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The basic reproduction number obtained from Jacobian and next generation matrices – A case study of dengue transmission modelling

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ABSTRACT

The basic reproduction number is a key parameter in mathematical modelling of transmissible diseases. From the stability analysis of the disease free equilibrium, by applying Routh–Hurwitz criteria, a threshold is obtained, which is called the basic reproduction number. However, the application of spectral radius theory on the next generation matrix provides a different expression for the basic reproduction number, that is, the square root of the previously found formula. If the spectral radius of the next generation matrix is defined as the geometric mean of partial reproduction numbers, however the product of these partial numbers is the basic reproduction number, then both methods provide the same expression. In order to show this statement, dengue transmission modelling incorporating or not the transovarian transmission is considered as a case study. Also tuberculosis transmission and sexually transmitted infection modellings are taken as further examples.

1. Introduction

Dengue virus, a *flavivirus* transmitted by arthropod of the genus *Aedes*, is prevalent in different parts of the world. As a result of being pathogenic for humans and capable of transmission in heavily populated areas, dengue virus (arbovirus) can cause widespread and serious epidemics, which constitute one of the major public health problems in many tropical and subtropical regions of the world where *Aedes aegypti* and other appropriate mosquito vectors are present.

In order to prevent dengue outbreak, periodic surveys designed to detect changes in key adult indices are important since they allow the detection of adult population fluctuations, which may prompt changes to vector control strategy. However, ecological, behavioral and control information on population size, distribution, survivorship, seasonal abundance and insecticide susceptibility are required for an understanding of epidemic potential and for the formulation of control strategies (Monath, 1989). By the means of dengue transmission modelling, the efforts of the eradication of dengue epidemics can be measured. These efforts are linked with the basic reproduction number denoted by R_0 (Nåsell, 1976).

The basic reproduction number is defined, *e.g.*, for a microparasite as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible, in the absence of density-dependent constraints (Anderson and May, 1991). This key epidemiological parameter is determined by assessing the stability of equilibrium points using the Routh–Hurwitz criteria to analyze the characteristic equation (Edelstein-Keshet, 1988). (Another way to obtain R_0 is done through an M-matrix, which is not considered here (Berman and Plemmons, 1979; Raimundo et al., 2010, 2014; Yang, 2012).) Recently, spectral radius theory has been applied to obtain the basic reproduction number (van den Driessche and Watmough, 2002). Hereafter, the application of Routh–Hurwitz criteria to obtain R_0 is referred to as the Jacobian method, while the recent approach is referred to as the next generation method.

The main goal of this paper is to compare R_0 obtained using Jacobian and next generation methods taking the dengue transmission modelling as a case study. The Jacobian method provides R_0 as the product of the partial reproduction numbers. The next generation method provides R_0 as the spectral radius, which is the (geometric) mean number of new infectives per infective in any class, per generation (Heffernan et al., 2005). Both methods yield the same mathematical expression if the product of the partial reproduction numbers defines

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the basic reproduction number, while the geometric mean of these partial reproduction numbers is the spectral radius of the next generation matrix. The paper is structured as follows. In Section 2, models for dengue transmission are presented, and the stability of the disease free equilibrium point is assessed. Section 3 presents discussion to compare the results obtained by applying Jacobian and next generation methods. Finally, conclusion is given in Section 4.

2. Models for dengue transmission

Dengue virus circulates due to the interaction between human and mosquito populations in urban areas. A unique serotype of dengue virus is being considered in the modelling.

With respect to population dynamics, the total human population is assumed to be constant, by taking the natality and mortality rates, both designated by μ_h, being equal. The life cycle of *A. aegypti* encompasses an aquatic phase (eggs, larva and pupa) followed by winged (adult) form (Yang et al., 2011). The number of eggs, which do not constitute a state variable (see (Yang, 2014a) for a model including this compartment), is determined by the oviposition rate $\varphi(M) = \phi m$, where ϕ is the per-capita oviposition rate and m, the number of female mosquitoes at time t. Defining as l the number of larvae (female) at time t, the effective larvae production rate is given by $qf(1 - l/C)\phi m$, where q and f are the fractions of eggs that are hatching to larva and that will originate female mosquitoes, respectively, and C is the total (carrying) capacity of the breeding sites. The number of larvae decreases according to change of larvae to pupae and death, described, respectively, by the changing σ_l and the mortality μ_l rates. The number of pupae in time t, p, increases with change of larvae to pupae (σ_l) and decreases according to transformation of pupae to adult mosquitoes and death, described, respectively, by the emerging σ_p and the mortality μ_p rates. Finally, the number of female mosquitoes increases according to the emerging of pupae (σ_p) and decreases according to the mortality rate μ_f.

With respect to dengue transmission, the human population is divided into four compartments according to the natural history of the disease: s, e, i and r, which are the fractions at time t of, respectively, susceptible, exposed, infectious and recovered persons, with $s + e + i + r = 1$. The constant total number of the human population is designated by N. The female mosquito population is divided into three compartments: m_1, m_2 and m_3, which are the numbers at time t of, respectively, susceptible, exposed and infectious mosquitoes. The size of mosquito population is given by $m = m_1 + m_2 + m_3$.

Dengue transmission is sustained by the flows among human and mosquito compartments according to the dengue epidemics cycle presented above. Susceptible humans are infected during the blood meal by infectious mosquitoes, with the transmission rate being designated by B_h, which depends on the frequency of bites on humans by mosquitoes. A very simple way to take into account the frequency of bites is by allowing it to be proportional to oviposition rate ϕ, that is, $B_h = \beta_h \phi$, where β_h is the transmission coefficient. The exposed persons are, then, transferred to an infectious class by rate γ_h, where $1/\gamma_h$ is the intrinsic incubation period. These infectious persons progress to recovered (immune) class at rate σ_h. Neither loss of immunity nor induced mortality due to the disease (a unique serotype infection) are considered. With respect to the vector, the susceptible mosquitoes are infected at a rate B_m. These exposed mosquitoes are transferred to infectious class at a rate γ_m, where $1/\gamma_m$ is the extrinsic incubation period, and remain infective until death.

To incorporate the feature that a particular human is bitten by a particular mosquito, the transmission coefficients β_h and β_m must be divided by N. The dynamics of dengue infection can incorporate or not the transovarian transmission.

2.1. Dengue infection without transovarian transmission

Here, the transovarian transmission is not considered, hence all emerging mosquitoes from pupa stage are classified as susceptible. Based on the foregoing descriptions of model parameters and dynamical states, dengue transmission is described by a system of differential equations

$$\begin{cases} \dfrac{d}{dt}m_2 = \beta_m \phi i m_1 - (\gamma_m + \mu_f)m_2 \\ \dfrac{d}{dt}m_3 = \gamma_m m_2 - \mu_f m_3 \\ \dfrac{d}{dt}e = \dfrac{\beta_h \phi}{N} m_3 s - (\gamma_h + \mu_h)e \\ \dfrac{d}{dt}i = \gamma_h e - (\sigma_h + \mu_h)i \\ \dfrac{d}{dt}l = qf\phi m(1 - \dfrac{l}{C}) - (\sigma_l + \mu_l)l \\ \dfrac{d}{dt}p = \sigma_l l - (\sigma_p + \mu_p)p \\ \dfrac{d}{dt}m_1 = \sigma_p p - (\beta_m \phi i + \mu_f)m_1 \\ \dfrac{d}{dt}s = \mu_h - (\dfrac{\beta_h \phi}{N} m_3 + \mu_h)s, \end{cases} \tag{1}$$

where the decoupled fraction of immune persons is given by $r = 1 - s - e - i$. In this system of equations, the infective classes were written in first place, different from the sequence of *A. aegypti* life cycle and the evolution of disease, that is, in the order l, p, m_1, m_2, m_3, s, e, and i.

There are two equilibrium points, assuming the existence of mosquito population. One is the trivial equilibrium P^0, or disease free equilibrium (DFE), given by

$$P^0 = (\overline{m}_2 = 0, \overline{m}_3 = 0, \overline{e} = 0, \overline{\imath} = 0, \overline{l} = l^*, \overline{p} = p^*, \overline{m}_1 = m^*, \overline{s} = 1),$$

where l^*, p^* and m^* are given by

$$\begin{cases} l^* = C\left(1-\dfrac{1}{Q_0}\right) \\ p^* = \dfrac{\sigma_l}{\sigma_p+\mu_p} C\left(1-\dfrac{1}{Q_0}\right) \\ m^* = \dfrac{\sigma_p}{\mu_f}\dfrac{\sigma_l}{\sigma_p+\mu_p} C\left(1-\dfrac{1}{Q_0}\right). \end{cases} \tag{2}$$

Clearly the mosquito population exists if $Q_0 > 1$, where

$$Q_0 = \frac{\sigma_l}{\sigma_l+\mu_l}\frac{\sigma_p}{\sigma_p+\mu_p}\frac{qf\phi}{\mu_f} \tag{3}$$

is the basic offspring number (Yang et al., 2011).

Other is a unique non-trivial equilibrium P^*, or endemic equilibrium, given by

$$P^* = (\overline{m}_2 = m_2^*, \overline{m}_3 = m_3^*, \overline{e} = e^*, \overline{\imath} = i^*, \overline{l} = l^*, \overline{p} = p^*, \overline{m}_1 = m_1^*, \overline{s} = s^*),$$

where l^* and p^* are given by Eq. (2), and the remaining values are

$$\begin{cases} m_1^* = \dfrac{\sigma_p}{\beta_m\phi i^*+\mu_f}\dfrac{\sigma_l}{\sigma_p+\mu_p} C\left(1-\dfrac{1}{Q_0}\right) \\ m_2^* = \dfrac{\beta_m\phi i^*}{\gamma_m+\mu_f}\dfrac{\sigma_p}{\beta_m\phi i^*+\mu_f}\dfrac{\sigma_l}{\sigma_p+\mu_p} C\left(1-\dfrac{1}{Q_0}\right) \\ m_3^* = \dfrac{\gamma_m}{\mu_f}\dfrac{\beta_m\phi i^*}{\gamma_m+\mu_f}\dfrac{\sigma_p}{\beta_m\phi i^*+\mu_f}\dfrac{\sigma_l}{\sigma_p+\mu_p} C\left(1-\dfrac{1}{Q_0}\right) \\ s^* = 1-\dfrac{(\sigma_h+\mu_h)(\gamma_h+\mu_h)}{\gamma_h\mu_h} i^* \\ e^* = \dfrac{\sigma_h+\mu_h}{\gamma_h} i^* \\ i^* = \dfrac{\mu_f(R_0-1)}{\beta_m\phi+\dfrac{\mu_f(\sigma_h+\mu_h)(\gamma_h+\mu_h)}{\gamma_h\mu_h}R_0}, \end{cases} \tag{4}$$

where the basic reproduction number R_0 is given by

$$R_0 = \frac{\gamma_m}{\gamma_m+\mu_f}\frac{\beta_h\phi}{\mu_f}\frac{\gamma_h}{\gamma_h+\mu_h}\frac{\beta_m\phi}{\sigma_h+\mu_h}\frac{m^*}{N}, \tag{5}$$

with the size of mosquito population m^* being given by Eq. (2).

The combination of s^*, m_1^* and m^*, given by Eqs. (2) and (4), results in

$$s^*\frac{m_1^*}{m^*} \equiv \chi_0 = \frac{1}{R_0}, \tag{6}$$

that is, in the endemic steady state, the product of the fractions of susceptible humans and mosquitoes (χ_0) is equal to the inverse of the basic reproduction number. This relationship is well established in directly transmitted infections (Anderson and May, 1991; Yang and Silveira, 1998).

The basic reproduction number R_0 given by Eq. (5) can be split in two partial reproduction numbers R_0^h and R_0^m defined by

$$\begin{cases} R_0^h = \dfrac{\beta_h\phi}{\mu_f}\dfrac{\gamma_h}{\gamma_h+\mu_h} \\ R_0^m = \dfrac{\beta_m\phi}{\sigma_h+\mu_h}\dfrac{m^*}{N}\dfrac{\gamma_m}{\gamma_m+\mu_f}, \end{cases} \tag{7}$$

thus $R_0 = R_0^h R_0^m$. Notice that the term $[(\beta_h\phi/N)N]/\mu_f$ of R_0^h is the average number of humans (in a susceptible population of size N) infected by one infectious mosquito during her entire lifespan; and the term $\gamma_h/(\gamma_h+\mu_h)$ is the probability of these infected persons to survive the exposed class and enter the infectious class. Hence, R_0^h is the average number of infectious humans produced by one infectious mosquito introduced in a community free of dengue. The term $[(\beta_m\phi/N)m^*]/(\sigma_h+\mu_h)$ of R_0^m is the average number of mosquitoes (in a susceptible population of size m^*) infected by one infectious human during his/her infectious period; and the term $\gamma_m/(\gamma_m+\mu_f)$ is the probability of these infected mosquitoes to survive the exposed class and enter to the infectious class. Thus, R_0^m is the average number of infectious mosquitoes produced by one infectious human introduced in a community free of dengue. Therefore, the basic reproduction number R_0 gives the average number of secondary infectious humans (or mosquitoes) produced by one primary infectious human (or mosquito) introduced in completely susceptible populations of humans and mosquitoes.

