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Infectious Disease Modeling

A Hybrid System Approach



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Preface

Human life expectancy has increased over the past three centuries, from approximately 30 years in 1700 to approximately 70 years in 1970 [4]; one of the main factors of this improvement is a result of the decline in deaths caused by infectious diseases. In contrast to this decline in mortality, both the magnitude and frequency of epidemics increased during the eighteenth and nineteenth centuries, principally as a result of an increase of large population centers in industrialized societies [4]. This trend then reversed in the twentieth century, mainly due to the development and widespread use of vaccines to immunize susceptible populations [4]. The human invasion of new ecosystems, global warming, increased international travel, and changes in economic patterns will continue to provide opportunities for the spread of new and existing infectious diseases [65].

New infectious diseases have emerged in the twentieth century and some existing diseases have reemerged [65]: Measles, a serious disease of childhood, still causes approximately one million deaths each year worldwide. Type A influenza led to the 1918 pandemic (a worldwide epidemic) that killed over 20 million people. Examples of newly emerging infectious diseases include Lyme disease (1975), Legionnaire's disease (1976), hepatitis C (1989), hepatitis E (1990), and hantavirus (1993). The appearance of the human immunodeficiency virus (HIV) in 1981, which leads to acquired immunodeficiency syndrome (AIDS), has become a significant sexually transmitted disease throughout the world. New antibiotic-resistant strains of tuberculosis, pneumonia, and gonorrhea have emerged. Malaria, dengue, and yellow fever have reemerged and, as a result of climate changes, are spreading into new regions. Plague, cholera, and hemorrhagic fevers (e.g., Ebola) continue to erupt occasionally.

In 1796, an English country doctor, Edward Jenner, observed that milkmaids who had been infected with cowpox did not get smallpox, and so he began inoculating people with cowpox to protect them from getting smallpox (this was the world's first vaccine, taken from the Latin word *vacca* for cow) [65]. Mathematical models have become important tools in analyzing both the spread and control of infectious diseases. The first known mathematical epidemiology model was formulated and solved by Daniel Bernoulli in 1760 [92]. The pioneering work on infectious

disease modeling by Kermack and McKendrick has had a major influence in the development of mathematical models of infectious diseases [116]. These authors were the first to obtain a threshold result that showed the density of susceptibles must exceed a critical value for an outbreak to occur [65]. In the early twentieth century, the foundations of modern mathematical epidemiology based on compartment models were laid, and mathematical epidemiology has grown exponentially since the middle of the previous century [92]. An extensive number of models have been formulated, analyzed, and applied to a variety of infectious diseases, including measles, rubella, chickenpox, whooping cough, smallpox, malaria, rabies, gonorrhea, herpes, syphilis, and HIV/AIDS [64].

Studying these somewhat simple mathematical epidemiology models is crucial in order to gain important knowledge of the underlying aspects of the spread of infectious diseases [64]; one such purpose of analyzing epidemiology models is to get a clear understanding of the similarities and differences in the behavior of solutions of the models, as this allows us to make decisions in choosing models for certain applications. Mathematical models and computer simulations are extremely useful tools for building and testing theories, assessing quantitative conjectures, answering qualitative questions, and estimating key parameters from data; epidemic modeling can help to identify trends, suggest crucial data that should be collected, make general forecasts, and estimate the uncertainty in forecasts [65].

The transmission of a disease, which depends on its intrinsic infectiousity as well as population behavior, is a crucial part in the medical and statistical study of an epidemic [38]. In mathematical modeling, these two aspects are summarized in the contact rate and the incidence rate of a disease, which are the average number of contacts between individuals that would be sufficient for transmitting the disease and the number of new cases of a disease per unit time, respectively [65]. Empirical studies have shown that there are seasonal variations in the transmission of many infections [69]. Examples include differences in the abundance of vectors due to weather changes (e.g., dry season vs rainy season), changes in the survivability of pathogens (outside hosts), differences in host immunity, and variations in host behavior (e.g., increased contacts between individuals in the winter season from being indoors) [39, 53]. For childhood infections such as measles, chickenpox, and rubella, it has been observed that the rates of transmission peak at the start of the school year and decline significantly during the summer months [69]. An analysis of measles data in New York demonstrates that sufficiently large seasonal variations in transmission can generate a biennial-looking cycle [134]. Data from England and Wales displays a four-year cycle in poliomyelitis incidence, while measles has been observed to have a biennial cycle for the same countries [134]. Reports have found that many diseases show periodicity in their transmission, such as measles, chickenpox, mumps, rubella, poliomyelitis, diphtheria, pertussis, and influenza [66]. Depending on the particular disease of interest and population behavior, an appropriate model of the disease's spread may require term-time forcing where the model parameters change abruptly in time.

The recent increase in seaborne trade and air travel has removed many geographic barriers to insect disease vectors [26]. For example, the vector responsible in part

for transmitting diseases such as chikungunya and, more recently, Zika virus, *Aedes albopictus*, has developed capabilities to adapt to nontropical regions and is now found in Southeast Asia, the Pacific and Indian Ocean islands, Europe, the USA, and Australia [41, 113, 114]. Consequently, studying mathematical models on the spread of vector-borne diseases has become a large focus in the literature, for example, the dengue virus [165, 166] and the chikungunya virus [7, 40–43, 113, 114]. Seasonal changes are an important factor in how these vector-borne diseases spread in a population and relate to changes in the abundance of vectors and the host population behavior. For example, Bacaër [7] noted that seasonality plays an important role in the spread of the chikungunya virus. The 2005 outbreak of chikungunya virus in Réunion occurred when the mosquito population was at its highest, the end of the hot season and beginning of the winter season [42]. The transmission of dengue fever is higher during wet and humid periods with high temperatures ideal for mosquitoes and lower when the temperature is low [126, 165].

One of the most important aspects of epidemic modeling is the application of control schemes to eradicate, or at least suppress, an impending epidemic. Infectious disease models are a vital component of comparing, implementing, evaluating, and optimizing various detection, prevention, and control programs [65]; epidemic models are useful in approximating vaccination levels needed for the control of a disease [116]. For example, in 1967, there were approximately 15 million cases of smallpox per year which led the World Health Organization (WHO) to develop an initiative against smallpox. The WHO strategy involved extensive vaccination programs, surveillance for outbreaks, and containment of these outbreaks by local vaccination programs [65]. This has been considered the most spectacular success of a vaccination program [101]; smallpox was eventually eradicated worldwide by 1977, and the WHO estimates that the elimination of smallpox worldwide saves over two billion dollars per year [65]. There are now vaccines that are effective in preventing rabies, yellow fever, poliovirus, hepatitis B, parotitis, and encephalitis B, among others [83].

Aside from seasonal changes in population behavior, the conduct of the population can shift due to, for example, psychological effects (widespread panic of an impending outbreak) or from public health campaigns to prevent a disease spread. The aim of this study is to mathematically model infectious diseases, which take these important factors into account, using a switched and hybrid systems framework. The scope of coverage includes background on mathematical epidemiology, including classical formulations and results; a motivation for seasonal effects and changes in population behavior; an investigation into term-time forced epidemic models with switching parameters; and a detailed account of several different control strategies. The main goal is to study these models theoretically and to establish conditions under which eradication or persistence of the disease is guaranteed. In doing so, the long-term behavior of the models is determined through mathematical techniques from switched systems theory. Numerical simulations are also given to augment and illustrate the theoretical results and to help study the efficacy of the control schemes.

The objective of this monograph is to formulate new epidemiology models with time-varying contact rates or time-varying incidence rate structures, and to study the long-time behavior of diseases. More specifically, we look to extend epidemiology models in the literature by the addition of switching, which is the abrupt change of the dynamics governing the systems at certain switching times. This switching framework allows the contact rate to be approximated by a piecewise constant function. Since relatively modest variations in the contact rate can result in large amplitude fluctuations in the transmission of a disease [69], this is an important phenomenon that requires attention. Switching is a new approach to this problem that has not been studied before as an application to epidemiology models. A specific incidence rate must be chosen appropriately based on the scenario and disease being modeled for any given infectious disease model. There are numerous incidence rates which have been used in models in the literature, for example, the standard incidence, psychological-effect incidences, saturation incidences, media coverage incidences, and more general nonlinear forms (see [38, 64, 73, 122]). With regard to different forms of the incidence rate, one of the possible causes of unexpected failures of a vaccination campaign may be the nonlinearity of the incidence rate not being properly modeled [38], which gives extra motivation in studying switching incidence rate structures. The focus of this monograph is to present new methods for formulating and analyzing epidemic models with time-varying model parameters and function forms, which are easily extendable to many different models, as will be shown.

The area of hybrid dynamical systems (HDS) is a new discipline which bridges applied mathematics, control engineering, and theoretical computer science [45]. HDS frameworks provide a natural fit for many problems scientists face as they seek to control complex physical systems using computers [45]. Indeed, there is a growing demand in industry for methods to model, analyze, and understand systems that combine continuous components with logic-based switching [136]. Practical examples of switched systems, a type of HDS, include areas as diverse as mechanical systems, the automotive industry, air traffic control, robotics, intelligent vehicle/highway systems, chaos generators, integrated circuit design, multimedia, manufacturing, high-level flexible manufacturing systems, power electronics, interconnected power systems, switched-capacitor networks, computer disk drives, automotive engine management, chemical processes, and job scheduling [31, 45, 54, 85]. Examples of systems which can be described by switching systems with abrupt changes at the switching instances include biological neural networks, optimal control modes in economics, flying object motions, bursting rhythm models in pathology, and frequency-modulated signal processing systems [54]. Impulsive systems will be important when we look to add pulse control to the switched models. As mentioned, switched systems are described using a mixture of continuous dynamics and logic-based switching, in that they evolve according to mode-dependent continuous dynamics and experience transitions between modes that are triggered by certain events [136]. There are typically two cases in which a switched system arises [31]: One is when there are abrupt changes in the structure or the

parameters of a dynamical system, which can be due to, for example, environmental factors (i.e., outside forces). The second is when a continuous system is controlled using a switched controller.

This monograph is not meant to be a comprehensive analysis of every modeling choice possible for mathematical models of infectious diseases. Rather, its aim is to provide theoretical tools which are applicable to a wide variety of problems in epidemic modeling. The mathematical methods are revealed one at a time as this monograph progresses. Aside from modeling the spread of an infectious disease using a hybrid and switched system, a new approach to mathematical disease modeling, the unique features of this monograph can be summarized as follows: (1) using techniques from switched systems theory to study the stability of epidemic models, (2) focusing on the role seasonality plays in the spread of infectious diseases, and (3) investigating how abrupt changes in model parameters or function forms affect control schemes. Accessible to individuals with a background in dynamical systems theory or mathematical modeling of epidemics, this work is intended as a graduate-level book for individuals with an interest in mathematical biology, epidemic models, and, more generally, physical problems exhibiting a mixture of continuous and discrete dynamics (i.e., hybrid behavior).

The reader gains the fundamentals of compartmental infectious disease modeling, as well as the necessary mathematical background (e.g., stability theory of ordinary and functional differential equations). The reader learns techniques from switched and hybrid systems, which are applicable to a variety of applications in engineering and computer science. Knowledge is gained regarding the roles seasonality and population behavior play in the spread of a disease, including the formulation and theoretical tools for analysis of epidemic models and infectious disease control strategies. In doing so, the reader learns about the concept of threshold conditions in epidemic modeling, such as the basic reproduction number, used to prove eradication or persistence of the disease based on model parameters. Numerical simulations are also given, to help illustrate the results to the reader.

The structure of the monograph is outlined as follows: In Part I, the theoretical framework is established for the remainder of the monograph. Chapter 2 details the necessary foundational material. Switching epidemic models are formalized and studied in Part II: The classic SIR model is investigated in Chap. 3 while extensions are studied in Chap. 4. Control methods to achieve eradication of the disease are presented and thoroughly analyzed in Part III. Switching control schemes are investigated in Chap. 5 while impulsive strategies are studied in Chap. 6. A case study is given in Chap. 7 detailing an outbreak of chikungunya virus and possible control strategies for its containment and eradication. Conclusions and future directions are given in Part IV.

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List of Symbols

\mathbb{R}^n	Euclidean space of n -dimensions
\mathbb{R}_+	Set of nonnegative real numbers
$\mathbb{R}^{m \times n}$	Vector space of $m \times n$ real-valued matrices
\mathbb{N}	Set of positive integers
$\ \cdot\ $	Euclidean norm: $\ x\ = \sqrt{x_1^2 + \dots + x_n^2}$ for $x \in \mathbb{R}^n$
$\text{cl } A$	Closure of a set $A \subset \mathbb{R}^n$
$\text{int } A$	Interior of a set $A \subset \mathbb{R}^n$
∂A	Boundary of a set $A \subset \mathbb{R}^n$
$\text{conv } A$	Convex hull of a set $A \subset \mathbb{R}^n$
$B_r(x)$	Open ball of radius $r > 0$ centered at $x \in \mathbb{R}^n$
$\lambda_{\min}(Q)$	Minimum eigenvalue of a symmetric matrix Q
$\lambda_{\max}(Q)$	Maximum eigenvalue of a symmetric matrix Q
$Df(x)$	Jacobian matrix of f evaluated at x
$C(D, \mathbb{R}^m)$	Continuous functions mapping $D \subset \mathbb{R}^n$ to \mathbb{R}^m
$C^1(D, \mathbb{R}^m)$	Continuously differentiable functions mapping $D \subset \mathbb{R}^n$ to \mathbb{R}^m
$C^k(D, \mathbb{R}^m)$	Continuously differentiable functions of order k
$\delta(\cdot)$	Dirac delta generalized function
\mathcal{K}_0	$\{w \in C(\mathbb{R}_+, \mathbb{R}_+) : w(0) = 0, w(s) > 0 \text{ for } s > 0\}$
\mathcal{K}_1	$\{w \in \mathcal{K}_0 : w \text{ is nondecreasing in } s\}$
\mathcal{K}	$\{w \in C(\mathbb{R}_+, \mathbb{R}_+) : w(0) = 0 \text{ and } w \text{ is strictly increasing}\}$
\mathcal{K}_∞	$\{w \in \mathcal{K} : w(s) \rightarrow \infty \text{ as } s \rightarrow \infty\}$
C_τ	Continuous functions mapping $[-\tau, 0] \subset \mathbb{R}$ to \mathbb{R}^m
$\text{PC}(D, \mathbb{R}^m)$	Piecewise continuous functions mapping D to \mathbb{R}^m
PC_τ	$\text{PC}([- \tau, 0], \mathbb{R}^m)$
$\ \cdot\ _\tau$	Usual sup norm: $\ \psi\ _\tau = \sup_{-\tau \leq s \leq 0} \ \psi(s)\ $ for $\psi \in \text{PC}$
\mathcal{S}	Set of all admissible switching rules
σ	Switching rule associated with a switched system
$\mathcal{S}_{\text{periodic}}$	Subset of \mathcal{S} that are periodic
$\mathcal{S}_{\text{dwell}}$	Subset of \mathcal{S} that admit a dwell-time
\mathcal{S}_{avg}	Subset of \mathcal{S} that admit an average dwell-time

\mathcal{P}	Finite index set of modes of switched system: $\mathcal{P} \equiv \{1, \dots, p\}$
\mathcal{M}	Finite index set of modes of switched system: $\mathcal{M} \equiv \{1, \dots, m\}$
\mathcal{N}	Finite index set of modes of switched system: $\mathcal{N} \equiv \{1, \dots, n\}$
\mathcal{F}	Finite index set of vector fields: $\mathcal{F} \equiv \{f_1, \dots, f_m\}$
$T_i(t^1, t^2)$	Total activation time of the i th mode on $[t^1, t^2]$
$T^+(t^1, t^2)$	Total activation time of the modes $\mathcal{M}^+ \subset \mathcal{M}$ on $[t^1, t^2]$
$T^-(t^1, t^2)$	Total activation time of the modes $\mathcal{M}^- \subset \mathcal{M}$ on $[t^1, t^2]$
$N(t^1, t^2)$	Number of switches activating the i th mode on $[t^1, t^2]$
$N^-(t^1, t^2)$	Number of switches activating modes in \mathcal{M}^- on $[t^1, t^2]$
$R_0^{(*)}$	Basic reproduction number of the infectious disease model $(*)$
$D^{(*)}$	Physical domain associated with epidemic model $(*)$
$Q_{\text{DFS}}^{(*)}$	Disease-free solution associated with epidemic model $(*)$
$Q_{\text{ES}}^{(*)}$	Endemic solution associated with epidemic model $(*)$
C_H^c	Cumulative number of infected humans with control
C_H^0	Cumulative number of infected humans without control
F_0	Control strategy efficacy rating ($F_0 \equiv 100C_H^c/C_H^0$)
Ψ	Total number of vaccinations administered during a campaign
χ	Cost-benefit rating of a control scheme ($\chi \equiv \Psi/(C_H^0 - C_H^c)$)

Part I

Mathematical Background

Chapter 1

Basic Theory

Necessary mathematical concepts are presented in this chapter. Background theory on ordinary differential equations, delay differential equations, impulsive dynamic systems, and stochastic differential equations is detailed. Stability theory is a focus throughout this chapter, although fundamental theory is also given in each of these topics. Section 1.2 draws upon the work by Hale [56] for the background material regarding ODE systems, while the concept of partial stability is from [57]. The reader is also referred to the excellent works [71, 109, 123] for classical ODE theory. Sufficient background regarding delay differential equations (DDEs) is presented in Sect. 1.4, highlighting the material in [58]. The short background in Sect. 1.3 on impulsive dynamic systems details the works [76] and [15].

1.1 Preliminaries

The following notation is used throughout this monograph. The set of positive integers is denoted by \mathbb{N} . \mathbb{R}_+ denotes the set of nonnegative real numbers. \mathbb{R}^n denotes the Euclidean space of n -dimensions (equipped with the Euclidean norm $\|\cdot\|$). The vector space of $n \times m$ matrices with real-valued entries is denoted by $\mathbb{R}^{n \times m}$ (equipped with the corresponding induced norm). A vector $x \in \mathbb{R}^n$ has i th component $x_i \in \mathbb{R}$ and can be written as

$$x \equiv \begin{bmatrix} x_1 \\ \vdots \\ x_n \end{bmatrix} \equiv (x_1, \dots, x_n).$$

A vector-valued function $f : \mathbb{R}^n \rightarrow \mathbb{R}^m$ can be similarly written as

$$f(x) \equiv f(x_1, \dots, x_n) \equiv \begin{bmatrix} f_1(x_1, \dots, x_n) \\ \vdots \\ f_m(x_1, \dots, x_n) \end{bmatrix} \equiv (f_1(x_1, \dots, x_n), \dots, f_m(x_1, \dots, x_n)).$$

Let I denote the $n \times n$ identity matrix and 0 denote the zero vector in \mathbb{R}^n (i.e., the origin); the dimensions of these objects will be clear from the context. Given a symmetric matrix $Q \in \mathbb{R}^{n \times n}$, let $\lambda_{\max}(Q)$ and $\lambda_{\min}(Q)$ denote its maximum and minimum eigenvalue, respectively. Let $B_r(x)$ denote the open ball of radius $r > 0$ centered at $x \in \mathbb{R}^n$. Let $\text{cl } A$, $\text{int } A$, ∂A , $\text{conv} A$ denote the closure, interior, boundary, and convex hull of a set $A \subset \mathbb{R}^n$. A set $A \subset \mathbb{R}^n$ is compact if it is closed and bounded. Given a set $A \subset \mathbb{R}^n$ and a point $x \in \mathbb{R}^n$,

$$\text{dist}(x, A) = \inf\{\|z - x\| : z \in A\}.$$

Let $f : D \subset \mathbb{R}^n \rightarrow \mathbb{R}^m$ be a function mapping an open set D to \mathbb{R}^m . f is called locally Lipschitz continuous in D if for each $x \in D$, there exists a neighborhood $N \subset D$ of x and a Lipschitz constant $L \geq 0$ such that

$$\|f(y) - f(z)\| \leq L\|y - z\|, \quad \forall y, z \in N.$$

f is called differentiable in D if for each $x \in D$, the Jacobian matrix $Df(x) \in \mathbb{R}^m \times n$ of f at x is well-defined, with (i, j) th entry given by

$$\left(\frac{\partial f_i}{\partial x_j}(x_1, \dots, x_n) \right).$$

If $m = 1$ (i.e., f is a scalar-valued function), then $\nabla f(x) \equiv (Df(x))^T \in \mathbb{R}^m$ denotes its gradient vector evaluated at x . f is called continuously differentiable (C^1) in D if for each $x \in D$ there exists a neighborhood $N \subset D$ of x such that Df is a continuous function in N . The space of continuous functions mapping D to \mathbb{R}^m is denoted by $C(D, \mathbb{R}^m)$. The space of C^1 functions mapping D to \mathbb{R}^m is denoted by $C^1(D, \mathbb{R}^m)$. Note that if f is continuously differentiable in D then it is locally Lipschitz in D . Let $\delta(\cdot)$ denote the Dirac delta generalized function. Suppose that $0 \in D$ and $V : D \rightarrow \mathbb{R}$. The function V is called positive definite in D if V is continuous in D , $V(0) = 0$, and $V(x) > 0$ for all $x \in D \setminus \{0\}$. Define the following \mathcal{K} -class functions.

$$\mathcal{K}_0 \equiv \{w \in C(\mathbb{R}_+, \mathbb{R}_+) : w(0) = 0, w(s) > 0 \text{ for } s > 0\},$$

$$\mathcal{K}_1 \equiv \{w \in \mathcal{K}_0 : w \text{ is nondecreasing in } s\},$$

$$\mathcal{K} \equiv \{w \in C(\mathbb{R}_+, \mathbb{R}_+) : w(0) = 0 \text{ and } w \text{ is strictly increasing}\},$$

$$\mathcal{K}_\infty \equiv \{w \in \mathcal{K} : w(s) \rightarrow \infty \text{ as } s \rightarrow \infty\}.$$

1.2 Ordinary Differential Equations

Classical theory is recounted regarding ODEs (i.e., existence and uniqueness) in Sect. 1.2.1. Stability theory is detailed for equilibria in Sect. 1.2.2. The notion of partial stability is given in Sect. 1.2.3. ODE systems with impulsive effects are introduced in Sect. 1.3. Functional differential equations (i.e., delay differential equations) are briefly discussed in Sect. 1.4. The theory of stochastic differential equations is highlighted in Sect. 1.5.

1.2.1 Fundamental Theory

Let $D \subset \mathbb{R}^{n+1}$ be an open and connected set and $f : D \rightarrow \mathbb{R}^n$ be a vector-valued function. Consider the following system of ordinary differential equations (ODEs):

$$\dot{x}(t) = f(t, x(t)), \quad (1.1)$$

(or, more briefly, $\dot{x} = f(t, x)$), where $t \in \mathbb{R}$ is the independent variable; $x \in \mathbb{R}^n$ is the dependent variable; $\dot{x} \equiv \frac{dx}{dt}$ is the derivative of x with respect to t ; $x(t) \equiv (x_1(t), \dots, x_n(t))$ is the state of the ODE system at time t ; and

$$f(t, x) \equiv (f_1(t, x_1, \dots, x_n), \dots, f_m(t, x_1, \dots, x_n)), \quad \forall (t, x) \in D.$$

For a given $(t_0, x_0) \in D$, an initial value problem (IVP) is formulated as follows:

$$\begin{aligned} \dot{x}(t) &= f(t, x(t)), \\ x(t_0) &= x_0. \end{aligned} \quad (1.2)$$

A solution of the IVP is defined next.

Definition 1.1 Let $T \subset \mathbb{R}$ be an interval containing t_0 . A function $\phi : T \rightarrow \mathbb{R}^n$ is called a solution of (1.2) in T if ϕ is C^1 in T , satisfies Eq. (1.1) for all $t \in T$, $\{(t, \phi(t)) : t \in T\} \subset D$, and $\phi(t_0) = x_0$.

The solution mapping ϕ outlined in Definition 1.1 may be written as $\phi \equiv \phi(\cdot; t_0, x_0)$ to denote its dependence on t_0 and x_0 . In this case, the solution is said to pass through (t_0, x_0) . Assuming that f is continuous in D , the IVP (1.2) is equivalent to the following integral equation:

$$x(t) = x_0 + \int_{t_0}^t f(s, x(s))ds,$$

where the integral is considered here in the Riemann sense. A weaker notion of a solution (i.e., absolutely continuous instead of continuously differentiable) exists if

the integral is considered in the Lebesgue sense. In this case, f is permitted to be measurable with respect to t (see [47] for details); this case is not pursued further in this section. Existence and uniqueness of classical solutions follows from continuity and Lipschitz continuity, as follows.

Theorem 1.1 *Assume that $(t_0, x_0) \in D$. If $f \in C(D, \mathbb{R}^n)$, then there exists at least one solution of (1.2) passing through (t_0, x_0) . If, in addition, f is locally Lipschitz continuous with respect to x , then there exists exactly one solution of (1.2) passing through (t_0, x_0) .*

If (1.2) is an autonomous ODE system (i.e., $f(t, x) \equiv f(x)$), the initial time t_0 is not significant and can be set to zero without loss of generality.

Definition 1.2 Let ϕ be a solution of (1.2) in T . If $\tilde{\phi}$ is a solution of (1.2) in $\tilde{T} \supset T$ (i.e., a strict superset) and $\phi(t) = \tilde{\phi}(t)$ for all $t \in T$, then $\tilde{\phi}$ is a continuation of ϕ . A solution $\hat{\phi}$ of (1.2) in \hat{T} is called noncontinuable if no such continuation exists; \hat{T} is called a maximal interval of existence.

In the general case (i.e., (1.2)), the solution need not exist globally. For example, the solution of the IVP

$$\begin{aligned}\dot{x}(t) &= 1 + x^2(t), \\ x(0) &= 0,\end{aligned}$$

is given by $x(t) \equiv \tan(t)$, whose maximal interval of existence is $(-\frac{\pi}{2}, \frac{\pi}{2})$. In this case, $|x(t)| \rightarrow \infty$ as $t \rightarrow \pm\frac{\pi}{2}$. Such a solution is often called to have a finite escape time (or finite blow-up time).

If (1.2) is a linear ODE system (i.e., $f(t, x) \equiv Ax$, for some $A \in \mathbb{R}^{n \times n}$), the unique noncontinuable solution is given by

$$x(t) \equiv \exp(A(t - t_0))x_0, \quad \forall t \in \mathbb{R}. \quad (1.3)$$

That is, $T = \mathbb{R}$ is the maximal interval of existence. A solution of the non-autonomous ODE (1.2) defined on a maximal interval of existence either reaches its boundary (i.e., escapes in finite time) or is defined globally.

Theorem 1.2 *Let $f \in C(D, \mathbb{R}^n)$ and ϕ be a solution of (1.2) in T . Then there is a continuation of ϕ to a maximal interval of existence $\hat{T} \equiv (t_*, t^*)$. Moreover, either $t^* = +\infty$ or $\lim_{t \rightarrow t^*}(t, \phi(t)) \in \partial D$ (i.e., it tends to its boundary). A similar result holds for t_* .*

Therefore, if $D = \mathbb{R}^{n+1}$ then either $t^* = +\infty$ or $\|\phi(t; x_0)\| \rightarrow \infty$ at $t \rightarrow t^*$. As a result, we get the next important corollary (where we focus on the autonomous case for the later results in this monograph); invariance of a compact set coupled with continuous differentiable of the right-hand side function implies global existence of a unique solution.

Definition 1.3 A set $W \subset D$ is called invariant to (1.2) if every solution $\phi(\cdot; t_0, x_0)$ of (1.2) in \tilde{T} with $(t_0, x_0) \in W$ satisfies $\{(t, \phi(t)) : t \in \tilde{T}\} \subset W$. W is called positively invariant to (1.2) if all solutions $\phi(\cdot; t_0, x_0)$ starting in W remain in W for all $t \in \tilde{T} \cap [t_0, \infty)$. (i.e., $(t_0, x_0) \in W$ implies $\{(t, \phi(t)) : t \in \tilde{T} \cap [t_0, \infty)\} \subset W$).

Theorem 1.3 Let $f \in C^1(\mathbb{R}^{n+1}, \mathbb{R}^n)$ and let $\phi(\cdot; t_0)$ be a solution of (1.2). Suppose $W \subset \mathbb{R}^{n+1}$ is a compact set that is positively invariant to the IVP (1.2). If $(t_0, x_0) \in W$, then the maximal right interval of existence is $\hat{T} = \mathbb{R}_+$.

1.2.2 Stability Theory

In general, (1.2) cannot be solved to yield a closed-form solution. To investigate the mathematically models set forth in this monograph, qualitative behavior of solutions of (1.2) are analyzed. Useful descriptions of solution behavior can be given via the following definitions and observations. Unless specified otherwise, the excellent book by Khalil [71] (particularly Sect. 4.5) forms the basis for the material in this section. Consider the ODE initial value problem (1.2) and suppose that $f : \mathbb{R}_+ \times D \rightarrow \mathbb{R}^n$, $D \subset \mathbb{R}^n$ is an open connected set containing the origin, and $t_0 \in \mathbb{R}_+$ for the remainder of this section.

Definition 1.4 A vector $\bar{x} \in D$ is called an equilibrium point (or equilibrium solution) of (1.2) if $f(t, \bar{x}) = 0$ for all $t \in \mathbb{R}_+$.

An equilibrium point \bar{x} of (1.2) is called such since, by inspection, $\phi : \mathbb{R}_+ \rightarrow \mathbb{R}^n : t \mapsto \bar{x}$ is a solution of (1.2). It is assumed, without loss of generality, that $f(t, 0) = 0$ for all $t \in \mathbb{R}_+$; if this is not true, then letting $z \equiv x - \bar{x}$ yields

$$\dot{z}(t) = f(t, z(t) + \bar{x}) \equiv \bar{f}(t, z),$$

where $\bar{f} : (t, z) \mapsto f(t, z + \bar{x})$. Thus, qualitative behavior of the ODE (1.2) can be discerned from $\dot{z}(t) = \bar{f}(t, z)$ with the initial condition $z(t_0) = x_0 - \bar{x}$. This argument extends to studying the stability of non-constant solutions of (1.2): supposing that $\phi : \mathbb{R}_+ \rightarrow D$ is a solution of (1.2) passing through (t_0, x_0) , let $z \equiv x - \phi$ and $\tau = t - t_0$. Then

$$\dot{z}(t) = f(t, x(t)) - \frac{d\phi}{dt}(t) = f(\tau + t_0, z(\tau) + \phi(\tau + t_0)) - \frac{d\phi}{d\tau}(\tau + t_0) \equiv \hat{f}(\tau, z(\tau)).$$

Observe that the origin is an equilibrium point of the transformed ODE system since

$$\frac{d\phi}{dt}(\tau + t_0) = f(\tau + t_0, \phi(\tau + t_0))$$

for all $\tau \in \mathbb{R}_+$. Without loss of generality then, assume that $\bar{x} \equiv 0$ is an equilibrium of (1.2).

Definition 1.5 Let $\phi \equiv \phi(\cdot; t_0, x_0)$ be a solution of (1.2) in \mathbb{R}_+ . Then the trivial solution is said to be

- (i) stable if for all $\epsilon > 0$, $t_0 \in \mathbb{R}_+$, there exists a $\delta = \delta(t_0, \epsilon) > 0$ such that $\|x_0\| < \delta$ implies $\|\phi(t)\| < \epsilon$ for all $t \geq t_0$;
- (ii) uniformly stable if δ in (i) is independent of t_0 , that is, $\delta(t_0, \epsilon) = \delta(\epsilon)$;
- (iii) attractive if there exists a $\beta = \beta(t_0) > 0$ such that $\|x_0\| < \beta$ implies that

$$\lim_{t \rightarrow \infty} \phi(t) = 0;$$

- (iv) uniformly attractive if there exists a $\beta > 0$, $\|x_0\| < \beta$ implies that for all $\eta > 0$, there exists a $T = T(\eta) > 0$ such that for all $t_0 \in \mathbb{R}$, $\|\phi(t)\| < \eta$ if $t \geq t_0 + T(\eta)$;
- (v) asymptotically stable if (i) and (iii) hold;
- (vi) uniformly asymptotically stable if (ii) and (iv) hold;
- (vii) exponentially stable if there exist constants $\beta, \gamma, C > 0$ such that if $\|x_0\| < \beta$ then $\|\phi(t)\| \leq C\|x_0\| \exp(-\gamma(t - t_0))$ for all $t \geq t_0$;
- (viii) (globally attractive) (uniformly attractive) (asymptotically stable) (uniformly asymptotically stable) (exponentially stable) if β in (iii) (iv) (v) (vi) (vii) can be made arbitrary;
- (ix) unstable if (i) fails to hold.

Exponential stability implies uniform asymptotic stability (and therefore asymptotic stability). In the autonomous case, uniform stability is equivalent to stability. The stability properties of a solution can be characterized by using the method of Lyapunov functions.

Definition 1.6 A function $W : D \rightarrow \mathbb{R}$ is said to be positive definite if $W(0) = 0$ and $W(x) > 0$ for all $x \in D \setminus \{0\}$. A function $V \in C^1(\mathbb{R}_+ \times D, \mathbb{R})$ is said to be positive definite if $V(t, 0) = 0$ and there exists a positive definite function $W : D \rightarrow \mathbb{R}$ such that $V(t, x) \geq W(x)$ for all $(t, x) \in \mathbb{R}_+ \times D$. It is further said to be radially unbounded if W is radially unbounded. The function V is said to be decrescent if there exists a positive definite function $Z : D \rightarrow \mathbb{R}$ such that $V(t, x) \leq Z(x)$ for all $(t, x) \in \mathbb{R}_+ \times D$.

An auxiliary function satisfying the properties of Definition 1.6 is a candidate Lyapunov function (so named after A.M. Lyapunov). In the case that (1.2) is a modeling a mechanical system, a candidate Lyapunov function is often given by an expression for the total energy of the system. Evaluating the time-derivative of V along trajectories of the ODE system (1.2) uncovers stability properties and is defined as follows:

$$\dot{V}_{(1.2)}(t, x) \equiv \frac{\partial V}{\partial t}(t, x) + \frac{\partial V}{\partial x}f(t, x). \quad (1.4)$$

This calculation is a Lie derivative of a function V along a vector field f .

Theorem 1.4 Consider (1.2) with $f : \mathbb{R}_+ \times D \subset \mathbb{R}^{n+1} \rightarrow \mathbb{R}^n$. Let $V \in C^1(\mathbb{R}_+ \times D, \mathbb{R})$ and $W_1, W_2 \in C(D, \mathbb{R})$ be positive definite. Assume that the following conditions hold:

- (i) $W_1(x) \leq V(t, x) \leq W_2(x)$ for all $(t, x) \in \mathbb{R}_+ \times D$;
- (ii) $\dot{V}_{(1.2)}(t, x) \leq 0$ for all $(t, x) \in \mathbb{R}_+ \times D$.

Then the trivial solution is uniformly stable. If (ii) is replaced by

- (ii)' $\dot{V}_{(1.2)}(t, x) \leq -W_3(x)$ for all $(t, x) \in \mathbb{R}_+ \times D$,

for some positive definite function $W_3 \in C(D, \mathbb{R})$, then the trivial solution is uniformly asymptotically stable. If in addition W_1 is radially unbounded and $D = \mathbb{R}^n$, then the trivial solution is globally uniformly asymptotically stable.

The trivial solution is uniformly (asymptotically) stable if there is a C^1 positive definite, decrescent function whose derivative along the trajectories is negative semidefinite (definite). The result becomes global if V is in addition radially unbounded. The versatility of Lyapunov's direct method lies in the fact that an analytic solution of (1.2) is not required. The results in Theorem 1.4 can be described intuitively: if $\dot{V}_{(1.2)}(x) = \nabla V(x) \cdot f(x) < 0$ for $x \in D \setminus \{0\}$ (i.e., in the non-autonomous case), then V is decreasing along the solution trajectory in $[t_0, \infty) \times (D \setminus \{0\})$ (i.e., V decreases along all orbits in the state space except at the origin, which is an equilibrium point); orbits therefore cut level sets of V inward toward the origin. This continues and the solution trajectory approaches the origin as $t \rightarrow \infty$.

Theorem 1.5 Consider (1.2) with $f : \mathbb{R}_+ \times D \rightarrow \mathbb{R}^n$. Let $V \in C^1(\mathbb{R}_+ \times D, \mathbb{R})$. Assume that there exist constants $a_1, a_2, a_3, p > 0$ such that the following conditions hold:

- (i) $a_1 \|x\|^p \leq V(t, x) \leq a_2 \|x\|^p$ for all $(t, x) \in \mathbb{R}_+ \times D$;
- (ii) $\dot{V}_{(1.2)}(t, x) \leq -a_3 \|x\|^p$ for all $(t, x) \in \mathbb{R}_+ \times D$.

Then the trivial solution is exponentially stable. If $D = \mathbb{R}^n$ and the assumptions still hold, then the trivial solution is globally exponentially stable.

Analogous autonomous Lyapunov theorems are presented in Sect. 4.1 in [71] while converse Lyapunov theorems are given in Sect. 4.7 in [71]. In the linear case (recall the analytical solution outlined in Eq. (1.3)), the following well-known result holds: if $A \in \mathbb{R}^{n \times n}$ is a Hurwitz matrix,¹ then the trivial solution of (1.2) is globally exponentially stable. If there exists an eigenvalue of A with positive real part, then the trivial solution is unstable. Although this is not immediately applicable to the general nonlinear setting, this result is useful thanks to the Hartman-Grobman theorem; the linearization of a nonlinear autonomous ODE system with C^1 right-hand side function $f : \mathbb{R}^n \rightarrow \mathbb{R}^n$ about an equilibrium point

¹All eigenvalues have negative real part.

provides local information about the qualitative behavior of the nonlinear system near said equilibrium point, as long as no eigenvalues of the linearization have zero real part. Supposing that $f(0) = 0$,

$$f(x) = f(0) + Df(0)x + R(x) = Df(0)x + R(x), \quad \forall x \in \mathbb{R}^n,$$

where R is the remainder function satisfying $\lim_{x \rightarrow 0} R(x)/\|x\| = 0$ by Taylor's Theorem. Let $A \equiv Df(0)$. The linearization of the ODE system

$$\dot{x}(t) = f(x(t)),$$

at the origin is given by

$$\dot{x}(t) = Ax(t),$$

which characterizes the solution behavior of the nonlinear ODE system locally. For example, if $Df(0)$ is a Hurwitz matrix, there exists a neighborhood U of the origin and $M, k > 0$ such that the solution $\phi \equiv \phi(\cdot; x_0)$ of the nonlinear ODE system with $\phi(0) = x_0$ satisfies

$$\|\phi(t)\| \leq M \exp(-kt) \|x_0\|, \quad \forall t \geq 0,$$

whenever $x_0 \in U$.

Unfortunately, there is no procedure to construct a Lyapunov function in the general nonlinear case. In some cases it is possible to construct Lyapunov functions such that the Lie derivative is negative semidefinite for all $(t, x) \in D$, only implying stability, yet the system displays asymptotic stability characteristics. To definitively prove asymptotic stability in these cases, the contributions of Barbashin, Krasovski, and LaSalle may be used in the form of LaSalle's Invariance Principle. First, some definitions are required (consider here the non-autonomous case of (1.2)).

Definition 1.7 A point $z \in D$ is called an ω -limit point of x_0 if there exists a sequence $\{t_j\}$ satisfying $\lim_{j \rightarrow \infty} t_j = \infty$ and $\lim_{j \rightarrow \infty} x(t_j) = z$. The set of all such ω -limit points of x_0 is called the ω -limit set of x_0 , denoted by $\omega(x_0)$.

Theorem 1.6 Consider (1.2) with $f : D \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$, where D is an open and connected set. Let $V \in C^1(D, \mathbb{R})$ and $W \subset D$ be a compact set. Assume that the following conditions hold:

- (i) $\dot{V}_{(1.2)}(x) \leq 0$ for all $x \in W$;
- (ii) W is positively invariant to (1.2).

Then for all $x_0 \in D$, the solution $\phi \equiv \phi(\cdot; x_0)$ of (1.2) satisfies

$$\lim_{t \rightarrow +\infty} \text{dist}(\phi(t), \Omega) = 0$$

where Ω is the largest invariant set in $\{x \in W : \nabla V(x) \cdot f(x) = 0\}$.

The following corollary can be given.

Corollary 1.1 Consider (1.2) with $f : D \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$, where D is an open and connected set containing the origin. Let $V \in C^1(D, \mathbb{R})$ be positively definite. Assume that the following conditions hold:

- (i) $\dot{V}_{(1.2)}(x) \leq 0$ for all $x \in D$;
- (ii) the set $\{x \in D : \nabla V(x) \cdot f(x) = 0\}$ does not contain any whole orbits except the trivial solution.

Then the trivial solution of (1.2) is asymptotically stable. If in addition $D = \mathbb{R}^n$ and V is radially unbounded, then the trivial solution of (1.2) is globally asymptotically stable.

Stability of periodic orbits is briefly detailed by highlighting Floquet theory as presented in Sect. 2.8 in [109]. This theory is concerned with the behavior of periodic time-varying linear ODE systems of the following form:

$$\begin{aligned}\dot{x}(t) &= A(t)x(t), \\ x(t_0) &= x_0.\end{aligned}\tag{1.5}$$

Equation (1.5) is an appropriate model for many physical systems and for the linearization of ODE systems about a periodic orbit. Focusing on the latter case, assume that A is a continuous mapping from \mathbb{R} to $\mathbb{R}^{n \times n}$ and $A(t) = A(t + T)$ for some $T > 0$ (called the period). Let $\Phi \equiv \Phi(\cdot; t_0)$ denote the fundamental matrix solution of (1.5), which is given as the solution of the auxiliary ODE matrix system:

$$\begin{aligned}\dot{\Phi}(t) &= A(t)\Phi(t), \\ \Phi(t_0) &= I.\end{aligned}\tag{1.6}$$

Recall Eq. (1.3), which provides the solution of the linear ODE system $\dot{x}(t) = Ax(t)$ as the matrix exponential; $\Phi(t; t_0) \equiv \exp(A(t - t_0))$ is the fundamental matrix solution. However, this does not generalize to (1.5) as expected. Furthermore, the eigenvalues of A do not describe the stability behavior of (1.5) as in the linear ODE case.

Definition 1.8 Let $\Phi \equiv \Phi(\cdot; t_0)$ be the unique solution of (1.6). Then $M \equiv \Phi(T, 0)$ is called the monodromy matrix of (1.5) and its eigenvalues are called the Floquet multipliers.

Floquet's Theorem is given as follows.

Theorem 1.7 Let M be the monodromy matrix of (1.5) and $\tilde{M} \equiv \frac{1}{T} \ln(M)$. Then the fundamental matrix solution of (1.5) is given by

$$\Phi(t, 0) \equiv P(t) \exp(i\tilde{M}),$$

where P is a matrix with period T .

This result is a useful tool in characterizing stability of a periodic orbit by linearizing (1.2) about a periodic orbit (see [109] for details). Noting that the linearization of an autonomous nonlinear system about a periodic orbit always produces a monodromy with at least one eigenvalue equal to one (see Theorem 4.19 in [109]), the following definition is made.

Definition 1.9 Let φ be a periodic orbit of (1.5). Then φ is said to be

- (i) linearly stable if all of its Floquet multipliers have magnitude less than or equal to one;
- (ii) linearly asymptotically stable if all of its Floquet multipliers apart from the unit multiplier have magnitude less than one.

By employing Poincaré maps (see Sect. 4.12 in [109]), a stability result can be described.

Theorem 1.8 *Let φ be a periodic orbit of a smooth vector field that is linearly asymptotically stable (i.e., the spectrum of its Poincaré map is inside the unit circle), then it is asymptotically stable.*

As remarked earlier, the stability definitions and criteria outlined above are also applicable to the case in which (1.2) admits a time-varying solution (e.g., an isolated² periodic orbit). This is of particular importance in the present monograph as disease-free periodic³ solutions are present in infectious disease models with pulse vaccination schemes. Such a periodic orbit may attract nearby solutions (i.e., pointwise, asymptotically), leading to a physical system which exhibits an oscillatory steady state.

Lastly, comparison theorems are presented which converts the study of the original ODE system into that of a simpler system [77].

Theorem 1.9 *Let $m \in C^1(J, \mathbb{R})$ and $g \in C(\mathbb{R}^2, \mathbb{R})$. Suppose that*

$$\dot{m}(t) \leq g(t, m(t)). \quad (1.7)$$

If for all $(t_0, u_0) \in J \times \mathbb{R}$, the IVP of the comparison system

$$\begin{aligned} \dot{u}(t) &= g(t, u(t)), \\ u(t_0) &= u_0, \end{aligned} \quad (1.8)$$

admits a unique solution u in J , then $m(t) \leq u(t)$ for all $t \in J \cap [t_0, \infty)$ if $m(t_0) \leq u_0$, where $u \equiv u(\cdot; t_0, u_0)$ is a solution of the comparison ODE system (1.8).

²An orbit is called isolated if there exists a neighborhood containing said orbit for which there exists no other periodic orbit. (This is not possible in linear ODE systems.)

³A solution $\phi \equiv \phi(\cdot; x_0)$ of (1.2) is said to be a periodic if there exists $T > 0$ such that $\phi(t + T; x_0) = \phi(t; x_0)$ for all time t . The smallest T for which this equality holds is called the period.

If in Theorem 1.9, $m \in C^1(J, \mathbb{R}^n)$ and $g \in C(\mathbb{R}^{n+1}, \mathbb{R}^n)$, the conclusion of the theorem remains valid under the additional assumption that $g(t, u)$ is quasi-monotone increasing in u (i.e., for each $i \in \{1, \dots, n\}$, $g_i(t, u) \leq g_i(t, v)$ whenever $u \leq v$ and $u_i = v_i$).

Theorem 1.10 *Let $m \in C^1(J, \mathbb{R}^n)$ and $g \in C(\mathbb{R}^{n+1}, \mathbb{R}^n)$ such that (1.7) holds (componentwise). If $g(t, u)$ is quasi-monotone increasing in u and for all $(t_0, u_0) \in J \times \mathbb{R}^n$, the IVP of the comparison system*

$$\begin{aligned}\dot{u}(t) &= g(t, u(t)), \\ u(t_0) &= u_0,\end{aligned}\tag{1.9}$$

admits a unique solution u in J , then $m(t) \leq u(t)$ for all $t \in J \cap [t_0, \infty)$ if $m(t_0) \leq u_0$, where $u \equiv u(\cdot; t_0, u_0)$ is a solution of the comparison ODE system (1.9).

The comparison theorems outlined above hold under relaxed assumptions on the function m (e.g., continuity) but have been restated in these useful forms for present purposes.

1.2.3 Partial Stability

Extending the stability concepts outlined in Definition 1.5, stability analysis of ODE systems with respect to a set of the state variables is known as partial stability. Arising in applications requiring performances of certain state variables, this concept was first formulated by A.M. Lyapunov and later by V.V. Rumyantsev. Consider again the ODE system (1.2) and let the components of the state variable x be partitioned into the following groups (based on the nature of the problem):

1. The set of basic variables $\{y_1, \dots, y_m\} \subset \{x_1, \dots, x_n\}$, $1 < m < n$, whose stability properties are of interest.
2. The remaining variables denoted by $\{z_1, \dots, z_p\}$, $p = n - m$, called the uncontrollable variables.

By construction, $\{y_1, \dots, y_m\} \cup \{z_1, \dots, z_p\} = \{x_1, \dots, x_n\}$ and, without loss of generality, suppose that a solution $x \equiv x(\cdot; t_0, x_0)$ of (1.2) can be written as $x \equiv (y_1, \dots, y_m, z_1, \dots, z_p) \equiv (y, z)$. Here the uncontrollable variables are not of interest in any stability analysis, however, the dynamics of the basic variables are related to the dynamics of the uncontrollable variables. As a result, the analysis of the partial stability of (1.2) requires an analysis of the behavior of all state variables. Consider the autonomous case of (1.2) (i.e., $f(t, x) \equiv f(x)$) and assume that $f(0) = 0$.

Definition 1.10 Let $\phi \equiv \phi(\cdot; x_0) \equiv (y(\cdot; x_0), z(\cdot; x_0))$ be the unique solution of solution of (1.2) in \mathbb{R}_+ and let $x_0 \equiv (y_0, z_0)$. Then the trivial solution of (1.2) is said to be

- (i) y -stable if for all $\epsilon > 0$, there exists a $\delta > 0$ such that $\|y_0\| < \delta$ implies $\|y(t; x_0)\| < \epsilon$ for all $t \geq 0$;
- (ii) asymptotically y -stable if (i) holds and there exists a $\beta > 0$ such that $\|y_0\| < \beta$ implies that

$$\lim_{t \rightarrow \infty} \|y(t; x_0)\| = 0;$$

- (ii) exponentially y -stable if there exist constants $\beta, \gamma, C > 0$ such that if $\|y_0\| < \beta$ then $\|y(t; x_0)\| < C\|y_0\| \exp(-\gamma t)$ for all $t \geq 0$;
- (iv) globally asymptotically (exponentially) y -stable if it is asymptotically (exponentially) stable and β is arbitrary,
- (v) unstable if (i) fails to hold.

Example 1.1 Consider (1.2) with $f : \mathbb{R}^3 \rightarrow \mathbb{R}^3$ and $x \equiv (y_1, y_2, z_1)$ (i.e., two basic variables and one uncontrollable variable). Partial (y_1, y_2) -stability of the trivial solution of (1.2) implies that for any $\epsilon > 0$, there exists $\delta > 0$ such that if

$$(y_{10}, y_{20}) \in \{(y_1, y_2) \in \mathbb{R}^2 : y_1^2 + y_2^2 < \delta^2\},$$

then $\{y(t; x_0) : t \in \mathbb{R}_+\} \subset H(\epsilon)$, where the ϵ -cylinder is defined as

$$H(\epsilon) \equiv \{(y_1, y_2) \in \mathbb{R}^2 : y_1^2 + y_2^2 < \epsilon^2\}.$$

This stability notion is not concerned with the behavior of the uncontrollable solution mapping $z_1(\cdot; x_0)$. Moreover, the initial condition is in a δ -cylinder (with δ depending on ϵ) that is independent of z_1 ; only the initial values of the basic variables are tied to ϵ .

1.3 Impulsive Systems

An impulsive differential equation (IDE) system is a natural way to model the evolution of a system which experiences instantaneous changes in the system state, called impulsive effects. Let $D \subset \mathbb{R}^n$ be open and connected, let $f : \mathbb{R} \times D \rightarrow \mathbb{R}^n$, and let $g_k : D \rightarrow \mathbb{R}^n$ for each $k \in \mathbb{N}$. Given $t_0 \in T$ and $x_0 \in D$, an IVP in IDEs is given by the following dynamic system:

$$\begin{aligned} \dot{x}(t) &= f(t, x(t)), & \forall t \notin \{T_k\}, \\ \Delta x(t) &= g_k(x(t^-)), & \forall t \in \{T_k\}, \\ x(t_0) &= x_0, & k \in \mathbb{N}, \end{aligned} \tag{1.10}$$

where $\Delta x(t) \equiv x(t) - \lim_{h \rightarrow 0^+} x(t-h)$ and $\{T_k\} \equiv \{T_k \in T : k \in \mathbb{N}\}$ is the set of impulsive times (also called impulsive moments). The impulsive times necessarily

satisfy $t_0 < T_1$ and $T_{k-1} < T_k$ for each $k \in \mathbb{N}$. For $t \neq T_k$, (1.10) evolves as an ODE system and at $t = T_k$, an impulsive effect is applied. A solution of (1.10) is defined as follows (see, e.g., [15]).

Definition 1.11 Let $T \subset \mathbb{R}$ contain t_0 . A function $\phi : T \rightarrow \mathbb{R}^n$ is a solution of (1.10) in T if it satisfies the following:

- (i) ϕ is C^1 from the right in T ;
- (ii) ϕ satisfies $\dot{\phi}(t) = f(t, \phi(t))$ for all $t \in T \setminus \{T_k\}$;
- (iii) ϕ satisfies $\phi(T_k) = \phi(T_k^-) + g_k(\phi(T_k^-))$ for each $k \in \mathbb{N}$;
- (iv) $\{\phi(t) : t \in T\} \subset D$.

Existence and uniqueness of the IDE IVP (1.10) is guaranteed for continuously differentiable right-hand side ODE functions (see Theorem 3.1 in [15]).

Theorem 1.11 If $f \in C^1(\mathbb{R} \times D, \mathbb{R}^n)$, g_k is continuous in D and $x + g_k(x) \in D$ for each $k \in \mathbb{N}$ and $x \in D$, then there exists a unique solution of (1.10).

Extending the comparison results outlined earlier (e.g., see Theorem 1.10), the next comparison result applies to impulsive systems [77].

Theorem 1.12 Let $m : J \rightarrow \mathbb{R}^n$ be piecewise smooth and $g \in C(\mathbb{R}^{n+1}, \mathbb{R}^n)$, $I_k \in C(\mathbb{R}^n, \mathbb{R}^n)$ for each k . Suppose that

$$\begin{aligned}\dot{m}(t) &\leq g(t, m(t)), \quad a.e. t \in J, \\ m(T_k) &\leq I_k(m(T_k^-)).\end{aligned}$$

If $g(t, u)$ is quasi-monotone increasing in u and for all $(t_0, u_0) \in J \times \mathbb{R}^n$, $I_k(u)$ is nondecreasing for each k , and the IVP of the comparison system

$$\begin{aligned}\dot{u}(t) &= g(t, u(t)), \\ u(T_k) &= I_k(u(T_k^-)), \\ u(t_0) &= u_0,\end{aligned}\tag{1.11}$$

admits a unique solution u in J . Then $m(t) \leq u(t)$ for all $t \in J \cap [t_0, \infty)$ if $m(t_0) \leq u_0$, where $u \equiv u(\cdot; t_0, u_0)$ is a solution of the comparison ODE system (1.11).

The IVP in IDEs (1.10) experiences impulses at the fixed times $\{T_k\}$. A more general formulation with variable impulsive moments is given by the system

$$\begin{aligned}\dot{x}(t) &= f(t, x), \quad \forall t \notin \{T_k(x)\}, \\ \Delta x(t) &= g_k(x(t^-)), \quad t \in \{T_k(x)\}, \\ x(t_0) &= x_0, \quad k \in \mathbb{N},\end{aligned}\tag{1.12}$$

where $T_k(x) < T_{k+1}(x)$ and $\lim_{k \rightarrow \infty} T_k(x) = \infty$. The impulsive moments depend here on the solution; solutions initialized at different points may therefore have different points of discontinuity. More details on IDEs, including variable impulsive moments, stability, and Lyapunov function methods, are given in [15, 76].

1.4 Delay Differential Equations

In this part, background material from delay differential equations is presented. For the remainder of this section, let $\tau > 0$ be a given real number and for notational convenience denote by $C_\tau \equiv C([-\tau, 0], \mathbb{R}^n)$ to be the space of continuous functions mapping $[-\tau, 0]$ to \mathbb{R}^n . Equip the space C_τ with the sup-norm: given $\phi \in C_\tau$, let

$$\|\phi\|_\tau \equiv \sup_{-\tau \leq s \leq 0} \|\phi(s)\|.$$

It follows that C_τ is a Banach space⁴. Given $t_0, t_f \in \mathbb{R}$, such that $t_0 < t_f$, and $x \in C([t_0 - \tau, t_0 + t_f], \mathbb{R}^n)$, let $x_t \in C_\tau$ denote the mapping $x_t(s) \equiv x(t + s)$ for $-\tau \leq s \leq 0$.

Let $D \subset C_\tau$, $f : \mathbb{R} \times D \rightarrow \mathbb{R}^n$, and consider the following delay differential equations (DDEs):

$$\dot{x}(t) = f(t, x_t), \quad (1.13)$$

where \dot{x} represents the right-hand time-derivative. The general form of (1.13) includes the following class of DDEs:

$$\dot{x}(t) = f(t, x(t), x(t - \tau_1(t)), \dots, x(t - \tau_p(t)))$$

where $0 \leq \tau_j(t) \leq \tau$ for $j = 1, 2, \dots, p$. It also includes types of integro-differential equations; for example,

$$\dot{x}(t) = \int_{-\tau}^0 g(t, s, x(t + s)) ds,$$

and

$$\dot{x}(t) = f(t, x) + \int_{t-\tau}^t g(t, s, x(s)) ds,$$

where g are suitably defined functions and $\tau > 0$ represents an upper bound on the distribution of delays. For theory devoted to systems of integro-differential equations (including those with unbounded delay), see [78]. Given $t_0 \in \mathbb{R}$ and an initial function $\phi_0 \in C_\tau$, the IVP associated with (1.13) is given by

$$\begin{aligned} \dot{x}(t) &= f(t, x_t), \\ x_{t_0}(s) &= \phi_0(s), \quad \forall s \in [-\tau, 0]. \end{aligned} \quad (1.14)$$

⁴Complete normed vector space.

Definition 1.12 Given $t_f > t_0$, a function $\phi : [t_0 - \tau, t_f] \rightarrow \mathbb{R}^n$ is called a solution of (1.14) in $[t_0 - \tau, t_f]$ if $\phi \in C([t_0 - \tau, t_f], \mathbb{R}^n)$, ϕ satisfies Eq. (1.13) for all $t \in [t_0, t_f]$, $\{x_t : t \in [t_0, t_f]\} \subset D$, and $x(t_0 + s) = \phi_0(s)$ for all $s \in [-\tau, 0]$.

As in the ODE system case, Definition (1.12) can be equivalently formulated as an integral equation:

$$\begin{aligned} x(t_0 + s) &= \phi_0(s), \quad \forall s \in [-\tau, 0], \\ x(t) &= \phi_0(0) + \int_{t_0}^t f(s, x_s) ds, \quad \forall t \geq t_0. \end{aligned} \tag{1.15}$$

For a DDE system with finite delay (as is the present setting), continuity of a function x ensures continuity of x_t ; if $x \in C([t_0 - \tau, t_0 + \alpha], \mathbb{R}^n)$ for some $\alpha > 0$ then the mapping $t \mapsto x_t$ is continuous in $[t_0, t_0 + \alpha]$. As in Theorem 1.1 for the ODE system, existence follows from continuity of the right-hand side function.

Theorem 1.13 If f is continuous in $\mathbb{R} \times D$, then there exists at least one solution of (1.14) with initial data (t_0, ϕ_0) .

As in Theorem 1.1, uniqueness of the solution requires Lipschitz continuity: given $t \in T, f(t, \cdot)$ is Lipschitz in $W \subset D$ if there exists $L \geq 0$ such that

$$\|f(t, \psi_1) - f(t, \psi_2)\| \leq L \|\psi_1 - \psi_2\|_\tau, \quad \forall \psi_1, \psi_2 \in W.$$

Theorem 1.14 If f is continuous in $\mathbb{R} \times D$ and $f(t, \cdot)$ is Lipschitz continuous for each compact subset in D and each fixed $t \in T$, then there exists a unique solution of (1.14) with initial data (t_0, ϕ_0) .

Assume that $f \in C^1(\mathbb{R}_+ \times D, \mathbb{R}^n)$, $f(t, 0) = 0$ for all $t \in \mathbb{R}_+$, and (1.14) has a unique solution in $[t_0 - \tau, \infty)$. Stability concepts for the DDE (1.14) are analogous to the ODE case in Definition 1.5 (e.g., see page 130 in [58]) and can be examined using a Lyapunov functional approach (an extension of Lyapunov stability in ODE theory). Consider an auxiliary function $V \in C^1(\mathbb{R} \times C_\tau, \mathbb{R})$ (e.g., a candidate Lyapunov functional). The time-derivative of V along trajectories of (1.14) is given by

$$\dot{V}_{(1.14)}(t, \psi) \equiv \frac{\partial V}{\partial t}(t, \psi) + \frac{\partial V}{\partial x}(t, \psi)f(t, \psi). \tag{1.16}$$

Theorem 1.15 Given any bounded subset $W \subset D$, assume that f maps $\mathbb{R} \times W$ to a bounded subset of \mathbb{R}^n . Let $c_1, c_2 \in \mathcal{K}_1$ and $c_3 : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ be a continuous nondecreasing function. Assume that there exists $V \in C^1(\mathbb{R} \times C_\tau, \mathbb{R})$ that satisfies

- (i) $c_1(\|\psi(0)\|) \leq V(t, \psi) \leq c_2(\|\psi\|_\tau)$ for all $(t, \psi) \in \mathbb{R} \times D$;
- (ii) $\frac{\partial V}{\partial t}(t, \psi) + \frac{\partial V}{\partial x}(t, \psi)f(t, \psi) \leq -c_3(\|\psi(0)\|)$ for all $(t, \psi) \in \mathbb{R} \times D$.

Then the trivial solution of (1.14) is uniformly stable. If in addition $c_3(s) > 0$ for all $s > 0$, then the trivial solution is uniformly asymptotically stable.

Stability of (1.14) can also be demonstrated via Lyapunov functions, which is the basis for Razumikhin-type theorems. The main idea is as follows: suppose that (1.14) has a unique solution $x \equiv x(\cdot; t_0, \phi_0)$ in $[t_0 - \tau, \infty)$. Suppose that initially the solution is contained inside a neighborhood of $\phi(0)$ but reaches its boundary at $t = t^* > t_0$; i.e., $\{x(t) : t \in [t_0, t^*)\} \subset B(\phi(0), r)$ for some $r > 0$ and

$$\|\dot{x}(t^*)\| \geq 0.$$

This case requires consideration of initial data satisfying such properties and the analysis then is concerned with investigating $t \mapsto x_t(0)$. In this way, the time-derivative of a function $V \in C^1(\mathbb{R} \times \mathbb{R}^n, \mathbb{R})$ along (1.14) can be defined as

$$\dot{V}_{(1.14)}(t, x) \equiv \frac{\partial V}{\partial t}(t, x) + \frac{\partial V}{\partial x}(t, x)f(t, x).$$

Theorem 1.16 *Given any bounded subset $W \subset D$, assume that f maps $\mathbb{R} \times W$ to a bounded subset of \mathbb{R}^n . Let $c_1 \in \mathcal{K}_1$, $c_2 \in \mathcal{K}$, and $c_3 : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ be a continuous nondecreasing function such that $c_3(s) > 0$ for $s > 0$. Let $q : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ be a continuous nondecreasing function such that $q(s) > 0$ for $s > 0$. If there is a function $V \in C^1(\mathbb{R} \times \mathbb{R}^n, \mathbb{R})$ that satisfies*

- (i) $c_1(\|x\|) \leq V(t, x) \leq c_2(\|x\|)$ for $(t, x) \in \mathbb{R} \times \mathbb{R}^n$;
- (ii) $\frac{\partial V}{\partial t}(t, \psi(0)) + \frac{\partial V}{\partial x}f(t, \psi(0)) \leq -c_3(\|\psi(0)\|)$ if $V(t + s, \psi(s)) < q(V(t, \psi(0)))$ for $s \in [-\tau, 0]$;

then the trivial solution of (1.14) is uniformly asymptotically stable.

1.5 Stochastic Differential Equations

A brief introduction to stochastic ODEs is presented here, with the work of Mao [106] as its basis. Let (Ω, \mathcal{F}, P) be a complete probability space; i.e., a set of events Ω , a σ -algebra of Ω denoted by \mathcal{F} , and a probability measure $P : \mathcal{F} \rightarrow [0, 1]$ such that $P(\Omega) = 1$ and, for any disjoint sequence $\{A_i : i \geq 1\} \subset \mathcal{F}$,

$$P\left(\bigcup_{i \geq 1} A_i\right) = \sum_{i=1}^{\infty} P(A_i).$$

Definition 1.13 Let $\{X_k : k \in \mathbb{N}\}$ and X be R^n -valued random variables.

- (i) If there exists a P -null set $\Omega_0 \in \mathcal{F}$ such that for all $\omega \notin \Omega_0$ the sequence $\{X_k(\omega)\}$ converges to $X(\omega)$, then $\{X_k\}$ is said to converge to X almost surely; $\lim_{k \rightarrow \infty} X_k = X$ almost surely (a.s.).

- (ii) If for every $\epsilon > 0$, $\lim_{k \rightarrow \infty} P\{\omega : \|X_k(\omega) - X(\omega)\| > \epsilon\} = 0$, then $\{X_k\}$ is said to converge to X in probability.
- (iii) If X_k and X belong to L^p (i.e., p th moment has finite value) and $\lim_{k \rightarrow \infty} \mathbb{E}[\|X_k - X\|^p] = 0$, then $\{X_k\}$ is said to converge to X in the p th moment.

Convergence in the p th moment or almost surely imply convergence in probability. Referring the reader to Chap. 1 in [106] for a full background treatment on the subject matter, we proceed by defining a stochastic process under the Itô interpretation, with a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ satisfying the usual conditions, as follows: let $B : \mathbb{R}_+ \rightarrow \mathbb{R}^m$ be an m -dimensional Brownian motion (i.e., mean zero and variance dt) defined on said probability space. Consider the following stochastic ODE system:

$$\begin{aligned} dx(t) &= f(x(t))dt + g(x(t))dB(t), \\ x(0) &= x_0, \end{aligned} \tag{1.17}$$

which is understood as the following stochastic integral equation:

$$x(t) = x_0 + \int_0^t f(x(s))ds + \int_0^t g(x(s))dB(t),$$

where $f : \mathbb{R}^n \rightarrow \mathbb{R}^n$ and $g : \mathbb{R}^n \rightarrow \mathbb{R}^{n \times m}$ and the integrals are understood as Itô integrals. A solution x is called an Itô process or stochastic process with stochastic differential dx (see Definition 2.1 in [106] for details). The functions f and g are assumed to be Borel measurable functions and must be L^1 and L^2 , respectively, when composed with a solution x of (1.17). Fundamental theory regarding existence and uniqueness of solutions is given in Sect. 2.3 in [106].

Supposing that $f(0) = 0$ and $g(0) = 0$, the direct method of Lyapunov outlined in Sect. 1.2.2 can be extended to stochastic ODEs. Here, stability in probability, moment stability, and almost sure stability are extensions of the classical stability notions (Definition 1.5).

Definition 1.14 Let $\phi \equiv \phi(\cdot; x_0)$ be a solution of (1.17) in \mathbb{R}_+ . Then the trivial solution is said to be

- (i) stable in probability if for every $\epsilon \in (0, 1)$ and $r > 0$ there exists $\delta = \delta(\epsilon, r) > 0$ such that $\|\phi(t)\| < \delta$ implies that

$$P\{\|\phi(t)\| < r \text{ for all } t \geq 0\} \geq 1 - \epsilon,$$

(otherwise it is stochastically unstable);

- (ii) stochastically asymptotically stable if it is stochastically stable and for every $\epsilon \in (0, 1)$ there exists $\beta = \beta(\epsilon) > 0$ such that $\|\phi(t)\| < \beta$ implies that

$$P\left\{\lim_{t \rightarrow \infty} \|\phi(t)\| = 0\right\} \geq 1 - \epsilon;$$

- (iii) stochastically asymptotically stable in the large if it is stochastically stable and for all $x_0 \in \mathbb{R}^n$,

$$P\left\{\lim_{t \rightarrow \infty} \|\phi(t)\| = 0\right\} = 1.$$

Letting $V \in C^2(\mathbb{R}^n, \mathbb{R}_+)$, Itô's formula gives the following stochastic differential of V along trajectories of (1.17):

$$\begin{aligned} d[V]_{(1.17)}(x(t)) &\equiv [\nabla V(x(t)) \cdot f(x(t)) + 0.5\text{trace}(g(x(t))^T HV(x)g(x(t)))]dt \\ &\quad + \nabla V(x(t)) \cdot (x(t))dB(t), \quad \text{a.s.}, \end{aligned}$$

where $HV(x)$ is the Hessian matrix of V evaluated at x . Similar to [106] (see page 110), the following notation is adopted:

$$L[V]_{(1.17)}(x) \equiv \nabla V(x) \cdot f(x) + 0.5\text{trace}(g(x)^T HV(x)g(x));$$

i.e.,

$$d[V]_{(1.17)}(x(t)) = L[V]_{(1.17)}(x(t))dt + \nabla V(x(t)) \cdot (x(t))dB(t).$$

Theorem 1.17 Let $V \in C^2(\mathbb{R}^n, \mathbb{R}_+)$ be positive definite and $\dot{V}_{(1.17)}(x) \leq 0$ for all $x \in \mathbb{R}^n$. Then the trivial solution of (1.17) is stochastically stable. If, in addition, V is decrescent and $LV_{(1.17)}(x) < 0$ for all $x \in \mathbb{R}^n \setminus \{0\}$, then the trivial solution is stochastically asymptotically stable. Further, if V is radially unbounded and $LV_{(1.17)}(x) < 0$ for all $x \in \mathbb{R}^n \setminus \{0\}$, then the trivial solution is stochastically asymptotically stable in the large.

Definition 1.15 Let $\phi \equiv \phi(\cdot; x_0)$ be a solution of (1.17) in \mathbb{R}_+ . Then the trivial solution of (1.17) is said to be p th moment exponentially stable if there exist $\gamma, C > 0$ such that for any $x_0 \in \mathbb{R}^n$,

$$\mathbb{E}[\|\phi(t)\|^p] \leq C\|x_0\|^p \exp(-\gamma t), \quad \forall t \in \mathbb{R}_+.$$

Theorem 1.18 Let $V \in C^2(\mathbb{R}^n, \mathbb{R}_+)$. Assume that there exist positive constants $c_1, c_2, \lambda > 0$ such that the following conditions hold:

- (i) $c_1\|x\|^p \leq V(x) \leq c_2\|x\|^p$ for all $x \in \mathbb{R}^n$;
- (ii) $LV_{(1.17)}(x) \leq -\lambda V(x)$ for all $x \in \mathbb{R}^n$;

Then the trivial solution of (1.17) is p th moment exponentially stable; $\mathbb{E}[\|\phi(t; x_0)\|^p] \leq \frac{c_2}{c_1}\|x_0\|^p \exp(-\lambda t)$ for all $t \in \mathbb{R}_+$ where $\phi \equiv \phi(\cdot; x_0)$ is a solution of (1.17).

For illustrative examples of these theorems, see Chap. 4 in [106].

Chapter 2

Hybrid and Switched Systems

The theory of hybrid and switched systems is reviewed here, with an emphasis on stability theory. The material presented in this section is mainly based on [84, 85]; the interested reader is also referred to the hybrid systems literature (e.g., [45, 136, 153]). Hybrid dynamical systems [45, 136, 153] are governed by a combination of continuous and discrete dynamics. Switched systems [23, 84, 144], a type of hybrid system, evolve according to mode-dependent continuous/discrete dynamics (e.g., modeled as differential equations) and experience abrupt transitions between modes according to a logic-based switching rule. Switched systems most often arise in two contexts [31]: (1) a natural system that experiences sudden changes in its dynamics based on, for example, environmental factors; and (2) when switching control is used to stabilize a continuous system. The following examples illustrate the mixture of continuous and discrete dynamics displayed by these types of systems:

1. *Multi-controller architecture*: Suppose a user is tasked with achieving a desired performance behavior for a complex dynamic process and no continuous feedback control exists. Given a family of controllers, each of which is designed for a particular task in the implementation, it may be possible to control the process by switching between controllers. As the system evolves, a decision maker determines which controller is active in the closed-loop system. In this way, the decision maker acts as a logic-based switching supervisor; the governing dynamics are naturally modeled as a switched system (see Fig. 2.1).
2. *Air conditioner (AC) unit*: Consider a climate-control system designed so that when the temperature T increases to some preset threshold $T = T_{\text{hot}}$, the AC is automatically turned on. This precipitates a decrease in the temperature and, once another threshold $T = T_{\text{cold}}$ is reached, the AC is automatically turned off. The temperature then changes according to the ambient temperature. The larger the difference between T_{hot} and T_{cold} , the less number of switches present in the system. See Fig. 2.2 for a simple illustration.
3. *Vehicle with manual transmission*: The motion of a vehicle along a fixed path at time t can be described by its position $x(t)$ and velocity $v(t)$. A simplified

Fig. 2.1 Process system with supervisory switching control

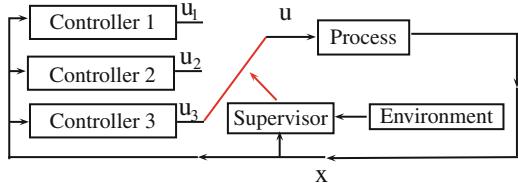


Fig. 2.2 Air conditioner unit as a switched system

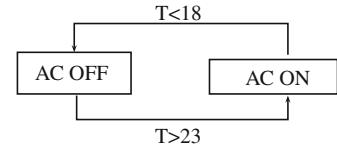
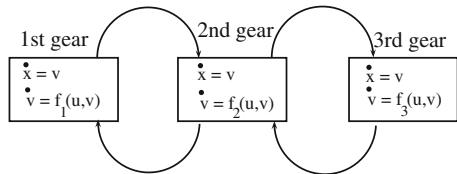


Fig. 2.3 Vehicle with manual transmission as a switched system



version of the model has two control inputs [136]: the current throttle angle, $u(t)$, and the current gear engaged, $g(t) \in \{1, 2, 3\}$ (i.e., the mode of the switched system); changing gears requires an abrupt action by the driver and represents a switch between modes. This situation is depicted in Fig. 2.3.

Switched systems can lead to interesting behavior, such as the instability of a switched system comprised solely of stable continuous subsystems [85] and the switched and impulsive control of unstable continuous subsystems that leads to a stable switched system [54, 55]. Due to its advantages in improving transient response and providing an effective mechanism to deal with highly complex systems and systems with large uncertainties, hybrid control has also received growing interest [54]. Further, even though the complex system behaviors may follow unpredictable patterns, impulsive and switching control is an effective method in achieving stabilization of complex systems using only small control impulses in different modes [54]. Having conditions which guarantee stability is a substantial part of the switched systems literature. Some common techniques to show stability of these systems are the switched invariance principle [12, 61, 62] and common/multiple Lyapunov function techniques [22, 23, 31, 124]. There is literature on families of subsystems that are triangularizable [112], as well as those that commute [119]. Work has been done on the control of discrete switched systems [28], the stabilization of nonlinear switched systems using control [115], and criteria for the instability of switched systems under arbitrary switching [135]. A general overview of hybrid and switched systems and its literature can be seen in [31, 32, 85, 136].

The mathematical framework of a switched system is characterized in this monograph by a set of continuous modes (i.e., ordinary differential equations) and a logical rule orchestrating switching between said modes. Consider a finite index set $\mathcal{P} \equiv \{1, \dots, p\}$ and a family of vector fields $\{f_i : i \in \mathcal{P}\}$ where each $f_i : D \rightarrow \mathbb{R}^n$ is a smooth function (i.e., C^1 in an open and connected set $D \subset \mathbb{R}^n$ containing the zero vector). The set of autonomous ODE systems

$$\dot{x}(t) = f_i(x(t)), \quad \forall i \in \mathcal{P}, \quad (2.1)$$

correspond to the modes of the switched system. Parameterized by an initial condition and a piecewise constant function, called the switching rule (or signal), $\sigma : \mathbb{R}_+ \rightarrow \mathcal{P}$, the switched system is written as the following dynamic system IVP:

$$\begin{aligned} \dot{x}(t) &= f_{\sigma}(x(t)), \\ x(0) &= x_0. \end{aligned} \quad (2.2)$$

Definition 2.1 Associated with the switching rule σ are the switching times $\{t_k\}$, assumed to satisfy $t_{k-1} < t_k$ for each $k \in \aleph \equiv \{1, \dots, n_s\}$, where $n_s \in \mathbb{N} \cup \{+\infty\}$ is the total number of switches (which may be finite or infinite). This is a piecewise constant function (assumed continuous from the right) that takes on values from a finite index set \mathcal{P} . Denote the set of all such switching rules by \mathcal{S} .

Note that the initial time t_0 has been shifted to zero, without loss of generality (simply redefine a new time as $h = t - t_0$ and a new switching time sequence accordingly). The corresponding intervals $[t_{k-1}, t_k)$, $k \in \aleph$, are called the switching intervals; $\sigma(t) = i_k \in \mathcal{P}$ for all $t \in [t_{k-1}, t_k)$. That is, the mode i_k is active on the interval $[t_{k-1}, t_k)$, so that (2.2) evolves according to

$$\dot{x}(t) = f_{i_k}(x(t)), \quad \forall t \in [t_{k-1}, t_k),$$

and the modes switch at $t = t_k$ where the active mode changes from $\sigma(t_k^-) := \lim_{h \rightarrow 0^+} \sigma(t_k - h) \in \mathcal{P}$ to $\sigma(t_k) \in \mathcal{P}$. (Note that $\sigma(t_{k-1}) = \sigma(t_k^-)$ and $\sigma(t_k^-) \neq \sigma(t_k)$ in general.) The switching times may be time-dependent (e.g., pre-specified event times), state-dependent (i.e., $t_k \equiv t_k(x)$), or a mixture of both; other types of switching rules, such as Markovian switching, are detailed in [85]. Unlike the ODE system (1.2), Eq. (2.2) admits a set of solutions parameterized by both the initial condition and switching rule σ . Formally, a solution of (2.2) is considered here as a piecewise smooth function $\phi(\cdot; x_0)$ satisfying the following [12].

Definition 2.2 Let $t_f \in \mathbb{R}_+ \cup \{+\infty\}$ and $\sigma \in \mathcal{S}$ with switching times $\{t_k\} \subset [0, t_f]$ and mode sequence $\{i_k\} \subset \mathcal{P}$, a function $\phi : [0, t_f] \rightarrow \mathbb{R}^n$ is called a solution of (2.2) if the function $\phi \equiv \phi(\cdot; x_0, \sigma)$ is a piecewise smooth function satisfying $\{\phi(t) : t \in [0, t_f]\} \subset D$ and is an integral curve of the switching vector field;

$$\phi(t) = x_0 + \int_0^t f_{\sigma(s)}(\phi(s))ds, \quad \forall t \in [0, t_f].$$

Equation (2.2) is often written in the alternative form

$$\begin{aligned}\dot{x}(t) &= f_{i_k}(x(t)), \quad t \in [t_{k-1}, t_k], k \in \mathbb{N}, \\ x(0) &= x_0,\end{aligned}$$

where $\sigma(t) = i_k \in \mathcal{P}$ for $t \in [t_{k-1}, t_k]$. The switched system (2.2) has an equilibrium point $\bar{x} \in D$ (also called a common equilibrium point) if $f_i(\bar{x}) = 0$ for all $i \in \mathcal{P}$. As it is possible to shift such a point to the origin by setting $y \equiv x - \bar{x}$, it is assumed, without loss of generality, that $f_i(0) = 0$ for all $i \in \mathcal{P}$ in the remainder of this section. The stability definitions for the trivial solution of (2.2) are analogous to the classical ones outlined earlier for ODE systems (see, e.g., [12]).

At this point, it is appropriate to define some fundamental objects associated with (2.2). More specifically, the set of switching rules exhibiting a nonvanishing dwell-time and the total activation time or switches into a mode (or set of modes).

Definition 2.3 Let $\mathcal{S}_{\text{dwell}} \subset \mathcal{S}$ denote the set of all switching rules σ which have nonvanishing dwell-times; for any x_0 , there exists $\eta > 0$ such that the switching times $\{t_k\}$ associated with σ satisfy

$$\inf_k \{t_k - t_{k-1}\} \geq \eta. \quad (2.3)$$

The notation $\mathcal{S}_{\text{dwell}}(\eta)$ is sometimes used and explicitly denotes the nonvanishing dwell-time $\eta > 0$.

Definition 2.4 Given $t^1, t^2 \in \mathbb{R}_+$, denote the activation time of the i th mode on (t^1, t^2) by $T_i(t^1, t^2) \equiv |\{t \in (t^1, t^2) : \sigma(t) = i\}|$. Denote the activation time of the subset of modes $\mathcal{P}^* \subset \mathcal{P}$ on (t^1, t^2) by $T_{\mathcal{P}^*} \equiv |\{t \in (t^1, t^2) : \sigma(t) \in \mathcal{P}^*\}|$. Denote the number of switches of the subset of modes $\mathcal{P}^* \subset \mathcal{P}$ on (t^1, t^2) by $N_{\mathcal{P}^*} \equiv |\{t_k \in [t^1, t^2] : \sigma(t_k) \in \mathcal{P}^*\}|$.

Detailed in the remaining parts of this section, the majority of the literature on switched systems stability can be categorized into one of the following problems [85]:

1. Finding conditions guaranteeing asymptotic stability of the trivial solution under arbitrary switching rules.
2. Identifying classes of switching rules under which the trivial solution is asymptotically stable.
3. Constructing switching rules guaranteeing asymptotic stability of the trivial solution.

For the remainder of this chapter, it is assumed that $\mathbb{N} = \mathbb{N}$ (i.e., $n_s = +\infty$).

2.1 Stability Under Arbitrary Switching

A brief overview of preservation of stability under arbitrary switching is given here. For more details regarding stability under arbitrary switching, the reader is encouraged to see Chap. 2 of [84], from which this material is adapted. A first observation is that if the j th mode of (2.2) is unstable, $\sigma(t) \equiv j$ for all t immediately gives instability; all modes of (2.2) being stable is thus a necessary condition for stability under arbitrary switching. However, this condition is not sufficient, as demonstrated in the following example adapted from [84].

Example 2.1 Consider (2.2) with two modes, i.e., $\mathcal{P} = \{1, 2\}$. Let $f_1(x) \equiv A_1x$ and $f_2(x) \equiv A_2x$ with

$$A_1 = \begin{pmatrix} -0.1 & 1 \\ -2 & -0.1 \end{pmatrix}, \quad A_2 = \begin{pmatrix} -0.1 & 2 \\ -1 & -0.1 \end{pmatrix}.$$

Both A_1 and A_2 are Hurwitz matrices; the trivial solution is globally exponentially stable for each mode in isolation. Suppose that σ is constructed according to the following rule: if $x_1x_2 < 0$, engage mode 1; if $x_1x_2 \geq 0$, engage mode 2. (Note that this switching rule construction is state-dependent.) The trivial solution of (2.2) is unstable in this scenario (see Fig. 2.4 for an illustration).

The existence of a so-called common Lyapunov function is a sufficient condition for asymptotic stability of the trivial solution of (2.2). The main idea is that the rate of decrease of a Lyapunov function along (2.2) is unaffected by the switching; asymptotic stability is uniform with respect to the switching rule σ .

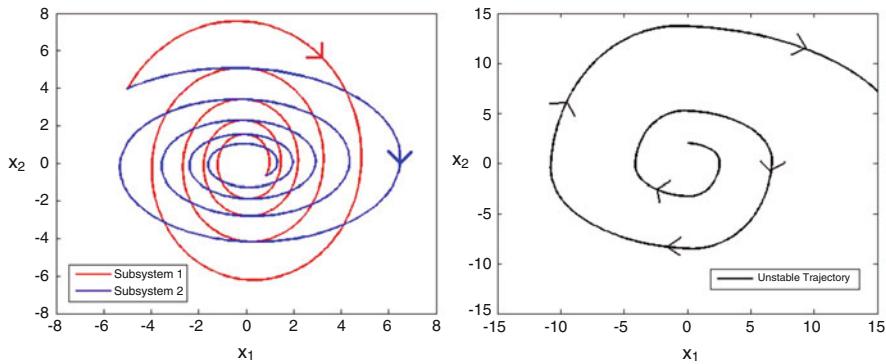


Fig. 2.4 Simulation of Example 2.1. Both modes are stable (left), however, the switched system is unstable (right)

Theorem 2.1 Let $V \in C^1(D, \mathbb{R}_+)$ and let $W \in C(D, \mathbb{R}_+)$ be a positive definite and radially unbounded¹ function. If

$$\nabla V(x) \cdot f_i(x) \leq -W(x), \quad \forall x \in D, \forall i \in \mathcal{P}, \quad (2.4)$$

then the trivial solution of (2.2) is globally asymptotically stable under arbitrary switching.

Observe that Eq. (2.4) is the Lie derivative of V with respect to each mode $i \in \mathcal{P}$ of the switched system. The level sets of V are cut inward by trajectories of (2.2) regardless of the mode sequence and switching times.

LaSalle's Invariance Principle from classical ODE theory (i.e., Theorem 1.6) fails to hold for the switched system (2.2) under arbitrary switching. However, Liu et al. [12] provided an invariance principle for switched systems possessing a so-called weak common Lyapunov function. Before presenting the switched invariance result, the following definitions are needed.

Definition 2.5 A set $\Omega \subset D$ is said to be weakly invariant with respect to (2.2) if for each $x_0 \in D$, there exists an index $i \in \mathcal{P}$ and constant $b > 0$ such that the solution $\phi_{f_i} \equiv \phi_{f_i}(\cdot; x_0)$ of the i th mode (in isolation) satisfies $\phi_{f_i}(t) \in \Omega$ for either $t \in [-b, 0]$ or $t \in [0, b]$.

Definition 2.6 A solution $\phi \equiv \phi(\cdot; x_0, \sigma)$ of the switched system (2.2) is said to be attracted by a compact set $\Omega \subset D$ if for each $\epsilon > 0$ there exists $T > 0$ such that $\{\phi(t) : t \geq T\} \subset B_\epsilon(\Omega)$, where

$$B_\epsilon(\Omega) = \bigcup_{x \in \Omega} B_\epsilon(x).$$

Definition 2.7 A function $V \in C^1(D, \mathbb{R}_+)$ is called a weak common Lyapunov function for (2.2) if V is positive definite and

$$\nabla V(x) \cdot f_i(x) \leq 0, \quad \forall x \in D, i \in \mathcal{P}. \quad (2.5)$$

Note that

$$\lim_{t \rightarrow \infty} \text{dist}(\phi(t), \Omega) = \liminf_{t \rightarrow \infty} \{\|\phi(t) - w\| : w \in \Omega\} = 0$$

is a necessary and sufficient condition for a solution $\phi \equiv \phi(\cdot; x_0, \sigma)$ of (2.2) to be attracted by Ω . The invariance principle mentioned above is stated as follows (see [12] for illustrative examples).

¹Recall this means that $W(x) \rightarrow \infty$ as $\|x\| \rightarrow \partial D$.

Theorem 2.2 Assume that V is a weak common Lyapunov function for (2.2). Let D_c be the connected component of the level set $\{x \in D : V(x) < c\}$ for some constant $c > 0$. Assume that D_c is bounded and let

$$Z \equiv \{x \in D : \exists i \in \mathcal{P} \text{ such that } \nabla V(x) \cdot f_i(x) = 0\}.$$

Further, let Ω be the union of all compact, weakly invariant sets which are contained in $Z \cap D_c$. Then the solution $\phi \equiv \phi(\cdot; x_0, \sigma)$ of (2.2) associated with $x_0 \in D_c$ and $\sigma \in \mathcal{S}_{\text{dwell}}$ is attracted by the union of all compact, weakly invariant sets which are contained in $Z \cap D_c$.

2.2 Stability Under Constrained Switching

Motivated by switched systems composed entirely of stable modes exhibiting instability (e.g., see Example 2.1), classes of switching rules are sought which avoid this unwanted behavior. This problem can be resolved by placing restrictions upon the rate of switching in the switched system (2.2), leading to the concept of stability under slow or dwell-time switching [85]. Multiple Lyapunov functions is one analysis technique to guarantee the switching is sufficiently slow. By assuming stability of each individual mode, there exists a Lyapunov function corresponding to each mode (i.e., its time-derivative decreases along the i th mode in isolation). Under certain conditions on the family of Lyapunov functions, asymptotic stability of the switched system (2.2) can be ensured. For example, see the result in [61], given as follows.

Theorem 2.3 Assume that there exist a family of Lyapunov functions $\{V_i \in C^1(D, \mathbb{R}_+) : i \in \mathcal{P}\}$ satisfying the following conditions:

- (i) $\nabla V_i(x) \cdot f_i(x) < 0$ for all $x \in D \setminus \{0\}$;
- (ii) at each $t = t_k$, $k \in \mathbb{N}$,

$$V_{i_{k+1}}(\phi(t_k)) \leq V_{i_k}(\phi(t_k)), \quad (2.6)$$

where $\sigma(t_k) = i_{k+1} \in \mathcal{P}$ and $\sigma(t_k^-) = i_k \in \mathcal{P}$, where $\phi \equiv \phi(\cdot; x_0, \sigma)$ is the unique solution of (2.2) passing through $x_0 \in D$.

Then the trivial solution of the switched system (2.2) is asymptotically stable.

Note here that the expression $\nabla V_i(x) \cdot f_i(x)$ in Theorem 2.3 is the Lie derivative of V_i along the vector field f_i . The set of multiple Lyapunov functions $\{V_i\}$ in Theorem 2.3 do not increase in value at the switching moments; the switching Lyapunov function $V_\sigma \equiv V_{i_k}$ decreases along the trajectories of (2.2) for all t . In fact, if $\{V_{i_k}(t_k)\}$ forms a decreasing sequence (saying nothing about the behavior of V_σ in between switching times), the result also holds.

Theorem 2.4 Assume there exist a family of Lyapunov functions $\{V_i \in C^1(D, \mathbb{R}_+) : i \in \mathcal{P}\}$, and positive definite continuous functions $\{W_i : i \in \mathcal{P}\}$ such that the following conditions hold:

- (i) $\nabla V_i(x) \cdot f_i(x) < 0$ for all $x \in D \setminus \{0\}$;
- (ii) for every pair of switching times (t_i, t_j) satisfying $i < j$, $\sigma(t_i) = \sigma(t_j) = q \in \mathcal{P}$, and $\sigma(t_k) \neq q$ for any t_k satisfying $t_i < t_k < t_j$, it holds that

$$V_q(\phi(t_j)) - V_q(\phi(t_i)) \leq -W_q(\phi(t_i)), \quad (2.7)$$

where $\phi \equiv \phi(\cdot; x_0, \sigma)$ is the unique solution of (2.2) passing through $x_0 \in D$.

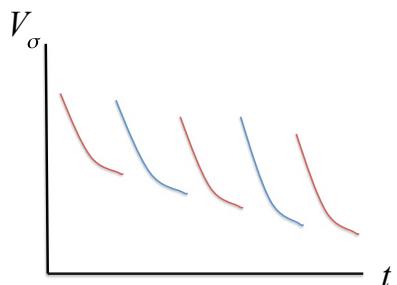
Then the trivial solution of the switched system (2.2) is asymptotically stable.

