A Study of Infectious Disease Models with Switching

by

Peter Stechlinski

A thesis
presented to the University of Waterloo
in fulfillment of the
thesis requirement for the degree of
Master of Mathematics
in
Applied Mathematics

Waterloo, Ontario, Canada, 2009

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Infectious disease models with switching are constructed and investigated in detail. Modelling infectious diseases as switched systems, which are systems that combine continuous dynamics with discrete logic, allows for the use of methods from switched systems theory. These methods are used to analyze the stability and long-term behaviour of the proposed switched epidemiological models.

Switching is first incorporated into epidemiological models by assuming the contact rate to be time-dependent and better approximated by a piecewise constant. Epidemiological models with switched incidence rates are also investigated. Threshold criteria are established that are sufficient for the eradication of the disease, and, hence, the stability of the disease-free solution. In the case of an endemic disease, some criteria are developed that establish the persistence of the disease.

Lyapunov function techniques, as well as techniques for stability of impulsive or non-impulsive switched systems with both stable and unstable modes are used. These methods are first applied to switched epidemiological models which are intrinsically one-dimensional. Multi-dimensional disease models with switching are then investigated in detail. An important part of studying epidemiology is to construct control strategies in order to eradicate a disease, which would otherwise be persistent. Hence, the application of controls schemes to switched epidemiological models are investigated. Finally, epidemiological models with switched general nonlinear incidence rates are considered.

Simulations are given throughout to illustrate our results, as well as to make some conjectures. Some conclusions are made and future directions are given.

Acknowledgements

First and foremost, I would like to thank my supervisor Dr. Xinzhi Liu, whose guidance has been invaluable in my time as a graduate student. I would like to extend a great thanks to my examining committee, Dr. Marek Stastna and Dr. Sue Ann Campbell, both of whom gave very helpful feedback, in the form of both corrections and suggestions. I would like to extend a thank you to the members of my research group: Mohamad Alwan, Jun Liu, Benjamin Turnbull, Hongtao Zhang and Lijun Wang, each of whom helped me either directly or indirectly with my research.

I am very grateful for all the help Helen Warren has given me during this process. I would like to thank Dr. Edward Vrscay for his helpful advice, beginning in my undergraduate days, and, finally, I would like to thank Dr. Hans De Sterck for being understanding.

Dedication

To my Mother and Father.

Contents

List of Tables

List of Figures

Chapter 1

Introduction

Over the past three centuries, human life expectancy has increased from approximately 30 years in 1700 to approximate 70 years in 1970 [2]. One of the main causes of this improvement has come from a decline in deaths as a result of infectious diseases [2]. In contrast to this decline in mortality, both the magnitude and frequency of epidemics has increased during the 18th and 19th centuries, principally as a result of an increase of large population centers in increasingly industrialized societies [2]. This trend then reversed in the 20th century, mainly due to the development and widespread use of vaccines to immunize susceptible populations [2]. Although chronic diseases, such as cancer and heart disease, now receive more attention in developed countries, infectious diseases are still important factors in causing suffering and mortality in developing countries [27]. 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 [28].

In the 20th century, new infectious diseases have emerged and some existing diseases have re-emerged [28]. Measles, a serious disease of childhood, still causes approximately one million deaths each year worldwide [28]. Type A influenza led to the 1918 pandemic (which is a worldwide epidemic) that killed over 20 million people worldwide [28]. Examples of newly emerging infectious diseases include Lyme disease (1975), Legionnaire's disease (1976), hepatitis C (1989), hepatitis E (1990), and hantavirus (1993) [28]. The appearance of the human immunodeficiency virus (HIV) in 1981, which leads to acquired immunodeficiency syndrome (AIDS), has become an important sexually transmitted disease throughout the world [28]. New antibiotic-resistant strains of tuberculosis, pneumonia, and gonorrhea have emerged [28]. Malaria, dengue, and yellow fever have re-emerged and, as a result of climate changes, are spreading into new regions [28]. Plague, cholera, and hemorrhagic fevers (for example, Ebola) continue to erupt occasionally [28]. For other detailed accounts of important emerging diseases in the 20th century, see [28].

Mathematical models have become important tools in analyzing both the spread and control of infectious diseases. An English country doctor, Edward Jenner,

observed that milkmaids who had been infected with cowpox did not get smallpox [28]. And so, beginning in 1796, he started vaccinating people with cowpox to protect them from smallpox [28]. This was the world's first vaccine, taken from the Latin word vacca for cow [28]. The first known mathematical epidemiology model was formulated and solved by Daniel Bernoulli in 1760 [43]. Theoretical papers on infectious disease models by Kermack and McKendrick (1927, 1932, 1933) have had a major influence in the development of mathematical epidemiology models [55]. These authors were the first to obtain a threshold result that showed the density of susceptibles must exceed a critical value for an epidemic outbreak to occur [28]. The foundations of modern mathematical epidemiology based on compartment models were laid in the early 20th century, and, since the middle of the 20th century, mathematical epidemiology has grown exponentially [43]. A tremendous number of models have been formulated, analyzed and applied to a variety of infectious diseases. Mathematical models have been formulated for diseases such as measles, rubella, chickenpox, whooping cough, smallpox, malaria, rabies, gonorrhea, herpes, syphillis, and HIV/AIDS [27]. For a review of mathematical models of infectious diseases, see [3, 27, 28, 31].

These models may be rather simple, but studying them is crucial in order to gain important knowledge of the underlying aspects of the spread of infectious diseases [27]. One purpose of analyzing epidemiology models is to get a clear understanding of the similarities and differences in the behaviour of solutions of the models, as this allows us to make decisions in choosing models for certain applications [27]. These models provide important conceptual results such as thresholds. For example, the basic reproduction number conceptualizes the rate of spread of a certain disease[28]. Mathematical models and computer simulations are extremely useful tools for building theories, testing them, assessing quantitative conjectures, answering qualitative questions and estimating key parameters from data [28]. Epidemiology modelling can identify trends and suggest crucial data that should be collected, make general forecasts, and estimate the uncertainty in forecasts [28]. Certainly, understanding the transmission characteristics of a communicable infectious disease in a region can lead to improved approaches to decreasing the transmission of said disease [28].

One of the most important aspects of epidemiology is the application of control schemes to eradicate, or at least supress, a disease. Infectious disease models are vital for comparing, implementing, evaluating, and optimizing various detection, prevention, and control programs [28]. These models are very useful in giving reasoned estimates for the level of vaccination required for the control of a disease [55]. For example, the World Health Organization (WHO) began an initiative against smallpox in 1967 when there were approximately 15 million cases per year. The WHO strategy involved extensive vaccination programs, surveillance for outbreaks, and containment of these outbreaks by local vaccination programs [28]. Smallpox was eventually eradicated worldwide by 1977 [28]. This has been considered the most spectacular success of a vaccination program [47]. The WHO estimates that the elimination of smallpox worldwide saves over two billion dollars per year [28]. There are now vaccines that are effective in preventing rabies, yellow fever,

poliovirus, hepatitis B, parotitis, and encephalitis B [41].

Recently, pulse vaccination has gained in prominence as a control scheme as a result of its successful application to the control of polyomyelitis and measles throughout Central and South America [67]. The strategy has also been examined in the United Kingdom, where children aged five to 16 years were offered a combined measles and rubella vaccine in 1994 [67]. Coverage of 90% or more was achieved in 133 of 172 districts, and the mean coverage in England and Wales reached 92% [67]. 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 [67]. Pulse vaccination has been illustrated to be an effective strategy in preventing such viral infections as rabies, yellow fever, poliovirus, and hepatitis B [61]. In 1988, the WHO set a goal of global polio eradication by the year 2000 [28]. 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 for acute flaccid paralysis [28]. Polio has disappeared from many countries from 1990-2000, and it is likely that polio will soon be eradicated worldwide [28]. The WHO estimates that eradicating polio will save approximately 1.5 billion dollars each year in immunization, treatment, and rehabilitation around the globe [28]. Eventually, it is possible that vaccines will prevent malaria, venereal diseases, and even some forms of heart disease and cancer [48].

A crucial part in the medical and statistical study of an epidemic is its transmission, which depends on the intrinsic infectiousity of the disease and on population behaviour [60]. In mathematical modelling, these two aspects are summarized in the contact rate and the incidence rate of a disease, which are, respectively, 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 [28]. Empirical studies have shown that the transmission of many infections varies seasonally [31]. For example, 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 [31]. For many diseases, seasonality is one of the main forces driving an epidemic outbreak. An analysis of the biennial pattern in New York demonstrates that sufficiently large seasonal variations in transmission can generate a biennial looking cycle [63]. It has also been observed that data from England and Wales displays a four-year cycle in poliomyelitis incidence, while measles has also been observed to have a biennial cycle for the same countries [63].

The objective of this thesis is to formulate new epidemiology models with time-varying contact rates or time-varying incidence rate structures, and to study the long-time behaviour of diseases. More specifically, we look to extend epidemiology models in the literature by the addition of switching, that is, the abrupt change of the dynamics governing the systems at certain switching times. This switching will allow the contact rate to be approximated by a piecewise constant function.

Though there have been some studies on models with time-dependent contact rates in the literature (for example, see [31, 49, 66]), analytical methods for analyzing models with time-dependent contact rates are lacking [31]. Since relatively modest variations in the contact rate can result in large amplitude fluctuations in the transmission of a disease [31], this is an important phenomenon that requires attention. Switching is a new approach to this problem and has not been studied before as an application to epidemiology models.

For a given infectious disease model, a specific incidence rate must be chosen appropriately based on the scenario and disease being modelled. There are numerous incidence rates which have been used in models in the literature; for example, the standard incidence, saturation incidences, weakly nonlinear incidences, psychological-effect incidences, media coverage incidences, and more general nonlinear forms (see [27, 33, 60, 61]). With regards 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 [60], which gives extra motivation in studying time-varying incidence rate structures. Thus, changing the structure of the incidence rate over time, which has not been investigated in the epidimiology literature, may be very useful in giving new insights and new directions for future work. Taking a switched systems approach will also allow us to easily extend switched infectious disease models to include control techniques, such as constant and pulse control. Hence, the contributions of this thesis will be a method to analyze epidemiology models with time-dependent parameters and function forms, which are easily extendable to many different models, as will be shown.

The idea of switching the dynamics of a system comes from the area of hybrid and switched systems. Hybrid and switched systems are described using a mixture of continuous dynamics and logic-based switching [64]. The classical view of such systems is that they evolve according to mode-dependent continuous dynamics, and experience transitions between modes that are triggered by certain events [64]. A switched system usually arises in two cases [12]: One is when there are abrupt changes in the structure or the parameters of a dynamical system, which can be due to, for example, variations in environmental factors. Second, when a continuous system is controlled using a switched controller, which can achieve better performance than a continuous controller in certain cases. It is also possible for a system to not be asymptotically stabilizable by a single continuous controller, but can be by a switched controller [42].

The area of hybrid dynamical systems (HDS) is a new discipline which bridges applied mathematics, control engineering, and theoretical computer science [17]. Many problems facing scientists as they seek to control complex physical systems using computers naturally fit into the HDS framework [17]. Indeed, there is a growing demand in industry for methods to model, analyze, and understand systems that combine continuous components with logic-based switching [64]. Practical examples of switched systems include areas as diverse as mechanical systems, the automotive industry, air traffic control, robotics, intelligent vehicle/highway systems, robotics, integrated circuit design, multimedia, manufacturing, power electronics,

switched-capacitor networks, chaos generators, computer disk drives, automotive engine management, high-level flexible manufacturing systems, job scheduling, interconnected power systems, and chemical processes [12, 17, 22, 42]. The majority of switched systems literature covers continuous and discrete switched systems, but these systems do not encompass real world applications which exhibit dynamics with an impulsive effect at switching points [22]. Examples of systems which can be described by switching states with abrupt changes at the switching instances include biological neural networks, bursting rhythm models in pathology, optimal control modes in economics, frequency-modulated signal processing systems, and flying object motions [22]. There are few reports dealing with hybrid impulsive and switched systems and the corresponding control problem [22]. Hybrid and impulsive systems will be important when we look to add pulse control to the switched models.

Switched systems can lead to interesting behaviour, such as the instability of a switched system comprised solely of stable continuous subsystems [42] and the switched and impulsive control of unstable continuous subsystems that leads to a stable switched system [22, 23]. Hybrid control has also received growing interest, due to its advantages in improving transient response, and providing an effective mechanism to deal with highly complex systems and systems with large uncertainties [22]. Further, impulsive and switching control is an effective method in achieving stabilization of complex systems using only small control impulses in different modes, even though the complex system behaviors may follow unpredictable patterns [22]. A substantial part of the switched systems literature is concerned with conditions guaranteeing stability. Some common techniques to show stability of these systems are the switched invariance principle [6, 24, 25] and common/multiple Lyapunov function techniques [8, 9, 12, 62]. There is literature on families of subsystems that are triangularizable [53], as well as those that commute [56]. Work has been done on the control of discrete switched systems [11], the stabilization of nonlinear switched systems using control [54], and criteria for the instability of switched systems under arbitrary switching [65]. A general overview of hybrid and switched systems and its literature can be seen in [12, 13, 42, 64].

This thesis is organized as follows: Chapter 2 establishes the necessary mathematical background for systems of ordinary differential equations, systems of impulsive differential equations, epidemiology models and switched systems. In Chapter 3, variations of the basic one dimensional SIS model with switching will be investigated in detail. Some sufficient conditions for the eradication of the disease are developed, as well as some results for the endemic case. In Chapter 4, disease models that are intrinsically at least two dimensional will be analyzed thoroughly, and threshold criteria for the eradication of the disease are established. In Chapter 5, control strategies are applied to switched epidemiology models and studied. In Chapter 6, more general switched epidemiology models will be developed and analyzed. Finally, some conclusions are drawn and future directions are given in Chapter 7. Simulations are given throughout the thesis.

Chapter 2

Mathematical Background

In order to analyze infectious disease models with switching, it is necessary to first establish some background theory from differential equations (DEs), impulsive differential equations (IDEs), mathematical epidemiology and switched systems theory. This background theory will help in mathematically formalizing the practical questions in epidemiology, such as: Will there be an epidemic? If so, how severe will it be? What will be the long-term behaviour of the disease? And so on.

In Section 2.1, some classical theory of ordinary differential equations will be given. This theory will be the backbone for the rest of the thesis. It will formalize the practical problems in a mathematical sense. It will also outline some important fundamental theories, such as existence and uniqueness, as well as some practical methods for proving stability, such as the Lyapunov function method and LaSalle's Invariance Principle. The concept of partial stability, which will be used in the thesis, is outlined in Section 2.1.2. In Section 2.1.3, impulsive differential equations will also be introduced and discussed in some detail.

In Section 2.2, the mathematical formulation of infectious disease models will be posed. The formulation taken will be deterministic continuous ordinary differential equations. Important concepts will be outlined, and illustrated, for some of the more classic epidemiology models from the literature. Finally, control schemes will be introduced, a vital part of epidemiology as it pertains to the control, prevention and eradication of diseases around the world.

In Section 2.3, switched systems will be introduced, with some practical applications and interesting results. The motivation for developing the switched systems theory will be for use in applying it to infectious disease models.

2.1 Preliminaries

2.1.1 Systems of Differential Equations

Unless otherwise specified, the material in this section is taken from [45]. Consider the following system of autonomous ordinary differential equations (ODEs):

$$x' = f(x), \tag{2.1}$$

where $x = (x_1(t), \ldots, x_n(t))^T$ and $f(x) = (f_1(x_1, \ldots, x_n), \ldots, f_n(x_1, \ldots, x_n))^T$. The system is said to be autonomous because the right-hand side of equation (2.1) does not explicitly depend on t. If the initial condition $x(t_0) = x_0 \in D \subset \mathbb{R}^n$, where D is an open set, $\mathbb{R}^n$ is the n-dimensional Euclidean space, and $t_0 \in \mathbb{R}$, is added to the system, the system becomes an initial value problem (IVP):

$$\begin{cases} x' = f(x), \\ x(t_0) = x_0. \end{cases} \tag{2.2}$$

A solution to this IVP is a differentiable function $\phi(t; x_0)$ if $\phi'(t; x_0) = f(\phi(t; x_0))$ and $\phi(t_0; x_0) = x_0$. Since the IVP is autonomous, without loss of generality we can take $t_0 = 0$. This can be seen easily by defining a new time variable $\tau = t - t_0$. It is desirable, for mathematical reasons and for real-world applications, to know whether or not there exists a unique solution to (2.2).

Theorem 2.1.1. *Let D be an open subset of $\mathbb{R}^n$ and assume that $f \in C^1[D, \mathbb{R}^n]$. Then for all $x_0 \in D$, there exists an $\alpha > 0$ such that the IVP (2.2) has a unique solution $x(t) = \phi(t; x_0)$ on the interval $[-\alpha, \alpha]$.*

Here $C^1[D, \mathbb{R}^n]$ is the space of continuously differentiable functions that map D to $\mathbb{R}^n$. In applications such as epidemiology, where the independent variable t represents the physical quantity of time, it is important that the model is mathematically and biologically well-posed, that is, there exists a unique solution which is defined for all time $t \geq 0$. In order to address this problem, the following definitions are needed:

Definition 2.1.1. *Let $x(t)$ by a solution of the IVP (2.2) defined on an interval J, then J is called a right-maximal interval of existence for $x(t)$ if there does not exist an extension of $x(t)$ over an interval J_1 so that $x(t)$ remains a solution of the IVP (2.2) on J_1, and J is a proper subset of J_1 with different right endpoints. A left-maximal interval of existence for $x(t)$ can be defined similarly. A maximal interval of existence for $x(t)$ is an interval which is both a left-maximal and right-maximal interval.*

The following theorems can now be stated, which establish global existence of a solution.

Theorem 2.1.2. *Let $f \in C^1[\mathbb{R}^n, \mathbb{R}^n]$ and $\phi(t; x_0)$ be a solution of (2.2) on a maximal interval J. Then $J = (-\infty, \infty)$ if one of the following is true:*

(i) $\phi(t; x_0)$ is bounded on J,

(ii) $f(x)$ is bounded on $\mathbb{R}^n$.

Theorem 2.1.3. *Let $f \in C^1[\mathbb{R}^n, \mathbb{R}^n]$, and let $\phi(t; x_0)$ be a solution of (2.2) on a maximal right interval J. Then, either $J = [0, \infty)$ or $J = [0, \beta^*)$ with $\beta^* < \infty$ and $\|\phi(t; x_0)\| \to \infty$ at $t \to \beta^*$.*

Here, the usual Euclidean norm is used, $\|x\| = \sqrt{x_1^2 + \ldots + x_n^2}$. A corollary of these theorems can be stated, which will give sufficient conditions for a solution to exist on a maximal interval of $J = [0, \infty)$.

Definition 2.1.2. *A subspace $\Gamma \subset D$ is said to be an invariant set of (2.2) if all solutions $\phi(t; x_0)$ starting in Γ remain in Γ for all time $t \in \mathbb{R}$.*

Definition 2.1.3. *A subspace $\Gamma \subset D$ is said to be a positively invariant set of (2.2) if all solutions $\phi(t; x_0)$ starting in Γ remain in Γ for all time $t \geq 0$.*

Definition 2.1.4. *A set $\Gamma \subset D$ is compact if it is closed (that is, contains all of its limit points) and bounded (that is, there exists an $M > 0$ such that $\|x\| \leq M$ for all $x \in \Gamma$).*

Corollary 2.1.4. *Let $f \in C^1[\mathbb{R}^n, \mathbb{R}^n]$, and let $\phi(t; x_0)$ be a solution of (2.2) on a maximal right interval J. Suppose Γ is a compact set that is positively invariant to the IVP (2.2). If $x_0 \in \Gamma$ then the maximal interval of existence is $J = [0, \infty)$.*

This follows from Theorem 2.1.3 which can be seen easily: if Γ is compact and positively invariant then the solution $\phi(t; x_0)$ will be bounded for all time $t \geq 0$, hence Theorem 2.1.3 can be applied and the maximal interval is $J = [0, \infty)$.

Now that the existence and uniqueness of the solution $x(t)$ to the IVP (2.2) has been established, the next important step is determining an analytical solution. In the special case that $f(x) = Ax$, where $A \in \mathbb{R}^{n \times n}$ is a constant matrix, a unique solution can be given explicitly.

Theorem 2.1.5. *Assume $f(x) = Ax$, $A \in \mathbb{R}^{n \times n}$, then the IVP (2.2) has a unique solution for all time $t \in \mathbb{R}$, which is given by*

$$x(t) = e^{At} x_0, \tag{2.3}$$

where e^{At} is the matrix exponential, defined as follows:

$$e^{At} := \sum_{k=0}^{\infty} \frac{A^k t^k}{k!},$$

which converges for all time $t \in \mathbb{R}$.

Unfortunately, there is no general method for solving the nonlinear IVP (2.2) analytically. However, in many real world applications (e.g. population, mechanical and infectious disease models) there are important qualitative features which may be gathered. Important questions one may ask are: What will the long-term behaviour of the solution be? Will the solution converge to a constant value, a periodic function, diverge, or something else? If two solutions of the IVP (2.2), $\phi_1(t; x_1)$ and $\phi_2(t; x_2)$, begin close to each other, that is, $\phi_1(0; x_1) = x_1 \approx \phi_2(0; x_2) = x_2$, will the solutions stay close to each other for all time? Many of these kinds of questions are answered by studying the stability of the IVP (2.2).

Definition 2.1.5. *A point $\bar{x}$ is said to be an equilibrium point of the IVP (2.2) if $f(\bar{x}) = 0$, since $x(t) = \bar{x}$ is then, by inspection, a solution to the IVP.*

Note that if $f(\bar{x}) = 0$ for $\bar{x} \neq 0$ then this equilibrium point can be shifted to the origin. Set $y = x - \bar{x}$, then $y' = x' = f(x) = f(y + \bar{x}) = \widetilde{f}(y)$ and then the IVP becomes

$$\begin{cases} y' = \widetilde{f}(y), \\ y(0) = y_0, \end{cases} \tag{2.4}$$

with $y_0 = x_0 - \bar{x}$, and the initial time has been taken to be zero, i.e. $t_0 = 0$. Then, without loss of generality, assume the equilibrium points are shifted to the origin, i.e. $f(0) = 0$. The equilibrium point $x = 0$ is often called the trivial solution. The long-term behaviour of the IVP (2.2) can be characterized using the following stability concepts.

Definition 2.1.6. *Consider the IVP (2.2). Assume $f(0) = 0$ and let $\phi(t; x_0)$ be the solution of the IVP such that $\phi(0; x_0) = x_0$ where $x_0 \in D$, then the origin, $x = 0$, is said to be*

(i) stable if for all $\epsilon > 0$ there exists a $\delta > 0$ such that $\|x_0\| < \delta$ implies $\|\phi(t; x_0)\| < \epsilon$ for all $t \geq 0$,

(ii) asymptotically stable if (i) holds and there exists a $\beta > 0$ such that $\|x_0\| < \beta$ implies

$$\lim_{t \to +\infty} \phi(t; x_0) = 0,$$

(ii) exponentially stable if there exist constants $\alpha, \gamma, C > 0$ such that if $\|x_0\| < \alpha$ then $\|\phi(t; x_0)\| < C\|x_0\|e^{-\gamma t}$ for any $t \geq 0$,

(iv) globally asymptotically (exponentially) stable if it is asymptotically (exponentially) stable and β (α) is arbitrary,

(v) unstable if (i) fails to hold.

Note that exponential stability implies asymptotic stability. Stability is useful in answering the question of whether two solutions will stay close to each other if

they begin close to each other. Asymptotic stability helps in giving a mathematical formulation for the long-term behaviour of the system, without necessarily knowing the analytical solution. Exponential stability is more attractive than asymptotic stability because it also gives information on the rate at which the solution converges to the origin.

The next step then is finding a procedure to show the solution of the IVP (2.2) satisfies any of the above definitions (2.1.6). In the linear case, $f(x) = Ax$, the following simple condition for the stability of the IVP (2.2) follows from Theorem 2.1.5.

Theorem 2.1.6. *Suppose $f(x) = Ax$ for the IVP (2.2), and $A \in \mathbb{R}^{n\times n}$ is a Hurwitz matrix*[1]*, then the origin of the system is asymptotically stable. If there exists an eigenvalue λ of A such that $Re(\lambda) > 0$, then the origin is unstable.*

In the more general case where the IVP is nonlinear, one approach is linearizing (2.2) about an equilibrium point. This gives information about the behaviour of trajectories of solutions to the IVP (2.2) near the equilibrium points. The approach is to consider the linear approximation of $f(x)$ at an equilibrium point. Assume that f has continuous partial derivatives with respect to x. The derivative of $f(x) = (f_1(x_1, \ldots, x_n), \ldots, f_n(x_1, \ldots, x_n))^T$ is an $n \times n$ matrix $Df(x)$, called the Jacobian matrix, defined by

$$Df(x) = \left(\frac{\partial f_i}{\partial x_j}\right), \qquad i, j = 1, 2, \ldots, n.$$

Suppose that x is close to the origin, and $f(0) = 0$ (that is, the origin is an equilibrium point of the IVP (2.2)), then by Taylor's theorem

$$\begin{aligned} f(x) &= f(0) + Df(0) \cdot x + R(x), \\ &= Df(0) \cdot x + R(x), \end{aligned}$$

with $R(x)$ the remainder such that $R(x)/\|x\| \to 0$ as $x \to 0$. Hence, the nonlinear system (2.1) can be written as

$$x' = Df(0) \cdot x + R(x).$$

This leads to the linearization of the nonlinear system (2.1),

$$z' = Df(0)z. \tag{2.5}$$

The linearized system (2.5), with initial condition $z(0) = x_0$ imposed, can give information about the nonlinear IVP (2.2), seen, for example, in the following theorem.

[1] All eigenvalues have real parts that are negative.

Theorem 2.1.7. *Suppose that $f(0) = 0$ and that the constant matrix $Df(0)$ is Hurwitz. Then there exists a neighbourhood U about the origin such that for some constants $M, k > 0$, the solution $\phi(t; x_0)$ of (2.2) satisfies*

$$\|\phi(t; x_0)\| \leq Me^{-kt}\|x\|, \quad \forall\, x \in U,\, t \geq 0.$$

Another technique to investigate the stability of the IVP (2.2) is the method of Lyapunov functions, developed by A.M. Lyapunov in the late 19th century. Consider an auxilliary function $V(x) \in C^1[D, \mathbb{R}]$, then the time-derivative of $V(x)$ along solutions of the IVP (2.2) is:

$$\dot{V}(x) = \frac{dV(x(t))}{dt} = \nabla V(x) \cdot f(x), \tag{2.6}$$

where ∇ is the gradient operator, and $\cdot$ is the dot product. Hence, V increases or decreases along solutions of the IVP (2.2) based on the sign of $\nabla V(x) \cdot f(x)$. In the case that the IVP (2.2) is a mechanical system, the auxilliary or Lyapunov function $V(x)$ often represents the total energy of the system.

Theorem 2.1.8. *Suppose that $f(0) = 0$ for the IVP (2.2), $D \subset \mathbb{R}^n$ an open set containing the origin, and $V \in C^1[D, \mathbb{R}]$ such that $V(x) > 0$ for all $x \neq 0$ and $V(0) = 0$, then*

(i) $\dot{V}(x) \leq 0$ for all $x \in D$ implies the origin is stable,

(ii) $\dot{V}(x) < 0$ for all $x \in D \setminus \{0\}$ implies the origin is asymptotically stable,

(iii) $\dot{V}(x) > 0$ for all $x \in D \setminus \{0\}$ implies the origin is unstable.

When the conditions $V(x) > 0$ for all $x \neq 0$ and $V(0) = 0$ are satisfied, the function V is said to be positive definite. This method does not require explicit knowledge of the analytical solution of the IVP (2.2), which is its main strength. Intuitively, if $\nabla V(x) \cdot f(x) < 0$ for $x \in D \setminus \{0\}$ then V decreases along all orbits in $D \setminus \{0\}$, and so orbits will cut the level sets of V inward. This should continue until the orbit is forced to approach the origin as $t \to \infty$, hence the origin is asymptotically stable. Similarly, the other cases can be described intuitively (see [45]). In the linear case, $f(x) = Ax$, there are methods for constructing a Lyapunov function of the system (see [45]), unfortunately, for the nonlinear IVP (2.2), there is no general method for constructing a Lyapunov function, which is this method's main weakness.

In some cases it is possible to construct Lyapunov functions such that $\dot{V}(x)$ is negative semi-definite, that is, $\dot{V}(x) \leq 0$ for all $x \in D$, which implies stability. Often, it is more desirable to find sufficient conditions for asymptotic stability, and this is possible for many problems thanks to the contributions of Barbashin and Krasovski in 1952 and then later by LaSalle. These are summarized in the following theorem, often called LaSalle's Invariance Principle. First, a few definitions are needed.

Definition 2.1.7. *A point $p \in D$ is called an ω-limit point of x_0, where $x_0 = x(0)$, if there exists a sequence $\{t_n\}$ such that $t_n \to \infty$ as $n \to \infty$ and*

$$\lim_{n\to\infty} x(t_n) = p.$$

The set of all ω-limit points of x_0 is called the ω-limit set of x_0, denoted $\omega(x_0)$.

Definition 2.1.8. *A function $V(x) : \mathbb{R}^n \to \mathbb{R}_+$ is said to be radially unbounded if $V(x) \to \infty$ as $\|x\| \to \infty$.*

Theorem 2.1.9. (LaSalle's Invariance Principle)
Let $V \in C^1[D, \mathbb{R}_+]$, where $D \subset \mathbb{R}^n$ is an open subset, and $\mathbb{R}_+$ is the nonnegative real line, be positive definite and radially unbounded. Assume that

(i) $\dot{V}(x) = \nabla V(x) \cdot f(x) \leq 0$ *for all* $x \in \Omega$ *such that* $cl(\Omega) \subset D$.

(ii) $x(t) = \phi(t; x_0)$ *is a solution of system (2.2) such that* $\phi(t; x_0) \in \Omega$ *for all* $t \geq 0$.

Then for some real number c, $\omega(x_0) \subseteq E \bigcap V^{-1}(c)$, where

$$E = \{x \in cl(\Omega) |\ \dot{V}(x) = 0\}, \text{ and } \quad V^{-1}(c) = \{x \in cl(\Omega) | V(x) = c\}.$$

Here $cl(\Omega)$ denotes the closure of the set Ω, and $\mathbb{R}_+$ denotes the positive real line. This theorem leads to the following corollary.

Corollary 2.1.10. *Assume that $f(0) = 0$. If*

(i) $D \subset \mathbb{R}^n$ *is a bounded and positively invariant set of (2.2),*

(ii) $V \in C^1[\mathbb{R}^n, \mathbb{R}]$ *is bounded from below and* $\dot{V}(x) \leq 0$ *for all* $x \in D$, *and*

(iii) the set $Z = \{x \in cl(D) |\ \dot{V}(x) = 0\}$ *does not contain any whole orbits except the origin,*

then for all $x_0 \in D$, the solution $\phi(t; x_0)$ of IVP (2.2) converges to the origin as $t \to \infty$.

Combining Theorem 2.1.8 with Corollary 2.1.10 leads to a weaker condition which guarantees asymptotic stability of the origin.

Theorem 2.1.11. *Suppose that $f(0) = 0$, $D \subset \mathbb{R}^n$ an open set containing the origin and $V(x) \in C^1[\mathbb{R}^n, \mathbb{R}_+]$ is positive definite. Then the trivial solution of the IVP (2.2) is asymptotically stable if the following two conditions hold:*

(i) $\dot{V}(x) \leq 0$ *for all* $x \in D$, *and*

(i) the set $Z = \{x \in cl(D) | \dot{V} = 0\}$ *does not contain any whole orbits except the trivial solution.*

In the discussion so far, we have considered the case where the IVP (2.2) has an equilibrium point. Another important possibility in many applications (including epidemiology) is the existence of an isolated periodic orbit. It is said to be isolated if the orbit contains a neighbourhood about it which contains no other periodic orbits. This is, in fact, only possible for a nonlinear system. This periodic solution may possibly attract nearby solutions, leading to a physical system which has an oscillatory steady state. The solution $\varphi(t; x_0)$ of the IVP (2.2) is said to be a periodic solution if there exists a $T > 0$ such that $\varphi(t + T; x_0) = \varphi(t; x_0)$ for all time $t \in \mathbb{R}$. The minimal T for which this equality holds is called the period of the periodic solution. Unfortunately, many of the methods for proving the existence of periodic orbits are only available in $\mathbb{R}^2$.

Theorem 2.1.12. (Dulac's Criterion)
Let $D \subset \mathbb{R}^2$ *be a simply connected open set and* $f(x) \in C^1[D, \mathbb{R}^2]$. *If there exists a function* $B \in C^1[D, \mathbb{R}^2]$ *such that*

$$\nabla \cdot Bf = div(Bf) = \frac{\partial(B_1 f_1)}{\partial x_1} + \frac{\partial(B_2 f_2)}{\partial x_2}$$

is nonzero and does not change sign in D, *then the system (2.1) has no periodic orbits lying entirely in* D.

Here $\nabla \cdot Bf$ is the divergence of Bf. It is also possible to eliminate the existence of periodic solutions using Lyapunov functions. The next method is applicable to the $\mathbb{R}^n$ case.

Theorem 2.1.13. *Let* $V \in C^1[D, \mathbb{R}]$, *where* $D \subset \mathbb{R}^n$ *is an open set. If* $\dot{V}(x) \leq 0$, $V(x)$ *is bounded from below on* D, *and the set* $Z = \{x \in cl(D) | \dot{V}(x) = 0\}$ *contains no whole orbits except possibly equilibrium points of (2.1), then the system (2.1) has no periodic solutions lying entirely in* D.

One of the most famous theorems in this area is the Poincaré-Bendixson Theorem, which gives sufficient conditions for the existence of a periodic solution.

Theorem 2.1.14. (Poincaré-Bendixson Theorem)
Let $f \in C^1[D, \mathbb{R}^n]$, *with* $D \subset \mathbb{R}^2$ *an open set. Let* $x_0 \in D$ *and* $\omega(x_0)$ *be a nonempty* ω*-limit set of (2.2) with* $x \in \mathbb{R}^2$. *If*

(i) $\omega(x_0) \subset D$ *is bounded, and*

(ii) $\omega(x_0)$ *contains no equilibrium points,*

then $\omega(x_0)$ *is a periodic orbit.*

From this theorem, we can get the following corollary.

Corollary 2.1.15. *Let* Γ *be a positively invariant compact set of (2.2) with* $x \in \mathbb{R}^2$, *then* Γ *contains an equilibrium point or a periodic solution of (2.2).*

2.1.2 Partial Stability

The material in this section is taken from [70]. In contrast to the stability concepts outlined in (2.1.6) for an ODE IVP (2.2), it is also possible to analyze the stability and stabilization of dynamical systems with respect to just a given part of the variables characterizing a system rather than all variables. This problem is often referred to as a problem of partial stability. These types of problems naturally arise in applications, for example from the requirement of proper performance of a system, certainly, a lot of actual phenomena can be formulated in terms of partial stability. For example, the concept of partial stability will be useful in our analysis of switched epidemiology systems, where the stability of the variables for the infected portion of the population is most important.

A.M. Lyapunov, the founder of the modern theory of stability, was the first to formulate the problem of partial stability. Later, works by V.V. Rumyantsev drew the attention of many mathematicians around the world to this problem, which resulted in it being intensively studied. The method of Lyapunov functions became the most useful method, which turned out to be very effective in analyzing both theoretical and applied problems. Consider again the ODE IVP (2.2). Suppose now that the variables constituting the state vector x of IVP (2.2) are divided into two groups:

1. the variables $y_1, \ldots, y_m$ with respect to which the stability of the trivial solution $x = 0$ is to be investigated;

2. the remaining variables $z_1, \ldots, z_p$.

That is, $x(t) = (y_1(t), \ldots, y_m(t), z_1(t), \ldots, z_p(t))^T = (y(t), z(t))^T$ with $m > 0, p \geq 0$ and $n = m + p$. This partitioning depends on the nature of the problem being investigated. It is assumed that the choice of the basic variables, $y_1, \ldots, y_m$, has already been made before studying the partial stability problem. This formulation means that the partial stability problem is a problem of stability with respect to a prescribed part of the variables, namely, the basic variables. Variables $z_1, \ldots, z_p$ are correspondingly called the uncontrollable variables.

The behaviour of the variables $z_1, \ldots, z_p$ of system (2.2) is, in principle, of no interest in the study of the partial stability problem. However, the dynamics of the basic variables $y_1, \ldots, y_m$ are related to the dynamics of the uncontrollable variables $z_1, \ldots, z_p$. As a result, the analysis of the partial stability problem requires a definite analysis of the behaviour of all the variables of system (2.2). Of course, the specifics of such a complete analysis stem from the desire to study only partial properties of the system, namely, the basic variables, $y_1, \ldots, y_m$.

Definition 2.1.9. *Assume $f(0) = 0$ and let $\phi(t; x_0) = (y(t; x_0), z(t; x_0))^T$ be the solution of the IVP (2.2) such that $\phi(0; x_0) = x_0 = (y_0, z_0)^T$ where $x_0 \in D$, then the origin, $x = 0$, 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 each solution $\phi(t; x_0)$ with $\|y_0\| < \beta$ implies

$$\lim_{t \to +\infty} y(t; x_0) = 0,$$

(ii) exponentially y-stable if there exist constants $\alpha, \gamma, C > 0$ such that if $\|y_0\| < \alpha$ then for a solution $\phi(t; x_0)$: $\|y(t; x_0)\| < C\|y_0\|e^{-\gamma t}$ for any $t \geq 0$,

(iv) globally asymptotically (exponentially) stable if it is asymptotically (exponentially) stable and β (α) is arbitrary,

(v) unstable if (i) fails to hold.

These definitions are based on those found in [70]. For an intuitive idea of partial stability, consider the case that $x = (y_1, y_2, z_1)^T \in \mathbb{R}^3$. Then, there are two basic variables of interest and one uncontrollable variable z_1. Partial stability of the origin $x = 0$ implies that for any $\epsilon > 0$ there exists a $\delta > 0$ such that if the initial conditions $(y_{10}, y_{20}) \in \{(y_1, y_2) \in \mathbb{R}^2 |\ y_1^2 + y_2^2 < \delta^2\}$ then the solution $y(t; x_0)$ remains in the ϵ-cylinder $H(\epsilon) = \{(y_1, y_2) |\ y_1^2 + y_2^2 < \epsilon^2\}$ for all time $t \geq 0$. The stability is not interested in what happens with the uncontrollable variable z_1. Further, the initial conditions must be in a δ-cylinder, which will depend on the ϵ chosen, but the δ will not give a required condition on the initial condition for z_1. Hence, only the initial values of the basic variables must be close to the origin for stability to be satisfied.

2.1.3 Systems of Impulsive Differential Equations

The material in this section, unless otherwise specified, is taken from [37]. Many evolution processes are characterized by a sudden change in the state of the system at certain times. These sudden abrupt changes have a duration that is negligible compared to the duration of the process. Hence, it is natural to assume that these perturbations of the system act instantaneously. This leads to the idea of impulsive differential equations (IDEs), differential equations involving impulsive effects. Many biological phenomena involving thresholds, bursting rhythm models in medicine and biology, optimal control models in economics, and frequency modulated systems exhibit impulsive effects. Certainly, IDEs appear as a natural description of observed evolution phenomena of several real world problem, including control schemes in epidemiology.

In order to construct a system of impulsive differential equations, we use the Dirac delta function. Construct it as follows [71]: consider the following function, for any $\epsilon > 0$,

$$I_\epsilon(t) = \begin{cases} \frac{1}{\epsilon}, & 0 \leq t \leq \epsilon, \\ 0, & t > \epsilon. \end{cases}$$

Then the Dirac delta function, which is not a function but rather a generalized function, can be regarded as the limit of the sequence of functions $\delta(t) = \lim_{\epsilon \to 0} I_\epsilon(t)$ and is defined by the integral:

$$\int_{-\infty}^{\infty} f(t)\delta(t)dt = f(0).$$

Further, it is also possible to translate this result,

$$\int_{-\infty}^{\infty} f(t)\delta(t-a)dt = f(a).$$

Introduce the Dirac function into the IVP (2.2) as an input control $u(t)$, similar to the procedure in [22]:

$$\begin{cases} x(t)' = f(x(t)) + u(t), \\ x(t_0) = x_0, \end{cases} \tag{2.7}$$

where

$$u(t) = c\sum_{k=1}^{\infty} x(t)\delta(t-t_k),$$

and $c > 0$ is a constant. The sequence of times $\{t_k\}_{k=1}^{\infty}$ are the moments of impulsive control, and $t_0 < t_1 < t_2 < \ldots < t_k < \ldots \to \infty$ as $k \to \infty$. When $t \neq t_k$, the system evolves as the ODE IVP (2.2). The intuitive idea is that this control acts as an impulsive force: at the times $t = t_k$, an impulsive force of magnitude c is applied to the system. Observe that, from (2.7),

$$\lim_{h\to 0^+} x(t_k+h) - x(t_k) = \lim_{h\to 0^+} \int_{t_k}^{t_k+h} \left[f(s) + p\sum_{k=1}^{\infty} x(s)\delta(s-t_k) \right] ds = px(t_k).$$

Define $x(t_k^+) := \lim_{h\to 0^+} x(t_k+h)$, and $\Delta x(t_k) := x(t_k^+) - x(t_k)$, then the IVP (2.7) can be re-written as:

$$\begin{cases} x' = f(x), & t \in (t_{k-1}, t_k], \\ \Delta x = cx, & t = t_k, \\ x(t_0^+) = x_0, & k = 1, 2, \ldots \end{cases} \tag{2.8}$$

This system has a difference equation which models the impulsive effect, and it is called an impulsive differential equation (IDE) IVP.

For a more general construction of impulsive differential equations, consider an evolution process described by an autonomous ODE IVP (2.2) (with $f : D \to \mathbb{R}^n$, $D \subset \mathbb{R}^n$ is an open set), combined with the following two mathematical objects:

(i) the sets $M(t), N(t) \in D$ for all $t \in \mathbb{R}_+$; and

(ii) the operator $A(t) : M(t) \to N(t)$ for all $t \in \mathbb{R}_+$.

Consider a solution $\phi(t;x_0)$ of the IVP (2.2) and consider the point $P_t = (t, \phi(t;x_0)) \in \mathbb{R}_+ \times D$ which behaves as follows: It begins its motion from an initial point $P_{t_0} = (t_0, x_0)$ and moves along the curve $\{(t,x) \in \mathbb{R}_+ \times D |\ t \geq t_0, x = \phi(t;x_0)\}$ until the first time t_1 when the point P_t meets the set $M(t)$. At time t_1, the operator $A(t)$ then acts on the point P_{t_1} by transferring it to $P_{t_1^+} = (t_1, x_1^+) \in \mathbb{R}_+ \times N(t_1)$, with $x_1^+ = A(t_1)x(t_1)$. The point P_t continues along the curve $x(t) = \phi(t, x_1^+)$ as the solution of the IVP (2.2) beginning at $P_{t_1} = (t_1, x_1^+)$ until it again meets the set $M(t)$ at the time $t_2 > t_1$. Then, at t_2, the operator $A(t)$ again acts on the point by transferring it to $P_{t_2^+} = (t_2, x_2^+) \in \mathbb{R}_+ \times N(t_2)$ with $x_2^+ = A(t_2)x(t_2)$. The process continues in this way, and the IVP (2.2) coupled with the two objects $(i), (ii)$ characterize an impulsive differential system.

The points described by P_t form an integral curve which defines a function that is a solution to the impulsive differential system. The moments t_k where the set $M(t)$ were crossed by the curve P_t are called the moments of impulsive effect. It should be apparent from this that the solution of the impulsive differential system is either continuous or piecewise continuous with discontinuities at the times t_k where P_t hits the set $M(t)$. The solution could possibly have no discontinuities if the integral curve P_t does not ever cross $M(t)$, it could have a finite number of discontinuities, or it could also have a countably infinite number of discontinuities. Assume, without loss of generality, that the solutions of the impulsive differential system are left continuous at the moments of impulse t_k, $k = 1, 2, \ldots$, that is,

$$x(t_k) = x(t_k^-) := \lim_{h \to 0^+} x(t_k - h), \quad x(t_k^+) := \lim_{h \to 0^+} x(t_k + h).$$

Consider the special case that $M(t)$ is a sequence of planes $t = t_k$, such that $t_k \to \infty$ as $k \to \infty$, and define the operator $A(t)$ only for times $t = t_k$ so that $A(t_k) = A(k) : D \to D, x \to A(t)x = x + I_k(x)$, where $I_k : D \to D$. Following from this, the set $N(t)$ is also defined only for $t = t_k$, and hence $N(k) = A(k)M(k)$. This leads to the IDE IVP:

$$\begin{cases} x' = f(x), & t \neq t_k, \\ \Delta x = I_k(x), & t = t_k, \\ x(t_0^+) = x_0, & k = 1, 2, \ldots \end{cases} \tag{2.9}$$

Notice that system (2.9) is a more general formulation than the impulsive system (2.8) because of the more general impulsive functions I_k. Any solution $\phi(t;x_0)$ on the interval (α, β) of the impulsive IVP (2.9) satisfies the following [7]:

(i) $(t, \phi(t;x_0)) \in \mathbb{R} \times D$ for $t \in (\alpha, \beta)$, and $\phi(t_0^+;x_0) = x_0$ where $x_0 \in D$.

(ii) For $t \in (\alpha, \beta)$, $t \neq t_k$, $\phi'(t;x_0) = f(\phi(t;x_0))$.

(iii) $\phi(t;x_0)$ is continuous from the left in (α, β) and if $t_k \neq \alpha \neq \beta$, then $\phi(t_k^+;x_0) = \phi(t_k;x_0) + I_k(\phi(t_k;x_0))$.

Next, we establish existence and uniqueness of the IDE IVP (2.9), based on Theorem 1.3 in [7] for the non-autonomous case.

Theorem 2.1.16. [7]
Assume $f \in C^1[D, \mathbb{R}^n]$ and $y + I_k(y) \in D$ for each $k = 1, 2, \ldots$, and $y \in D$. Then for each $x_0 \in D$ there exists a unique solution $\phi(t; x_0)$ of the IVP (2.9) which is defined in an interval of the form (t_0, ω), where ω is a constant, and is not continuable to the right of ω.

Denote $J^+ = J^+(t_0^+, x_0)$ the maximal interval of the form (t_0, ω) in which the solution $\phi(t; x_0)$ is defined. Now we are prepared to establish sufficient conditions for global existence of a solution, based on Theorem 1.4 of [7].

Theorem 2.1.17. [7]
Assume $f \in C^1[D, \mathbb{R}^n]$ and $y + I_k(y) \in D$ for each $k = 1, 2, \ldots$, and $y \in D$. Let $\phi(t; x_0)$ be a unique solution of the IVP (2.9) on a maximal interval J^+. If there exists a compact set $\Omega \subset D$ such that $\phi(t; x_0) \in \Omega$ for $t \in J^+(t_0^+, x_0)$ then $J^+ = (t_0, \infty)$

Actually, in the case of IDE IVPs of the form (2.9), uniqueness is straightforward, it follows from the non-impulsive case. The following theorem is based on Corollary 2.2.1 of [37] for the non-autonomous case.

Theorem 2.1.18. *Uniqueness of solutions of the IVP (2.2) for every (t_0, x_0) implies the uniqueness of solutions of the IVP (2.9).*

One final note is that if $t_0 \neq 0$, it is possible to shift the initial time to zero using $\tau = t - t_0$,

$$\begin{cases} x' = f(x), & \tau \in (h_{k-1}, h_k], \\ \Delta x = px, & \tau = h_k, \\ x(0^+) = x_0, \end{cases} \tag{2.10}$$

with $h_k = t_k - t_0$. Hence, without loss of generality, in the case of IDEs with impulses at fixed times, we may take $t_0 = 0$. For both a broader and more in depth discussion of impulsive differential systems, including systems with variable impulse times, global existence, stability, and Lyapunov function methods, see [7, 37].

2.2 Epidemiology

2.2.1 Model Formulation

The continuous deterministic approach is taken here, where the spread of the infectious disease is modelled as a system of ordinary differential equations. For an example of a stochastic or discrete time approach, see [31]. 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 [27]. Because there are many choices for these various components, based on the situation being modelled, the combinatorial possibilities are enormous [27]. Certainly, there are many modifications and extensions which depend critically on the disease being modelled and should be incorporated [55]. The interest of this thesis is dealing with the spread of acute communical infectious diseases, rather than chronic diseases, that is, those diseases which are conferred to individuals and have a relatively short lifespan. Examples of acute diseases are rubella, measles, influenza, gonorrhea, etc. Acute diseases have a relatively shorter lifespan because the individuals have a natural immune response and eventually eliminate the disease.

In classic deterministic epidemiological models, the population is split into different compartments. These compartments are well established in the literature and describe the current state of the individual. The notation for the various compartments has become somewhat standard [27]. The most common compartments are the susceptible class, S, for individuals that are healthy and can obtain the disease, the infected class, I, for individuals that are infected with the disease and capable of spreading it, the exposed class, E, for individuals exposed to the disease but not yet infectious, the removed class, R, for individuals who have immunity, or have been removed from the general population, the passively immune class, M, for individuals who have been transferred immunity through birth and finally the vaccinated class V for individuals who have gained a vaccine immunity through some type of control program. Often, the disease models are named based on which compartments are used and the flow of individuals in these compartments, for example the SIS, SIR, SIRS, and SEIR models, which will be introduced in the next section.

It has been observed that acute infections have infectious periods that are distributed around a mean value [31]. This implies the probability an individual moves from the infected class to another class is dependent on how long they have been infected [31]. A usual simplifying assumption made is that the period of infection is a constant, which leads to an exponentially distributed infectious period [31]. Taking the common assumption that the infected are removed linearly with removal rate $g > 0$ gives that the fraction of infectives still infected t units after becoming infectious are $P(t) = e^{-gt}$, and this corresponds to an average waiting time of $1/g$ [28]. For example, the average infectious period for measles is about one week [28]. Alternatively to the exponential waiting time construction outlined above, another possibility is assuming the waiting time distribution is a step function [28]:

$$P(t) = \begin{cases} 1, & 0 \leq t \leq \tau \\ 0, & t \geq \tau. \end{cases}$$

Here, individuals have the disease for exactly a time $\tau > 0$ and then are immediately recovered. This leads to a delay-differential equation [28]. A more general construction of the waiting time is assuming the fraction $P(t)$ of infectives still infected after t units is a nonincreasing, piecewise continuous function with $P(0) = 1$

and $lim_{t\to\infty}P(t) = 0$ [28]. This leads to the rate of individuals leaving the compartment at time t as $-P'(t)$, and the mean waiting time in the compartment is $\int_0^\infty t(-P'(t))dt = \int_0^\infty P(t)dt$ [28]. For example, substituting the usual assumption of $P(t) = e^{-gt}$ leads to the waiting time of $1/g$, as expected. Motivated by this discussion, a common assumption is that the movements between the M, E, and I compartments are governed by terms like $\delta M, aE$, and gI in an ordinary differential equations model [28].

