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ORIGINAL ARTICLE

Approximation of the Basic Reproduction Number R_0 for Vector-Borne Diseases with a Periodic Vector Population

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Abstract The main purpose of this paper is to give an approximate formula involving two terms for the basic reproduction number R_0 of a vector-borne disease when the vector population has small seasonal fluctuations of the form $p(t) = p_0(1 + \varepsilon \cos(\omega t - \phi))$ with $\varepsilon \ll 1$. The first term is similar to the case of a constant vector population p but with p replaced by the average vector population p_0. The maximum correction due to the second term is $(\varepsilon^2/8)\%$ and always tends to decrease R_0. The basic reproduction number R_0 is defined through the spectral radius of a linear integral operator. Four numerical methods for the computation of R_0 are compared using as example a model for the 2005/2006 chikungunya epidemic in La Réunion. The approximate formula and the numerical methods can be used for many other epidemic models with seasonality.

Keywords Epidemics · Basic reproduction number · Seasonality
MSC 92D30 · 45C05 · 47A55

1. Introduction

Since March 2005, an epidemic of chikungunya has hit for the first time the island of La Réunion, a French overseas territory located in the Indian Ocean. After a first peak of above 400 new human cases per week in May 2005, the epidemic slowed down (Fig. 1, top) because of the winter season, which is cooler and less rainy (Fig. 1, bottom) and therefore less favorable to the proliferation of *Aedes albopictus*, the mosquito transmitting the virus causing chikungunya to humans. Notice that La Réunion is in the southern hemisphere. *Aedes albopictus* was also responsible for a small epidemic of dengue that started in April 2004 and stopped in July of the same year, that is at the beginning of winter (Pierre et al., 2005). This probably led local epidemiologists to believe that the scenario of the dengue

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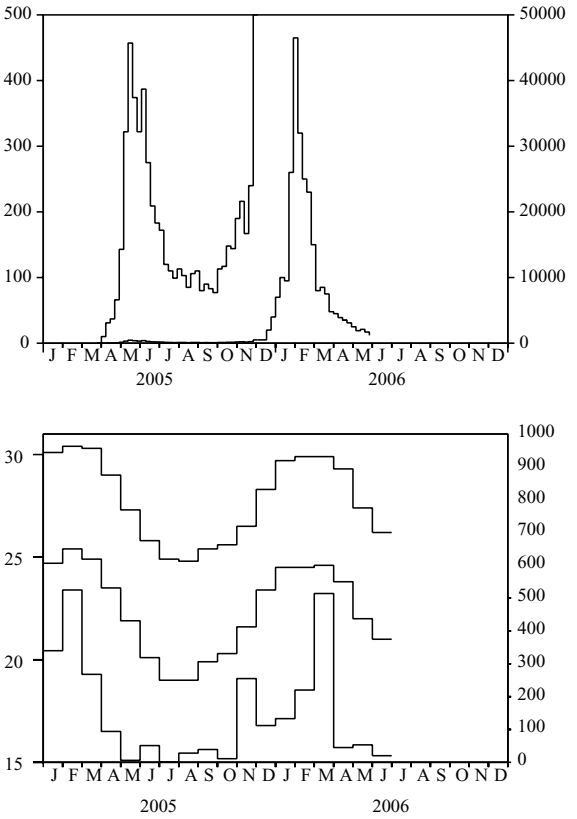

Fig. 1 (*Top*) Estimated number of new cases per week plotted with two different scales. Using the left axis, we can see clearly the epidemic curve for the year 2005. Using the right axis, we can see how it continued during the year 2006. Data from Institut de Veille Sanitaire (www.invs.sante.fr/surveillance/chikungunya). (*Bottom*) Maximum/minimum temperature in degree Celsius (*upper and middle curves*, left axis) and rainfall in millimeters per month (*lower curve*, right axis) in the city of Sainte-Marie, La Réunion. Data from Météo France (www.acreunion.fr/pedagogie/cotamarp/temps/temperatures.html).

epidemic would repeat for chikungunya, and that the small-scale vector control associated with the active search for human cases would be sufficient to stop the epidemic before the end of the winter. This was not the case. After reaching a minimum under 100 new cases per week in September 2005, the chikungunya epidemic started to grow again and reached an astonishing peak in February 2006 of over 40,000 new cases per week. By that time, the epidemic had become a subject of scientific and political controversy: why weren't epidemiologists able to predict what would happen, and why didn't the Ministry of Health in Paris launch a large-scale vector control campaign early enough? By now (July 2006), more than 260,000 people have suffered from the disease since the beginning of the epidemic, that is about one-third of the island's population. About 200 death certificates have mentioned chikungunya as one of the causes of death. Besides, the epidemic has had

an important impact on the economy of the island, and particularly on tourism, which is one of the main industries. Because of the combined effect of winter and vector control, the number of new cases per week has now fallen below 1000.

An important but difficult question is: will the epidemic cross the winter season one more time and cause a new important peak next summer? A popular scientific but simplified way of thinking at this kind of question is the following. There is a key parameter associated with the epidemic which is the basic reproduction number R_0, loosely defined as the average number of secondary cases caused by a primary case at the beginning of the epidemic. If $R_0 > 1$, the epidemic can develop. If $R_0 < 1$, it will stop. Following the work of Ronald Ross on malaria (Ross, 1911), the following formula for R_0 has been derived for vector-borne diseases:

$$R_0 = \frac{\beta^2 q q' p}{\alpha \mu P}, \tag{1}$$

where β is the biting rate of the vector, q and q' are the transmission probabilities per bite from vector to human and from human to vector, p is the vector population, P is the human population, $1/\alpha$ is the average infectious period in humans, and $1/\mu$ is the life expectation of adult vectors (see Bailey, 1982, Anderson and May, 1991, and Heesterbeek, 2002 for a historical perspective). This formula shows, in particular, that R_0 is proportional to the vector population p. So if a surveillance system could follow the evolution of the vector density before and during the epidemic, and if the numerical value of R_0 were known from a previous epidemic or could be estimated using Eq. (1), then one would expect the epidemic to stop once large-scale vector control has divided the vector density by R_0. But since no surveillance system presently follows the density of *Aedes albopictus* in La Réunion, the approach just described cannot work. Therefore, it seems just impossible to answer reasonably the question of whether the chikungunya epidemic will cross the winter season once again.

In this paper, we focus our attention on the more theoretical part of the problem, namely the estimation of the basic reproduction number R_0. A striking feature of the chikungunya epidemic is the role played by seasonality. Equation (1) is based on the inappropriate assumption that the vector population p is constant all through the year. Several questions arise: what is the definition of R_0 when seasonality is taken into account, for example, if we assume that the vector population is a periodic function of time $p(t)$? How to compute R_0? Are there some special cases where simple formulas similar to (1) can be obtained? These questions are of course not specific to chikungunya. They arise, for example, in connection with the emergence of other vector-borne diseases, and more generally with problems of population dynamics (epidemiology (Altizer et al., 2006), ecology, demography, immunology, population genetics, etc.) influenced by seasonality.

The recent work (Bacaër and Guernaoui, 2006) has been able to answer some of these questions. It contains a definition of R_0 in a periodic environment as the spectral radius of a linear integral operator on a space of periodic functions. The definition was inspired by earlier work on age-structured population dynamics with periodic coefficients (Coale, 1972; Thieme, 1984; Jagers and Nerman, 1985; Anita

et al., 1998) and by the book of Diekmann and Heesterbeek (2000) which emphasizes the "next-generation matrix" and "next-generation operator" approach to the definition of R_0. Bacaër and Guernaoui (2006) also contains an algorithm to compute R_0 based on the discretization of the integral operator. This algorithm was used to estimate R_0 for an epidemic of cutaneaous leishmaniasis in Morocco, for which the fluctuations of the vector population were known precisely thanks to field work.

The present paper is organized as follows. In Section 2, we introduce a slight modification to the definition of R_0 given in Bacaër and Guernaoui (2006, Section 5). The spectral radius of the "next-generation operator" is now called r_0, and R_0 is defined by $R_0 = r_0^n$, where n is the number of "infected" compartments in the model. This point has already been briefly discussed in Heesterbeek and Roberts (1995b, Section 2.1) for the case of the "next-generation matrix". We also show for a certain class of models, which may be called "cyclic", that the n-dimensional integral eigenvalue problem can be reduced to a one-dimensional problem. In most of the paper, we focus on the special case where the kernel of the reduced problem takes the form $K(x,t) = f(t)\,G(x)$, where $f(t)$ is a periodic function. This case includes already many models for vector-borne diseases and for directly transmitted diseases.