See Fig. 2.5 for an illustration of condition (2.7). Theorems 2.3 and 2.4 require conditions on the multiple Lyapunov functions at the switching times (i.e., via (2.6) and (2.7)). These conditions can be restrictive in general, requiring knowledge of the solution state at the switching times. However, it is often the case that said conditions are trivially satisfied or the switching rule is constructed with these conditions in mind [124]. If $f_i(x) \equiv A_i x$ for all $i \in \mathcal{P}$, where each $A_i \in \mathbb{R}^{n \times n}$ is a Hurwitz matrix, then a Lyapunov function associated with each mode is given by $V_i(x) \equiv x^T P_i x$, where P_i are positive definite matrices which can be calculated from the Lyapunov equations $A_i^T P_i + P_i A_i^T = -Q_i$ for any positive definite matrix Q_i .

The problem of sufficiently slow switching can be alternatively resolved from the perspective of finding sets of admissible switching rules. This is especially convenient when the switching rules depend on the solution trajectory (i.e., state-dependent switching) [62]. Stability can be established based on the lower bound of a dwell-time satisfying switching rule (see Theorem 2.5).

Theorem 2.5 Consider the switched system (2.2) with $\mathcal{P} = \{1, 2\}$. Assume that there exist functions $V_1, V_2 \in C^1(D, \mathbb{R}_+)$ and constants $a_1, a_2, b_1, b_2, c_1, c_2 > 0$

Fig. 2.5 Multiple Lyapunov functions which satisfy Eq. (2.7). The red line corresponds to the first mode being active and the blue line corresponds to the second mode being active



such that the following conditions hold:

- (i) $a_i\|x\|^2 \leq V_i(x) \leq b_i\|x\|^2$ for all $x \in D$ and $i \in \{1, 2\}$;
- (ii) $\nabla V_i(x) \cdot f_i(x) \leq -c_i\|x\|^2$ for all $x \in D$ and $i \in \{1, 2\}$;
- (iii) $\sigma \in \mathcal{S}_{\text{dwell}}(\eta)$ such that

$$\left(\frac{c_1}{b_1} + \frac{c_2}{b_2} \right) \ln \left(\frac{b_1 b_2}{a_1 a_2} \right) < \eta.$$

Then the trivial solution of the switched system (2.2) is asymptotically stable.

The dwell-time switching condition in Theorem 2.5 can be too restrictive for certain applications. For example, if the switching rule is constructed to select modes for optimizing a particular behavior, the performance may deteriorate in time (e.g., from system failures) to an unacceptable level (necessitating a switch) before the required dwell-time has passed. Average dwell-time switching allows for fast switching in some instances and demands a particular switching rate, on average. As a result, average dwell-time satisfying switching rules alleviate this problem [60] while still being able to achieve the desired performance.

Recall the set of dwell-time satisfying switching rules in Definition 2.3, where the notation $\mathcal{S}_{\text{dwell}}(\eta)$ explicitly denotes the nonvanishing dwell-time $\eta > 0$, but $\mathcal{S}_{\text{dwell}}$ may be appropriately used depending on the context. See Fig. 2.6 for an illustration of dwell-time.

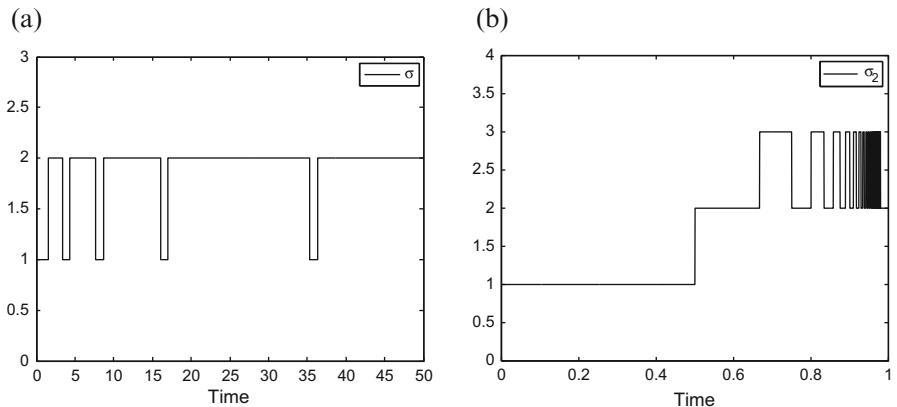


Fig. 2.6 Switching rules with nonvanishing and vanishing dwell-times. **(a)** Switching rule with nonvanishing dwell-time (i.e., $\sigma \in \mathcal{S}_{\text{dwell}}$). **(b)** Switching rule with vanishing dwell-time (i.e., $\sigma_2 \notin \mathcal{S}_{\text{dwell}}$)

Definition 2.8 Let $\mathcal{S}_{\text{avg}} \equiv \mathcal{S}_{\text{avg}}(\tau_a, N_0) \subset \mathcal{S}$ denote the set of all switching rules σ which have average dwell-time τ_a and chatter bound N_0 ; for any x_0 , there exist constants $N_0, \tau_a > 0$ such that

$$N_\sigma(t^1, t^2) \leq N_0 + \frac{t^2 - t^1}{\tau_a}, \quad \text{for all } t \in [t^1, t^2], \quad (2.8)$$

where $N_\sigma(t^1, t^2)$ is defined to be the number of total switches of the switching rule σ on the interval (t^1, t^2) .

Theorem 2.6 Consider the switched system (2.2) with $\mathcal{P} = \{1, 2\}$. Assume that there exist functions $V_1, V_2 \in C^1(D, \mathbb{R}_+)$, $\alpha_1, \alpha_2 \in \mathcal{K}_\infty$ and constants $\mu, \lambda > 0$ such that the following conditions hold:

- (i) $\alpha_1(\|x\|) \leq V_i(x) \leq \alpha_2(\|x\|)$ for all $x \in D$ and $i \in \{1, 2\}$;
- (ii) $\nabla V_i(x) \cdot f_i(x) \leq -\lambda V_i(x)$ for all $x \in D$ and $i \in \{1, 2\}$;
- (iii) $V_i(x) \leq \mu V_j(x)$ for all $x \in D$ and $(i, j) \in \{1, 2\}^2$;
- (iv) $\sigma \in \mathcal{S}_{\text{avg}}(\tau_a, N_0)$ such that $\tau_a > \ln(\mu)/\lambda$.

Then the trivial solution of the switched system (2.2) is globally asymptotically stable.

(For the extension of Theorem 2.6 to the general case \mathcal{P} , see Theorem 3.2 in [84].) For more background on the stability of switched systems with dwell-time and average dwell-time, see [60, 84, 136]. For examples of some other classes of switching rules, the reader is referred to [62] for an overview. For details regarding demonstrating instability of a switched system, see [135]. Often used in the epidemic material in this work is the class of periodic switching rules.

Definition 2.9 Let $\mathcal{S}_{\text{periodic}} \equiv \mathcal{S}_{\text{periodic}}(\omega) \subset \mathcal{S}$ denote the set of all periodic switching rules σ with period $\omega > 0$; for any x_0 , there exists $\omega > 0$ such that $t_k - t_{k-1} \equiv \tau_k$ satisfies $\tau_{k+m} = \tau_k$, $\sum_{i=1}^m \tau_i = \omega$ and $\sigma(t + \omega) = \sigma(t)$.

2.3 Switching Control

Of importance to the present monograph, the third problem can be viewed as a control problem in which switching control is used to stabilize an unstable continuous system. As discussed elsewhere, this may be a requirement if continuous control is not suitable (e.g., due to the nature of the problem), unavailable (e.g., because of model uncertainty), or cannot be implemented (e.g., due to sensor and/or actuator limitations). Moreover, switching control can improve performance compared to a fixed continuous controller [31] and be easier to find for a desired task [45].

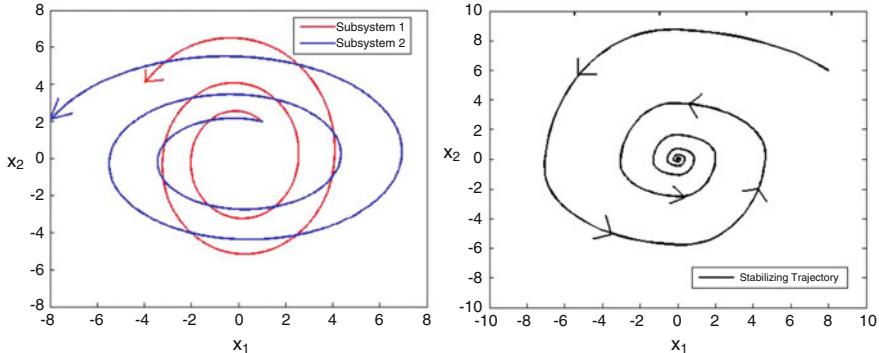


Fig. 2.7 Each mode is unstable (left figure). The switching rule outlined in Example 2.2 is stabilizing (right figure)

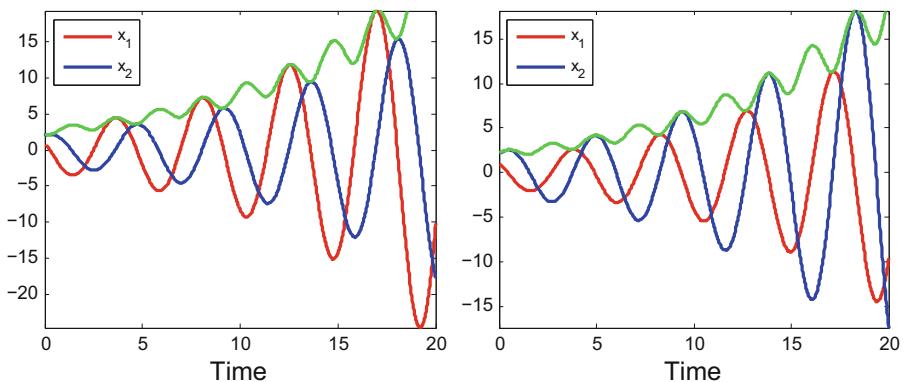


Fig. 2.8 The solution trajectories of mode 1 (left figure) and mode 2 (right figure); both modes are unstable but their solutions' norms (green curves) do not increase monotonically

Example 2.2 Consider the switched system (2.2) from [85] with $\mathcal{P} = \{1, 2\}$, $f_1(x) \equiv A_1x$, $f_2(x) \equiv A_2x$,

$$A_1 = \begin{pmatrix} 0.1 & -1 \\ 2 & 0.1 \end{pmatrix}, \quad A_2 = \begin{pmatrix} 0.1 & -2 \\ 1 & 0.1 \end{pmatrix}.$$

The eigenvalues of A_1 and A_2 have positive real parts; each mode is unstable. Design a stabilizing switching rule as follows: let $\sigma = 1$ if $x_1x_2 < 0$, otherwise choose subsystem 2 to be active. The results are illustrated in Figs. 2.7 and 2.8. The increase in norm of solutions of each mode in isolation increases but not monotonically; the switching rule is constructed with this observation in mind.

Wickes et al. [162] developed stabilizing state-dependent switching rule theory for linear switched systems. Consider the switched system (2.2) with $\mathcal{P} = \{1, 2\}$, $f_1(x) \equiv A_1x$, and $f_2(x) \equiv A_2x$, where $A_1 \in \mathbb{R}^{n \times n}$ and $A_2 \in \mathbb{R}^{n \times n}$ have eigenvalues with positive real parts. The method is outlined as follows: if a convex combination

$\tilde{A} \equiv \alpha A_1 + (1 - \alpha)A_2$ (also called matrix pencil), for some $\alpha \in (0, 1)$, is Hurwitz, then a stabilizing switching rule for (2.2) can be constructed as follows:

1. Let P be a positive definite matrix that solves the Lyapunov equation $\tilde{A}^T P + P \tilde{A} = -Q$ for some positive definite matrix Q .
2. Partition the state space into the switching regions

$$\begin{aligned}\Omega_1 &\equiv \{x \in \mathbb{R}^n : x^T (A_1^T P + PA_1^T) x < 0\}, \\ \Omega_2 &\equiv \{x \in \mathbb{R}^n : x^T (A_2^T P + PA_2^T) x < 0\}.\end{aligned}$$

3. Design the switching rule as follows:

$$\sigma \equiv \begin{cases} 1 & \text{if } x \in \Omega_1, \\ 2 & \text{if } x \in \Omega_2. \end{cases} \quad (2.9)$$

By this construction, the Lyapunov function $V(x) \equiv x^T Px$ satisfies $\nabla V(x) A_1 x < 0$ for $x \in \Omega_1 \setminus \{0\}$ and $\nabla V(x) A_2 x$ for $x \in \Omega_2 \setminus \{0\}$. Moreover, it can be shown that $\Omega_1 \cup \Omega_2 = \mathbb{R}^2$. This approach can be extended to linear switched systems with p modes if there exist constants $\alpha_i > 0$ satisfying $\sum_{i \in \mathcal{P}} \alpha_i = 1$ such that the convex combination matrix $\tilde{A} \equiv \sum_{i \in \mathcal{P}} \alpha_i A_i$ is Hurwitz. For a more detailed account of the linear case, see the book Chapter 3 in [84] and the survey paper [86]. Geometrically, the state space partitioning dictates the current active mode; when the solution trajectory crosses from one region to another, a switch is made (see Fig. 2.9).

The state-dependent switching rule in Eq. (2.9) raises concerns over its well-posedness. Namely, if the solution crosses a boundary and switches, the trajectory could then immediately cross over the same boundary depending on the vector field of the new mode (and thus forcing another switch). This raises the possibility of chattering, Zeno, or sliding motion behavior. (For more details, see [84, 90].) These behaviors are undesirable practically as it results in excessive equipment wear. This situation is illustrated in Fig. 2.10.

In [90], Liu et al. extended this line of research to the nonlinear switched system (2.2). Suppose that there exists a Lyapunov function $V \in C^1(D, \mathbb{R}_+)$ that is positive definite and radially unbounded, and constants $\alpha_i > 0$ satisfying $\sum_{i \in \mathcal{P}} \alpha_i = 1$ such that

Fig. 2.9 Solution trajectories for a switched system with a state-dependent switching rule. A switch occurs whenever the state trajectory crosses a switching region boundary

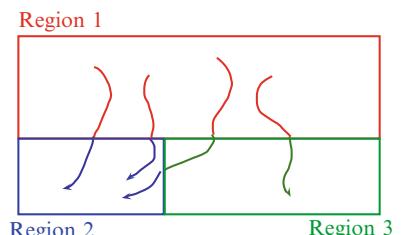
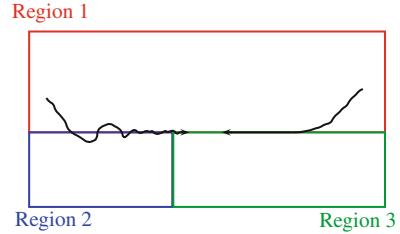


Fig. 2.10 Chattering and sliding motion behaviors in a state-dependent switching rule



$$\nabla V(x) \cdot \left(\sum_{i \in \mathcal{P}} \alpha_i f_i(x) \right) \leq -\lambda(\|x\|), \quad \forall x \in D,$$

for some \mathcal{K} -class function $\lambda \in \mathcal{K}$. Then it is necessarily true that the domain D can be partitioned into switching regions such that, for any $x \neq 0$, there is at least one index $j \in \mathcal{P}$ (and associated vector field f_j) such that the state of the switched system (2.2) is being stabilized if mode j is active. This immediately motivates the following construction of the switching regions:

$$\widetilde{\Omega}_i \equiv \{x \in D : \nabla V(x) \cdot f_i(x) \leq -\lambda(\|x\|)\}, \quad \forall i \in \mathcal{P}.$$

This can be interpreted as follows: if the trajectory of the switched system (2.2) associated with x_0 are in the region $\widetilde{\Omega}_i$ then activate mode i . If the solution crosses a boundary into another region, switch to the appropriate mode. With this observation in mind, along with remarks earlier on chattering and Zeno behavior, Liu et al. [90] provided the following minimum rule algorithm (restated slightly here for the present setting).

Theorem 2.7 Assume that there exist constants $\alpha_i > 0$ satisfying $\sum_{i \in \mathcal{P}} \alpha_i = 1$, $\lambda > 0$, functions $c_1, c_2 \in \mathcal{K}_\infty$, $V \in C^1(D, \mathbb{R}_+)$ such that

- (i) $c_1(\|x\|) \leq V(x) \leq c_2(\|x\|)$ for all $x \in D$;
- (ii) $\nabla V(x) \cdot \left(\sum_{i \in \mathcal{P}} \alpha_i f_i(x) \right) \leq -\lambda(\|x\|)$ for all $x \in D$.

Then the trivial solution of (2.2) is globally asymptotically stable under the following state-dependent switching rule construction called the minimum rule (MR):

- (MR0) Choose $\xi > 1$.
- (MR1) Choose the active mode such that $\sigma(x_0) \in \arg \min_{i \in \mathcal{P}} \nabla V(x_0) \cdot f_i(x_0)$.
- (MR2) Remain in the active mode while

$$x(t) \in \Omega_i \equiv \left\{ x \in \mathbb{R}^n : \nabla V(x) \cdot f_i(x) \leq -\frac{\lambda(\|x\|)}{\xi} \right\}.$$

- (MR3) If $x(t)$ crosses the boundary of Ω_i at $t = t_c$, set $x_0 \equiv x(t_c)$ and return to step (MRI).

There is trade-off in the choice of the constant ξ in Theorem 2.7: the larger the value of ξ , the more overlap between the switching regions Ω_i , resulting in a decrease in chattering behavior. On the other hand, the rate of stabilization decreases as ξ increases. The authors Liu et al. [90] also investigated the following complications: non-autonomous vector fields f_i , two-measure stability, and extending the minimum rule to a generalized rule by adding a so-called wandering rule component (to avoid Zeno behavior). The underlying state-dependent switching approach using a minimum rule and switching regions remains unchanged for these obstacles.

The state-dependent stabilizing switching rule is closed-loop in nature; the changes in active mode depend on feedback of the system state. On the other hand, an open-loop approach is also possible to stabilize a switched system composed entirely of unstable modes. Since each mode is unstable, it reasons that the switching rule should not dwell for too long in any single mode. That is, the rate of switching should be high-frequency instead of the dwell-time approach in the previous section where the system dwells in a particular mode for sufficiently long. Sun et al. [144] detailed the idea of fast-switching stabilization via periodic time-dependent switching rules for linear systems.

Example 2.3 Consider the switched system (2.2) with $\mathcal{P} = \{1, 2\}$, $f_1(x) \equiv A_1x$, $f_2(x) \equiv A_2x$,

$$A_1 = \begin{bmatrix} -9 & 1 \\ 3 & 2 \end{bmatrix}, \quad A_2 = \begin{bmatrix} 1 & -1 \\ 3 & -8 \end{bmatrix}.$$

A_1 and A_2 have eigenvalues with positive real part. The matrix $\tilde{A} \equiv 0.5A_1 + 0.5A_2$ is Hurwitz. If the modes are switched every 0.05 time units, the solution converges to the origin (see Fig. 2.11 for a simulation).

The existence of a high-frequency locally stabilizing switching rule for (2.2) is proved using the Campbell–Baker–Hausdorff [13]. The result is highlighted as follows: Given $x_0 \in \mathbb{R}^n$ and vector fields $\{f_i : i \in \mathcal{P}\}$, we seek to construct a switching rule which ensures asymptotic stability of the trivial solution of (2.2). Said another way, the switching times and switching mode sequences, i.e., the set $\{(t_k, i_k) : k \in \mathbb{N}\}$ are designed to stabilize the system and said design can be based on the current state of the system. Whenever this is possible, a similar construct for switching between feedback controllers yields a stabilizing result in the control setting. The technique is to relate the solution trajectory of (2.2) to a solution trajectory of a smooth ODE via the Campbell–Baker–Hausdorff formula (see [20, 154]). Results in this area can be found regarding nonlinear systems [13], impulsive and nonlinear systems [141], linear systems [144], eventually periodic switching rules [14], and open-loop switching stabilization control with respect to a compact set [105]. The sufficient conditions developed by Bacciotti and Mazzi [13] are highlighted here.

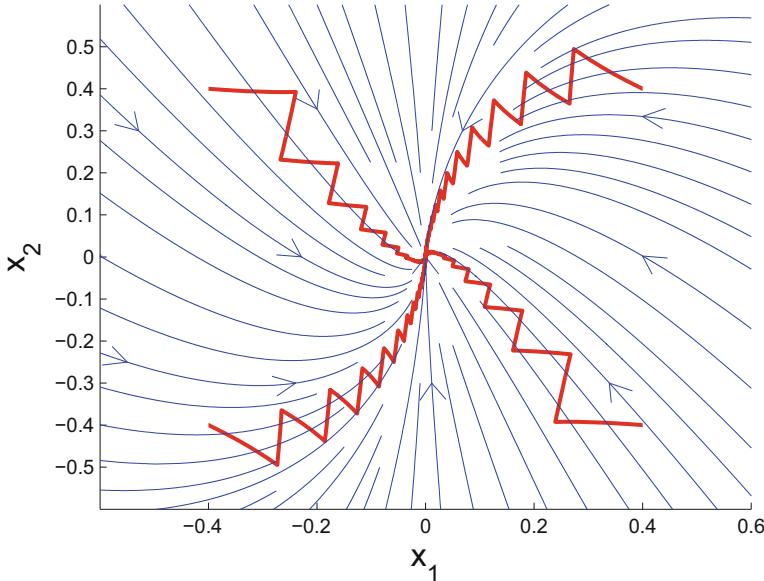


Fig. 2.11 Simulation of Example 2.3. The blue lines are solution trajectories of the ODE system $\dot{x}(t) = Ax(t)$. The red lines are solution trajectories of the switched system under periodic high-frequency switching

Theorem 2.8 Consider (2.2) and suppose that $f_i \in \mathcal{H}$ for each $i \in \mathcal{P}$ where \mathcal{H} is the space of bounded, analytic vector fields on $B_r(0)$ for some constant $r > 0$. Assume that there exist constants $\alpha_i > 0$ satisfying $\sum_{i \in \mathcal{P}} \alpha_i = 1$ such that the trivial solution of the ODE system

$$\begin{aligned} \dot{x}(t) &= \sum_{i \in \mathcal{P}} \alpha_i f_i(x(t)), \\ x(0) &= x_0, \end{aligned} \tag{2.10}$$

is asymptotically stable. Then there exists a switching rule with $\{(t_k, i_k) : i \in \mathbb{N}\}$ only depending on x_0 , such that the trivial solution of system (2.2) is asymptotically stable.

If the high-frequency switching control is inadequate, impulsive control used in combination with high-frequency switching control can achieve stabilization [141]. Consider the following switched impulsive system:

$$\begin{aligned} \dot{x}(t) &= f_\sigma(x(t)), & \forall t \notin \{T_k\}, \\ \Delta x &= g_k(x(t^-)), & \forall t \in \{T_k\}, \\ x(0) &= x_0, & k \in \mathbb{N}, \end{aligned} \tag{2.11}$$

where $\{f_i : i \in \mathcal{P}\}$ is a set of sufficiently smooth functions satisfying $f_i : D \rightarrow \mathbb{R}^n$ and $f_i(0) = 0$ for all $i \in \mathcal{P}$. (Each mode is assumed to be unstable here.) The impulsive functions $\{g_k : k \in \mathbb{N}\}$ are assumed to satisfy $x + g_k(x) \in D$ for all $x \in D$ and $g_k(0) = 0$ for all $k \in \mathbb{N}$.

Theorem 2.9 Consider the switched system (2.11) and assume that there exist constants $\alpha_i > 0$ satisfying $\sum_{i \in \mathcal{P}} \alpha_i = 1$, constants $\lambda, \delta_k, \chi_k > 0$, $\zeta_k \in (0, 1)$, and functions $c_1, c_2 \in \mathcal{K}$, $V \in C^1(D, \mathbb{R}_+)$ such that the following conditions hold:

- (i) $c_1(\|x\|) \leq V(x) \leq c_2(\|x\|)$ for all $x \in D$;
- (ii) $\nabla V(x) \cdot (\sum_{i \in \mathcal{P}} \alpha_i f_i(x)) \leq \lambda V(x)$ for all $x \in D$;
- (iii) $V(x + g_k(x)) \leq \delta_k V(x)$ for all $x \in D$ and $k \in \mathbb{N}$;
- (iv) $\ln(\delta_k) + \lambda(1 + \chi_k)(T_k - T_{k-1}) < \ln(\zeta_k)$ for all $k \in \mathbb{N}$.

Then there exists a switching rule with $\{(t_k, i_k) : i \in \mathbb{N}\}$ only depending on x_0 , such that the trivial solution of system (2.11) is asymptotically stable.

The notion that $\{(t_k, i_k)\}$ only depends on x_0 and not on the current state of the system $x(t)$ implies that this approach is an open-loop stabilizing switching rule. Moreover, it can be said to be a high-frequency approach, because of the Campbell–Baker–Hausdorff lemma only applies when the switching is sufficiently fast, which could be more desirable than a closed-loop stabilizing switching rule (i.e., the state-dependent minimum rule approach). This makes sense intuitively since each mode is assumed to be unstable here, so dwelling in any individual mode for too long should lead to instability. In the open-loop approach, chattering behavior is not an inherent issue, sensors are not required (since the information is pre-programmed), and a Lyapunov function is not required [13]. On the other hand, the frequency of switching demanded could be unrealistic for a physical system. Moreover, there is a cost associated with switching controllers, which could be a large drawback to the open-loop strategy. In the closed-loop approach, chattering can be avoided in theory by choosing ξ appropriately, though this may result in an inefficient stabilization (i.e., requiring too long for the problem at hand). Consider the following example which illustrates both methods.

Example 2.4 Consider the switched nonlinear system (2.2) and assume that $\mathcal{P} = \{1, 2\}$ with mode right-hand side functions

$$\begin{aligned} f_1(x_1, x_2) &\equiv \begin{pmatrix} 5x_1 + 2x_2^5 - x_2^2 \exp(\sin(x_1)) \\ -3x_2 - 2x_1x_2^4 \end{pmatrix}, \\ f_2(x_1, x_2) &\equiv \begin{pmatrix} -6x_1 - x_2^5 \\ 2x_2 + x_1x_2^4 + x_1x_2 \exp(\sin(x_1)) \end{pmatrix}. \end{aligned}$$

Both modes are unstable; the Jacobian matrices are evaluated as

$$Df_1(0) = \begin{bmatrix} 5 & 0 \\ 0 & -3 \end{bmatrix}, \quad Df_2(0) = \begin{bmatrix} -6 & 0 \\ 0 & 2 \end{bmatrix}.$$

Let $\alpha_1 = \alpha_2 = 0.5$ so that

$$\alpha_1 f_1(x_1, x_2) + \alpha_2 f_2(x_1, x_2) = \frac{1}{2} \begin{pmatrix} -x_1 + x_2^5 - x_2^2 \exp(\sin(x_1)) \\ -x_2 - x_1 x_2^4 + x_1 x_2 \exp(\sin(x_1)) \end{pmatrix}.$$

Letting $V(x_1, x_2) \equiv x_1^2 + x_2^2$, it follows that for any $(x_1, x_2) \in \mathbb{R}^2$,

$$\nabla V(x_1, x_2) \cdot (\alpha_1 f_1(x_1, x_2) + \alpha_2 f_2(x_1, x_2)) = -(x_1^2 + x_2^2) = -\|(x_1, x_2)\|^2.$$

The conditions of Theorem 2.7 are satisfied with $c_1(s) \equiv c_2(s) \equiv s^2$ and $\lambda(s) \equiv s^2$. The state-dependent switching rule constructed according to the minimum rule algorithm outlined in Theorem 2.7 (choose $\xi = 2$) stabilizes the system with the overlapping switching regions:

$$\begin{aligned} \Omega_1 &= \{(x_1, x_2) \in \mathbb{R}^2 : 10x_1^2 - 6x_2^2 - 2x_1 x_2^2 \exp(\sin(x_1)) \leq -(x_1^2 + x_2^2)/2\}, \\ \Omega_2 &= \{(x_1, x_2) \in \mathbb{R}^2 : -12x_1^2 + 4x_2^2 + 2x_1 x_2^2 \exp(\sin(x_1)) \leq -(x_1^2 + x_2^2)/2\}. \end{aligned}$$

The conditions of Theorem 2.8 are also satisfied, guaranteeing the existence of a high-frequency stabilizing switching rule. See Fig. 2.12 for a simulation (where a periodic switching rule with period 0.05 time units is used for the high-frequency approach).

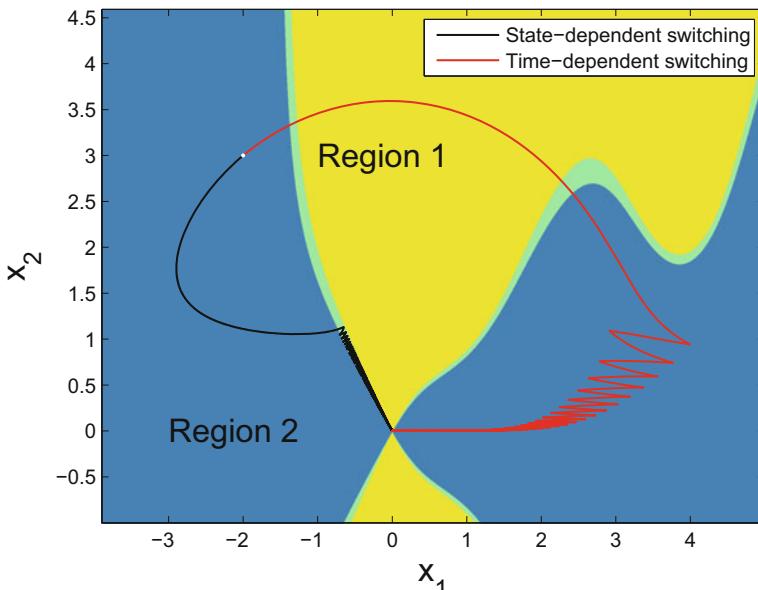


Fig. 2.12 Simulation of (2.4) with initial condition $x_0 = (-2, 3)$. The yellow regions are Ω_1 , the blue regions are Ω_2 , and the green region is the overlapping region. The solution governed by the state-dependent switching rule is given in black while the solution governed by the high-frequency switching rule is given in red

Table 2.1 Comparison of convergence times and number of switches for the state-dependent switching approach versus the high-frequency switching approach

	State-dependent switching rule		High-frequency switching rule	
	Avg. (min, max)	Std.	Avg. (min, max)	Std.
$\inf\{t : \ x\ < 0.5\ x_0\ \}$	0.051 ($\approx 0, 0.29$)	0.07	12.6 (12.1, 13.1)	0.502
Number of switches	0.147 (0, 5)	0.76	28.0 (27, 29)	1.00
$\inf\{t : \ x\ < 0.1\ x_0\ \}$	0.311 ($\approx 0, 1.92$)	0.58	44.6 (44.1, 45.1)	0.502
Number of switches	15.951 (0, 139)	43.9	92.0 (91, 93)	1.00
$\inf\{t : \ x\ < 10^{-3}\ x_0\ \}$	3.10 ($\approx 0, 11.1$)	4.46	136.7 (136, 137)	0.499
Number of switches	170.7 (0, 642)	241	276.1 (275, 277)	1.00

Given the initial condition $x_0 = (-2, 3)$, and a stabilizing threshold of $\|x(t)\| < 0.01$, the state-dependent switching rule requires 510 switches and takes a total time of 10.1. In contrast, the high-frequency switching rule requires only 229 switches, but takes a total time of 113.1. From this simulation, the state-dependent approach achieves stabilization faster, but requires more controller switching (which is disadvantageous practically). To further investigate these characteristics, Example 2.4 was simulated for 100 different initial conditions; see Table 2.1 where the mean, minimum, maximum, and standard deviation is given for $\inf\{t : \|x(t)\| < \epsilon\}$ for different values of $\epsilon > 0$. The number of switches required (as well as minimum, maximum, and standard deviation) is also tallied; this scenario is illustrated in Fig. 2.13.

The number of total switches required in the high-frequency approach depends entirely on the rate of switching that is chosen (e.g., every 0.05 time units in Fig. 2.12). In the state-dependent approach, the number of switches is less, on average, but the variance is significantly higher. Intuitively, for initial conditions close to or inside the overlapping regions (green regions in Fig. 2.12), a large difference in the number of switches can be demanded. Because of the state-dependent switching rule construction, the minimum number of switches needed can be also zero (i.e., if the initial condition is far from the boundaries). The variance in the high-frequency approach for different initial conditions is negligible since the switching rule is not state-dependent.

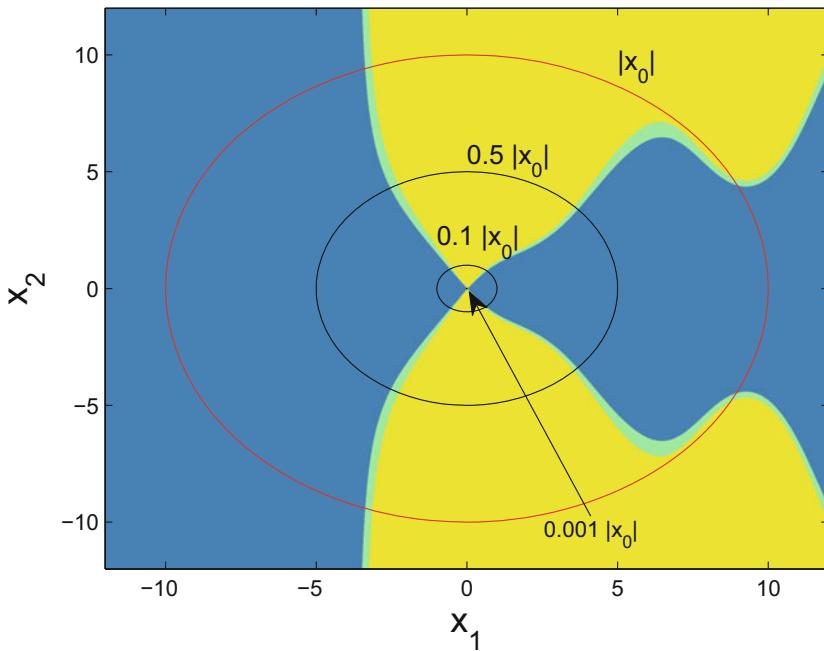


Fig. 2.13 Initial conditions used in Example 2.4 for construction of Table 2.1. The red circle contains all initial conditions considered ($x_0 \in \{(x_1, x_2) \in \mathbb{R}^2 : x_1^2 + x_2^2 = 100\}$) and the black circles represent the different convergence thresholds ($\{(x_1, x_2) \in \mathbb{R}^2 : x_1^2 + x_2^2 = \epsilon\}$)

Part II

Hybrid Infectious Disease Models

Chapter 3

The Switched SIR Model

The modeling of epidemics by hybrid and switched systems is introduced and analyzed. To begin, the classical SIR model is derived and its defining features are detailed. Motivated by variations in the contact rate between members of the population, a switched SIR model is formulated. The flexibility of the switched systems framework and its accompanying theory is highlighted by relaxing some of the population demographics and epidemiological assumptions. A switching incidence rate function form is considered to model abrupt changes in population behavior. The incorporation of stochastic perturbations into the model is also investigated. The findings here focus on the qualitative behavior of the models (i.e., stability theory). More specifically, global attractivity and partial stability are demonstrated, as well as persistence of the disease.

3.1 Model Formulation

The continuous deterministic modeling approach is taken here, where the spread of an infectious disease is modeled using switched systems of ordinary differential equations. For an example of a stochastic or discrete time approach, see [69]. Mathematical infectious disease models are built from various components that represent the physical spread of the disease. Some of these components are the epidemiological compartment structure, the incidence rate form, the compartmental waiting time distributions, the population demographic structure, and the epidemiological-demographic interactions [64]. Because there are many choices for these various components, the combinatorial possibilities are enormous. There are a number of modifications and extensions which depend critically on the disease being modeled [116]. The interest of this monograph is dealing with the spread of acute infectious diseases, which are conferred to individuals and have a relatively short lifespan. In this chapter, the classical epidemic models

are briefly reviewed. Motivated by seasonal variations, a new switched systems framework is introduced and applied. Stability of the so-called disease-free solution is investigated using switched systems techniques. The flexibility of this modeling approach is highlighted through modeling shifting public perception of an oncoming or current epidemic, which is accomplished by switched incidence rate function forms. Stochasticity is also considered here via noise in the contact patterns between individuals in a population.

The spread of an infectious disease is modeled by dividing the population into appropriate compartments (or groups) which display different characteristics relative to the disease, and considering interactions and movements between the compartments. The reader is assumed to be familiar with the classical epidemic modeling and analysis (see the excellent references [2, 4, 34, 69, 116]). Suppose that the population of individuals (e.g., humans) at a snapshot in time (e.g., $t = 0$) is given by N_0 (a positive integer). The population can be subdivided into individuals that are infected with the disease, I_0 , individuals that are susceptible, S_0 , and those who have recovered from the disease or are removed altogether from the disease-spreading interactions, R_0 . That is,

$$S_0 + I_0 + R_0 = N_0.$$

At a later time, suppose that some individuals have moved from the susceptible group to the infected (i.e., new infections), while some infected have moved to the removed group (e.g., via naturally conferred immunity, disease-induced death, etc.). Then

$$S_1 + I_1 + R_1 = N_0$$

where $S_1 < S_0$ and $R_1 > R_0$. Without more information, it is not clear whether $I_1 \leq I_0$ (decrease in cases of infection) or $I_1 > I_0$ (increase in cases of infection); the mechanisms with which individuals move between the compartments need to be modeled more precisely to understand the time-evolution of the disease. A number of assumptions on these interactions are made to build the full dynamic model. Consider the continuous-time case under the assumption that the total population, N_0 , is sufficiently large. Similarly, let the number of infected at an arbitrary time $t > 0$ be denoted by $I(t) > 0$. Under the continuum assumption, $I(t)$ need not be integral here, but fractional values are understood as approximations for the number of infected.

Begin as follows [65]: Define the fraction of individuals remaining in the infected group at time $t > 0$ by

$$P(t) \equiv \frac{I(t)}{I_0},$$

and the rate at which the infected are removed by

$$L(t) \equiv -\frac{dP}{dt}(t).$$

It follows that the average infectious period is given by

$$W \equiv \int_0^\infty tL(t)dt = \int_0^\infty t(-\frac{dP}{dt}(t))dt.$$

Assuming that it is a well-defined operation, integrating by parts yields that

$$W = [-tP(t)]_{t=0}^{t=\infty} + \int_0^\infty P(t)dt.$$

If $\lim_{t \rightarrow \infty} tP(t) = 0$, which necessarily requires that $\lim_{t \rightarrow \infty} P(t) = 0$, it follows that

$$W = \int_0^\infty P(t)dt.$$

As a simplifying assumption, suppose that the period of infection is distributed around a mean value; let $P(t) \equiv \exp(-gt)$ for some $g > 0$. Then

$$W = \frac{\exp(-gt)}{g} \Big|_{t=0}^{t \rightarrow \infty} = \frac{1}{g};$$

the infected are removed linearly, with removal rate g . This leads to the first modeling assumption:

- (A1) The rate of removal of infected is $g > 0$ with an exponential distributed waiting time.

This assumption gives the following dynamic relationship:

$$\frac{dI}{dt}(t) = -gI(t). \quad (3.1)$$

Equation (3.1) details the rate of removal of infected individuals due to the infectious period passing. If the infected gain natural immunity at time t , they enter the recovered (or removed) class, denoted by $R(t)$ at time t ,

$$\frac{dR}{dt}(t) = gI(t). \quad (3.2)$$

Before proceeding, we should mention another possibility for P is a step function:

$$P(t) \equiv \begin{cases} 1, & \text{if } 0 \leq t \leq \tau, \\ 0, & \text{if } t \geq \tau, \end{cases}$$

for some $\tau > 0$, corresponding to a mean waiting time of τ and leading to a delay differential equation. This modeling choice leads to a time-delayed differential

equation formulation, which will be revisited later. In general, P can be a piecewise differentiable, nonincreasing function satisfying $P(0) = 1$ and

$$\lim_{t \rightarrow \infty} tP(t) = 0.$$

The mechanism of the disease spread is modeled by horizontal transmission (i.e., due to interactions between individuals in the population) between infected individuals and the susceptible, denoted by $S(t)$ at time t . (Other possibilities, such as mother-newborn vertical transmission or mosquito-human vector-borne transmission, are discussed in Chap. 4). From basic principles, the incidence rate is constructed as follows: let $\beta_c > 0$ be the average number of contacts between individuals in the population per unit time, $p_c \in [0, 1]$ be the probability that an average contact is sufficient for transmission. Letting $N(t)$ denote the total population at time t , the incidence rate of new infections per unit time at t is equal to

$$\beta_c p_c S(t) \frac{I(t)}{N(t)},$$

since $I(t)/N(t)$ represents the probability the susceptible is coming into contact with an infected. The underlying assumptions being made are as follows:

- (A2) The rate of increase of infected (and decrease of susceptible) is proportional to the number of susceptible and fraction of infected present.
- (A3) The population mixes homogeneously.

Assumption (A2) corresponds to the so-called standard incidence rate (rather than, e.g., the mass-action incidence rate, among others discussed in Sect. 3.5). The assumption (A3) is made implicitly by the above arguments. A more realistic assumption is to separate the population into different age groups and assign appropriate contact rates $\beta_c^{(i,j)}$ for age group i mixing with age group j . For now, the homogeneous assumption is made. Other physiological mechanisms that are not being considered include the following:

- (A4) The duration of the disease incubation period is negligible compared to the other dynamics of the disease.
- (A5) The population dynamics are negligible when considering the timescale for the dynamics of the disease.

Assumption (A4) corresponds to the absence of an exposed group (i.e., those in the latent stage but not yet infectious); when a susceptible individual makes adequate contact with an infected individual, they enter the infected group immediately. Assumption (A5) corresponds to a closed population; births/deaths and immigration/emigration are not being considered. Piecing together Eqs. (3.1) and (3.2), along with an appropriate differential equation for S , gives the following ODE system:

$$\begin{aligned}\frac{dS}{dt}(t) &= -\beta S(t) \frac{I(t)}{N(t)}, \\ \frac{dI}{dt}(t) &= \beta S(t) \frac{I(t)}{N(t)} - gI(t), \\ \frac{dR}{dt}(t) &= gI(t).\end{aligned}\tag{3.3}$$

Since the population is closed, and without considering any other groups, the total population $N(t) = S(t) + I(t) + R(t)$ is expected to equal a constant value for all t . Indeed,

$$\begin{aligned}\frac{dN}{dt}(t) &= \frac{dS}{dt}(t) + \frac{dI}{dt}(t) + \frac{dR}{dt}(t), \\ &= -\beta S(t) \frac{I(t)}{N(t)} + \beta S(t) \frac{I(t)}{N(t)} - gI(t) + gI(t), \\ &= 0,\end{aligned}$$

so that $N(t) = N_0$ for all t . Alternatively, the population dynamics could be taken into account by modeling unbounded exponential growth or decay:

$$\frac{dN}{dt}(t) = (b - d)N(t),$$

where $b > d > 0$ or $d > b > 0$, respectively. The assumption above corresponds to $b, d \approx 0$ (i.e., the dynamics of the disease are much shorter than the average human life-span). This is not appropriate when the timescale involved is much longer (i.e., the so-called endemic case) or when disease-induced deaths are significant.

Comparing the density-dependent (also called mass-action) incidence rate, ηSI , with the above formulation $\beta S \frac{I}{N}$ gives that the mass-action coefficient,

$$0 < \eta \equiv \frac{\beta}{N_0}.$$

That is, the contact rate $\beta = \eta N$ increases linearly with the population size. However, as detailed by Hethcote [65], this is a naive assumption: the daily contact patterns of individuals in a human population are mostly unaffected once a threshold population is reached (i.e., when considering medium-sized cities to large-sized cities). This assumption will be further explored when general switched incidence rates are analyzed in Sect. 3.5.

Initial conditions are added to the ODE system (3.3) to form an initial value problem. Moreover, the variables are normalized to represent fractions of individuals in each class: $\hat{S} \equiv S/N_0$, $\hat{I} \equiv I/N_0$, and $\hat{R} \equiv R/N_0$. Thus,

$$\frac{d\widehat{S}}{dt}(t) = \frac{dS}{dt}(t) \frac{1}{N_0} = -\beta S(t) \frac{I(t)}{N(t)} \frac{1}{N_0} = -\beta \frac{S(t)}{N_0} \frac{I(t)}{N_0} = -\beta \widehat{S}(t) \widehat{I}(t).$$

With similar calculations for the differential equations governing \widehat{I} and \widehat{R} , and after dropping the hats, the ODE initial value problem is given by the following system:

$$\begin{aligned}\dot{S}(t) &= -\beta S(t) I(t), \\ \dot{I}(t) &= \beta S(t) I(t) - g I(t), \\ \dot{R}(t) &= g I(t),\end{aligned}\tag{3.4}$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

which is sometimes called the classical epidemic model. The notation $\dot{S} \equiv \frac{dS}{dt}$ is adopted going forward. The initial conditions are assumed to satisfy $S_0, I_0, R_0 \in [0, 1]$ and $S_0 + I_0 + R_0 = 1$ and the initial time has been set as $t_0 \equiv 0$ without loss of generality (since the right-hand side function is autonomous). $S_0 > 0$ and $I_0 > 0$ is generally assumed to make the problem biologically interesting. The domain of the right-hand side function in (3.4), i.e.,

$$(S, I, R) \mapsto \begin{bmatrix} -\beta SI \\ \beta SI - gI \\ gI \end{bmatrix}$$

is the physically meaningful domain

$$D_{(3.4)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\}$$

from the physiological considerations outlined above. The notation convention for the physically meaningful domain, $D_{(*)}$, will persist through this monograph; $(*)$ corresponds to the ODE system associated with the domain. It is straightforward to see that $D_{(3.4)}$ is positively invariant to (3.4):

$$\dot{S}|_{S=0} = \mu > 0, \quad \dot{I}|_{I=0} = 0, \quad \dot{R}|_{R=0} = gI \geq 0,$$

and

$$[\dot{S} + \dot{I} + \dot{R}]|_{S+I+R=0} = 0.$$

As a result of the positive invariance of the compact set $D_{(3.4)}$, along with the continuous differentiability of the right-hand side functions in the SIR model (3.4), Theorem 1.3 implies that a unique solution exists on \mathbb{R}_+ for each

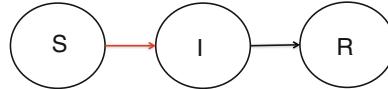


Fig. 3.1 Flow diagram of the SIR system (3.4). The *red line* represents horizontal transmission of the disease and the *black line* represents recovery

$(S_0, I_0, R_0) \in D_{(3.4)}$. It should also be noted that the differential equation for R is often omitted for simplification, since the other equations do not depend directly on R . See Fig. 3.1 for the flow diagram associated with (3.4).

Remark 3.1 The positive invariance of the meaningful domain can be demonstrated more formally by defining the auxiliary functions $V^{(1)}(S, I, R) \equiv S$, $V^{(2)}(S, I, R) \equiv I$, $V^{(3)}(S, I, R) \equiv R$, $V^{(4)}(S, I, R) \equiv S + I + R$. It follows that

$$\begin{aligned}\dot{V}_{(3.4)}^{(1)}(0, I, R) &= \mu > 0, \\ \dot{V}_{(3.4)}^{(2)}(S, 0, R) &= 0, \\ \dot{V}_{(3.4)}^{(3)}(S, I, 0) &= gI \geq 0, \\ \dot{V}_{(3.4)}^{(4)}(S, I, R) &= 0.\end{aligned}$$

For the remainder of this monograph, the more informal notation is used to demonstrate positive invariance of the physically meaningful domains with this understanding in mind.

3.2 Threshold Criteria: The Basic Reproduction Number

To analyze the short and long-term behavior of the classical epidemic model (3.4), a mathematical analysis is needed to reveal the underlying mechanisms driving the spread of the disease and yield conclusions with respect to its qualitative behavior. For example, if there is an epidemic (i.e., an outbreak of the disease among the population), it is desirable to estimate its duration and severity. From this, measures can be taken to prevent, or at least limit, an epidemic. To uncover the principles dictating the answers to these questions, we turn to some important qualitative features of the classical epidemic model (3.4). First, we detail the basic reproduction number of (3.4):

$$R_0^{(3.4)} \equiv \frac{\beta}{g};$$

this ratio is the mean number of secondary infections caused by a single infected individual, during their infectious period, when exposed to a wholly susceptible population. Observe that

$$R_0^{(3.4)} = \frac{d(\beta_c p_c I)}{dI}(0) \frac{1}{S_0} = \beta_c p_c \frac{1}{g}$$

since $S_0 = 1$ in a wholly susceptible population ($I_0 = 0, R_0 = 0$) and

$$\frac{d(\beta_c p_c I)}{dI}(0) = 1$$

(i.e., rate of change of infected at introduction of a single infected). The mapping $I \mapsto \beta_c p_c I$ is called the force of infection and varies for different infectious diseases of interest (i.e., epidemiological assumptions) and population behaviors.

Other threshold values in epidemic modeling include [65]: the contact number (not to be confused with the contact rate as outlined earlier) and the replacement number. These two numbers are, respectively, the average number of adequate contacts of a typical infected during their infectious period and the average number of secondary infections produced by one infected during their infectious period (i.e., the number of secondary cases caused by one infected). The basic reproduction number, contact number, and replacement number are all equal at $t = 0$. As detailed in [65]: the contact number remains constant (and equal to the basic reproduction number) for most epidemiological models (the model of pertussis in Sect. 8 of [65] is a counter-example), while the replacement number becomes strictly less than the contact number after invasion (because the susceptible fraction is reduced to less than one and thus subsequent sufficient contacts between individuals may be between two infected).

The focus of the analyses here will be on threshold criteria involving the basic reproduction number. Basic reproduction numbers for a variety of real-world diseases are listed in Table 3.1 (other real-world epidemiological data of interest can be found in [4]). Theory for the calculation and approximation of basic reproduction numbers for autonomous epidemic models [35, 152] and periodic epidemic models [7, 8, 11, 159] has been developed.

Table 3.1 Epidemiological data [4]

Disease	Infectious period (days)	Average age at infection (years)	R_0
Measles	6–7	4.4–5.6	13.7–18.0
Whooping cough	21–23	4.1–5.9	14.3–17.1
Rubella	11–12	10.5	6.7
Chicken pox	10–11	6.7	9.0
Poliomyelitis	14–20	11.2	6.2

In some cases, closed-form expressions can be obtained for the basic reproduction number, as is the case for the classical epidemic model. In the notation of [152], $F = \beta$ and $V = g$ so that the next-generation matrix for the model (3.4) is $FV^{-1} = \beta/g$; F is the rate at which infected individuals produce new infections (which is derived from the linearization of (3.4) about the disease-free solution, as above) and V^{-1} is the average period of infection. In general, the basic reproduction number is defined as the spectral radius of the next-generation matrix (i.e., $R_0^{(3.4)} = \beta/g$, as above). See Sect. 4.2 for a more complex derivation of a basic reproduction number using the next-generation matrix.

Remark 3.2 The notation $R_0^{(*)}$ is reserved for the basic reproduction number associated with the epidemic model (*) throughout this monograph.

At $t = 0$,

$$\dot{I}(0) = I_0(\beta S_0 - g).$$

Hence, $\dot{I}(0) > 0$ if $S_0 > g/\beta$ and $\dot{I}(0) \leq 0$ if $S_0 \leq g/\beta$. For all $t \geq 0$, $\dot{S}(t) \leq 0$ implies that $S(t) \leq S_0$ and thus $\dot{I}(t) = I(t)(\beta S(t) - g) \leq I(t)(\beta S_0 - g) \leq 0$. From this it follows that $I(t) \leq I_0$ for all $t \geq 0$ if $S_0 - g/\beta \leq 0$ which is equivalent to $R_0^{(3.4)}S_0 \leq 1$. We are now in a position to make some important observations regarding the classical epidemic model (3.4) [116]:

1. The basic reproduction number acts as a threshold criteria as there is no epidemic/outbreak (in the sense that $I(t)$ does not increase at any time during the evolution of the disease) if $R_0^{(3.4)}S_0 \leq 1$.
2. If $R_0^{(3.4)}S_0 > 1$, the severity of the epidemic can be determined as follows:

$$\frac{\dot{I}}{\dot{S}} = \frac{\beta SI - gI}{\beta SI} = -1 + \frac{g}{\beta S},$$

for $S > 0$, from which it follows that

$$I(t) + S(t) - \frac{g \ln(S(t))}{\beta} = I_0 + S_0 - \frac{g \ln(S_0)}{\beta}.$$

The maximum value of I , i.e., the most severe stage of the epidemic, occurs when the rate of change of infected is zero, which occurs when $S = g/\beta$, implying that

$$I_{\max} \equiv \frac{g}{\beta} \ln\left(\frac{g}{\beta}\right) - \frac{g}{\beta} + I_0 + S_0 - \frac{g}{\beta} \ln S_0 = 1 - \frac{g}{\beta} + \frac{g}{\beta} \ln\left(\frac{g}{\beta S_0}\right),$$

assuming that $R_0 = 0$.

3. The long-term behavior of the susceptible population can be analyzed by noting that

$$\frac{\dot{S}}{\dot{R}} = -\frac{\beta S}{g},$$

so that

$$S(t) = S_0 \exp(-\beta R(t)/g).$$

From this, it is possible to conclude that [116]

$$\lim_{t \rightarrow \infty} S(t) = S^*$$

where $S^* \in (0, g/\beta)$ is the root of the nonlinear equation system

$$S_0 \exp\left(-\frac{\beta(1 - S^*)}{g}\right) = S^*.$$

The disease eventually dies out from a lack of infected, not a lack of susceptible individuals.

3.3 Seasonal Variations in Disease Transmission: Term-Time Forcing

Epidemic models traditionally assume that the contact rate is constant [63, 65, 69, 116], as was the case in the SIR model (3.4) with β . However, seasonal variations play an important role in the spread of a disease. Empirical studies have demonstrated seasonal variation in the transmission of many infections, for example, the transmission of childhood infections peak at the start of the school year and decline significantly in the summer months [69]. Measles, mumps, rubella, chickenpox, poliomyelitis, diphtheria, pertussis, and influenza all display periodicity in their transmission [66]. Disease-spreading factors affected by seasonality include the following [3, 34, 39, 53, 69]:

- (a) changes in host immunity (physiological changes in host susceptibility) and differences in host behavior (e.g., summer breaks for children of school age);
- (b) changes in the abundance of vector agents (e.g., mosquito population from weather and temperature differences throughout the seasons);
- (c) changes in the survivability of pathogens;
- (d) seasonal timing of reproduction in some animal populations.

There has been some work done in the literature on models which assume that the contact rate is a smoothly varying function. For example, a periodic HIV model was studied in [168], a periodic tuberculosis model was analyzed in [91], a seasonal model of cutaneous leishmaniasis was investigated in [11], and a pulse model with seasonality was studied in [68]. Other studies can be found in [6, 10, 52, 53, 69, 87, 103, 118, 128, 138] and the references therein. In this modeling framework, the

time-constant contact rate assumption is replaced by a smoothly varying contact rate given as

$$\beta(t) \equiv \beta_0(1 + \epsilon \cos(2\pi t)), \quad (3.5)$$

where $\beta_0 > 0$ is the base contact rate and $\epsilon > 0$ captures seasonal variations.

It is important to acknowledge that the transmission data has been shown in some cases to more accurately match a term-time forcing model (where the contact rate changes abruptly in time) [44]. Schenzle first considered this type of epidemic model in [133] (see also [44, 70] for example). Analytical methods for dealing with time-dependent contact rates are lacking, in general, and are an important phenomenon to explore further since relatively modest variations in the contact rate can result in large amplitude fluctuations in the disease incidence [69]. A term-time forcing contact rate is modeled as

$$\beta(t) \equiv \beta_0(1 + \epsilon)^{\text{term}(t)} = \begin{cases} \beta_0(1 + \epsilon), & \text{during school terms,} \\ \frac{\beta_0}{1+\epsilon}, & \text{otherwise,} \end{cases} \quad (3.6)$$

i.e.,

$$\text{term}(t) \equiv \begin{cases} 1, & \text{during school terms,} \\ -1, & \text{otherwise.} \end{cases}$$

The main focus of this monograph is on the latter term-time forcing approach. Along this line, suppose that

$$\beta(t) \equiv \beta_1, \quad \forall t \in [0, t_1),$$

where $t_1 > 0$ is a time at which there is a shift in the contact rate (e.g., due to a school closure or the beginning of a rainy season for a vector-borne disease). Suppose that

$$\beta(t) \equiv \beta_2, \quad \forall t \in [t_1, t_2),$$

where $t_2 > t_1$ denotes the next time of interest with respect to a change in population interactions. Continuing this model design, this naturally fits into a switched systems framework: Define the finite index set $\mathcal{M} \equiv \{1, \dots, m\}$ and the switching times $\{t_k\}$ satisfying $t_{k-1} < t_k$ for all $k \in \mathbb{N}$ and $t_k \rightarrow \infty$ as $k \rightarrow \infty$ such that $\beta(t)$ is piecewise constant taking values from the set of possible contact rate values

$$\{\beta_i > 0 : i \in \mathcal{M}\} = \{\beta_1, \dots, \beta_m\}.$$

That is,

$$\beta(t) \equiv \beta_{i_k}, \quad \forall t \in [t_{k-1}, t_k),$$

where $i_k \in \mathcal{M}$ and $\beta_{i_k} \in \{\beta_1, \dots, \beta_m\}$ for each $k \in \mathbb{N}$ (i.e., a piecewise constant formulation). This leads to a switched ODE system reformulation of the classical epidemic model (3.4):

$$\begin{aligned}\dot{S}(t) &= -\beta_\sigma S(t)I(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t), \\ \dot{R}(t) &= gI(t),\end{aligned}\tag{3.7}$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

where $\beta_\sigma : \mathbb{R}_+ \rightarrow \{\beta_1, \dots, \beta_m\}$ ($\beta_\sigma \equiv \beta_{\sigma(t)}$ is used for notational brevity) and $\sigma \in \mathcal{S}_{\text{dwell}}$ is a dwell-time satisfying switching rule, mapping \mathbb{R}_+ to \mathcal{M} (piecewise constant, continuous from the right). This formulation includes the term-time forced contact rate outlined above with $\mathcal{M} = \{1, 2\}$ and the set of contact rates $\{\beta_0(1 + \epsilon), \beta_0/(1 + \epsilon)\}$, and

$$\sigma(t) \equiv \begin{cases} 1, & \text{during school terms,} \\ 2, & \text{otherwise.} \end{cases}$$

Remark 3.3 The meaningful domain of (3.7), $D_{(3.7)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\}$, is positively invariant to (3.7). As a consequence of the positive invariance of the compact set $D_{(3.7)}$; the continuous differentiability of each mode of (3.7), i.e., the mappings

$$(S, I, R) \mapsto \begin{bmatrix} \beta_i SI \\ \beta_i SI - gI \\ gI \end{bmatrix}, \quad \forall i \in \mathcal{M};$$

and the dwell-time satisfying switching rule σ , the method of steps (i.e., solving the initial value problem for the current switching interval followed by a reinitialization at the switching time) may be applied to conclude a unique solution of (3.7) exists on \mathbb{R}_+ . Henceforth, any mention of a solution corresponds to the unique solution existing on \mathbb{R}_+ and passing through an initial condition in $D_{(3.7)}$ and parameterized by a particular switching rule σ . This result persists throughout this monograph, but is not always mentioned explicitly (in special cases such as the case of stochastic perturbations, more careful consideration is given). $t_0 = 0$ is taken without loss of generality and σ will be assumed to be dwell-time satisfying for the epidemic models in this monograph (though not always mentioned explicitly).

3.4 Adding Population Dynamics: The Classical Endemic Model

Next we revisit assumption (A5) and consider the SIR ODE system (3.4) with population dynamics. Incorporate births/deaths by assuming that the mean lifetime of an individual is distributed about a mean value of $1/\mu > 0$. That is, the birth rate is given by $\mu > 0$ per unit time. For now, we make the following assumptions: there are no disease-induced deaths and all offspring are born susceptible. Mathematically, this is translated into the classical epidemic model (3.4) as follows: the rate of change of susceptible population from population dynamics is

$$\dot{S}(t) = \mu(S(t) + I(t) + R(t)) = \mu N(t)$$

where $N(t)$ is the total population. Similarly, $\dot{I}(t) = -\mu I(t)$ and $\dot{R}(t) = -\mu R(t)$. $\dot{N}(t) = 0$ still holds in this case, implying that $S(t) + I(t) + R(t) = S_0 + I_0 + R_0$ for all $t \geq 0$, as before. Hence, after normalization, the full model with switching contact rate is given by

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0).\end{aligned}\tag{3.8}$$

The flow of (3.8), including the population dynamics, is shown in Fig. 3.2. Positive invariance of the meaningful physical domain,

$$D_{(3.8)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\},$$

to (3.8) follows exactly as in Sect. 3.1 for the classical epidemic model;

$$\dot{S}|_{S=0} = \mu > 0, \quad \dot{I}|_{I=0} = 0, \quad \dot{R}|_{R=0} = gI \geq 0,$$

and $S(t) + I(t) + R(t) = 1$ for all $t \geq 0$ given that $(S_0, I_0, R_0) \in D_{(3.8)}$.

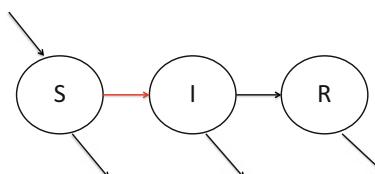


Fig. 3.2 Flow diagram of the SIR model (3.8) with population dynamics. The *red line* represents horizontal transmission of the disease. The *black lines* represent recovery and births/deaths

Before analyzing the long-term behavior of the SIR model (3.8), the qualitative behavior of the time-constant version (i.e., the classical endemic model) is presented. Namely, the so-called classical endemic model

$$\begin{aligned}\dot{S}(t) &= \mu - \beta S(t)I(t) - \mu S(t), \\ \dot{I}(t) &= \beta S(t)I(t) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0).\end{aligned}\tag{3.9}$$

To find equilibria, consider the following nonlinear equation system:

$$\begin{aligned}0 &= \mu - \beta SI - \mu S, \\ 0 &= \beta SI - (g + \mu)I, \\ 0 &= gI - \mu R,\end{aligned}\tag{3.10}$$

which admits two solutions:

$$\left\{(1, 0, 0), \left(\frac{\mu + g}{\beta}, \frac{\mu(\beta - g - \mu)}{\beta(\mu + g)}, \frac{g(\beta - g - \mu)}{\beta(\mu + g)}\right)\right\}$$

The vector

$$Q_{\text{DFS}}^{(3.9)} \equiv (1, 0, 0) \in D_{(3.9)} = D_{(3.8)}$$

is called the disease-free equilibrium or disease-free solution (DFS) of (3.9). The vector

$$\begin{aligned}&\left(\frac{\mu + g}{\beta}, \frac{\mu(\beta - g - \mu)}{\beta(\mu + g)}, \frac{g(\beta - g - \mu)}{\beta(\mu + g)}\right) \\ &= \left(\frac{1}{R_0^{(3.9)}}, \frac{\mu}{\mu + g} \left(1 - \frac{1}{R_0^{(3.9)}}\right), \frac{g}{\mu + g} \left(1 - \frac{1}{R_0^{(3.9)}}\right)\right) \\ &\equiv Q_{\text{ES}}^{(3.9)}\end{aligned}$$

is called the endemic equilibrium or endemic solution (ES), where

$$R_0^{(3.9)} \equiv \frac{\beta}{\mu + g}\tag{3.11}$$

is the basic reproduction number of the classical endemic model (the contact rate, β , multiplied by the average death-adjusted infectious period, $1/(\mu + g)$). The endemic solution satisfies

$$Q_{\text{ES}}^{(3.9)} \in D_{(3.9)}$$

if and only if $R_0^{(3.9)} \geq 1$ (and there is a bifurcation $Q_{\text{DFS}}^{(3.9)} = Q_{\text{ES}}^{(3.9)}$ at $R_0^{(3.9)} = 1$). The disease-free solution and endemic solution are given their names precisely because the disease is absent in the disease-free solution and is present in the endemic solution.

Remark 3.4 The notation $Q_{\text{DFS}}^{(*)}$ and $Q_{\text{ES}}^{(*)}$ is adopted here as the disease-free solution and endemic solution of the epidemic model (*), respectively.

The classical endemic model (3.9) experiences a bifurcation at $R_0^{(3.9)} = 1$: if $R_0^{(3.9)} \leq 1$, then the disease-free solution is globally asymptotically stable (GAS) in the meaningful domain $D_{(3.9)}$, while if $R_0^{(3.9)} > 1$ then the endemic solution is GAS in $D_{(3.9)}$ [63]. Intuitively, $R_0^{(3.9)} < 1$ implies that a single infected produces less than one infection, during their infectious period, when introduced into a wholly susceptible population. Consequently, if a large fraction of the population is infected, the replacement number should be less than one, dictating eradication of the disease.

On the other hand, if $R_0^{(3.9)} > 1$, then the solution trajectory of (3.9) approaches the endemic solution with damped oscillations, with period of oscillations approximately equal to [69]:

$$2\pi \sqrt{\left(\frac{1}{\mu(R_0^{(3.9)} - 1)}\right)\left(\frac{1}{\mu + g}\right)}$$

where

$$\frac{1}{\mu(R_0^{(3.9)} - 1)}$$

is the average age of infection and $\frac{1}{\mu+g}$ is the death-adjusted average period of infectiousness. This part can be explained with a biological interpretation [65]: when $R_0^{(3.9)} > 1$, the contact and replacement numbers are necessarily greater than one at the initial time. At the introduction of an infected population $I_0 > 0$, each infected is infecting more than one susceptible, on average, resulting in a decrease of the susceptible population S_0 . This process continues until the susceptible population is sufficiently low so as to have a slowing affect on the spread of the disease.

The population dynamics replenish the susceptible population and the remaining infected restart the process (i.e., once the contact number multiplied by the fraction of susceptible $S(t)$ is sufficiently large for another epidemic to occur). Here “sufficiently large” is precisely the point at which the replacement number is equal to one, which occurs when the contact number multiplied by the susceptible population is equal to one. This is the balancing point of the disease (i.e., the endemic equilibrium) since otherwise if the replacement number were greater than or less than one, the infected population would increase or decrease, respectively. See Fig. 3.3 for an illustration of these concepts (also Figs. 5 and 6 in [65]).

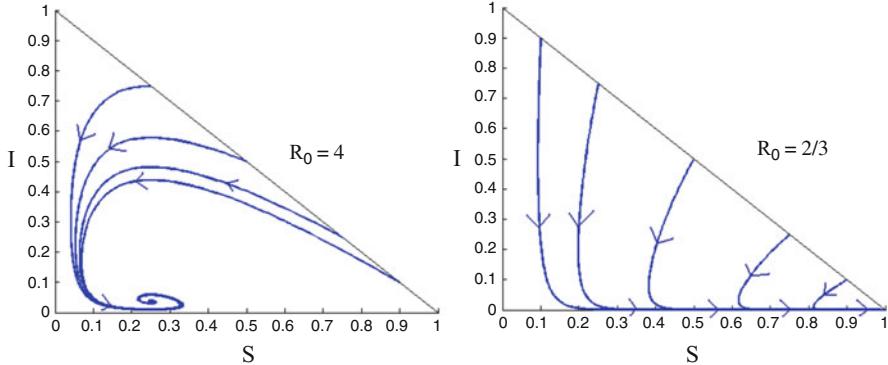


Fig. 3.3 Phase plane portraits of SIR model (3.9) with different initial conditions and basic reproduction numbers

Returning to the switched SIR model (3.8), the following observations are made:

1. Equation (3.8) admits the steady-state solution $(S(t), I(t), R(t)) \equiv (1, 0, 0)$ (i.e., the disease free solution is a common equilibrium of (3.8)).
2. Each mode of (3.8) admits the equilibrium

$$\left(\frac{\mu + g}{\beta_i}, \frac{\mu(\beta_i - g - \mu)}{\beta_i(\mu + g)}, \frac{g(\beta_i - g - \mu)}{\beta_i(\mu + g)} \right).$$

Again $D_{(3.8)}$ is positively invariant to the SIR model (3.8). The expression $R_0^{(3.9)}$ is no longer the basic reproduction number for the switched SIR system (3.8) due to the time-varying contact rate. Define the mode basic reproduction numbers

$$R_0^{(3.8),i} \equiv \frac{\beta_i}{\mu + g}, \quad \forall i \in \mathcal{M}, \quad (3.12)$$

then the endemic solution for each mode can be rewritten as

$$Q_{ES}^{(3.8),i} \equiv \left(\frac{1}{R_0^{(3.8),i}}, \frac{\mu}{\mu + g} \left(1 - \frac{1}{R_0^{(3.8),i}} \right), \frac{g}{\mu + g} \left(1 - \frac{1}{R_0^{(3.8),i}} \right) \right). \quad (3.13)$$

Any one of these endemic solutions are in the meaningful domain $D_{(3.8)}$ if and only if $R_0^{(3.8),i} \geq 1$, and are equal to the DFS whenever $R_0^{(3.8),i} = 1$. It is not true that $R_0^{(3.8),i}$ are the basic reproduction numbers of (3.8), though they do play a role in the behavior of (3.8). For example, if $R_0^{(3.8),i} < 1$ for all $i \in \mathcal{M}$, then $\beta_{\max} \equiv \max\{\beta_1, \dots, \beta_m\} > g + \mu$. From this it follows that $\lim_{t \rightarrow \infty} I(t) = 0$ since

$$\dot{I}(t) = \beta_\sigma S(t)I(t) - (g + \mu)I(t) \leq (\beta_{\max} - g - \mu)I(t) < 0,$$

and, furthermore, $\dot{I}(t) < 0$ unless $S(t) = 1$ or $I(t) = 0$. That is, the disease is eradicated. Alternatively, if $R_0^{(3.8),i} > 1$ for all $i \in \mathcal{M}$, then

$$\dot{I}(t) \geq (\beta_{\min} S(t) - \mu - g)I(t) = (\min\{R_0^{(3.8),i}\}S(t) - 1)I(t).$$

However, in the case that $R_0^{(3.8),i} \leq 1$ for some $i \in \mathcal{M}$ and $R_0^{(3.8),i} \geq 1$ for the remaining modes, the characteristic long-term behavior needs to be formally analyzed.

Motivated by the periodicity in the smoothly varying and term-time forcing contact rates outlined earlier, recall that $\mathcal{S}_{\text{periodic}}$ is the set of switching rules for which $\sigma(t + \omega) = \sigma(t)$, with switching times satisfying $t_k - t_{k-1} = \tau_k$ and $\tau_{k+m} = \tau_k$. The dependence of $\mathcal{S}_{\text{periodic}}$ on ω may be given explicitly or not. Note that $\mathcal{S}_{\text{periodic}}(\omega) \subset \mathcal{S}_{\text{dwell}}(\tau^*)$ where $\tau^* \equiv \min\{\tau_i : i \in \mathcal{M}\}$; periodic switching rules are dwell-time satisfying and therefore furnish a solution that exists globally given initial conditions in the meaningful domain (which is positively invariant to (3.8)). If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ in (3.8), then $\beta_{\sigma(t)} = \beta_k$ for all $t \in [t_{k-1}, t_k]$, $k \in \mathbb{N}$, with $\beta_{k+m} = \beta_k$. That is, the contact rate is periodic, with period ω : $\beta_{\sigma(t+\omega)} = \beta_{\sigma(t)}$. In this case, the basic reproduction number can be calculated according to the theory of [8, 159] and disease eradication can be shown.

Theorem 3.1 *Let $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and*

$$R_0^{(3.8)} \equiv \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < 1, \quad (3.14)$$

Then, given $(S_0, I_0, R_0) \in D_{(3.8)}$, the unique solution of the switched SIR system (5.4) converges to the disease-free solution $Q_{\text{DFS}}^{(3.8)}$.

Proof Given $(S_0, I_0, R_0) \in D_{(3.8)}$, the unique solution of (3.8) satisfies

$$\dot{I}(t) \leq \beta_\sigma S(t)I(t) - (g + \mu)I(t) \leq (\beta_\sigma - g - \mu)I(t), \quad (3.15)$$

since $S(t) \in [0, 1]$ for all $t \geq 0$. It follows that

$$I(t) \leq I_0 + \int_0^t \lambda_\sigma I(s)ds, \quad (3.16)$$

where $\lambda_i \equiv \beta_i - g - \mu$ for each $i \in \mathcal{M}$, and, by Gronwall's Inequality,

$$\begin{aligned} I(\omega) &\leq I_0 \exp\left(\sum_{i=1}^m \lambda_i \tau_i\right), \\ &= I_0 \exp\left((\mu + g) \sum_{i=1}^m (R_0^{(3.8),i} - 1) \tau_i\right), \\ &= I_0 \exp(\eta), \end{aligned}$$

where $\eta \equiv \exp\left((\mu + g) \sum_{i=1}^m (R_0^{(3.8),i} - 1)\tau_i\right) < 1$ from the basic reproduction number threshold (3.14). Thus, $I(\omega) \leq I_0\eta < I_0$. It can be similarly shown that $I(2\omega) \leq I(\omega)\eta < I(\omega)$ and, in general, $I(h\omega) \leq I((h-1)\omega)$ for any $h \in \mathbb{N}$. Therefore,

$$I(h\omega) \leq \eta^h I_0, \forall h \in \mathbb{N},$$

and the sequence $\{I(h\omega)\}$ is monotonically decreasing and converges to zero.

Define $v(t) = \exp[\lambda_{i_1}(t_1) + \dots + \lambda_{i_k}(t - t_{k-1})]$ for $t \in [t_{k-1}, t_k]$ and suppose that $t_k \in (0, \omega]$. Then since $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$,

$$\begin{aligned} v(t + \omega) &= v(t) \exp[\lambda_k(t_k - t) + \lambda_{k+1}\tau_{k+1} + \dots + \lambda_m\tau_m] \\ &\quad \times \exp[\lambda_{m+1}\tau_{m+1} + \lambda_{m+2}\tau_{m+2} + \dots + \lambda_{m+k}(t + \omega - (t_{k-1} + \omega))], \\ &= v(t) \exp[\lambda_k(t_k - t) + \lambda_{k+1}\tau_{k+1} + \dots + \lambda_m\tau_m] \\ &\quad \times \exp[\lambda_1\tau_1 + \lambda_2\tau_2 + \dots + \lambda_k(t - t_{k-1})], \\ &= v(t) \exp\left[\sum_{i=1}^m \lambda_i\tau_i\right]. \end{aligned}$$

That is, $v(t + \omega) < v(t)$ for $t \in [t_{k-1}, t_k]$. By repeating the arguments, $\{I(\epsilon + h\omega)\}$ converges to zero for any $\epsilon \in [0, \omega)$. Hence,

$$\lim_{t \rightarrow \infty} I(t) = 0.$$

The limiting system of (3.8) with $I(t) \equiv 0$ is given by

$$\begin{aligned} \dot{S}(t) &= \mu - \mu S(t), \\ \dot{R}(t) &= -\mu R(t), \end{aligned} \tag{3.17}$$

from which it follows that $\lim_{t \rightarrow \infty} R(t) = 0$, and, by the invariance of $S + I + R = 1$, implies that $\lim_{t \rightarrow \infty} S(t) = 1$, as required.

In the periodic switching rule case, the threshold criteria for disease eradication in Eq. (3.14) can be reformulated in terms of the mode basic reproduction numbers;

$$\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} = \frac{1}{\omega} \sum_{i=1}^m R_0^{(3.8),i} \tau_i = R_0^{(3.8)},$$

the basic reproduction number equals the time-weighted average of the mode basic reproduction numbers.

Remark 3.5 The basic reproduction number $R_0^{(3.8)}$ is defined as above only if $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and thus $R_0^{(3.8)} = R_0^{(3.8)}(\sigma)$. With this understanding in place, notation giving explicit dependence on the switching rule is avoided going forward. On the other hand, the notation $R_0^{(*),i}$ is reserved for mode basic reproduction numbers associated with the switched epidemic model (*).

Furthermore, if $m = 1$ (i.e., time-constant contact rate), then $\tau_1 = \omega$ and

$$R_0^{(3.8)} = \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} = \frac{\beta_1(\tau_1)}{\omega(\mu + g)} = R_0^{(3.9)},$$

the basic reproduction of the classical endemic model (3.9) is recovered. Seeking an expression that estimates the peak number of cases of the disease, we let

$$\begin{aligned}\mathcal{M}^+ &\equiv \{i \in \mathcal{M} : R_0^{(3.8),i} \geq 1\}, \\ \mathcal{M}^- &\equiv \{i \in \mathcal{M} : R_0^{(3.8),i} < 1\}.\end{aligned}$$

From (3.16),

$$I(t) \leq I_0 \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i \right) = I_0 \exp \left((\mu + g) \sum_{i \in \mathcal{M}^+} (R_0^{(3.8),i} - 1) \tau_i \right) \equiv I_{\max}, \quad \forall t \geq 0,$$

whenever $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, since $\{I(h\omega)\}$ is a monotonically decreasing sequence and $I(t) \leq I(\omega)$ for all $t \geq \omega$. The severity of the epidemic is bounded as

$$I(t) \leq I_{\max} < 1, \quad \forall t \geq 0.$$

Moreover, given $\epsilon > 0$, choosing $\delta = \epsilon \exp(-\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i)$ implies that $|I(t)| = I(t) < \epsilon$ whenever $|I_0| = I_0 < \delta$. As a result of these observations, the following corollary can be given.

Corollary 3.1 *If the conditions of Theorem 3.1 hold, then in addition the disease-free solution $Q_{\text{DFS}}^{(3.8)}$ is globally asymptotically I -stable in the physically meaningful domain $D_{(3.8)}$.*

Theorem 3.1 states that, given an initial condition $(S_0, I_0, R_0) \in D_{(3.8)}$, the unique solution passing through (S_0, I_0, R_0) that exists on \mathbb{R}_+ satisfies $\lim_{t \rightarrow \infty} (S(t), I(t), R(t)) = (1, 0, 0)$; the disease-free solution $Q_{\text{DFS}}^{(3.8)}$ is globally attractive in the physically meaningful domain $D_{(3.8)}$ and disease eradication is achieved. Corollary 3.1 provides information on the possible severity of an epidemic; given an initial condition (S_0, I_0, R_0) with I_0 relatively small then I remains relatively small (i.e., partial stability).

In the non-periodic case, a time-weighted average of the mode basic reproduction numbers gives an appropriate threshold condition for disease eradication. Recall that the total activation time of the i th mode on $[0, t]$ is denoted by

$$T_i(0, t) \equiv T_i(t) \equiv |\{t \in [0, t] : \sigma(t) = i\}|.$$

Theorem 3.2 *If $\sigma \in \mathcal{S}_{\text{dwell}}$ and*

$$\left\langle R_0^{(3.8)} \right\rangle \equiv \sup_{t \geq h} \frac{\sum_{i=1}^m \beta_i T_i(t)}{t(\mu + g)} < 1, \quad (3.18)$$

for some $h > 0$, then $Q_{\text{DFS}}^{(3.8)}$ is globally attractive and exponentially I-stable in the physically meaningful domain $D_{(3.8)}$.

Proof By Eq. (3.15),

$$I(t) \leq I(t_{k-1}) \exp(\lambda_{i_k}(t - t_{k-1})), \quad \forall t \in [t_{k-1}, t_k], \quad (3.19)$$

for any $k \in \mathbb{N}$, where $\lambda_i \equiv \beta_i - \mu - g$ for each $i \in \mathcal{M}$. Applying this inequality successively gives that $I(t) \leq I_0 \exp(\lambda_{i_1} t)$ for all $t \in [0, t_1]$,

$$I(t) \leq I(t_1) \exp(\lambda_{i_2}(t - t_1)) \leq I_0 \exp(\lambda_{i_1} t_1 + \lambda_{i_2}(t - t_1)), \quad \forall t \in [t_1, t_2],$$

and, in general,

$$I(t) \leq I_0 \exp(\lambda_{i_1} t_1 + \dots + \lambda_{i_k}(t - t_{k-1})), \quad (3.20)$$

$$= I_0 \exp \left[\sum_{i=1}^m \lambda_i T_i(t) \right], \quad (3.21)$$

for all $t \in [t_{k-1}, t_k]$.

The threshold $\left\langle R_0^{(3.8)} \right\rangle < 1$ in (3.18) implies the existence of $\epsilon > 0$ such that

$$\sum_{i=1}^m \beta_i T_i(t) < (1 - \epsilon)(\mu + g)t, \quad \forall t \geq h.$$

Hence,

$$\sum_{i=1}^m (\beta_i - \mu - g) T_i(t) < -\epsilon(\mu + g)t$$

since $t = \sum_{i=1}^m T_i(t)$. Thus,

$$\sum_{i=1}^m \lambda_i T_i(t) < -\epsilon(\mu + g)t, \quad \forall t \geq h, \quad (3.22)$$

Returning to the bound on I , it follows from Eq. (3.22) that

$$\begin{aligned} I(t) &\leq I_0^* \exp\left(\sum_{i=1}^m \lambda_i T_i(t)\right), \\ &\leq I_0^* \exp(-\epsilon(\mu + g)t), \quad \forall t \geq h, \end{aligned}$$

where $I_0^* \equiv I_0 \sum_{i=1}^m \lambda_i T_i(h)$. The result follows since

$$\dot{R}(t) = gI(t) - gR(t) \leq I_0 \exp(-\epsilon(\mu + g)t) - gR(t)$$

for all $t \geq h$ and $S(t) = 1 - R(t) - I(t)$ for all t .

The mode sets \mathcal{M}^+ and \mathcal{M}^- introduced earlier can be used to give a worst-case approximation of the contact rate variations (and their occurrence) as these sets roughly represent the unstable and unstable modes, respectively. Note that $\mathcal{M} = \mathcal{M}^+ \cup \mathcal{M}^-$ and $\mathcal{M}^+ \subseteq \mathcal{M}$ and $\mathcal{M}^- \subseteq \mathcal{M}$. Defining the sets

$$\begin{aligned} T^+(t) &\equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^+\}|, \\ T^-(t) &\equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^-\}|, \end{aligned}$$

this leads to a more easily verifiable condition on the model parameters, as compared to the previous result.

Theorem 3.3 *If $\sigma \in \mathcal{S}_{\text{dwell}}$ satisfies $T^+(t) \leq N_0 + qT^-(t)$ for some $q \in (0, 1)$ and $N_0 \geq 0$ such that*

$$q\lambda^+ < \lambda^-, \tag{3.23}$$

where $\lambda^- \equiv |\max\{\lambda_i : i \in \mathcal{M}^-\}|$ and $\lambda^+ \equiv \max\{\lambda_i : i \in \mathcal{M}^+\}$, then the conclusions of Theorem 3.2 hold; the disease is eradicated.

Proof Note that $t = T^+(t) + T^-(t) \leq N_0 + (1 + q)T^-(t)$. Starting from Eq. (3.15),

$$\begin{aligned} I(t) &\leq I_0 \exp\left(\sum_{i=1}^m \lambda_i T_i(t)\right), \\ &= I_0 \exp\left(\sum_{i \in \mathcal{M}^+} \lambda_i T_i(t) + \sum_{i \in \mathcal{M}^-} \lambda_i T_i(t)\right), \\ &\leq I_0 \exp(\lambda^+ T^+(t) - \lambda^- T^-(t)), \\ &\leq I_0 \exp(\lambda^+ (N_0 + qT^-(t)) - \lambda^- T^-(t)), \end{aligned}$$

$$\begin{aligned}
&= \leq I_0 \exp(\lambda^+ N_0 + (q\lambda^+ - \lambda^-) T^-(t)), \\
&\leq I_0^* \exp\left(\left(\frac{q\lambda^+ - \lambda^-}{1+q}\right)t\right),
\end{aligned}$$

where $I_0^* \equiv I_0 \exp(\lambda^+ N_0 - N_0(q\lambda^+ - \lambda^-)/(1+q))$. Exponential I -stability holds and global attractivity follows as in the proof of Theorem 3.1.

Returning to the definitions of the mode basic reproduction numbers in (3.12),

$$\langle R_0^{(3.8)} \rangle = \sup_{t \geq h} \frac{\sum_{i=1}^m \beta_i T_i(t)}{t(\mu + g)} = \sup_{t \geq h} \frac{1}{t} \left(\sum_{i=1}^m R_0^{(3.8),i} T_i(t) \right) = \sup_{t \geq h} \frac{1}{t} \left(\int_0^t R_0^{(3.8),\sigma(s)} ds \right)$$

is a time-weighted average of the mode basic reproduction numbers. Similarly, $\lambda^- - q\lambda^+ < 0$ is equivalently written as

$$(\beta^- - \mu - g) < q(\beta_{\max} - \mu - g)$$

where $\beta_{\max} \equiv \max\{\beta_1, \dots, \beta_m\}$ and $\beta^- \equiv \max\{\beta_i : i \in \mathcal{M}^-\}$ represent the worst-case contact rate and most conservative estimate of a “stabilizing” contact rate (i.e., one for which the disease would die out given no other contact rate variations), respectively. Equivalently,

$$R_0^{(3.8),-} - 1 < q(R_0^{(3.8),+} - 1),$$

where $R_0^{(3.8),+} \equiv \max\{R_0^{(3.8),i} : i \in \mathcal{M}^+\}$ and $R_0^{(3.8),-} \equiv \max\{R_0^{(3.8),i} : i \in \mathcal{M}^-\}$ represent the worst-case mode basic reproduction number and most conservative estimate of mode basic reproduction numbers that display “stabilizing” behavior whenever the set of modes \mathcal{M}^- are active. The ratio of time spent in the stable modes versus the unstable modes must be sufficiently large (captured by the constant q).

The threshold conditions outlined above are sufficient for disease eradication. Whenever they do not hold or cannot be evaluated in a straightforward way from the data available, it is of interest to conclude persistence of the disease (see [148]).

Definition 3.1 The disease is said to persist uniformly in (3.8) if there exists $\eta > 0$ (independent of initial conditions in $D_{(3.8)}$ which are assumed to satisfy $I_0 > 0$) such that the solution satisfies $\liminf_{t \rightarrow \infty} I(t) \geq \eta$.

Theorem 3.4 If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(3.8)} > 1$, then the disease persists uniformly in (3.8).

Proof The proof proceeds in two parts. First it is shown that the disease is weakly uniformly persistent; i.e., there exists $c > 0$ for which $\limsup_{t \rightarrow \infty} I(t) > c$. If this were not true, then for any $\epsilon > 0$ it must be true that $\limsup_{t \rightarrow \infty} I(t) < \epsilon$. From the switched SIR system (3.8),

$$\dot{S}(t) = \mu - \beta_\sigma S(t)I(t) - \mu S(t) \geq \mu - \beta_{\max}\epsilon - \mu S(t), \quad \forall t \geq 0,$$

where $\beta_{\max} \equiv \max\{\beta_1, \dots, \beta_m\}$. The ODE system

$$\begin{aligned}\dot{S}_m(t) &= \mu - \beta^*\epsilon - \mu S_m(t), \\ S_m(t_0) &= S_0,\end{aligned}$$

admits the unique solution

$$S_m(t) \equiv \left(S_0 - 1 + \frac{\beta_{\max}\epsilon}{\mu} \right) \exp(-\mu t) + 1 - \beta_{\max}$$

on \mathbb{R}_+ such that $\lim_{t \rightarrow \infty} S_m(t) = 1 - \beta_{\max}$. $S(t) \geq S_m(t)$ for all $t \geq 0$ by the comparison theorem (i.e., Theorem 1.9), from which it follows that for any $\epsilon > 0$, there must exist a time t^* for which $S(t) \geq 1 - \beta_{\max}\epsilon/\mu - \epsilon$ for $t \geq t^*$.

Then

$$\dot{I}(t) = \beta_k(S, I) - (g + \mu)I(t) \geq (\beta_k - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_k)I(t), \quad \forall t \in [t_{k-1}, t_k],$$

such that $t_{k-1} > t^*$, and thus,

$$\begin{aligned}I(t) &\geq I(t^*) \exp \left(\int_{t^*}^t (\beta_\sigma - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_\sigma) ds \right), \\ &= I(t^*) \exp \left(\int_{t^*}^{t^* + (k-1)\omega} (\beta_\sigma - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_\sigma) ds \right) \\ &\quad + I(t^*) \exp \left(\int_{t^* + (k-1)\omega}^t (\beta_\sigma - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_\sigma) ds \right), \\ &\geq I^* \exp \left((k-1) \int_0^\omega (\beta_\sigma - g - \mu) ds - (k-1)\omega\epsilon(1 + \beta_{\max}/\mu)\beta_{\max} \right),\end{aligned}$$

where $I^* \equiv I(t^*) \exp(-(g + \mu)\omega - \epsilon(1 + \beta_{\max}/\mu)\beta_{\max}\omega)$. Choose ϵ to satisfy

$$0 < \epsilon \leq \frac{\int_0^\omega (\beta_\sigma - g - \mu) ds}{2\beta_{\max}(1 + \beta_{\max}/\mu)} = \frac{(\int_0^\omega (g + \mu) ds)(R_0^{(3.8)} - 1)}{2\beta_{\max}(1 + \beta_{\max}/\epsilon)}.$$

It follows that $\lim_{t \rightarrow \infty} I(t) = \infty$, which is a contradiction; the disease is weakly uniformly persistent.