Assume that the disease can be obtained two ways: sufficient direct or indirect contact of infected individuals (known as horizontal transmission) and the transfer of a disease from a mother to her newborn or unborn child transplacentally (known as vertical transmission) [33]. Vertical incidence is usually included in epidemiology models by assuming that a fixed fraction of newborns are infected vertically (transplacentally) [28]. For examples of literature studying models with vertical transmission, see [32, 40, 43, 48, 51, 57]. The horizontal incidence, on the other hand, is more complicated to construct and varies from model to model. The most common horizontal incidence rate, usually called the standard incidence, is constructed as follows from basic principles [28]: assume that $\beta > 0$ is the average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit time. That is, β is the product of the nominal contact rate and transmission probability [31], and is commonly called the contact rate or transmission rate. Suppose I_c and S_c denote the number of susceptibles and individuals, respectively, in a population, denoted by N, then $\beta I_c/N$ is the average number of adequate contacts with infectives per unit time of one susceptible, which is the force of infection for this particular horizontal incidence rate; the per capita rate of new infections in susceptible individuals [31]. Then, $(\beta I_c/N)S_c = \beta NSI$ $(I = I_c/N, S = S_c/N)$ is the standard incidence rate; the number of new cases per unit time due to the $S_c = NS$ susceptibles. This horizontal incidence rate is also sometimes referred to as frequency dependent transmission or mass action transmission [31]. For a more detailed derivation of the standard horizontal incidence rate, see page 18 of [31].

The simplest horizontal incidence is the density dependent (or pseudo mass action) rate $\eta S_c I_c = \eta N^2 SI$, with η as a mass action coefficient, which has sometimes been used in models [28]. The parameter η has no direct epidemiological interpretation, but comparing it with the standard formulation gives $\beta = \eta N$, and hence, this form implicitly assumes that the contact rate increases linearly with the population size [28]. It might seem plausible that the population the contact rate would increase with population size, but this is naive because the daily contact patterns of people are often similar in large and small communities [28]. For example, we should not expect an infected individual who lives in New York (population 8 million) to transmit a disease 50 times more than someone who lives in Cambridge, Massachusetts (population 100,000) [31]. Indeed, for human diseases the contact rate seems to be only very weakly dependent on the population size [28]. On the other hand, the standard incidence rate is consistent with the concept that individuals are infected through their daily encounters, which are largely independent of community size [28]. The distinction between these two incidence

rates becomes especially pronounced when the $1/N$ term cannot be absorbed into the constant, that is, when the total population size is varying [31]. There are other possible incidence rates which have been conceived and are possibly more realistic in certain scenarios. For example, saturation incidence rates, incidence rates which take into account psychological effects, time-dependent incidence rates and density-dependent incidence rates. For examples of literature discussing and analyzing different incidence rates, see [19, 27, 33, 34, 39, 41, 43, 44, 52, 60, 61].

Another important feature is the population dynamics of a model, which becomes important when the spread of the disease is measured in years. In this case, births and deaths should be considered. The most common assumption is an exponential growth or decay population model $N' = (b - d)N$, where N is the total population, $b > 0$ is the birth rate and $d > 0$ is the death rate. Often it is assumed that the birth rate is equal to the death rate, $b = d = \mu$. This leads to an average lifetime of $1/\mu$, and it also means the population size is constant [28]. These models are appropriate when the time period of the disease is relatively short or when the natural births balance the natural deaths [27]. Infectious disease models with constant population size are not suitable when the disease-related deaths are significant or when the inflow and outflow are not balanced [27]. In these cases, models with a variable total population size are needed, which are often more difficult to analyze mathematically because the population size is an additional variable which is governed by a differential equation [27]. There have been many infectious diseases which have caused enough deaths so that the population size has not remained even approximately constant [27]. Infectious diseases which have debilitated and regulated human populations include plague (the black plague resulted in the deaths of a quarter of the world population), measles, scarlet fever, diptheria, tuberculosis, smallpox, malaria and the pneumonias [27]. Further, diseases caused by viruses, bacteria, and protozoans, combined with low nutritional status still cause significant childhood mortality in developing countries [27]. When disease-induced mortality cannot be ignored, it is usally included in the models by the addition of a disease-induced mortality rate, $\alpha > 0$, into the population dynamics, for example, $N' = (b-d)N - \alpha I_c$. There are many different models for the population dynamics, which have been studied in the literature. For examples of models with different demographic structures and their analyses, see [18, 20, 27, 28, 30, 38, 49, 58].

2.2.2 Threshold Criteria

One of the main goals of studying epidemiology models is to analyze the spread of a disease in order to try to understand its underlying principles. The reason for this is to be able to come to some conclusions about the severity and duration of the epidemic. Certainly, it is desired to be able to answer important questions such as: Will there be an epidemic? If so, how long will it last? How severe might it be? Can the disease be eradicated through some type of control scheme? Mathematically, most of these questions translate to studying the stability properties of the models' disease-free solution.

Thresholds that dictate the persistence or eradication of a disease are very important in epidemiology [72]. Hence, one of the main goals of disease modelling is to establish criteria based on the parameters and structure of the system that will ensure disease eradication. This has been done in many of the classical models in the literature, and there are three commonly used threshold numbers. The following descriptions of the threshold numbers in this section is taken from [28], unless otherwise specified.

The first number, which is most often used, is the basic reproduction number, usually denoted $\mathcal{R}_0$, which is defined as the average number of secondary infections produced by one infected individual in a wholly susceptible population. It is assumed that the infected individual is present in the host population for their entire infectious period and, further, that the infected individual mixes with susceptibles in a normal way. The second threshold number sometimes considered is the contact number σ, which is defined as the average number of adequate contacts of a typical infective during their infectious period. Here, an adequate contact means one that is sufficient for transmitting the disease, if the individual contacted by a susceptible is infected. The last threshold number considered is the replacement number $\mathcal{R}$, which is defined to be the average number of secondary infections produced by a typical infective during the entire infectious period. This is the actual number of secondary cases coming from a typical infective.

These three threshold numbers are all equal at the beginning of the spread of a disease when there is only one infective present. Although $\mathcal{R}_0$ is only defined at the time of invasion, the other threshold numbers, σ and $\mathcal{R}$, are defined for all time. For most models, the contact number remains constant as the infection spreads, and is equal to the basic reproduction number. For an example of a model where this is not true, see the model for pertussis in Section 8 of [28]. Finally, after the introduction of infectives into a population, the susceptible fraction should be less than one, so that not all subsequent adequate contacts will result in a new case. This leads to the fact that the replacement number $\mathcal{R}$ is always less than the contact number σ after the invasion. Combining these results:

$$\mathcal{R} \leq \sigma \leq \mathcal{R}_0.$$

The equality comes at the time of invasion, $\mathcal{R}_0 = \sigma$ in most models, and $\mathcal{R} < \sigma$ after the invasion for all models.

Often in mathematical epidemiology, threshold theorems establish that if a particular model's basic reproduction number satisfies $\mathcal{R}_0 \leq 1$, then the disease will eventually be eradicated. The threshold criteria theorems in this thesis will be established based on $\mathcal{R}_0$, since if $\mathcal{R}_0 \leq 1$ then it is also true that $\mathcal{R} \leq \sigma \leq 1$. See Table 2.1 for a list of basic reproduction numbers, $\mathcal{R}_0$, for some real-world diseases, and see [2] for more real-world epidemiological data. For a table of the mathematical expression of basic reproduction numbers for common infectious disease models (based on the models' parameters), some of which will be discussed in detail in the next section, see [44]. For an explicit derivation of the basic reproduction num-

bers for general compartmental disease models, as the spectral radius of a next generation matrix, see [14, 16].

Alternatively, in the case that the disease is not eradicated, there is usually an endemic equilibrium, which represents a persistent population of infected individuals. In the literature, threshold theorems usually establish that $\mathcal{R}_0 > 1$ implies that the endemic equilibrium is asymptotically stable. This might not always be straightforward to prove, and alternative method of illustrating the endemicity of a disease are the persistence or permanence of the disease. These concepts are common in the literature and are outlined in, for example, [19, 51, 69]. Let I represent the fraction of individuals in the infectived class, then we define persistence and permanence similarly as in [19]:

Definition 2.2.1. *In an epidemiology system, a disease is said to be persistent if there is an $\eta > 0$ (independent of initial conditions) such that the solution $I(t)$ of the system with initial condition $I(0) = I_0 > 0$ satisfies*

$$\liminf_{t\to\infty} I(t) \geq \eta.$$

Definition 2.2.2. *In an epidemiology system, a disease is said to be permanent if there exists a compact region $\Omega_0 \in int(\Omega)$[2] such that every solution $I(t)$ of the epidemiology system with initial condition $I(0)$ will eventually enter and remain in the region Ω_0.*

Disease	Infectious period (days)	Average age at infection (years)	$\mathcal{R}_0$
Measles	6 to 7	4.4 to 5.6	13.7 to 18.0
Whooping cough	21 to 23	4.1 to 5.9	14.3 to 17.1
Rubella	11 to 12	10.5	6.7
Chicken pox	10 to 11	6.7	9.0
Poliomyelitis	14 to 20	11.2	6.2

Table 2.1: Epidemiological data from [2].

2.2.3 Classical Models

The SIR Model without Population Dynamics

For the classic epidemic model, the population is split into three compartments: susceptibles, S_c, infectives, I_c and removed, R_c. Assume that the total population is $N = S_c + I_c + R_c$. To formulate this model, we assume that:

[2] $int(\Omega)$ is the interior of the meaningful domain Ω

1. The rate of increase of infectives (and loss of susceptibles) is proportional to the number of infectives and susceptibles present, normalized by the total population. That is, assume that the incidence rate takes the standard form $\beta S_c I_c/N$, with $\beta > 0$ as the contact rate, the average number of contacts of a person per unit time.

2. The rate of removal of infectives is proportional to the number of infectives. That is, assume an exponentially distributed waiting time with a removal rate $g > 0$, and hence, the average infectious period will be $1/g$.

3. The incubation period of the disease is negligible in length, hence when a susceptible is infected, they are immediately infectious and able to spread the disease.

4. All individuals in the population mix homogeneously, so that every pair of individuals has an equal probability of coming into contact with one another.

5. The dynamics of the disease are short enough such that population dynamics are negligible, that is, assume a closed population.

The flow of the model is $S \to I \to R$, hence the name SIR model. This formulation leads to the the SIR model without population dynamics, sometimes called the classical epidemic model because the duration of the disease is assumed to be short compared to the time scale of the population dynamics. This model was initially studied in depth by Kermack and McKendrick in 1927 [31], has since been studied extensively, for example in [28, 29, 31, 55], and is given by

$$\begin{cases} \dot{S}_c = -\beta \dfrac{S_c I_c}{N}, \\ \dot{I}_c = \beta \dfrac{S_c I_c}{N} - g I_c, \\ \dot{R}_c = g I_c. \end{cases} \tag{2.11}$$

This model is good for acute diseases with relatively short lifespans, for example influenza [55]. Notice that $\dot{S}_c + \dot{I}_c + \dot{R}_c = 0$, hence total population satisfies $N' = 0$, that is, the constant population assumption is built into the model. Since this is an autonomous differential equation system, it is assumed, without loss of generality, that $t_0 = 0$. Use $S = S_c/N$, $I = I_c/N$, $R = R_c/N$ to get

$$\begin{cases} \dot{S} = -\beta S I, \\ \dot{I} = \beta S I - g I, \\ \dot{R} = g I, \end{cases} \tag{2.12}$$

where the variables now represent the fraction of individuals in each class. Since $S + I + R = 1$, the initial conditions are $S(0) = S_0$, $I(0) = I_0$, $R(0) = R_0$ such that $S_0 + I_0 + R_0 = 1$. It is assumed that $S_0 > 0$, $I_0 > 0$ to make the problem

biologically interesting, and it is often assumed that $R_0 = 0$. Note that $S+I+R = 1$ and the physical domain of interest is $\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S + I + R = 1\}$, which is invariant to the system. This follows from $\{\dot{S} + \dot{I} + \dot{R}\}_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$, and $\dot{R}\,|_{R=0} = gI \geq 0$. Note that since $S + I + R = 1$, the model is intrinsically two dimensional, and the equation for R is often omitted, which simplifies the system.

This model is well-posed, both mathematically and epidemiologically, and has a unique solution which exists for all positive time given certain initial conditions [28]. There are infinitely many equilibrium points on the S-axis. Given S_0, I_0, g, β, it is desired to determine how the disease will spread in time. More specifically, a question which arises is whether or not there will be an epidemic, that is, whether or not I ever increases. Observe that at the initial time $t_0 = 0$,

$$\left.\frac{dI}{dt}\right|_{t=0} = \begin{cases} I_0(\beta S_0 - g) > 0, & \text{if } S_0 > g/\beta, \\ I_0(\beta S_0 - g) < 0, & \text{if } S_0 < g/\beta. \end{cases} \tag{2.13}$$

If $S_0 > g/\beta$ then I initially increases, and hence there is an epidemic. Notice $S' \leq 0$ for all time, which implies that $S \leq S_0$, and it follows that if $S_0 < g/\beta$ then $\dot{I} = I(\beta S - g) \leq I(\beta S_0 - g) \leq 0$ for all $t \geq 0$. Hence, in this case, $I \leq I_0$ for all time and I converges to zero [55]. Hence, for this model, the basic reproduction number can be defined as

$$\mathcal{R}_0 = \frac{\beta}{g}, \tag{2.14}$$

and, based on the above discussions, if $\mathcal{R}_0 < 1/S_0$ there is no epidemic, whereas if $\mathcal{R}_0 > 1/S_0$ there will be an epidemic.

It is possible to determine the severity of the epidemic as follows,

$$\frac{dI}{dS} = -\frac{I(\beta S - g)}{\beta S I} = -1 + \frac{g}{\beta S},$$

and, upon integration, the phase plane trajectories are [55]:

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

The maximum of I occurs when $\dot{I} = 0$, that is, at $S = g/\beta$, therefore [55],

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

In this case we are assuming $R_0 = 0$, and hence $S_0 + I_0 = 1$. It is also possible to investigate the long-term behaviour of the susceptibles and removed as follows:

$$\frac{dS}{dR} = -\frac{\beta S}{g}.$$

Hence, $S = S_0 e^{-\beta R/g}$, which can be used (see [55]) to determine that $lim_{t\to\infty} S(t)$ is the positive root $0 < z < g/\beta$ of the equation

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

Hence, we see the disease does not die out due to a lack of susceptibles, but rather a lack of infectives [55].

The SIR Model with Population Dynamics

For the classical endemic model, the same assumptions are made as above except now the duration of the disease is assumed to be long enough such that population dynamics become important. More specifically, choose to now incorporate the births and deaths of individuals. The assumption that the disease lasts long is what gives the model its endemic name. Assume that the birth rate $\mu > 0$ is equal to the natural death rate, hence the mean lifetime of an individual is $1/\mu$. Assume that all individuals may have children, and, all the children are born healthy, and hence are born into the susceptible class. Assume that there is no disease induced mortality rate. The endemic SIR model is a good model for nonfatal diseases such as hepatitis B and measles [47]. The flow of this model again is $S \to I \to R$ (see Figure 2.1).

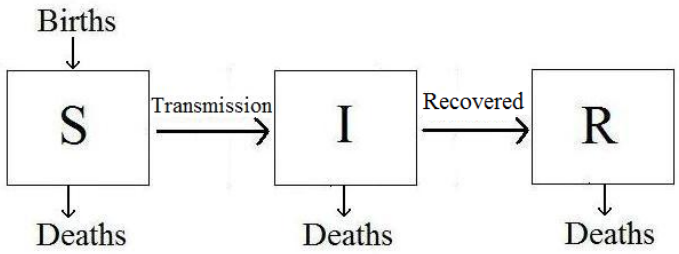

Figure 2.1: **Flow of SIR System (2.16).**

This model has been studied extensively in the literature, for example [28, 29, 31, 35], and is given by:

$$\begin{cases} \dot{S}_c = \mu N - \beta \dfrac{S_c I_c}{N} - \mu S_c, \\ \dot{I}_c = \beta \dfrac{S_c I_c}{N} - g I_c - \mu I_c, \\ \dot{R}_c = g I_c - \mu R_c, \end{cases} \tag{2.15}$$

with $S_c + I_c + R_c = N$. Since $\dot{S}_c + \dot{I}_c + \dot{R}_c = 0$, normalize the variables again such that $S + I + R = 1$ to get:

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S, \\ \dot{I} = \beta SI - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{2.16}$$

where $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = 0$. The meaningful domain for this system is the plane $\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S+I+R = 1\}$, and so $S_0+I_0+R_0 = 1$ must be satisfied. Since $\{\dot{S} + \dot{I} + \dot{R}\}_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$, and $\dot{R}\,|_{R=0} = gI \geq 0$, this domain is invariant to the system, hence the model is well-posed biologically.

Since $S + I + R = 1$, the model is intrinsically two dimensional, it is possible for us to omit the equation for R and then to use the meaningful two dimensional domain $\Omega^l_{SI} = \{(S, I) \in \mathbb{R}^2_+ | S + I \leq 1\}$. Along these boundaries, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$, and $\{\dot{S} + \dot{I}\}\,|_{S+I=1} = -gI \leq 0$ and so this domain is also invariant to the system. The usual approach in this thesis will be to use the domain Ω_{SIR} and not the domain S^l_{SI} associated with a reduced system. Define

$$\mathcal{R}_0 = \sigma = \frac{\beta}{\mu + g}, \tag{2.17}$$

which is the contact rate times the mean death-adjusted infectious period in a wholly susceptible population. This quantity is the model's basic reproduction number, an important threshold criteria, as discussed earlier, as it is the average number of secondary infections produced by a single infected individual in a wholly susceptible population. There is a disease-free solution $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ and an endemic solution

$$\mathbf{Q}^* = (S^*, I^*, R^*) = \left(\frac{1}{\mathcal{R}_0}, \frac{\mu}{\mu + g} \left(1 - \frac{1}{\mathcal{R}_0} \right), \frac{g}{\mu + g} \left(1 - \frac{1}{\mathcal{R}_0} \right) \right). \tag{2.18}$$

It is called the endemic solution because at this equilibrium the disease persists. Notice that the endemic solution is in the physically reasonable domain only if $\mathcal{R}_0 \geq 1$. In fact, there is a bifurcation when $\mathcal{R}_0 = 1$, for this value we get that $\bar{\mathbf{Q}} = \mathbf{Q}^*$.

In this model, the long-term behaviour is completely dictated by the value of $\mathcal{R}_0$. If $\mathcal{R}_0 \leq 1$ then $\bar{\mathbf{Q}}$ is globally asymptotically stable in the meaningful domain Ω_{SIR}, while if $\mathcal{R}_0 > 1$ then $\mathbf{Q}^*$ is globally asymptotically stable in the meaningful domain [29]. This is reasonable intuitively, if $\mathcal{R}_0 < 1$ then each infected individual is passing the infection on to less than one susceptible, on average. An investigation into the stability of the endemic solution (see [31]) shows that the solution approaches the endemic equilibrium with damped oscillations when $\mathcal{R}_0 > 1$. It can be shown that the period of oscillations is approximately $2\pi\sqrt{AG}$, where $A = 1/(\mu(\mathcal{R}_0 - 1))$ is the mean age of infection and $G = 1/(\mu + g)$ is the mean period of a host's infectivity.

The approach to the endemic equilibrium with damped oscillations has a biological interpretation [28]: when $\mathcal{R}_0 = \sigma > 1$ (recall that σ is the contact number), each infected individual is infecting more than one susceptible person, on average, then for some small initial number of infectives $I_0 > 0$, the susceptible population will decrease as the virus spreads, until the susceptible population is at a low level. At this point, there are few susceptibles and it is hard for infectives to spread the disease, hence the infectives decrease. After the infective fraction has decreased to a low level, the slow processes of the natural deaths of the recovered and the births of new susceptibles gradually increase the susceptible fraction until σS is large enough such that that another smaller epidemic occurs [28]. This process continues, alternating between epidemics and slow regeneration of susceptibles, until the solution approaches the endemic equilibrium. At the endemic equilibrium, the replacement number $\mathcal{R} = \sigma S^*$ is 1, which makes sense intuitively since if the replacement number were greater than or less than 1, the infectives would be increasing or decreasing, respectively [28]. See Figure 2.2, or Figures 5 and 6 in [28], for phase plane portraits of the SIR model.

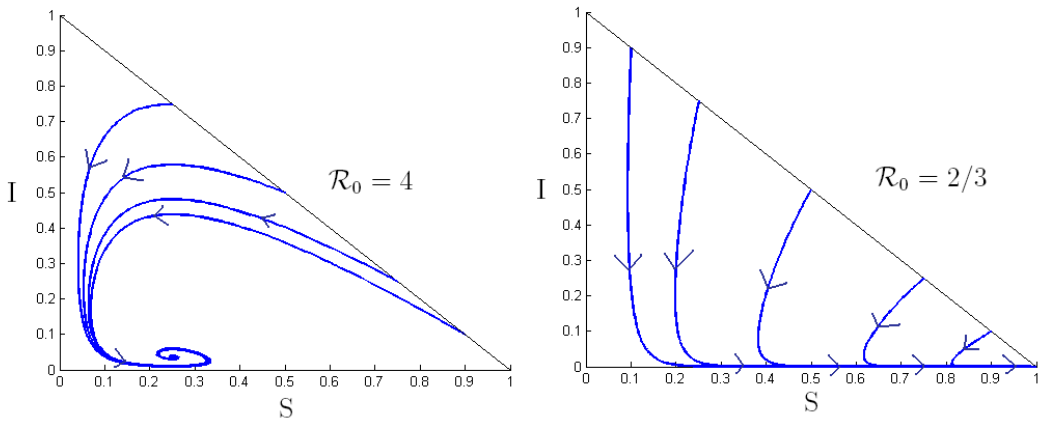

Figure 2.2: Phase plane portraits of SIR system (2.16) with different initial conditions and basic reproduction numbers. Simulation done in MATLAB©.

The SIS Model

Another prominent model in the literature is the SIS model, it has been analyzed extensively, for example, in [29, 30, 31, 35, 55]. In this model, susceptibles become infected with the disease and once recovered return to the susceptible class immediately. Hence, there is no natural immunity conferred from being infected by the disease. Some infections, for example gonorrhea and other sexually transmitted diseases [72], do not give rise to acquired immunity in the host. Hence, there is no removed class in this model. Include population dynamics as in (2.16), assuming the birth rate, $\mu > 0$, is equal to the natural death rate. The flow of this model is $S \to I \to S$ (see Figure 2.3).

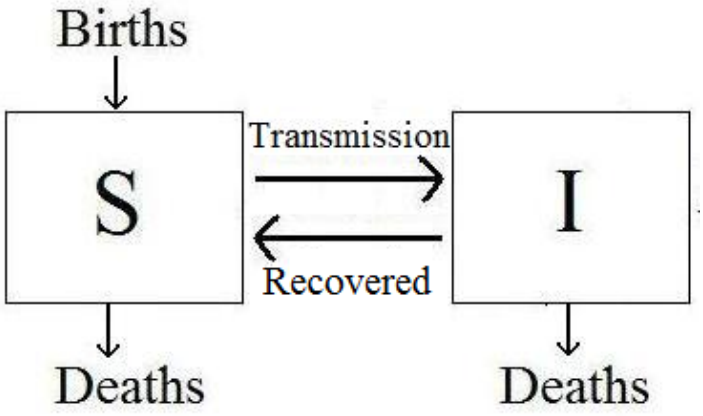

Figure 2.3: **Flow of SIS System (2.19).**

Mathematically, after normalizing the variables by the total population (which is again a constant), the SIS model is given as:

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S + gI, \\ \dot{I} = \beta SI - gI - \mu I, \end{cases} \tag{2.19}$$

where S, I represent the fractions of the population in each class. The initial conditions are $S(0) = S_0 > 0, I(0) = I_0 > 0$ such that $S_0 + I_0 = 1$. The normalized variables satisfy $S+I = 1$ and hence the meaningful domain for this system is $\Omega_{SI} = \{(S, I) \in \mathbb{R}^2_+ | S + I = 1\}$. Notice that $\{\dot{S} + \dot{I}\}|_{S+I=1} = 0$, $\dot{S}|_{S=0} = \mu + gI > 0$, and $\dot{I}|_{I=0} = 0$, and so this domain is invariant to the system. The basic reproduction number for this model is the same as for the SIR models,

$$\mathcal{R}_0 = \frac{\beta}{\mu + g}. \tag{2.20}$$

There is a disease-free solution $\bar{\mathbf{Q}} = (1, 0)$ and an endemic solution

$$\mathbf{Q}^* = (S^*, I^*) = (1/\mathcal{R}_0, 1 - 1/\mathcal{R}_0)\,. \tag{2.21}$$

Since $S + I = 1$, the model is intrinsically one-dimensional and we may omit the equation for S and solely focus on the equation for I:

$$\dot{I} = -\beta I^2 + (\beta - g - \mu)I, \tag{2.22}$$

with $0 \leq I \leq 1$ and $I(0) = I_0 > 0$. This equation has equilibrium points $I = 0$ and $I = 1 - 1/\mathcal{R}_0$, which are associated with the disease-free solution $\bar{\mathbf{Q}}$ and the endemic solution $\mathbf{Q}^*$, respectively.

The equation (2.22) is a Bernoulli differential equation which has a unique solution that can be found explicitly [29], as follows: define $\lambda := \beta - \mu - g$, then,

for $\mathcal{R}_0 \neq 1$, $\dot{I} - \lambda I = -\beta I^2$, and hence

$$\frac{\dot{I}}{I^2} - \frac{\lambda}{I} = -\beta.$$

Use the substitution $y = I^{-1}$ to get $\dot{y} = -\frac{1}{I^2}\dot{I}$. This change of variables gives $\dot{y} + \lambda y = \beta$ which can be solved to get $y = Ce^{-\lambda t} + \beta/\lambda$ for some constant C to be determined. Use the initial condition $I(0) = I_0 > 0$ to get $C = 1/I_0 - \beta/\lambda$. Then,

$$I(t) = \frac{1}{(\frac{1}{I_0} - \frac{\beta}{\lambda})e^{-\lambda t} + \frac{\beta}{\lambda}} = \frac{e^{(\mu+g)(\mathcal{R}_0-1)t}}{\mathcal{R}_0(e^{(\mu+g)(\mathcal{R}_0-1)t} - 1)/(\mathcal{R}_0 - 1) + 1/I_0}.$$

For $\mathcal{R}_0 = 1$: $\dot{I} = -\beta I^2$ implies $\int \frac{dI}{I^2} = \int -\beta dt$, which, after intergration, gives $-1/I = -\beta t + C$ where C is a constant to be determined. Use the initial condition $I(0) = I_0$ to get $C = -1/I_0$. This implies $I(t) = 1/(\beta t + 1/I_0)$. Combining the cases,

$$I(t) = \begin{cases} \dfrac{e^{(\mu+g)(\mathcal{R}_0-1)t}}{\mathcal{R}_0(e^{(\mu+g)(\mathcal{R}_0-1)t} - 1)/(\mathcal{R}_0 - 1) + 1/I_0}, & \text{for } \mathcal{R}_0 \neq 1, \\ \dfrac{1}{\beta t + 1/I_0}, & \text{for } \mathcal{R}_0 = 1. \end{cases} \tag{2.23}$$

By inspection, if $\mathcal{R}_0 \leq 1$ then $I(t)$ converges to zero and hence $\bar{\mathbf{Q}}$ is asymptotically stable. For $\mathcal{R}_0 > 1$, $I(t)$ converges to $1 - 1/\mathcal{R}_0$, and so $\mathbf{Q}^*$ is asymptotically stable. Therefore, the number $\mathcal{R}_0$ entirely determines the long-term behaviour of the disease. Notice that the basic reproduction number (2.20) is the same in the SIR model with population dynamics (2.17), this implies that the disease spreads at the same rate in these two models.

The SIRS Model

The SIRS model is also prominent in the literature, for example, see [31, 35]. This infectious disease model makes the same assumptions as the SIR model with population dynamics (2.16), with the important difference that individuals do recover from the disease with immunity, as in the SIR model, but only do so temporarily. For example, herpes simplex tends to relapse after recovery [40]. In fact, following recovery, many sexually transmitted diseases such as gonorrhea and chlamydia are known to result in little or no acquired immunity [18]. Assume individuals lose immunity at rate $\theta > 0$, hence, the average period of immunity is $1/\theta$. Along with the other assumptions of the SIR model (2.16), this leads to

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S + \theta R, \\ \dot{I} = \beta SI - gI - \mu I, \\ \dot{R} = gI - \mu R - \theta R, \end{cases} \tag{2.24}$$

with $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, such that $S_0 + I_0 + R_0 = 1$. The flow of this model is $S \to I \to R \to S$. The variables have been normalized such that $S + I + R = 1$, and hence represent the fractions of individuals in each class. The meaningful physical domain for this system is $\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ | S + I + R = 1\}$, which is invariant since $\{\dot{S} + \dot{I} + \dot{R}\}|_{S+I+R=1} = 0$, $\dot{S}|_{S=0} = \mu + gI > 0$, $\dot{I}|_{I=0} = 0$ and $\dot{R}|_{R=0} = gI \geq 0$. Note that the SIS model can be regarded as the limiting case of the SIRS model in the limit $1/\theta \to 0$. The basic reproduction number for this model is [44]:

$$\mathcal{R}_0 = \frac{\beta}{\mu + g}. \tag{2.25}$$

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$. and an endemic equilibrium

$$\mathbf{Q}^* = (S^*, I^*, R^*) = \left(\frac{1}{\mathcal{R}_0}, \frac{\mu + \theta}{\mu + \theta + g} \left(1 - \frac{1}{\mathcal{R}_0} \right), \frac{g}{\mu + \theta + g} \left(1 - \frac{1}{\mathcal{R}_0} \right) \right). \tag{2.26}$$

Since $S + I + R = 1$, the equation for R can be omitted, and the model can be made intrinsically two dimensional. Notice that if $\mathcal{R}_0 \leq 1$ then $I' < 0$ in Ω_{SIR} unless $S = 1$ or $I = 0$, hence the disease is eradicated. The SIRS model has the same basic reproduction number as the SIR model with population dynamics (2.17), and hence spreads at the same rate fundamentally. 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 equilibrium increases dramatically, and the period of the damped oscillations decreases [31]. Further, we expect the convergence rate to the equilibrium points will be different in the SIR and SIRS models. The SIS is the limiting case of this phenomenon ($1/\theta \to 0$) and hence the prevalence of the disease will also be dramatically increased in the SIS model (2.19) as compared to the SIR model (2.16).

The SEIR Model

Many diseases incubate inside the hosts for a period of time before the hosts become infectious, hence the assumption that the incubating period is negligible may be a very poor one. Examples of such diseases include hepatitis B, Chagas' disease, HIV/AIDS and tuberculosis, the last two having latent stages that may last for years [49, 40]. Motivated by this, assume that once a susceptible makes an adequate contact with an infective they enter a latent period before becoming infectious. In this stage, an individual has been exposed but is not yet infectious. Denote this class of exposed individuals as E. Assume that individuals who have been exposed become infectious at a rate $a > 0$, and so, the infection has an average incubating period $1/a$. This leads to the SEIR model, which is common in the literature, for example, see [31, 32, 38, 39, 49, 63]. It uses the same assumptions on the infectious

period, incidence rate and population dynamics as the SIR model (2.16) and is given by:

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S, \\ \dot{E} = \beta SI - aE - \mu E, \\ \dot{I} = aE - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{2.27}$$

with $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $E(0) = E_0$, $R(0) = R_0$, such that $S_0 + I_0 + E_0 + R_0 = 1$ and the variables have been normalized to be fractions of individuals in each class. The flow of this model is $S \to E \to I \to R$. The meaningful physical domain for this system is

$$\Omega_{SEIR} = \{(S, E, I, R) \in \mathbb{R}^4_+ | S + E + I + R = 1\},$$

which is invariant to the system since $\{\dot{S}+\dot{E}+\dot{I}+\dot{R}\}\,|_{S+I+E+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{E}\,|_{E=0} = \beta SI \geq 0$, $\dot{I}\,|_{I=0} = 0$, and $\dot{R}\,|_{R=0} = gI \geq 0$. For this model, define the basic reproduction number [44]:

$$\mathcal{R}_1 = \frac{\beta a}{(\mu + g)(\mu + a)}. \tag{2.28}$$

Intuitively, this threshold is the product of the contact rate β, the average fraction $a/(a + \mu)$ surviving the latent period, and the average infectious period $1/(\mu + g)$ [28]. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{E}, \bar{I}, \bar{R}) = (1, 0, 0, 0)$ and an endemic equilibrium

$$\mathbf{Q}^* = (S^*, E^*, I^*, R^*) = \left(\frac{1}{\mathcal{R}_1}, \frac{\mu(\mu + g)}{\beta a}(\mathcal{R}_1 - 1), \frac{\mu}{\beta}(\mathcal{R}_1 - 1), \frac{g}{\beta}(\mathcal{R}_1 - 1) \right). \tag{2.29}$$

Since $S + E + I + R = 1$, the equation for R can be omitted, hence this model is intrinsically three dimensional. Recall the reproduction number $\mathcal{R}_0 = \beta/(\mu + g)$ for the SIS (2.19), SIR (2.16) and SIRS (2.24) models. Notice that for the SEIR model, the reproduction number

$$\mathcal{R}_1 = \mathcal{R}_0 \cdot \frac{a}{\mu + a},$$

which implies that $\mathcal{R}_1 \leq \mathcal{R}_0$. Further, since the mean lifetime of an individual $1/\mu$ is usually much greater than the incubation period $1/a$, then $a >> \mu$ and hence $a/(a + \mu) \approx 1$ [31], and so the reproduction number is close to the SIR model's reproduction number $\mathcal{R}_0$ (2.17). If the latent period is small compared to the infectious period ($a/g >> 1$), which is usually the case, the latent period can be ignored [49]. In this limit, the model becomes the SIR model [49]. Again, the dynamics of the model are determined by the reproduction number, if $\mathcal{R}_1 \leq 1$ then disease-free solution is asymptotically stable, and if $\mathcal{R}_1 > 1$ then the endemic solution is asymptotically stable [38], and is approached with damped oscillations

[31]. In fact, it can be shown that the period of oscillations is approximately $2\pi\sqrt{AG}$, where $A = 1/(\mu(\mathcal{R}_1 - 1))$ is the mean age of infection and $G = 1/(\mu + g) + 1/(\mu + a)$ is the mean period of a host's infectivity [31]. The SEIR model has a slower rate of growth of the disease after its introduction because of the latent period delaying an exposed person in becoming infectious [31].

2.2.4 Control Schemes

Constant Control

Most developed countries have cohort immunization programs in place with varying degress of success [4]. These program, sometimes also called constant immunization, are based on the concept of time-constant immunization [66], in which members of the susceptible population are continuously vaccinated. For example, recently, the strategy for measles immunization in many areas of the Western world recommends a vaccination dose at 15 months of age and a second dose at around 6 years of age [67]. There are a lot of studies on constant control schemes in the literature, for example, see [2, 31, 36, 41, 43, 46, 47, 48, 51, 66, 68, 73].

Consider the constant vaccination of a fraction $0 \leq p \leq 1$ of susceptible newborn infants, moving them to the removed class R with permanent immunity. Hence, assume that the immunity acquired naturally or from the vaccination are the same. This scheme has been studied in, for example, [31, 66, 73], and, when applied to the SIR model (2.16), the model becomes:

$$\begin{cases} \dot{S} = (1-p)\mu - \beta SI - \mu S, \\ \dot{I} = \beta SI - gI - \mu I, \\ \dot{R} = gI + \mu p - \mu R, \end{cases} \tag{2.30}$$

where the variables have been normalized such that $S + I + R = 1$, and the initial conditions are $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, with $S_0 + I_0 + R_0 = 1$. The meaningful domain is $\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S + I + R = 1\}$, which is invariant to the system. The effect of this strategy reduces the birth rate μ of susceptibles, which can be seen from the model in the $(1-p)\mu$ term. There are two equilibrium points, a disease-free solution $\bar{\mathbf{Q}} = (1-p, 0, p)$ and an endemic solution

$$\mathbf{Q}^* = (S^*, I^*, R^*) = \left(\frac{\mu + g}{\beta}, \frac{\mu}{\beta}(\mathcal{R}_0^p - 1), \frac{g}{\beta}(\mathcal{R}_0^p - 1) + p \right). \tag{2.31}$$

Consider the linear change of variables [31]: $S = \hat{S}(1-p), I = \hat{I}(1-p), R =$

$\hat{R}(1-p)+p$. Apply these to the system to get [31]:

$$\begin{cases} \dfrac{d\hat{S}}{dt} = \mu - \beta(1-p)\hat{S}\hat{I} - \mu\hat{S}, \\ \dfrac{d\hat{I}}{dt} = \beta(1-p)\hat{S}\hat{I} - g\hat{I} - \mu\hat{I}, \\ \dfrac{d\hat{R}}{dt} = g\hat{I} - \mu\hat{R}. \end{cases} \tag{2.32}$$

From this, it is apparent that changing the birth rate has the effect of transforming the contact rate from β to $\beta(1-p)$. Indeed, the basic reproduction number for this model is [31]

$$\mathcal{R}_0^p = \frac{\beta}{\mu+g} \cdot (1-p). \tag{2.33}$$

Notice that $\mathcal{R}_0^p = (1-p)\mathcal{R}_0$ from the non-vaccination SIR model (2.17), and hence, the basic reproduction rate has been reduced by a factor $1-p$. If $\mathcal{R}_0^p < 1$ then the disease-free solution $\bar{\mathbf{Q}}$ of system (2.30) is locally asymptotically stable in the meaningful domain Ω_{SIR}, if $\mathcal{R}_0^p > 1$ then endemic solution $\mathbf{Q}^*$ of system (2.30) is locally asymptotically stable in the meaningful domain Ω_{SIR} [67]. Note that the requirement $\mathcal{R}_0^p < 1$ implicitly defines a minimum vaccination rate which must be reached to achieve what is commonly referred to as herd immunity [29]. More specifically, for this strategy to successfully eradicate the disease, we require $p > p_{\text{crit}} := 1 - 1/\mathcal{R}_0$, where $\mathcal{R}_0$ is the basic reproduction number of the non-vaccination SIR model (2.16).

Pulse Control

Pulse vaccination strategies are based on the suggestion that an epidemic can be more effectively controlled when the natural temporal process of the epidemics is antagonized by a temporal process [4, 66]. Theoretical results show that a pulse vaccination strategy can be distinguished from conventional constant immunization in leading to disease eradication at relatively low values of vaccination [4]. Recently, pulse vaccination has gained prominence for its highly successful control of poliomyelitis and measles throughout Central and South America [41]. This technique was first proposed as a control scheme for measles in [4] by Shulgin et. al and has since been further developed, for example in [19, 21, 43, 48, 51, 58, 61, 66, 67, 73].

More specifically, pulse vaccination is the control technique of immunizing a portion of all age cohorts of the susceptible population in a very short time period with respect to the dynamics of the disease. This is in contrast to the constant control scheme outlined in the previous section, where the vaccinations are applied continuously in time. The motivation for this strategy [66] is to notice that in the SIR model (2.16) $I' = \beta SI - \mu I - gI = I(\beta S - \mu - g) < 0$ if

$$S < \frac{\mu+g}{\beta} := S_{\text{crit}}. \tag{2.34}$$

That is, so long as the susceptible population is controlled such that it is always less than some critical value S_{crit}, then $I' < 0$ in Ω_{SIR} for all $t \geq 0$ unless $I = 0$, which means the infection will burn out and there will be no epidemic.

And so, applying this scheme to the SIR model (2.16) by impulsively vaccinating a portion $0 \leq p \leq 1$ of the susceptible population every T time units, giving them permanent immunity. In mathematical terms, discrete time vaccination can be represented by Dirac δ functions as inputs to the above system, causing discontinuous jumps in the state of the systems [4], see [66] for a derivation from first principles. This leads to an IDE system:

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S, & t \in ((k-1)T, kT] \\ \dot{I} = \beta SI - gI - \mu I, \\ \dot{R} = gI - \mu R, \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t), \\ R(t^+) = R(t) + pS(t), \end{cases} \tag{2.35}$$

where $k = 1, 2, \ldots$, and the total population is constant. Here

$$S(kT^+) := \lim_{h \to 0^+} S(kT + h).$$

The initial conditions are $S(0^+) = S_0 > 0$, $I(0^+) = I_0 > 0$, $R(0^+) = R_0$. The meaningful domain is Ω_{SIR}, which is invariant.

The following derivations and analyses in this section are taken from [66]. Since $(1, 0, 0)$ is no longer an equilibrium point of the system, we begin the analysis by showing the existence of a periodic disease-free solution, motivated by the fact that $I \equiv 0$ is a solution to the differential equation for I. Under these conditions, the system becomes:

$$\begin{cases} \dot{S} = \mu(1 - S), & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t) + pR(t). \end{cases} \tag{2.36}$$

For $(k-1)T < t \leq kT$, integrate and solve the equation for S between pulses, and use $S + R = 1$ (since $I = 0$):

$$\begin{cases} S(t) = 1 + (S((k-1)T) - 1)e^{-\mu(t-(k-1)T)}, \\ R(t) = 1 - S(t). \end{cases} \tag{2.37}$$

Immediately after the pulse vaccination,

$$S(kT^+) = (1-p)[1 + (S((k-1)T) - 1)e^{-\mu T}] := F(S((k-1)T)).$$

This defines a stroboscopic mapping $S_k = F(S_{k-1})$ where $S_{k-1} := S((k-1)T)$. This mapping has a unique fixed point:

$$S^* = F(S^*) = \frac{(1-p)(1-e^{-\mu T})}{1-(1-p)e^{-\mu T}}.$$

Further, notice that

$$\left|\frac{dF(S(kT))}{dS(kT)}\right|_{S(kT)=S^*} = (1-p)e^{-\mu T} < 1,$$

which implies that the fixed point is globally asymptotically stable in Ω_{SIR} (follows from Lemma 2.1 of [43]). Set $S^* = S((k-1)T)$ to get the periodic disease-free solution [66], for $(k-1)T < t \leq kT$:

$$\begin{cases} \widetilde{S}(t) = 1 - \dfrac{pe^{-\mu(t-(k-1)T)}}{1-(1-p)e^{-\mu T}}, \\ \widetilde{I}(t) = 0, \\ \widetilde{R}(t) = 1 - \widetilde{S}(t). \end{cases} \tag{2.38}$$

For the pulse SIR model (2.35), define the basic reproduction number:

$$\mathcal{R}_0(T) = \frac{\beta}{\mu+g}\frac{1}{T}\int_0^T \widetilde{S}(t)dt. \tag{2.39}$$

It can be shown, using Floquet theory (see [50] for background material on Floquet theory), that if $\frac{1}{T}\int_0^T \widetilde{S}(t)dt < \frac{g+\mu}{\beta} := S_{\text{crit}}$, that is, if $\mathcal{R}_0(T) < 1$, then the periodic disease-free solution $(\widetilde{S}(t), 0, \widetilde{R}(t))$ is locally asymptotically stable [66]. Notice that

$$\mathcal{R}_0(T) = \mathcal{R}_0\frac{1}{T}\int_0^T \widetilde{S}(t)dt < \mathcal{R}_0,$$

with $\mathcal{R}_0$ the basic reproduction number of the SIR model without pulse vaccination (2.17). Hence, the reproduction number of this model has been reduced, as expected.

Since $\widetilde{S}(t)$ is explicitly known, we can evaluate the integral in (2.39) as is done in [66],

$$\begin{aligned} \frac{1}{T}\int_0^T \widetilde{S}(t)dt &= \frac{1}{T}\int_0^T \left[1 - \frac{pe^{-\mu t}}{1-(1-p)e^{-\mu T}}\right]dt = \frac{1}{T}\left[t + \frac{pe^{-\mu t}}{\mu[1-(1-p)e^{-\mu T}]}\right]_0^T, \\ &= 1 + \frac{p - pe^{\mu t}}{\mu T[e^{\mu T} + p - 1]} = \frac{(\mu T - p)(e^{\mu T} - 1) + \mu pT}{\mu T(e^{\mu T} + p - 1)}. \end{aligned}$$

Then, for $\mathcal{R}_0(T) < 1$, T and p need to satisfy [66]:

$$\frac{(\mu T - p)(e^{\mu T} - 1) + \mu pT}{\mu T(e^{\mu T} + p - 1)} < \frac{\mu + g}{\beta} := S_{\text{crit}}, \tag{2.40}$$

in order for the disease to be eradicated. From this, the tradeoff between how large the interpulse time T can be and how small the proportion of population vaccinated p needs to be is more clear. Further, the maximum allowable interpulse time T (given a vaccination portion p) can be calculated by noticing that the function on the left in (2.40) is an increasing function of T [66] and so reaches $T_{\max}$ at equality. Simplify using Taylor expansions, by reasonably assuming the period of pulses is much shorter than the mean life-time, $T << 1/\mu$, and by assuming the duration of the disease is much shorter than the average mean life-time, $1/g << 1/\mu$. After neglecting higher order terms this leads to [66]:

$$T^1_{\max} \approx \frac{gp}{\mu\beta} \frac{1}{1 - p/2 - g/\beta}. \tag{2.41}$$

Returning to the earlier pulse vaccination motivation of requiring that $S(t) < S_{\text{crit}}$ from (2.34) for all $t \geq 0$, the maximum allowable interpulse time, $T^2_{\max}$, can be calculated for this constraint. Recall that the minimum number of susceptibles occurs immediately after pulse vaccinations (S^*), while the maximum number of susceptibles occurs just before the vaccination ($S^*/(1-p)$). Thus, to guarantee $S(t) < S_{\text{crit}}$, $S^*/(1-p) < S_{\text{crit}}$ is required. We can arrive at the expression for $T^2_{\max}$ by evaluating this at equality, that is, $S^* = (1-p)S_{\text{crit}}$, to get [66]:

$$T^2_{\max} = \frac{1}{\mu} \ln\left(1 + \frac{pS_{\text{crit}}}{1 - S_{\text{crit}}}\right).$$

It is important to note that, as expected, $T^2_{\max} \geq T^1_{\max}$ for all $0 \leq p \leq 1$ [66].

Comparison of Control Schemes

Before implementing any control scheme, it is important to investigate the strategy's advantages and disadvantages. Certainly, in choosing control strategies for the eradication of a disease, the possible schemes should be analyzed rigorously and compared in detail. In practice, a range of constraints and trade-offs influence the choice of control strategy, and hence their inclusion in any modelling investigation is important [31]. These limitations may be logistical, 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 [31]. Economic considerations should also be included in epidemiological models, since control schemes should be judged through cost-benefit analyses [31]. Ultimately, the desirability of implementing a new type of control strategy (such as pulse control) depends on two factors [4]: the risks attached to the scheme and the costs of implementation and long-term maintenance.

In a constant vaccination scheme, the vaccination affects the amplitude and the period of the epidemic, but it does not antagonize the underlying dynamics of the disease [67]. It can be seen easily from the constant vaccination model introduced in the previous section (2.30) that, in effect, it reduces the birth rate of susceptibles

[66]. Indeed, this is equivalent to an unvaccinated population with a reduced basic reproduction number [31]. In most countries, pediatric immunization programs are already established and any pulse vaccination strategy is likely to be in addition to constant immunization rather than an alternative [31].

Many countries have encountered difficulties in eliminating the spread of diseases with cohort immunization, even when the vaccination coverage is relatively high [4]. This is largely due to the persistence of pockets of susceptible individuals, often in poor communities in large urban centers [4]. For example, the critical vaccination level required for measles eradication is about 94%, and 86% for rubella [28]. Further, the vaccine efficacy for these diseases is approximately 0.95, which means 5% of those who are immunized do not gain immunity [28]. Therefore, to reach the levels necessary to achieve what is referred to as herd immunity, at least 0.99 would need to be immunized for measles and 0.91 for rubella [28]. It would be both difficult and expensive to implement a cohorti mmunization for such a high coverage of the population [66]. In fact, it is unrealistic practically, and it usually leads to a two-dose program as an attractive alternative, which has been implemented in some countries [28]. It is noted that even if a constant vaccination program does not eradicate a disease, it can still be useful in reducing the prevalence of the infection [31].

As discussed in the previous section, in contrast to constant control, a pulse control strategy is based on the suggestion that in some cases epidemics can be more efficiently controlled when its natural temporal process is antagonized by another temporal process, that is, by a vaccination process that is pulsed in time rather than continuous [66, 67]. Recent research shows that pulse vaccination strategy (PVS) might be an optimal choice in cases of highly infectious diseases outbreaks, such as a new smallpox epidemic [60]. 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 [66]) parotitis, and phthisis [51]. Another well-publicized example is PVS's success in controlling poliomyelitis and measles in Central and South America [31].

Results show that pulse vaccination strategies can be distinguished from time-constant immunization strategies in leading to disease eradication at relatively low values of vaccination [4]. Indeed, this is one of this scheme's main benefits compared to the continuous control schemes. Compared to continual pediatric vaccination (2.30), it also has the additional advantage that it is often logistically simpler to implement [31]. On a practical level, it seems essential to determine before hand the time between successive pulses required for the effective implementation of the pulse strategy (2.35) [67]. This is actually not a major problem, as for many pulse models, an explicit relation between the pulse vaccination portion p and the interpulse time T can be established explicitly. In some cases, such as developing countries, where levels of vaccine coverage are often low (for example, less than 65% by age 5 years), analyses suggest that the interpulse times may be too short to make a pulse program a sensible strategy [4]. Even in this case, a pulse strategy can still be useful in reducing the prevalence of the infection. For other types of

control schemes, such as quarantine, ring vaccination and targeted vaccination, as well as how they compare, see [31].