In Section 3, we present four numerical methods for the computation of R_0 associated with such one-dimensional integral eigenvalue problems. The first one has already been presented in Bacaër and Guernaoui (2006, Section 4): it is a simple discretization of the integral operator. The second one uses Fourier series and was inspired by Williams and Dye (1997), which focuses on the Malthusian parameter instead of the basic reproduction number. These two methods work for a general function $G(x)$ and a general periodic function $f(t)$. The third method is designed for the special case where $f(t) = 1 + \varepsilon\cos(\omega t - \phi)$, and combines Fourier series with a perturbation method for small ε. It is similar to the one used in Coale (1972, Chap. 6), which also focuses on the Malthusian parameter instead of the basic reproduction number. The fourth method works for "cyclic" next-generation operators associated to systems of linear ordinary differential equations with periodic coefficients. It uses Floquet theory as in Heesterbeek and Roberts (1995a,b) but in a different way.

In Section 4, we consider vector-borne diseases and assume that the vector population is given by

$$p(t) = p_0[1 + \varepsilon\cos(\omega t - \phi)]. \tag{2}$$

Using first a simple model for malaria and the results of Section 3.3, we show that with the same notations as in Eq. (1), the basic reproduction number is given by

$$R_0 \simeq \frac{\beta^2\, q\, q'\, p_0}{\alpha\,\mu\,P}\left(1 - \frac{\alpha\mu}{\omega^2 + (\alpha+\mu)^2}\,\frac{\varepsilon^2}{2}\right) \tag{3}$$

when ε is small. This apparently new formula generalizes the formula represented by Eq. (1). The first term is similar to the case of a constant vector population p

but with p replaced by the average vector population p_0. The maximum correction due to the second term is $(\varepsilon^2/8)\%$ and always tends to decrease R_0. We then turn to the chikungunya epidemic using a slightly more complicated model. The simple form, represented by Eq. (2), for the vector population seems not too unreasonable when we look back at the temperature and rainfall curves in La Réunion (Fig. 1, bottom), both having only one maximum each year around February. After having estimated the parameters of the model, we compare the four numerical methods of Section 3 for the computation of R_0. However, the numerical value of R_0 obtained for the chikungunya epidemic should not be taken too seriously since the parameter values are imprecisely known and because of the simplicity of the assumption, represented by Eq. (2). It can be seen as an exercise to test the different numerical methods, as a source of inspiration for developing the theory, or as a first modeling attempt waiting for field work concerning the fluctuations of the population of *Aedes albopictus*.

The last section discusses the applicability of the method of Section 3.3 to get approximate formulas for R_0 for other mathematical models of infectious diseases with periodic coefficients, especially the much studied SIR model with periodic contact rate and fixed infectious period, and also the SEIR model with periodic contact rate and exponentially distributed latent and infectious periods. We also present some preliminary indications on the meaning of R_0 in stochastic epidemic models with seasonality.

2. Definition of R_0

For all $t \in \mathbb{R}$ and $x \geq 0$, let $K(t, x)$ be a nonnegative $n \times n$ matrix. Assume that $K(t, x)$ is a periodic function of t of period θ for all $x \geq 0$.

The idea behind the function $K(t, x)$ is an epidemic model with n "infected" compartments $(I_1, I_2, \ldots, I_n)$, which may be infectious or latent. The coefficient $K_{i,j}(t, x)$ in row i and column j represents the expected number of individuals in compartment I_i that one individual in compartment I_j "generates" at the beginning of an epidemic per unit time at time t if it has been in compartment I_j for x units of time. The verb "generates" covers the case where individuals in compartment I_j infect individuals in compartment I_i, but also the case where individuals in compartment I_j just move to compartment I_i. The periodicity assumption on $K(t, x)$ is designed to represent a periodic environment.

Consider the linear integral operator $\mathcal{K}$ defined by

$$(\mathcal{K}v)(t) = \int_0^\infty K(t, x)\, v(t - x)\, \mathrm{d}x \tag{4}$$

and acting on a space of θ-periodic functions with values in $\mathbb{R}^n$. To be more specific, we notice that because of the periodicity assumptions on $K(t, x)$ and $v(t)$, Eq. (4) can be rewritten as

$$(\mathcal{K}v)(t) = \int_0^\theta \widehat{K}(t, s)\, v(s)\, \mathrm{d}s$$

where

$$\widehat{K}(t,s) = \begin{cases} \sum_{k=0}^{+\infty} K(t, t-s+k\theta) & \text{if } s < t, \\ \sum_{k=1}^{+\infty} K(t, t-s+k\theta) & \text{if } s > t. \end{cases}$$

We assume that $\widehat{K}$ belongs to the space $L^2((0,\theta)\times(0,\theta),\mathbb{R}^{n\times n})$. A simple extension of Theorem 7 in Hochstadt (1973, p. 51) shows that $\mathcal{K}$ is a compact operator on $L^2((0,\theta),\mathbb{R}^n)$. As in Diekmann and Heesterbeek (2000, p. 77), $\mathcal{K}$ can be called the "next-generation operator," and $K(t,x)$ the associated kernel. Let r_0 be the spectral radius of $\mathcal{K}$. We define the basic reproduction number R_0 by the formula $R_0 = r_0^n$. We refer to Heesterbeek and Roberts (1995b, Section 2.1) for a discussion of why it is sometimes more convenient to take $R_0 = r_0^n$ instead of $R_0 = r_0$. We also refer to Bacaër and Guernaoui (2006, Section 5) for a discussion of why this definition of R_0 generalizes the usual one without seasonality based on the "next-generation matrix" (Diekmann and Heesterbeek, 2000, p. 74).

The operator $\mathcal{K}$ is positive. If $r_0 > 0$, it follows from the theorem of Krein and Rutman (see, for instance, Theorem 9.2 in Krasnosel'skij et al. (1980, p. 87)) that r_0 is an eigenvalue of $\mathcal{K}$ and that there is a nonnegative eigenfunction $v(t) \in L^2((0,\theta),\mathbb{R}^n)$ associated with r_0. Extending $v(t)$ by periodicity to $\mathbb{R}$, we can write that

$$\int_0^\infty K(t,x)\, v(t-x)\, \mathrm{d}x = r_0\, v(t)\,. \tag{5}$$

Conditions ensuring that $r_0 > 0$ can be found in Krasnosel'skij et al. (1980) or Schaefer (1974, p. 377).

In the rest of this paper, we will consider "cyclic" models that have the following special form (Fig. 2): all elements $K_{i,j}(t,x)$ of the kernel are zero except $K_{1,n}(t,x)$ and $K_{j+1,j}(t,x)$ for all $1 \le j \le n-1$.

This includes, in particular, the general "one-dimensional" case $n = 1$ with arbitrary kernel $K(t,x)$. Set $v(t) = (v_1(t),\dots,v_n(t))$. The integral eigenvalue problem, represented by Eq. (5), can be rewritten as

$$\begin{aligned} \int_0^\infty K_{1,n}(t,x)\, v_n(t-x)\, \mathrm{d}x &= r_0\, v_1(t), \\ \int_0^\infty K_{j+1,j}(t,x)\, v_j(t-x)\, \mathrm{d}x &= r_0\, v_{j+1}(t), \quad 1 \le j \le n-1. \end{aligned}$$

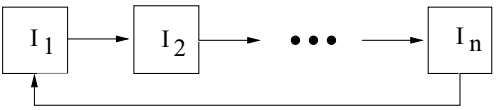

Fig. 2 Infected compartments in a "cyclic" model.

Replacing successively the equation with $j = n-1$, $j = n-2, \ldots j = 1$ in the first equation, and recalling that $R_0 = r_0^n$, it follows that

$$\int_0^\infty \cdots \int_0^\infty K_{1,n}(t, x_1)\, K_{n,n-1}(t - x_1, x_2) \ldots\ K_{2,1}(t - x_1 - \cdots - x_{n-1}, x_n)$$
$$v_1(t - x_1 - \cdots - x_n)\, \mathrm{d}x_1 \ldots \mathrm{d}x_n = R_0\, v_1(t).$$

Notice the important property: if any of the nonzero element $K_{i,j}(t, x)$ is multiplied by a certain constant, then R_0 is also multiplied by the same constant. The change of variable ($x_1 = x_1, \ldots, x_{n-1} = x_{n-1}$, $x = x_1 + \cdots + x_n$) leads to

$$\int_0^\infty \widetilde{K}(t, x)\, v_1(t - x)\, \mathrm{d}x = R_0\, v_1(t), \tag{6}$$

where $\widetilde{K}(t, x)$ is the hypersurface integral

$$\widetilde{K}(t, x) = \int_{\sigma_x^n} K_{1,n}(t, x_1)\, K_{n,n-1}(t - x_1, x_2) \ldots\ K_{2,1}(t - x_1 - \cdots - x_{n-1}, x_n)\, \mathrm{d}\sigma_x^n$$

and $\sigma_x^n = \{(x_1, \ldots, x_n) \in \mathbb{R}^n;\quad x_1 + \cdots + x_n = x,\quad x_1 \geq 0, \ldots, x_n \geq 0\}$. Hence, the n-dimensional integral eigenvalue problem, represented by Eq. (5) has been reduced to the one-dimensional problem, represented by Eq. (6).