Next uniform persistence is demonstrated. By weak uniform persistence, there exists $\hat{t} > 0$ for which $I(\hat{t}) > c$ is satisfied. Two cases need to be analyzed to move towards uniform persistence: (i) $I(t) \geq c$ for all $t \geq \hat{t}$ and (ii) $I(t)$ oscillates about c for large t . In case (i), letting $\eta \equiv c$ leads to the desired result. In considering (ii),

choose $t^2 > t^1 > \hat{t}$ such that $I(t^1) = I(t^2) = c$ and $I(t) < c$ for $t \in (t^1, t^2)$. Let $A \equiv S + I$ so that

$$\dot{A}(t) = \mu - \beta_\sigma S(t)I(t) - \mu S(t) + \beta_\sigma S(t)I(t) - (g + \mu)I(t) = \mu - gI(t) - \mu A(t).$$

If $I(t) \leq c$ holds, then

$$\dot{A}(t) = \mu - gI(t) - \mu A(t) > \mu - gc - \mu A(t).$$

Let

$$c \equiv \frac{\mu(R_0^{(3.8)} - 1)}{2gR_0^{(3.8)}}.$$

In this case,

$$\dot{A}(t) > \mu - g \frac{\mu(R_0^{(3.8)} - 1)}{2gR_0^{(3.8)}} - \mu A(t) = \frac{\mu}{2} \left(1 + \frac{1}{R_0^{(3.8)}} \right) - \mu A(t).$$

The ODE system

$$\begin{aligned}\dot{A}_m(t) &= \frac{\mu}{2} \left(1 + \frac{1}{R_0^{(3.8)}} \right) - \mu A_m(t), \\ A_m(t^1) &= A(t^1),\end{aligned}$$

admits a unique solution on $[t^1, \infty)$ which satisfies

$$\lim_{t \rightarrow \infty} A_m(t) = 0.5(1 + 1/R_0^{(3.8)}) \equiv A_m^*$$

and $A_m(t) \downarrow A_m^*$ as $t \rightarrow \infty$ (i.e., approaches from above), by inspection. Therefore, there exists $\bar{t} > 0$ such that

$$A(t) > 0.5(1 + 1/R_0^{(3.8)}), \quad \forall t > t^1 + \bar{t}. \quad (3.24)$$

Without loss of generality, let $h \in \mathbb{N}$ be such that $t^1 \in [t_{h-1}, t_h)$. For any $k \in \mathbb{N}$ satisfying $k > h$,

$$\begin{aligned}\dot{I}(t) &= \beta_k(A(t) - I(t))I(t) - (g + \mu)I(t) \\ &> \beta_k \left(\frac{1}{2} \left(1 + \frac{1}{R_0^{(3.8)}} \right) - I(t) \right) I(t) - (g + \mu)I(t), \quad \forall t \in [t_{k-1}, t_k].\end{aligned}$$

Define the mapping

$$I_m(t) \equiv \frac{c \exp \left(\int_{t^1}^{t_h} \lambda_h ds + \int_{t_h}^{t_{h+1}} \lambda_{h+1} ds + \dots + \int_{t_{k-1}}^t \lambda_k ds \right)}{1 + c\Phi(t)}, \quad t \in [t_{k-1}, t_k),$$

where

$$\lambda_i \equiv \frac{1}{2} \left(1 + \frac{1}{R_0^{(3.8)}} \right) \beta_i - g - \mu, \quad \forall i \in \mathcal{M},$$

and

$$\begin{aligned} \Phi(t) \equiv & \int_{t^1}^{t_h} \beta_h \exp(\lambda_h(s - t^1)) ds \\ & + \int_{t_h}^{t_{h+1}} \beta_{h+1} \exp(\lambda_h(t_h - t^1) + \lambda_{h+1}(s - t_h)) ds \\ & + \dots + \int_{t_{k-1}}^t \beta_k \exp(\lambda_h(t_h - t^1) + \dots + \lambda_k(s - t_{k-1})) ds. \end{aligned}$$

Then I_m is the solution of the ODE system

$$\begin{aligned} \dot{I}_m(t) &= \beta_k \left(\frac{1}{2} \left(1 + \frac{1}{R_0^{(3.8)}} \right) - I_m(t) \right) I_m(t) - (g + \mu) I_m(t), \quad \forall t \in [t_{k-1}, t_k), \\ I_m(t^1) &= c, \end{aligned} \tag{3.25}$$

on $[t^1, \infty)$, since there is no finite blow-up time in the closed-form solution.

Note also that (3.25) admits the following periodic solution:

$$\tilde{I}(t) \equiv \frac{I^* \exp(\lambda_h(t_h - t^1) + \lambda_{h+1}(t_{h+1} - t_h) + \dots + \lambda_k(t - t_{k-1}))}{1 + I^* \Phi(t)},$$

where

$$I^* \equiv \frac{\exp(\sum_{i=1}^m \lambda_i \tau_i) - 1}{\Phi(t^h + \omega)}.$$

Noting that

$$\sum_{i=1}^m \lambda_i \tau_i = \omega(g + \mu)(R_0^{(3.8)} - 1) > 0,$$

$\lim_{t \rightarrow \infty} \Phi(t) = \infty$ and

$$\lim_{t \rightarrow \infty} \exp \left(\int_{t^1}^{t_h} \lambda_h ds + \int_{t_h}^{t_{h+1}} \lambda_{h+1} ds + \dots + \int_{t_{k-1}}^t \lambda_k ds \right) = \infty.$$

Then,

$$\lim_{t \rightarrow \infty} |I_m(t) - \tilde{I}(t)| = 0,$$

from which it follows that there exists $\tilde{t} > 0$ satisfying

$$I_m(t) > \rho \equiv 0.5 \min\{\tilde{I}(t) : t \in [t^1, t^1 + \omega]\} > 0, \quad \forall t \geq t^1 + \tilde{t}.$$

Let $q \equiv \max\{\tilde{t}, \tilde{t}\}$ and

$$\eta \equiv \min \left(\rho, c \exp \left(- \left(\int_{t^1}^{t^2} (g + \mu) ds \right) \right) \right).$$

If $t^2 - t^1 < q$ holds, then

$$\dot{I}(t) = \beta_k(A(t) - I(t))I(t) - (g + \mu)I(t) > -(g + \mu)I(t), \quad \forall t \in [t_{k-1}, t_k], \quad (3.26)$$

so that

$$I(t) \geq c \exp \left(- \left(\int_{t^1}^t (g + \mu) ds \right) \right) \geq c \exp \left(- \left(\int_{t^1}^{t^2} (g + \mu) ds \right) \right).$$

Thus, $I(t) \geq \eta$ for all $t \in (t^1, t^2)$. On the other hand, if $t^2 - t^1 > q$, let $H_1 \equiv [t^1, t^1 + q]$ and $H_2 \equiv [t^1 + q, t^2]$. By repeating the above arguments, $I(t) \geq \eta$ holds for all $t \in H_1$. From (3.24) and (3.26),

$$\dot{I}(t) \geq \beta_k \left(0.5 \left(1 + \frac{1}{R_0^{(3.8)}} \right) - I(t) \right) I(t) - (g + \mu)I(t), \quad \forall t \in [t_{k-1}, t_k],$$

which implies that $I(t) \geq I_m(t) \geq \rho \geq \eta$ for all $t \in H_2$. As $[t^1, t^2]$ was chosen arbitrarily and η does not depend on the solution of (3.8), the result holds.

Example 3.1 Motivated by seasonal variations, consider the following periodic switching rule:

$$\sigma(t) \equiv \begin{cases} 1, & \text{during the winter months,} \\ 2, & \text{otherwise.} \end{cases}$$

That is, $\mathcal{M} = \{1, 2\}$, $\tau_1 = 0.25$, $\tau_2 = 0.75$ and $\omega = 1$. Let $S_0 = 0.7$, $I_0 = 0.3$, and $R_0 = 0$, with model parameters $\beta_1 = 3$ during the winter months, $\beta_2 = 1$ during other seasons, $\mu = 0.1$, and $g = 0.9$. Hence, $R_0^{(3.8).1} = 3$ and $R_0^{(3.8).2} = 1$;

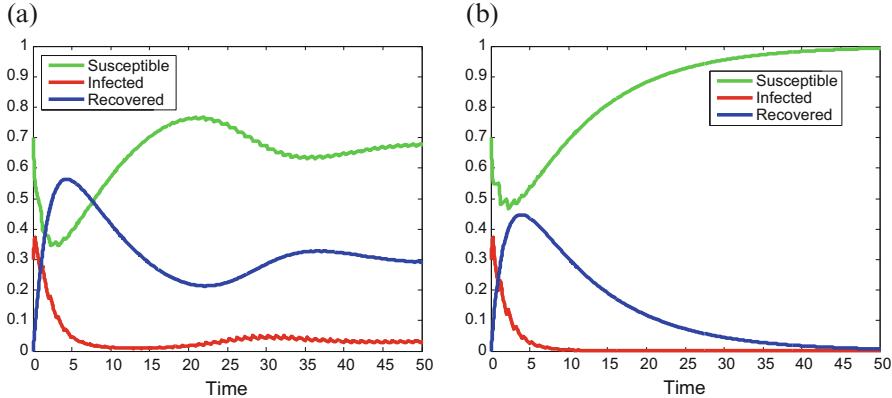


Fig. 3.4 Simulations of (3.8). **(a)** $\beta_1 = 3$ and $\beta_2 = 1$. **(b)** $\beta_1 = 3$ and $\beta_2 = 0.3$

$$R_0^{(3.8)} = \frac{1}{\omega} \left(R_0^{(3.8),1} \tau_1 + R_0^{(3.8),2} \tau_2 \right) = 1.5,$$

implying persistence of the disease by Theorem 3.4. If $\beta_2 = 0.3$, then $R_0^{(3.8)} = 0.975$ and the disease is eradicated by Theorem 3.1. See Fig. 3.4 for a simulation with these model parameters.

3.5 Generalizing the Incidence Rate of New Infections

Variations in the contact rate alters the spread of the disease, and therefore its basic reproduction number. It is not correct to characterize the switched SIR system (3.8) as having m basic reproduction numbers given by $R_0^{(3.8),i}$ or as having the basic reproduction number $R_0^{(3.8),ik}$ on the switching interval $[t_{k-1}, t_k]$. (It is reasonable to discuss the mode-specific reproduction numbers when considering the modes of the switched system in isolation). For example, for a general dwell-time satisfying switching rule $\sigma \in \mathcal{S}_{\text{dwell}}$,

$$R_0^{(3.8)} \neq \sup_{t \geq h} \frac{\sum_{i=1}^m \beta_i T_i(t)}{t(\mu + g)} = \langle R_0^{(3.8)} \rangle;$$

the basic reproduction number is not equal to the weighted average outlined in (3.18) under general switching.

In general, the basic reproduction number of a general compartmental infectious disease model is defined as the spectral radius of a next-generation matrix [35, 152]. Closed-form expressions for a variety of compartmental models have been found

(see [93] for a list). The basic reproduction number of (3.8) is implicitly defined as the spectral radius of a next-generation integral operator:

$$R_0^{(3.8)} \equiv \rho(L),$$

where the operator L acts on the space of continuous functions:

$$L(\phi) \equiv \int_0^\infty K(t, s)\phi(t - s)ds,$$

with $K(t, s)$ being the rate of secondary infections produced at time t by an infected at time $t - s$ [10, 11]. For example, in the classical endemic SIR model (3.9) [10],

$$K(t, s) = \beta \exp\left(-\int_{t-s}^t (g + \mu)ds\right) = \beta \exp(-(g + \mu)s) = \beta \tilde{P}(s),$$

where the derivative of $\tilde{P}(s) \equiv \exp(-(g + \mu)s)$ represents the rate at which infected are removed (recall the definition $P(t) \equiv \exp(-gt)$ in Sect. 3.1).

Again, this may be interpreted as the average secondary number of infections produced by a single infected, during their entire infectious period, when introduced into a wholly susceptible population. However, in the periodic switching case (i.e., given that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$), the basic reproduction number of (3.8) can be calculated as follows:

$$\frac{\frac{1}{\omega} \int_0^\omega \beta_\sigma dt}{\frac{1}{\omega} \int_0^\omega (g + \mu)dt} = \frac{\sum_{i=1}^m \beta_i}{\omega(\mu + g)} = \frac{1}{\omega} \sum_{i=1}^m R_0^{(3.8),i} \tau_i = R_0^{(3.8)}.$$

Observe that $R_0^{(3.8)} < 1$ if and only if (3.14) holds.

The mapping $f_{\text{standard}}(S, I) \equiv \beta SI$ used so far to model horizontal transmission in the population is called the standard incidence rate (or proportionate mixing incidence rate). However, it is not always the most appropriate modeling choice. For example, a saturation incidence rate is given by the function

$$f_{\text{sat}}(S, I) \equiv \frac{\beta SI}{1 + \nu S},$$

for some $\nu \in (0, 1)$ (see, e.g., [49, 92, 122]). It is called a saturation incidence rate because there is a saturating effect as the number of susceptible increases:

$$\frac{\partial^2 f_{\text{sat}}}{\partial S^2}(S, I) \equiv \frac{-2\beta\nu I}{(1 + \nu S)^3} \leq 0.$$

When the fraction of infected is relatively high in a population, exposure to the disease is almost certain and the transmission rate slows [73, 74]. Compare this to the standard incidence rate $f_{\text{standard}}(S, I)$, which satisfies

$$\frac{\partial^2 f_{\text{standard}}}{\partial S^2}(S, I) \equiv 0.$$

Incorporate this into the switched SIR model (3.8) by replacing the switching standard incidence rate with a switching saturation incidence rate to yield the following ODE system:

$$\begin{aligned}\dot{S}(t) &= \mu - \frac{\beta_\sigma S(t)I(t)}{1 + \nu S(t)} - \mu S(t), \\ \dot{I}(t) &= \frac{\beta_\sigma S(t)I(t)}{1 + \nu S(t)} - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0).\end{aligned}\tag{3.27}$$

System (3.27) again admits the DFS $(1, 0, 0)$ and has the meaningful domain

$$D_{(3.27)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\} = D_{(3.8)},$$

which is positively invariant. Therefore, a unique solution of (3.27) exists in \mathbb{R}_+ given $(S_0, I_0, R_0) \in D_{(3.27)}$ and a dwell-time satisfying switching rule $\sigma \in \mathcal{S}_{\text{dwell}}$. Supposing that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, the basic reproduction number of (3.27) is calculated as

$$R_0^{(3.27)} \equiv \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)(1 + \nu)}.$$

The relationship

$$R_0^{(3.27)} < R_0^{(3.8)}$$

holds for $\sigma \in \mathcal{S}_{\text{periodic}}$, which can be explained by the saturating effect in a wholly susceptible population. Observe that

$$\dot{I}(t) = \frac{\beta_\sigma S(t)I(t)}{1 + \nu S(t)} - (g + \mu)I(t) \leq \left(\frac{\beta_\sigma}{1 + \nu} - (g + \mu) \right) I(t), \quad \forall t \geq 0.\tag{3.28}$$

Replacing $\lambda_i \equiv \beta_i - \mu - g$ by $\lambda_i \equiv \beta_i/(1 + \nu) - \mu - g$ for each $i \in \mathcal{M}$ in the proof of Theorem 3.1, it follows that the solution of (3.27) converges to the DFS if $R_0^{(3.27)} < 1$. In fact, on the basis of (3.28), the other eradication results in the previous section are easily extended to this model using instead the mode basic reproduction numbers

$$R_0^{(3.27),i} \equiv \frac{\beta_i}{(\mu + g)(1 + \nu)}.$$

As discussed earlier, the (pseudo) mass-action incidence rate is inconsistent with the known result that daily contact patterns are largely independent of community size [65]. On the other hand, the standard incidence rate f_{standard} is consistent with this observed result [73] but homogeneous mixing is assumed. Alternative nonlinear incidence rate modeling choices include the following:

1. *Saturating incidence rates.* For example, $f(S, I) \equiv \beta S^p I^q$, $\beta > 0$, $0 < p < 1$ [73, 74], $f(S, I) \equiv SI(a - bc^{-vI})$ with constants a , b , c , v [38], and $f(S, I) \equiv \beta I(1 - cI)S$, where c is a constant [64].
2. *Nonstandard incidence rates.* For example, $f(S, I) \equiv \beta S I^p (1 - I)^{q-1}$ with $p > 1$, $q \geq 1$, $\beta > 0$ [38], and $f(S, I) \equiv \beta S I(1 - vI^p)$, $\beta > 0$, $v > 0$, $p \geq 0$ [151], which take into account psychological effects in which the susceptible take extra measures to avoid infection during the occurrence of a severe epidemic. This results in a decrease in the incidence of new cases as the infected fraction increases [38].
3. *General incidence rate formulations.* For example, $f(t, S, I) \equiv h(t, I)S$, where $h(t, I)$ is called the force of infection satisfying, e.g., $h(t, I) \leq \frac{dh}{dt}(t, 0)I$ [38].

This motivates an analysis of (3.8) with a switching incidence rate of a general form. Let \mathcal{F} denote the set of incidence rates $\{f_i : i \in \mathcal{M}\}$ which necessarily satisfy, for each $i \in \mathcal{M}$, the following conditions:

- (a) $f_i(S, I)$ is smooth in S and I ;
- (b) $f_i(S, I) > 0$ for all $(S, I) \in (0, 1]^2$;
- (c) $f_i(0, I) = 0$ for $I \in [0, 1]$ and $f_i(S, 0) = 0$ for $S \in [0, 1]$;
- (d) $\frac{\partial f}{\partial I}(S, I) \geq 0$ and $\frac{\partial f}{\partial S}(S, I) \geq 0$ for $(S, I) \in [0, 1]^2$.

For other examples of compartmental epidemic models with various incidence rate forms, see [38, 64, 73, 80, 83, 92, 93, 111].

Under the above assumptions, the switched SIR model takes on the following form:

$$\begin{aligned} \dot{S}(t) &= \mu - f_\sigma(S(t), I(t)) - \mu S(t), \\ \dot{I}(t) &= f_\sigma(S(t), I(t)) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t), \end{aligned} \tag{3.29}$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0).$$

The meaningful domain for system (3.29) is

$$D_{(3.29)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\} = D_{(3.8)}.$$

By the assumptions on \mathcal{F} ,

$$\{\dot{S} + \dot{I} + \dot{R}\}|_{S+I+R=1} = 0,$$

$\dot{S}|_{S=0} = \mu > 0$, $\dot{I}|_{I=0} = 0$, and $\dot{R}|_{R=0} = gI \geq 0$; $D_{(3.29)}$ is positively invariant to (3.29). Moreover, (3.29) admits the disease-free solution $(1, 0, 0)$. From the non-switched study in [73], if

$$\frac{\partial^2 f_i}{\partial I^2}(S, I) \leq 0$$

for each $(S, I) \in [0, 1]^2$, then each mode $i \in \mathcal{M}$ of (3.29) admits an endemic solution $Q_{ES}^{(3.29),i} \equiv (S_i^*, I_i^*, R_i^*)$ satisfying the nonlinear equation system:

$$\begin{aligned} \mu &= f_i(S_i^*, I_i^*) + \mu S_i^* + g I_i^*, \\ (\mu + g)I_i^* &= f_i(S_i^*, I_i^*), \\ R_i^* &= 1 - S_i^* - I_i^*. \end{aligned} \tag{3.30}$$

Again, these points are called endemic solutions/equilibria since the disease persists above a positive level. The notion of the basic reproduction number is extended to (3.29) as follows: In the non-switched case, i.e., $\mathcal{F} = \{f(S, I)\}$, the basic reproduction number of (3.29) is calculated as

$$R_0^{(3.29)} \equiv \frac{1}{\mu + g} \frac{\partial f}{\partial I}(1, 0),$$

assuming that $\frac{\partial f}{\partial I}(1, 0)$ exists [73]. This ratio can be interpreted physiologically as before: $\frac{\partial f}{\partial I}(1, 0)$ represents the rate of new infections when the system state is at its disease-free solution and a single infected is introduced while $1/(\mu + g)$ is the average death-adjusted infectious period. Extensions of the eradication and endemic persistence results in the previous section (i.e., Theorems 3.1 and 3.4) to the general incidence rate case are possible (see Theorems 2.1 and 2.4 in [96], respectively): Assume that, in addition, \mathcal{F} satisfies

$$\gamma_i SI \leq f_i(S, I) \leq \beta_i SI, \quad \forall i \in \mathcal{M}, \forall (S, I) \in \{(S, I) \in \mathbb{R}_+^2 : S + I \leq 1\},$$

for some $\beta_i, \gamma_i > 0$. Given $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, define the following basic reproduction number bounds:

$$\begin{aligned} \overline{R}_0^{(3.29)} &= \frac{\sum_{i=1}^m \gamma_i \tau_i}{\omega(\mu + g)}, \\ \widehat{R}_0^{(3.29)} &= \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)}. \end{aligned}$$

The following results hold for the switched SIR model (3.29):

1. If $\widehat{R}_0^{(3.29)} < 1$, then $Q_{\text{DFS}}^{(3.29)}$ is globally attractive and asymptotically I -stable in the physically meaningful domain $Q_{\text{DFS}}^{(3.29)}$.
2. If $\overline{R}_0^{(3.29)} > 1$, then the disease persists uniformly in (3.29).

The full proofs follow similarly as those of Theorems 3.1 and 3.4 (see [96] for details). The bounds are approximations of the basic reproduction number of (3.8), in the following sense:

$$\overline{R}_0^{(3.29)} \leq R_0^{(3.29)} \leq \widehat{R}_0^{(3.29)}.$$

Extensions of Theorems 3.2 and 3.3 are also possible using the approximate mode basic reproduction numbers

$$\widehat{R}_0^{(3.29),i} \equiv \frac{\beta_i}{\omega(\mu + g)}, \quad \forall i \in \mathcal{M}.$$

Example 3.2 Consider (3.29) with $\mathcal{M} = \{1, 2, 3, 4\}$ and switching rule

$$\sigma(t) \equiv \begin{cases} 1, & \text{if } t \in [k, k + 0.25), \quad k = 0, 1, 2, 3, 4, \\ 2, & \text{if } t \in [k + 0.25, k + 1), \quad k = 0, 1, 2, 3, 4, \\ 3, & \text{if } t \in [k, k + 0.25), \quad k = 5, 6, 7, 8, \dots, \\ 4, & \text{if } t \in [k + 0.25, k + 1), \quad k = 5, 6, 7, 8, \dots. \end{cases} \quad (3.31)$$

Let $f_1(S, I) \equiv \beta_1 SI$, $f_2(S, I) \equiv \beta_2 SI$, $f_3(S, I) \equiv \beta_1 SI(1 - I)$, and $f_4(S, I) \equiv \beta_2 SI(1 - I)$; f_1 and f_2 are standard incidence rates (with different contact rates), while f_3 and f_4 take psychological effects into account. From (3.31), the disease spreads with standard incidence rate and term-time forcing (switching contact rate). At $t = 5$, there is a shift in the transmission of the disease, resulting in a structural change to $(t, S, I) \mapsto \beta_o SI(1 - I)$. Let $\beta_1 = 2.5$, $\beta_2 = 0.5$, $\mu = 0.125$, and $g = 1$. As $f_i(S, I) \leq \beta_i I$ for all $i \in \{1, 2, 3, 4\}$,

$$\left\langle R_0^{(3.29)} \right\rangle = 0.991$$

(with $h = 3$) and the solution of (3.29) converges to the disease-free solution (see Fig. 3.5a).

3.6 Uncertainty in the Model: Stochastic Transmission

In modeling the spread of a disease, there are external, environmental forces at play which partially drive the spread of a disease, modeled as perturbations in a model's parameters. There are real benefits gained in using a stochastic model formulation

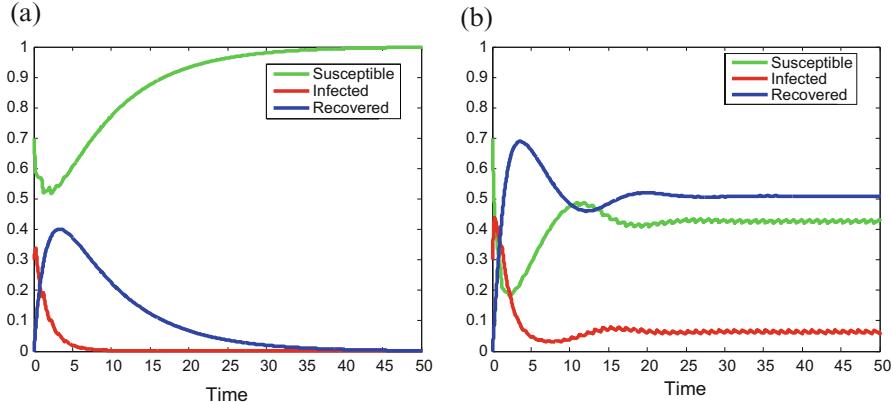


Fig. 3.5 Simulations of Example 3.2. (a) $\beta_1 = 2.5$ and $\beta_2 = 0.5$. (b) $\beta_1 = 4.5$ and $\beta_2 = 2.25$

for the spread of an infectious disease [30, 169]. This is true specifically when modeling biological phenomena, an example being internal HIV viral dynamics [30]. Further, the behavior of the corresponding deterministic evolution of the system [149] can be modified by noise which induces non-trivial effects in physical and biological systems.

There is some literature available on stochastic epidemic models with white noise perturbations. Tornatore et al. [149] investigated the stability of the disease-free equilibrium of a stochastic SIR model with distributed time delay. White noise stochastic perturbations around positive endemic equilibria of epidemic models with time delays influenced by probability was analyzed by Beretta et al. [18]. A two-group SIR model with white noise stochastic perturbations around its positive endemic equilibrium is introduced and studied in [169]. The stability properties of a stochastic model for phage-bacteria interaction in open marine environment were investigated by Carletti [25]. Dalal et al. [29, 30] studied a model of AIDS and HIV by analyzing condom use in a stochastic epidemic model with parameter perturbations. This was motivated by the inherent randomness associated with HIV and AIDS. A Fokker-Planck equation or Master equation is the result of a stochastic process intrinsic noise formulation (see, for example, [69, 131]).

In this part, the role external perturbations play in an epidemic is investigated. More specifically, the contact rate is assumed to be distributed about a switching contact rate β_σ in the form $\beta_{\sigma(t)} + \beta_v n(t)$, where $\beta_v > 0$ is a volatility parameter and $n(\cdot)$ is Gaussian white noise. The incidence rate takes the stochastic form

$$(\beta_{\sigma(t)} + \beta_v n(t))SI = \beta_{\sigma(t)}SI + \beta_v n(t)SI;$$

the contact rate is equal to an estimated mean plus or minus an error term (scaled by β_v) which follows a normal distribution. The analysis to follow considers such a parameter perturbation. Adding this effect into (3.8) yields the following system of

stochastic differential equations:

$$\begin{aligned} dS(t) &= (\mu N(t) - \beta_\sigma S(t)I(t) - \mu S(t)) dt - \beta_v S(t)I(t)dB(t), \\ dI(t) &= (\beta_\sigma S(t)I(t) - gI(t) - \mu I(t)) dt + \beta_v S(t)I(t)dB(t), \\ dR(t) &= (gI(t) - \mu R(t))dt, \end{aligned} \quad (3.32)$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

where B is a Brownian motion with mean equal to zero and variance equal to dt . This process is defined, under the Itô interpretation, on a complete probability space (Ω, \mathcal{F}, P) with a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ satisfying the usual conditions [106]. As per usual, $S_0 + I_0 + R_0 = 1$ is assumed (no noise is present in the initial conditions). Note that (3.32) admits the disease-free solution $Q_{\text{DFS}}^{(3.32)} \equiv (1, 0, 0)$. Existence, uniqueness, and nonnegativity of solutions of (3.32) is derived.

Theorem 3.5 Given $(S_0, I_0, R_0) \in D_{(3.32)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 \mid S + I + R = 1\}$ satisfying $S_0, I_0 > 0$, there is a unique solution (S, I, R) of (3.32) on \mathbb{R}_+ , which satisfies $\{(S(t), I(t), R(t)) : t \in \mathbb{R}_+\} \subset D_{(3.32)}$ such that $S(t) > 0$ and $I(t) > 0$ for all $t \in \mathbb{R}_+$ almost surely.

Proof From integrating (3.32) it is clear that $S + I + R = 1$ is positively invariant to (3.32) almost surely. The proof can therefore be divided into two parts: (1) proving global existence of solutions and (2) proving positivity of (S, I) and nonnegativity of R almost surely. The right-hand side functions of (3.32) are smooth in S, I, R and piecewise continuous in t ; there exists a unique solution of (3.32) by standard arguments on $[0, t_U)$ almost surely (where $t_U \in (0, \infty) \cup \{+\infty\}$ is called the explosion time [48]). It is claimed that $t_U = +\infty$ almost surely. By positivity of S_0 and I_0 , there exists $j_0 \geq 0$ that satisfies $S_0 \in [1/j_0, j_0]$ and $I_0 \in [1/j_0, j_0]$. For each $j \in \mathbb{N}, j \geq j_0$, define the stopping time as

$$t^{(j)} \equiv \inf\{t \in [0, t_U) : (S(t), I(t), R(t)) \notin (1/j, j)^3\}.$$

Note that $t^{(j)}$ increases as j increases. Let $t^\infty \equiv \lim_{j \rightarrow +\infty} t^{(j)}$ and note that $t^\infty \leq t_U$ almost surely. It is claimed that $t^\infty = +\infty$. If not, there exists $\tilde{t} > 0$ and $\epsilon \in (0, 1)$ such that $P[t^\infty \leq \tilde{t}] > \epsilon$. In this case, there must exist $j_1 \geq j_0$ for which

$$P[t^{(j)} \leq \tilde{t}] \geq \epsilon, \quad \forall j \geq j_1. \quad (3.33)$$

Define the mapping $V(S, I, R) \equiv S + 1 - \ln(S) + I + 1 - \ln(I) + R + 1 - \ln(R)$, which satisfies $V(S, I, R) > 0$ for $(S, I, R) \in D_{(3.32)} \cap \{(S, I, R) : I \neq 0\}$. By Itô's formula,

$$\begin{aligned} dV_{(3.32)}(S(t), I(t), R(t)) &= (4\mu - \mu(S(t) + I(t)) - \mu/S(t) + \beta_\sigma(I(t) - S(t)) + g)dt \\ &\quad + (0.5\beta_v^2(S^2(t) + I^2(t)) - \mu R(t) - gI(t)/R(t))dt + \beta_v(S(t) - I(t))dB(t). \end{aligned}$$

Let $\eta \equiv \min\{\tilde{t}, t^{(j)}\}$. Then

$$\begin{aligned} dV_{(3.32)}(S(t), I(t), R(t)) \\ \leq [(\beta_\sigma + g)I(t) + 4\mu + g + 0.5\beta_v^2(S(t) + I(t) + R(t))^2]dt + \beta_v(S(t) - I(t))dB(t), \\ = [(\beta_\sigma + g)I(t) + 4\mu + g + 0.5\beta_v^2]dt + \beta_v(S(t) - I(t))dB(t), \quad \forall t \in [0, \eta]. \end{aligned}$$

For any $(x, y) \in \{(x, y) \in \mathbb{R}_+^2 : x + y \leq 1\}$,

$$y \leq 2(y + 1 - \ln(y) - (4 - 2\ln(2))) \leq 2(x + 1 - \ln(x + y + 1) - \ln(y)) = 2V(x, y).$$

Using this fact,

$$\begin{aligned} dV_{(3.32)}(S(t), I(t), R(t)) \\ \leq (2(\beta_\sigma + g)V(S(t), I(t)) + 4\mu + g + 0.5\beta_v^2)dt + \beta_v(S(t) - I(t))dB(t), \\ \leq \lambda(1 + V(t))dt + \beta_v(S(t) - I(t))dB(t), \end{aligned}$$

where $\lambda \equiv \max\{2(\beta_1 + g), \dots, 2(\beta_m + g), 0.5\beta_v^2 + 4\mu + g\}$. Hence,

$$\begin{aligned} \int_0^\eta dV(S(t), I(t), R(t)) &\leq \lambda \int_0^\eta (1 + V(S(t), I(t), R(t)))dt \\ &\quad + \lambda \mathbb{E} \left[\int_0^\eta (1 + V(S(t), I(t), R(t)))dt \right], \end{aligned}$$

which implies that

$$\begin{aligned} \mathbb{E}[V(S(\eta), I(\eta), R(\eta))] &\leq V_0 + \mathbb{E} \left[\int_0^\eta \lambda(1 + V(S(t), I(t), R(t)))dt \right], \\ &\leq V_0 + \lambda t^* + \lambda \mathbb{E} \left[\int_0^\eta V(S(t), I(t), R(t))dt \right], \\ &\leq V_0 + \widetilde{\lambda t} + \lambda \mathbb{E} \left[\int_0^{t^*} V(S(\eta), I(\eta), R(\eta))dt \right], \\ &= V_0 + \widetilde{\lambda t} + \lambda \int_0^{t^*} \mathbb{E}[V(S(\eta), I(\eta), R(\eta))]dt, \end{aligned}$$

where $V_0 \equiv V(S_0, I_0, R_0)$. Gronwall's Inequality can be applied to yield that

$$\mathbb{E}[V(S(\eta), I(\eta), R(\eta))] \leq [V_0 + \widetilde{\lambda t}] \exp(c_2 \widetilde{t}), \quad (3.34)$$

where $c_2 \equiv \exp(\lambda t^*)$.

Denote the proposition that $(t^{(j)} \leq \tilde{t})$ for $j \geq j_1$ by Ω_j . Equation (3.33) implies that $P(\Omega_j) \geq \epsilon$. Since for all $B \in \Omega_N$,

$$\{S(t^{(j)}, B)\} = \{j\} \cup \{1/j\},$$

or

$$\{I(t^{(j)}, B)\} = \{j\} \cup \{1/j\},$$

or

$$\{R(t^{(j)}, B)\} = \{j\} \cup \{1/j\},$$

it must be that

$$\{V(S(t^{(j)}, B), I(t^{(j)}, B), R(t^{(j)}, B))\} \geq \{j + 1 - \ln(j)\} \cup \{1/j + 1 - \ln(1/j)\}.$$

That is,

$$V(S(t^{(j)}, B), I(t^{(j)}, B), R(t^{(j)}, B)) \geq \min\{j + 1 - \ln(j), 1/j + 1 - \ln(1/j)\}.$$

Equations (3.33) and (3.34) imply that

$$(V_0 + \lambda \tilde{t}) \exp(\lambda \tilde{t}) \geq \mathbb{E}[\mathbf{1}_{\Omega_j}(B)V(S(t^{(j)}, B), I(t^{(j)}, B), R(t^{(j)}, B))], \quad (3.35)$$

$$\geq \epsilon(\min\{j + 1 - \ln(j), 1/j + 1 - \ln(1/j)\}), \quad (3.36)$$

where $\mathbf{1}_{\Omega_j}(\cdot)$ denotes the indicator function with respect to the set Ω_j . Letting $j \rightarrow +\infty$, $c_3 = (V_0 + \lambda \tilde{t}) \exp(\lambda \tilde{t})$ satisfies $+\infty > c_3 = +\infty$, a contradiction, from which it follows that $t^\infty = +\infty$.

Positivity of solutions is shown as follows: given that $S_0 > 0$ and $I_0 > 0$, there exists $t_\Delta > 0$ sufficiently small so that $S(t_\Delta) > 0$ and $I(t_\Delta) > 0$ almost surely. Itô's formula yields that

$$d[\ln I]_{(3.32)}(t) = (\beta_\sigma S(t) - \mu - g - 0.5\beta_v^2 S^2(t)I^2(t))dt + \beta_v S(t)I(t)dB(t).$$

Thus,

$$I(t) = I_0 \exp\left(\int_0^t (\beta_\sigma S(u) - \mu - g - 0.5\beta_v^2 S^2(u)I^2(u))du + \beta_v \int_0^t S(u)I(u)dB(u)\right).$$

Similarly,

$$d[\ln S]_{(3.32)}(t) = (\mu/S(t) - \beta_\sigma I(t) - \mu - 0.5\beta_v^2 S^2(t)I^2(t))dt + \beta_v S(t)I(t)dB(t),$$

so that

$$S(t) = S_0 \exp \left(\int_0^t (\mu/S(u) - \beta_\sigma I(u) - \mu - 0.5\beta_v^2 S^2(u)I^2(u))du + \int_0^t \beta_v S(u)I(u)dB(u) \right).$$

By shifting the initial time from $t = 0$ to $t = t_\Delta$, and using the fact that solutions exist for all $t \geq 0$ almost surely, it follows without loss of generality that $I(t) > 0$ and $S(t) > 0$ for all $t \in \mathbb{R}_+$ almost surely. Lastly, since the differential equation for R is absent of a Brownian motion term, and $I(t) > 0$ almost surely, it follows that $R(t) \geq 0$ for all $t \in \mathbb{R}_+$ almost surely. Hence, $(S(t), I(t), R(t)) \in \mathbb{R}_+^3$ for $t \in \mathbb{R}_+$ almost surely.

Threshold conditions involving the basic reproduction number can be extended to the stochastic case (recall Definition 1.13).

Theorem 3.6 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and*

$$R_0^{(3.32)} \equiv \frac{(\sum_{i=1}^m \beta_i \tau_i) + 0.5\omega\beta_v^2}{\omega(\mu + g)} < 1,$$

then the solution of the switched SIR stochastic system (3.32) converges in the second moment to the disease-free solution $Q_{\text{DFS}}^{(3.32)}$.

Before proceeding to the proof, notice that if $\beta_v = 0$ (i.e., no stochastic perturbations), then it holds that $R_0^{(3.32)} = R_0^{(3.8)}$, where $R_0^{(3.8)}$ is the basic reproduction number of the switched SIR system, as expected.

Proof An application of Itô's formula to the mapping $I \mapsto I^2$ along trajectories of (3.32) yields

$$d[I^2]_{(3.32)}(t) = (I^2(t)(\beta_\sigma S(t) - \mu - g) + 0.5\beta_v^2 S^2(t)I^2(t))dt + 2\beta_v S(t)I^2(t)dB(t).$$

Integrating gives

$$\begin{aligned} I^2(t) &= I_0^2 + \int_0^t ((\beta_{\sigma(u)} S(u) - \mu - g)I^2(u) + 0.5\beta_v^2 S^2(u)I^2(u))du \\ &\quad + \int_0^t 2\beta_v S(u)I^2(u)dB(u), \\ &\leq I_0^2 + \int_0^t \lambda_{\sigma(u)} I^2(u)du + \int_0^t 2\beta_v S(u)I^2(u)dB(u), \end{aligned}$$

where $\lambda_i \equiv \beta_i - \mu - g + 0.5\beta_v^2$ for each $i \in \mathcal{M}$. The expected value of I^2 is bounded above as follows:

$$\mathbb{E}[I^2(t)] \leq I_0^2 + \int_0^t \lambda_{\sigma(u)} \mathbb{E}[I^2(u)]du,$$

since $\mathbb{E}[\int_0^t 2\beta_v S(u)I^2(u)dB(u)] = 0$. It follows that

$$\mathbb{E}[I^2(t)] \leq I_0^2 \exp\left(\int_0^t \lambda_{\sigma(u)} du\right).$$

Hence,

$$\mathbb{E}[I^2(\omega)] \leq I_0^2 \exp\left(\sum_{i=1}^m \lambda_i \tau_i\right) = I_0^2 \exp\left(\omega(\mu + g)(R_0^{(3.32)} - 1)\right).$$

Defining

$$\eta \equiv \exp\left(\omega(\mu + g)(R_0^{(3.32)} - 1)\right) < 1,$$

it is readily seen that $\mathbb{E}[I^2(\omega)] \leq \eta I_0^2 < I_0^2$, and, similarly, $\mathbb{E}[I^2(h\omega)] \leq \eta \mathbb{E}[I^2((h-1)\omega)]$ for any $h \in \mathbb{N}$. In general,

$$\mathbb{E}[I^2(h\omega)] \leq \eta \mathbb{E}[I^2((h-1)\omega)] \leq \eta(\eta \mathbb{E}[I^2((h-2)\omega)]) \leq \dots \leq \eta^h I_0^2.$$

The sequence $\{\mathbb{E}[I^2(h\omega)]\}$ converges to zero and $\mathbb{E}[I^2(t)]$ is bounded on each interval of the form $[(h-1)\omega, h\omega)$; I^2 converges to zero in probability. Note that $R^2(t) = R_0^2 + \int_0^t 2R(u)(gI(u) - \mu R(u))du$. By Holdér's Inequality,

$$\begin{aligned} \mathbb{E}[R^2(t)] &= R_0^2 + \int_0^t (2g\mathbb{E}[I(u)R(u)] - 2\mu\mathbb{E}[R^2(u)])du, \\ &\leq R_0^2 + \int_0^t (2g\sqrt{\mathbb{E}[I^2(u)]\mathbb{E}[R^2(u)]} - 2\mu\mathbb{E}[R^2(u)])du. \end{aligned}$$

Since $\mathbb{E}[I^2(t)] \rightarrow 0$ as $t \rightarrow +\infty$, it follows that $\mathbb{E}[R^2(t)]$ converges to zero. $S(t) = 1 - I(t) - R(t)$ for all $t \in \mathbb{R}_+$ implies that

$$\mathbb{E}[S^2(t)] = 1 + \mathbb{E}[I^2(t)] + \mathbb{E}[R^2(t)] - 2\mathbb{E}[I(t)] - 2\mathbb{E}[R(t)] + 2\mathbb{E}[I(t)R(t)].$$

Another application of Holdér's Inequality yields that $\mathbb{E}[S^2(t)]$ converges to one; the solution of (3.32) converges in the second moment to $Q_{\text{DFS}}^{(3.32)}$.

Example 3.3 Consider the switched SIR model (3.32) with initial conditions $S_0 = 0.2$, $I_0 = 0.8$, and $R_0 = 0$. Assume that the switching rule takes the periodic seasonal form:

$$\sigma(t) \equiv \begin{cases} 1, & \text{if } t \in [k, k + 0.25), \quad k = 0, 1, 2, \dots, \\ 2, & \text{if } t \in [k + 0.25, k + 1), \end{cases} \quad (3.37)$$

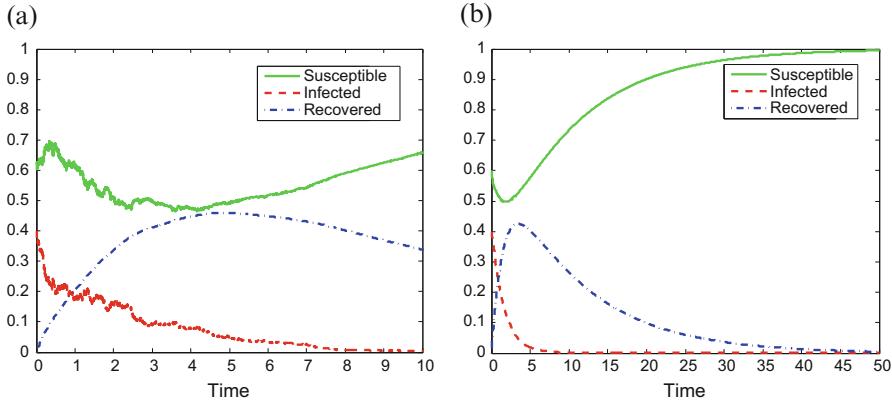


Fig. 3.6 Simulations of Example 3.3. (a) Realization of (3.32). (b) Ensemble average of (3.32)

which implies $\tau_1 = 0.25$, $\tau_2 = 0.75$, and $\omega = 1$. Let $\beta_1 = 1$ during the winter, $\beta_2 = 0.7$ during other seasons, $\mu = 0.1$, $g = 0.9$, and noise parameter $\beta_v = 0.5$. Then $R_0^{(3.32)} = 0.9$ and the solution of (3.32) converges to the disease-free solution in the second moment by Theorem 3.6. See Fig. 3.6.

3.7 Discussions

For traditional analyses of infectious disease models with constant contact rates, the reader is referred to [63, 65, 69, 116] and the references within. The so-called classical endemic SIR model is an important first modeling step for a number of diseases; measles, scarlet fever, diphtheria, tuberculosis, smallpox, malaria and the pneumonias also fall into this category [64]. The derivations in Sect. 3.1, as well as some notions raised in Sect. 3.2, are largely inspired by the excellent review article [65].

Studies of disease models with smoothly varying contact rates [i.e., (3.5)] can be found in [138], where Shulgin et al. analyzed a pulse vaccination SIR model with sinusoidal forcing; [168], where Yang and Xiao studied an HIV model with periodicity; [11], in which Baca  r and Souad analyzed a seasonal model of cutaneous leishmaniasis; [68], where the authors Jin et al. detailed a pulse control model with seasonality and [103], where Ma and Ma studied a seasonally forced SEIR model (susceptible, exposed, infected, and recovered groups). Other examples are found in [6, 10, 11, 52, 53, 69, 87, 91, 118, 128, 138, 168].

Citing cases where transmission data is more accurately reflected by term-time forced contact rates (i.e., (3.6)) [44], there have been a number of studies analyzing the behavior of epidemics using this modeling approach. For example, see [44, 70]; [94, 96] formed the basis for the analyses in Sects. 3.4 and 3.5; [95] provided

the framework for the results in Sect. 3.6 (and also extends the work to control strategies). As noted by [69], relatively small contact rate variations can cause large fluctuations in a disease's incidence; this phenomenon warrants more attention since current analytic methods are lacking.

Switched systems techniques found in [54, 55] are used to prove the threshold conditions found in this chapter (in particular, those provided in Sect. 3.4). The persistence result in Theorem 3.4 was accomplished by extending the methods of [68] (see Lemma 4.1 and Theorem 4.1). The well-posedness results in Sect. 3.6 (i.e., Theorem 3.5) were derived along the lines of [29, 30], where the authors looked at HIV/AIDS models with stochastic perturbations, by adjusting the methods to include switching.

Regarding the various threshold condition theorems presented in this chapter, the following observations are made:

1. Extensions of the threshold conditions to a time-varying recovery rate (i.e., $g_\sigma \in \{g_1, \dots, g_m\}$) and natural death/birth rate (i.e., $\mu_\sigma \in \{\mu_1, \dots, \mu_m\}$) are straightforward. In fact, extensions to switching time-dependent functions, i.e., $g_i(t)$, $\mu_i(t)$, and $f_i(t, S, I)$ for the switching incidence rate studies, are also possible in this framework. The reader is referred to [96] for details.
2. Taking $\mathcal{M} = \{1, \dots, m\}$ in this case is without loss of generality; if we considered $\{\beta_1, \dots, \beta_{m_1}\}$ and $\{g_1, \dots, g_{m_2}\}$, then we could write $m = m_1 m_2$ and construct $\{\beta_1, \dots, \beta_m\}$ and $\{g_1, \dots, g_m\}$ by repeating elements as necessary.
3. Returning to the motivating discussion in Sect. 3.3, the term-time forcing contact rate outlined in Eq. (3.6) is included as a special case in the switched systems formulation of the SIR model (3.8). Namely, the results in Sect. 3.4 are applicable with basic reproduction number

$$R_0^{(3.8)} = \frac{\beta_0}{\mu + g} [(1 + \epsilon) \times \text{days of school per year} \\ + (1 + \epsilon)^{-1} \times \text{days of school closure per year}].$$

4. The assumptions that $\sigma \in \mathcal{S}_{\text{dwell}}$, which was made to invoke well-posedness of the epidemic models (i.e., global existence of a unique solution), will either be explicitly stated throughout this monograph (i.e., in the eradication results) or implicitly assumed in the models.
5. Since an outbreak is the main point of interest, results on attractivity of the disease-free solution are useful in establishing the long-term behavior of the outbreak (namely, eradication). Partial I -stability results yield information on the behavior of the infected population as the disease dies out. More specifically, said results eliminate the possibility of instability with respect to $I = 0$ and exponential I -stability yields a rate of convergence to zero.
6. The techniques here are straightforward mathematically but versatile in the different classes of switching rules and across different epidemic models (as will be shown in the remainder of this monograph).

Chapter 4

Epidemic Models with Switching

In this chapter, the methods developed thus far are applied to a variety of infectious disease models with different physiological and epidemiological assumptions. Many of the previous results are immediately applicable, thanks to the flexibility of the simple techniques used here. However, some complicating modeling assumptions lead to a need for different switched systems techniques and results not present in the previous chapter. First, the so-called SIS model is considered, followed by incorporation of media coverage, network epidemic models with interconnected cities (or patches), and diseases spread by vector agents (e.g., mosquitoes) which are modeled using time delays. Straightforward extensions of eradication results are given for models with vertical transmission, disease-induced mortality, waning immunity, passive immunity, and a model with general compartments.

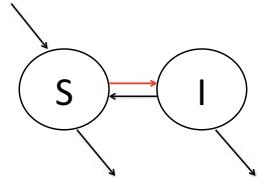
4.1 Absence of Conferred Natural Immunity: The SIS Model

Consider the set-up of a two-compartment disease model where the infected, once recovered, immediately return to the susceptible class (i.e., only the susceptible, S , and the infected, I , are considered). Implicitly, the assumption of conferred natural immunity in the switched SIR model (3.8) is being discarded. Invoking the other assumptions of Sects. 3.1 and 3.3 yield the switched SIS model:

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) + gI(t) - \mu S(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (g + \mu)I(t), \\ (S(0), I(0)) &= (S_0, I_0),\end{aligned}\tag{4.1}$$

Fig. 4.1 Flow diagram of the switched SIS system (4.1).

The red line represents horizontal transmission of the disease



where $\sigma \in \mathcal{S}_{\text{dwell}}$ designates a switching rule; $\sigma(t) \in \mathcal{M} \equiv \{1, \dots, m\}$ and $\beta_{\sigma(t)} \in \{\beta_1, \dots, \beta_m\}$ for each t . Again, the variables have been normalized by the constant total population and $(S_0, I_0) \in D_{(4.1)} \equiv \{(S, I) \in \mathbb{R}_+^2 : S + I = 1\}$, the meaningful domain which is positively invariant to (4.1);

$$\{\dot{S} + \dot{I}\}|_{S+I=1} = 0, \quad \dot{S}|_{S=0} = \mu + gI > 0, \quad \dot{I}|_{I=0} = 0.$$

The flow of (4.1) is outlined in Fig. 4.1. Since the domain is positively invariant and the switched system has continuously differentiable functions on the right-hand side in each mode, the model is well-posed, biologically and mathematically.

The disease-free solution of (4.1) is $Q_{\text{DFS}}^{(4.1)} \equiv (1, 0)$. There exist m endemic equilibria, each associated with a mode of (4.1), given by

$$Q_{\text{ES}}^{(4.1),i} \equiv \left(\frac{\mu + g}{\beta_i}, 1 - \frac{\mu + g}{\beta_i} \right). \quad (4.2)$$

Since $S + I = 1$ is an invariant to (4.1), the differential equation for S may be omitted:

$$\begin{aligned} \dot{I}(t) &= -\beta_\sigma I^2(t) + (\beta_\sigma - g - \mu)I(t), \\ I(0) &= I_0. \end{aligned} \quad (4.3)$$

For any $i \in \mathcal{M}$,

$$\dot{I}(t) = -\beta_i I^2(t) + (\beta_i - g - \mu)I(t),$$

is a Bernoulli switched differential equation. With this in mind for the piecewise switching case, the SIS model (4.1) admits the following solution (adopted from [63]):

$$I(t) \equiv \begin{cases} \frac{I(t_{k-1}) \exp(\lambda_{i_k}(t-t_{k-1}))}{I(t_{k-1})\beta_{i_k}(\exp(\lambda_{i_k}(t-t_{k-1}))-1)/\lambda_{i_k}+1}, & \text{if } \lambda_{i_k} \neq 0, \\ \frac{I(t_{k-1})}{I(t_{k-1})\beta_{i_k}(t-t_{k-1})+1}, & \text{if } \lambda_{i_k} = 0, \end{cases}$$

for all $t \in [t_{k-1}, t_k]$, where $\lambda_i \equiv \beta_i - g - \mu$ for each $i \in \mathcal{M}$. The solution can be given in a closed-form expression, as a function of parameters (i.e., initial condition and switching rule) and t : if $\lambda_{i_1} \neq 0$, then

$$I(t_1) = \frac{I_0 \exp(\lambda_{i_1}(t_1))}{I_0 \beta_{i_1}(\exp(\lambda_{i_1}(t_1))-1)/\lambda_{i_1}+1}.$$

If $\lambda_{i_2} \neq 0$, then

$$\begin{aligned} I(t_2) &= \frac{I(t_1) \exp(\lambda_{i_2}(t_2 - t_1))}{I(t_1)\beta_{i_2}(\exp(\lambda_{i_2}(t_2 - t_1)) - 1)/\lambda_{i_2} + 1}, \\ &= \frac{I_0 \exp(\lambda_{i_1}(t_1) + \lambda_{i_2}(t_2 - t_1))}{\left(\frac{I_0 \beta_{i_2} \exp(\lambda_{i_1}(t_1))(\exp(\lambda_{i_2}(t_2 - t_1)) - 1)}{\lambda_{i_2}} \right) + \left(\frac{I_0 \beta_{i_1} (\exp(\lambda_{i_1}(t_1)) - 1)}{\lambda_{i_1}} \right) + 1}. \end{aligned}$$

Assuming that $\lambda_{i_k} \neq 0$ for each k , then the solution is given by

$$I(t) \equiv \frac{I_0 \exp\left(\sum_{j=1}^{k-1} \lambda_{i_j}(t_j - t_{j-1}) + \lambda_{i_k}(t - t_{k-1})\right)}{I_0 \left(\beta_{i_k} B_{i_k}(t) + \sum_{j=1}^{k-1} \beta_{i_j} A_{i_j}\right) + 1}, \quad \forall t \in [t_{k-1}, t_k], \quad (4.4)$$

where

$$\begin{aligned} B_{i_k}(t) &\equiv \exp\left(\sum_{j=1}^{k-1} \lambda_{i_j}(t_j - t_{j-1}) + \lambda_{i_k}(t - t_{k-1})\right) \frac{\exp(\lambda_{i_k}(t - t_{k-1})) - 1}{\lambda_{i_k}}, \\ A_{i_j} &\equiv \widehat{A}_{i_j} \exp(\lambda_{i_1}(t_1) + \dots + \lambda_{i_{j-1}}(t_{j-1} - t_{j-2})), \end{aligned}$$

and,

$$\widehat{A}_{i_j} \equiv \begin{cases} \frac{\exp(\lambda_{i_j}(t_j - t_{j-1})) - 1}{\lambda_{i_j}}, & \text{if } \lambda_{i_j} \neq 0, \\ t_j - t_{j-1}, & \text{if } \lambda_{i_j} = 0. \end{cases}$$

Compare this result to the time-constant contact rate SIS model:

$$\begin{aligned} \dot{S}(t) &= \mu - \beta S(t)I(t) - \mu S(t) + gI(t), \\ \dot{I}(t) &= \beta S(t)I(t) - (g + \mu)I(t), \end{aligned} \quad (4.5)$$

which has basic reproduction number

$$R_0^{(4.5)} \equiv \frac{\beta}{\mu + g}, \quad (4.6)$$

and, after eliminating the equation for S via the invariant $S + I = 1$, simplifies to the Bernoulli differential equation

$$\begin{aligned} \dot{I}(t) &= -\beta I^2(t) + (\beta - g - \mu)I(t), \\ I(0) &= I_0 > 0. \end{aligned} \quad (4.7)$$

Equation (4.7) has two equilibria: $Q_{\text{DFS}}^{(4.7)} \equiv 0$ and $Q_{\text{ES}}^{(4.7)} \equiv 1 - 1/R_0^{(4.5)}$, corresponding to the disease-free solution and endemic solution of (4.5), respectively. Equation (4.7) admits a unique solution [63] which can be found analytically. The details are explored to draw comparisons with the switched contact rate case outlined above. Letting $\lambda \equiv \beta - \mu - g$,

$$\dot{I}(t) - \lambda I(t) = -\beta I^2(t),$$

if $R_0^{(4.5)} \neq 1$ (i.e., $\lambda \neq 0$). In this case,

$$\frac{\dot{I}}{I^2} - \frac{\lambda}{I} = -\beta.$$

The substitution $y \equiv I^{-1}$, which is valid for $I \neq 0$, yields

$$\dot{y} = -\frac{\dot{I}}{I^2}.$$

Hence,

$$\begin{aligned}\dot{y}(t) &= -\lambda y(t) + \beta, \\ y(0) &= I_0 > 0,\end{aligned}$$

(where $I_0 > 0$ has been assumed to make the problem interesting) which admits a unique solution given by

$$y(t) \equiv \left(I_0 - \frac{\beta}{\lambda} \right) \exp(-\lambda t) + \frac{\beta}{\lambda}, \quad \forall t \in \mathbb{R}_+.$$

Consequently, the unique solution is

$$\begin{aligned}I(t) &\equiv \frac{1}{\left(I_0 - \frac{\beta}{\lambda} \right) \exp(-\lambda t) + \frac{\beta}{\lambda}}, \\ &= \frac{\exp((\mu + g)(R_0^{(4.5)} - 1)t)}{R_0^{(4.5)}(\exp((\mu + g)(R_0^{(4.5)} - 1)t) - 1)/(R_0^{(4.5)} - 1) + 1/I_0}, \quad \forall t \in \mathbb{R}_+.\end{aligned}$$

In the case that $R_0^{(4.5)} = 1$, $\dot{I}(t) = -\beta I^2(t)$ which is readily solved to get the unique solution

$$I(t) \equiv \frac{1}{\beta t + \frac{1}{I_0}}, \quad \forall t \in \mathbb{R}_+.$$

Combining the cases,

$$I(t) \equiv \begin{cases} \frac{\exp((\mu+g)(R_0^{(4.5)}-1)t)}{R_0^{(4.5)}(\exp((\mu+g)(R_0^{(4.5)}-1)t)-1)/(R_0^{(4.5)}-1)+1/I_0}, & \text{if } R_0^{(4.5)} \neq 1, \\ \frac{1}{\beta t+1/I_0}, & \text{if } R_0^{(4.5)} = 1. \end{cases} \quad (4.8)$$

As $\lambda = 0$ is equivalent to $R_0^{(4.5)} = 1$, notice that (4.4) reduces to (4.8) when $\beta_\sigma = \beta$. By inspection, if $R_0^{(4.5)} \leq 1$, it follows that

$$\lim_{t \rightarrow \infty} I(t) = 0,$$

and $Q_{\text{DFS}}^{(4.7)}$ is asymptotically stable in the meaningful domain. If $R_0^{(4.5)} > 1$ then

$$\lim_{t \rightarrow \infty} I(t) = 1 - 1/R_0^{(4.5)} > 0$$

and $Q_{\text{ES}}^{(4.7)}$ is asymptotically stable in the meaningful domain. The basic reproduction number completely determines the long-term behavior of (4.7) (and therefore (4.5)).

In light of these findings, let us return to (4.3) in order to study its qualitative behavior.

Theorem 4.1 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and*

$$R_0^{(4.1)} \equiv \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < 1,$$

then the disease-free solution $Q_{\text{DFS}}^{(4.1)} \equiv (1, 0)$ of the switched SIS model (4.1) is globally asymptotically stable in the meaningful domain $D_{(4.1)}$.

Proof Since $A_i > 0$ for each $i \in \mathcal{M}$ and $B_i(t) > 0$ for each $i \in \mathcal{M}$ and $t \in \mathbb{R}_+$, Eq. (4.4) implies that

$$I(t) \leq I_0 \exp \left(\sum_{j=1}^{k-1} \lambda_{i_j}(t_j - t_{j-1}) + \lambda_{i_k}(t - t_{k-1}) \right), \quad \forall t \in [t_{k-1}, t_k], \quad (4.9)$$

and, from $\sigma \in \mathcal{S}_{\text{periodic}}$,

$$I(\omega) \leq I_0 \exp \left(\sum_{i=1}^m \lambda_i \tau_i \right),$$

where $\sum_{i=1}^m \lambda_i \tau_i < 0$ since $R_0^{(4.1)} < 1$. Letting

$$\eta \equiv \exp \left(\sum_{i=1}^m \lambda_i \tau_i \right) < 1,$$

$I(h\omega) \leq I_0\eta^h$ for any $h \in \mathbb{N}$ and the sequence $\{I(h\omega)\}$ is monotonically decreasing and converges to zero, and, similarly to the proof of Theorem 3.1, $\lim_{t \rightarrow \infty} I(t) = 0$. Moreover, (4.9) gives that $I(t) \leq I_0 M \equiv I_{\max}$ for all $t \in \mathbb{R}_+$ where

$$M \equiv \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i \right),$$

with $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i > 0\}$. The result follows from the fact that $S = 1 - I$.

From the proof of Theorem 4.1, an approximation of the epidemic severity is given as

$$I_{\max} \equiv I_0 \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i \right),$$

which is greater than I_0 but may not be achieved. Importantly, a small amount of initial infected cases results in a small number of infections in time and the disease is eventually eradicated. However, in the case that the basic reproduction number $R_0^{(4.1)}$ is greater than one, a result on the persistence of the disease can be established along the lines of the proof of Theorem 3.3 in [83] and Lemma 4.1 and Theorem 4.1 in [68]. If weak uniform persistence does not hold, then for any $\epsilon > 0$,

$$\limsup_{t \rightarrow \infty} I(t) < \epsilon.$$

In this case,

$$\dot{S}(t) = \mu - \beta_k S(t)I(t) + gI(t) - \mu S(t) > \mu - \beta_{\max}\epsilon - \mu S(t), \quad \forall t \in [t_{k-1}, t_k],$$

where $\beta_{\max} \equiv \max\{\beta_1, \dots, \beta_m\}$. The comparison ODE system

$$\begin{aligned} \dot{S}_m(t) &= \mu - \beta_{\max}\epsilon - \mu S_m(t), \\ S_m(0) &= S_0, \end{aligned} \tag{4.10}$$

has a unique solution converging to $S^* \equiv 1 - \beta_{\max}\epsilon/\mu$. Hence, there exists a time $t^* > 0$ for which $S(t) \geq 1 - \beta_{\max}\epsilon/\mu - \epsilon$ for all $t \geq t^*$ and, for any $k \in \mathbb{N}$ satisfying $t^* < t_{k-1} < t \leq t_k$,

$$\dot{I}(t) = \beta_k S(t)I(t) - (g + \mu)I(t) \geq (\beta_k - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_k)I(t).$$

For $t \in [t^* + (k-1)\omega, t^* + k\omega]$,

$$\begin{aligned}
I(t) &\geq I(t^*) \exp \left(\int_{t^*}^t (\beta_{\sigma(s)} - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_{\sigma(s)}) ds \right), \\
&= I(t^*) \exp \left(\int_{t^*}^{t^* + (k-1)\omega} (\beta_{\sigma(s)} - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_{\sigma(s)}) ds \right) \\
&\quad \times \exp \left(\int_{t^* + (k-1)\omega}^t (\beta_{\sigma(s)} - g - \mu - \epsilon(1 + \beta_{\max}/\mu)\beta_{\sigma(s)}) ds \right), \\
&\geq M \exp \left\{ (k-1) \left[\int_0^\omega (\beta_{\sigma(s)} - g - \mu) ds - \epsilon \omega \beta_{\max} (1 + \beta_{\max}/\mu) \right] \right\},
\end{aligned}$$

where $M \equiv I(t^*) \exp(-\omega(g + \mu) - \epsilon \omega \beta_{\max} (1 + \beta_{\max}/\mu))$. Choosing ϵ to satisfy

$$0 < \epsilon \leq \frac{\int_0^\omega (\beta_{\sigma(s)} - g - \mu) ds}{2\omega \beta_{\max} \left(1 + \frac{\beta_{\max}}{\mu} \right)},$$

$$\phi(\epsilon) \equiv \left(\int_0^\omega (\beta_{\sigma(s)} - g - \mu) ds - \epsilon \omega \beta_{\max} (1 + \beta_{\max}/\mu) \right) > 0,$$

and $I(t) \geq M \exp((k-1)\phi(\epsilon))$, which contradicts the boundedness of I ; there exists a time $t^1 > t^*$ such that $I(t^1) \geq \eta$. Uniform persistence is then shown along the lines of the proof of Theorem 3.4 to give the following result.

Theorem 4.2 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(4.1)} > 1$, then the disease persists uniformly in (4.1).*

A permanence result (see [148] for the original definition, also see [49]) can be derived in terms of the endemic equilibria associated with each mode of (4.1), i.e., $Q_{\text{ES}}^{(4.1),i}$ as outlined in (4.2).

Definition 4.1 The disease is said to be permanent in (4.1) if there exists a compact set $\Omega \subset \text{int}(D_{(4.1)})$ such that for every initial condition in $D_{(4.1)}$, $I(t)$ eventually enters and remains in Ω .

Note that permanence implies persistence. Periodicity of the switching rule is not required in this case.

Theorem 4.3 *If $\sigma \in \mathcal{S}_{\text{dwell}}$ and $\min\{R_0^{(4.1),i} : i \in \mathcal{M}\} > 1$, then the disease is permanent in (4.1); $I(t)$ converges to $\text{conv}\{Q_{\text{ES}}^{(4.1),1}, \dots, Q_{\text{ES}}^{(4.1),m}\}$.*

Proof Note that $\min\{R_0^{(4.1),i} : i \in \mathcal{M}\} > 1$ implies that

$$\frac{\beta_{\min}}{\mu + g} > 1,$$

where $\beta_{\min} \equiv \min\{\beta_i : i \in \mathcal{M}\}$. Let $\Lambda \equiv \text{conv}\{Q_{\text{ES}}^{(4.1),1}, \dots, Q_{\text{ES}}^{(4.1),m}\}$ and $\lambda_i \equiv \beta_i - \mu - g$ for each $i \in \mathcal{M}$. For each $i \in \mathcal{M}$, $Q_{\text{ES}}^{(4.1),i} = (S_i^*, I_i^*, R_i^*)$ where $I_i^* \equiv \lambda_i / \beta_i$. Then

$$\Lambda = \{(S, I) \in \mathbb{R}_+^2 : I_{\min}^* \leq I \leq I_{\max}^*, S = 1 - I\},$$

where $I_{\min} \equiv \min\{I_1^*, \dots, I_m^*\}$ and $I_{\max} \equiv \max\{I_1^*, \dots, I_m^*\}$. For any $i \in \mathcal{M}$,

$$\dot{I}|_{I=I_{\min}^*} = -\beta_i \left(\frac{\lambda_{\min}}{\beta_{\min}} \right)^2 + \lambda_i \frac{\lambda_{\min}}{\beta_{\min}} = \frac{\lambda_{\min}}{\beta_{\min}} \beta_i \left(\frac{\lambda_i}{\beta_i} - \frac{\lambda_{\min}}{\beta_{\min}} \right) \geq 0,$$

since $\min\{R_0^{(4.1),i} : i \in \mathcal{M}\} > 1$. Similarly, for any $i \in \mathcal{M}$,

$$\dot{I}|_{I=I_{\max}^*} = -\beta_i \left(\frac{\lambda_{\max}}{\beta_{\max}} \right)^2 + \lambda_i \frac{\lambda_{\max}}{\beta_{\max}} = \frac{\lambda_{\max}}{\beta_{\max}} \beta_i \left(\frac{\lambda_i}{\beta_i} - \frac{\lambda_{\max}}{\beta_{\max}} \right) \leq 0.$$

The invariance of $S + I = 1$ immediately implies that Λ is positively invariant to (4.1); if $I_0 \in \Lambda$, $\{I(t) : t \in \mathbb{R}_+\} \subset \Lambda$. If $0 < I_0 < \lambda_{\min}/\beta_{\min}$, then

$$\dot{I}(t) = -\beta_\sigma I^2(t) + \lambda_\sigma I(t) = \beta_\sigma I(t) \left(\frac{\lambda_\sigma}{\beta_\sigma} - I(t) \right) > 0, \quad \forall t \in \mathbb{R}_+,$$

implying that either $I(t) \in \Lambda$ in finite time or $\lim_{t \rightarrow \infty} I(t) = I_{\min}^* \in \Lambda$. Similar arguments can be used for the case $\lambda_{\max}/\beta_{\max} < I_0 \leq 1$.

Example 4.1 Consider the switched SIS model (4.1) with switching in all model parameters:

$$\begin{aligned} \dot{S}(t) &= \mu_\sigma - \beta_\sigma S(t)I(t) + g_\sigma I(t) - \mu_\sigma S(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (g_\sigma + \mu_\sigma)I(t), \\ (S(0), I(0)) &= (S_0, I_0), \end{aligned} \tag{4.11}$$

where $\mathcal{M} = \{1, 2\}$ and σ is defined by the seasonal switching rule (3.37) (which is periodic with $\tau_1 = 0.25$, $\tau_2 = 0.75$ and $\omega = 1$). Letting $\beta_1 = 1/4$, $\beta_2 = 1/12$, $g_1 = 1/10$, $g_2 = 1/8$, $\mu_1 = 1/70$, and $\mu_2 = 1/60$ (motivated by the parameter values in [173]), there is an increase in the contact rate and decrease in the recovery rate in the winter seasons and the birth rate increases during the summer months. The basic reproduction number is calculated as

$$R_0^{(4.1)} = \frac{\sum_{i=1}^2 \beta_i \tau_i}{\sum_{i=1}^2 (\mu_i + g_i) \tau_i} = 0.927$$

and, by a straightforward extension of Theorem 4.1 (see Theorem 2.1 in [98]), the disease-free solution is globally asymptotically stable in the meaningful domain.

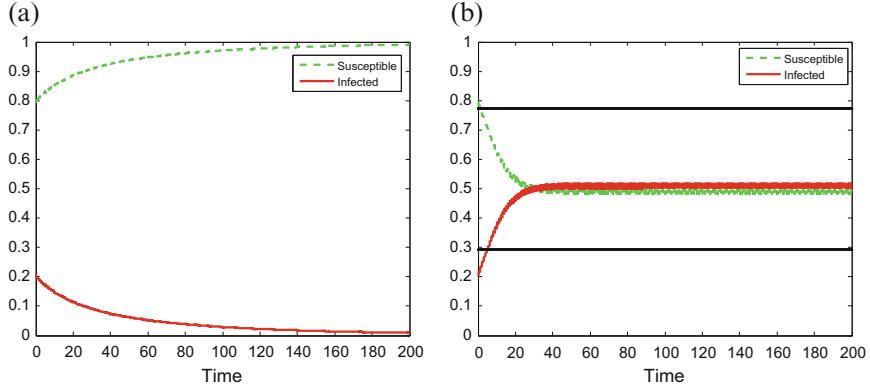
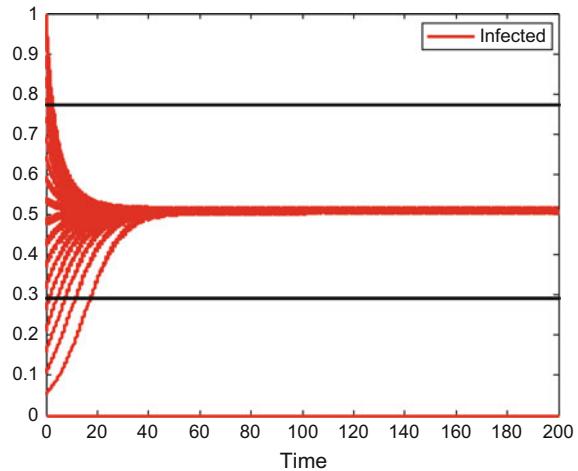


Fig. 4.2 Simulation of Example 4.1. (a) $R_0^{(4.11)} = 0.927$. (b) $\min\{R_0^{(4.11),i} : i \in \mathcal{M}\} = 1.41$; the black lines are I_{\min}^* and I_{\max}^*

Fig. 4.3 Simulations of Example 4.1 with different initial conditions. The solution eventually satisfies $I(t) \in [I_{\min}^*, I_{\max}^*]$ unless $I_0 = 0$



If instead $\beta_1 = 1/2$, $\beta_2 = 1/5$, $g_1 = 1/10$, $g_2 = 1/8$, $\mu_1 = 1/70$, and $\mu_2 = 1/60$, then $R_0^{(4.11)} = 2.04$ and the disease persists according to an extension of Theorem 4.2 (Theorem 2.3 in [98]). In fact, $\min\{R_0^{(4.1),1}, R_0^{(4.1),2}\} = 1.41$ and the solution converges to the convex hull of the endemic equilibria according to an extension of Theorem 4.3 (Theorem 2.4 in [98]). See Fig. 4.2 for an illustration with $(S_0, I_0) = (0.8, 0.2)$ and Fig. 4.3 for simulations with different initial conditions.

The spread of an infectious disease in a population depends crucially on two factors: (1) properties of its transmission mechanisms; and (2) the behavior of the host population. These two items are manifested in the infectious disease models via incidence rate constructions. In this part, we consider the following two generalizations of the standard incidence rate studied thus far: first, the standard incidence rate as

$$(S, I) \mapsto \beta(S + I)^{\alpha-1}SI = \beta N^\alpha \frac{SI}{N},$$

where $\alpha \in [0, 1]$ represents the pattern of daily encounters by individuals in the population $N = S + I$ ($\alpha = 0$ corresponds to the standard incidence rate) and the variables are non-normalized here. According to studies [171], $\alpha \approx 0.05 \pm 0.02$, justifying the choice of using the standard incidence rate thus far compared to the mass-action incidence rate (which corresponds to $\alpha = 1$). To see the effect of α on the switched SIS model, we proceed in this part with $\alpha \in [0, 1]$. Second, the host population's psychological behavior is taken into account by considering media coverage of an epidemic. The authors Li and Cui [83] considered the incidence rate

$$(S, I) \mapsto \left(\beta - \gamma \frac{I}{b + I} \right) SI,$$

where the variables are normalized, $\beta \equiv \rho c_1$, $\gamma \equiv \rho c_2$, $\rho > 0$ is the transmission probability if a contact is made between individuals, $c_1 > 0$ is the average number of contacts, and $c_2 > 0$ is the reduction in average number of contacts due to media coverage. Knowledge of an impending severe epidemic in a population via increased media coverage shifts the population behavior. Here $\beta \geq \gamma > 0$ is assumed to hold (the average number of new cases per unit time cannot become negative). The term $I/(b + I)$, $b > 0$, captures the relationship between the media coverage and psychological behavior of the susceptible population. This motivates the following switched incidence rate form:

$$(t, S, I) \mapsto \left(\beta_\sigma - \gamma_\sigma \frac{I}{b + I} \right) (S + I)^{\alpha-1} SI,$$

where $\beta_i \geq \gamma_i > 0$ for each $i \in \mathcal{M}$, and the corresponding switched SIS model:

$$\begin{aligned} \dot{S}(t) &= A - \left(\beta_\sigma - \frac{\gamma_\sigma I}{b + I} \right) (S(t) + I(t))^{\alpha-1} S(t) I(t) + g I(t) - \mu S(t), \\ \dot{I}(t) &= \left(\beta_\sigma - \frac{\gamma_\sigma I(t)}{b + I(t)} \right) (S(t) + I(t))^{\alpha-1} S(t) I(t) - (g + \mu) I(t), \\ (S(0), I(0)) &= (S_0, I_0), \end{aligned} \tag{4.12}$$

where the emigration rate $A > 0$ satisfies $0 < S_0 + I_0 \leq A/\mu$. Note that

$$\dot{N}(t) = \dot{S}(t) + \dot{I}(t) = A - \mu N(t)$$

and S and I are not fractions here as they have been up to this point; the meaningful physical domain is given by

$$D_{(4.12)} \equiv \{(S, I) \in \mathbb{R}_+^2 : S + I \leq A/\mu\},$$

whose positive invariance to (4.12) follows from

$$\{\dot{S} + \dot{I}\}|_{S+I=1} = 0, \quad \dot{S}|_{S=0} = A + gI > 0, \quad \dot{I}|_{I=0} = 0.$$

Here the disease-free equilibria is given by $Q_{\text{DFS}}^{(4.12)} \equiv (A/\mu, 0)$, whose stability can be shown by incorporating the comparison theorem into the methods previously outlined.

Theorem 4.4 *If $\sigma \in \mathcal{S}_{\text{periodic}}$ and*

$$R_0^{(4.12)} \equiv \left(\frac{A}{\mu}\right)^\alpha \left(\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)}\right) < 1$$

then the disease is eradicated; the solution of the switched SIS system (4.12) converges to the disease-free solution $Q_{\text{DFS}}^{(4.12)}$. If

$$\widehat{R}_0^{(4.12)} \equiv \left(\frac{A}{\mu}\right)^\alpha \left(\frac{\beta_{\max}}{\mu + g}\right) < 1$$

then the disease-free solution $Q_{\text{DFS}}^{(4.12)}$ is globally asymptotically stable in the meaningful domain $D_{(4.12)}$.

With the techniques of the previous chapter, combined with the intrinsic one-dimensionality of the model, global asymptotic stability of $Q_{\text{DFS}}^{(4.12)}$ in the meaningful domain is shown.

Proof The differential equation for I satisfies

$$\begin{aligned} \dot{I}(t) &= \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)}\right)(S(t) + I(t))^{\alpha-1} S(t) I(t) - (g + \mu)I(t), \\ &\leq \beta_k (A/\mu)^{\alpha-1} (A/\mu) I(t) - (g + \mu)I(t), \\ &= \beta_k (A/\mu)^\alpha I(t) - (g + \mu)I(t), \\ &= \lambda_k I(t), \quad \forall t \in [t_{k-1}, t_k], \end{aligned}$$

where $\lambda_i \equiv \beta_i (A/\mu)^\alpha - g - \mu$ for all $i \in \mathcal{M}$. It follows that

$$I(t) \leq I(t_{k-1}) \exp(\lambda_k(t - t_{k-1})), \quad \forall t \in [t_{k-1}, t_k], \quad (4.13)$$

which gives that

$$I(h\omega) \leq I_0 \exp\left(h \left(\sum_{i=1}^m \lambda_i \tau_i\right)\right), \quad \forall h \in \mathbb{N}. \quad (4.14)$$

Hence, $\{I(h\omega)\}$ is a monotonically decreasing sequence that converges to zero and, by the arguments in the proof of Theorem 3.1, $\lim_{t \rightarrow \infty} I(t) = 0$. The differential equation for the total population $\dot{N}(t) = A - \mu N(t)$ implies that

$$S(t) + I(t) = (S_0 + I_0 - A/\mu) \exp(-\mu t) + A/\mu, \quad \forall t \in \mathbb{R}_+,$$

so that $\lim_{t \rightarrow \infty} S(t) = A/\mu$. More than that, the solution can be given an upper bound in terms of the initial condition and a constant:

$$I(t) \leq I_0 \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i \right), \quad \forall t \geq 0,$$

where $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$; for any $\epsilon > 0$ choose $\delta = 0.5\epsilon \exp(-\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i)$, then

$$|(S(t), I(t)) - (1, 0)| \leq |S(t) - 1| + |I(t)| = 2I(t) < \epsilon.$$

Using the Generalized Binomial Theorem, a persistence result can be established for the endemic case.

Theorem 4.5 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(4.12)} > 1$, then the disease persists uniformly; there exists $\eta > 0$ such that $\liminf_{t \rightarrow \infty} I(t) \geq \eta$.*

Proof If $I(t) < \epsilon$ for $t \in [t_e, +\infty)$ for some $t_e > 0$ then $\dot{S}(t) > A - \beta_{\max}(A/\mu)^{\alpha-1}(A/\mu)\epsilon - \mu S(t)$ for all $t \in [t_e, +\infty)$. The ODE system

$$\begin{aligned} \dot{S}_m(t) &= \left(A - \epsilon \beta_{\max} \left(\frac{A}{\mu} \right)^\alpha \right) - \mu S_m(t), \\ S_m(t_e) &= S_0, \end{aligned} \tag{4.15}$$

has a unique solution S_m on $[t_e, +\infty)$ which satisfies

$$\lim_{t \rightarrow \infty} S_m(t) = \frac{A}{\mu} - \frac{\epsilon \beta_{\max} A^\alpha}{\mu^{\alpha+1}}.$$

The existence of $t^* \geq t_e$ follows such that

$$S(t) \geq \frac{A}{\mu} - \frac{\epsilon \beta_{\max} A^\alpha}{\mu^{\alpha+1}} - \epsilon, \quad \forall t \geq t^*.$$

For $k \in \mathbb{N}$ satisfying $t^* < t_{k-1} < t \leq t_k$,

$$\begin{aligned} \dot{I}(t) &= \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)} \right) (S(t) + I(t))^{\alpha-1} S(t) I(t) - (g + \mu) I(t), \\ &\geq \left(\beta_k - \frac{\gamma_{\max} \epsilon}{b + \epsilon} \right) \left(\frac{A}{\mu} - \frac{\epsilon \beta_{\max} A^\alpha}{\mu^{\alpha+1}} - \epsilon \right)^\alpha I(t) - (g + \mu) I(t), \end{aligned}$$

where $\gamma_{\max} \equiv \max\{\gamma_i : i \in \mathcal{M}\}$. Defining

$$B \equiv \frac{\beta^* A^\alpha}{\mu^{\alpha+1}} + 1,$$

$A/\mu > B\epsilon$ implies that $(A/\mu - B\epsilon)^\alpha$ can be expanded using the Generalized Binomial Theorem:

$$\begin{aligned} \left(\frac{A}{\mu} - B\epsilon\right)^\alpha &= \sum_{k=0}^{\infty} \binom{\alpha}{k} \left(\frac{A}{\mu}\right)^{\alpha-k} (-B\epsilon)^k, \\ &= \left(\frac{A}{\mu}\right)^\alpha - \epsilon\alpha B \left(\frac{A}{\mu}\right)^{\alpha-1} + \sum_{k=2}^{\infty} \binom{\alpha}{k} \left(\frac{A}{\mu}\right)^{\alpha-k} (-B\epsilon)^k. \end{aligned}$$

Then, if $A/\mu > B\epsilon$ and $\epsilon < 1$,

$$\begin{aligned} \sum_{k=2}^{\infty} \binom{\alpha}{k} \left(\frac{A}{\mu}\right)^{\alpha-k} (-B\epsilon)^k &= \left(\frac{A}{\mu}\right)^\alpha \sum_{k=2}^{\infty} \binom{\alpha}{k} \left(\frac{-\epsilon B \mu}{A}\right)^k, \\ &\geq \frac{-\alpha(\alpha-1)}{2} \left(\frac{B\mu}{A}\right). \end{aligned}$$

Thus,

$$\begin{aligned} \left(\frac{A}{\mu} - B\epsilon\right)^\alpha &\geq \left(\frac{A}{\mu}\right)^\alpha - \epsilon \left(\frac{A}{\mu}\right)^\alpha \left(\frac{B\mu}{A} + \frac{\alpha(\alpha-1)B\mu}{2A}\right), \\ &= \left(\frac{A}{\mu}\right)^\alpha - \epsilon B \left(\frac{A}{\mu}\right)^{\alpha-1} \left(1 + \frac{\alpha(\alpha-1)}{2}\right), \end{aligned}$$

which yields that

$$\begin{aligned} I(t) &\geq I(t^*) \exp \left(\int_{t^*}^t \left\{ \left[\beta_{\sigma(s)} - \frac{\gamma_{\max}\epsilon}{b+\epsilon} \right] \left[\frac{A}{\mu} - B\epsilon \right]^\alpha - (g + \mu) \right\} ds \right), \\ &\geq I(t^*) \exp \left(\int_{t^*}^t \left\{ \left[\beta_{\sigma(s)} - \frac{\gamma_{\max}\epsilon}{b+\epsilon} \right] \left(\frac{A}{\mu} \right)^\alpha \right\} ds \right) \\ &\quad \times \exp \left[- \int_{t^*}^t \left\{ \left[\beta_{\sigma(s)} - \frac{\gamma_{\max}\epsilon}{b+\epsilon} \right] \left[\epsilon B \left(\frac{A}{\mu} \right)^{\alpha-1} \left[1 + \frac{\alpha(\alpha-1)}{2} \right] \right] \right\} ds \right] \\ &\quad \times \exp \left[- \int_{t^*}^t (g + \mu) ds \right], \\ &= I(t^*) \exp \left[\int_{t^*}^t \left(\beta_{\sigma(s)} \left(\frac{A}{\mu} \right)^\alpha - g - \mu + G(\epsilon) \right) ds \right], \end{aligned}$$

for all $t \in [t^* + (k-1)\omega, t^* + k\omega]$, where

$$G(\epsilon) \equiv -\frac{\gamma_{\max}\epsilon}{a+\epsilon} \left[\left(\frac{A}{\mu}\right)^\alpha + \epsilon B \left(\frac{A}{\mu}\right)^{\alpha-1} \left[1 + \frac{\alpha(\alpha-1)}{2} \right] \right] \\ - \epsilon \beta_{\max} B \left(\frac{A}{\mu}\right)^{\alpha-1} \left[1 + \frac{\alpha(\alpha-1)}{2} \right].$$

It follows that

$$I(t) \geq I(t^*) \exp \left\{ \int_{t^*}^{t^* + (k-1)\omega} (\beta_{\sigma(s)}(A/\mu)^\alpha - g - \mu + G(\epsilon)) ds \right\} \\ \times \exp \left\{ \int_{t^* + (k-1)\omega}^t (\beta_{\sigma(s)}(A/\mu)^\alpha - g - \mu + G(\epsilon)) ds \right\}, \\ \geq M \exp \left\{ (k-1) \left[\int_0^\omega (\beta_{\sigma(s)}(A/\mu)^\alpha - g - \mu) ds + \omega G(\epsilon) \right] \right\},$$

where $M \equiv I(t^*) \exp(-\omega(g + \mu) + \omega G(\epsilon))$. $R_0^{(4.12)} > 1$ implies the existence of $\epsilon_1 > 0$ such that

$$\phi(\epsilon_1) \equiv \left((A/\mu)^\alpha \sum_{i=1}^m \beta_i \tau_i - \omega(g + \mu) + \omega G(\epsilon_1) \right) > 0.$$

Choosing $\epsilon \equiv 0.5 \min\{\epsilon_1, A/(\mu B), 1\}$ yields that $I(t) \geq M \exp((k-1)\phi(\epsilon))$, a contradiction. There must exist a time $t^1 > t^*$ for which $I(t^1) \geq \eta$; weak uniform persistence of I holds. Uniform persistence can then be shown by observing that $\dot{I}(t) \geq -(g + \mu)(t)$ and using similar arguments as in the proof of Theorem 3.4.

From a practical point of view, it can be difficult to approximate the basic reproduction number, and even more so when it is changing over time. Moreover, the switching rule may not always be exactly periodic. Defining the mode basic reproduction numbers

$$R_0^{(4.12),i} \equiv \left(\frac{A}{\mu} \right)^\alpha \left(\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} \right),$$

the results in Sect. 3.4 are easily mirrored (i.e., Theorems 3.2 and 3.3) via the bound (4.13). Namely, $Q_{\text{DFS}}^{(4.12)}$ is globally attractive and exponentially I -stable in the physically meaningful domain $D_{(4.12)}$ if either of the following conditions hold:

(1) $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$\left\langle R_0^{(4.12)} \right\rangle \equiv \sup_{t \geq h} \sum_{i=1}^m R_0^{(4.12),i} T_i(t) < 1,$$

for some $h > 0$;

- (2) $\sigma \in \mathcal{S}_{\text{dwell}}$ satisfies $T^+ \leq N_0 + qT^-(t)$ for some $q \in (0, 1)$ and $N_0 \geq 0$ such that

$$R_0^{(4.12),-} - 1 < q(R_0^{(4.12),+} - 1),$$

where $R_0^{(3.8),-} \equiv \max\{R_0^{(3.8),i} : i \in \mathcal{M}^-\}$ and $R_0^{(3.8),+} \equiv \max\{R_0^{(3.8),i} : i \in \mathcal{M}^+\}$ and

$$\begin{aligned} T^+(t) &\equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^+\}|, \\ T^-(t) &\equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^-\}|. \end{aligned}$$

Example 4.2 Consider the switched SIS model with media coverage incidence rate (4.12) and assume that $\mathcal{M} = \{1, 2\}$ follows the switching rule

$$\sigma(t) = \begin{cases} 1, & \text{if } t \in [2k, 2k+2), \quad k = 0, 1, 2, \dots, \\ 2, & \text{if } t \in [2k+2, 2k+4), \end{cases} \quad (4.16)$$

which is periodic with $\tau_1 = 2$, $\tau_2 = 2$ and $\omega = 4$. Motivated by the parameter values of [171], let $A = 3000$, $\beta_1 = 1/10$, $\beta_2 = 1/5$, $\gamma_1 = 1/30$, $\gamma_2 = 1/7$, $g = 1/5$, $\mu = 1/10$, $b = 0.5$, and $\alpha = 0.07$. The contact rate varies every 2 years and, accordingly, there is an increase in media coverage (and hence reduction in the real, media-adjusted contact rate). Let $(S_0, I_0) = (12, 000, 2000)$ (i.e., $N_0 = 14,000$) and $\alpha = 0.07$ to reflect the daily contact patterns of individuals. Then $R_0^{(4.12)} = 3.50$ and the disease persists by Theorem 4.5 (see Fig. 4.4a). If instead, $A = 300$, $\beta_1 = 1/10$, $\beta_2 = 1/5$, $\gamma_1 = 1/20$, $\gamma_2 = 1/10$, $g_1 = 9/10$, $g_2 = 2/5$, (i.e., switching recovery rates) $\mu = 1/10$, $b = 0.5$, and $\alpha = 0.5$, then $R_0^{(4.12)} = 11.0$ and the disease persists by an extension of Theorem 4.5 (Theorem 3.2 in [98]). Here $\alpha = 0.5$ reflects the influence of the smaller community size on daily encounters. Given the initial conditions $(S_0, I_0) = (1800, 15)$, see Fig. 4.4b for an illustration.

4.2 Multi-City Epidemics: Modeling Traveling Infections

Travel has created an easy way for many infectious diseases to be transmitted from one region to another. The SARS outbreak in 2003 is a clear example of the effects of travel on the spread of a disease as it initially began in only one area of China and eventually spread to most of the country as well as other cities in the world due to travel of infected individuals [100]. A second example can be seen in the outbreak of measles in Iceland due, in part, to infected individuals traveling to the country [147]. More recently, in April 2009, the H1N1 influenza virus appeared in Mexico, and soon spread to other countries all over the world [167]. In many developing

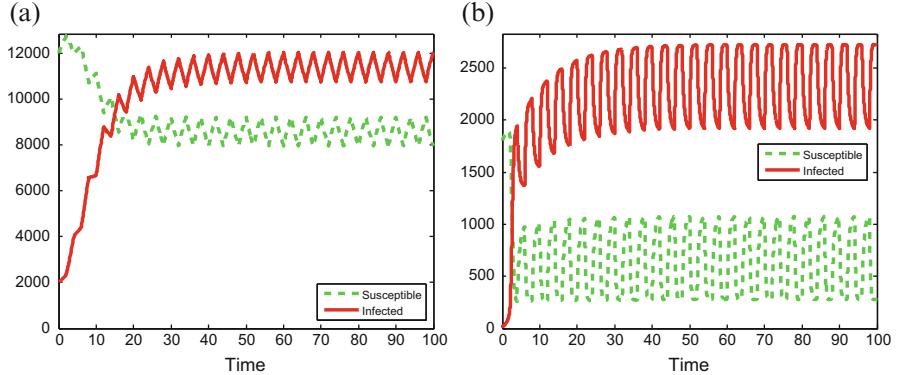


Fig. 4.4 Simulations of Example 4.2. (a) $R_0^{(4.12)} = 3.50$. (b) $R_0^{(4.12)} = 11.0$

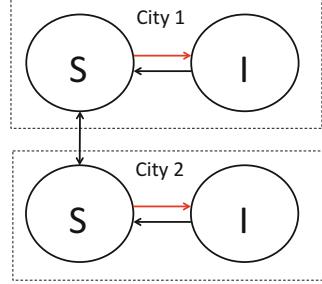
countries, poor traveling conditions in mass transit, such as limited sanitation, leads to an increase in the spread of diseases due to infected individuals using transit [146].