The following cost-effectiveness analysis is taken from [66]. It is important to know the cost-effectiveness of schemes when deciding which control strategy to implement. For example, the number of people requiring the vaccination every pulse interval time T in the pulse strategy (2.35) might be close to the number of newborns requiring vaccination over the same period T in the constant vaccination scheme (2.30). As is done in [66], the cost here is taken to be the mean number of individuals per time unit requiring vaccination.

In the constant vaccination scheme (2.30), the number of individuals vaccinated per time unit is $N(p) = p\mu$, from the system equations. For the pulse vaccination scheme (2.35), the average number of people requiring vaccination per time unit is

$$N(p,T) = \frac{1}{T} p\widetilde{S}(kT^-),$$

with $k = 1, 2, \ldots$, and where $p\widetilde{S}(kT^-)$ is the number of people impulsively vaccinated at time kT. From earlier, and using a Taylor series expansion,

$$\widetilde{S}(kT^-) = \frac{e^{\mu T} - 1}{p - 1 + e^{\mu T}} \approx \frac{\mu T}{p + \mu T}.$$

And hence we have

$$N(p,T) \approx \frac{p\mu}{p + \mu T},$$

which is minimized when T is at a maximum, that is, $T = T^1_{\max}$ from (2.41), which gives:

$$N(p, T^1_{\max}) \approx \mu - \frac{\mu g}{\beta(1 - p/2)} \approx \mu.$$

And so, the minimum number of vaccinations required for pulse vaccination is approximately μ, and is approximately independent of p. One interesting note is that regardless of the vaccination portion p (and associated interpulse time $T_{\max}$ used) roughly the same number of people will be vaccinated under this pulse scheme. Compared to the constant control scheme cost $N(p) = p\mu$, we see the two costs are approximately equal when $p \approx 1$, which is usually the case from eradication requirements.

2.3 Switched and Hybrid Systems

2.3.1 Introduction

Hybrid and switched systems, which have applications in disciplines such as computer science, control engineering and applied mathematics, usually arise in two

contexts [12]: When there is a natural system that experiences abrupt changes based on factors (for example, environmental) governing the system. The second scenario is using switching controllers to stabilize a non-switched dynamical system. In both cases, switched systems evolve according to mode-dependent continuous dynamics, and experience transitions between modes that are triggered by events [64]. Consider the following motivating example from [64]:

Example 2.3.1. *Consider a car that has a manual gearbox. Travelling along a certain fixed path, the motion of the car can be characterized by its velocity $v(t)$ and its position $s(t)$. The system has two control inputs: the current angle of the throttle (u) and the current engaged gear (g). The response of the velocity to the current throttle input depends on which gear is currently engaged. The dynamics of this vehicle system can be interpreted as a hybrid system. Each mode (engaged gear) evolves the dynamics in a continuous manner according to a differential equation. The transitions between modes are abrupt and are triggered by the driver in the form of gear changes. See Figure 2.4.*

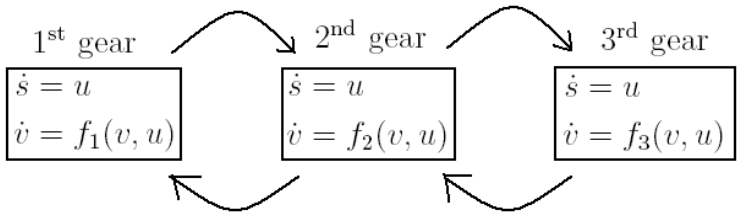

Figure 2.4: A hybrid model of a car with a manual gearbox, based on an image from [64].

Another simple example is a home climate-control system. Due to its on-off nature, a thermostat can be modelled as a discrete-event system, whereas the furnace or air conditioner is modelled as a continuous time-system [17]. For more examples, see [64]. For a review of the literature on hybrid and switched systems, see [12, 13, 42, 64].

Switched systems typically arise in the context of hybrid systems, which are systems that combine continuous dynamics (typcally modelled by differential or difference equations) and event-driven logic (typically modelled by finite or infinite-state automaton) [25]. For an example of a simple hybrid system, see [25]. As discussed above, switched systems are dynamical systems consisting of continuous-time subsystems (or modes) and a logical rule that orchestrates switching between them [17]. Mathematically, a switched system can be described by a family of ordinary differential equations [17]:

$$\begin{cases} x' = f_i(x), \\ x(t_0) = x_0, \end{cases} \tag{2.42}$$

where $\{f_i : i \in \aleph\}$ is a family of sufficiently regular functions from $\mathbb{R}^n \to \mathbb{R}^n$ that is parameterized by an index set $\aleph$ and a piecewise constant function of time $\sigma(t) : \mathbb{R}_+ \to \aleph$, usually called a switching signal or switching rule [42]. The switched system works as follows: the $i's$ are picked based on the switching rule, that is, $i = \sigma(t) : \mathbb{R}_+ \to \aleph : (t_{k-1}, t_k] \to \aleph$ and the system evolves according to the current value of σ. We assume that the switching rule is left-continuous, that is, $\sigma(t_k^-) := lim_{h \to 0^+} \sigma(t_k - h) = \sigma(t_k)$. For an illustration of a simple switching rule, see Figure 2.5.

The set $\aleph$ is usually a compact, finite subset of a finite-dimensional linear vector space [42]. The times $t_0 < t_1 < \ldots < t_k < \ldots \to \infty$ form the switching time sequence $\{t_k\}_{k=0}^{\infty}$. The case of infinitely fast switching, usually called chattering [42], is not considered here. The switching rule may be time-dependent (synchronous switching), state-dependent (asynchronous switching), Markovian, or something more sophisticated such as hybrid feedback with memory in the loop [42]. To be clear, for a particular choice $i = p$ with $p \in \aleph$, $x' = f_p(x)$ is called a subsystem or mode of the switched system (2.42).

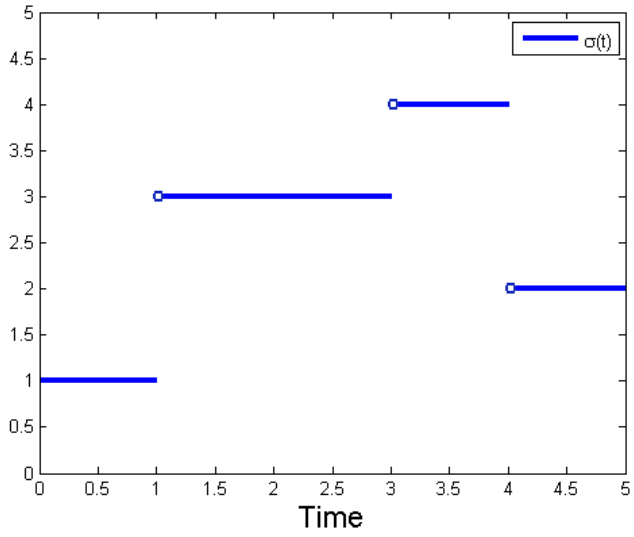

Figure 2.5: Example of a switching rule $\sigma(t)$ with switch times $t_k = 0, 1, 3, 4$.

Recall that an ODE IVP (2.2) admits a family of solutions that can be parameterized solely by the initial condition x_0, whereas the switched system (2.42) admits a family of solutions that is parameterized both by the initial condition x_0 and the switching signal σ [25]. Hence, one initialization of the switched system (2.42) is

$$\begin{cases} x' = f_\sigma(x), \\ x(t_0) = x_0. \end{cases} \tag{2.43}$$

It is also possible to construct switched systems from a control systems approach.

Consider the control ODE system

$$\dot{x}(t) = u(t), \tag{2.44}$$

with state $x \in \mathbb{R}^n$, and controller $u \in \mathbb{R}^n$. Following the method of [17], assume that there is a collection of nonlinear state feedback controllers: $u(t) \in \{f_1(x), \ldots, f_m(x)\}$, where $f_i(x)$ are continuously differentiable vector-valued functions such that $f_i(0) \equiv 0$ for all i. Incorporate these controllers into the system (2.44) by constructing the control input as follows, following the procedure of [22]:

$$u(t) = \sum_{k=1}^{\infty} f_{i_k}(x) l_k(t), \qquad \text{where } l_k(t) = \begin{cases} 1, & \text{if } t \in (t_{k-1}, t_k], \\ 0, & \text{otherwise,} \end{cases}$$

with discontinuity points $t_1 < \ldots < t_k < \ldots \to \infty$ as $k \to \infty$ and where $i_k \in \{1, 2, \ldots, m\} = \aleph$. Based on the contruction of $l_k(t)$, it is apparent that the controller switches its value at every t_k, hence it is a switching controller. The system can then be rewritten as:

$$\begin{cases} \dot{x} = f_{i_k}(x), & t \in (t_{k-1}, t_k], \\ x(t_0) = x_0 & k = 1, 2, \ldots \end{cases} \tag{2.45}$$

where $i_k \in \{1, 2, \ldots, m\} = \aleph$. Based on the construction of the switched controller, we say the switching times t_k are governed by a switching signal $\sigma = \sigma(t) : \mathbb{R}_+ \to \{1, 2, \ldots, m\}$ i.e. $(t_{k-1}, t_k] \to i_k \in \{1, 2, \ldots, m\}$, where σ is a piecewise continuous function. It is apparent that the control system (2.45) is a switched system.

A solution of the switched system (2.42) is a continuous function $\varphi(t) : \mathbb{R}_+ \to \mathbb{R}^n$ which satisfies the following: there exists a switching sequence $\{t_k\}_{k=0}^{\infty}$ and indices $i_1, i_2, i_3, \ldots$, with $i_k \in \aleph$, associated with a switching rule σ such that $\varphi(t)$ is an integral curve of the vector field $f_{i_k}(x)$ for $t \neq t_k$ [6]. The switched system has an equilibrium point $\bar{x}$ if $f_i(\bar{x}) = 0$ for all i. Sometimes in this thesis we refer to such a point as a common equilibrium point, or equilibrium point common to all subsystems. Without loss of generality, it is possible to shift such a point to the origin using $y = x - \bar{x}$ as before (see Section 2.1.1). The definitions of stability for switched systems (for example, found in [6]) are analogous to the definitions (2.1.6) from the classical theory of ODEs. For a switched system (2.42), it is also possible to assume, without loss of generality, that $t_0 = 0$, since, if this is not the case, it is possible shift the time by defining a new time variable $\tau = t - t_0$ and new switching times $h_k = t_k - t_0$.

Since analytical solutions of the switched system (2.42) are, in general, not known explicitly, there are three basic problems most often studied in switched systems literature [42]:

1. Find conditions that guarantee that the origin of the switched system (2.42) is asymptotically stable for any switching signal σ.

2. Identify those classes of switching signals σ for which the origin of the switched system (2.42) is asymptotically stable.

3. Construct a switching signal σ that makes the origin of the switched system (2.42) asymptotically stable.

Problem 1

The first problem is of particular importance in the area of feedback control, where a given plant is being controlled by switching between a set of stabilizing controllers. This process is usually governed by a decision maker (supervisor) such as a computer-controlled system [42]. This plant-multicontroller system is illustrated in Figure 2.6.

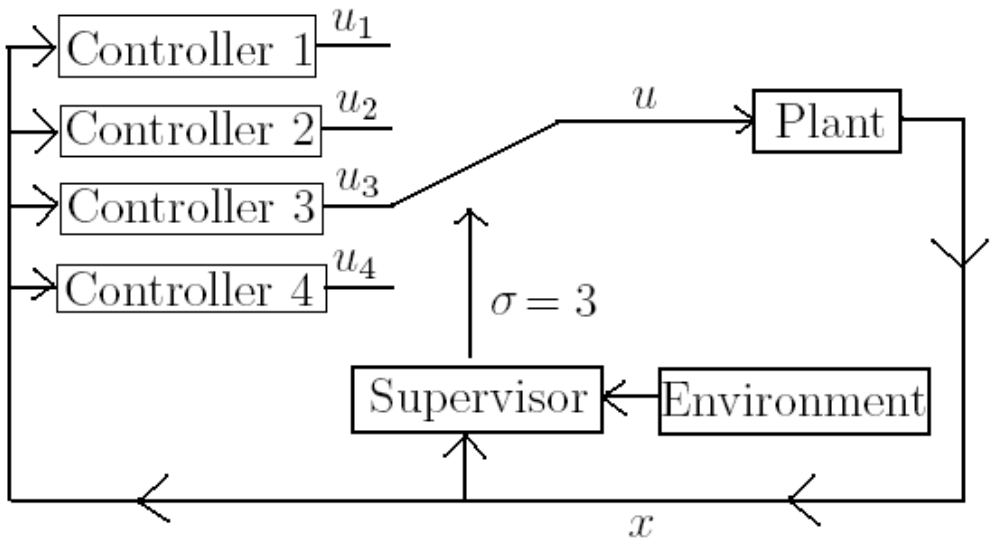

Figure 2.6: Multicontroller architechture, based on image from [42].

Certainly, if any one of the stabilizing controllers leads to instability of the system then one switching rule that guarantees instability is the supervisor choosing that particular controller to be in the system's loop indefinitely [42]. This raises the first important point of this problem, which is that all subsystems (or modes) of a switched system must be stable in order for asymptotic stability to be possible for an arbitrary switching signal σ [42]. It is often the case that if each stabilizing controller is kept in the loop for a sufficient amount of time, then the origin of the switched system will be asymptotically stable [42]. This raises the second important point for switched systems, the stability of all individual subsystems (or modes) is not a sufficient condition for asymptotic stability of the origin of the overall switched system (2.42) for an arbitrary switching signal σ. This interesting phenomenon is illustrated in the following example, where a switched system with

two stable subsystems is switched in such a way that the solution trajectory is unstable, taken from [42].

Example 2.3.2. *Consider the switched system (2.42) with $f_i(x) = A_i x$, $i = 1, 2$, and*

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

These matrices are Hurwitz, hence, the trivial solution is asymptotically stable for each subsystem. It is possible to construct a switching signal for these matrices that results in an unstable trajectory: if $x_1 x_2 < 0$ choose subsystem 1 to be active, otherwise choose subsystem 2 to be active. See Figure 2.7 for an illustration of this example, or see Figure 2 of [42].

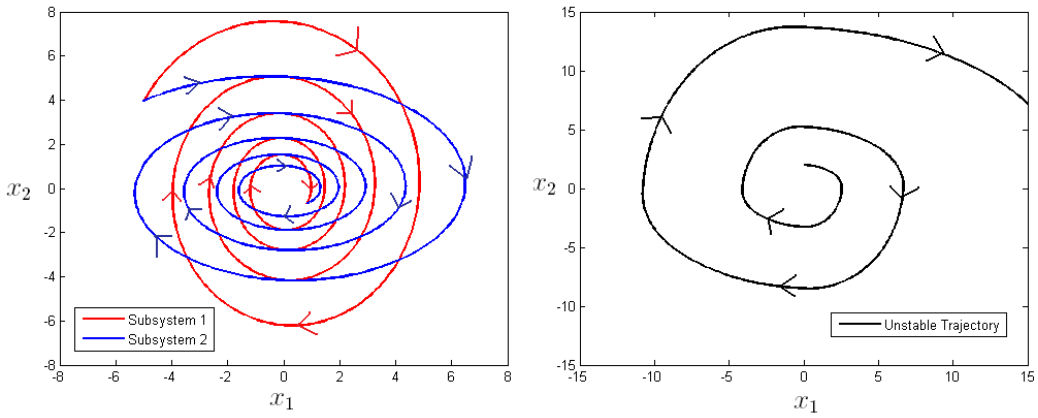

Figure 2.7: The instability of a switched system with two stable subsystems. The left pictures shows the (stable) dynamics of the two subsystems: subsystem 1 ($x' = A_1 x$) and subsystem 2 ($x' = A_2 x$) from Example 2.3.2. The right picture shows a trajectory of the switched system under a partilcular switching signal leading to isntability. Simulations done in MATLAB©.

One condition which does guarantee the asymptotic stability of the origin of the switched system (2.42) under arbitrary switching is the existence of a so-called common strict Lyapunov function.

Definition 2.3.1. [6]
The auxilliary function $V(x) \in C^1[D, \mathbb{R}_+]$, where $D \subset \mathbb{R}^n$ is an open set, is a common strict Lyapunov function for the switched system (2.42) if V is positive definite and if

$$\nabla V(x) \cdot f_i(x) < 0 \tag{2.46}$$

for all $x \in D \setminus \{0\}$ and for all $i \in \aleph$.

Then the following theorem then can be given.

Theorem 2.3.1. [42]
If the switched system (2.42) has a common strict Lyapunov function $V(x)$ then the origin of system (2.42) is globally asymptotically stable for arbitrary switching.

Problem 2

The second problem arises out of the first. Illustrated by the example of the instability of a switched system with stable subsystems, conditions are desired on the switching signal such that the overall switched system is asymptotically stable. This usually leads to restrictions on the rate at which the system can switch modes [42]. More specifically, if all subsystems are stable and if the switching is sufficiently slow, asymptotic stability is guaranteed [42]. Motivated by this, we are interested in formalizing the concept of sufficiently slow switching.

One important concept in this area is that of multiple Lyapunov functions. In this problem, it is assumed that all the subsystems are stable and that each subsystem has a Lyapunov function. The family of individual Lyapunov functions for each subsystem gives rise to the concept of multiple Lyapunov functions, defined as follows.

Definition 2.3.2. [6]
A switched system (2.42) has multiple strict Lyapunov functions if, for each $i \in \aleph$, *there exists a function* $V_i \in C^1[D, \mathbb{R}_+]$, $D \subset \mathbb{R}^n$ *an open set, that is positive definite, and for all* $x \in D \setminus \{0\}$, $\nabla V_i(x) \cdot f_i(x) < 0$.

Then, so long as the switched system's energy (measured by the Lyapunov functions) is not increasing at the switching times, asymptotic stability is ensured.

Theorem 2.3.2. [24]
If the switched system (2.42) has multiple strict Lyapunov functions $\{V_i : i \in \aleph\}$ *such that*

$$V_{p_2}(x(t_k)) \leq V_{p_1}(x(t_k)) \tag{2.47}$$

at every switching time t_k *where the switching rule* σ *switches from* p_1 *to* p_2, *then the trivial solution of system (2.42) is globally asymptotically stable for arbitrary switching.*

It is possible to weaken the condition (2.47) on the value of the Lyapunov functions at the switching times. If the switched system (2.42) has multiple strict Lyapunov functions $\{V_i : i \in \aleph\}$ such that, for any times $t_j > t_k$, where t_k is the last time the system switched out of mode i and t_j is the next time that the system switches back into mode i,

$$V_i(x(t_j)) \leq V_i(x(t_k)), \tag{2.48}$$

then the switched system (2.42) is stable [64]. See Figure 2.8 for an illustration.

Further, it is possible to weaken the condition (2.48) even further. Denote $V_{\sigma(t)}$ to be the multiple Lyapunov function that is active at the time t, based on the switching rule σ. If there exists a constant $\epsilon > 0$ with the property that for any two switching times t_i and t_j such that $i < j$ and $\sigma(t_i) = \sigma(t_j)$, the following is true

$$V_{\sigma(t_j)}(x(t_{j+1})) - V_{\sigma(t_i)}(x(t_{i+1})) \leq -\epsilon \|x(t_{i+1})\|^2, \tag{2.49}$$

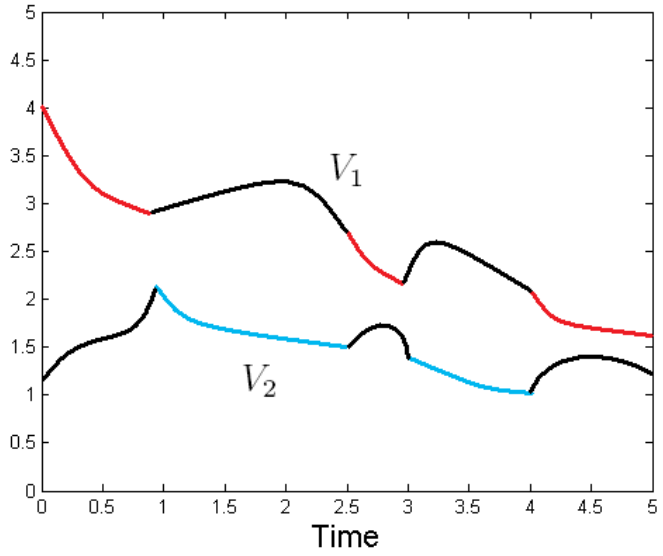

Figure 2.8: An example of possible trajectories of two Lyapunov functions along solutions to a switched system (2.42), based on image from [64]. The red line corresponds to the first Lyapunov function being active, the blue line corresponds to the second Lyapunov function being active. Switch times are $t_k = 0, 1, 2.5, 3, 4$. The condition (2.48) is satisfied by these multiple Lyapunov functions.

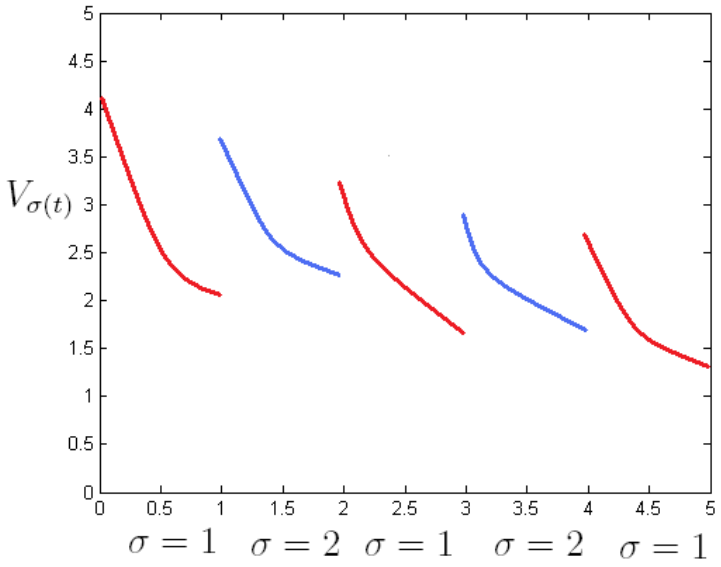

Figure 2.9: An example of possible trajectories of two Lyapunov functions along solutions to (2.42), based on image from [42]. The red line corresponds to the Lyapunov function V_1 being active. The blue line corresponds to the Lyapunov function V_2 being active. The condition (2.49) is satisfied.

then the origin of the switched system (2.42) is asymptotically stable. See Figure 2.9 for an illustration of this condition.

In the case that the switched system (2.42) is linear, $f_i(x) = A_i x$, it is possible to construct Lyapunov functions with a general procedure (for example, see [42]), however, as in the case of conventional Lyapunov theory in ODEs (see Section 2.1.1), there is no general method for constructing either a common or multiple Lyapunov function(s) for a nonlinear switched system (2.42). Further, and unlike the case of conventional ODEs theory, the multiple Lyapunov theorems here require explicit knowledge of the solution trajectory at the switching points t_k, when there are switches from one auxilary function to another [62]. This might seem to defeat the purpose of this approach, but often the case is that either the energy conditions (such as (2.47), (2.48), or (2.49)) are trivially satisfied or that the switching signal is constructed exactly with these energy conditions in mind. That is, the system is a switching controller system and the rule is specially constructed so that the non-increasing energy requirements outlined above are satisfied. See problem 3 for a more detailed account of stabilizing switching controllers.

Alternatively, another approach to guaranteeing the switching is sufficiently slow is to restrict the admissable switching signals. This is especially convenient when the switching signals are trajectory dependent [25]. The switching signal of system (2.42) is said to have a dwell time if there exists a constant $\eta > 0$ such that $t_k - t_{k-1} \geq \eta$ for all switching times t_k. When the switched system (2.42) is linear, that is, $f_i(x) = A_i x$ for all i, such that all matrices A_i are Hurwitz, the required lower bound on η to ensure asymptotic stability of the switched system (2.42) can be calculated explicitly from the parameters of the individual subsystems (see [42]). In the general nonlinear case of the switched system (2.42), it is also possible to make suitable assumptions under which a sufficiently large dwell-time will ensure asymptotic stability of the switched system [42]. If there exists constants $a, b \geq 0, T > 0$ such that $N_\sigma(T) \leq a + bT$ where $N_\sigma(T)$ is defined to be the number of discontinuities of a switching signal σ on the interval $[0, T)$, then the switching signal σ is said to have an average dwell-time (in this case, it is $1/b$) [42]. Note that this is more general than a dwell-time: in the case where $a = 0, b = 1/\eta$, the system has dwell-time $\eta > 0$. Intuitively, a switching signal has an average dwell-time $\eta_{avg} > 0$ if it switches more quickly than η_{avg} on some switch intervals, but on average it switches no faster than η_{avg}. If the switched system (2.42) has a switching signal which satisfies this average dwell-time property, then conditions can be established based on the parameters of the switched system such that the trivial solution will be globally asymptotically stable (see [42]). For more on the stability of switched systems with average-dwell time, see [26, 64]. To review other sets of admissable switching signals see [25].

Problem 3

The third problem is mainly a control problem. In this case, conditions are desired such that the switching signal σ stabilizes a switched system with entirely unstable

subsystems. Consider the switched system (2.42) in the linear case, $f_i(x) = A_i x$, and assume that $\aleph = [1, 2]$, then one condition that leads to a a stabilizing switching signal is if the matrix pencil $\gamma_\alpha(A_1, A_2) := \alpha A_1 + (1 - \alpha)A_2$, for $\alpha \in [0, 1]$ contains a stable matrix [42]. This problem leads to a linear matrix inequality which must be solved. Consider the following example from [42].

Example 2.3.3. *Consider the switched system (2.42) with $f_i(x) = A_i x$, $i = 1, 2$. Take*

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

The eigenvalues of both of these matrices have positive real parts. It is possible to construct a stabilizing switching signal for these matrices: if $x_1 x_2 < 0$ choose subsystem 1 to be active, otherwise choose subsystem 2 to be active. See Figure 2.10 for an illustration of this example, or see Figure 5 of [42].

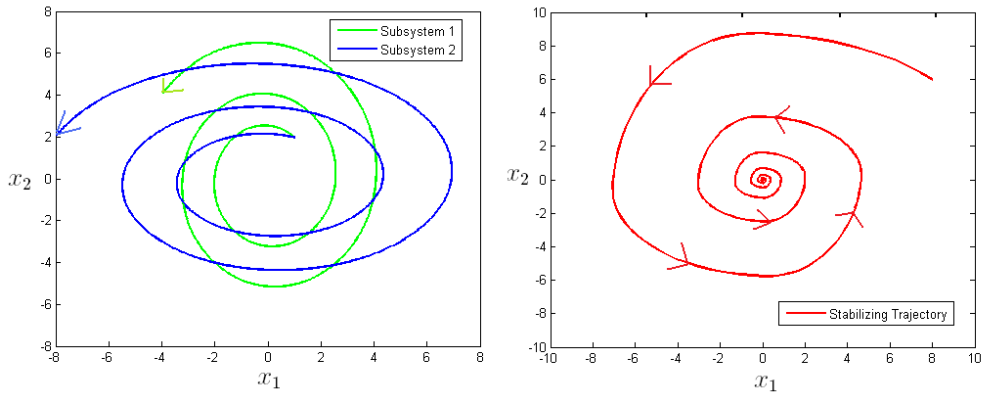

Figure 2.10: The stabilization of a switched system with two unstable subsystems. The left pictures shows the (unstable) dynamics of the two subsystems: subsystem 1 ($x' = A_1 x$) and subsystem 2 ($x' = A_2 x$) from Example 2.3.3. The right picture shows a trajectory of the switched system under the stabilizing switching signal outlined in the example. Simulations done in MATLAB©.

In other words, it is possible to construct a positive definite matrix P such that $\mathbb{R}^n \setminus \{0\}$ is covered by the union of two open conic regions $\Omega_1 := \{x |\ x^T(A_1^T P + PA_1^T)x < 0\}$ and $\Omega_2 := \{x |\ x^T(A_2^T P + PA_2^T)x < 0\}$ [42]. The function $V(x) = x^T P x$ decreases along solutions of the first system ($x' = A_1 x$) in the region Ω_1 and decreases along solutions of the second system ($x' = A_2 x$) in the region Ω_2 [42]. Using this property, it is possible to construct a stabilizing switching signal such that V decreases along solutions of the switched system, which implies asymptotic stability [42].

There are many results on stabilizing switching signals in the case that there exists a stable convex combination of the linear subsystems, for some other examples, see [42]. Other examples of stabilizing switching signals can be found in [62]

(where asynchronous switching is considered) and [17] (where both asynchronous and synchronous switching are considered). It is important to note that not only can switching signals stabilize switched systems with unstable subsystems [42], but switching between controllers in a certain way can also improve performance over a fixed continuous controller [12]. It can also prove to be easier to find a switching controller to perform a desired task versus finding a continuous one [17].

2.3.2 Invariance Principle for Switched Systems

The invariance principle in classical ODE theory (see Theorem 2.1.9) fails to hold for switched systems under completely arbitrary switching [6]. Appropriate restrictions need to be applied to the admissible trajectories, and hence to the switching signal σ [6]. Here, we look to establish an invariance principle for switched systems which exhibit a weak common Lyapunov function, and the following material is taken from [6], unless otherwise stated.

Assume, without loss of generality, $t_0 = 0$ and denote the set of all switching signals $\sigma(t) : [0, +\infty) \to \aleph$ by $\mathcal{S}$. Denote $\mathcal{S}_{\text{inf-dwell}} \subset \mathcal{S}$ the set of all switching signals σ which have nonvanishing dwell times, that is, there exists a $\eta > 0$, dependent on the specific solution $\phi(t; x_0)$ of switched system (2.42) such that

$$\inf_k t_k - t_{k-1} \geq \eta, \tag{2.50}$$

for all $k = 1, 2, \ldots$, where $\{t_k\}$ is the sequence of switching times associated to $\phi(t; x_0)$. We require the following definitions in order to state an invariance principle for switched systems.

Definition 2.3.3. *A set Ω is said to be weakly invariant with respect to the switched system (2.42) if for each $x_0 \in D$, D an open subset of $\mathbb{R}^n$ containing the origin, there exists an index $i \in \aleph$, a solution $\phi(t; x_0)$ of the vector field $f_i(x)$ and a real number $b > 0$ such that $\phi(0; x_0) = x_0$ and $\phi(t; x_0) \in \Omega$ for either $t \in [-b, 0]$ or $t \in [0, b]$.*

Definition 2.3.4. *A solution $\phi(t; x_0)$ of the switched system (2.42) is said to be attracted by a compact set Ω if for each $\epsilon > 0$ there exists a time $T > 0$ such that for all $t \geq T$, $\phi(t; x_0) \in \mathcal{B}(\epsilon, \Omega)$, where $\mathcal{B}(\epsilon, x)$ is the open ball of radius ϵ centered on x and*

$$\mathcal{B}(\epsilon, \Omega) = \bigcup_{x \in \Omega} \mathcal{B}(\epsilon, x).$$

Note that if $\phi(t; x_0)$ is attracted by Ω, then it is necessary and sufficient that

$$\lim_{t \to +\infty} dist(\phi(t; x_0), \Omega) = 0.$$

Definition 2.3.5. *The auxilliary function $V(x) \in C^1[D, \mathbb{R}_+]$, where $D \subset \mathbb{R}^n$ is an open set, is a common weak Lyapunov function for the switched system (2.42) if V is positive definite and if*

$$\nabla V(x) \cdot f_i(x) \leq 0 \tag{2.51}$$

for all $x \in D$ and for all $i \in \aleph$.

We are now in a position to state an invariance principle for switched systems that have a common weak Lyapunov function.

Theorem 2.3.3. [6]
Let $V(x) : D \to [0, +\infty)$ be a weak common Lyapunov function for the switched system (2.42). Let D_l be the connected component of the level set $\{x \in D | \ V(x) < l\}$ for some constant $l > 0$. Assume that D_l is bounded and let $Z = \{x \in D | \ \exists i \in \aleph$ 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 $Z \bigcap D_l$. Then every solution $\phi(t; x_0)$ associated with a switching signal $\sigma \in \mathcal{S}_{inf\text{-}dwell}$ and with $x_0 \in D_l$ is attracted by Ω.

For examples of applying this invariance principle to switched systems, see the examples in [6].

Chapter 3

One-Dimensional Switched Epidemiological Models

The epidemiological models discussed in Section 2.2 can be made more realistic by using time-varying parameters. As discussed in Chapter 1, the contact rate has been observed to vary over the seasons periodically [31]. Another possibility is to consider the seasonal variation in the birth rate, but since μ is usually relatively small, this will not effect the model in the same way as a seasonal variation in the contact rate. Further, changes in the birth rate or removal rate are not as destabilizing as a change in the contact rate with respect to causing changes in the dynamics [31]. The approach of using a temporally forced model with $\beta = \beta(t)$ has been studied in the literature for some models, for example, see [31, 49, 57, 58, 59, 60, 63, 66]. This approach's drawback is that for more complicated models alternative methods of analysis are needed [31].

The alternative approach studied here is to approximate the contact rate as a piecewise constant. For example, taking into account the cyclical variation in the contact rate over a one year period, consider the approximation:

$$\beta = \begin{cases} \beta_1 & \text{during the winter,} \\ \beta_2 & \text{during the other seasons.} \end{cases} \tag{3.1}$$

This gives a better approximation of the contact rate and it allows the use of a multitude of techniques from switched systems theory (some of which are detailed in Section 2.3). Further, it is possible to easily extend this method to approximate the birth rate μ, the removal rate g, or any other parameter in these epidemiological models as piecewise constants.

Another benefit of a switched systems approach is that it allows for the epidemiological structures of the compartments to change in time. For example, as discussed in Section 2.2, there are different choices for the horizontal incidence rate, and it is apparent that the choice depends on the circumstances of the specific disease considered. There can be both advantages and disadvantages to a specific

choice of incidence rate, and hence, it can be beneficial, for example, to be able to use one incidence rate for some time and different one entirely at a later time. Using a switched systems approach allows for this possibility:

$$f(S,I) = \begin{cases} f_1(S,I) & \text{for the earlier periods of a disease,} \\ f_2(S,I) & \text{for the later period.} \end{cases}$$

Switching the incidence rate will be the focus of Chapter 6.

This chapter is structured as follows: In Section 3.1, the one-dimensional model SIS model with switching will be introduced and studied. Threshold criteria ensuring stability of the disease-free solution will be established. The permanence of the disease will then be investigated. In Section 3.2, a switched SIS model with vertical transmission will be considered. Then, in Section 3.3, SIS models with varying total population sizes will be studied. The generalization to switching the contact rate, removal rate and birth rate will be examined in Section 3.4. Finally, simulations will be given in Section 3.5.

3.1 Switching the Contact Rate in the SIS Model

The contact rate, which is the average number of adequate contacts of a person per unit time, is traditionally assumed to be a constant in these epidemic models [28, 29, 31]. Introduce switching into the SIS model (2.19) by assuming the contact rate, β, is a parameter which varies over time. Assume it varies in a simple way: it is a piecewise constant that switches its value at the switching times t_k, where $t_0 = 0 < t_1 < \ldots < t_k \to \infty$ as $k \to \infty$. Here we have assumed, without loss of generality, that the initial time is zero. Assume there are m different contact rates $\beta_i > 0$ with which to approximate β as a piecewise constant parameter, that is, $i \in \{1, \ldots, m\}$. Consider a switching rule $\sigma = \sigma(t) : \mathbb{R}_+ \to \{1, 2, \ldots, m\}$, where σ is a piecewise continuous function, assumed to be continuous from the left. Denote the set of all such switching rules as $\mathcal{S}$. Then the value of i follows the switching rule, and hence, β_i follows the switching rule. This leads to the following new switched SIS model:

$$\begin{cases} \dot{S}_c = \mu N - \dfrac{\beta_i S_c I_c}{N} + g I_c - \mu S_c, \\ \dot{I}_c = \dfrac{\beta_i S_c I_c}{N} - g I_c - \mu I_c, \end{cases} \tag{3.2}$$

where $i \in \{1, \ldots, m\}$ follows the switching rule $\sigma(t)$. The variables S_c, I_c are, respectively, the number of susceptible and infected individuals, and $N = S_c + I_c$ is the total population. Since $\dot{S}_c + \dot{I}_c = 0$, the total population is constant and the variables may be normalized using $S = S_c/N$ and $I = I_c/N$,

$$\begin{cases} \dot{S} = \mu - \beta_i S I - \mu S + g I, \\ \dot{I} = \beta_i S I - g I - \mu I. \end{cases} \tag{3.3}$$

The meaningful physical domain for this system is $\Omega_{SI} = \{(S, I) \in \mathbb{R}^2_+ |\ S + I = 1\}$. Notice that $\{\dot{S} + \dot{I}\}\,|_{S+I=1} = 0,\ \dot{S}\,|_{S=0} = \mu + g > 0$ and $\dot{I}\,|_{I=0} = 0$ which implies the domain is invariant to each subsystem, and hence is invariant to the switched system (3.3). Suppose the initial conditions satisfy $S(0) = S_0 > 0, I(0) = I_0 > 0$, such that $(S_0, I_0) \in \Omega_{SI}$.

Since the domain is invariant and the switched system has continuously differentiable functions on the right-hand side, the model is well-posed, biologically and mathematically. For each subsystem, define the basic reproduction number, from the non-switched case (2.20)

$$\mathcal{R}_i = \frac{\beta_i}{\mu + g}, \tag{3.4}$$

the average number of secondary infections produced by a single infected individual in a wholly susceptible population. Note that each subsystem has its own basic reproduction number, this stems from the fact that as the contact rate changes, so does the rate at which the disease spreads. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}) = (1, 0)$ that is common to all subsystems. Each subsystem also has its own unique endemic equilibrium

$$\mathbf{Q}^*_\mathbf{i} = (S^*_i, I^*_i) = \left(\frac{1}{\mathcal{R}_i}, 1 - \frac{1}{\mathcal{R}_i}\right), \tag{3.5}$$

which exist in the meainingful domain only if $\mathcal{R}_i \geq 1$. Since $S + I = 1$, the system is intrinsically one-dimensional:

$$\dot{I} = (\beta_i - g - \mu)I - \beta_i I^2. \tag{3.6}$$

Each subsystem (i.e., each i) is a Bernoulli differential equation, whose full solution can be found [29], as was done in Section 2.2.3. For $t \in (t_{k-1}, t_k]$, $k = 1, 2, \ldots$, with switching rule $\sigma(t) = i_k$ on this interval:

$$I(t) = \begin{cases} \dfrac{e^{(\mu+g)(\mathcal{R}_{i_k}-1)t}}{\mathcal{R}_{i_k}(e^{(\mu+g)(\mathcal{R}_{i_k}-1)t} - 1)/(\mathcal{R}_{i_k} - 1) + 1/I(t_{k-1})}, & \text{for } \mathcal{R}_{i_k} \neq 1, \\ \dfrac{1}{\beta_{i_k} t + 1/I(t_{k-1})}, & \text{for } \mathcal{R}_{i_k} = 1. \end{cases} \tag{3.7}$$

If $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$, then it is apparent, from system (3.3), that $I' < 0$ in Ω_{SI} for $I \neq 0$. Thus, since $S + I = 1$, the disease-free solution $\bar{\mathbf{Q}}$ is asymptotically stable in the meaningful domain Ω_{SI}. It is important to note that the requirement $\mathcal{R}_i \leq 1$ for all i is restrictive from a biological standpoint. This requirement states that the disease can never spread fast enough for one infective to, on average, infect more than one susceptible. For many diseases this is simply not true (see Table 2.1), and so, in a more realistic case, conditions are desired for the eradication of the disease when some of the basic reproduction numbers are greater than one. This idea can be captured with the following definition: for some switching rule $\sigma(t)$, define, for any time $t \geq 0$, the time-weighted mean:

$$\langle R_\sigma \rangle := \frac{1}{t} \int_0^t R_{\sigma(s)} ds. \tag{3.8}$$

Define $T_i(t)$ to be the total activation time in the i^{th} subsystem in the interval $(0, t]$. The following lemma is needed before we establish stability conditions, in order to make the threshold criteria biologically meaningful.

Lemma 3.1.1. *Consider a general switched epidemiology system with basic reproduction numbers $\mathcal{R}_i = A_i/B$ for $i = 1, 2, \ldots, m$ where $A_1, \ldots, A_m, B > 0$ are constants. If*

$$\langle R_\sigma \rangle < 1 - \epsilon, \tag{3.9}$$

for $t \geq h$, with constants $\epsilon > 0, h \geq 0$ and switching rule $\sigma \in \mathcal{S}$, then it follows that $\sum_{i=1}^{m}(A_i - B)T_i(t) < -ct$ for $t \geq h$, with $c > 0$ a constant.

Proof. (3.9) implies, from the definition,

$$\frac{1}{t}\int_0^t \frac{A_{\sigma(s)}}{B} ds < 1 - \epsilon,$$

for $t \geq h$, which implies

$$\frac{1}{t}\int_0^t (A_{\sigma(s)} - B) ds < -\epsilon B.$$

Define $c = \epsilon B$, then

$$\int_0^t (A_{\sigma(s)} - B) ds < -ct.$$

Thus,

$$\int_0^{T_1(t)} (A_1 - B) ds + \cdots + \int_0^{T_m(t)} (A_m - B) ds < -ct,$$

and

$$\sum_{i=1}^{m} \int_0^{T_i(t)} (A_i - B) ds < -ct.$$

Hence

$$\sum_{i=1}^{m} (A_i - B) T_i(t) < -ct \tag{3.10}$$

for $t \geq h$. □

We are now ready to establish a less restrictive threshold criteria for the eradication of the disease.

Theorem 3.1.2. *If $\langle R_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease-free solution $\bar{\mathbf{Q}}$ of system (3.3) is exponentially stable in the meaningful domain Ω_{SI}.*

Proof. This proof has been adapted from one in [22]. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = -\beta_{i_k} I^2 + (\beta_{i_k} - \mu - g)I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Then, for $t \in (t_{k-1}, t_k]$,

$$I(t) \leq I(t_{k-1}) \exp[\lambda_{i_k}(t - t_{k-1})], \tag{3.11}$$

Thus, since $I \geq 0$ for all $t \geq 0$, I is bounded in the 1-norm, based on the effects of the switching rule. Apply (3.11) successively on each subinterval.

For $t \in (0, t_1]$:

$$I(t) \leq I_0 \exp[\lambda_{i_1} t], \text{ hence } I(t_1) \leq I_0 \exp\left[\lambda_{i_1} t_1\right].$$

For $t \in (t_1, t_2]$:

$$I(t) \leq I(t_1) \exp\left[\lambda_{i_2}(t - t_1)\right] \leq I_0 \exp\left[\lambda_{i_1} t_1 + \lambda_{i_2}(t - t_1)\right].$$

$\vdots$

For $t \in (t_{k-1}, t_k]$:

$$I(t) \leq I_0 \exp\left[\lambda_{i_1} t_1 + \ldots + \lambda_{i_k}(t - t_{k-1})\right], \tag{3.12}$$

$$= I_0 \exp\left[\sum_{i=1}^{m} \lambda_i T_i(t)\right]. \tag{3.13}$$

It then follows from Lemma 3.1.1 with $A_i = \beta_i$ and $B = \mu + g$ that $I(t) \leq I_0 \exp(-ct)$ for some $c > 0$ and for all $t \geq 0$. Thus, since the system is intrinsically one-dimensional with $S = 1 - I$, the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.3) is exponentially stable in the meaningful domain Ω_{SI}. □

Intuitively, it makes sense that $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ results in the eradication of the disease. During some seasons, the disease may be spreading rapidly, but on average, one infective is infecting less than one susceptible during their infectious period. The requirement that $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ instead of $\langle \mathcal{R}_\sigma \rangle < 1$ stems from the fact that there is a possible limiting case where

$$lim_{t \to \infty} \langle \mathcal{R}_\sigma \rangle = 1.$$

This is a very pathological case, it is meaningful mathematically but not biologically, and so to avoid it the ϵ requirement is added. Practically, the basic reproduction numbers will not be exactly one, and so this extra condition is not restrictive.

Further, one may ask, what if the average basic reproduction number is not below one to begin with, but is eventually below one, that is, $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for $t \geq h$, with $h \geq 0$. We should expect that the disease is still eventually eradicated, which is indeed the case.

Corollary 3.1.3. *If $\langle R_\sigma \rangle < 1 - \epsilon$ for all $t \geq h$, with constants $\epsilon > 0, h \geq 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ of system (3.3) in the meaningful domain Ω_{SI}.*

Proof. From the proof of Theorem 3.1.2, beginning with equation (3.13), we have $I(t) \leq I_0 \exp\left[\sum_{i=1}^{m} \lambda_i T_i(t)\right]$ for $t \geq h$, then, by Lemma 3.1.1, we have that $I(t) \leq I_0 \exp(-ct)$ for some $c > 0$ and $t \geq h$. Then, since $S = 1 - I$, it is apparent that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SI}. □

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. Motivated by this, suppose that, without loss of generality, $\mathcal{R}_1, \ldots, \mathcal{R}_r < 1$ and $\mathcal{R}_{r+1}, \ldots, \mathcal{R}_m \geq 1$, and define

$$\mathcal{R}^- = \max_{i=1,\ldots,r} \mathcal{R}_i, \qquad \mathcal{R}^+ = \max_{i=r+1,\ldots,m} \mathcal{R}_i. \tag{3.14}$$

Further, define $T^-(t)$ and $T^+(t)$ to be the total activation times in stable subsystems $1, \ldots r+1$, and unstable subsystems $r+1, \ldots m$, during the interval $(0, t]$, respectively. Now conditions can be given that require only knowledge of at most two reproduction numbers (one from the first set, another from the second set), that ensure exponential stability in the meaningful domain.

Theorem 3.1.4. *If $T^+(t) \leq qT^-(t)$ for some constant $q \geq 0$ then $(\mathcal{R}^- - 1) + q(\mathcal{R}^+ - 1) < 0$ implies the disease-free solution $\bar{\mathbf{Q}}$ of system (3.3) is exponentially stable in the meaningful domain Ω_{SI}.*

Proof. This proof has been adapted from one in [23]. Note that $t = T^- + T^+ \leq (1+q)T^-$. Proceed from equation (3.12), for $t \in (t_{k-1}, t_k]$:

$$\begin{aligned}
I(t) &\leq I_0 \exp\left[\lambda_{i_1} t_1 + \ldots + \lambda_{i_k}(t - t_{k-1})\right], \\
&= I_0 \exp\left[(\mu+g)((\mathcal{R}_{i_1} - 1)t_1 + \ldots + (\mathcal{R}_{i_k} - 1)(t - t_{k-1}))\right], \\
&\leq I_0 \exp\left[(\mu+g)((\mathcal{R}^- - 1)T^-(t) + (\mathcal{R}^+ - 1)T^+(t))\right], \\
&\leq I_0 \exp\left[(\mu+g)((\mathcal{R}^- - 1) + q(\mathcal{R}^+ - 1))T^-(t)\right], \\
&\leq I_0 \exp\left[(\mu+g)((\mathcal{R}^- - 1) + q(\mathcal{R}^+ - 1))\frac{t}{q+1}\right],
\end{aligned}$$

Then, since $S = 1 - I$, it follows that the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.3) is exponentially stable in the meaningful domain Ω_{SI}. □

Since it has been observed that the contact rate varies seasonally, as discussed earlier, we should consider a switching rule that is periodic, motivated by [22]. Suppose that the switching rule σ satisfies $t_k - t_{k-1} = \tau_k$ with $\tau_{k+m} = \tau_k$. Further, assume that $\mathcal{R}_i = \mathcal{R}_k$ for $t \in (t_{k-1}, t_k]$, and $\mathcal{R}_{k+m} = \mathcal{R}_k$. Finally, define one period of the switching rule $T := \tau_1 + \tau_2 + \ldots + \tau_m$. Denote the set of switching rules that satisfy this property $\mathcal{S}_{\text{periodic}} \subset \mathcal{S}$. Then, motivated by a theorem in [22], we state the following theorem.

Theorem 3.1.5. *If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1-1)\tau_1+\ldots+(\mathcal{R}_m-1)\tau_m<0$, then the disease-free solution $\bar{\mathbf{Q}}$ of system (3.3) is asymptotically stable in the domain Ω_{SI}.*

Proof. First we show convergence. It follows from equation (3.12), that for $t \in (0,T]$:

$$I(t) \leq I_0 \exp\left[\lambda_1\tau_1 + \ldots + \lambda_m(t-(T-\tau_m))\right],$$

where, from before, $\lambda_i := \beta_i - \mu - g$. From this,

$$\begin{aligned} I(T) &\leq I_0 \exp\left[\lambda_1\tau_1 + \ldots + \lambda_m\tau_m\right], \\ &= I_0 \exp\left[(\mu+g)((\mathcal{R}_1-1)\tau_1 + \ldots + (\mathcal{R}_m-1)\tau_m)\right]. \end{aligned}$$

Define $\eta := \exp\left[(\mu+g)((\mathcal{R}_1-1)\tau_1 + \ldots + (\mathcal{R}_m-1)\tau_m)\right]$. Then $I(T) \leq \eta I_0 < I_0$ since $\eta < 1$ from the conditions of the theorem. Similarly, it can be shown that $I(hT) \leq \eta I((h-1)T)$ for any integer $h = 1, 2, \ldots$, then

$$I(hT) \leq \eta I((h-1)T) \leq \eta(\eta I((h-2)T)) \leq \ldots \leq \eta^h I_0,$$

and hence the sequence $\{I(hT)\}$ converges to zero as $h \to \infty$.

Furthermore, without loss of generality, take $t \in (t_{k-1}, t_k]$, with $hT < t_k \leq (h+1)T$, then

$$I(t) \leq I(hT)\exp[\lambda_1\tau_1 + \ldots + \lambda_k(t-t_k)] \leq I(hT)e^M, \tag{3.15}$$

with $M > 0$ a constant, and since at the switching times the sequence $I(hT)$ is converging to zero, then as $k, h \to \infty$ the solution I(t) is converging to zero.