In the rest of the paper except in Section 3.4, we consider the more special case where

$$K_{1,n}(t, x) = f(t)\, g_n(x), \quad K_{j+1,j}(t, x) = g_j(x), \quad 1 \leq j \leq n-1. \tag{7}$$

Equation (6) takes the form

$$f(t) \int_0^\infty G(x)\, v_1(t - x)\, \mathrm{d}x = R_0\, v_1(t), \tag{8}$$

with

$$G(x) = \int_{\sigma_x^n} g_1(x_1) \ldots g_n(x_n)\, \mathrm{d}\sigma_x. \tag{9}$$

Notice that if $n = 1$, the kernel reduces to $K(t, x) = f(t)\, g_1(x)$ so that $G(x) = g_1(x)$. Notice also that if

$$g_j(x) = a_j\, \mathrm{e}^{-b_j x}, \quad 1 \leq j \leq n, \tag{10}$$

it can be shown (see Appendix), starting from Eq. (9), that

$$G(x) = a_1 \ldots a_n \sum_{j=1}^{n} \frac{\mathrm{e}^{-b_j x}}{\prod_{k \neq j}(b_k - b_j)}\,. \tag{11}$$

This formula also holds for $n = 1$ with the usual convention that a product over an empty set is equal to 1.

3. Numerical methods to compute R_0

3.1. Discretization of the integral eigenvalue problem

This method consists in discretizing the integral eigenvalue problem, represented by Eq. (8). It was presented in Bacaër and Guernaoui (2006, Section 4), so we just recall it briefly. Let N be a large integer and set $t_k = (k-1)\,\theta/N$, where $k = 1, 2, \ldots, N$. Set

$$\widehat{G}(x) = \sum_{k=0}^{+\infty} G(x + k\theta). \tag{12}$$

Let $\mathcal{R}_0$ be the spectral radius of the ordinary matrix eigenvalue problem

$$f(t_k)\,\frac{\theta}{N}\left[\sum_{j=1}^{k-1} \widehat{G}(t_k - t_j)\,\mathcal{V}_j + \sum_{j=k}^{N} \widehat{G}(t_k - t_j + \theta)\,\mathcal{V}_j\right] = \mathcal{R}_0\,\mathcal{V}_k\,, \tag{13}$$

where $\mathcal{V}_i$ is an eigenvector, then $\mathcal{R}_0 \to R_0$ as $N \to +\infty$. The numerical computation of $\mathcal{R}_0$ can be done using, e.g., Scilab (`www.scilab.org`), a free mathematical software similar to Matlab. Notice that if $g_j(x) = a_j\,\mathrm{e}^{-b_j x}$ for all $1 \le j \le n$, it follows from Eq. (11) that

$$\widehat{G}(x) = a_1 \ldots a_n \sum_{j=1}^{n} \frac{\mathrm{e}^{-b_j x}}{(1 - \mathrm{e}^{-b_j\,\theta})\,\prod_{i\neq j}(b_i - b_j)}\,. \tag{14}$$

3.2. Fourier series: general periodic case

Set $\omega = 2\pi/\theta$. Consider the Fourier decomposition of the periodic function $f(t)$:

$$f(t) = \sum_{j\in\mathbb{Z}} f_j\,\mathrm{e}^{ji\omega t}, \qquad f_j = \frac{1}{\theta}\int_0^\theta f(t)\,\mathrm{e}^{-ji\omega t}\,\mathrm{d}t\,, \tag{15}$$

where $\mathbb{Z}$ is the set of integers (positive or negative) and $i^2 = -1$. The f_j's are complex numbers such that $f_{-j} = f_j^*$ (the superscript * stands for the complex conjugate). We look for a real (and even positive) solution of Eq. (8) of the form

$$v_1(t) = \sum_{j\in\mathbb{Z}} c_j\,\mathrm{e}^{ji\omega t}. \tag{16}$$

The c_j's are also complex numbers such that $c_{-j} = c_j^*$. Replacing Eqs. (15) and (16) in Eq. (8) yields

$$\left(\sum_{j\in\mathbb{Z}} f_j\, \mathrm{e}^{ji\omega t}\right)\left(\sum_{j\in\mathbb{Z}} G_j\, c_j\, \mathrm{e}^{ji\omega t}\right) = R_0 \sum_{j\in\mathbb{Z}} c_j\, \mathrm{e}^{ji\omega t}\,, \tag{17}$$

where we set

$$G_j = \int_0^\infty G(x)\, \mathrm{e}^{-ji\omega x}\, \mathrm{d}x\,. \tag{18}$$

It follows from Eq. (9) that

$$G_j = \left(\int_0^\infty g_1(x)\, \mathrm{e}^{-ji\omega x}\, \mathrm{d}x\right) \cdots \left(\int_0^\infty g_n(x)\, \mathrm{e}^{-ji\omega x}\, \mathrm{d}x\right). \tag{19}$$

If $g_j(x) = a_j\, \mathrm{e}^{-b_j x}$ for all $1 \le j \le n$, then

$$G_j = \frac{a_1 \ldots a_n}{(b_1 + ji\omega)\cdots(b_n + ji\omega)} \tag{20}$$

for all $j \in \mathbb{Z}$. Equation (17) can be rewritten as

$$\sum_{j\in\mathbb{Z}} \left(\sum_{k\in\mathbb{Z}} f_{j-k}\, G_k\, c_k\right) \mathrm{e}^{ji\omega t} = R_0 \sum_{j\in\mathbb{Z}} c_j\, \mathrm{e}^{ji\omega t}.$$

Such an equality is true if and only if

$$\sum_{k\in\mathbb{Z}} f_{j-k}\, G_k\, c_k = R_0\, c_j \tag{21}$$

for all $j \in \mathbb{Z}$. This is an "infinite matrix" eigenvalue problem. Notice that $f_k \to 0$ and $G_k \to 0$ as $k \to \pm\infty$. So if we let N be a large integer and $\mathcal{R}_0$ be the spectral radius of the "truncated" square matrix $(f_{j-k}\, G_k)_{-N\le j,k\le N}$, then $\mathcal{R}_0 \to R_0$ as $N \to +\infty$.

3.3. Fourier series: sinusoidal case

Assume that

$$f(t) = 1 + \varepsilon \cos\bigl(\omega t - \phi\bigr), \tag{22}$$

where $0 \le \varepsilon \le 1$ and $0 \le \phi < 2\pi$. This is what we call a "sinusoidal" function. Looking at the eigenvalue problem, represented by Eq. (8), we see that a shift in time of $f(t)$ does not change R_0. Indeed, if R_0 is the spectral radius associated with $f(t)$ with eigenfunction $v_1(t)$, then R_0 is still the spectral radius associated with

$\hat{f}(t) = f(t-h)$ with the eigenfunction $\hat{v}_1(t) = v_1(t-h)$. For the computation of R_0, we may therefore assume that $\phi = 0$, so that

$$f(t) = 1 + \frac{\varepsilon}{2}\,\mathrm{e}^{i\omega t} + \frac{\varepsilon}{2}\,\mathrm{e}^{-i\omega t}.$$

Obviously, $f_0 = 1$, $f_1 = f_{-1} = \frac{\varepsilon}{2}$, and $f_k = 0$ for $|k| > 1$. The system, represented by Eq. (21), becomes

$$\frac{\varepsilon}{2}\,G_{j-1}\,c_{j-1} + G_j\,c_j + \frac{\varepsilon}{2}\,G_{j+1}\,c_{j+1} = R_0\,c_j \tag{23}$$

for all $j \in \mathbb{Z}$. Since $G(x)$ is real-valued, G_j given by Eq. (18) satisfies $G_{-j} = G_j^*$. From this fact, it follows that Eq. (23) with c_{-j} on the right-hand side is just the complex conjugate of Eq. (23) with c_j on the right-hand side. We can therefore forget about Eq. (23) for $j < 0$. Recalling that $c_{-1} = c_1^*$, and $G_{-1} = G_1^*$, the eigenvalue problem, represented by Eq. (23), with $j \in \mathbb{Z}$ reduces to

$$\begin{cases} \frac{\varepsilon}{2}\,G_1^*\,c_1^* \quad + G_0\,c_0 + \quad \frac{\varepsilon}{2}\,G_1\,c_1 \quad = R_0\,c_0\,, \\ \frac{\varepsilon}{2}\,G_{j-1}\,c_{j-1} + G_j\,c_j + \frac{\varepsilon}{2}\,G_{j+1}\,c_{j+1} = R_0\,c_j\,, \ (j \ge 1). \end{cases} \tag{24}$$

