Vector-borne diseases with nonstationary vector populations: The case of growing and decaying populations

Àlex Giménez-Romero [1], Rosa Flaquer-Galmés [1,2] and Manuel A. Matías [1]

[1] *Instituto de Física Interdisciplinar y Sistemas Complejos IFISC (UIB-CSIC), 07122 Palma de Mallorca, Spain*

[2] *Grup de Física Estadística, Departament de Física. Facultat de Ciències, Universitat Autònoma de Barcelona, 08193 Bellaterra (Barcelona), Spain*

(Received 30 May 2022; accepted 5 October 2022; published 1 November 2022)

Since the last century, deterministic compartmental models have emerged as powerful tools to predict and control epidemic outbreaks, in many cases helping to mitigate their impacts. A key quantity for these models is the so-called basic reproduction number, R_0, that measures the number of secondary infections produced by an initial infected individual in a fully susceptible population. Some methods have been developed to allow the direct computation of this quantity provided that some conditions are fulfilled, such that the model has a prepandemic disease-free equilibrium state. This condition is fulfilled only when the populations are stationary. In the case of vector-borne diseases, this implies that the vector birth and death rates need to be balanced. This is not fulfilled in many realistic cases in which the vector population grows or decreases. Here we develop a vector-borne epidemic model with growing and decaying vector populations that in the long term converge to an asymptotic stationary state, and study the conditions under which the standard methods to compute R_0 work and discuss an alternative when they fail. We also show that growing vector populations produce a delay in the epidemic dynamics when compared to the case of the stationary vector population. Finally, we discuss the conditions under which the model can be reduced to the Susceptible, Infectious, and/or Recovered (SIR) model with fewer compartments and parameters, which helps in solving the problem of parameter unidentifiability of many vector-borne epidemic models.

DOI: 10.1103/PhysRevE.106.054402

I. INTRODUCTION

Vector-borne diseases are caused by infectious agents transmitted by living organisms, called vectors, frequently insects. These diseases represent a significant threat to global human health [1], causing diseases such as malaria, dengue, yellow fever, Zika, trypanosomiasis, and leishmaniasis [2]. Vector-borne human diseases are responsible of more than 17% of all human infectious diseases, causing millions of cases and more than 700 000 deaths annually [3]. Moreover, crop production and farm profitability are also affected by bacterial [4] and viral [5] vector-borne diseases. Some examples are the Pierce's disease of grapevines, which has resulted in an annual cost of approximately $100 million in California alone [6], the olive quick decline syndrome, which could cause about US$5 and US$17 billion of losses in Italy and Spain over the next 50 years in the absence of disease control measures [7], and the multiple diseases caused by viruses [8], with diseases like tobacco mosaic, tomato spotted wilt, etc., transmitted by aphids and other vectors.

Compartmental deterministic models, e.g., the well-known Susceptible, Infectious, and/or Recovered (SIR) model [9], have been widely used in the modeling of vector-borne diseases after the seminal work of Ross and Macdonald [10], which opened the way to controlling malaria outbreaks by acting on the vectors of the disease (the *Anopheles* mosquito). These models consider that both host and vector populations can be divided into different compartments describing different states of the individuals, such as susceptible, infected, or removed (recovered or dead) [11], and the time evolution of these compartments is expressed as a system of ordinary differential equations, defining a dynamical system. Compartmental models provide a mean-field description that imply well-mixed (in practice spatially homogeneous) populations. The well-mixed approximation will be valid whenever the mean distance among hosts is smaller than the mixing length of vectors before they die. In the case of vector-borne diseases it is also equivalent to every vector effectively interacting with all the hosts and every host with all the vectors. A mean-field description is not always valid in spatially extended systems, but still it is often the first step before writing a spatially explicit description.

The most relevant piece of information about a disease is whether an epidemic outbreak will take place or not. The basic reproduction number, R_0, measures the number of secondary infections caused by an initial infected individual in a fully susceptible population, defining the epidemic threshold [12,13], that determines the emergence (or not) of an outbreak. If $R_0 > 1$ an epidemic outbreak will occur, while there will be no outbreak otherwise. The standard way of computing R_0 in deterministic compartmental models is based on the existence of an initial disease-free (prepandemic) equilibrium, represented by the absence of infected hosts and vectors [14,15]. Some standard methods based on the linear stability condition of this equilibrium have been developed

to allow the direct computation of R_0, such as the next-generation matrix (NGM) method [16].

In the case of vector-borne diseases, some models assume that populations (both hosts and vectors) do not change with time (see, e.g., [10,17,18]), thus assuming equal birth and death rates. This guarantees the existence of a disease-free equilibrium and the proper use of standard methods to determine R_0. However, this assumption could be far from reality in several pathosystems. For example, the interaction between temperature, precipitation variations, and other factors may lead to strong variations in the vector population [19,20], implying that the prepandemic state may not be an equilibrium state and that standard methods cannot be applied.

Compartmental models of vector-borne diseases have another feature that may hinder their practical applicability, namely the fact that these models have many compartments, which describe the different states of both hosts and vectors, and as a consequence a relatively large number of parameters. This may lead to an issue known as parameter identifiability and uncertainty [21], depending on the available data, that is more likely to be found in models with many compartments and parameters [22]. Usually, parameter estimation procedures are needed to connect the models with disease data, mainly using incidence or prevalence over time in the host population. Unfortunately, under many circumstances the underlying model parameters are unidentifiable, so that many different sets of parameter values produce the same model fit [23]. Moreover, these parameters can be really difficult to determine from the available experimental data. Nevertheless, in some cases, mathematical manipulations can be performed to reduce the model complexity using exact or approximate relations [24]. In such cases, the number of parameters of the models can be usually reduced in terms of new parameters defined as combinations of some of the original parameters.

The plan of this paper is as follows. In Sec. II we develop a compartmental model of vector-borne transmitted diseases with constant, but different, birth and death rates for the vectors, which we will use to describe the case of growing and decaying vector populations. For simplicity, the model assumes that there is no host to host direct transmission and that the development of the disease is faster than host recruitment, which is also a realistic assumption in many cases, like plant diseases. Section III contains the main results of the study. In particular, we show that the asymptotic approach fails to estimate the R_0 of the model, overlooking outbreaks if some conditions are fulfilled. Here we provide an alternative method to compute R_0 based on the average number of secondary host infections produced by a primary infected host in one generation. It turns out that the validity of the asymptotic approach depends, among other things, on some timescales of the model. Furthermore, we discuss and apply some approximations that allow us to reduce the model in favor of simpler ones, with both fewer compartments and fewer parameters. In particular, we show that if some of the parameters fulfill certain conditions, it is possible to reduce the original model with five compartments and four parameters to a SIR model, with three compartments and two parameters. It is expected that model reductions like this one significantly help in solving possible problems of parameter unidentifiability that plague these models. It is interesting to note that a model in which hosts do not interact directly, but only through vectors, in a certain limit becomes described as if hosts would infect directly one to each other, which is assumed in some studies without suitable confirmation. Finally, the main concluding remarks of the study are presented in Sec. IV.