The effective reproduction number R_{ef} can be defined as product of partial effective reproduction numbers $R_0^h s$ and $R_0^m m_1/m$ as

$$R_{ef} = \left(R_0^h s\right)\left(R_0^m\frac{m_1}{m}\right). \tag{8}$$

Suppose that at $t=0$ one infectious case (does not matter if human or mosquito) is introduced in a completely susceptible populations of humans and mosquitoes. Then, when $t \leq 0$, before and just at the time of the beginning of epidemics, $R_{ef} = R_0$ because $s=1$ and $m_1 = m$. Notwithstanding, when $t \to \infty$, the epidemics reaches a steady state, which occurs due to $R_{ef} = 1$, and Eq. (6) can be obtained.

Details of all above calculations can be found in Yang et al. (2014).

The main goal of this work is the comparison of R_0 obtained using the Routh–Hurwitz criteria and the spectral radius of next generation matrix. Hence, the stability analysis will be restricted to the DFE. Details of the calculations are presented in order to compare both methods.

2.1.1. Jacobian method – Routh–Hurwitz criteria

Here, the basic reproduction number is obtained applying Routh–Hurwitz criteria (Edelstein-Keshet, 1988).

The Jacobian matrix evaluated at DFE, named $J = J(P^0)$, results in

$$J = \begin{bmatrix} F & 0 \\ J_1 & J_2 \end{bmatrix},$$

where the matrices F and J_2 are

$$F = \begin{bmatrix} -(\gamma_m + \mu_f) & 0 & 0 & \beta_m \phi m^* \\ \gamma_m & -\mu_f & 0 & 0 \\ 0 & \dfrac{\beta_h \phi}{N} & -(\gamma_h + \mu_h) & 0 \\ 0 & 0 & \gamma_h & -(\sigma_h + \mu_h) \end{bmatrix} \text{ and } J_2 = \begin{bmatrix} M & 0 \\ 0 & H \end{bmatrix}, \tag{9}$$

with the matrices M and H being given by

$$M = \begin{bmatrix} -(\sigma_l + \mu_l)Q_0 & 0 & qf\phi \dfrac{1}{Q_0} \\ \sigma_l & -(\sigma_p + \mu_p) & 0 \\ 0 & \sigma_p & -\mu_f \end{bmatrix} \text{ and } H = [-\mu_h], \tag{10}$$

and the matrix J_1 is

$$J_1 = \begin{bmatrix} qf\phi \dfrac{1}{Q_0} & qf\phi \dfrac{1}{Q_0} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\beta_m \phi m^* \\ 0 & -\dfrac{\beta_h \phi}{N} & 0 & 0 \end{bmatrix}. \tag{11}$$

Notice that F is the disease transmission matrix, and M and H are the vital dynamics matrices of mosquito and human populations. The vital dynamics of human population is Malthusian with constant population, hence H is an 1×1 matrix. The local stability of DFE is assessed by the eigenvalues of the characteristic equation $\det(J - \lambda I) = 0$, where

$$\det(J - \lambda I) \equiv \det(F - \lambda I)\det(M - \lambda I)\det(H - \lambda I).$$

The eigenvalue corresponding to vital dynamics matrix of humans H is $\lambda_1 = -\mu_h$.

The characteristic equation corresponding to vital dynamics matrix of mosquitoes M is

$$\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0,$$

where the coefficients are

$$\begin{cases} a_2 = (\sigma_l + \mu_l)Q_0 + (\sigma_p + \mu_p) + \mu_f \\ a_1 = (\sigma_l + \mu_l)(\sigma_p + \mu_p + \mu_f)Q_0 + (\sigma_p + \mu_p)\mu_f \\ a_0 = (\sigma_l + \mu_l)(\sigma_p + \mu_p)\mu_f(Q_0 - 1), \end{cases}$$

with Q_0 being given by Eq. (3). The difference $a_2a_1 - a_0$ can be evaluated, resulting in

$$a_2a_1 - a_0 = a_1[(\sigma_l + \mu_l)Q_0 + (\sigma_p + \mu_p)] + \frac{qf\phi}{Q_0}\sigma_l\sigma_p + [(\sigma_l + \mu_l)Q_0 + (\sigma_p + \mu_p)]\mu_f^2 > 0.$$

Hence, the eigenvalues $\lambda_{2,3,4}$ have negative real part since all the Routh–Hurwitz criteria (for a third degree polynomial they are $a_0 > 0$, $a_2 > 0$ and $a_2a_1 > a_0$) are satisfied when $Q_0 > 1$, which is the condition for the existence of mosquito population. With this condition, matrix M is an M-matrix (van den Driessche and Watmough (2002), in their proof, assumed that matrix J_2 had all eigenvalues with negative real part).

The characteristic equation corresponding to dengue transmission matrix F is

$$\lambda^4 + b_3\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0,$$

where the coefficients are

$$\begin{cases} b_3 = \gamma_h + \sigma_h + \gamma_m + 2\mu_h + 2\mu_f \\ b_2 = (\gamma_h + \mu_h)(\sigma_h + \mu_h) + (\gamma_h + \sigma_h + 2\mu_h) \times (\gamma_m + 2\mu_f) + (\gamma_m + \mu_f)\mu_f \\ b_1 = (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + 2\mu_f) + (\gamma_h + \sigma_h + 2\mu_h)(\gamma_m + \mu_f)\mu_f \\ b_0 = (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + \mu_f)\mu_f(1 - R_0), \end{cases} \tag{12}$$

with R_0 being given by Eq. (5). The Routh–Hurwitz criteria for a fourth degree polynomial are $b_3 > 0, b_1 > 0, b_0 > 0$ and $b_3 b_2 b_1 > b_1^2 + b_3^2 b_0$. The first two conditions are true, while the third condition is satisfied if $R_0 < 1$. The last inequality can be rewritten as $\delta = b_3 b_2 b_1 - b_1^2 - b_3^2 b_0 > 0$, or, splitting b_0,

$$\delta = b_3 b_2 b_1 - b_1^2 - b_3^2 \Upsilon + b_3^2 \Upsilon R_0 = \Delta + b_3^2 \Upsilon R_0,$$

where $\Upsilon = (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + \mu_f)\mu_f > 0$. However, Δ is

$$\begin{aligned} \Delta &= b_3 b_2 b_1 - b_1^2 - b_3^2 \Upsilon \\ &= b_3 \left\{ (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_h + \sigma_h + 2\mu_h) \times \left[\left(\gamma_m + \mu_f\right)^2 + \mu_f^2 + (\gamma_m + \mu_f)\mu_f \right] + (\gamma_m + 2\mu_f)(\gamma_m + \mu_f) \right. \\ &\quad \left. \times \mu_f \left[(\gamma_h + \mu_h)^2 + (\sigma_h + \mu_h)^2 + (\gamma_h + \mu_h)(\sigma_h + \mu_h) \right] \right\} + b_1 \left\{ (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + \sigma_h + 2\mu_h) \right. \\ &\quad \left. + (\gamma_m + 2\mu_f)(\gamma_m + \mu_f)\mu_f \right\} > 0, \end{aligned}$$

resulting in $\delta > 0$. Hence, for $R_0 < 1$, all the Routh–Hurwitz criteria are satisfied, and the eigenvalues $\lambda_{5,6,7,8}$ have negative real part. Therefore, DFE is locally asymptotically stable for $R_0 < 1$, and at $R_0 = 1$ occurs bifurcation.

The independent term b_0 was obtained, using definition given in Eq. (5), from

$$b_0 = (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + \mu_f)\mu_f \times \left(1 - \frac{\gamma_m \gamma_h \beta_h \phi \beta_m \phi m^*/N}{(\gamma_m + \mu_f)(\gamma_h + \mu_h)(\sigma_h + \mu_h)\mu_f} \right).$$

Notice that this expression is one of the way to write b_0 in the form $K_1(1 - K_2/K_1)$, where K_1 and K_2 are functions of the model parameters, and K_2/K_1 is defined as R_0. But, there are many other ways to do this. For instance, defining $K_2/K_1 = \sqrt{R_0}$, or $(K_2 + K)/(K_1 + K) = R_0$, because in all cases, they give the same threshold at $R_0 = 1$ (Li et al., 2011). For this reason, let a recipe (named Procedure 1) with two steps be defined:

1. Write a positive K_1 in terms of the model parameters, excluding all transmission parameters, in order to write b_0 in the form $K_1(1 - K_2/K_1)$.
2. Define the ratio K_2/K_1 as the basic reproduction number R_0.

This procedure defines a unique R_0.

Another threshold parameter comes from Eq. (6), which states that the product of the fractions of susceptible humans and mosquitoes (χ_0) is equal to the inverse of the basic reproduction number. This parameter can also be obtained from the independent term b_0 following a recipe (named Procedure 2) with two steps:

1. Write a positive K_3 in terms of the model parameters, including vertical transmission parameters, in order to write b_0 in the form $K_3(1 - R_h/K_4)$, where R_h contains only horizontal transmission parameters (not necessarily the basic reproduction number R_0).
2. Define the ratio R_h/K_4 as the inverse of the product of fractions χ_0^{-1}.

This procedure defines a unique χ_0^{-1}.

Following the Procedure 2, b_0 can be written as

$$b_0 = (\gamma_h + \mu_h)(\sigma_h + \mu_h)(\gamma_m + \mu_f)\mu_f \left(1 - \frac{R_0}{1} \right),$$

that is, $K_3 = K_1$ and $K_4 = 1$, resulting in $\chi_0^{-1} = R_0$, the basic reproduction number, since there is only horizontal transmission. Notice that DFE is stable if $\chi_0^{-1} < 1$, and bifurcates at $\chi_0^{-1} = 1$, and above this value a unique non-trivial (endemic) equilibrium appears. The condition $\chi_0^{-1} < 1$, or $\chi_0 > 1$, shows that the product of fractions is greater than one, which is biologically unfeasible, and DFE is stable.

2.1.2. Next generation method – Spectral radius theory

Here, the basic reproduction number is obtained calculating the spectral radius of next generation matrix (van den Driessche and Watmough, 2002). In this method, the next generation matrix is constructed by a subsystem of (1) taking into account the states-at-infection (m_2,e) and the states-of-infectiousness (m_3,i) (Diekmann et al., 2010).

First, consider only states-of-infectiousness variables in the vector f (van den Driessche and Watmough, 2002). In matrix form, the dynamical system (1) is written as

$$\frac{d}{dt} x_p = f_p(x) - v_p(x), \quad p = 1, \ldots, 8,$$

where

$$x = \begin{bmatrix} m_2 \\ m_3 \\ e \\ i \\ l \\ p \\ m_1 \\ s \end{bmatrix}, \quad f = \begin{bmatrix} \beta_m \phi i m_1 \\ 0 \\ \frac{\beta_h \phi}{N} m_3 s \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

and

$$v = \begin{bmatrix} (\gamma_m + \mu_f) m_2 \\ -\gamma_m m_2 + \mu_f m_3 \\ (\gamma_h + \mu_h) e \\ -\gamma_h e + (\sigma_h + \mu_h) i \\ -qf\phi m \left(1 - \frac{l}{C}\right) + (\sigma_l + \mu_l) l \\ -\sigma_l l + (\sigma_p + \mu_p) p \\ -\sigma_p p + (\beta_m \phi i + \mu_f) m_1 \\ -\mu_h + \left(\frac{\beta_h \phi}{N} m_3 + \mu_h\right) s \end{bmatrix}.$$

The partial derivatives of f and v, with respect to m_2, m_3, e and i, evaluated at the DFE are partitioned as

$$Df = \frac{\partial f_p}{\partial x_n} = \begin{bmatrix} F_1 & 0 \\ 0 & 0 \end{bmatrix} \text{ and } Dv = \frac{\partial v_p}{\partial x_n} = \begin{bmatrix} V & 0 \\ -J_1 & -J_2 \end{bmatrix}, \quad 1 \le p, n \le 8,$$

where the transmission matrix F_1 and transition matrix V are

$$F_1 = \begin{bmatrix} 0 & 0 & 0 & \beta_m \phi m^* \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_h \phi}{N} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} (\gamma_m + \mu_f) & 0 & 0 & 0 \\ -\gamma_m & \mu_f & 0 & 0 \\ 0 & 0 & (\gamma_h + \mu_h) & 0 \\ 0 & 0 & -\gamma_h & (\sigma_h + \mu_h) \end{bmatrix},$$

and J_2 and J_1 are given by Eqs. (9) and (11). Notice that $J = Df - Dv$ and $F = F_1 - V$, where J and F are, respectively, the Jacobian and the disease transmission matrices obtained in the foregoing section.

The eigenvalues $\lambda_{1,2,3,4}$ of matrix J_2, solutions of $\det(J_2 - \lambda I) \equiv \det(M - \lambda I)\det(H - \lambda I) = 0$, where matrices M and H are given by Eq. (10), were already evaluated in the preceding section.