The eigenfunction $v_1(t)$ can be normalized so that $c_0 = 1$. This is possible because $v_1(t)$ is positive so that $c_0 = \frac{1}{\theta}\int_0^\theta v_1(t)\,\mathrm{d}t > 0$. Let us look for a solution of the system represented by Eq. (24), of the form

$$R_0 = \sum_{k\ge 0} \rho_k\,\varepsilon^k, \quad c_j = \sum_{k\ge 0} c_{j,k}\,\varepsilon^k, \tag{25}$$

which we expect to hold at least for ε small. Because $c_0 = 1$, notice that $c_{0,0} = 1$ and that $c_{0,k} = 0$ for all $k \ge 1$. Inserting Eq. (25) in the first equation of Eq. (24) and separating the powers of ε^k, one arrives at $G_0 = \rho_0$ and

$$\frac{G_1^*}{2}\,c_{1,k-1}^* + \frac{G_1}{2}\,c_{1,k-1} = \rho_k \tag{26}$$

for all $k \ge 1$. Similarly, inserting Eq. (25) in the second equation of Eq. (24), one arrives at $G_j\,c_{j,0} = \rho_0\,c_{j,0}$ for all $j \ge 1$ and

$$\frac{G_{j-1}}{2}\,c_{j-1,k-1} + G_j\,c_{j,k} + \frac{G_{j+1}}{2}\,c_{j+1,k-1} = \sum_{l=0}^{k} \rho_l\,c_{j,k-l} \tag{27}$$

for all $j \ge 1$ and $k \ge 1$. For all $j \ge 1$, it follows that $(G_0 - G_j)\,c_{j,0} = 0$, so $c_{j,0} = 0$ because $G(x)$ is nonnegative and nonzero and hence $G_0 - G_j = \int_0^\infty (1 - \mathrm{e}^{-ji\omega x})\,G(x)\,\mathrm{d}x \ne 0$. Knowing that

$$\rho_0 = G_0, \quad c_{j,0} = 0\ (j \ge 1), \quad c_{0,0} = 1, \quad c_{0,k} = 0\ (k \ge 1),$$

it follows from Eqs. (26) and (27) that the coefficients ρ_k and $c_{j,k}$ for all $j \geq 1$ and $k \geq 1$ can be computed recursively:

$$\rho_k = \Re(G_1\, c_{1,k-1})\,, \tag{28}$$

$$c_{j,k} = \frac{1}{G_0 - G_j}\left[\frac{G_{j-1}}{2}\, c_{j-1,k-1} + \frac{G_{j+1}}{2}\, c_{j+1,k-1} - \sum_{l=1}^{k-1} \rho_l\, c_{j,k-l}\right], \tag{29}$$

where $\Re(z)$ stands for the real part of the complex number z. More precisely, if the coefficients ρ_l and $c_{j,l}$ have been computed for all $l \leq k-1$ and all $j \geq 1$, then the formulas provide an expression for ρ_k and $c_{j,k}$ for all $j \geq 1$. The algorithm can start because ρ_0 and the coefficients $c_{j,0}$ are known. Using Eqs. (28) and (29), it is easily seen that $c_{j,k} = 0$ for all $j > k$, that $\rho_k = 0$ for all odd integer k, and that $c_{j,k} = 0$ when $j \geq 1$ is odd while $k \geq 1$ is even.

In practice, fix an integer $\kappa > 1$ and consider the vector $(\rho_k)_{0\leq k\leq \kappa}$ and the rectangular matrix $(c_{j,k})_{0\leq j\leq \kappa+1,\, 0\leq k\leq \kappa}$. Set $\rho_0 = G_0$, $c_{0,0} = 1$, $c_{j,k} = 0$ for all $j > k$ in the matrix, and $c_{0,k} = 0$ for $1 \leq k \leq \kappa$. The algorithm runs as follows:

```
for k=1 to κ,
|   compute ρ_k using Eq. (28)
|   for j=1 to k,
|   |   compute c_{j,k} using Eq. (29)
|   end;
end.
```

This way, one easily gets

$$\rho_1 = 0, \quad c_{1,1} = \frac{G_0}{2(G_0 - G_1)}, \quad \rho_2 = \frac{1}{2}\,\Re\Big(\frac{G_0\, G_1}{G_0 - G_1}\Big), \tag{30}$$

Finally, we get

$$R_0 \simeq G_0 + \frac{\varepsilon^2}{2}\,\Re\left(\frac{G_0\, G_1}{G_0 - G_1}\right) \tag{31}$$

for ε small, i.e., the lowest order correction to the basic reproduction number when small amplitude seasonal variations are taken into account. Let us make now some additional remarks:

- We notice that

$$1 - \varepsilon\cos\big(\omega t - \phi\big) = 1 + \varepsilon\cos\big(\omega(t + \theta/2) - \phi\big).$$

  Hence, changing ε in $-\varepsilon$ corresponds to a time shift in $f(t)$. So, according to the remark made at the beginning of Section 3.3, R_0 should stay unchanged. This explains why the odd terms ρ_{2k+1} $(k \geq 0)$ in the series expansion of R_0 vanish.

- The sinusoidal function, represented by Eq. (22), is not as special as it might seem at first look. Indeed, for any given nonnegative θ-periodic function $f(t)$ with, e.g., a mean equal to 1, the first terms of the Fourier expansion are $1 + f_1 \cos(\omega t) + f_1' \sin(\omega t)$, which can be put in the form $1 + \varepsilon \cos(\omega t - \phi)$ with $\varepsilon = \sqrt{(f_1)^2 + (f_1')^2}$ and $\phi = \arctan(f_1'/f_1)$.
- It seems difficult to determine the convergence radii of the power series, represented by Eq. (25). It follows from general theorems on analytic perturbations of linear operators (Kato, 1984) that these radii are positive because r_0 is a simple isolated eigenvalue of the "next-generation operator." Some nontrivial methods have also been developed to give lower bounds for these radii (Kato, 1984): further work is needed to try to apply them to the present case. In practice, the algorithm of this section can easily provide ρ_k for say $k \le 20$ or $k \le 50$. If inspection of the result suggests that ρ_k tends to 0 as $k \to +\infty$, there is a good chance that the convergence radius of the series giving R_0 is greater than or equal to 1.
- The formal perturbation method used in this section can be considered from the point of view of the general mathematical theory developed in Kato (1984). Consider, for example, the left-hand side of Eq. (8) with $f(t)$ given by Eq. (22) as a linear operator $\mathcal{L}_\varepsilon$ acting on the Hilbert space of square-integrable θ-periodic real valued functions with the usual scalar product $\langle \psi_1, \psi_2 \rangle = \int_0^\theta \psi_1(t)\, \psi_2(t)\, \mathrm{d}t$. Consider the unperturbed eigenvalue problem $\mathcal{L}_0\, \psi = \lambda\, \psi$, i.e.,

$$\int_0^\infty G(x)\, \psi(t - x)\, \mathrm{d}x = \lambda\, \psi(t)\,.$$

Looking for a solution of the form $\psi(t) = \sum_{k\in\mathbb{Z}} a_k\, \mathrm{e}^{ki\omega t}$, we find that $(\lambda - G_k)\, a_k = 0$ for all k. So the eigenvalues are given by $\lambda_k = G_k$ for $k \in \mathbb{Z}$, and the eigenspace associated with λ_k is spanned by $\psi_k(t) = \mathrm{e}^{ki\omega t}$. The ψ_k's form a basis. Consider the "dual basis" $\widehat{\psi}_k(t) = \mathrm{e}^{-ki\omega t}/\theta$ $(n \in \mathbb{Z})$, which is such that $\langle \psi_j, \widehat{\psi}_k \rangle = 1$ for $j = k$ and 0 for $j \ne k$. The operator $\mathcal{L}_\varepsilon$ is of the form $\mathcal{L}_0 + \varepsilon\, \mathcal{L}'$, where

$$(\mathcal{L}'\psi)(t) = \cos(\omega t - \phi) \int_0^\infty G(x)\, \psi(t - x)\, \mathrm{d}x\,.$$