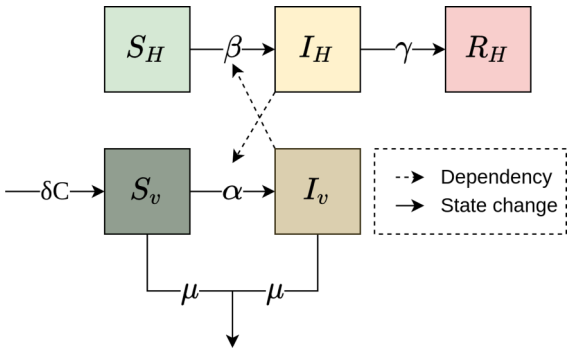

FIG. 1. Schematic representation of the model in Eq. (2). Boxes are the compartments in which the population is divided, solid arrows represent changes in state (so transitions between compartments), and dashed arrows depict the crossed interaction between hosts and vectors.

II. THE MODEL

The compartment model for vector-borne diseases that we will use to illustrate the points to be discussed in this study consists of five compartments, three of which describe the host population (susceptible, S_H, infected, I_H, and removed, R_H), while the other two describe the vector population (susceptible S_V and infected vectors, I_V). Thus, we consider that the pathogen affects only the hosts and do not consider exposed compartments. In addition, no direct host to host or vertical (or mother to offspring for vectors) transmission is assumed. The model could be also generalized to include an exposed host compartment and the above mentioned transmission modes, which would hinder the theoretical analysis without altering the qualitative conclusions of the study. Finally, for the host population we consider neither recruitment nor natural death, and then the total host population, N_H, is constant, $N_H = S_H + I_H + R_H$. Finally, we assume that infected hosts do not have a mechanism to combat the disease and become susceptible again. These assumptions are reasonable in the case of many phytopathologies.

The model is defined according to the following processes:

$$S_H + I_V \xrightarrow{\beta} I_H + I_V, \quad I_H \xrightarrow{\gamma} R_H,$$
$$S_V + I_H \xrightarrow{\alpha} I_V + I_H, S_V \xrightarrow{\mu} \varnothing, \quad I_V \xrightarrow{\mu} \varnothing, \tag{1}$$

which are graphically described in Fig. 1, being the birth of new susceptible vectors described as a source term. Thus, the host-vector compartmental model is written as

$$\begin{aligned}
\dot{S}_H &= -\beta S_H I_v / N_H, \\
\dot{I}_H &= \beta S_H I_v / N_H - \gamma I_H, \\
\dot{R}_H &= \gamma I_H, \\
\dot{S}_v &= \delta C - \alpha S_v I_H / N_H - \mu S_v, \\
\dot{I}_v &= \alpha S_v I_H / N_H - \mu I_v,
\end{aligned} \tag{2}$$

where the crossed nonlinear terms, $S_x I_y$, are written divided by the total host population, N_H, which corresponds to the so-called standard incidence, which differs from the purely bilinear form known as mass action incidence [25].

The model describes infection of susceptible hosts, S_H, at a rate β through their interaction with infected vectors, I_v, while susceptible vectors, S_v, are infected at a rate α through their interaction with infected hosts I_H. Infected hosts exit the infected compartment at rate γ, while infected vectors stay infected the rest of their lifetime, as we consider that the pathogen does not affect them, as is customary. Vectors die naturally (or disappear from the population by some mechanism) at rate μ and are born (appear) at a constant rate δ being susceptible. The constant term C sets the scale of the stationary value of the vector population. Figure 1 shows an schematic representation of the model, and we refer to [17] for a similar model of vector-borne diseases. However, the model in [17] includes exposed compartments and direct host to host transmission, but assumes that the birth and death rate of vectors are identical, and thus, the population does not change with time and stays as fixed by the initial condition.

A. Preliminary analysis of the model

From Eq. (2) it is straightforward to verify that the population of hosts remains constant over time, $N_H = S_H + I_H + R_H$, while the vector population fulfills

$$\dot{N}_v = \dot{S}_v + \dot{I}_v = -\mu(S_v + I_v) + \delta C = -\mu N_v + \delta C, \qquad (3)$$

with the solution

$$N_v(t) = \frac{\delta}{\mu} C + \left(N_v(0) - \frac{\delta}{\mu} C \right) e^{-\mu t}. \qquad (4)$$

From Eq. (4) one can write the stationary value for the vector population, N_v^*,

$$N_v^* = \lim_{t\to\infty} N_v(t) = \frac{\delta}{\mu} C. \qquad (5)$$

Thus, if the initial population of vectors is below (above) the stationary value, the vector population will grow (decrease) until it reaches the stationary value. On the other hand, if $N_v(0) = N_v^* = \delta C/\mu$, the initial population of vectors is already at the stationary state. The initial condition for the vector population can be written in terms of its stationary value (5), $N_v(0) = f N_v^*$, where both $f < 1$ and $f > 1$ are possible, so that one gets

$$N_v(t) = N_v^*[1 + (f-1)e^{-\mu t})]. \qquad (6)$$

We note that vector-borne disease models that assume constant vector populations (e.g., [17]) can be recovered by setting $\delta = \mu$ and $C = N_v(0)$, so that any initial condition for the vector population is stationary, i.e., $\dot{N}_v = 0$ in Eq. (3) and $N_v(t) = N_v(0)$. We note that our model describes populations with an asymptotic stationary vector population and cannot describe periodic vector populations.

III. RESULTS

A. The effect of nonstationary vector populations into the epidemic threshold and disease dynamics

Let us start with the cases in which any initial condition for the vector population is stationary and the total vector population remains unchanged. This will happen when the birth δ and death μ vector rates are identical, independently on the initial condition of the vector population, or the case in which the initial condition of the vector population is already at its stationary value, $N_v(0) = N_v^*$, independently of the values of δ and μ. In such a case, the initial disease-free state of the model, given by $I_H(0) = I_v(0) = 0$, is a fixed point (equilibrium state) of the dynamical system (2) independently of the other initial conditions for the host and vector populations. This allows the definition of the basic reproduction number, R_0, using standard methods such as linear stability analysis or the next-generation matrix (NGM) method [16] (see Appendix A).

In other cases, the total vector population will vary with time provided that the initial condition, $N_v(0)$, is not identical to the asymptotic value at large times, N_v^*. In these cases, an initial disease-free state is not an equilibrium (fixed point) of the model. However, in the literature it is customary to apply the standard techniques, i.e., NGM, to compute R_0 using the vector population in the asymptotic state, that is the post-pandemic disease-free equilibrium [26–30]. The use of these methods is supported by the fact that the asymptotic dynamics of the model converges to the dynamics of the subsystem where the vector population is stationary [31,32]. In both cases the basic reproduction number is given by

$$R_0 = \frac{\beta\alpha}{\mu\gamma} \frac{S_H(0)}{{N_H}^2} N_v^*. \qquad (7)$$

As usual, R_0 accounts for the number of secondary infections produced by an infected individual in one generation and controls the threshold behavior of the model: for $R_0 < 1$ the epidemic dies out, and for $R_0 > 1$ an outbreak occurs. By one generation we refer to the typical time in which new infections can be produced, being the generation time in our model

$$t_g = 1/\gamma + 1/\mu. \qquad (8)$$

Now we will show that Eq. (7) is not always predictive about the onset of the epidemic. In Fig. 2 the final size of the epidemic, R_∞/N_H, is plotted as a function of R_0, where R_∞ is the number of dead individuals at the end of the epidemic. Figures 2(a)–2(d) show that Eq. (7) does indeed regulate the onset of an epidemic when the initial vector population is in its stationary value or below it. This result is general and does not depend on the timescales of the system, $1/\gamma$ and $1/\mu$, and so all curves in these panels behave similarly. In contrast, Figs. 2(e) and 2(f) show that Eq. (7) does not predict the onset of epidemic outbreak when the initial vector population is larger than the stationary value. Thus, for $R_0 < 1$ [computed using Eq. (7)] severe outbreaks appear, yielding mortalities even above 80% of the total population. However, one can observe that as μ is increased, or γ decreased, the predictive power of Eq. (7) is progressively recovered.

