



# Computing the basic reproductive numbers for epidemiological models in nonhomogeneous environments



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## ABSTRACT

In this paper, we present a numerical method to calculate the basic reproductive number, commonly denoted as  $R_0$ , for a class of compartmental epidemiological models in nonhomogeneous environments. We focus our attention on time-periodic models that incorporate seasonal variation and heterogeneity into disease dynamics. Our numerical algorithm is based on a procedure that efficiently transforms the operator eigenvalue problem into a matrix eigenvalue problem. In addition to time-periodic ODE models, the proposed computational approach can also be applied to spatially heterogeneous epidemic models represented by reaction–diffusion PDE systems. We present several examples to demonstrate the validity and application of this algorithm, and we compare the method with existing approaches for the calculation of  $R_0$ .

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## 1. Introduction

Mathematical models for infectious diseases play an important role in understanding basic disease mechanisms, and have long provided useful guidelines for preventing and controlling disease outbreaks. A fundamental concept in epidemiology is the basic reproductive number, commonly denoted as  $R_0$ , which measures the average number of secondary infections that occur when one infective is introduced into a completely susceptible host population. Many mathematical epidemiological models exhibit threshold dynamics characterized by the basic reproductive number: a disease will die out if  $R_0$  is lower than unity, while an epidemic will occur if  $R_0$  exceeds unity. This theoretical principle has been extensively applied to measure the effectiveness of vaccination strategy and antibiotic treatment, to estimate the likelihood of eradicating a disease, and to guide public health administrations to properly scale their efforts [14].

In this study, we are concerned with compartmental epidemiological models formulated by systems of differential equations. These systems typically have several parameters that appear as coefficients in front of model variables, representing various rates related to disease transmission, such as the contact rate, recovery rate, pathogen growth rate, and disease caused death rate. Most existing epidemiological models assume that these parameters are constants and that all population sets are uniformly mixed; i.e., under a homogeneous setting. Such an assumption of homogeneity results in simplified, autonomous ordinary differential equation (ODE) systems that allow detailed mathematical analysis on stabilities and bifurcations. In particular, the basic reproduction number  $R_0$  has been established as a sharp threshold for disease dynamics in a large class of these models (see review [14] and references therein). Meanwhile, calculation of  $R_0$  using the theory of next generation matrices, developed by van den Driessche and Watmough [23] and Diekmann et al. [10], has been widely

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accepted and regarded as standard framework in mathematical epidemiology. No doubt these studies are valuable and inspiring. However, disease transmission mechanisms are usually more complex than described by autonomous model systems. Particularly, seasonal variations and climatic events cause periodic fluctuation of the contact and exposure rates, pathogen growth/death rates, etc., which in turn have strong impacts on disease dynamics. To better reflect such periodic epidemic oscillations, related model parameters could be periodic functions of time instead of simply being constants. Such epidemic models with time-periodic parameters can deepen our understanding of the complex disease mechanism and potentially provide more useful guidelines for public health administration.

Currently, mathematical analysis of periodic epidemic models, especially the study of threshold dynamics, remains a challenge [1], and there have been relatively few studies devoted to this direction. Moneim and Greenhalgh [17] derived an upper bound and a lower bound for  $R_0$  in a periodic epidemic model with vaccination. Wesley and Allen [26] showed that for some epidemic models with periodic coefficients and constant population size, the time-averaged basic reproduction number is a threshold for disease extinction. The authors of [16] analyzed the threshold dynamics for some periodic SEIR (Susceptible–Exposed–Infectious–Recovered) models using the long-term averaged system. Other related work includes [2,6,9,27]. We note that many of these studies are concerned with relatively simple systems where useful information of the solutions can be obtained through direct integration, and it could be difficult to extend the analysis to general model systems of non-autonomous equations. Recently, Wang and Zhao [24] investigated threshold dynamics for a wider range of epidemic models in periodic environments and developed a general framework for determining  $R_0$ . Their approach is based on a rigorous functional analysis on a Banach space and  $R_0$  is defined as the spectral radius of the next infection operator (see Appendix A for a summary). Through several examples, the authors in [24] demonstrated that this  $R_0$  gives a sharper threshold than the basic reproduction number of the time-averaged autonomous system, as the latter might underestimate or overestimate the infection risks. With a focus on mathematical analysis, however, the work of [24] did not provide an explicit way to compute  $R_0$ . In addition, Bacaër and coworkers [3–5] proposed another definition of  $R_0$  for a class of periodic epidemic models and presented several methods to calculate it. It was also observed in their studies that the time-averaged reproduction number inaccurately predict disease risks.

In the present paper, we describe a new and efficient numerical algorithm to calculate the value of  $R_0$  for a class of epidemiological models in nonhomogeneous environments. We focus our attention on time-periodic models and make use of the fundamental formula established in [24]. Our numerical method is based on a procedure that transforms the operator eigenvalue problem into a matrix eigenvalue problem; the method is natural and easy for implementation. This approach will enable practical evaluation of the basic reproduction numbers and, consequently, threshold determination, for various periodic epidemiological models. We use several examples to demonstrate the application of the proposed method. We also make comparison with existing numerical approaches to validate our method.

In addition to the time-periodic ODE models, we will also use an example to illustrate the application of our approach to epidemic models in a spatially heterogeneous setting (another type of nonhomogeneous environments). We present a new PDE model for cholera dynamics which is based on a reaction–diffusion system, taking into account the spatial movement of human hosts and pathogens. We then compute the basic reproduction number of this PDE model using a similar procedure of reducing an operator eigenvalue problem to a matrix eigenvalue problem. To our knowledge, rigorous definition and analysis of the basic reproduction number for a reaction–diffusion PDE epidemic model only appear in a very recent study [25] published in 2012, and our numerical approach will be first of its kind in providing a systematical way to compute  $R_0$  for such nonhomogeneous epidemiological models.

## 2. The method

We now describe the numerical procedure in the context of time-periodic epidemiological models. In the well-known work of van den Driessche and Watmough [23], a general approach based on the next-generation matrix is proposed to compute the basic reproduction number  $R_0$  for autonomous ODE models. Wang and Zhao [24] extended this framework to a large class of epidemic models in periodic environments; a brief review of their work is provided in Appendix A.

Consider a compartmental epidemic model  $\frac{dx_i}{dt} = f_i(t, x)$  with  $f_i(t, x) = f_i(t + \omega, x)$  for some  $\omega > 0$ ,  $1 \leq i \leq J$ . Let  $m$  be the dimension of the subsystem that includes all the infected compartments. Essentially, the authors in [24] introduced the next infection operator

$$(L\phi)(t) = \int_0^\infty Y(t, t-s)F(t-s)\phi(t-s)ds, \quad (1)$$

where  $Y(t, s)$  is the evolution operator of the linear  $\omega$ -periodic system  $dy/dt = -V(t)y$ ,  $F(t)$  and  $V(t)$  are the next-generation matrices associated with the epidemic system, and  $\phi(t) \geq 0$  is a  $\omega$ -periodic function representing the initial distribution of the infectious individuals (see Appendix A for details). It is assumed that  $F(t)$  and  $V(t)$  are continuous and  $\omega$ -periodic functions of  $t$ ,  $F(t)$  is an  $m \times m$  non-negative matrix, and  $-V(t)$  is an  $m \times m$  cooperative matrix. The basic reproduction number is then defined as the spectral radius of  $L$ ; i.e.,

$$R_0 = \rho(L). \quad (2)$$

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