We are interested in the perturbation $R_0 = \rho_0 + \varepsilon\, \rho_1 + \varepsilon^2\, \rho_2 + \cdots$ of the eigenvalue $\lambda_0 = \rho_0 = G_0$, whose associated eigenfunction $\psi_0 = 1$ is positive. Using the formulas given in Kato (1984, p. 81) in the finite-dimensional case (these formulas also hold in the infinite-dimensional case and are well known in quantum mechanics (Cohen-Tannoudji et al., 1986, Chapter XI) but for selfadjoint operators), one gets

$$\rho_1 = \langle \mathcal{L}'\psi_0, \widehat{\psi}_0 \rangle = \frac{G_0}{\theta} \int_0^\theta \cos(\omega t - \phi)\, \mathrm{d}t = 0\,,$$

and

$$\rho_2 = \sum_{k\neq 0} \frac{\langle \mathcal{L}'\psi_0, \widehat{\psi}_k\rangle \langle \mathcal{L}'\psi_k, \widehat{\psi}_0\rangle}{\lambda_0 - \lambda_k}$$
$$= \frac{1}{\theta^2} \sum_{k\neq 0} \frac{G_0\, G_k}{G_0 - G_k} \left| \int_0^\theta \cos(\omega t - \phi) \mathrm{e}^{ki\omega t}\, \mathrm{d}t \right|^2 = \frac{1}{2}\, \Re\left(\frac{G_0\, G_1}{G_0 - G_1}\right),$$

which is the same as Eq. (30). The expressions for higher order corrections are more complicated: the *ad hoc* method we used and the algorithm we propose for computing the ρ_k's seem more practical.

3.4. Application of Floquet theory

In this section, we consider the system of linear ordinary differential equations

$$\frac{\mathrm{d}I_1}{\mathrm{d}t} = -\alpha_1(t)\, I_1(t) + \beta_n(t)\, I_n(t), \tag{32}$$
$$\frac{\mathrm{d}I_{j+1}}{\mathrm{d}t} = -\alpha_{j+1}(t)\, I_{j+1}(t) + \beta_j\, I_j(t), \quad 1 \leq j \leq n-1, \tag{33}$$

where all the functions $\alpha_j(t)$ and $\beta_j(t)$ are θ-periodic. Such a system can arise as the linearization near the diseasefree steady state of a nonlinear epidemic model. The kernel of the associated next-generation operator is given by

$$K_{1,n}(t,x) = \beta_n(t)\, \mathrm{e}^{-\int_{x-t}^{x} \alpha_n(s)\, \mathrm{d}s},$$
$$K_{j+1,j}(x,t) = \beta_j(t)\, \mathrm{e}^{-\int_{x-t}^{x} \alpha_{j+1}(s)\, \mathrm{d}x}, \quad 1 \leq j \leq n-1,$$

and $K_{i,j}(t,x) = 0$ for all other indices. It is therefore a "cyclic" model of the general kind introduced in Section 2. It follows from a remark in that section that if, for example, $\beta_n(t)$ is multiplied by a certain constant, then R_0 is multiplied by the same constant.

The Floquet theory applied to the system, represented by Eqs. (32) and (33) says that the zero-steady state is unstable if and only if the spectral radius of the "next-year matrix" (also called the monodromy matrix) is greater than 1. So the basic reproduction number R_0 is also the unique positive real number such that the spectral radius of the $n \times n$ matrix $X(\theta)$ is equal to 1, where $X(\theta)$ is the solution at

time $t = \theta$ of the system of differential equations

$$\frac{\mathrm{d}X}{\mathrm{d}t}(t) = \begin{pmatrix} -\alpha_1(t) & 0 & \cdots & 0 & \frac{\beta_n(t)}{R_0} \\ \beta_1(t) & \ddots & \ddots & & 0 \\ 0 & \ddots & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & \beta_{n-1}(t) & -\alpha_n(t) \end{pmatrix} X(t)$$

with the initial condition $X(0) = 1_n$ (the $n \times n$ identity matrix). Hence, R_0 can be found by combining a dichotomy method with a numerical solver of ordinary differential equations such as the one included in Scilab.

4. Vector-borne diseases

4.1. Malaria

In this section, we consider a very simple model for malaria, namely a variation on one of the first models proposed by Ronald Ross (1911) but with a periodic vector population. Let us introduce the following notations: $S(t)$ is the susceptible human population; $I(t)$ is the infectious human population; $P = S(t) + I(t)$ is the total human population. Similarly, $s(t)$ is the susceptible vector population, $i(t)$ the infectious vector population, and $p(t) = s(t) + i(t)$ the total vector population. Besides, we consider the following parameters: α is the rate of recovery of humans; β is the biting rate of the vectors; q (resp. q') is the transmission probability per bite from vector to human (resp. from human to vector); $\lambda(t)$ is the number of new adult vectors that emerge per unit time, assumed to be a θ-periodic function; μ is the death rate of vectors. The model is the following:

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \lambda(t) - \beta\, q'\, s(t)\, \frac{I(t)}{P} - \mu\, s(t), \tag{34}$$

$$\frac{\mathrm{d}i}{\mathrm{d}t} = \beta\, q'\, s(t)\, \frac{I(t)}{P} - \mu\, i(t), \tag{35}$$

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta\, q\, i(t)\, \frac{S(t)}{P} + \alpha\, I(t)\,, \tag{36}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta\, q\, i(t)\, \frac{S(t)}{P} - \alpha\, I(t)\,. \tag{37}$$

Adding Eqs. (34) and (35), we see that $\frac{\mathrm{d}p}{\mathrm{d}t} = \lambda(t) - \mu\, p(t)$. We assume that $p(t)$ is given by

$$p(t) = p_0[1 + \varepsilon \cos(\omega t - \phi)].$$

Given μ, this determines $\lambda(t)$. Linearizing the system, represented by Eqs. (34)–(37), near the disease-free steady state, we get

$$\frac{\mathrm{d}i_*}{\mathrm{d}t} = \beta\, q'\, p(t)\, \frac{I_*(t)}{P} - \mu\, i_*(t)\,, \qquad \frac{\mathrm{d}I_*}{\mathrm{d}t} = \beta\, q\, i_*(t) - \alpha\, I_*(t)\,. \tag{38}$$

The kernel of the associated next-generation operator is

$$K(t,x) = \begin{pmatrix} 0 & \frac{\beta\, q'\, p(t)}{P}\, \mathrm{e}^{-\alpha\, x} \\ \beta\, q\, \mathrm{e}^{-\mu\, x} & 0 \end{pmatrix}, \tag{39}$$

which is "cyclic" of the special form, represented by Eq. (7), with the functions $g_j(x)$ $(1 \le j \le 2)$ of the form of Eq. (10) and $f(t) = 1 + \varepsilon \cos(\omega t - \phi)$. Equation (20) yields

$$G_j = \frac{\beta^2\, q\, q'\, p_0}{(\alpha + ji\omega)(\mu + ji\omega)P} \tag{40}$$

for all $j \in \mathbb{Z}$. Finally, Eq. (31) takes the form

$$R_0 \simeq \frac{\beta^2\, q\, q'\, p_0}{\alpha\, \mu\, P}\Big(1 - \frac{\alpha\mu}{\omega^2 + (\alpha+\mu)^2}\, \frac{\varepsilon^2}{2}\Big). \tag{41}$$

This is the lowest order correction to Eq. (1). Notice that the inequality

$$0 \le \frac{\alpha\mu}{\omega^2 + (\alpha+\mu)^2}\, \frac{\varepsilon^2}{2} \le \frac{\varepsilon^2}{8}$$

holds. The upper bound is reached when $\alpha \simeq \mu \gg \omega$. Hence, we arrive at the following conclusion:

> *The first term in the formula for R_0 is the same as for the case of a constant vector population p but with p replaced by the average vector population p_0. The maximum correction due to the second term is $(\varepsilon^2/8)\%$ and always tends to decrease R_0. So, it is slightly more difficult for a vector-borne pathogen to invade a population with such fluctuations.*

We also recall two fundamental properties of R_0 in the context of vector-borne diseases: an epidemic can develop if and only if $R_0 > 1$; an epidemic can be prevented if the vector population $p(t)$ is uniformly divided by R_0 all through the year.