Consider complicating the switched SIS system (4.1) by adding geographic factors. To begin, suppose that there are two cities (or patches) and the susceptible population is permitted to travel at a per capita rate $\alpha > 0$ (called the dispersal rate) between the cities. With the other modeling assumptions of the switched SIS system (4.1), the multi-city model is given as

$$\begin{aligned} \dot{S}^{(1)}(t) &= \mu N^{(1)}(t) - \beta_\sigma \frac{S^{(1)}(t)I^{(1)}(t)}{N^{(1)}(t)} - \mu S^{(1)}(t) \\ &\quad + gI^{(1)}(t) - \alpha S^{(1)}(t) + \alpha S^{(2)}(t), \\ \dot{I}^{(1)}(t) &= \beta_\sigma \frac{S^{(1)}(t)I^{(1)}(t)}{N^{(1)}(t)} - gI^{(1)}(t) - \mu I^{(1)}(t), \\ \dot{S}^{(2)}(t) &= \mu N^{(2)}(t) - \frac{S^{(2)}(t)I^{(2)}(t)}{N^{(2)}(t)} - \mu S^{(2)}(t) \\ &\quad + gI^{(2)}(t) - \alpha S^{(2)}(t) + \alpha S^{(1)}(t), \\ \dot{I}^{(2)}(t) &= \beta_\sigma \frac{S^{(2)}(t)I^{(2)}(t)}{N^{(2)}(t)} - gI^{(2)}(t) - \mu I^{(2)}(t), \\ (S^{(j)}(0), I^{(j)}(0)) &= (S_0^{(j)}, I_0^{(j)}), \quad \forall j \in \{1, 2\}, \end{aligned} \tag{4.17}$$

where $N^{(1)} \equiv S^{(1)} + I^{(1)}$ and $N^{(2)} \equiv S^{(2)} + I^{(2)}$. In this way, homogeneity of the population mixing has been changed; the groups $S^{(1)}$ and $S^{(2)}$ interact with the infected group $I^{(1)}$ in vastly different ways. The flow of the model can be seen in Fig. 4.5.

Fig. 4.5 Flow diagram of the Multi-city SIS model (4.17)



Next, suppose that infected individuals also travel and, due to dense crowds on mass transportation (which may have relatively poor sanitary conditions in developing countries [146]), the disease is transmitted between traveling individuals. More specifically, assume that the disease is transmitted at a contact rate $\gamma > 0$ during travel. The traveling incidence rate therefore takes the form

$$\gamma \frac{(\alpha S^{(j)}) (\alpha I^{(j)})}{\alpha N^{(j)}} = \gamma \frac{(\alpha S^{(j)}) (\alpha I^{(j)})}{(\alpha S^{(j)}) + (\alpha I^{(j)})} = \gamma \alpha \frac{S^{(j)} I^{(j)}}{S^{(j)} + I^{(j)}}.$$

This leads to the following model:

$$\begin{aligned}
\dot{S}^{(1)}(t) &= \mu N^{(1)}(t) - \beta_\sigma \frac{S^{(1)}(t) I^{(1)}(t)}{N^{(1)}(t)} - \mu S^{(1)}(t) + g I^{(1)}(t) \\
&\quad - \alpha S^{(1)}(t) + \alpha S^{(2)}(t) - \alpha \gamma \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)}, \\
\dot{I}^{(1)}(t) &= \beta_\sigma \frac{S^{(1)}(t) I^{(1)}(t)}{N^{(1)}(t)} - g I^{(1)}(t) - \mu I^{(1)}(t) - \alpha I^{(1)}(t) \\
&\quad + \alpha I^{(2)}(t) + \alpha \gamma \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)}, \\
\dot{S}^{(2)}(t) &= \mu N^{(2)}(t) - \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)} - \mu S^{(2)}(t) + g I^{(2)}(t) \\
&\quad - \alpha S^{(2)}(t) + \alpha S^{(1)}(t) - \alpha \gamma \frac{S_{c_1(t)} I^{(1)}(t)}{N^{(1)}(t)}, \\
\dot{I}^{(2)}(t) &= \beta_\sigma \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)} - g I^{(2)}(t) - \mu I^{(2)}(t) - \alpha I^{(2)}(t) \\
&\quad + \alpha I^{(1)}(t) + \alpha \gamma \frac{S^{(1)}(t) I^{(1)}(t)}{N^{(1)}(t)}, \\
(S^{(j)}(0), I^{(j)}(0)) &= (S_0^{(j)}, I_0^{(j)}), \quad \forall j \in \{1, 2\}.
\end{aligned} \tag{4.18}$$

The total population, $N \equiv N^{(1)} + N^{(2)}$, satisfies

$$\dot{N}(t) = \dot{S}^{(1)}(t) + \dot{I}^{(1)}(t) + \dot{S}^{(2)}(t) + \dot{I}^{(2)}(t) = 0,$$

though $N^{(1)}$ and $N^{(2)}$ need not be constant (the system is closed when considering both cities together).

The meaningful physical domain of (4.18) is given by

$$D_{(4.18)} \equiv \{(S^{(1)}, S^{(2)}, I^{(1)}, I^{(2)}) \in \mathbb{R}_+^4 : S^{(1)} + I^{(1)} + S^{(2)} + I^{(2)} = N\},$$

which is positively invariant to (4.18). Observe that

$$\alpha S^{(j)} - \alpha \gamma \frac{S^{(j)} I^{(j)}}{S^{(j)} + I^{(j)}} \geq 0, \quad \forall j \in \{1, 2\},$$

as long as $(S^{(j)}, I^{(j)}) \in \mathbb{R}_+^2$; the difference between the number of susceptible individuals traveling from city j and those being infected while traveling from city j is nonnegative. From this, invariance of $D_{(4.18)}$ to (4.18) is shown as follows:

$$\{\dot{S}^{(1)} + \dot{I}^{(1)} + \dot{S}^{(2)} + \dot{I}^{(2)}\}_{|S^{(1)}+I^{(1)}+S^{(2)}+I^{(2)}=N} = 0,$$

$$\dot{S}^{(1)}|_{S^{(1)}=0} = (\mu + g)I^{(1)} + \alpha S^{(2)} - \alpha \gamma \frac{S^{(2)}I^{(2)}}{N^{(2)}} \geq 0, \quad \dot{I}^{(1)}|_{I^{(1)}=0} = \alpha I^{(2)} + \alpha \gamma \frac{S^{(2)}I^{(2)}}{N^{(2)}} \geq 0,$$

$$\dot{S}^{(2)}|_{S^{(2)}=0} = (\mu + g)I^{(2)} + \alpha S^{(1)} - \alpha \gamma \frac{S^{(1)}I^{(1)}}{N^{(1)}} \geq 0,$$

$$\dot{I}^{(2)}|_{I^{(2)}=0} = \alpha I^{(1)} + \alpha \gamma \frac{S^{(1)}I^{(1)}}{N^{(1)}} \geq 0.$$

If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and the basic reproduction number

$$R_0^{(4.18)} \equiv \frac{(\sum_{i=1}^m \beta_i \tau_i) + \omega \alpha \gamma}{\omega(\mu + g)} < 1$$

then $Q_{\text{DFS}}^{(4.18)} \equiv (N/2, 0, N/2, 0)$ is attractive in the meaningful domain $D_{(4.12)}$. A more precise characterization is that $Q_{\text{DFS}}^{(4.18)}$ is exponentially $(I^{(1)}, I^{(2)})$ -stable in $D_{(4.12)}$, which can be shown using the techniques detailed thus far:

$$\begin{aligned} \frac{d(I^{(1)} + I^{(2)})}{dt}(t) &= \beta_\sigma \left(\frac{S^{(1)}(t)I^{(1)}(t)}{S^{(1)}(t) + I^{(1)}(t)} + \frac{S^{(2)}(t)I^{(2)}(t)}{S^{(2)}(t) + I^{(2)}(t)} \right) \\ &\quad - (g + \mu)(I^{(1)}(t) + I^{(2)}(t)) \end{aligned}$$

$$\begin{aligned}
& + \alpha\gamma \left(\frac{S^{(1)}(t)I^{(1)}(t)}{S^{(1)}(t) + I^{(1)}(t)} + \frac{S^{(2)}(t)I^{(2)}(t)}{S^{(2)}(t) + I^{(2)}(t)} \right), \\
& \leq (\beta_\sigma + \alpha\gamma - g - \mu)(I^{(1)}(t) + I^{(2)}(t)), \\
& = \lambda_\sigma(I^{(1)}(t) + I^{(2)}(t)),
\end{aligned} \tag{4.19}$$

where $\lambda_i \equiv \beta_i + \alpha\gamma - g - \mu$ for each $i \in \mathcal{M}$. It is straightforward to show that the 1-norm satisfies

$$|(I^{(1)}(t), I^{(2)}(t))|_1 = I^{(1)}(t) + I^{(2)}(t) \leq (I_0^{(1)} + I_0^{(2)}) \exp(-ct)$$

for some $c > 0$. The limiting equations for $S^{(1)}$ and $S^{(2)}$ are given by the system

$$\begin{aligned}
\dot{S}^{(1)}(t) &= -\alpha S^{(1)}(t) + \alpha S^{(2)}(t), \\
\dot{S}^{(2)}(t) &= -\alpha S^{(2)}(t) + \alpha S^{(1)}(t).
\end{aligned} \tag{4.20}$$

$S^{(1)} + S^{(2)} = N$ is an invariant of (4.20), from which it follows that

$$\lim_{t \rightarrow \infty} S^{(1)}(t) = \lim_{t \rightarrow \infty} S^{(2)}(t) = N/2.$$

Note that traveling infected can cause the disease to become endemic in both cities while eradication would be the outcome in either city if travel were to be restricted (i.e., $\alpha = 0$). This can be observed in the basic reproduction number via the $\alpha\gamma$ term and motivates the notion of limiting the spread of a disease by restricting travel and screening individuals (this idea will be revisited in Chap. 5).

Extending the model to $n \in \mathbb{N}$ cities or patches is natural at this point: let $S^{(j)}$, $I^{(j)}$, $R^{(j)}$, and $N^{(j)}$ denote the susceptible, infected, recovered, and total population in city $j \in \mathcal{N} \equiv \{1, \dots, n\}$, respectively. Motivated by the analysis of (3.29), consider a general switched incidence rate for its flexibility in modeling a term-time forcing contact rate or a change in the fundamental structure of the disease spread. Assume that, in city $j \in \mathcal{N}$, the birth/death rate is given by $\mu^{(j)} > 0$ and the recovery rate by $g^{(j)} > 0$. Individuals do not die, recover, or give birth while traveling between cities. The per capita dispersal rate from city $l \in \mathcal{N}$ to city $j \in \mathcal{N} \setminus \{l\}$ is given by $\alpha^{(l,j)} \geq 0$. Let $-\alpha^{(j,j)} \geq 0$ denote the emigration rate from city j to all other cities. The general switched incidence rate in city $j \in \mathcal{N}$ is denoted by the function

$$(t, S^{(j)}, I^{(j)}) \mapsto f_\sigma^{(j)}(S^{(j)}, I^{(j)})$$

(only individuals in city j affect the spread of the disease there), where $\sigma \in \mathcal{S}_{\text{dwell}}$ is a switching rule, and dependence on $N^{(j)}$ is not explicitly stated but is understood. The generalized traveling incidence rate from city $l \in \mathcal{N}$ to city $j \in \mathcal{N} \setminus \{l\}$ is denoted by the function

$$(t, S^{(l)}, I^{(l)}) \mapsto h_\sigma^{(l,j)}(S^{(l)}, I^{(l)}).$$

Omitting the arguments for the switched incidence rate functions, the model is thus formulated as the following ODE system:

$$\begin{aligned}
\dot{S}^{(j)}(t) &= \mu^{(j)}N^{(j)}(t) - f_\sigma^{(j)} - \mu^{(j)}S^{(j)}(t) \\
&\quad + \sum_{l \in \mathcal{N}} \alpha^{(l,j)}S^{(l)}(t) - \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)}h_\sigma^{(l,j)}, \quad \forall j \in \mathcal{N} \\
\dot{I}^{(j)}(t) &= f_\sigma^{(j)} - g^{(j)}I^{(j)}(t) - \mu^{(j)}I^{(j)}(t) \\
&\quad + \sum_{l \in \mathcal{N}} \alpha^{(l,j)}I^{(l)}(t) + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)}h_\sigma^{(l,j)}, \quad \forall j \in \mathcal{N}, \\
\dot{R}^{(j)}(t) &= g^{(j)}I^{(j)}(t) - \mu^{(j)}R^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)}R^{(l)}(t), \quad \forall j \in \mathcal{N}, \\
(S^{(j)}(0), I^{(j)}(0), R^{(j)}(0)) &= (S_0^{(j)}, I_0^{(j)}, R_0^{(j)}), \quad \forall j \in \mathcal{N}.
\end{aligned} \tag{4.21}$$

The following observations are made (some of which are extended from [146, 167]):

1. $h_i^{(l,j)}(S^{(l)}, I^{(l)}) = h_i^{(j,l)}(S^{(l)}, I^{(l)})$ for each $l, j \in \mathcal{N}$; the transportation method between cities l and j is identical in either direction.
2. $S^{(j)}(t) + I^{(j)}(t) + R^{(j)}(t) = N^{(j)}(t)$ for all t and $\sum_{j \in \mathcal{N}} N^{(j)} \equiv N \in \mathbb{R}_+$.
3. Most often it is assumed that $S_0^{(j)} > 0$ for all $j \in \mathcal{N}$ (all cities begin with some number of susceptible) and $I_0^{(j^*)} > 0$ for some $j^* \in \mathcal{N}$ (at least one city begins with some infected).
4. The meaningful domain is positively invariant and given by

$$D_{(4.21)} \equiv \left\{ (S, I, R) \in \mathbb{R}_+^{3n} : N = \sum_{j \in \mathcal{N}} S^{(j)} + I^{(j)} + R^{(j)} \right\},$$

where the notation

$$(S, I, R) \equiv (S^{(1)}, S^{(2)}, \dots, S^{(n)}, I^{(1)}, I^{(2)}, \dots, I^{(n)}, R^{(1)}, R^{(2)}, \dots, R^{(n)})$$

is adopted for the rest of this section.

5. $\sum_{l \in \mathcal{N}} \alpha^{(l,j)} = 0$ for each $j \in \mathcal{N}$ (sum of immigration must equal emigration);
6. The matrix formed with entries $(\alpha^{(l,j)})_{1 \leq l, j \leq n}$ in row l and column j is irreducible (the n cities cannot be separated into two groups of cities such that there is no immigration from one group of cities to the other).
7. For each $l \in \mathcal{N}, j \in \mathcal{N} \setminus \{l\}, i \in \mathcal{M}$, the traveling condition

$$\alpha^{(l,j)}S^{(j)} - \alpha^{(l,j)}h_i^{(l,j)}(S^{(l)}, I^{(l)}) \geq 0, \tag{4.22}$$

holds (the number of susceptible individuals traveling to city $j \in \mathcal{N}$ must enter city j as either susceptible or infected);

8. The function $f_i^{(j)}$ is assumed to be smooth for each $j \in \mathcal{N}$ and each $i \in \mathcal{M}$ and satisfies physically reasonable restrictions; i.e.,

$$f_i^{(j)}(S^{(j)}, I^{(j)}) > 0,$$

and

$$f_i^{(j)}(S^{(j)}, 0) = 0,$$

for physically realizable values of $(S^{(j)}, I^{(j)})$.

9. The function $h_i^{(j,l)}$ is assumed to be smooth for each $l \in \mathcal{N}, j \in \mathcal{N} \setminus \{l\}$, and $i \in \mathcal{M}$ and satisfies similar physically reasonable restrictions.

Figure 4.6 illustrates the flow diagram of (4.21). Observe that $D_{(4.21)}$ is positively invariant to (4.21) under the above assumptions:

$$\left(\sum_{j \in \mathcal{N}} \dot{S}^{(j)} + \dot{I}^{(j)} + \dot{R}^{(j)} \right) \Big|_{\sum_{j \in \mathcal{N}} S^{(j)} + I^{(j)} + R^{(j)} = N} = 0,$$

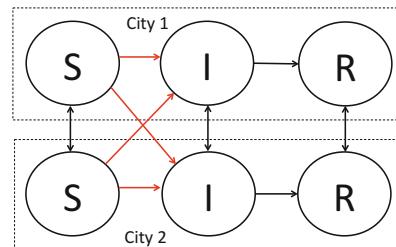
$\dot{S}^{(j)}|_{S^{(j)}=0} \geq 0$, $\dot{I}^{(j)}|_{I^{(j)}=0} \geq 0$, and $\dot{R}^{(j)}|_{R^{(j)}=0} \geq 0$. The flow of (4.21) is detailed in Fig. 4.6.

We detail the basic reproduction number of (4.21) by working from a simplified version of the model (i.e., restricted travel and time-invariant incidence rates) up to the full model.

1. *Restricted travel and time-invariant incidence rates:* When $\alpha^{(l,j)} = 0$ for all $i, j \in \mathcal{N}$ and $f_\sigma^{(j)}(S^{(j)}, I^{(j)}) \equiv f^{(j)}(S^{(j)}, I^{(j)})$ for all $j \in \mathcal{N}, i \in \mathcal{M}$, the switched multi-city system (4.21) models n closed cities which do not interact. The basic reproduction number of each city is given by the closed-form expression [73]:

$$R_0^{(4.21),(j)} = \frac{1}{\mu + g} \left(\frac{\partial f^{(j)}}{\partial I^{(j)}}(N^{(j)}, 0) \right), \quad \forall j \in \mathcal{N},$$

Fig. 4.6 Flow of multi-city SIR model (4.21) for $n = 2$. The red lines represent new infections



where $N^{(j)}$ is constant in this case since

$$\dot{N}^{(j)}(t) = \dot{S}^{(j)}(t) + \dot{I}^{(j)}(t) + \dot{R}^{(j)}(t) = 0, \quad \forall t.$$

As expected, the long-term behavior is dictated by $R_0^{(4.21),(j)}$ as follows: $R_0^{(4.21),(j)} < 1$ yields global asymptotic stability of $(N^{(j)}, 0)$ in each city, while $R_0^{(4.21),(j)} > 1$ yields global asymptotic stability of an endemic equilibrium (the results of [73] are applicable to each city individually).

2. *Restricted travel and switching incidence rates*: If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, then the basic reproduction number of each city in the switched multi-city model (4.21) is given by [11]:

$$R_0^{(4.21),(j)} = \sum_{i=1}^m \frac{\partial f^{(j)}}{\partial I^{(j)}}(N^{(j)}, 0) \tau_i \frac{1}{\omega(\mu + g)}, \quad \forall j \in \mathcal{N},$$

where $N^{(j)}$ is constant, as above, and has the usual physical interpretation; $R_0^{(4.21),(j)}$ is the average number of secondary infections resulting from the introduction of an infected individual into city j with a wholly susceptible population.

3. *Unrestricted travel and time-invariant incidence rates*: The basic reproduction number of the multi-city model (4.21) in this case is the spectral radius of its next-generation matrix [152]:

$$R_0^{(4.21)} = \rho(FV^{-1}),$$

where

$$F \equiv \begin{bmatrix} \frac{\partial f^{(1)}}{\partial I^{(1)}} & \alpha^{(2,1)} \frac{\partial h^{(2,1)}}{\partial I^{(2)}} & \dots & \alpha^{(n,1)} \frac{\partial h^{(n,1)}}{\partial I^{(n)}} \\ \alpha^{(1,2)} \frac{\partial h^{(1,2)}}{\partial I^{(2)}} & \frac{\partial f^{(2)}}{\partial I^{(2)}} & \dots & \alpha^{(n,2)} \frac{\partial h^{(n,1)}}{\partial I^{(n)}} \\ \vdots & & \ddots & \vdots \\ \alpha^{(1,n)} \frac{\partial h^{(1,n)}}{\partial I^{(2)}} & \dots & \alpha^{(n-1,n)} \frac{\partial h^{(n-1,n)}}{\partial I^{(n-1)}} & \frac{\partial f^{(n)}}{\partial I^{(n)}} \end{bmatrix},$$

and

$$V \equiv \begin{bmatrix} \mu^{(1)} + g^{(1)} + \alpha^{(1,1)} & -\alpha^{(2,1)} & \dots & -\alpha^{(n,1)} \\ -\alpha^{(1,2)} & \mu^{(2)} + g^{(2)} + \alpha^{(2,2)} & \dots & -\alpha^{(n,2)} \\ \vdots & & \ddots & \vdots \\ -\alpha^{(1,n)} & \dots & -\alpha^{(n-1,n)} & \mu^{(n)} + g^{(n)} + \alpha^{(n,n)} \end{bmatrix},$$

where the argument of $h^{(l,j)}$ in the matrix F is $(\tilde{S}^{(l)}, 0)$ (the disease-free solution, whose existence is guaranteed from the irreducibility and cooperativeness of the matrix A but whose full form is omitted; see [170] for details).

Here, the (i,j) entry of F represents the rate of new infections in city $j \in \mathcal{N}$ caused by infected individuals in city $i \in \mathcal{N}$ and the (i,j) entry of V^{-1} represents the average period of time spent in city $j \in \mathcal{N}$ during an average lifetime (assuming the population remains near the disease-free solution) [152].

4. *Unrestricted travel and switching incidence rates:* The basic reproduction number is complicated by multiple infected compartments flowing into one another and can only be implicitly defined as the spectral radius of its next-generation integral operator, $R_0^{(4.21)} = \rho(L)$. However, the disease is eradicated in each city under a threshold condition on the model parameters, which may be interpreted as an approximation of the basic reproduction number.

Theorem 4.6 Assume that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and there exist $\beta_i, \gamma_i > 0$ such that $f_i^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \leq \beta_i S^{(j)} I^{(j)} / N^{(j)}$ and $h_i^{(l,j)}(S^{(l)}, I^{(l)}, N^{(l)}) \leq \gamma_i S^{(l)} I^{(l)} / N^{(l)}$ for each $j \in \mathcal{N}, l \in \mathcal{N}, i \in \mathcal{M}$. If

$$\widehat{R}_0^{(4.21)} \equiv \frac{\sum_{i=1}^m (\beta_i + (n-1)\alpha_{\max} \gamma_i) \tau_i}{\omega(\mu_{\min} + g_{\min})} < 1, \quad (4.23)$$

where $\alpha_{\max} \equiv \max\{\alpha^{(l,j)} : l \in \mathcal{N}, j \in \mathcal{N} \setminus \{l\}\}$, $\mu_{\min} \equiv \min\{\mu^{(j)} : j \in \mathcal{N}\}$, and $g_{\min} \equiv \min\{g^{(j)} : j \in \mathcal{N}\}$, then the solution of the switched multi-city (4.21) satisfies

$$\lim_{t \rightarrow \infty} I(t) = \lim_{t \rightarrow \infty} (I^{(1)}(t), \dots, I^{(n)}(t)) = 0;$$

the disease is eradicated in each city.

Proof Let $I \equiv \sum_{j \in \mathcal{N}} I^{(j)}$. Then

$$\begin{aligned} \dot{I}(t) &= \sum_{j \in \mathcal{N}} (f_\sigma^{(j)}(S^{(j)}(t), I^{(j)}(t), N^{(j)}(t)) - (g^{(j)} + \mu^{(j)}) I^{(j)}(t)) \\ &\quad + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} h_\sigma^{(l,j)}(S^{(l)}(t), I^{(l)}(t), N^{(l)}(t)), \\ &\leq \sum_{j \in \mathcal{N}} \left((\beta_\sigma - g_{\min} - \mu_{\min}) I^{(j)}(t) + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma I^{(l)}(t) \right), \\ &\leq (\beta_\sigma - g_{\min} - \mu_{\min} + (n-1)\alpha_{\max} \gamma_\sigma) \sum_{j \in \mathcal{N}} I^{(j)}(t), \\ &= \lambda_\sigma I(t), \end{aligned} \quad (4.25)$$

where $\lambda_i \equiv \beta_i + (n-1)\alpha_{\max} \gamma_i - g_{\min} - \mu_{\min}$ for each $i \in \mathcal{M}$. Successive applications of Eq. (4.25) on each subinterval $[t_{k-1}, t_k]$, $k \in \mathbb{N}$, and noting that (4.23) implies $\sum_{i=1}^m \lambda_i \tau_i < 0$ yield

$$I(\omega) \leq \left(\sum_{j \in \mathcal{N}} I_0^{(j)} \right) \exp \left(\sum_{i=1}^m \lambda_i \tau_i \right). \quad (4.26)$$

The usual approach can thus be applied (i.e., the proof of Theorem 3.1) to conclude that $\{\sum_{j=1}^n I^{(j)}(h\omega)\}_{h=0}^\infty$ converges to zero and, moreover,

$$\lim_{t \rightarrow \infty} I^{(j)}(t) = 0, \quad \forall j \in \mathcal{N}.$$

Example 4.3 Consider the multi-city SIR system (4.21) with $n = 2$ cities. Suppose that the dynamics in city 1 are governed by the following switched system:

$$\begin{aligned} \dot{S}^{(1)}(t) &= \mu^{(1)} \left(1 + \delta \exp \left(\frac{t}{L} \right) \right) N^{(1)}(t) - f_\sigma^{(1)} - \mu^{(1)} \left(1 + \delta \exp \left(\frac{t}{L} \right) \right) S^{(1)}(t) \\ &\quad + \alpha^{(1,1)} S^{(1)}(t) + \alpha^{(2,1)} S^{(2)}(t) - \alpha^{(2,1)} \gamma \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)}, \\ \dot{I}^{(1)}(t) &= f_\sigma^{(1)} - g^{(1)} \left(1 - \xi \exp \left(\frac{t}{L} \right) \right) I^{(1)}(t) - \mu^{(1)} \left(1 + \delta \exp \left(\frac{t}{L} \right) \right) I^{(1)}(t) \\ &\quad + \alpha^{(1,1)} I^{(1)}(t) + \alpha^{(2,1)} I^{(2)}(t) + \alpha^{(2,1)} \gamma \frac{S^{(2)}(t) I^{(2)}(t)}{N^{(2)}(t)}, \\ \dot{R}^{(1)}(t) &= g^{(1)} \left(1 - \xi \exp \left(\frac{t}{L} \right) \right) I^{(1)}(t) - \mu^{(1)} \left(1 + \delta \exp \left(\frac{t}{L} \right) \right) R^{(1)}(t) \\ &\quad + \alpha^{(1,1)} R^{(1)}(t) + \alpha^{(2,1)} R^{(2)}(t), \end{aligned} \quad (4.27)$$

and, in city 2,

$$\begin{aligned} \dot{S}^{(2)}(t) &= \mu^{(2)} N^{(2)}(t) - f_\sigma^{(2)} - \mu^{(2)} S^{(2)}(t) \\ &\quad + \alpha^{(2,2)} S^{(2)}(t) + \alpha^{(1,2)} S^{(1)}(t) - \alpha^{(1,2)} \gamma \frac{S^{(1)}(t) I^{(1)}(t)}{N^{(1)}(t)}, \\ \dot{I}^{(2)}(t) &= f_\sigma^{(2)} - g^{(2)} I^{(2)}(t) - \mu^{(2)} I^{(2)}(t) \\ &\quad + \alpha^{(1,2)} I^{(1)}(t) + \alpha^{(2,2)} I^{(2)}(t) + \alpha^{(1,2)} \gamma \frac{S^{(1)}(t) I^{(1)}(t)}{N^{(1)}(t)}, \\ \dot{R}^{(2)}(t) &= g^{(2)} I^{(2)}(t) - \mu^{(2)} R^{(2)}(t) \\ &\quad + \alpha^{(2,2)} R^{(2)}(t) + \alpha^{(1,2)} R^{(1)}(t). \end{aligned} \quad (4.28)$$

Let σ be defined as the periodic switching rule,

$$\sigma(t) \equiv \begin{cases} 1, & \text{if } t \in [k, k + 0.25), \quad k = 0, 1, 2, 3, 4, \\ 2, & \text{if } t \in [k + 0.25, k + 1), \quad k = 0, 1, 2, 3, 4, \\ 3, & \text{if } t \in [k, k + 0.25), \quad k = 5, 6, 7, 8, \dots, \\ 4, & \text{if } t \in [k + 0.25, k + 1), \quad k = 5, 6, 7, 8, \dots. \end{cases}$$

Let

$$\begin{aligned} f_1^{(j)} &\equiv f_1^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \equiv \beta_1 \frac{S^{(j)} I^{(j)}}{N^{(j)}}, \quad j = 1, 2, \\ f_2^{(j)} &\equiv f_2^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \equiv \beta_2 \frac{S^{(j)} I^{(j)}}{N^{(j)}}, \quad j = 1, 2, \\ f_3^{(j)} &\equiv f_3^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \equiv \beta_1 \frac{S^{(j)} I^{(j)}}{N^{(j)}}, \quad j = 1, 2, \\ f_4^{(j)} &\equiv f_4^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \equiv \beta_2 \frac{S^{(j)} I^{(j)} (1 - I^{(j)})}{N^{(j)}}, \quad j = 1, 2, \end{aligned}$$

with $\beta_1 > \beta_2 > 0$. Here $f_1^{(j)}, f_2^{(j)}, f_3^{(j)}$ are standard incidence rates with term-time forced contact rates while $f_4^{(j)}$ takes psychological effects into account. For $t \in [0, 5]$, the disease is transmitted by standard incidence rate with seasonal variations in both cities. After $t = 5$, city 2 exhibits a shift in population behavior (e.g., due to media coverage resulting in widespread aversion). The traveling incidence rates $h^{(l,j)}(S^{(l)}, I^{(l)}, N^{(l)}) = \gamma \frac{S^{(l)} I^{(l)}}{N^{(l)}}$ satisfy (4.22) if $\gamma \in [0, 1]$ and it follows from the derivation in [146]:

$$\gamma \frac{(\alpha^{(l,j)} S^{(l)}) (\alpha^{(l,j)} I^{(l)})}{\alpha^{(l,j)} N^{(l)}} = \gamma \alpha^{(l,j)} \frac{S^{(l)} I^{(l)}}{N^{(l)}}.$$

Let $(S_0^{(1)}, I_0^{(1)}, R_0^{(1)}) = (0.5, 0, 0)$ and $(S_0^{(2)}, I_0^{(2)}, R_0^{(2)}) = (0.3, 0.2, 0)$ (i.e., the epidemic begins in city 2), and model parameters $\beta_1 = 2, \beta_2 = 0.5, g^{(1)} = 1.5, g^{(2)} = 2, \gamma = 0.8, \mu^{(1)} = 0.125, \mu^{(2)} = 0.1, -\alpha^{(1,1)} = \alpha^{(1,2)} = 0.6, -\alpha^{(2,2)} = \alpha^{(2,1)} = 0.3, \zeta = 0.2, \delta = 0.5$, and $L = 10$. These model parameters can be interpreted as follows:

1. In city 2, individuals recover faster from the disease and the death rate is less.
2. The dispersal rate indicates that individuals in the population favor traveling from city 1 to city 2.
3. The birth rate, death rate, and infectious period decrease over time in city 1 (i.e., socioeconomic advancements).

Let $\alpha = \max\{\alpha^{(1,2)}, \alpha^{(2,1)}\}$, $g = \min\{\inf\{g_1(1 - \zeta e^{-t/L}) : t \geq 0\}, g_2\} = g_2$, $\mu = \min\{\inf\{\mu_1(1 + \delta e^{-t/L}) : t \geq 0\}, \mu_2\} = \mu_2$. The value

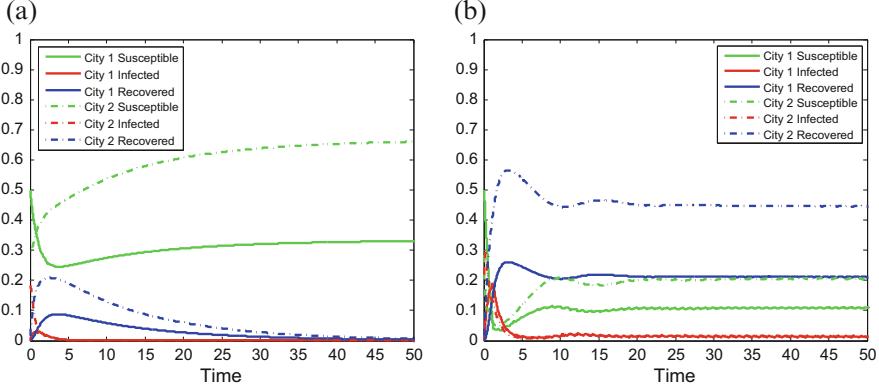


Fig. 4.7 Simulations of Example 4.3. (a) $\langle R_0^{(4.21)} \rangle = 0.955$. (b) $\langle R_0^{(4.21)} \rangle > 3.7$

$$\langle R_0^{(4.21)} \rangle \equiv \sup_{t \geq 2.25} \frac{\int_0^t \beta_\sigma ds + \alpha \gamma t}{(g + \mu)t} = 0.955$$

ensures eradication of the disease across both cities by a straightforward extension of Theorem 3.2 to the multi-city case (see Theorem 2.1 in [97]). If $\beta_1 = 10$, $\beta_2 = 4$, then $\langle R_0^{(4.21)} \rangle > 3.7$ for any value of h and the disease persists in both cities. The two cases are illustrated in Fig. 4.7.

4.3 Vector-Borne Diseases with Seasonality

The assumption of horizontal transmission of infections between members of the population is reconsidered here. More specifically, vector agents which are outside the host population transmit the disease (e.g., via mosquito–human interactions). By considering fast and slow timescales of the dynamics involved, and seasonal variations in transmission, infectious disease dynamics are modeled using switched delay differential equations. We begin by considering a host population (e.g., humans) modeled using an SIR compartmental model (with compartments denoted by $S^{(H)}$, $I^{(H)}$, and $R^{(H)}$, respectively). Assume that the vector population (e.g., mosquitoes) is split into two groups: the susceptible, denoted by $S^{(M)}$, and the infected, denoted by $I^{(M)}$. The following demographic and epidemiological assumptions are made [16, 145]:

1. The host population birth rate $\mu^{(H)} > 0$ is equal to the host population natural death rate.
2. The vector population birth rate $\mu^{(M)} > 0$ is equal to the vector population natural death rate.

3. The average number of contacts sufficient for disease transmission between susceptible host individuals and infected vector agents is given by $\beta^{(H)} > 0$.
4. The average number of contacts sufficient for disease transmission between susceptible vector agents and infected host individuals is given by $\beta^{(M)} > 0$.
5. Infected individuals in the host population recover at a per unit time rate $g^{(H)} > 0$ and, once infected, a vector agent remains infected until death.
6. At the time of infection, a susceptible vector agent exhibits a periodic of incubation, denoted by $u > 0$, before becoming infectious.
7. The timescale of the vector agent vital dynamics is much faster than that of the host population.

Some conclusions can be drawn from these assumptions: the total host and vector populations, denoted by $N^{(H)} \equiv S^{(H)} + I^{(H)} + R^{(H)}$ and $N^{(M)} \equiv S^{(M)} + I^{(M)}$, respectively, are constant in time. The ratio $\epsilon \equiv N^{(H)}/N^{(M)} \ll 1$, implying that $\mu^{(M)} \gg \mu^{(H)}$. The corresponding ODE system is written as follows:

$$\begin{aligned}\dot{S}^{(H)}(t) &= \mu^{(H)}(N^{(H)} - S^{(H)}(t)) - \beta^{(H)}S^{(H)}(t)I^{(M)}(t), \\ \dot{I}^{(H)}(t) &= \beta^{(H)}S^{(H)}(t)I^{(M)}(t) - (g^{(H)} + \mu^{(H)})I^{(H)}(t), \\ \dot{R}^{(H)}(t) &= g^{(H)}I^{(H)}(t) - \mu^{(H)}R^{(H)}(t), \\ \dot{S}^{(M)}(t) &= \mu^{(M)}N^{(M)} - \beta^{(M)} \exp(-\mu^{(M)}u)I^{(H)}(t-u)S^{(M)}(t-u) - \mu^{(M)}S^{(M)}(t), \\ \dot{I}^{(M)}(t) &= \beta^{(M)} \exp(-\mu^{(M)}u)I^{(H)}(t-u)S^{(M)}(t-u) - \mu^{(M)}I^{(M)}(t), \\ (S^{(H)}(0), I^{(H)}(0), R^{(H)}(0), S^{(M)}(0), I^{(M)}(0)) &= (S_0^{(H)}, I_0^{(H)}, R_0^{(H)}, S_0^{(M)}, I_0^{(M)}). \end{aligned}\quad (4.29)$$

There exist two dimensionless timescales: a slow timescale, corresponding to the dynamics of the host population ($t^{(H)}(t) \equiv \beta^{(M)}N^{(H)}t$), and a fast timescale, corresponding to the dynamics of the vector population ($t^{(M)}(t) \equiv \beta^{(M)}N^{(M)}t$). The flow diagram is shown in Fig. 4.8.

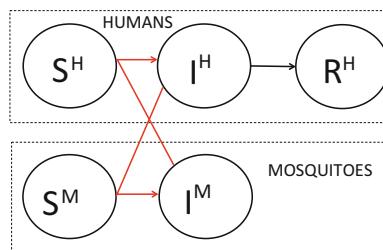


Fig. 4.8 Flow of the vector-borne model (4.29). The *red lines* represent human–mosquito interactions leading to new infections; an infected mosquito must interact with a susceptible human or an infected human with a susceptible mosquito to produce a new infection. The population dynamics are omitted here

Consideration of the dynamics on the slower timescale yields an equivalent DDE system (see [145] for the details): introduce the dimensionless variables $s^{(H)} \equiv S^{(H)}/N^{(H)}$, $i^{(H)} \equiv I^{(H)}/N^{(H)}$, $r^{(H)} \equiv R^{(H)}/N^{(H)}$, $s^{(M)} \equiv S^{(M)}/N^{(M)}$, $i^{(M)} \equiv I^{(M)}/N^{(M)}$. On the fast timescale, the differential equations corresponding to $s^{(M)}$ and $i^{(M)}$ can be rewritten as

$$\begin{aligned}\frac{ds^{(M)}}{dt^{(M)}}(t) &= -\frac{di^{(M)}}{dt^{(M)}}(t), \\ \frac{di^{(M)}}{dt^{(M)}}(t) &= \epsilon \left(\exp(-\mu^{(M)} u) i^{(H)}(t-u) s^{(M)}(t-u) - \frac{\mu^{(M)}}{\beta^{(M)} N^{(H)}} i^{(M)}(t) \right),\end{aligned}\tag{4.30}$$

where $s^{(M)}(t) + i^{(M)}(t) = 1$ and $s^{(H)}(t) + i^{(H)}(t) + r^{(H)}(t) = 1$ hold for all t . Equation (4.30) yields that

$$-\frac{\epsilon \mu^{(M)}}{\beta^{(M)} N^{(H)}} \leq \frac{di^{(M)}}{dt^{(M)}}(t) \leq \epsilon \exp(-\mu^{(M)} u), \quad \forall t.\tag{4.31}$$

and, as $\epsilon \rightarrow 0$,

$$\frac{ds^{(M)}}{dt^{(M)}}(t) = -\frac{di^{(M)}}{dt^{(M)}}(t) = 0$$

so that $i^{(M)}$ and $i^{(S)}$ approach their equilibria values:

$$\begin{aligned}i^{(M)}(t) &= \frac{\beta^{(M)} N^{(H)}}{\mu^{(M)}} \exp(-\mu^{(M)} u) i^{(H)}(t-u) s^{(M)}(t-u), \\ s^{(M)}(t) &= 1 - i^{(M)}(t).\end{aligned}\tag{4.32}$$

From this it is apparent that the vector agent variables $s^{(H)}$ and $i^{(H)}$ approach their equilibria since $i^{(H)}(t-u)$ is approximately equal to a constant on the fast timescale. If

$$\frac{\beta^{(M)} N^{(H)}}{\mu^{(M)}} \exp(-\mu^{(M)} u) \ll 1,$$

then $s^{(M)}(t) \approx 1$. Hence,

$$i^{(M)}(t) \approx \frac{\beta^{(M)} N^{(H)}}{\mu^{(M)}} \exp(-\mu^{(M)} u) i^{(H)}(t-u)$$

so that $S^{(M)}(t) \approx N^{(H)}$ and

$$I^{(M)}(t) \approx \frac{\beta^{(M)} N^{(M)} \exp(-\mu^{(M)} u)}{\mu^{(M)}} I^{(H)}(t-u)$$

where $I^{(H)}(t-u)$ evolves on the slow timescale (and thus constant in this setting).

Omitting $S^{(M)}$ and $I^{(M)}$ (which no longer appear in the equations for the host population) and normalizing the host population variables by $N^{(H)}$ (and dropping their superscripts) leads to the slow timescale reformulation of the epidemic model (4.29) as the following DDE system:

$$\begin{aligned}\dot{S}(t) &= \mu(1 - S(t)) - \beta S(t)I(t - u), \\ \dot{I}(t) &= \beta S(t)I(t - u) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t),\end{aligned}\tag{4.33}$$

$$(S(s), I(s), R(s)) = (S_0, I_0(s), R_0), \quad \forall s \in [-u, 0],$$

where $S_0 \in \mathbb{R}_+$, $R_0 \in \mathbb{R}_+$, and the function $I_0 \in \text{PC}([-u, 0], \mathbb{R}_+)$, and where

$$\beta \equiv \frac{\beta^{(H)} N^{(M)} \exp(-\mu^{(M)} u)}{\mu^{(M)}}, \quad g \equiv \frac{g^{(H)}}{\beta_M^{(M)} N}, \quad \mu = \frac{\mu_H}{\beta_M N}.$$

A more realistic assumption is that the period of incubation, u , follows a distribution: $u \in [0, d]$ for some $d > 0$ (i.e., the upper bound for the incubation time) [145]. After u units of time, it is assumed that a fraction $f(u)$ of the vector population becomes infectious; the force of infection is given by

$$\beta S(t) \int_0^d f(u) I(t - u) du.$$

Here, f is assumed to satisfy the following conditions:

- (a) f is a nonnegative, square integrable function on $[0, d]$ (the force of infection is positive and the distribution is well-defined);
- (b) $\int_0^d f(u) du = 1$ (the distribution is normalized);
- (c) $\int_0^d u f(u) du < +\infty$ (finite average incubation time until vector agents become infectious after adequate contact).

The vector-borne disease model is a system of integro-differential equations:

$$\begin{aligned}\dot{S}(t) &= \mu(1 - S(t)) - \beta S(t) \int_0^d f(u) I(t - u) du, \\ \dot{I}(t) &= \beta S(t) \int_0^d f(u) I(t - u) du - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t),\end{aligned}\tag{4.34}$$

$$(S(s), I(s), R(s)) = (S_0, I_0(s), R_0), \quad \forall s \in [-d, 0],$$

Considering seasonal variations in the contact rate pattern between host and vector populations leads to the following dynamic system:

$$\begin{aligned}\dot{S}(t) &= \mu(1 - S(t)) - \beta_\sigma S(t) \int_0^d f(u)I(t-u)du, \\ \dot{I}(t) &= \beta_\sigma S(t) \int_0^d f(u)I(t-u)du - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t), \\ (S(s), I(s), R(s)) &= (S_0, I_0(s), R_0), \quad \forall s \in [-d, 0].\end{aligned}\tag{4.35}$$

A detailed stability analysis of (4.35) is presented in Part III under a number of control strategies (switching control in Sect. 5.5 and impulsive control in Sect. 6.1.7).

4.4 Other Epidemiological Considerations

In this part, other physiological and epidemiological assumptions are considered, leading to complications in the infectious disease models. Straightforward variations in the switched systems techniques used thus far overcome the difficulties and lead to appropriate eradication results. That is, once the assumption is properly incorporated into the model, the methods of the previous sections become applicable. The new transmission or population behaviors play a role in the spread of a disease and manifest themselves in the basic reproduction number of the models. The following complications are considered here:

1. Vertical transmission of infections, in addition to horizontal transmission.
2. Varying total population sizes (i.e., a model with disease-induced mortality).
3. Waning immunity (i.e., an SIRS model).
4. The introduction of a passively immune class (i.e., an MSIR model).
5. A model with general compartments.

Since the switched systems techniques already established are applied in a straightforward way to these model variations, the eradication results are reserved for the end of this section (see Sect. 4.4.6). In some cases, model parameters yielding persistence and permanence are also easily found.

4.4.1 Vertical Transmission

One complication to the SIS model (4.1) is to consider both horizontal and vertical transmission, which is the direct transmission of communicable diseases by an infected mother to her newborn or unborn child. A typical vertical incidence term in a deterministic model is the product of the probability of transmission per birth,

the birth rate and the number of infected women [64]. Assume that $0 \leq \rho \leq 1$ is the probability that a mother with the disease does not transmit it transplacentally, then $(1 - \rho)$ is the probability that a child gains the infection transplacentally. This vertical transmission is incorporated into the model then by assuming that a flux $\mu(1 - \rho)I$ enters the infected group through birth and the remaining births from infected mothers which are not infected, $\mu\rho I$, enters the susceptible group as normal. The switched SIS model with vertical transmission then is

$$\begin{aligned}\dot{S}(t) &= \mu(S(t) + \rho I(t)) - \beta_\sigma S(t)I(t) - \mu S(t) + gI(t), \\ \dot{I}(t) &= \mu(1 - \rho)I(t) + \beta_\sigma SI - (g + \mu)I(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0).\end{aligned}\tag{4.36}$$

As in the switched SIS model (4.1), the meaningful domain, which is positively invariant, is given by

$$D_{(4.36)} \equiv \{(S, I) \in \mathbb{R}_+^2 : S + I = 1\} = D_{(4.1)},$$

with initial conditions satisfying $(S_0, I_0) \in D_{(4.36)}$. In the limit $\rho \rightarrow 1$, the model (4.36) becomes the SIS model (4.1), and in the limit $\rho \rightarrow 0$, all infected pass on the infection to offspring. For each mode, the basic reproduction number (from the time-invariant case, e.g., [102]) is given as

$$R_0^{(4.36),i} \equiv \frac{\beta_i}{\rho\mu + g}, \quad \forall i \in \mathcal{M},\tag{4.37}$$

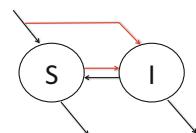
which biologically represent the average number of secondary infections produced by a single infected individual. Notice that these reproduction numbers are greater than when there is only horizontal transmission (i.e., the mode basic reproduction numbers of (4.1)).

$$R_0^{(4.1),i} = \frac{\beta_i}{\mu + g} \leq \frac{\beta_i}{\rho(\mu + g)} = R_0^{(4.36),i}, \quad \forall i \in \mathcal{M}.$$

This makes sense biologically, as there are now infected individuals being recruited through birth. Figure 4.9 shows the flow diagram of (4.36).

There is a single disease-free equilibrium point $Q_{\text{DFS}}^{(4.36)} \equiv (1, 0)$ that is common to all modes and each mode also has endemic equilibrium

Fig. 4.9 Flow of the SIS model (4.36). The red lines represent new infections (some newborns are born infected)



$$Q_{\text{ES}}^{(4.36),i} \equiv \left(\frac{1}{R_0^{(4.36),i}}, 1 - \frac{1}{R_0^{(4.36),i}} \right), \quad \forall i \in \mathcal{M}, \quad (4.38)$$

which exists in the meaningful domain if $R_0^{(4.36),i} \geq 1$. Again, since $S + I = 1$, the system is intrinsically one-dimensional. In the case that

$$R_0^{(4.36),1}, \dots, R_0^{(4.36),m} \leq 1,$$

then $\dot{I}(t) < 0$ in the domain $D_{(4.36)}$ for $I \neq 0$, and since $S + I = 1$, the disease-free equilibrium $Q_{\text{DFS}}^{(4.36)}$ is asymptotically stable in the meaningful domain. From (4.36),

$$\dot{I}(t) = \beta_\sigma S(t)I(t) - gI(t) - \rho\mu I(t) \leq (\beta_\sigma - \rho\mu - g)I(t) = \lambda_\sigma I(t), \quad (4.39)$$

where $\lambda_i \equiv \beta_i - \rho\mu - g$ for all $i \in \mathcal{M}$; the eradication and persistence results from Sect. 4.1 are applicable to (4.36) (see Sect. 4.4.6).

Example 4.4 Consider (4.36) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), $\beta_1 = 0.8$, $\beta_2 = 0.2$, $\rho = 0.4$, $\mu = 0.07$ and $g = 0.3$ (from [102]). In this case, $R_0^{(4.36)} = 1.067$ and the disease persists. If instead $\rho = 0$, then the disease is eradicated; the vertical transmission is driving persistence of the disease. See Fig. 4.10 for a simulation.

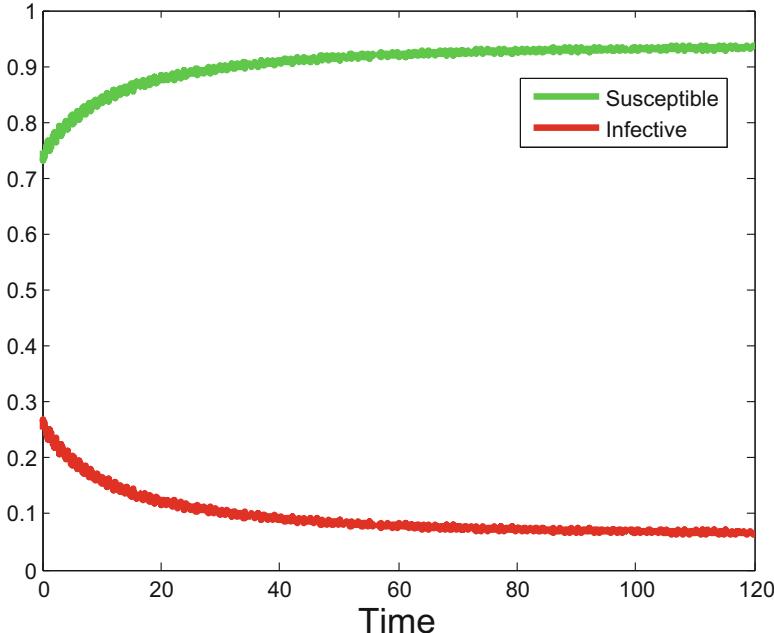


Fig. 4.10 Simulation of Example 4.4

4.4.2 Disease-Induced Mortality: Varying Population Size

In this section, two different population demographic structures are investigated here. First, we revisit the assumption that the natural birth and death rates are equal. Assume a simple birth–death demographic structure for the total population N based on the differential equation

$$\dot{N}(t) = (b - d)N(t), \quad (4.40)$$

where bN are births and dN are the natural deaths. In the absence of births and deaths, i.e. $b = d = 0$, the model is suitable for describing an epidemic in a short time period, for example less than 1 year [64]. This leads to models without population dynamics, such as the classical epidemic model (3.4) studied earlier. If $b = d \neq 0$, then there is an inflow of susceptibles from births, but the population size is a constant because of the corresponding deaths. This is the demographic structure that is most often assumed in the literature and has been assumed up until this point. If $b - d \neq 0$, then the population is exponentially growing or decaying. Applied to the switched SIS model (4.1),

$$\begin{aligned} \dot{S}_c(t) &= bN(t) - \frac{\beta_\sigma S_c(t)I_c(t)}{N(t)} + gI_c(t) - dS_c(t), \\ \dot{I}_c(t) &= \frac{\beta_\sigma S_c(t)I_c(t)}{N(t)} - gI_c(t) - dI_c(t), \end{aligned} \quad (4.41)$$

where S_c, I_c are the number of infected and susceptible individuals (i.e., not fractions), and the total population is $N \equiv S_c + I_c$, which is not necessarily constant and satisfies the differential equation (4.40). The flow associated with (4.41) is shown in Fig. 4.11.

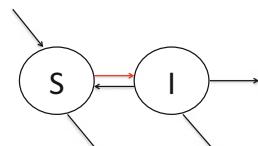
Normalizing the equations using $I \equiv I_c/N$ and $S \equiv S_c/N$ gives $S + I = 1$,

$$\dot{S}(t) = \frac{\dot{S}_c(t)}{N(t)} - S(t)\frac{\dot{N}(t)}{N(t)},$$

and

$$\dot{I}(t) = \frac{\dot{I}_c(t)}{N(t)} - I(t)\frac{\dot{N}(t)}{N(t)}.$$

Fig. 4.11 Flow of the SIS model (4.41). New infections are represented by the red line



Hence, the switched model is rewritten as

$$\begin{aligned}\dot{S}(t) &= b - \beta_\sigma S(t)I(t) + gI(t) - dS(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t) - dI(t), \\ (S(0), I(0)) &= (S_0, I_0),\end{aligned}\tag{4.42}$$

with initial conditions $(S_0, I_0) \in D_{(4.42)} \equiv \{(S, I) \in \mathbb{R}_+^2 : S + I = 1\}$, the positively invariant meaningful domain. The mode basic reproduction numbers are thus given by

$$R_0^{(4.42),i} \equiv \frac{\beta_i}{b + g}, \quad \forall i \in \mathcal{M}.\tag{4.43}$$

Equation (4.42) admits a single disease-free equilibrium point $Q_{\text{DFS}}^{(4.42)} \equiv (1, 0)$ common to all modes. Each mode also has an endemic equilibrium

$$Q_{\text{ES}}^{(4.42),i} \equiv \left(\frac{1}{R_0^{(4.42),i}}, 1 - \frac{1}{R_0^{(4.42),i}} \right), \quad \forall i \in \mathcal{M}.\tag{4.44}$$

Again, since $S + I = 1$ is an invariant to (4.42), the system (4.42) is intrinsically one-dimensional. In the case that

$$\max\{R_0^{(4.42),i} : i \in \mathcal{M}\} \leq 1,$$

then $\dot{I}(t) < 0$ for all t and $(S, I) \in D_{(4.42)} \setminus \{(S, I) : I = 0\}$; the disease-free solution $Q_{\text{DFS}}^{(4.42)}$ is thus globally asymptotically stable in the meaningful domain. Notice that system (4.42) is identical to the switched SIS model (4.1) if b is replaced by μ . Therefore, the theorems in Sect. 4.1 apply to this system, with the following caveat: the fraction I converges to zero, but it does not necessarily mean the total infected individuals, $I_c \equiv I/N$, converge to zero since the population is not constant, and possibly growing without bound. From $I_c \equiv IN$, $S_c \equiv SN$, if $b = d$ it follows that the population N is constant, and the results for the switched SIS model (4.1) are recovered. If $b < d$, then the total population N converges to zero exponentially, and so $\lim_{t \rightarrow \infty} I(t) = 0$ implies that $\lim_{t \rightarrow \infty} I_c(t) = 0$. In the final case when $b > d$, the population is growing exponentially but, since $S \rightarrow 1$ as $t \rightarrow \infty$, it is apparent that $\lim_{t \rightarrow \infty} S_c(t) = \lim_{t \rightarrow \infty} N(t)$ and hence $\lim_{t \rightarrow \infty} I_c(t) = 0$ since $N = S_c + I_c$.

Next, we consider a population demographic structure which includes a disease-induced mortality rate, $\alpha > 0$. In this setting, the population satisfies the differential equation

$$\dot{N}(t) = (b - d)N(t) - \alpha I_c(t).\tag{4.45}$$

The epidemic model is given as

$$\begin{aligned}\dot{S}_c(t) &= bN(t) - \frac{\beta_\sigma S_c(t)I_c(t)}{N(t)} - dS_c(t) + gI_c(t), \\ \dot{I}_c(t) &= \frac{\beta_\sigma S_c(t)I_c(t)}{N(t)} - gI_c(t) - dI_c(t) - \alpha I_c(t),\end{aligned}\tag{4.46}$$

where S_c , I_c are the number of infected and susceptible individuals, respectively, and $N \equiv S_c + I_c$. Again normalizing the equations using $I \equiv I_c/N$ and $S \equiv S_c/N$ leads to

$$\begin{aligned}\dot{S}(t) &= b - \beta_\sigma S(t)I(t) - bS(t) + gI(t) + \alpha S(t)I(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t) - bI(t) - \alpha I(t) + \alpha I^2(t), \\ (S(0), I(0)) &= (S_0, I_0).\end{aligned}\tag{4.47}$$

The meaningful domain is the same as (4.42). The αSI and αI^2 terms are nonlinear positive feedbacks induced by the disease-related death rate α : At any time that individuals die from the disease, the population size N decreases resulting in the fraction of individuals in each group increasing [103]. Define the mode basic reproduction numbers as

$$R_0^{(4.47),i} \equiv \frac{\beta_i}{b + g + \alpha}, \quad \forall i \in \mathcal{M},\tag{4.48}$$

the disease-free solution $Q_{\text{DF}}^{(4.47)} \equiv (1, 0)$ and mode-dependent endemic equilibria:

$$Q_{\text{ES}}^{(4.47),i} \equiv (S_i^*, I_i^*) \equiv \left(\frac{b + g}{\beta_i - \alpha}, \frac{b + g + \alpha}{\beta_i - \alpha} (R_0^{(4.47),i} - 1) \right), \quad \forall i \in \mathcal{M},\tag{4.49}$$

which are in the meaningful domain only when $R_0^{(4.47),i} \geq 1$. (Again, since $S+I = 1$, the system is intrinsically one-dimensional.)

Linearizing (4.47) about the disease-free solution gives the following system:

$$\begin{aligned}\dot{S}_L(t) &= -\beta_\sigma I_L(t) - bS_L(t) + gI_L(t) + \alpha I_L(t), \\ \dot{I}_L(t) &= \beta_\sigma I_L(t) - gI_L(t) - bI_L(t) - \alpha I_L(t), \\ (S_L(0), I_L(0)) &= (S_0, I_0).\end{aligned}\tag{4.50}$$

Therefore,

$$\dot{I}_L(t) = (\beta_\sigma - g - b - \alpha)I_L(t) = \lambda_\sigma I_L(t),\tag{4.51}$$

where $\lambda_i \equiv \beta_i - g - b - \alpha$ for all $i \in \mathcal{M}$. Applying the previous switching techniques implies similar eradication thresholds but are local in nature. For example,

$$R_0^{(4.47)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(4.47),i} \tau_i < 1$$

implies local asymptotic stability of $Q_{\text{DFS}}^{(4.47)}$ if $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$. Global results can be achieved under stronger conditions, i.e., if

$$\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} = R_0^{(4.1)} < R_0^{(4.47)} < 1.$$

This follows from the observation that

$$\dot{I}_L(t) = \beta_\sigma S(t) I_L(t) - g I_L(t) - b I_L(t) - \alpha I_L(t) + \alpha I^2(t) \leq (\beta_\sigma - b - g) I_L(t).$$

As before, such eradication results only establish that the fractions of infected individuals in the population $I \rightarrow 0$ as $t \rightarrow \infty$, but not necessarily that the actual number of infected individuals, I_c , go to zero. Recall that the infected fraction is $I \equiv I_c/N$ so that $I_c \equiv IN$, but if $I \rightarrow 0$ and $N \rightarrow \infty$, it is not immediately clear what will happen to the actual infected number of individuals. The different cases must be investigated: Recalling the equation for the population dynamics (4.45), $b < d$ implies that the total population is going to zero, and hence $I \rightarrow 0$ implies $I_c \rightarrow 0$. The case $b = d$ gives $\dot{N}(t) = -\alpha I(t)N(t) \leq 0$, from which it follows that the total population approaches a constant value since $I \rightarrow 0$. Hence, $I_c \rightarrow 0$ in this case. Finally, if $b > d$, then the total population grows without bound since $I \rightarrow 0$. In this case, since $S \rightarrow 1$, $S_c \equiv SN$ gives $S_c \rightarrow N$ and then $N \equiv S_c + I_c$ implies $I_c \rightarrow 0$.

Lastly, permanence of the disease can be established once again by simply adjusting the switching system techniques as in Theorem 4.3: If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$\min\{R_0^{(4.47),i} : i \in \mathcal{M}\} > 1,$$

then the solution of the SIS system with disease-induced deaths (4.47) converges to the convex hull of the set of endemic points $\{Q_{\text{ES}}^{(4.47),1}, \dots, Q_{\text{ES}}^{(4.47),m}\}$ (i.e., the disease is permanent). The endemic equilibria,

$$I_i^* \equiv (\beta_i - g - b - \alpha)/(\beta_i - \alpha), \quad \forall i \in \mathcal{M},$$

imply that

$$\text{conv}\{Q_{\text{ES}}^{(4.47),1}, \dots, Q_{\text{ES}}^{(4.47),m}\} = \{(S, I) \in \mathbb{R}_+^2 : I_{\min}^* \leq I \leq I_{\max}^*, S = 1 - I\},$$

where

$$I_{\min}^* \equiv \min\{I_i^* : i \in \mathcal{M}\} = \frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha},$$

and

$$I_{\max}^* \equiv \max\{I_i^* : i \in \mathcal{M}\} = \frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha}.$$

Moreover, the differential equation for I can be rewritten as

$$\dot{I}(t) = (\beta_\sigma - g - b - \alpha)I(t) - (\beta_\sigma - \alpha)I^2(t),$$

so that at $I = I_{\min}^*$,

$$\begin{aligned} \dot{I}|_{I=I_{\min}^*} &= (\beta_i - g - b - \alpha)I_{\min}^* - (\beta_i - \alpha)(I_{\min}^*)^2, \\ &= I_{\min}^* \left(\beta_i - g - b - \alpha - (\beta_i - \alpha) \frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha} \right), \\ &= (\beta_i - \alpha)I_{\min}^* \left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - \frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha} \right] \geq 0. \end{aligned}$$

For any i , at $I = I_{\max}^*$:

$$\begin{aligned} \dot{I}|_{I=I_{\max}^*} &= (\beta_i - g - b - \alpha)I_{\max}^* - (\beta_i - \alpha)(I_{\max}^*)^2, \\ &= I_{\max}^* \left(\beta_i - g - b - \alpha - (\beta_i - \alpha) \frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha} \right), \\ &= (\beta_i - \alpha)I_{\max}^* \left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - \frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha} \right] \leq 0. \end{aligned}$$

Since $S = 1 - I$,

$$I_0 \in \text{conv}\{Q_{\text{ES}}^{(4.47),1}, \dots, Q_{\text{ES}}^{(4.47),m}\}$$

implies that I remains in the set for all $t \in \mathbb{R}_+$, regardless of the switching rule. If $0 < I_0 < I_{\min}^*$,

$$\begin{aligned} \dot{I}(t) &= (\beta_\sigma - g - b - \alpha)I(t) - (\beta_\sigma - \alpha)I^2(t), \\ &= (\beta_\sigma - \alpha) \left[\frac{\beta_\sigma - g - b - \alpha}{\beta_\sigma - \alpha} - I(t) \right] I(t) > 0, \quad \forall t \in \mathbb{R}_+, \end{aligned}$$

and the rest of the argument follows similarly as in the proof of Theorem 4.3.

Example 4.5 Consider (4.47) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), $\beta_1 = 1.5$, $\beta_2 = 1$, $b = 0.07$, $d = 0.01$, $\alpha = 1$, $g = 0.3$. From this, $R_0^{(4.47)} = 0.821$. If $\alpha = 0$ and $b = d = \mu = 0.07$ then the disease persists; disease-induced mortality helps in achieving eradication of the disease. See Fig. 4.12 for a simulation.

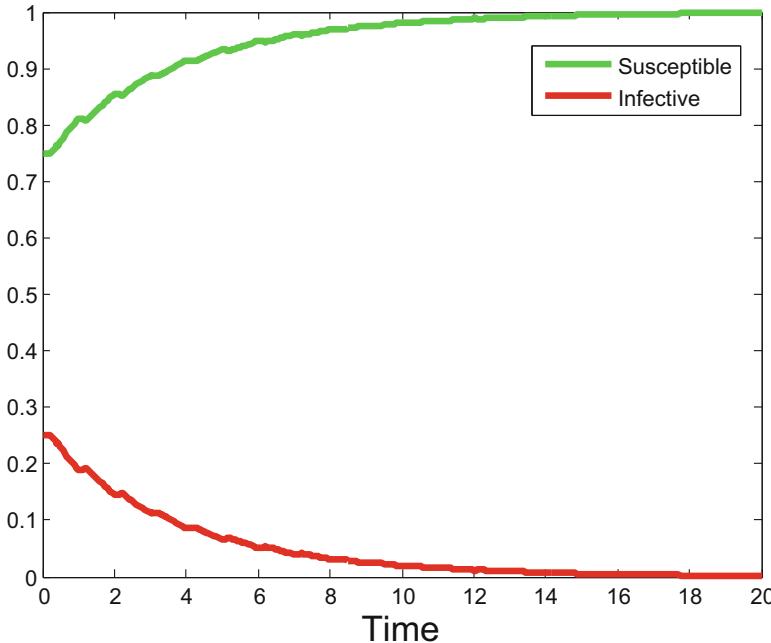


Fig. 4.12 Simulation of Example 4.5

4.4.3 Waning Immunity: The Switched SIRS Model

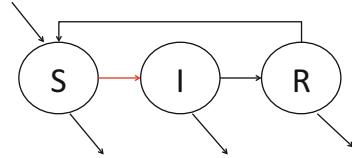
Individuals that recover from infection and lose immunity over time is reconsidered here. More precisely, assume that individuals lose immunity at rate $\theta > 0$ (thus giving an average period of immunity by $1/\theta$). Along with the other assumptions of the switched SIR model (3.8), the model is given as

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) + \theta R(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t) - \mu I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t) - \theta R(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0),\end{aligned}\tag{4.52}$$

The flow of this model is now given by $S \rightarrow I \rightarrow R \rightarrow S$. The mode basic reproduction numbers are the same as from the SIR model (i.e., the mode reproduction numbers $R_0^{(3.8),i}$ in (3.12)):

$$R_0^{(4.52),i} \equiv \frac{\beta_i}{\mu + g} = R_0^{(3.8),i}, \quad \forall i \in \mathcal{M}.\tag{4.53}$$

Fig. 4.13 Flow of the SIRS model (4.52). New infections are represented by the red line



Fundamentally, the disease spreads at the same rate in the switched SIR and SIRS models, whether the immunity is temporary or permanent. If there is no immunity at all (switched SIS model (4.1)), the basic reproduction rate still does not change. Furthermore, the meaningful domain is the same as the switched SIR model (3.8), i.e., $D_{(4.52)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\}$, and remains positively invariant: $\{\dot{S} + \dot{I} + \dot{R}\}|_{S+I+R=1} = 0$, $\dot{S}|_{S=0} = \mu + \theta R > 0$, $\dot{I}|_{I=0} = 0$ and $\dot{R}|_{R=0} = gI \geq 0$. Note that the SIS model (4.1) can be regarded as the limiting case of the SIRS model as $1/\theta \rightarrow 0$ (i.e., the average immunity period goes to zero). Figure 4.13 shows the flow diagram of (4.52).

Because of these observations, the eradication conditions for (4.52) are the same as those outlined for (3.8) (i.e., Theorems 3.1 and 3.4). For example, it is straightforward to show that if $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(4.52)} \equiv \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < 1,$$

then the solution of (4.52) satisfies $\lim_{t \rightarrow \infty} (S(t), I(t), R(t)) = (1, 0, 0) \equiv Q_{\text{DFS}}^{(4.52)}$ (the disease-free solution) and global asymptotic I -stability in the meaningful domain, while if $R_0^{(4.52)} > 1$ then the disease persists uniformly in (4.52).

One important difference between these models arises from the waning immunity rate θ : as the waning immunity is increased (and hence the immunity period $1/\theta$ is reduced), the prevalence of disease at the endemic equilibria increases and the period of the damped oscillations decreases [69]. Observe that in this case,

$$\begin{aligned} Q_{\text{ES}}^{(4.52),i} &\equiv (S_i^*, I_i^*, R_i^*), \\ &\equiv \left(\frac{1}{R_0^{(4.52),i}}, \frac{\mu + \theta}{\mu + \theta + g} \left(1 - \frac{1}{R_0^{(4.52),i}} \right), \frac{g}{\mu + \theta + g} \left(1 - \frac{1}{R_0^{(4.52),i}} \right) \right), \end{aligned}$$

for all $i \in \mathcal{M}$. Indeed, when the disease is persistent, the endemic points I_i^* are greater than the corresponding endemic points in the switched SIR model with permanent immunity (i.e., $Q_{\text{ES}}^{(3.8),i}$ in (3.13)). This is reasonable biologically, because the loss of immunity should result in more individuals being infected when the disease is persistent. Moreover, the expected rate of convergence to equilibria are different in the SIR and SIRS models. This is because the removed class is being sent back into the susceptible class, because of the temporary immunity. As a result of this, the infectives have more susceptibles to infect.

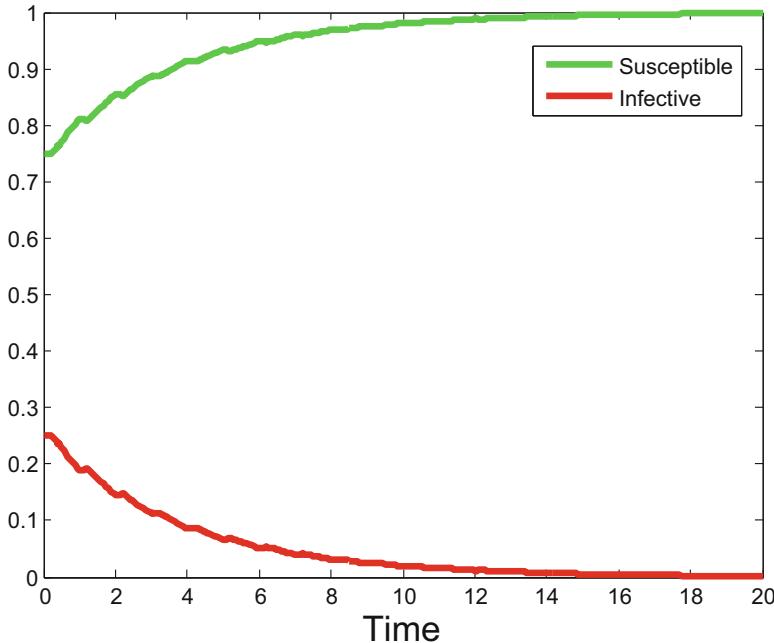


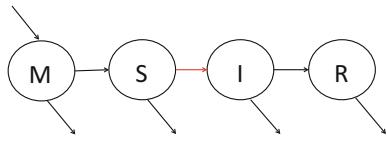
Fig. 4.14 Simulation of Example 4.5

Example 4.6 Consider (4.52) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37). Let $\beta_1 = 3$, $\beta_2 = 0.2$, $g = 1$, $\mu = 0.02$, and $\theta = 1$ so that $R_0^{(4.52)} = 0.882$. See Fig. 4.14 for an illustration with initial conditions $S_0 = 0.75$, $I_0 = 0.25$, $R_0 = 0$. Compared to the SIR case, it takes longer for the disease to become eradicated (even though the susceptible population converges to one more quickly). As the recovered class filters back into the susceptible class from the temporary immunity, the pool of susceptibles becomes larger for the infected to come into contact with.

4.4.4 Passive Immunity: The Switched MSIR Model

Suppose that all mothers who are infected (infected class) or have been infected in the past (recovered/removed class) give birth to children with temporary passive immunity, denoted by the passively immune class M . Assume that individuals born into the passively immune class lose immunity at a rate $\delta > 0$ (hence an average passive immunity period of $1/\delta$). Introducing these assumptions into the switched SIR model (3.8) gives the following epidemic model:

Fig. 4.15 Flow of the MSIR model (4.54). New infections are represented by the *red line*



$$\begin{aligned}\dot{M}(t) &= \mu(M(t) + I(t) + R(t)) - \delta M(t) - \mu M(t), \\ \dot{S}(t) &= \mu S(t) - \beta_\sigma S(t)I(t) - \mu S(t) + \delta M(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t) - \mu I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t),\end{aligned}\tag{4.54}$$

$(M(0), S(0), I(0), R(0)) = (M_0, S_0, I_0, R_0).$

Here, the positively invariant meaningful domain is given as

and the total population is constant (variables have been normalized). Notice that $\dot{M} + \dot{S} + \dot{I} + \dot{R}|_{M+S+I+R=1} = 0$, $\dot{S}|_{S=0} = \delta M \geq 0$, $\dot{I}|_{I=0} = 0$, $\dot{R}|_{R=0} = gI \geq 0$ and $\dot{I}|_{I>0} > 0$. We tested this in Fig. 4.15 in the file [ode45.m](#).

For this model, again define the mode basic reproduction numbers according to

$$R_0^{(4.54),i} \equiv \frac{\beta_i}{\mu + a}, \quad \forall i \in \mathcal{M},$$

which are the same as the switched SIS model, switched SIR model, and switched SIRS model. Hence, the addition of the M class does not alter the spread of the disease physically but there are differences here. There is a single common disease-free equilibrium point $Q_{\text{DFS}}^{(4,54)} \equiv (0, 1, 0, 0)$ and each mode also has an endemic equilibrium point $Q_{\text{ES}}^{(4,54),i} \equiv (M_i^*, S_i^*, I_i^*, R_i^*)$ with

$$\begin{aligned} M_i^* &\equiv \frac{\mu}{\delta + \mu} \left(1 - 1/R_0^{(4.54),i} \right), \\ S_i^* &\equiv \frac{1}{R_0^{(4.54),i}}, \\ I_i^* &\equiv \frac{\delta}{\delta + \mu} \frac{\mu}{\mu + g} \left(1 - 1/R_0^{(4.54),i} \right), \\ R_i^* &\equiv \frac{g}{\delta + \mu} \frac{\mu}{\mu + g} \left(1 - 1/R_0^{(4.54),i} \right). \end{aligned}$$

The endemic equilibria points are again different from the SIR and SIRS cases. From the differential equation for I , it is apparent that if

$$\max\{R_0^{(4.54),i} : i \in \mathcal{M}\} \leq 1$$

then $\dot{I}(t) < 0$ in the physical domain unless $I = 0$ or $S = 1$. Hence the disease will be eradicated. Inspection of the system (4.54) with an absence of infection, $I(t) \equiv 0$, gives that R converges to zero, from which it follows that M converges to zero. By constant total population then, S converges to one and the reduced system converges to the disease-free solution. Hence, the eradication results of the switched SIR model (3.8) may be applied. For example, if $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(4.54)} \equiv \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < 1,$$

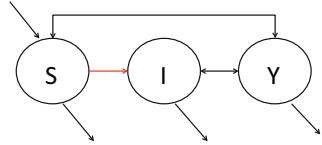
then the solution of (4.54) satisfies $\lim_{t \rightarrow \infty} (M(t), S(t), I(t), R(t)) = (0, 1, 0, 0) = Q_{\text{DFS}}^{(4.54)}$.

4.4.5 Infectious Disease Model with General Compartments

As highlighted in the previous sections, there are a number of compartments and interactions that can be considered in an epidemic model, based on the population behavior and the disease dynamics. Here, we consider an epidemic model with general compartments with the following assumptions:

1. There is a susceptible and infected compartment, labeled by S and I , respectively.
2. Individuals in the susceptible group move to the infected class with switched incidence rate $(t, S, I) \mapsto h_\sigma(I)S$, where $\{h_i : i \in \mathcal{M}\}$ is a family of forces of infection with appropriate assumptions. Namely, the forces of infection h_i are assumed to be sufficiently smooth functions satisfying $h_i(t, I) > 0$ for $I > 0$ and $h_i(t, 0) = 0$ for $t \geq 0$ and $i \in \mathcal{M}$ from physical considerations.
3. The birth rate is given by the switched constant $\mu_\sigma > 0$, which is equal to the death rate.
4. There are n_Y other epidemiological compartments $Y^{(1)}, Y^{(2)}, \dots, Y^{(n_Y)}$, representing various other stages in the progression of the disease.
5. It is possible for said n_Y compartments to filter back into the susceptible class (e.g., due to waning immunity) at a switched rate $\theta_\sigma^{(j)} \geq 0$ for each $j \in \{1, 2, \dots, n_Y\}$.
6. The infected class moves to the $Y^{(j)}$ compartments (e.g., due to natural recovery) via a switched function $(t, I, Y) \mapsto \Psi_\sigma(I, Y)$, where $Y \equiv (Y^{(1)}, Y^{(2)}, \dots, Y^{(n_Y)})$.
7. The progression of the disease in compartment $Y^{(j)}$ is governed by a switched vector function $(t, S, I, Y) \mapsto \Upsilon_\sigma(S, I, Y)$.

Fig. 4.16 Flow of the epidemic model with general compartments (4.55). The red line represents horizontal transmission



Putting together these modeling assumptions, the switched system is given by

$$\begin{aligned}\dot{S}(t) &= \mu_\sigma - h_\sigma(I(t))S(t) - \mu_\sigma S(t) + \sum_{j=1}^{n_Y} \theta_\sigma^{(j)} Y^{(j)}(t), \\ \dot{I}(t) &= h_\sigma(I(t))S(t) - \mu_\sigma I + \Psi_\sigma(I(t), Y(t)), \\ \dot{Y}(t) &= \Upsilon_\sigma(S(t), I(t), Y(t)), \\ (S(0), I(0), Y(0)) &= (S_0, I_0, Y_0),\end{aligned}\tag{4.55}$$

with $S_0, I_0 \in \mathbb{R}_+$ and $Y_0 \in \mathbb{R}_+^{n_Y}$. The flow between the general compartments is shown in Fig. 4.16. The variables have been normalized by the total population so that

$$S(t) + I(t) + \sum_{j=1}^{n_Y} Y^{(j)}(t) = 1, \quad \forall t.$$

Assume that $\Upsilon_i \equiv (\Upsilon_i^{(1)}, \Upsilon_i^{(2)}, \dots, \Upsilon_i^{(n_Y)})$ is a sufficiently smooth vector function satisfying $\Upsilon_i^{(j)}(S, I, 0) \geq 0$ for each $i \in \mathcal{M}$ and $j \in \{1, \dots, n_Y\}$ and

$$\begin{aligned}&(\Upsilon_i^{(1)}(S, 0, Y), \dots, \Upsilon_i^{(n_Y)}(S, 0, Y)) \\ &= -(\phi_i^{(1)}(S, Y), \dots, \phi_i^{(n_Y)}(S, Y)), \\ &= -\phi_i(S, Y), \quad \forall (S, I, Y) \in D_{(4.55)}, \quad \forall i \in \mathcal{M}, \quad \forall j \in \{1, \dots, n_Y\}, \quad \forall t \in \mathbb{R}_+, \end{aligned}$$

where

$$D_{(4.55)} \equiv \{(S, I, Y) \in \mathbb{R}_+^{2+n_Y} : S + I + \sum_{j=1}^{n_Y} Y^{(j)} = 1\},$$

$\phi_i^{(j)}(S, Y) \geq 0$ are sufficiently smooth functions. Assume that $\Psi_i : \mathbb{R}^{n_Y+1} \rightarrow \mathbb{R}_+$ is a sufficiently smooth scalar function satisfying $\Psi_i(0, Y) = 0$ for suitable Y and all $i \in \mathcal{M}$. Lastly, assume that $\theta_i^{(j)} \geq 0$ for each $i \in \mathcal{M}$ and $j \in \{1, \dots, n_Y\}$. The normalization of the variables implies that the functions satisfy

$$\mu_i - \mu_i(S(t) + I(t)) + \sum_{j=1}^{n_Y} \Upsilon_i^{(j)}(t) + \Psi_i(I(t), Y(t)) + \sum_{j=1}^{n_Y} \theta_i^{(j)} Y^{(j)}(t) = 0$$

for all $i \in \mathcal{M}$, $j \in \{1, \dots, n_Y\}$, and $t \in \mathbb{R}_+$. Along with the conditions on the functions outlined above, this implies the meaningful domain is invariant to system (4.55), and hence the model is mathematically and physically well-posed. System (4.55) admits a disease-free equilibrium

$$Q_{\text{DFS}}^{(4.55)} \equiv (1, 0, \underbrace{0, \dots, 0}_{n_Y}).$$

Even in this general setting, the previously outlined switching systems methods can be applied to give eradication results based on the model parameters. One such result is highlighted in detail.

Theorem 4.7 Suppose that there exist $\beta_i \geq 0$ and $\alpha_i \geq 0$ such that $h_i(I) \leq \beta_i I$ and $\Psi_i(I, Y) \leq -\alpha_i I$ for $i \in \mathcal{M}$. If either of the following conditions hold:

(i) $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$\left\langle R_0^{(4.55)} \right\rangle \equiv \sup_{t \geq h} \sum_{i=1}^m T_i(t) \frac{\beta_i}{\mu_i + \alpha_i} < 1,$$

(ii) $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$\widehat{R}_0^{(4.55)} \equiv \sum_{i=1}^m \tau_i \frac{\beta_i}{\mu_i + \alpha_i} < 1,$$

then the solution of (4.55) converges to the disease-free solution $Q_{\text{DFS}}^{(4.55)}$.

Proof First we prove case (i). From the system (4.55), let i_k follow a switching rule $\sigma \in \mathcal{S}$, then for $t \in [t_{k-1}, t_k)$,

$$\begin{aligned} \dot{I}(t) &= h_\sigma(I(t))S(t) - \mu_\sigma I(t) + \Psi_\sigma(I(t), Y(t)), \\ &\leq (\beta_\sigma - \mu_\sigma - \alpha_\sigma)I(t), \\ &= \lambda_\sigma I(t), \end{aligned} \tag{4.56}$$

where $\lambda_i \equiv \beta_i - \mu_i - \alpha_i$ for each $i \in \mathcal{M}$. Equation (4.56) and the proof of Theorem 3.2 gives that $\lim_{t \rightarrow \infty} I(t) = 0$. Since $\Upsilon_i(S, 0, Y) = -\phi_i(S, Y)$, it is clear that the variables Y_1, \dots, Y_k converge to zero. Finally, $S = 1 - I - \sum_{j=1}^{n_Y} Y^{(j)}$ implies that S converges to one. Hence, the solution converges to the disease-free equilibrium. Case (ii) follows from Eq. (4.56) and the proof of Theorem 3.1.

4.4.6 Summary of Mode Basic Reproduction Numbers and Eradication Results

One consistently revisited theme of this chapter is the ease of application of the switched systems techniques to epidemic models with different epidemiological and physiological assumptions. The main reason for this flexibility is the focus on global attractivity and partial I -stability or that the models involved are intrinsically of dimension one (strengthening the results to global stability). In either case, establishable differential equation bounds of the form

$$\dot{I}(t) \leq \lambda_i I(t),$$

where λ_i is defined different for each model, makes the following results possible.

Theorem 4.8 Consider the epidemic models with vertical transmission, varying population size, and disease-induced mortality ((4.36), (4.42), and (4.47), respectively) and their corresponding mode basic reproduction numbers $R_0^{(*),i}$ and disease-free solutions $Q_{\text{DFS}}^{(*)}$. Then the following statements hold:

(i) If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(*)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(*),i} \tau_i < 1,$$

then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally asymptotically stable in the meaningful domain $D_{(*)}$ (locally asymptotically stable if $(*) = (4.47)$).

(ii) If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$\left\langle R_0^{(*)} \right\rangle \equiv \sup_{t \geq h} \frac{1}{t} \sum_{i=1}^m R_0^{(*),i} T_i(t) < 1, \quad (4.57)$$

for some $h > 0$, then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally exponentially stable in the domain $D_{(*)}$ (locally exponentially stable if $(*) = (4.47)$).

(iii) If $\sigma \in \mathcal{S}_{\text{dwell}}$ satisfies $T^+ \leq N_0 + qT^-(t)$ for some $q \in (0, 1)$ and $N_0 \geq 0$ such that

$$R_0^{(*),-} - 1 < q(R_0^{(*),+} - 1),$$

where $R_0^{(*),-} \equiv \max\{R_0^{(*),i} : i \in \mathcal{M}^-\}$, $R_0^{(*),+} \equiv \max\{R_0^{(*),i} : i \in \mathcal{M}^+\}$, $\mathcal{M}^- \equiv \{i \in \mathcal{M} : R_0^{(*),i} < 1\}$, $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : R_0^{(*),i} \geq 1\}$, and

$$T^+(t) \equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^+\}|,$$

$$T^-(t) \equiv |\{t \in [0, t] : \sigma(t) \in \mathcal{M}^-\}|,$$

then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally exponentially stable in the domain $D_{(*)}$ (locally exponentially stable if $(*) = (4.47)$).

- (iv) If $\sigma \in \mathcal{S}_{\text{dwell}}$ and $\min\{R_0^{(*),i} : i \in \mathcal{M}\} > 1$, then the disease is permanent in $(*)$; $I(t)$ converges to $\text{conv}\{Q_{\text{ES}}^{(*),1}, \dots, Q_{\text{ES}}^{(*),m}\}$.

Similarly for the epidemic models of intrinsic dimension greater than or equal to two, the following theorem is given.

Theorem 4.9 Consider the epidemic models with waning immunity, passive immunity, and general compartments ((4.52), (4.54), and (4.55), respectively) and their corresponding mode basic reproduction numbers $R_0^{(*),i}$ and disease-free solutions $Q_{\text{DFS}}^{(*)}$. Then the following statements hold:

- (i) If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(*)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(*),i} \tau_i < 1,$$

then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally attractive and asymptotically I-stable in the meaningful domain $D_{(*)}$.

- (ii) If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$\left\langle R_0^{(*)} \right\rangle \equiv \sup_{t \geq h} \frac{1}{t} \sum_{i=1}^m R_0^{(*),i} T_i(t) < 1, \quad (4.58)$$

for some $h > 0$, then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally attractive and exponentially I-stable in the meaningful domain $D_{(*)}$.

- (iii) If $\sigma \in \mathcal{S}_{\text{dwell}}$ satisfies $T^+ \leq N_0 + qT^-(t)$ for some $q \in (0, 1)$ and $N_0 \geq 0$ such that

$$R_0^{(*),-} - 1 < q(R_0^{(*),+} - 1),$$

where $R_0^{(*),-} \equiv \max\{R_0^{(*),i} : i \in \mathcal{M}^-\}$, $R_0^{(*),+} \equiv \max\{R_0^{(*),i} : i \in \mathcal{M}^+\}$, then the disease-free solution $Q_{\text{DFS}}^{(*)}$ is globally attractive and exponentially I-stable in the meaningful domain $D_{(*)}$.

The results are summarized in Table 4.1. It should be noted that although some epidemic models share the same mode basic reproduction numbers, they may possess differing qualitative behaviors (i.e., via different mode-dependent endemic equilibria and therefore different permanence sets in Theorem 4.8 (iv), for example).

Table 4.1 Mode basic reproduction numbers of the outlined disease models

Epidemiological assumption	Disease model	Mode basic reproduction numbers	DFS stability
Vertical transmission (SIS)	(4.36)	$\beta_i/(\rho\mu + g)$	Global
Varying population size (SIS)	(4.42)	$\beta_i/(b + g)$	Global
Disease-induced mortality (SIS)	(4.47)	$\beta_i/(b + g + \alpha)$	Local
Waning immunity (SIRS)	(4.52)	$\beta_i/(\mu + g)$	GA and PS
Passive immunity (MSIR)	(4.54)	$\beta_i/(\mu + g)$	GA and PS
General compartments	(4.55)	$\beta_i/(\mu_i + \alpha_i)$	GA and PS

The stability results obtained for $Q_{\text{DFS}}^{(*)}$ in the meaningful domain are global (i.e., global asymptotic or exponential stability), local (i.e., local asymptotic stability), or GA and PS (global attractivity and partial stability)

4.5 Discussions

The SIS model (4.1) with time-constant contact rate has been analyzed extensively in the literature [63, 67, 69, 73, 116]. In Sect. 4.1, an SIS model with term-time forced parameters is analyzed and the analytic solution is explicitly provided. Results on persistence of the disease in the endemic case are given, including some criteria guaranteeing the convergence of the solution to the convex hull of the endemic equilibria. A term-time forced SIS model is also studied that considers an incidence rate which takes media coverage and the pattern of daily encounters in a local community into account. This investigation contributes to the existing literature by extending the studies in [83, 171] through the switching incidence rates and term-time forced seasonal variations, and is based on the work in [98]. The persistence result derived in Theorem 4.2 is established along the lines of the proof of Theorem 3.3 in [83] and Lemma 4.1 and Theorem 4.1 in [68]. The authors Li and Cui [83] considered the incidence rate

$$(S, I) \mapsto \left(\beta - \gamma \frac{I}{b + I} \right) SI,$$

and therefore the autonomous (non-switched) version of (4.12).

As mentioned, infectious diseases like influenza (e.g., the subtype H1N1 in 2009) and SARS are easily transmitted from one geographic region to another due to population dispersal from individuals traveling; the effect of travel on the spread of a disease should be considered [156]. The compartmental epidemic model literature contains formulations and studies of epidemic models with population dispersal;

for example, Sattenspiel and Dietz [132] studied the transmission of measles in the Caribbean island of Dominica using a multi-city SIR model with travel between populations. Arino and van den Driessche [5] developed and studied a multi-city SIS model to study the spatial spread of a disease. A multi-city SIS model with a general nonlinear birth-rate term was studied by Wang and Zhao in [157]. Wang and Mulone explored a two-city SIS model with population dispersal in [156]. Wang and Zhao studied a multi-city SIS model with age structure and time delay in [158]. A two-city SIS model with transport-related infection has been studied by Cui et al. in [146] and some results were extended by Takeuchi et al. in [147]. Wan and Cui analyzed a two-city SEIS model in [155], and Liu and Zhou studied a two-city SIRS model in [88], both with transport-related infection.

There are few reports analyzing multi-city models with seasonality in the literature; Zhang and Zhao studied a multi-city SIS model with general nonlinear birth-rate and periodic model parameters, including the contact rate, in [170]. The multi-city SIR model, suitable for modeling infections such as hepatitis B, measles, influenza, and chickenpox [88, 101], is extended to switched seasonal variations and general incidence rates in (4.21), which is inspired by the work in [97]. The analysis of multi-city epidemic models in Sect. 4.2 naturally leads to age group considerations, which are not presently considered but the interested reader is referred to [65, 82, 107, 129, 130, 137]. The authors Röst and Wu [130] considered age-dependent mixing and provided global asymptotic stability of the disease-free equilibrium. In [107], McCluskey resolved the endemic case and showed global asymptotic stability of the endemic equilibrium, using a Lyapunov functional, whenever the basic reproduction number is greater than one. In the paper [129], Röst analyzed an SEI (susceptible-exposed-infected) model with distributed delays and a death rate for the infected class that depends on the age of infection. A heterogeneous host population can be divided into homogeneous groups according to transmission characteristics (modes of transmission, contact patterns, geographic distributions, etc.) [82]. Motivated by this, a multi-group SEIR (susceptible-exposed-infected-recovered) model with unbounded delay was studied in [82] by Li et al. to model within-group and inter-group interactions separately. The authors found global asymptotic stability results for the disease-free equilibrium and endemic equilibrium based on the spectral radius of the next-generation matrix using Lyapunov functionals. These results were extended by Shu et al. in [137] to model generalized nonlinear transmission rates. Lyapunov functionals were used to give sufficient conditions for global asymptotic stability of the disease-free equilibrium and endemic equilibrium based on the basic reproduction number.

