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# Threshold dynamics for compartmental epidemic models with impulses☆

Youping Yang*, Yanni Xiao

*Department of Applied Mathematics, Xi'an Jiaotong University, Xi'an 710049, PR China*

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ABSTRACT

The basic reproductive number and its calculation for general impulsive compartmental epidemic models, with pulses on both the infected and the uninfected compartments, are established. Theoretical results show that the basic reproductive number serves as a threshold parameter: the disease dies out if the basic reproductive number is smaller than unity, and breaks out if it is larger than unity. The global dynamics of a viral dynamical model with impulsive immune response is analyzed to study how the vaccination strength and the vaccination interval affect the basic reproductive number and virus progression.



## 1. Introduction

The basic reproductive number ($R_0$) is defined as the expected number of secondary infections produced by an index case in a completely susceptible population. This concept is now widely used in the study of epidemiology and within-host pathogen dynamics. Usually, the basic reproductive number serves as a threshold parameter that determines whether the disease breaks out or not. If $R_0$ is smaller than unity, then the disease dies out; else, if $R_0$ is bigger than unity, the disease is established in the population. See [1,2] for recent reviews of the use of $R_0$. For autonomous compartmental epidemic models, Van den Driessche and Watmough [3] presented general approaches for the calculations of the basic reproductive number as the spectral radius of the next generation matrix. Wang and Zhao [4] extended the calculation of the basic reproductive number to periodic systems as the spectral radius of the next infection operator.

Recently, pulse vaccination has gained remarkable achievements for its highly successful application in the control of poliomyelitis and measles throughout Central and South America [5,6]. Theoretical results show that pulse vaccination strategies can be distinguished from conventional strategies in leading to disease eradication at relatively low values of vaccination [7,8]. Another application is the vaccines that stimulate the cytotoxic T-lymphocyte (CTL) response, which represents the best hope for the control of Human Immunodeficiency Virus (HIV) [9–12]. The authors of [9] proposed a post-infection programme to regularly boost CTLs, in order to stimulate the immune system's natural defenses. The author concluded that a post-infection CTL vaccine would be highly desirable: the number of infected T cells is driven towards zero if the vaccine is sufficiently strong or is given sufficiently often. At the very least, this vaccine would offer an alternative to the daily pill burden of antiretroviral drug therapy. Note that these vaccinations lead to impulsive differential equations, mathematically.

Periodic replanting of healthy plants or removing (roguing) infected plants in plant-virus disease epidemics are widely used to minimize losses and maximize returns [13]. These strategies also lead to impulsive differential equations. Yang and Xiao [14] gave the definition of the basic reproductive number for compartmental epidemic models with the uninfected

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* Corresponding author. Tel.: +86 0 29 82663938; fax: +86 0 29 82668559.
*E-mail addresses:* yangyouping841022@163.com (Y. Yang), yxiao@mail.xjtu.edu.cn (Y. Xiao).

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compartments pulsed at fixed time moments. An interesting question then arises, namely, how to define and calculate the basic reproductive number for general impulsive epidemic models. Our purpose then is to establish the basic reproductive number for such models, and meanwhile, to show that it is a threshold parameter that determines the local stability of the disease-free periodic solution and even the global stability (we illustrate this point by analyzing a viral dynamical model with impulsive immune response, explicitly).

In the section that follows, we give the definition and the calculation of the basic reproductive number for general impulsive systems; meanwhile, we present an example to show the application. In Section 3, we study a viral dynamical model with impulsive immune response, define its basic reproductive number, and further illustrate that the basic reproductive number serves as a threshold parameter that determines the global stability of the virus-free periodic solution. Finally, we present our conclusions.

