha_2+m_{12})^{-1}$ and $(d_2+\varepsilon_2+\gamma_2)^{-1}$ correspond to the the average time spent in nodes 3 and 4, respectively.

As a second example, consider the patch WNv model presented in Sect. 5.3. The digraph shown in Fig. 7b, corresponds to an intermediate step in the reduction of the digraph in Fig. 7a. The self loop $-a_{ii}$ at each node in Fig. 7b has a_{ii} given by Eq. (26), from which the lower bounds

$$\mathcal{R}_0 > \sqrt{\frac{\alpha_V \alpha_R \beta_{Ri}^2 \kappa_V N_V}{d_V(\kappa_V + d_V)\left(\delta_R + \gamma_R + \sum_{j=1}^{3} m_{ji}\right) N_R}} \tag{30}$$

for $i = 1, 2, 3$ result. The difference between the basic reproduction number for the single patch WNv (Eq. (25)) and the 3 patch model (Eq. (29)), lies in the patch outflow $(\sum_{j=1}^{3} m_{ji})$ in the denominator.

The method presented here is analogous to the one in [3,4] for discrete systems (also known as matrix population models). In a discrete system, the movement between compartments is described as probabilities in discrete time steps as opposed to rates in continuous-time epidemiological models. However, the digraph reduction procedures are related. The examples presented show how the digraph reduction method applied to large ordinary differential equation models can simplify the calculation of the net reproduction number. Additionally, these examples illustrate that the intermediate digraph reduction steps can give lower bounds on $\mathcal{R}_0$ and also can assist in the interpretation of the basic reproduction number.

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