4.2. The chikungunya epidemic in La Réunion

Chikungunya is a viral disease that seems to lead to lasting immunity. Moreover, if we want to take into account the incubation period in humans and in vectors, the

following model seems appropriate:

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \lambda(t) - \beta\, s(t)\, \frac{I(t)}{P} - \mu\, s(t), \tag{42}$$

$$\frac{\mathrm{d}e}{\mathrm{d}t} = \beta\, s(t)\, \frac{I(t)}{P} - (\gamma + \mu)\, e(t), \quad \frac{\mathrm{d}i}{\mathrm{d}t} = \gamma\, e(t) - \mu\, i(t), \tag{43}$$

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta\, i(t)\, \frac{S(t)}{P}\,, \tag{44}$$

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \beta\, i(t)\, \frac{S(t)}{P} - \delta\, E(t)\,, \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \delta\, E(t) - \alpha\, I(t)\,, \tag{45}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \alpha\, I(t)\,, \tag{46}$$

where $e(t)$ (resp. $E(t)$) is the population of infected but noninfectious vectors (resp. humans), $1/\gamma$ (resp. $1/\delta$) is the average incubation period in vectors (resp. humans), and $R(t)$ is the immune human population. Notice that the transmission probabilities from compartments e and E have been set to 0 and those from compartments i and I to 1. The total human population $P = S(t) + E(t) + I(t) + R(t)$ is constant, while the total vector population $p(t) = s(t) + e(t) + i(t)$ still satisfies $\frac{\mathrm{d}p}{\mathrm{d}t} = \lambda(t) - \mu\, p(t)$.

We use this model to try to estimate R_0 for the 2005/2006 chikungunya epidemic in La Réunion. Since the fluctuations of the vector population are unknown, we assume for $p(t)$ the simple form $p(t) = p_0(1 + \varepsilon\, \cos(\omega t - \phi))$, which seems not too unreasonable when we look back at the temperature and rainfall curves in La Réunion (Fig. 1, bottom), both having only one maximum each year around February and a minimum around July. Hence, the periodicity $\theta = \frac{2\pi}{\omega}$ is 1 year and we can take $\phi = \frac{2\pi}{12}$. The function $s(t)$ can be eliminated from the system, represented by Eqs. (42)–(46), since $s(t) = p(t) - e(t) - i(t)$. The other parameter values used for simulation are summarized in Table 1. Notice that, e.g., www.chikungunya.net/faq/faq.htm, see #83 refers to question 83 in the list of frequently asked questions on the web site (www.chikungunya.net/faq/faq.htm), a web site set up by epidemiologists and dedicated to the chikungunya epidemic in La Réunion.

The incubation period in humans is estimated between 3 and 7 days (Duhamel et al., 2006, p. 6), or between 4 and 7 days (www.chikungunya.net/faq/faq.htm;

Table 1 Parameter values used for the simulation

Parameter	Symbol	Value
Incubation period in vectors	$1/\gamma$	7 days
Life expectation of vectors	$1/\mu$	1 month
Incubation period in humans	$1/\delta$	4 days
Infectious period in humans	$1/\alpha$	7 days
Period between two bites	$1/\beta$	4 days
Population of La Réunion	P	785,000
Shift in time	ϕ	$\frac{2\pi}{12}$

see #101). But according to (www.chikungunya.net/faq/faq.htm; see #156), humans can start being infectious 2 to 3 days before symptoms. So, we took 4 days for the incubation period. The infectious period in humans after symptoms is estimated around 5 days (Duhamel et al., 2006, p. 7) or between 5 and 7 days (www.chikungunya.net/faq/faq.htm; see #49,52). Given the previous remark, we took the value 7 days for the entire infectious period. The incubation period in vectors is estimated between 9 and 14 days (www.chikungunya.net/faq/faq.htm; see #83), between 4 and 5 days (www.chikungunya.net/faq/faq.htm; see #253), or between 1 and 2 weeks (www.chikungunya.net/faq/faq.htm; see #395). We chose 7 days. Once infected, the vectors are believed to stay so until they die (www.chikungunya.net/faq/faq.htm; see #83). The life expectation of adult vectors is estimated between 4 and 10 weeks (www.chikungunya.net/faq/faq.htm; see #83) or "several" weeks (www.chikungunya.net/faq/faq.htm; see #404). We chose 1 month. The vector can bite five or six times during its life (www.chikungunya.net/faq/faq.htm; see #404): we chose an average of one bite every 4 days. It is not clear whether the infected vector can transmit the virus to its eggs (www.chikungunya.net/faq/faq.htm; see #83/385/442): the present model does not take this possibility into account. Infection in humans leads to a state of immunity (www.chikungunya.net/faq/faq.htm; see #10/385) that can probably last at least several years since nobody seems to have suffered twice from chikungunya during the epidemic in La Réunion. Asymptomatic cases (between 10 and 15% according to www.chikungunya.net/faq/faq.htm, see #385), which do not seem to be included in the estimation of the number of cases in Fig. 1, are not taken into account in the model.

The first case of chikungunya in La Réunion was detected on February 22, 2005. It seems to have been imported from Comoros where already several thousand people had been infected. Taking the incubation and infectious periods into account, we assume for the simulation that one human in compartment E is introduced in the population of La Réunion at the beginning of the 5th week of 2005. The simulation of the model is performed until the beginning of February 2006, when large-scale vector control started as a response to the high peak; such a control is not included in the model. Small-scale vector control before this date is considered as negligible in the model.

The parameters p_0 and ε for the vector population are essentially unknown and have to be fitted using the epidemic curve (Fig. 1). Let us introduce $p_{\max} = p_0(1+\varepsilon)$ and $p_{\min} = p_0(1-\varepsilon)$. Using a rudimentary method of trial and error, we found that a not too bad fit to the epidemic curve—given the simplicity of the model—was obtained with a maximum number of bites received per human per week equal to $\beta\, p_{\max}/P = 1.2$ and a minimum number of bites per human per week equal to 6% of the maximum, i.e., $p_{\min}/p_{\max} = 6\%$ (Fig. 3). From this we get $p_{\max}$, $p_{\min}$, $p_0 = (p_{\max} + p_{\min})/2$ and $\varepsilon = (p_{\max} - p_{\min})/(p_{\max} + p_{\min})$. Numerically, $\varepsilon \simeq 0.887$. It can be easily checked that $\lambda(t) = \mathrm{d}p/\mathrm{d}t + \mu\, p(t)$ stays positive because $\varepsilon \leq 1/\sqrt{1+(\omega/\mu)^2}$.

Now that all the parameters of the model have been fixed, we turn to the estimation of R_0. Linearizing Eqs. (43) and (45) near the disease-free steady state, we

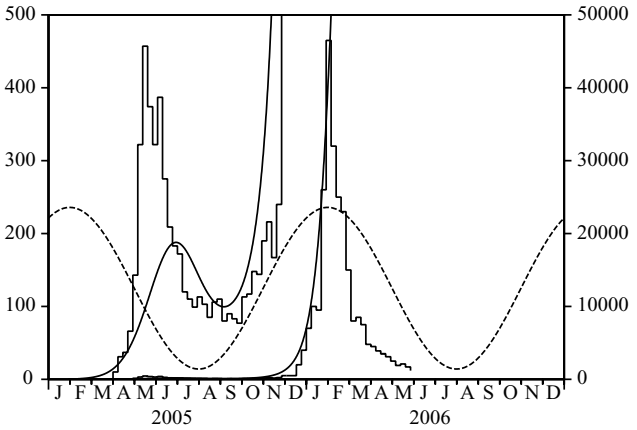

Fig. 3 Estimation of the parameters p_0 and ε by fitting the smooth solid curve produced by the model to the epidemic curve before large-scale vector control (February 2006). The dotted curve shows the assumed variation of the vector population (scale not shown).

get

$$\frac{\mathrm{d}e_*}{\mathrm{d}t} = \beta\, p(t)\, \frac{I_*(t)}{P} - (\gamma+\mu)\, e_*(t), \quad \frac{\mathrm{d}i_*}{\mathrm{d}t} = \gamma\, e_*(t) - \mu\, i_*(t),$$
$$\frac{\mathrm{d}E_*}{\mathrm{d}t} = \beta\, i_*(t) - \delta\, E_*(t)\,, \quad \frac{\mathrm{d}I_*}{\mathrm{d}t} = \delta\, E_*(t) - \alpha\, I_*(t)\,.$$

The kernel of the associated next-generation operator is

$$K(t,x) = \begin{pmatrix} 0 & 0 & 0 & \frac{\beta p(t)}{P}\,\mathrm{e}^{-\alpha x} \\ \gamma\,\mathrm{e}^{-(\gamma+\mu)x} & 0 & 0 & 0 \\ 0 & \beta\,\mathrm{e}^{-\mu x} & 0 & 0 \\ 0 & 0 & \delta\,\mathrm{e}^{-\delta x} & 0 \end{pmatrix}, \tag{47}$$

which is "cyclic" and of the special form, represented by Eq. (7), with $f(t) = 1 + \varepsilon\cos(\omega t - \phi)$ while the functions $g_j(x)$ $(1 \le j \le 4)$ are of the form represented by Eq. (10). Hence $G(x)$ is given by Eq. (11), $\widehat{G}(x)$ by Eq. (14), and G_k by Eq. (20).