Thus, only if the vector population reaches its stationary value before infected hosts have produced new infections

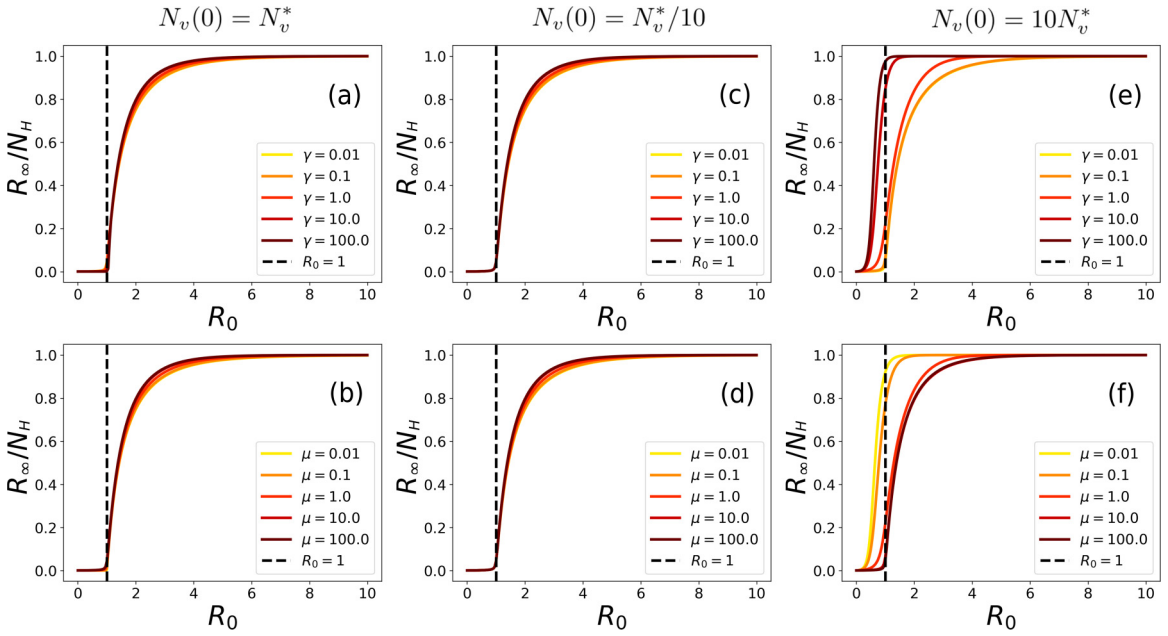

FIG. 2. Numerical verification of the predictive power of the basic reproduction number relation by plotting the final size of the epidemic, R_∞/N_H, as function of R_0. In panels (a) and (b) the initial vector population is in the stationary value, in panels (c) and (d) is below, $N_V^*/10$, and in panels (e) and (f) above, $10N_V^*$. Panels (a), (c), and (e) show realisations for different γ values with a fixed $\mu = 1$ baseline value. Panels (b), (d), and (f) show realizations for different μ values with a fixed $\gamma = 1$ baseline value.

can the onset of an epidemic be characterized by Eq. (7). Let us discuss separately the cases $f > 1$ and $f < 1$, with $N_v(0) = fN_v^*$, namely, when the initial vector population is above and below its stationary value, that is, decaying and growing vector populations towards the asymptotic state.

If $f > 1$ Eq. (6), the time to approach the stationary value, t^*, is

$$(1+\epsilon)N_v^* = N_v^*[1 + (f-1)e^{-\mu t^*}], \tag{9}$$

where $\epsilon \to 0$ is a small parameter controlling the amount by which the vector population differs from its asymptotic value at time t^*. Thus, the time to approach the stationary value, with precision ϵ, is given by

$$t^* = -\frac{1}{\mu}\ln\left(\frac{\epsilon}{f-1}\right) = \frac{1}{\mu}\left|\ln\frac{\epsilon}{f-1}\right|, \tag{10}$$

where the last equality assumes that the small parameter ϵ satisfies $\epsilon < (f-1) > 0$.

If the vector population reaches its stationary value before infected hosts have had time to generate new infections, then R_0 as determined from Eq. (7) is a good prediction of the onset for an epidemic, which is equivalent to the condition that t^* is much smaller than the host's infectious period, $t^* \ll 1/\gamma$,

$$\frac{1}{\gamma} \gg \frac{1}{\mu}\left|\ln\frac{\epsilon}{f-1}\right| \quad \text{or} \quad \frac{\mu}{\gamma} \gg \left|\ln\frac{\epsilon}{f-1}\right|. \tag{11}$$

Otherwise, Eq. (7) will not be predictive of the epidemic onset, and as shown in Figs. 2(e) and 2(f) one may have outbreaks with a substantial final size with $R_0 < 1$.

In the case of growing vector populations, $f < 1$, if $R_0 < 1$ an outbreak cannot occur at all, because R_0 is calculated with the asymptotic population, N_v^*, that is larger than the vector population at any finite time, $N_v(t) < N_v^*\ \forall t$, and so the threshold condition is never attained. In the $R_0 > 1$ case the behavior will be richer, and it will depend on the initial condition, $N_v(0)$. One can define an instantaneous basic reproductive number,

$$R_0^{(i)}(t) = \frac{\beta\alpha}{\mu\gamma}\frac{S_H(0)}{{N_H}^2}N_v(t) = R_0\frac{N_v(t)}{N_v^*}, \tag{12}$$

using $N_v(t)$ instead of N_v^*, with $R_0^{(i)}(t) < R_0\ \forall t$ because the vector population grows. In particular, if $R_0^{(i)}(0) > 1$ there will be an outbreak occurring for short times, and the population of infected hosts will start growing. If instead, $R_0^i(0) < 1$, and as $R_0 > 1$ with R_0 being calculated with the asymptotic state, there must be an intermediate time, say, t_D, for which $R_0^{(i)}(t_D) = 1$. Thus, from $t > t_D$ an outbreak will occur, not initially but after a finite time, that induces a delay in the outbreak, and the infected host population will start growing.

The difference between the original and the delayed dynamics stems from the waiting time to reach $R_0^{(i)} = 1$, t_D, plus the nonlinear effect associated with a new initial condition for the epidemic outbreak at t_D. Thus, in the case that $R_0 > 1$ and $R_0^{(i)}(0) < 1$, from Eq. (12) and Eq. (6) we can analytically approximate the delay as the time needed to reach $R_0^{(i)}(t_D) = 1$,

$$1 + (f-1)e^{-\mu t_D} = \frac{1}{R_0}, \tag{13}$$

which yields the relation

$$t_D = -\frac{1}{\mu}\ln\left[\frac{1-R_0}{(f-1)R_0}\right], \tag{14}$$

where the argument of the logarithm is always positive because $R_0 > 1$ and $f < 1$. Equation (14) is valid only if