The next step is to show stability of the solution (recall definition 2.1.6). We will assume the worst case scenario for growth of the disease in a periodic scenario, where the disease spreads the most during the first r intervals. More specifically, suppose that, $\mathcal{R}_1, \ldots, \mathcal{R}_r \geq 1$ and $\mathcal{R}_{r+1}, \ldots, \mathcal{R}_m < 1$. Then, $\lambda_1, \ldots, \lambda_r \geq 0$ and $\lambda_{r+1}, \ldots, \lambda_m < 0$. It follows that, during the interval $(0,T]$, the maximum value I can attain is

$$I_{\max} = I_0 e^{\lambda_1\tau_1 + \ldots + \lambda_r\tau_r} := I_0 B.$$

For any $\epsilon > 0$, choose $\delta = \epsilon/B$ and suppose that $I_0 < \delta$, then it follows that in the interval $(0,T]$, $I(t) \leq I_{\max} = I_0 B < \delta B = \epsilon$. This can be generalized easily to any interval $(t_{k-1}, t_k]$, with $hT < t_k \leq (h+1)T$, $h = 1, 2, \ldots$, since on this interval, $I(t) \leq I(hT)B < I_0 B < \delta B = \epsilon$. Hence, the solution is also stable. Therefore, since $S = 1 - I$ and the system is intrinsically one-dimensional, the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.3) is asymptotically stable in the meaningful domain Ω_{SI}. □

Finally, in the scenario that the reproduction numbers are greater than one, which is an important realistic case, the permanence and persistence (see definition 2.2.2 and definition 2.2.1) of the disease should be investigated.

Theorem 3.1.6. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$ then the solution of system (3.3) will converge to the convex hull of the set of endemic points $\Gamma = \{Q_1^*, \ldots, Q_m^*\}$, that is, the disease will be permanent.*

Proof. Recall the endemic equilibrium points $I_i^* = 1 - 1/\mathcal{R}_i$. The convex hull is $co(\Gamma) = \{(S, I) \in \mathbb{R}_+^2 |\ I_{\min}^* \leq I \leq I_{\max}^*, S = 1 - I\}$, where $I_{\min}^* = 1 - 1/\mathcal{R}_{\min}$ and $I_{\max}^* = 1 - 1/\mathcal{R}_{\max}$ are, respectively, the minimum and maximum endemic equilibrium points. Rewrite the equation for I as $\dot{I} = (\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2$. First show this set is positively invariant when $\mathcal{R}_i > 1$ for all i. For any i, at $I = I_{\min}^*$:

$$\begin{aligned}
\dot{I} &= (\mu + g)(\mathcal{R}_i - 1)I_{\min}^* - \beta_i (I_{\min}^*)^2, \\
&= (\mu + g)I_{\min}^* \left[(\mathcal{R}_i - 1) - \mathcal{R}_i I_{\min}^*\right], \\
&= (\mu + g)I_{\min}^* \left[\frac{\mathcal{R}_i}{\mathcal{R}_{\min}} - 1\right] \geq 0.
\end{aligned}$$

For any i, at $I = I_{\max}^*$:

$$\begin{aligned}
\dot{I} &= (\mu + g)(\mathcal{R}_i - 1)I_{\max}^* - \beta_i (I_{\max}^*)^2, \\
&= (\mu + g)I_{\max}^* \left[(\mathcal{R}_i - 1) - \mathcal{R}_i I_{\max}^*\right], \\
&= (\mu + g)I_{\max}^* \left[\frac{\mathcal{R}_i}{\mathcal{R}_{\max}} - 1\right] \leq 0.
\end{aligned}$$

Since $S = 1 - I$, $co(\Gamma)$ is positively invariant. Thus, if $I_0 \in co(\Gamma)$ then $I(t) \in co(\Gamma)$ for all $t \geq 0$, regardless of the switching rule. Now consider $0 < I < I_{\min}^*$ (recall the initial condition is $I_0 > 0$, and so $I = 0$ is not considered), then for any i,

$$\dot{I} = (\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I \left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right) > \beta_i I \left(\frac{1}{\mathcal{R}_{\min}} - \frac{1}{\mathcal{R}_i}\right) \geq 0,$$

until possibly $I = I_{\min}^*$ and at this point I enters $co(\Gamma)$. It is also possible, based on a switching rule such as $\sigma(t) \equiv \text{argmin}_i\, \beta_i$ for all $t \geq 0$, that the solution will asymptotically converge to $co(\Gamma)$. Similarly, for $I_{\max}^* < I \leq 1$,

$$\dot{I} = (\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I \left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right) < \beta_i I \left(\frac{1}{\mathcal{R}_{\max}} - \frac{1}{\mathcal{R}_i}\right) \leq 0,$$

until possibly $I = I_{\max}^*$, where I enters $co(\Gamma)$. As before, it is also possible to asymptotically approach it. Thus, the solution converges to the convex hull of the set Γ.

□

Recall the definition for persistence (2.2.1).

Conjecture 3.1.7. *If $\langle \mathcal{R}_\sigma \rangle > 1$ for all $t \geq h$, with $h \geq 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease of system (3.3) will be persistent.*

Recall that in the non-switching disease models (see Section 2.2), it is easy to analyze the endemic solution because it is a single equilibrium. Here, the solution will move between the m different endemic equilibriums based on the switching signal. Though the dynamics might be complicated, the disease will be permanent and the solution will converge to the convex hull of Ω_{SI}. See the simulations in Section 3.5 for illustrations.

3.2 Switched SIS Model with Vertical Transmission

A complication to the SIS model is to consider both horizontal and vertical transmission. Recall that vertical transmission is the direct transmission of communicable diseases by an infected mother to her newborn or unborn child, transplacentally [33]. Examples of human diseases that transmit both horizontally and vertically are rubella, hepatitis and AIDS [57]. 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 [27]. 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 I through birth and the remaining births from infected mothers which are not infected, $\mu\rho I$, enters the S class as normal. The switched SIS model with vertical transmission then is,

$$\begin{cases} \dot{S} = \mu(S+\rho I) - \beta_i SI - \mu S + gI, \\ \dot{I} = \mu(1-\rho)I + \beta_i SI - gI - \mu I. \end{cases} \tag{3.16}$$

with $i \in \{1, \ldots, m\}$ according to a switching rule σ and the variables have been normalized, as before, since the total population is constant. As before, the meaningful domain is Ω_{SI}, and the initial conditions considered are $S(0) = S_0 > 0$, $I_0 = I(0) > 0$. Notice that $\{\dot{S}+\dot{I}\}\,|_{S+I=1} = 0$, $\dot{S}\,|_{S=0} = \mu\rho + g > 0$ and $\dot{I}\,|_{I=0} = 0$, hence the domain is invariant to each subsystem. In the limit $\rho = 1$, the model becomes the SIS model (3.3), and in the limit $\rho = 0$, all infectives give birth to infected babies. For each subsystem, use the modified basic reproduction numbers from the non-switched case (for example, found in [48]):

$$\mathcal{R}_i = \frac{\beta_i}{\rho\mu + g}. \tag{3.17}$$

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 (3.4). This makes sense biologically, as there are now infected individuals being recruited through birth. There is a single

disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}) = (1, 0)$ that is common to all subsystems and each subsystem also has an endemic equilibrium

$$\mathbf{Q_i^*} = (S_i^*, I_i^*) = \left(\frac{1}{\mathcal{R}_i}, 1 - \frac{1}{\mathcal{R}_i}\right), \tag{3.18}$$

which exists in the meaningful domain if $\mathcal{R}_i \geq 1$. Again, since $S+I = 1$, the system is intrinsically one-dimensional. In the case that $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$, then $I' < 0$ in the domain Ω_{SI} for $I \neq 0$, and since $S + I = 1$, the disease-free equilibrium $\bar{\mathbf{Q}}$ is asymptotically stable in the meaningful domain Ω_{SI}.

Theorem 3.2.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.16) is exponentially stable in the domain Ω_{SI}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the disease-free equilibrium $\bar{\mathbf{Q}}$ is asymptotically stable in the domain Ω_{SI}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$, then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - gI - \rho\mu I \leq (\beta_{i_k} - \rho\mu - g)I = \lambda_{i_k} I, \tag{3.19}$$

where $\lambda_{i_k} := \beta_{i_k} - \rho\mu - g$. Then, since $S + I = 1$, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), and using Lemma (3.1.1) with $A_i = \beta_i$ and $B = \rho\mu + g$, that the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.16) is exponentially stable in the meaningful domain Ω_{SI}. If the switching rule is periodic then the proof follows from inequality (3.19) and the proof of Theorem 3.1.5. □

Again, it is important to outline the permanence of the disease in the case that the basic reproduction numbers are large.

Theorem 3.2.2. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$ then the solution of system (3.16) will converge to the convex hull of the set of endemic points $\Gamma = \{Q_1^*, \ldots, Q_m^*\}$, that is, the disease will be permanent.*

Proof. Recall the endemic equilibrium points $I_i^* = 1 - 1/\mathcal{R}_i$. The convex hull is $co(\Gamma) = \{(S, I) \in \mathbb{R}_+^2 |\ I_{\min}^* \leq I \leq I_{\max}^*, S = 1 - I\}$, where $I_{\min}^* = 1 - 1/\mathcal{R}_{\min}$ and $I_{\max}^* = 1 - 1/\mathcal{R}_{\max}$ are, respectively, the minimum and maximum endemic equilibrium points. Rewrite the equation for I as $\dot{I} = (\rho\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2$. First show this set is positively invariant when $\mathcal{R}_i > 1$ for all i. For any i, at $I = I_{\min}^*$:

$$\begin{aligned}
\dot{I} &= (\rho\mu + g)(\mathcal{R}_i - 1)I_{\min}^* - \beta_i (I_{\min}^*)^2, \\
&= (\rho\mu + g)I_{\min}^* \left[(\mathcal{R}_i - 1) - \mathcal{R}_i I_{\min}^*\right], \\
&= (\rho\mu + g)I_{\min}^* \left[\frac{\mathcal{R}_i}{\mathcal{R}_{\min}} - 1\right] \geq 0.
\end{aligned}$$

For any i, at $I = I^*_{\max}$:

$$\begin{aligned}\dot{I} &= (\rho\mu + g)(\mathcal{R}_i - 1)I^*_{\max} - \beta_i (I^*_{\max})^2, \\ &= (\rho\mu + g)I^*_{\max}\left[(\mathcal{R}_i - 1) - \mathcal{R}_i I^*_{\max}\right], \\ &= (\rho\mu + g)I^*_{\max}\left[\frac{\mathcal{R}_i}{\mathcal{R}_{\max}} - 1\right] \leq 0.\end{aligned}$$

Since $S = 1 - I$, $co(\Gamma)$ is positively invariant. Thus, if $I_0 \in co(\Gamma)$ then $I(t) \in co(\Gamma)$ for all $t \geq 0$, regardless of the switching rule. Now consider $0 < I < I^*_{\min}$, then for any i,

$$\dot{I} = (\rho\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I\left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right) > \beta_i I\left(\frac{1}{\mathcal{R}_{\min}} - \frac{1}{\mathcal{R}_i}\right) \geq 0,$$

until possibly $I = I^*_{\min}$ and at this point I enters or asymptotically approaches $co(\Gamma)$. Similarly, for $I^*_{\max} < I \leq 1$,

$$\dot{I} = (\rho\mu + g)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I\left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right)\beta_i I\left(\frac{1}{\mathcal{R}_{\max}} - \frac{1}{\mathcal{R}_i}\right) \leq 0,$$

until possibly $I = I^*_{\max}$, where I enters $co(\Gamma)$. It is also possible to asymptotically approach $co(\Gamma)$ based on the switching rule. Thus, the solution converges to the convex hull of the set Γ. □

3.3 Switched SIS Model with Varying Population Size

It is commonly postulated in mathematical epidemiology that the births and deaths are equal, and hence balance each other [35]. However, for many acute infectious diseases, such as measles, chickenpox, and pertussis, the susceptible class is mainly composed of young people whose rate of natural mortality does not necessarily coincide with that of the population as a whole [33]. In developed countries, due to relatively low child mortality, the natural mortality rate is considerably lower than the birth rate and can be neglected [33], whereas for developing countries, where child mortality is commonly high, the mortality rate may exceed the birth rate [35]. Indeed, as discussed in Section 2.2, there have been many real-world examples where infectious diseases have resulted in the population size not being even approximately constant [27]. Therefore, it is desired to investigate the case where the birth rate $b > 0$ is not necessarily equal to the natural death rate $d > 0$. Two different population demographic structures will be investigated here.

For the first model, assume a simple birth-death demographic structure for the total population N based on the differential equation $N' = (b - d)N$, 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 one year [27]. This leads to models without population dynamics, such as the classical epidemic model (2.12) 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, that is, births $b = \mu > 0$ and natural deaths $d = \mu > 0$. If $b - d \neq 0$, then the population is exponentially growing or decaying. Then, the model is, with switching,

$$\begin{cases} \dot{S}_c = bN - \dfrac{\beta_i S_c I_c}{N} + gI_c - dS_c, \\ \dot{I}_c = \dfrac{\beta_i S_c I_c}{N} - gI_c - dI_c, \end{cases} \tag{3.20}$$

where S_c, I_c are the actual number of infected and susceptible individuals, and the total population is $N = S_c + I_c$, which is not necessarily constant and satisfies the differential equation $N' = (b - d)N$. Normalize the equations using $I = I_c/N$ and $S = S_c/N$. Then $S + I = 1$, and

$$S' = \frac{S_c'}{N} - S\frac{N'}{N}, \qquad I' = \frac{I_c'}{N} - I\frac{N'}{N},$$

hence, the model becomes,

$$\begin{cases} \dot{S} = b - \beta_i SI + gI - bS, \\ \dot{I} = \beta_i SI - gI - bI, \end{cases} \tag{3.21}$$

with $i \in \{1, \dots, m\}$ and initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$ in the meaningful domain Ω_{SI}. The domain is invariant to each subsystem, since $\{\dot{S} + \dot{I}\}\,|_{S+I=1} = 0$, $\dot{S}\,|_{S=0} = b + g > 0$, and $\dot{I}\,|_{I=0} = 0$. Define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i}{b + g}. \tag{3.22}$$

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}) = (1, 0)$ that is common to all subsystems. Each subsystem also has an endemic equilibrium

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*) = \left(\frac{1}{\mathcal{R}_i}, 1 - \frac{1}{\mathcal{R}_i}\right). \tag{3.23}$$

Again, since $S + I = 1$, the system is intrinsically one-dimensional. In the case that $\mathcal{R}_1, \dots, \mathcal{R}_m \leq 1$ then $I' < 0$ in Ω_{SI} for $I \neq 0$, hence the disease-free equilibrium $\bar{\mathbf{Q}}$ is asymptotically stable in the meaningful domain Ω_{SI}. Notice that system (3.21) is identitcal to the switched SIS model (3.3) if b is replaced with μ. Then, the theorems in Section 3.1 apply to this system, with an important caveat, that is, the theorems will guarantee that the fraction I converges to zero, but it does not necessarily mean the total infected individuals, $I_c = I/N$, will converge to zero since the population is now non-constant, and possibly growing without bound. From $I_c = IN$, $S_c = SN$, then if $b - d = 0$ it follows that the population

N is constant, and hence I_c will converge to zero if I converges to zero. In the case that $b - d < 0$, then the total population N will exponentially converge to zero, and so I converging to zero certainly implies that I_c will converge to zero. In the final case, that is, when $b - d > 0$, then the population is growing exponentially. In this case, since $S \to 1$ as $t \to \infty$, it is apparent that $S_c \to N$ and hence $I_c \to 0$, since $N = S_c + I_c$.

The constraint $b = d = \mu$, which is often used in this thesis, might seem too restrictive based on the introductory discussions of this section. Certainly, since births and deaths occur independently in real populations [33], this might seem to be a very poor approximation, but this assumption is justified by the fact that for many infectious dieases the processes occur on a considerably shorter time-scale than the populational demographic process (perhaps HIV is the only exception among human diseases) [33].

In the case of infectious diseases such as AIDS, one should modify the constant population assumption to incorporate disease-related deaths [40]. Disease-related deaths and persistence of a disease can actually reverse a naturally growing population into a stable or decaying population [27]. Assume the birth rate $b > 0$ is different from the death rate $d > 0$. Assume that there is also a disease-induced mortality rate $\alpha > 0$, then the population satisfies $N' = (b-d)N - \alpha I_c$. This leads to the switched model,

$$\begin{cases} \dot{S}_c = bN - \dfrac{\beta_i S_c I_c}{N} - dS_c + gI_c, \\ \dot{I}_c = \dfrac{\beta_i S_c I_c}{N} - gI_c - dI_c - \alpha I_c, \end{cases} \tag{3.24}$$

where S_c, I_c are the number of infected and susceptible individuals, and $N = S_c + I_c$. Normalize the equations using $I = I_c/N$ and $S = S_c/N$. This leads to

$$\begin{cases} \dot{S} = b - \beta_i SI - bS + gI + \alpha SI, \\ \dot{I} = \beta_i SI - gI - bI - \alpha I + \alpha I^2, \end{cases} \tag{3.25}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I_0 = I(0) > 0$, and meaningful physical domain Ω_{SI}. The domain invariance follows from $\{\dot{S}+\dot{I}\}\,|_{S+I=1} = 0$, $\dot{S}\,|_{S=0} = b + g > 0$, and $\dot{I}\,|_{I=0} = 0$. The αSI and αI^2 terms are nonlinear positive feedbacks induced by α. At any time that individuals die from the disease, the population size decreases and hence the fraction of individuals in each class increases [49]. Define the basic reproduction numbers,

$$\mathcal{R}_i = \frac{\beta_i}{b + g + \alpha}. \tag{3.26}$$

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}) = (1, 0)$ that is common to all subsystems. Each subsystem also has an endemic equilibrium

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*) = \left(\frac{b+g}{\beta_i - \alpha}, \frac{b+g+\alpha}{\beta_i - \alpha}(\mathcal{R}_i - 1) \right). \tag{3.27}$$

Notice that the endemic solution is only in the meaningful domain when $\mathcal{R}_i \geq 1$. Again, since $S + I = 1$, the system is intrinsically one-dimensional.

Theorem 3.3.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$ then the disease-free solution $\bar{\mathbf{Q}}$ of system (3.25) is locally exponentially stable in the meaningful domain Ω_{SI}.*

Proof. Linearize the system (3.25) about the disease-free equilibrium $\bar{\mathbf{Q}} = (1, 0)$:

$$\begin{cases} \dot{S} = -\beta_i I - bS + gI + \alpha I, \\ \dot{I} = \beta_i I - gI - bI - \alpha I. \end{cases} \tag{3.28}$$

Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$, then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = (\beta_{i_k} - g - b - \alpha)I = \lambda_{i_k} I, \tag{3.29}$$

where $\lambda_{i_k} := \beta_{i_k} - g - b - \alpha$. Thus, following the proof of Theorem 3.1.2, beginning at equation (3.11), and using $S = 1 - I$ the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.25) is locally exponentially stable in the domain Ω_{SI}. □

Notice that in this theorem, the criteria using the basic reproduction number (3.26) only give local results. Unfortunately, it is only possible to conject that if $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$, the solution will converge to the disease-free solution in the entire meaningful domain Ω_{SI}. If we consider the non-physical basic reproduction numbers

$$\mathcal{R}_i^{non} = \frac{\beta_i}{\mu + g}$$

instead, we will get the desired results globally in the domain Ω_{SI} (see Theorem 3.3.2). These reproduction numbers do not contain the disease-induced death rate α and hence it is not being used in expressing how fast or slow the disease will spread. The disease-induced death should actually help to eradicate the disease and thus it should be used in the threshold criteria. Hence, these reproduction numbers may not adequately describe how the disease spreads, from a biological viewpoint; they may be too strict. Whenever this is the case, the notation $\mathcal{R}_i^{non}$ will be used, with the superscript *non* signifying possible non-physical basic reproduction numbers. In this case, using these non-physical reproduction number leads to global results but at the cost of stricter criteria.

Theorem 3.3.2. *If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and $\sigma \in \mathcal{S}$, then the disease-free solution $\bar{\mathbf{Q}}$ of system (3.25) is exponentially stable in the meaningful domain Ω_{SI}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_i SI - gI - bI - \alpha I + \alpha I^2 \leq (\beta_{i_k} - b - g)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - g - b$. Thus, following the proof of Theorem 3.1.2, beginning at equation (3.11), and using $S = 1 - I$, the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (3.25) is exponentially stable in domain Ω_{SI}. □

Theorems 3.3.1 and 3.3.2 establish that the fractions of infected individuals in the population $I \to 0$ as $t \to \infty$, but again, since the population is non-constant, this does not necessarily imply that the actual number of infected individuals, I_c, go to zero. Recall that the infected fraction is $I = I_c/N$, and hence $I_c = IN$, but if $I \to 0$ and $N \to \infty$ it is not immediately clear what will happen to the actual infected number of individuals. We must again look at the different cases.

Recall the equation for the population dynamics, $N' = (b-d)N - \alpha I_c = (b - d - \alpha I)N$. Then, if $b < d$, it is clear that the total population is going to zero, and hence $I \to 0$ implies $I_c \to 0$. If $b = d$, then $N' = -\alpha IN \leq 0$, and hence the total population should approach a constant since $I \to 0$, and hence $I_c \to 0$. Finally, if $b > d$, then the total population will grow without bound since $I \to 0$. In this case, since $S \to 1$ use $S_c = SN$ to get $S_c \to N$ and then $N = S_c + I_c$ implies $I_c \to 0$.

Theorem 3.3.3. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$ then the solution of system (3.25) will converge to the convex hull of the set of endemic points $\Gamma = \{Q_1^*, \ldots, Q_m^*\}$, that is, the disease will be permanent.*

Proof. The endemic equilibrium points can be written as $I_i^* = (\beta_i - g - b - \alpha)/(\beta_i - \alpha)$. The convex hull is $co(\Gamma) = \{(S, I) \in \mathbb{R}^2_+ |\ I^*_{\min} \leq I \leq I^*_{\max}, S = 1 - I\}$, where

$$I^*_{\min} = \frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha}, \qquad I^*_{\max} = \frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha}$$

are, respectively, the minimum and maximum endemic equilibrium points. Rewrite the equation for I as $\dot{I} = (\beta_i - g - b - \alpha)I - (\beta_i - \alpha)I^2$. First show this set is positively invariant when $\mathcal{R}_i > 1$ for all i. For any i, at $I = I^*_{\min}$:

$$\begin{aligned}
\dot{I} &= (\beta_i - g - b - \alpha)I^*_{\min} - (\beta_i - \alpha)(I^*_{\min})^2, \\
&= I^*_{\min}\left(\beta_i - g - b - \alpha - (\beta_i - \alpha)\frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha}\right), \\
&= (\beta_i - \alpha)I^*_{\min}\left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - \frac{\beta_{\min} - g - b - \alpha}{\beta_{\min} - \alpha}\right] \geq 0.
\end{aligned}$$

For any i, at $I = I^*_{\max}$:

$$\begin{aligned}
\dot{I} &= (\beta_i - g - b - \alpha)I^*_{\max} - (\beta_i - \alpha)(I^*_{\max})^2, \\
&= I^*_{\max}\left(\beta_i - g - b - \alpha - (\beta_i - \alpha)\frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha}\right), \\
&= (\beta_i - \alpha)I^*_{\max}\left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - \frac{\beta_{\max} - g - b - \alpha}{\beta_{\max} - \alpha}\right] \leq 0.
\end{aligned}$$

Since $S = 1 - I$, $co(\Gamma)$ is positively invariant. Thus, if $I_0 \in co(\Gamma)$ then $I(t) \in co(\Gamma)$ for all $t \geq 0$, regardless of the switching rule. Now consider $0 < I < I^*_{\min}$, then for any i,

$$\dot{I} = (\beta_i - g - b - \alpha)I - (\beta_i - \alpha)I^2 = I(\beta_i - \alpha)\left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - I\right] > 0,$$

until possibly $I = I^*_{\min}$ and at this point I enters $co(\Gamma)$. It is also possible, based on a switching rule such as $\sigma(t) \equiv \text{argmin}_i\, \beta_i$ for all $t \geq t_0$, that the solution will asymptotically converge to $co(\Gamma)$. Similarly, for $I^*_{\max} < I \leq 1$,

$$\dot{I} = (\beta_i - g - b - \alpha)I - (\beta_i - \alpha)I^2 = I(\beta_i - \alpha)\left[\frac{\beta_i - g - b - \alpha}{\beta_i - \alpha} - I\right] < 0,$$

until possibly $I = I^*_{\max}$, where I enters $co(\Gamma)$. As before, it is also possible to asymptotically approach it. Thus, the solution converges to the convex hull of the set Γ. □

3.4 Switching the Contact Rate, Removal Rate and Birth Rate in the SIS Model

There are other seasonal variations in these models that can be considered, aside from the contact rate. For example, fluctuations in birth rates is another possibility [49]. The switched systems approach does not require these variations to be seasonal or periodic, so we could also consider the case where the infectious period of a disease could decrease steadily over a long period of time, due to advancements in medicine. Motivated by this, suppose that the contact rate can take on values from $\beta_1, \ldots, \beta_m > 0$, the birth rate (assumed to be equal to the death rate) can take on values $\mu_1, \ldots, \mu_j > 0$ and the removal rate is approximated by the constants $g_1, \ldots, g_l > 0$, then the switched SIS model is

$$\begin{cases} \dot{S} = \mu_i - \beta_i SI - \mu_i S + g_i I, \\ \dot{I} = \beta_i SI - g_i I - \mu_i I, \end{cases} \tag{3.30}$$

with $i \in \{1, \ldots, h\}$ where $h = m \cdot j \cdot l$, and the variables have been normalized under the assumption of a constant population. The initial conditions are $S(0) = S_0 > 0$, $I(0) = I_0 > 0$. Here $\{\dot{S} + \dot{I}\}\,|_{S+I=1} = 0$, $\dot{S}\,|_{S=0} = \mu_i + g_i > 0$, and $\dot{I}\,|_{I=0} = 0$. And so, Ω_{SI} is invariant to each subsystem. Define the basic reproduction number

$$\mathcal{R}_i = \frac{\beta_i}{\mu_i + g_i}. \tag{3.31}$$

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}) = (1, 0)$ that is common to all subsystems. Each subsystem also has an endemic equilibrium

$$\mathbf{Q}^*_\mathbf{i} = (S^*_i, I^*_i) = \left(\frac{1}{\mathcal{R}_i}, 1 - \frac{1}{\mathcal{R}_i}\right), \tag{3.32}$$

which exist in the meaningful domain if $\mathcal{R}_i \geq 1$. Since $S + I = 1$, the system is intrinsically one-dimensional. Observe from (3.30), that if $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$, then it is apparent, from the system (3.3), that $I' < 0$ in Ω_{SI} for $I \neq 0$. Therefore, since $S + I = 1$, the disease-free solution $\bar{\mathbf{Q}}$ is asymptotically stable in the meaningful domain

Ω_{SI}. A less restrictive condition is again desired, such that some reproduction numbers are greater than one. Recall that $T_i(t)$ is defined as the total activation time in subsystem i during the interval $(0, t]$.

Theorem 3.4.1. *If $\sum_{i=1}^{h}(\beta_i - \mu_i - g_i)T_i(t) \leq -ct$ for all $t \geq 0$, with constant $c > 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease-free solution $\bar{\mathbf{Q}}$ of system (3.30) is exponentially stable in the meaningful domain Ω_{SI}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - g_{i_k} I - \mu_{i_k} I \leq (\beta_{i_k} - \mu_{i_k} - g_{i_k})I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - \mu_{i_k} - g_{i_k}$. Then, for $t \in (t_{k-1}, t_k]$, from (3.13)

$$I(t) \leq I(t_{k-1}) \exp[\lambda_{i_k}(t - t_{k-1})], \tag{3.33}$$

Thus, since $I \geq 0$ for all $t \geq 0$, I is bounded in the 1-norm, based on the effects of the switching rule. Then, from the proof of Theorem 3.1.2, applying (3.33) successively on intervals, it follows that for $t \in (t_{k-1}, t_k]$:

$$\begin{aligned} I(t) &\leq I_0 \exp\left[\lambda_{i_1} t_1 + \ldots + \lambda_{i_k}(t - t_{k-1})\right], \\ &= I_0 \exp\left[\sum_{i=1}^{m} \lambda_i T_i(t)\right], \end{aligned}$$

Hence $I(t) \leq I_0 \exp(-ct)$ for all $t \geq 0$. Thus, since $S = 1 - I$, the disease-free solution $\bar{\mathbf{Q}}$ of system (3.30) is exponentially stable in the meaningful domain Ω_{SI}. □

Theorem 3.4.2. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$ then the solution of system (3.30) will converge to the convex hull of the set of endemic points $\Gamma = \{Q_1^*, \ldots, Q_m^*\}$, that is, the disease will be persistent.*

Proof. Recall the endemic equilibrium points are $I_i^* = 1 - 1/\mathcal{R}_i$. The convex hull is $co(\Gamma) = \{(S, I) \in \mathbb{R}_+^2 |\ I_{\min}^* \leq I \leq I_{\max}^*, S = 1 - I\}$, where $I_{\min}^* = 1 - 1/\mathcal{R}_{\min}$, and $I_{\max}^* = 1 - 1/\mathcal{R}_{\max}$ are, respectively, the minimum and maximum endemic equilibrium points. Rewrite the equation for I as $\dot{I} = (\mu_i + g_i)(\mathcal{R}_i - 1)I - \beta_i I^2$. First show this set is positively invariant when $\mathcal{R}_i > 1$ for all i. For any i, at $I = I_{\min}^*$:

$$\begin{aligned} \dot{I} &= (\mu_i + g_i)(\mathcal{R}_i - 1)I_{\min}^* - \beta_i (I_{\min}^*)^2, \\ &= (\mu_i + g_i) I_{\min}^* \left[(\mathcal{R}_i - 1) - \mathcal{R}_i I_{\min}^*\right], \\ &= (\mu_i + g_i) I_{\min}^* \left[\frac{\mathcal{R}_i}{\mathcal{R}_{\min}} - 1\right] \geq 0. \end{aligned}$$

For any i, at $I = I^*_{\max}$:

$$\begin{aligned}\dot{I} &= (\mu_i + g_i)(\mathcal{R}_i - 1)I^*_{\max} - \beta_i (I^*_{\max})^2, \\ &= (\mu_i + g_i)I^*_{\max}\left[(\mathcal{R}_i - 1) - \mathcal{R}_i I^*_{\max}\right], \\ &= (\mu_i + g_i)I^*_{\max}\left[\frac{\mathcal{R}_i}{\mathcal{R}_{\max}} - 1\right] \leq 0.\end{aligned}$$

Since $S = 1 - I$, $co(\Omega_{SI})$ is positively invariant. Thus, if $I_0 \in co(\Omega_{SI})$ then $I(t) \in co(\Omega_{SI})$ for all $t \geq 0$, regardless of the switching rule. Now consider $0 < I < I^*_{\min}$, then for any i,

$$\dot{I} = (\mu_i + g_i)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I\left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right) > \beta_i I\left(\frac{1}{\mathcal{R}_{\min}} - \frac{1}{\mathcal{R}_i}\right) \geq 0,$$

until possibly $I = I^*_{\min}$ and at this point I enters $co(\Gamma)$. Hence the solution enters or asymptotically converges to $co(\Gamma)$. Similarly, for $I^*_{\max} < I \leq 1$,

$$\dot{I} = (\mu_i + g_i)(\mathcal{R}_i - 1)I - \beta_i I^2 = \beta_i I\left(\frac{\mathcal{R}_i - 1}{\mathcal{R}_i} - I\right) < \beta_i I\left(\frac{1}{\mathcal{R}_{\max}} - \frac{1}{\mathcal{R}_i}\right) \leq 0,$$

until possibly $I = I^*_{\max}$, where I enters $co(\Gamma)$. As before, it is also possible to asymptotically approach it. Thus, the solution converges to the convex hull of the set Γ. □

3.5 Simulations

The simulations in Chapters 3-6 of this thesis were done in MATLAB© using a built-in ODE solver, for example, as is done in [1]. That is, an ODE-solver was used on whichever subsystem was currently active to numerically solve the ODE system. For the simulations here, take $t_0 = 0$, $S_0 = 0.75$, $I_0 = 0.25$ and $i \in \{1, 2\}$. For the switching signal use

$$\sigma(t) = \begin{cases} 1 & \text{during winter,} \\ 2 & \text{otherwise.} \end{cases} \tag{3.34}$$

Recall that the variables have been normalized so that $S + I = 1$. The constants $\mu = 0.07$ and $g = 0.3$ are used here, taken from [48]. The simulations are in non-dimensional units.

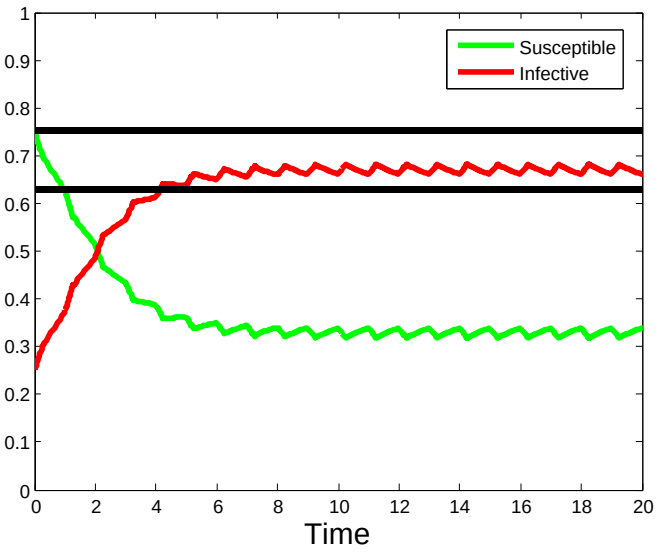

Figure 3.1: **Switched SIS System (3.3).** Simulation with $\beta_1 = 1.5$ and hence $\mathcal{R}_1 = 4.054$ during the winter season and $\beta_2 = 1$ and hence $\mathcal{R}_2 = 3.041$ during the other seasons, hence $\langle \mathcal{R}_\sigma \rangle = 3.041$ for t large. Here we see that the solution I converges to the convex hull of the two endemic equilibriums $I = 0.630$ and $I = 0.753$, marked by the black lines. This follows from Theorem 3.1.6. The effects from seasonal changes in the contact rate are apparent from the jagged trajectories.

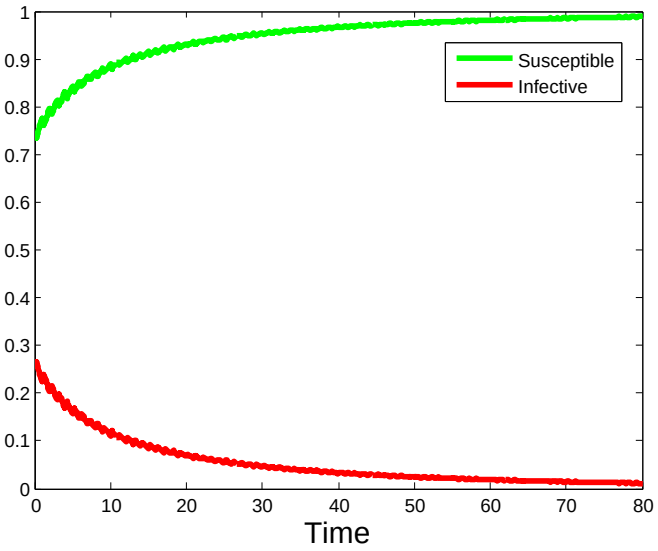

Figure 3.2: **Switched SIS System (3.3)** Simulation with $\beta_1 = 0.8$ (and hence $\mathcal{R}_1 = 2.162$) during the winter season and $\beta_2 = 0.2$ (and hence $\mathcal{R}_2 = 0.5$) during the other seasons, hence $\langle \mathcal{R}_\sigma \rangle = 0.946$ for t large. We see the solution converges to the disease-free equilibrium, following from Theorem 3.1.5.

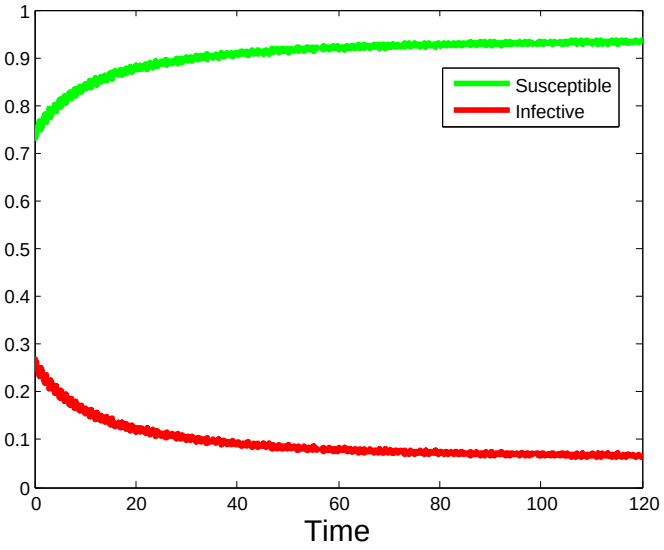

Figure 3.3: **Switched SIS System with Vertical Transmission (3.16).** Simulation with $\beta_1 = 0.8$, $\beta_2 = 0.2$, $\rho = 0.4$, which give $\mathcal{R}_1 = 2.439$ and $\mathcal{R}_2 = 0.610$, and hence $\langle \mathcal{R}_\sigma \rangle = 1.067$ for t large. Here we see that the disease is persistent. Notice that if $\rho = 0$ then the disease dies out (see Figure 3.2), hence, the addition of vertical transmission results in the persistence of the disease.

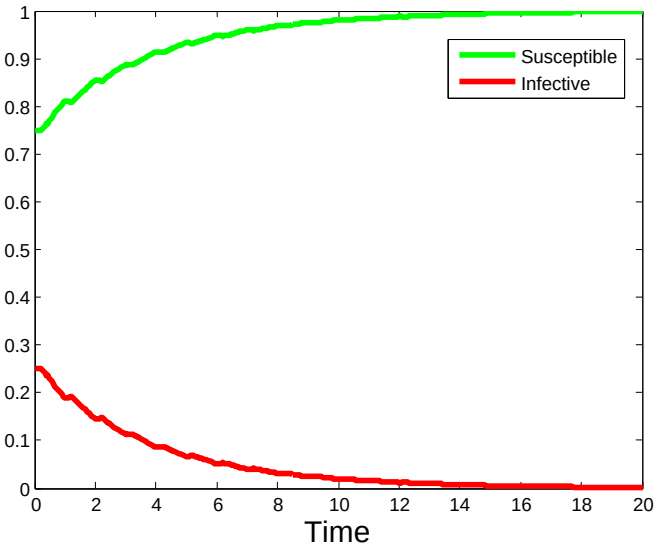

Figure 3.4: **Switched SIS System with Disease-Induced Mortality (3.25).** Parameters $b = 0.07$, $d = 0.01$, $\alpha = 1$, $\beta_1 = 1.5$, $\beta_2 = 1$. Hence, $\mathcal{R}_1 = 1.095$ and $\mathcal{R}_2 = 0.730$, then $\langle \mathcal{R}_\sigma \rangle = 0.821$ for t large. The solution converges to the disease-free solution, which is ensured, at least locally, by Theorem 3.3.1. Notice that if $\alpha = 0$ and we take $b = d = \mu = 0.07$ then $\langle \mathcal{R}_\sigma \rangle = 3.041$ for t large, as in Figure 3.1. It is apparent that the disease-induced mortality helps in achieving the eradication of the disease.

Chapter 4

Multi-Dimensional Switched Epidemiological Models

In this chapter, switching will be introduced in infectious disease models that cannot be reduced to one dimension. That is, they are intrinsically at least two dimensional. Switching will be incorporated into these models in the same way as Chapter 3; the contact rate will be assumed to vary in time as a piecewise constant. First, a switched SIR model with population dynamics will be considered in Section 4.1. In Section 4.2, a switched SIR model is considered without population dynamics. In Section 4.3, a switched SIR model with vertical transmission is considered. Sections 4.4 and 4.5 will study switched SIRS and MSIR models. Section 4.6 investigates switched models where the incubating period is not negligible, that is, SEIR models. Switched SIR models with different population demographic structures, such that the total population is non-constant, are considered in Section 4.7. Finally, some interesting switched transport models are considered in Section 4.8, where transport between multiple cities is possible. The endemicity of diseases for these multi-dimensional models are discussed briefly in Section 4.9. Simulations are given in Section 4.10.

4.1 Switching the Contact Rate in the SIR Model

Introduce switching into the SIR model with population dynamics (2.16) by assuming the contact rate, β, is a parameter which varies over time. Assume there are m different contact rates $\beta_1, \ldots, \beta_m > 0$ with which to approximate β as a piecewise constant parameter. Consider a switching rule $\sigma = \sigma(t) : \mathbb{R}_+ \to \{1, 2, \ldots, m\}$, and denote the set of all such switching rules is $\mathcal{S}$. This leads to the following new switched SIR model:

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S, \\ \dot{I} = \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{4.1}$$

with $i \in \{1, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0, R(0) = R_0$, and the variables have been normalized, i.e. $S + I + R = 1$, since the population is constant. The meaningful physical domain for this system is

$$\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S + I + R = 1\}.$$

Notice that

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

hence this domain is invariant to the switched system. For this model, define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i}{\mu + g}, \tag{4.2}$$

for each subsystem, from the non-switched case (2.17). These reproduction numbers are the same as for the switched SIS model (3.3), this is because in both models the disease spreads biologically at the same rate. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\mathbf{Q}^*_\mathbf{i} = (S^*_i, I^*_i, R^*_i) = \left(\frac{1}{\mathcal{R}_i}, \frac{\mu}{\mu + g}\left(1 - \frac{1}{\mathcal{R}_i}\right), \frac{g}{\mu + g}\left(1 - \frac{1}{\mathcal{R}_i}\right)\right). \tag{4.3}$$

An endemic equilibrium is only physically meaningful when $\mathcal{R}_i \geq 1$, and when $\mathcal{R}_i = 1$, the endemic solution is equal to the disease-free solution. Since $S+I+R = 1$, the system is intrinsically two-dimensional and it is possible to omit the equation for R, though, in the work of this thesis, this is not required. If $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$ then, from system (4.1), $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$, hence the solution will converge to the disease-free solution.

Theorem 4.1.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.1) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.1) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \mu I - gI \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{4.4}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, for some $c > 0$, and hence the disease-free solution is exponentially I-stable in the domain Ω_{SIR}. Then, by inspection of system (4.1) with $I = 0$, the solution will converge to the disease-free solution $\bar{\mathbf{Q}}$. If the switching signal is periodic, then it follows from the bound (4.4) and the proof of Theorem 3.1.5 that the disease-free solution is asymptotically I-stable and the solution will converge to the disease-free solution, in the meaningful domain Ω_{SIR}. □

Recall, from Definition 2.1.9, that the asymptotic I-stability of the disease-free equilibrium $\bar{\mathbf{Q}}$ implies that for all $\epsilon > 0$, there exists a $\delta > 0$ such that $I_0 < \delta$ implies that $I(t) < \epsilon$ for all $t \geq 0$ and, for any $0 < I_0 \leq 1$,

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

The physical interpretation is that if the initial number of infectives is small then the number of infectives will stay small, and that, perhaps most importantly, the disease will eventually be eradicated for any initial condition of infectives.

Since the reproduction numbers (4.2) are the same as those of the SIS model (3.4), the criteria for disease eradication is the same. Fundamentally, the disease spreads at the same rate for both the switched SIS (3.3) and switched SIR (4.1) models. There are, however, a few differences between these models. First, we expect the convergence rates to be different in these two models. Specifically, since there is no immunity in the switched SIS model, infectives are moved back into the susceptible class and hence the disease should take longer to die out. Moreover, in the endemically persistent case, notice that the endemic level I_i^* in the switched SIR model (4.3) is lower than the corresponding endemic level I_i^* in the switched SIS model (3.5).

Furthermore, since this model is intrinsically two-dimensional, the mathematical analysis in the case $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$ is not as straightforward. Recall that in the non-switching SIR model (2.16), when $\mathcal{R}_0 > 1$, the solution converges to the endemic solution in an oscillatory fashion. Hence, in this switched case, when $\mathcal{R}_1, \ldots, \mathcal{R}_m > 1$, because of the oscillatory nature of the solution, it is possible to start in the convex hull of the endemic points $\Gamma = \{Q_1^*, \ldots, Q_m^*\}$ and to leave this set, but we conjecture that the disease will be persistent in this case (see Section 4.9). In the switched SIS model (3.3), the solutions approaches the equilibriums exponentially, and not with oscillations, because it is intrinsically one-dimensional and hence oscillations are not possible.

4.2 Switched SIR Model without Population Dynamics

Introduce switching into the SIR model without population dynamics (2.12). Here, the time scale of the disease is assumed to be short compared to the time scale of the population demographics such that they can be ignored. Assume the contact rate is approximate by $\beta_1, \ldots, \beta_m > 0$:

$$\begin{cases} \dot{S} = -\beta_i SI, \\ \dot{I} = \beta_i SI - gI, \\ \dot{R} = gI, \end{cases} \tag{4.5}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0, R(0) = R_0$, and the variables have been normalized since the population is constant. The meaningful physical domain for this system is Ω_{SIR}. Notice that $\{\dot{S}+\dot{I}+\dot{R}\}\,|_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = 0$, $\dot{I}\,|_{I=0} = 0$ and $\dot{R}\,|_{R=0} = gI > 0$, hence this domain is invariant to the system. For this model, define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i}{g}, \tag{4.6}$$

for each subsystem, from the non-switched system (2.14).

There are an infinite number of equilibrium points on the S-axis and there are no endemic equilibriums. And so, instead of considering the stability of any equilibrium point, we instead focus on two questions: Will the disease die out (i.e., $\lim_{t\to\infty} I = 0$)? Will there be an epidemic (i.e. will $I > I_0$ at any time $t \geq 0$)? From the equation for S', it is clear that $S \leq S_0$ for all time $t \geq 0$. Thus, $I' = \beta_i SI - gI \leq (\beta_i S_0 - g)I$. Hence, if $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1/S_0$ then $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$. Since $I_0 > 0$ and $S \leq S_0$, then $S = 1$ is not possible, hence the disease dies out.

Theorem 4.2.1. *If $\langle \mathcal{R}_\sigma \rangle < 1/S_0 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease will be eradicated ($\lim_{t\to\infty} I = 0$) and there will be no epidemic ($I \leq I_0$ for all time $t \geq 0$). If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1/S_0)\tau_1 + \ldots + (\mathcal{R}_m - 1/S_0)\tau_m < 0$ then, again, the disease will be eradicated and there will be no epidemic.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - gI \leq (\beta_{i_k} S_0 - g)I = \lambda_{i_k} I, \tag{4.7}$$

where $\lambda_{i_k} := \beta_{i_k} S_0 - g$. Thus, by the proof of Theorem 3.1.2, beginning with equation (3.11), $I(t) \leq I_0 \exp(-ct)$ for some $c > 0$. Hence $I \leq I_0$ for all time $t \geq 0$ and so there is no epidemic. The periodic switching case follows from the bound (4.7) and the proof of Theorem 3.1.5. □

4.3 Switched SIR Model with Vertical Transmission

Consider the SIR model with population dynamics (2.16) but now with vertical transmission as well as horizontal. Assume $0 \leq \rho \leq 1$ to be the fraction of newborns that are born healthy from infected mothers. Assume the contact rate is approximated by $\beta_1, \ldots, \beta_m > 0$, then the switched model is

$$\begin{cases} \dot{S} = \mu(S + R + \rho I) - \beta_i SI - \mu S, \\ \dot{I} = \mu(1 - \rho)I + \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{4.8}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and the variables have been normalized. Since

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

the meaningful domain Ω_{SIR} is invariant to each subsystem. For this model, the basic reproduction numbers are

$$\mathcal{R}_i = \frac{\beta_i}{\rho\mu + g}, \tag{4.9}$$

for each subsystem. These are identical to the reproduction numbers (3.17) from the SIS model with vertical transmission. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems. Each subsystem also has a unique endemic solution

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*, R_i^*) = \left(\frac{1}{\mathcal{R}_i}, \frac{\mu}{\mu+g}\left(1-\frac{1}{\mathcal{R}_i}\right), \frac{g}{\mu+g}\left(1-\frac{1}{\mathcal{R}_i}\right)\right). \tag{4.10}$$

Since $S+I+R = 1$, the model is intrinsically two-dimensional. If $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$, then, from (4.8), $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$, hence the disease will be eradicated.

Theorem 4.3.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.8) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.8) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \rho\mu I - gI \leq (\beta_{i_k} - \rho\mu - g)I = \lambda_{i_k} I, \tag{4.11}$$

where $\lambda_{i_k} := \beta_{i_k} - \rho\mu - g$. Thus, it follows from the proof of Theorem 3.1.2, beginning with equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence the disease-free solution is exponentially I-stable in Ω_{SIR}. Further, system (4.8) with $I = 0$ will converge to the disease-free solution, by inspection. If the switching signal is periodic, then it follows from the bound (4.11), the proof of Theorem 3.1.5 and a similar analysis as above, that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain Ω_{SIR}. □

4.4 Switched SIRS Model

Assume now that the infectious disease confers a temporary immunity to individuals once they eliminate the disease. Assume individuals lose their temporary immunity

at a rate $\theta > 0$, hence the immune period is $1/\theta$. That is, consider the SIRS model (2.24) with switching in the contact rate:

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S + \theta R, \\ \dot{I} = \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R - \theta R, \end{cases} \tag{4.12}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and the variables have been normalized such that $S+I+R = 1$, since the population is constant. The meaningful physical domain for this system is Ω_{SIR}, which is invariant to each subsystem since $\{\dot{S} + \dot{I} + \dot{R}\}\,|_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu + \theta R > 0$, $\dot{I}\,|_{I=0} = 0$ and $\dot{R}\,|_{R=0} = gI \geq 0$. This model is intrinsically two-dimensional. For this model, the basic reproduction numbers for each subsystem are the same as from the SIR model (4.2), $\mathcal{R}_i = \beta_i/(\mu + g)$ Fundamentally the disease spreads at the same rate in the SIR and SIRS models, whether the immunity is temporary or permanent. In fact, if there is no immunity at all (switched SIS model (3.3)), the basic reproduction rate still does not change.

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*, R_i^*) = \left(\frac{1}{\mathcal{R}_i}, \frac{\mu + \theta}{\mu + \theta + g}\left(1 - \frac{1}{\mathcal{R}_i}\right), \frac{g}{\mu + \theta + g}\left(1 - \frac{1}{\mathcal{R}_i}\right)\right). \tag{4.13}$$

The endemic solution is only physically meaningful when $\mathcal{R}_i \geq 1$. Observe that if $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$ then $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$, hence the disease will be eradicated.