With the numerical values of the parameters as above, we obtain $R_0 \simeq 3.4$ using any one of the four methods of Section 3. The program can de downloaded from `www.bondy.ird.fr/~bacaer/chikungunya.sci`. The convergence of the first three methods is shown in Table 2. The first method (Section 3.1) seems to converge more slowly than the other methods. But this is probably because it replaces the function $f(t)$ by a step function $(f(t_k))_{1\le k\le N}$, which is not a good approximation for the special case where $f(t)$ is sinusoidal. The second method (Section 3.2) uses the Fourier coefficients f_k of $f(t)$, which are in the present case simply $f_0 = 1$, $f_1 = f_{-1} = \frac{\varepsilon}{2}$, and $f_k = 0$ for $|k| > 1$. Because of this, the convergence of the method is very fast. These two methods require the computation of

Table 2 Convergence of the first three numerical methods

1st method					
N	12	25	50	100	200
R_0	3.100	3.399	3.392	3.389	3.389
2nd method					
N	0	1	2	3	4
R_0	3.868	3.496	3.418	3.389	3.389
3rd method					
κ	0	2	4	10	12
R_0	3.868	3.461	3.409	3.390	3.389

the spectral radius of a certain matrix. On the contrary, the third method (Section 3.3) requires only elementary operations and could almost be performed with a simple calculator. Recall that κ is the number of terms kept in the expression of R_0 as a series of powers of ε. It should be noticed that the approximation given by Eq. (1) with p replaced by the average vector population p_0 corresponds to $\kappa = 0$ in the table. The difference with the "exact" value of R_0 is 14%. If we include the term of order ε^2 as in Eq. (31), the difference reduces to 2% even though ε is not very small. The convergence of the fourth method (Section 3.4) is determined by the discretization of the differential equation. This is usually controlled by the ODE solver. With Scilab's standard ODE solver, one easily gets the correct value $R_0 \simeq 3.389$ after a certain number of iterations of the dichotomy.

Let us repeat. The numerical value of R_0 obtained for the chikungunya epidemic should not be taken too seriously since the parameter values are imprecisely known and because of the simplicity of assumption, represented by Eq. (2). It can be seen as a numerical exercise to test the different numerical methods, as a source of inspiration for developing the theory, or as a first modeling attempt waiting for field work concerning the fluctuations of the population of *Aedes albopictus*.

5. Concluding remarks

5.1. Other applications

5.1.1. Epidemic models with $n = 1$

Consider an epidemic model with one infected compartment and a kernel of the form

$$K(t, x) = [1 + \varepsilon \cos(\omega t - \phi)]\, g(x). \tag{48}$$

Then $G(x) = g(x)$ as already noticed in Section 2, and R_0 can be approximated by Eq. (31). The kernel, represented by Eq. (48), arises for example in SIS/SIR/SIRS epidemic models with a sinusoidal contact rate.

If the infectious period is exponentially distributed as in Dietz (1976); Grossman et al. (1977); Kuznetsov and Piccardi (1994), then $G(x) = a\,\mathrm{e}^{-bx}$ and it is easily checked that $G_0 = a/b$, that the term of order ε^2 in Eq. (31) vanishes, so that $R_0 \simeq a/b$. Using the same definition of R_0 as in the present paper, it was shown in Bacaër

and Guernaoui (2006, Section 5) that the exact formula $R_0 = a/b$ holds in this case. Of course, this "result" had been noticed for a long time, since the kernel, represented by Eq. (48), arises in connection with the equation

$$\frac{\mathrm{d}I}{\mathrm{d}t} = a(1 + \varepsilon\,\cos(\omega t - \phi))\,I(t) - b\,I(t),$$

which can be solved explicitly, and which is easily seen to have an unstable zero steady state if and only if $a/b > 1$. By analogy with the trivial case $\varepsilon = 0$, several people were thus led to set $R_0 = a/b$ as a definition, to notice that this R_0 is the time average of the function $\mathcal{R}_0(t) = a(1 + \varepsilon\,\cos(\omega t - \phi))/b$, and to believe that such an averaging property holds for more complicated models (this is not the case).

If the infectious period is a fixed constant τ as in Cooke and Kaplan (1976); Smith (1977); Nussbaum (1977, 1978); Grossman (1980), then $G(x) = a$ for $x < \tau$ and $G(x) = 0$ for $x > \tau$. Then $G_0 = a\,\tau$, $G_1 = a\,\frac{1-\mathrm{e}^{-i\omega\tau}}{i\omega}$, and (31) yields

$$R_0 \simeq a\,\tau + \varepsilon^2\,\frac{2\,a\,\tau\,\sin^2(\omega\tau/2)}{[\omega\tau - \sin(\omega\tau)]^2 + [1 - \cos(\omega\tau)]^2}\left[\frac{\omega\tau/2}{\tan(\omega\tau/2)} - 1\right]. \tag{49}$$

This formula shows that, contrary to the case of the model for malaria considered in Section 4.1, seasonality can either increase or decrease R_0, depending on the numerical value of $\omega\tau$. Notice that for the rather exceptional case $\omega = 2\pi$ and $a = 1$ considered in Cooke and Kaplan (1976); Smith (1977); Nussbaum (1977, 1978), Eq. (49) tells that $R_0 = 1 + o(\varepsilon^2)$ when $\tau = 1$. We expect the exact formula $R_0 = 1$ to hold for all ε when $\tau = 1$, since periodic solutions of the full nonlinear epidemic model were shown to exist if and only if $\tau > 1$ (Nussbaum, 1977; Smith, 1977).

5.1.2. Epidemic models with $n = 2$

Consider an epidemic model with two infected compartments which, once linearized near the disease-free steady state, takes the form

$$\frac{\mathrm{d}I_1}{\mathrm{d}t} \simeq -b_1\,I_1(t) + a_2\,[1 + \varepsilon\,\cos(\omega t - \phi)]\,I_2(t), \qquad \frac{\mathrm{d}I_2}{\mathrm{d}t} \simeq a_1\,I_1(t) - b_2\,I_2(t).$$

Notice that the system, represented by Eq. (38), was of this form. The kernel of the associated next-generation operator is

$$K(t,x) = \begin{pmatrix} 0 & [1 + \varepsilon\,\cos(\omega t - \phi)]\,a_2\,\mathrm{e}^{-b_2 x} \\ a_1\,\mathrm{e}^{-b_1 x} & 0 \end{pmatrix}. \tag{50}$$

Equation (31) yields

$$R_0 \simeq \frac{a_1\,a_2}{b_1\,b_2}\left(1 - \frac{b_1\,b_2}{\omega^2 + (b_1 + b_2)^2}\,\frac{\varepsilon^2}{2}\right). \tag{51}$$

One such example is the model for malaria considered in Anderson and May (1991, p. 404). The numerical values used in this reference are: $\omega = 2\pi$, $\varepsilon = 15/25$, $a_1 = 20$ per year, $a_2 = 20 \times 25$ per year, $b_1 = 50$ per year and $b_2 = 4$ per year. All four numerical methods of Section 3, as well as the simple approximate formula, represented by Eq. (51), yield $R_0 \simeq 49.4$. Notice that the lowest order term is $\rho_0 = 50$.

Another example is the SEIR/SEIRS epidemic model with a sinusoidal contact rate considered for example in Schwartz and Smith (1983); Aron and Schwartz (1984); Kuznetsov and Piccardi (1994), Altizer et al. (2006, Box 1), and Ma and Ma (2006, Section 4). The numerical values used in Ma and Ma (2006, Section 4) are: $\omega = 1$, $\varepsilon = 0.8$, $a_1 = 0.3$ $a_2 = 1$, $b_1 = 0.3$, and $b_2 = 0.99$ (units not specified). A numerical simulation showed that no epidemic can develop in this case. But for $\varepsilon = 0$, it was noticed that $R_0 = \rho_0 = (a_1\, a_2)/(b_1\, b_2) = 1/0.99 > 1$. The conclusion was that averaging the contact rate is not a correct way of determining the epidemic threshold. Indeed, any one of the four numerical methods of Section 3 of the present paper yields $R_0 \simeq 0.973 < 1$ for $\varepsilon = 0.8$. The simple approximate formula, represented by Eq. (51), yields $R_0 \simeq 0.974$.