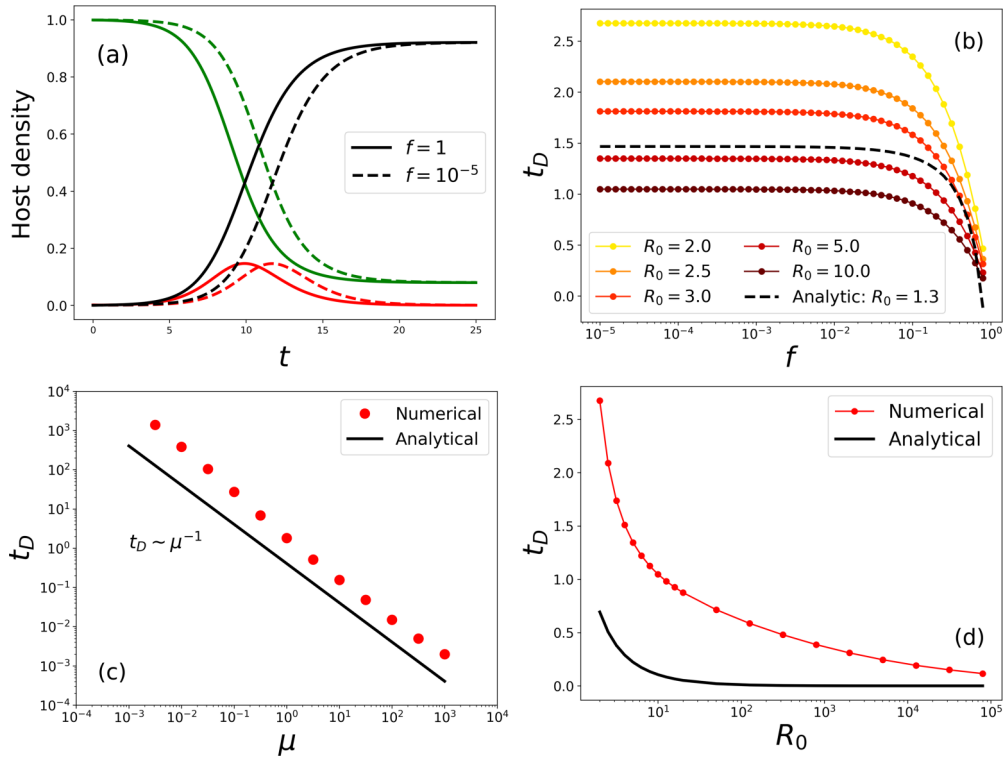

FIG. 3. Numerical study of the delay induced by growing vector populations. (a) Comparison of host's dynamics for a stationary vector population ($f = 1$) and a growing vector population ($f = 10^{-5}$). (b) Time delay as function of f for different values of the basic reproduction number R_0. (c) Time delay as function of the vector natural death rate. (d) Time delay as function of the basic reproduction number, R_0, with $f = 10^{-5}$.

$f < 1/R_0$, for $R_0^{(i)}(0) = fR_0 < 1$, as if otherwise $R_0^{(i)} > 1$ the outbreak would already occur initially.

From Eq. (14) one can see that when the initial vector population is far enough from its stationary value, $f \to 0$, the delay saturates to a constant value, instead of increasing, that is,

$$\lim_{f\to 0} t_D = \frac{1}{\mu} \ln\left(\frac{R_0}{R_0 - 1}\right). \tag{15}$$

In addition, for increasing values of the basic reproduction number, R_0, the delay tends to vanish, and from Eq. (15), this is

$$\lim_{R_0\to\infty} t_D = \frac{1}{\mu} \ln(1) = 0, \tag{16}$$

where the limit $f \to 0$ is taken simultaneously to guarantee that $R_0^{(i)}(0) = fR_0 < 1$. On the other hand the delay, t_D, scales with the vector's lifetime

$$t_D \sim \frac{1}{\mu} = \tau_v. \tag{17}$$

Figure 3(a) shows an example of the time delay caused in the host's dynamics when the vector population grows from an initial condition far from the stationary value. In Fig. 3(b) we can qualitatively observe that all the predicted properties of the delay are fulfilled, namely, the time delay saturates for low f values and decreases with increasing R_0. Although the analytical expression (black dashed line) is clearly not exact due to nonlinear effects, Eq. (14) captures the basic trends of the time delay, t_D. This is clear from Fig. 3(c), which shows that the delay scales with $1/\mu$, and in Fig. 3(d), which shows that the delay tends to 0 in the limit $R_0 \to \infty$, in agreement with the prediction of Eq. (16).

B. The basic reproduction number for nonstationary vector populations

As shown in the previous section, traditional methods to compute the basic reproduction number fail in the case of epidemic models with decaying vector populations, $f > 1$, unless the timescale of vector population fulfills the strong inequality condition (11), as illustrated in Sec. III A. Here we introduce an effective, average definition of R_0, useful to predict the epidemic onset for vector-borne diseases with decaying vector populations, i.e., the case where traditional methods fail. It is defined as the average number of infections produced by an infected individual in one generation [Eq. (8)],

$$\overline{R_0} = \left\langle R_0^i(t) \right\rangle \Big|_0^{t_g} = R_0 \left[1 - \frac{1}{\tau}(f-1)(e^{-\tau} - 1)\right] = R_0 \mathcal{F}, \tag{18}$$

where $\tau = 1 + \mu/\gamma$ and $\mathcal{F}$ accounts for the effect of the decaying vector population on the stationary R_0 [see Appendix B for the full derivation of Eq. (18)].

A first observation is that $\overline{R_0} > R_0$ always (for $f > 1$). This stems from the fact that $\tau = 1 + \mu/\gamma > 1$, so that $e^{-\tau} - 1 < 0$, and $f - 1 > 0$, which yields $\mathcal{F} > 1$. This discussion unravels why standard methods fail to predict the onset of an

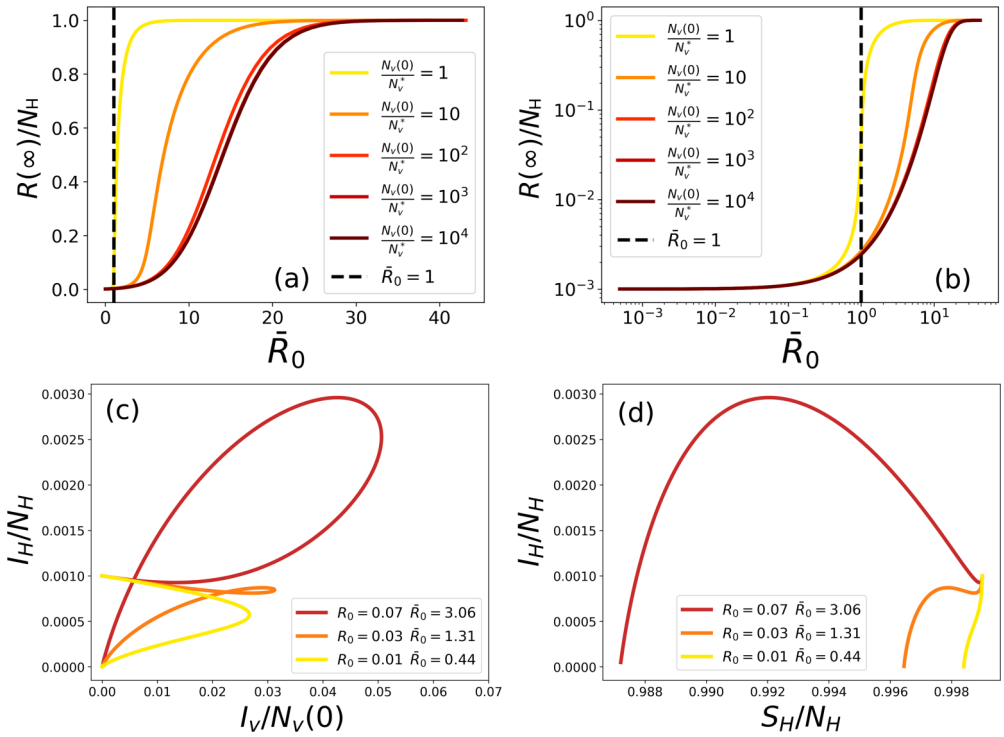

FIG. 4. Numerical verification of the expression for the basic reproduction number for vector-borne diseases with decaying vector populations (18). Final size of the epidemic as a function of the basic reproduction number: (a) linear scale; (b) logarithmic scale. Phase space trajectories: (c) I_H/N_H vs $I_v/N_v(0)$ and (d) I_H/N_H vs S_H/N_H, where an initial condition $I_H(0)/N_H = 0.01$, $S_H(0)/N_H = 0.99$, and $I_v(0)/N_V(0) = 0$ has been used for the three cases. $\mu = \gamma$ has been used in all the simulations.