Theorem 4.4.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.12) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.12) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \mu I - gI \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{4.14}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Thus, it follows from the proof of Theorem 3.1.2, $I(t) \leq I_0 \exp(-ct)$, and hence the disease-free solution is exponentially I-stable. Then, looking at system (4.12) with $I = 0$, by inspection, R and S, converge to zero and one, respectively. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. If the switching signal is periodic, then it follows from the bound (4.14) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

The analysis of this model might seem to be identical to the switched SIR model (4.1), since the reproduction numbers are the same, but one difference which should be highlighted is that in this case, when the disease is persistent, the endemic points I_i^* (4.13) are higher than the corresponding endemic points in the switched SIR model with permanent immunity (4.3). This is reasonable biologically, because the loss of immunity should result in more individuals being infected when the disease is persistent. Another difference is that when $\langle \mathcal{R}_\sigma \rangle < 1$, we should expect the infection to be eradicated more slowly and the susceptible fraction to converge to one faster. 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. See the simulation of this model in Section 4.10 (Figure 4.4) for a comparison.

4.5 Switched MSIR Model

Some diseases, such as chickenpox, result in the transfer of antibodies across the placenta if the mother has been infected [28]. Suppose that all mothers who are infected (infected class) or have been infected in the past (removed class) give birth to children with temporary passive immunity, denoted by the passively immune class M. Realistically, all women should be out of the passively immune class before they give birth to a child, but theoretically a passively immune mother would also transfer some antibodies to her newborn child [28]. For an example of an MSEIR model with non-constant population, see [28].

Assume that individuals born into the passively immune class lose immunity at a rate $\delta > 0$, hence the passive immunity has average period $1/\delta$. Assume birth rate $\mu > 0$ equal to natural death rate, assume removal rate $g > 0$, and assume the immunity acquired by defeating the infection is permanent. Introduce switching into this model by assuming the contact rate $\beta_i > 0$ switches, and hence is approximated by a peicewise constant. This switched model then is,

$$\begin{cases} \dot{M} = \mu(M + I + R) - \delta M - \mu M, \\ \dot{S} = \mu S - \beta_i SI - \mu S + \delta M, \\ \dot{I} = \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{4.15}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $M(0) = M_0$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0, R(0) = R_0$, and the total population is constant. The variables have been normalized and the meaningful domain for this system is

$$\Omega_{MSIR} = \{(M, S, I, R) \in \mathbb{R}^4_+ |\ M + S + I + R = 1\}.$$

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 $\dot{M}|_{M=0} = \mu I + \mu R \geq 0$, hence this domain is invariant to

each subsystem. For this model, again define the basic reproduction numbers $\mathcal{R}_i = \beta_i/(\mu+g)$ for each subsystem, which are the same as the switched SIS model (3.4), switched SIR model (4.2), and switched SIRS model (4.12). Hence, the addition of the M class actually does not biologically alter the spread of the disease. There is a single common disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{M}, \bar{S}, \bar{I}, \bar{R}) = (0, 1, 0, 0)$ and each subsystem also has an endemic equilibrium $\mathbf{Q_i^*} = (M_i^*, S_i^*, I_i^*, R_i^*)$, with,

$$\begin{aligned} M_i^* &= \frac{\mu}{\delta+\mu}\left(1 - 1/\mathcal{R}_i\right), \\ S_i^* &= \frac{1}{\mathcal{R}_i}, \\ I_i^* &= \frac{\delta}{\delta+\mu}\frac{\mu}{\mu+g}\left(1 - 1/\mathcal{R}_i\right), \\ R_i^* &= \frac{g}{\delta+\mu}\frac{\mu}{\mu+g}\left(1 - 1/\mathcal{R}_i\right). \end{aligned}$$

Here we see the endemic equilibrium points are again different from the SIR and SIRS cases. From the equation for I', it is apparent that if $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$, then $I' < 0$ in Ω_{MSIR} unless $I = 0$ or $S = 1$. Hence the the disease will be eradicated.

Theorem 4.5.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.15) will converge to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{MSIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.15) will converge to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{MSIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \mu I - gI \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{4.16}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Thus, it follows from the proof of Theorem 3.1.2, $I(t) \leq I_0 \exp(-ct)$, and hence the disease-free solution is exponentially I-stable. Then, looking at the system (4.15) with $I = 0$, it is apparent, by inspection, that R converges to zero. Then, it is obvious that M will converges to zero, and hence S converges to one. Therefore, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the domain Ω_{MSIR}. If the switching signal is periodic, then it follows from the bound (4.16) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically stable, in the meaningful domain. □

4.6 Switched SEIR Model

Assume that the infection has an incubating period. In this stage, an individual has been exposed but is not yet infectious. We denote this compartment by E.

That is, consider the SEIR model (2.27) with switching in the contact rate,

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S, \\ \dot{E} = \beta_i SI - aE - \mu E, \\ \dot{I} = aE - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{4.17}$$

with $i \in \{1, 2, \ldots, m\}$, initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $E(0) = E_0$, $R(0) = R_0$, and the total population is constant. The variables have been normalized to represent fractions of individuals in each class. The meaningful physical domain for this system is

$$\Omega_{SEIR} = \{(S, E, I, R) \in \mathbb{R}^4_+ |\ S + E + I + R = 1\}.$$

For this system,

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

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

hence this domain is invariant to each subsystem. For this model, use the basic reproduction numbers from the non-switching case (2.28),

$$\mathcal{R}_i = \frac{\beta_i a}{(\mu + g)(\mu + a)} \tag{4.18}$$

for each subsystem.

There is a common single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{E}, \bar{I}, \bar{R}) = (1, 0, 0, 0)$ and each subsystem also has an endemic equilibrium

$$\mathbf{Q}^*_\mathbf{i} = (S^*_i, E^*_i, I^*_i, R^*_i) = \left(\frac{1}{\mathcal{R}_i}, \frac{\mu(\mu + g)}{\beta_i a}(\mathcal{R}_i - 1), \frac{\mu}{\beta_i}(\mathcal{R}_i - 1), \frac{g}{\beta_i}(\mathcal{R}_i - 1) \right). \tag{4.19}$$

Since $S + E + I + R = 1$, the system is intrinsically three-dimensional. For the switched SEIR model (4.17), when $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$ it is not obvious whether or not I converges to zero. Here, Lyapunov functions from the non-switced case are used to prove stability of the disease-free solution using common weak Lyapunov techniques, specifically, the invariance principle for switched systems (see Section 2.3.2). Denote the set $\mathcal{S}_{\text{inf-dwell}} \subset \mathcal{S}$ to be all switching signals σ which have nonvanishing dwell times, that is, there exists an $\eta > 0$, dependent on the specific solution of the switched system, such that

$$\inf_k t_k - t_{k-1} \geq \eta, \tag{4.20}$$

where $\{t_k\}$ is the sequence of switching times associated to the switching signal.

Theorem 4.6.1. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1$ for any dwell-time switching rule $\sigma \in \mathcal{S}_{\text{inf-dwell}}$, then the solution of system (4.17) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SEIR}.*

Proof. Consider the Lyapunov function $V(E,I) = aE + (a+\mu)I$, similar to the one from [40]. Define $\Omega^l_{EI} = \{(E,I) \in \mathbb{R}^2_+ |\ E + I \leq 1\}$, which is invariant to system (4.17). This Lyapunov function satisfies $V(0,0) = 0$ and $V(E,I) > 0$ for $(E,I) \in \Omega^l_{EI} \setminus \{(0,0)\}$. Along trajectories of subsystem i:

$$\begin{aligned}\dot{V} &= a(\beta_i SI - aE - \mu E) + (a+\mu)(aE - gI - \mu I),\\ &= \beta_i aSI - (\mu+g)(\mu+a)I,\\ &= (\mathcal{R}_i S - 1)(\mu+g)(\mu+a)I.\end{aligned}$$

Hence, if $\mathcal{R}_i < 1$ for all i then $\dot{V} \leq 0$ and hence $V(E,I)$ is a common weak Lyapunov function. Then, since $Z = \{(E,I) \in \Omega^l_{EI} |\ V' = 0\}$ is the set $(E,I) = (c,0)$ for any $0 \leq c \leq 1$ and by inspecting the limiting equations of (4.17) with $I = 0$, it follows that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ by Theorem 2.3.3. □

Many infectious diseases transmit through both horizontal and vertical modes, for example, rubella, herpes simplex, hepatitis B, and Chagas' disease [40]. Hence, consider the SEIR model (2.27) with the addition of vertical transmission and switching in the contact rate. Suppose that a portion $0 \leq \rho \leq 1$ of exposed and a portion $0 \leq q \leq 1$ of infectives are born directly into the exposed class E. The switched model then is,

$$\begin{cases}\dot{S} = \mu(1 - \rho E - qI) - \beta_i SI - \mu S,\\ \dot{E} = \mu(\rho E + qI) + \beta_i SI - aE - \mu E,\\ \dot{I} = aE - gI - \mu I,\\ \dot{R} = gI - \mu R,\end{cases} \tag{4.21}$$

with meaningful domain Ω_{SEIR}, $i \in \{1, 2, \ldots, m\}$, and initial conditions as before. Observe that

$$\{\dot{S} + \dot{E} + \dot{I} + \dot{R}\}\,|_{S+I+E+R=1} = 0, \quad \dot{S}\,|_{S=0} = \mu(1 - \rho E - qI) \geq 0,$$

$$\dot{E}\,|_{E=0} = \mu qI + \beta_i SI \geq 0, \quad \dot{I}\,|_{I=0} = aE \geq 0, \quad \dot{R}\,|_{R=0} = gI \geq 0,$$

thus the domain is invariant to each subsystem. For this model, define the basic reproduction numbers, from the non-switched case [40]:

$$\mathcal{R}_i = \frac{\beta_i a}{(\mu+g)(\mu+a) - \mu\rho(\mu+g) - \mu qa} \tag{4.22}$$

for each subsystem. An interesting interpretation of this basic reproduction number, as the Taylor series expansion of all the generations of offspring and how they transmit the disease, can be found in [40].

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{E}, \bar{I}, \bar{R}) = (1,0,0,0)$ that is common to all subsystems. Further, each subsystem also has an endemic

equilibrium $\mathbf{Q_i^*} = (S_i^*, E_i^*, I_i^*, R_i^*)$ [40]:

$$\begin{aligned}
S_i^* &= \frac{1}{\mathcal{R}_i}, \\
E_i^* &= 1 - S_i^* - I_i^* - R_i^*, \\
I_i^* &= \frac{a\mu\mathcal{R}_i}{\beta_i a + \rho\mu(g+\mu)\mathcal{R}_i + q\mu a\mathcal{R}_i}(1 - 1/\mathcal{R}_i), \\
R_i^* &= \frac{ag\mathcal{R}_i}{\beta_i a + \rho\mu(g+\mu)\mathcal{R}_i + q\mu a\mathcal{R}_i}(1 - 1/\mathcal{R}_i).
\end{aligned}$$

Theorem 4.6.2. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1$ for any dwell-time switching rule $\sigma \in \mathcal{S}_{inf\text{-}dwell}$, then the solution of system (4.21) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SEIR}.*

Proof. Consider the Lyapunov function $V(E, I) = aE + (a + \mu - \rho\mu)I$ from [40]. This Lyapunov function satisfies $V(0, 0) = 0$ and $V(E, I) > 0$ when $(E, I) \in \Omega_{EI}^l \setminus \{(0, 0)\}$. Along trajectories of subsystem i:

$$\begin{aligned}
\dot{V} &= a(\beta_i SI + \rho\mu E + q\mu I - aE - \mu E) + (a + \mu - \rho\mu)(aE - gI - \mu I), \\
&= \beta_i aSI - [(\mu + g)(\mu + a - \rho\mu) - \mu qa]I, \\
&= (\mathcal{R}_i S - 1)(\mu + g)(\mu + a - \rho\mu - \mu qa)I.
\end{aligned}$$

Hence, if $\mathcal{R}_i < 1$ for all i then $\dot{V} \leq 0$ and, therefore, $V(E, I)$ is a common weak Lyapunov function. Then, since $Z = \{(E, I) \in \Omega_{EI}^l |\ V' = 0\}$ is the set $(E, I) = (c, 0)$ for $0 \leq c \leq 1$, and by inspecting the limiting equations of (4.21) with $I = 0$, it follows that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ by Theorem 2.3.3. □

Assume now that the birth rate $b > 0$ is different from the death rate $d > 0$. Also assume that there is a disease-induced mortality rate $\alpha > 0$. Certainly, AIDS is an example of a disease with an incubating period and disease-induced mortality [40]. Assume switching in the contact rate, then this leads to:

$$\begin{cases}
\dot{S}_c = b - \beta_i \dfrac{S_c I_c}{N} - dS_c, \\
\dot{E}_c = \beta_i \dfrac{S_c I_c}{N} - aE_c - dE_c, \\
\dot{I}_c = aE_c - gI_c - dI_c - \alpha I_c, \\
\dot{R}_c = gI_c - dR_c,
\end{cases} \tag{4.23}$$

with S_c, E_c, I_c, R_c representing the number of individuals in the susceptible, exposed, infectious and removed class, respectively. Further, the total population $N = S_c + E_c + I_c + R_c$ satisfies the differential equation $N' = (b - d)N - \alpha I_c$.

Normalize the equations using $S = S_c/N, E = E_c/N, I = I_c/N, R = R_c/N$. This gives:

$$\begin{cases} \dot{S} = b - \beta_i SI - bS + \alpha SI, \\ \dot{E} = \beta_i SI - aE - bE + \alpha EI, \\ \dot{I} = aE - gI - bI - \alpha I + \alpha I^2, \\ \dot{R} = gI - bR + \alpha RI, \end{cases} \tag{4.24}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $E(0) = E_0$, $R(0) = R_0$, and the normalized variables satisfy $S + E + I + R = 1$. The αSI, αEI, αIR and αI^2 terms are positive feedback terms due to the disease-induced mortality. The meaningful physical domain for this system is Ω_{SEIR}. Notice that $\{\dot{S} + \dot{E} + \dot{I} + \dot{R}\}\,|_{S+I+E+R=1} = 0$, $\dot{S}\,|_{S=0} = b > 0, \dot{E}\,|_{E=0} = \beta_i SI \geq 0, \dot{I}\,|_{I=0} = aE \geq 0$ and $\dot{R}\,|_{R=0} = gI \geq 0$, hence this domain is invariant to each subsystem. For this model, define the basic reproduction numbers, from the non-switched case [38]:

$$\mathcal{R}_i = \frac{\beta_i a}{(b + g + \alpha)(b + a)} \tag{4.25}$$

for each subsystem. These are smaller than the corresponding ones from the SEIR system (4.18) because of the disease-induced mortality.

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{E}, \bar{I}, \bar{R}) = (1, 0, 0, 0)$ that is common to all subsystems. Further, each subsystem also has a unique endemic equilibrium $\mathbf{Q_i^*} = (S_i^*, E_i^*, I_i^*, R_i^*)$ where I_i^* satisfies the cubic [38]:

$$\left(1 - \frac{\alpha}{a+b} I_i^*\right)\left(1 - \frac{\alpha}{\alpha + g + b} I_i^*\right)\left(1 + \frac{\beta_i - \alpha}{b} I_i^*\right) = \mathcal{R}_i, \tag{4.26}$$

and the other endemic states satisfy

$$\begin{aligned} S_i^* &= \frac{b}{b + \beta_i I_i^* - \alpha I_i^*}, \\ E_i^* &= \frac{g + \alpha + b - \alpha I_i^*}{a} I_i^*, \\ R_i^* &= 1 - S_i^* - E_i^* - I_i^*. \end{aligned}$$

It was shown in the non-switched case [38] that when $\mathcal{R}_i > 1$ this system has a unique solution such that $I_i^* > 0$. For the proof of the stability of the disease-free solution, the following lemma is needed.

Lemma 4.6.3. [38]
Let $\Delta = \{(x, y) \in \mathbb{R}_+^2 |\ x + y \leq 1\}$ and define the function $h(x, y) = (a_1 - b_1)x + (c_1 - b_1)y + b_1$, where the constants $a_1, b_1, c_1 > 0$. The maximum of $h(x, y)$ in the domain Δ then is,

$$\max_{(x,y) \in \Delta} h(x, y) = \max\{a_1, b_1, c_1\}.$$

Now, we can state a theorem for the eradication of the disease.

Theorem 4.6.4. *If $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1$ for any dwell-time switching rule $\sigma \in \mathcal{S}_{inf\text{-}dwell}$, then the solution of system (4.24) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SEIR}.*

Proof. Consider the Lyapunov function $V(E, I) = aE + (a + b)I$ from [38]. This Lyapunov function satisfies $V(0, 0) = 0$ and $V(E, I) > 0$ for $(E, I) \in \Omega^l_{EI} \setminus \{(0, 0)\}$. Along trajectories of subsystem i:

$$\begin{aligned}
\dot{V} &= a(\beta_i SI - aE - bE + \alpha EI) + (a + b)(aE - gI - bI - \alpha I + \alpha I^2),\\
&= [\beta_i aS - (a + b)(g + \alpha + b) + \alpha aE + \alpha(a + b)I]I,\\
&\leq [\beta_i a(1 - E - I) - (a + b)(g + \alpha + b) + \alpha aE + \alpha(a + b)I]I,\\
&= [h_i(E, I) - (a + b)(g + \alpha + b)]I,
\end{aligned}$$

where $h_i(E, I) = (\alpha a - \beta_i a)E + (\alpha(a + b) - \beta_i a)I + \beta_i a$. Then, applying Lemma 4.6.3 in the domain Ω^l_{EI},

$$\dot{V} \leq [\max\{\alpha a, \beta_i a, \alpha(a + b)\} - (a + b)(g + \alpha + b)]I,$$

and so, since $\mathcal{R}_i < 1$, it follows that $V' \leq 0$. Therefore, $V(E, I)$ is a common weak Lyapunov function. Notice that $V' = 0$ if $(E, I) = (c, 0)$ or possibly if $\max\{\alpha a, \beta_i a, \alpha(a + b)\} = (a + b)(g + \alpha + b)$, which implies $\mathcal{R}_i = 1$, but we assumed $\mathcal{R}_i < 1$. Then, it follows that $Z = \{(E, I) \in \Omega^l_{EI} |\ V' = 0\}$ is the set $(E, I) = (c, 0)$, with $0 \leq c \leq 1$, and by inspecting the limiting equations of (4.24) with $I = 0$, it follows that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ by Theorem 2.3.3. □

Theorem 4.6.4 gives sufficient conditions for the eradication of the infected fraction of the population. From $I_c = IN$ and since the population, N, is non-constant and possibly growing without bound, this does not necessarily imply that the actual number of infected individuals, I_c, go to zero. Recall the equation for the population dynamics is $N' = (b - d)N - \alpha I_c = (b - d - \alpha I)N$. Then, if $b < d$, it is clear that the total population is going to zero, and hence $I \to 0$ implies $I_c \to 0$. If $b = d$, then $N' = -\alpha IN \leq 0$, and hence the total population should approach a constant since $I \to 0$. Thus, in this case, $I_c \to 0$. Finally, if $b > d$, then the total population will grow without bound since $I \to 0$. In this case, since $S \to 1$ use $S_c = SN$ to get $S_c \to N$ and then $N = S_c + E_c + I_c + R_c$ implies $I_c \to 0$. It also follows that E_c and R_c both approach zero as well.

4.7 Switched SIR Models with Varying Total Population

Assume that the birth rate $b > 0$ is different from the death rate $d > 0$. Assume also that there is a disease-induced mortality $\alpha > 0$, then the population satisfies

$N' = (b-d)N - \alpha I_c$. Apply this to the SIR model with switching in the contact rate,

$$\begin{cases} \dot{S}_c = bN_c - \dfrac{\beta_i S_c I_c}{N} - dS_c, \\ \dot{I}_c = \dfrac{\beta_i S_c I_c}{N} - gI_c - dI_c - \alpha I_c, \\ \dot{R}_c = gI_c - dR_c, \end{cases} \tag{4.27}$$

where S_c, I_c, and R_c are the number of susceptible, infected and removed individuals, respectively, and $N = S_c + I_c + R_c$. Normalize the equations using $I = I_c/N$ and $S = S_c/N$. This leads to

$$\begin{cases} \dot{S} = b - \beta_i SI - bS + \alpha SI, \\ \dot{I} = \beta_i SI - gI - bI - \alpha I + \alpha I^2, \\ \dot{R} = gI - bR + \alpha IR, \end{cases} \tag{4.28}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and $S+I+R = 1$. The meaningful physical domain for this system is $\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S+I+R = 1\}$. The domain is invariant to each subsystem:

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

The αSI,αIR and αI^2 terms are positive feedback terms due to mortality from the disease. For each subsystem, define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i}{b+g+\alpha}. \tag{4.29}$$

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems.

Theorem 4.7.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.28) locally converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is locally exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.28) locally converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is locally asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Linearize the system (4.28) about the disease-free equilibrium $\bar{\mathbf{Q}} = (1, 0, 0)$:

$$\begin{cases} \dot{S} = -\beta_i I - bS + gI + \alpha I, \\ \dot{I} = \beta_i I - gI - bI - \alpha I, \\ \dot{R} = gI - bR, \end{cases} \tag{4.30}$$

Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$, then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = (\beta_{i_k} - g - b - \alpha)I = \lambda_{i_k} I, \tag{4.31}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g - \alpha$. Thus, it follows from the proof of Theorem 3.1.2, beginning at (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence the disease-free solution $\bar{\mathbf{Q}}$ is exponentially I-stable. Then, by inspection of system (4.30) with $I = 0$, R and S, converge to zero and one, respectively. Hence, the solution converges locally to the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (4.28) in the domain Ω_{SIR}. If the switching signal is periodic, then it follows from the bound (4.31) and the proof of Theorem 3.1.5 that the solution converges locally to the disease-free solution, which is locally asymptotically I-stable, in the meaningful domain. □

It is conjectured here that if $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for some constant $\epsilon > 0$, then the solution will converge to the disease-free solution $\bar{\mathbf{Q}}$ of system (4.28) in the meaningful domain Ω_{SIR}, that is, the disease will be eradicated. If we again demand that the more strict non-physical reproduction numbers $\mathcal{R}_i^{non} = \beta_i/(b+g)$ are used (similar to the analysis in Section 3.3), we will get the desired result of exponential stability in the entire domain Ω_{SIR}.

Theorem 4.7.2. *If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.28) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the meaningful domain Ω_{SIR}.*

Proof. Let i_k follow the dwell-time switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_i SI - gI - bI - \alpha I + \alpha I^2 \leq (\beta_{i_k} - b - g)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - b - g$. Thus, following the proof of Theorem 3.1.2, the disease-free solution $\bar{\mathbf{Q}}$ of system (4.28) is exponentially I-stable, and, inspecting system (4.28) with $I = 0$, the solution converges to $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. □

Theorems 4.7.1 and 4.7.2 give sufficient conditions for the eradication of the infected fraction of the population. From $I_c = IN$ and since the population is non-constant, and potentially growing without bound, this does not necessarily mean that the actual number of infected individuals vanishes. Recall the equation for the population dynamics $N' = (b - d)N - \alpha I_c = (b - d - \alpha I)N$. If $b < d$, it is clear that the total population is going to zero, and hence $I \to 0$ implies $I_c \to 0$. If $b = d$, then $N' = -\alpha IN \leq 0$, and hence the total population should approach a constant since $I \to 0$, and hence $I_c \to 0$. Finally, if $b > d$, then the total population will grow without bound since $I \to 0$. In this case, since $S \to 1$ use $S_c = SN$ to get $S_c \to N$ and then $N = S_c + I_c + R_c$ implies $I_c \to 0$. It also follows that R_c approaches zero as well.

Another possible demographic model is $N' = A - dN - \alpha I_c$, where $A > 0$ is the rate of immigration of individuals, $d > 0$ is the rate of natural mortality, and α is the disease-induced mortality. Without the disease, the population size N approaches

A/d. There have been models of HIV/AIDS that have used this structure [27]. Applying this structure to the SIR model with switched contact rate gives:

$$\begin{cases} \dot{S}_c = A - \dfrac{\beta_i S_c I_c}{N} - dS_c, \\ \dot{I}_c = \dfrac{\beta_i S_c I_c}{N} - gI_c - dI_c - \alpha I_c, \\ \dot{R}_c = gI_c - dR_c, \end{cases} \tag{4.32}$$

where S_c, I_c, and R_c are the actual number of susceptible, infected and removed individuals, respectively, and $N = S_c + I_c + R_c$. The initial conditions are $S_c(0) = S_0 > 0$, $I_c(0) = I_0 > 0$, $R_c(0) = R_0$. From the differential equation for $N(t)$, it is apparent that $A - (d+\alpha)N(t) \leq N'(t) \leq A - dN(t)$. Then it follows that [20]:

$$\frac{A}{d+\alpha} \leq \liminf_{t\to\infty} N(t) \leq \limsup_{t\to\infty} N(t) \leq \frac{A}{d}.$$

Hence, the meaningful physical domain for this system is

$$T_{SIR} = \{(S_c, I_c, R_c) \in \mathbb{R}^3_+ |\ S_c + I_c + R_c \leq A/d\}.$$

We choose to use the notation T for the domain, instead of the usual Ω, here because the variables have not been normalized. To show it is invariant, observe that

$$\{\dot{S}_c + \dot{I}_c + \dot{R}_c\}\,|_{S_c+I_c+R_c=A/d} = -\alpha I_c \leq 0,$$

$$\dot{S}_c\,|_{S_c=0} = A > 0, \quad \dot{I}_c\,|_{I_c=0} = 0, \quad \dot{R}_c\,|_{R_c=0} = gI_c \geq 0.$$

Therefore, the domain is invariant. For this model, the basic reproduction numbers are $\mathcal{R}_i = \beta_i/(d+g+\alpha)$ for each subsystem, which are the same the other SIR model with varying population size modelled in this section (4.29).

There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (A/d, 0, 0)$ that is common to all subsystems. Since $S_c + I_c + R_c = N$ and because N is varying, this model is intrinsically three-dimensional. It is interesting to note in this case that the normalization of variables $S = S_c/N$, $I = I_c/N$ and $R = R_c/N$ does not help to simplify the system. In the case that $\mathcal{R}_1, \ldots, \mathcal{R}_m \leq 1$ then $I' < 0$ in T_{SIR} unless $I_c = 0$ or $S_c = N$, hence the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain T_{SIR}.

Theorem 4.7.3. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.32) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain T_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.32) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain T_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I_c' = (\beta_{i_k} S_c/N - g - d - \alpha)I_c \leq (\beta_{i_k} - g - d - \alpha)I_c = \lambda_{i_k} I_c, \tag{4.33}$$

where $\lambda_{i_k} := \beta_{i_k} - g - d - \alpha$. Thus, it follows from the proof of Theorem 3.1.2, beginning with equation (3.11), that $I_c(t) \leq I_0 \exp(-ct)$, and hence the disease-free equilibrium $\bar{\mathbf{Q}}$ is exponentially I-stable. The limiting equation for R then can be written as $\dot{R}_c = -dR_c$ which implies R_c converges to zero. Since $N' = A - dN - \alpha I_c$, then $I_c \to 0$ implies that $N \to A/d$, and $N = S_c + I_c + R_c$ then implies that $S_c \to A/d$. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (4.32) in the domain T_{SIR}. If the switching signal is periodic, then it follows from the bound (4.33) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the meaningful domain. □

4.8 Switched Multi-City SIS Models

Communicable infectious diseases such as influenza, foot-and-mouth disease, SARS and sexually transmitted diseases (STDs) can be easily transmitted from one geographic region to another due to population dispersal from individuals travelling, and so, the effect of travel on the spread of a disease should be considered [72]. In 2003, SARS began in one province in China and spread to most parts of China and some other cities in the world due to the travel of infected individuals [46]. Another example is the outbreak of measles in Iceland due, in part, to new infectives entering the country from other regions [68]. There has been some work done on transport models in the literature for the non-switched case, for example, see [10, 46, 68, 72], and the switched models in this section are motivated by these works.

To begin an analysis of this situation, assume that there are two cities and that only susceptibles may travel between the two cities at a per capita rate $\alpha > 0$, sometimes called the dispersal rate. Assume the standard incidence rate $\beta_i S_c I_c/N$ in both cities, where $\beta_i > 0$ follows a switching rule $\sigma(t) \in \mathcal{S}$. Furthermore, assume that individuals do not die, recover or give birth while travelling. Assume that the removal rate is $g > 0$ for both cities, and the birth rate is $\mu > 0$ for both cities. Let S_{c_1}, S_{c_2} be the number of susceptible individuals in the first and second city, respectively. Similarly define I_{c_1}, I_{c_2}. Assume there is no immunity conferred from recovery. That is, each city is modelled as a switched SIS model, with extra terms

from travelling,

$$\begin{cases} \dot{S}_{c_1} = \mu N_1 - \beta_i \dfrac{S_{c_1} I_{c_1}}{N_1} - \mu S_{c_1} + g I_{c_1} - \alpha S_{c_1} + \alpha S_{c_2}, \\ \dot{I}_{c_1} = \beta_i \dfrac{S_{c_1} I_{c_1}}{N_1} - g I_{c_1} - \mu I_{c_1}, \\ \dot{S}_{c_2} = \mu N_2 - \dfrac{S_{c_2} I_{c_2}}{N_2} - \mu S_{c_2} + g I_{c_2} - \alpha S_{c_2} + \alpha S_{c_1}, \\ \dot{I}_{c_2} = \beta_i \dfrac{S_{c_2} I_{c_2}}{N_2} - g I_{c_2} - \mu I_{c_2}, \end{cases} \tag{4.34}$$

where $i \in \{1, 2, \ldots, m\}$, $N_1 = S_{c_1} + I_{c_1}$, $N_2 = S_{c_2} + I_{c_2}$, and $N_1 + N_2 = N$. Notice that $\dot{S}_{c_1} + \dot{S}_{c_1} + \dot{S}_{c_1} + \dot{S}_{c_1} = 0$, which gives $N' = 0$, and hence the total population, N, is constant, though N_1 and N_2 are not necessarily constant. The initial conditions are $S_{c_1}(0) = S_{c_1,0} > 0$, $S_{c_2}(0) = S_{c_2,0} > 0$, $I_{c_1}(0) = I_{c_1,0} > 0$, $I_{c_2}(0) = I_{c_2,0} > 0$. The meaningful physical domain for this system is $T_{SISI} = \{(S_{c_1}, I_{c_1}, S_{c_2}, I_{c_2}) \in \mathbb{R}^4_+ |\ S_{c_1} + I_{c_1} + S_{c_2} + I_{c_2} = N\}$. Observe that

$$\{\dot{S}_{c_1} + \dot{I}_{c_1} + \dot{S}_{c_2} + \dot{I}_{c_2}\} \,|_{S_{c_1}+I_{c_1}+S_{c_2}+I_{c_2}=N} = 0,$$

$$\dot{S}_{c_1} \,|_{S_{c_1}=0} = (\mu + g) I_{c_1} + \alpha S_{c_2} \geq 0, \quad \dot{I}_{c_1} \,|_{I_{c_1}=0} = 0,$$

$$\dot{S}_{c_2} \,|_{S_{c_2}=0} = (\mu + g) I_{c_2} + \alpha S_{c_1} \geq 0, \quad \dot{I}_{c_2} \,|_{I_{c_2}=0} = 0,$$

hence this domain is invariant. For this model, define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i}{\mu + g} \tag{4.35}$$

for each subsystem. There is a disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}_{c_1}, \bar{I}_{c_1}, \bar{S}_{c_2}, \bar{I}_{c_2}) = (N/2, 0, N/2, 0)$$

that is common to all subsystems. Notice that in the case that there is no dispersal from travelling, that is, $\alpha = 0$, the model becomes two independent cities that are modelled by the switched SIS model (3.3). Also note that, since each city is modelled as a switched SIS model, the reproduction numbers considered are the same as for the SIS model (3.4). If $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1$ then, in the domain T_{SISI}, $I'_{c_1} < 0$ unless $I_{c_1} = 0$ and $I'_{c_2} < 0$ unless $I_{c_2} = 0$, hence the disease is eradicated in both cities.

Theorem 4.8.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.34) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.34) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}.*

Proof.

Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}(I_{c_1} + I_{c_2})' &= \beta_{i_k}\left(\frac{S_{c_1}I_{c_1}}{N_1} + \frac{S_{c_2}I_{c_2}}{N_2}\right) - (g+\mu)(I_{c_1} + I_{c_2}),\\ &\leq (\beta_{i_k} - g - \mu)(I_{c_1} + I_{c_2}),\\ &= \lambda_{i_k}(I_{c_1} + I_{c_2}),\end{aligned} \tag{4.36}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Then, by the proof of Theorem 3.1.2, beginning with equation (3.11), we have that $I_{c_1} + I_{c_2} \leq (I_{c_1,0} + I_{c_2,0})\exp(-ct)$ for some $c > 0$. Since $I_{c_1}, I_{c_2} \geq 0$, the solution $\bar{\mathbf{Q}}$ is exponentially (I_{c_1}, I_{c_2})-stable in T_{SISI}. Since I_{c_1} and I_{c_2} are converging to zero, the limiting equations for S_{c_1} and S_{c_2} are

$$\begin{cases}\dot{S}_{c_1} = -\alpha S_{c_1} + \alpha S_{c_2},\\ \dot{S}_{c_2} = -\alpha S_{c_2} + \alpha S_{c_1}.\end{cases} \tag{4.37}$$

$S_{c_1} + S_{c_2} = N$ then implies that S_{c_1} and S_{c_2} both converge to $N/2$. Hence, the solution of system (4.34) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain T_{SISI}. If the switching signal is periodic, then it follows from the bound (4.36) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically (I_{c_1}, I_{c_2})-stable, in the meaningful domain. □

In developing countries, there can be dense crowds on trains, airplanes, and other mass transportation, which may have relatively poor sanitary conditions. Under these conditions, the transmission of the virus between travelling individuals may be an important factor for the outbreak of infectious diseases [10]. This leads to an important question: how do transport-related infections affect the dynamics and spread of infectious diseases [10]? Assume, as above, that there are two cities modelled as switched SIS systems and that susceptibles and infectives may both travel between the two cities at a per capita rate $\alpha > 0$. Assume additionally that the disease is transmitted at a contact rate $0 \leq \gamma \leq 1$ during travel. Assume a standard incidence rate for individuals travelling from city j, then the travelling incidence rate should be

$$\gamma\frac{(\alpha S_{c_j})(\alpha I_{c_j})}{\alpha N_j} = \gamma\frac{(\alpha S_{c_j})(\alpha I_{c_j})}{(\alpha S_{c_j}) + (\alpha I_{c_j})} = \gamma\alpha\frac{S_{c_j}I_{c_j}}{S_{c_j} + I_{c_j}}.$$

Also, assume that infectives do not recover, die or give birth during travel. Then the switched model is:

$$\begin{cases}\dot{S}_{c_1} = \mu N_1 - \beta_i\dfrac{S_{c_1}I_{c_1}}{N_1} - \mu S_{c_1} + gI_{c_1} - \alpha S_{c_1} + \alpha S_{c_2} - \alpha\gamma\dfrac{S_{c_2}I_{c_2}}{N_2},\\ \dot{I}_{c_1} = \beta_i\dfrac{S_{c_1}I_{c_1}}{N_1} - gI_{c_1} - \mu I_{c_1} - \alpha I_{c_1} + \alpha I_{c_2} + \alpha\gamma\dfrac{S_{c_2}I_{c_2}}{N_2},\\ \dot{S}_{c_2} = \mu N_2 - \beta_i\dfrac{S_{c_2}I_{c_2}}{N_2} - \mu S_{c_2} + gI_{c_2} - \alpha S_{c_2} + \alpha S_{c_1} - \alpha\gamma\dfrac{S_{c_1}I_{c_1}}{N_1},\\ \dot{I}_{c_2} = \beta_i\dfrac{S_{c_2}I_{c_2}}{N_2} - gI_{c_2} - \mu I_{c_2} - \alpha I_{c_2} + \alpha I_{c_1} + \alpha\gamma\dfrac{S_{c_1}I_{c_1}}{N_1},\end{cases} \tag{4.38}$$

where $i \in \{1, 2, \ldots, m\}$, $N_1 = S_{c_1} + I_{c_1}$, $N_2 = S_{c_2} + I_{c_2}$, and $N_1 + N_2 = N$. The total population, N, is constant, and the initial conditions are $S_{c_1}(0) = S_{c_{1,0}} > 0, S_{c_2}(0) = S_{c_{2,0}} > 0, I_{c_1}(0) = I_{c_{1,0}} > 0, I_{c_2}(0) = I_{c_{2,0}} > 0$. The flow of the model can be seen in Figure 4.1.

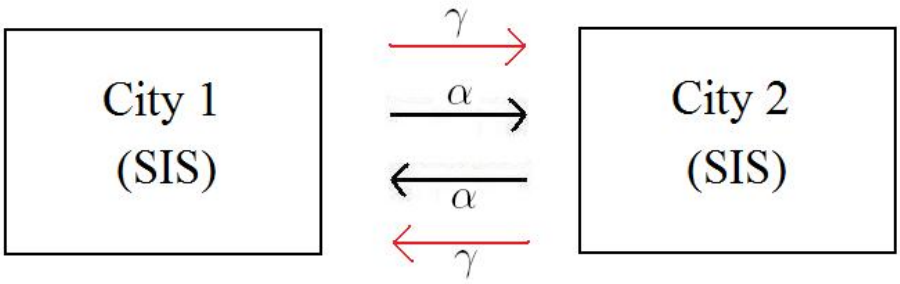

Figure 4.1: **Flow of Switched Multi-city System (4.38).**

The meaningful physical domain for this system is T_{SISI}. Because $0 \leq \gamma \leq 1$, it follows that

$$\alpha S_{c_j} - \alpha\gamma \frac{S_{c_j} I_{c_j}}{S_{c_j} + I_{c_j}} \geq 0.$$

This is reasonable physically since these terms represent the difference between the number of susceptible individuals travelling from city j and those being infected while travelling from city j. This requirement is also needed for the well-posedness of the system, observe that T_{SISI} is invariant because

$$\{\dot{S}_{c_1} + \dot{I}_{c_1} + \dot{S}_{c_2} + \dot{I}_{c_2}\} \,|_{S_{c_1}+I_{c_1}+S_{c_2}+I_{c_2}=N} = 0,$$

$$\dot{S}_{c_1} \,|_{S_{c_1}=0} = (\mu + g) I_{c_1} + \alpha S_{c_2} - \alpha\gamma \frac{S_{c_2} I_{c_2}}{N_2} \geq 0, \quad \dot{I}_{c_1} \,|_{I_{c_1}=0} = \alpha I_{c_2} + \alpha\gamma \frac{S_{c_2} I_{c_2}}{N_2} \geq 0,$$

$$\dot{S}_{c_2} \,|_{S_{c_2}=0} = (\mu + g) I_{c_2} + \alpha S_{c_1} - \alpha\gamma \frac{S_{c_1} I_{c_1}}{N_1} \geq 0, \quad \dot{I}_{c_2} \,|_{I_{c_2}=0} = \alpha I_{c_1} + \alpha\gamma \frac{S_{c_1} I_{c_1}}{N_1} \geq 0.$$

Consider the basic reproduction numbers, from the non-switched case [10]:

$$\mathcal{R}_i = \frac{\beta_i + \alpha\gamma}{\mu + g}. \tag{4.39}$$

There is a disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}_{c_1}, \bar{I}_{c_1}, \bar{S}_{c_2}, \bar{I}_{c_2}) = (N/2, 0, N/2, 0)$ that is common to all subsystems.

Theorem 4.8.2. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.38) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then the solution of system (4.38) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}.*

Proof.

Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}(I_{c_1} + I_{c_2})' &= \beta_{i_k}\left(\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} + \frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}}\right) - (g+\mu)(I_{c_1}+I_{c_2}) \\ &\quad + \alpha\gamma\left(\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} + \frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}}\right), \\ &\leq (\beta_{i_k} + \alpha\gamma - g - \mu)(I_{c_1}+I_{c_2}), \\ &= \lambda_{i_k}(I_{c_1}+I_{c_2}), \end{aligned} \tag{4.40}$$

where $\lambda_{i_k} := \beta_{i_k} + \alpha\gamma - g - \mu$. Then, by the proof of Theorem 3.1.2, beginning with equation (3.11), it follows that $I_{c_1} + I_{c_2} \leq (I_{c_1,0} + I_{c_2,0})\exp(-ct)$ for some $c > 0$. Since $I_{c_1}, I_{c_2} \geq 0$, the solution $\bar{\mathbf{Q}}$ is exponentially (I_{c_1}, I_{c_2})-stable in T_{SISI}. Then, I_{c_1} and I_{c_2} are converging to zero, and the limiting equations for S_{c_1} and S_{c_2} are

$$\begin{cases} \dot{S}_{c_1} = -\alpha S_{c_1} + \alpha S_{c_2}, \\ \dot{S}_{c_2} = -\alpha S_{c_2} + \alpha S_{c_1}. \end{cases} \tag{4.41}$$

From $S_{c_1} + S_{c_2} = N$, by inspection, S_{c_1} and S_{c_2}, both converge to $N/2$. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (4.38) in the meaningful domain T_{SISI}. If the switching signal is periodic, then it follows from the bound (4.40) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically (I_{c_1}, I_{c_2})-stable in the meaningful domain. □

One important remark is that it is possible for the disease to be endemic in both cities because of travelling infections, seen in the reproduction numbers (4.39) in the $\alpha\gamma$ term, and to be eradicated in the same scenario with a restriction on travelling infections ($\gamma = 0$). That is, the travelling infections alone can result in the disease being endemic. Further, if there are no travelling infections, the reproduction numbers are reduced to the ones for the previous multi-city model (4.35). If $\alpha = 0$, the cities are isolated and act as two separate switched SIS models, and hence the disease will spread in the same way as the switched SIS model (3.3) in both cities. This gives rise to the idea of controlling the spread of a disease by limiting travel and screening individuals, which will be discussed in Section 5.1.7.

Another factor which can affect the spread of a disease in a city is its media coverage. Motivated by a media coverage model for an SIS model found in [41], which is a good model for influenza [41], we incorporate media coverage into these switched multi-city models. Consider a model of two cities and assume that city 1 has a media coverage $c_1 > 0$, and that city 2 has media coverage $c_2 > 0$. Assume a standard incidence rate for horizontal transmission of the disease, with a reduced contact rate $\beta_i - c_1$ and $\beta_i - c_2$ in city 1 and city 2, respectively, due to the cities'

media coverage. Assume that the contact rates β_i satisfy $\beta_i \geq c_1$ and $\beta_i \geq c_2$ for all i, so that the media coverage cannot make the contact rate negative. The higher the media coverage number, the more efficient the city is at spreading knowledge of the disease, and hence the lower the contact rate with infected individuals.

Assume that susceptibles and infectives may travel between the two cities at two different rates. This is reasonable as the vital and epidemiological parameters may depend on the cities [72]. Assume individuals travel from city 1 to 2 at a rate α_1 and from city 2 to city 1 at a rate α_2. Assume a travelling contact rate of $0 \leq \gamma \leq 1$, and a standard incidence for travelling infections:

$$\gamma \frac{(\alpha_j S_{c_j})(\alpha_j I_{c_j})}{\alpha_j N_j} = \gamma \alpha_j \frac{S_{c_j} I_{c_j}}{S_{c_j} + I_{c_j}},$$

where α_j is the dispersal rate from city j. Furthermore, assume that the disease has infectious period $1/g_1$ in city 1, and $1/g_2$ in city 2. Assume that in city 1 the birth rate is $\mu_1 > 0$, which is equal to the death rate, and in city 2 the birth rate is $\mu_2 > 0$, which is again equal to the death rate. Then the switched multi-city model is:

$$\begin{aligned}
\dot{S}_{c_1} &= \mu_1 N_1 - (\beta_i - c_1)\frac{S_{c_1} I_{c_1}}{N_1} - \mu_1 S_{c_1} + g_1 I_{c_1} - \alpha_1 S_{c_1} + \alpha_2 S_{c_2} - \alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2}, \\
\dot{I}_{c_1} &= (\beta_i - c_1)\frac{S_{c_1} I_{c_1}}{N_1} - g_1 I_{c_1} - \mu_1 I_{c_1} - \alpha_1 I_{c_1} + \alpha_2 I_{c_2} + \alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2}, \\
\dot{S}_{c_2} &= \mu_2 N_2 - (\beta_i - c_2)\frac{S_{c_2} I_{c_2}}{N_2} - \mu_2 S_{c_2} + g_2 I_{c_2} - \alpha_2 S_{c_2} + \alpha_1 S_{c_1} - \alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1}, \\
\dot{I}_{c_2} &= (\beta_i - c_2)\frac{S_{c_2} I_{c_2}}{N_2} - g_2 I_{c_2} - \mu_2 I_{c_2} - \alpha_2 I_{c_2} + \alpha_1 I_{c_1} + \alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1},
\end{aligned} \tag{4.42}$$

where $i \in \{1, 2, \ldots, m\}$, $N_1 = S_{c_1} + I_{c_1}$, $N_2 = S_{c_2} + I_{c_2}$ and $N_1 + N_2 = N$. The total population, N, is constant and the initial conditions are $S_{c_1}(0) = S_{c_1,0} > 0, S_{c_2}(0) = S_{c_2,0} > 0, I_{c_1}(0) = I_{c_1,0} > 0, I_{c_2}(0) = I_{c_2,0} > 0$. The meaningful physical domain for this system is T_{SISI}. Since $0 \leq \gamma \leq 1$,

$$\alpha_j S_{c_j} - \gamma \alpha_j \frac{S_{c_j} I_{c_j}}{S_{c_j} + I_{c_j}} \geq 0,$$

and hence the model is well-posed:

$$\{\dot{S}_{c_1} + \dot{I}_{c_1} + \dot{S}_{c_2} + \dot{I}_{c_2}\} \,|_{S_{c_1} + I_{c_1} + S_{c_2} + I_{c_2} = N} = 0,$$

$$\dot{S}_{c_1} \,|_{S_{c_1}=0} = (\mu_1 + g_1) I_{c_1} + \alpha_2 S_{c_2} - \alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2} \geq 0, \quad \dot{I}_{c_1} \,|_{I_{c_1}=0} = \alpha_2 I_{c_2} + \alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2} \geq 0,$$

$$\dot{S}_{c_2} \,|_{S_{c_2}=0} = (\mu_2 + g_2) I_{c_2} + \alpha_1 S_{c_1} - \alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1} \geq 0, \quad \dot{I}_{c_2} \,|_{I_{c_2}=0} = \alpha_1 I_{c_1} + \alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1} \geq 0,$$

and hence the domain is invariant to the switched system (4.42). Define the non-physical basic reproduction numbers

$$\mathcal{R}_i^{non} = \frac{\beta_i - c_{\min} + \alpha_{\max} \gamma}{\mu_{\min} + g_{\min}}, \tag{4.43}$$

where $\alpha_{\max} = \max\{\alpha_1, \alpha_2\}$, $c_{\min} = \min\{c_1, c_2\}$, $\mu_{\min} = \min\{\mu_1, \mu_2\}$, and $g_{\min} = \min\{g_1, g_2\}$. There is a disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}_{c_1}, \bar{I}_{c_1}, \bar{S}_{c_2}, \bar{I}_{c_2}) = \left(\frac{\alpha_2}{\alpha_1+\alpha_2}N, 0, \frac{\alpha_1}{\alpha_1+\alpha_2}N, 0\right) \tag{4.44}$$

that is common to all subsystems. Since $S_{c_1} + I_{c_1} + S_{c_2} + I_{c_2} = N$, the system is intrinsically three-dimensional.

Theorem 4.8.3. *If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (4.42) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0$ then the solution of system (4.42) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically (I_{c_1}, I_{c_2})-stable, in the domain T_{SISI}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}
(I_{c_1} + I_{c_2})' &= (\beta_{i_k} - c_1)\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} + (\beta_{i_k} - c_2)\frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}} - (g_1+\mu_1)I_{c_1}, \\
&\quad - (g_2+\mu_2)I_{c_2} + \alpha_1\gamma\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} + \alpha_2\gamma\frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}}, \\
&\leq (\beta_{i_k} - c_{\min} + \alpha_{\max}\gamma - g_{\min} - \mu_{\min})(I_{c_1} + I_{c_2}), \\
&= \lambda_{i_k}(I_{c_1} + I_{c_2}),
\end{aligned} \tag{4.45}$$

where $\lambda_{i_k} := \beta_{i_k} - c_{\min} + \alpha_{\max}\gamma - g_{\min} - \mu_{\min}$. Then, by the proof of Theorem 3.1.2, we have that $I_{c_1} + I_{c_2} \leq (I_{c_1,0} + I_{c_2,0})\exp(-ct)$ for some $c > 0$. Since $I_{c_1}, I_{c_2} \geq 0$, the solution $\bar{\mathbf{Q}}$ is exponentially (I_{c_1}, I_{c_2})-stable in T_{SISI}. So, I_{c_1} and I_{c_2} are converging to zero, and the limiting equations for S_{c_1} and S_{c_2} are

$$\begin{cases} \dot{S}_{c_1} = -\alpha_1 S_{c_1} + \alpha_2 S_{c_2}, \\ \dot{S}_{c_2} = -\alpha_1 S_{c_2} + \alpha_2 S_{c_1}. \end{cases} \tag{4.46}$$

Then, since $S_{c_1} + S_{c_2} = N$, S_{c_1} and S_{c_2}, converge to

$$\bar{S}_{c_1} = \frac{\alpha_2}{\alpha_1+\alpha_2}N, \quad \bar{S}_{c_2} = \frac{\alpha_1}{\alpha_1+\alpha_2}N.$$

Hence, the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (4.42) is exponentially (I_{c_1}, I_{c_2})-stable in the meaningful domain T_{SISI}. If the switching signal is periodic, then it follows from the bound (4.45) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically (I_{c_1}, I_{c_2})-stable, in the meaningful domain. □

Notice since $c_1, c_2 > 0$, and if we take $g_1 = g_2 = g$, $\mu_1 = \mu_2 = \mu$, then the basic reproductions of this model (4.43) are less than the previous model without

media coverage (4.39). This is expected because the media coverage should help in eradicating the disease. It is important to remark that the reproduction numbers (4.43) are non-physical in the sense that they don't have a biological interpretation. Indeed, it is conjectured that these reproduction numbers are too restrictive, the disease does not actually spread this fast. Hence, even when $\langle \mathcal{R}_\sigma^{non} \rangle > 1$, it may be possible to achieve stability of the disease-free solution (see Figure 4.10).