The next generation matrix (or, operator (Diekmann and Heesterbeek, 2000)) is defined by $F_1 V^{-1}$. The inverse of the matrix V exists and is

$$V^{-1} = \begin{bmatrix} \frac{1}{\gamma_m + \mu_f} & 0 & 0 & 0 \\ \frac{\gamma_m}{\mu_f(\gamma_m + \mu_f)} & \frac{1}{\mu_f} & 0 & 0 \\ 0 & 0 & \frac{1}{\gamma_h + \mu_h} & 0 \\ 0 & 0 & \frac{\gamma_h}{(\gamma_h + \mu_h)(\sigma_h + \mu_h)} & \frac{1}{\sigma_h + \mu_h} \end{bmatrix},$$

and the next generation matrix F_1V^{-1} is, then,

$$F_1V^{-1} = \begin{bmatrix} 0 & 0 & N\overline{R}_0^m & \frac{\gamma_h+\mu_h}{\gamma_h}N\overline{R}_0^m \\ 0 & 0 & 0 & 0 \\ \frac{1}{N}\overline{R}_0^h & \frac{\gamma_m+\mu_f}{\gamma_m}\frac{1}{N}\overline{R}_0^h & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \tag{13}$$

where the partial contributions from human and mosquito populations $\overline{R}_0^h$ and $\overline{R}_0^m$ are defined by

$$\begin{cases} \overline{R}_0^h = \dfrac{\gamma_m}{\gamma_m+\mu_f}\dfrac{\beta_h\phi}{\mu_f} \\ \overline{R}_0^m = \dfrac{\gamma_h}{\gamma_h+\mu_h}\dfrac{\beta_m\phi}{\sigma_h+\mu_h}\dfrac{m^*}{N}. \end{cases} \tag{14}$$

The interpretation follows similar to the partial reproduction numbers given by Eq. (7), that is, $\overline{R}_0^h$ (or $\overline{R}_0^m$) is the average number of exposed humans (or mosquitoes) originated by one exposed mosquito (or human). The difference is that the partial reproduction numbers given by Eq. (7) are defined in function of infectious classes. The four eigenvalues corresponding to F_1V^{-1} are $\lambda_{5,6}=0$ and $\lambda_{7,8}=\pm\sqrt{R_0}$, with R_0 being given by Eq. (5). The spectral radius of a matrix A is denoted by $\rho(A)$, which is the dominant eigenvalue, hence $\rho(F_1V^{-1})=\sqrt{R_0}$. If $\rho(F_1V^{-1})<1$, then all eigenvalues corresponding to matrix F_1-V have negative real part, and DFE is locally asymptotically stable (van den Driessche and Watmough, 2002), assuming that all eigenvalues corresponding to J_2 have negative real part. Hence, the spectral radius, which is the basic reproduction number R_0^{ng}, is

$$R_0^{ng} \equiv \rho(F_1V^{-1}) = \sqrt{R_0}. \tag{15}$$

This square root arises from the two 'generations' required for an infected vector or host to 'reproduce' itself (van den Driessche and Watmough, 2002).

Now, let the states-at-infection be included in the vector f, that is,

$$f = \left(\beta_m\phi im_1,\ \gamma_m m_2,\ \frac{\beta_h\phi}{N}m_3 s,\ \gamma_h e,\ 0,\ 0,\ 0,\ 0\right)^T,$$

where T stands for the transposition of a matrix. In this case, the next generation matrix F_1V^{-1} is

$$\begin{aligned} F_1V^{-1} &= \begin{bmatrix} 0 & 0 & 0 & \frac{\beta_m\phi m^*}{\sigma_h+\mu_h} \\ \frac{\gamma_m}{\gamma_m+\mu_f} & 0 & 0 & 0 \\ 0 & \frac{1}{N}\frac{\beta_h\phi}{\mu_f} & 0 & 0 \\ 0 & 0 & \frac{\gamma_h}{\gamma_h+\mu_h} & 0 \end{bmatrix} \\ &= \begin{bmatrix} 0 & 0 & 0 & R^4 \\ R^1 & 0 & 0 & 0 \\ 0 & R^2 & 0 & 0 \\ 0 & 0 & R^3 & 0 \end{bmatrix}, \end{aligned}$$

with R^p, $p=1,\ldots,4$, being the partial reproduction numbers. The corresponding eigenvalues are $\lambda_{5,6}=\pm im\sqrt[4]{R^1R^2R^3R^4}$, with im standing for imaginary part, and $\lambda_{7,8}=\pm\sqrt[4]{R^1R^2R^3R^4}$, where $R_0=R^1R^2R^3R^4$, with R_0 being given by Eq. (5). Hence, the spectral radius, which is the basic reproduction number $\overline{R}_0^{ng}$, is

$$\overline{R}_0^{ng} \equiv \overline{\rho}(F_1V^{-1}) = \sqrt[4]{R_0}. \tag{16}$$

This fourth order root arises from the four 'generations' required for an infected vector or host to 'reproduce' itself.

2.1.3. Comparison

Currently, the spectral radius of the next generation matrix, which is defined as the basic reproduction number, is obtained as the geometric mean of entries. This formalism is largely accepted, and the majority of papers treating epidemiological modellings apply this definition. There are few exceptions, for instance, Hyman and Li (2005) they applied next generation and Jacobian (M-matrix theory) methods, while in Hyman and Li (2007) they applied the Jacobian method.

Instead of that definition, let the product of the partial reproduction numbers be the basic reproduction number (Anderson and May, 1991). By the fact that the spectral radius is obtained as the geometric mean of the entries (or partial reproduction numbers), the basic reproduction number is the square of the spectral radius (if there are n entries, then the basic reproduction number is the n-th order of the spectral radius). In Appendix A, this definition is tested considering tuberculosis transmission.

To assess the stability of DFE by the Jacobian method, Routh–Hurwitz criteria were applied, and a threshold parameter R_0 was obtained, given by Eq. (5), as the product of partial reproduction numbers. The biological interpretation was done for R_0, and concluded that it is the basic reproduction number. The next generation method, however, resulted in two different expressions for the spectral radius, that is, R_0^{ng} and $\overline{R}_0^{ng}$, given by Eqs. (15) and (16), which are composed by two and four mean numbers of new infectives, respectively. Or, the spectral radius is the geometric mean of partial reproduction numbers. If the definition that the basic reproduction number is indeed the product of partial reproduction numbers is applied, then $\rho\left(F_1V^{-1}\right)^2 = \overline{\rho}\left(F_1V^{-1}\right)^4$, which is R_0 yielded by the Jacobian method. As a consequence, the different manners to construct vectors f and v in the next generation method are not determinant in the process of obtaining the basic reproduction number.

Another detail observed in the next generation matrix F_1V^{-1} given by Eq. (13) is that the elements are not exactly the partial reproduction numbers. Roberts and Heesterbeek (2003) stated that each element of the matrix F_1V^{-1} provides the expected number of secondary cases in host type p that would arise from a typical primary case in host type n in a susceptible population. Or, in another words, the partial reproduction numbers. This fact is one of the reasons to consider that the threshold obtained from the next generation method is indeed the basic reproduction number. But, to be in accordance with above definition, the elements must be multiplied or divided by the size of human population N. Another minor detail is that the elements of the next generation matrix consider exposed classes, not infectious classes.

2.2. Dengue infection with transovarian transmission

The model dealing with transovarian transmission simplifies the previous one. The exposed classes of humans and mosquitoes are not considered, hence $s+i+r=1$ and $m=m_1+m_2$, where m_2 is now the infectious class of mosquitoes. Another simplification is gathering larva and pupa forms in the aquatic phase, hence σ_a is the rate of adult emerging from aquatic phase, and μ_a is the mortality rate of aquatic phase Yang et al. (2009). The number of uninfected aquatic forms is denoted by l_1, and l_2 is the number of infected aquatic forms, where the total size is $l=l_1+l_2$. It is assumed that infected aquatic forms behave equally as uninfected. The infected aquatic forms that emerge as male mosquitoes are not considered here, in order to simplify the model, for instance, the mating between male and female mosquitoes is not taken into account (Esteva and Yang, 2000).

Taking into account above simplifications, and based on the foregoing descriptions of model parameters and dynamical states, the dengue transmission encompassing transovarian transmission is described by the system of differential equations

$$\begin{cases} \dfrac{d}{dt}m_2 = \sigma_a l_2 + \beta_m\phi i m_1 - \mu_f m_2 \\ \dfrac{d}{dt}i = \dfrac{\beta_h\phi}{N}m_2 s - (\sigma_h+\mu_h)i \\ \dfrac{d}{dt}l_2 = qf\phi j m_2\left(1-\dfrac{l_1+l_2}{C}\right) - (\sigma_a+\mu_a)l_2 \\ \dfrac{d}{dt}l_1 = qf\phi[m_1+(1-j)m_2]\left(1-\dfrac{l_1+l_2}{C}\right) - (\sigma_a+\mu_a)l_1 \\ \dfrac{d}{dt}m_1 = \sigma_a l_1 - (\beta_m\phi i+\mu_f)m_1 \\ \dfrac{d}{dt}s = \mu_h - \left(\dfrac{\beta_h\phi}{N}m_2+\mu_h\right)s, \end{cases} \tag{17}$$

where j is the fraction of eggs with dengue virus from all eggs laid by infected mosquitoes.

There are two equilibrium points, assuming the existence of mosquito population. One is the trivial equilibrium P^0, or disease free equilibrium (DFE), given by

$$P^0 = (\overline{m}_2 = 0, \bar{\imath} = 0, \bar{l}_2 = 0, \bar{l}_1 = l^*, \overline{m}_1 = m^*, \bar{s} = 1),$$

where l^* and m^* are given by

$$\begin{cases} l^* = C\left(1-\dfrac{1}{Q_0}\right) \\ m^* = \dfrac{\sigma_a}{\mu_f}C\left(1-\dfrac{1}{Q_0}\right). \end{cases} \tag{18}$$

Clearly the mosquito population exists if $Q_0 > 1$, where

$$Q_0 = \frac{\sigma_a}{\sigma_a+\mu_a}\frac{qf\phi}{\mu_f} \tag{19}$$

is the basic offspring number.

Other is a unique non-trivial equilibrium P^*, or endemic equilibrium, given by

$$P^* = (\overline{m}_2 = m_2^*, \bar{\imath} = i^*, \bar{l}_2 = l_2^*, \bar{l}_1 = l_1^*, \overline{m}_1 = m_1^*, \bar{s} = s^*),$$

with the coordinates being given by

$$\begin{cases} l_1^* = (1-j)\dfrac{\beta_m\phi i^* + \mu_f}{\beta_m\phi i^* + (1-j)\mu_f} C\left(1 - \dfrac{1}{Q_0}\right) \\ l_2^* = j\dfrac{\beta_m\phi i^*}{\beta_m\phi i^* + (1-j)\mu_f} C\left(1 - \dfrac{1}{Q_0}\right) \\ m_1^* = (1-j)\dfrac{\mu_f}{\beta_m\phi i^* + (1-j)\mu_f}\dfrac{\sigma_a}{\mu_f} C\left(1 - \dfrac{1}{Q_0}\right) \\ m_2^* = \dfrac{\beta_m\phi i^*}{\beta_m\phi i^* + (1-j)\mu_f}\dfrac{\sigma_a}{\mu_f} C\left(1 - \dfrac{1}{Q_0}\right) \\ s^* = 1 - \dfrac{\sigma_h + \mu_h}{\mu_h} i^* \\ i^* = \dfrac{\mu_f(R_e - 1)}{\beta_m\phi + \dfrac{\mu_f(\sigma_h + \mu_h)}{\mu_h} R_0}, \end{cases} \tag{20}$$

where the basic reproduction number R_e, which encompasses transovarian transmission, is defined as

$$R_e = R_0 + j. \tag{21}$$

This number is the sum of the basic reproduction number R_0 for the horizontal transmission, given by

$$R_0 = \frac{\beta_h\phi}{\mu_f}\frac{\beta_m\phi}{\sigma_h + \mu_h}\frac{m^*}{N}, \tag{22}$$

with the size of mosquito population m^* being given by Eq. (18), and the contribution due to the vertical transmission j. With respect to R_0, which can be obtained from Eq. (5) by letting $\gamma_h \to \infty$ and $\gamma_m \to \infty$, this horizontal transmission parameter can be written as the product of two partial reproduction numbers R_0^h and R_0^m defined by

$$\begin{cases} R_0^h = \dfrac{\beta_h\phi}{\mu_f} \\ R_0^m = \dfrac{\beta_m\phi}{\sigma_h + \mu_h}\dfrac{m^*}{N}, \end{cases} \tag{23}$$

resulting in $R_e = R_0^h R_0^m + j$.

The basic reproduction number R_e, given by Eq. (21), is interpreted as follows. R_0 is the average number of secondary infectious humans (or mosquitoes) produced by one primary infectious human (or mosquito) introduced in a completely susceptible populations of humans and mosquitoes. That is, R_0 gives the average number of secondary cases due to horizontal transmission. The term j is the average number of infectious mosquitoes (daughters) generated by a single infectious mosquito by transovarian (vertical) transmission. Hence R_e is the overall number of infectious humans (or mosquitoes) generated by a single infectious human (or mosquito) due to horizontal and vertical transmissions.

The combination of s^*, m_1^* and m^*, given by Eqs. (18) and (20), results in

$$s^*\frac{m_1^*}{m^*} \equiv \chi_e = \frac{1-j}{R_0}, \tag{24}$$

that is, in the endemic steady state, the product of the fractions of susceptible humans and mosquitoes encompassing the transovarian transmission (χ_e) is not equal to the inverse of the basic reproduction number R_e, differently from that one obtained in the previous modelling. If $j = 1$, then $m_1^* = 0$ and $s^* m_1^*/m^* = 0$.

Details of all above calculations and discussions of the results are left to a further work (Yang, 2014b).

Again, the stability analysis will be restricted to the DFE considering the Routh–Hurwitz criteria and the spectral radius of next generation matrix.