## 2. The definition of the basic reproductive number for general impulsive systems

We first present the definition for systems with impulses at fixed times [15]. Suppose that there are two sets $M(t), N(t) \subset \Omega$, for each $t \in R^+$; $\Omega \in R^n$ is an open set. Define the operator $A(t) : M(t) \to N(t)$ for each $t \in R^+$. Now, let the set $M(t)$ represent a sequence of planes $t = t_k$, where $t_k$ is a sequence of times such that $t_k \to \infty$ as $k \to \infty$. Define the operator $A(t)$ for $t = t_k$ only, so that the sequence of operators $A(k)$ is given by

$$A(k) : \Omega \to \Omega, \qquad x \to A(t)x = x + I_k(x),$$

where $I_k : \Omega \to \Omega$. $N(t)$ is also defined for $t = t_k$; therefore, we have $N(k) = A(k)M(k)$. With the choices of $M(k)$, $N(k)$ and $A(k)$, a mathematical model of impulsive differential systems in which impulses occur at fixed times may be described by the following equations:

$$\begin{cases} \dfrac{dx(t)}{dt} = f(t, x), & t \neq t_k, \\ \Delta x = I_k(x), & t = t_k, \end{cases} \tag{1}$$

where $f : R^+ \times \Omega \to R^n$, for $t = t_k$, $\Delta x(t_k) = x(t_k^+) - x(t_k)$, and $x(t_k^+) = \lim_{h \to 0^+} x(t_k + h)$, $k \in N, N = 1, 2, \ldots$.

Refer to [16] for the existence and the uniqueness of solutions for system (1).

Since we are concerned with compartmental epidemic models, we use

$$f(t, x) = \mathcal{F}(t, x) - \mathcal{V}(t, x),$$

where $\mathcal{F}(t, x)$ denotes the newly infected rate, $\mathcal{V}^+(t, x)$ the input rate of individuals by other means, and $\mathcal{V}^-(t, x)$ the rate of transfer of individuals out of compartments; then, $\mathcal{V} = \mathcal{V}^- - \mathcal{V}^+$ denotes the net transfer rate out of compartments. We suppose that $x(t_k)$ immediately after pulses equals

$$x(t_k^+) = x(t_k) + \Delta x(t_k) = \psi(x(t_k)),$$

where $\psi : \Omega \to \Omega$, $\Omega \in R^n$, $\psi \in C^1(\Omega, \Omega)$.

We write

$$x = (x_1, x_2, \ldots, x_n)^T,$$
$$\mathcal{F}(t, x) = (\mathcal{F}_1(t, x), \mathcal{F}_2(t, x), \ldots, \mathcal{F}_n(t, x))^T,$$
$$\mathcal{V}(t, x) = (\mathcal{V}_1(t, x), \mathcal{V}_2(t, x), \ldots, \mathcal{V}_n(t, x))^T,$$

where $A^T$ denotes the transpose of $A$. We consider that $x_1, x_2, \ldots, x_n$ are $n$ homogeneous compartments in a heterogeneous population [3], with each $x_i \geq 0$ being the number of individuals in each compartment. We assume that the compartments can be sorted by two types, with the first $m$ compartments $\{x_1, x_2, \ldots, x_m\}$ the infected individuals, and $\{x_{m+1}, \ldots, x_n\}$ the uninfected individuals. Denote

$$X = (x_1, \ldots, x_m), \qquad Y = (x_{m+1}, \ldots, x_n),$$
$$\psi = (h, g)^T, \quad h = (\psi_1, \ldots, \psi_m), \quad g = (\psi_{m+1}, \ldots, \psi_n),$$
$$h \in C^1(\Omega, R^m), \quad g \in C^1(\Omega, R^{n-m}).$$

Further, we assume that the pulses are applied with time interval $T$ ($t_{k+1} - t_k = T$). Then system (1) now can be written as

$$\begin{cases} \dfrac{dx_i(t)}{dt} = \mathcal{F}_i(t, x) - \mathcal{V}_i(t, x), & i = 1, 2, \ldots, n,\ t \neq nT,\ n \in N, \\ \left.\begin{aligned} X(nT^+) &= h(x(nT)), \\ Y(nT^+) &= g(x(nT)), \end{aligned}\right\} & t = nT,\ n \in N. \end{cases} \tag{2}$$

Define $X_s$ to be the set

$$X_s = \{x \geq 0 | x_i = 0,\ i = 1, \ldots, m\}.$$

We make the following assumptions, which share the same meanings as those by Van den Driessche and Watmough [3] and Wang and Zhao [4].