Finally, consider a model with n different cities and assume the contact rate is $\beta_i > 0$ in all cities. Assume that susceptibles and infectives both travel from city j at a per capita rate α. Assume the disease has removal rate $g > 0$ and it does not confer immunity. Assume the birth rate and death rate are $\mu > 0$ for all individuals and assume that individuals travelling may get infected at a rate $0 \leq \gamma \leq 1$. Assume a standard incidence rate, as in the other switched transport models. Assume that individuals do not die, give birth or become removed while travelling. The switched model then is

$$
\begin{aligned}
\dot{S}_{c_1} &= \mu N_1 - \beta_i \frac{S_{c_1} I_{c_1}}{N_1} - \mu S_{c_1} + g I_{c_1} - \alpha S_{c_1} + \frac{\alpha}{n-1} \left[\sum_{j=2}^{n} S_{c_j} - \gamma \sum_{j=2}^{n} \frac{S_{c_j} I_{c_j}}{N_j} \right], \\
\dot{I}_{c_1} &= \beta_i \frac{S_{c_1} I_{c_1}}{N_1} - g I_{c_1} - \mu I_{c_1} - \alpha I_{c_1} + \frac{\alpha}{n-1} \left[\sum_{j=2}^{n} I_{c_j} + \gamma \sum_{j=2}^{n} \frac{S_{c_j} I_{c_j}}{N_j} \right], \\
\dot{S}_{c_2} &= \mu N_2 - \beta_i \frac{S_{c_2} I_{c_2}}{N_2} - \mu S_{c_2} + g I_{c_2} - \alpha S_{c_2} + \frac{\alpha}{n-1} \left[\sum_{\substack{j=1 \\ j \neq 2}}^{n} S_{c_j} - \gamma \sum_{\substack{j=1 \\ j \neq 2}}^{n} \frac{S_{c_j} I_{c_j}}{N_j} \right], \\
\dot{I}_{c_2} &= \beta_i \frac{S_{c_2} I_{c_2}}{N_2} - g I_{c_2} - \mu I_{c_2} - \alpha I_{c_2} + \frac{\alpha}{n-1} \left[\sum_{\substack{j=1 \\ j \neq 2}}^{n} I_{c_j} + \gamma \sum_{\substack{j=1 \\ j \neq 2}}^{n} \frac{S_{c_j} I_{c_j}}{N_j} \right], \\
&\vdots \\
\dot{S_{c_n}} &= \mu N_n - \beta_i \frac{S_{c_n} I_{c_n}}{N_n} - \mu S_{c_n} + g I_{c_n} - \alpha S_{c_n} + \frac{\alpha}{n-1} \left[\sum_{j=1}^{n-1} S_{c_j} - \gamma \sum_{j=1}^{n-1} \frac{S_{c_j} I_{c_j}}{N_j} \right], \\
\dot{I_{c_n}} &= \beta_i \frac{S_{c_n} I_{c_n}}{N_n} - g I_{c_n} - \mu I_{c_n} - \alpha I_{c_n} + \frac{\alpha}{n-1} \left[\sum_{j=1}^{n-1} I_{c_j} + \gamma \sum_{j=1}^{n-1} \frac{S_{c_j} I_{c_j}}{N_j} \right],
\end{aligned} \tag{4.47}
$$

where $i \in \{1, 2, \ldots, m\}$, $N_j = S_{c_j} + I_{c_j}$ and $\sum_{j=1}^{n} S_{c_j} + I_{c_j} = N$, with the total population N a constant. The initial conditions are $S_{c_j}(0) = S_{c_{j,0}} > 0, I_{c_j}(0) = I_{c_{j,0}} > 0$, for $j = 1, \ldots, n$. The meaningful physical domain for this system is

$$
T_{multi} = \left\{ (S_{c_1}, \ldots, S_n, I_{c_1}, \ldots, I_n) \in \mathbb{R}_+^{2n} | \sum_{j=1}^{n} S_{c_j} + I_{c_j} = N \right\}.
$$

Notice that

$$\left(\sum_{j=1}^{n} \dot{S}_{c_j} + \dot{I}_{c_j}\right) |_{\sum_{j=1}^{n} S_i + I_i = N} = 0,$$

$\dot{S}_{c_j} |_{S_{c_j}=0} \geq 0$ since $0 \leq \gamma \leq 1$, and $\dot{I}_{c_j} |_{I_{c_j}=0} \geq 0$, hence this domain is invariant to the switched system. For this model, define the basic reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i + \alpha\gamma}{\mu + g} \tag{4.48}$$

for each subsystem. There is a disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}_{c_1}, \ldots, \bar{S}_{c_n}, \bar{I}_{c_1}, \ldots, \bar{I}_{c_n}) = (N/n, \ldots, N/n, 0, \ldots, 0) \tag{4.49}$$

that is common to all subsystems. Notice that this system has intrinsic dimension $2n - 1$.

Theorem 4.8.4. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the disease will be eradicated in all cities of system (4.47). If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$ then, again, the disease will be eradicated in all cities of system (4.47).*

Proof.

Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}
\sum_{j=1}^{n} \dot{I}_{c_j} &= \beta_{i_k} \sum_{j=1}^{n} \frac{S_{c_j} I_{c_j}}{S_{c_j} + I_{c_j}} - (g + \mu) \sum_{j=1}^{n} I_{c_j} + \gamma \sum_{j=1}^{n} \alpha \frac{S_{c_j} I_{c_j}}{S_{c_j} + I_{c_j}}, \\
&\leq (\beta_{i_k} - g - \mu + \gamma\alpha) \sum_{j=1}^{n} I_{c_j}, \\
&= \lambda_{i_k} \sum_{j=1}^{n} I_{c_j},
\end{aligned} \tag{4.50}$$

where $\lambda_{i_k} := \beta_{i_k} - g - \mu + \gamma\alpha$. Then, by the proof of Theorem 3.1.2, and since $I_{c_j} \geq 0$ for all j, it follows that I_{c_j} converges to zero for all $j = 1, 2, \ldots, n$. If the switching signal is periodic, then it follows from the bound (4.50) and the proof of Theorem 3.1.5 that the infectives converge to zero in the meaningful domain. □

4.9 Persistence of the Disease

As discussed in Section 4.1, when the reproduction numbers are above one for systems that are intrinsically at least two-dimensional, the solution will approach the endemic equilibriums with damped oscillations. This stems from the non-switched case and was discussed earlier in Section 2.2. The following conjecture is made on the endemicity of the disease for switched models in this chapter.

Conjecture 4.9.1. *For any model in this chapter with physically meaningful reproduction numbers and for any switching signal $\sigma \in \mathcal{S}$ such that $\langle \mathcal{R}_\sigma \rangle > 1$, the disease is persistent, that is there exists a positive constant $\eta > 0$ (independent of I_0) such that every solution with $I(0) = I_0 > 0$ satisfies*

$$\liminf_{t\to\infty} I(t) \geq \eta.$$

4.10 Simulations

For the switching rule in these simulations, motivated by practical applications, we use

$$\sigma(t) = \begin{cases} 1 & \text{during winter,} \\ 2 & \text{otherwise,} \end{cases} \tag{4.51}$$

as in Section 3.5. The variables in these simulations are normalized by total population, the initial condition is taken to be $t_0 = 0$, and the units are non-dimensional. The initial conditions are $S_0 = 0.75$, $I_0 = 0.25$, $R_0 = 0$, unless otherwise specified.

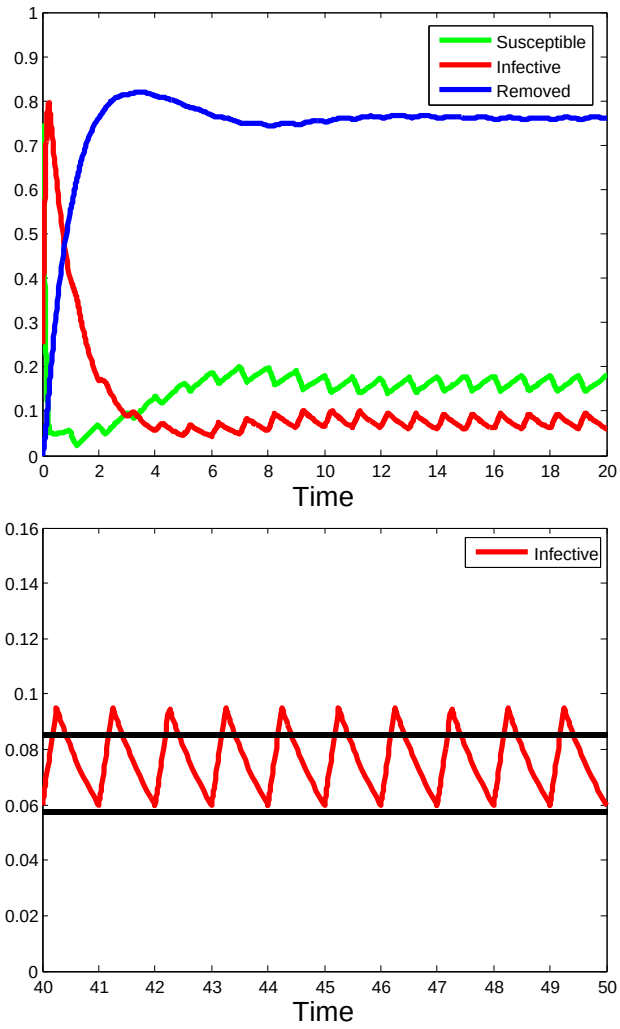

Figure 4.2: **Switched SIR System (4.1).** Motivated by the measles parameters of [66], which give relatively high reproduction numbers, use the parameters $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$. This implies $\langle \mathcal{R}_\sigma \rangle = 6.136$ for t large. Though the solution is not contained between the endemic minimum and maximum, $I_{\min} = 0.0576$ and $I_{\max} = 0.0854$, it is clear that the solution is persistent.

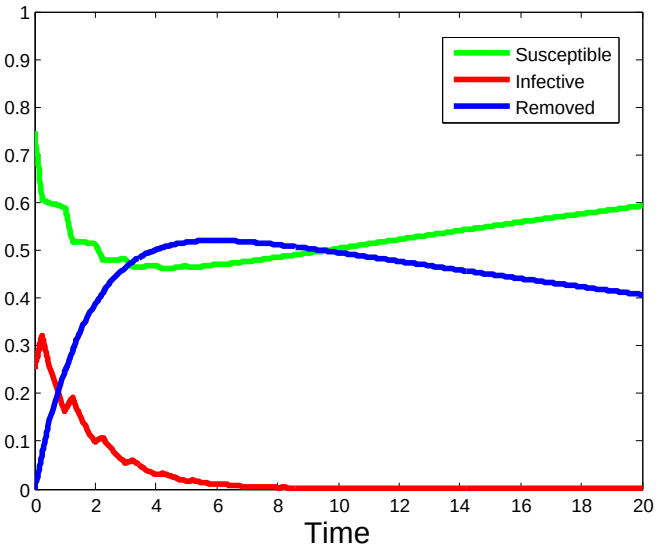

Figure 4.3: **Switched SIR System (4.1).** The parameters used here are $\beta_1 = 3$, $\beta_2 = 0.2$, $g = 1$, $\mu = 0.02$. These give $\mathcal{R}_1 = 2.941$, $\mathcal{R}_2 = 0.196$ and thus $\langle \mathcal{R}_\sigma \rangle = 0.882$ for large t. The disease is eradicated by Theorem 4.1.1

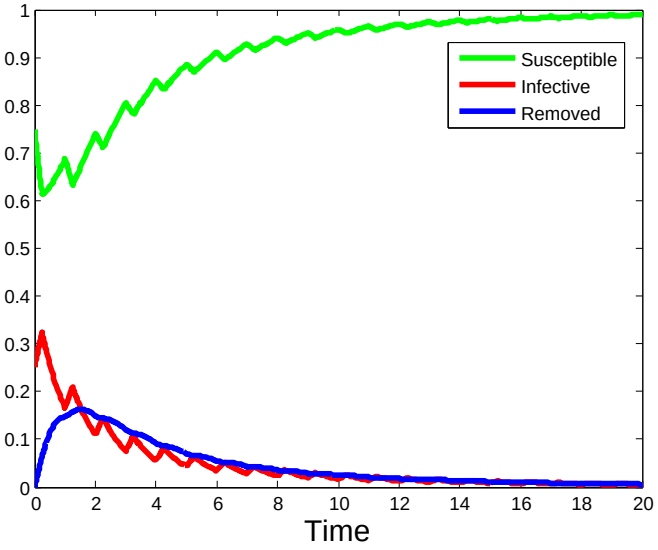

Figure 4.4: **Switched SIRS System (4.12).** Parameters are $\beta_1 = 3$, $\beta_2 = 0.2$, $g = 1$, $\mu = 0.02$, $\theta = 1$ and hence $\langle \mathcal{R}_\sigma \rangle = 0.882$ for t large, and the disease is eradicated by Theorem 4.4.1. Comparing this figure with Figure 4.3 of the switched SIR simulation with the same parameters, it seems as though it takes longer for the disease to die out, even though the susceptible population seems to converge to one faster. Physically, as the removed class moves back into the susceptible class due to the temporary immunity, this leads to more susceptibles for the infectives to infect.

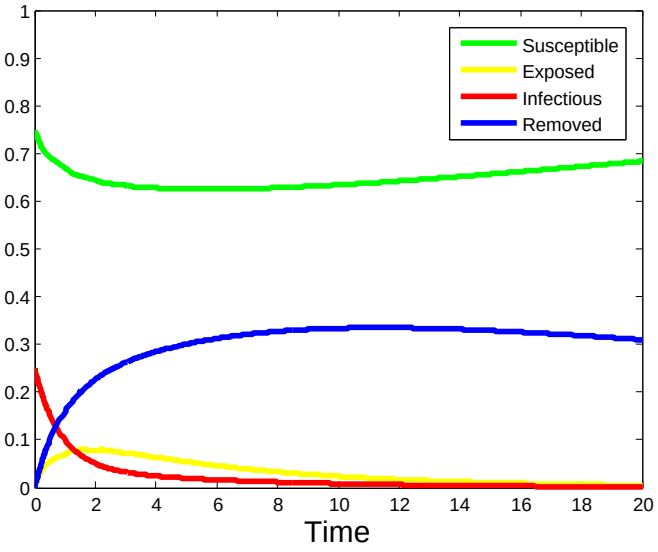

Figure 4.5: **Switched SEIR System (4.17).** Here $1/a = 1/0.3$ for the latent period from [49], with other parameters $\beta_1 = 1$, $\beta_2 = 0.6$, $a = 0.3$, $g = 1$, $\mu = 0.02$. Initial conditions are $S_0 = 0.75$, $I_0 = 0.25$, $E_0 = 0$, $R_0 = 0$. Hence, $\mathcal{R}_1 = 0.919$ and $\mathcal{R}_2 = 0.551$, then by Theorem 4.6.1, the solution converges to the disease-free equilibrium.

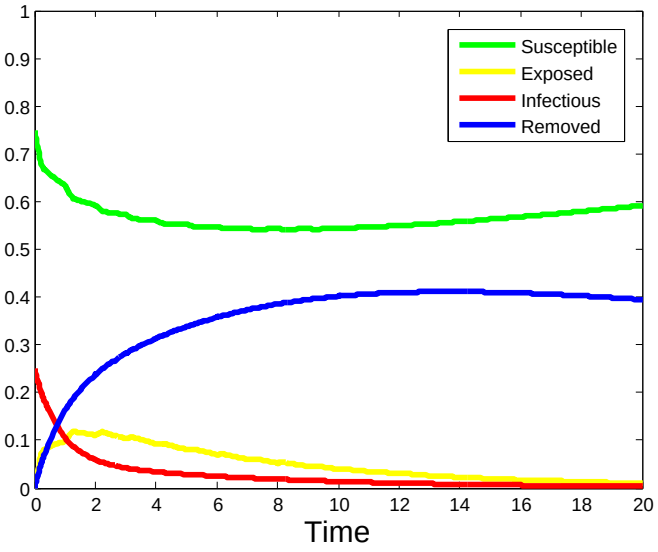

Figure 4.6: **Switched SEIR System (4.17).** Here $1/a = 1/0.3$ for the latent period from [49], with other parameters $\beta_1 = 2$, $\beta_2 = 0.6$, $a = 0.3$, $g = 1$, $\mu = 0.02$. Initial conditions are $S_0 = 0.75$, $I_0 = 0.25$, $E_0 = 0$, $R_0 = 0$. Hence, $\mathcal{R}_1 = 1.838$ and $\mathcal{R}_2 = 0.551$, which implies $\langle \mathcal{R}_\sigma \rangle = 0.873$ for t large. Hence, we can conject that $\langle \mathcal{R}_\sigma \rangle < 1$ is a sufficient condition for the eradication of the disease.

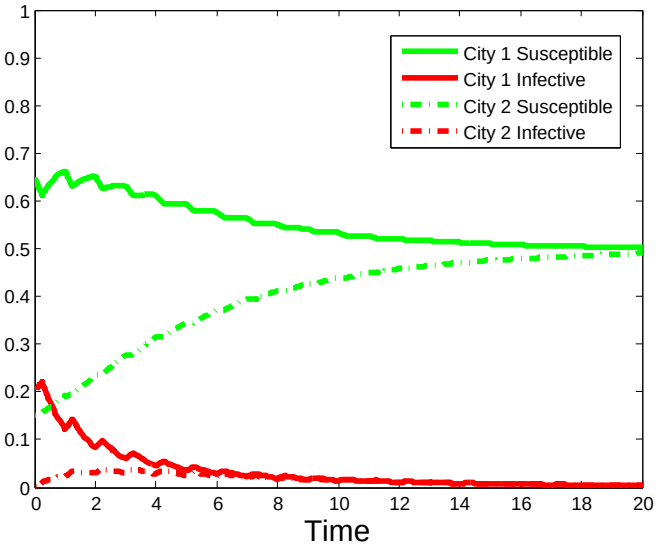

Figure 4.7: **Multi-city Switched System (4.38).** Parameters are $\beta_1 = 2$, $\beta_2 = 0.4$, $g = 1$, $\mu = 0.02$ and the transport parameters are $\alpha = 0.1$ and $\gamma = 1$, similar to the ones from [10]. In this case, we have normalized the variables by the total population, since it is a constant, and the initial conditions are $S_{1_0} = 0.65$, $I_{1_0} = 0.2$, $S_{2_0} = 0.15$, $I_{2_0} = 0$. From the parameters, $\langle \mathcal{R}_\sigma \rangle = 0.882$ for t large, and the solution converges to $S_1 = S_2 = 0.5$, $I_1 = I_2 = 0$ by Theorem 4.8.2.

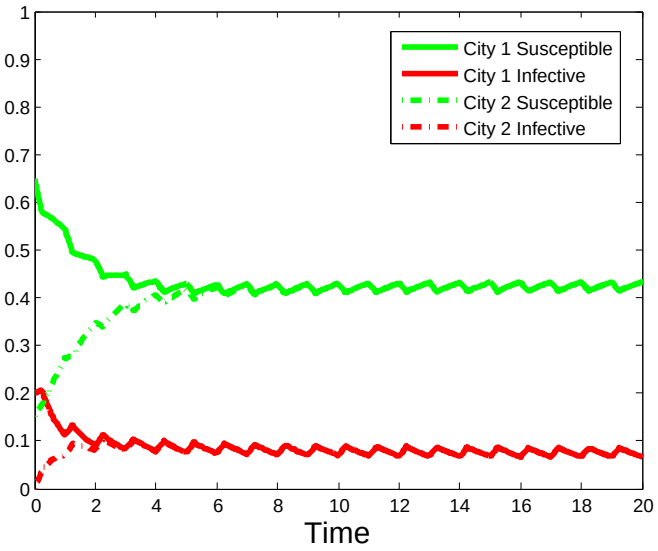

Figure 4.8: **Multi-city Switched System (4.38).** Same parameters as Figure 4.7 only now $\alpha = 0.4$, that is, individuals are travelling at a higher rate. Because of this, we have $\langle \mathcal{R}_\sigma \rangle = 1.176$, for t large, and we see the disease persists. Notice that if travel was restricted, $\alpha = 0$, then the time average of the reproduction numbers would drop to $\langle \mathcal{R}_\sigma \rangle = 0.784$ for t large and the disease would be eradicated in both cities.

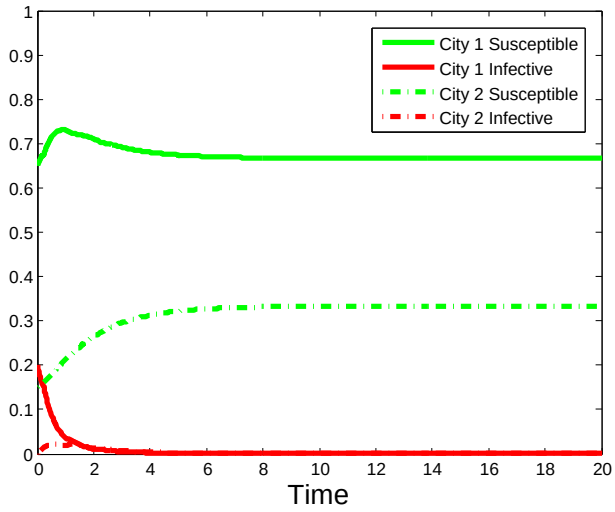

Figure 4.9: **Multi-city Switched System (4.42).** The variables have been normalized by the total population, which is constant, and the initial conditions are $S_{1_0} = 0.65$, $I_{1_0} = 0.2$, $S_{2_0} = 0.15$, $I_{2_0} = 0$. For city 1: $\mu_1 = 0.02$, $g_1 = 2$, $\alpha_1 = 0.2$, and $c_1 = 0.3$. For city 2: $\mu_2 = 0.05$, $g_2 = 1$, $\alpha_2 = 0.4$, and $c_2 = 0.1$. In both cities $\beta_1 = 1.5$, $\beta_2 = 0.4$, and $\gamma = 1$. We see the media coverage, life expectancy and removal rates are all better in city 1, and, more people want to travel from city 2 to city 1. Here $\langle \mathcal{R}_\sigma^{non} \rangle = 0.956$ for t large, the infectives drop to zero in both cities and $S_1 \to 2/3$, $S_2 \to 1/3$ by Theorem 4.8.3.

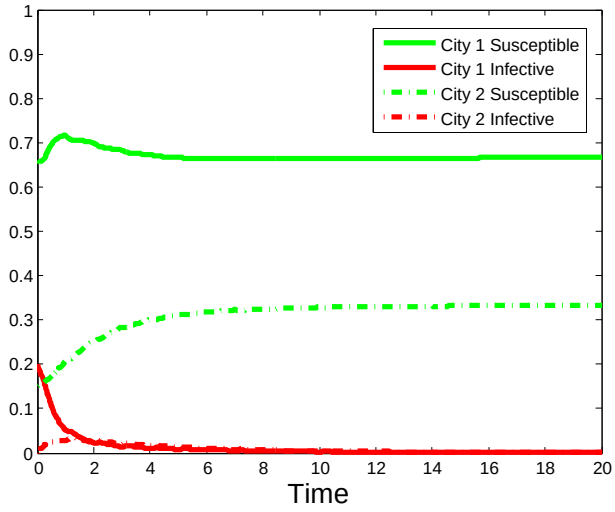

Figure 4.10: **Multi-city Switched System (4.42).** Same parameters as Figure 4.9 only now $\beta_1 = 2$, $\beta_2 = 0.8$, and hence $\langle \mathcal{R}_\sigma^{non} \rangle = 1.373$ for large t. This illustrates the fact that since the reproduction numbers are non-physical, they are indeed too strict in this case, as we can see the disease is eradicated in both cities and $S_1 \to 2/3$, $S_2 \to 1/3$.

Chapter 5

Control Schemes Applied to Switched Epidemiological Models

As outlined in Section 2.2, control strategies are extremely important in epidemiology as practical applications. Indeed, control schemes can eradicate diseases which are otherwise persistent. In this chapter, both constant and pulse control schemes with contact rate switching will be introduced, analyzed, and discussed. In Section 5.1, constant control schemes are investigated. The schemes include constant vaccination of newborns (Section 5.1.1), constant vaccination of a portion of susceptibles (Section 5.1.2), constant treatment of infectives (Section 5.1.3), constant treatment of infectives with waning immunity (Section 5.1.4), constant vaccination with progressive immunity (Section 5.1.5), constant treatment of infectives with progressive immunity (Section 5.1.6), and finally a screening process applied to a multi-city transport model (Section 5.1.7). In Section 5.2, pulse control strategies are studied. The pulse schemes considered are pulse treatment (Section 5.2.1), pulse vaccination (Section 5.2.2), pulse vaccination with vaccine failure (Section 5.2.3), and finally a pulse vaccination with a reduced infective class (Section 5.2.4). Simulations are presented in Section 5.3.

5.1 Constant Control Schemes

5.1.1 Switched SIR with Constant Vaccination of Newborns

Introduce switching into the SIR model with constant vaccination of newborns (2.30). Here, a fraction $0 \leq p \leq 1$ of the newborns are continuously vaccinated and removed from the population. This model also assumes that the permanent immunity acquired through vaccination is the same as the natural immunity obtained from infected individuals eliminating the disease naturally. Add switching by approximating the contact rate by a piecewise constant. More specifically, assume it is approximated by the values $\beta_1, \ldots, \beta_m > 0$, which follow a switching rule

$\sigma = \sigma(t) : \mathbb{R}_+ \to \{1, 2, \ldots, m\}$, where $\sigma \in \mathcal{S}$ is a piecewise continuous function. Then the switched model with constant control is:

$$\begin{cases} \dot{S} = \mu(1-p) - \beta_i SI - \mu S, \\ \dot{I} = \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R + p\mu, \end{cases} \tag{5.1}$$

with $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, $i \in \{1, \ldots, m\}$ and the total population is constant. One of the main benefits of this model is that it is straightforward to implement: simply vaccinate a portion p of all susceptible newborns. The method's main drawback is that it can be very expensive as the portion of newborns required to be vaccinated can be very high (recall from 2.2.4). The meaningful physical domain for this system is

$$\Omega_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ |\ S + I + R = 1\}.$$

Notice that

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

$\dot{S}\,|_{S=0} = \mu(1-p) \geq 0$, $\dot{I}\,|_{I=0} = 0$, and $\dot{R}\,|_{R=0} = gI + p\mu \geq 0$, hence this domain is invariant. The constant vaccination appears in the μp terms, in the limit $p = 0$, the model becomes the normal non-vaccinating switched SIR model (4.1). Define the basic reproduction numbers

$$\mathcal{R}_i^p = \frac{\beta_i}{\mu + g}(1-p) \tag{5.2}$$

for each subsystem. The superscript p indicates that the reproduction numbers are associated with a particular control scheme. Observe that $\mathcal{R}_i^p \leq \mathcal{R}_i = \beta_i/(\mu + g)$ from the switched SIR system (4.2) without vaccination. Equality is only achieved in the limit $p = 0$, that is, when there is no vaccination. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1-p, 0, p)$ that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*, R_i^*) = \left(\frac{\mu + g}{\beta_i}, \frac{\mu}{\beta_i}(\mathcal{R}_i^p - 1), \frac{g}{\beta_i}(\mathcal{R}_i^p - 1) + p \right). \tag{5.3}$$

Recall from Section 2.2.4 that the linear change of variables, $S = \hat{S}(1-p), I = \hat{I}(1-p), R = \hat{R}(1-p) + p$, transforms this model into the switched SIR model (4.1) with contact rates $\beta_i(1-p)$ instead of β_i. Hence, we make the following conjecture.

Conjecture 5.1.1. *If $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.1) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.1) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Notice that, as in the non-switched case (see Section 2.2.4), the constraint $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ implicitly defines a critical vaccination portion $p > p_{\text{crit}}$ that must be achieved for eradication, where

$$p_{\text{crit}} := 1 - \frac{1 - \epsilon}{\langle \mathcal{R}_\sigma \rangle},$$

with $\mathcal{R}_\sigma = \beta_\sigma/(\mu + g)$ from the unvaccinated switched SIR model (4.2). Due to the efficacy of different vaccinations, this critical value may be unrealistically high, as discussed in Section 2.2.4.

5.1.2 Switched SIR Model with Constant Vaccination of Susceptibles

Consider the control technique of constant vaccination of susceptibles. In this scheme a fraction $0 \leq p \leq 1$ of the entire susceptible population, not just the newborns, is being continuously vaccinated. Assume that the permanent immunity acquired through vaccination is the same as the natural immunity obtained from infected individuals defeating the disease. Apply this to the switched SIR model (4.1):

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S - pS, \\ \dot{I} = \beta_i SI - gI - \mu I, \\ \dot{R} = gI - \mu R + pS, \end{cases} \tag{5.4}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and the total population is constant. The meaningful physical domain for this system is Ω_{SIR}. Notice that $\{\dot{S} + \dot{I} + \dot{R}\}\,|_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$ and $\dot{R}\,|_{R=0} = gI + pS > 0$, hence this domain is invariant to each subsystem. For this model, define the basic reproduction numbers (from non-switched case [73]):

$$\mathcal{R}_i^p = \frac{\beta_i}{\mu + g} \frac{\mu}{\mu + p} \tag{5.5}$$

for each subsystem. There is a single disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = \left(\frac{\mu}{\mu + p}, 0, \frac{p}{\mu + p} \right) \tag{5.6}$$

that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\begin{aligned} \mathbf{Q}_\mathbf{i}^* &= (S_i^*, I_i^*, R_i^*), \\ &= \left(\frac{\mu + g}{\beta_i}, \frac{\mu}{\mu + g} \left(1 - \frac{1}{\mathcal{R}_i^p} \right), \frac{\mu}{\mu + g} \left(1 - \frac{1}{\mathcal{R}_i^p} \right) + \frac{p}{\mu} \frac{\mu + g}{\beta_i} \right). \end{aligned} \tag{5.7}$$

Observe that $\mathcal{R}_i^p \leq \mathcal{R}_i$ from the non-vaccinated switched SIR system (4.1) again, as expected.

Conjecture 5.1.2. *If $\langle \mathcal{R}_\sigma^p \rangle < 1-\epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.4) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.4) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Comparing this model to the constant vaccination of newborns model with switching (5.1), it is apparent that instead of constantly vaccinating a portion of newborns, a portion of the entire susceptible population is now being continuously vaccinated. Since the natural birth rate μ is usually very small, the fraction μp of newborns being continuously vaccinated in (5.1) will be small, whereas in this model, a larger group of susceptibles can be continuously vaccinated in this model because it is a portion of the entire susceptible population, pS. Due to this, we expect that this model should require a smaller value of p to achieve eradication (see the simulations in Section 5.3). Furthermore, the requirement $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ implicitly defines a critical vaccination portion $p > p_{\text{crit}}$, which we expect will result in disease eradication, where

$$p_{\text{crit}} := (\langle \mathcal{R}_\sigma \rangle - 1)\left(\frac{\mu}{1-\epsilon}\right),$$

with $\mathcal{R}_i = \beta_i/(\mu + g)$ from the unvaccinated switched SIR model (4.2).

5.1.3 Switched SIR Model with Constant Treatment of Infectives

Consider the control technique of constantly treating (curing) a fraction $0 \leq p \leq 1$ of infected individuals. Assume that when they are treated, they are immediately cured with permanent immunity and hence are moved to the removed class R. Apply this to the switched SIR model (4.1):

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S, \\ \dot{I} = \beta_i SI - gI - \mu I - pI, \\ \dot{R} = gI - \mu R + pI, \end{cases} \tag{5.8}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and the total population is constant. The pI terms represent the constant treatment of infectives. The meaningful physical domain for this system is Ω_{SIR}. Notice that $\{\dot{S} + \dot{I} + \dot{R}\}|_{S+I+R=1} = 0$, $\dot{S}|_{S=0} = \mu \geq 0$, $\dot{I}|_{I=0} = 0$ and $\dot{R}|_{R=0} = gI + pI \geq 0$, hence this domain is invariant to each subsystem. For this model, define the basic reproduction numbers

$$\mathcal{R}_i^p = \frac{\beta_i}{\mu + g + p} \tag{5.9}$$

for each subsystem. Here $\mathcal{R}_i^p \leq \mathcal{R}_i$ from the non-vaccination system (4.1). There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*, R_i^*) = \left(\frac{1}{\mathcal{R}_i^p}, \frac{\mu}{\beta_i}(\mathcal{R}_i^p - 1), \frac{g+p}{\beta_i}(\mathcal{R}_i^p - 1) \right). \tag{5.10}$$

If $\mathcal{R}_1^p, \ldots, \mathcal{R}_m^p \leq 1$, then $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$, hence, the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ and the disease will be eradicated.

Theorem 5.1.3. *If $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.8) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.8) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \mu I - gI - pI \leq (\beta_{i_k} - \mu - g - p)I = \lambda_{i_k} I, \tag{5.11}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g - p$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence the disease-free solution $\bar{\mathbf{Q}}$ is exponentially I-stable. Then, by inspection of system (5.8) with $I = 0$, R and S, converge to zero and one, respectively. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. If the switching signal is periodic, then it follows from the bound (5.11) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

Mathematically, this model is simpler to analyze than the constant vaccination models discussed in the previous two sections, (5.1) and (5.4), because the treatment is being applied to the infected population directly. Practically, this model has a drawback that it may be more difficult to implement, as it might not be straightforward to identify the infected individuals and treat them directly. It could also be expensive, and unrealistic to implement (see simulations). As before, the constraint $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ implicitly defines a critical treatment portion $p > p_{\text{crit}}$ in order to achieve eradication, where

$$p_{\text{crit}} := \frac{\langle \beta_\sigma \rangle}{1 - \epsilon} - \mu - g. \tag{5.12}$$

5.1.4 Switched SIR Model with Constant Treatment of Infectives and Waning Immunity

Consider again the control scheme of constant treatment applied to a switched SIR model (5.8). Suppose that the immunity, gained naturally or from the treatment

process, is temporary. Assume the immunity has waning rate $\theta > 0$, hence the immune period is $1/\theta > 0$. Then the model now is

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S + \theta R, \\ \dot{I} = \beta_i SI - gI - \mu I - pI, \\ \dot{R} = gI + pI - \mu R - \theta R, \end{cases} \tag{5.13}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0$, and the total population is constant. The meaningful physical domain for this system is Ω_{SIR}. Notice that $\{\dot{S} + \dot{I} + \dot{R}\}\,|_{S+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu + \theta R > 0$, $\dot{I}\,|_{I=0} = 0$ and $\dot{R}\,|_{R=0} = gI + pI \geq 0$, hence this domain is invariant. Define the basic reproduction numbers

$$\mathcal{R}_i^p = \frac{\beta_i}{\mu + g + p} \tag{5.14}$$

for each subsystem. These reproduction numbers are the same as for the switched constant treatment model (5.9), as the disease will still spread at the same rate with or without temporary immunity. There is a single disease-free equilibrium point $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1, 0, 0)$ that is common to all subsystems. Further, each subsystem also has an endemic equilibrium

$$\begin{aligned} \mathbf{Q_i^*} &= (S_i^*, I_i^*, R_i^*), \\ &= \left(\frac{1}{\mathcal{R}_i^p}, \frac{\mu + \theta}{\mu + g + p + \theta} \left(1 - \frac{1}{\mathcal{R}_i^p} \right), \frac{g + p}{\mu + g + p + \theta} \left(1 - \frac{1}{\mathcal{R}_i^p} \right) \right). \end{aligned} \tag{5.15}$$

If $\mathcal{R}_1^p, \ldots, \mathcal{R}_m^p \leq 1$, then $I' < 0$ in Ω_{SIR} unless $I = 0$ or $S = 1$, hence, the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ and the disease will be eradicated.

Theorem 5.1.4. *If $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.13) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.13) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{i_k} SI - \mu I - gI - pI \leq (\beta_{i_k} - \mu - g - p)I = \lambda_{i_k} I, \tag{5.16}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g - p$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence $\bar{\mathbf{Q}}$ is exponentially I-stable. Then, by inspection of system (5.13) with $I = 0$, R and S, converge to zero and one, respectively. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the domain domain Ω_{SIR}. If the switching signal is periodic, then it follows from the bound (5.16) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

Notice that even with waning immunity, the same critical treatment rate is required. That is, the critical treatment portion for this model $p > p_{\text{crit}}$ is the same as for the critical treatment level for the treatment model without waning immunity (5.12). The difference between the constant treatment with and without waning immunity is that the endemic level I_i^* for waning immunity (5.15) is higher than the corresponding endemic infective level I_i^* without waning immunity (5.10) from the system without waning immunity. We should also expect that the convergence rate will be different between these two systems, more specifically, that the disease will be eradicated faster in the constant treatment model without waning immunity (5.8) compared to the model with waning immunity (5.13).

5.1.5 Switched SIR Model with Constant Vaccination and Progressive Immunity

The constant vaccination or treatment models discussed so far have assumed that as soon as individuals begin either the treatment or vaccination process, they are immediately vaccinated or cured. These models have ignored the time it takes for individuals to obtain immunity by completing a vaccination or treatment process. In constrast to this, consider the usual proposed vaccination schedule for hepatitis B: individuals are vaccinated immediately, then again in one month, then a third time in 6 months [47]. Usually $30-50\%$ of individuals will gain anti-HB antibodies after the first dose, $80-90\%$ will gain them after the second dose, and virtually all the individuals will have them one month after the last dose [47]. The anti-HB antibdody concentrations may decline slowly, but will stay at effective levels for protection possibly for more than 10 years [47].

Motivated by the above discussion, instead of assuming that individuals who are vaccinated gain immunity immediately, assume they begin the vaccination process in a class V, and take time to complete the program to gain immunity and enter the removed class R. Begin from a basic SIR model (2.16) and suppose that susceptible individuals begin the vaccination process at a constant rate $0 \leq p \leq 1$. Suppose the mean period of vaccine-induced immunity is $1/\gamma$ before the vaccinated susceptibles acquire permanent immunity, hence they move into the removed class at an average rate of $\gamma > 0$. Introduce switching into the model by assuming that while they are in the vaccinated class, individuals can still possibly contract the disease and do so at the rate $\beta_{2i} > 0$. Assume that susceptible individuals normally contract the disease with contact rate $\beta_{1i} > 0$ and standard incidence rate. Then, reasonably assume that $\beta_{2i} < \beta_{1i}$ for all i, since the individuals being vaccinated may have partial immunity during the vaccination process [47]. The efficacy of the vaccine will determine the values β_{2i} and γ, the better the vaccine, the lower the partially immune contact rates β_{2i} and the faster the vaccination process is, hence the higher the value of γ. This model was based on the non-switched version from [47], which is a good model for diseases such as hepatitis B and measles [47]. In model, we use the notation $SVIR$ for the model instead of $SIRV$, because of the flow of

the model: the susceptibles flow into both the vaccinated and infective class, the vaccinated flows into the infective class and removed class and the infected class flows into the removed class. With switching, the model is

$$\begin{cases} \dot{S} = \mu - \beta_{1i} SI - \mu S - pS, \\ \dot{V} = pS - \beta_{2i} VI - \gamma V - \mu V, \\ \dot{I} = \beta_{1i} SI + \beta_{2i} VI - gI - \mu I, \\ \dot{R} = gI + \gamma V - \mu R, \end{cases} \tag{5.17}$$

with $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $V(0) = V_0$, $R(0) = R_0$, $i \in \{1, \ldots, m\}$ and the total population is constant. Often it is assumed that $V_0 = 0$. The meaningful physical domain for this system is

$$\Omega_{SVIR} = \{(S, V, I, R) \in \mathbb{R}^4_+ |\ S + V + I + R = 1\}.$$

Notice that

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

$\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$, $\dot{V}\,|_{V=0} = pS \geq 0$ and $\dot{R}\,|_{R=0} = gI + \gamma V \geq 0$, hence this domain is invariant to each subsystem. For this model, define the basic reproduction numbers for each subsystem [47],

$$\mathcal{R}_i^p = \frac{\beta_{1i}\mu}{(\mu + g)(\mu + p)} + \frac{\beta_{2i} p \mu}{(\mu + \gamma)(\mu + g)(\mu + p)} \tag{5.18}$$

Notice that as the efficacy of the vaccine goes up, and hence β_{2i} goes down or γ goes up, in the limit as $\beta_{2i} \to 0$ or $\gamma \to \infty$, the reproduction numbers will approach the reproduction numbers of the SIR model with constant vaccination of susceptibles (5.4). However, it is noted in [47] that it is much more difficult to increase the efficacy of the vaccine as compared to controlling the vaccination rate p. There is a single disease-free equilibrium point [47],

$$\bar{\mathbf{Q}} = (\bar{S}, \bar{V}, \bar{I}, \bar{R}) = \left(\frac{\mu}{\mu + p}, \frac{p\mu}{(\mu + \gamma)(\mu + p)}, 0, \frac{p\gamma}{(\mu + \gamma)(\mu + p)} \right) \tag{5.19}$$

that is common to all subsystems. Further, if $\mathcal{R}_i^p > 1$ then the subsystem i also has an endemic equilibrium $\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*, R_i^*, V_i^*)$, where I_i^* is the positive root of $g(I) = A_1 I^2 + A_2 I + A_3(1 - \mathcal{R}_i)$ [47], with

$$\begin{aligned} A_1 &= (\mu + g)\beta_{1i}\beta_{2i} > 0, \\ A_2 &= (\mu + g)[(\mu + p)\beta_{2i} + (\mu + \gamma)\beta_{1i}] - \beta_{2i}\beta_{1i}\mu, \\ A_3 &= (\mu + g)(\mu + p)(\mu + \gamma) > 0, \end{aligned}$$

and

$$\begin{aligned} S_i^* &= \frac{\mu}{\mu + p + \beta_{1i} I_i^*}, \\ V_i^* &= \frac{p\mu}{(\mu + p + \beta_{1i} I_i^*)(\mu + \gamma + \beta_{2i} I_i^*)} \\ R_i^* &= 1 - S_i^* - I_i^* - V_i^*. \end{aligned}$$

Conjecture 5.1.5. *If $\langle \mathcal{R}_\sigma^p \rangle < 1-\epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.17) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SVIR}. If the switching rule is periodic $\sigma \in \mathcal{S}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.17) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SVIR}.*

The constraint $\langle \mathcal{R}_\sigma^p \rangle < 1-\epsilon$ implicitly defines a critical vaccination level $p > p_{\text{crit}}$ that must be achieved in order for the disease to be eradicated by the control scheme. Define another basic reproduction number for each subsystem:

$$\mathcal{R}_i^{non} = \frac{\beta_{1i} + \beta_{2i}}{\mu + g}.$$

Notice that these reproduction numbers do not consider the vaccination rate p, and further, $\mathcal{R}_i^{non} \geq \mathcal{R}_i^p$ for all i. Hence, this is a stricter assumption of how quickly the disease will spread; based on the actual structure of the system, the disease should spread slower than this.

Theorem 5.1.6. *If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and $\sigma \in \mathcal{S}$, then the solution of system (5.17) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SVIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0$ then the solution of system (5.17) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SVIR}.*

Proof. Let i_k follow the dwell-time switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{1i_k} SI + \beta_{2i_k} VI - gI - \mu I \leq (\beta_{1i_k} + \beta_{2i_k} - \mu - g)I = \lambda_{i_k} I, \tag{5.20}$$

where $\lambda_{i_k} := \beta_{1i_k} + \beta_{2i_k} - \mu - g$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence $\bar{\mathbf{Q}}$ is exponentially I-stable. Then, the limiting equation for S is $S' = \mu - \mu S - pS$, which, by inspection, converges to $\bar{S}$. Further, the equation for V becomes $V' = p\bar{S} - \gamma V - \mu V$, and hence V converges to $\bar{V}$. Finally, using $R = 1 - S - I - V$, it is clear that R converges to $\bar{R}$. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in Ω_{SVIR}. If the switching signal is periodic, then it follows from the bound (5.20) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

5.1.6 Switched SIR Model with Constant Treatment and Progressive Immunity

Consider again the progessively immune switched $SVIR$ model (5.17), but now consider the constant treatment of infectives at a rate $0 \leq p \leq 1$, instead of constant

vaccination of susceptibles. Assume that infected individuals enter a treatment process, which takes on average $1/\gamma$, and while they are in this process they are able to be infected at a reduced rate $\beta_{2i} < \beta_{1i}$, as before. Then the switched model is,

$$\begin{cases} \dot{S} = \mu - \beta_{1i} SI - \mu S, \\ \dot{V} = pI - \beta_{2i} VI - \gamma V - \mu V, \\ \dot{I} = \beta_{1i} SI + \beta_{2i} VI - gI - \mu I - pI, \\ \dot{R} = gI + \gamma V - \mu R, \end{cases} \tag{5.21}$$

with $i \in \{1, 2, \ldots, m\}$, $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $V(0) = 0$, $R(0) = R_0$, and the total population is constant. Again, this model requires explicit knowledge of the infected individuals in the population. The meaningful physical domain for this system is Ω_{SVIR}. Notice that $\{\dot{S} + \dot{V} + \dot{I} + \dot{R}\}\,|_{S+V+I+R=1} = 0$, $\dot{S}\,|_{S=0} = \mu > 0$, $\dot{I}\,|_{I=0} = 0$, $\dot{R}\,|_{R=0} = gI + \gamma V \geq 0$ and $\dot{V}\,|_{V=0} = pI \geq 0$ hence this domain is invariant. For this model, define the basic reproduction numbers for each subsystem,

$$\mathcal{R}_i^p = \frac{\beta_{1i} + \beta_{2i}}{(\mu + g + p)}. \tag{5.22}$$

There is a single disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}, \bar{V}, \bar{I}, \bar{R}) = (1, 0, 0, 0) \tag{5.23}$$

that is common to all subsystems. If $\mathcal{R}_1^p, \ldots, \mathcal{R}_m^p < 1$, then $I' < 0$ in Ω_{SVIR} unless $I = 0$, hence, the disease will be eradicated.

Theorem 5.1.7. *If $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.21) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SVIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^p - 1)\tau_1 + \ldots + (\mathcal{R}_m^p - 1)\tau_m < 0$ then the solution of system (5.21) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SVIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \beta_{1i_k} SI + \beta_{2i_k} VI - gI - \mu I - pI \leq (\beta_{1i_k} + \beta_{2i_k} - \mu - g - p)I = \lambda_{i_k} I, \tag{5.24}$$

where $\lambda_{i_k} := \beta_{1i_k} + \beta_{2i_k} - \mu - g - p$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I(t) \leq I_0 \exp(-ct)$, and hence $\bar{\mathbf{Q}}$ is exponentially I-stable. Then, the limiting equation for S is $S' = \mu - \mu S$, which, by inspection, converges to one. Further, the equation for V becomes $V' = -\gamma V - \mu V$, and hence V converges to zero. Finally, using $R = 1 - S - I - V$, R converges to zero. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (5.21) in Ω_{SVIR}. If the switching signal is periodic, then it follows from the bound (5.24) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

The constraint $\langle \mathcal{R}_\sigma^p \rangle < 1 - \epsilon$ implicitly defines a critical treatment portion $p > p_{\text{crit}}$ in order to achieve eradication, where

$$p_{\text{crit}} := \frac{\langle \beta_{1\sigma} + \beta_{2\sigma} \rangle}{1 - \epsilon} - \mu - g. \tag{5.25}$$

5.1.7 Switched Multi-City Model with a Screening Process

It has been suggested (for example in [46, 68]) that restricting the travel of infected individuals is important in controlling the spread of a disease. For many diseases, it may be difficult to identify infected individuals in order to restrict their travel. However, the recent case of the SARS epidemic was a good example of a case where it was possible, due to the global awareness of the seriousness of this disease [46]. In 2003, when SARS was spreading, entry and exit screenings, including visual inspection to detect symptoms, temperature screening via thermal scanning, distributing health alert notices and administering questionnaires to assess symptoms and possible exposure were done at mass transit centers to identify infected individuals [46]. In fact, it is possible to eradicate a disease that is led by transport-related infection using entry screening even when the disease would be endemic in both isolated cities [46]. The switched model in this section was motivated by the non-switched entry screening models studied in [46, 68].

Assume that there are two cities and that susceptibles and infectives may travel between the two cities as follows: assume individuals travel from city 1 to 2 at a rate α_1, and from city 2 to city 1 at a rate α_2. Assume there is a screening process with $0 \leq p \leq 1$ being the probability of successfully detecting an infected individual during the screening process. Assume that susceptible individuals are never falsely identified as being infected (no false positives). Do not consider population dynamics for the screened classes V_{c_1} and V_{c_2}, that is, individuals who are being screened do not die or give birth. When the infected individuals are identified, assume that they will be isolated for treatment (for example in hospitals) as was done for the SARS infection in 2003 [46]. Assume that individuals in the screened classes are removed at a constant rate $f > 0$ and re-enter the susceptible population. As before, assume that individuals do not give birth or die, or recover while they are travelling. Assume a standard incidence rate for the horizontal incidence of the disease while individuals are travelling, with travelling contact rate $0 \leq \gamma \leq 1$.