2.2.1. Jacobian method – Routh–Hurwitz criteria

The Jacobian matrix evaluated at DFE, named $J = J(P^0)$, results in

$$J = \begin{bmatrix} F & 0 \\ J_1 & J_2 \end{bmatrix},$$

where the matrices F and J_2 are

$$F = \begin{bmatrix} -\mu_f & \beta_m\phi m^* & \sigma_a \\ \beta_h\dfrac{\phi}{N} & -(\sigma_h + \mu_h) & 0 \\ jq f\phi\dfrac{1}{Q_0} & 0 & -(\sigma_a + \mu_a) \end{bmatrix} \text{ and } J_2 = \begin{bmatrix} M & 0 \\ 0 & H \end{bmatrix}, \tag{25}$$

with the matrices M and H being given by

$$M = \begin{bmatrix} -qf\phi m^* - (\sigma_a + \mu_a) & qf\phi\dfrac{1}{Q_0} \\ \sigma_a & -\mu_f \end{bmatrix} \text{ and } H = [-\mu_h], \tag{26}$$

and the matrix J_1 is

$$J_1 = \begin{bmatrix} (1-j)qf\phi\dfrac{1}{Q_0} & 0 & qf\phi m^* \\ 0 & -\beta_m\phi m^* & 0 \\ -\dfrac{\beta_h\phi}{N} & 0 & 0 \end{bmatrix}. \tag{27}$$

The local stability of DFE is assessed by the eigenvalues of the characteristic equation $\det(J-\lambda I)=0$, where

$$\det(J-\lambda I) \equiv \det(F-\lambda I)\det(M-\lambda I)\det(H-\lambda I).$$

The eigenvalue corresponding to vital dynamics matrix of humans H is $\lambda_1 = -\mu_h$.

The characteristic equation corresponding to vital dynamics matrix of mosquitoes M is

$$\lambda^2 + a_1\lambda + a_0 = 0,$$

where the coefficients are

$$\begin{cases} a_1 = qf\phi m^* + \sigma_a + \mu_a + \mu_f \\ a_0 = (\sigma_a + \mu_a)\mu_f(Q_0 - 1), \end{cases}$$

with Q_0 being given by Eq. (19). The eigenvalues $\lambda_{2,3}$ have negative real part since all the Routh–Hurwitz criteria (for a second degree polynomial they are $a_0 > 0$ and $a_1 > 0$) are satisfied when $Q_0 > 1$, which is the condition for the existence of mosquito population.

The characteristic equation corresponding to dengue transmission matrix F is

$$\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0,$$

where the coefficients are

$$\begin{cases} b_2 = \sigma_h + \mu_h + \sigma_a + \mu_a + \mu_f \\ b_1 = (\sigma_h + \mu_h)[\sigma_a + \mu_a + \mu_f(1-R_0)] + (1-j)\mu_f(\sigma_a + \mu_a) \\ b_0 = (\sigma_h + \mu_h)(\sigma_a + \mu_a)\mu_f(1-R_e), \end{cases} \tag{28}$$

with R_e and R_0 being given by Eqs. (21) and (22), respectively. The difference $b_2b_1 - b_0$ can be evaluated, resulting in

$$b_2b_1 - b_0 = (\sigma_h + \mu_h)\{(\sigma_h + \mu_h + \mu_f)[(\sigma_a + \mu_a) + \mu_f \times (1-R_0)] + (\sigma_a + \mu_a)(\sigma_a + \mu_a + \mu_f)\} + (1-j)\mu_f(\sigma_a + \mu_a)(\sigma_a + \mu_a + \mu_f) > 0$$

for $R_0 < 1$. For $j < 1$, when $R_e < 1$, which implies that $R_0 < 1$, the eigenvalues $\lambda_{4,5,6}$ have negative real part since all the Routh–Hurwitz criteria are satisfied, and DFE is locally asymptotically stable. For $j = 1$, $b_0 = -(\sigma_h + \mu_h)(\sigma_a + \mu_a)\mu_f R_0 < 0$ and DFE is always unstable for $R_0 > 0$.

The independent term $b_0 = \det(F)$ in Eq. (28) was obtained, using the definition given in Eq. (21), from

$$b_0 = (\sigma_a + \mu_a)(\sigma_h + \mu_h)\mu_f \times \left[1 - \frac{\beta_h\phi\beta_m\phi\frac{m^*}{N} + (\sigma_h + \mu_h)\mu_f j}{(\sigma_h + \mu_h)\mu_f}\right].$$

Notice that the Procedure 1 already defined in the foregoing section was applied ($K_1 = (\sigma_a + \mu_a)(\sigma_h + \mu_h)\mu_f$ and $K_2/K_1 = R_e$), defining a unique R_e.

It is important to stress the fact that R_e, given by Eq. (21), is not a good parameter to be related to the product of fractions of susceptible populations χ_e, given by Eq. (24). Following Procedure 2 presented in the foregoing section, b_0 given by Eq. (28) is written in the form $K_3(1 - R_0/K_4)$, that is,

$$b_0 = (\sigma_h + \mu_h)(\sigma_a + \mu_a)\mu_f(1-j)(1 - \chi_e^{-1}),$$

for $j < 1$, where the inverse of the product of susceptible fractions χ_e is

$$\chi_e^{-1} = \frac{R_0}{1-j}. \tag{29}$$

Notice that DFE is stable if $\chi_e^{-1} < 1$, and bifurcates at $\chi_e^{-1} = 1$, and above this value a unique non-trivial (endemic) equilibrium appears. The condition $\chi_e^{-1} < 1$ is equivalent to $R_e < 1$. For $j = 1$, the Procedure 2 can not be used, due to $m_1^*/m^* = 0$ (all mosquitoes are infectious), resulting in $\chi_e = 0$.

Interestingly, χ_e brings implicitly the idea of the basic reproduction number, as it must do. The equation relating susceptible fractions, given by Eq. (24), can be rewritten as

$$s^*\frac{m_1^*}{m^*} \equiv \chi_e = \frac{1}{R_0} - \frac{j}{R_0},$$

which has clearly a biological interpretation. The term $1/R_0$ is the decreasing fractions of susceptible populations due to the horizontal transmission, while the term j/R_0 is the additional decrease due to vertical transmission. The appearance of R_0 in the latter term shows that vertical transmission is a consequence of horizontal transmission. Additionally, this latter term is such that the sum of numerator and denominator results in R_e, hence χ_e brings indirectly the idea of the basic reproduction number, as expected. In this particular modelling, the contribution of the vertical transmission (j) does not depend on the horizontal transmission parameters β_h and β_m (see Appendix B for a modelling which does).

2.2.2. Next generation method – Spectral radius theory

The next generation matrix is constructed by a subsystem of (17) taking into account the state-at-infection (l_2) and the states-of-infectiousness (m_2,i) (Diekmann et al., 2010).

2.2.2.1. Considering only states-of-infectiousness. In matrix form, the dynamical system (17) is written as

$$\frac{d}{dt}x_p = f_p(x) - v_p(x), \quad p = 1, \ldots, 6,$$

where

$$x = \begin{bmatrix} m_2 \\ i \\ l_2 \\ l_1 \\ m_1 \\ s \end{bmatrix}, \quad f = \begin{bmatrix} \beta_m \phi i m_1 \\ \frac{\beta_h \phi}{N} m_2 s \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

and

$$v = \begin{bmatrix} -\sigma_a l_2 + \mu_f m_2 \\ (\sigma_h + \mu_h) i \\ -qf\phi j m_2 \left(1 - \frac{l_1 + l_2}{C}\right) + (\sigma_a + \mu_a) l_2 \\ -qf\phi [m_1 + (1-j) m_2] \left(1 - \frac{l_1 + l_2}{C}\right) + (\sigma_a + \mu_a) l_1 \\ -\sigma_a l_1 + (\beta_m \phi i + \mu_f) m_1 \\ -\mu_h + \left(\frac{\beta_h \phi}{N} m_2 + \mu_h\right) s \end{bmatrix}.$$

The partial derivatives of f and v, with respect to m_2, i and l_2, evaluated at the DFE are partitioned as

$$Df = \frac{\partial f_p}{\partial x_n} = \begin{bmatrix} F_1 & 0 \\ 0 & 0 \end{bmatrix} \text{ and } Dv = \frac{\partial v_p}{\partial x_n} = \begin{bmatrix} V & 0 \\ -J_1 & -J_2 \end{bmatrix}, \quad 1 \le p, n \le 6,$$

where F_1 and V are

$$F_1 = \begin{bmatrix} 0 & \beta_m \phi m^* & 0 \\ \frac{\beta_h \phi}{N} & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \mu_f & 0 & -\sigma_a \\ 0 & \sigma_h + \mu_h & 0 \\ -jqf\phi \frac{1}{Q_0} & 0 & \sigma_a + \mu_a \end{bmatrix},$$

and J_2 and J_1 are given by Eqs. (25) and (27).

The eigenvalues $\lambda_{1,2,3}$ of matrix J_2, solution of $\det(J_2 - \lambda I) \equiv \det(M - \lambda I)\det(H - \lambda I) = 0$, where matrices M and H are given by Eq. (25), were already evaluated in the preceding section.

The inverse of the matrix V for $j < 1$ exists and is

$$V^{-1} = \begin{bmatrix} \frac{1}{(1-j)\mu_f} & 0 & \frac{\sigma_a}{(1-j)\mu_f(\sigma_a + \mu_a)} \\ 0 & \frac{1}{\sigma_h + \mu_h} & 0 \\ \frac{1}{(1-j)\sigma_a} & 0 & \frac{1}{(1-j)(\sigma_a + \mu_a)} \end{bmatrix},$$

and the next generation matrix F_1V^{-1} is

$$F_1V^{-1} = \begin{bmatrix} 0 & NR_0^m & 0 \\ \frac{1}{1-j}\frac{1}{N}R_0^h & 0 & \frac{1}{1-j}\frac{\sigma_a}{\sigma_a+\mu_a}\frac{1}{N}R_0^h \\ 0 & 0 & 0 \end{bmatrix}, \tag{30}$$

where the partial reproduction numbers R_0^h and R_0^m are given by Eq. (23). The eigenvalues corresponding to F_1V^{-1} are $\lambda_4 = 0$ and $\lambda_{5,6} = \pm\sqrt{\chi_e^{-1}}$, with χ_e^{-1} being given by Eq. (29), and the spectral radius is $\overline{\rho}(F_1V^{-1}) = \sqrt{\chi_e^{-1}}$. If $\overline{\rho}(F_1V^{-1}) < 1$, then all eigenvalues corresponding to matrix $F_1 - V$ have negative real part, and DFE is locally asymptotically stable (van den Driessche and Watmough, 2002), assuming that all eigenvalues corresponding to J_2 have negative real part. Hence, the spectral radius, which is the basic reproduction number $\overline{R}_e^{ng}$, is

$$\overline{R}_e^{ng} \equiv \overline{\rho}(F_1V^{-1}) = \sqrt{\chi_e^{-1}}, \tag{31}$$

and χ_e^{-1} can be written as the product of the partial reproduction numbers, for instance, $R_0^h/(1-j)$ and R_0^m. See below the reason why basic reproduction number and partial reproduction numbers are inappropriate for χ_e^{-1}.

For $j = 1$, $\det(V) = 0$ and V is not invertible, and the next generation matrix is not defined.

2.2.2.2. Adding state-at-infection. Now, let the state-at-infection be included in the vector f, that is,

$$f = \left(\beta_m\phi i m_1 + \sigma_a l_2, \frac{\beta_h\phi}{N}m_2 s, qf\phi j m_2\left(1 - \frac{l_1+l_2}{C}\right), 0, 0, 0\right)^T,$$

where T stands for the transposition of a matrix. In this case, the next generation matrix F_1V^{-1} is

$$F_1V^{-1} = \begin{bmatrix} 0 & NR_0^m & \frac{\sigma_a}{\sigma_a+\mu_a} \\ \frac{1}{N}R_0^h & 0 & 0 \\ j\frac{\sigma_a+\mu_a}{\sigma_a} & 0 & 0 \end{bmatrix}.$$

The corresponding eigenvalues are $\lambda_4 = 0$ and $\lambda_{5,6} = \pm\sqrt{R_e}$, with R_e being given by (21), and the spectral radius is $\rho(F_1V^{-1}) = \sqrt{R_e}$. Hence, the spectral radius, which is the basic reproduction number R_0^{ng}, is

$$R_e^{ng} \equiv \rho(F_1V^{-1}) = \sqrt{R_e}, \tag{32}$$

and R_e can be written as the product of partial reproduction numbers, for instance, R_0^h and $R_0^m + j/R_0^h$.

The substitution of $R_e = R_0 + j$ in Eq. (32), for $j = 1$, results in $\rho(F_1V^{-1}) = \sqrt{R_0+1}$, showing that DFE is always unstable for $R_0 > 0$.

Vector f can be constructed in more two different ways, by removing $qf\phi j m_2[1-(l_1+l_2)/C]$ or $\sigma_a l_2$, that is,

$$f = \left(\beta_m\phi i m_1 + \sigma_a l_2, \frac{\beta_h\phi}{N}m_2 s, 0, 0, 0, 0\right)^T,$$

or

$$f = \left(\beta_m\phi i m_1, \frac{\beta_h\phi}{N}m_2 s, qf\phi j m_2\left(1 - \frac{l_1+l_2}{C}\right), 0, 0, 0\right)^T,$$

where T stands for the transposition of a matrix. In both cases, diagonal element corresponding to the vertical transmission appears in the next generation matrix. The eigenvalues of F_1V^{-1} are $\lambda_4 = 0$ and $\lambda_{5,6}$ given by the solution of

$$\lambda^2 - j\lambda - R_0 = 0.$$

Hence, the spectral radius is given by

$$\rho(F_1V^{-1}) = \frac{1}{2}(j + \sqrt{j^2 + 4R_0}), \tag{33}$$

which is very difficult to interpret biologically.