In Sect. 4.3, infectious diseases which spread by vector agents are detailed, motivated by the work in [143]. In particular, those diseases which display a finite incubation time before vector agents become infectious (see, e.g., [16, 17, 19, 27, 50, 104, 108, 145]). Chikungunya virus is usually transmitted via *Aedes aegypti*, however, in recent outbreaks transmission has been observed via *Aedes albopictus* (e.g., in Réunion [114]). Capable of transmitting diseases such as dengue (see the studies [165, 166] for mathematical models of dengue), *Aedes aegypti* is a tropical and subtropic species but *Aedes albopictus* has recently been observed adapting

to non-tropic regions in Southeast Asia, islands in the Pacific and Indian oceans, China, Europe, USA, and Australia [41, 113, 114]. Italy experienced an outbreak in 2007 [127]; globalization of vector-borne disease is of great interest at present, pronounced by recent outbreaks of Zika virus. The author Cooke [27] first proposed a version of the vector-borne disease model (4.34) for study. Beretta and Takeuchi [16, 17] analyzed the stability of the disease-free equilibrium of vector-borne disease models similar to (4.34). Takeuchi et al. [145] and Beretta et al. [19] extended these works to the endemic case. Ma et al. [104] analyzed the permanence of (4.34). Gao et al. [50] investigated a vaccination scheme for an SIR vector-borne disease model with distributed delays. The work on stability of the endemic equilibrium of (4.34), with birth rate unequal to death rate, was completed by McCluskey in [108].

The vector agent population, and thus interactions between host and vector populations, is absent in (4.35); the qualitative behavior of the disease with respect to the host population is the main focus. This is in contrast with the case study in Chap. 7, where the full dynamics between host and vector populations are modeled. The drawback to this omission is the introduction of time delays (leading to theoretical complications) and the exclusion of the vector population for vector-focused control measures (e.g., destruction of breeding sites cannot be adequately modeled in (4.35)). On the other hand, integro-differential equations, as appearing in Sect. 4.3, arise frequently in modeling physical and biological phenomena. Examples are found in [24, 78]: biological population models, predator-prey models with a past hereditary influence, grazing systems, chemical oscillations, nuclear reactors, and heat flow problems [24, 78].

A number of different epidemic models are presented and examined in Sect. 4.4. First, vertical transmission was incorporated into the model in Sect. 4.4.1, which is an important transmission mechanism in a variety of diseases like hepatitis and AIDS [37]. The switched SIS model (4.1) and switched SIS model with vertical transmission (4.36) made the common assumption that births and deaths are equal (leading to a population balance) [73], which is reasonable when considering the often shorter time scales involved in the epidemics when compared to the population dynamics. However, infectious diseases like measles, chickenpox, and pertussis display the characteristic that the susceptible class is mostly composed of younger individuals whose rate of natural mortality does not necessarily coincide with that of the rest of the population [73]. Non-constant population size has been displayed in a number of real-world examples, motivating the analysis of the SIS model with non-constant population (4.42).

In the case of infectious diseases like AIDS, disease-related deaths should be taken into account by modifying the constant-population assumption [140]. As disease-related deaths and persistence of a disease can have the effect of reversing a naturally growing population into a stable or decaying population [64], the switched SIS model with disease-induced mortality (4.47) is investigated. When there is natural recovery from the disease for a non-negligible amount of time yet the immunity wanes in time, the SIRS model is appropriate (see [69, 73]). The modeling assumptions of the SIR model (3.9) are taken with the distinction that individuals recovering from the disease do so temporarily. Examples include the

herpes simplex virus, which tends to relapse after recovery [140]. This has also been demonstrated in a number of sexually transmitted diseases (e.g., gonorrhea and chlamydia) [46]. The switched SIRS model (4.52) is the focus of Sect. 4.4.3 to address these concerns. Diseases in which antibodies are transferred from an infected mother to unborn child (e.g., chickenpox) [65] are modeled according to the so-called switched MSIR model (4.54). Lastly, the seasonally varying epidemic model with generalized compartments in Sect. 4.4.5 was motivated by the time-invariant epidemic model studied in [36].

Part III

Control Strategies

Chapter 5

Switching Control Strategies

This chapter is motivated by the application of control strategies to eradicate epidemics. The previous switched epidemic models are reintroduced with continuous control (e.g., vaccination of newborns continuously in time) or switching control (i.e., piecewise continuous application of vaccination or treatment schemes) for evaluation and optimization. As discussed earlier, infectious disease models are a crucial component in designing and implementing detection, prevention, and control programs (e.g., WHO's program against smallpox, leading to its global eradication by 1977). The switched SIR model is first returned to analyze vaccination of the susceptible group (e.g., newborns or the entire cohort). Subsequently, the developed theoretical methods are applied to the switched SIR model with a treatment program in effect. Common Lyapunov functions are used to provide controlled eradication of diseases modeled by the so-called SEIR (Susceptible-Exposed-Infected-Recovered) model with seasonal variations captured by switching. A screening process, where traveling individuals are examined for infection, is proposed and studied for the switched multi-city model of the previous chapter. Switching control of diseases such as dengue and chikungunya, which are spread via mosquito–human interactions, is also investigated.

5.1 Vaccination of the Susceptible Group

The majority of developed countries have in place cohort immunization programs (also called time-constant immunization or vaccination programs here) for a number of diseases with varying degrees of success [1]. For example, measles immunization in many areas of the Western world recommends vaccinations at 15 months of age and 6 years of age [139]. Studies analyzing this type of program mathematically can be found in, for example, [4, 69, 75, 83, 92, 100–102, 110, 138, 147, 173].

The mathematical formulation of a newborn continuous vaccination strategy takes the following form [69, 138, 173]: assume that a fraction $\rho \in [0, 1]$ of susceptible newborns are vaccinated, moving them to the recovered class R , continuously in time. In this model, natural and vaccine-acquired immunity are viewed as the same. Applied to the classical endemic model SIR model (3.9) gives

$$\begin{aligned}\dot{S}(t) &= (1 - \rho)\mu - \beta S(t)I(t) - \mu S(t), \\ \dot{I}(t) &= \beta S(t)I(t) - (g + \mu)I(t), \\ \dot{R}(t) &= \mu\rho + gI(t) - \mu R(t).\end{aligned}\tag{5.1}$$

Newborn vaccinations reduce the birth rate μ of the susceptible population to $(1 - \rho)\mu$. Equation (5.1) admits the following equilibria: a disease-free solution $(1 - \rho, 0, \rho) \equiv Q_{\text{DFS}}^{(5.1)}$ and an endemic solution

$$Q_{\text{ES}}^{(5.1)} \equiv \left(\frac{\mu + g}{\beta}, \frac{\mu}{\beta} (R_0^{(5.1)} - 1), \frac{g}{\beta} (R_0^{(5.1)} - 1) + \rho \right),\tag{5.2}$$

where

$$R_0^{(5.1)} \equiv \frac{\beta(1 - \rho)}{\mu + g}$$

is the basic reproduction number of (5.1). The underlying mechanics of the newborn vaccination can be translated into something more familiar by the following change of variables [69]: let $S \equiv \widehat{S}(1 - \rho)$, $I \equiv \widehat{I}(1 - \rho)$, and $R \equiv \widehat{R}(1 - \rho) + \rho$. Then (5.1) is equivalently written as

$$\begin{aligned}\frac{d\widehat{S}}{dt}(t) &= \mu - \beta(1 - \rho)\widehat{S}(t)\widehat{I}(t) - \mu\widehat{S}(t), \\ \frac{d\widehat{I}}{dt}(t) &= \beta(1 - \rho)\widehat{S}(t)\widehat{I}(t) - (g + \mu)\widehat{I}(t), \\ \frac{d\widehat{R}}{dt}(t) &= g\widehat{I}(t) - \mu\widehat{R}(t).\end{aligned}\tag{5.3}$$

This control strategy therefore has the effect of transforming the contact rate from β to $\beta(1 - \rho)$. This is most clearly reflected in the basic reproduction number $R_0^{(5.1)}$, which dictates the usual threshold for long-term behavior (i.e., disease eradication versus endemicity). The condition $R_0^{(5.1)} < 1$ yields a critical vaccination rate to achieve herd immunity [63]:

$$\rho_{\text{crit}} \equiv 1 - 1/R_0^{(5.1)} \in [0, 1).$$

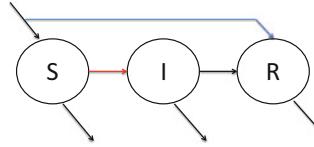


Fig. 5.1 Flow of the switched SIR system with newborn vaccinations (5.4). The red line represents the horizontal transmission and the blue line represents the vaccination scheme

With seasonality modeled by a switched contact rate β_σ (where $\sigma \in \mathcal{S}_{\text{dwell}}$), the model is given by

$$\begin{aligned}\dot{S}(t) &= \mu(1 - \rho) - \beta_\sigma S(t)I(t) - \mu S(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t) + \rho\mu,\end{aligned}\tag{5.4}$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

with physical domain

$$D_{(5.4)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\} = D_{(3.8)}$$

(which is positively invariant to (5.4)). See Fig. 5.1 for the flow diagram associated with (5.4).

Although the present focus is on disease eradication by control, we mention that each mode admits an endemic equilibria of the form

$$Q_{\text{ES}}^{(5.4),i} \equiv \left(\frac{\mu + g}{\beta_i}, \frac{\mu}{\beta_i} (R_0^{(5.4),i} - 1), \frac{g}{\beta_i} (R_0^{(5.4),i} - 1) + \rho \right), \quad \forall i \in \mathcal{M}, \tag{5.5}$$

with mode basic reproduction numbers

$$R_0^{(5.4),i} \equiv \frac{\beta_i}{\mu + g} (1 - \rho) = (1 - \rho) R_0^{(3.8),i}, \quad \forall i \in \mathcal{M}. \tag{5.6}$$

Recall Theorem 3.1, in which the switched SIR model (3.8) was shown to achieve eradication if

$$R_0^{(3.8)} = \frac{1}{\omega} \sum_{i=1}^m R_0^{(3.8),i} \tau_i = \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < 1$$

whenever $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ (in such a way that the disease-free solution is globally asymptotically *I*-stable). Moreover, $R_0^{(3.8)} > 1$ implies persistence of the disease (see Theorem 3.4). In contrast, consider the following theorem.

Theorem 5.1 If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(5.4)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(5.4),i} \tau_i = \frac{\sum_{i=1}^m \beta_i (1 - \rho) \tau_i}{\omega(\mu + g)} < 1,$$

then the disease-free solution $Q_{\text{DFS}}^{(5.4)} \equiv (1 - \rho, 0, \rho)$ of the switched SIR system with newborn vaccination (5.4) is globally attractive and globally asymptotically I-stable in the meaningful domain.

Proof By (5.4),

$$\begin{aligned} \dot{S}(t) &= \mu(1 - \rho) - \beta_\sigma S(t)I(t) - \mu S(t), \\ &\leq \mu(1 - \rho) - \mu S(t). \end{aligned}$$

Consider the comparison system

$$\begin{aligned} \dot{x}(t) &= \mu(1 - \rho) - \mu x(t), \\ x(0) &= S_0, \end{aligned} \tag{5.7}$$

which has unique solution $x(t) \equiv (S_0 - (1 - \rho)) \exp(-\mu t) + (1 - \rho)$ that satisfies

$$\lim_{t \rightarrow \infty} x(t) = 1 - \rho.$$

By the comparison theorem, for any $\epsilon > 0$ there exists a time $t^* > 0$ such that $S(t) \leq x(t) \leq 1 - \rho + \epsilon$ for $t \geq t^*$, and so

$$\begin{aligned} \dot{I}(t) &= \beta_\sigma S(t)I(t) - (\mu + g)I(t), \\ &\leq (\beta_\sigma([1 - \rho + \epsilon] - \mu - g)I(t), \\ &\equiv \lambda_{\sigma, \epsilon} I(t), \end{aligned}$$

where $\lambda_{i,\epsilon} \equiv \beta_i(1 - \rho) - g - \mu + \epsilon\beta_i$ for each $i \in \mathcal{M}$. Choose N to be the smallest integer such that $N\omega > t^*$. Then, as in the proof of Theorem 3.1,

$$\begin{aligned} I((N+1)\omega) &\leq I(N\omega) \exp \left(\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i \right), \\ &= \eta(\epsilon) I(N\omega), \end{aligned}$$

where

$$\eta(\epsilon) \equiv \exp \left(\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i \right).$$

Now, $R_0^{(5.4)} < 1$ gives that $\sum_{i=1}^m \lambda_i \tau_i < 0$. Then it holds that $\sum_{i=1}^m \lambda_i \tau_i < -\delta$ for some $\delta > 0$, and

$$\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i = \sum_{i=1}^m \lambda_i \tau_i + \epsilon \sum_{i=1}^m \beta_i \tau_i < -\delta + \epsilon \sum_{i=1}^m \beta_i \tau_i.$$

Choosing

$$\epsilon = \frac{\delta}{2 \sum_{i=1}^m \beta_i \tau_i}$$

implies that $\eta(\epsilon) < 1$. It can be similarly shown that $I((N+h+1)\omega) \leq \eta I((N+h)\omega)$ for any integer $h \in \mathbb{N}$ and the rest of the proof of Theorem 3.1 may be applied to produce the result.

The threshold condition $R_0^{(5.4)} < 1$ defines a critical newborn vaccination rate:

$$R_0^{(5.4)} = \frac{\sum_{i=1}^m \beta_i (1-\rho) \tau_i}{\omega(\mu+g)} < 1$$

implies that

$$(1-\rho) \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu+g)} = (1-\rho) R_0^{(3.8)} < 1,$$

and hence the critical rate is given as

$$\rho_{\text{crit}} \equiv 1 - 1/R_0^{(3.8)} = 1 - \frac{\omega(\mu+g)}{\sum_{i=1}^m \beta_i \tau_i} \in [0, 1),$$

which guarantees disease eradication. That is, if the disease persists in the switched SIR model ($R_0^{(3.8)} > 1$), then disease eradication can be achieved by newborn vaccinations as long as $\rho \geq \rho_{\text{crit}}$. If $R_0^{(3.8)} = 1$ then $\rho_{\text{crit}} = 0$ and as $R_0^{(3.8)} \rightarrow \infty$ then $\rho_{\text{crit}} \rightarrow 1$. Other controlled eradication results can also be shown under different classes of switching rules, as in Sect. 3.4 (i.e., if $\sigma \in \mathcal{S}_{\text{dwell}}$ according to Theorems 3.2 and 3.3).

Example 5.1 Consider (5.4) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), and initial conditions $(S_0, I_0, R_0) = (0.75, 0.25, 0)$. Motivated by the measles parameters of [138], let $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$, and $\rho = 0$ which give that $R_0^{(5.4)} = 6.136$ and persistence of the disease, i.e., by Theorem 3.4 (see Fig. 5.2 for an illustration; the solution I oscillates approximately between the endemic minimum and maximum, $I_{\min} = 0.0576$ and $I_{\max} = 0.0854$). With $\rho = 0.85$ ($\rho_{\text{crit}} = 0.84$), $R_0^{(5.4)} = 0.920$ and the disease is eradicated according to Theorem 5.1 (see Fig. 5.3).

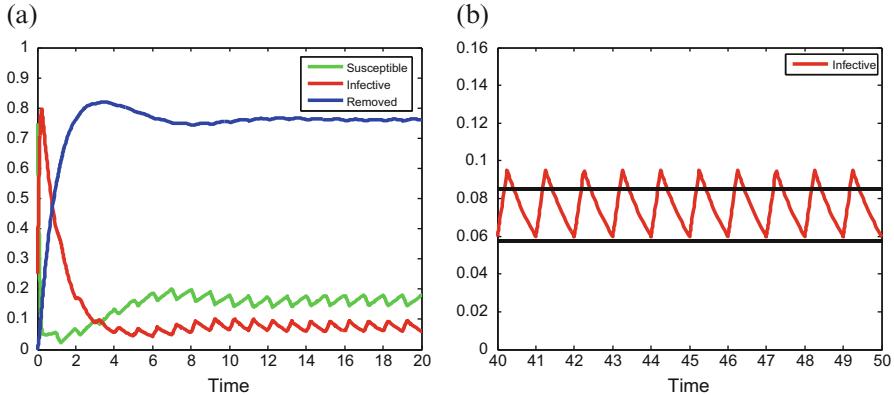


Fig. 5.2 Simulation of Example 5.1. (a) $\rho = 0$. (b) The black lines represent $I_{\min} = 0.0576$ and $I_{\max} = 0.0854$

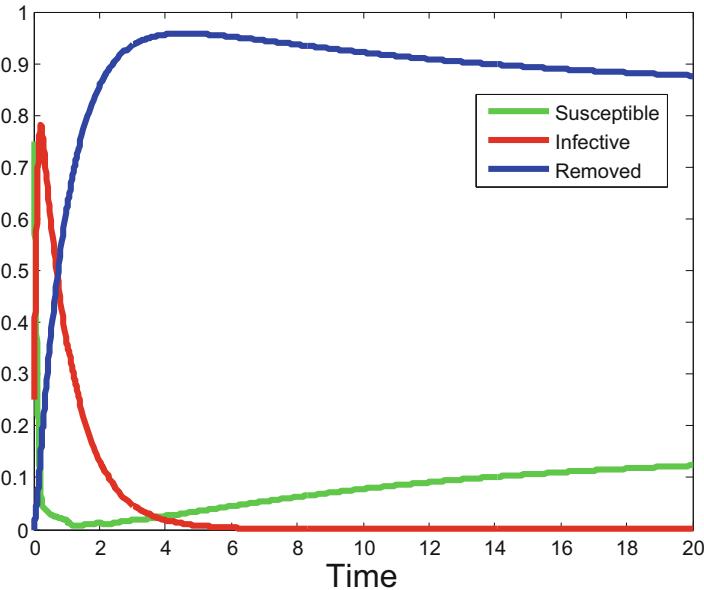


Fig. 5.3 Simulation of Example 5.1 with $\rho = 0.85$

Instead of a newborn vaccination strategy, consider an immunization strategy applied to the entire susceptible cohort in an SIR model (3.8). Mathematically, suppose that the susceptible population is vaccinated at a rate $v \geq 0$ per unit time and again assume permanent immunity is acquired through vaccination (which is

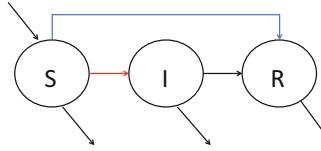


Fig. 5.4 Flow of the switched SIR system with susceptible vaccinations (5.8). The *red line* represents the horizontal transmission and the *blue line* represents the vaccination scheme

indistinguishable from naturally acquired immunity). Thus, the dynamics of the model

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) - vS(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (g + \mu)I(t), \\ \dot{R}(t) &= gI(t) + vS(t) - \mu R(t),\end{aligned}\tag{5.8}$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

are investigated. The flow diagram for (5.8) is shown in Fig. 5.4.

As before, the meaningful domain is unchanged ($D_{(5.8)} = D_{(3.8)}$) and positively invariant (thus giving a global unique solution for appropriate initial conditions). However, the set of mode basic reproduction numbers of (5.8) is changed from the uncontrolled switched SIR model (as expected):

$$R_0^{(5.8),i} \equiv \frac{\beta_i}{\mu + g} \frac{\mu}{\mu + v}, \quad \forall i \in \mathcal{M},\tag{5.9}$$

while the disease-free solution is calculated as

$$Q_{\text{DFS}}^{(5.8)} \equiv \left(\frac{\mu}{\mu + v}, 0, 1 - \frac{\mu}{\mu + v} \right).\tag{5.10}$$

Each mode $i \in \mathcal{M}$ admits an endemic equilibrium:

$$Q_{\text{ES}}^{(5.8),i} \equiv \left(\frac{\mu + g}{\beta_i}, \frac{\mu}{\mu + g} \left(1 - \frac{1}{R_0^{(5.8),i}} \right), \frac{\mu}{\mu + g} \left(1 - \frac{1}{R_0^{(5.8),i}} \right) + \frac{v}{\mu} \frac{\mu + g}{\beta_i} \right).\tag{5.11}$$

Different from the newborn vaccination scheme, (5.8) gives that

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) - vS(t), \\ &\leq \mu - (\mu + v)S(t),\end{aligned}$$

which motivates analyzing the comparison system

$$\begin{aligned}\dot{x}(t) &= \mu - (\mu + v)x(t), \\ x(0) &= S_0,\end{aligned}\tag{5.12}$$

that has unique solution

$$x(t) \equiv \left(S_0 - \frac{\mu}{\mu + v} \right) \exp(-(\mu + v)t) + \frac{\mu}{\mu + v},$$

satisfying

$$\lim_{t \rightarrow \infty} x(t) = \frac{\mu}{\mu + v}$$

(the first component of the disease-free solution). Thus, the same analysis as in Theorem 5.1 yields that the solution of (5.8) converges to the disease-free solution $\mathcal{Q}_{\text{DFS}}^{(5.8)}$ (which is globally asymptotically L -stable in the meaningful domain) if

$$R_0^{(5.8)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(5.8),i} \tau_i = \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} \frac{\mu}{\mu + v};$$

the critical cohort immunization rate as

$$v_{\text{crit}} \equiv \mu(R_0^{(3.8)} - 1) = \mu \left(\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} - 1 \right) \in \mathbb{R}_+$$

(assuming that $R_0^{(3.8)} \geq 1$).

Example 5.2 Consider (5.8) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), and initial conditions $(S_0, I_0, R_0) = (0.75, 0.25, 0)$. Motivated by the measles parameters of [138], let $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$, and $v = 0.57$ ($v_{\text{crit}} = 0.51$). Then $R_0^{(5.8)} = 0.92$ (see Fig. 5.5 for an illustration).

The vaccination models thus far assume immediate movement from susceptible to vaccinated. This ignores the time it takes to obtain immunity by completing a vaccination program. The following assumptions are made [101]:

1. The mean period of vaccine-induced immunity is $1/\gamma$ for some $\gamma > 0$.
2. Individuals in the vaccinated class contract the disease at a reduced rate β_σ^V (i.e., $\beta_\sigma^V < \beta_i$ for each $i \in \mathcal{M}$ since individuals may have partial immunity during the vaccination process).

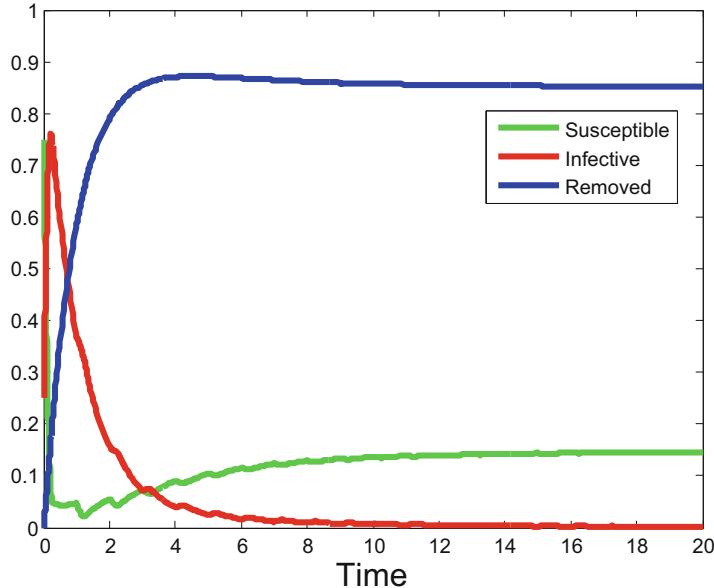


Fig. 5.5 Simulation of Example 5.2 with $v = 0.57$

Under these assumptions, the SVIR model with switching is written as

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) - vS(t), \\ \dot{V}(t) &= vS(t) - \beta_\sigma^V V(t)I(t) - \gamma V(t) - \mu V(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) + \beta_\sigma^V V(t)I(t) - gI(t) - \mu I(t), \\ \dot{R}(t) &= gI(t) + \gamma V(t) - \mu R(t),\end{aligned}\quad (5.13)$$

$$(S(0), V(0), I(0), R(0)) = (S_0, V_0, I_0, R_0).$$

For (5.13), the set of mode basic reproduction numbers can be calculated as follows:

$$R_0^{(5.13),i} \equiv \left(\frac{\beta_i}{\mu + g} + \frac{\beta_i^V}{\mu + g} \frac{v}{\mu + \gamma} \right) \frac{\mu}{\mu + v}, \quad \forall i \in \mathcal{M}. \quad (5.14)$$

The flow diagram of (5.13) is illustrated in Fig. 5.6.

Observe that as the efficacy of the vaccine is increased (i.e., β_i^V decreases or γ increases), the mode reproduction numbers reduce to those of the SIR model (3.8) (and are equal in the limit $\beta_i^V \rightarrow 0$ for each i or $\gamma \rightarrow \infty$). However, as noted in [101], increasing the efficacy of the vaccine is usually more difficult than controlling the vaccination rate v . There is a single disease-free equilibrium point [101]:

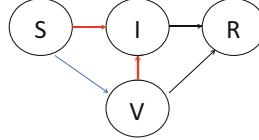


Fig. 5.6 Flow diagram of the switched SVIR system (5.13). The *red line* represents the transmission of the disease and the *blue line* represents the vaccination

$$\mathcal{Q}_{\text{DFS}}^{(5.13)} \equiv (\bar{S}, \bar{V}, \bar{I}, \bar{R}) \equiv \left(\frac{\mu}{\mu + v}, \frac{v\mu}{(\mu + \gamma)(\mu + v)}, 0, \frac{v\gamma}{(\mu + \gamma)(\mu + v)} \right) \quad (5.15)$$

and, as per usual, any mode for which $R_0^{(5.8),i} \geq 1$ admits an endemic equilibrium

$$\mathcal{Q}_{\text{ES}}^{(5.13),i} \equiv (S_i^*, V_i^*, I_i^*, R_i^*), \quad \forall i \in \mathcal{M},$$

where I_i^* is the positive root of the function $I \mapsto A_1 I^2 + A_2 I + A_3 (1 - R_0^{(5.8),i})$ where

$$A_1 \equiv (\mu + g)\beta_i\beta_i^V > 0, \quad \forall i \in \mathcal{M},$$

$$A_2 \equiv (\mu + g)[(\mu + v)\beta_i^V + (\mu + \gamma)\beta_i] - \beta_i^V\beta_i\mu, \quad \forall i \in \mathcal{M},$$

$$A_3 \equiv (\mu + g)(\mu + v)(\mu + \gamma) > 0, \quad \forall i \in \mathcal{M},$$

and

$$S_i^* \equiv \frac{\mu}{\mu + v + \beta_i I_i^*}, \quad \forall i \in \mathcal{M},$$

$$V_i^* \equiv \frac{v\mu}{(\mu + v + \beta_i I_i^*)(\mu + \gamma + \beta_i^V I_i^*)}, \quad \forall i \in \mathcal{M},$$

$$R_i^* \equiv 1 - S_i^* - I_i^* - V_i^*, \quad \forall i \in \mathcal{M}.$$

Theorem 5.2 If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$R_0^{(5.13)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(5.13),i} \tau_i < 1,$$

then the disease-free solution $\mathcal{Q}_{\text{DFS}}^{(5.13)}$ of the switched SIR system with progressive immunity (5.13) is globally attractive and globally asymptotically I-stable in the meaningful domain.

Proof Observe from (5.8) that

$$\begin{aligned} \dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) - vS(t), \\ &\leq \mu - (\mu + v)S(t). \end{aligned}$$

Similarly,

$$\begin{aligned}\dot{V}(t) &= vS(t) - \beta_\sigma^V V(t)I(t) - \gamma V(t) - \mu V(t), \\ &\leq vS(t) - \gamma V(t) - \mu V(t).\end{aligned}$$

The comparison system

$$\begin{aligned}\dot{x}(t) &= \mu - (\mu + v)x(t), \\ \dot{y}(t) &= vx(t) - (\gamma + \mu)y(t), \\ (x(0), y(0)) &= (S_0, V_0),\end{aligned}\tag{5.16}$$

gives the appropriately needed result; for any $\epsilon > 0$, there exists $t^* > 0$ such that $S(t) \leq x(t) \leq \bar{S} + \epsilon$ and $V(t) \leq y(t) \leq \bar{V} + \epsilon$ for $t \geq t^*$. Returning to the differential equation for I ,

$$\begin{aligned}\dot{I}(t) &= \beta_\sigma S(t)I(t) + \beta_\sigma^V V(t)I(t) - gI(t) - \mu I(t), \\ &\leq (\beta_\sigma[\bar{S} + \epsilon] + \beta_\sigma^V[\bar{V} + \epsilon] - \mu - g)I(t), \\ &= \lambda_{\sigma, \epsilon}I(t),\end{aligned}$$

where $\lambda_{i, \epsilon} \equiv \beta_\sigma[\bar{S} + \epsilon] + \beta_\sigma^V[\bar{V} + \epsilon] - \mu - g$ for each $i \in \mathcal{M}$. The condition $R_0^{(5.4)} < 1$ gives that

$$\sum_{i=1}^m (\beta_i \bar{S} + \beta_\sigma^V \bar{V} - \mu - g) \tau_i < 0.$$

As in the proof of Theorem 5.1, $\epsilon > 0$ can be chosen sufficiently small so that $\sum_{i=1}^m \lambda_{i, \epsilon} \tau_i < 0$ and it follows that $\lim_{t \rightarrow \infty} I(t) = 0$. The limiting equation for S is $\dot{S}(t) = \mu - \mu S(t) - vS(t)$; S converges to $\bar{S} = \mu/(\mu + v)$, and the limiting equation for V is $\dot{V}(t) = v\mu/(\mu + v) - \gamma V(t) - \mu V(t)$, from which it follows that V converges to \bar{V} . Finally, the limiting equation for R is $\dot{R}(t) = \gamma v\mu/[(\mu + v)(\gamma + \mu)] - \mu R(t)$, from which convergence of R to \bar{R} follows. Therefore, the solution of system (5.13) converges to the disease-free equilibrium $Q_{\text{DFS}}^{(5.13)}$. Asymptotic I -stability follows as usual.

The critical vaccination rate in the case of progressive immunity is calculated by setting

$$R_0^{(5.13)} = \frac{1}{\omega} \left(\frac{\sum_{i=1}^m \beta_i \tau_i}{\mu + g} + \frac{\sum_{i=1}^m \beta_i^V \tau_i}{\mu + g} \frac{v}{\mu + \gamma} \right) \frac{\mu}{\mu + v} = 1.$$

Namely,

$$v_{\text{crit}} \equiv \mu \left(\frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} - 1 \right) \left(1 - \mu \frac{\sum_{i=1}^m \beta_i^V \tau_i}{\omega(\mu + g)} \right)^{-1}.$$

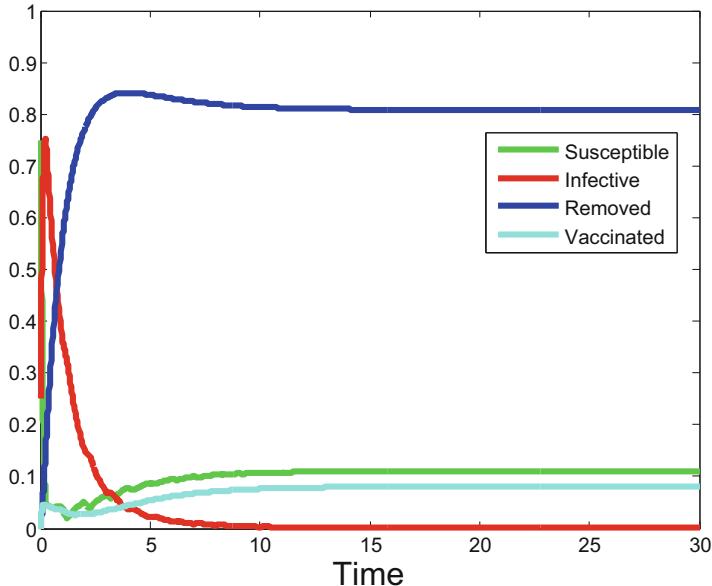


Fig. 5.7 Simulation of Example 5.3 with $v = 0.8$

Example 5.3 Consider (5.13) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), and initial conditions $(S_0, V_0, I_0, R_0) = (0.75, 0, 0.25, 0)$. Given $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$, $\gamma = 1$ and vaccine-reduced contact rates $\beta_1^V = 1$ and $\beta_2^V = 0.17$. Then $v = 0.8$ ($v_{\text{crit}} = 0.51$) implies that $R_0^{(5.13)} = 0.580$ (see Fig. 5.7 for an illustration).

5.2 Treatment Schedules for Classes of Infected

The control strategy of treating infections is investigated. More specifically, a piecewise constant switching control is presented. Assume that $p_i \geq 0$, $i \in \mathcal{M}$, are treatment rates, per unit time, of the infected population which may be applied to the infected population. The value p_i can be broken down as $p_i = v_i/q$ where $1/q > 0$ is average treatment period and $v_i > 0$ is the treatment success rate. Assuming movement to the recovered class from the treatment process, the switched system is written as follows:

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t), \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - gI(t) - \mu I(t) - p_\sigma I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t) + p_\sigma I(t).\end{aligned}\tag{5.17}$$

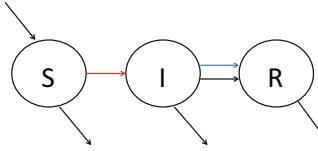


Fig. 5.8 Flow of the switched SIR system with treatment (5.17). The red line represents the horizontal transmission and the blue line represents the treatment strategy

The variables here have been normalized by the total population (since $S+I+R=1$ is an invariant of (5.17)). Indeed, the physically meaningful domain of (5.17) is equal to

$$D_{(5.17)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\} = D_{(3.8)}.$$

See Fig. 5.8 for an illustration of the flow diagram for (5.17).

The treatment rate acts to reduce the average infectious period (from an average of $1/(\mu + g)$ to $1/(\mu + g + p_i)$); the set of mode basic reproduction numbers are reduced as

$$R_0^{(5.17),i} \equiv \frac{\beta_i}{\mu + g + p_i} \leq \frac{\beta_i}{\mu + g} = R_0^{(3.8),i}, \quad \forall i \in \mathcal{M}. \quad (5.18)$$

Disease eradication by switching treatment can immediately be proved from the techniques of Sect. 3.4 by making the following observation:

$$\dot{I}(t) = \beta_\sigma S(t)I(t) - gI(t) - \mu I(t) - p_\sigma I(t) \leq \lambda_i I(t),$$

where $\lambda_i \equiv \beta_i - g - \mu - p_i$ for each i . By repeating the standard attractivity and partial stability switched systems methods already used, the following result is provided.

Theorem 5.3 Consider the switched SIR model with switching treatment (5.17). Global attractivity of the disease-free solution $Q_{\text{DFS}}^{(5.17)} \equiv (1, 0, 0)$ holds under any of the following conditions:

- (i) $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(5.17)} \equiv \frac{1}{\omega} \sum_{i=1}^m R_0^{(5.17),i} \tau_i < 1$;
- (ii) $\sigma \in \mathcal{S}_{\text{dwell}}$ and there exists $h > 0$ such that

$$\left\langle R_0^{(5.17)} \right\rangle \equiv \sup_{t \geq h} \frac{\sum_{i=1}^m \beta_i T_i(t)}{t(\mu + g) + \sum_{i=1}^m p_i T_i(t)} < 1; \quad (5.19)$$

- (iii) $\sigma \in \mathcal{S}_{\text{dwell}}$ satisfies $T^+ \leq N_0 + qT^-(t)$ for some $q \in (0, 1)$ and $N_0 \geq 0$ such that

$$\max\{R_0^{(5.17),i} : i \in \mathcal{M}^-\} - 1 < q(\max\{R_0^{(5.17),i} : i \in \mathcal{M}^+\} - 1),$$

where $\mathcal{M}^- \equiv \{i \in \mathcal{M} : R_0^{(5.17),i} < 1\}$ and $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : R_0^{(5.17),i} \geq 1\}$.

On the other hand, if $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(5.17)} > 1$, then the disease persists uniformly in (5.17).

In the setting of Theorem 5.3, case (i) also implies asymptotic I -stability of $Q_{\text{DFS}}^{(5.17)}$ in the meaningful domain. Cases (ii)-(iii) give exponential I -stability.

Example 5.4 Consider (5.17) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), initial conditions $(S_0, I_0, R_0) = (0.75, 0.25, 0)$, and model parameters $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$. Given $p = 1$ (recall $v = 0.57$ ensured disease eradication in the cohort immunization scheme (5.8)), then $R_0^{(5.17)} = 3.21$ and the scheme is ineffective (see Fig. 5.9 for an illustration).

This treatment strategy can be extended to generalized forces of infections (recall the formulation in the switched SIR model with general switched incidence rates (3.29)): suppose that the incidence rate takes the form $(t, S, I) \mapsto h_\sigma(I)S$ to give the system

$$\begin{aligned}\dot{S}(t) &= \mu - h_\sigma(I(t))S(t) - \mu S(t), \\ \dot{I}(t) &= h_\sigma(I(t))S(t) - (g + \mu + p_\sigma)I(t), \\ \dot{R}(t) &= (g + p_\sigma)I(t) - \mu R(t), \\ (S(0), I(0), R(0)) &= (S_0, I_0, R_0),\end{aligned}\tag{5.20}$$

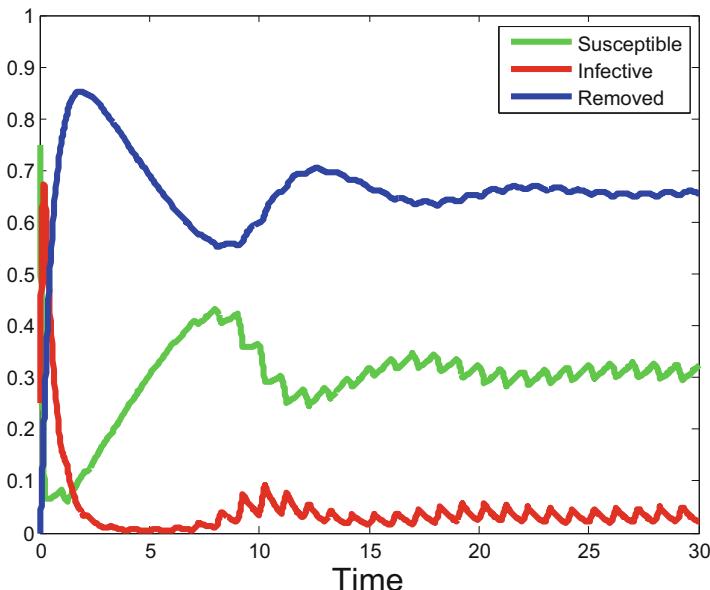


Fig. 5.9 Simulation of Example 5.4 with $p = 1$

where the forces of infection h_i are assumed to satisfy necessary physical conditions (i.e., so that (a)–(d) in Sect. 3.5 are satisfied by $f_i(S, I) \equiv h_i(I)S$). The treatment rate can be used to control the disease to eradication, via the set of mode reproduction numbers

$$R_0^{(5.20),i} \equiv \frac{1}{\mu + g + p_i} \frac{dh_i}{dI}(0), \quad \forall i \in \mathcal{M},$$

as follows.

Theorem 5.4 Assume that $h_i \in C^2([0, 1], \mathbb{R}_+)$ satisfies $\frac{d^2 h_i}{dI^2}(I) \leq 0$ for all $I \in [0, 1]$, $i \in \mathcal{M}$. If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$p_i > \frac{dh_i}{dI}(0) - (\mu + g), \quad \forall i \in \mathcal{M}, \quad (5.21)$$

then $Q_{\text{DFS}}^{(5.20)} \equiv (1, 0, 0)$ is globally asymptotically stable in the meaningful domain

$$D_{(5.20)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\};$$

the disease is eradicated by the switching treatment control.

Proof Define the mapping

$$V(S, I) \equiv S - \ln(S) + I - 1$$

which is continuously differentiable on

$$\Omega_{SI}^\epsilon \equiv \{(S, I) \in \mathbb{R}_+^2 : S + I \leq 1\} \cap \{(S, I) : S \geq \epsilon\} = \{(S, I) : S \geq \epsilon, S + I \leq 1\},$$

for $\epsilon > 0$ [73]. Observe that $V(1, 0) = 0$, $V > 0$ for $(S, I) \in \Omega_{SI}^\epsilon \setminus \{(1, 0)\}$,

$$\frac{\partial V}{\partial S}(S, I) = 1 - 1/S, \quad \frac{\partial^2 V}{\partial S^2}(S, I) = 1/S^2, \quad \frac{\partial V}{\partial I}(S, I) = 1, \quad \frac{\partial^2 V}{\partial I^2}(S, I) = 0,$$

implying that $(S, I) = (1, 0)$ is the unique (global) minimum of the Lyapunov function in Ω_{SI}^ϵ . The time-derivative of V along trajectories of (5.20) yields that

$$\begin{aligned} \dot{V}_{(5.20)}(t, S, I, R) &= (1 - 1/S)(\mu - h_\sigma(I)S - \mu S) + h_\sigma(I)S - (\mu + g + p_\sigma)I, \\ &= \mu [(1 - 1/S)(1 - S)] + (\mu + g + p_\sigma)I \left(\frac{h_\sigma(I)}{(\mu + g + p_\sigma)I} - 1 \right). \end{aligned}$$

Proceed by arguments in [73]: observe that $(1 - 1/S)(1 - S) < 0$ for $\epsilon \leq S < 1$; $(1 - 1/S)(1 - S) = 0$ if $S = 1$. The concavity condition on the set of functions h_i

implies that $h_i(I)/I \leq \frac{dh_i}{dI}(0)$ for all $I > 0$. It follows that

$$\frac{h_i(I)}{(\mu + g + p_i)I} \leq \frac{1}{\mu + g + p_i} \frac{dh_i}{dI}(0) \leq R_0^{(5.20),i}, \quad \forall i \in \mathcal{M}.$$

The condition (5.21) implies that

$$R_0^{(5.20),i} < 1, \quad \forall i \in \mathcal{M}.$$

Moreover, $h_i(I)/[(\mu_i + g_i)I] - 1 < 0$ for each $i \in \mathcal{M}$, so that $\dot{V}_{(5.20)}(t, S, I, R) < 0$ holds unless $(S, I) = (1, 0)$ and the arbitrary choice of ϵ yields global asymptotic stability of $(1, 0)$ in $\Omega_{SI}^{\epsilon \rightarrow 0}$. The equation $R = 1 - I - S$ implies the conclusion holds in $D_{(5.20)}$.

Example 5.5 Consider (5.20) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), initial conditions $(S_0, I_0, R_0) = (0.75, 0.25, 0)$, and $h_i(I) = \beta_i \sin(\pi I/2)$ for $i = 1, 2$. Let $\beta_1 = 4$, $\beta_2 = 1.6$, $g = 1.9$, $\mu = 0.1$. Observe that $f_i(S, I) \equiv h_i(I)S$ satisfies $f_i(t, S, I) > 0$ for $S, I \neq 0$, $f_i(t, S, 0) = f_i(t, 0, I) = 0$, $\frac{\partial f_i(t, S, I)}{\partial I} > 0$ for $0 \leq I < 1$. Then $p_1 = 5$ and $p_2 = 1$ imply that (5.21) holds and global asymptotic stability of the disease-free solution by Theorem 5.4. On the other hand, if $p_1 = p_2 = 0$ then, since $\beta_i \sin(\pi I/2)S \geq \beta_i SI$ for each i , the disease persists by a straightforward calculation of

$$\overline{R}_0^{(3.29)} = 1.1$$

(where $\overline{R}_0^{(3.29)}$ is outlined in Sect. 3.5). The situation is illustrated in Fig. 5.10.

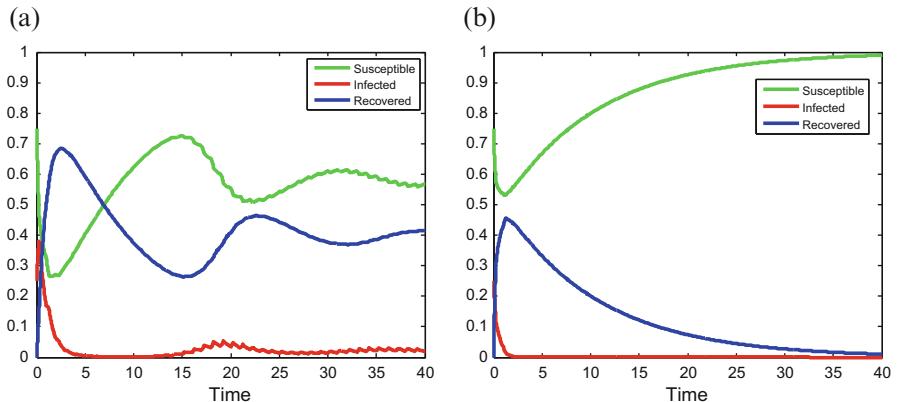


Fig. 5.10 Simulations of Example 5.5. (a) $p_1 = p_2 = 0$. (b) $p_1 = 5, p_2 = 1$

5.3 Introduction of the Exposed: A Controlled SEIR Model

A number of diseases exhibit a period of latency where individuals have been infected but are not yet infectious. (An incubation period is the time between infection and clinical onset of the disease; i.e., appearance of symptoms.) Motivated by this fact, we re-examine the assumption made earlier of a negligible latency period; assume that once a susceptible individual makes an adequate contact with an infected individual they enter a latent period before becoming infectious. Let E denote the class of individuals who have been exposed but are not yet infectious. Assume that individuals who have been exposed become infectious at a rate $a > 0$ (i.e., average incubating period of $1/a$). With other physiological and epidemiological assumptions matching those of the classical endemic model (i.e., (3.9)), the model is given by the following dynamic system:

$$\begin{aligned}\dot{S}(t) &= \mu - \beta S(t)I(t) - \mu S(t), \\ \dot{E}(t) &= \beta S(t)I(t) - aE(t) - \mu E(t), \\ \dot{I}(t) &= aE(t) - gI(t) - \mu I(t), \\ \dot{R}(t) &= gI(t) - \mu R(t),\end{aligned}\tag{5.22}$$

$$(S(0), E(0), I(0), R(0)) = (S_0, E_0, I_0, R_0),$$

where

$$(S_0, E_0, I_0, R_0) \in D_{(5.22)} \equiv \{(S, E, I, R) \in \mathbb{R}_+^4 : S + E + I + R = 1\},$$

which is invariant to (5.22); $\{\dot{S} + \dot{E} + \dot{I} + \dot{R}\}|_{S+E+I+R=1} = 0$, $\dot{S}|_{S=0} = \mu > 0$, $\dot{E}|_{E=0} = \beta SI \geq 0$, $\dot{I}|_{I=0} = 0$, and $\dot{R}|_{R=0} = gI \geq 0$. The basic reproduction number of (5.22) is calculated as

$$R_0^{(5.22)} \equiv \frac{\beta a}{(\mu + g)(\mu + a)};\tag{5.23}$$

the average number of new cases is the product of the contact rate, β , the average fraction surviving the latent period, $a/(a + \mu)$, and the average infectious period $1/(\mu + g)$ [65]. There is a single disease-free equilibrium

$$Q_{\text{DFS}}^{(5.22)} \equiv (1, 0, 0, 0)$$

and an endemic equilibrium:

$$Q_{\text{ES}}^{(5.22)} \equiv \left(\frac{1}{R_0^{(5.22)}}, \frac{\mu(\mu + g)}{\beta a} (R_0^{(5.22)} - 1), \frac{\mu}{\beta} (R_0^{(5.22)} - 1), \frac{g}{\beta} (R_0^{(5.22)} - 1) \right).$$

The invariant $S + E + I + R = 1$ implies that the equation for R can be omitted (i.e., (5.22) is intrinsically three-dimensional).

Recall the basic reproduction number of the classical endemic SIR model (see Eq. (3.11)) and note that for the SEIR model, the reproduction number

$$R_0^{(5.22)} = R_0^{(3.9)} \frac{a}{\mu + a},$$

which implies that $R_0^{(5.22)} \leq R_0^{(3.9)}$. Moreover, since the mean lifetime of an individual is much greater than the average latency period (i.e., $1/\mu \gg 1/a$) then $a \gg \mu$ so that $a/(a + \mu) \approx 1$ [69]. Thus, $R_0^{(5.22)} \approx R_0^{(3.9)}$ in most cases. If the latent period is small compared to the infectious period (i.e., $a/g \gg 1$), which is often the case, the latent period can be ignored [103], which justifies the assumption made for the classical endemic model. The dynamics of (5.22) are again dictated by the basic reproduction number:

$$R_0^{(5.22)} \leq 1$$

implies asymptotic stability of the disease-free equilibrium $Q_{\text{DFS}}^{(5.22)}$ in $D_{(5.22)}$;

$$R_0^{(5.22)} > 1$$

implies asymptotic stability of the endemic equilibrium $Q_{\text{ES}}^{(5.22)}$ in $D_{(5.22)}$ (see, e.g., [81]) and is approached in a damped oscillatory fashion [69]. In fact, the period of oscillations is approximately equal to

$$2\pi \sqrt{\frac{1}{\mu(R_0^{(5.22)} - 1)} \left(\frac{1}{\mu + g} + \frac{1}{\mu + a} \right)}$$

where [69]:

1. The term $1/(\mu(R_0^{(5.22)} - 1))$ is the average age of infection.
2. The term $1/(\mu + g) + 1/(\mu + a)$ is the average period of host's infectivity.

In effect, the SEIR model (5.22) admits a slower rate of growth of the disease after its introduction because the latent period delays an exposed person from becoming infectious [69].

With seasonal variations in (5.22), and a treatment of infected by the switching rate p_σ ($p_1, \dots, p_m \geq 0$), the model is given by

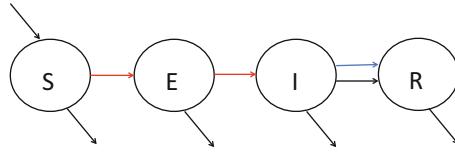


Fig. 5.11 Flow of the switched SEIR system with treatment (5.24). The red line represents the horizontal transmission and the blue line represents the treatment strategy

$$\begin{aligned}
 \dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t), \\
 \dot{E}(t) &= \beta_\sigma S(t)I(t) - aE(t) - \mu E(t), \\
 \dot{I}(t) &= aE(t) - gI(t) - \mu I(t) - p_\sigma I(t), \\
 \dot{R}(t) &= gI(t) + p_\sigma I(t) - \mu R(t), \\
 (S(0), E(0), I(0), R(0)) &= (S_0, E_0, I_0, R_0).
 \end{aligned} \tag{5.24}$$

Here, it is assumed that infected individuals seek treatment but those who have been exposed and are in the latent period (possibly asymptomatic) do not seek treatment. See Fig. 5.11 for the flow of individuals in the population. The mode basic reproduction numbers are thus

$$R_0^{(5.24),i} \equiv \frac{\beta_i a}{(\mu + g + p_i)(\mu + a)}, \quad \forall i \in \mathcal{M}. \tag{5.25}$$

Intuitively, the basic reproduction number in each isolated mode equal to $\beta_i/(\mu + g + p_i)$ (average contact rate times average period of infection) multiplied by $1/(\mu + a)$ (average latent period). Equation (5.24) still admits a common disease-free equilibrium

$$Q_{\text{DFS}}^{(5.24)} \equiv (1, 0, 0, 0) = Q_{\text{DFS}}^{(5.22)},$$

while each mode admits an endemic equilibrium:

$$Q_{\text{ES}}^{(5.24),i} \equiv \left(\frac{1}{R_0^{(5.24),i}}, \frac{\mu(\mu + g + p_i)}{\beta_i a} (R_0^{(5.24),i} - 1), \frac{\mu}{\beta_i} (R_0^{(5.24),i} - 1), \frac{g + p_i}{\beta_i} (R_0^{(5.24),i} - 1) \right),$$

for each $i \in \mathcal{M}$. The long-term behavior of (5.24) is characterized via common Lyapunov function techniques and the switching invariance principle.

Theorem 5.5 If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$p_i > \frac{\beta_i a}{\mu + a} - (\mu + g), \quad \forall i \in \mathcal{M}, \tag{5.26}$$

then $Q_{\text{DFS}}^{(5.24)}$ is globally attractive in the meaningful domain; the disease is eradicated by the switching treatment control.

Proof Define the mapping $V(E, I) \equiv aE + (a + \mu)I$ (similar to the one from [140]) and define the following set:

$$\Omega_{EI} = \{(E, I) \in \mathbb{R}_+^2 : E + I \leq 1\}.$$

Observe that $V(0, 0) = 0$ and $V(E, I) > 0$ for $(E, I) \in \Omega_{EI} \setminus \{(0, 0)\}$. The time-derivative of V along trajectories of (5.24) is given by:

$$\begin{aligned}\dot{V}_{(5.24)}(t, S, E, I, R) &= a(\beta_\sigma SI - aE - \mu E) + (a + \mu)(aE - gI - \mu I - p_\sigma I), \\ &= \beta_\sigma aSI - (\mu + g + p_\sigma)(\mu + a)I, \\ &= (R_0^{(5.24)}S - 1)(\mu + g + p_\sigma)(\mu + a)I.\end{aligned}$$

Condition (5.26) precisely implies that $R_0^{(5.24),i} < 1$ for all $i \in \mathcal{M}$. From this it follows that $\dot{V}_{(5.24)}(t, S, E, I, R) \leq 0$; $V(E, I)$ is a common weak Lyapunov function of (5.24). The set

$$\{(E, I) \in \Omega_{EI} : \dot{V}_{(5.24)} = 0\} = \{(E, I) \in \Omega_{EI} : (E, I) = (c, 0), \quad \forall 0 \leq c \leq 1\}$$

and, by inspection of the limiting equations of (5.24) with $I = 0$, the solution converges to the disease-free equilibrium $Q_{\text{DFS}}^{(5.24)}$ by Theorem 2.2.

Example 5.6 Consider (5.24) with $\mathcal{M} = \{1, 2\}$, σ defined as in (3.37), initial conditions $(S_0, E_0, I_0, R_0) = (0.9, 0, 0.1, 0)$, and $\beta_1 = 8$, $\beta_2 = 1.6$, $g = 0.9$, $\mu = 0.1$. Let the latent period equal $1/a = 1/0.3$ from [103]. Given $p_1 = 6$ and $p_2 = 1$, then

$$6 = p_1 > \frac{\beta_1 a}{\mu + a} - (\mu + g) = 5,$$

and

$$1 = p_2 > \frac{\beta_2 a}{\mu + a} - (\mu + g) = 0.2;$$

the conditions of Theorem 5.5 are satisfied and $Q_{\text{DFS}}^{(5.24)}$ is globally attractive in the meaningful domain. See Fig. 5.12 for an illustration.

Motivated by the number of infectious diseases transmitted by both horizontal and vertical modes (e.g., rubella, herpes simplex, hepatitis B, Chagas' disease [140]), consider (5.24) with the additional assumption of vertical transmission:

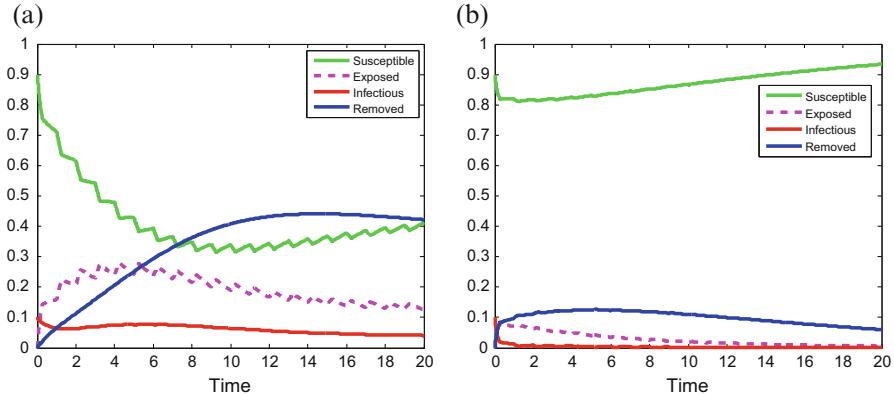


Fig. 5.12 Simulations of Example 5.5. (a) $p_1 = p_2 = 0$. (b) $p_1 = 6, p_2 = 1$

$$\begin{aligned}
 \dot{S}(t) &= \mu(1 - \rho E(t) - qI(t)) - \beta_\sigma S(t)I(t) - \mu S(t), \\
 \dot{E}(t) &= \mu(\rho E(t) + qI(t)) + \beta_\sigma S(t)I(t) - aE(t) - \mu E(t), \\
 \dot{I}(t) &= aE(t) - gI(t) - \mu I(t) - p_\sigma I(t), \\
 \dot{R}(t) &= gI(t) + p_\sigma I(t) - \mu R(t), \\
 (S(0), E(0), I(0), R(0)) &= (S_0, E_0, I_0, R_0),
 \end{aligned} \tag{5.27}$$

where $\rho \in [0, 1]$ and $q \in [0, 1]$ represent vertical transmission via exposed and infected individuals, respectively. The set

$$D_{(5.27)} \equiv \{(S, E, I, R) \in \mathbb{R}_+^4 : S + E + I + R = 1\}$$

is the meaningful domain (which is positively invariant). The mode basic reproduction numbers are (from the case [140]):

$$R_0^{(5.27),i} \equiv \frac{\beta_i a}{(\mu + g + p_i)(\mu(1 - \rho) + a) - \mu qa}, \quad \forall i \in \mathcal{M}, \tag{5.28}$$

which can be interpreted via a Taylor expansion of the transmission of diseases through the generations of offspring in each mode [140] (where the authors also present the endemic equilibria and stability results for the time-invariant and uncontrolled version of (5.27)). Equation (5.27) admits a disease-free equilibrium $Q_{\text{DFS}}^{(5.27)} \equiv (1, 0, 0, 0)$ and mode-dependent endemic equilibria $Q_{\text{ES},i}^{(5.27)} \equiv (S_i^*, E_i^*, I_i^*, R_i^*)$ where, for each $i \in \mathcal{M}$,

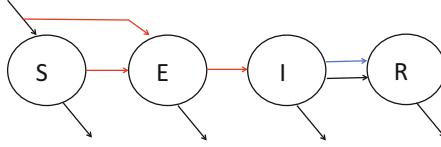


Fig. 5.13 Flow of the switched SEIR system with vertical transmission and treatment (5.27). The red lines represent the horizontal and vertical transmission and the blue line represents the treatment strategy

$$S_i^* \equiv \frac{1}{R_0^{(5.27),i}},$$

$$E_i^* \equiv 1 - S_i^* - I_i^* - R_i^*,$$

$$I_i^* \equiv \frac{a\mu R_0^{(5.27),i}}{\beta_i a + \rho\mu(g + \mu + p_i)R_0^{(5.27),i} + q\mu a R_0^{(5.27),i}}(1 - 1/R_0^{(5.27),i}),$$

$$R_i^* \equiv \frac{a(g + p_i)R_0^{(5.27),i}}{\beta_i a + \rho\mu(g + \mu + p_i)R_0^{(5.27),i} + q\mu a R_0^{(5.27),i}}(1 - 1/R_0^{(5.27),i}).$$

The flow of (5.27) is illustrated in Fig. 5.13. Eradication is established as follows.

Theorem 5.6 If $\sigma \in \mathcal{S}_{\text{dwell}}$ and

$$p_i > \frac{(\beta_i + \mu q)a}{\mu(1 - \rho) + a} - (\mu + g), \quad \forall i \in \mathcal{M}, \quad (5.29)$$

then $Q_{\text{DFS}}^{(5.27)}$ is globally attractive in the meaningful domain; the disease is eradicated by the switching treatment control.

Proof The proof proceeds similar to the proof of Theorem 5.5 by replacing the Lyapunov candidate function with

$$V(E, I) \equiv aE + (a + \mu - \rho\mu)I$$

(adopted from one in [140]). Observe that $V(0, 0) = 0$ and $V(E, I) > 0$ when $(E, I) \in \Omega_{EI} \setminus \{(0, 0)\}$ (where Ω_{EI} is defined in the proof of Theorem 5.5). The time-derivative of V along trajectories of (5.27) is given by

$$\begin{aligned} \dot{V}_{(5.27)}(t, S, E, I, R) &= a(\beta_\sigma SI + \rho\mu E + q\mu I - aE - \mu E) \\ &\quad + (a + \mu - \rho\mu)(aE - gI - p_\sigma I - \mu I), \\ &= \beta_\sigma aSI - [(\mu + g + p_\sigma)(\mu + a - \rho\mu) - \mu qa]I, \\ &= (R_0^{(5.27)}S - 1)(\mu + g + p_\sigma)(\mu + a - \rho\mu - \mu qa)I. \end{aligned}$$

Hence, if $R_0^{(5.27),i} < 1$ for all i , then $\dot{V}_{(5.27)}(t, S, E, I, R) \leq 0$. The remaining part follows by similar arguments to the proof of Theorem 5.5.

Appropriate for a disease like AIDS [140], suppose that the assumptions on the population dynamics and disease-induced mortality are relaxed; assume that the birth rate is $b > 0$, the natural death rate is $d > 0$ and the disease-induced death rate is $\alpha > 0$. Applied to (5.24) yields the following dynamic system:

$$\begin{aligned}\dot{S}_c(t) &= b - \beta_\sigma \frac{S_c(t)I_c(t)}{N(t)} - dS_c(t) \\ \dot{E}_c(t) &= \beta_\sigma \frac{S_c(t)I_c(t)}{N(t)} - aE_c(t) - dE_c(t), \\ \dot{I}_c(t) &= aE_c(t) - gI_c(t) - dI_c(t) - \alpha I_c(t) - p_\sigma I_c(t), \\ \dot{R}_c(t) &= gI_c(t) + p_\sigma I_c(t) - dR_c(t),\end{aligned}\tag{5.30}$$

where S_c, E_c, I_c, R_c represent the number of individuals in the susceptible, exposed, infectious, and removed classes, respectively. The total population $N \equiv S_c + E_c + I_c + R_c$ satisfies the differential equation

$$\dot{N}(t) = (b - d)N(t) - \alpha I_c(t).$$

Normalizing the equations via $S \equiv S_c/N$, $E \equiv E_c/N$, $I \equiv I_c/N$, $R \equiv R_c/N$ yields the following switching system:

$$\begin{aligned}\dot{S}(t) &= b - \beta_\sigma S(t)I(t) - bS(t) + \alpha S(t)I(t), \\ \dot{E}(t) &= \beta_\sigma S(t)I(t) - aE(t) - bE(t) + \alpha E(t)I(t), \\ \dot{I}(t) &= aE(t) - gI(t) - bI(t) - \alpha I(t) - p_\sigma I(t) + \alpha I^2(t), \\ \dot{R}(t) &= gI(t) + p_\sigma I(t) - bR(t) + \alpha R(t)I(t), \\ (S(0), E(0), I(0), R(0)) &= (S_0, E_0, I_0, R_0),\end{aligned}\tag{5.31}$$

where the normalized variables satisfy $S(t) + E(t) + I(t) + R(t) = 1$. The initial conditions satisfy $(S_0, E_0, I_0, R_0) \in D_{(5.31)} = D_{(5.24)}$, which is invariant to (5.31); $\{\dot{S} + \dot{E} + \dot{I} + \dot{R}\}|_{S+E+I+R=1} = 0$, $\dot{S}|_{S=0} = b > 0$, $\dot{E}|_{E=0} = \beta_\sigma SI \geq 0$, $\dot{I}|_{I=0} = aE \geq 0$ and $\dot{R}|_{R=0} = gI \geq 0$. A consequence of the disease-induced mortality, the terms αSI , αEI , αIR , and αI^2 act as positive feedback in the dynamic system. The mode basic reproduction numbers are

$$R_0^{(5.31),i} \equiv \frac{\beta_i a}{(b + g + \alpha + p_i)(b + a)}, \quad \forall i \in \mathcal{M},\tag{5.32}$$

which reflect the time-invariant case [81]. Comparing (5.32) to (5.25) reveals a reduction in the mode-dependent basic reproduction numbers; the disease-induced mortality reduces the infectious period and therefore the rate of transmission. As in the previously studied SEIR models, (5.31) again admits a disease-free equilibrium

$Q_{\text{DFS}}^{(5.31)} \equiv (1, 0, 0, 0)$ and m endemic equilibria $Q_{\text{ES}}^{(5.31),i} \equiv (S_i^*, E_i^*, I_i^*, R_i^*)$. Here, I_i^* satisfies the following cubic equation [81]:

$$\left(1 - \frac{\alpha}{a+b} I_i^*\right) \left(1 - \frac{\alpha}{\alpha + g + b + p_i} I_i^*\right) \left(1 + \frac{\beta_i - \alpha}{b} I_i^*\right) = R_0^{(5.31),i}, \quad (5.33)$$

for each $i \in \mathcal{M}$. If $R_0^{(5.31),i} > 1$, then (5.33) admits a unique positive solution [81]. The other endemic equilibria states satisfy

$$\begin{aligned} S_i^* &\equiv \frac{b}{b + \beta_i I_i^* - \alpha I_i^*}, \\ E_i^* &\equiv \frac{g + \alpha + b + p_i - \alpha I_i^*}{a} I_i^*, \\ R_i^* &\equiv 1 - S_i^* - E_i^* - I_i^*, \end{aligned}$$

for each $i \in \mathcal{M}$. Stability of the disease-free solution can be established using the following lemma from [81].

Lemma 5.1 *Let $\Omega \equiv \{(x, y) \in \mathbb{R}_+^2 : x+y \leq 1\}$ and $h(x, y) \equiv (a-b)x + (c-b)y + b$, where $a, b, c > 0$ are constants. Then it follows that*

$$\max\{h(x, y) : (x, y) \in \Omega\} = \max\{a, b, c\}.$$

Theorem 5.7 *If $\sigma \in \mathcal{S}_{\text{dwell}}$ and*

$$p_i > \frac{\beta_i a}{b+a} - (\mu + g + \alpha), \quad \forall i \in \mathcal{M}, \quad (5.34)$$

then $Q_{\text{DFS}}^{(5.31)}$ is globally attractive in the meaningful domain. Moreover, the total number of infected individuals approaches zero (i.e., $\lim_{t \rightarrow \infty} I_c(t) = 0$).

Proof Define the mapping $V(E, I) \equiv aE + (a+b)I$ [81], which satisfies $V(0, 0) = 0$ and $V(E, I) > 0$ for $(E, I) \in \Omega_{EI} \setminus \{(0, 0)\}$ (where Ω_{EI} is outlined in the proof of Theorem 5.5). The time-derivative of V trajectories of (5.31) is given by

$$\begin{aligned} \dot{V}_{(5.27)}(t, S, E, I, R) &= a(\beta_\sigma SI - aE - bE + \alpha EI) \\ &\quad + (a+b)(aE - gI - bI - \alpha I - p_\sigma I + \alpha I^2), \\ &= [\beta_\sigma aS - (a+b)(g + \alpha + b + p_\sigma) + \alpha aE + \alpha(a+b)I]I, \\ &\leq [\beta_\sigma a(1 - E - I) - (a+b)(g + \alpha + b + p_\sigma) \\ &\quad + \alpha aE + \alpha(a+b)I]I, \\ &= [h_\sigma(E, I) - (a+b)(g + \alpha + b + p_\sigma)]I, \end{aligned}$$

where

$$h_i(E, I) \equiv (\alpha a - \beta_i a)E + (\alpha(a+b) - \beta_i a)I + \beta_i a, \quad \forall i \in \mathcal{M}.$$

Applying Lemma 5.1 with the function h_i and set Ω_{EI} gives that

$$\dot{V}_{(5.27)} \leq [\max\{\alpha a, \beta_\sigma a, \alpha(a+b)\} - (a+b)(g + \alpha + b + p_\sigma)]I.$$

Then, since $R_0^{(5.31),i} < 1$ for each $i \in \mathcal{M}$ by Eq. (5.34), it follows that $\dot{V}_{(5.27)} \leq 0$. Note that $\dot{V} = 0$ if $(E, I) = (c, 0)$ or if $\max\{\alpha a, \beta_i a, \alpha(a+b)\} = (a+b)(g + \alpha + b + p_i)$, which implies $R_0^{(5.31),i} = 1$ (and is therefore not possible). It then follows by similar arguments to the proof of Theorem 5.5 that $\lim_{t \rightarrow \infty} I(t) = 0$. Recall that $I_c \equiv IN$ and

$$\dot{N}(t) = (b - d)N(t) - \alpha I_c(t) = (b - d - \alpha I(t))N(t).$$

The case $b < d$ is straightforward. The case $b = d$ yields that $\dot{N}(t) = -\alpha I(t)N(t) \leq 0$, from which it follows that N is bounded for all t since $I \rightarrow 0$. The case $b > d$ gives that N grows without bound since $I \rightarrow 0$. Then, $S_c \equiv SN$ and $S \rightarrow 1$ implies that $S_c \rightarrow N$. The fact that $N \equiv S_c + E_c + I_c + R_c$ yields the result.

Equations (5.26), (5.29), and (5.34) define mode-dependent critical control rates for the SEIR model (5.24), SEIR model with vertical transmission (5.27), and SEIR model with disease-induced mortality (5.31), respectively:

$$\begin{aligned} p_i^{(5.26),\text{crit}} &\equiv \frac{\beta_i a}{\mu + a} - (\mu + g), \quad \forall i \in \mathcal{M}, \\ p_i^{(5.29),\text{crit}} &\equiv \frac{(\beta_i + \mu q)a}{\mu(1 - \rho) + a} - (\mu + g), \quad \forall i \in \mathcal{M}, \\ p_i^{(5.34),\text{crit}} &\equiv \frac{\beta_i a}{b + a} - (\mu + g + \alpha), \quad \forall i \in \mathcal{M}. \end{aligned}$$

Observe that

$$p_i^{(5.34),\text{crit}} \leq p_i^{(5.26),\text{crit}} \leq p_i^{(5.29),\text{crit}}, \quad \forall i \in \mathcal{M},$$

as expected; the disease-induced mortality effectively reduces the average infectious period (making the disease easier to control and thus a decrease in the critical treatment rates) while the vertical transmission has the effect of increasing the basic reproduction number of each mode (hence an increase in the critical treatment rates).

5.4 Screening of Traveling Individuals

In this part, we return to (4.21) and consider restricting the travel of infected individuals as a control method for preventing epidemics. We consider the following control strategy:

1. Assume that $\theta^{(j)} \in [0, 1]$ is the probability of successfully detecting an infected individual entering city $j \in \mathcal{N} \equiv \{1, \dots, n\}$ by travel.
2. Assume that susceptible individuals are not falsely identified as being infected. Denote infected individuals traveling to city j who are properly screened by $Q^{(j)}$.
3. Assume that individuals who are being screened do not die or give birth.
4. When the infected individuals are identified, assume that they will be isolated for treatment.
5. Assume that individuals in the screened classes recover at a switched rate $q_\sigma^{(j)} > 0$ in city j and enter the recovered population.

With the additional assumptions that the immigration rate is $m^{(j)}$ in city j and the functions $f_i^{(j)}$ and $h_i^{(j)}$ having standard incidence rate structures, the controlled version of (4.21) becomes the following switching system:

$$\begin{aligned}
\dot{S}^{(j)}(t) &= m^{(j)} - \beta_\sigma^{(j)} \frac{S^{(j)}(t)I^{(j)}(t)}{N^{(j)}(t)} - \mu^{(j)}S^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(j)}(t) \\
&\quad - \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma^{(j)} \frac{S^{(l)}(t)I^{(l)}(t)}{N^{(l)}(t)}, \\
\dot{I}^{(j)}(t) &= \beta_\sigma^{(j)} \frac{S^{(j)}(t)I^{(j)}(t)}{N^{(j)}(t)} - g^{(j)}I^{(j)}(t) - \mu^{(j)}I^{(j)}(t) + \alpha^{(j,j)} I^{(j)}(t) \\
&\quad + (1 - \theta^{(j)}) \left[\sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} I^{(l)}(t) + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma^{(j)} \frac{S^{(l)}(t)I^{(l)}(t)}{N^{(l)}(t)} \right], \\
\dot{Q}^{(j)}(t) &= -q_\sigma^{(j)} Q^{(j)} + \theta^{(j)} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} I^{(l)}(t) \\
&\quad + \theta^{(j)} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma^{(j)} \frac{S^{(l)}(t)I^{(l)}(t)}{N^{(l)}(t)}, \\
\dot{R}^{(j)}(t) &= g^{(j)}I^{(j)}(t) + q_\sigma^{(j)}Q^{(j)}(t) - \mu^{(j)}R^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} R^{(l)}(t), \\
(S^{(j)}(0), I^{(j)}(0), Q^{(j)}(0), R^{(j)}(0)) &= (S_0^{(j)}, I_0^{(j)}, Q_0^{(j)}, R_0^{(j)}),
\end{aligned} \tag{5.35}$$

for all $j \in \mathcal{N}$. The flow diagram for the model with screening is given in Fig. 5.14.

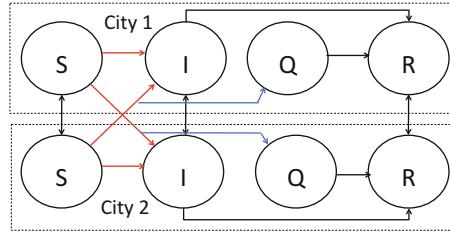


Fig. 5.14 Flow of the multi-city model with screening (5.35) with $n = 2$. The red lines represent new infections (including from traveling individuals) and the blue lines represent the screening process. The population dynamics in each city have been omitted here

The meaningful physical domain for this system is

$$D_{(5.35)} \equiv \{(S, I, Q, R) \in \mathbb{R}_+^{4n} : \sum_{j \in \mathcal{N}} S^{(j)} + I^{(j)} + Q^{(j)} + R^{(j)} \leq N^*\},$$

where

$$N^* = \frac{\sum_{j=1}^n m^{(j)}}{\min\{\mu^{(1)}, \mu^{(2)}, \dots, \mu^{(n)}\}} > 0.$$

For a given initial condition, the solution of (5.35) enters $D_{(5.35)}$ (in finite or infinite time); $D_{(5.35)}$ is positively invariant to (5.35) (see Proposition 2.1 in [167]).

Let us next consider the existence of a disease-free solution of (5.35) with $I^{(j)}(t) \equiv 0$ for all $j \in \mathcal{N}$: It is apparent that the screening class converges to zero, and thus the recovered class (since $\mu^{(j)} > 0$ for each $j \in \mathcal{N}$). The limiting system is given by

$$\dot{S}^{(j)}(t) = m^{(j)} - \mu^{(j)} S^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(l)}(t), \quad \forall j \in \mathcal{N}. \quad (5.36)$$

Using the notation and methodology in [167], define the irreducible matrices $A \equiv (\alpha^{(l,j)})_{1 \leq l,j \leq n}$ and $U \equiv \text{diag}\{\mu^{(1)}, \dots, \mu^{(n)}\}$ and the vector $m = (m^{(1)}, \dots, m^{(n)})$. Then (5.36) is in vector form as

$$\dot{S}(t) = m + (A - U)S(t),$$

whose unique solution satisfies

$$S(t) \equiv (S_0 + (A - U)^{-1}m) \exp((A - U)t) - (A - U)^{-1}m,$$

and

$$\lim_{t \rightarrow \infty} S(t) = -(A - U)^{-1}m \equiv S^*,$$

where $A - U$ is nonsingular and m has nonnegative components (i.e., $(A - U)^{-1}m$ has nonnegative entries). Hence, Eq. (5.35) admits the disease-free solution

$$Q_{\text{DFS}}^{(5.35)} \equiv (S^*, 0, 0, 0).$$

The basic reproduction number of (5.35) is, in general, the spectral radius of an integral operator. It is possible to provide a threshold theorem involving an approximation of the basic reproduction number, as follows.

Theorem 5.8 *Let $\alpha_{\min} \equiv \min\{\alpha^{(l,j)} : l, j \in \mathcal{N}, l \neq j\}$, $\alpha_{\max} \equiv \max\{\alpha^{(l,j)} : l, j \in \mathcal{N}, l \neq j\}$, $\theta_{\min} \equiv \min\{\theta^{(j)} : j \in \mathcal{N}\}$, $g_{\min} \equiv \min\{g^{(j)} : j \in \mathcal{N}\}$ and $\mu_{\min} \equiv \min\{\mu^{(j)} : j \in \mathcal{N}\}$. For each $i \in \mathcal{M}$, let $\beta_i \equiv \max\{\beta_i^{(j)} : j \in \mathcal{N}\}$, and $\gamma_i \equiv \max\{\gamma_i^{(j)} : j \in \mathcal{N}\}$. If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and*

$$\widehat{R}_0^{(5.35)} \equiv \frac{\sum_{i=1}^m (\beta_i S^* + (n-1)(1-\theta_{\min})\alpha_{\max}\gamma_i S^*)\tau_i}{\omega(g_{\min} + \mu_{\min} + (n-1)\theta_{\min}\alpha_{\min})} < 1, \quad (5.37)$$

then $Q_{\text{DFS}}^{(5.35)}$ is globally attractive in the meaningful domain; the disease is eradicated by the screening control.

Proof From Eq. (5.35) note that

$$\dot{S}^{(j)}(t) \leq m^{(j)} - \mu_j S^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(j)}(t).$$

Consider the comparison system

$$\begin{aligned} \dot{x}^{(j)}(t) &= m^{(j)} - \mu^{(j)} x^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} x^{(j)}(t), \\ x(0) &= (S_0^{(1)}, \dots, S_0^{(n)}) = S_0. \end{aligned} \quad (5.38)$$

As remarked above, the solution of this system converges to $-(A - U)^{-1}m = S^*$. Choose

$$0 < \epsilon = \frac{(1 - \widehat{R}_0^{(5.35)}) (\omega(g_{\min} + \mu_{\min} + (n-1)\theta_{\min}\alpha_{\min}))}{2 \sum_{i=1}^m (\beta_i S^* + (n-1)(1-\theta_{\min})\alpha_{\max}\gamma_i)\tau_i}.$$

By comparison theorem, there exists a time $t^* > 0$ such that $S^{(j)}(t) \leq x^{(j)}(t) \leq S^* + \epsilon$ for $t \geq t^*$ and each $j \in \mathcal{N}$ (i.e., by Theorem 1.10). Choose $N \in \mathbb{N}$ as the smallest integer such that $N\omega > t^*$. The following inequalities follow from (5.35) for each $j \in \mathcal{N}$:

$$\sum_{j \in \mathcal{N}} \dot{I}_j(t) = \sum_{j \in \mathcal{N}} [\beta_\sigma^{(j)} \frac{S^{(j)}(t) I^{(j)}(t)}{N^{(j)}(t)} - g^{(j)} I^{(j)}(t) - \mu^{(j)} I^{(j)}(t)]$$

$$\begin{aligned}
& -\theta^{(j)} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} I^{(l)}(t) + (1 - \theta^{(j)}) \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma^{(j)} \frac{S^{(l)}(t) I^{(l)}(t)}{N^{(l)}(t)}, \\
& \leq \sum_{j \in \mathcal{N}} [\beta_\sigma \frac{S^{(j)}(t) I^{(j)}(t)}{N^{(j)}(t)} - g_{\min} I^{(j)}(t) - \mu_{\min} I^{(j)}(t) - \theta^{(j)} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} I^{(j)}(t) \\
& \quad + (1 - \theta^{(j)}) \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_\sigma^{(j)} \frac{S^{(l)}(t) I^{(l)}(t)}{N^{(l)}(t)}].
\end{aligned}$$

Since

$$\sum_{j \in \mathcal{N}} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} S^{(l)} I^{(l)} = \sum_{j \in \mathcal{N}} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} S^{(j)} I^{(j)} \leq \sum_{j \in \mathcal{N}} (n-1) \alpha_{\max} S^{(j)} I^{(j)},$$

then

$$\begin{aligned}
\sum_{j \in \mathcal{N}} \dot{I}_j(t) & \leq \sum_{j \in \mathcal{N}} [\beta_\sigma (S^* + \epsilon) - g_{\min} - \mu_{\min} \\
& \quad - (n-1)\theta_{\min} \alpha_{\min} + (n-1)(1-\theta_{\min})\alpha_{\max} \gamma_\sigma (S^* + \epsilon)] I^{(j)}(t), \\
& \leq \sum_{j \in \mathcal{N}} [\beta_\sigma S^* + (n-1)(1-\theta_{\min})\alpha_{\max} \gamma_\sigma S^* \\
& \quad + \epsilon (\beta_\sigma + (n-1)(1-\theta_{\min})\alpha_{\max} \gamma_\sigma) - g_{\min} - \mu_{\min} - (n-1)\theta_{\min} \alpha_{\min}] I^{(j)}(t), \\
& = \lambda_{k,\epsilon} \sum_{j \in \mathcal{N}} I^{(j)}(t),
\end{aligned} \tag{5.39}$$

where

$$\begin{aligned}
\lambda_{i,\epsilon} & \equiv \beta_i S^* + (n-1)(1-\theta_{\min})\alpha_{\max} \gamma_i S^* \\
& \quad + \epsilon (\beta_i + (n-1)(1-\theta_{\min})\alpha_{\max} \gamma_i) - g_{\min} - \mu_{\min} - (n-1)\theta_{\min} \alpha_{\min}.
\end{aligned} \tag{5.40}$$

Equation (5.39) implies

$$\begin{aligned}
\sum_{j \in \mathcal{N}} I^{(j)}((N+1)\omega) & \leq \sum_{j \in \mathcal{N}} I^{(j)}(N\omega) \exp \left(\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i \right) \\
& = \exp \left(\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i \right) \sum_{j \in \mathcal{N}} I^{(j)}(N\omega),
\end{aligned}$$

from which it follows that $\sum_{j \in \mathcal{N}} I^{(j)}((N+1)\omega) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}(N\omega)$, where

$$\eta \equiv \exp \left(\sum_{i=1}^m \lambda_{i,\epsilon} \tau_i \right).$$

Note that $\eta \in (0, 1)$ since $\widehat{R}_0^{(5.35)} < 1$ and by the choice of ϵ above. Thus,

$$\sum_{j \in \mathcal{N}} I^{(j)}((N+1)\omega) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}(N\omega) < \sum_{j \in \mathcal{N}} I^{(j)}(N\omega).$$

Similarly, it can be shown that

$$\sum_{j \in \mathcal{N}} I^{(j)}((N+h+1)\omega) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h)\omega), \quad \forall h \in \mathbb{N},$$

and so

$$\begin{aligned} \sum_{j \in \mathcal{N}} I^{(j)}((N+h+1)\omega) &\leq \eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h)\omega), \\ &\leq \eta(\eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h-1)\omega)), \\ &\vdots \\ &\leq \eta^{h+1} \sum_{j \in \mathcal{N}} I^{(j)}(N\omega). \end{aligned}$$

Therefore the sequence $\{\sum_{j \in \mathcal{N}} I^{(j)}((N+h)\omega)\}_{h=0}^\infty$ converges to zero as $h \rightarrow \infty$. Since $I^{(j)}(t)$ is bounded on $t \in [0, N\omega]$ for each j and since $\sum_{j \in \mathcal{N}} I^{(j)}$ is bounded on each interval $[t_0 + (N+h)\omega, (N+h+1)\omega]$ for $h \in \mathbb{N} \cup \{0\}$, then it follows that $I^{(j)}$ converges to zero as $h \rightarrow \infty$ for each j . The limiting system is given by Eq. (5.36), which converges to the disease-free solution $Q_{\text{DFS}}^{(5.35)}$.

Requiring that $\widehat{R}_0^{(5.35)} < 1$ in Eq. (5.37) defines a critical screening rate θ_{crit} that guarantees disease eradication. More precisely,

$$\theta_{\text{crit}} \equiv \frac{\sum_{i=1}^m (\beta_i S^* m - g_{\min} - \mu_{\min} + (n-1)\alpha_{\max} \gamma_i S^*) \tau_i}{\sum_{i=1}^m (\alpha_{\max} \gamma_i) \tau_i + \omega \alpha_{\min}}. \quad (5.41)$$

Example 5.7 Consider (5.35) with $\mathcal{N} = \{1, 2\}$ and $\mathcal{M} = \{1, 2\}$. Suppose that σ follows the seasonal switching rule outlined in (3.37) and the initial conditions are given by $(S^{(1)}, I^{(1)}, Q^{(1)}, R^{(1)}, S^{(2)}, I^{(2)}, Q^{(2)}, R^{(2)}) = (0.5, 0.1, 0, 0, 0.4, 0, 0, 0)$ (i.e., the disease begins in city 1). The following model parameters are used: $\beta_1 = 4.5$,

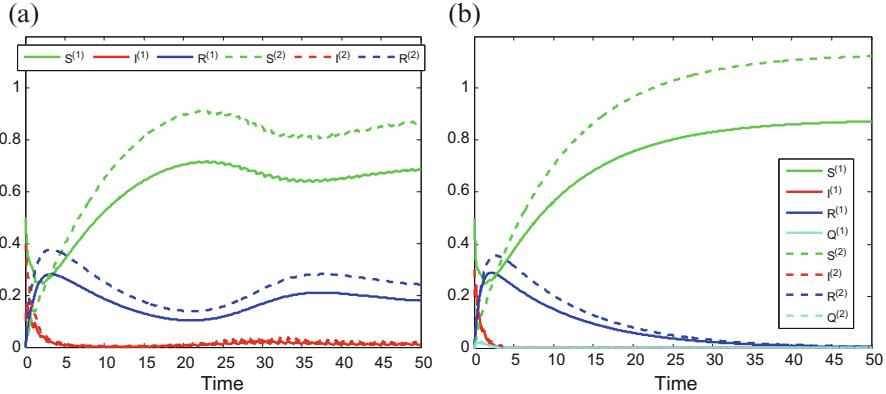


Fig. 5.15 Simulations of Example 5.7. (a) $\theta^{(1)} = \theta^{(2)} = 0$. (b) $\theta^{(1)} = 0.95, \theta^{(2)} = 0.9$

$\beta_2 = 0.5, g^{(1)} = 1.5, g^{(2)} = 1.2, m^{(1)} = 0.1, m^{(2)} = 0.09, \mu^{(1)} = 0.1, \mu^{(2)} = 0.09, \gamma = 1, \alpha^{(1,1)} = -0.4, \alpha^{(1,2)} = 0.4, \alpha^{(2,2)} = -0.3, \alpha^{(2,1)} = 0.3$. That is,

$$A = \begin{bmatrix} -0.4 & 0.3 \\ 0.4 & -0.3 \end{bmatrix}, \quad U = \text{diag}\{0.1, 0.09\}, \quad m = (0.1, 0.09),$$

giving that $S^* = (0.880, 1.13)$. If $\theta^{(1)} = \theta^{(2)} = 0$ then $\widehat{R}_0^{(5.35)} = 1.47$ (see Fig. 5.15a). If $\theta^{(1)} = 0.95$ and $\theta^{(2)} = 0.9$ then $\widehat{R}_0^{(5.35)} = 0.987$ (see Fig. 5.15b); in this case, the critical screening rate is given by $\theta_{\text{crit}} = 0.871$.

5.5 Switching Control for Vector-borne Diseases

In this part we return to the vector-borne model (4.35) for control strategy analysis. Switching cohort immunization is considered here: assume that a switching vaccination control is applied at a rate $v_\sigma > 0$ to the susceptible population (where immunization immediately moves an individual to the vaccinated class, V). Assume also that a switching treatment control is applied at a rate $p_\sigma > 0$. Motivated by realistic difficulties and failures of a vaccine program, the probability that a vaccinated individual can still become infected through transmission is assumed to be nonzero (but reduced when compared to the susceptible individuals); let

$$\xi \beta_\sigma V(t) \int_0^d f(u) I(t-u) du,$$

where $\xi \in [0, 1]$, correspond to such a reduced transmission between vaccinated and infected (i.e., ξ is a measure of the vaccine efficacy). Applied to (4.35), the control model is given by

$$\begin{aligned}
\dot{S}(t) &= \mu(1 - S(t)) - \beta_\sigma S(t) \int_0^d f(u) I(t-u) du - v_\sigma S(t) + \theta V(t), \\
\dot{I}(t) &= \beta_\sigma(S(t) + \xi V(t)) \int_0^d f(u) I(t-u) du - (g + \mu + p_\sigma) I(t), \\
\dot{R}(t) &= gI(t) + p_\sigma I(t) - \mu R(t), \\
\dot{V}(t) &= v_\sigma S(t) - \xi \beta_\sigma V(t) \int_0^d f(u) I(t-u) du - (\theta + \mu) V(t),
\end{aligned}$$

$(S(s), I(s), R(s), V(s)) = (S_0, I_0(s), R_0, V_0), \quad \forall s \in [-d, 0].$

(5.42)

The physical domain of interest for (5.42) is given by

$$D_{(5.42)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : S + I + R + V = 1\},$$

and it is assumed that $(S_0, I_0(0), R_0, V_0) \in D_{(5.42)}$. Equation (5.42) admits m disease-free equilibria due to the time-varying vaccination rates:

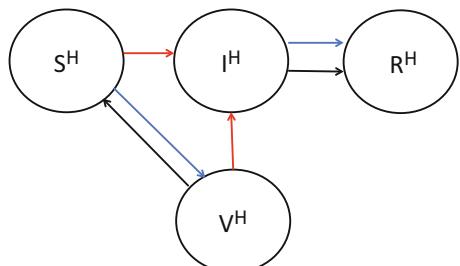
$$Q^{(5.42)} \equiv (S_i^*, I_i^*, R_i^*, V_i^*) \equiv \left(\frac{\mu(\theta + \mu)}{\mu + v_i(1 - \theta)}, 0, 0, \frac{v_i S_i^*}{\theta + \mu} \right),$$

for all $i \in \mathcal{M}$. The movement of the population between compartments is illustrated in Fig. 5.16.