Still another example is the model for cholera with a sinusoidal contact rate with the water or a sinusoidal contamination rate of the water considered in Codeço (2001). This reference also considers the case where the coefficient b_2 representing the decay rate of *Vibrio cholerae* in water might also be a sinusoidal function of time. The present paper does not provide an approximate formula for the basic reproduction number in this last case, but R_0 can still be computed numerically using, for example, the method of Section 3.4.

We also mention the "conjecture" of Moneim and Greenhalgh (2005), suggesting that a basic reproduction number R_0 (with threshold at 1) in an SEIRS model with periodic vaccination and periodic contact rate can be computed by a simple formula after having taken the average of the coefficients of the linearized system over one period. No numerical example is given in this reference. But if we assume that the contact rate is constant and that the vaccination rate is such that the susceptible population in the diseasefree situation is sinusoidal, then $K(t, x)$ is exactly of the form of Eq. (50) and R_0 is given by Eq. (51). If averaging were correct, the result should not depend on ε. So the "conjecture" seems to be wrong.

5.2. The stochastic case

For the chikungunya epidemic in La Réunion, it would be useful to have some estimate of the probability for the epidemic to go extinct because of the winter season knowing the size of the infected human population at the beginning of the winter. To answer such a question, a stochastic model is obviously needed. But stochastic models for vector-borne diseases with seasonality are difficult to handle. In this section, we try to emphasize the link between the extinction probability at time t and the basic reproduction number R_0 using a very simple epidemic model with seasonality.

Consider the simple "birth and death process" with θ-periodic coefficients $a(t)$ and $b(t)$:

$$\frac{\mathrm{d}W_k}{\mathrm{d}t} = a(t)\,(k-1)\,W_{k-1}(t) - [a(t)+b(t)]\,k\,W_k(t) + b(t)\,(k+1)\,W_{k+1}(t), \quad k \geq 1$$

and $dW_0/\mathrm{d}t = b(t)\,W_1(t)$. Here, $W_k(t)$ is the probability of having k infected people at time t. If Z infected people ($Z \geq 1$) are introduced or present at time $t = T$, then $W_Z(T) = 1$ and $W_k(T) = 0$ for $k \neq Z$. The probability $W_0(t)$ of extinction at time $t \geq T$ can be computed by solving the first-order partial differential equation satisfied by the generating function $g(t,x) = \sum_{k\geq 0} W_k(t)x^k$. The result, given in Bartlett (1960), holds even if $a(t)$ and $b(t)$ are not periodic:

$$W_0(t) = \left[1 - \frac{\mathrm{e}^{-\int_T^t (b(\tau)-a(\tau))\,\mathrm{d}\tau}}{1 + \int_T^t a(\tau)\,\mathrm{e}^{-\int_\tau^t (b(\sigma)-a(\sigma))\,\mathrm{d}\sigma}\,\mathrm{d}\tau}\right]^Z.$$

Notice that the expected number $I(t)$ of infected people at time t is given by

$$I(t) = \sum_{k\geq 1} k\,W_k(t), \quad \frac{\mathrm{d}I}{\mathrm{d}t} = a(t)\,I(t) - b(t)\,I(t).$$

As can be guessed from this differential equation, and as shown in Bacaër and Guernaoui (2006, Section 5) for periodic functions $a(t)$ and $b(t)$, the basic reproduction number R_0, if defined as in Section 2, is then given by

$$R_0 = \left(\int_0^\theta a(\tau)\,\mathrm{d}\tau\right) / \left(\int_0^\theta b(\tau)\,\mathrm{d}\tau\right).$$

Now notice that if $R_0 < 1$, then $W_0(t) \to 1$ as $t \to +\infty$: the epidemic will go extinct. If $R_0 > 1$, then

$$W_0(t) \underset{t\to+\infty}{\longrightarrow} \left[1 - 1/\int_T^\infty a(\tau)\,\mathrm{e}^{\int_T^\tau (b(\sigma)-a(\sigma))\,\mathrm{d}\sigma}\,\mathrm{d}\tau\right]$$

and there is a certain probability that the epidemic will persist.

Hence, the basic reproduction number R_0 is also a threshold between the situation where the epidemic will go extinct with probability 1 whatever the initial time of introduction of the first infected cases, and the situation where the epidemic will go extinct with a probability between 0 and 1 depending on the initial time. One may expect a similar threshold result for stochastic models of vector-borne diseases with seasonality, but further work is needed to check this point.

Notice that this section "avoids" the introduction of a time-dependent basic reproduction number "$R_0(t)$," defined, e.g., for the case of vector-borne diseases by Eq. (1) with p replaced by $p(t)$. This expression seems a good candidate to discuss invasion as a function of the time of introduction of the pathogen. But the example in Hale (1980, p. 121), mentioned in Diekmann and Heesterbeek (2000,

p. 149), already suggests that the following case may well happen: $R_0(t) < 1$ for all t, but the diseasefree steady state is unstable (i.e., $R_0 > 1$, with R_0 defined as in the present paper). Besides, R_0 is generally not the average over time of "$R_0(t)$" (with the notable exception of the case $K(t, x) = a(t)\,\mathrm{e}^{-bx}$ already discussed in Section 5.1.1). From a biological point of view, the possibility of invasion of a pathogen in a seasonally varying environment obviously depends on the time of introduction of the pathogen during the year. Because invasion is completely determined by R_0 in deterministic models (unlike in stochastic models), this gives the impression that deterministic models are just not suitable to discuss invasion as a function of the time of introduction of the pathogen.

Appendix

Starting from the definition given by Eq. (9) of $G(x)$ and assuming Eq. (10), we prove Eq. (11) by induction. Obviously, no generality is lost by assuming that $a_j = 1$ for all j. For $n = 2$, a simple computation shows that

$$G(x) = \int_0^x \mathrm{e}^{-\lambda_1 x_1 - \lambda_2 (x - x_1)}\,\mathrm{d}x_1 = \frac{\mathrm{e}^{-\lambda_1 x}}{\lambda_2 - \lambda_1} + \frac{\mathrm{e}^{-\lambda_2 x}}{\lambda_1 - \lambda_2}\,.$$

Now assume that Eq. (11) is true for a certain integer n. Then

$$\begin{aligned}
G(x) &= \int_{\sigma_x^{n+1}} \mathrm{e}^{-\lambda_1 x_1 - \cdots - \lambda_n x_n - \lambda_{n+1} x_{n+1}}\,\mathrm{d}\sigma_x^{n+1} \\
&= \int_0^x \left(\int_{\sigma_{x-x_{n+1}}^n} \mathrm{e}^{-\lambda_1 x_1 - \cdots - \lambda_n x_n}\,\mathrm{d}\sigma_{x-x_{n+1}}^n \right) \mathrm{e}^{-\lambda_{n+1} x_{n+1}}\,\mathrm{d}x_{n+1} \\
&= \int_0^x \left(\sum_{j=1}^n \frac{\mathrm{e}^{-\lambda_j (x - x_{n+1})}}{\prod_{\substack{k \neq j \\ k \leq n}} (\lambda_k - \lambda_j)} \right) \mathrm{e}^{-\lambda_{n+1} x_{n+1}}\,\mathrm{d}x_{n+1} \\
&= \sum_{j=1}^n \frac{\mathrm{e}^{-\lambda_j x}}{\prod_{\substack{k \neq j \\ k \leq n}} (\lambda_k - \lambda_j)} \int_0^x \mathrm{e}^{(\lambda_j - \lambda_{n+1}) x_{n+1}}\,\mathrm{d}x_{n+1} \\
&= \sum_{j=1}^n \frac{\mathrm{e}^{-\lambda_j x}}{\prod_{\substack{k \neq j \\ k \leq n+1}} (\lambda_k - \lambda_j)} + \mathrm{e}^{-\lambda_{n+1} x} \sum_{j=1}^n \frac{1}{(\lambda_j - \lambda_{n+1}) \prod_{\substack{k \neq j \\ k \leq n}} (\lambda_k - \lambda_j)}\,.
\end{aligned}$$

Notice that the second sum in the last line is the partial fraction expansion of the rational function of λ_{n+1}

$$\frac{1}{\prod_{1 \leq j \leq n} (\lambda_j - \lambda_{n+1})}\,.$$

So

$$G(x) = \sum_{j=1}^{n+1} \frac{\mathrm{e}^{-\lambda_j x}}{\prod_{\substack{k\neq j \\ k\leq n+1}} (\lambda_k - \lambda_j)},$$

and Eq. (11) is true for $n+1$. QED.

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