2.2.3. Comparison

With respect to the next generation method, all comments provided in the foregoing section are valid here. However, due to the exclusion of exposed classes, the partial reproduction numbers are related to infectious classes. Additionally, the vertical transmission did not appear as a element of diagonal. Roberts and Heesterbeek (2003) established that the infection from one host to itself must appear as a diagonal element. Sexually transmitted infection presented in Appendix B, however, presents the vertical transmission as a diagonal element.

In the dengue modelling with transovarian transmission, two different threshold parameters were obtained from the Jacobian method. One was the basic reproduction number given by $R_e = R_0 + j$, Eq. (21). Other was χ_e^{-1}, Eq. (29), which is useful to relate the product of the fractions of susceptibles at endemic steady state, bringing implicitly the basic reproduction number R_e.

Depending on the construction of vectors f and v, the next generation method yielded two different spectral radius $\overline{\rho}(F_1V^{-1})$ and $\rho(F_1V^{-1})$, given by Eqs. (31) and (32), respectively. Remember that the product of partial reproduction numbers is the basic reproduction number, and the spectral radius is the geometric mean of these quantities. Then, $R_e = \rho\left(F_1V^{-1}\right)^2$, for the basic reproduction number. Other threshold, $\overline{\rho}(F_1V^{-1}) = \sqrt{R_0/(1-j)}$, is not defined at $j=1$, where $\overline{\rho}(F_1V^{-1}) \to \infty$, hence $\overline{\rho}(F_1V^{-1})$ must not be defined as the basic reproduction number. Rather, it is more convenient to link this threshold with the product of fraction of susceptibles, by the fact that $\overline{\rho}\left(F_1V^{-1}\right)^2 = \chi_e^{-1}$.

3. Discussion

In the analysis of the stability of DFE, the common calculation in Jacobian and next generation methods was the eigenvalues of J_2. Under certain conditions, J_2 satisfies all criteria to be M-matrix, and all eigenvalues have negative real part.

The difference relies in the assessment of the eigenvalues of matrices F (disease transmission matrix, dimension $time^{-1}$) and F_1V^{-1} (next generation matrix, dimensionless), remembering that $F = F_1 - V$. The Jacobian method applied the Routh–Hurwitz criteria on the characteristic equation corresponding to F, while the next generation method evaluated the spectral radius of matrix F_1V^{-1}. Each method presents inherent challenges with respect to calculations.

The stability of DFE by the Jacobian method in dengue modellings (with and without transovarian transmission) established that if $b_0 = \det(F) > 0$, then the Routh–Hurwitz criteria were satisfied. By two different procedures of writing b_0, two threshold parameters were obtained: the basic reproduction number (R_0 or R_e) and the product of the fractions of susceptible populations ($\chi_0 = 1/R_0$ or $\chi_e = (1-j)/R_0$). Likewise, the next generation method yielded also two threshold parameters depending on the construction of the vectors f and v. The spectral radii of the next generation matrix resulted in $\sqrt{R_e}$ (or $\sqrt{R_0}$) and $\sqrt{\chi_e^{-1}}$.

Roberts and Heesterbeek (2003) stated that "although a quantity derived in this way (Jacobian method) will have the same threshold behaviour as the dominant eigenvalue of the next-generation matrix, it does not have the same biological interpretation and can therefore not be called the basic reproduction ratio or denoted by R_0", with which Heffernan et al. (2005) agreed. To shed some lights in this statement, let the results form Jacobian and next generation methods be discussed.

Let the results from the Jacobian method be summarized:

1. The disease related parameters were the entries of the matrix F, which was the reason to call F as the disease transmission matrix.
2. By applying the Routh–Hurwitz criteria, there is a procedure to obtain a threshold parameter denoted R_0 (or R_e) that determines the stability of DFE. When $R_0 < 1$ (or $R_e < 1$), all Routh–Hurwitz criteria are satisfied. Hence, R_0 (or R_e) alone plays a fundamental role in the stability analysis.
3. The model parameters in R_0 (or horizontal transmission part of R_e) can be arranged as the product of two partial reproduction numbers R_0^h and R_0^m.
4. In dengue model with transovarian route besides the horizontal transmission, the product of the fractions of susceptible populations was not related to R_e. Another threshold parameter was obtained to attain this purpose (χ_e). The threshold parameter χ_e latently brought R_e.

Therefore, based on these four statements, the threshold value R_0 (or R_e), supporting clearly a biological interpretation, was identified as the basic reproduction number.

The main reasons for which the spectral radius of next generation matrix $\rho(F_1V^{-1})$ has biologically meaningful are (Roberts and Heesterbeek, 2003):

1. For two types of hosts, each elements of the matrix F_1V^{-1} provides the expected number of secondary cases in host type p that would arise from a typical primary case in host type n in a susceptible population. Hence, F_1V^{-1} is named the next generation matrix.
2. The spectral radius of the next generation matrix $\rho(F_1V^{-1})$, the geometric mean of partial reproduction numbers, was defined as the basic reproduction number.
3. The expected number of secondarily infected humans that result from a single infected human is R_0^2, as two generations are required to transmit an infection from human to human, the first being from human to mosquito and the second being from mosquito to human.

These statements deserve some comments.

With respect to the statement 1, the elements a_{31} and a_{13} of the next generation matrix F_1V^{-1}, given by Eq. (13), are different of the partial reproduction numbers R_0^h and R_0^m, given by Eq. (7). However, a_{31} multiplied by N, and a_{13} divided by N are such that Na_{31} and a_{13}/N are the expected number of secondary exposed (not infectious) cases in humans and mosquitoes, respectively, that would arise from a typical primary exposed case in mosquito and human, respectively, in completely susceptible populations of humans and mosquitoes. The elements a_{31} and a_{13} were denoted as K_{np} in Roberts and Heesterbeek (2003).

The above comment is valid for dengue with transovarian transmission modelling, but the elements are regarded to infectious populations, since exposed classes were removed. Moreover, the term regarding the vertical transmission did not appear as the diagonal element in the next generation matrix. In Roberts and Heesterbeek (2003), vertically infected mosquitoes were introduced in the next generation matrix as an element in the diagonal (K_{55}), because this kind of infection occurs among individuals of the same species (mosquito to mosquito).

Let the statements 3 and 2, in this order, be considered.

3.1. About generation

Remember that R_0 obtained as the spectral radius is the geometric mean of the secondary cases in humans (or mosquitoes) originated from a single infectious mosquito (or human). To encompass the complete cycle of transmission, Heesterbeek and Roberts (2007) introduced the type reproduction number T, interpreting it as "the expected number of cases in individuals of type 1, caused by one infected individual of type 1 in a completely susceptible population, either directly or through chains of infection passing through any sequence of the other types". The type reproduction number was defined as $T = R_0^2$ in order to provide the expected number of secondary infections in humans (or mosquitoes) that would arise from a primary infected human (or mosquito), in fully susceptible populations (Adams and Boots, 2010; Heesterbeek and Roberts, 2007; Roberts, 2007). They also argued that T provides a direct link with the control effort required to eliminate infection.

For macroparasites, the basic reproduction number is defined as the average number of female offsprings per adult female worm that survive to reproduction in the absence of density-dependent constraints (Anderson and May, 1991). This definition clearly establishes the notion that one species is generating offspring of the same species.

For instance, schistosomiasis is the human infection, which involves at least two host species (human and snail), two free-living transmission stages of the parasite (cercariae and miracidia) and distinct environments. Humans are the principal definitive host for the five Schistosome species. Adult worms live in the venous system of intestine (*S. mansoni, S. japonicum, S. mekongi* and *S. intercalatum*) or the urinary bladder (*S. haematobium*). Eggs laid by adult worms are eliminated to an aquatic environment, where they hatch and become miracidia. Miracidia must infect snails (intermediate host) that, after a period of time, release cercariae, which are the aquatic form that infect humans (definitive host). Once in the human body, cercaria suffer transformations until becoming adult worm. Two successive infective events in different hosts must occur to close the cycle of schistosome transmission. Hence, one generation implies the closing of the transmission cycle, and the basic reproduction number is the average number of secondary adult worms that one adult worm produces during her entire lifespan, disregarding what happens inside the infected snails (in fact, hundred of thousands of cercaria are released by one infected snail) (Yang and Coutinho, 1999; Yang, 2003).

Differently, dengue is a viral infection, but requires a vector to close its transmission cycle. First, an infectious human must be bitten by susceptible mosquitoes, which become infectious and, then, bite susceptible humans. (The cycle can be initiated with one infectious mosquito.) Due to infections by the same virus in two different populations, two generations were evoked (van den Driessche and Watmough, 2002). However, these two steps are partial contributions to close the transmission cycle, hence one generation must encompass occurrence of infections in both populations, that is, one species originating infection in the same species. It is not reasonable that the average number of mosquitoes infected by one infected human is the first generation, and the second generation is the average number of infected humans originated by one infectious mosquito (or, vice-versa).

The notion of one generation can be corroborated by Eq. (6) or (24), for instance, $s^* m_1^*/m^* = 1/R_e$. If the basic reproduction number R_e could be estimated, this value is the product of two fractions of susceptible populations. In another words, the indistinguishability between two susceptible populations demands that what happens in these populations must be considered as one generation.

The life cycle of *A. aegypti* is another example. There are two different forms living in two different environments. The female mosquito lay eggs, which hatch in aquatic environment, and suffer successive transformations until emerging as adult mosquitoes. Hence, one generation must be understood when newly emerged mosquitoes replace the old population, despite the aquatic forms they have passed by. This notion is found in the basic offspring number Q_0.

3.2. Spectral radius, geometric mean and partial reproduction numbers

In order to remove the divergence in the threshold parameters provided by Jacobian and next generation methods the following definition was introduced. The spectral radius of next generation matrix is in fact the geometric mean of the partial reproduction numbers, but is not the basic reproduction number; rather the product of these numbers is the basic reproduction number.

The partial reproduction numbers arise because dengue transmission is not a directly transmitted infection, but needs a vector to close the cycle. Whenever mosquito population is demanded to close the transmission cycle in humans, the threshold parameters are determined by the product between two partial reproduction numbers that characterize the infection in each population. But, this is also true when an intermediate host is required to complete the transmission cycle, such as in the majority of macroparasite infections.

Roberts (2007) stated that "taking a geometric mean number of humans and mosquitoes seems a strange thing to do, although it is a valid threshold quantity". However, Williams (1937) stated that geometric mean in some biological experiments (estimation of number of insects based on a series of collected data) provides a more exact interpretation of the results. Following this assertion, the definition that spectral radius is the geometric mean of partial reproduction numbers, but not the basic reproduction number, seems natural.

The suitability of the above definition is assessed considering tuberculosis (Appendix A). Under this new definition, in all three examples, the basic reproduction number is given by Eq. (36). This result is totally expected because the model is the same, and the basic reproduction number must be uniquely determined, despite of different ways to construct transmission F_1 and transition V matrices from vectors $\tilde{f}$ and $\tilde{v}$. In sexually transmitted infection with vertical transmission (Appendix B), different threshold parameters were obtained depending on the construction (or factorization) of vectors $\tilde{f}$ and $\tilde{v}$.

3.3. Further discussion

The Jacobian method provided Procedures 1 and 2 to obtain two different threshold parameters: The Procedure 1 yield the basic reproduction number (R_*, a generic notation for the basic reproduction number obtained from models), and the Procedure 2, the product of the fractions of susceptible populations at steady state (χ_*, a generic notation). The next generation method also provided two thresholds, which were obtained by constructing different vectors f and v:

1. From the analysis of models, specially those with vertical transmission, the spectral radius provided $\sqrt{\chi_*^{-1}}$, when vector f contains only states-of-infectiousness (corresponding to the Procedure 2 in the Jacobian method – the product of the fractions of susceptibles).
2. If a particular combination of states-at-infection is introduced in vector f, the spectral radius was $\sqrt{R_*}$ (corresponding to the Procedure 1 in the Jacobian method – the basic reproduction number).

However, in modellings presenting only the horizontal route of transmission, the Procedures 1 and 2 of the Jacobian method provided a unique threshold parameter, which is the basic reproduction number R_0. The product of the fractions of susceptible populations χ_0 was obtained as the inverse of the basic reproduction number. Similarly, the next generation method, depending on the construction of vector f, provided a unique threshold given by the spectral radius $\sqrt[n]{R_0}$, with $n = 1, \ldots, 4$.

From horizontally transmitted infections (dengue without transovarian transmission in Section 2.1 and tuberculosis in Appendix A) and infections with additional vertical transmission route (dengue with transovarian transmission in Section 2.2 and sexually transmitted infection in Appendix B) modellings, a unique non-trivial equilibrium was obtained. This steady state became biologically feasible if $R_* > 1$. In the assessment of the stability of DFE by Jacobian and next generation methods, this steady state was locally asymptotically stable when $R_* < 1$, otherwise, unstable. Hence, at $R_* = 1$ occurs forward bifurcation (backward bifurcation does not occur (Yang and Raimundo, 2010), hence sub-thresholds do not exist).