This gives the model:

$$\begin{aligned}
\dot{S}_{c_1} &= \mu N_1 - \beta_i \frac{S_{c_1} I_{c_1}}{N_1} - \mu S_{c_1} + g I_{c_1} + f V_{c_1} - \alpha_1 S_{c_1} + \alpha_2 S_{c_2} - \alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2}, \\
\dot{I}_{c_1} &= \beta_i \frac{S_{c_1} I_{c_1}}{N_1} - g I_{c_1} - \mu I_{c_1} - \alpha_1 I_{c_1} + (1-p)\alpha_2 I_{c_2} + (1-p)\alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2}, \\
\dot{V}_{c_1} &= p\alpha_2 I_{c_2} + p\alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{N_2} - f V_{c_1}, \\
\dot{S}_{c_2} &= \mu N_2 - \beta_i \frac{S_{c_2} I_{c_2}}{N_2} - \mu S_{c_2} + g I_{c_2} + f V_{c_2} - \alpha_2 S_{c_2} + \alpha_1 S_{c_1} - \alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1}, \\
\dot{I}_{c_2} &= \beta_i \frac{S_{c_2} I_{c_2}}{N_2} - g I_{c_2} - \mu I_{c_2} - \alpha_2 I_{c_2} + (1-p)\alpha_1 I_{c_1} + (1-p)\alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1}, \\
\dot{V}_{c_2} &= p\alpha_1 I_{c_1} + p\alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{N_1} - f V_{c_2},
\end{aligned} \tag{5.26}$$

where $i \in \{1, 2, \ldots, m\}$, $N_1 = S_{c_1} + I_{c_1}$, $N_2 = S_{c_2} + I_{c_2}$ and $N_1 + V_{c_1} + N_2 + V_{c_2} = N$. The total population, N, is constant and the initial conditions are $S_{c_1}(0) = S_{c_{1,0}} > 0, S_{c_2}(0) = S_{c_{2,0}} > 0, I_{c_1}(0) = I_{c_{1,0}} > 0, I_{c_2}(0) = I_{c_{2,0}} > 0, V_{c_1}(0) = V_{c_{1,0}}, V_{c_2}(0) = V_{c_{2,0}}$. The meaningful physical domain for this system is

$$T_{SIVSIV} = \{(S_{c_1}, I_{c_1}, V_{c_1}, S_{c_2}, I_{c_2}, V_{c_2}) \in \mathbb{R}^6_+ | S_{c_1} + I_{c_1} + V_{c_1} + S_{c_2} + I_{c_2} + V_{c_2} = N\}.$$

Notice that, since $0 \leq \gamma \leq 1$, we have that

$$\{\dot{S}_{c_1} + \dot{I}_{c_1} + \dot{V}_{c_1} + \dot{S}_{c_2} + \dot{I}_{c_2} + \dot{V}_{c_2}\} \big|_{S_{c_1}+I_{c_1}+V_{c_1}+S_{c_2}+I_{c_2}+V_{c_2}=N} = 0,$$

$$\dot{S}_{c_1}\Big|_{S_{c_1}=0} = (\mu+g)I_{c_1} + fV_{c_1} + \alpha_2 S_{c_2} - \alpha_2\gamma\frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}} \geq 0,$$

$$\dot{S}_{c_2}\Big|_{S_{c_2}=0} = (\mu+g)I_{c_2} + fV_{c_2} + \alpha_2 S_{c_1} - \alpha_2\gamma\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} \geq 0,$$

$$\dot{I}_{c_1}\Big|_{I_{c_1}=0} = (1-p)\alpha_2 I_{c_2} + (1-p)\alpha_2\gamma\frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}} \geq 0,$$

$$\dot{I}_{c_2}\Big|_{I_{c_2}=0} = (1-p)\alpha_1 I_{c_1} + (1-p)\alpha_1\gamma\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} \geq 0,$$

$$\dot{V}_{c_1}\Big|_{V_{c_1}=0} = p\alpha_2 I_{c_2} + p\alpha_2\gamma\frac{S_{c_2}I_{c_2}}{S_{c_2}+I_{c_2}} \geq 0, \quad \dot{V}_{c_2}\Big|_{V_{c_2}=0} = p\alpha_1 I_{c_1} + p\alpha_1\gamma\frac{S_{c_1}I_{c_1}}{S_{c_1}+I_{c_1}} \geq 0,$$

which implies the domain is invariant to the switched system. For this model, define the non-physical basic reproduction numbers

$$\mathcal{R}_i^{p,non} = \frac{\beta_i + (1-p)\alpha_{\max}\gamma}{\mu + g + p\alpha_{\min}} \tag{5.27}$$

for each subsystem, where $\alpha_{\max} = \max\{\alpha_1, \alpha_2\}$ and $\alpha_{\min} = \min\{\alpha_1, \alpha_2\}$. These reproduction numbers do take into account the screening probability p, but they

are not physically meaningful because of the use of the max and min functions. Hence the theorems established are sufficient but we conject they are not necessary. There is a disease-free equilibrium point

$$\bar{\mathbf{Q}} = (\bar{S}_{c_1}, \bar{I}_{c_1}, \bar{V}_{c_1}, \bar{S}_{c_2}, \bar{I}_{c_2}, \bar{V}_{c_2}) = \left(\frac{\alpha_2}{\alpha_1 + \alpha_2} N, 0, 0, \frac{\alpha_1}{\alpha_1 + \alpha_2} N, 0, 0 \right) \tag{5.28}$$

that is common to all subsystems.

Theorem 5.1.8. *If $\langle \mathcal{R}_\sigma^{p,non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.26) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is exponentially (I_{c_1}, I_{c_2})-stable, in the domain T_{SIVSIV}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^{p,non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{p,non} - 1)\tau_m < 0$ then the solution of system (5.26) converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically (I_{c_1}, I_{c_2})-stable in the domain T_{SIVSIV}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}
(I_{c_1} + I_{c_2})' &= \beta_{i_k} \left(\frac{S_{c_1} I_{c_1}}{S_{c_1} + I_{c_1}} + \frac{S_{c_2} I_{c_2}}{S_{c_2} + I_{c_2}} \right) - (g + \mu)(I_{c_1} + I_{c_2}) - p\alpha_2 I_{c_2} - p\alpha_1 I_{c_1} \\
&\quad + (1-p)\alpha_1 \gamma \frac{S_{c_1} I_{c_1}}{S_{c_1} + I_{c_1}} + (1-p)\alpha_2 \gamma \frac{S_{c_2} I_{c_2}}{S_{c_2} + I_{c_2}}, \\
&\leq (\beta_{i_k} + (1-p)\alpha_{\max}\gamma - g - \mu - p\alpha_{\min})(I_{c_1} + I_{c_2}), \\
&= \lambda_{i_k}(I_{c_1} + I_{c_2}),
\end{aligned} \tag{5.29}$$

where $\lambda_{i_k} := \beta_{i_k} + (1-p)\alpha_{\max}\gamma - g - \mu - p\alpha_{\min}$. Thus, it follows from the proof of Theorem 3.1.2, beginning at equation (3.11), that $I_{c_1} + I_{c_2} \leq (I_{c_{1,0}} + I_{c_{2,0}}) \exp(-ct)$ for some $c > 0$. Since $I_{c_1}, I_{c_2} \geq 0$, the solution $\bar{\mathbf{Q}}$ is exponentially (I_{c_1}, I_{c_2})-stable in T_{SIVSIV}. The limiting equations for V_{c_1} and V_{c_2} then are $V'_{c_1} = -fV_{c_1}$ and $V'_{c_2} = -fV_{c_2}$, respectively, and hence, by inspection, V_{c_1} and V_{c_2} both converge to zero. The limiting equations for S_{c_1}, S_{c_2} are

$$\begin{cases} \dot{S}_{c_1} = -\alpha_1 S_{c_1} + \alpha_2 S_{c_2}, \\ \dot{S}_{c_2} = -\alpha_1 S_{c_2} + \alpha_2 S_{c_1}. \end{cases} \tag{5.30}$$

Then, since $S_{c_1} + S_{c_2} = N$, S_{c_1} and S_{c_2} converge to $\bar{S}_{c_1}$ and $\bar{S}_{c_2}$. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (5.26) in the meaningful domain T_{SIVSIV}. If the switching signal is periodic, then it follows from the bound (5.29) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain. □

Again, notice that the constraint $\langle \mathcal{R}_\sigma^{p,non} \rangle < 1 - \epsilon$ will implicitly define a critical vaccination rate p_{crit} such that $p > p_{\text{crit}}$ will ensure that the disease is eradicated. In this case, because of the non-physicalality of the reproduction numbers, the critical vaccination rate may be higher than necessary for eradication.

5.2 Pulse Control Schemes

5.2.1 Switched SIR Model with Pulse Treatment

Introduce switching into a SIR model with pulse control, similar to the model (2.35). Instead of impulsively vaccinating a portion p of susceptibles, this strategy impulsively treats a portion of infectives. More specifically, at certain times t_k assume a fraction of the infected population is cured of the disease. Assume that immediately after the pulse treatment the individuals are healthy and permanently immune (and hence removed). Though it might seem unreasonable physically for individuals to be cured instantaneously, as discussed in Section 2.2.4, it is assumed that the time scale of the treatment is very short (for example, given a needle with the cure) compared to the time scale for the dynamics of the disease.

Suppose that there are m different pulses, that is, $0 \leq p_1, \ldots, p_m \leq 1$, and at the pulse times t_k, $k = 1, 2, \ldots$, it is possible to apply one of the pulses. Hence, these pulses can have varying strengths. The switching times are $t_0 = 0 < t_1 < t_2 < \ldots < t_k < \ldots \to \infty$. At each switch time t_k, $k = 1, 2, \ldots$, an impulsive cure is applied to a fraction $0 \leq p_i \leq 1$ of the infected population. This is an impulsive type of control, and, combined with switching in the contact rate, $\beta_1, \ldots, \beta_m > 0$, leads to a new impulsive switching model:

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S, & t \in (t_{k-1}, t_k] \\ \dot{I} = \beta_i SI - gI - \mu I, & \\ \dot{R} = gI - \mu R, & \\ S(t^+) = S(t), & t = t_k \\ I(t^+) = I(t) - p_i I(t), & \\ R(t^+) = R(t) + p_i I(t) & \end{cases} \tag{5.31}$$

where $k = 1, 2, \ldots$, and $i \in \{1, \ldots, m\}$ follows the piecewise continuous switching rule $\sigma \in \mathcal{S}$. Since the population is constant, the variables have been normalized so that $S + I + R = 1$, hence the meaningful domain of interest is Ω_{SIR}. Assume that for all switched pulse control models in Section 5.2 that the solutions are continuous from the left at the moments of impulse t_k, that is,

$$(S(t_k), I(t_k), R(t_k)) = (S(t_k^-), I(t_k^-), R(t_k^-)) = lim_{h \to 0^+}(S(t_k - h), I(t_k - h), R(t_k - h)),$$

and

$$(S(t_k^+), I(t_k^+), R(t_k^+)) = lim_{h \to 0^+}(S(t_k + h), I(t_k + h), R(t_k + h)).$$

This domain is invariant since

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

Further, the impulsive difference equations will not move the solution to outside the meaningful domain. As discussed briefly in Section 2.1.3, we assume for these

disease models that there is no impulsive effect at the initial time t_0, which can be taken to be zero without loss of generality. Assume initial conditions $S(0^+) = S_0 > 0$, $I(0^+) = I_0 > 0$ and $R(0^+) = R_0$ such that $(S_0, I_0, R_0) \in \Omega_{SIR}$. In this model, the basic reproduction numbers are the SIR reproduction numbers (4.2),

$$\mathcal{R}_i = \frac{\beta_i}{\mu + g}. \tag{5.32}$$

The switched system (5.31) has a disease-free solution $\bar{\mathbf{Q}} = (1, 0, 0)$ common to all subsystems. Since $S + I + R = 1$, the system is intrinsically two-dimensional. Recall that $T_i(t)$ is defined to be the total activation time of the i^{th} subsystem in the interval $(0, t]$.

Theorem 5.2.1. *Let $p_i = p$ for all i. If $(k-1)\ln(1-p)+\sum_{i=1}^{m}(\beta_i-\mu-g)T_i(t) \leq -ct$ for $t \in (t_{k-1}, t_k]$, with constant $c > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (5.31) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the domain Ω_{SIR}.*

Proof. This proof follows from a proof in [22]. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\dot{I} = \beta_i SI - gI - \mu I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{5.33}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Then, for $t \in (t_{k-1}, t_k]$:

$$I(t) \leq I({t_{k-1}}^+) \exp[\lambda_{i_k}(t - t_{k-1})], \tag{5.34}$$

Thus, since $I \geq 0$ for all $t \geq 0$, I is bounded in the 1-norm, based on the effects of the switching rule. Furthermore, immediately after each t_k,

$$I({t_k}^+) = (1 - p)I(t_k) \tag{5.35}$$

Now apply (5.34) and (5.35) successively on each subinterval.

For $t \in (0, t_1]$:
Using (5.34), $I(t) \leq I_0 \exp[\lambda_{i_1} t] \Rightarrow I(t_1) \leq I_0 \exp[\lambda_{i_1} t_1]$.
Using (5.35), $I({t_1}^+) = (1 - p)I(t_1)$.
Combining gives $I({t_1}^+) \leq I_0(1 - p) \exp[\lambda_{i_1} t_1]$.

For $t \in (t_1, t_2]$:
Using (5.34), $I(t) \leq I(t_1^+) \exp[\lambda_{i_2}(t - t_1)] \leq I_0(1 - p) \exp[\lambda_{i_1} t_1 + \lambda_{i_2}(t - t_1)]$.
Using (5.35), $I({t_2}^+) = (1 - p)I(t_2)$.
Combining gives $\rightarrow I({t_2}^+) \leq I_0(1 - p)^2 \exp[\lambda_{i_1} t_1 + \lambda_{i_2}(t_2 - t_1)]$.
$\vdots$
For $t \in (t_{k-1}, t_k]$:

$$\begin{aligned} I(t) &\leq I_0(1 - p)^{k-1} \exp[\lambda_{i_1} t_1 + \ldots + \lambda_{i_k}(t - t_{k-1})], \\ &= I_0 \exp\left[(k - 1)\ln(1 - p) + \sum_{i=1}^{m} \lambda_i T_i(t)\right], \\ &\leq I_0 \exp(-ct). \end{aligned}$$

Thus, $\bar{\mathbf{Q}}$ is exponentially I-stable in Ω_{SIR}. Then, from the limiting equations of system (5.31) with $I = 0$, it is apparent that the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. □

The condition $(k-1)\ln(1-p) + \sum_{i=1}^{m} \lambda_i T_i(t) \leq -ct$ is not easily verified. To improve this, consider the situation where $\mathcal{R}_i \geq 1$ for all i, which implies $\lambda_i := \beta_i - \mu - g \geq 0$ for all i. For many diseases, this is the case, see Table 2.1. A switching signal is considered to have a dwell-time if there exists an $\eta > 0$ such that $t_k - t_{k-1} \geq \eta$. Define the set of all such switch rules to be $\mathcal{S}_{\text{dwell}} \subset \mathcal{S}$. This is reasonable biologically, as the contact rate should not switch too quickly, for example, seasonal switching. Then, in this scenario, more easily verifiable conditions can be established.

Theorem 5.2.2. *Suppose $0 \leq p_i < 1$ for all i and $\mathcal{R}_1, \ldots, \mathcal{R}_m \geq 1$. If the switch rule satisfies $\sigma \in \mathcal{S}_{dwell}$ and there exists a constant $\alpha > 1$ such that $\ln(\alpha(1-p_i)) + \eta(\mu+g)(\mathcal{R}_i - 1) \leq 0$ for all i then the solution of system (5.31) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.*

Proof. This proof is motivated from one in [23]. Let i_k follow the switching rule $\sigma \in \mathcal{S}_{\text{dwell}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\dot{I} = \beta_i SI - gI - \mu I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{5.36}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Notice $\mathcal{R}_i \geq 1$ for all i implies $\lambda_i \geq 0$. Since $\dot{I} \leq \lambda_{i_k} I$, for $t \in (t_{k-1}, t_k]$:

$$I(t) \leq I({t_{k-1}}^+) \exp[\lambda_{i_k}(t - t_{k-1})], \tag{5.37}$$

Thus, since $I \geq 0$ for all $t \geq 0$, I is bounded in the 1-norm, based on the effects of the switching rule. Furthermore, immediately after each t_k,

$$I({t_k}^+) = (1 - p_{i_k}) I(t_k) \tag{5.38}$$

Now apply (5.37) and (5.38) successively on each subinterval.

For $t \in (0, t_1]$:
Using (5.37), $I(t) \leq I_0 \exp[\lambda_{i_1} t]$ hence $I(t_1) \leq I_0 \exp[\lambda_{i_1} t_1]$.
Using (5.38), $I({t_1}^+) = (1 - p_{i_1}) I(t_1)$.
Combining gives $I({t_1}^+) \leq (1 - p_{i_1}) I_0 \exp[\lambda_{i_1} t_1]$.

For $t \in (t_1, t_2]$:
Using (5.37), $I(t) \leq I(t_1^+) \exp[\lambda_{i_2}(t - t_1)] \leq I_0 \exp[\lambda_{i_1} t_1 + \lambda_{i_2}(t - t_1)]$.
Using (5.38), $I({t_2}^+) = (1 - p_{i_2}) I(t_2)$.
Combining gives $I({t_2}^+) \leq (1 - p_{i_1})(1 - p_{i_2}) I_0 \exp[\lambda_{i_1} t_1 + \lambda_{i_2}(t_2 - t_1)]$.
⋮

For $t \in (t_{k-1}, t_k]$:

$$\begin{aligned}
I(t) &\leq I_0(1-p_{i_1})\cdots(1-p_{i_{k-1}})\exp\left[\lambda_{i_1}t_1+\ldots+\lambda_{i_k}(t-t_{k-1})\right],\\
I(t) &\leq I_0(1-p_{i_1})\cdots(1-p_{i_{k-1}})\exp\left[\lambda_{i_1}t_1+\ldots+\lambda_{i_k}(t-t_{k-1})\right],\\
&\leq I_0(1-p_{i_1})\cdots(1-p_{i_{k-1}})\exp\left[\lambda_{i_1}\eta+\ldots+\lambda_{i_k}\eta\right],\\
&= I_0\frac{1}{\alpha^k(1-p_{i_k})}\alpha(1-p_{i_1})e^{(\lambda_{i_1}\eta)}\cdots\alpha(1-p_{i_k})e^{(\lambda_{i_k}\eta)},\\
&= I_0\frac{1}{\alpha^k(1-p_{i_k})}\alpha(1-p_{i_1})e^{(\mu+g)(\mathcal{R}_{i_1}-1)\eta}\cdots\alpha(1-p_{i_k})e^{(\mu+g)(\mathcal{R}_{i_k}-1)\eta},\\
&\leq I_0\frac{1}{\alpha^k(1-p_{i_k})},
\end{aligned}$$

Thus, $\bar{\mathbf{Q}}$ is asymptotically I-stable. Then, from the limiting equations of system (5.31) with $I = 0$, it is apparent that the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. □

Now consider the case where the switching signal is periodic, that is $t_k - t_{k-1} = \tau_k$, with $\tau_{k+m} = \tau_k$. Further, assume that $\mathcal{R}_i = \mathcal{R}_k$, on the interval $(t_{k-1}, t_k]$, $\mathcal{R}_{k+m} = \mathcal{R}_k$, and $p_i = 0$ unless $t = kT$ where $T := \tau_1 + \ldots + \tau_m$, $k = 1, 2, \ldots$, and $p_i = p$. The period of the switching signal is T, hence, pulses are applied at the end of each period. Denote the set of all periodic switching signals for impulsive switched systems that satisfy the above as $\mathcal{S}_{\text{periodic-pulse}} \subset \mathcal{S}$.

Theorem 5.2.3. *If switching rule is periodic $\sigma \in \mathcal{S}_{periodic\text{-}pulse}$ and*

$$\frac{\ln(1-p)}{\mu+g} + (\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0,$$

then the solution of system (5.31) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the domain Ω_{SIR}.

Proof. First we show convergence. Since there are no impulses applied until after one period, T, is complete, proceed from equation (3.12) from the proof of Theorem 3.1.2, for $t \in (0, T]$:

$$I(t) \leq I_0 \exp\left[\lambda_1\tau_1 + \ldots + \lambda_m(t - (T - \tau_m))\right], \tag{5.39}$$

where $\lambda_i := \beta_i - \mu - g$. Immediately after T, apply the first impulse,

$$\begin{aligned}
I(T^+) &\leq I_0(1-p)\exp\left[\lambda_1\tau_1+\ldots+\lambda_m\tau_m\right],\\
&= I_0\exp\left[\ln(1-p)+\lambda_1\tau_1+\ldots+\lambda_m\tau_m\right],\\
&= \eta I_0,
\end{aligned}$$

where $\eta := \exp\left[\ln(1-p)+\lambda_1\tau_1+\ldots+\lambda_m\tau_m\right] < 1$ from the conditions of the theorem. Similarly, it can be shown that $I(hT^+) \leq \eta I((h-1)T^+)$ for any integer $h = 1, 2, \ldots$. Then $I(hT^+) \leq \eta I((h-1)T^+) \leq \eta(\eta I((h-2)T^+)) \leq \ldots \leq \eta^h I_0$, and

hence the sequence $\{I(hT^+)\}$ converges to zero as $h \to \infty$. Furthermore, without loss of generality, take $t \in (t_{k-1}, t_k]$ with $hT < t_k \leq (h+1)T$,

$$I(t) \leq I(hT^+)(1-p)^h \exp[\lambda_1\tau_1 + \ldots + \lambda_k(t-t_k)]. \tag{5.40}$$

Since the exponents are finite numbers, $I(t) \leq I(hT^+)(1-p)^h e^M$ for some constant $M > 0$ where the sequence $\{I(hT^+)\}$ is converging to zero, hence the solution is converging to zero as $h \to \infty$.

It remains to show stability of the solution. We will look at the worst case scenario for growth of the disease in a periodic scenario, with the disease spreading fastest at the beginning: suppose that $\mathcal{R}_1, \ldots, \mathcal{R}_m \geq 1$ and $\mathcal{R}_{r+1}, \ldots, \mathcal{R}_m < 1$, then it follows that $\lambda_1, \ldots, \lambda_r \geq 0$ and $\lambda_{r+1}, \ldots, \lambda_m < 0$. Then, during the interval $(0, T]$, the maximum value I can attain is

$$I_{\max} = I_0 e^{\lambda_1\tau_1 + \ldots + \lambda_r\tau_r} := I_0 B.$$

For any $\epsilon > 0$, choose $\delta = \epsilon/B$ and suppose that $I_0 < \delta$. It follows that in the interval $(0, T]$, $I \leq I_{\max} = I_0 B < \delta B = \epsilon$. More generally, in the interval $(t_{k-1}, t_k]$, where $hT < t_k \leq (h+1)T$, it follows that $I(t) \leq I(hT^+)(1-p)^h B < I_0(1-p)^h B < \delta B = \epsilon$. Hence, the solution is also stable.

Therefore, $\bar{\mathbf{Q}}$ is asymptotically I-stable. Then, from the limiting equations of system for (5.31) with $I = 0$, it is apparent that the solution converges to the disease-free solution $\bar{\mathbf{Q}}$ in the domain Ω_{SIR}. □

Recall the condition for eradication for the non-pulse treatment system (4.1) for a periodic switching rule in Theorem 4.1.1: $(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$. By inspection, it is now easier to obtain eradication of the disease using the pulse treatment. This follows from the fact that the pulse treatment is affecting the disease eradication criteria with the $\ln(1-p) < 0$ terms, which are helping to achieve eradication, as expected. In the case of periodic switching, the conditions on p required for eradication are easier to evaluate. The theorem defines a critical value for the pulse treatment that must be achieved in order to eradicate the disease, p must satisfy

$$(1-p)e^{(\mu+g)[(\mathcal{R}_1-1)\tau_1 + \ldots + (\mathcal{R}_m-1)\tau_m]} < 1,$$

and hence, for eradication,

$$p > 1 - e^{-(\mu+g)[(\mathcal{R}_1-1)\tau_1 + \ldots + (\mathcal{R}_m-1)\tau_m]} := p_{\text{crit}}.$$

5.2.2 Switched SIR Model with Pulse Vaccination and Pulse Treatment

Consider now the control strategy of applying impulsive vaccinations to a fraction of the susceptible population at certain times t_k, as well as impulsive treatments.

As in Section 2.2.4, the motivation for this strategy is to notice that in the switched SIR model (4.1), $\dot{I} = I(\beta_i S - \mu - g) < 0$ if $S < (\mu + g)/\beta_i := S_{\text{crit}}$. That is, so long as size of the susceptible population is controlled so that it is always less than some critical value S_{crit}, then $\dot{I} < 0$ for all $t \geq 0$. This means the infection will burn out and there will be no epidemic. Apply impulses periodically every T time units to a portion p of the susceptible population (with vaccinations) and a portion p of the infected population (with treatments), giving them permanent immunity, and sending them to the immune class R. Hence this scheme combines pulse vaccination with pulse treatment. In this case, demand that the switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$. Hence, after m intervals an impulse is applied and the switching rule repeats itself. Since the motivation for periodicity of the switching rule is the seasonal (yearly) variations in the contact rate, this means applying a vaccination pulse yearly, which is not unrealistic. Apply this technique to the switched SIR model (4.1):

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S, & t \in (t_{k-1}, t_k] \\ \dot{I} = \beta_i SI - gI - \mu I, & \\ \dot{R} = gI - \mu R, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) - pI(t), & \\ R(t^+) = R(t) + pS(t) + pI(t), & \end{cases} \tag{5.41}$$

where $k = 1, 2, \ldots,$ and $i \in \{1, \ldots, m\}$ follows the switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$, that is, $T = \tau_1 + \ldots + \tau_m$. The initial conditions are $S(0^+) = S_0 > 0, I(0^+) = I_0 > 0, R(0^+) = R_0$ and the variables have been normalized, since the population is constant. The meaningful domain is Ω_{SIR}, which is invariant to the switched system, since

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

and the impulsive difference equations will not move the solution to outside the meaningful domain. The basic reproduction numbers are

$$\mathcal{R}_i = \frac{\beta_i}{\mu + g}, \tag{5.42}$$

unchanged from the non-pulse switched SIR model (4.2). Observe that the usual disease-free solution $(1, 0, 0)$ is no longer an equilibrium point of the system. As in Section (2.2.4), motivated by the fact that $I = 0$ is an equilibrium solution to the differential equation I', begin the analysis of this system by showing the existence of a periodic disease-free solution, denoted $\mathbf{Q}(\mathbf{t})$, in which $I(t) = 0$ for all $t \geq 0$. Under these conditions, the system reduces to:

$$\begin{cases} \dot{S} = \mu(1 - S), & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t) + pS(t). & \end{cases} \tag{5.43}$$

where $T = \tau_1 + \ldots + \tau_m$. This reduced system is not a switched system, and was shown to asymptotically converge to the periodic disease-free solution $\mathbf{Q(t)} = (\widetilde{S}(t), 0, \widetilde{R}(t))$ in Section (2.2.4), where, from equation (2.38),

$$\begin{cases} \widetilde{S}(t) = 1 - \dfrac{pe^{-\mu(t-(k-1)T)}}{1-(1-p)e^{-\mu T}}, & (k-1)T < t \leq kT \\ \widetilde{R}(t) = 1 - \widetilde{S}(t). \end{cases} \tag{5.44}$$

Theorem 5.2.4. *If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic\text{-}pulse}$ and*

$$\frac{\ln(1-p)}{\mu+g} + (\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0,$$

then the solution of system (5.41) will converge to the periodic disease-free solution $\mathbf{Q(t)}$, which is asymptotically I-stable, in the meaningful domain Ω_{SIR}.

Proof. Let i_k follow the periodic switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\dot{I} = \beta_i SI - gI - \mu I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{5.45}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Additionally, after each time T: $I(kT^+) = I(kT) - pI(kT)$. Then, from the proof of Theorem 5.2.3, beginning at equation (5.39), $\mathbf{Q(t)}$ is asymptotically I-stable. The limiting system then becomes

$$\begin{cases} \dot{S} = \mu(1-S), & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t) + pS(t). & \end{cases}$$

where $T = \tau_1 + \ldots + \tau_m$. This is the reduced system (5.43), which converges to the periodic disease-free solution $\mathbf{Q(t)}$ in the meaningful domain Ω_{SIR}. □

Notice that when the system is in equilibrium, it is a non-switched system, hence the cost of this scheme is comparable to the cost of the constant vaccination of newborns scheme (5.1) (see Section 2.2.4). Though, when the infectives have not been treated, there will be an extra cost incurred in their pulse treatment, hence this model should be costlier, from a standpoint of number of individuals which must be vaccinated or treated, compared to the constant vaccination of newborns scheme.

The advantage of this scheme is that it is possible to eradicate a disease with a relatively lower vaccination rate p as compared to the constant control schemes. This comes from the fact that if the inter-pulse period is relatively short, then the pulse scheme can be applied often enough such that the susceptibles are kept below a critical threshold. In the case of constant control schemes, as discussed in

Section 2.2.4, because of the efficacy of the vaccine, the vaccination levels required for eradication might be unrealistically high and not feasible.

Finally, the constraint in Theorem 5.2.4 implicitly defines a critical vaccination portion p_{crit} such that

$$p > 1 - e^{-(\mu+g)[(\mathcal{R}_1-1)\tau_1+\ldots+(\mathcal{R}_m-1)\tau_m]} := p_{\text{crit}},$$

with reproduction numbers (5.42), in order for this pulse control scheme to achieve disease eradication.

5.2.3 Switched SIR Model with Pulse Control and Vaccine Failure

Two important aspects should be considered with regards to a switched pulse vaccination and treatment model such as (5.41): the temporal duration and the efficacy [58]. With regards to the temporal duration of the vaccine, assume for this model that the immune period is finite. As for the efficacy, no vaccine can guarantee immunization, indeed, the probability of a vaccinated person becoming infected after a critical contact with an infected individual should be considerably reduced, but it is not zero [58]. This is a serious problem in vaccination programs, for example, it is particularly relevant in the case of vaccination against measles [58].

We introduce these two aspects into a pulse control SIR model as in [58]: use a reduced force of infection for the vaccinated to become infected, $g(I) = \omega\beta_i I$, which is reduced by a factor $0 \leq \omega \leq 1$ with respect to the regular force of infection $g(I) = \beta_i I$ for the susceptible individuals. In the limit $\omega = 1$, the vaccine is completely failing and when $\omega = 0$ the vaccine has a perfect efficacy. Since the duration of the immune period is finite, suppose individuals in the vaccinated class V have immune period $1/\theta$, with $\theta > 0$ the removal rate of the immunity, and hence θV is the flux of vaccinated subjects into the susceptible class. Then, combined with the SIR model with switched contact rate β_i (4.1), the model is

$$\begin{cases} \dot{S} = \mu - \beta_i SI - \mu S + \theta V, & t \in (t_{k-1}, t_k] \\ \dot{I} = \beta_i SI + \omega\beta_i VI - gI - \mu I, & \\ \dot{R} = gI - \mu R, & \\ \dot{V} = -\omega\beta_i VI - \mu V - \theta V, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) - pI(t), & \\ R(t^+) = R(t), & \\ V(t^+) = V(t) + pS(t) + pI(t), & \end{cases} \tag{5.46}$$

where $i \in \{1, \ldots, m\}$ follows a switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$, $T = \tau_1 + \ldots + \tau_m$, and the variables have been normalized since the population is constant. The

initial conditions are $S(0^+) = S_0 > 0, I(0^+) = I_0 > 0, R(0^+) = R_0, V(0^+) = V_0$. The meaningful domain, which is invariant, is $\Omega_{SIRV} = \{(S, I, R, V) \in \mathbb{R}^4_+ |\ S + I + R + V = 1\}$. This can be seen since

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

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

and, further, the impulsive difference equations will not move the solution to outside the meaningful domain. Define the reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i(1+\omega)}{\mu + g} \tag{5.47}$$

for each subsystem. In seeking a disease-free solution, set $I = 0$ and observe that R converges to zero in this case, hence the limiting system becomes

$$\begin{cases} \dot{S} = (\mu + \theta)(1 - S), & t \in ((k-1)T, kT] \\ \dot{V} = -(\mu + \theta)V, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ V(t^+) = V(t) + pS(t). & \end{cases} \tag{5.48}$$

where $T = \tau_1 + \ldots + \tau_m$. This reduced system is not a switched system, and a similar approach as in Section (2.2.4) gives that this system converges to the periodic solution, for $(k-1)T < t \leq kT$,

$$\begin{cases} \widetilde{S}(t) = 1 - \dfrac{pe^{-(\mu+\theta)(t-(k-1)T)}}{1 - (1-p)e^{-(\mu+\theta)T}}, \\ \widetilde{V}(t) = 1 - \widetilde{S}(t). \end{cases} \tag{5.49}$$

Hence, system (5.46) has the periodic disease-free solution $\mathbf{Q}(t) = (\widetilde{S}(t), \widetilde{I}(t), \widetilde{R}(t), \widetilde{V}(t)) = (\widetilde{S}(t), 0, 0, 1 - \widetilde{S}(t))$.

Theorem 5.2.5. *If the switching rule is periodic $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$ and*

$$\frac{\ln(1-p)}{\mu + g} + (\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$$

then the solution of system (5.46) converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$, which is asymptotically I-stable, in the meaningful domain Ω_{SIRV}.

Proof. Let i_k follow the periodic switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned} I' &= [\beta_{i_k}(S + \omega V) - (g + \mu)]I, \\ &\leq [\beta_{i_k}(1 + \omega) - (\mu + g)]I, \\ &= \lambda_{i_k} I, \end{aligned}$$

where $\lambda_{i_k} := \beta_{i_k}(1+\omega) - (\mu+g)$. Additionally, after each time T: $I(kT^+) = I(kT) - pI(kT)$. Then, from the proof of Theorem 5.2.3, beginning at equation (5.39), $\mathbf{Q}(\mathbf{t})$ is asymptotically I-stable. Then the limiting equations are

$$\begin{cases} \dot{S} = \mu(1-S) + \theta V, & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, \\ \dot{V} = -\mu V - \theta V, \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t), \\ V(t^+) = V(t) + pS(t). \end{cases}$$

where $k = 1, 2, \ldots,$ and $T = \tau_1 + \ldots + \tau_m$. By inspection, R converges to zero, and the equations for S and V form the reduced system (5.48), therefore, the solution converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$ of system (5.46) in the meaningful domain Ω_{SIRV}. □

The constraint on the reproduction numbers in Theorem 5.2.5 implicitly defines a critical vaccination portion p_{crit} such that

$$p > 1 - e^{-(\mu+g)[(\mathcal{R}_1-1)\tau_1 + \ldots + (\mathcal{R}_m-1)\tau_m]} := p_{\text{crit}},$$

with reproduction numbers (5.47), is required in order for this pulse control scheme to achieve disease eradication.

5.2.4 Switched SIR Model with Pulse Control and a Reduced Infective Class

There is another possibility in a model of vaccine failure, instead of vaccine failures causing infection, suppose that vaccinees who are infected become infectious, but with a reduced level of infectivity. This leads to, from [58], the addition of a second class of infected individuals, who have a reduced contact rate $\beta_{vi} < \beta_i$, with $\beta_{vi} > 0$, and an increased removal rate $g_v \geq g > 0$. Represent this reduced class by I_v. These assumptions are physically reasonable, the individuals in the reduced infective class should have a reduced level of infectivity, and hence contact rate, and should also have a reduced infectious period, hence an increased removal rate. Assume, as in the model (5.46), reduced forces of infection for the vaccinated individuals to become infected: $g(I) = \omega\beta_i I$, and $g(I_v) = \omega\beta_{vi} I_v$, which are reduced by a factor $0 \leq \omega \leq 1$ with respect to the regular force of infection $\beta_i I$ for the susceptible individuals. In the limit $\omega = 1$, the vaccine is completely failing and when $\omega = 0$ the vaccine has a perfect efficacy. Assume that individuals who have been vaccinated successfully, represented by the class V, only have temporary immunity, that is, assume an average vaccine-induced immunity period $1/\theta$. Applying this scheme to

the switched SIR model (4.1) gives:

$$\begin{cases} \dot{S} = \mu - (\beta_i I + \beta_{vi} I_v) S - \mu S + \theta V, & t \in (t_{k-1}, t_k] \\ \dot{I} = S(\beta_i I + \beta_{vi} I_v) - gI - \mu I, \\ \dot{I}_v = \omega V(\beta_i I + \beta_{vi} I_v) - g_v I_v - \mu I_v, \\ \dot{R} = gI + g_v I_v - \mu R, \\ \dot{V} = -\omega V(\beta_i I + \beta_{vi} I_v) - \mu V - \theta V, \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) - pI(t), \\ I_v(t^+) = I_v(t) - pI(t), \\ R(t^+) = R(t), \\ V(t^+) = V(t) + pS(t) + pI(t) + pI_v(t), \end{cases} \tag{5.50}$$

where $k = 1, 2, \ldots$, $i \in \{1, \ldots, m\}$ follows a switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$ with $T = \tau_1 + \ldots + \tau_m$, and the variables have been normalized since the population is constant. The initial conditions are $S(0^+) = S_0 > 0$, $I(0^+) = I_0 > 0$, $I_v(0^+) = I_{v_0}$, $R(0^+) = R_0$, $V(0^+) = V_0$. The meaningful domain, which is invariant, is

$$\Omega_{SII_vRV} = \{(S, I, I_v, R, V) \in \mathbb{R}^5_+ |\ S + I + I_v + V + R = 1\}.$$

The invariances follows from

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

$$\dot{S} \Big|_{S=0} = \mu + \theta V > 0, \quad \dot{I} \Big|_{I=0} = \beta_{vi} S I_v \geq 0, \quad \dot{I}_v |_{I_v=0} = \omega \beta_{vi} V I_v \geq 0,$$

$$\dot{R} \Big|_{R=0} = gI + g_v I_v \geq 0, \quad \dot{V} |_{V=0} = 0.$$

Further, the impulsive difference equations will not move the solution to outside the meaningful domain. Define the reproduction numbers

$$\mathcal{R}_i = \frac{\beta_i (1 + \omega)}{\mu + g} \tag{5.51}$$

for each subsystem. Again, seek a disease-free solution by setting $I = 0$, $I_v = 0$, and, following the procedure as in Section 5.2.2, the disease-free solution is the periodic solution $\mathbf{Q}(\mathbf{t}) = (\widetilde{S}(t), \widetilde{I}(t), \widetilde{I}_v(t), \widetilde{R}(t), \widetilde{V}(t)) = (\widetilde{S}(t), 0, 0, 0, 1 - \widetilde{S}(t))$, with $\widetilde{S}(t)$ as in (5.49).

Theorem 5.2.6. *If the switching rule is periodic $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$ and*

$$\frac{\ln(1-p)}{\mu + g} + (\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m < 0$$

then the solution of system (5.50) converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$, which is asymptotically (I, I_v)-stable, in the meaningful domain Ω_{SII_vRV}.

Proof. Let i_k follow the periodic switching rule $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\begin{aligned}(I + I_v)' &= [\beta_{i_k}(S + \omega V) - (\mu + g)]I + [\beta_{vi_k}(S + \omega V) - (\mu + g_v)]I_v, \\ &\leq [\beta_{i_k}(S + \omega V) - (\mu + g)](I + I_v), \\ &\leq [\beta_{i_k}(1 + \omega) - (\mu + g)](I + I_v), \\ &= \lambda_{i_k} I,\end{aligned}$$

where $\lambda_{i_k} := \beta_{i_k}(1 + \omega) - (\mu + g)$. Additionally, after each time T: $I(kT^+) + I_v(kT^+) = I(kT) + I_v(kT) - p(I(kT) + I_v(kT))$. Then, from the proof of Theorem 5.2.3, beginning at equation (5.39), it follows that $\mathbf{Q(t)}$ is asymptotically (I, I_v)-stable. The limiting equations of the system then are

$$\begin{cases} \dot{S} = \mu(1 - S) + \theta V, & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, \\ \dot{V} = -\mu V - \theta V, \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t), \\ V(t^+) = V(t) + pS(t). \end{cases}$$

where $T = \tau_1 + \ldots + \tau_m$. By inspection, R converges to zero, and the equations for S and V form the reduced system (5.48), therefore, the solution converges to the disease-free periodic solution $\mathbf{Q(t)}$ of system (5.50), in the meaningful domain Ω_{SII_vRV}. □

Again, the constraint in Theorem 5.2.6 implicitly defines a critical vaccination portion p_{crit} such that

$$p > 1 - e^{-(\mu+g)[(\mathcal{R}_1 - 1)\tau_1 + \ldots + (\mathcal{R}_m - 1)\tau_m]} := p_{\text{crit}},$$

with reproduction numbers (5.51), is required in order for this pulse control scheme to achieve disease eradication.

5.3 Simulations

For the switching rule in these simulations, motivated by practical applications, we use

$$\sigma(t) = \begin{cases} 1 & \text{during winter,} \\ 2 & \text{otherwise,} \end{cases} \tag{5.52}$$

as in Section 3.5. The variables in these simulations are normalized by total population, the initial condition is taken to be $t_0 = 0$, and the units are non-dimensional. Initial conditions are $S_0 = 0.75$, $I_0 = 0.25$, $R_0 = 0$ unless otherwise specified.

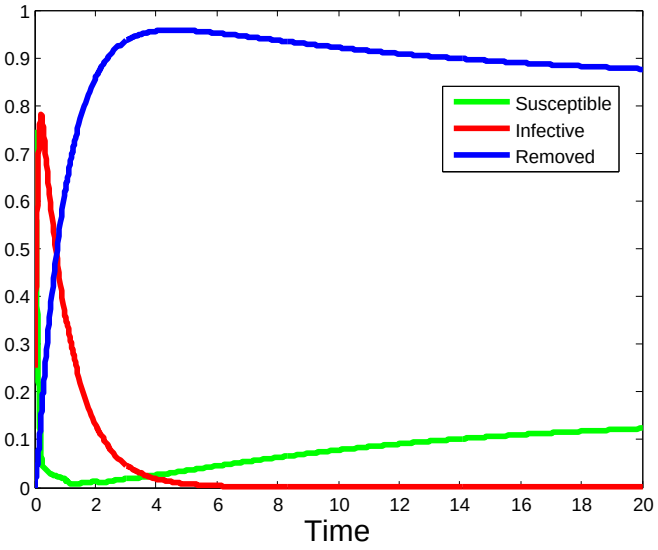

Figure 5.1: **Constant Vaccination of Newborns Switched System (5.1).** Parameters used are motivated by the measles parameters of [66], $\beta_1 = 18$, $\beta_2 = 3$, $g = 1$, $\mu = 0.1$. This gives $\langle \mathcal{R}_\sigma \rangle = 6.136$ for t large (same parameters as Figure 4.10 with $p = 0$). With $p = 0.85$ ($p_{\text{crit}} = 0.84$), we get $\langle \mathcal{R}_\sigma^p \rangle = 0.920$ for t large, and the disease is eradicated.

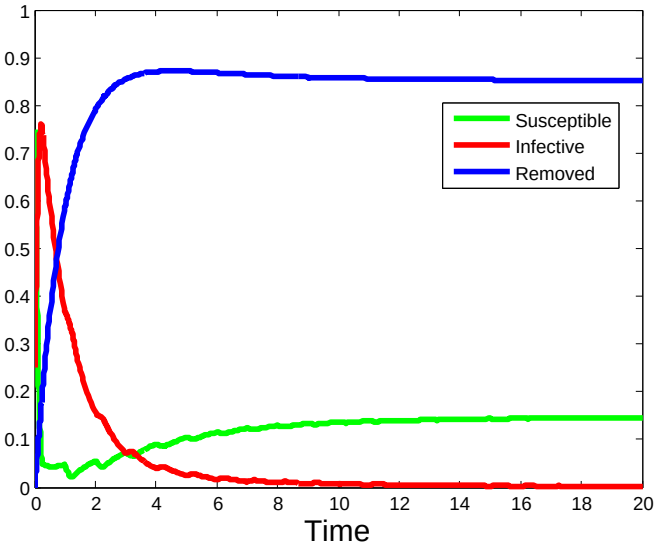

Figure 5.2: **Constant Vaccination of Susceptibles Switched System (5.4).** Parameters are the same as in Figure 5.1 except now the vaccination rate is $p = 0.57$ ($p_{\text{crit}} = 0.51$), leading to $\langle \mathcal{R}_\sigma^p \rangle = 0.92$ for t large and the disease is eradicated.

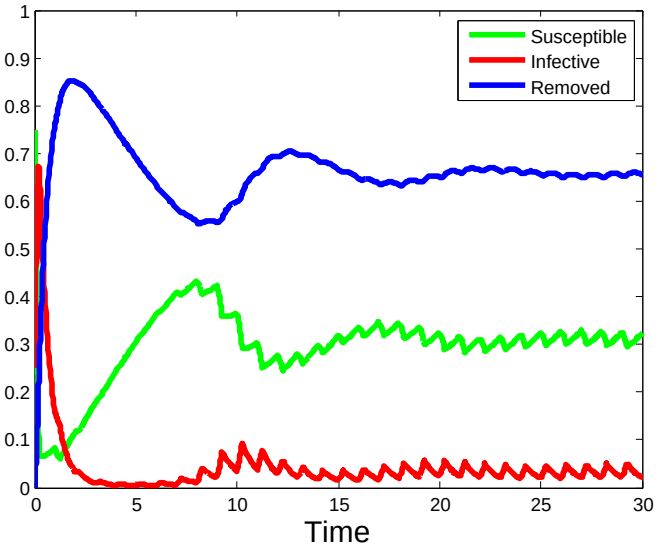

Figure 5.3: **Constant Treatment of Infectives Switched System (5.8).** Parameters are the same as in Figure 5.1 except now, even with $p = 1$, we have that $\langle \mathcal{R}_\sigma^p \rangle = 3.214$ for t large. It seems as though this scheme is less effective than the constant vaccination schemes, where eradication is possible.

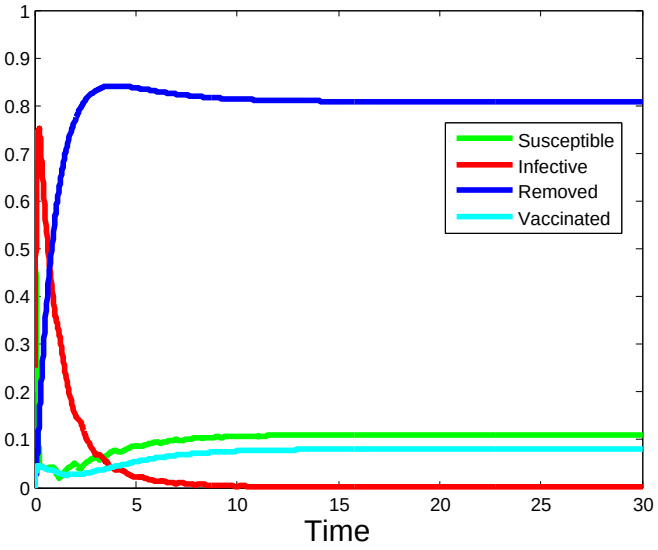

Figure 5.4: **Constant Vaccination Switched System with Progressive Immunity (5.17).** $V_0 = 0$ and parameters are $\beta_{1_1} = 18$, $\beta_{1_2} = 3$ for the susceptibles contracting the disease, $\beta_{2_1} = 1$, $\beta_{2_2} = 0.17$ for the vaccinated contracting the disease, and $g = 1$, $\mu = 0.1$, $\gamma = 1$. The vaccination rate is $p = 0.8$ and this leads to $\langle \mathcal{R}_\sigma^p \rangle = 0.71$ for t large and the disease is eradicated. If $p = 0$ then we would have $\langle \mathcal{R}_\sigma^p \rangle = 6.136$ for large t and the disease would persist.

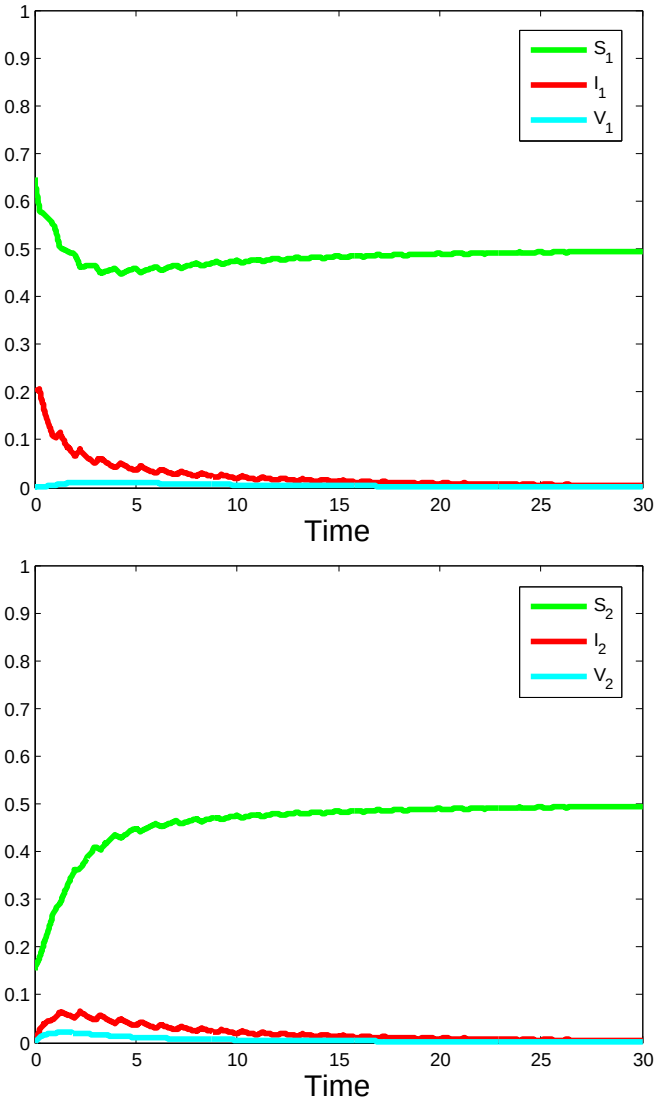

Figure 5.5: **Screening Process in Switched Multi-city System (5.26).** Initial conditions are $S_{1,0} = 0.65$, $I_{1,0} = 0.2$, $V_{1,0}$=0, $S_{2,0} = 0.15$, $I_{2,0} = 0$, $V_{2,0} = 0$. Parameters are $\beta_1 = 2$, $\beta_2 = 0.4$, $\alpha_1 = \alpha_2 = 0.4$, $\gamma = 1$, $f = 1$, $\mu = 0.02$, $g = 1$, and the screening rate is $p = 0.3$, that is, 30% of infected individuals travelling are properly screened. There are no false positive screens. The screening process leads to $\langle \mathcal{R}_\sigma^{p,non} \rangle = 0.947$ for large t and the disease is eradicated by Theorem 5.1.8. If $p = 0$ then we would have $\langle \mathcal{R}_\sigma^{non} \rangle = 1.176$ for large t and the disease would persist (see Figure 4.10).