In the absence of infection, the solution of (5.42) traverses between the disease-free equilibria as the vaccination rates vary with respect to time. This observation motivates studying convergence to a disease-free set: when $I(t) \equiv 0$, the number of individuals in the recovered class approaches zero exponentially and the reduced model is given by

$$\begin{aligned}
\dot{S}(t) &= \mu(1 - S(t)) - v_\sigma S(t) + \theta V(t), \\
\dot{V}(t) &= v_\sigma S(t) - (\mu + \theta) V(t).
\end{aligned}$$
(5.43)

Fig. 5.16 Flow of the vector-borne model with treatment and vaccination (5.42). The red lines represent the horizontal transmission and the blue lines represent the treatment and vaccination strategies. Births/deaths are omitted here for illustrative purposes



Define $v_{\min} \equiv \min\{v_i : i \in \mathcal{M}\}$ and $v_{\max} \equiv \max\{v_i : i \in \mathcal{M}\}$. Since $S + V = 1$ is invariant to (5.43),

$$\begin{aligned}\dot{S}(t) &\leq \mu - (\mu + v_{\min})S(t) + \theta(1 - S(t)), \\ &= (\mu + v_{\min} + \theta) \left(\frac{\bar{S}_{\max}}{S(t)} - 1 \right) S(t),\end{aligned}$$

so that $\dot{S}(t) \leq 0$ if $1 \geq S(t) \geq \bar{S}_{\max}$ where

$$\bar{S}_{\max} \equiv \frac{\mu + \theta}{\mu + v_{\min} + \theta}.$$

Similarly, if $0 < S(t) \leq \bar{S}_{\min} \equiv \mu(1 + \theta)/(\mu + v_{\max} + \theta)$, then $\dot{S}(t) \geq 0$ since

$$\begin{aligned}\dot{S}(t) &\geq \mu - (\mu + v_{\max})S(t) + \theta(1 - S(t)), \\ &= (\mu + v_{\max} + \theta) \left(\frac{\bar{S}_{\min}}{S(t)} - 1 \right) S(t).\end{aligned}$$

Further, $\dot{V}(t) \leq 0$ whenever $1 \geq V(t) \geq \bar{V}_{\max} \equiv v_{\max}/(\mu + v_{\max} + \theta)$ since

$$\begin{aligned}\dot{V}(t) &\leq v_{\max}(1 - V(t)) - (\mu + \theta)V(t), \\ &= (\mu + v_{\max} + \theta) \left(\frac{\bar{V}_{\max}}{V(t)} - 1 \right) V(t).\end{aligned}$$

Finally, if $0 < V(t) \leq \bar{V}_{\min} \equiv v_{\min}/(\mu + v_{\min} + \theta)$, then $\dot{V}(t) \geq 0$ since

$$\begin{aligned}\dot{V}(t) &\geq v_{\min}(1 - V(t)) - (\mu + \theta)V(t), \\ &= (\mu + v_{\min} + \theta) \left(\frac{\bar{V}_{\min}}{V(t)} - 1 \right) V(t).\end{aligned}$$

The solution of (5.43) converges to the set

$$\{(S, V) \in \mathbb{R}_+^2 : \bar{S}_{\min} \leq S \leq \bar{S}_{\max}, \bar{V}_{\min} \leq V \leq \bar{V}_{\max}\},$$

which can be shown as follows: Consider the comparison system

$$\dot{x}(t) = \begin{cases} (\mu + v_{\min} + \theta) \left(\frac{\bar{S}_{\max}}{x(t)} - 1 \right) x(t), & \text{if } x(t) \neq 0, \\ \mu + \theta, & \text{if } x(t) = 0, \end{cases} \quad (5.44)$$

$$x(0) = S_0.$$

The solution of (5.44) converges to \bar{S}_{\max} . By the comparison theorem,, for any $\epsilon > 0$ there exists $t^* > 0$ such that $S(t) \leq x(t) \leq \bar{S}_{\max} + \epsilon$ for all $t \geq t^*$. Similarly, the comparison system

$$\dot{x}(t) = \begin{cases} (\mu + v_{\max} + \theta) \left(\frac{\bar{S}_{\min}}{x(t)} - 1 \right) x(t), & \text{if } x(t) \neq 0, \\ \mu - (\mu + v_{\max})x(t) + \theta(1 - x(t)), & \text{if } x(t) = 0, \end{cases} \quad (5.45)$$

$$x(0) = S_0,$$

yields that $\lim_{t \rightarrow \infty} S(t) \geq \bar{S}_{\min}$, with similar arguments with respect to V giving the desired result. Therefore, under the assumption that $I(t) \equiv 0$, the solution of (5.42) converges to the disease-free convex set

$$\Psi_{\text{cohort}} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : \bar{S}_{\min} \leq S \leq \bar{S}_{\max}, I = 0, R = 0, \bar{V}_{\min} \leq V \leq \bar{V}_{\max}\}.$$

Define the following constants:

$$\lambda_i \equiv \beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_i), \quad \forall i \in \mathcal{M}.$$

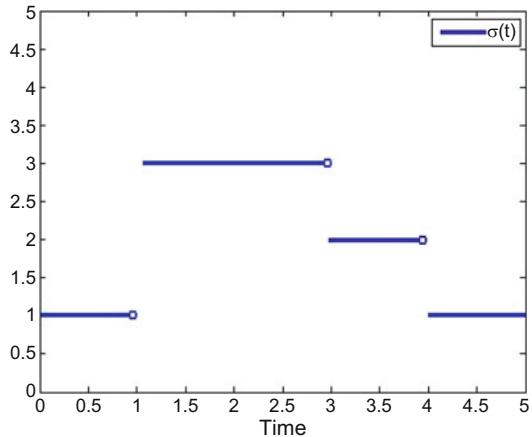
$\mathcal{M}^- \equiv \{i \in \mathcal{M} : \lambda_i < 0\}$ and $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$. The idea here is that the switched system is composed of a mixture of stable and unstable modes, where \mathcal{M}^- and \mathcal{M}^+ denote the stable and unstable modes, respectively. To prove threshold conditions for disease eradication, we focus on the set Ψ_{cohort} . Before proceeding, we remind the reader of some switched systems notions: let $\sigma \in \mathcal{S}_{\text{dwell}}$, $t^2 > t^1 \geq 0$, and let

$$\begin{aligned} T_i(t^1, t^2) &\equiv |\{t \in [t^1, t^2] : \sigma(t) = i\}|, \\ T^+(t^1, t^2) &\equiv |\{t \in [t^1, t^2] : \sigma(t) \in \mathcal{M}^+\}|, \\ T^-(t^1, t^2) &\equiv |\{t \in [t^1, t^2] : \sigma(t) \in \mathcal{M}^-\}|, \\ N_i(t^1, t^2) &\equiv |\{t_k \in [t^1, t^2] : \sigma(t_k) = i\}|, \\ N(t^1, t^2) &\equiv |\{t_k \in [t^1, t^2]\}|, \\ N^-(t^1, t^2) &\equiv |\{t_k \in [t^1, t^2] : \sigma(t_k) \in \mathcal{M}^-\}|. \end{aligned}$$

Roughly, these are the activation time in the i th mode, set \mathcal{M}^+ , set \mathcal{M}^- , and the number of switches activating the i th mode, the total number of switches, and the number of switches activating modes in the set \mathcal{M}^+ , respectively. Note that $\bigcup_{i=1}^m T_i(t_0, t) = [t_0, t]$. As an illustration, consider the switching rule in Fig. 5.17, which gives that

$$\begin{aligned} T_1(0, 5) &= 2, & T_1(0, 4) &= 1, & T_2(3, 3.5) &= 0.5, & T_3(0, 5) &= 2 \\ N_1(0, 5) &= 2, & N_1(0, 4) &= 1, & N_2(3, 3.5) &= 1, & N_3(0, 5) &= 1. \end{aligned}$$

Fig. 5.17 Example of a switching rule $\sigma \in \mathcal{S}_{\text{dwell}}$ with switch times $t_k = 1, 3, 4$ and $\mathcal{M} = \{1, 2, 3\}$



Some necessary Halanay-like results are needed for the disease eradication proofs and are reviewed here. In [174], Zhu used the following Halanay-like lemma to study switched system stability.

Lemma 5.2 Assume that $\beta, \alpha > 0$ and the function $u : [t_0 - d, \infty) \rightarrow \mathbb{R}_+$ satisfies the following delay differential inequality:

$$\dot{u}(t) \leq \beta \|u_t\|_d - \alpha u(t), \quad \forall t \geq t_0.$$

If $\beta - \alpha \geq 0$, then

$$u(t) \leq \|u_{t_0}\|_d \exp((\beta - \alpha)(t - t_0)), \quad \forall t \geq t_0.$$

If $\beta - \alpha < 0$, then there exists a positive constant η satisfying $\eta + \beta \exp(\eta d) - \alpha < 0$ such that

$$u(t) \leq \|u_{t_0}\|_d \exp(-\eta(t - t_0)), \quad \forall t \geq t_0,$$

where $\|u_t\|_d \equiv \sup_{-d \leq s \leq 0} u(t + s)$.

For completeness, an impulsive delayed version of a switching Halanay-like result is presented here without proof (see Proposition 1 in [142]).

Proposition 5.1 For $i \in \mathcal{M}$, let $a_i, b_i, g_i, h_i \geq 0$ be constants and assume that a function $u : [t_0 - d, +\infty) \rightarrow \mathbb{R}_+$ satisfies

$$\begin{aligned} \dot{u}(t) &\leq b_\sigma \|u_t\|_d - a_\sigma u(t), & t \neq t_k, \quad t \geq t_0, \\ u(t) &\leq g_\sigma u(t^-) + h_\sigma \|u_t\|_d, & t = t_k, \quad k \in \mathbb{N}, \end{aligned} \tag{5.46}$$

for some $\sigma \in \mathcal{S}_{\text{dwell}}(d)$ (i.e., $t_k - t_{k-1} \geq d$ for all $k \in \mathbb{N}$). Then, for $t \geq t_0$,

$$u(t) \leq \|u_{t_0}\|_d \left(\prod_{j=1}^{N(t_0,t)} \delta_{i_j} \right) \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i T_i(t_0, t) - \sum_{i \in \mathcal{M}^-} \eta_i \tilde{T}_i(t_0, t) \right), \quad (5.47)$$

where $\tilde{T}_i(t_0, t) \equiv T_i(t_0, t) - N_i(t_0, t)d$, $\lambda_i \equiv b_i \max_{i \in \mathcal{M}} \{1/\delta_i, 1\} - a_i$, $\delta_i \equiv g_i + h_i \exp(\xi d)$, $\xi \equiv \max\{\xi_i : i \in \mathcal{M}^-\}$, $\xi_i > 0$ is chosen for $i \in \mathcal{M}^-$ so that $\xi_i + b_i \exp(\xi_i d) - a_i < 0$, $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$, $\mathcal{M}^- \equiv \{i \in \mathcal{M} : \lambda_i < 0\}$, and $\eta_i > 0$ is chosen for $i \in \mathcal{M}^-$ so that $\eta_i + b_i \max_{i \in \mathcal{M}} \{1/\delta_i, 1\} \exp(\eta_i d) - a_i < 0$.

Proposition 5.1 is placed into the following useful form for this section (set $g_i = 1$, $h_i = 0$, and $\delta_i = 1$ for each $i \in \mathcal{M}$).

Proposition 5.2 For $i \in \mathcal{M}$, let $\beta_i \geq 0$ and $\alpha_i \geq 0$. Assume that a function $u : [t_0 - d, \infty) \rightarrow \mathbb{R}_+$ satisfies the following switching delay differential inequality:

$$\dot{u}(t) \leq \beta_\sigma \|u_t\|_d - \alpha_\sigma u(t),$$

and $\sigma \in \mathcal{S}_{\text{dwell}}(d)$. Let $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$ and $\mathcal{M}^- \equiv \{i \in \mathcal{M} : \lambda_i < 0\}$ where $\lambda_i \equiv \beta_i - \alpha_i$ for each $i \in \mathcal{M}$. For each $i \in \mathcal{M}^-$, choose $\eta_i > 0$ such that

$$\eta_i + \beta_i \exp(\eta_i d) - \alpha_i < 0.$$

Then,

$$u(t) \leq \|u_{t_0}\|_d \exp \left(\sum_{i \in \mathcal{M}^+} \lambda_i T_i(t_0, t) - \sum_{i \in \mathcal{M}^-} \eta_i (T_i(t_0, t) - N_i(t_0, t)d) \right), \quad \forall t \geq t_0. \quad (5.48)$$

Note that if $\lambda_i = \beta_i - \alpha_i < 0$ for $i \in \mathcal{M}$ then it is always possible to choose $\eta_i > 0$ satisfying $\eta_i + \beta_i \exp(\eta_i d) - \alpha_i < 0$. Letting $F_i(x) \equiv x + \beta_i \exp(xd) - \alpha_i$, $F(0) = \beta_i - \alpha_i < 0$ and $F'(\eta_i) = 1 + \beta_i d \exp(\eta_i d) > 0$. By continuity of F_i , there exists $\eta_i^* > 0$ such that $F(\eta_i^*) = 0$ and η_i can be chosen as $0 < \eta_i < \eta_i^*$.

Proposition 5.3 Assume that $\beta_i \geq 0$ and $\alpha_i \geq 0$ for $i \in \mathcal{M}$. Assume that a function $u : [t_0 - d, \infty) \rightarrow \mathbb{R}_+$ satisfies the following switching delay differential inequality:

$$\dot{u}(t) \leq \beta_\sigma \|u_t\|_d - \alpha_\sigma u(t),$$

and $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$. Let $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$ and $\mathcal{M}^- \equiv \{i \in \mathcal{M} : \lambda_i < 0\}$ where $\lambda_i \equiv \beta_i - \alpha_i$ for each $i \in \mathcal{M}$. For each $i \in \mathcal{M}^-$, choose $\eta_i > 0$ such that

$$\eta_i + \beta_i \exp(\eta_i d) - \alpha_i < 0.$$

Then, u is bounded on any compact interval and satisfies

$$u(t_0 + j\omega) \leq \|u_{t_0}\|_d \chi^j, \quad \forall j \in \mathbb{N}, \quad (5.49)$$

where

$$\chi = \exp \left[\sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d) \right].$$

Proof The boundedness of u on any compact interval follows immediately from Theorem 5.2. From Eq. (5.48), for $j \in \mathbb{N}$

$$\begin{aligned} & u(t_0 + j\omega) \\ & \leq \|u_{t_0}\|_d \exp \left[\sum_{i \in \mathcal{M}^+} \lambda_i T_i(t_0, t_0 + j\omega) - \sum_{i \in \mathcal{M}^-} \eta_i (T_i(t_0, t_0 + j\omega) - N_i(t_0, t_0 + j\omega)d) \right], \\ & = \|u_{t_0}\|_d \exp \left[\sum_{i \in \mathcal{M}^+} \lambda_i j T_i(t_0, t_0 + \omega) - \sum_{i \in \mathcal{M}^-} \eta_i j (T_i(t_0, t_0 + \omega) - N_i(t_0, t_0 + \omega)d) \right], \\ & = \|u_{t_0}\|_d \exp \left[j \sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - j \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d) \right], \\ & = \|u_{t_0}\|_d \chi^j, \end{aligned}$$

since $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ implies that $T_i(t_0, t_0 + j\omega) = jT_i(t_0, t_0 + \omega)$ and $N_i(t_0, t_0 + j\omega) = jN_i(t_0, t_0 + \omega)$.

We are now in a position to prove some eradication results.

Theorem 5.9 For each $i \in \mathcal{M}^-$, let $\eta_i > 0$ satisfy

$$\eta_i + \beta_i (\bar{S}_{\max} + \xi \bar{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i) < 0.$$

Let $\lambda^+ \equiv \max\{\lambda_i : i \in \mathcal{M}^+\}$ and $\lambda^- \equiv \min\{\eta_i : i \in \mathcal{M}^-\}$. Let $\sigma \in \mathcal{S}_{\text{dwell}}(d)$ such that there exists $M > 0$ and $\tilde{t} > 0$ satisfying

$$\sup_{t \geq \tilde{t}} \frac{t - \tilde{t}}{T^-(\tilde{t}, t) - N^-(\tilde{t}, t)d} \leq M. \quad (5.50)$$

If there exists $q \geq 0$ such that

$$T^+(\tilde{t}, t) \leq q(T^-(\tilde{t}, t) - N^-(\tilde{t}, t)d), \quad (5.51)$$

$$q\lambda^+ < \lambda^-, \quad (5.52)$$

then the solution of (5.42) satisfies $\lim_{t \rightarrow \infty} (S(t), I(t), R(t), V(t)) \in \Psi_{\text{cohort}}$; the solution converges to the disease-free set and is therefore eradicated.

Proof From the switched model of a vector-borne disease (5.42),

$$\begin{aligned}\dot{S}(t) &= \mu - \beta_\sigma S(t) \int_0^d f(u) I(t-u) du - v_\sigma S(t) + \theta V(t), \\ &\leq \mu(1 - S(t)) - v_\sigma S(t) + \theta V(t), \\ &\leq \mu(1 - S(t)) - v_{\min} S(t) + \theta V(t), \\ &\leq \mu + \theta - (\mu + \theta + v_{\min}) S(t),\end{aligned}$$

since $V(t) = 1 - S(t) - I(t) - R(t) \leq 1 - S(t)$. Similarly,

$$\begin{aligned}\dot{V}(t) &= v_\sigma S(t) - \xi \beta_\sigma V(t) \int_0^d f(u) I(t-u) du - (\mu + \theta) V(t), \\ &\leq v_\sigma S(t) - (\mu + \theta) V(t), \\ &\leq v_{\max} S(t) - (\mu + \theta) V(t), \\ &\leq v_{\max} (1 - V(t)) - (\mu + \theta) V(t), \\ &\leq v_{\max} - (v_{\max} + \mu + \theta) V(t).\end{aligned}$$

For any $\epsilon > 0$, there exists a time $t^* > 0$ for which $S(t) \leq \bar{S}_{\max} + \epsilon$ and $V(t) \leq \bar{V}_{\max} + \epsilon$ for all $t \geq t^*$. Let l be the smallest positive integer such that $t_l > \max\{t, t^*\}$. Then,

$$\begin{aligned}\dot{I}(t) &= \beta_\sigma (S(t) + \xi V(t)) \int_0^d f(u) I(t-u) du - (\mu + g + p_\sigma) I(t), \\ &\leq \beta_{\max} (1 + \xi) \sup_{t-d \leq s \leq t} I(s) - (\mu + g + p_{\min}) I(t), \quad \forall t \in [0, t_l].\end{aligned}$$

By inspection, $I(t) \leq \|I_0\|_d \exp(\eta t)$ for all $t \in [0, t_l]$ where $\eta > 0$ satisfies

$$\eta + \beta_{\max} (1 + \xi) \exp(\eta d) - (\mu + g + p_{\min}) > 0$$

by Lemma 5.2. In general,

$$\dot{I}(t) \leq \beta_\sigma [(\bar{S}_{\max} + \epsilon) + \xi (\bar{V}_{\max} + \epsilon)] \sup_{t-d \leq s \leq t} I(s) - (\mu + g + p_\sigma) I(t), \quad (5.53)$$

for all $t \in [t_{k-1}, t_k)$ and $k-1 \geq l$, where $I_{t_l} \in \text{PC}([-d, 0], \mathbb{R}_+)$. Define the constants

$$\lambda_{i,\epsilon} \equiv \beta_i [(\bar{S}_{\max} + \epsilon) + \xi (\bar{V}_{\max} + \epsilon)] - (\mu + g + p_i), \quad \forall i \in \mathcal{M}.$$

For each $i \in \mathcal{M}^-$, let $\eta_{i,\epsilon} > 0$ satisfy

$$\eta_{i,\epsilon} + \beta_i [(\bar{S}_{\max} + \epsilon) + \xi (\bar{V}_{\max} + \epsilon)] \exp(\eta_{i,\epsilon} d) - (\mu + g + p_i) < 0.$$

Proposition 5.2 thus implies that

$$I(t) \leq I_0^* \exp \left[\sum_{i \in \mathcal{M}^+} \lambda_{i,\epsilon} T_i(t_l, t) - \sum_{i \in \mathcal{M}^-} \eta_{i,\epsilon} (T_i(t_l, t) - N_i(t_l, t)d) \right], \quad (5.54)$$

for all $t \in [t_{k-1}, t_k]$, $k-1 \geq l$, where $I_0^* \equiv \|I_0\|_d \exp(\eta t_l)$.

Define $\lambda_\epsilon^+ \equiv \max\{\lambda_{i,\epsilon} : i \in \mathcal{M}^+\}$ and $\lambda_\epsilon^- \equiv \{\eta_{i,\epsilon} : i \in \mathcal{M}^-\}$. Then, by definition,

$$\beta_i[(\bar{S}_{\max} + \epsilon) + \xi(\bar{V}_{\max} + \epsilon)] \exp(\eta_{i,\epsilon} d) - (\mu + g + p_i) < -\eta_{i,\epsilon} \leq -\lambda_\epsilon^-, \quad \forall i \in \mathcal{M},$$

which can be rewritten as

$$\beta_i(\bar{S}_{\max} + \xi\bar{V}_{\max}) \exp(\eta_{i,\epsilon} d) - (\mu + g + p_i) + G_i \epsilon < -\eta_{i,\epsilon} \leq -\lambda_\epsilon^-, \quad \forall i \in \mathcal{M},$$

where

$$G_i \equiv \beta_i(1 + \xi) \exp(\eta_{i,\epsilon} d), \quad \forall i \in \mathcal{M}.$$

Also,

$$\beta_i(\bar{S}_{\max} + \xi\bar{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i) < -\eta_i \leq -\lambda^-, \quad \forall i \in \mathcal{M}.$$

Therefore, there exists a constant F_1 such that $-\lambda_\epsilon^+ \leq -\lambda^- + F_1 \epsilon$. Letting $v \in \arg \max\{\lambda_i : i \in \mathcal{M}^+\}$,

$$q\lambda_\epsilon^+ \leq q\lambda^+ + F_2 \epsilon,$$

where

$$F_2 \equiv q\beta_v(\bar{S}_{\max} + \xi\bar{V}_{\max}) - (\mu + g + c_v).$$

Hence,

$$q\lambda_\epsilon^+ - \lambda_\epsilon^- \leq q\lambda^+ - \lambda^- + (F_1 + F_2)\epsilon.$$

Since $q\lambda^+ - \lambda^- < 0$, there exists a positive constant δ such that $q\lambda_\epsilon^+ - \lambda_\epsilon^- \leq -0.5\delta$. Choose

$$\epsilon = \frac{\delta(F_1 + F_2)}{2},$$

then $q\lambda_\epsilon^+ - \lambda_\epsilon^- \leq -0.5\delta$.

It thus follows from Eqs. (5.50), (5.51), and (5.54) that

$$\begin{aligned}
I(t) &\leq I_0^* \exp \left[\lambda_\epsilon^+ \sum_{i \in \mathcal{M}^+} T_i(t_l, t) - \lambda_\epsilon^- \sum_{i \in \mathcal{M}^-} (T_i(t_l, t) - N_i(t_l, t)d) \right], \\
&= I_0^* \exp[\lambda_\epsilon^+ T^+(t_l, t) - \lambda_\epsilon^- (T^-(t_l, t) - N^-(t_l, t)d)], \\
&\leq I_0^* \exp[q\lambda_\epsilon^+ (T^-(t_l, t) - N^-(t_l, t)d) - \lambda_\epsilon^- (T^-(t_l, t) - N^-(t_l, t)d)], \\
&= I_0^* \exp[(q\lambda_\epsilon^+ - \lambda_\epsilon^-)(T^-(t_l, t) - N^-(t_l, t)d)], \\
&\leq I_0^* \exp \left[(q\lambda_\epsilon^+ - \lambda_\epsilon^-) \frac{(t - t_l)}{M} \right], \quad \forall t \geq t_l.
\end{aligned}$$

Equation (5.51) guarantees that $T^-(t_l, t) - N^-(t_l, t)d \geq 0$. Therefore,

$$I(t) \leq I_0^* \exp[-0.5\delta(t - t_l)], \quad \forall t \geq t_l.$$

It follows that $\lim_{t \rightarrow \infty} R(t) = 0$ and (5.42) reduces to system (5.43), from which the result follows.

Intuitively, Eqs. (5.51) and (5.52) describe the time spent in the unstable mode \mathcal{M}^+ , with corresponding worst-case growth rate λ^+ , versus the time spent in the stable modes \mathcal{M}^- , with corresponding most conservative decay rate λ^- . The constant q characterizes said relationships. If Eq. (5.52) holds, then

$$\begin{aligned}
&q \max_{i \in \mathcal{M}^+} \{\beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_i)\} \\
&+ \min_{i \in \mathcal{M}^-} \{\beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i)\} < 0.
\end{aligned}$$

Let $v \in \arg \max \{\lambda_i : i \in \mathcal{M}^+\}$ and $\zeta \in \arg \min \{\eta_i : i \in \mathcal{M}^+\}$. Then

$$\lambda^+ = \beta_v(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_v)$$

and

$$\lambda^- = \beta_\zeta(\bar{S}_{\max} + \xi \bar{V}_{\max}) \exp(\eta_\zeta d) - (\mu + g + p_\zeta).$$

Hence, (5.52) implies that

$$\overline{R}_0^{(5.42)} \equiv q \frac{(\beta_v + \beta_\zeta \exp(\eta_\zeta d))(\bar{S}_{\max} + \xi \bar{V}_{\max})}{2\mu + 2g + p_v + p_\zeta} < 1, \quad (5.55)$$

an approximation of the disease's basic reproduction number. In fact, (5.52) implies (5.55); (5.52) is a stricter requirement on the model parameters. Controlled eradication under periodic variations can be established as follows.

Theorem 5.10 *For each $i \in \mathcal{M}^-$, let $\eta_i > 0$ satisfy*

$$\eta_i + \beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i) < 0.$$

If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$\Lambda_{\text{cohort}} \equiv \sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d) < 0, \quad (5.56)$$

then the solution of (5.42) satisfies $\lim_{t \rightarrow \infty} (S(t), I(t), R(t), V(t)) \in \Psi_{\text{cohort}}$; the solution converges to the disease-free set and is therefore eradicated.

Proof Beginning from Eq. (5.53) in the proof of Theorem 5.9, choose the smallest positive integer B such that $B\omega > \max\{\tilde{t}, t^*\}$. By Proposition 5.3, $I((B+j)\omega) \leq \|I_{B\omega}\|_d \delta^j$ for each $j \in \mathbb{N}$, where

$$\delta \equiv \exp \left[\sum_{i \in \mathcal{M}^+} \lambda_{i,\epsilon} \tau_i - \sum_{i \in \mathcal{M}^-} \eta_{i,\epsilon} (\tau_i - d) \right]$$

and $\|I_{B\omega}\|_d \leq K$ for some constant $K > 0$. It follows from (5.56) and the arguments in the proof of Theorem 5.9 that $\epsilon > 0$ can be chosen sufficiently small to guarantee that $0 < \delta < 1$. Thus, $\lim_{t \rightarrow \infty} I(t) = 0$, from which $\lim_{t \rightarrow \infty} R(t) = 0$ follows. Equation (5.42) reduces to (5.43) and the result holds.

Equation (5.56) implies that

$$\begin{aligned} & \sum_{i \in \mathcal{M}^+} [\beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_i)] \tau_i \\ & + \sum_{i \in \mathcal{M}^-} [\beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i)] (\tau_i - d), \\ & < \sum_{i \in \mathcal{M}^+} [\beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_i)] \tau_i + \sum_{i \in \mathcal{M}^-} (-\eta_i)(\tau_i - d), \\ & = \sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d), \\ & < 0. \end{aligned}$$

That is, (5.56) implies that $\overline{R}_0^{(5.42)} < 1$ where

$$\overline{R}_0^{(5.42)} \equiv \frac{\sum_{i \in \mathcal{M}^+} \beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) \tau_i + \sum_{i \in \mathcal{M}^-} \beta_i \exp(\eta_i d) (\bar{S}_{\max} + \xi \bar{V}_{\max})(\tau_i - d)}{\sum_{i \in \mathcal{M}^+} (\mu + g + p_i) \tau_i + \sum_{i \in \mathcal{M}^-} (\mu + g + p_i)(\tau_i - d)}. \quad (5.57)$$

Table 5.1 Epidemiological parameters

Parameter	Description	Value
β_σ	Average number of contacts per unit time	[8, 1.6]
μ	Natural birth/death rate	1
g	Recovery rate	1.5
d	Upper bound on the incubation time	0.1

The parameter values given in brackets represent the switching value associated with $\sigma = 1$ and $\sigma = 2$, respectively

$\bar{R}_0^{(5.42)}$ may be viewed as an approximate basic reproduction number and it should be noted that the theorem condition is stricter than requiring $\bar{R}_0^{(5.42)} < 1$. A comparison of these switching control strategies (i.e., switching vaccination and switching treatment) is reserved for Sect. 6.2.1.

The results of this section are illustrated with simulation. Consider the initial conditions $(S_0, I_0, R_0, V_0) = (0.9, 0.1, 0, 0)$, baseline model parameters in Table 5.1, and dwell-time satisfying periodic switching rule

$$\sigma = \begin{cases} 1, & \text{if } t \in [k, k + \frac{3}{12}), k \in \mathbb{N} \cup \{0\}, \\ 2, & \text{if } t \in [k + \frac{3}{12}, k + 1), \end{cases} \quad (5.58)$$

which is motivated from seasonal variations in the model parameters. The period of the switching rule is $\omega = 1$ with $\tau_1 = 3/12$ (modeling a winter season or rainy season, depending on climate) and $\tau_2 = 9/12$ (summer seasons or dry season). As in [104], let

$$f(u) \equiv \frac{\exp(-u)}{1 - \exp(-d)}.$$

Let $v_1 = 3$, $v = 2$, $p = 2$, $p = 0.5$. For the susceptible cohort immunization program, the model parameters give $\bar{S}_{\max} = 0.3548$, $\bar{V}_{\max} = 0.7317$, and $\lambda_1 = 0.8948$ (i.e., $\mathcal{M}^+ = \{1\}$). Letting $\eta_2 = 1$ (i.e., $\mathcal{M}^- = \{2\}$) implies that

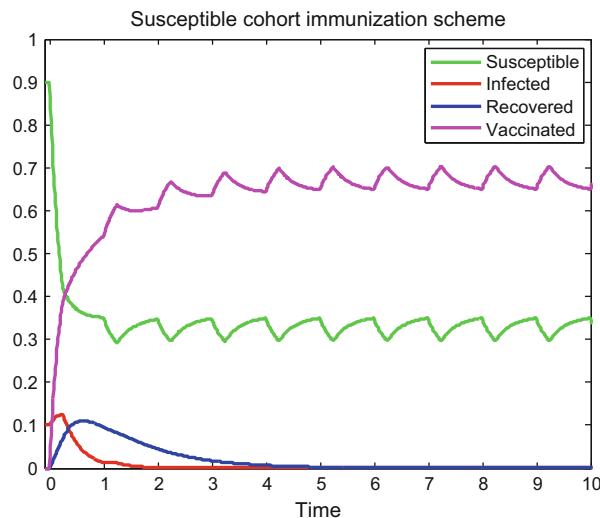
$$\Lambda_{\text{cohort}} = -0.4263,$$

and convergence to the disease-free set Ψ_{cohort} by Theorem 5.10 (Fig. 5.18).

5.6 Discussions

Cohort immunization (i.e., time-constant vaccination) has been implemented by a number of countries, as discussed earlier. As mentioned, the predominant strategy for measles immunization follow a recommendation of doses at 15 months of

Fig. 5.18 Simulations of the switching control scheme (5.42) with parameters in Table 5.1



age and approximately 6 years of age in many parts of the Western world [139]. For background studies in the literature on epidemic models with such a control program, the reader is referred to [4, 69, 102, 138] and the references therein. The control strategies considered in Sect. 5.1 assume immediate movement from susceptible classes to the recovered class. This ignores the time involved to obtain immunity by completing a vaccination program. Motivated by this, consider the usual vaccination schedule for hepatitis B where individuals are given three vaccinations separated by 1 month and 6 months [101]. The authors further note that approximately 30–50% of individuals will gain anti-HB antibodies after the first dose, 80–90% after the second dose, and virtually all 1 month after the final dose. Based on their work on hepatitis B and measles in [101], the model (5.13) was analyzed. The application of vaccination and treatment schemes to switched SIR models in Sects. 5.1 and 5.2 are largely based on, and extend, the works in [94, 96].

Hepatitis B, Chagas' disease, HIV/AIDS, and tuberculosis are examples of diseases displaying latency periods [103, 140] and therefore appropriately modeled by the SEIR model (5.22), which has been extensively studied in the literature (e.g., see [69, 72, 80, 81, 103, 134]). The SEIR model with vertical transmission (5.27) was analyzed with switching because of the number of infectious diseases with latency period that are transmitted by both horizontal and vertical modes (e.g., rubella, herpes simplex, hepatitis B, Chagas' disease [140]). The SEIR model with disease-induced deaths (i.e., Eq. (5.31)) is an appropriate modeling choice for disease like AIDS [140]. A summary of the critical control rates guaranteeing eradication in the various theorems provided in Sects. 5.1, 5.2, and 5.3 is given in Table 5.2.

In the mathematical epidemic modeling literature, a time-constant entry/exit screening strategy was studied by Liu and Takeuchi [100] consisting of a two-city SIS model with transport-related infections and a screening process. Entry and

Table 5.2 Critical control rates of the epidemic models with periodic switching

Control strategy	Disease model	Critical control rate
Newborn vaccinations	(5.4)	$\rho_{\text{crit}} \equiv 1 - \omega(\mu + g) / (\sum_{i=1}^m \beta_i \tau_i)$
Susceptible vaccinations	(5.8)	$v_{\text{crit}} \equiv \mu (\sum_{i=1}^m \beta_i \tau_i / (\omega(\mu + g)) - 1)$
Vaccinations with progressive immunity	(5.13)	$v_{\text{crit}} \equiv \frac{\mu (\sum_{i=1}^m \beta_i \tau_i / (\omega(\mu + g)) - 1)}{1 - \mu \sum_{i=1}^m \beta_i^V \tau_i / (\omega(\mu + g))}$
Treatment of infected	(5.17)	$p_{\text{average-crit}} \equiv \sum_{i=1}^m \beta_i \tau_i / \omega - (\mu + g)$
SIR with general FOI and treatments	(5.20)	$p_i^{\text{crit}} \equiv h'_i(0) - (\mu + g)$
SEIR with treatments	(5.24)	$p_i^{\text{crit}} \equiv \beta_i a / (\mu + a) - (\mu + g)$
Vertical SEIR with treatments	(5.27)	$p_i^{\text{crit}} \equiv \frac{(\beta_i + \mu q)a}{\mu(1-\rho)+a} - (\mu + g)$
Disease-induced mortality SEIR with treatments	(5.31)	$p_i^{\text{crit}} \equiv \beta_i a / (b + a) - (\mu + g + \alpha)$

Note that $p_{\text{average-crit}} \equiv \frac{\sum_{i=1}^m p_i^{\text{crit}} \tau_i}{\omega}$. The critical rates indexed by i are mode-dependent

exit screening were performed during the spread of SARS in 2003; temperature screening using thermal scanning and questionnaires were given to assess symptoms for possible exposure at mass transit centers [100]. More recently, global travel has been a major factor in the spread of the H1N1 strain of influenza in 2009, Ebola virus in 2015, and Zika virus in 2016. Motivated by this and the time-invariant entry screening models investigated in [100, 147], screening strategies were considered in Sect. 5.4. The formulation and analysis of the screening strategy for a switched multi-city model in Sect. 5.4. In Sect. 5.5, Halanay-like switching results were used to prove convergence to disease-free sets (and thus disease eradication). Halanay-like inequalities have been generalized to include switching (for example, [164]), time-varying parameters (for example, [120, 172]), and impulsive effects (for example, [160, 163]). The works [142, 143] form the basis for the derivations and results found in Sect. 5.5. Other switching control strategies (e.g., reduced contact rates) are detailed later in this monograph, while other possibilities (e.g., purposeful shifts in population behavior) are theoretically unlocked by the findings here.

Chapter 6

Pulse Control Strategies

Building upon the previous chapter, impulsive control in switched epidemic models is formulated and analyzed. Pulse vaccination, which is the control technique of applying vaccinations to a portion of the susceptible population in a relatively short time period (with respect to the dynamics of the disease) is considered. This strategy is applied to the switched SIR model previously set forth in this monograph. Complications such as general switched incidence rates, vaccine failures, media coverage, and traveling individuals are considered. Conditions are found which guarantee eradication under the pulse schemes and an evaluation and comparison of control strategies (switching and impulsive) is performed in the context of a general vector-borne disease model.

6.1 Public Immunization Campaigns: Control by Pulse Vaccination and Treatment

Pulse vaccination has recently gained prominence as a control scheme due to its successful application to the control of poliomyelitis and measles throughout Central and South America [139]. The strategy has been examined in the United Kingdom, where children aged 5–16 years were offered a combined measles and rubella vaccine in 1994 [139]; coverage of 90% or more was achieved in 133 of 172 districts, and the mean coverage in England and Wales reached 92%. Consequently, it was concluded that the pulse vaccination of all children of school age is likely to have a dramatic effect on the transmission of measles and should prevent a substantial toll of morbidity and mortality [139]. Pulse vaccination has been illustrated to be an effective strategy in preventing such viral infections as rabies, yellow fever, poliovirus, and hepatitis B [122]. In 1988, the WHO set a goal of global polio eradication by the year 2000 [65]. The WHO strategy has included routine vaccination, national immunization days (during which many

people in a region are vaccinated on a certain day in order to interrupt transmission, i.e., pulse vaccination), mopping-up vaccinations, and surveillance [65]. Polio has disappeared from many countries from 1990–2000, and it is likely that polio will soon be eradicated worldwide [65]. The WHO estimates that eradicating polio will save approximately 1.5 billion dollars each year in immunization, treatment, and rehabilitation around the globe [65]. Eventually, it is possible that vaccines will prevent malaria, venereal diseases, and even some forms of heart disease and cancer [102].

In this section, the control strategies of pulse vaccination and treatment are detailed. The control is assumed to be given to a fraction of the population in a relatively short period of time. The mathematical framework for this scheme is impulsive control. Since its initial proposal in [1] by Shulgin et al., this technique has been developed further in, for example, [36, 49, 51, 92, 102, 110, 122, 138, 139, 173]. Theoretical results show that as a distinction from conventional strategies, pulse vaccination strategies can lead to disease eradication at relatively low values of vaccination [1]. In Sect. 6.1.1, the classical endemic model is revisited for highlighting the workings of the strategy in the time-invariant case. Then, the pulse vaccination strategy is applied to a switched SIR model with standard incidence rates, followed by application of a pulse treatment strategy in Sect. 6.1.2. Demonstrating the flexibility of the framework, a switched SIR model with general incidence rates is controlled with both vaccination and treatment pulse control in Sect. 6.1.3. Complications such as vaccine failure (Sect. 6.1.4) and media coverage (Sect. 6.1.5) are analyzed. Previously studied models are revisited with pulse control strategies (the multi-city model in Sect. 6.1.6 and the general vector-borne disease model in Sect. 6.1.7).

6.1.1 Impulsive Control Applied to the Classical Endemic Model

In contrast to the switching control strategies of Chap. 5, pulse strategies are based on the idea that an epidemic is more effectively controlled when its natural temporal process is antagonized [1, 138]; vaccinations are given to a portion of all age cohorts of the susceptible population in a very short time period with respect to the dynamics of the disease.

The motivating observation here is by noticing that in the SIR model (3.9),

$$\frac{dI}{dt}(t) = \beta S(t)I(t) - (\mu + g)I(t) < 0$$

if

$$S < \frac{\mu + g}{\beta} \equiv S_{\text{crit.}} \quad (6.1)$$

If this is the case, then $\dot{I}(t) < 0$ for $(S, I, R) \in D_{(3.9)} = \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\}$ unless $I = 0$; the disease is eradicated and there cannot be an epidemic outbreak. Assume that a portion $v \in [0, 1]$ of the susceptible population is given a vaccination at each time $t = kT$, $k \in \mathbb{N}$, where $T > 0$ is the inter-pulse period. The mathematical model is given by the following impulsive ODE system:

$$\left. \begin{array}{l} \dot{S}(t) = \mu - \beta S(t)I(t) - \mu S(t) \\ \dot{I}(t) = \beta S(t)I(t) - (\mu + g)I(t) \\ \dot{R}(t) = gI(t) - \mu R(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{array}{l} S(t) = (1-v)S(t^-) \\ I(t) = I(t^-) \\ R(t) = R(t^-) + vS(t^-) \end{array} \right\} \forall t \in \{kT\},$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$
(6.2)

Recall the notation $S(t^-) \equiv \lim_{h \rightarrow 0^+} S(t-h)$ in the impulsive (or difference) equations. The meaningful domain is unchanged from the classical SIR model $D_{(3.9)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\}$, which is positively invariant to (6.2) since

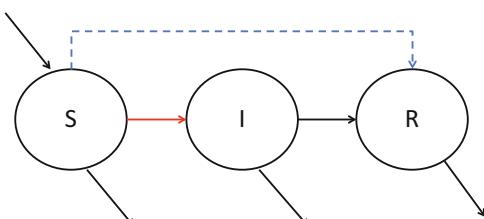
$$\{\dot{S} + \dot{I} + \dot{R}\}|_{S+I+R=1} = 0,$$

$\dot{S}|_{S=0} = \mu > 0$, $\dot{I}|_{I=0} = 0$, $\dot{R}|_{R=0} = gI \geq 0$, and the impulsive equations do not move the solution to outside the meaningful domain. A vaccinated class V could be introduced in (6.2) for which susceptible individuals could enter upon vaccination. This group is omitted here since there is no distinction between vaccine-induced and naturally conferred immunity in this model. In the case of vaccine failure, which is studied later (see Sect. 6.1.4), such a distinction is added. The initial time has been shifted to zero again, without loss of generality. For the flow diagram of (6.2), see Fig. 6.1.

The typical disease-free point $(1, 0, 0)$ is not an equilibrium of (6.2). However, there exists a periodic disease-free solution, which can be furnished as follows (see the derivation in [138]): $I(t) \equiv 0$ is a solution of the differential equation for I . Under this assumption, (6.2) becomes the reduced system

Fig. 6.1 Flow diagram of the switched SIR system (6.2).

The red line represents horizontal transmission of the disease and the dashed blue line represents pulse vaccination



$$\begin{aligned} \dot{S}(t) &= \mu(1 - S(t)) \\ \dot{R}(t) &= -\mu R(t) \end{aligned} \left\{ \begin{array}{l} \forall t \in \mathbb{R}_+ \setminus \{kT\}, \\ S(t) = (1 - v)S(t^-) \\ R(t) = R(t^-) + vS(t^-) \end{array} \right\} \forall t \in \{kT\},$$

$$(S(0), R(0)) = (S_0, R_0).$$
(6.3)

Integrating the equations between the pulse vaccinations gives that

$$\begin{aligned} S(t) &= 1 + (S((k-1)T) - 1) \exp(-\mu(t - (k-1)T)), \\ R(t) &= 1 - S(t), \end{aligned}$$

for $t \in [(k-1)T, kT]$, since $S + R = 1$ is an invariant when $I(t) \equiv 0$. Immediately after the pulse vaccination, it holds that

$$S(kT) = (1 - v)[1 + (S((k-1)T) - 1) \exp(-\mu T)] \equiv F(S((k-1)T)). \quad (6.4)$$

Using the notation $S_k \equiv S(kT)$ for each $k \in \mathbb{N}$, Eq. (6.4) defines a stroboscopic mapping $S_k = F(S_{k-1})$, which has a unique fixed point that can be calculated as

$$S^* \equiv F(S^*) = \frac{(1 - v)(1 - \exp(-\mu T))}{1 - (1 - v)\exp(-\mu T)}.$$

Moreover, the derivative of the mapping evaluated at the fixed point satisfies

$$\frac{dF}{dS}(S^*) = (1 - v)\exp(-\mu T) < 1,$$

implying that S^* is asymptotically stable in $D_{(3.9)}$ (see Lemma 2.1 in [92], for example).

The periodic disease-free solution of (6.2),

$$Q_{\text{DFS}}^{(6.2)}(t) \equiv (\tilde{S}(t), 0, \tilde{R}(t))$$

can be found by setting $S^* = S((k-1)T)$ [138]:

$$\begin{aligned} \tilde{S}(t) &\equiv 1 - \frac{v \exp(-\mu(t - (k-1)T))}{1 - (1 - v)\exp(-\mu T)}, \\ \tilde{R}(t) &\equiv 1 - \tilde{S}(t), \end{aligned} \quad (6.5)$$

for $t \in [(k-1)T, kT]$. The basic reproduction number associated with (6.2) is given by

$$R_0^{(6.2)} \equiv \frac{\beta}{\mu + g} \frac{1}{T} \int_0^T \tilde{S}(t) dt, \quad (6.6)$$

and, if

$$\frac{1}{T} \int_0^T \tilde{S}(t) dt < \frac{g + \mu}{\beta} = S_{\text{crit}},$$

(i.e., if $R_0^{(6.2)} < 1$) then the periodic disease-free solution is locally asymptotically stable; this result follows from an application of Floquet theory (see [109] for background on Floquet and [138] for the full derivation).

Observe that the basic reproduction number of the uncontrolled classical endemic SIR model (3.9) satisfies

$$R_0^{(6.2)} = R_0^{(3.9)} \frac{1}{T} \int_0^T \tilde{S}(t) dt < R_0^{(3.9)},$$

as expected. The impulsive control mechanism suppresses the spread of the disease, and thus basic reproduction number, by controlling the susceptible population; the steady-state periodic solution satisfies $\tilde{S}(t) < 1$ for all t . As the closed-form expression of \tilde{S} is known, the following can be calculated:

$$\begin{aligned} \frac{1}{T} \int_0^T \tilde{S}(t) dt &= \frac{1}{T} \int_0^T \left[1 - \frac{v \exp(-\mu t)}{1 - (1-v) \exp(-\mu T)} \right] dt, \\ &= \frac{1}{T} \left[t + \frac{v \exp(-\mu t)}{\mu [1 - (1-v) \exp(-\mu T)]} \right]_0^T, \\ &= 1 + \frac{v - v \exp(\mu T)}{\mu T [\exp(\mu T) + v - 1]}, \\ &= \frac{(\mu T - v)(\exp(\mu T) - 1) + \mu v T}{\mu T (\exp(\mu T) + v - 1)}. \end{aligned}$$

Therefore, if T and v satisfy the inequality

$$\frac{(\mu T - v)(\exp(\mu T) - 1) + \mu v T}{\mu T (\exp(\mu T) + v - 1)} < \frac{\mu + g}{\beta} \equiv S_{\text{crit}}, \quad (6.7)$$

it follows that $R_0^{(6.2)} < 1$ (and hence the disease is eradicated). From this, an apparent trade-off can be established between T and v ; the larger the inter-pulse period (i.e., fewer public campaigns for vaccination), the large v must be (i.e., a larger fraction must be vaccinated).

Given a vaccination rate v , the maximum inter-pulse period T for which eradication can be achieved can be calculated: the function

$$T \mapsto \frac{(\mu T - v)(\exp(\mu T) - 1) + \mu v T}{\mu T(\exp(\mu T) + v - 1)}$$

is an increasing function on \mathbb{R}_+ . The maximum such inter-pulse period, T_{\max} , therefore occurs when the left-hand and right-hand sides of (6.7) are equal. Assuming that the inter-pulse period and average duration of the disease are much smaller than the average life-time (i.e., $T \ll 1/\mu$ and $1/g \ll 1/\mu$), neglecting higher-order terms in a Taylor series expansion yields the following [138]:

$$T_{\max} \approx \widehat{T}_{\max} \equiv \frac{gv}{\mu\beta} \frac{1}{1 - v/2 - g/\beta}. \quad (6.8)$$

The outlined strategy from earlier, i.e., requiring that $S(t) < S_{\text{crit}}$ from (6.1) for all t , the maximum allowable inter-pulse period can also be calculated from this constraint. The minimum number of susceptibles at steady state occurs immediately after a pulse vaccination is applied (i.e., S^*) and the maximum number occurs immediately before the vaccination ($S^*/(1-v)$). Thus, to guarantee that $S(t) < S_{\text{crit}}$, the inequality

$$S^*/(1-p) < S_{\text{crit}}$$

must hold. At equality, this relationship gives that [138]

$$T_{\max} \approx \bar{T}_{\max} \equiv \frac{1}{\mu} \ln \left(1 + \frac{vS_{\text{crit}}}{1 - S_{\text{crit}}} \right).$$

And, as expected, $\bar{T}_{\max} \geq \widehat{T}_{\max}$ for all $v \in [0, 1]$ [138].

Applied to the switched SIR model with seasonal variations (3.8), the pulse vaccination control strategy is given by the following model:

$$\begin{aligned} \dot{S}(t) &= \mu - \beta_\sigma S(t)I(t) - \mu S(t) \\ \dot{I}(t) &= \beta_\sigma S(t)I(t) - (\mu + g)I(t) \\ \dot{R}(t) &= gI(t) - \mu R(t) \\ S(t) &= (1-v)S(t^-) \\ I(t) &= I(t^-) \\ R(t) &= R(t^-) + vS(t^-) \end{aligned} \quad \left. \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\}, \quad (6.9)$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0),$$

where $\sigma \in \mathcal{S}_{\text{periodic}}(T)$ here and the inter-pulse period is T . (Later we will see how to deal with the case where $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $T \neq \omega$.) The domain

$$D_{(6.9)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\},$$

which is positively invariant to (6.9) for the same reasons as outlined above for (6.2). The basic reproduction number of (6.9) is given by

$$R_0^{(6.9)} \equiv \frac{\int_0^T \beta_\sigma \tilde{S}(t) dt}{T(\mu + g)}. \quad (6.10)$$

Noting that (6.9) reduces to (6.3) with $I(t) \equiv 0$ and prompted by the earlier observations regarding the disease-free solution, (6.9) also admits the periodic disease-free solution $Q_{\text{DFS}}^{(6.9)}(t) \equiv (\tilde{S}(t), 0, \tilde{R}(t)) = Q_{\text{DFS}}^{(6.2)}(t)$. Accordingly, the following eradication result can be given.

Theorem 6.1 *If $\sigma \in \mathcal{S}_{\text{periodic}}(T)$ and $R_0^{(6.9)} < 1$, then the solution of (6.9) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.9)}$.*

Proof From (6.9), it follows that

$$\dot{S}(t) = \mu - \beta_\sigma S(t)I(t) - \mu S(t) \leq \mu(1 - S(t)), \quad \forall t \in \mathbb{R}_+ \setminus \{kT\}.$$

Consider the following comparison system:

$$\begin{aligned} \dot{x}(t) &= \mu(1 - x(t)), & t \neq kT, \\ x(t) &= (1 - v)x(t^-), & t = kT, \\ x(0) &= S_0, & k \in \mathbb{N}, \end{aligned}$$

which converges to \tilde{S} by the analysis above; for any $\epsilon > 0$ there exists a time $t^* > 0$ such that $S(t) \leq x(t) \leq \tilde{S}(t) + \epsilon$ for $t \geq t^*$ by the impulsive comparison theorem (i.e., Theorem 1.12). Choose N to be the smallest integer such that $NT > t^*$, then for $NT < t_{k-1} < t \leq t_k$,

$$\begin{aligned} \dot{I}(t) &= \beta_k S(t)I(t) - (\mu + g)I(t), \\ &\leq (\beta_k([\tilde{S}(t) + \epsilon] - \mu - g) - \mu - g)I, \\ &\equiv \lambda_{k,\epsilon}(t)I, \end{aligned}$$

where $\lambda_{i,\epsilon}(t) \equiv \beta_i \tilde{S}(t) - g - \mu + \epsilon \beta_i$ for all $i \in \mathcal{M}$. Then by similar arguments found in the proof of Theorem 3.1,

$$\begin{aligned} I((N+1)T) &\leq I(NT) \exp \left(\int_{NT}^{t_1+NT} \lambda_{1,\epsilon}(t) dt + \dots + \int_{t_{m-1}+NT}^{t_m+NT} \lambda_{m,\epsilon}(t) dt \right), \\ &= I(NT) \exp \left[\int_0^{t_1} \lambda_{1,\epsilon}(t) dt + \dots + \int_{T-\tau_m}^T \lambda_{m,\epsilon}(t) dt \right], \end{aligned}$$

since $\tilde{S}(t) = \tilde{S}(t+T)$ and $\beta_{\sigma(t)} = \beta_{\sigma(t+T)}$. This implies that $I((N+1)T) \leq \eta I(NT)$ where

$$\eta(\epsilon) \equiv \exp \left[\int_0^{t_1} \lambda_{1,\epsilon}(t) dt + \dots + \int_{T-\tau_m}^T \lambda_{m,\epsilon}(t) dt \right].$$

Importantly, $R_0^{(6.9)} < 1$ gives that

$$\exp \left[\int_0^T (\beta_{\sigma(t)} \tilde{S}(t) - g - \mu) dt \right] < 1,$$

which implies the existence of $\delta > 0$ satisfying

$$\int_0^T (\beta_{\sigma(t)} \tilde{S}(t) - g - \mu) dt < -\delta.$$

Choose ϵ so that

$$0 < \epsilon = \frac{\delta}{2 \sum_{i=1}^m \beta_i \tau_i}$$

where $\sum_{i=1}^m \tau_i = T$, then

$$\eta(\epsilon) = \exp \left[\int_0^T (\beta_{\sigma(t)} (\tilde{S}(t) + \epsilon) - g - \mu) dt \right] < 1.$$

It can be similarly shown that $I((N + h + 1)T) \leq \eta I((N + h)T)$ for any integer $h \in \mathbb{N}$; the sequence $\{I((N + h)z^+)\}_{h=0}^\infty$ is monotonically decreasing and converges to zero, and, by boundedness of I , it follows that I converges to zero. The limiting system is given by the reduced system (6.3), from which the result follows.

Comparing Theorem 6.1 to Theorem 3.1 with $\sigma \in \mathcal{S}_{\text{periodic}}(T)$ for the uncontrolled version of the switched SIR model (i.e., absence of a pulse vaccination program), there is a parameter regime in which disease eradication can be achieved only under application of control. Since $\tilde{S}(t) < 1$ for all t ,

$$R_0^{(6.9)} = \frac{1}{T} \int_0^T R_0^{(3.8),\sigma(t)} \tilde{S}(t) dt < \frac{1}{T} \int_0^T R_0^{(3.8),\sigma(t)} dt = \frac{1}{T} \sum_{i=1}^m R_0^{(3.8),i} \tau_i = R_0^{(3.8)}.$$

6.1.2 Incorporating Impulsive Treatment into the Public Campaigns

Instead of impulsively vaccinating a portion v of susceptibles, consider the impulsive treatment of the infected. Different from the previous model, we assume here that a fraction of the population is treated at the switching times $t = t_k$, conferring immunity and moving them to the recovered class. That is, when there is a shift in the model parameters (i.e., β_{k-1} to β_k), an impulsive treatment is applied. Again,

the timescale of the treatment is considered to be relatively short as compared to the timescale of the disease dynamics. Consider m different pulse treatment levels, $p_i \in [0, 1)$ for all $i \in \mathcal{M}$, one of which is applied at the impulsive time. That is, a fraction $p \in \{p_1, \dots, p_m\}$ of the infected population is treated during each public campaign. Applied to the SIR model with seasonal variations (3.8), the impulsive switching model is given by

$$\left. \begin{array}{l} \dot{S}(t) = \mu - \beta_\sigma S(t)I(t) - \mu S(t) \\ \dot{I}(t) = \beta_\sigma S(t)I(t) - (\mu + g)I(t) \\ \dot{R}(t) = gI(t) - \mu R(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{t_k\},$$

$$\left. \begin{array}{l} S(t) = S(t^-) \\ I(t) = (1 - p_\sigma)I(t^-) \\ R(t) = R(t^-) + p_\sigma I(t^-) \end{array} \right\} \forall t \in \{t_k\},$$

$$(S(0), I(0), R(0)) = (S_0, I_0, R_0).$$
(6.11)

Recall that the total population is constant; the variables have been normalized. The meaningful domain of interest is

$$D_{(6.11)} \equiv \{(S, I, R) \in \mathbb{R}_+^3 : S + I + R = 1\} = D_{(6.9)},$$

which is assumed to contain the initial conditions (i.e., $(S_0, I_0, R_0) \in D_{(6.11)}$), and is positively invariant to (6.11) for the same reasons as the previous section. In this model, the mode basic reproduction numbers match the switched SIR reproduction numbers (i.e., (3.12)),

$$R_0^{(6.11),i} \equiv \frac{\beta_i}{\mu + g};$$
(6.12)

the underlying mechanisms driving the spread of the disease are unchanged within each mode. However, the impulsive treatment has an overall affect on the disease dynamics, as will be seen. The switched system (6.11) admits a disease-free equilibrium $Q_{\text{DFS}}^{(6.11)} \equiv (1, 0, 0)$ (common to all modes).

Recall the notation $T_i(t)$ for the total activation time of the i th mode of (6.11) in the interval $[0, t]$ and $N(t)$ for the total number of switches of (6.11) on the interval $[0, t]$.

Theorem 6.2 *Suppose that $\sigma \in \mathcal{S}_{\text{dwell}}$ with $\sigma = i_k$ on $[t_{k-1}, t_k)$. If there exists $c > 0$ such that*

$$\prod_{j=1}^{N(t)} \ln(1 - p_{ij}) + \sum_{i=1}^m (\beta_i - \mu - g)T_i(t) \leq -ct, \quad \forall t \geq 0,$$
(6.13)

then the solution of (6.11) converges to the disease-free equilibrium $Q_{\text{DFS}}^{(6.11)}$. Moreover, $Q_{\text{DFS}}^{(6.11)}$ is globally exponentially L -stable in the meaningful domain.

Proof Letting $\lambda_i \equiv \beta_i - \mu - g$,

$$\dot{I}(t) = \beta_\sigma S(t)I(t) - (\mu + g)I(t) \leq \lambda_\sigma I(t), \quad \forall t \in \mathbb{R}_+ \setminus \{t_k\}.$$

Therefore,

$$I(t) \leq I(t_{k-1}) \exp[\lambda_{i_k}(t - t_{k-1})], \quad t \in [t_{k-1}, t_k]. \quad (6.14)$$

Furthermore, at each impulsive time $t = t_k$,

$$I(t_k) = (1 - p_\sigma)I(t_k^-) \quad (6.15)$$

Let $\sigma(t) = i_k$ on $[t_{k-1}, t_k]$. Then an application of (6.14) and (6.15) successively on each subinterval leads to the following:

$$I(t) \leq I_0 \exp[\lambda_{i_1} t], \quad \forall t \in [0, t_1].$$

Then, $I(t_1^-) \leq I_0 \exp[\lambda_{i_1} t_1]$ and $I(t_1) = (1 - p_{i_1})I(t_1)$ so that $I(t_1) \leq I_0(1 - p_{i_1}) \exp[\lambda_{i_1} t_1]$. In general, for $t \in [t_{k-1}, t_k]$,

$$\begin{aligned} I(t) &\leq I_0(1 - p_{i_1}) \cdots (1 - p_{i_{k-1}}) \exp[\lambda_{i_1} t_1 + \dots + \lambda_{i_k}(t - t_{k-1})], \\ &= I_0 \exp \left[\prod_{j=1}^{N(t)} \ln(1 - p_{i_j}) + \sum_{i=1}^m \lambda_i T_i(t) \right], \\ &\leq I_0 \exp(-ct). \end{aligned}$$

Thus, $\lim_{t \rightarrow \infty} I(t) = 0$ and, from the limiting equations of system (6.11) with $I(t) \equiv 0$, it is apparent that the solution converges to the disease-free solution $Q_{\text{DFS}}^{(6.11)}$ in the domain $D_{(6.11)}$.

Motivated by an epidemic scenario and the data in Table 3.1 on the reproduction numbers of diseases, suppose that the mode reproduction numbers are greater than one in the switched SIR model (6.11) (i.e., $R_0^{(6.11),i} \geq 1$ for all $i \in \mathcal{M}$). A verifiable condition based on the model parameters ensures controlled disease eradication in this scenario.

Theorem 6.3 Suppose that $\sigma \in \mathcal{S}_{\text{dwell}}$ such that $t_k - t_{k-1} \leq \chi$ for some $\chi > 0$. If $R_0^{(6.11),i} \geq 1$ for all $i \in \mathcal{M}$ and there exists $\alpha > 1$ such that

$$\ln(\alpha(1 - p_i)) + (\mu + g)(R_0^{(6.11),i} - 1)\chi \leq 0, \quad \forall i \in \mathcal{M},$$

then the solution of (6.11) converges to the disease-free equilibrium $Q_{\text{DFS}}^{(6.11)}$. Moreover, $Q_{\text{DFS}}^{(6.11)}$ is globally asymptotically I -stable in the meaningful domain.

Proof Let $\lambda_i \equiv \beta_i - \mu - g$ for each $i \in \mathcal{M}$ and $\sigma(t) = i_k$ on $[t_{k-1}, t_k]$. Then an application of (6.14) and (6.15) successively on each subinterval leads to the following, for $t \in [t_{k-1}, t_k]$,

$$\begin{aligned} I(t) &\leq I_0(1-p_{i_1}) \cdots (1-p_{i_{k-1}}) \exp [\lambda_{i_1} t_1 + \dots + \lambda_{i_k} (t - t_{k-1})], \\ &\leq I_0(1-p_{i_1}) \cdots (1-p_{i_{k-1}}) \exp [\lambda_{i_1} \chi + \dots + \lambda_{i_k} \chi], \\ &= I_0 \frac{1}{\alpha^k (1-p_{i_k})} \alpha(1-p_{i_1}) \exp (\lambda_{i_1} \chi) \cdots \alpha(1-p_{i_k}) \exp (\lambda_{i_k} \chi), \\ &= I_0 \frac{1}{\alpha^k (1-p_{i_k})} \prod_{j=1}^k \alpha(1-p_{i_j}) \exp((\mu+g)(R_0^{(6.11),i_j} - 1)\chi), \\ &\leq I_0 \frac{1}{\alpha^k (1 - \max\{p_1, \dots, p_m\})}. \end{aligned}$$

I -partial asymptotic stability of the disease-free solution follows immediately since $\alpha > 1$. The result holds by the limiting equations for (6.11).

Finally, the case is considered in which the switching rule is periodic and a pulse treatment is applied once, at the end of each period.

Theorem 6.4 *Let $\sigma \in \mathcal{S}_{\text{periodic}}(T)$ and suppose that $p_1 = \dots = p_{m-1} = 0$ and let $p_m = p$. If*

$$R_0^{(6.11)} \equiv \frac{\ln(1-p) + \sum_{i=1}^m \beta_i \tau_i}{T(\mu+g)} < 1, \quad (6.16)$$

then the solution of (6.11) converges to the disease-free equilibrium $Q_{\text{DFS}}^{(6.11)}$. Moreover, $Q_{\text{DFS}}^{(6.11)}$ is globally asymptotically I -stable in the meaningful domain.

Proof The first impulse is applied at $t = T$; from the proof of Theorem 3.1,

$$I(t) \leq I_0 \exp [\lambda_1 \tau_1 + \dots + \lambda_m (t - (T - \tau_m))],$$

for $t \in [T - \tau_m, T]$, where $\lambda_i \equiv \beta_i - g - \mu$ for each $i \in \mathcal{M}$. At $t = T$,

$$I(T) \leq I_0(1-p) \exp \left(\sum_{i=1}^m \lambda_i \tau_i \right) = I_0 \exp \left(\ln(1-p) + \sum_{i=1}^m \lambda_i \tau_i \right) = \eta I_0,$$

where $\eta \equiv (\ln(1-p) + \sum_{i=1}^m \lambda_i \tau_i) < 1$ from (6.16). Similarly, it can be shown that $I(hT) \leq \eta I((h-1)T)$ for any integer $h \in \mathbb{N}$. Thus,

$$I(hT) \leq \eta I((h-1)T) \leq \eta(\eta I((h-2)T)) \leq \dots \leq \eta^h I_0;$$

the sequence $\{I(hT)\}_{h=0}^\infty$ converges to zero. As I is bounded, it follows that $\lim_{t \rightarrow \infty} I(t) = 0$ and the result follows from the limiting equations.

Comparing the results in the present section to the uncontrolled case [i.e., (3.8)] and using that $T = \omega$ and $p_1 = \dots = p_{m-1}$ and $p_m = p$,

$$R_0^{(6.11)} = \frac{\ln(1-p) + \sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} < \frac{\sum_{i=1}^m \beta_i \tau_i}{\omega(\mu + g)} = R_0^{(3.8)};$$

as expected, the impulsive control can guarantee disease eradication when it is usually not possible. Theorem 6.4 defines a critical value p_{crit} for the pulse treatment to guarantee eradication:

$$(1-p) \exp(\mu + g)[(R_0^{(6.11),1} - 1)\tau_1 + \dots + (R_0^{(6.11),m} - 1)\tau_m] < 1,$$

implies that (6.16) holds. Thus, if

$$p > 1 - \exp(-(\mu + g)[(R_0^{(6.11),1} - 1)\tau_1 + \dots + (R_0^{(6.11),m} - 1)\tau_m]) \equiv p_{\text{crit}},$$

(6.16) holds. Written another way, the critical treatment rate can be expressed in terms of the model's parameters by

$$p_{\text{crit}} \equiv 1 - \exp[(\mu + g - \beta_1)\tau_1 + \dots + (\mu + g - \beta_m)\tau_m];$$

there is a trade-off between the inter-pulse period T and the control rate p since increasing T requires a higher control rate p (and vice versa).

6.1.3 The SIR Model with General Switched Incidence Rates

Consider the application of impulsive control to the SIR model with switching incidence rates (3.29) in Sect. 3.5 (with functions f_i satisfying the physical conditions outlined there). To move the modeling efforts towards complications such as vaccine failure, suppose here that a pulse vaccination (which is applied periodically every $T > 0$ time units to a fraction $v \in [0, 1]$ of the susceptible population) sends the individual to the vaccinated class, denoted by V . Assume also that a fraction $p \in [0, 1]$ of the infected population is impulsively treated (moving them to the recovered class). Realistically, the treatment control rate is broken down as $p = q\zeta$, where ζ represents the success rate and q is the fraction of individuals treated. (The vaccination control rate can be broken down similarly.) Then, the control model is given by

$$\left. \begin{array}{l} \dot{S}(t) = \mu - f_\sigma(S(t), I(t)) - \mu S(t) \\ \dot{I}(t) = f_\sigma(S(t), I(t)) - (g + \mu)I(t) \\ \dot{R}(t) = gI(t) - \mu R(t) \\ \dot{V}(t) = -\mu V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{array}{l} S(t) = (1 - v)S(t^-) \\ I(t) = (1 - p)I(t^-) \\ R(t) = R(t^-) + pI(t^-) \\ V(t) = V(t^-) + vS(t^-) \end{array} \right\} \forall t \in \{kT\},$$

$$(S(0), I(0), R(0), V(0)) = (S_0, I_0, R_0, V_0).$$
(6.17)

The physical domain associated with (6.17) is $D_{(6.17)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : S + I + R + V = 1\}$, which is invariant since $\{\dot{S} + \dot{I} + \dot{R} + \dot{V}\}|_{S+I+R+V=1} = 0$, $\dot{S}|_{S=0} = \mu > 0$, $\dot{I}|_{I=0} = 0$, $\dot{R}|_{R=0} = gI \geq 0$, $\dot{V}|_{V=0} = 0$, and the impulsive equations do not move the solution to outside the meaningful domain. Notice that $(1, 0, 0, 0)$ is not an equilibrium of (6.17), however, letting $I(t) \equiv 0$, (6.17) reduces to

$$\left. \begin{array}{l} \dot{S}(t) = \mu(1 - S(t)) \\ \dot{R}(t) = -\mu R(t) \\ \dot{V}(t) = -\mu V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{array}{l} S(t) = (1 - v)S(t^-) \\ R(t) = R(t^-) \\ V(t) = V(t^-) + vS(t^-) \end{array} \right\} \forall t \in \{kT\},$$

$$(S(0), R(0), V(0)) = (S_0, R_0, V_0).$$
(6.18)

It is apparent that R converges to zero and the resulting reduced system is equivalent to (6.3) (with R replaced by V); (6.17) admits the periodic disease-free solution $Q_{\text{DFS}}^{(6.17)}(t) \equiv (\tilde{S}(t), 0, 0, \tilde{V}(t))$ where $\tilde{V}(t) \equiv 1 - \tilde{S}(t)$ and \tilde{S} is outlined in Eq. (6.5). An eradication result can be given which contains both vaccination rate and treatment rate, where the impulsive times do not have to coincide with the switching times.

Theorem 6.5 Assume that there exist $\beta_i > 0$ such that $f_i(S, I) \leq \beta_i SI$ for all $i \in \mathcal{M}$ and $(S, I) \in \{(S, I) \in \mathbb{R}_+^2 : S + I \leq 1\}$. If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$\overline{R}_0^{(6.17)} \equiv \frac{\frac{1}{z} \int_0^z \beta_\sigma \tilde{S}(t) dt}{g + \mu - \frac{1}{T} \ln(1 - p)} < 1,$$
(6.19)

where $z \equiv \text{lcm}(\omega, T)$, then the solution of (6.17) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.17)}$.

Proof From Eq. (6.17), $\dot{S}(t) = \mu - f_\sigma(S(t), I(t)) - \mu S(t) \leq (1 - S(t))\mu$. Consider the comparison system

$$\begin{aligned}\dot{x}(t) &= \mu(1 - x(t)), \quad t \neq kT, \\ x(t) &= (1 - v)x(t^-), \quad t = kT, \\ x(0) &= S_0, \quad k \in \mathbb{N},\end{aligned}\tag{6.20}$$

whose solution converges to \tilde{S} in Eq. (6.5). Choose

$$0 < \epsilon = \frac{(1 - \bar{R}_0^{(6.9)})(g + \mu - \frac{1}{T} \ln(1 - p))}{\frac{2}{\omega} \sum_{i=1}^m \beta_i \tau_i}.$$

Since $S(t) \leq x(t)$, there exists a time $t^* > 0$ such that $S(t) \leq \tilde{S}(t) + \epsilon$ for $t \geq t^*$. Choose N to be the smallest integer such that $Nz > t^*$ and let i_k follow the switching rule $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$. Then for $Nz \leq t_{k-1} \leq t < t_k$,

$$\begin{aligned}\dot{I}(t) &= f_k(S(t), I(t)) - (g + \mu)I(t), \\ &\leq (\beta_k S(t) - g - \mu)I(t), \\ &\leq (\beta_k [\tilde{S}(t) + \epsilon] - g - \mu)I(t), \\ &= \lambda_{k,\epsilon}(t)I(t),\end{aligned}\tag{6.21}$$

where $\lambda_{i,\epsilon}(t) \equiv \beta_i[\tilde{S}(t) + \epsilon] - g - \mu$ for each $i \in \mathcal{M}$. It follows that

$$\begin{aligned}I((N+1)z) &\leq I(Nz)(1-p)^{z/T} \exp\left\{\int_{Nz}^{t_1+Nz} \lambda_{1,\epsilon}(t)dt + \dots + \int_{t_{m-1}+Nz}^{t_m+Nz} \lambda_{m,\epsilon}(t)dt\right. \\ &\quad \left.+ \dots + \int_{(N+1)z-\omega}^{(N+1)z-\omega+\tau_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{(N+1)z-\tau_m}^{(N+1)z} \lambda_{m,\epsilon}(t)dt\right\}, \\ &= I(Nz) \exp\left[\frac{z}{T} \ln(1-p) + \int_0^{t_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t)dt\right],\end{aligned}$$

which implies $I((N+1)z^+) \leq \eta I(Nz^+) < I(Nz^+)$ where

$$\eta(\epsilon) \equiv \exp\left[\frac{z}{T} \ln(1-p) + \int_0^{t_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t)dt\right]$$

satisfies $\eta(\epsilon) < 1$ since $\bar{R}_0^{(6.9)} < 1$ and the choice of ϵ above.

It can be similarly shown that $I((N+h+1)z) \leq \eta I((N+h)z)$ for any integer $h \in \mathbb{N}$;

$$I((N+h+1)z) \leq \eta I((N+h)z) \leq \eta(\eta I((N+h-1)z)) \leq \dots \leq \eta^{h+1} I(Nz).$$

Thus, the sequence $\{I((N + h))\}_{h=0}^{\infty}$ is monotonically decreasing and converges to zero. Since I is bounded for $0 \leq t \leq Nz$ and on each interval of the form $[(N + h - 1)z, (N + h)z]$ for any $h \in \mathbb{N}$, $\lim_{t \rightarrow \infty} I(t) = 0$. The limiting system, with $I(t) \equiv 0$, is given by the reduced system (6.18), which converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.17)}$.

Some remarks are in order:

1. It is straightforward to extend Theorem 6.5 to the case in which the switched incidence rates (i.e., $f_i(t, S, I)$) and model parameters are time-varying (e.g., the recovery rate, the birth/death rates); in this case, $\overline{R}_0^{(6.17)}$ is replaced by

$$R_0^{(6.17)*} \equiv \frac{\frac{1}{z} \int_0^z \beta_\sigma(t) \widetilde{S}(t) dt}{\frac{1}{z} \int_0^z g_\sigma(t) dt + \mu - \frac{1}{T} \ln(1-p)}.$$

(See [96] for details.)

2. If $f_i(S, I) \equiv \beta_i SI$ for each $i \in \mathcal{M}$ and $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, the reproduction number given in Eq. (6.19) reduces to the appropriate basic reproduction number of the model (i.e., $\overline{R}_0^{(6.17)} = R_0^{(6.9)}$) [150].
3. Given a vaccination rate v , the condition $\overline{R}_0^{(6.17)} < 1$ in Eq. (6.19) defines a critical pulse treatment rate p_{crit} for which $p > p_{\text{crit}}$ guarantees disease eradication. More specifically,

$$p_{\text{crit}} \equiv 1 - \exp \left[-\frac{T}{z} \left(\int_0^{t_1} \lambda_1(t) dt + \dots + \int_{z-\tau_m}^z \lambda_m(t) dt \right) \right], \quad (6.22)$$

where $\lambda_i(t) \equiv \beta_i \widetilde{S}(t) - g - \mu$ for each $i \in \mathcal{M}$. Similarly, given a treatment rate p , the condition $\overline{R}_0^{(6.9)} < 1$ defines a critical pulse vaccination rate v_{crit} , which may also be found explicitly in terms of the model parameters.

4. Observe that there is an apparent trade-off between p , v , and T : if T is decreased (i.e., apply impulses more frequently) then p and v may be decreased (i.e., less individuals must be treated/vaccinated to achieve the same effects). Similarly, if T is increased then p or v must also be increased, given the model parameters, in order to achieve eradication.
5. It is also possible to establish some criteria guaranteeing disease persistence along the lines of the proof of Theorem 3.4 (see [96] for details): Assume that there exist $\gamma_i > 0$ such that $\gamma_i SI \leq f_i(S, I)$ for all $i \in \mathcal{M}$ and $(S, I) \in \{(S, I) \in \mathbb{R}_+^2 : S + I \leq 1\}$. If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, $v > p$, and

$$\widehat{R}_0^{(6.17)} \equiv \frac{\frac{1}{z} \int_0^z \gamma_\sigma \widetilde{S}(t) dt}{g + \mu - \frac{1}{T} \ln(1-p)} < 1, \quad (6.23)$$

where $z \equiv \text{lcm}(\omega, T)$, then the disease persists uniformly in (6.17); there exists $\eta > 0$ such that $\liminf_{t \rightarrow +\infty} I(t) \geq \eta$.

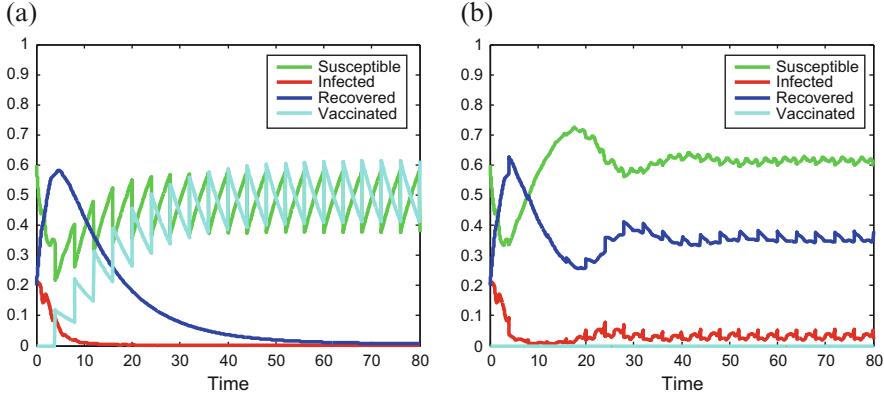


Fig. 6.2 Simulations of Example 6.1. (a) $v = 0.35, p = 0$. (b) $p = 0.6, v = 0$

Example 6.1 Consider (6.17) with $\mathcal{M} = \{1, 2\}$, periodic switching rule

$$\sigma(t) \equiv \begin{cases} 1, & \text{if } t \in [2k, 2k+1], \quad k = 0, 1, 2, \dots, \\ 2, & \text{if } t \in [2k+1, 2k+2), \end{cases} \quad (6.24)$$

(i.e., $\tau_1 = \tau_2 = 1$ and $\omega = 2$), and initial conditions $(S_0, I_0, R_0, V_0) = (0.6, 0.2, 0.2, 0)$. Let $f_i(t, S, I) \equiv \beta(1 + \eta_i \cos(2\pi t))SI$ for $i = 1, 2$ (i.e., smoothly varying seasonal variations that switch from year to year). Given model parameters $\beta = 2$, $\mu = 0.1$, $\eta_1 = 0.1$, $\eta_2 = 1$, and time-varying recovery rate $g(t) \equiv g(1 + \delta \sin(2\pi t))$ where $g = 0.9$ and $\delta = 0.1$, a vaccination rate $v = 0.35$ gives $R_0^{(6.17)*} = 0.978$ ($v_{\text{crit}} = 0.337$). On the other hand, a pulse treatment rate $p = 0.6$ gives $R_0^{(6.17)*} = 1.63$ (the disease persists; an unrealistically high critical treatment rate of $p_{\text{crit}} = 0.982$ is needed in this case). The results are illustrated in Fig. 6.2.

6.1.4 Vaccine Failures

In an impulsive vaccination scheme, two important factors that should be analyzed include [36]:

1. The duration of the immunity gained through immunization.
2. The efficacy of the vaccination.

Incorporate these two items into the previously analyzed models as follows [36]:

1. Assume that the temporal duration of the immune period is finite; vaccinated individuals move back into the susceptible class at a rate $\theta > 0$ (i.e., $1/\theta$ is the average duration of the vaccine-induced immunity).

2. The probability that a vaccinated individual becomes infected after a sufficient contact with an infected individual should be considerably reduced from the normal probability, but it is not zero practically [36]; this is a serious concern in immunization programs and is relevant in vaccinating against, for example, measles.

Motivated by this discussion, assume that a fraction $p \in [0, 1]$ of susceptible individuals are successfully given a pulse treatment/vaccination periodically (with inter-pulse period T), entering the recovered/vaccinated class, respectively. Assume that susceptible individuals that have received the vaccination can still become infected, with an incidence rate of new infections given by

$$(t, S, I, N) \mapsto \frac{\xi \beta_\sigma SI}{N},$$

where $N \equiv S + I + R + V$, which is reduced by a factor $\xi \in [0, 1]$ as compared to the usual switching standard incidence rate. ($\xi = 1$ corresponds to complete failure of the vaccination scheme while $\xi = 0$ corresponds to perfect efficacy.) After normalizing the variables by the constant total population, the switched model is given by

$$\left. \begin{array}{l} \dot{S}(t) = \mu - \beta_\sigma S(t)I(t) - \mu S(t) + \theta V(t) \\ \dot{I}(t) = \beta_\sigma S(t)I(t) + \xi \beta_\sigma V(t)I(t) - (g + \mu)I(t) \\ \dot{R}(t) = gI(t) - \mu R(t) \\ \dot{V}(t) = -\xi \beta_\sigma V(t)I(t) - \mu V(t) - \theta V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{array}{l} S(t) = (1-p)S(t^-) \\ I(t) = (1-p)I(t^-) \\ R(t) = R(t^-) + pI(t^-) \\ V(t) = V(t^-) + pS(t^-) \end{array} \right\} \forall t \in \{kT\}, \quad (6.25)$$

$$(S(0), I(0), R(0), V(0)) = (S_0, I_0, R_0, V_0).$$

Here the switching rule is assumed to take the form $\sigma \in \mathcal{S}_{\text{periodic}}(T)$; i.e., the inter-pulse period satisfies $T = \tau_1 + \dots + \tau_m$ such that $\tau_k \equiv t_k - t_{k-1}$ for each $k \in \mathbb{N}$. The meaningful domain, which is invariant to system (6.25), is

$$D_{(6.25)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : S + I + R + V = 1\},$$

which follows from the following:

$$\{\dot{S} + \dot{I} + \dot{R} + \dot{V}\}|_{S+I+R+V=1} = 0,$$

$\dot{S}|_{S=0} = \mu + \theta V > 0$, $\dot{I}|_{I=0} = 0$, $\dot{R}|_{R=0} = gI \geq 0$, $\dot{V}|_{V=0} = 0$, and, further, the impulsive equations do not move the solution to outside the meaningful domain. The flow of the compartments is shown in Fig. 6.3.

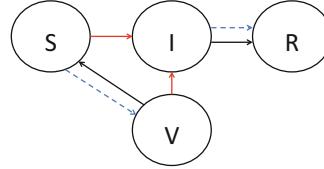


Fig. 6.3 Flow diagram of the switched SIRV system (6.25). The *red lines* represent new cases of infection via horizontal transmission and vaccine failure. The *dashed blue lines* represent pulse vaccination/treatment

In seeking a periodic disease-free solution, the limiting system of (6.25) (with $I(t) \equiv 0$ and $R(t) \equiv 0$) is given by:

$$\begin{aligned} \dot{S}(t) &= (\mu + \theta)(1 - S(t)) \\ \dot{V}(t) &= -(\mu + \theta)V(t) \end{aligned} \quad \left\{ \begin{array}{l} \forall t \in \mathbb{R}_+ \setminus \{kT\}, \\ S(t) = (1 - p)S(t^-) \\ V(t) = V(t^-) + pS(t^-) \end{array} \right\} \quad (6.26)$$

$$(S(0), V(0)) = (S_0, V_0).$$

The solution of system (6.26), for any initial conditions in $D_{(6.25)}$, converges to the periodic solution,

$$\begin{aligned} \widetilde{S}(t) &\equiv 1 - \frac{p \exp(-(\mu + \theta)(t - (k - 1)T))}{1 - (1 - p) \exp(-(\mu + \theta)T)}, \quad \forall t \in [(k - 1)T, kT), \\ \widetilde{V}(t) &\equiv 1 - \widetilde{S}(t), \quad k \in \mathbb{N}, \end{aligned} \quad (6.27)$$

which again follows from the previous derivations above (see also, for example, Lemma 2.2 of [49]). Hence, system (6.25) admits the periodic disease-free solution $Q_{\text{DFS}}^{(6.25)}(t) \equiv (\widetilde{S}(t), 0, 0, \widetilde{V}(t))$. Given that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ in the switched system (6.25) and that a solution satisfies $S(t) + I(t) \leq 1$,

$$\begin{aligned} \dot{S}(t) &\leq \mu - \mu S(t) + \theta V(t) \leq (\mu + \theta)(1 - S(t)), \\ \dot{V}(t) &\leq -(\mu + \theta)V(t). \end{aligned}$$

Thus, by a similar comparison theorem approach as in Theorem 6.5, for any $\epsilon > 0$ there exists $t^* > 0$ such that $S(t) \leq \widetilde{S}(t) + \epsilon$ and $V(t) \leq \widetilde{V}(t) + \epsilon$ for $t \geq t^*$. Then, by using the bound

$$\begin{aligned} \dot{I}(t) &= [\beta_\sigma(S(t) + \xi V(t)) - (g + \mu)]I(t), \\ &\leq [\beta_\sigma((\widetilde{S}(t) + \epsilon) + \xi(\widetilde{V}(t) + \epsilon)) - (g + \mu)]I(t), \\ &= \lambda_\sigma I(t), \end{aligned}$$

where $\lambda_{i,\epsilon}(t) \equiv \beta_i[\widetilde{S}(t) + \xi\widetilde{V}(t)] - g - \mu + \beta_i\epsilon(1 + \xi)$ for each $i \in \mathcal{M}$, the following result follows by proceeding as in Theorem 6.5.

Theorem 6.6 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and*

$$R_0^{(6.25)} \equiv \frac{\frac{1}{z} \int_0^z \beta_\sigma(\widetilde{S}(t) + \xi\widetilde{V}(t))dt}{g + \mu - \frac{1}{T} \ln(1 - p)} < 1, \quad (6.28)$$

where $z \equiv \text{lcm}(\omega, T)$, then the solution of system (6.25) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.25)}$.

6.1.5 Pulse Control Applied to an Epidemic Model with Media Coverage

In this section we return to the SIS model with media coverage (4.12) for application of impulsive control strategies. As in Sect. 6.1.4, waning immunity and vaccine failure are considered here; a vaccinated individual can become infected with a reduced probability $\xi \in [0, 1]$. As the nonlinearity of the incidence rate not being properly taken into account is a possible cause of vaccination program failure [38], consider (4.12) with $\alpha = 0$ (recall that $\alpha \approx 0.05 \pm 0.02$ [171]). The incidence rate takes the form

$$(t, S, I, V) \mapsto h_\sigma(I)(S + \xi V),$$

with forces of infection

$$h_i(I) \equiv \left(\beta_i - \frac{\gamma_i I}{b + I} \right) I, \quad \forall i \in \mathcal{M}.$$

Here we also take vertical transmission into account; assume that a fraction $\rho \in [0, 1]$ of newborns are born infected (i.e., with transmission from an infected mother). The switched and impulsive model is given by

$$\left. \begin{aligned} \dot{S}(t) &= \mu(1 - \rho I(t)) - h_\sigma(I(t))S(t) + gI(t) + \theta V(t) - \mu S(t) \\ \dot{I}(t) &= \mu\rho I(t) + h_\sigma(I(t))(S(t) + \xi V(t)) - gI(t) - \mu I(t) \\ \dot{V}(t) &= -\xi h_\sigma(I(t))V(t) - \theta V(t) - \mu V(t) \end{aligned} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{aligned} S(t) &= (1 - v)S(t^-) \\ I(t) &= I(t^-) \\ V(t) &= V(t^-) + vS(t^-) \end{aligned} \right\} \forall t \in \{kT\},$$

$$(S(0), I(0), V(0)) = (S_0, I_0, V_0), \quad (6.29)$$

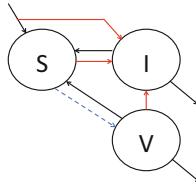


Fig. 6.4 Flow of the switched SIS model with media coverage (6.29). The red lines represent disease transmission (from horizontal transmission, vertical transmission, and vaccine failure) and the dashed blue line represents the pulse vaccination scheme

where the variables have been normalized by the total population. Assume that the initial conditions satisfy

$$(S_0, I_0, V_0) \in D_{(6.29)} \equiv \{(S, I, V) \in \mathbb{R}_+^3 : S + I + V = 1\}.$$

Note that $\{\dot{S} + \dot{I} + \dot{V}\}|_{S+I+V=1} = 0$, $\dot{S}|_{S=0} = \mu(1 - \rho I) + gI + \theta V > 0$, $\dot{I}|_{I=0} = 0$, $\dot{V}|_{V=0} = 0$, and the impulsive equations do not move the solution to outside the meaningful domain; $D_{(6.29)}$ is positively invariant to system (6.29). Figure 6.4 shows the flow diagram associated with the dynamics in (6.29).

Consistent with the theme of this chapter, $(1, 0, 0)$ is not an equilibrium point of (6.29), however, we begin the analysis of system (6.29) by showing the existence of a periodic disease-free solution in which $I(t) \equiv 0$ for all $t \geq 0$. Under this assumption, system (6.29) becomes (6.26), which admits the periodic solution outlined in (6.27). Hence, (6.29) admits the disease-free periodic solution given by $Q_{\text{DFS}}^{(6.29)}(t) \equiv (\widetilde{S}(t), 0, \widetilde{V}(t))$, where \widetilde{S} and \widetilde{V} are outlined in (6.27). If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, then the basic reproduction number of (6.29) is given by:

$$R_0^{(6.29)} \equiv \frac{\frac{1}{z} \int_0^z [\beta_\sigma(\widetilde{S}(t) + \xi \widetilde{V}(t))] dt}{\mu(1 - \rho) + g}, \quad (6.30)$$

where $z \equiv \text{lcm}(\omega, T)$ (see, e.g., the methodology in [150]). Using this threshold value, global asymptotic stability can be shown using Floquet theory in combination with the previously applied methods.

Theorem 6.7 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, $g \leq \rho\mu + \theta$, and $R_0^{(6.29)} < 1$, then the solution of (6.29) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.29)}$. If in addition*

$$\widetilde{R}_0^{(6.29)} \equiv \frac{\frac{1}{z} \int_0^z [\beta_{\max}(\widetilde{S}(t) + \xi \widetilde{V}(t))] dt}{\mu(1 - \rho) + g} < 1$$

then $Q_{\text{DFS}}^{(6.29)}$ is globally asymptotically stable in the meaningful domain $D_{(6.29)}$.