In all models taken into account here, it is easy to observe that the independent term of the characteristic equation $b_0 = \det(F)$, where F is the disease transmission matrix, determined the stability of DFE (Leite et al., 2000). If $b_0 > 0$, then all other Routh–Hurwitz criteria were automatically satisfied. Therefore, in the modellings presenting a unique non-trivial equilibrium point which appears when $R_* > 1$ and DFE is stable when $R_* < 1$, otherwise unstable, the following conjecture can be stated: The threshold parameters can be obtained by calculating b_0 as $\det(F)$ and writing it according to the Procedures 1 and 2. This conjecture establishes that the task of obtaining the threshold parameters by applying the Jacobian method is easy.

Notwithstanding, the next generation method has also a simplified version to calculate the basic reproduction number. Wesley et al. (2010) obtained a spectral radius in the form $\rho(A) = \frac{1}{2}(a_1 + \sqrt{a_1^2 + 4a_2})$, but used a simplified threshold $R_{sim} = a_1 + a_2$. This usage can be generalized as a conjecture: Let the characteristic equation of order n corresponding to the next generation matrix F_1V^{-1} be written as

$$\lambda^n - a_{n-1}\lambda^{n-1} - \cdots - a_1\lambda - a_0 = 0, \tag{34}$$

with $a_i \geq 0$, for $i = 0, \cdots, n-1$. Then, the basic reproduction number could be defined by the sum

$$R_* = a_{n-1} + \cdots + a_1 + a_0. \tag{35}$$

In dengue transmission modellings, above conjecture was validated for the spectral radius obtained in Eqs. (15), (16), (32) and (33) which are the basic reproduction numbers. This definition is also valid for Eq. (31), which provided the product of the fractions of susceptibles. In tuberculosis and sexually transmitted infection modellings, the conjecture could also be validated for the basic reproduction number, see Eqs. (36), (37), (38), (50), (51), (52) and (53).

Above conjecture was obtained considering a single infection. When coinfections occur, let the characteristic equation corresponding to the next generation matrix F_1V^{-1} be written as

$$\Lambda_1(\lambda)\Lambda_2(\lambda) - \Lambda_3(\lambda) = 0,$$

where $\Lambda_1(\lambda)$ and $\Lambda_2(\lambda)$ are the characteristic polynomials corresponding to species 1 and 2, and $\Lambda_3(\lambda)$ is the characteristic polynomial involving cross infections. First, the basic reproduction numbers R_1 and R_2 corresponding to species 1 and 2 could be obtained by applying the above conjecture, and the basic reproduction number R_0 could the maximum between R_1 and R_2, that is,

$$R_0 = \max\{R_1, R_2\}.$$

Second, letting $\lambda = 1$, the characteristic equation can be written as

$$\Lambda_1(1)\Lambda_2(1)\left[1 - \frac{\Lambda_3(1)}{\Lambda_1(1)\Lambda_2(1)}\right] = 0,$$

and the quocient $\Lambda_3(1)/[\Lambda_1(1)\Lambda_2(1)]$ could be defined as the overall reproduction number R_t, that is,

$$R_t = \frac{\Lambda_3(1)}{(R_1 - 1)(R_2 - 1)}.$$

From the drug sensitive and resistant strains modelling of *M. tuberculosis* proposed by Raimundo et al. (2014), by analyzing the independent term of the characteristic equation and also by applying the M-matrix theory, they obtained the basic reproduction numbers for sensitive and resistant strains of tuberculosis R_0^s and R_0^r. Another threshold was $R_t = R_c/[(R_0^s - 1)(R_0^r - 1)]$, where R_c is the reproduction number of appearance of resistant strain due to failure of drug treatment among sensitive tuberculosis individuals. Applying the next generation method,[1] the characteristic equation corresponding to the next generation matrix is obtained as

$$(\lambda^2 - R_0^s)(\lambda^2 - R_0^r) - R_c\lambda = 0.$$

[1] S.M. Raimundo – personal communication.

The reproduction numbers R_0^s and R_0^r can be obtained by applying above conjecture, Eq. (35). Letting $\lambda = 1$, and writing the characteristic equation as

$$(1 - R_0^s)(1 - R_0^r)\left[1 - \frac{R_c}{(R_0^s - 1)(R_0^r - 1)}\right] = 0,$$

then $R_t = R_c/[(R_0^s - 1)(R_0^r - 1)]$.

4. Conclusion

The basic reproduction number is the expected (average) number of secondary cases. When two hosts are involved in the transmission, the magnitude of the transmission from one host to other, and vice-versa, can vary greatly (several orders of magnitude). In this situation, the spectral radius being interpreted as the geometric mean sounds reasonable in the biological world. However, defining the spectral radius of next generation matrix as the basic reproduction number resulted in some troubles. One is the explanation that the square root in the spectral radius is due to the requirement of two generations to close the disease transmission. Another is the discrepancy with the Jacobian method.

In this paper, the definition that the basic reproduction number is the product of the partial reproduction numbers was maintained in two methods. This definition eliminated an apparent conflict between Jacobian and next generation methods in predicting the basic reproduction number: By the fact that the spectral radius is the geometric mean of partial reproduction numbers, both methods predicted the same basic reproduction number. Moreover, the ambiguous definition of two basic reproduction numbers presented in Table 1 in van den Driessche and Watmough (2002) can be removed. Also, there is no need to state that "the expected number of secondarily infected humans that result from a single infected human is R_0^2, as two generations are required to transmit an infection from human to human, the first being from human to mosquito and the second being from mosquito to human" (Roberts and Heesterbeek, 2003). Therefore, the introduction of type reproduction number is unnecessary.

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Appendix A. Directly transmitted infection

To present further discussions about the definition that spectral radius is the geometric mean of partial reproduction numbers, but this product is the basic reproduction number, a tuberculosis model is studied. The model is slightly different that used as an example in van den Driessche and Watmough (2002): one more infectious compartment is introduced (E_1) in order to present a didactic example.

The tuberculosis transmission model considers that the population is divided into five compartments, namely, individuals susceptible to tuberculosis (S), exposed individuals without immune response (E), latent individuals (E_1), infectious individuals (I) and treated individuals (T_b). Latent individuals are those who mounted an effective immune response, restricting *M. tuberculosis* in granulomas (Yang, 2012). Susceptible and treated individuals enter the exposed compartment at rates $\beta_1 I/N$ and $\beta_1 T_b/N$, respectively, where the constant population is $N = E + E_1 + I + S + T_b$. Infected individuals progress to the latent compartment at the rate ν_1, which in turn progress to the infectious class at the rate ν_2. Infectious individuals are treated at rate g. All newborns are susceptible, and all individuals die at the rate d. Then, tuberculosis transmission model is given by

$$\begin{cases} \dfrac{d}{dt}E = \beta_1 \dfrac{SI}{N} + \beta_2 \dfrac{T_b I}{N} - (d + \nu_1)E \\ \dfrac{d}{dt}E_1 = \nu_1 E - (d + \nu_2)E_1 \\ \dfrac{d}{dt}I = \nu_2 E_1 - (d + g)I \\ \dfrac{d}{dt}S = dN - dS - \beta_1 \dfrac{SI}{N} \\ \dfrac{d}{dt}T_b = gI - dT_b - \beta_2 \dfrac{T_b I}{N}. \end{cases}$$

DFE is given by ($\overline{E} = 0, \overline{E}_1 = 0, \overline{I} = 0, \overline{S} = N, \overline{T}_b = 0$).

Let the next generation method be applied. The infective classes are E, E_1 and I. Hence, instead of full vectors f and v, only the first three elements are shown, designated by vectors $\tilde{f}$ and $\tilde{v}$, which are

$$\tilde{f} = \begin{bmatrix} \beta_1 \dfrac{SI}{N} + \beta_2 \dfrac{T_b I}{N} \\ 0 \\ 0 \end{bmatrix} \text{ and } \tilde{v} = \begin{bmatrix} (d + \nu_1)E \\ -\nu_1 E + (d + \nu_2)E_1 \\ -\nu_2 E_1 + (d + g)I \end{bmatrix}.$$

Matrices F_1 and V are derived as

$$F_1 = \begin{bmatrix} 0 & 0 & \beta_1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} d+\nu_1 & 0 & 0 \\ -\nu_1 & d+\nu_2 & 0 \\ 0 & -\nu_2 & d+g \end{bmatrix},$$

and the matrices V^{-1} and F_1V^{-1} can be evaluated, resulting in

$$V^{-1} = \begin{bmatrix} \frac{1}{d+\nu_1} & 0 & 0 \\ \frac{\nu_1}{(d+\nu_1)(d+\nu_2)} & \frac{1}{d+\nu_2} & 0 \\ \frac{R_0}{\beta_1} & \frac{\nu_2}{(d+\nu_2)(d+g)} & \frac{1}{d+g} \end{bmatrix} \text{ and } F_1V^{-1} = \begin{bmatrix} R_0 & \frac{\beta_1\nu_2}{(d+\nu_2)(d+g)} & \frac{\beta_1}{d+g} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

where the basic reproduction number R_0 is given by

$$R_0 = \frac{\beta_1\nu_1\nu_2}{(d+\nu_1)(d+\nu_2)(d+g)}. \tag{36}$$

The eigenvalues corresponding to the next generation matrix F_1V^{-1} are $\lambda_{1,2}=0$ and $\lambda_3=R_0$, and, hence $\rho(F_1V^{-1})=R_0$. This same threshold can be obtained applying the Jacobian method (there is only horizontal transmission, then Procedures 1 and 2 defined in the main text yield $R_0=\chi_0^{-1}$). Hence, the spectral radius is exactly the basic reproduction number, because the geometric mean of a number is itself.

Next two examples treat the cases where the terms ν_1E and ν_2E_1 are removed from $\tilde{v}$ and put in $\tilde{f}$.

A.1. Adding one state-at-infection

In this example, the progression to latent class is considered as an infective event, where Diekmann et al. (2010) called E as the state-at-infection, while I as the state-of-infectiousness. In this case, $\tilde{f}$ and $\tilde{v}$ are

$$\tilde{f} = \begin{bmatrix} \beta_1\frac{SI}{N} + \beta_2\frac{T_bI}{N} \\ \nu_1E \\ 0 \end{bmatrix} \text{ and } \tilde{v} = \begin{bmatrix} (d+\nu_1)E \\ (d+\nu_2)E_1 \\ -\nu_2E_1 + (d+g)I \end{bmatrix},$$

from which F_1 and V are derived as

$$F_1 = \begin{bmatrix} 0 & 0 & \beta_1 \\ \nu_1 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} d+\nu_1 & 0 & 0 \\ 0 & d+\nu_2 & 0 \\ 0 & -\nu_2 & d+g \end{bmatrix}.$$

The matrices V^{-1} and F_1V^{-1} can be evaluated, resulting in

$$V^{-1} = \begin{bmatrix} \frac{1}{d+\nu_1} & 0 & 0 \\ 0 & \frac{1}{d+\nu_2} & 0 \\ 0 & \frac{\nu_2}{(d+\nu_2)(d+g)} & \frac{1}{d+g} \end{bmatrix} \text{ and } F_1V^{-1} = \begin{bmatrix} 0 & \frac{\beta_1\nu_2}{(d+\nu_2)(d+g)} & \frac{\beta_1}{d+g} \\ \frac{\nu_1}{d+\nu_1} & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

The eigenvalues corresponding to the next generation matrix F_1V^{-1} are $\lambda_1=0$, $\lambda_{2,3}=\pm\sqrt{R_0}$, where R_0 is given by Eq. (36), and, hence, $\rho(F_1V^{-1})=\sqrt{R_0}$. Defining the partial reproduction numbers as $R_0^{\beta_1}=\beta_1\nu_2/[(d+\nu_2)(d+g)]$ and $R_0^{\nu_1}=\nu_1/(d+\nu_1)$, then $R_0=R_0^{\beta_1}R_0^{\nu_1}$, and the spectral radius is written as

$$\rho(F_1V^{-1}) = \sqrt{R_0^{\beta_1}R_0^{\nu_1}}. \tag{37}$$

In the case of adding one state-at-infection, the same threshold obtained before is retrieved if the spectral radius and the reproduction number obey $R_0=\rho\left(F_1V^{-1}\right)^2$.

A.2. Adding two states-at-infection

In this example, the progressions to latent and to infectious classes E and E_1 are considered the states-at-infection. In this case, $\tilde{f}$ and $\tilde{v}$ are

$$\tilde{f} = \begin{bmatrix} \beta_1 \dfrac{SI}{N} + \beta_2 \dfrac{T_b I}{N} \\ \nu_1 E \\ \nu_2 E_1 \end{bmatrix} \text{ and } \tilde{v} = \begin{bmatrix} (d+\nu_1)E \\ (d+\nu_2)E_1 \\ (d+g)I \end{bmatrix},$$

from which F_1 and V are derived as

$$F_1 = \begin{bmatrix} 0 & 0 & \beta_1 \\ \nu_1 & 0 & 0 \\ 0 & \nu_2 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} d+\nu_1 & 0 & 0 \\ 0 & d+\nu_2 & 0 \\ 0 & 0 & d+g \end{bmatrix}.$$

The matrices V^{-1} and F_1V^{-1} can be evaluated, resulting in

$$V^{-1} = \begin{bmatrix} \dfrac{1}{d+\nu_1} & 0 & 0 \\ 0 & \dfrac{1}{d+\nu_2} & 0 \\ 0 & 0 & \dfrac{1}{d+g} \end{bmatrix} \text{ and } F_1V^{-1} = \begin{bmatrix} 0 & 0 & \dfrac{\beta_1}{d+g} \\ \dfrac{\nu_1}{d+\nu_1} & 0 & 0 \\ 0 & \dfrac{\nu_2}{d+\nu_2} & 0 \end{bmatrix}.$$

The eigenvalues corresponding to the next generation matrix F_1V^{-1} are $\lambda_{1,2,3} = \sqrt[3]{R_0}$, where R_0 is given by Eq. (36), and, hence, $\rho(F_1V^{-1}) = \sqrt[3]{R_0}$. Defining the partial reproduction numbers as $R_0^{\beta_1} = \beta_1/(d+g)$, $R_0^{\nu_1} = \nu_1/(d+\nu_1)$ and $R_0^{\nu_2} = \nu_2/(d+\nu_2)$, then $R_0 = R_0^{\beta_1}R_0^{\nu_1}R_0^{\nu_2}$, and the spectral radius is written as

$$\rho(F_1V^{-1}) = \sqrt[3]{R_0^{\beta_1}R_0^{\nu_1}R_0^{\nu_2}}. \tag{38}$$

In the case of adding two states-at-infection, the same threshold obtained before is retrieved if the spectral radius and the reproduction number obey $R_0 = \rho\left(F_1V^{-1}\right)^3$.