epidemic under decaying vector populations. Another important point is that if $\mu/\gamma \gg 1$, which implies $\tau \gg 1$,

$$\lim_{\tau\gg 1} \mathcal{F} = \lim_{\tau\gg 1}\left[1 - \frac{1}{\tau}(f-1)(e^{-\tau}-1)\right] = 1 + \frac{f-1}{\tau}, \quad (19)$$

and if furthermore $\tau \sim \frac{\mu}{\gamma} \gg (f-1)$ then $\mathcal{F} \to 1$ and $\overline{R_0} \to R_0$. This is in agreement with the discussion in Sec. III A showing that the R_0 computed from standard methods works if $\mu \gg \gamma$.

Figures 4(a) and 4(b) contrast numerically the validity of Eq. (18) to predict the final size of the epidemic as a function of the general basic reproduction number, $\overline{R_0}$, in linear and logarithmic scale, respectively. We observe that, independently of the initial condition of vectors, the outbreak occurs for $\overline{R_0} > 1$. However, we may notice that for large values of the initial condition of vectors the final size of the epidemic grows more slowly, so that larger values of $\overline{R_0}$ are needed to produce a proper outbreak. This can be explained by the fact that for $\overline{R_0}$ slightly above the threshold, $\overline{R_0} = 1$, and large values of $f = N_v(0)/N_v^*$, infections are produced only in the transient period of the dynamics, as $R_0 < 1$. That is, while the vector population is decaying to its stationary value, the vectors are able to produce new infections, but once the vector population reaches the stationary value, the epidemics stops. This transmission mechanism is radically different from that of vector-borne diseases with stationary vector populations in which the prepandemic disease-free state is an equilibrium of the system. The phase-space plots in Figs. 4(c) and 4(d) show that the time-averaged basic reproduction number $\overline{R_0}$ is able to accurately predict the conditions under which the infected host population will grow, in contrast with R_0 computed in the post-pandemic fixed point. In essence, for $\overline{R_0} > 1$ the infected host population, I_H, grows before reaching the absorbing state, $I_H = I_v = 0$, while for $\overline{R_0} < 1$ the infected host population is monotonically decreasing. We note that Eq. (18) is similar to the time-averaged basic reproduction number presented in [33] for the periodic case, which is a first-order approximation to the true basic reproductive number [34].

C. Fast-slow approximation

The original 5D Eq. (2) model is certainly not amenable to mathematical analyses due to its high phase-space dimensionality and the fact that it depends on four parameters. Moreover, in a real-case application, if the parameters conforming the model are not known, the model could suffer from parameter unidentifiability. However, some approximations can be performed to reduce the mathematical complexity of the model, such as a fast-slow (or adiabatic) approximation.

If the timescale of the vector population evolution is much faster than that of the infected hosts, which is expected to be a good approximation in many practical cases, the vector population will almost instantaneously adapt to its stationary value. Thus, if $1/\mu \ll 1/\gamma$, or equivalently if $\gamma/\mu \ll 1$, we can rewrite the time derivative of the vector-infected population as

$$\epsilon \dot{I}_v = \frac{\alpha}{\mu} S_v \frac{I_H}{N_H} - I_v, \quad (20)$$

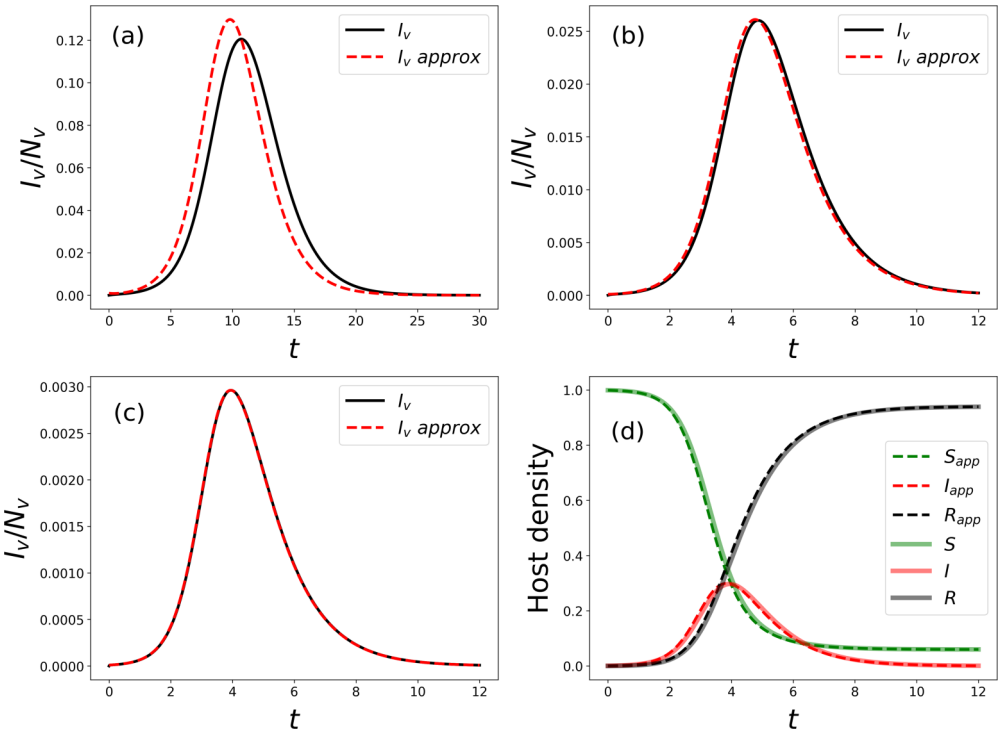

FIG. 5. Numerical verification of the timescale approximation [Eq. (21)] with $N_H = 100$, $\alpha = \gamma = 1$. β is chosen such that $R_0 = 3$. (a) $\mu = 1$, (b) $\mu = 10$, (c) $\mu = 100$. Panel (d) shows a comparison between the approximate and original models for the parameters used in (c), where the approximated models are expected to represent well the original one.

where time has been rescaled to $t' \to \gamma t$ and $\epsilon = \gamma/\mu$ is a small parameter. Then $\dot{I}_v$ can be neglected and the infected vector population can be obtained from the relationship

$$I_v \approx \frac{\alpha}{\mu}\frac{S_v I_H}{N_H}. \tag{21}$$

Substituting Eq. (21) into the original system (2) and the identity $N_v(t) = S_v(t) + I_v(t)$, considering the conditions for which the timescale approximation is valid, $\mu \gg \gamma$, implies that the vector population will reach its stationary value almost instantaneously, so that $N_v(t) \approx N_v^*$, and we obtain the following reduced system:

$$\begin{aligned}
\dot{S}_H &= -\beta' \frac{S_H I_H}{\lambda N_H + I_H}, \\
\dot{I}_H &= \beta' \frac{S_H I_H}{\lambda N_H + I_H} - \gamma I_H, \\
\dot{R}_H &= \gamma I_H,
\end{aligned} \tag{22}$$

where $\beta' = \beta N_v^*/N_H$ and $\lambda = \mu/\alpha$.