Proof Global attractivity of $Q_{\text{DFS}}^{(6.29)}$ is shown as follows: on the interval $[t_{k-1}, t_k)$,

$$\begin{aligned}\dot{S}(t) &= \mu(1 - \rho I(t)) - \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)}\right) S(t)I(t) + gI(t) + \theta V(t) - \mu S(t), \\ &\leq \mu(1 - S(t)) + (g - \rho\mu)I(t) + \theta(1 - S(t) - I(t)), \\ &= (\mu + \theta)(1 - S(t)) + (g - \rho\mu - \theta)I(t), \\ &\leq (\mu + \theta)(1 - S(t)),\end{aligned}$$

as $g \leq \rho\mu + \theta$. Also, $\dot{V}(t) \leq -(\mu + \theta)V(t)$. Thus, the following comparison system may be considered:

$$\begin{aligned}\begin{cases} \dot{x}(t) = (\mu + \theta)x(t) \\ \dot{y}(t) = -(\mu + \theta)y(t) \end{cases} &\forall t \in \mathbb{R}_+ \setminus \{kT\}, \\ \begin{cases} x(t) = (1 - v)x(t^-) \\ y(t) = y(t^-) + vx(t^-) \end{cases} &\forall t \in \{kT\}, \\ (x(0), y(0)) &= (S_0, V_0),\end{aligned}\tag{6.31}$$

whose unique solution satisfies $\lim_{t \rightarrow \infty} \|(x(t), y(t)) - (\tilde{S}(t), \tilde{V}(t))\| = 0$. Since $S(t) \leq \tilde{x}(t)$ and $V(t) \leq \tilde{y}(t)$ for all $t \in \mathbb{R}_+$, there exists a time $t^* > 0$ such that $S(t) \leq \tilde{S}(t) + \epsilon$ and $V(t) \leq \tilde{V}(t) + \epsilon$ for $t \geq t^*$. Choosing N as the smallest integer satisfying $Nz > t^*$,

$$\begin{aligned}\dot{I}(t) &= \mu\rho I(t) + \left(\beta_k - \frac{\gamma_k I(t)}{a + I(t)}\right) (S(t)I(t) + \xi V(t)I(t)) - gI(t) - \mu I(t), \\ &\leq (\beta_k([\tilde{S}(t) + \epsilon] + \xi[\tilde{V}(t) + \epsilon]) + \rho\mu - g - \mu)I(t), \\ &= \lambda_{k,\epsilon}(t)I(t),\end{aligned}$$

for $Nz < t_{k-1} \leq t < t_k$, where $\lambda_{i,\epsilon}(t) \equiv \beta_i(\tilde{S}(t) + \xi\tilde{V}(t)) + \rho\mu - g - \mu + \epsilon\beta_i(1 + \xi)$ for each $i \in \mathcal{M}$. The rest of this part of the proof proceeds similarly as in the proof of Theorem 6.1: note that

$$\begin{aligned}I((N+1)z^+) &\leq I(Nz^+) \exp\left\{\int_{Nz}^{t_1+Nz} \lambda_{1,\epsilon}(t)dt + \dots + \int_{t_{m-1}+Nz}^{t_m+Nz} \lambda_{m,\epsilon}(t)dt\right. \\ &\quad \left.+ \dots + \int_{(N+1)z-\omega}^{(N+1)z-\omega+\tau_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{(N+1)z-\tau_m}^{(N+1)z} \lambda_{m,\epsilon}(t)dt\right\}, \\ &= I(Nz^+) \exp\left[\int_0^{t_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t)dt\right].\end{aligned}$$

which gives that $I((N + 1)z^+) \leq \eta(\epsilon)I(Nz^+)$ where

$$\eta(\epsilon) \equiv \exp \left[\int_0^{t_1} \lambda_{1,\epsilon}(t) dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t) dt \right].$$

The condition $R_0^{(6.29)} < 1$ implies that

$$\exp \left[\int_0^z (\beta_{\sigma(t)} [\tilde{S}(t) + \xi \tilde{V}(t)] - g - \mu(1 - \rho)) dt \right] < 1,$$

from which the existence of a constant $\delta > 0$ satisfying

$$\int_0^z (\beta_{\sigma(t)} [\tilde{S}(t) + \xi \tilde{V}(t)] - g - \mu(1 - \rho)) dt \leq -\delta,$$

is guaranteed. Letting $\epsilon > 0$ be chosen so that

$$\epsilon \leq \frac{\delta}{2(1 + \xi) \sum_{i=1}^m \beta_i \tau_i}$$

ensures that $\eta(\epsilon) < 1$. It can be similarly shown that $I((N + h + 1)z^+) \leq \eta I((N + h)z^+)$ for any integer $h \in \mathbb{N}$. Hence,

$$I((N + h + 1)z^+) \leq \eta I((N + h)z^+) \leq \eta(\eta I((N + h - 1)z^+)) \leq \dots \leq \eta^{h+1} I(Nz^+).$$

Therefore, the sequence $\{I((N + h)z^+)\}_{h=0}^\infty$ converges to zero, and, since I is bounded, it follows that $\lim_{t \rightarrow \infty} I(t) = 0$. The limiting system with $I = 0$ is given by the reduced system (6.26), which converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.29)}$.

To demonstrate stability, the comparison system

$$\left. \begin{aligned} \dot{x}(t) &= \mu(1 - \rho y(t)) - \beta_{\max} x(t)y(t) + gy(t) + \theta z(t) - \mu x(t) \\ \dot{y}(t) &= \mu \rho y(t) + \beta_{\max}(x(t)y(t) + \xi z(t)y(t)) - gy(t) - \mu y(t) \\ \dot{z}(t) &= -\xi \beta_{\max} z(t)y(t) - \theta z(t) - \mu z(t) \end{aligned} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{aligned} x(t) &= (1 - v)x(t^-) \\ y(t) &= y(t^-) \\ z(t) &= z(t^-) + vx(t^-) \end{aligned} \right\} \forall t \in \{kT\},$$

$$(x(0), y(0), z(0)) = (S_0, I_0, V_0), \quad (6.32)$$

gives that $S(t) \leq x(t)$, $I(t) \leq y(t)$, and $V(t) \leq z(t)$ for all $t \geq 0$. Introduce the new variables $S_L \equiv S - \bar{S}$ and $V_L \equiv \bar{V}$. Linearizing the system (6.29) about $Q_{\text{DFS}}^{(6.29)}$ yields the following ODE system:

$$\begin{aligned}\dot{S}_L(t) &= -\mu S_L(t) - (\beta_\sigma \tilde{S}(t) - \rho\mu + g)I(t) + \theta V_L(t), \\ \dot{I}(t) &= (\beta_{\max}(\tilde{S}(t) + \xi \tilde{V}(t)) + \rho\mu - g - \mu)I(t), \\ \dot{V}_L(t) &= -\beta_\sigma \xi \tilde{V}(t)I(t) - (\mu + \theta)V_L(t),\end{aligned}\tag{6.33}$$

which, when combined with the impulsive dynamics, motivates the following appropriate ODE comparison system:

$$\begin{aligned}\dot{x}(t) &= -\mu S_L(t) - (\beta_{\max} \tilde{S}(t) - \rho\mu + g)I(t) + \theta V_L(t), \\ \dot{y}(t) &= (\beta_{\max}(\tilde{S}(t) + \xi \tilde{V}(t)) + \rho\mu - g - \mu)I(t), \\ \dot{z}(t) &= -\beta_{\max} \xi \tilde{V}(t)I(t) - (\mu + \theta)V_L(t).\end{aligned}\tag{6.34}$$

It is possible to rewrite (6.34) as a linear time-varying ODE system $(\dot{x}(t), \dot{y}(t), \dot{z}(t)) = F(t)(x(t), y(t), z(t))$ where

$$F(t) \equiv \begin{pmatrix} -\mu & -(\beta_{\max} \tilde{S}(t) - \rho\mu + g) & \theta \\ 0 & (\beta_{\max}(\tilde{S}(t) + \xi \tilde{V}(t)) + \rho\mu - g - \mu) & 0 \\ 0 & -\beta_{\max} \xi \tilde{V}(t) & -(\mu + \theta) \end{pmatrix}$$

satisfies $F(t) = F(t + T)$. Letting

$$E \equiv \begin{pmatrix} (1-v) & 0 & 0 \\ 0 & 0 & 0 \\ v & 0 & 1 \end{pmatrix},$$

the monodromy matrix associated with (6.34) is thus given by

$$M \equiv \begin{pmatrix} (1-v) \exp(-z\mu) & * & * \\ 0 & H(z) & 0 \\ 0 & * & \exp(-z(\mu + \theta)) \end{pmatrix},$$

where

$$H(z) \equiv \exp \left(\int_0^z \beta_{\max}(\tilde{S}(t) + \xi \tilde{V}(t)) dt + (\rho\mu - g - \mu)z \right)$$

and the $*$ entries are not required explicitly for subsequent calculations. The eigenvalues of M are given by

$$\begin{aligned}\phi_1 &\equiv (1-v) \exp(-\mu\omega), \\ \phi_2 &\equiv \exp \left(\int_0^z \beta_{\max}(\tilde{S}(t) + \xi \tilde{V}(t)) dt + (\rho\mu - g - \mu)z \right), \\ \phi_3 &\equiv \exp(-(\mu + \theta)z).\end{aligned}$$

By inspection, $\phi_1 < 1$ and $\phi_3 < 1$. Furthermore, $R_0^{(6.29)} < 1$ implies that $\phi_2 < 1$. Hence, $Q_{\text{DFS}}^{(6.29)}$ is locally asymptotically stable with respect to (6.34), according to Floquet theory, and the result follows.

A persistence result can also be provided for the endemic scenario, using the Generalized Binomial Theorem.

Theorem 6.8 *If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and $R_0^{(6.29)} > 1$ then the disease persists uniformly in (6.29); there exists $\eta > 0$ such that the solution of (6.29) satisfies $\liminf_{t \rightarrow \infty} I(t) \geq \eta$.*

Proof Begin by showing weak uniform persistence as follows: it is claimed that there exists $c > 0$ satisfying $\limsup_{t \rightarrow \infty} I(t) > c$. If not, then for any given $\epsilon > 0$, $\limsup_{t \rightarrow \infty} I(t) < \epsilon$. For $t \in [t_{k-1}, t_k)$, (6.29) implies that

$$\begin{aligned}\dot{S}(t) &= \mu(1 - \rho I(t)) - \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)} \right) S(t)I(t) + gI(t) + \theta V(t) - \mu S(t), \\ &> \mu(1 - \rho\epsilon) - \beta_{\max}\epsilon S(t) - \mu S(t) + \theta(1 - \epsilon - S(t)), \\ &\geq [\mu(1 - \rho\epsilon) + \theta(1 - \epsilon) - \beta_{\max}\epsilon] - (\mu + \theta)S(t),\end{aligned}$$

where $\beta_{\max} \equiv \max\{\beta_i : i \in \mathcal{M}\}$. Consider the comparison system

$$\begin{aligned}\dot{x}(t) &= [\mu(1 - \rho\epsilon) + \theta(1 - \epsilon) - \beta_{\max}\epsilon] - (\mu + \theta)x(t), & t \neq kT, \\ x(t) &= (1 - v)x(t^-), & t = kT, \\ x(0) &= S_0,\end{aligned}\tag{6.35}$$

whose unique solution satisfies $\lim_{t \rightarrow \infty} |x(t) - \tilde{x}(t)| = 0$, where

$$\tilde{x}(t) \equiv \left[1 - \epsilon \left(\frac{\beta_{\max} + \rho\mu + \theta}{\mu + \theta} \right) \right] \left[1 - \frac{v \exp(-(\mu + \theta)(t - (k - 1)T))}{1 - (1 - v) \exp(-(\mu + \theta)T)} \right].$$

By definition of \tilde{S} and \tilde{x} ,

$$\tilde{S}(t) - \tilde{x}(t) = \alpha\epsilon \left[1 - \frac{v \exp(-(\mu + \theta)(t - (k - 1)T))}{1 - (1 - v) \exp(-(\mu + \theta)T)} \right],$$

where $\alpha \equiv (\beta_{\max} + \rho\mu + \theta)/(\mu + \theta)$. Let

$$\Delta \equiv \max_{0 \leq t \leq T} \left[1 - \frac{v \exp(-(\mu + \theta)t)}{1 - (1 - v) \exp(-(\mu + \theta)T)} \right].$$

Then, there exists $t^* > 0$ such that $S(t) \geq x(t) \geq \tilde{x}(t) - \epsilon \geq \tilde{S}(t) - \alpha\Delta\epsilon - \epsilon$ for all $t \geq t^*$. Therefore, for $t^* < t_{k-1} \leq t < t_k$,

$$\begin{aligned}\dot{I}(t) &= \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)} \right) (S(t)I(t) + \xi V(t)I(t)) - gI(t) - \mu(1 - \rho)I(t), \\ &= \left(\beta_k - \frac{\gamma_k I(t)}{b + I(t)} \right) (S(t)I(t)(1 - \xi) + \xi I(t) - \xi I^2(t)) - gI(t) - \mu(1 - \rho)I(t), \\ &\geq \beta_k (\tilde{S}(t) - \alpha\Delta\epsilon - \epsilon)(1 - \xi)I(t) + \xi I(t) - \xi\epsilon I(t) - gI(t) - \mu(1 - \rho)I(t), \\ &\geq (\beta_k (\tilde{S}(t)(1 - \xi) + \xi) - g - \mu(1 - \rho))I(t) + G(\epsilon)I,\end{aligned}$$

where $\gamma_{\max} \equiv \max\{\gamma_i : i \in \mathcal{M}\}$ and

$$G(\epsilon) \equiv -\frac{\gamma_{\max}\epsilon}{a + \epsilon} [(\tilde{S}(t) - \alpha\Delta\epsilon - \epsilon)(1 - \xi) + \xi - \xi\epsilon] + \beta_{\max}[(-\alpha\Delta\epsilon - \epsilon)(1 - \xi) - \xi\epsilon].$$

For $t \in [t^* + (k-1)z, t^* + kz]$, $k \in \mathbb{N}$,

$$\begin{aligned}I(t) &\geq I(t^*) \exp \left\{ \int_{t^*}^t (\beta_{\sigma(s)}(\tilde{S}(s)(1 - \xi) + \xi) - g - \mu(1 - \rho) + G(\epsilon)) ds \right\}, \\ &= I(t^*) \exp \left\{ \int_{t^*}^{t^* + (k-1)z} (\beta_{\sigma(s)}(\tilde{S}(s)(1 - \xi) + \xi) - g - \mu(1 - \rho) + G(\epsilon)) ds \right\} \\ &\quad \times \exp \left\{ \int_{t^* + (k-1)z}^t (\beta_{\sigma(s)}(\tilde{S}(s)(1 - \xi) + \xi) - g - \mu(1 - \rho) + G(\epsilon)) ds \right\}, \\ &\geq M \exp \left\{ (k-1) \left[\int_0^z (\beta_{\sigma(s)}(\tilde{S}(s)(1 - \xi) + \xi) - g - \mu(1 - \rho)) ds + zG(\epsilon) \right] \right\},\end{aligned}$$

where $M \equiv I(t^*) \exp[-z(g + \mu(1 - \rho)) + zG(\epsilon)]$. As $R_0^{(6.29)} > 1$, it is possible to choose $\epsilon > 0$ so that

$$\phi(\epsilon) \equiv \left[\int_0^z (\beta_{\sigma(s)}(\tilde{S}(s)(1 - \xi) + \xi) - g - \mu(1 - \rho)) ds - zG(\epsilon) \right] > 0.$$

This leads to the contradiction that $I(t) \geq M \exp[(k-1)\phi(\epsilon)]$. Thus, there exists a time $t^1 > t^*$ such that $I(t^1) \geq \eta$ and the disease is weakly uniformly persistent. Since $\dot{I}(t) \geq -(g + \mu(1 - \rho))I(t)$, the rest of the proof follows similarly to the proof of Theorem 4.5.

Example 6.2 Consider (6.29) with $\mathcal{M} = \{1, 2\}$ and periodic switching rule outlined in (3.37). Let the initial conditions be given by $(S_0, I_0, V_0) = (0.8, 0.2, 0)$ and suppose that the model parameters are given as $\beta_1 = 1/3$, $\beta_2 = 1/10$, $\gamma_1 = \gamma_2 = 1/20$, $g = 1/8$, $\mu = 1/60$, $\rho = 1/20$, $\theta = 1$, and $b = 0.5$. In the uncontrolled case

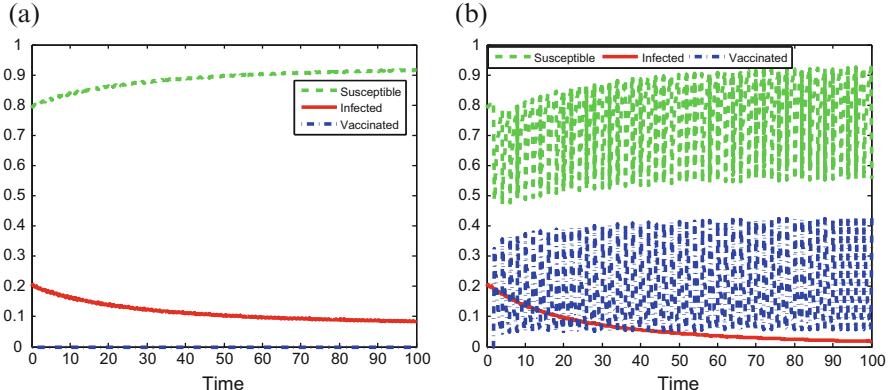


Fig. 6.5 Simulations of Example 6.2. (a) $v = 0$. (b) $v = 0.4$

($v = 0$), $\tilde{R}_0^{(6.29)} = 1.12$ (see Fig. 6.5a). However, vaccination rate $v = 0.4$, inter-pulse period $T = 2$, and vaccine failure rate $\xi = 0.1$ implies that $\tilde{R}_0^{(6.29)} = 0.91$ (see Fig. 6.5b).

6.1.6 Multi-City Vaccination Efforts

In Sect. 5.4, the strategy of exit and entry screening was discussed as restricting travel is an important tool for preventing epidemic outbreaks. Those findings are compared in this section to an impulsive control strategy. A pulse vaccination scheme applied to a multi-city SIR model with population dispersal was investigated by, for example, Yang and Xiao [167]. Assume that a fraction $0 \leq p^{(j)} \leq 1$ of infected individuals in city $j \in \mathcal{N} \equiv \{1, \dots, n\}$ are given a pulse treatment periodically (i.e., every $T > 0$ time units), immediately moving them to the recovered class. Similarly, assume that a fraction $0 \leq v^{(j)} \leq 1$ of susceptible individuals in city $j \in \mathcal{N}$ are successfully given a pulse vaccination every T time units, and enter the vaccinated class, denoted by $V^{(j)}$. As in the previous sections, vaccine failure is considered here: assume that individuals who have been vaccinated exhibit an incidence rate of new cases that is reduced by a switching constant $\xi_{\sigma}^{(j)}$ in city $j \in \mathcal{N}$, where $\xi_i^{(j)} \in [0, 1]$ for each $i \in \mathcal{M}$ and $j \in \mathcal{N}$. Moreover, suppose that the incidence rate of new infections takes on the general form $f_{i_k}^{(j)}$ in city $j \in \mathcal{N}$ on the k th switching interval. With these assumptions and an immigration rate of $m^{(j)} \geq 0$ in city $j \in \mathcal{N}$, (4.21) is given by the following switched impulsive system:

$$\begin{aligned}
\dot{S}^{(j)}(t) &= m^{(j)} - f_\sigma^{(j)}(S^{(j)}(t), I^{(j)}(t), N^{(j)}(t)) - \mu^{(j)} S^{(j)}(t) \\
&\quad + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(l)}(t) - \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} h_\sigma^{(l,j)}(S^{(l)}(t), I^{(l)}(t), N^{(l)}(t)), \\
\dot{I}^{(j)}(t) &= f_\sigma^{(j)}(S^{(j)}(t), I^{(j)}(t), N^{(j)}(t)) + \xi_\sigma^{(j)} f_\sigma^{(j)}(V^{(j)}(t), I^{(j)}(t), N^{(j)}(t)) \\
&\quad - (g^{(j)} + \mu^{(j)}) I^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} I^{(l)}(t) \\
&\quad + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} h_\sigma^{(l,j)}(S^{(l)}(t), I^{(l)}(t), N^{(l)}(t)), \\
\dot{R}^{(j)}(t) &= g^{(j)} I^{(j)}(t) - \mu^{(j)} R^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} R^{(l)}(t), \\
\dot{V}^{(j)}(t) &= -\xi_\sigma^{(j)} f_\sigma^{(j)}(V^{(j)}(t), I^{(j)}(t), N^{(j)}(t)) - \mu^{(j)} V^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} V^{(l)}(t),
\end{aligned} \tag{6.36}$$

for all $t \in \mathbb{R}_+ \setminus \{kT\}$ and $j \in \mathcal{N}$, with impulsive equations

$$\begin{aligned}
S^{(j)}(t) &= (1 - v^{(j)}) S^{(j)}(t^-), & I^{(j)}(t) &= (1 - p^{(j)}) I^{(j)}(t^-), \\
V^{(j)}(t) &= V^{(j)}(t^-) + v^{(j)} S^{(j)}(t^-), & R^{(j)}(t) &= R^{(j)}(t^-) + p^{(j)} I^{(j)}(t^-),
\end{aligned}$$

for $t \in \{kT\}$, and initial conditions

$$(S^{(j)}(0), I^{(j)}(0), R^{(j)}(0), V^{(j)}(0)) = (S_0^{(j)}, I_0^{(j)}, R_0^{(j)}, V_0^{(j)}), \quad \forall j \in \mathcal{N}.$$

Each city or patch has population $N^{(j)} \equiv S^{(j)} + I^{(j)} + R^{(j)} + V^{(j)}$. The meaningful physical domain for (6.36) is given as

$$D_{(6.36)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^{4n} : \sum_{j \in \mathcal{N}} S^{(j)} + I^{(j)} + R^{(j)} + V^{(j)} \leq N^*\},$$

where

$$N^* \equiv \frac{\sum_{j \in \mathcal{N}} m^{(j)}}{\min\{\mu^{(1)}, \mu^{(2)}, \dots, \mu^{(n)}\}} > 0.$$

Given an initial condition, the unique solution of (6.36) enters (in finite or infinite time) $D_{(6.36)}$; $D_{(6.36)}$ is positively invariant to (6.36) (this follows from Proposition 2.1 in [167]). The flow associated with (6.36) is given in Fig. 6.6.

Assuming that $I^{(j)} \equiv 0$ for all $j \in \mathcal{N}$, it is apparent that each $R^{(j)}$ converges to zero. Then, the limiting system is given by

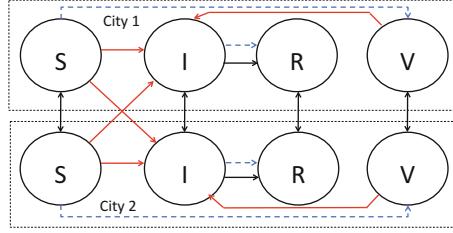


Fig. 6.6 Flow of the switched multi-city system (6.36) with $n = 2$. The red lines represent disease transmission (within cities, from traveling individuals, and from vaccine failures) and the dashed blue lines represent the pulse treatment/vaccination schemes. The population dynamics within each city have been omitted here

$$\left. \begin{aligned} \dot{S}^{(j)}(t) &= m^{(j)} - \mu^{(j)} S^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(j)}(t), \\ \dot{V}^{(j)}(t) &= -\mu^{(j)} V^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} V^{(j)}(t), \end{aligned} \right\} \quad t \neq t_0 + kT, \quad (6.37)$$

$$\left. \begin{aligned} S^{(j)}(t) &= (1 - v^{(j)}) S^{(j)}(t^-), \\ V^{(j)}(t) &= V^{(j)}(t^-) + v S^{(j)}(t^-), \end{aligned} \right\} \quad t = t_0 + kT.$$

Following the procedure of [167], we adopt the following notation: let $A \equiv (\alpha_{lj})_{1 \leq l, j \leq n}$, $P \equiv \text{diag}\{v_1, v_2, \dots, v_n\}$, $m \equiv (m_1, m_2, \dots, m_n)$, and $U \equiv \text{diag}\{\mu_1, \mu_2, \dots, \mu_n\}$. Lemma 2.2 in [167] implies that the solution of (6.37) converges to the periodic solution given by

$$\begin{aligned} \widetilde{S}(t) &\equiv [E + \exp((A - U)(t - kT))[((E - P^{-1}) \\ &\quad - \exp((A - U)T))^{-1} [\exp((A - U)T) - E] + E]](A - U)^{-1}m, \\ \widetilde{V}(t) &\equiv \exp((A - U)(t - kT))(E - \exp((A - U)T))^{-1}P[-(A - U)^{-1}m \\ &\quad + \exp((A - U)T)(W^* + (A - U)^{-1}m)], \end{aligned} \quad (6.38)$$

for $t \in [(k - 1)T, kT]$, where

$$W^* \equiv ((E - P)^{-1} - \exp((A - U)T))^{-1}(\exp((A - U)T) - E)(A - U)^{-1}m,$$

E is the $n \times n$ identity matrix, and the notation is understood as $\widetilde{S} \equiv (\widetilde{S}^{(1)}, \widetilde{S}^{(2)}, \dots, \widetilde{S}^{(n)})$ and $\widetilde{V} \equiv (\widetilde{V}^{(1)}, \widetilde{V}^{(2)}, \dots, \widetilde{V}^{(n)})$. The original system of interest (6.36) thus admits the periodic disease-free solution

$$Q_{\text{DFS}}^{(6.36)}(t) \equiv (\widetilde{S}(t), 0, 0, \widetilde{V}(t)).$$

The basic reproduction number associated with (6.36) can again be defined as the spectral radius of an integral operator, using a next-generation derivation, but cannot be calculated explicitly. Instead, an eradication theorem is derived via an approximate basic reproduction number.

Theorem 6.9 Assume that there exist $\beta_i > 0$, $\gamma_i > 0$, and $\xi_i \in [0, 1]$ such that $f_i^{(j)}(S^{(j)}, I^{(j)}, N^{(j)}) \leq \beta_i S^{(j)} I^{(j)} / N^{(j)}$, $h_i^{(l,j)}(S^{(l)}, I^{(l)}, N^{(l)}) \leq \gamma_i S^{(l)} I^{(l)} / N^{(l)}$, and $\xi_i^{(j)} \leq \xi_i$ for each $i \in \mathcal{M}$, $l, j \in \mathcal{N}^2$ such that $l \neq j$. Assume that there exist constants α_{\max} , α_{\min} , p , v , and continuous functions \tilde{S}^* and \tilde{V}^* such that $\alpha_{\min} \leq \alpha^{(l,j)} \leq \alpha_{\max}$, $p \leq p^{(j)}$, $v \leq v^{(j)}$, $\tilde{S}^{(j)}(t) \leq \tilde{S}^*(t)$ and $\tilde{V}^{(j)}(t) \leq \tilde{V}^*(t)$ for $j \in \mathcal{N}$ and $t \geq 0$. If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$\overline{R}_0^{(6.36)} \equiv \frac{\frac{1}{z} \int_0^z (\beta_\sigma [\tilde{S}^*(t) + \xi_\sigma \tilde{V}^*(t)] + (n-1)\alpha_{\max} \gamma_\sigma \tilde{S}^*(t)) dt}{g + \mu - \frac{1}{T} \ln(1-p)} < 1, \quad (6.39)$$

and $z \equiv \text{lcm}(T, \omega)$, then the solution of system (6.36) converges to the disease-free solution $Q_{\text{DFS}}^{(6.36)}$.

Proof From Eq. (6.36),

$$\begin{aligned} \dot{S}^{(j)}(t) &\leq m_j - \mu_j S^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} S^{(j)}(t), \\ \dot{V}^{(j)}(t) &\leq -\mu^{(j)} V^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} V^{(j)}(t), \end{aligned}$$

for each $j \in \mathcal{N}$. Consider the following comparison system (compare to the reduced system):

$$\begin{aligned} \dot{x}^{(j)}(t) &= m_j - \mu^{(j)} x^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} x^{(j)}(t), & t \neq kT, \\ \dot{y}^{(j)}(t) &= -\mu^{(j)} y^{(j)}(t) + \sum_{l \in \mathcal{N}} \alpha^{(l,j)} y^{(j)}(t), \\ x^{(j)}(t) &= (1 - v^{(j)}) x^{(j)}(t^-), & t = kT, \\ y^{(j)}(t) &= y^{(j)}(t^-) + v^{(j)} x^{(j)}(t^-), \\ (x^{(j)}(0), y^{(j)}(0)) &= (S_0^{(j)}, V_0^{(j)}). \end{aligned} \quad (6.40)$$

The unique solution of (6.40) satisfies

$$\lim_{t \rightarrow \infty} \|(x^{(j)}(t), y^{(j)}(t)) - (\tilde{S}^{(j)}(t), \tilde{V}^{(j)}(t))\| = 0, \quad \forall j \in \mathcal{N}.$$

Choose ϵ to satisfy

$$0 < \epsilon = \frac{(1 - \overline{R}_0^{(6.36)})(g + \mu - \frac{1}{T} \ln(1-p))}{\frac{2}{z} \int_0^z (\beta_\sigma (1 + \xi_\sigma) + (n-1)\alpha_{\max} \gamma_\sigma) dt}.$$

Then, there exists a time t^* such that $S^{(j)}(t) \leq x^{(j)}(t) \leq \tilde{S}^{(j)}(t) + \epsilon$ and $V^{(j)}(t) \leq y^{(j)}(t) \leq \tilde{V}^{(j)}(t) + \epsilon$ for $t \geq t^*$. Let N be the smallest integer satisfying $Nz > t^*$ and let i_k follow the switching rule $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$. For $t \in [t_{k-1}, t_k]$,

$$\begin{aligned} \sum_{j \in \mathcal{N}} \dot{I}^{(j)}(t) &= \sum_{j \in \mathcal{N}} [f_k^{(j)}(S^{(j)}(t), I^{(j)}(t)) + \xi_k^{(j)} f_k^{(j)}(V^{(j)}(t), I^{(j)}(t)) - g^{(j)} I^{(j)} - \mu^{(j)} I^{(j)} \\ &\quad + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} h_k^{(l,j)}(S^{(l)}(t), I^{(l)}(t))], \\ &\leq \sum_{j \in \mathcal{N}} (\beta_k [S^{(j)}(t) I^{(j)}(t) + \xi_k V^{(j)}(t) I^{(j)}(t)] - g I^{(j)}(t) - \mu I^{(j)}(t) \\ &\quad + \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} \gamma_k S^{(l)}(t) I^{(l)}(t)). \end{aligned}$$

Observe that

$$\begin{aligned} \sum_{j \in \mathcal{N}} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} S^{(l)} I^{(l)} &= \sum_{j \in \mathcal{N}} \sum_{l \in \mathcal{N} \setminus \{j\}} \alpha^{(l,j)} S^{(l)} I^{(l)}, \\ &\leq \sum_{j \in \mathcal{N}} (n-1) \alpha_{\max} S^{(l)} I^{(l)}, \end{aligned}$$

from which it follows that

$$\begin{aligned} \sum_{j \in \mathcal{N}} \dot{I}^{(j)}(t) &\leq \sum_{j \in \mathcal{N}} [\beta_k ((\tilde{S}^{(j)}(t) + \epsilon) + \xi_k (\tilde{V}^{(j)}(t) + \epsilon)) - g - \mu \\ &\quad + (n-1) \alpha_{\max} \gamma_k (\tilde{S}^{(j)}(t) + \epsilon)] I^{(j)}(t), \\ &\leq \sum_{j \in \mathcal{N}} [\beta_k (\tilde{S}^*(t) + \xi_k (\tilde{V}^*(t))) + (n-1) \alpha_{\max} \gamma_k \tilde{S}^*(t) \\ &\quad + \epsilon (\beta_k (1 + \xi_k) + (n-1) \alpha_{\max} \gamma_k) - g - \mu] I^{(j)}(t), \\ &= \lambda_{k,\epsilon}(t) \sum_{j \in \mathcal{N}} I_j(t), \end{aligned} \tag{6.41}$$

for $t \in [t_{k-1}, t_k)$, where

$$\begin{aligned} \lambda_{i,\epsilon}(t) &\equiv \beta_i (\tilde{S}^*(t) + \xi_k \tilde{V}^*(t)) + (n-1) \alpha_{\max} \gamma_i \tilde{S}^*(t) \\ &\quad + \epsilon (\beta_i (1 + \xi_i) + (n-1) \alpha_{\max} \gamma_i) - g - \mu, \end{aligned} \tag{6.42}$$

for each $i \in \mathcal{M}$. Equation (6.41) thus implies

$$\begin{aligned} & \sum_{j \in \mathcal{N}} I^{(j)}((N+1)z) \\ & \leq \sum_{j \in \mathcal{N}} I^{(j)}(Nz)(1-p)^{z/T} \exp\left\{\int_{Nz}^{t_1+Nz} \lambda_{1,\epsilon}(t)dt + \dots + \int_{t_{m-1}+Nz}^{t_m+Nz} \lambda_{m,\epsilon}(t)dt\right. \\ & \quad \left.+ \dots + \int_{(N+1)z-\omega}^{(N+1)z-\omega+\tau_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{(N+1)z-\tau_m}^{(N+1)z} \lambda_{m,\epsilon}(t)dt\right\}, \\ & = \exp\left\{\frac{z}{T} \ln(1-p) + \int_0^{t_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t)dt\right\} \sum_{j \in \mathcal{N}} I^{(j)}(Nz), \end{aligned}$$

from which it follows that $\sum_{j \in \mathcal{N}} I^{(j)}((N+1)z) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}(Nz)$, where

$$\eta(\epsilon) \equiv \exp\left\{\frac{z}{T} \ln(1-p) + \int_0^{t_1} \lambda_{1,\epsilon}(t)dt + \dots + \int_{z-\tau_m}^z \lambda_{m,\epsilon}(t)dt\right\}.$$

The condition $\overline{R}_0^{(6.36)} < 1$ implies that $\eta(\epsilon) < 1$ by the choice of ϵ above. Thus,

$$\sum_{j \in \mathcal{N}} I^{(j)}((N+1)z) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}(Nz) < \sum_{j \in \mathcal{N}} I^{(j)}(Nz).$$

Similarly, it can be shown that $\sum_{j \in \mathcal{N}} I^{(j)}((N+h+1)z) \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h)z)$ for any integer $h \in \mathbb{N}$. Therefore,

$$\begin{aligned} \sum_{j \in \mathcal{N}} I^{(j)}((N+h+1)z) & \leq \eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h)z), \\ & \leq \eta(\eta \sum_{j \in \mathcal{N}} I^{(j)}((N+h-1)z)), \\ & \vdots \\ & \leq \eta^{h+1} \sum_{j \in \mathcal{N}} I^{(j)}(Nz). \end{aligned}$$

Hence, the sequence $\{\sum_{j \in \mathcal{N}} I^{(j)}((N+h)z^+)\}_{h=0}^\infty$ converges to zero monotonically. Since $I^{(j)}$ is bounded on $0 \leq t \leq Nz$ for each $j \in \mathcal{N}$ and since $\sum_{j \in \mathcal{N}} I^{(j)}$ is bounded on each interval $[(N+h)z, (N+h+1)z]$ for $h \in \mathbb{N} \cup \{0\}$,

$$\lim_{t \rightarrow \infty} I^{(j)}(t) = 0, \quad \forall j \in \mathcal{N}.$$

The limiting system of (6.36) is then given by Eq. (6.37), from which the result follows by the analysis above.

Given a vaccination rate $v \leq v^{(j)}$, requiring $\widehat{R}_0^{(6.36)} < 1$ in Eq. (6.39) defines a critical pulse treatment portion p_{crit} such that $p^{(j)} \geq p > p_{\text{crit}}$ guarantees disease eradication, where

$$p_{\text{crit}} \equiv 1 - \exp \left[-\frac{T}{z} \left(\int_0^{t_1} \lambda_{1,0}(t) dt + \dots + \int_{z-\tau_m}^z \lambda_{m,0}(t) dt \right) \right], \quad (6.43)$$

with $\lambda_{i,0}(t)$ given in Eq. (6.42). Similarly, given a pulse treatment rate $p \leq p^{(j)}$, $\widehat{R}_0^{(6.36)} < 1$ defines a critical pulse vaccination rate v_{crit} , which may be found explicitly depending on the model's parameters. Moreover, the familiar trade-off between the pulse treatment rates, the pulse vaccination rates, and the inter-pulse period T is again apparent: if T is decreased then eradication can be achieved with decreased impulsive control rates (i.e., $p^{(j)}$ and $v^{(j)}$). Similarly, if T is increased then the impulsive control rates must also be increased, given the model's parameters, in order to achieve eradication. This motivates the consideration of different inter-pulse periods in different patches (i.e., $T^{(j)}$ in city $j \in \mathcal{N}$).

Example 6.3 Consider (6.36) with $\mathcal{N} = \{1, 2\}$, $\mathcal{M} = \{1, 2\}$ and suppose that σ follows the seasonal switching rule outlined in (3.37). Let the initial conditions be given by $(S^{(1)}, I^{(1)}, R^{(1)}, V^{(1)}, S^{(2)}, I^{(2)}, R^{(2)}, V^{(2)}) = (0.5, 0.1, 0, 0, 0.4, 0, 0, 0)$ (i.e., the disease begins in city 1). The following model parameters are used: $\beta_1 = 4.5$, $\beta_2 = 0.5$, $g^{(1)} = 1.5$, $g^{(2)} = 1.2$, $m^{(1)} = 0.1$, $m^{(2)} = 0.09$, $\mu^{(1)} = 0.1$, $\mu^{(2)} = 0.09$, $\gamma = 1$, $\alpha^{(1,1)} = -0.4$, $\alpha^{(1,2)} = 0.4$, $\alpha^{(2,2)} = -0.3$, $\alpha^{(2,1)} = 0.3$. Let the inter-pulse period be given by $T = 2$ and suppose that $p^{(1)} = p^{(2)} = 0.5$, then $\widehat{R}_0^{(6.36)} = 0.958$ and eradication is achieved by Theorem 6.9 (see Fig. 6.7a). If instead $v^{(1)} = 0.25$, $v^{(2)} = 0.2$, and the vaccine failure rate is given by $\xi = 0.1$, then $\widehat{R}_0^{(6.36)} = 0.930$ (see Fig. 6.7b). The critical control rates are calculated as $p_{\text{crit}} = 0.457$ and $v_{\text{crit}} = 0.186$, respectively; pulse vaccination requires a significantly lower control rate as compared to the pulse treatment scheme. Moreover, both strategies have the advantage of being able to reduce the control rate by pulsing more often (compare to the screening process in Example 5.7).

6.1.7 Pulse Vaccination Strategies for a Vector-Borne Disease

Returning to the vector-borne disease model outlined in Sect. 4.3, impulsive control applied at pre-specified times, as well as state-dependent impulsive control, is proposed and analyzed in this part.

1. Assume that at the pre-specified times $\{T_k\}$, a fraction $v_k \in [0, 1]$ of the susceptible population is given a vaccination (and immediately move to the vaccinated class, V).

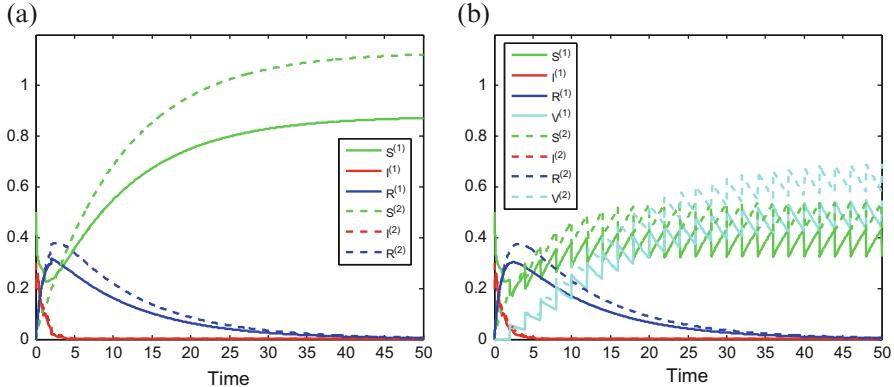


Fig. 6.7 Simulations of Example 6.3. (a) $p^{(1)} = p^{(2)} = 0.5$. (b) $v^{(1)} = 0.25, v^{(2)} = 0.2$

2. Assume that the pulse vaccination scheme is periodic; let $T > 0$ and $N \in \mathbb{N}$ such that the following conditions are satisfied:
 - (a) $\sum_{k=1}^N \bar{T}_k = T$ with $T_k - T_{k-1} \equiv \bar{T}_k$;
 - (b) $T_{k+N} = T_k + T$ and $v_{k+N} = v_k$ for each $k \in \mathbb{N}$;
 - (c) $\bar{T}_k \geq d$ for each $k \in \mathbb{N}$.
3. Adopt vaccine failure (with probability $\xi \in [0, 1]$), waning immunity (with rate $\theta > 0$), and a switching treatment control $p_\sigma \geq 0$.

Applying the control strategy to (4.35) gives the following switched and impulsive system:

$$\left. \begin{array}{l} \dot{S}(t) = \mu(1 - S(t)) - \beta_\sigma S(t) \int_0^d f(u) I(t-u) du + \theta V(t) \\ \dot{I}(t) = \beta_\sigma S(t) \int_0^d f(u) I(t-u) du - (\mu + g + p_\sigma) I(t) \\ \dot{R}(t) = (g + p_\sigma) I(t) - \mu R(t) \\ \dot{V}(t) = -\beta_\sigma \xi V(t) \int_0^d f(u) I(t-u) du - (\mu + \theta) V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{T_k\},$$

$$\left. \begin{array}{l} S(t) = (1 - v_k) S(t^-) \\ I(t) = I(t^-) \\ R(t) = R(t^-) \\ V(t) = V(t^-) + v_k S(t^-) \end{array} \right\} \forall t \in \{T_k\},$$

$$(S(s), I(s), R(s), V(s)) = (S_0, I_0(s), R_0, V_0), \quad \forall s \in [-d, 0], \tag{6.44}$$

where $S_0, R_0, V_0 \in \mathbb{R}_+$ and $I_0 \in PC([-d, 0], \mathbb{R}_+)$ such that

$$(S_0, I_0(0), R_0, V_0) \in D_{(6.44)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : S + I + R + V = 1\}.$$

The existence of a disease-free solution is sought before performing a stability analysis. As has been the case in the pulse vaccination strategies outlined in this chapter, $(1, 0, 0, 0)$ is not an equilibrium point of (6.44) but $I(t) \equiv 0$ is a solution for the equations governing the variable I . Under this assumption, the fraction of individuals in the recovered class approaches zero and (6.44) reduces to

$$\begin{aligned} \dot{\bar{S}}(t) &= \mu(1 - S(t)) + \theta V(t) \\ \dot{\bar{V}}(t) &= -(\mu + \theta)V(t) \\ S(t) &= (1 - v_k)S(t^-) \\ V(t) &= V(t^-) + v_k S(t^-) \\ (S(0), V(0)) &= (S_0, V_0), \end{aligned} \quad \left. \begin{array}{l} \dot{\bar{S}}(t) = (\mu + \theta)(1 - S(t)) \\ \dot{\bar{V}}(t) = -(\mu + \theta)V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{T_k\}, \quad (6.45)$$

where $S + V = 1$ is an invariant of (6.45). Rewriting the differential equation for S as

$$\dot{\bar{S}}(t) = (\mu + \theta)(1 - S(t))$$

reveals that (6.45) converges to (\bar{S}, \bar{V}) defined by

$$\begin{aligned} \bar{S}(t) &\equiv 1 + (\bar{S}_{j-1} - 1) \exp(-(\mu + \theta)(t - kT - T_j)), \quad \forall t \in [kT + T_{j-1}, kT + T_j], \\ \bar{V}(t) &\equiv 1 - \bar{S}(t), \quad \forall j \in \{1, 2, \dots, N\}, \forall k \in \mathbb{N}, \end{aligned} \quad (6.46)$$

where

$$\begin{aligned} \bar{S}_j &\equiv \sum_{l=1}^j \left\{ (1 - v_l)(1 - \exp(-(\mu + \theta)\bar{T}_l)) \prod_{q=l+1}^N [(1 - v_q) \exp(-(\mu + \theta)\bar{T}_q)] \right\} \\ &\quad + \left\{ \prod_{l=1}^j [(1 - v_l) \exp(-(\mu + \theta)\bar{T}_l)] \right\} \bar{S}_0, \quad \forall j \in \{1, 2, \dots, N\}, \end{aligned}$$

and

$$\bar{S}_0 \equiv \frac{\sum_{l=1}^N \left\{ (1 - v_l)(1 - \exp(-(\mu + \theta)\bar{T}_l)) \prod_{q=l+1}^N [(1 - v_q) \exp(-(\mu + \theta)\bar{T}_q)] \right\}}{1 - \exp(-(\mu + \theta)T) \prod_{l=1}^N (1 - v_l)}.$$

(This follows from Lemma 2.2 [59].) Equation (6.44) therefore admits the periodic disease-free solution $Q_{\text{DFS}}^{(6.44)}(t) \equiv (\bar{S}(t), 0, 0, \bar{V}(t))$. Disease eradication under a dwell-time condition on the switching is derived.

Before proceeding, the following definitions are needed:

$$\lambda_i \equiv \beta_i(\bar{S}_{\max} + \xi \bar{V}_{\max}) - (\mu + g + p_i), \quad \forall i \in \mathcal{M},$$

where $\widetilde{S}_{\max} \equiv \max\{\widetilde{S}(t) : 0 \leq t \leq T\}$ and $\widetilde{V}_{\max} \equiv \max\{\widetilde{V}(t) : 0 \leq t \leq T\}$. Let $\mathcal{M}^- \equiv \{i \in \mathcal{M} : \lambda_i < 0\}$ and $\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \lambda_i \geq 0\}$ (i.e., the set of stable and unstable modes, respectively). The reader is reminded here of the following switched systems notions: given $\sigma \in \mathcal{S}_{\text{dwell}}$, $t^2 > t^1 \geq 0$, let

$$\begin{aligned} T^+(t^1, t^2) &\equiv |\{t \in (t^1, t^2) : \sigma(t) \in \mathcal{M}^+\}|, \\ T^-(t^1, t^2) &\equiv |\{t \in (t^1, t^2) : \sigma(t) \in \mathcal{M}^-\}|, \\ N^-(t^1, t^2) &\equiv |\{t_k \in [t^1, t^2] : \sigma(t_k) \in \mathcal{M}^-\}|. \end{aligned}$$

Theorem 6.10 *For each $i \in \mathcal{M}^-$, let η_i satisfy*

$$\eta_i + \beta_i(\widetilde{S}_{\max} + \xi\widetilde{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i) < 0.$$

Let $\lambda^+ \equiv \max\{\lambda_i : i \in \mathcal{M}^+\}$ and $\lambda^- \equiv \min\{\eta_i : i \in \mathcal{M}^-\}$. If $\sigma \in \mathcal{S}_{\text{dwell}}(d)$ such that there exists $M > 0$ and $\widetilde{t} > 0$ satisfying Eq. (5.50) and there exists $q \geq 0$ such that $T^+(\widetilde{t}, t) \leq q(T^-(\widetilde{t}, t) - N^-(\widetilde{t}, t)d)$ and $q\lambda^+ < \lambda^-$, then the solution of (6.44) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.44)}$.

Proof The differential equation for S in (6.44) implies that

$$\begin{aligned} \dot{S}(t) &= \mu(1 - S(t)) - \beta_\sigma S(t) \int_0^d f(u)I(t-u)du + \theta V(t), \\ &\leq \mu(1 - S(t)) + \theta(1 - S(t) - I(t)), \\ &\leq (\mu + \theta)(1 - S(t)), \quad \forall t \in \mathbb{R}_+ \setminus \{T_k\}, \end{aligned}$$

and

$$\dot{V}(t) \leq -(\mu + \theta)V(t), \quad \forall t \in \mathbb{R}_+ \setminus \{T_k\}.$$

These observations invoke the use of the following comparison system:

$$\begin{cases} \dot{x}(t) = (\mu + \theta)(1 - x(t)) \\ \dot{y}(t) = -(\mu + \theta)y(t) \end{cases} \quad \forall t \in \mathbb{R}_+ \setminus \{T_k\},$$

$$\begin{cases} x(t) = (1 - v_k)x(t^-) \\ y(t) = V(t^-) + v_kx(t^-) \end{cases} \quad \forall t \in \{T_k\},$$

$$(x(0), y(0)) = (S_0, V_0),$$

which, by the observations above regarding (6.45), admits a unique solution on \mathbb{R}_+ that converges to $(\widetilde{S}, \widetilde{V})$. Since $S(t) \leq x(t)$ and $V(t) \leq y(t)$ for all $t \geq 0$, then for any $\epsilon > 0$ there exists a time $t^* \geq 0$ such that $S(t) \leq \widetilde{S}(t) + \epsilon \leq \widetilde{S}_{\max} + \epsilon$ and $V(t) \leq \widetilde{V}(t) + \epsilon \leq \widetilde{V}_{\max} + \epsilon$ for $t \geq t^*$. Without loss of generality, supposing that

$t^* \in [t_l, t_{l+1})$ for some $l \in \mathbb{N}$. Then

$$\dot{I}(t) \leq \beta_\sigma [\tilde{S}_{\max} + \epsilon] + \xi (\tilde{V}_{\max} + \epsilon) - (\mu + g + p_\sigma), \quad \forall t \geq t_l. \quad (6.47)$$

The remainder of the proof follows from the proof of Theorem 5.10 and by the properties of the reduced system (6.45) as outlined above.

In the case that the inter-pulse period and vaccination rates are constant in time (i.e., $T_k \equiv kT$ and $v_k \equiv v$ for each $k \in \mathbb{N}$), the periodic disease-free solution $Q_{\text{DFS}}^{(6.44)}$ of (6.44) simplifies to

$$\begin{aligned} \tilde{S}(t) &= 1 - \frac{v \exp(-(\mu + \theta)(t - (k-1)T))}{1 - (1-v) \exp(-(\mu + \theta)T)}, \quad \forall t \in [(k-1)T, kT), \\ \tilde{V}(t) &= 1 - \tilde{S}(t), \quad \forall k \in \mathbb{N}. \end{aligned} \quad (6.48)$$

(See, for example, Lemma 2.2 of [49].) A disease eradication condition can be given which can be proved similarly as Theorem 5.10 using the bound from Eq. (6.47).

Theorem 6.11 Suppose that $T_k \equiv kT$, $v_k \equiv v$ and $\sigma \in \mathcal{S}_{\text{periodic}}$ such that $\tau_i \geq d$ for each $i \in \mathcal{M}$. Let $\lambda_i \equiv \beta_i(\tilde{S}_{\max} + \xi \tilde{V}_{\max}) - (\mu + g + p_i)$ for all $i \in \mathcal{P}$ where

$$\tilde{S}_{\max} \equiv 1 - \frac{v \exp(-(\mu + \theta)T)}{1 - (1-v) \exp(-(\mu + \theta)T)}, \quad \tilde{V}_{\max} \equiv \frac{v}{1 - (1-v) \exp(-(\mu + \theta)T)}.$$

For each $i \in \mathcal{M}^-$, let $\eta_i > 0$ satisfy

$$\eta_i + \beta_i(\tilde{S}_{\max} + \xi \tilde{V}_{\max}) \exp(\eta_i d) - (\mu + g + p_i) < 0.$$

If

$$\Lambda_{\text{time-pulse}} \equiv \sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d) < 0, \quad (6.49)$$

then the solution of system (6.44) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.44)}$, where \tilde{S} and \tilde{V} are given in (6.48).

Of note, Eq. (6.49) implies that an approximate basic reproduction number $\widehat{R}_0^{(6.44)} < 1$ where

$$\widehat{R}_0^{(6.44)} \equiv \frac{\sum_{i \in \mathcal{M}^+} \beta_i (\tilde{S}_{\max} + \xi \tilde{V}_{\max}) h_i + \sum_{i \in \mathcal{M}^-} \beta_i \exp(\eta_i \tau) (\tilde{S}_{\max} + \xi \tilde{V}_{\max}) (h_i - \tau)}{\sum_{i \in \mathcal{M}^+} (\mu + g + c_i) h_i + \sum_{i \in \mathcal{M}^-} (\mu + g + c_i) (h_i - \tau)}. \quad (6.50)$$

The method of state-dependent pulse vaccination has been first studied recently and not analyzed as extensively as the classical pulse vaccination and treatment methods (for example, Nie et al. [121] proposed and analyzed such a control scheme for an SIR model). The strategy is motivated by the observations in Sect. 6.1

(in particular, (6.1)): whenever $S \geq S_{\text{crit}}$ at some time $t = t_{\text{crit}}^-$, apply an impulsive vaccination to reduce the susceptible population below the appropriate threshold, i.e., so that $S(t_{\text{crit}}) = (1 - v)S_{\text{crit}}$. Along with the other assumptions of waning immunity and vaccine failure (dictated here by a coefficient $\xi \in [0, 1]$ multiplied by the time-varying contact rate), the vector-borne disease model (4.35) takes the following form:

$$\left. \begin{array}{l} \dot{S}(t) = \mu(1 - S(t)) - \beta_\sigma S(t) \int_0^d f(u)I(t-u)du + \theta V(t) \\ \dot{I}(t) = \beta_\sigma(S(t) + \xi I(t)) \int_0^d f(u)I(t-u)du - (\mu + g - p_\sigma)I(t) \\ \dot{R}(t) = (g + p_\sigma)I(t) - \mu R(t) \\ \dot{V}(t) = -\beta_\sigma \xi V(t) \int_0^d f(u)I(t-u)du - (\mu + \theta)V(t) \end{array} \right\} S < S_{\text{crit}},$$

$$\left. \begin{array}{l} S(t) = (1 - v)S(t^-) \\ I(t) = I(t^-) \\ R(t) = I(t^-) \\ V(t) = V(t^-) + vS(t^-) \end{array} \right\} S \geq S_{\text{crit}}, \quad (6.51)$$

with initial condition

$$(S(s), I(s), R(s), V(s)) = (S_0, I_0(s), R_0, V_0), \quad \forall s \in [-d, 0],$$

where $S_0, R_0, V_0 \in \mathbb{R}_+$ and $I_0 \in PC([-u, 0], \mathbb{R}_+)$ satisfy

$$(S_0, I_0(0), R_0, V_0) \in D_{(6.51)} \equiv \{(S, I, R, V) \in \mathbb{R}_+^4 : S + I + R + V = 1\}.$$

Here it is assumed that $v > 0$ to make (6.51) mathematically well-posed at the vaccination moments. If $S_0 > S_{\text{crit}}$, then the initial time is a critical time and, according to (6.51), an impulse is immediately applied. Depending on the magnitude of the vaccination rate v , it may be that $\lim_{t \rightarrow 0^+} S(t) > S_{\text{crit}}$ is still satisfied, necessitating another pulse vaccination to be applied. Mathematically, multiple impulses (i.e., $l \in \mathbb{N}$) could be required at the initial time. In practical terms, this translates to a single pulse vaccination with magnitude equal to the summation of the vaccination rates lv applied at the initial time so that $\lim_{t \rightarrow 0^+} S(t) < S_{\text{crit}}$. Assuming that $S_0 < S_{\text{crit}}$ is therefore reasonable here and the solution S of (6.51) must satisfy $S(t) \leq S_{\text{crit}}$ for all $t > 0$ under this scheme.

Given that $I(t) \equiv 0$, (6.51) reduces to the following ODE system with state-dependent impulses:

$$\left. \begin{array}{l} \dot{S}(t) = (\mu + \theta)(1 - S(t)), \\ \dot{V}(t) = -(\mu + \theta)V(t), \end{array} \right\} S < S_{\text{crit}},$$

$$\left. \begin{array}{l} S(t) = (1 - v)S(t^-), \\ V(t) = V(t^-) + vS(t^-), \end{array} \right\} S \geq S_{\text{crit}}, \quad (6.52)$$

From this, it follows that the periodic disease-free solution is given by the following functions:

$$\begin{aligned}\widetilde{S}(t) &\equiv 1 + ((1-v)S_{\text{crit}} - 1) \exp(-(\mu + \theta)(t - T_{k-1})), \quad t \in [T_{k-1}, T_k), \\ \widetilde{V}(t) &\equiv 1 - \widetilde{S}(t), \quad k = 1, 2, \dots,\end{aligned}\tag{6.53}$$

which is globally attractive in the meaningful domain associated with (6.52). As a consequence, (6.51) has a periodic disease-free solution given by $Q_{\text{DFS}}^{(6.51)} \equiv (\widetilde{S}, 0, 0, \widetilde{V})$. The impulsive times $\{T_k\}$ outlined in (6.53) are the critical times detailed above and are functions of the susceptible state, i.e., $t_{\text{crit}} = T_k(S)$. The impulsive times are not known a priori because of this, however, the inter-pulse period for the steady-state disease-free solution can be calculated as

$$T_k - T_{k-1} = \frac{\ln(1 - (1-v)S_{\text{crit}}) - \ln(1 - S_{\text{crit}})}{\mu + \theta}, \quad \forall k \in \mathbb{N}.$$

Let $V_{\text{crit}} \equiv 1 - (1-v)S_{\text{crit}}$ and $\lambda_i \equiv \beta_i(S_{\text{crit}} + \xi V_{\text{crit}}) - (\mu + g + p_i)$ for each $i \in \mathcal{M}$. A dwell-time eradication condition can be established as follows.

Theorem 6.12 *For each $i \in \mathcal{M}^-$, let $\eta_i > 0$ satisfy*

$$\eta_i + \beta_i(S_{\text{crit}} + \xi V_{\text{crit}}) \exp(\eta_i d) - (\mu + g + p_i) < 0.$$

If $\sigma \in \mathcal{S}_{\text{dwell}}(d)$ and there exist $M > 0$, $\tilde{t} > 0$, and $q \geq 0$ such that Eq. (5.50) holds and

$$T^+(\tilde{t}, t) \leq q(T^-(\tilde{t}, t) - N^-(0, t)d), \tag{6.54}$$

$$q\lambda^+ < \lambda^-, \tag{6.55}$$

then the solution of (6.51) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.51)}$.

Proof By construction, the solution of (6.51) satisfies $S(t) \leq S_{\text{crit}}$ and $V(t) \leq V_{\text{crit}}$ for all $t \in \mathbb{R}_+$. It follows that for any $t \in [t_{k-1}, t_k]$,

$$\dot{I}(t) \leq (\beta_\sigma[S_{\text{crit}} + \xi V_{\text{crit}}] - (\mu + g))I(t). \tag{6.56}$$

Therefore, $\lim_{t \rightarrow \infty} I(t) = 0$ and, by the same arguments as the proof of Theorem 5.9, the system reduces to (6.52). The result then follows by global attractivity of $Q_{\text{DFS}}^{(6.51)}$.

A periodic result can also be given in the state-dependent pulse vaccination case (along the lines of the proof of Theorem 5.10 using the bound (6.56) established above).

Theorem 6.13 Define V_{crit} , λ_i , \mathcal{M}^- , \mathcal{M}^+ , and η_i as in Theorem 6.12. If $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$ and

$$\Lambda_{\text{state-pulse}} \equiv \sum_{i \in \mathcal{M}^+} \lambda_i \tau_i - \sum_{i \in \mathcal{M}^-} \eta_i (\tau_i - d) < 0, \quad (6.57)$$

then the solution of (6.51) converges to the periodic disease-free solution $Q_{\text{DFS}}^{(6.51)}$.

From Eq. (6.57), it follows that $\tilde{R}_0^{(6.51)} < 1$ where

$$\tilde{R}_0^{(6.51)} \equiv \frac{\sum_{i \in \mathcal{M}^+} \beta_i (S_{\text{crit}} + \xi V_{\text{crit}}) \tau_i + \sum_{i \in \mathcal{M}^-} \beta_i (S_{\text{crit}} + \xi V_{\text{crit}}) (\tau_i - d)}{\sum_{i \in \mathcal{M}^+} (\mu + g + p_i) \tau_i + \sum_{i \in \mathcal{M}^-} (\mu + g + p_i) (\tau_i - d)} \quad (6.58)$$

and $\tilde{R}_0^{(6.51)}$ can be interpreted as an approximate basic reproduction number.

6.2 Discussions

Some of the impulsive switched systems stability techniques here follow the lines of [54, 55] (e.g., Theorems 6.2 and 6.3). In Sect. 6.1, a number of vaccination strategies were analyzed: Application of pulse vaccination to the classical SIR model (3.9) (where derivations from [138] were used to illustrate the mechanisms of pulse vaccination) and switched SIR model (3.8) in Sect. 6.1.1. The addition of pulse treatment was considered in Sect. 6.1.2, extensions to general switched incidence rates were considered in Sect. 6.1.3, and the role vaccine failures play was studied in Sect. 6.1.4. These findings largely reflect and extend the works in [94, 96].

The impulsive control of an SIS model with media coverage and switching was proposed and analyzed in Sect. 6.1.5, based on the theory in [98]. More specifically, an SIVS model with pulse vaccination, vertical transmission, term-time forcing, waning immunity, and media coverage is explored, where the inter-pulse period does not necessarily equal the period of term-time forcing (extending the work in [36, 83]). The strategies outlined in Sects. 6.1.6 and 6.1.7, vaccination strategies for multi-city and vector-borne models, extend the screening scheme and switching control schemes in the previous chapter and are drawn from the analyses in [97] and [143], respectively.

Some of the discussions made in Sect. 3.7 are also applicable to the material in this chapter (and the previous one on switching control). For example, extensions of the results to time-varying switching model parameters are straightforward (and have been made in some of the aforementioned works above). Moreover, extensions to epidemic models with other underlying physical assumptions is also possible due to the flexibility of the theory here. For example, echoing the complications with progressive immunity (see (5.13)), consider the following complication: individuals that are vaccinated can become infected, but at a reduced level of infectivity. Motivated by the study in [36], [94] considered a switched SIR model with an

additional compartment for the infected, I^R , for the reduced infectives. Due to inefficacy of the vaccination, individuals in this group exhibit a reduced contact rate β_i^R which satisfies $\beta_i^R < \beta_i$ for each $i \in \mathcal{M}$ (i.e., a reduced transmission rate). Furthermore, suppose the recovery rate in this class, $g^R > 0$, satisfies $g^R > g$ (i.e., a reduced average infectious period). The incidence rate associated with this group is given by $\xi\beta_i SI(S + I + I^R + R + V)$, for each $i \in \mathcal{M}$, where $\xi \in [0, 1]$ represents the inefficacy of the vaccination. Assume that the vaccination gives temporary immunity (with a mean vaccine-induced immunity period $1/\theta > 0$). The dynamic system is written as

$$\left. \begin{array}{l} \dot{S}(t) = \mu - (\beta_\sigma I(t) + \beta_\sigma^R I^R(t))S(t) - \mu S(t) + \theta V(t) \\ \dot{I}(t) = S(t)(\beta_\sigma I(t) + \beta_\sigma^R I^R(t)) - (g + \mu)I(t) \\ \dot{I}^R(t) = \xi V(t)(\beta_\sigma I(t) + \beta_\sigma^R I^R(t)) - (g^R + \mu)I^R(t) \\ \dot{R}(t) = (g + g^R)I(t) - \mu R(t) \\ \dot{V}(t) = -\xi V(t)(\beta_\sigma I(t) + \beta_\sigma^R I^R(t)) - (\mu + \theta)V(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{kT\},$$

$$\left. \begin{array}{l} S(t) = (1-p)S(t^-) \\ I(t) = (1-p)I(t^-) \\ I^R(t) = (1-p)I^R(t^-) \\ R(t) = R(t^-) + pI(t^-) + pI^R(t^-) \\ V(t) = V(t^-) + pS(t^-) \end{array} \right\} \forall t \in \{kT\},$$

$$(S(0), I(0), I^R(0), R(0), V(0)) = (S_0, I_0, I_0^R, R_0, V_0), \quad (6.59)$$

with physical domain

$$D_{(6.59)} \equiv \{(S, I, I^R, R, V) \in \mathbb{R}_+^5 : S + I + I^R + V + R = 1\}.$$

(which is an invariant of (6.59)). The basic reproduction number associated with each mode is

$$R_0^{(6.59),i} \equiv \frac{\beta_i}{\mu + g} + \frac{\xi\beta_i^R}{\mu + g^R}. \quad (6.60)$$

Eradication results can be shown by observing the following bound:

$$\begin{aligned} \dot{I}(t) + \dot{I}^R(t) &= [\beta_\sigma(S(t) + \xi V(t)) - (\mu + g)]I(t) \\ &\quad + [\beta_\sigma^R(S(t) + \xi V(t)) - (g^R + \mu)]I^R(t). \end{aligned}$$

(See Sect. 3.4 in [94].)

In [89], Liu et al. presented a switched and impulsive system invariance principle applicable to an SEIR model under hybrid control (see Theorem 5.1 in [89]). More specifically, the SEIR switching model (5.24) is considered, but with an impulsive

treatment control strategy and switching parameters for the birth/death rate μ_i , recovery rate g_i , average incubating period $1/a_i$ (in addition to switching parameters for the contact rate β_i):

$$\left. \begin{array}{l} \dot{S}(t) = \mu_\sigma - \beta_\sigma S(t)I(t) - \mu_\sigma S(t) \\ \dot{E}(t) = \beta_\sigma S(t)I(t) - a_\sigma E(t) - \mu_\sigma E(t) \\ \dot{I}(t) = a_\sigma E(t) - g_\sigma I(t) - \mu_\sigma I(t) \\ \dot{R}(t) = g_\sigma I(t) - \mu_\sigma R(t) \end{array} \right\} \forall t \in \mathbb{R}_+ \setminus \{t_k\},$$

$$\left. \begin{array}{l} S(t) = S(t^-) \\ E(t) = (1 - p_k)E(t^-) \\ I(t) = (1 - p_k)I(t^-) \\ R(t) = R(t^-) + p_k E(t^-) + p_k I(t^-) \end{array} \right\} \forall t \in \{t_k\},$$

$$(S(0), E(0), I(0), R(0)) = (S_0, E_0, I_0, R_0), \quad (6.61)$$

i.e., $p_k \in [0, 1]$ for all $k \in \mathbb{N}$ represents the treatment. Recall the mode basic reproduction numbers of (6.61), as outlined in (5.25),

$$R_0^{(6.61),i} \equiv \frac{\beta_i a_i}{(\mu_i + g_i)(\mu_i + a_i)}, \quad \forall i \in \mathcal{M},$$

and disease-free solution as the point $Q_{\text{DFS}}^{(6.61)} \equiv (1, 0, 0, 0)$. Using a multiple Lyapunov functions approach and switching invariance principle, a suitable theorem can be given which guarantees eradication under pulse treatment using the multiple Lyapunov functions $V_i(E, I) \equiv a_i E + (a_i + \mu_i)I$ for $i \in \mathcal{M}$ and the impulsive control to satisfy Assumption 2.1 in [89]. The reader is also referred to the work [117] for a study of pulse vaccination of SEIR models with time delays.

6.2.1 Comparison of Control Schemes

A range of constraints and trade-offs influence the choice of control strategy in practice and must be considered. For example [69]:

1. There may be logistical limitations, in terms of the maximum number of units of vaccine that can be given in a certain time frame, or epidemiological, such as adverse reactions to a particular vaccine.
2. Economic considerations should also be included in epidemiological models, since control schemes should be judged through cost-benefit analyses.

The desirability of implementing a new type of control strategy depends on two factors [1]: the risks attached to the scheme and the costs of implementation and long-term maintenance.

In the continuous vaccination schemes of the previous chapter, the vaccination affects the amplitude and the period of the epidemic, but it does not antagonize the underlying dynamics of the disease [139]. For example, in the newborn vaccination model (5.1), the birth rate of susceptibles is effectively reduced. Pediatric immunization programs are already established in many countries, and any pulse vaccination strategy is likely to be in addition to a continuous immunization strategy rather than an alternative [69]. However, many countries have encountered difficulties in eliminating the spread of diseases with cohort immunization, even when the vaccination coverage is relatively high [1]. The critical vaccination level required for measles eradication is about 94%, and 86% for rubella, and the vaccine efficacy for these diseases is approximately 95% (5% of those who are immunized do not gain immunity) [65]. (Therefore, to reach the necessary levels to achieve herd immunity, at least 99% would need to be immunized for measles and 91% for rubella.) As a result, a two-dose program is usually employed, which has been implemented in some countries [65]. Of course, even if a vaccination program does not eradicate a disease, it can still be useful in reducing the prevalence of the infection [69].

In contrast to (switching) continuous control, pulse control strategies are based on the suggestion that epidemics can be more effectively controlled when the involved temporal processes are antagonized [138, 139], and have been shown to lead to disease eradication at relatively low values of vaccination [1]. Recent research shows that pulse vaccination strategy might be an optimal choice in cases of highly infectious diseases outbreaks, such as a new smallpox epidemic [38]. Pulse vaccination is gaining prominence as a strategy for the elimination of childhood infections such as measles, rubella (for example, the UK vaccination campaign in 1994 [138]) parotitis, and phthisis [110]. Pulse vaccination strategies also have the additional advantage of often being simpler to implement logically [69] (compare to continuous newborn vaccination (5.1)). For other types of control schemes, such as quarantine, ring vaccination and targeted vaccination, as well as how they compare, see [69].

In this section, we highlight some of the differences in cost-effectiveness of control strategies. To begin, we detail the analysis from the important work [138]. Here we are motivated by an interest in calculating total number of vaccinations required in the newborn vaccination scheme versus a pulse vaccination strategy; the number of people requiring the vaccination every inter-pulse period T in the pulse vaccination strategy might be close to the number of newborns requiring vaccination over the same period in the newborn continuous vaccination scheme.

Let the cost of a vaccination control program be equal to the number of individuals requiring vaccination (following [138]). In the constant vaccination scheme (5.1), the number of individuals vaccinated per time unit is $N(v) \equiv v\mu$. In the pulse vaccination scheme, the average number of people requiring vaccination per time unit is

$$N(v, T) \equiv \frac{1}{T} v \widetilde{S}(kT^-), \quad k \in \mathbb{N},$$

where $p\widetilde{S}(kT^-)$ is the number of individuals in the susceptible population that are given a pulse vaccination at $t = kT$. Using a Taylor series expansion,

$$\widetilde{S}(kT^-) = \frac{\exp(\mu T) - 1}{v - 1 + \exp(\mu T)} \approx \frac{\mu T}{v + \mu T}.$$

Thus,

$$N(v, T) \approx \frac{v\mu}{v + \mu T},$$

which is minimized when T is maximized; i.e., when $T = T_{\max}^1$ from (6.8), giving that

$$N(v, T_{\max}^1) \approx \mu - \frac{\mu g}{\beta(1 - v/2)} \approx \mu.$$

The minimum number of vaccinations required for pulse vaccination is approximately μ (independent of v). Note that regardless of the vaccination rate v (and associated inter-pulse time T_{\max}), roughly the same number of individuals are vaccinated. Compared to the newborn continuous control scheme cost $N(v) = v\mu$, the costs associated with the strategies are approximately equal when $v \approx 1$.

Returning to the switched vector-borne disease models (i.e., in Sects. 5.5 and 6.1.7), we proceed with a cost-benefit analysis to evaluate the different control strategies outlined (i.e., switching immunization in (5.42), pulse control at pre-specified moments in (6.44), and state-dependent pulse vaccination in (6.51)). In the following simulations, the initial conditions are taken as $(S_0, I_0, R_0, V_0) = (0.9, 0.1, 0, 0)$ and the model parameters are those found in Sect. 5.5 (see Table 5.1).

The effects of varying the switching contact rate, recovery rate, birth/death rate, and upper bound on the distributed delays are investigated next. As the total number of infected cases is of interest, a total constant population of $N_0 = 1,000,000$ is considered. The effects of these model parameters on the disease spread are illustrated in Fig. 6.8. An increase in the number of contacts results in a significant increase in the disease spread, while increasing the rate of recovery or natural death rate leads to a decrease in total number of infections. If the natural birth/death rate is sufficiently low, then the total number of infective cases decreases due to a decrease in the influx of new susceptibles. As the incubation times are increased (by increasing the upper bound d), the epidemic worsens.

For the control schemes we differentiate between cohort immunization of the susceptible population ($p_\sigma > 0, \rho_\sigma = 0$) and cohort immunization of newborns ($p_\sigma = 0, \rho_\sigma > 0$). See Table 6.1 for the values of the control parameters (the epidemiological parameters in Table 5.1 are used again here).

The maximum thresholds for the pulse vaccination scheme at pre-specified times are $\widetilde{S}_{\max} = 0.8698$ and $\widetilde{V}_{\max} = 0.3911$ (i.e., $\lambda_1 = 4.1971$ and $\eta_2 = 1.7$). In this case, $\Lambda_{\text{time-pulse}} = -0.0557$ for this control strategy and the solution converges to

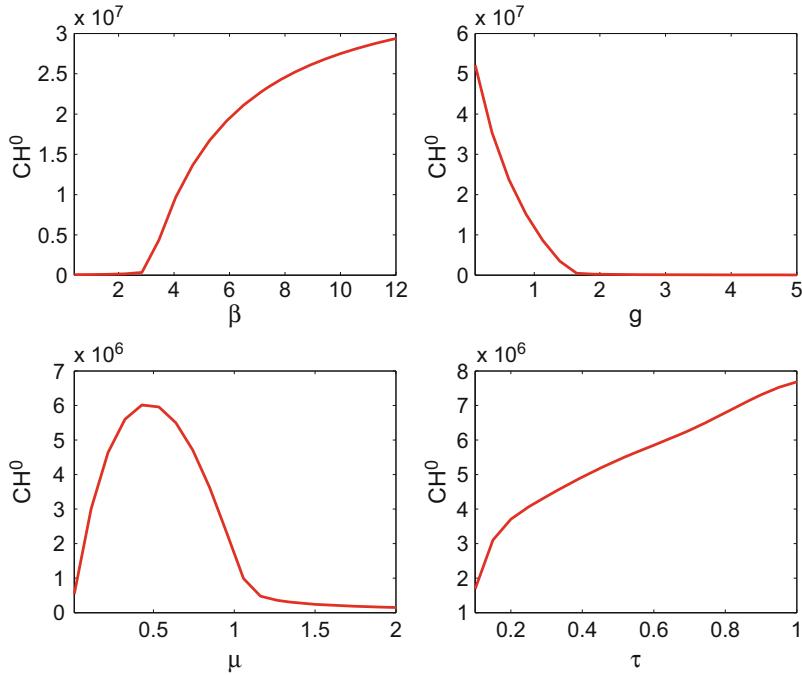


Fig. 6.8 Cumulative number of infections, C_H^0 , of system (4.35) as different model parameters are varied. Here β is the average contact rate over the period ω (i.e., $\beta = \beta_1 \times \tau_1 + \beta_2 \times \tau_2$)

Table 6.1 Control parameters

Control parameter	Description	Value
p_σ	Immunization rate for the susceptible population	[3, 2]
θ	Rate of waning immunity	0.1
ρ_σ	Immunization rate for newborns	[0.6, 0.4]
c_σ	Treatment rate	[2, 0.5]
ξ	Vaccine failure	0.3
v_k	Pulse vaccination rate	0.3
$T_k - T_{k-1}$	Inter-pulse period	1
S_{crit}	Critical threshold	0.3

The parameter values given in brackets represent the switching value associated with $\sigma = 1$ and $\sigma = 2$, respectively

the periodic disease-free solution by Theorem 6.11. In the state-dependent pulse vaccination scheme, $S_{\text{crit}} = 0.3$, $V_{\text{crit}} = 0.79$, $\lambda_1 = 0.5960$, and $\eta_2 = 0.25$. By Theorem 6.13, the disease is eradicated since $\Lambda_{\text{state-pulse}} = -0.0135$. For the simulations, see Fig. 6.9.

We proceed by measuring the efficacy of the aforementioned control schemes, considering the difference between the number of infected cases with and without

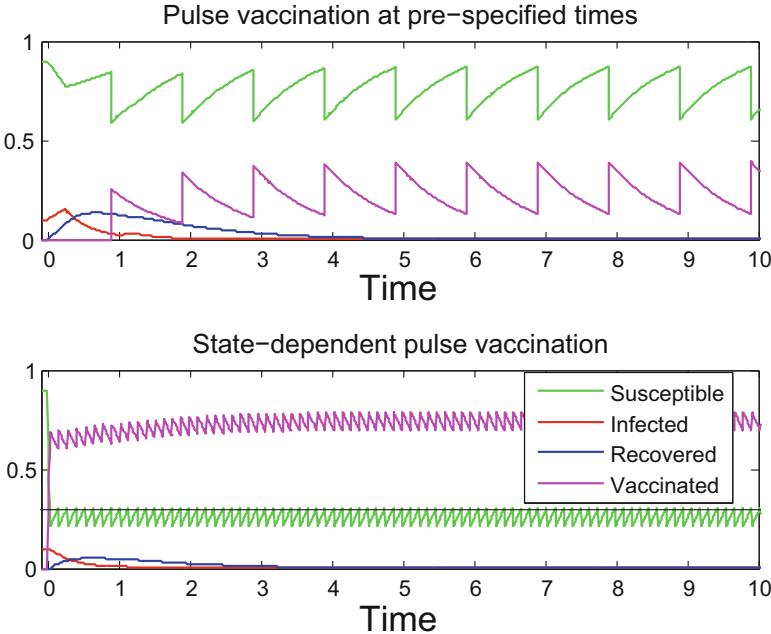


Fig. 6.9 Simulations of the different control schemes with parameters given in Tables 5.1 and 6.1. The *horizontal black line* in the state-dependent pulse vaccination simulation represents the critical threshold S_{crit}

control. The control efficacy rating [41] used is given by

$$F_0 \equiv 100 \frac{C_H^c}{C_H^0},$$

where C_H^c and C_H^0 are the cumulative number of humans infected with control and without control, respectively. For the simulations we use the epidemiological parameter values in Table 5.1, with β_σ replaced as $\beta_1 = 30$ and $\beta_2 = 6$. For the switching cohort immunization strategy, the relationship between the control rates (p_σ) and the duration of the strategy (denoted by t_c) and the efficacy measure F_0 is studied. For the pulse vaccination scheme at pre-specified times, different inter-pulse periods $T_k - T_{k-1} = T$ and vaccination rates $v_k = v$ are considered. In the state-dependent pulse vaccination scheme, F_0 is calculated under varying vaccination rates $v_k = v$ and varying critical thresholds for the susceptible population, S_{crit} .

The following observations on the control efficacy ratings (as illustrated in Fig. 6.10) are made:

1. Aside from the state-dependent pulse vaccination scheme, the control strategies have an inverse relationship between F_0 and their control rate (p_σ and v).

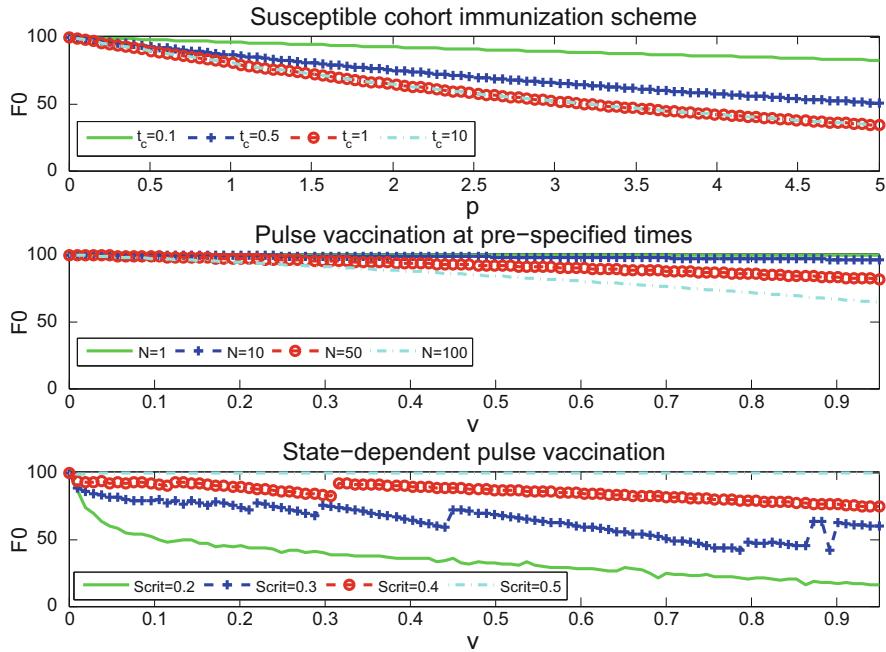


Fig. 6.10 Control efficacy ratings for the vector-borne control strategies; the parameters p and v represent averages of p_σ and v_σ , respectively, over one period ω of the switching rule σ

2. In the state-dependent pulse vaccination scheme, the relationship is roughly inverse but F_0 is not strictly decreasing as a function of v . Because of this, it may be possible to achieve greater control efficacies at lower rates of control.
3. The efficacy increases (i.e., F_0 decreases) in all strategies by either increasing the duration of the scheme (in the case of cohort immunization), increasing the total number of impulses (in the case of pulse vaccination at pre-specified times), or decreasing the threshold pulse value S_{crit} (in the case of state-dependent pulse vaccination).
4. The cohort scheme seems to have a maximum efficient duration, above which increasing the duration has negligible effects; the response during the initial epidemic outbreak is the most important.
5. The best control efficacy ratings are achieved in the state-dependent pulse vaccination strategy.

To take economic costs of the control programs into account (which is not accomplished by the control efficacy measure F_0), assume that the cost of administering a vaccination to the susceptible population is the same across the control strategies. For $C_H^0 \neq C_H^c$, let

$$\chi \equiv \frac{\psi}{C_H^0 - C_H^c}$$

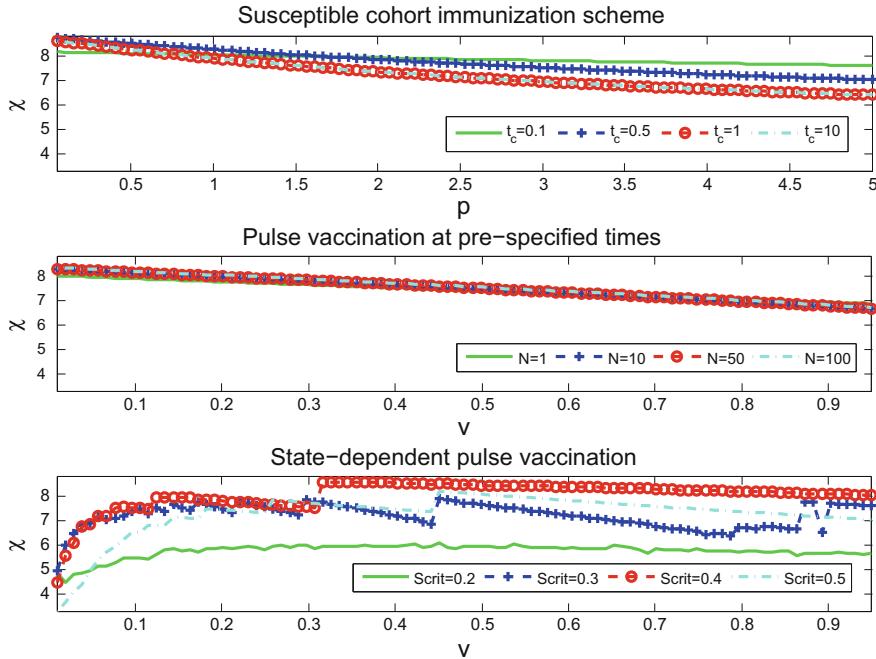


Fig. 6.11 Cost-benefit analysis

where Ψ is the total number of vaccinations administered from the beginning of the control scheme to the end; χ can be viewed as the cost of the control scheme (measured in total vaccinations administered) normalized by the program benefit (as measured by the number of individuals that do not contract the disease because of the control scheme). See Fig. 6.11 for the results.

From Fig. 6.11, we are in a position to make some observations and draw some conclusions regarding the cost-benefit scenarios of the control strategies outlined above:

1. From a cost-benefit perspective, state-dependent pulse vaccination performs the best.
2. Increasing the vaccination rate is not necessarily the best course of action when costs are taken into account. In some cases, the costs can outweigh the benefits for high vaccination rates (this is particularly apparent in the state-dependent pulse case).
3. For the pulse vaccination scheme at pre-specified times, the benefit of increasing the number of total impulses seems to be offset by the cost of increased vaccinations. On the other hand, increasing the vaccination rate v seems to have a non-negligible positive impact on the cost-benefit ratio of the scheme.

4. In the switching cohort program, increasing the duration or the control rate outweighs the cost of additional vaccinations and is therefore beneficial for the population.
5. The state-dependent vaccination strategy cost-benefit ratios behave differently from the other strategies; the graphs are neither strictly increasing nor strictly decreasing. Decreasing the critical threshold S_{crit} seems to increase the benefit (decreases χ), indicating that the best possible strategy is to apply a pulse vaccination to a small fraction of the susceptible population with a small critical value for S_{crit} . The results on the state-dependent pulse vaccination scheme warrant further investigations.

Chapter 7

A Case Study: Chikungunya Outbreak in Réunion

This chapter is devoted to analyzing the spread of the chikungunya virus, a vector-borne disease, modeled here according to interactions between human and mosquito populations. After introducing the full model, the remainder of this chapter focuses on studying the efficacy of different control strategies. This modeling approach is in contrast to the study of a general vector-borne disease model in Sect. 4.3, where the different time scales involved for the human and mosquito populations evolution allowed for a modeling simplification via a decoupling of the vector dynamics. The motivation for studying both approaches is to properly frame the problem by building an intuition of both models' underlying dynamics and to be able to see the differences between the two modeling methods. Once the model is formulated and analyzed, a case study of the 2005–06 chikungunya outbreak in Réunion is completed. Here, the mosquito birth rate is modeled as a time-varying switching parameter, to incorporate differences between the rainy season and dry season. Variations in the contact rate between mosquitoes and humans are also considered, as well as a genetic mutation in the virus. Control strategies are analyzed and evaluated for comparison (e.g., destruction of breeding sites, reduced contact rates).

7.1 Background

Transmitted primarily by mosquitoes of the *Aedes* genus (i.e., *Aedes aegypti* and *Aedes albopictus* [114, 125]), the chikungunya virus is a vector-borne viral disease. Symptoms of a chikungunya infection usually include a sudden onset of fever and incapacitating arthralgia (i.e., non-inflammatory joint pain) and are often accompanied by rash, headache, and muscle pain with less frequent symptoms of nausea and vomiting [125, 126]. First isolated in 1953 in Tanzania [126], a series of outbreaks have occurred in the past decade over a geographic area including African islands in the Indian Ocean and the Indian subcontinent: the first outbreak was in

Kenya in 2004, followed by outbreaks on the Comoros Islands in early 2005 and in India in 2005–06 where the World Health Organization reported an estimated 1.3 million cases [26, 125–127].

On April 29, 2005 a confirmed case of chikungunya virus was reported on the island of Réunion (a French island located east of Madagascar), the virus was imported from Grande-Comore. This resulted in an outbreak of chikungunya virus in Réunion in 2005 and 2006, which consisted of two epidemic waves: the first occurred in May 2005, with 450 reported cases. The second, and much larger wave, began in December 2005, peaking in January and February 2006 with more than 47,000 estimated cases [126]. In total, there were about 244,000 estimated cases during the outbreak [113, 126], which is approximately one third of the island's population [41]. This chapter's main focus is studying the outbreak in Réunion as a case study.

A crucial role in the spread of vector-borne diseases are seasonal fluctuations in the environment. For example, the transmission of dengue (transmitted by *Aedes aegypti*) is low when the temperature is low [126, 165] and similarly transmission is high when the temperature is high, during wet and humid periods. The island of Réunion experienced an outbreak in 2005 between March and June, which corresponds to the beginning of the winter season and the end of the hot season (when the mosquito population is at a maximum) [42]. In Réunion, another factor that played an important role in the outbreaks was that two strains of the virus appeared [41]: the first strain was isolated in May 2005 during the first outbreak while the second strain, isolated in November 2005, had a higher rate of transmission from human to mosquito. As a result it was demonstrated by those authors [41] that the probability of a mosquito contracting the infection by biting an infected human increased from 37% for the first strain to 95% for the second strain.

Conventional strategies for preventing chikungunya outbreaks involve the interruption of contact between humans and vectors (e.g., individual protection against mosquito bites) or the control of the mosquito population [114]. Measures to control the *Aedes albopictus* vector population were used in Réunion when the DRASS (an agency of the French government for disease prevention and vector control) conducted several interventions [41]. These included massive spraying of Deltamethrin (a chemical adulticide) and localized treatment of a chemical larvicide BTI (*Bacillus thuringiensis israelensis*), as well as the mechanical destruction of breeding sites by eliminating standing water in rain gutters, buckets, plastic covers, tires, tree holes, or any other potential breeding site for mosquitoes. In [41], Dumont and Chiroleu noted that compared to adulticide, larvicide treatments do not have a relatively large impact on a chikungunya epidemic. A potential explanation was given by the authors, that this may be because only breeding sites are treated with the larvicide, which can be very localized. Adulticides can cause harm to the environment [41, 114, 126] and in some areas *Aedes* have rapidly developed resistances to adulticides (for example, up to 60% resistances for Deltamethrin) [114]. Mechanical controls are effective with the cooperation of the local population and are sustainable, relatively cheap, and can be effective depending on the duration and time of initiation [41]. A new strategy has been recently proposed and studied called the sterile insect technique where sterile male insects are periodically released into the wild to control the vector population [40, 43].

There has been an increased interest in studying chikungunya, motivated by the outbreaks in the last decade and the possibility for chikungunya virus to re-emerge after an absence of years or even decades [126]. Dumont et al. [42] were the first authors to analyze a mathematical model based on the chikungunya outbreak in Réunion. The authors computed the basic reproduction number of the disease, proved a necessary condition for eradication of the disease, and presented several simulations of the outbreak in different cities on the island. Dumont and Chiroleu [41] were the first authors to consider vector control for the outbreak in Réunion. The authors did this by analyzing and comparing the use of adulticide, larvicide, and mechanical control. In [43], Dumont and Tchuench, by analyzing the use of sterile insects, helped prevent the spread of chikungunya disease by vector population control. Dufourd and Dumont [40] more recently have studied the effects of periodic parameters on the temporal and spatio-temporal evolution of a vector population under the sterile insect technique. In [113], Moulay et al. investigated a chikungunya model for the outbreak in Réunion with embryonic, larvae, and adult stages for the vector population. Stability was proven by the authors using the theory of competitive systems and Lyapunov function methods. The authors Moulay et al. [114] studied optimal control of the chikungunya disease by considering vector control (using larvicide, larvivore fish, and water traps) reducing the number of vector-host contacts, and treatment of individuals (such as by isolating infected patients in hospitals). The authors Bowong et al. [21] investigated a multi-city model for chikungunya-like diseases where humans are able to travel between the cities.

By considering a periodic model of chikungunya disease and approximating the basic reproduction number numerically, Bacaër[7] studied the Réunion outbreak. Bacaër noted that many chikungunya models in the literature make the inappropriate assumption that the vector population is constant in time, however, seasonality plays an important role in the spread of the disease [7]. From Réunion weather data (e.g., see Fig. 1 in [7]), rainfall and temperature appear to achieve a maximum around February and a minimum around July. Therefore, it is reasonable to suppose that there is a peak in the vector population each year when rainfall is high [7]. Indeed, Dumont et al. [42] stated that one way to improve their work would be to add weather parameters, such as humidity and temperature. Dumont and Chiroleu [41] concluded that due to changes in temperature and humidity, one possible improvement to their model would be to consider periodicity in some of the parameters in the mosquito population. In [33], Delatte showed that the survival rate of adult *Aedes albopictus* is inversely correlated to the temperature. Hence, the vector is therefore able to survive the dry season, which could be a possible explanation for why the chikungunya virus survived from June to October 2005 in Réunion [41].