Summarizing, the definition that the spectral radius is the geometric mean of partial reproduction numbers, but the product of these partial numbers is the basic reproduction number, provided the same R_0, given by Eq. (36), for three different manners of constructing vectors $\tilde{f}$ and $\tilde{v}$.

Appendix B. Vertical transmission in sexually transmitted infections

Diekmann et al. (2010) analyzed a model for sexually transmitted infection with vertical transmission (see end of this Appendix for criticism to this modelling). They considered an SIR model for a heterosexually transmitted infectious disease that may also be transmitted vertically. The indices 1 and 2 stand for, respectively, female and male populations with sizes N_1 and N_2. As new-born individuals are not immediately sexually active, they took J_1 and J_2 to be the numbers of infected juveniles. For adults, they took S_1 and S_2 to be the numbers of susceptible adults, and I_1 and I_2 to be the numbers of infected adults. They assumed that both the length of the pre-sexual period (ν_1^{-1} and ν_2^{-1}) and the length of the infectious period (γ_1^{-1} and γ_2^{-1}) are large compared to the latency period, so they neglected the latter. They assumed that all females are generating descendants without considering mating, and the sex ratio of offspring is one-to-one, but here different ratio is considered: k for the fraction of females, and $1-k$, for males. A fraction p of offspring is vertically infected by infected mothers. The population was considered constant, then natality and mortality rates are considered equal, denoted by μ.

Based on above descriptions, the infected subsystem comprised by the states-at-infection (J_1J_2) and the states-of-infectiousness (I_1,I_2) is given by

$$\begin{cases} \dfrac{d}{dt}J_1 = kp\mu I_1 - (\nu_1+\mu)J_1 \\ \dfrac{d}{dt}I_1 = \nu_1 J_1 + \beta_1 \dfrac{I_2}{N_2} S_1 - (\gamma_1+\mu)I_1 \\ \dfrac{d}{dt}J_2 = (1-k)p\mu I_1 - (\nu_2+\mu)J_2 \\ \dfrac{d}{dt}I_2 = \nu_2 J_2 + \beta_2 \dfrac{I_1}{N1} S_2 - (\gamma_2+\mu)I_2, \end{cases} \tag{39}$$

where the equations for susceptible populations were not shown.

Let special epidemiological parameters be introduced. These parameters are divided according to horizontal and vertical transmissions.

1 **Horizontal transmission**. The partial reproduction numbers R_0^f and R_0^m are defined by

$$\begin{cases} R_0^m = \dfrac{\beta_2 \dfrac{1}{N_1} N_2}{\gamma_1 + \mu} \\ R_0^f = \dfrac{\beta_1 \dfrac{1}{N_2} N_1}{\gamma_2 + \mu}, \end{cases} \tag{40}$$

and the basic reproduction number R_0 corresponding to horizontal transmission is the product of these numbers, or

$$R_0 = R_0^f R_0^m = \frac{\beta_1 \beta_2}{(\gamma_1 + \mu)(\gamma_2 + \mu)}. \tag{41}$$

R_0^f (or R_0^m) is the average number of women (or men) infected by one infected man (or woman), during his (or her) infectious period, introduced in a completely susceptible populations of men and woman. Hence, R_0 is the average number of secondary infectious women originated by horizontal transmission from one primary infectious woman introduced in a completely susceptible populations of men and woman.

2. **Vertical transmission**. The vertical reproduction numbers R_v^f and R_v^m are defined by

$$\begin{cases} R_v^m = \dfrac{(1-k)p\mu}{\gamma_1 + \mu} \dfrac{\nu_2}{\nu_2 + \mu} R_0^f \\ R_v^f = \dfrac{kp\mu}{\gamma_1 + \mu} \dfrac{\nu_1}{\nu_1 + \mu}, \end{cases} \tag{42}$$

where the first term is the average number of male ($(1-k)p\mu/(\gamma_1+\mu)$) or female ($kp\mu/(\gamma_1+\mu)$) offsprings from an infected woman, and the second term is the probability of surviving male ($\nu_2/(\nu_2+\mu)$) or female ($\nu_1/(\nu_1+\mu)$) juvenile class and entering in the adult class. Hence, R_v^f is the average number of infected daughters originated from one infectious woman that become adults, and R_v^m is the average number of infected women originated from infected sons of one infectious woman that become adults and infect women during their infectious period, in a completely susceptible populations of men and women. Notice that R_v^m encompasses vertical and horizontal transmissions. Additionally, it is clear that $R_v^f < 1$, and R_v^m can assume any value.

DFE is given by ($J_1^* = 0, I_1^* = 0, J_2^* = 0, I_2^* = 0$), plus ($S_1^* = N_1, S_2^* = N_2$) for the susceptible populations. The stability of DFE is assessed by Jacobian and next generation methods.

B.1. Jacobian method

Let the Jacobian method be considered. The matrices F_1 and V are given by

$$F_1 = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_1 \dfrac{N_1}{N_2} \\ 0 & 0 & 0 & 0 \\ 0 & \beta_2 \dfrac{N_2}{N_1} & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \nu_1 + \mu & -kp\mu & 0 & 0 \\ -\nu_1 & \gamma_1 + \mu & 0 & 0 \\ 0 & -(1-k)p\mu & \nu_2 + \mu & 0 \\ 0 & 0 & -\nu_2 & \gamma_2 + \mu \end{bmatrix}, \tag{43}$$

from which the matrix $F = F_1 - V$ is obtained as

$$F = \begin{bmatrix} -(\nu_1 + \mu) & kp\mu & 0 & 0 \\ \nu_1 & -(\gamma_1 + \mu) & 0 & \beta_1 \dfrac{N_1}{N_2} \\ 0 & (1-k)p\mu & -(\nu_2 + \mu) & 0 \\ 0 & \beta_2 \dfrac{N_2}{N_1} & \nu_2 & -(\gamma_2 + \mu) \end{bmatrix}.$$

The characteristic equation corresponding to disease transmission matrix F is

$$\lambda^4 + b_3\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0, \tag{44}$$

where the coefficients are

$$\begin{cases} b_3 = \nu_1 + \gamma_1 + \nu_2 + \gamma_2 + 4\mu \\ b_2 = g_2 \left\{ 1 - (\gamma_1 + \mu) \left[R_0 \dfrac{(\gamma_2 + \mu)}{g_2} + R_v^f \dfrac{(\nu_1 + \mu)}{g_2} \right] \right\} \\ b_1 = g_1 \left\{ 1 - (\gamma_1 + \mu) \left[R_0 \dfrac{(\nu_1 + \nu_2 + 2\mu)(\gamma_2 + \mu)}{g_1} + R_v^f \dfrac{(\nu_2 + \gamma_2 + 2\mu)(\nu_1 + \mu)}{g_1} + R_v^m \dfrac{(\gamma_2 + \mu)(\nu_2 + \mu)}{g_1} \right] \right\} \\ b_0 = g_0(1 - R_v), \end{cases} \tag{45}$$

with the auxiliary parameters g_2, g_1 and g_0 being given by

$$\begin{cases} g_2 = (\gamma_1+\mu)(\nu_1+\mu)+(\gamma_2+\mu)(\nu_2+\mu)+(\gamma_1+\nu_1+2\mu)(\gamma_2+\nu_2+2\mu) \\ g_1 = (\gamma_1+\mu)(\nu_1+\mu)(\gamma_2+\nu_2+2\mu)+(\gamma_2+\mu)(\nu_2+\mu)(\gamma_1+\nu_1+2\mu) \\ g_0 = (\gamma_1+\mu)(\gamma_2+\mu)(\nu_1+\mu)(\nu_2+\mu), \end{cases}$$

and the basic reproduction number R_ν is given by

$$R_\nu = R_0 + R_\nu^f + R_\nu^m, \tag{46}$$

where R_0, R_ν^f and R_ν^m are given by Eqs. (41) and (42). Notice that all quocients appearing in b_2 and b_1 are lower than 1.

The Routh–Hurwitz criteria for the polynomial (44) are $b_3>0, b_1>0, b_0>0$ and $b_3b_2b_1 > b_1^2+b_3^2b_0$. Defining Δ as $\Delta = b_3b_2b_1 - b_1^2 - b_3^2b_0$, it is given by

$$\begin{aligned} \Delta = {} & b_1R_\nu^m\frac{\nu_1(\gamma_1+\mu)(\nu_2+\mu)(\gamma_2+\mu)}{\nu_2} + b_3^2g_0(R_0+R_\nu^f+R_\nu^m) + b_1h_1\left\{1-(\gamma_1+\gamma_2+2\mu)(\gamma_1+\mu)\times\left[R_0\frac{(\gamma_2+\mu)}{h_1}+R_\nu^f\frac{(\nu_1+\mu)}{h_1}\right]\right\} \\ & + b_3h_2\times\left\{1-(\gamma_1+\nu_1+2\mu)(\gamma_2+\nu_2+2\mu)(\gamma_1+\mu)\left[R_0\frac{(\nu_1+\nu_2+2\mu)(\gamma_2+\mu)}{h_2}\right.\right. \\ & \left.\left. + R_\nu^f\frac{(\gamma_2+\nu_2+2\mu)(\nu_1+\mu)}{h_2}+R_\nu^m\frac{(\gamma_2+\mu)(\nu_2+\mu)}{h_2}\right]\right\}, \end{aligned}$$

where

$$\begin{cases} h_1 = (\gamma_1+\nu_1+2\mu)(\gamma_1+\mu)(\nu_1+\mu)+(\gamma_2+\nu_2+2\mu)(\gamma_2+\mu)(\nu_2+\mu) \\ h_2 = (\gamma_1+\nu_1+2\mu)(\gamma_1+\mu)(\nu_1+\mu)\times\left[(\gamma_2+\mu)(\nu_2+\mu)+(\gamma_2+\mu)^2+(\nu_2+\mu)^2\right]+(\gamma_2+\nu_2+2\mu)(\gamma_2+\mu)(\nu_2+\mu) \\ \quad\times\left[(\gamma_1+\mu)(\nu_1+\mu)+(\gamma_1+\mu)^2+(\nu_1+\mu)^2\right]. \end{cases}$$

Notice that if $R_\nu<1$, all the Routh–Hurwitz criteria are satisfied, and DFE is locally asymptotically stable.

The independent term $b_0 = \det(F)$ in Eq. (45) was obtained, using the definition given in Eq. (46), from

$$b_0 = g_0\left[1-\frac{\beta_1\beta_2(\nu_1+\mu)(\nu_2+\mu)}{g_0}-\frac{\beta_1\frac{N_1}{N_2}\nu_2(1-k)p\mu(\nu_1+\mu)+kp\mu\nu_1(\gamma_2+\mu)(\nu_2+\mu)}{g_0}\right].$$

Notice that the Procedure 1 defined in the main text were applied ($K_1 = g_0$ and $K_2/K_1 = R_\nu$). By this procedure, there is a unique way to define R_ν, the secondary cases. From the foregoing stability analysis, DFE is stable if $R_\nu<1$, and bifurcates at $R_\nu=1$, and this parameter was called the basic reproduction number.

The basic reproduction number R_ν given by Eq. (46) has a clear biological interpretation. Let one infectious woman be introduced in a completely susceptible populations of men and women, and count the average number of secondary infectious women originated by this infected woman. This woman can infect other women by infecting directly adults. On average, this woman infects R_0^m men, and each man infects R_0^f women. Hence, there is R_0 infected women originated from a single woman by horizontal transmission. The other route of infection is through vertical transmission. Vertically infected daughters from a single infected woman must grow up and become adults, which number on average is given by R_ν^f. Notwithstanding, each vertically infected man must grow up and, then, infects on average R_0^f women, resulting in a total of R_ν^m infected women. Hence, the overall average infectious women originated from a single infectious woman by horizontal and vertical transmissions is given by R_ν.