Moreover, if $f \neq 1$ the above mentioned timescales relationship must fulfill $\frac{\mu}{\gamma} \gg |\ln \frac{\epsilon}{f-1}|$ [cf. Eq. (11)] and not only $\frac{\mu}{\gamma} \gg 1$. It is important to notice that the presence of direct host-to-host transmission would simply rescale the coefficient β', and the SIR reduction (22) would keep its validity.

In Fig. 5 we numerically verify the validity of the presented fast-slow approximation. As expected, we observe that the approximation breaks down for $\mu \sim \gamma$ [Fig. 5(a)], while as μ becomes larger than γ the approximation improves Fig. 5(b), and it becomes quantitative when $\mu \gg \gamma$ [Fig. 5(c)]. Finally, we show in Fig. 5(d) a comparison between the dynamics of the hosts using both the original and the approximated model using the same parameters than in Fig. 5(c), where the results of both models are expected to converge.

D. Reduction to a SIR model

In addition to the previous condition, $\gamma/\mu \ll 1$, if one has that $\lambda N_H \gg I_H$ also holds (which is indeed plausible in this limit) (22), then the model can be written as a standard SIR model,

$$\begin{aligned}
\dot{S}_H &= -\beta_{\text{eff}} \frac{S_H I_H}{N_H}, \\
\dot{I}_H &= \beta_{\text{eff}} \frac{S_H I_H}{N_H} - \gamma I_H, \\
\dot{R}_H &= \gamma I_H,
\end{aligned} \tag{23}$$

where $\beta_{\text{eff}} = \frac{\beta'}{\lambda} = \frac{\beta \alpha N_v^*}{\mu N_H}$.

In Fig. 6 we show the validity of the reduced models (22) and (23). Figure 6(a) shows that the SIR-like model [Eq. (22)] works when the timescale approximation can be performed (as $\mu/\gamma \gg 1$), but the SIR model fails when the condition $\lambda N_H \gg I_H$ is not fulfilled. Conversely, in Fig. 6(b) we show that as $\lambda N_H \gg I_H$ is fulfilled, then the SIR model perfectly matches the original model. Finally, Fig. 6(c) shows the decrease in the mean squared error of the approximation as the condition (11) is fulfilled for different values of f.

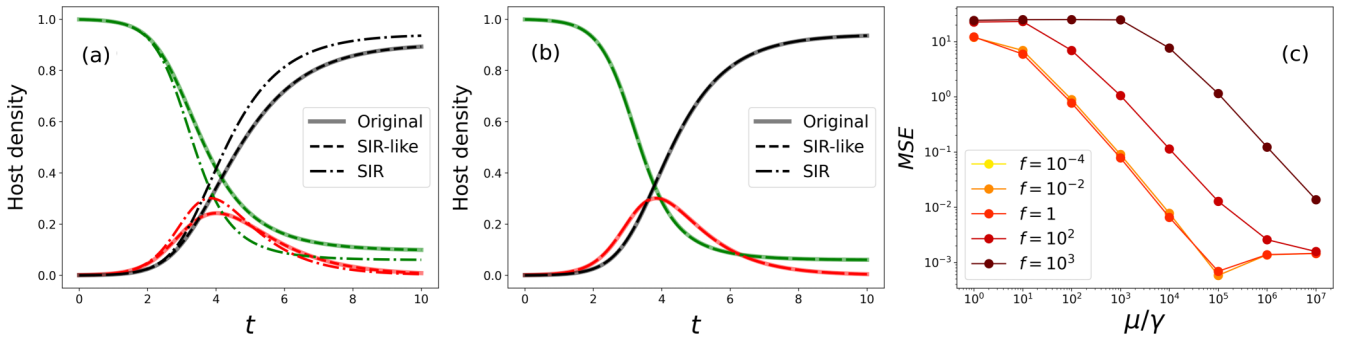

FIG. 6. Comparison between the original model and the reductions, Eq. (22) (SIR-like) and Eq. (23) (SIR) with $N = 100$, $\mu/\gamma = 10^3$, and $f = 1$. β was chosen such that $R_0 = 3$. (a) $\lambda = 1$, (b) $\lambda = 10^3$, (c) mean-squared error between the original model and the SIR approximations as function of the ratio μ/γ and f.

IV. CONCLUSIONS

In the present work we have analyzed several features of a compartmental deterministic model for vector-borne diseases with three compartments for hosts and two for vectors, that does not consider either direct host to host or vertical transmission. The goal is to study the behavior of the model in the case that the vector population is not stationary. In this case, the prepandemic disease-free state is not a fixed point (equilibrium state) of the dynamical system, and, in principle, the methods that are customarily used to determine the basic reproduction number, R_0, do not work. This is so because these methods determine the onset of an outbreak by performing a linear stability analysis of the disease-free state, assuming that it is a fixed point of the model. A common assumption made in the literature is to determine R_0 from the asymptotic state for the vectors (if it is not an extinction state), a fixed point of the model.

We have analyzed several initial conditions of the vector population, characterizing different regimes. In the case that the initial condition for the number of vectors is below the asymptotic state, implying that the vector population overall grows, then R_0 as determined from the asymptotic state correctly predicts the existence (or not) of an epidemic outbreak, but with a temporal delay in its appearance. This result contrasts with the situation in which the initial state is above the asymptotic state, with an overall decrease in the vector population. In this case R_0 determined from the asymptotic state may fail badly, predicting no outbreak while a large fraction of the population might get infected. We present a simple, albeit useful, generalization of R_0 that is able to give a reasonable prediction of the epidemic threshold for decaying populations, including the case in which vectors become extinct, a case in which the asymptotic estimation to determine R_0 cannot be applied.

Compartmental models of vector-borne diseases usually have many compartments and parameters, which can lead to a problem of parameter unidentifiability. The model analyzed here is not an exception, and when applied to real-world cases many different combinations of the parameters could be able to reproduce the available data. Thus, in order to facilitate the application of the model to experimental data, we have studied a useful fast-slow (or adiabatic) approximation that allows us to reduce the model if the parameters fulfill certain conditions. In particular, our study shows that under quite realistic assumptions (the typical timescale of host's infection and death is much slower than vector timescales) it is possible to obtain a reduced SIR model. We recall that this reduction implies that, under these assumptions, the process by which hosts (that could be immobile) get infected through the action of vectors is equivalent to a direct interaction among hosts.

The deterministic compartmental model analyzed here, with some modifications, is a clear candidate to study many vector-borne diseases, in particular phytopathologies. Furthermore, in the case of parameter unidentifiability the model reductions performed in this work could be useful to solve this issue. In any case, this description is still idealized, as compartmental models imply a well-mixed assumption in which space is not explicitly described. This kind of representation is not always applicable to real-world scenarios although are useful as a first approximation. Thus, future research should focus on the integration of space and vector mobility in the model to account for more realistic situations.