By analyzing control schemes with time-varying parameters, we aim to provide a more detailed model of the chikungunya disease outbreak in Réunion. More specifically, the birth rate of the vector population is assumed to be a switching parameter (to model a time-varying birth rate from wet season to dry season) and the transmission rate of the disease is assumed to change in time (due to shifts in the contact rate between humans and mosquitoes throughout the year). The possibility

of a genetic mutation is also taken into account in the model as a switching parameter. Mechanical control of breeding sites and a reduction of contact rates between humans and mosquitoes are considered. The contributions of this chapter are to further extend current knowledge on vector population control methods and human–mosquito interaction interruption methods.

7.2 Human–Mosquito Interaction Mechanisms

To begin, a stage structured compartmental dynamic model of the vector population is formulated. It is noted that for *Aedes albopictus*, the vector roughly remains in the area in which it was born, given that it has suitable conditions to develop and survive (e.g., blood and sugar meals). Moreover, it has an expected adult life of approximately 10–11 days [41]. The life cycle of a vector consists of four stages (in order):

1. embryonic stage;
2. larvae stage;
3. pupae stage; and
4. adult stage.

The first three stages require significant amounts of water while the final stage does not [113]. Motivated by the chikungunya model in [113], assume that the vector population is broken into three distinct compartments: the embryonic stage, denoted by E , which consists of eggs; the aquatic stage, denoted by Q , which includes the larvae and pupae stages; and the adult stage, denoted by A . Note that the main motivation for separating the embryonic stage from the aquatic stage is because mechanical control of breeding sites is not successful in destroying eggs, since they can cling to surfaces and are desiccation-resistant [113]. The following assumptions are made:

1. The embryonic and aquatic life cycles of the vector population have a limited carrying capacity (due to the constraints on water levels and nutrients). (This was first considered in [42] and also in [41, 113].)
2. The carrying capacity of the habitat for the eggs is given by $\Gamma_E > 0$ and the carrying for the aquatic stages is given by $\Gamma_Q > 0$.
3. The rate of transfer from embryonic stage to aquatic stage is $\eta_E > 0$ and the rate of transfer from aquatic stage to adult stage is $\eta_Q > 0$.
4. The death rate of mosquitoes in the embryonic stage is $d_E > 0$ and the death rate of aquatic mosquitoes is $d_Q > 0$.

For a large mosquito population, the number of exposed but not yet infectious vectors is a negligible part of the total population [113]. As a consequence, two adult mosquito population compartments are considered ($A \equiv S^{(M)} + I^{(M)}$):

- (a) the susceptible vector population, denoted by $S^{(M)}$, for adult mosquitoes that do not carry the virus but are able to contract the disease from biting an infected human; and
- (b) the infected vector population, denoted by $I^{(M)}$, for adult mosquitoes that are infected with the virus and able to transmit it to healthy humans.

Assume that the death rate of susceptible mosquitoes is given by $d_S > 0$ and the death rate of infected mosquitoes is given by $d_I > 0$. As noted in [7, 41], the average lifespan of infected mosquitoes is approximately 5 days, and, after contracting the disease, the vectors of chikungunya remain infected until they die. Since the average lifespan of susceptible adult mosquitoes is approximately 10 days (detailed above), assume that $1/d_S > 1/d_I$ so that $d_I > d_S$.

The rainy season lasts from November until March in Réunion, during which the climatic conditions lead to an increase in the number of breeding sites for *Aedes albopictus* (and hence a larger population of susceptible mosquitoes). As a result, the carrying capacity of the vector population increases [42]. Studying the re-emergence of chikungunya virus in 2001–2003 in Indonesia, Laras et al. [79] observed a negligible variability in average monthly 24-h maximum–minimum ambient temperatures but did note significant seasonal fluctuations in rainfall. In August 2001, there was an increase in rainfall, which corresponds to the start of an epidemic outbreak lasting from September to December 2001 [79]. The Asian tiger mosquito's life-span is also strongly related to the temperature and humidity, which can vary greatly depending on the region [42].

Motivated by these seasonal fluctuations in the vector population, consider a term-time forced vector birth rate b_σ (i.e., the birth rate is a switching parameter assuming values in the set $\{b_1, b_2, \dots, b_m\}$ where $b_i > 0$). The parameter changes values at the switching times t_k , which depend on changes from the rainy season to dry season. Throughout this chapter, it is assumed that the switching rule satisfying a nonvanishing dwell-time (i.e., $\sigma \in \mathcal{S}_{\text{dwell}}$). The dynamics of the vector population is modeled by the switched system

$$\begin{aligned}\dot{E}(t) &= b_\sigma \left(1 - \frac{E(t)}{\Gamma_E}\right) A(t) - (\eta_E + d_E) E(t), \\ \dot{Q}(t) &= \eta_E \left(1 - \frac{Q(t)}{\Gamma_Q}\right) E(t) - (\eta_Q + d_Q) Q(t), \\ \dot{A}(t) &= \eta_Q Q(t) - d_I I^{(M)}(t) - d_S S^{(M)}(t).\end{aligned}\tag{7.1}$$

In [41, 42, 113, 114], the authors made the assumption that the average number of contacts per day, which results in a mosquito becoming infected, is constant in time (i.e., $\gamma > 0$). Moreover, that the per capita incidence rate among mosquitoes is modeled by

$$\gamma \frac{I^{(H)}}{N^{(H)}}$$

where $I^{(H)}$ represents the infected human population (individuals who have been infected with the disease and are able to transmit it to a mosquito if they are bitten) and $N^{(H)}$ is the total human population. Such an incidence rate structure takes into account frequency of bites and encounters between susceptible mosquitoes and infectious humans. This is extended here by considering an effective contact rate that varies in time. Assume that the contact rate sufficient for transmission of the disease from human to mosquito is equal to the switching parameter $\gamma_\sigma > 0$.

A genetic mutation in the chikungunya virus in Réunion resulted in a reduction in the extrinsic incubation period in *Aedes albopictus* to 2 days (from about 7–12 days) [41]. Furthermore, the genetic mutation also affected the death rate of infected mosquitoes and the transmission probability from human to mosquito [41]. See the works [41, 42] for studies of this genetic mutation. Motivated by this, we consider a mutation parameter that switches in time, $\delta_\delta \geq 0$, to reflect a possible genetic mutation in the virus causing a shift in the transmission rate. The adult vector population is modeled as follows:

$$\begin{aligned}\dot{S}^{(M)}(t) &= \eta_Q Q(t) - \delta_\sigma \gamma_\sigma \frac{S^{(M)}(t) I^{(H)}(t)}{N^{(H)}(t)} - d_S S^{(M)}(t), \\ \dot{I}^{(M)}(t) &= \delta_\sigma \gamma_\sigma \frac{S^{(M)}(t) I^{(H)}(t)}{N^{(H)}(t)} - d_I I^{(M)}(t).\end{aligned}\tag{7.2}$$

Lastly, the life cycle of the human population is considered. The susceptible, infected, and recovered classes of humans are denoted by $S^{(H)}$, $I^{(H)}$, and $R^{(H)}$, respectively. Vertical transmission of chikungunya did not play a key role in the spread of the virus in Réunion [41]. After a period of 4–7 days, a human infected with the disease is able to transmit it to vectors agents [113]. Disease-induced mortality from chikungunya is negligible; by April 2006, 203 death certificates mentioned the chikungunya infection as the direct or indirect cause of death (a mortality rate of about 3 per 10,000 persons [126]). Once a human recovers from the disease, they are assumed to move to the recovered class; most patients infected with chikungunya recover quickly without any long-lasting chronic effects and acquire immunity against the virus [126]. The recovery rate is assumed to be $g > 0$ and the contact rate sufficient for transmission from a mosquito to a human is given as the switching parameter $\beta_\sigma > 0$. The mosquito and human populations are governed by the following switched system:

$$\begin{aligned}\dot{S}^{(H)}(t) &= \mu N^{(H)}(t) - \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t)}{N^{(H)}(t)} - \mu S^{(H)}(t), \\ \dot{I}^{(H)}(t) &= \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t)}{N^{(H)}(t)} - (g + \mu) I^{(H)}(t), \\ \dot{R}^{(H)}(t) &= g I^{(H)}(t) - \mu R^{(H)}(t),\end{aligned}\tag{7.3}$$

where $N^{(H)} \equiv S^{(H)} + I^{(H)} + R^{(H)}$ is constant in time.

Remark 7.1 In the above formulation, the incidence rate is given by $\beta_\sigma S^{(H)} I^{(M)} / N^{(H)}$ which is the switching form of the incidence rate $\beta S^{(H)} I^{(M)} / N^{(H)}$ used in [41, 42]. In [113, 114], the authors instead adopted for an incidence rate of the form $\beta S^{(H)} I^{(M)} / A$, which takes into account the vector dynamics with non-constant population size and a contact rate dependent on the size of the vector population [113].

7.3 Chikungunya Virus Model Dynamics

Before combining the equations to form the full chikungunya model, first normalize equations (7.2) and (7.3) using $\bar{S}^{(M)} \equiv S^{(M)} / A$, $\bar{I}^{(M)} \equiv I^{(M)} / A$, $\bar{S}^{(H)} \equiv S^{(H)} / N^{(H)}$, $\bar{I}^{(H)} \equiv I^{(H)} / N^{(H)}$, $\bar{R}^{(H)} \equiv R^{(H)} / N^{(H)}$. Then,

$$\begin{aligned} \frac{d\bar{I}^{(M)}}{dt}(t) &= \frac{\dot{I}^{(M)}(t)A(t) - \dot{A}(t)I^{(M)}(t)}{A^2(t)}, \\ &= \left[\delta_\sigma \gamma_\sigma \frac{S^{(M)}(t)I^{(H)}(t)}{N^{(H)}} - d_I I^{(M)}(t) \right] \frac{1}{A} \\ &\quad - [\eta_Q Q(t) - d_I I^{(M)}(t) - d_s S^{(M)}(t)] \frac{I^{(M)}(t)}{A^2(t)}, \\ &= \delta_\sigma \gamma_\sigma \bar{S}^{(M)}(t) \bar{I}^{(H)}(t) - d_I \bar{I}^{(M)}(t) - \eta_Q \frac{Q(t)}{A(t)} \bar{I}^{(M)}(t) \\ &\quad + d_I (\bar{I}^{(M)}(t))^2 + d_s \bar{S}^{(M)}(t) \bar{I}^{(M)}(t), \\ &= \delta_\sigma \gamma_\sigma \bar{I}^{(H)}(t) - \delta_\sigma \gamma_\sigma \bar{I}^{(M)}(t) \bar{I}^{(H)}(t) - \eta_Q \frac{Q(t)}{A(t)} \bar{I}^{(M)}(t) \\ &\quad - d_I \bar{I}^{(M)}(t) + d_I (\bar{I}^{(M)}(t))^2 + d_s \bar{I}^{(M)}(t) - d_s (\bar{I}^{(M)}(t))^2, \\ &= - \left(\eta_Q \frac{Q(t)}{A(t)} + \delta_\sigma \gamma_\sigma \bar{I}^{(H)}(t) \right) \bar{I}^{(M)}(t) + \delta_\sigma \gamma_\sigma \bar{I}^{(H)}(t) \\ &\quad + (d_s - d_I) \bar{I}^{(M)}(t) + (d_I - d_s) (\bar{I}^{(M)}(t))^2, \end{aligned}$$

where the invariant $\bar{S}^{(M)} + \bar{I}^{(M)} = 1$ has been used. Similarly,

$$\begin{aligned} \frac{d\bar{S}^{(M)}}{dt}(t) &= \left[\eta_Q Q(t) - \delta_\sigma \gamma_\sigma \frac{S^{(M)}(t)I^{(H)}(t)}{N^{(H)}} - d_s S^{(M)}(t) \right] \frac{1}{A(t)} \\ &\quad - [\eta_Q Q(t) - d_I I^{(M)}(t) - d_s S^{(M)}(t)] \frac{S^{(M)}(t)}{A^2(t)}, \end{aligned}$$

$$\begin{aligned}
&= \eta_Q \frac{Q(t)}{A(t)} - \delta_\sigma \gamma_\sigma \bar{S}^{(M)}(t) \bar{I}^{(H)}(t) - d_S \bar{S}^{(M)}(t) - \eta_Q \frac{Q(t)}{A(t)} \bar{S}^{(M)}(t) \\
&\quad + d_S (\bar{S}^{(M)}(t))^2 + d_I \bar{S}^{(M)}(t) \bar{I}^{(M)}(t), \\
&= \eta_Q \frac{Q(t)}{A(t)} \bar{I}^{(M)}(t) - \delta_\sigma \gamma_\sigma (1 - \bar{I}^{(M)}(t)) \bar{I}^{(H)}(t) - d_S \bar{S}^{(M)}(t) \\
&\quad + d_S (\bar{S}^{(M)}(t))^2 + d_I \bar{S}^{(M)}(t) (1 - \bar{S}^{(M)}(t)), \\
&= \left(\eta_Q \frac{Q(t)}{A(t)} + \delta_\sigma \gamma_\sigma \bar{I}^{(H)}(t) \right) \bar{I}^{(M)}(t) - \delta_\sigma \gamma_\sigma \bar{I}^{(H)}(t) \\
&\quad + (d_I - d_S) \bar{S}^{(M)}(t) + (d_S - d_I) (\bar{S}^{(M)}(t))^2.
\end{aligned}$$

Since $\dot{N}^{(H)}(t) = 0$, the differential equations associated with $\bar{S}^{(H)}$, $\bar{I}^{(H)}$, and $\bar{R}^{(H)}$ are straightforward to calculate. Dropping the bars, the dynamic system is modeled by the following:

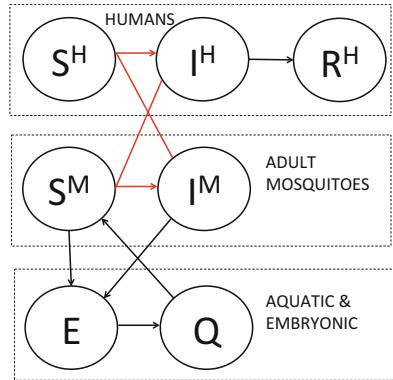
$$\begin{aligned}
\dot{E}(t) &= b_\sigma \left(1 - \frac{E}{\Gamma_E} \right) A(t) - (\eta_E + d_E) E(t), \\
\dot{Q}(t) &= \eta_E \left(1 - \frac{Q(t)}{\Gamma_Q} \right) E(t) - (\eta_Q + d_Q) Q(t),
\end{aligned} \tag{7.4a}$$

$$\begin{aligned}
\dot{A}(t) &= \eta_Q Q(t) - d_I I^{(M)}(t) A(t) - d_S S^{(M)}(t) A(t), \\
\dot{S}^{(M)}(t) &= \left(\eta_Q \frac{Q(t)}{A(t)} + \delta_\sigma \gamma_\sigma I^{(H)}(t) \right) I^{(M)}(t) - \delta_\sigma \gamma_\sigma I^{(H)}(t) \\
&\quad + (d_I - d_S) (1 - S^{(M)}(t)) S^{(M)}(t), \\
\dot{I}^{(M)}(t) &= - \left(\eta_Q \frac{Q(t)}{A(t)} + \delta_\sigma \gamma_\sigma I^{(H)}(t) + (d_S - d_I) (1 - I^{(M)}(t)) \right) I^{(M)}(t) + \delta_\sigma \gamma_\sigma I^{(H)}(t), \\
\dot{S}^{(H)}(t) &= \mu - \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}} - \mu S^{(H)}(t), \\
\dot{I}^{(H)}(t) &= \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}(t)} - (g + \mu) I^{(H)}(t), \\
\dot{R}^{(H)}(t) &= g I^{(H)}(t) - \mu R^{(H)}(t).
\end{aligned} \tag{7.4b}$$

The initial conditions $E(0) = E_0$, $Q(0) = Q_0$, $A(0) = A_0$, $S^{(H)}(0) = S_0^{(H)}$, $I^{(H)}(0) = I_0^{(H)}$, $R^{(H)}(0) = R_0^{(H)}$, $S^{(M)}(0) = S_0^{(M)}$, and $I^{(M)}(0) = I_0^{(M)}$ are nonnegative and necessarily satisfy $S_0^{(M)} + I_0^{(M)} = 1$ and $S_0^{(H)} + I_0^{(H)} + R_0^{(H)} = 1$. See Fig. 7.1 for the flow of the model. The physical domain is given by

$$D_{(7.4)} \equiv \{(E, Q, A, S^{(M)}, I^{(M)}, S^{(H)}, I^{(H)}, R^{(H)}) \in \mathbb{R}_+^8 : 0 \leq E \leq \Gamma_E, 0 \leq Q \leq \Gamma_Q,$$

Fig. 7.1 Flow of the switched chikungunya disease model (7.4). The red lines represent disease transmission (from human–mosquito interactions) and the black lines show the population dynamics of the mosquitoes. The population dynamics of the human population has been omitted here



$$0 \leq A \leq \frac{\eta_Q \Gamma_Q}{d_S}, S^{(M)} + I^{(M)} = 1, S^{(H)} + I^{(H)} + R^{(H)} = N^{(H)}\}.$$

The domain $D_{(7.4)}$ is the region of physical interest. If

$$(E_0, Q_0, A_0, S_0^{(M)}, I_0^{(M)}, S_0^{(H)}, I_0^{(H)}, R_0^{(H)}) \in D_{(7.4)},$$

then the solution remains in $D_{(7.4)}$. Moreover, given nonnegative initial conditions and

$$(E_0, Q_0, A_0, S_0^{(M)}, I_0^{(M)}, S_0^{(H)}, I_0^{(H)}, R_0^{(H)}) \notin D_{(7.4)},$$

the solution eventually enters and remains in $D_{(7.4)}$. (Such results are proved in the non-switched vector-borne disease model in [113] and are easily adopted to the current setting.) In Eq. (7.4), the spread of the chikungunya virus is modeled by considering the interaction between the human and mosquito population. The main focus of the present chapter is studying the efficacy of different control strategies when applied to model (7.4). First, destruction of breeding sites is analyzed in Sect. 7.4, followed by a reduction in contact rates strategy in Sect. 7.5.

7.4 Control via Mechanical Destruction of Breeding Grounds

As discussed at the beginning of this chapter, mechanical control of the mosquito breeding sites is a powerful tool to prevent the spread of chikungunya. The main vector of chikungunya, *Aedes albopictus*, is a container-inhabiting species that lays its eggs in any water-containing receptacle in urban, suburban, forest, or rural area [113]. The development of immature *Aedes albopictus* depends vitally on the availability of water, as the mosquitoes rely on rainfall to raise water levels

in containers so that the eggs may hatch [113]. Furthermore, an increase in larval density or decrease in food/water may lead to a reduced number of adult mosquitoes [113]. Mechanical control consists of destruction of the breeding sites (and thus a reduction in the carrying capacity of the aquatic population). Methods of application include the recommendation for people to search their properties after a rainfall to clean and empty water containers where mosquitoes could lay eggs [114].

Assume that the carrying capacity of the aquatic stage (larvae and pupae populations) of the mosquitoes is reduced to $\alpha\Gamma_Q$, where $\alpha \in (0, 1]$. Applied to the chikungunya model (7.4),

$$\begin{aligned}\dot{E}(t) &= b_\sigma \left(1 - \frac{E(t)}{\Gamma_E}\right) A(t) - (\eta_E + d_E) E(t), \\ \dot{Q}(t) &= \eta_E \left(1 - \frac{Q(t)}{\alpha\Gamma_Q}\right) E(t) - (\eta_Q + d_Q) Q(t), \\ \dot{A}(t) &= \eta_Q Q - d_I I^{(M)}(t) A(t) - d_S S^{(M)}(t) A(t),\end{aligned}\tag{7.5a}$$

$$\begin{aligned}\dot{S}^{(H)}(t) &= \mu - \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}} - \mu S^{(H)}(t), \\ \dot{I}^{(H)}(t) &= \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}} - (g + \mu) I^{(H)}(t), \\ \dot{R}^{(H)}(t) &= g I^{(H)}(t) - \mu R^{(H)}(t), \\ \dot{I}^{(M)}(t) &= - \left(\eta_Q \frac{Q(t)}{A(t)} + \delta_\sigma \gamma_\sigma I^{(H)}(t) + (d_S - d_I)(1 - I^{(M)}(t)) \right) I^{(M)}(t) + \delta_\sigma \gamma_\sigma I^{(H)}(t).\end{aligned}\tag{7.5b}$$

The equation for $S^{(M)}$ is omitted since $S^{(M)} + I^{(M)} = 1$. The physical domain is given by

$$\begin{aligned}D_{(7.5)} &\equiv \{(E, Q, A, I^{(M)}, S^{(H)}, I^{(H)}, R^{(H)}) \in \mathbb{R}_+^7 : 0 \leq E \leq \Gamma_E, 0 \leq Q \leq \alpha\Gamma_Q, \\ 0 \leq A &\leq \frac{\alpha\eta_Q\Gamma_Q}{d_S}, 0 \leq I^{(M)} \leq 1, S^{(H)} + I^{(H)} + R^{(H)} = N^{(H)}\}.\end{aligned}$$

To analyze the long-term behavior of (7.5), we first focus on the dynamics of the vector population given by Eq. (7.5a). System (7.5a) has an equilibrium $(0, 0, 0)$ common to all modes, which is the mosquito-free equilibrium. Each mode also has an endemic equilibrium

$$\mathcal{Q}_{ES}^{(7.5a),i} \equiv (E_i^*, Q_i^*, A_i^*) \equiv \left(1 - \frac{1}{r_{(7.5a),i}}\right) \left(\frac{\Gamma_E}{v_i}, \frac{\alpha\Gamma_Q}{\kappa_i}, \frac{\eta_Q}{d_I} \frac{\alpha\Gamma_Q}{\kappa_i}\right),$$

where

$$r_{(7.5a),i} \equiv \frac{b_i}{\eta_E + d_E} \frac{\eta_E}{\eta_Q + d_Q} \frac{\eta_Q}{d_I} \tag{7.6}$$

and

$$\nu_i \equiv 1 + \frac{(\eta_E + d_E)d_I\Gamma_E}{b_i\eta_Q\alpha\Gamma_Q}, \quad \kappa_i \equiv 1 + \frac{(\eta_Q + d_Q)\Gamma_Q}{b_i\eta_E\alpha\Gamma_E}.$$

Because of the time-varying model parameters (i.e., the switching), it may be possible that solution trajectories move between the endemic equilibria and do not converge to a point. Define the minimum and maximum vector birth rates as

$$b_{\max} \equiv \max\{b_i : i \in \mathcal{M}\}, \quad b_{\min} \equiv \min\{b_i : i \in \mathcal{M}\}.$$

Define the minimum and maximum endemic equilibria

$$E_{\max} \equiv \max\{E_i^* : i \in \mathcal{M}\}, \quad E_{\min} \equiv \min\{E_i^* : i \in \mathcal{M}\}.$$

Define Q_{\max} , Q_{\min} , A_{\max} , and A_{\min} similarly. The long-term behavior of the mosquito population is characterized as follows.

Proposition 7.1 *If*

$$\bar{r} \equiv \frac{b_{\min}}{\eta_E + d_E} \frac{\eta_E}{\eta_Q + d_Q} \frac{\eta_Q}{d_I} > 1, \quad (7.7)$$

then the solution of (7.5a) converges to the set

$$\begin{aligned} \Delta_{\text{mechanical}} = & \{(E, Q, A) \in \mathbb{R}_+^3 : E_{\min} \leq E \leq E_{\max}, Q_{\min} \leq Q \leq Q_{\max}, \\ & A_{\min} \leq A \leq A_{\max}\}. \end{aligned} \quad (7.8)$$

Proof From

$$\begin{aligned} \dot{E}(t) & \geq b_{\min} \left(1 - \frac{E(t)}{\Gamma_E}\right) A(t) - (\eta_E + d_E)Q(t), \\ \dot{A}(t) & \geq \eta_Q Q(t) - d_I I^{(M)}(t)A(t) - d_I S^{(M)}(t)A(t) = \eta_Q Q(t) - d_I A(t), \end{aligned}$$

we may consider the following comparison system:

$$\begin{aligned} \dot{x}(t) & = b_{\min} \left(1 - \frac{x(t)}{\Gamma_E}\right) z(t) - (\eta_E + d_E)x(t), \\ \dot{y}(t) & = \eta_E \left(1 - \frac{y(t)}{\Gamma_Q}\right) x(t) - (\eta_Q + d_Q)y(t), \\ \dot{z}(t) & = \eta_Q y(t) - d_I z(t), \\ (x(0), y(0), z(0)) & = (E_0, Q_0, A_0). \end{aligned} \quad (7.9)$$

The condition $\bar{r} > 1$ implies that the solution of (7.9) converges to $(E_{\min}, Q_{\min}, A_{\min})$ by Proposition 4.7 in [113]. Note that

$$b_{\min} \left(1 - \frac{x(t)}{\Gamma_E} \right) z(t) \geq 0$$

for $0 \leq x(t) \leq \Gamma_E$ and $z(t) \geq 0$,

$$\eta_E \left(1 - \frac{y(t)}{\Gamma_Q} \right) x(t) \geq 0$$

for $0 \leq y(t) \leq \Gamma_Q$ and $x(t) \geq 0$, and

$$\eta_Q y(t) \geq 0$$

for $y(t) \geq 0$. Then by the comparison theorem (i.e., the switched extension of Theorem 1.10), there exists $t^* > 0$ such that $E(t) \geq x(t) \geq E_{\min} - \epsilon$, $Q(t) \geq y(t) \geq Q_{\min} - \epsilon$ and $A(t) \geq z(t) \geq A_{\min} - \epsilon$ for $t \geq t^*$.

Similarly,

$$\begin{aligned} \dot{E}(t) &\leq b_{\max} \left(1 - \frac{E(t)}{\Gamma_E} \right) A(t) - (\eta_E + d_E) E(t), \\ \dot{A}(t) &\leq \eta_Q Q(t) - d_S I^{(M)}(t) A(t) - d_S S^{(M)}(t) A(t) = \eta_Q Q(t) - d_S A(t), \end{aligned}$$

motivating the comparison system

$$\begin{aligned} \dot{x}(t) &= b_{\max} \left(1 - \frac{x(t)}{\Gamma_E} \right) z(t) - (\eta_E + d_E) x(t), \\ \dot{y}(t) &= \eta_E \left(1 - \frac{y(t)}{\Gamma_Q} \right) x(t) - (\eta_Q + d_Q) y(t), \\ \dot{z}(t) &= \eta_Q y(t) - d_S z(t), \\ (x(0), y(0), z(0)) &= (E_0, Q_0, A_0). \end{aligned} \tag{7.10}$$

Now, $\bar{r} > 1$ implies that $r^{(7.5a),i} > 1$ for each $i \in \mathcal{M}$, so that

$$\frac{b_{\max}}{\eta_E + d_E} \frac{\eta_E}{\eta_Q + d_Q} \frac{\eta_Q}{d_I} > 1$$

and (7.10) converges to $(E_{\max}, Q_{\max}, A_{\max})$ by Proposition 4.7 in [113]. Hence, there exists $\hat{t} > 0$ such that $E(t) \leq E_{\max} + \epsilon$, $Q(t) \leq Q_{\max} + \epsilon$ and $A(t) \leq A_{\max} + \epsilon$ for $t > \hat{t}$. Thus, for $t \geq \max\{t^*, \hat{t}\}$, $E_{\min} - \epsilon \leq E(t) \leq E_{\max} + \epsilon$, $Q_{\min} - \epsilon \leq Q(t) \leq Q_{\max} + \epsilon$ and $A_{\min} - \epsilon \leq A(t) \leq A_{\max} + \epsilon$. It is clear that the solution of system (7.5a) converges to the set $\Delta_{\text{mechanical}}$.

In the special case that $b_\sigma \equiv b$, $d_S \equiv d_I \equiv d$, system (7.5a) has two equilibria: the mosquito-free equilibrium $(0, 0, 0)$, and the endemic equilibrium,

$$Q_{\text{ES}}^{(7.5a)} = (E^*, Q^*, A^*) = \left(1 - \frac{1}{r}\right) \left(\frac{\Gamma_E}{v}, \frac{\alpha \Gamma_Q}{\kappa}, \frac{\eta_Q}{d}\right), \quad (7.11)$$

where

$$v \equiv 1 + \frac{(\eta_E + d_E)d_I \Gamma_E}{b \eta_Q \alpha \Gamma_Q}, \quad \kappa = 1 + \frac{(\eta_Q + d_Q)\Gamma_Q}{b \eta_E \alpha \Gamma_E},$$

and the basic offspring number is defined as

$$r^{(7.5a)} \equiv \frac{b}{\eta_E + d} \frac{\eta_E}{\eta_Q + d} \frac{\eta_Q}{d}, \quad (7.12)$$

which represents the average number of offspring per mosquito during an average lifetime. In [113], the authors showed that if $r < 1$ then $(0, 0, 0)$ is globally asymptotically stable in the meaningful domain and if $r > 1$ then (E^*, Q^*, A^*) is globally asymptotically stable. Here the approximation \bar{r} is a lower bound for the average number of offspring from each mosquito when the mosquito birth rate is time-varying.

Shifting our focus to the long-term dynamics of the human population, observe that $(S^{(H)}(t), I^{(H)}(t), R^{(H)}(t), I^{(M)}(t)) \equiv (1, 0, 0, 0)$ is a solution to the differential equations for $S^{(H)}$, $I^{(H)}$, $R^{(H)}$, and $I^{(M)}$ in (7.5a). Motivated by this, define the set

$$\begin{aligned} \Psi_{\text{mechanical}} = \{(E, Q, A, I^{(M)}, S^{(H)}, I^{(H)}, R^{(H)}) \in \mathbb{R}_+^7 : (E, Q, A) \in \Delta_{\text{mechanical}}, \\ S^{(H)} = 1, I^{(H)} = 0, R^{(H)} = 0, I^{(M)} = 0\}. \end{aligned} \quad (7.13)$$

The basic reproduction number for a vector-borne disease model is defined as the average number of secondary cases produced by one primary infectious case by the vectors in a wholly susceptible population. For periodic models, the rate of infection varies based on the time of year and the basic reproduction number can be interpreted as an asymptotic per generation growth rate of the epidemic model linearized about the disease-free equilibrium [9].

When the model parameters in (7.5) are constant in time, there is no mutation factor ($\delta_\sigma = 1$) and the death rates of susceptible and infected mosquitoes are equal ($d_S = d_I = d$), the basic reproduction number of the epidemic model can be given explicitly in terms of the model parameters [114]:

$$R_0^{(7.5)} \equiv \frac{\beta}{g + \mu} \frac{\gamma}{d} \frac{A^*}{N^{(H)}} \quad (7.14)$$

where A^* is given in Eq. (7.11). The physical interpretation is as follows [41, 42]: the fraction

$$R_0^{(7.5),(M,H)} \equiv \frac{\beta}{g + \mu}$$

represents the rate of spread from mosquito to humans, while

$$R_0^{(7.5),(H,M)} \equiv \frac{\gamma}{d} \frac{A^*}{N^{(H)}}$$

represents the rate of spread from humans to mosquitoes. The basic reproduction number is then

$$R_0^{(7.5)} = R_0^{(7.5),(M,H)} \times R_0^{(7.5),(H,M)}.$$

As $0 = \eta_Q Q^* - dA^*$, we can rewrite $R_0^{(7.5)}$ as

$$R_0^{(7.5)} = \frac{\beta}{g + \mu} \frac{\gamma}{\eta_Q \frac{Q^*}{A^*} N^{(H)}} = \frac{\beta}{g + \mu} \frac{\gamma}{\eta_Q} \frac{(A^*)^2}{Q^* N^{(H)}}.$$

Motivated by this, consider system (7.5) and the following approximate basic reproduction numbers for each mode

$$\tilde{R}_0^{(7.5),i} = \frac{\beta_i \delta_i \gamma_i}{\eta_Q (g + \mu)} \frac{A_{\max}^2}{Q_{\min} N^{(H)}} \quad (7.15)$$

for each $i \in \mathcal{M}$. Verifiable threshold conditions guaranteeing disease eradication under mechanical destruction are presented after reminding the reader of the following switched systems notions. $T_i(t^1, t^2)$ denotes the total activation time of the i^{th} mode during the interval $[t^1, t^2]$. Define the sets

$$\mathcal{M}^- \equiv \{i \in \mathcal{M} : \frac{\eta_Q Q_{\min}}{A_{\max}} \tilde{R}_0^{(7.5),i} + \delta_i \gamma_i < 1\}$$

and

$$\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \frac{\eta_Q Q_{\min}}{A_{\max}} \tilde{R}_0^{(7.5),i} + \delta_i \gamma_i \geq 1\}.$$

Let $T^-(t^1, t^2)$ and $T^+(t^1, t^2)$ be the total time such that $\sigma(t) \in \mathcal{M}^-$ and $\sigma(t) \in \mathcal{M}^+$ on the interval (t^1, t^2) , respectively.

Theorem 7.1 Assume that there exists a constant $q \geq 0$ such that $T^+(0, t) \leq qT^-(0, t)$. Assume that $\bar{r} > 1$ and

$$q\lambda^+ < \lambda^-, \quad (7.16)$$

where

$$\lambda_i \equiv \frac{1 + \widetilde{R}_0^{(7.5),i}}{2\widetilde{R}_0^{(7.5),i}} \frac{1}{\left(1 + \frac{\eta_Q Q_{\min}}{\delta_i \gamma_i A_{\max}}\right)} \left[\frac{\eta_Q Q_{\min}}{A_{\max}} \widetilde{R}_0^{(7.5),i} + \delta_i \gamma_i - 1 \right], \quad (7.17)$$

$\lambda^- \equiv \max\{\lambda_i : i \in \mathcal{M}^-\}$ and $\lambda^+ \equiv \max\{\lambda_i : i \in \mathcal{M}^+\}$. Then the solution of system (7.5) converges to the disease-free set $\Psi_{\text{mechanical}}$.

Proof Define the functions $V_i(I^{(M)}, I^{(H)}) \equiv a_i I^{(M)} + b_i I^{(H)}$ for each $i \in \mathcal{M}$, where

$$a_i \equiv \frac{1 + \widetilde{R}_0^{(7.5),i}}{2\left(\delta_i \gamma_i + \eta_Q \frac{Q_{\min}}{A_{\max}}\right)} \left(\frac{\delta_i \gamma_i}{\widetilde{R}_0^{(7.5),i}} + \eta_Q \frac{Q_{\min}}{A_{\max}} \right), \quad b_i \equiv \eta_Q \frac{Q_{\min} N^{(H)}}{A_{\max}^2} \frac{1 + \widetilde{R}_0^{(7.5),i}}{2\beta_i}.$$

Take the time-derivative of the i th Lyapunov function along system (7.5),

$$\begin{aligned} \dot{V}_i &= a_i \left[- \left(\eta_Q \frac{Q}{A} + \delta_i \gamma_i I^{(H)} \right) I^{(M)} + \delta_i \gamma_i I^{(H)} + (d_S - d_I) I^{(M)} + (d_I - d_S) (I^{(M)})^2 \right] \\ &\quad + b_i \left[\beta_i \frac{I^{(M)} S^{(H)} A}{N^{(H)}} - (g + \mu) I^{(H)} \right], \end{aligned}$$

where the argument of \dot{V} , $I^{(M)}$, and $I^{(H)}$ are omitted here. Since $\bar{r} > 1$, for any $\epsilon > 0$ there exists a $t^* > 0$ such that $E \geq E_{\min} - \epsilon$, $Q \geq Q_{\min} - \epsilon$ and $A \leq A_{\max} + \epsilon$ for $t \geq t^*$. Also, since $d_I > d_S$ and $0 \leq I^{(M)}(t) \leq 1$,

$$(d_S - d_I) I^{(M)}(t) + (d_I - d_S) (I^{(M)}(t))^2 \leq (d_S - d_I) I^{(M)}(t) + (d_I - d_S) I^{(M)}(t) = 0.$$

Then

$$\begin{aligned} \dot{V}_i &\leq a_i \left[- \left(\eta_Q \frac{Q_{\min} - \epsilon}{A_{\max} + \epsilon} + \delta_i \gamma_i I^{(H)} \right) I^{(M)} + \delta_i \gamma_i I^{(H)} \right] \\ &\quad + b_i \left[\beta_i I^{(M)} S^{(H)} \left(\frac{A_{\max} + \epsilon}{N^{(H)}} \right) - (g + \mu) I^{(H)} \right], \\ &= -a_i \eta_Q \left(\frac{Q_{\min} - \epsilon}{A_{\max} + \epsilon} \right) I^{(M)} + a_i \delta_i \gamma_i (1 - I^{(M)}) I^{(H)} \\ &\quad + b_i \beta_i I^{(M)} S^{(H)} \left(\frac{A_{\max} + \epsilon}{N^{(H)}} \right) - b_i (\mu + g) I^{(H)}, \\ &= \left[a_i \delta_i \gamma_i (1 - I^{(M)}) - \eta_Q \frac{Q_{\min} N^{(H)}}{A_{\max}^2} \left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) \left(\frac{g + \mu}{\beta_i} \right) \right] I^{(H)} \\ &\quad + \left[\eta_Q \frac{Q_{\min}}{A_{\max}} \left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) S^{(H)} - a_i \eta_Q \left(\frac{Q_{\min} - \epsilon}{A_{\max} + \epsilon} \right) + b_i \beta_i \frac{S^{(H)}}{N^{(H)}} \epsilon \right] I^{(M)}. \end{aligned}$$

Note that

$$\frac{Q_{\min}}{A_{\max} + \epsilon} = \frac{Q_{\min}}{A_{\max}} \left[\frac{1}{1 + \frac{\epsilon}{A_{\max}}} \right] = \frac{Q_{\min}}{A_{\max}} [1 + f_1(\epsilon)],$$

where

$$f_1(\epsilon) \equiv \frac{\frac{-\epsilon}{A_{\max}}}{1 + \frac{\epsilon}{A_{\max}}}.$$

Therefore,

$$\begin{aligned} -\eta_Q \left(\frac{Q_{\min} - \epsilon}{A_{\max} + \epsilon} \right) &= -\eta_Q \frac{Q_{\min}}{A_{\max}} [1 + f_1(\epsilon)] + \eta_Q \frac{\epsilon}{A_{\max} + \epsilon}, \\ &\leq -\eta_Q \frac{Q_{\min}}{A_{\max}} + \eta_Q \frac{Q_{\min}}{A_{\max}} \left(\frac{\epsilon}{A_{\max}} \right) + \frac{\eta_Q \epsilon}{A_{\max}}, \\ &= -\eta_Q \frac{Q_{\min}}{A_{\max}} + \eta_Q \frac{Q_{\min}}{A_{\max}} f_2(\epsilon), \end{aligned}$$

where

$$f_2(\epsilon) \equiv \epsilon \left(\frac{1}{A_{\max}} + \frac{1}{Q_{\min}} \right).$$

Thus

$$\begin{aligned} \dot{V}_i &\leq \left[a_i (1 - I^{(M)}) - \eta_Q \frac{Q_{\min} N^{(H)}}{A_{\max}^2} \frac{(\mu + g)}{\beta_i \delta_i \gamma_i} \left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) \right] \delta_i \gamma_i I^{(H)} \\ &\quad + \left[\eta_Q \frac{Q_{\min}}{A_{\max}} \left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) S^{(H)} - a_i \eta_Q \frac{Q_{\min}}{A_{\max}} + a_i \eta_Q \frac{Q_{\min}}{A_{\max}} f_2(\epsilon) + \frac{b_i \beta_i}{N^{(H)}} \epsilon \right] I^{(M)}, \\ &= \left[a_i (1 - I^{(M)}) - \frac{1}{\widetilde{R}_0^{(7.5),i}} \left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) \right] \delta_i \gamma_i I^{(H)} \\ &\quad + \left[\left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) S^{(H)} - a_i + a_i f_2(\epsilon) + \frac{b_i \beta_i A_{\max}}{\eta_Q Q_{\min} N^{(H)}} \epsilon \right] \eta_Q \frac{Q_{\min}}{A_{\max}} I^{(M)}, \\ &\leq \left[a_i - \frac{1}{2} \left(\frac{1}{\widetilde{R}_0^{(7.5),i}} + 1 \right) \right] \delta_i \gamma_i I^{(H)} \\ &\quad + \left[\left(\frac{1 + \widetilde{R}_0^{(7.5),i}}{2} \right) - a_i + a_i f_2(\epsilon) + \frac{b_i \beta_i A_{\max}}{\eta_Q Q_{\min} N^{(H)}} \epsilon \right] \eta_Q \frac{Q_{\min}}{A_{\max}} I^{(M)}, \\ &= \lambda_i (I^{(M)} + I^{(H)}) + G_i(\epsilon) I^{(M)}, \end{aligned}$$

where

$$G_i(\epsilon) \equiv a_i \eta_Q \frac{Q_{\min}}{A_{\max}} \left[f_2(\epsilon) + \frac{b_i \beta_i}{N^{(H)}} \epsilon \right].$$

Defining

$$c \equiv \frac{1}{\min\{a_1, a_2, \dots, a_m, b_1, b_2, \dots, b_m\}},$$

it follows that

$$\begin{aligned} \frac{1}{c} \frac{d(I^{(M)} + I^{(H)})}{dt}(t) &\leq \frac{d(a_i I^{(M)} + b_i I^{(H)})}{dt}(t), \\ &\leq \lambda_i(I^{(M)}(t) + I^{(H)}(t)) + G_i(\epsilon)I^{(M)}(t), \\ &\leq (\lambda_i + G_i(\epsilon))(I^{(M)}(t) + I^{(H)}(t)). \end{aligned} \quad (7.18)$$

Let $N > 1$ be the smallest integer such that $t_{N-1} > t^*$. Then for $t \in [t_{N-1}, t_N]$,

$$I^{(H)}(t) + I^{(M)}(t) \leq c(I^{(H)}(t_{N-1}) + I^{(M)}(t_{N-1})) \exp[(\lambda_{i_N} + G_{i_N}(\epsilon))(t - t_{N-1})].$$

For $t \in [t_N, t_{N+1}]$,

$$\begin{aligned} I^{(H)}(t) + I^{(M)}(t) &\leq c(I^{(H)}(t_N) + I^{(M)}(t_N)) \exp[(\lambda_{i_{N+1}} + G_{i_{N+1}}(\epsilon))(t - t_N)], \\ &\leq c(I^{(H)}(t_{N-1}) + I^{(M)}(t_{N-1})) \exp[(\lambda_{i_N} + G_{i_N}(\epsilon))(t_N - t_{N-1})] \\ &\quad + (\lambda_{i_{N+1}} + G_{i_{N+1}}(\epsilon))(t - t_N)], \end{aligned}$$

The bounds $0 \leq I^{(M)} \leq 1$ and $0 \leq I^{(H)} \leq N^{(H)}$ give that $0 \leq I^{(H)}(t_{N-1}) + I^{(M)}(t_{N-1}) \leq M$ where $M \equiv 1 + N^{(H)}$. On a general time interval $t \in [t_{N-1+j}, t_{N+j}]$ for $j \in \mathbb{N}$,

$$\begin{aligned} I^{(H)}(t) + I^{(M)}(t) &\leq cM \exp \left[\sum_{l=1}^{j-1} (\lambda_{i_{N+l}} + G_{i_{N+l}}(\epsilon))(t_{N+l} - t_{N-1+l}) \right] \\ &\quad \times \exp[(\lambda_{i_{N+j}} + G_{i_{N+j}}(\epsilon))(t - t_{N-1+j})], \end{aligned}$$

and so

$$\begin{aligned} I^{(H)}(t) + I^{(M)}(t) &\leq cM \exp \left[\sum_{i=1}^m (\lambda_i + G_i(\epsilon))T_i(t_N, t) \right], \\ &= cM \exp \left[\sum_{i \in \mathcal{M}^-} (\lambda_i + G_i(\epsilon))T_i(t_N, t) + \sum_{i \in \mathcal{M}^+} (\lambda_i + G_i(\epsilon))T_i(t_N, t) \right]. \end{aligned}$$

It follows that

$$\begin{aligned}
I^{(H)}(t) + I^{(M)}(t) &\leq cM \exp \left[\sum_{i \in \mathcal{M}^-} (-\lambda^- + G_i(\epsilon)) T_i(t_N, t) + \sum_{i \in \mathcal{M}^+} (\lambda^+ + G_i(\epsilon)) T_i(t_N, t) \right], \\
&= cM \exp \left[-\lambda^- T^-(t_N, t) + \lambda^+ T^+(t_N, t) + \sum_{i=1}^m G_i(\epsilon) T_i(t_N, t) \right], \\
&\leq cM \exp \left[-\lambda^- T^-(t_N, t) + q\lambda^+ T^-(t_N, t) + \epsilon G_{\max}(t - T_N) \right], \\
&= cM \exp \left[(-\lambda^- + q\lambda^+) T^-(t_N, t) + \epsilon G_{\max}(t - T_N) \right],
\end{aligned}$$

where

$$G_{\max} \equiv \max_{i=1,2,\dots,m} a_i \eta_Q \frac{Q_{\min}}{A_{\max}} \left(\frac{1}{A_{\max}} + \frac{1}{Q_{\min}} + \frac{b_i \beta_i}{N^{(H)}} \right).$$

Then, since $t - t_N = T^-(t_N, t) + T^+(t_N, t) \leq (1 + q)T^-(t_N, t)$,

$$\begin{aligned}
I^{(H)}(t) + I^{(M)}(t) &\leq cM \exp \left[(-\lambda^- + q\lambda^+) \left(\frac{t - t_N}{1 + q} \right) + \epsilon G_{\max}(t - T_N) \right], \\
&= cM \exp \left[(-\lambda^- + q\lambda^+ + \epsilon G_{\max}(1 + q)) \left(\frac{t - t_N}{1 + q} \right) \right].
\end{aligned}$$

The condition $-\lambda^- + q\lambda^+ < 0$ implies the existence of a positive constant χ such that $-\lambda^- + q\lambda^+ \leq -\chi$. Choose $0 < \epsilon = \frac{1}{2} \frac{\chi}{G_{\max}(1+q)}$, from which it follows that $-\lambda^- + q\lambda^+ + \epsilon G_{\max}(1 + q) \leq \frac{-\chi}{2} < 0$ and it follows that $I^{(H)}$ and $I^{(M)}$ converge to zero. Then from the reduced system with $I^{(H)} = I^{(M)} = 0$, it is clear that $R^{(H)}$ converges to zero and $S^{(H)} = 1 - I^{(H)} - R^{(H)}$ implies that $S^{(H)}$ converges to one. Therefore the solution converges to the set $\Psi_{\text{mechanical}}$.

From the definitions of λ^+ and λ^- , the set \mathcal{M}^+ represents the set of contact rates such that the disease may be spreading (unstable modes) while the set \mathcal{M}^- represents modes where the disease is being eradicated (stable modes). Moreover, the condition $T^+(0, t) \leq qT^-(0, t)$ provides insight into the necessary relationship between the time spent in the unstable modes versus the stable modes. The threshold condition (7.16) depends on the mechanical destruction rate α via A_{\max} , Q_{\min} , and $\widetilde{R}_0^{(7.5),i}$. The approximate basic reproduction numbers for each mode, $\widetilde{R}_0^{(7.5),i}$, are analytic approximations to $R_0^{(7.5)}$ in Eq. (7.14) (rather than a numerical approximation, for example see [7]). Furthermore, the approximations are overestimates since

$$R_0^{(7.5)} \leq \max_{i=1,\dots,m} \widetilde{R}_0^{(7.5),i}.$$

Disease eradication can be shown for periodicity in the contact rates (e.g., dry season vs rainy season).

Theorem 7.2 Assume that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, $\bar{r} > 1$, and

$$\Lambda_{\text{mechanical}} \equiv \sum_{i=1}^m \lambda_i \tau_i < 0 \quad (7.19)$$

where λ_i is given in Eq. (7.17). Then the solution of system (7.5) converges to the disease-free set $\Psi_{\text{mechanical}}$.

Proof Beginning from Eq.(7.18) and letting $N > 1$ be the smallest integer satisfying $t_{N-1} > t^*$ and $\text{mod}(N, m) = 0$. Along the lines of the proof of Theorem 7.1, it holds that

$$\begin{aligned} I^{(H)}(t_{N-1} + \omega) + I^{(M)}(t_{N-1} + \omega) \\ \leq c(I^{(H)}(t_{N-1}) + I^{(M)}(t_{N-1})) \exp \left[\sum_{l=1}^m (\lambda_l + G_l(\epsilon)) \tau_l \right]. \end{aligned}$$

By Eq.(7.19) and since $G_i(\epsilon) \rightarrow 0$ as $\epsilon \rightarrow 0$, it is possible to choose $\epsilon > 0$ sufficiently small so that

$$\exp \left[\sum_{l=1}^m (\lambda_l + G_l(\epsilon)) \tau_l \right] < \chi$$

for some constant $0 < \chi < 1$. Since $0 \leq I^{(M)} \leq 1$ and $0 \leq I^{(H)} \leq N^{(H)}$, it follows that $0 \leq I^{(H)}(t_{N-1}) + I^{(M)}(t_{N-1}) \leq M$ where $M = 1 + N^{(H)}$. Hence

$$0 \leq I^{(H)}(t_{N-1} + \omega) + I^{(M)}(t_{N-1} + \omega) \leq cM\chi.$$

Similarly,

$$0 \leq I^{(H)}(t_{N-1} + 2\omega) + I^{(M)}(t_{N-1} + 2\omega) \leq cM\chi^2.$$

In general,

$$I^{(H)}(t_{N-1} + h\omega) + I^{(M)}(t_{N-1} + h\omega) \leq cM\chi^h,$$

and so the sequence $\{I^{(H)}(t_{N-1} + h\omega) + I^{(M)}(t_{N-1} + h\omega)\}_{h=1}^{\infty}$ converges to zero. Since the solutions do not blow up on any interval of the form $[t_{k-1}, t_k]$, it follows that $I^{(H)}$ and $I^{(M)}$ converge to zero. From the reduced system with $I^{(H)} = I^{(M)} = 0$, it is clear that the solution converges to the set $\Psi_{\text{mechanical}}$.

7.5 Control via Reduction in Contact Rate Patterns

As discussed at the beginning of Chap. 7, another possible control effort involves interrupting the interaction between humans and mosquitoes. Assume that the following conditions hold:

1. There is a public health campaign to reduce the contact rate between humans and mosquitoes at certain key times in the spread of the disease. This can be achieved by, for example, staying indoors during peak mosquito hours, reducing skin exposure, and using mosquito nets.
2. The contact rates β_σ and γ_σ are reduced by a control factor $\theta_\sigma \in [0, 1]$.

Under this construction, model (7.4) becomes the controlled switched system

$$\dot{E}(t) = b_\sigma \left(1 - \frac{\Gamma_E}{\Gamma_E}\right) A(t) - (\eta_E + d_E) E(t),$$

$$\dot{Q}(t) = \eta_E \left(1 - \frac{\Gamma_Q}{\Gamma_Q}\right) E(t) - (\eta_Q + d_Q) Q(t), \quad (7.20a)$$

$$\dot{A}(t) = \eta_Q Q(t) - d_I I^{(M)}(t) A(t) - d_S S^{(M)}(t) A(t),$$

$$\dot{S}^{(H)}(t) = \mu - \theta_\sigma \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}} - \mu S^{(H)}(t),$$

$$\dot{I}^{(H)}(t) = \theta_\sigma \beta_\sigma \frac{S^{(H)}(t) I^{(M)}(t) A(t)}{N^{(H)}} - (g + \mu) I^{(H)}(t),$$

$$\dot{R}^{(H)}(t) = g I^{(H)}(t) - \mu R^{(H)}(t),$$

$$\dot{I}^{(M)}(t) = - \left(\eta_Q \frac{\Gamma_Q}{A(t)} + \theta_\sigma \delta_\sigma \gamma_\sigma I^{(H)}(t) + (d_S - d_I)(1 - I^{(M)}(t)) \right) I^{(M)}(t) + \theta_\sigma \delta_\sigma \gamma_\sigma I^{(H)}(t). \quad (7.20b)$$

The physical domain is given by $D_{(7.20a)} = D_{(7.4)}$. System (7.20a) has the mosquito-free equilibrium $(0, 0, 0)$ and m endemic equilibria

$$Q_{ES}^{(7.20),i} \equiv (E_i^*, Q_i^*, A_i^*) \equiv \left(1 - \frac{1}{r^{(7.5a),i}}\right) \left(\frac{\Gamma_E}{v_i}, \frac{\Gamma_Q}{\kappa_i}, \frac{\eta_Q}{d_I} \frac{\Gamma_Q}{\kappa_i}\right), \quad (7.21)$$

where $r^{(7.5a),i}$ is given in Eq. (7.6) and

$$v_i \equiv 1 + \frac{(\eta_E + d_E)d_I\Gamma_E}{b_i\eta_Q\Gamma_Q}, \quad \kappa_i = 1 + \frac{(\eta_Q + d_Q)\Gamma_Q}{b_i\eta_E\Gamma_E}.$$

Define the minimum and maximum endemic equilibria as in the previous section. If $\bar{r} > 1$, with \bar{r} defined in (7.7), it follows similarly to the proof of Proposition 7.1 that the solution of (7.20a) converges to the set

$$\begin{aligned}\Delta_{\text{reduced}} = \{(E, Q, A) \in \mathbb{R}_+^3 : E_{\min} \leq E \leq E_{\max}, Q_{\min} \leq Q \leq Q_{\max}, \\ A_{\min} \leq A \leq A_{\max}\}.\end{aligned}\quad (7.22)$$

Observe that the values of E_{\max} , E_{\min} , Q_{\max} , Q_{\min} , A_{\max} , and A_{\min} defined above are different from those in Sect. 7.4 due to the fact that $\alpha = 1$ here (since there is no mechanical control applied in this scheme).

Define the following approximate basic reproduction numbers for each mode of (7.20)

$$\widehat{R}_0^{(7.20),i} \equiv \frac{\theta_i^2 \beta_i \delta_i \gamma_i}{\eta_Q(g + \mu)} \frac{A_{\max}^2}{Q_{\min} N^{(H)}}, \quad (7.23)$$

for $i \in \mathcal{M}$. Define the sets

$$\mathcal{M}^- \equiv \{i \in \mathcal{M} : \frac{\eta_Q Q_{\min}}{A_{\max}} (\widehat{R}_0^{(7.20),i})^2 + \theta_i \delta_i \gamma_i < 1\}$$

and

$$\mathcal{M}^+ \equiv \{i \in \mathcal{M} : \frac{\eta_Q Q_{\min}}{A_{\max}} (\widehat{R}_0^{(7.20),i})^2 + \theta_i \delta_i \gamma_i \geq 1\}.$$

Then the following results can be given, whose proofs are similar to that of Theorems 7.1 and 7.2, respectively.

Theorem 7.3 Assume that there exists a constant $q \geq 0$ such that $T^+(0, t) \leq qT^-(0, t)$. Assume that $\bar{r} > 1$ and

$$q\lambda^+ < \lambda^-, \quad (7.24)$$

where

$$\lambda_i \equiv \frac{1 + (\widehat{R}_0^{(7.5),i})^2}{2(\widehat{R}_0^{(7.5),i})^2} \frac{1}{\left(1 + \frac{\eta_Q Q_{\min}}{\theta_i \delta_i \gamma_i A_{\max}}\right)} \left[\frac{\eta_Q Q_{\min}}{A_{\max}} (\widehat{R}_0^{(7.5),i})^2 + \theta_i \delta_i \gamma_i - 1 \right], \quad (7.25)$$

where λ^+ and λ^- are defined as in Theorem 7.1. Then the solution of system (7.20) converges to the disease-free set

$$\begin{aligned}\Psi_{\text{reduced}} \equiv \{(E, Q, A, I^{(M)}, S^{(H)}, I^{(H)}, R^{(H)}) \in \mathbb{R}_+^7 : (E, Q, A) \in \Delta_{\text{reduced}}, \\ S^{(H)} = 1, I^{(H)} = 0, R^{(H)} = 0, I^{(M)} = 0\}.\end{aligned}\quad (7.26)$$

Theorem 7.4 Assume that $\sigma \in \mathcal{S}_{\text{periodic}}(\omega)$, $\bar{r} > 1$, and

$$\Lambda_{\text{reduced}} \equiv \sum_{i=1}^m \lambda_i \tau_i < 0 \quad (7.27)$$

where λ_i is given in Eq. (7.25). Then the solution of system (7.20) converges to the disease-free set Ψ_{reduced} .

7.6 Control Analysis: Efficacy Ratings

In this part, the control strategies outlined above are compared and contrasted using an efficacy measure introduced in [41]. Define

$$F_0 \equiv 100 \frac{C_H^c}{C_H^0},$$

where C_H^c and C_H^0 are the cumulative number of infected humans with control and without control, respectively. F_0 measures the efficacy of the control scheme on suppressing the total number of humans infected as it represents how many fewer humans would be infected in an outbreak by using the particular control strategy. In the simulations, the initial time is taken to coincide with the beginning of the dry season in March 2004 (approximately 1 year before the outbreak in Réunion). The initial conditions are given by $E_0 = c_1 \times N^{(H)}$, $Q_0 = c_1 \times N^{(H)}$, $A_0 = c_2 \times N^{(H)}$, $S_0^{(H)} = N^{(H)}$, $S_0^{(M)} = c_2 \times N^{(H)}$ where $N^{(H)} = 136,000$ is the population of the capital, Saint-Denis. The parameters are chosen to be $c_1 = 2$ and $c_2 = 5$ (as in [41], we focus on the outbreak in the capital).

Assume that the per capita number of eggs at each deposit (per day) is a switching parameter modeled by the switching rule

$$\sigma \equiv \begin{cases} 1, & \text{if } t \in [365k, 365(k + \frac{7}{12})) , k \in \mathbb{N} \cup \{0\} \\ 2, & \text{if } t \in [365(k + \frac{7}{12}), 365(k + 1)). \end{cases} \quad (7.28)$$

The switching rule is periodic with $\tau_1 = \frac{7}{12} \times 365$ (dry season), $\tau_2 = \frac{5}{12} \times 365$ (rainy season) and $\omega = 365$ (one period). That is, $b = b_{\text{dry}}$ whenever $\sigma = 1$ (dry season) and $b = b_{\text{rainy}}$ when $\sigma = 2$ (rainy season). The entomological model parameters are given in Table 7.1. The time-average of the dry season and rainy season eggs per day is given by $b_{\text{dry}} \times \tau_1 + b_{\text{rainy}} \times \tau_2 = b$, hence the choice of b_{dry} and b_{rainy} .

Table 7.1 Entomological and human demographic parameters

Parameter	Description	Average value	Source
$N^{(H)}$	Total human population in Saint-Denis	136000	[42]
b	Per capita number of eggs at each deposit (per day)	6	[41]
b_{dry}	Per capita number of eggs at each deposit (per day) in the dry season	3.27	
b_{rainy}	Per capita number of eggs at each deposit (per day) in the rainy season	9.82	
Γ_Q	Carrying capacity of aquatic mosquito population	$2 \times N^{(H)}$	[41]
Γ_E	Carrying capacity of embryonic mosquito population	$2 \times N^{(H)}$	
η_Q	Rate of maturation from embryonic to aquatic (per day)	0.1	[42]
η_E	Rate of maturation from aquatic to adult (per day)	0.1	
d_Q	Aquatic stage natural mortality rate (per day)	0.25	[42]
d_E	Embryonic stage natural mortality rate (per day)	0.25	[42]
$1/\mu$	Natural lifespan of human (days)	78×365	[41]

The epidemiological parameters of the models are outlined in Table 7.2. The simulation throughout this section reflects the following assumptions and observations:

1. The contact rates follow the seasonal switching rule (7.28) where $\beta_{\text{dry}} \times \tau_1 + \beta_{\text{rainy}} \times \tau_2 = \beta$ and $\gamma_{\text{dry}} \times \tau_1 + \gamma_{\text{rainy}} \times \tau_2 = \gamma$. As the vector *Aedes albopictus* is sensitive to weather conditions (e.g., temperature and humidity), changes in seasonal weather patterns (i.e., dry season versus rainy season) also have an effect on the behavior of the human population (e.g., individuals are more active outside during the dry season in the late afternoon when *Aedes albopictus* is active, skin exposure is higher during the dry season versus the rainy season due to clothing).
2. Assume that $\beta_{\text{dry}} > \beta_{\text{rainy}}$ and $\gamma_{\text{dry}} > \gamma_{\text{rainy}}$ to model a higher pattern of average contacts during the dry season.
3. The chikungunya disease is introduced into the simulation around March 2005 (which occurs at $t = 365$ in our simulations).
4. As mentioned at the beginning of Chap. 7, there was a genetic mutation in the virus approximately 30 weeks after March 2005 ($t = 575$) which shifted γ from 0.375 to about 0.95 [41]. Hence, for the switching mutation parameter we assume that

$$\delta_\sigma = \begin{cases} 1 & \text{if } t < 575, \\ 2.53 & \text{if } t \geq 575. \end{cases} \quad (7.29)$$

Table 7.2 Epidemiological parameters

Parameter	Description	Average value	Source
d_s	Natural death rate of susceptible adult mosquitoes (per day)	0.1	[41]
d_I	Natural death rate of infected adult mosquitoes (per day)	0.2	[41]
β	Contact rate resulting in human infection (per day)	0.375	[41]
β_1	Contact rate resulting in human infection in dry season (per day)	0.4737	
β_2	Contact rate resulting in human infection in rainy season (per day)	0.2368	
γ	Contact rate resulting in mosquito infection (per day)	0.375	[41]
γ_1	Contact rate resulting in mosquito infection in dry season (per day)	0.4737	
γ_2	Contact rate resulting in mosquito infection in rainy season (per day)	0.2368	
g	Human natural recovery rate (per day)	3	[41]

That is, $\delta_\sigma \gamma_{\text{dry}} \times \tau_1 + \delta_\sigma \gamma_{\text{rainy}} \times \tau_2 = 0.375$ for $t < 575$ and $\delta_\sigma \gamma_{\text{dry}} \times \tau_1 + \delta_\sigma \gamma_{\text{rainy}} \times \tau_2 = 0.95$ for $t \geq 575$.

7.6.1 Assessment of Mechanical Destruction of Breeding Sites

Consider the mechanical destruction of breeding sites model (7.5), in which public campaigns to clean, remove, and destroy water receptacles are enacted. As in [41], the scheme is analyzed with

- (a) varying starting times (with respect to the timing of the outbreak), denoted here by t_c ;
- (b) different durations, denoted by h ; and
- (c) adjustments to the rate of breeding site destruction (accomplished via varying the parameter α).

The spread of the virus occurs around $t = 365$ days. Suppose that the control scheme is initiated at $t = t_c = 250$ and continued for a duration of $h = 150$ (until $t = 400$). Consider $\alpha = 0.49$ (i.e., approximately half of the breeding sites are destroyed) and note that $\bar{r} = 1.34$ in this case, implying persistence of the mosquito population by Proposition 7.1. After the genetic mutation and while the control scheme is being applied, the approximate mode basic reproduction numbers are calculated as $(R_0^{(7.5),1})^2 = 3.94$ (corresponding to the dry season) and $(\widetilde{R}_0^{(7.5),2})^2 = 2.50$ (corresponding to the rainy season). From this, $\Lambda_{\text{mechanical}} = -78.54$ and the disease is eradicated by Theorem 7.2 (see Fig. 7.2).

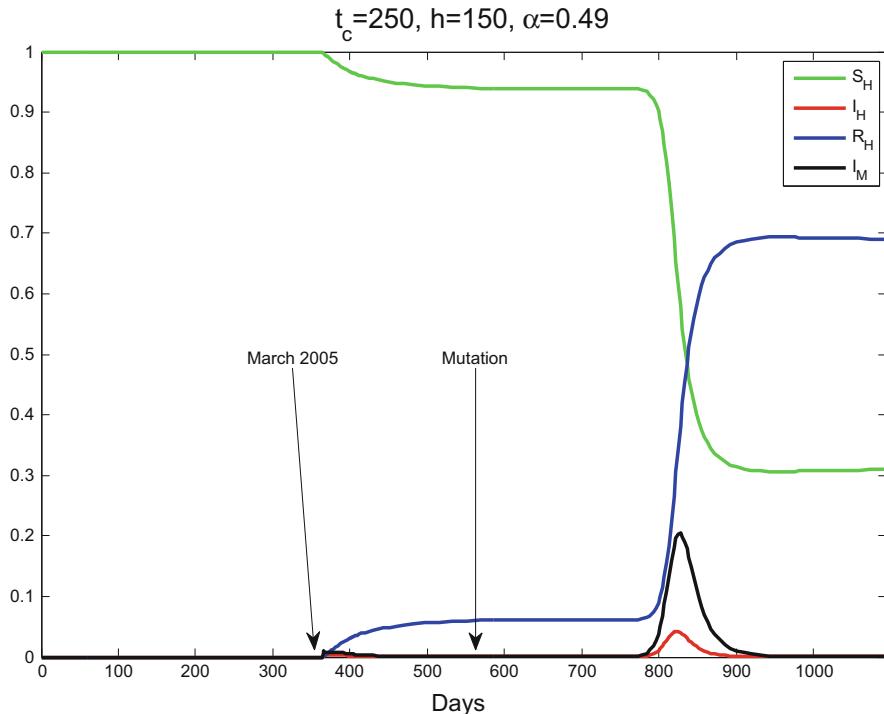


Fig. 7.2 Mechanical destruction model (7.5)

The outbreak in Réunion began with the first wave in May 2005 and was followed by a much larger epidemic wave in January and February of 2006. Dumont and Chiroleu [41] simulated a two-wave outbreak, separated by approximately 40 weeks, with the first wave being much smaller than the second wave. In line with this, after an initial small epidemic outbreak, there is a second much stronger epidemic outbreak (about 66 weeks later) in Fig. 7.3. Decreasing the number of aquatic mosquitoes (via the mechanical destruction) causes a reduction in the strength of the second epidemic wave (peak value of approximately 5800, compared to about 13,000 in the simulations in [41]). Moreover, it seems to also cause a delay between the two epidemic waves.

Remark 7.2 Presently, the mechanical destruction is assumed to affect only the aquatic stage and not the embryonic stage, which is reflected in the reduction of the carrying capacity Γ_Q to $\alpha\Gamma_Q$ but Γ_E remaining unaffected. However, since the females lay eggs in the containers, if the mechanical control for a particular container includes the actual destruction/removal of the container, the capacity of eggs deposited would also be reduced (and therefore Γ_E affected). The authors Dumont et al. [41] consider one compartment for both the aquatic/embryonic stage and assume that mechanical control affects both stages of life for the vector. This is a possible explanation for the delay between the epidemic waves mentioned above.

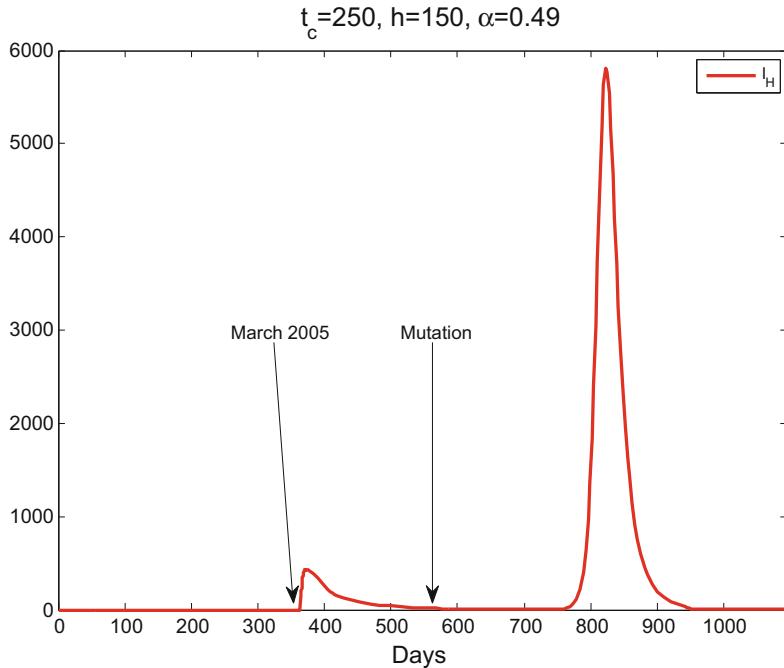


Fig. 7.3 Total number of infected humans in model (7.5) for different control rates α

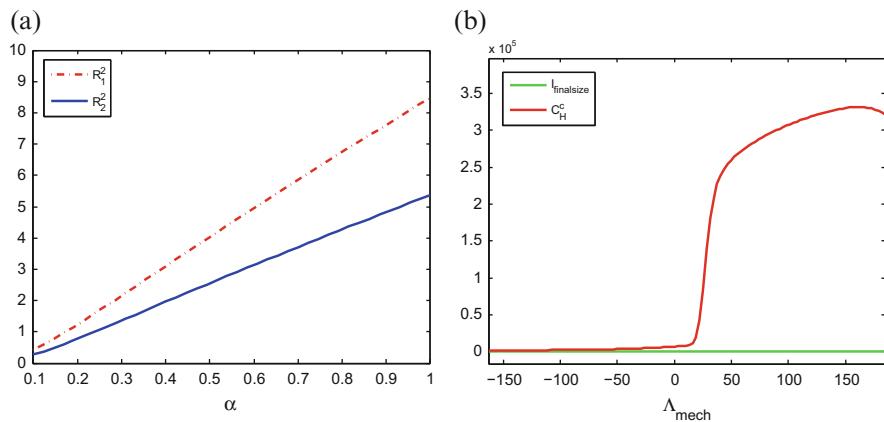


Fig. 7.4 Mechanical destruction model (7.5). (a) Values of $(\tilde{R}_0^{(7.5),1})^2$ (for the dry season, labelled as R_1^2 in the figure) and $(\tilde{R}_0^{(7.5),2})^2$ (rainy season, labelled as R_2^2) for varying values of α . (b) Final number of infected humans and cumulative infected humans

The relationship between the approximate mode basic reproduction numbers $\tilde{R}_0^{(7.5),i}$ and α are seen in Fig. 7.4a; $(\tilde{R}_0^{(7.5),1})^2 > (\tilde{R}_0^{(7.5),2})^2$ for all α from increases in human-mosquito contact during the dry season. As a further illustration of the

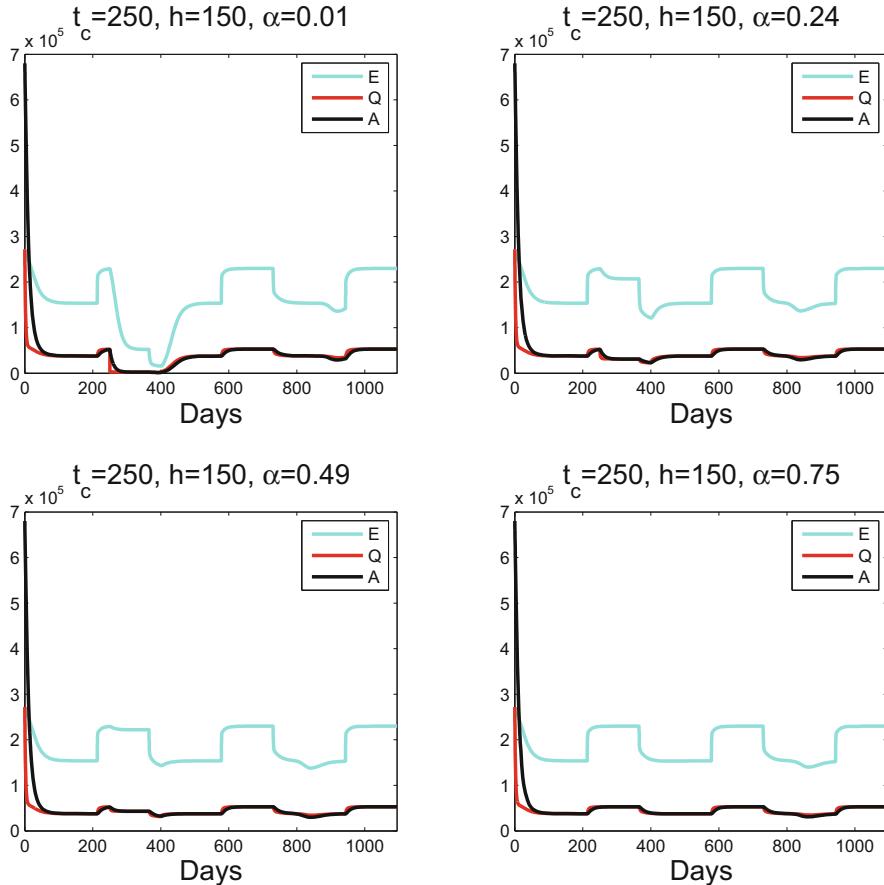


Fig. 7.5 Dynamics of the mosquito population for the mechanical destruction model (7.5)

eradication condition in Theorem 7.2, consider Fig. 7.4b which shows the final size of the epidemic ($I_{\text{finalsize}}$) and the cumulative number of infected humans under mechanical control (C_H^c) for different values of $\Lambda_{\text{mechanical}}$. As $\Lambda_{\text{mechanical}}$ decreases, the total number of infected humans also decreases and there is a transition around $\Lambda_{\text{mechanical}} \approx 25$ where the cumulative infected humans decreases sharply. The timing (t_c), duration (h), and strength (α) of the breeding site destruction play an important role in the dynamics of the mosquito population (see Fig. 7.5).

For further illustration, we consider evaluating the control efficacy number F_0 for mechanical control. The importance of α , t_c , and h is apparent in Fig. 7.6. If the duration is short, the scheme is not effective while if the scheme is initiated too early, the scheme is only successful if the duration is very long ($h = 365$). If the campaign is sufficiently long ($h = 365$) and is started before the first outbreak ($t_c = 300$) or soon after ($t_c = 400$), then the control strategy shows promise with

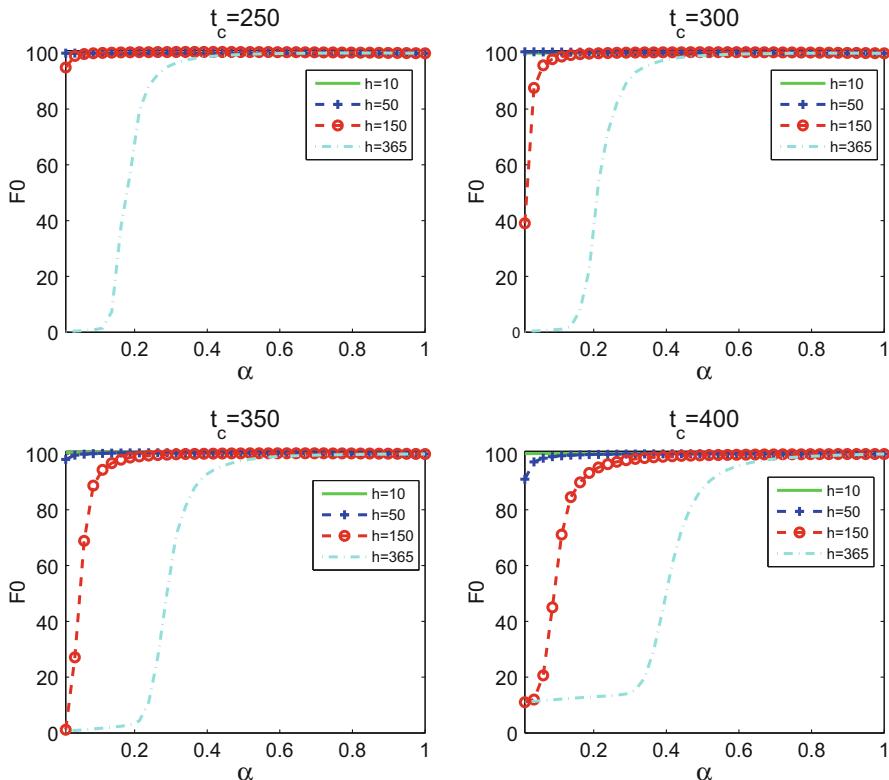


Fig. 7.6 The efficacy measure F_0 for different values of the destruction rate α under the mechanical destruction control strategy (7.5)

$F_0 \approx 20$ for mechanical destruction rates of $\alpha \approx 0.15$ or $\alpha \approx 0.30$, respectively. The most effective approach appears to be initiating the strategy before the second epidemic wave ($t_c = 700$), with $F_0 \approx 20$ achievable for different durations. There are sharp decreases in the efficacy rate F_0 at particular values of α for the above-mentioned successful cases, which is important from a cost-benefit perspective since decreasing α slightly can cause a significant improvement in the efficacy rate.

7.6.2 Assessment of Reduction in Contact Rate Patterns

Next we analyze (7.20), where the interaction between humans and mosquitoes is purposefully interrupted for a period of time. The following possibilities are considered here:

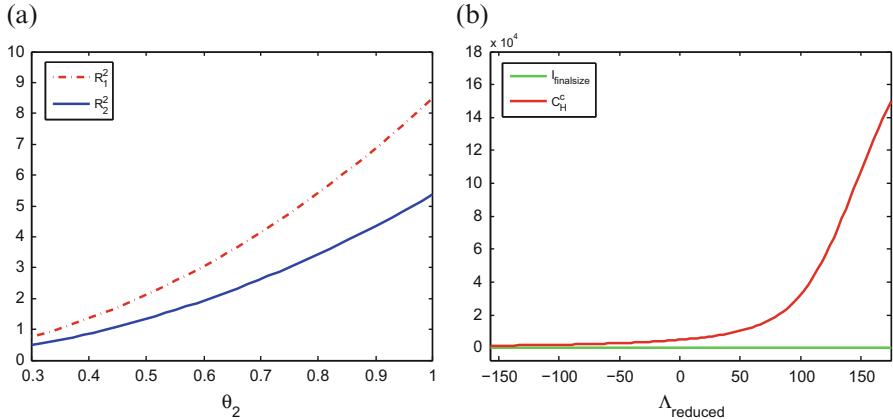


Fig. 7.7 Reduced contact rate model (7.20). **(a)** Values of $(\widehat{R}_0^{(7.5),1})^2$ (for the dry season, labelled as R_1^2 in the figure) and $(\widehat{R}_0^{(7.5),2})^2$ (rainy season, labelled as R_2^2) for varying values of θ_2 . **(b)** Final number of infected humans and cumulative infected humans for $\theta_2 = 0.64$

- (a) different reduction values (varying θ_i);
- (b) different timings for commencement of the strategy (denoted by t_c); and
- (c) different durations for the period of reduction (denoted by h).

The parameters t_c and h are altered by assuming that θ_σ follows the switching rule σ outlined as follows:

$$\theta_\sigma = \begin{cases} \theta_1 = 1, & \text{if } t < t_c \text{ or } t > t_c, \\ \theta_2, & \text{if } t_c \leq t \leq t_c + h. \end{cases} \quad (7.30)$$

Given that $\theta_2 = 0.64$ and the genetic mutation has occurred, then for the duration of the control scheme the thresholds can be calculated as $(\widehat{R}_0^{(7.5),1})^2 = 3.47$ and $(\widehat{R}_0^{(7.5),2})^2 = 2.20$. As a result, $\Lambda_{reduced} = -116.75$ and the disease is eradicated according to Theorem 7.4.

To illustrate how θ_2 factors into the approximate basic reproduction numbers $(\widehat{R}_0^{(7.5),i})^2$, see Fig. 7.7a. The final size of the epidemic ($I_{finalsize}$) and the cumulative number of infected humans (C_H^c) for different levels of $\Lambda_{reduced}$ under the reduced contact rates strategy with $\theta_2 = 0.64$ can be seen in Fig. 7.7b. As $\Lambda_{mechanical}$ increases, the total number of infected humans increases which is undesirable.

The timing (t_c), duration (h), and magnitude of contact rate reduction (θ_2) play an important role in the dynamics of the disease spreading (see Fig. 7.8). If the reduced contact strategy is initiated before or too early after an outbreak ($t_c = 300$ or $t_c = 400$), the scheme is not beneficial. If $t_c = 700$, then a duration $h = 90$ is relatively successful in controlling the disease, which may be unrealistically long for an intrusive strategy. The most effective approach ($F_0 \approx 20$) is to initiate the strategy during the second outbreak at $t_c = 800$, and for a duration of 60 days (90

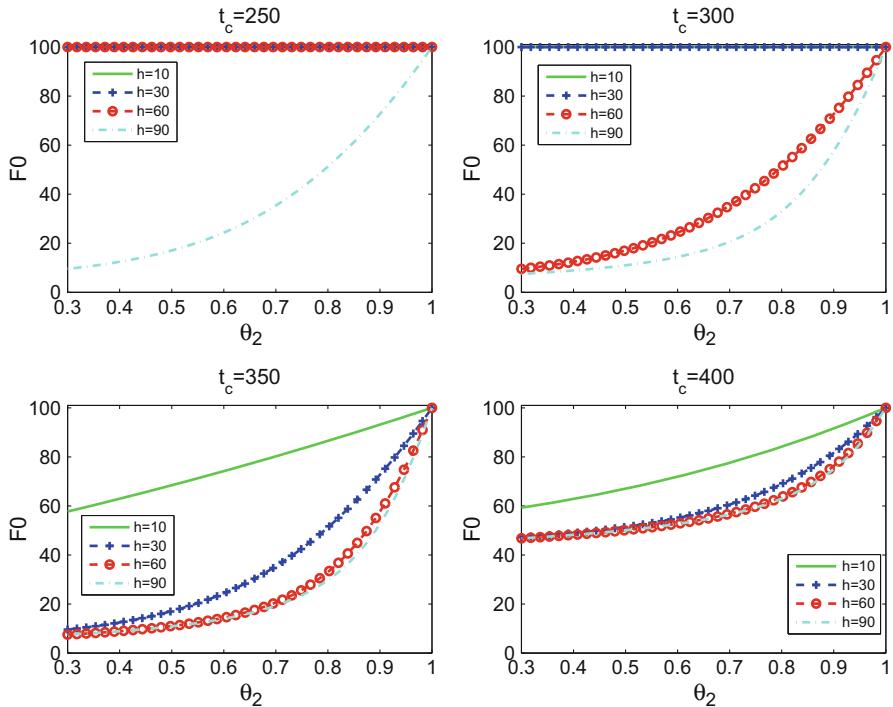


Fig. 7.8 The efficacy measure F_0 for the reduced contact rate scheme

days achieves similar results). Unlike the mechanical destruction efficacy analysis, there are no sharp decreases in F_0 for small increases in the control rate, and so the best approach from a cost-benefit point of view is not as obvious.

7.7 Discussions

From the investigations above, some observations and conclusions are drawn regarding the control strategies:

1. If either the mechanical destruction scheme or the reduced contact scheme is initiated too early, then the other control parameters must be at the upper end of their ranges. For example, the mechanical scheme requires $h = 365$ and $\alpha \approx 0.20$ to achieve $F_0 \approx 40$ if $t_c = 300$, which might be unrealistic (a public campaign of 80% breeding site destruction lasting a year). The reduced contact strategy is ineffective for a starting time of $t_c = 300$.
2. If the mechanical destruction scheme is applied for a short duration ($h = 10$ or $h = 50$), the scheme is not successful at all ($F_0 \approx 100$) regardless of the

breeding site destruction rate. Similarly, if the reduced contact rate strategy has a short duration ($h = 10$ or $h = 30$), the scheme is not impactful.

3. If contact rates are reduced during the second outbreak ($t_c = 800$), desirable efficacy rates can be achieved (such as $F_0 \approx 50$) for reasonable control rates (e.g., $\theta_2 \approx 0.60$). Unfortunately, the scheme's duration would need to be a possibly unrealistic 90 days (3 months of a 40% reduction in human–mosquito interactions).
4. In general, the mechanical destruction strategy requires the control rate α to be exceptionally low and the duration h to be large to achieve a desirable control efficacy (e.g., $F_0 < 50$). The comparatively low socioeconomic cost of this strategy, compared to a reduction in contact rates, might make this desirable.
5. The observation that the mechanical strategy seems to do well when initiated after the first outbreak ($t_c = 400$) if the duration is sufficiently long ($h = 365$) may be related to the delay in the epidemic peak mentioned earlier. This warrants further investigation (possibly from an optimal control point of view).
6. Mentioned only briefly, the above analyses do not factor in the socioeconomic cost of the control strategies. For example, mechanical destruction of breeding sites can be relatively cheap since it can be made up of a public-driven campaign. However, the reduced contact rate strategy may be quite intrusive to the daily lives of the human population.

From these notes, it seems that the best course of action to combat future chikungunya outbreaks in Réunion or other similar regions is to commence public campaigns of mechanical destruction of breeding sites in conjunction with a reduction in contact rate strategy in response to an outbreak. Since mechanical destruction may be comparatively cheap, the length and destruction rate should be made as high as possible. In addition, a reduced contact rate strategy should be commenced immediately after an outbreak with a high reduction rate (low value of θ_2) for a short duration (e.g., $h = 10$ days), followed by a period of longer duration with a lower reduction rate (higher value of θ_2).

In [99], which formed the basis for this chapter, a pulse vaccination strategy for controlling chikungunya outbreaks was also analyzed theoretically (with smoothly varying contact rates via Floquet theory) and numerically. The findings concluded that the best course of action to combat chikungunya outbreaks in Réunion or similar regions was a pulse vaccination strategy. The authors emphasized that although no commercially viable vaccines currently exist (Table 1 in [161] provides relevant information on the state of vaccine research), efforts should be continued towards finding a relatively cheap and viable commercial vaccine. Moreover, the cost-basis associated with initiating and maintaining such a pulse vaccination strategy (along with the other controls strategies) would have to be evaluated but that vaccines are cost-effective in general as compared to post-exposure treatments and disease management efforts [161].

Part IV

Conclusions and Future Work

Chapter 8

Conclusions and Future Directions

Invaluable for building and testing theory, epidemic models are useful in designing, implementing, and evaluating control programs. In this monograph, we have constructed and analyzed a new type of switched model for the spread of infectious diseases. Broadly, the focus was on studying the qualitative behavior of epidemics by establishing threshold criteria using stability and switched systems theory. Infectious disease models with time-varying parameters and nonlinear incidence rates which may change functional forms in time have been analyzed. The approach taken is to introduce switching into infectious disease models by assuming that the model's parameters are time-varying functions that switch in time, and the model's incidence rate switches functional forms due to either environmental factors (such as seasonality) or behavioral factors (such as a shift in the population's behavior). In order to model the incidence rate this way, the infectious disease is modeled as a switched system of differential equations. This included developing theory for ensuring disease eradication by virtue of techniques from switched systems (e.g., Halanay-like inequalities, dwell-time methods, common and multiple Lyapunov functions). Results have been put forth concerning convergence of solutions to a disease-free set or periodic disease-free solutions. Often, this was achieved in the form of global attractivity of a disease-free solution and partial I -stability, which has been argued to be useful in the setting of epidemic modeling. At times, fundamental theory was shown in the form of mathematical and biological well-posedness of models.

In Part II, the switched systems formulation of epidemic models was introduced and studied. For these purposes, necessary concepts and background material from switched systems theory (including basic theory on ordinary differential equations, etc.) were presented in Part I. After its classical derivation, the SIR model was used to demonstrate this switched systems modeling framework in Chap. 3. Following this, we looked at other epidemic models in Chap. 4 that are found in the mathematical epidemiology literature and analyzed these models with switching introduced. Part III investigated the application of control schemes to the switched epidemic

models. Namely, continuous and switching control (e.g., newborn vaccinations) in Chap. 5 and impulsive control (e.g., pulse vaccination) in Chap. 6. The classical epidemic models studied, and their corresponding analyses, were extended in three ways: (1) the consideration of seasonality in the disease spread via switching model parameters; (2) the analysis of shifts in population behavior, captured by switched general incidence rate functions; and (3) the application of switching and impulsive control strategies for eradication. This included applying stability results to switched epidemic models with time delays and a case study of the chikungunya virus in Chap. 7, as a new model of the disease's outbreak in Réunion in 2005–06, where control strategies were considered (mechanical destruction of mosquito breeding sites, contact rate reduction), accompanied by analytic and numerical investigations to evaluate the schemes. By comparing the control schemes from an analytical perspective and through simulations observations were made regarding an appropriate response to an impending epidemic from a cost-benefit perspective. This work is especially timely given that mosquitoes of the *Aedes* genus (i.e., *Aedes albopictus*) are also responsible for the recent spread of the Zika virus.

There are a number of benefits to a switched systems approach to infectious disease modeling. The contact rate can be approximated as a time-varying parameter without requiring a non-autonomous ODE modeling approach, where the analytical methods can be more difficult and unavailable for some modeling assumptions. Instead, switched systems techniques can be applied to easily prove verifiable eradication criteria for time-varying contact rates. The switching rule considered in this monograph is restricted to those satisfying a nonvanishing dwell-time, which is not restrictive. Different classes of such rules are considered (e.g., periodic). Switching and impulsive control can be incorporated into this framework in a straightforward way; the impulsive effects can be applied at the switching times, or can be independently applied to the populations. Another benefit of this modeling framework is seen in the epidemic models presently studied with general switched incidence rates (first presented in Sect. 3.5). Moreover, although the switching rules presently considered admit switching times that are time-dependent, extensions to those that are state-dependent are possible in this framework (the exception being the state-dependent pulse vaccination scheme studied in Sect. 6.1.7).

The switched systems methods can be adapted to numerous epidemic models, as illustrated in this monograph; application to other types of infectious disease models as future work is promising. One area that can be further investigated is epidemic models with time delays (e.g., arising from latent periods of the disease), where switched systems with time delays has been studied less extensively in the literature. The homogeneous mixing assumption was revisited at times in this monograph but was used in the majority of the modeling efforts. This leaves room for more analysis of models with heterogeneous mixing of the population (e.g., age-dependent mixing, which matches the data better; see [65, 69, 116] for details). Alternatively, the multi-city models could instead consider a spatial dimension (instead of nodes on a network). In both cases, this would lead to switched systems of partial differential equations, which is a relatively new area of work. In the cases where common or multiple Lyapunov functions are not easily found, other

techniques can be developed for use in the analysis of switched epidemic models. Hence, one possible direction is to generalize the present methods centered on stable and unstable modes captured in the differential equation for I whenever more compartments are involved in the spread of the disease (e.g., SEIR models). Other directions for future work include more fundamental extensions of theory; establishing basic theory for stochastic switched systems with time delays and adjusting the so-called Razumikhin-type theorems for use in switched epidemic models are two such examples. Another important avenue of work warranting future investigations is found in the optimal hybrid control setting, motivated by some of the observations at the end of Chap. 6 (specifically, Sect. 6.2.1) and the case study analysis in Chap. 7 (specifically, Sects. 7.6 and 7.7.).

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