Remember that R_ν, given by Eq. (46), is not a good parameter to be related to the fractions of susceptible populations χ_ν. Following the Procedure 2 defined in the main text, the coefficient b_0 given by Eq. (45) is written in the form $K_3(1-R_0/K_4)$, that is,

$$b_0 = g_0[1-(R_\nu^f+R_\nu^m)](1-\chi_\nu^{-1}),$$

where the inverse of the product of susceptible populations χ_ν^{-1} is

$$\chi_\nu^{-1} = \frac{R_0}{1-(R_\nu^f+R_\nu^m)}, \tag{47}$$

with R_0, R_ν^f and R_ν^m being given by Eqs. (41) and (42). ($K_3>0$ implies that $R_\nu^f+R_\nu^m<1$, and for $R_\nu^f+R_\nu^m=1$, $\chi_\nu=0$.) From foregoing stability analysis, DFE is stable if $\chi_\nu^{-1}<1$, and bifurcates at $\chi_\nu^{-1}=1$.

Notice that χ_ν^{-1} must appear (not verified) in the product of the susceptibles in the steady state which could be

$$\frac{S_1^*}{N_1}\frac{S_2^*}{N_2} \equiv \chi_\nu = \frac{1-(R_\nu^f+R_\nu^m)}{R_0} \equiv \frac{1}{R_0}-\frac{R_\nu^f+R_\nu^m}{R_0},$$

with clear biological interpretation. The term $1/R_0$ is the decreasing in the fractions of susceptible populations due to the horizontal transmission, while the term $(R_\nu^f+R_\nu^m)/R_0$ is the additional decreasing due to vertical transmission. Again, the sum of the numerator and denominator in the last term is the basic reproduction number, hence χ_ν^{-1} brings indirectly this idea. The appearance of R_0 in latter term shows that the vertical transmission is a consequence of horizontal transmission. The partial number R_ν^f does not depend on the horizontal transmission rates β_1 and β_2, but R_ν^m depends only on R_0^f, that is, on β_1. Vertically infected males must grow up, and then, infect females. For this reason the diminishing in the susceptible populations by vertical transmission depends on R_0^f.

B.2. Next generation method

The next generation matrix is constructed taking into account the states-at-infection (J_1J_2) and the states-of-infectiousness (I_1,I_2).

B.2.1. Considering only states-of-infectiousness

Considering only the states-of-infectiousness, the vectors f and v from system of equations (39) are given by

$$f = \begin{bmatrix} 0 \\ \beta_1 \dfrac{I_2}{N_2} S_1 \\ 0 \\ \beta_2 \dfrac{I_1}{N_1} S_2 \end{bmatrix} \text{ and } v = \begin{bmatrix} -kp\mu I_1 + (\nu_1 + \mu) J_1 \\ -\nu_1 J_1 + (\gamma_1 + \mu) I_1 \\ -(1-k)p\mu I_1 + (\nu_2 + \mu) J_2 \\ -\nu_2 J_2 + (\gamma_2 + \mu) I_2 \end{bmatrix},$$

from which F_1 and V are derived, given by Eq. (43).

The matrices V^{-1} and F_1V^{-1} can be evaluated, resulting in

$$V^{-1} = \begin{bmatrix} \dfrac{\gamma_1 + \mu}{\alpha} & \dfrac{kp\mu}{\alpha} & 0 & 0 \\ \dfrac{\nu_1}{\alpha} & \dfrac{\nu_1 + \mu}{\alpha} & 0 & 0 \\ \xi_1 \nu_1 & \xi_1(\nu_1 + \mu) & \dfrac{1}{\nu_2 + \mu} & 0 \\ \dfrac{\xi_1 \nu_1 \nu_2}{\gamma_2 + \mu} & \dfrac{\xi_1(\nu_1 + \mu)\nu_2}{\gamma_2 + \mu} & \dfrac{\nu_2}{(\nu_1 + \mu)(\nu_2 + \mu)} & \dfrac{1}{\gamma_2 + \mu} \end{bmatrix},$$

where $\xi_1 = (1-k)p\mu/[(\nu_2 + \mu)\alpha]$, and

$$F_1V^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 \\ \dfrac{R_v^m}{1 - R_v^f} \dfrac{\nu_1}{\nu_1 + \mu} & \dfrac{R_v^m}{1 - R_v^f} & R_0^f \dfrac{\nu_2}{\nu_2 + \mu} & R_0^f \\ 0 & 0 & 0 & 0 \\ \dfrac{R_0^m}{1 - R_v^f} \dfrac{\nu_1}{\nu_1 + \mu} & \dfrac{R_0^m}{1 - R_v^f} & 0 & 0 \end{bmatrix}.$$

The eigenvalues of F_1V^{-1} are $\lambda_{1,2} = 0$ and $\lambda_{3,4}$ given by the solution of

$$\lambda^2 - \frac{R_v^m}{1 - R_v^f}\lambda - \frac{R_0}{1 - R_v^f} = 0.$$

Hence, spectral radius corresponding to the next generation matrix F_1V^{-1}, $\overline{\rho}(F_1V^{-1})$, is given by

$$\overline{\rho}(F_1V^{-1}) = \frac{1}{2}\left\{ \frac{R_v^m}{1 - R_v^f} + \sqrt{\left[\frac{R_v^m}{1 - R_v^f}\right]^2 + 4\frac{R_0}{1 - R_v^f}} \right\}, \tag{48}$$

which does not have an easy and direct biological interpretation. R_0, R_v^f and R_v^m are given by Eqs. (41) and (42).

According to Eq. (35) regarding to the conjecture formulated in the main text, the product of the fraction of susceptibles could be given by

$$\chi_v^{-1} = \frac{R_0 + R_v^m}{1 - R_v^f}, \tag{49}$$

which seems wrong (R_v^m appears in the numerator).

B.2.2. Adding states-at-infection

In this case, the vectors f and v from system of equations (39) are given by

$$f = \begin{bmatrix} kp\mu I_1 \\ \beta_1 \dfrac{I_2}{N_2} S_1 \\ (1-k)p\mu I_1 \\ \beta_2 \dfrac{I_1}{N_1} S_2 \end{bmatrix} \text{ and } v = \begin{bmatrix} (\nu_1 + \mu) J_1 \\ -\nu_1 J_1 + (\gamma_1 + \mu) I_1 \\ (\nu_2 + \mu) J_2 \\ -\nu_2 J_2 + (\gamma_2 + \mu) I_2 \end{bmatrix}.$$

The eigenvalues of F_1V^{-1} (F_1 and V are not shown) are $\lambda_{1,2} = 0$ and $\lambda_{3,4}$ given by the solution of

$$\lambda^2 - R_v^f \lambda - (R_0 + R_v^m) = 0.$$

Hence, the spectral radius of the next generation matrix F_1V^{-1} is

$$\rho(F_1V^{-1}) = \frac{1}{2}\left[R_v^f + \sqrt{\left(R_v^f\right)^2 + 4(R_0 + R_v^m)}\right], \tag{50}$$

substantially different from that given by Eq. (48). The application of Eq. (35) regarding to the conjecture formulated in the main text results in the basic reproduction number $R_v = R_0 + R_v^m + R_v^f$.

However, if the term of growing up of females is introduced in vector f, then

$$f = \begin{bmatrix} kp\mu I_1 \\ \beta_1 \frac{I_2}{N_2} S_1 + \nu_1 J_1 \\ (1-k)p\mu I_1 \\ \beta_2 \frac{I_1}{N_1} S_2 \end{bmatrix} \text{ and } v = \begin{bmatrix} (\nu_1+\mu)J_1 \\ (\gamma_1+\mu)I_1 \\ (\nu_2+\mu)J_2 \\ -\nu_2 J_2 + (\gamma_2+\mu)I_2 \end{bmatrix},$$

and the next generation matrix F_1V^{-1} is given by

$$F_1V^{-1} = \begin{bmatrix} 0 & R_v^f \frac{\nu_1+\mu}{\nu_1} & 0 & 0 \\ \frac{\nu_1}{\nu_1+\mu} & 0 & R_0^f \frac{\nu_2}{\nu_2+\mu} & R_0^f \\ 0 & R_v^f \frac{\nu_2+\mu}{\nu_2} \frac{1}{R_0^f} & 0 & 0 \\ 0 & R_0^m & 0 & 0 \end{bmatrix}.$$

The spectral radius corresponding to this next generation matrix, $\rho(F_1V^{-1})$, is given by

$$\rho(F_1V^{-1}) = \sqrt{R_0 + R_v^f + R_v^m}, \tag{51}$$

where R_0, R_v^f and R_v^m are given by Eqs. (41) and (42). Two eigenvalues of F_1V^{-1} are $\lambda_{1,2} = 0$.

There are other two ways of constructing vector f. One is

$$f = \left(kp\mu I_1, \beta_1 \frac{I_2}{N_2} S_1, (1-k)p\mu I_1, \beta_2 \frac{I_1}{N_1} S_2 + \nu_2 J_2\right)^T,$$

where T stands for the transposition of a matrix. One of the eigenvalues is $\lambda_1 = 0$, and $\lambda_{2,3,4}$ are solutions of the characteristic equation

$$\lambda^3 - R_v^f \lambda^2 - R_0 \lambda - R_v^m = 0. \tag{52}$$

Other is

$$f = \left(kp\mu I_1, \beta_1 \frac{I_2}{N_2} S_1 + \nu_1 J_1, (1-k)p\mu I_1, \beta_2 \frac{I_1}{N_1} S_2 + \nu_2 J_2\right)^T,$$

where T stands for the transposition of a matrix. One of the eigenvalues is $\lambda_1 = 0$, and $\lambda_{2,3,4}$ are solutions of the characteristic equation

$$\lambda^3 - (R_0 + R_v^f)\lambda - R_v^m = 0. \tag{53}$$

In both situations, Eq. (35) regarding to the conjecture formulated in the main text results in the basic reproduction number $R_v = R_0 + R_v^m + R_v^f$, given by Eq. (46).

B.3. Comparison

The basic reproduction number R_v given by Eq. (46) can be related to the spectral radius $\rho(F_1V^{-1})$ given by Eq. (51) through $R_v = \rho\left(F_1V^{-1}\right)^2$. Again, the definition of the spectral radius as the geometric mean of partial reproduction numbers, but not the basic reproduction number, resulted in same expression for R_v.

However, the inverse of the product of susceptible populations χ_v^{-1}, Eq. (47), obtained from the Jacobian method is different from that obtained from the next generation method $\overline{\rho}(F_1V^{-1})$, given by Eq. (48), or the simplified threshold given by Eq. (49). Maybe the difference arises due to infeasibility of the modelling.

Let the full model be considered. The model assumes constant population of female and male populations. This assumption is guaranteed if additional births (Φ_1 and Φ_2) replenish deaths, that is, $\Phi_1 = \mu(B_1 + J_1)$ and $\Phi_2 = \mu N_2 - (1-k)\phi(S_1 + I_1 + R_1)$. Additionally, natality and mortality rates must obey the relation $\phi = \mu/k$. Another assumption is that all adult females (susceptible, infectious and recovered) are able

to generate descendants disregarding mating with male. Hence, the system of equations (39) should be completed including the equations for susceptible juveniles (B) and adults (S), and recovered persons (R). The full dynamical system becomes

$$\begin{cases} \dfrac{d}{dt}B_1 = \mu J_1 + \mu[S_1 + (1-p)I_1 + R_1] - \nu_1 B_1 \\ \dfrac{d}{dt}J_1 = p\mu I_1 - (\nu_1 + \mu)J_1 \\ \dfrac{d}{dt}S_1 = \nu_1 B_1 - \beta_1 \dfrac{I_2}{N_2} S_1 - \mu S_1 \\ \dfrac{d}{dt}I_1 = \nu_1 J_1 + \beta_1 \dfrac{I_2}{N_2} S_1 - (\gamma_1 + \mu)I_1 \\ \dfrac{d}{dt}R_1 = \gamma_1 I_1 - \mu R_1, \end{cases} \tag{54}$$

for female population, and

$$\begin{cases} \dfrac{d}{dt}B_2 = \mu(B_2 + J_2 + S_2 + I_2 + R_2) - \dfrac{1-k}{k} p\mu I_1 - (\nu_2 + \mu)B_2 \\ \dfrac{d}{dt}J_2 = \dfrac{1-k}{k} p\mu I_1 - (\nu_1 + \mu)J_2 \\ \dfrac{d}{dt}S_2 = \nu_2 B_2 - \beta_2 \dfrac{I_1}{N_1} S_2 - \mu S_2 \\ \dfrac{d}{dt}I_2 = \nu_2 J_2 + \beta_2 \dfrac{I_1}{N_1} S_2 - (\gamma_2 + \mu)I_2 \\ \dfrac{d}{dt}R_2 = \gamma_2 I_2 - \mu R_2, \end{cases} \tag{55}$$

for male population. The infective classes J_1 and J_2 are slightly different from Eq. (39).

To the system of equations (39) juvenile and recovered compartments were added, resulting in Eqs. (54) and (55). In this modelling, the infectious periods of female and male adults are γ_1^{-1} and γ_2^{-1}, respectively, which are the periods of time from the infection to recovery. However, the newborns must spend first ν_1^{-1} and ν_2^{-1} periods of time to become adults, and then spend additional γ_1^{-1} and γ_2^{-1} periods of time to become recovered. That is, the infected but not infectious juveniles never can be recovered from the infection during the periods of time ν_1^{-1} and ν_2^{-1}, which are approximately 13–18 years. If the model is applied to HIV (human immunodeficiency syndrome) infection, it seems that infected children, if reaching adulthood (Yang et al., 2003), may not transmit infection by using appropriate protection mechanisms. By improving the model, maybe the square of the spectral radius $\overline{\rho}(F_1 V^{-1})$ and χ_v^{-1} could be equal.

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