ACKNOWLEDGMENTS

A.G.R. and M.A.M. acknowledge financial support from Grants No. RTI2018-095441-B-C22 (SuMaEco) and No. PID2021-123723OB-C22 (CYCLE) funded by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe" and Grant No. MDM-2017-0711 (María de Maeztu Program for Units of Excellence in R&D) funded by MCIN/AEI/10.13039/501100011033.

APPENDIX A: CALCULATION OF R_0 FROM STANDARD METHODS

The standard methods of calculation of R_0 are based in the linear stability analysis of the disease-free equilibrium, either directly, through the linear analysis of the fixed point, that yields the stability condition from which R_0 can be obtained, or using the next-generation method (NGM) [16] that provides directly R_0 by solving a suitable linear problem. Customarily these methods are applied to a prepandemic disease-free equilibrium, but as there is no such state in the case of nonstationary populations, here a similar approach is applied to a post-pandemic or asymptotic disease-free equilibrium.

1. Linear stability analysis

In order to perform the linear stability analysis of the fixed point ($I_H = I_v = 0$) we first need to compute the Jacobian matrix, J,

$$J = \begin{pmatrix} -\beta\frac{I_v}{N_H} & 0 & 0 & -\beta\frac{S_H}{N_H} \\ \beta\frac{I_v}{N_H} & -\gamma & 0 & \beta\frac{S_H}{N_H} \\ 0 & -\alpha\frac{S_v}{N_H} & -\alpha\frac{I_H}{N_H} - \mu & 0 \\ 0 & \alpha\frac{S_v}{N_H} & \alpha\frac{I_H}{N_H} & -\mu \end{pmatrix}. \quad \text{(A1)}$$

Then we evaluate the Jacobian at the fixed point (or disease-free equilibrium, DFE), yielding

$$J|_{DFE} = \begin{pmatrix} 0 & 0 & 0 & -\beta \\ 0 & -\gamma & 0 & \beta \\ 0 & -\alpha\frac{C}{N_H}\frac{\delta}{\mu} & -\mu & 0 \\ 0 & \alpha\frac{C}{N_H}\frac{\delta}{\mu} & 0 & -\mu \end{pmatrix}, \quad \text{(A2)}$$

where $S_H = N_H$ has been considered.

The eigenvalues of Eq. (A2) are

$$\lambda_0 = 0,$$
$$\lambda_\mu = -\mu,$$
$$\lambda_\pm = -\frac{(\gamma+\mu)}{2} \pm \frac{1}{2}\sqrt{(\gamma-\mu)^2 + 4\beta\alpha\frac{C}{N_H}\frac{\delta}{\mu}}. \quad \text{(A3)}$$

It is straightforward to see that all eigenvalues are real and the stability of the disease-free equilibrium is determined by the sign of the eigenvalues. $\lambda_\mu = -\mu < 0$ as μ is defined positive, so in order to discuss the stability of this fixed point, we need to study the $\lambda_\pm$ eigenvalues. λ_- is always negative, but λ_+ changes sign depending on the values of the parameters. The threshold condition $\lambda_+ = 0$ leads to

$$\lambda_+ = 0 \;\Rightarrow\; \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} = 1. \quad \text{(A4)}$$

So, for $\frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} < 1 \Rightarrow \lambda_+ < 0$ the fixed point is stable and for $\frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} > 1 \Rightarrow \lambda_+ > 0$ a perturbation will grow in the direction of the eigenvector associated with λ_+. Thus, this threshold defines the basic reproduction number,

$$R_0 = \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu}. \quad \text{(A5)}$$

If instead of $S_H = N_H$ one considers any initial condition of hosts, $S_H(0)$, the basic reproduction number is given by

$$R_0 = \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu}\frac{S_H(0)}{N_H}. \quad \text{(A6)}$$

2. Next-generation matrix method

The previous result can also be obtained by means of the NGM method, which is explained in detail in [16]. Basically the method is based on decomposing the Jacobian in the form $\mathbf{J} = \mathbf{T} + \mathbf{\Sigma}$, where $\mathbf{T}$ is the transmission part, which describes the production of new infections, and $\mathbf{\Sigma}$ the transition part, which describes changes of state (including death). Then it can be proved [16] that the basic reproduction number R_0 is given by the spectral radius (i.e., the largest eigenvalue) of the (next-generation) matrix $\mathbf{K} = -\mathbf{T}\mathbf{\Sigma}^{-1}$:

$$\mathbf{K} = -\mathbf{T}\mathbf{\Sigma}^{-1} = \begin{pmatrix} \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} & \frac{\beta}{\mu} \\ 0 & 0 \end{pmatrix} \quad \text{(A7)}$$

with

$$\mathbf{T} = \begin{pmatrix} 0 & \beta\frac{N_H}{N_H} \\ 0 & 0 \end{pmatrix}, \quad \mathbf{\Sigma} = \begin{pmatrix} -\gamma & 0 \\ \alpha\frac{C}{N_H}\frac{\delta}{\mu} & -\mu \end{pmatrix}$$

and $$-\mathbf{\Sigma}^{-1} = \begin{pmatrix} \frac{1}{\gamma} & 0 \\ \frac{\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} & \frac{1}{\mu} \end{pmatrix}.$$

The basic reproduction number is the spectral radius of this matrix, so

$$\det(\mathbf{K} - \sigma\mathbb{I}) = 0 \Rightarrow \begin{vmatrix} \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} - \sigma & \frac{\beta}{\mu} \\ 0 & -\sigma \end{vmatrix}$$
$$= (-\sigma)\left(\frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu} - \sigma\right) = 0\,.$$

Solving for σ one obtains the solutions

$$\sigma_1 = \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}, \quad \sigma_2 = 0. \quad \text{(A8)}$$

Therefore, the basic reproduction number is

$$R_0 = \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu}. \quad \text{(A9)}$$

If instead of $S_H = N_H$ one considers any initial condition of hosts, $S_H(0)$, the basic reproduction number is given by

$$R_0 = \frac{\beta\alpha}{\gamma\mu}\frac{C}{N_H}\frac{\delta}{\mu}\frac{S_H(0)}{N_H}. \quad \text{(A10)}$$

APPENDIX B: CALCULATION OF R_0 FOR NONSTATIONARY VECTOR POPULATIONS

We extend the computation of R_0 in the case of nonstationary and nonperiodic vector populations by following the natural definition of basic reproductive number. Thus, R_0 is computed by averaging the number of secondary infections produced by an infected individual along one generation, which is equivalent to averaging the instantaneous definition of R_0, namely, R_0^i, over one generation,

$$\overline{R_0} = \left\langle R_0^i(t)\right\rangle\Big|_0^{t_g} = \frac{R_0}{N_v^*}\langle N_v(t)\rangle\Big|_0^{t_g} = \frac{R_0}{N_v^*}\frac{1}{t_g}\int_0^{t_g} N_v(t)\,dt, \quad \text{(B1)}$$

where the integral in Eq. (B1) is solved as

$$\int_0^{t_g} N_v(t)\,dt = \left[N_v^* t - \frac{1}{\mu}(N_v(0) - N_v^*)e^{-\mu t}\right]_0^{t_g}$$
$$\times N_v^* t_g - \frac{1}{\mu}(N_v(0) - N_v^*)[e^{-\mu t_g} - 1]. \quad \text{(B2)}$$

Thus, the basic reproduction number for nonstationary vector populations is given by

$$\overline{R_0} = \frac{R_0}{N_v^*}\left\{N_v^* - \frac{1}{\mu t_g}[N_v(0) - N_v^*][e^{-\mu t_g} - 1]\right\}, \quad \text{(B3)}$$

where the generation time, t_g, is Eq. (8). Equation (B3) can be rewritten as

$$\overline{R_0} = \left\langle R_0^i(t) \right\rangle \Big|_0^{t_g} = R_0 \left[1 - \frac{1}{\tau}(f-1)(e^{-\tau} - 1) \right] = R_0 \mathcal{F}, \quad \text{(B4)}$$

where $\tau = 1 + \mu/\gamma$ and $\mathcal{F}$ is the expression in brackets, which accounts for the effect of the decaying vector population on the stationary R_0.

In our approach, a generation is defined as the time elapsed in the following sequence of processes: (1) a host individual becomes infected; (2) the infected host passes the disease to a susceptible vector; (3) the infected vector dies. Basically, the time elapsed from the first to the last process is the time in which new infections can be produced, i.e., t_g [Eq. (8)].

[1] T. Athni *et al.*, How vector-borne disease shaped the course of human history, Authorea (2020), doi: 10.22541/au.159135318.82566392.

[2] S. K. Schumacher and J. I. Campbell, Travel medicine, in *Urgent Care Medicine Secrets*, edited by R. P. Olympia, R. M. O'Neill, and M. L. Silvis (Elsevier, Amsterdam, 2018), pp. 352–357.

[3] WHO, *Fact Sheets of Vector-Borne Diseases* (WHO, Geneva, 2020).

[4] W. Huang, P. Reyes-Caldas, M. Mann, S. Seifbarghi, A. Kahn, R. P. Almeida, L. Béven, M. Heck, S. A. Hogenhout, and G. Coaker, Bacterial vector-borne plant diseases: Unanswered questions and future directions, Mol. Plant **13**, 1379 (2020).

[5] C. Bragard, P. Caciagli, O. Lemaire, J. Lopez-Moya, S. MacFarlane, D. Peters, P. Susi, and L. Torrance, Status and prospects of plant virus control through interference with vector transmission, Annu. Rev. Phytopathol. **51**, 177 (2013).

[6] K. B. Tumber, J. M. Alston, and K. B. Fuller, Pierce's disease costs California $104 million per year, Calif. Agr. **68**, 20 (2014).

[7] K. Schneider, W. van der Werf, M. Cendoya, M. Mourits, J. A. Navas-Cortés, A. Vicent, and A. Oude Lansink, Impact of *Xylella fastidiosa* subspecies *pauca* in European olives, Proc. Natl. Acad. Sci. USA **117**, 9250 (2020).

[8] E. P. Rybicki, A top ten list for economically important plant viruses, Arch. Virol. **160**, 17 (2015).

[9] W. O. Kermack and A. G. McKendrick, A contribution to the mathematical theory of epidemics, Proc. R. Soc. London A **115**, 700 (1927).

[10] G. Macdonald, *The Epidemiology and Control of Malaria* (Oxford University Press, Oxford, 1957).

[11] F. Brauer, Compartmental models in epidemiology, in *Mathematical Epidemiology*, edited by F. Brauer, P. van den Driessche, and J. Wu (Springer, Berlin, 2008), pp. 19–79.

[12] R. M. Anderson, Discussion: The Kermack-McKendrick epidemic threshold theorem, Bull. Math. Biol. **53**, 3 (1991).

[13] P. van den Driessche, Reproduction numbers of infectious disease models, Infect. Dis. Model. **2**, 288 (2017).

[14] I. G. Laukó, Stability of disease free sets in epidemic models, Math. Comput. Model. **43**, 1357 (2006).

[15] J. C. Kamgang and G. Sallet, Computation of threshold conditions for epidemiological models and global stability of the disease-free equilibrium (DFE), Math. Biosci. **213**, 1 (2008).

[16] O. Diekmann, J. A. P. Heesterbeek, and M. G. Roberts, The construction of next-generation matrices for compartmental epidemic models, J. R. Soc. Interface **7**, 873 (2010).

[17] F. Brauer, C. Castillo-Chavez, A. Mubayi, and S. Towers, Some models for epidemics of vector-transmitted diseases, Infect. Dis. Model. **1**, 79 (2016).

[18] F. Van den Bosch and M. J. Jeger, The basic reproduction number of vector-borne plant virus epidemics, Virus Res. **241**, 196 (2017).

[19] R. Garms, J. F. Walsh, and J. B. Davies, Studies on the reinvasion of the *Onchocerciasis* control programme in the Volta River Basin by *Simulium damnosum* s.I. with emphasis on the south-western areas, Tropenmed. Parasitol. **30**, 345 (1979).

[20] J. Rocklöv and R. Dubrow, Climate change: An enduring challenge for vector-borne disease prevention and control, Nat. Immunol. **21**, 479 (2020).

[21] G. Chowell, Fitting dynamic models to epidemic outbreaks with quantified uncertainty: A primer for parameter uncertainty, identifiability, and forecasts, Infect. Dis. Model. **2**, 379 (2017).

[22] K. Roosa and G. Chowell, Assessing parameter identifiability in compartmental dynamic models using a computational approach: Application to infectious disease transmission models, Theor. Biol. Med. Model. **16**, 1 (2019).

[23] Y.-H. Kao and M. C. Eisenberg, Practical unidentifiability of a simple vector-borne disease model: Implications for parameter estimation and intervention assessment, Epidemics **25**, 89 (2018).

[24] À. Giménez-Romero, A. Grau, I. E. Hendriks, and M. A. Matias, Modelling parasite-produced marine diseases: The case of the mass mortality event of *Pinna nobilis*, Ecol. Model. **459**, 109705 (2021).

[25] M. Martcheva, *An Introduction to Mathematical Epidemiology* (Springer, New York, 2015).

[26] H.-M. Wei, X.-Z. Li, and M. Martcheva, An epidemic model of a vector-borne disease with direct transmission and time delay, J. Math. Anal. Appl. **342**, 895 (2008).

[27] A. A. Lashari and G. Zaman, Global dynamics of vector-borne diseases with horizontal transmission in host population, Comput. Math. Appl. **61**, 745 (2011).

[28] N. Shah and G. Jyoti, SEIR model and simulation for vector borne diseases, Appl. Math. **04**, 13 (2013).

[29] S. Zhao, S. S. Musa, J. T. Hebert, P. Cao, J. Ran, J. Meng, D. He, and J. Qin, Modelling the effective reproduction number of vector-borne diseases: The yellow fever outbreak in Luanda, Angola 2015–2016 as an example, PeerJ **8**, e8601 (2020).

[30] L. Esteva and C. Vargas, Analysis of a dengue disease transmission model, Math. Biosci. **150**, 131 (1998).

[31] H. R. Thieme, Convergence results and a Poincaré-Bendixson trichotomy for asymptotically autonomous differential equations, J. Math. Biol. **30**, 755 (1992).

[32] C. Castillo-Chavez and H. R. Thieme, Asymptotically autonomous epidemic models, in *Mathematical Population Dynamics: Analysis of Heterogeneity, Vol. I, Theory of Epidemics*, edited by D. Arino, O. Axelrod, M. Kimmel, and M. Langlais (Wuerz Publishing, Winnipeg, 1995), pp. 33–50.

[33] C. L. Wesley and L. J. Allen, The basic reproduction number in epidemic models with periodic demographics, J. Biol. Dyn. **3**, 116 (2009).

[34] N. Bacaër and S. Guernaoui, The epidemic threshold of vector-borne diseases with seasonality, J. Math. Biol. **53**, 421 (2006).