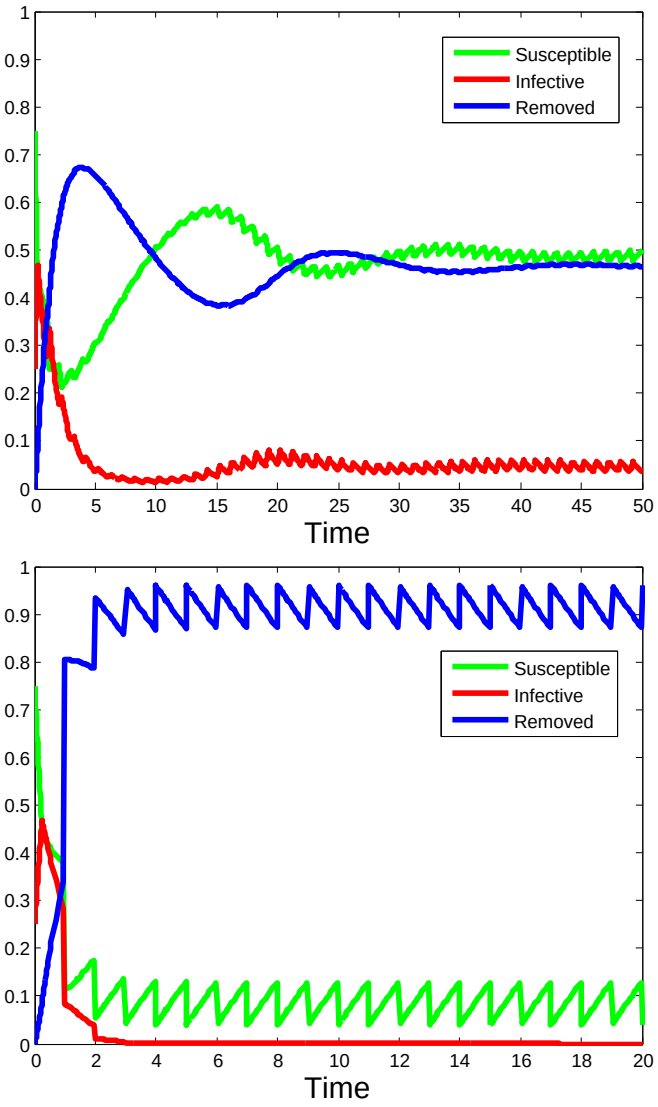

Figure 5.6: **Switched SIR Model with Pulse Vaccination and Treatment (5.41).** Parameters used are $\beta_1 = 6$, $\beta_2 = 1$, $g = 1$, $\mu = 0.1$. The top picture is the switched SIR system (4.1) with $p = 0$, and $\langle \mathcal{R}_\sigma \rangle = 2.046$ for large t; we see the disease persists. In the bottom picture, we use $p = 0.7$ ($p_{\text{crit}} = 0.68$), $\tau_1 = 0.25$, and $\tau_2 = 0.75$ which implies we pulse vaccinate and treat 70% of susceptibles and infectives every 1 time unit. The disease is eradicated which follows from Theorem 5.2.4.

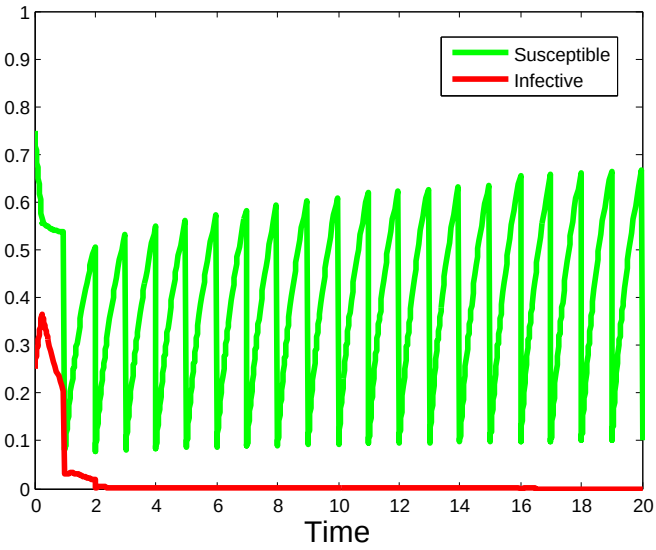

Figure 5.7: **Switched SIR Model with Pulse Vaccination and Treatment and Vaccine Failure (5.46).** Parameters used are $\beta_{1_1} = 4$, $\beta_{1_2} = 0.5$, $g = 1$, $\theta = 1$, $\mu = 0.1$ with vaccine failure rate $\omega = 0.5$. Then, $\langle \mathcal{R}_\sigma \rangle = 1.7045$ for t large and the disease persists. Apply pulse vaccination and treatment with $p = 0.85$ ($p_{\text{crit}} = 0.847$) and the disease is eradicated by Theorem 5.2.5.

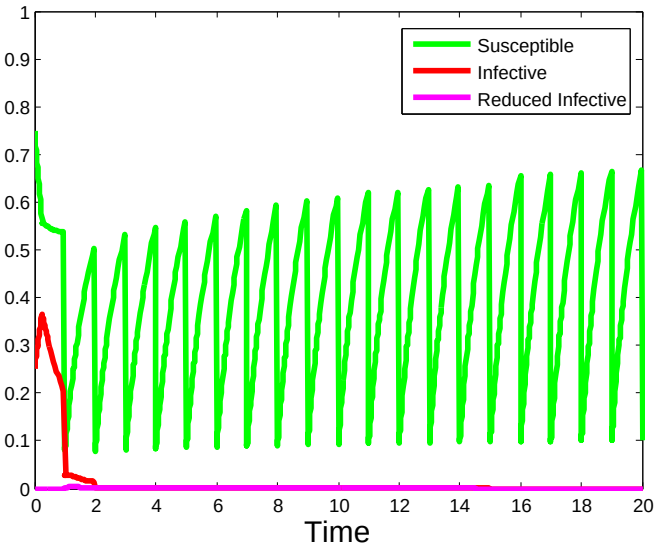

Figure 5.8: **Switched SIR Model with Pulse Vaccination and Treatment and a Reduced Infective Class (5.50).** Parameters used are $\beta_{1_1} = 4$, $\beta_{1_2} = 0.5$, $g = 1$, $\theta = 1$, $\mu = 0.1$ with vaccine failure rate $\omega = 0.5$. Now, we also have reduced infective class, use $\beta_{v_1} = 2 < \beta_1$, $\beta_{v_2} = 0.2 < \beta_2$, $g_v = 3 > g$. Then, $\langle \mathcal{R}_\sigma \rangle = 1.7045$ for large t and the disease persists. Apply pulse vaccination and treatment with $p = 0.85$ (we need $p_{\text{crit}} = 0.847$) and the disease is eradicated by Theorem 5.2.6.

Chapter 6

Switched Epidemiological Models with General Nonlinear Incidences

As discussed in Chapter 1, a vital issue in the study of an epidemic is its transmission, which depends on how infectious a disease is and on the population behaviour [60]. These two aspects are summarized in what is commonly referred to as the incidence rate. Recall from Section 2.2 that the horizontal incidence rate in an epidemiological model is the flow rate of susceptible individuals from the susceptible class into the infected class (or into the exposed class if the latent period is significant and not being ignored) because of direct contact between susceptible and infectious individuals. A vital part of vaccination strategy planning is determining the minimum number of individuals that need to be vaccinated in order to eradicate the disease at hand. In medical literature, there are some reported cases in which high levels of vaccination have not resulted in disease eradication [60]. These unexpected failures might be due to the inefficacy of the vaccine, or due to an unusually higher contact rate, but it has been pointed out it could also be because the nonlinear dependence on the number of infected individuals was not properly accounted for in the incidence rate [60]. Hence, it is important to investigate models with nonlinear incidence rates.

As throughout the thesis, we denote S_c, I_c the number of individuals in the susceptible class and infected class, respectively, S and I the fractions of individuals in the susceptible and infected class, respectively, and N is the total population. The pseudo mass-action incidence rate $f(S_c, I_c) = \eta S_c I_c$, which is linearly dependent with respect to the number of infected individuals, might be unrealistic in scenarios for certain diseases, for example, it is not consistent with the known result that daily contact patterns are largely independent of community size [28]. On the other hand, the standard incidence rate $f(S_c, I_c) = \beta S_c I_c / N$ is consistent with this observed result, though it is not perfect either. One possible need for modification of this incidence rate is the inclusion of a saturating effect, that is, when the fraction of infectives is relatively high in a population, exposure to the disease is virtually certain and the transmission rate might respond slower than linear to further increases in the number of infectives (a saturating effect) [33]. Further, the

underlying assumption of homogeneous mixing may be invalid [33]. This effect was observed in a study on the spread of the cholera epidemic in 1973 [33]. Finally, large epidemics also certainly induce psychological effects: when there is a high fraction of infected individuals in a population, the susceptibles, wary of the disease, will go to extra lengths to avoid infection, resulting in a possible decrease in the incidence rate as the infective fraction increases [60].

In the literature, there have been many studies on nonlinear incidence rates aside from the standard incidence, some of which we detail here. One common nonlinear incidence rate which has been studied takes the form $f(S,I) = \beta I^p S^q$, with $p, q > 0$ [34]: The case $p \leq 1$ represents the saturation effect, since, when the fraction of infectives is relatively high, transmission of the disease will respond slower than linearly with respect to I. If $p > 1$, the incidence rate is convex with respect to I, which can arise in particular cases as a consequence of community effects but is hardly common. There are many other examples of saturating incidence rates: $f(S_c, I_c) = \beta I_c(1 - kI_c)S_c$, k a constant, has been used, for example, in models for measles [27].

$$f(S_c, I_c) = \frac{\beta S_c I_c}{1 + kI_c}$$

was used in the modelling of cholera [27]. Other examples of saturation incidences are $f(S,I) = \beta SI/(1 + \alpha S)$, $\alpha > 0, \beta > 0$ [19], $f(S,I) = SI(a - bE^{-vI})$ [60], and

$$f(S,I) = \frac{kSI^l}{1 + \alpha I^h},$$

which has a saturating behaviour for $l = h$, a maximum and then decreases when $l < h$, and a saturating contact rate for $h = l - 1$ [60]. Some other interesting examples of nonstandard incidence rates are $f(S,I) = \beta SI^p(1 - I)^{q-1}$ with $p > 1, q \geq 1, \beta > 0$ [15], and $f(S,I) = \beta SI(1 + vI^p)$, $\beta > 0, v > 0, p \geq 0$ [15], which take into account the psychological effects of an epidemic [60].

A more general formulation is $f(S,I) = g(I)S$, where $g(I)$ is called the force of infection. For example, consider the family: $g(I) = kI(1 + h(I)), h(0) = 0, h'(I) > 0$, and $h''(I) \leq 0$ for $I > 0$ [60]. In the paper [60], more general classes of forces of infection are considered: $g(I,t) \leq q(t)I$ such that $q(t) = g_I(0,t) > 0$, as well as generic forces of infection $g(I,t)$ such that there exists a $\lambda(t) > 0$ with $g(I,t) \leq \lambda(t)I$. For example, the force of infection

$$g(I) = kI\left(1 + \frac{vI^2}{1 + vI^2}\right)$$

has asymptote $2kI$ as $I \to \infty$ and satisfies $g(I) \leq 2kI$ [60].

In this chapter, models with switched incidence rates will be investigated, beginning with a switched SIR model with a weakly nonlinear incidence rate in Section 6.1. Threshold conditions are also established for a switched SIR model with concave nonlinear forces of infection. A more generalized switched epidemiological model with weakly nonlinear incidence rate and contact switching is considered in

Section 6.2. In Section 6.3, a switched SIR model with weakly nonlinear incidence and pulse control is investigated. Finally, a more general epidemiological model with weakly nonlinear incidence, contact switching and pulse control is considered in Section 6.4.

6.1 Switched SIR Model with General Nonlinear Incidences

One example of an incidence rate, different from the standard incidence rate assumption, is the saturation incidence rate $f(S,I) = \beta SI/(1+\nu S)$, with $0 < \nu < 1$, studied in, for example [19, 43, 61]. Notice $f(0,I) = f(S,0) = 0$, $f(S,I) > 0$ for $S, I \neq 0$ and $f_I, f_S \geq 0$. Use this saturation incidence in replace of the standard incidence in the switched SIR model (4.1),

$$\begin{cases} \dot{S} = \mu - \dfrac{\beta_i SI}{1+\nu S} - \mu S, \\ \dot{I} = \dfrac{\beta_i SI}{1+\nu S} - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{6.1}$$

with $i \in \{1, 2, \ldots, m\}$ following a switching rule $\sigma \in \mathcal{S}$, initial conditions $S(0) = S_0 > 0, I(0) = I_0 > 0, R(0) = R_0$, and normalized variables since the population is constant. The meaningful domain is

$$\Omega_{SIR} = \{(S,I,R) \in \mathbb{R}^3_+ |\ S + I + R = 1\},$$

which is invariant to the system since

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

The basic reproduction numbers are

$$\mathcal{R}_i = \frac{\beta_i}{(\mu+g)(1+\nu)}$$

for each subsystem, and the disease-free equilibrium is $\bar{\mathbf{Q}} = (1,0,0)$.

Theorem 6.1.1. *If $\langle \mathcal{R}_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (6.1) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the meaningful domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t)$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = \frac{\beta_i SI}{1+\nu S} - gI - \mu I \leq (\beta_{i_k}/(1+\nu) - \mu - g)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k}/(1+\nu) - \mu - g$. Then, by proof of Theorem 3.1.2, beginning at equation (3.11), the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (6.1) is exponentially I-stable. By inspecting the system with $I = 0$, it is apparent that S and R converge to one and zero, respectively. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SIR}. □

As outlined in the introduction to this chapter, there are many possible nonlinear incidence rates, each of which have advantages and disadvantages depending on the disease being modelled and the behaviour of the population. Motivated by this and the illustration in system (6.1), assume that the incidence rate can change forms $f_1(S,I), \ldots, f_m(S,I)$ by switching. That is, assume the horizontal incidence rate is the switched function $f_i(S,I)$, with $i \in \{1,\ldots,m\}$ which follows a switching rule $\sigma \in \mathcal{S}$. Apply this to the switched SIR model (4.1):

$$\begin{cases} \dot{S} = \mu - f_i(S,I) - \mu S + gI, \\ \dot{I} = f_i(S,I) - gI - \mu I, \\ \dot{R} = gI - \mu R, \end{cases} \tag{6.2}$$

with $i \in \{1,2,\ldots,m\}$, initial conditions $S(0) = S_0 > 0, I(0) = I_0 > 0, R(0) = R_0$, and the variables have been normalized by the total population, which is constant. From physical considerations, assume that $f_i(S,0) = f_i(0,I) = 0$ for all $(S,I) \in \Omega_{SI}^l = \{(S,I) \in \mathbb{R}_+^2 |\ S + I \leq 1\}$, then meaningful domain Ω_{SIR} is invariant to system (6.2). The disease-free solution $\bar{\mathbf{Q}} = (\bar{S}, \bar{I}, \bar{R}) = (1,0,0)$ is a common equilibrium point of the system. From the non-switched version of system (6.2) studied in [33], if

$$\frac{\partial f_i}{\partial I} > 0, \quad \frac{\partial f_i}{\partial S} > 0, \quad \frac{\partial^2 f_i}{\partial I^2} \leq 0,$$

then there exist unique endemic equilibriums $\mathbf{Q}_\mathbf{i}^* = (S_i^*, I_i^*)$ for each subsystem when $\mathcal{R}_i \geq 1$ [33], which are the solutions to

$$\mu = f_i(S_i^*, I_i^*) + \mu S_i^* + gI_i^*, \quad (\mu+g)I_i^* = f_i(S_i^*, I_i^*), \quad R_i^* = 1 - S_i^* - I_i^*. \tag{6.3}$$

The basic reproduction numbers of this system are [33]:

$$\mathcal{R}_i = \frac{1}{\mu+g}\frac{\partial f_i(\bar{S},\bar{I})}{\partial I}. \tag{6.4}$$

Recall the biological meaning of the reproduction number; it is the average number of secondary infections produced by a single infected individual in a wholly susceptible population. Then this reproduction number makes sense intuitively,

$$\frac{\partial f_i(\bar{S},\bar{I})}{\partial I}$$

represents the rate of change of the infectives present when the system is at its disease-free solution and a single infective is introduced into a wholly susceptible population. Further, $1/(\mu+g)$ normalizes the spread by the average disease-adjusted lifetime of an infective person.

Notice that many of the rates outlined in the first section in this chapter satisfy the weakly nonlinear property $f(S,I) \leq \beta I$, for some constant $\beta > 0$. Motivated by this, we consider the non-physical reproduction numbers for system (6.2):

$$\mathcal{R}_i^{non} = \frac{\beta_i}{\mu + g},$$

which might be too strict, but can be used to establish criteria for the eradication of the disease.

Theorem 6.1.2. *Assume $f_i(S,I) \in C^1[\Omega_{SI}^l, \mathbb{R}_+]$ and $f_i(S,I) \leq \beta_i I$ for all $(S,I) \in \Omega_{SI}^l$ and all $i = 1, 2, \ldots, m$. If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma \in \mathcal{S}$, then the solution of system (6.2) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is exponentially I-stable, in the meaningful domain Ω_{SIR}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0$, then the solution of system (6.2) converges to the the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the meaningful domain Ω_{SIR}.*

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = f_{i_k}(S,I) - gI - \mu I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I, \tag{6.5}$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Then, by proof of Theorem 3.1.2, starting at equation (3.11), the disease-free equilibrium $\bar{\mathbf{Q}}$ of system (6.2) is exponentially I-stable in the meaningful domain Ω_{SIR}. Then, by looking at the limiting equations of system (6.2) with $I = 0$, it is apparent that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$. In the case that the switch signal is periodic, then it follows from the bound (6.5) and the proof of Theorem 3.1.5 that the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the meaningful domain Ω_{SIR}. □

Next, consider the case where the incidence rates are not necessarily weakly nonlinear, but instead the forces of infection, $h(I)$ from $f(S,I) = h(I)S$, satisfy a concavity condition. Recall that the set $\mathcal{S}_{\text{inf-dwell}} \subset \mathcal{S}$ denotes the set of all switching signals σ which have nonvanishing dwell times, that is, there exists a $\eta > 0$, dependent on the specific solution of the switched system, such that

$$\inf_k t_k - t_{k-1} \geq \eta, \tag{6.6}$$

where $\{t_k\}$ is the sequence of switching times associated to the switching signal.

Theorem 6.1.3. *Assume $f_i(S,I) = h_i(I)S$ with $h_i(0) = 0$, $h_i(I) > 0$ for $I \neq 0$, $h_i(I) \in C^1[[0,1], \mathbb{R}_+]$, and*

$$\frac{dh_i}{dI} > 0, \qquad \frac{d^2 h_i}{dI^2} \leq 0.$$

If $\mathcal{R}_1, \ldots, \mathcal{R}_m < 1$ for a switching rule $\sigma \in \mathcal{S}_{\text{inf-dwell}}$, then the solution of system (6.2) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically (S,I)-stable, in the meaningful domain Ω_{SIR}.

Proof. This proof follows similarly from the non-switched SIR model with concave general nonlinear incidence rates [33]. Consider the Lyapunov function $V(S,I) = S - lnS + I - 1$, which is continuously differentiable for $S \geq \epsilon$. Define $\Omega_{SI}^{\epsilon} = \{(S,I) \in \mathbb{R}_+^2 |\ S \geq \epsilon, S+I \leq 1\}$, then $V(1,0) = 0$ and $V > 0$ for $(S,I) \in \Omega_{SI}^{\epsilon} \setminus \{(1,0)\}$. Further,

$$\frac{\partial V}{\partial S} = 1 - 1/S, \quad \frac{\partial^2 V}{\partial S^2} = 1/S^2, \quad \frac{\partial V}{\partial I} = 1, \quad \frac{\partial^2 V}{\partial I^2} = 0,$$

which implies $(S,I) = (1,0)$ is the only minimum of the Lyapunov function in the domain Ω_{SI}^{ϵ}. Take the time-derivative along solutions to the subsystem i:

$$\begin{aligned} \frac{dV}{dt} &= (1 - 1/S)\frac{dS}{dt} + \frac{dI}{dt} \\ &= (1 - 1/S)\left(\mu - h_i(I)S - \mu S\right) + h_i(I)S - (\mu + g)I, \\ &= \mu \underbrace{\left[(1 - 1/S)\left(1 - S\right)\right]}_{A} + (\mu + g)I \underbrace{\left(\frac{h_i(I)}{(\mu+g)I} - 1\right)}_{B_i}. \end{aligned} \tag{6.7}$$

First notice that since $0 \leq S \leq 1$, $(1 - 1/S)(1 - S) \leq 0$, and hence $\mathbf{A} < 0$ for $\epsilon \leq S < 1$ and $\mathbf{A} = 0$ only if $S = 1$. Next, consider the $\mathbf{B}_i$ term. From the concavity condition on h_i, it follows that $h_i(I)/I \leq \frac{\partial h_i(0)}{\partial I}$ for all $I > 0$, hence, following [33],

$$\frac{h_i(I)}{(\mu+g)I} \leq \frac{1}{\mu+g}\frac{\partial h_i(0)}{\partial I} = \mathcal{R}_i.$$

Thus $\mathcal{R}_i < 1$ gives $\mathbf{B}_i < 0$ for all i. Therefore, it follows that $V' < 0$ unless $(S,I) = (1,0)$. Hence, $V(S,I)$ is a common strict Lyapunov function. Since ϵ is arbitrary, consider the limit $\epsilon \to 0$, then the disease-free solution is asymptotically (S,I)-stable by Theorem 2.3.1 in Ω_{SIR}. Further, by inspection of system (6.2) with $S = 1, I = 0$, it is apparent that the solution will converge to the disease-free equilibrium $\bar{\mathbf{Q}}$. □

Example 6.1.1. *Consider the switched SIR system (6.2) with general nonlinear incidence rates $f_i(S,I) = h_i(I)S$ with $i \in \{1,2,3,4\}$ following a dwell-time satisfying switching rule $\sigma \in \mathcal{S}_{inf\text{-}dwell}$. Consider the standard forces of infections $h_1(I) = \beta_1 I$, and $h_2(I) = \beta_2 I$, and the saturating forces of infection $h_3(I) = \beta_3 \sin(\pi I/2)$ and $h_4(I) = \beta_4 \sin(\pi I/2)$. Notice that for all i:*

$$\frac{\partial^2 h_i}{\partial I^2} \leq 0.$$

Hence by inspection, each f_i satisfies the necessary conditions of Theorem 6.1.3. Furthermore, the reproduction numbers are

$$\mathcal{R}_1 = \frac{\beta_1}{\mu+g}, \quad \mathcal{R}_2 = \frac{\beta_2}{\mu+g}, \quad \mathcal{R}_3 = \frac{\pi}{2}\frac{\beta_3}{\mu+g}, \quad \mathcal{R}_4 = \frac{\pi}{2}\frac{\beta_4}{\mu+g}.$$

If $\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4 < 1$ then, by Theorem 6.1.3, the solution converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically (S,I)-stable, in the domain Ω_{SIR}. This example is illustrated Figure 6.1.

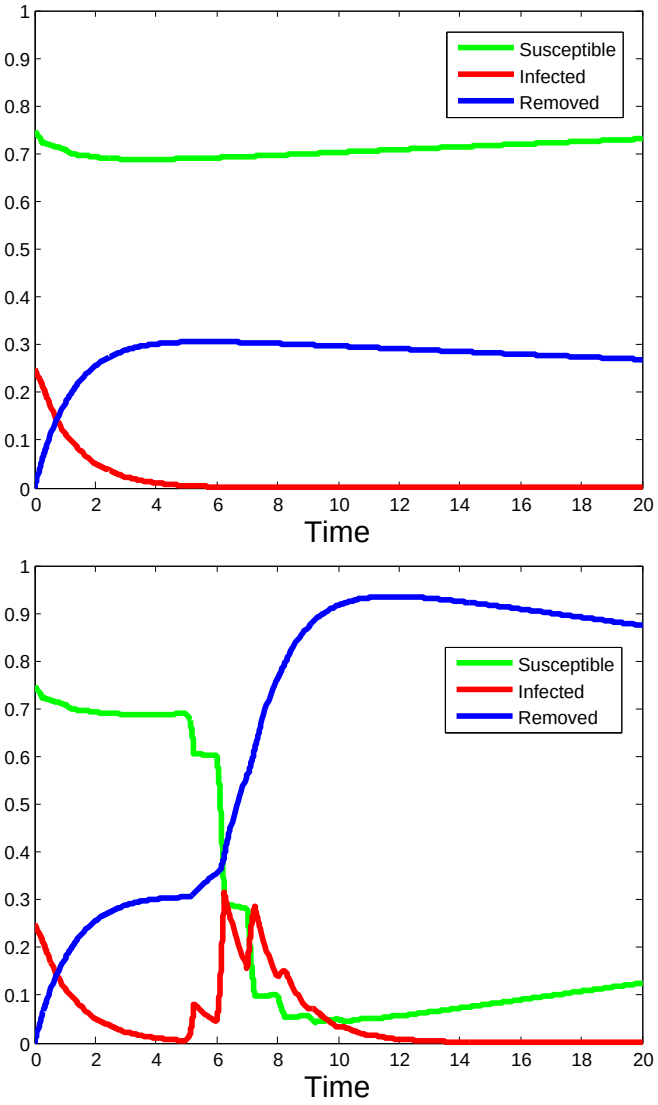

Figure 6.1: **Switched Concave Incidences Example.** In the top image, parameters are $g = 1$, $\mu = 0.01$, $\beta_1 = 0.6$, $\beta_2 = 0.2$, $\beta_3 = 0.6$, $\beta_4 = 0.2$. The incidence rates are $f_1 = \beta_1 SI$, $f_2 = \beta_2 SI$, $f_3 = \beta_3 S \sin(\pi I/2)$ and $f_4 = \beta_4 S \sin(\pi I/2)$. From $t = 0$ to $t = 5$, the standard incidence rates f_1 and f_2 are switched between seasonally. After $t = 5$, the saturating incidence rates f_3 and f_4 are switched between seasonally. Then the reproduction numbers are $\mathcal{R}_1 = 0.594$, $\mathcal{R}_2 = 0.198$, $\mathcal{R}_3 = 0.933$, $\mathcal{R}_4 = 0.311$, hence all the conditions of Theorem 6.1.3 are satisfied and the disease is eradicated. In the bottom image, the parameters are the same except $\beta_3 = 12$, which implies $\mathcal{R}_3 = 18.66$ and the disease is still eradicated.

6.2 Switched General Epidemiological Model with Weakly Nonlinear Incidences

Consider a more general epidemiological model now, based on a non-switched model in [58]. Assume that there are susceptible and infective compartments, and that susceptibles move into the infective class with horizontal incidence rate $g_i(I)S$. Assume the birth rate is $\mu > 0$, which is equal to the death rate. Assume that there are n_Y other compartments $Y_1, Y_2, \ldots, Y_{n_Y}$ which represent the various compartmental stages in the progression of the specific disease of interest. Assume that it is possible for these Y_j compartments to filter back into the susceptible class, with a rate $\theta_j \geq 0$. Furthermore, assume that the infective class filters into the Y_j compartments through a function $\Psi(I, Y)$. Assume that the spread of the disease in compartments Y_j are governed by a vector function $\Upsilon(S, I, Y)$. Then, the switched model is,

$$\begin{cases} \dot{S} = \mu - g_i(I)S - \mu S + \sum_{j=1}^{n_Y} \theta_j Y_j, \\ \dot{I} = g_i(I)S - \mu I + \Psi(I, Y), \\ \dot{Y} = \Upsilon(S, I, Y), \end{cases} \tag{6.8}$$

with $i \in \{1, 2, \ldots, m\}$ following a switching rule $\sigma \in \mathcal{S}$, $Y \in \mathbb{R}_+^{n_Y}$, and initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $Y(0) = Y_0 \in \mathbb{R}_+^{n_Y}$. The variables have been normalized by the total population so that $S + I + \sum_{j=1}^{n_Y} Y_j = 1$. The force of infections $g_i(I)$, $i = 1, \ldots, m$, are assumed to be sufficiently smooth functions satisfying $g_i(0) = 0$ and $g_i(I) > 0$ for $I > 0$ from physical considerations. Assume that $\Upsilon = (\Upsilon_1, \Upsilon_2, \ldots, \Upsilon_{n_Y})^T$ is a sufficiently regular vector function, such that $(\Upsilon_1(S, 0, Y), \ldots, \Upsilon_{n_Y}(S, 0, Y))^T = -(f_1(S, Y), \ldots, f_{n_Y}(S, Y))^T$ where $f_j \geq 0$ for all S, Y for $j = 1, \ldots, n_Y$. That is, $\Upsilon(S, 0, Y) = -f(S, Y)$ for some vector function $f \in \mathbb{R}_+^{n_Y}$ that satisfies $f \geq 0$ component-wise for all S, Y. Further, assume that $\Upsilon_1(S, I, 0), \ldots, \Upsilon_{n_Y}(S, I, 0) \geq 0$ for all S, I. Assume that $\Psi(I, Y)$ is a sufficiently smooth scalar function that maps a vector to a real number and that $\Psi(0, Y) = 0$. Finally, assume $\theta_k \geq 0$ for $k = 1, \ldots, n_Y$. For example, for the switched SIRS model (4.12), $g_i(I) = \beta_i I, \theta_1 = \theta, \Psi(I, Y) = -gI, \Upsilon(S, I, Y) = gI - \mu Y$, where $Y = R \in \mathbb{R}_+$.

The condition $S + I + \sum_{j=1}^{n_Y} Y_j = 1$ implicitly assumes that the functions satisfy $\mu - \mu(S + I) + \Upsilon_1 + \Upsilon_2 + \ldots + \Upsilon_{n_Y} + \Psi + \sum_{j=1}^{n_Y} \theta_j Y_j = 0$. This, along with the conditions on the functions outlined above, implies the meaningful domain $\Omega_{SIY} = \{(S, I, Y) \in \mathbb{R}_+^{2+n_Y} |\ S + I + \sum_{j=1}^{n_Y} Y_j = 1\}$ is invariant, and hence the model is physically and mathematically well-posed. From the assumptions on the functions, the disease-free solution is

$$\bar{\mathbf{Q}} = (1, 0, \underbrace{0, \ldots, 0}_{n_Y}).$$

Recall the notation $\Omega_{SI}^l = \{(S, I) \in \mathbb{R}_+^2 |\ S + I \leq 1\}$.

Theorem 6.2.1. *Assume $g_i \in C^1[\Omega_{SI}^l, \mathbb{R}_+]$, $g_i(I) \leq \beta_i I$ for all i and $\Psi(I,Y) \leq -CI$, with $C > 0$ a constant. If $\langle \mathcal{R}_\sigma^{non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$, switching rule $\sigma \in \mathcal{S}$, and non-physical reproduction numbers*

$$\mathcal{R}_i^{non} = \frac{\beta_i}{\mu + C},$$

then the solution of system (6.8) converges to the disease-free solution $\bar{\mathbf{Q}}$ of system (6.8), which is exponentially I-stable, in the meaningful domain Ω_{SIY}. If the switching rule is periodic $\sigma \in \mathcal{S}_{periodic}$ and $(\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0$, and the solution of system (6.8) converges to the disease-free solution $\bar{\mathbf{Q}}$, which is asymptotically I-stable, in the meaningful domain Ω_{SIY}.

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}$. Then for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$I' = g_{i_k}(I)S - \mu I + \Psi(I,Y) \leq \beta_{i_k} SI - \mu I - CI \leq (\beta_{i_k} - \mu - C)I = \lambda_{i_k} I, \quad (6.9)$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - C$. Then, by proof of Theorem 3.1.2, beginning with equation (3.11), $\bar{\mathbf{Q}}$ is exponentially I-stable. Then from $\Upsilon(S, 0, Y) = -f(S,Y)$, it is clear that all the variables $Y_1, \ldots, Y_k$ converge to zero. And $S = 1 - I - \sum_{j=1}^{n_Y} Y_j$ implies S converges to one. Hence, the solution converges to the disease-free equilibrium $\bar{\mathbf{Q}}$ in the meaningful domain Ω_{SIY}. In the case that the switching rule is periodic, then it follows from the bound (6.9) and the proof of Theorem 3.1.5 that the solution converges to the disease-free solution, which is asymptotically I-stable, in the meaningful domain Ω_{SIY}. □

6.3 Switched SIR Model with Pulse Vaccination and Treatment and Weakly Nonlinear Incidences

Now consider adding pulse treatment and pulse vaccination (see Section 5.2.2) to a switched SIR model with general nonlinear incidence rates $f_i(S,I)$. The incidences follow a switching rule, which is assumed to be periodic, that is, $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$. The model then is,

$$\begin{cases} \dot{S} = \mu - f_i(S,I) - \mu S, & t \in (t_{k-1}, t_k] \\ \dot{I} = f_i(S,I) - gI - \mu I, & \\ \dot{R} = -\mu R + gI, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) - pI(t), & \\ R(t^+) = R(t) + pS(t) + pI(t), & \end{cases} \quad (6.10)$$

where $k = 1, 2, \ldots$, $i \in \{1, \ldots, m\}$ according to a switching rule $\mathcal{S}_{\text{periodic-pulse}}$, $T = \tau_1 + \ldots + \tau_m$, and we have normalized the variables by the total population ($S + I + R = 1$), which is constant. The initial conditions are $S(0^+) = S_0 > 0, I(0^+) = I_0 > 0, R(0^+) = R_0$. Notice that

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

and the impulsive difference equations do not move the solution to outside the domain at the times kT, hence the domain is invariant to the switched system. From physical considerations, assume that $f_i(S, 0) = f_i(0, I) = 0$, and $f_i(S, I) > 0$, for all $(S, I) \in \Omega^l_{SI} = \{(S, I) \in \mathbb{R}^2_+ |\ S + I \leq 1\}$. From these conditions, it follows that there exists a periodic disease-free periodic solution $\mathbf{Q}(\mathbf{t}) = (\widetilde{S}(t), \widetilde{I}(t), \widetilde{R}(t)) = (\widetilde{S}(t), 0, 1 - \widetilde{S}(t))$, given in (5.44). The basic reproduction numbers of this system are [33]:

$$\mathcal{R}_i = \frac{1}{\mu + g} \frac{\partial f_i(\bar{S}, \bar{I})}{\partial I}. \tag{6.11}$$

Theorem 6.3.1. *Assume $f_i(S, I) \in C^1[\Omega^l_{SI}, \mathbb{R}_+]$ and $f_i(S, I) \leq \beta_i I$ for all i. If the switching rule is periodic $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$ and*

$$\frac{\ln(1-p)}{\mu + g} + (\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0,$$

where

$$\mathcal{R}_i^{non} = \frac{\beta_i}{\mu + g},$$

then the solution of system (6.10) converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$ of system (6.10), which is asymptotically I-stable, in the meaningful domain Ω_{SIR}.

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}_{\text{periodic-pulse}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\dot{I} = f_i(S, I) - gI - \mu I \leq (\beta_{i_k} - \mu - g)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - g$. Additionally, after each time T: $I(kT^+) = I(kT) - pI(kT)$. Then, from the proof of Theorem 5.2.3, beginning at equation (5.39), it follows that $\mathbf{Q}(\mathbf{t})$ is asymptotically I-stable. The limiting system then becomes

$$\begin{cases} \dot{S} = \mu(1 - S), & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R, & \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t) + pS(t). & \end{cases}$$

where $T = \tau_1 + \ldots + \tau_m$. This is the reduced system (5.43), which converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$ of system (6.10) in the meaningful domain Ω_{SIR}. □

6.4 Switched General Epidemiological Model with Pulse Control and Weakly Nonlinear Incidences

Consider the general epidemiological model with switched forces of infections (6.8), but now incorporate pulse vaccination and pulse treatment control schemes by introducing a vaccinated class V. Here it is assumed that the immunity gained through vaccination is permanent. Assume that the switching signal is periodic, $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$.

$$\begin{cases} \dot{S} = \mu - g_i(I)S - \mu S + \sum_{j=1}^{n_Y} \theta_j Y_j, & t \in (t_{k-1}, t_k] \\ \dot{I} = g_i(I)S - \mu I + \Psi(I, Y), \\ \dot{Y} = \Upsilon(S, I, Y), \\ V = 1 - S - I - \sum_{j=1}^{n_Y} Y_j, \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) - pI(t), \\ Y(t^+) = Y(t), \\ V(t^+) = V(t) + pS(t) + pI(t), \end{cases} \tag{6.12}$$

with $i \in \{1, 2, \ldots, m\}$, $Y \in \mathbb{R}_+^{n_Y}$, initial conditions $S(0^+) = S_0 > 0$, $I(0^+) = I_0 > 0$, $Y(0^+) = Y_0$, and the variables have been normalized so that $S+I+V+\sum_{j=1}^{n_Y} Y_j = 1$. Here $T = \tau_1 + \ldots + \tau_m$ is one period of the periodic switching rule $\sigma_{\text{periodic-pulse}}$. From natural considerations, assume $g_i(0) = 0$ and $g_i(I) > 0$ for $I > 0$. Assume that Υ, Ψ and θ_j satisfy the same conditions as in Section 6.2.

The meaningful domain for this system is $\Omega_{SIYV} = \{(S, I, Y) \in \mathbb{R}_+^{3+n_Y} \mid S + I + V + \sum_{j=1}^{n_Y} Y_j = 1\}$. The conditions on the functions outlined above, along with the fact that the impulsive difference equations do not move solutions to outside this meaningful domain, imply the domain Ω_{SIYV} is invariant to this impulsive switched system. Hence, the model is physically well-posed. There is not a disease-free equilibrium point for this system, but motivated by $I = 0$ being a solution to the differential equation for I, set $I = 0$ and seek the long-term solution,

$$\begin{cases} \dot{S} = \mu - g_i(I)S - \mu S, & t \in (t_{k-1}, t_k] \\ V = 1 - S, \\ S(t^+) = S(t) - pS(t), & t = kT \\ V(t^+) = V(t), \end{cases} \tag{6.13}$$

with $T = \tau_1 + \ldots + \tau_m$. This leads to the disease-free periodic solution

$$\mathbf{Q}(\mathbf{t}) = (\widetilde{S}(t), \widetilde{I}(t), \widetilde{Y}_1(t), \ldots, \widetilde{Y}_{n_Y}(t), \widetilde{V}(t)) = (\widetilde{S}(t), 0, \underbrace{0, \ldots, 0}_{n_Y}, 1 - \widetilde{S}(t)),$$

with $\widetilde{S}(t)$ given in (5.44). Recall the notation $\Omega_{SI}^l = \{(S, I) \in \mathbb{R}_+^2 |\ S + I \leq 1\}$.

Theorem 6.4.1. *Assume $g_i \in C^1[\Omega_{SI}^l, \mathbb{R}_+]$, $g_i(I) \leq \beta_i I$ for all i, and $\Psi(I, Y) \leq -CI$, for a constant $C > 0$. If the switching rule is periodic $\sigma \in \mathcal{S}_{\text{periodic-pulse}}$ and*

$$\frac{\ln(1-p)}{\mu + C} + (\mathcal{R}_1^{non} - 1)\tau_1 + \ldots + (\mathcal{R}_m^{non} - 1)\tau_m < 0,$$

where

$$\mathcal{R}_i^{non} = \frac{\beta_i}{\mu + C},$$

then the solution of system (6.12) converges to the periodic disease-free solution $\mathbf{Q}(\mathbf{t})$, which is asymptotically I-stable, in the meaningful domain Ω_{SIYV}.

Proof. Let i_k follow the switching rule $\sigma(t) \in \mathcal{S}_{\text{periodic-pulse}}$. Then, for $t \in (t_{k-1}, t_k]$, $i_k = \sigma(t)$ and,

$$\dot{I} = g_i(I)S - \mu I + \Psi(I, Y) \leq (\beta_{i_k} - \mu - C)I = \lambda_{i_k} I,$$

where $\lambda_{i_k} := \beta_{i_k} - \mu - C$. Additionally, after each time T: $I(kT^+) = I(kT) - pI(kT)$. Then, from the proof of Theorem 5.2.3, beginning at equation (5.39), $\mathbf{Q}(\mathbf{t})$ is asymptotically I-stable. Then, from $\Upsilon(S, 0, Y) = -f(S, Y)$, it is clear that the variables $Y_1, \ldots, Y_{n_Y}$ converge to zero. The system then reduces to (6.13) and hence the solution converges to the disease-free periodic solution $\mathbf{Q}(\mathbf{t})$ in the meaningful domain Ω_{SIYV}. □

Chapter 7

Conclusions and Future Directions

Infectious disease models are invaluable for both the building and testing of theories [27]. Certainly, they are used in comparing, planning, implementing and evaluating various detection, prevention and control programs [27]. Indeed, one of the most important issues in epidemiology is the controlled eradication of a disease. In this thesis we constructed and analyzed a new type of switched model for the spread of diseases. Threshold criteria were established ensuring the eradication of the disease and hence convergence to the so-called disease-free solution for many different models. Considering the importance of control strategies, switched models with control schemes were also considered. We looked at classical and interesting models that are found in the mathematical epidemiology literature and analyzed these models when switching was introduced to them.

In Chapter 3 the basic SIS model with switching was studied. This model, which is intrinsically one-dimensional, was analyzed under basic switching, switching with vertical transmission, switching with varying total population, and switching in the contact rate, removal rate and birth rate. Threshold criteria ensuring the eradication of the disease, that are mathematically straightforward to evaluate, were established in the chapter. Proofs were also given for permanence of the disease in the endemic case. Simulations were given at the end of the chapter.

In Chapter 4, multi-dimensional models with switching were studied. The most common models, SIR, SIRS, and SEIR were all investigated with switching. We also looked at a switched MSIR for transplacental antibody transfer, as well as SIR models with varying population and some interesting switched multi-city transport models. Similarly to Chapter 3, some intuitively reasonable, and straightforward to evaluate, threshold criteria were established for the eradication of the disease. Since these models were all intrinsically at least two dimensional, the persistence of the disease was conjectured when the reproduction numbers were all greater than one. Simulations were again given at the end of this chapter.

Chapter 5 investigated models with control schemes. In Section 5.1, the constant control strategy of vaccination or treatment was considered with switching. This investigation encompassed the switched SIR model with constant vaccination of

newborns, constant vaccination of susceptibles, constant treatment of infectives and constant treatment of infectives with waning immunity. Some other interesting models were investigated with switching, such as constant control models with progressive immunity and a screening process for infected individuals travelling in a switched multi-city model. In Section 5.2, the pulse control strategy applied to the SIR model was considered with the addition of switching in the contact rate. Both pulse treatment and pulse vaccination systems were studied, including models with vaccine failure and a reduced infective classes. Finally, some simulations were given to illustrate the benefits of control strategies.

In Chapter 6, more general epidemiological models with switching were studied. First, models with switched weakly nonlinear incidence rates were considered, as well as models with switched concave forces of infection. A general epidemiology with switching was also discussed, with general compartments and switching weakly nonlinear forces of infection. Pulse control schemes applied to these generalized switched epidemiological models were also investigated. Threshold criteria were given that were relatively simple to verify.

There are many benefits to a switching approach in infectious disease models. It allows us to approximate the contact rate to be a time-varying parameter without needing to change the models into non-autonomous systems. Because of this, we have relatively straightforward methods from switched systems theory to prove easily verifiable eradication criteria for time-varying contact rates. More specifically, it enables us to vary the contact rates such that the reproduction numbers can be larger than one temporarily, by using a proof for switched systems with stable and unstable modes. In the temporally forced non-autonomous approach, $\beta = \beta(t)$, the analytical methods are more difficult and for some models and scenarios not available. The switching rule considered can be restricted, for example to periodic switching, to guarantee disease eradication for these switched epidemiological models, including pulse control models with switching. These methods are easily extendible so that any parameter can be approximated by a piecewise constant, including the level of vaccination in the pulse control models.

Further, another benefit to a switched systems approach can be seen in Chapter 6, where switching in the structure of the incidence rate is considered. This is an interesting possibility in that the horizontal incidence rate can change over time, which could be advantageous for certain infectious disease scenarios. This is not trivial in the non-switched approach, and to the author's knowledge has not been studied. Another flexibility is that the switching in these models does not necessarily need to be time-dependent, it could also be state-dependent. That is, the parameters or incidence rate structure could switch values based on the state of the epidemiological compartments.

Since these methods are easily adapted to many different infectious disease models, as illustrated in this thesis, there is a great possibility for future work with this approach. Certainly, one area which could be investigated is infectious models with delay. These systems of delay differential equations, which can arise from a

latent period of the disease, lead to some interesting behaviour (see [19, 20, 21, 30, 61]). These models could be considered as delay switched systems, which is a new area in switched systems that is being investigated currently (for example, see [5]).

Another area for future direction is to consider infectious models without the homogeneous mixing assumption. Realistic epidemiological models include both time and age as independent variables, as it has been observed that age groups mix heterogeneously, risks from an infection may be age related, vaccination programs often focus on specific ages, and epidemiological data is often age specific [28]. Then, considering epidemiological models with age structure and switching would lead to switched systems of partial differential equations, which is an area currently in its infancy. Epidemiological models with age structure can be found in [28, 31, 55].

One disadvantage to the approaches taken in this thesis is that if the dynamic structure of the disease spread is not captured in the differential equation for I, then the method used in proofs for both stable and unstable subsystems fails to establish threshold criteria. Other methods must be resorted to, such as multiple and common Lyapunov function techniques (for example, in the switched SEIR models in Section 4.6). In the cases where a Lyapunov function is not easily constructed, conjectures were made (for example, in the constant vaccination of newborns scheme in Section 5.1.1). Hence, one possible direction is to generalize the method for stable and unstable subsystems to deal with models where the dynamics of the disease are captured in other compartments.

Finally, epidemiological models with a spatial structure could be also considered as switched systems. That is, models with both a temporal dependence and spatial dependence. Such models lead to systems of partial differential equations which may exhibit interesting phenomena, such as spatial waves (travelling waves), rather than temporal waves [55].

References

[1] L.J.S. Allen. *An Introduction to Mathematical Biology.* Prentice Hall, 2006. 68

[2] R. M. Anderson and R. M. May. *Directly Transmitted Infectious Diseases: Control by Vaccination.* Science, New Series, 215(4536) (1982), pp. 1053-1060. ix, 1, 22, 23, 33

[3] R.M. Anderson and R. M. May. *Infectious Diseases of Humans.* Oxford University Press, 1991. 2

[4] Z. Agur, L. Cojocaru, G. Mazor, R. M. Anderson, and Y. L. Danon *Pulse mass measles vaccination across age cohorts.* Proc. Natl. Acad. Sci. USA, 90 (1993), pp. 11698-11702. 33, 34, 35, 37, 38

[5] M. S. Alwan and X. Liu. *On stability of linear and weakly nonlinear switched systems with time delay.* Mathematical and Computer Modelling, 48(7-8) (2008), pp. 1150-1157. 146

[6] A. Bacciotti and L. Mazzi. *An invariance principle for nonlinear switched systems.* Systems Control Letters, 54 (2005), pp. 1109-1119. 5, 42, 44, 45, 49, 50

[7] D.D. Bainov and P.S. Simeonov. *Impulsive Differential Equations: Asymptotic Properties of the Solutions.* World Scientific Publishing co. Pte. Ltd., 1995. 17, 18

[8] M. S. Branicky. *Multiple Lyapunov Functions and Other Analysis Tools for Switched and Hybrid Systems.* IEEE Transactions on Automatic Control, 43(4) (1998), pp. 475-482. 5

[9] M. S. Branicky. *Stability of Switched and Hybrid Systems.* Proceedings of the 33rd Conference on Decision and Control (1994). 5

[10] J. Cui, Y. Takeuchi, and Y. Saito. *Spreading disease with transport-related infection.* Journal of Theoretical Biology, 239 (2006), pp. 376-290. 87, 89, 90, 100

[11] J. Daafouz, P. Riedinger, and C. Iung. *Stability Analysis and Control Synthesis for Switched Systems: A Switched Lyapunov Function Approach.* IEEE Transactions on Automatic Control, 47(11) (2002), pp. 1883-1887. 5

[12] G. Davrazos and N. T. Koussoulas. *A Review of Stability Results for Switched and Hybrid Systems.* Mediterrenean conferences on control and automation (2001). 4, 5, 40, 49

[13] R. A. Decarlo, M. S. Branicky, S. Pettersson, and B. Lennartson. *Perspectives and Results on the Stability and Stabilizability of Hybrid Systems.* Proceedings of the IEEE, 88(7) (2000), pp. 1069-1082. 5, 40

[14] O. Diekmann, J. A. P. Heesterbeek, and J. A. J. Metz. *On the defintion and the computation of the basic reproduction ratio $\mathcal{R}_0$ in models for infectious diseases in heterogeneous populations.* Journal of Mathematical Biology, 28 (1990), pp. 365-382 23

[15] P. van den Driessche and J. Watmough. *A simple SIS epidemic model with a backward bifurcation.* Mathematical Biology, 40 (2000), pp. 525-540. 133

[16] P. van den Driessche and J. Watmough. *Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission.* Mathematical Biosciences, 180 (2002), pp. 29-48. 23

[17] R. J. Evans and A. V. Savkin. *Hybrid Dynamical Systems.* Birkhauser, 2002. 4, 5, 40, 42, 49

[18] M. Fan, M. Y. Li, and K. Wang. *Global stability of an SEIS epidemic model with recruitment and a varying total population size.* Mathematical Biosciences, 170 (2001), pp. 199-208. 21, 30

[19] S. Gao, L. Chen, J. J. Neito, and A. Torres. *Analysis of a Delayed Epidemic Model with Pulse Vaccination and Saturation Incidence.* Vaccine, 24(35-36) (2006), pp. 6037-6045. 21, 23, 34, 133, 134, 146

[20] S. Gao, L. Chen, and Z. Teng. *Impulsive Vaccination of an SEIRS Model with Time Delay and Varying Total Population Size.* Bulletin of Mathematical Biology, 69 (2007), pp. 731-745. 21, 86, 146

[21] S. Gao, L. Chen, and Z. Teng. *Pulse vaccination of an SEIR epidemic model with time delay.* Nonlinear Analysis: Real World Applications, 9 (2006), pp. 599-607. 34, 146

[22] Z.H. Guan, D. Hill, and X. Shen. *On Hybrid Impulsive and Switching Systems and Application to Nonlinear Control.* IEEE Transactions on Automatic Control, 50(7) (2005), pp. 1058-1062. 5, 16, 42, 55, 56, 116

[23] Z.H. Guan, D. Hill, and J. Yao. *A Hybrid Impulsive and Switching Control Strategy for Synchronization of Nonlinear Systems and Application to Chua's Chaotic Circuit.* International Journal of Bifurcation and Chaos, 16(1) (2006), pp. 229-238. 5, 56, 117

[24] J. P. Hespanha. *Extending LaSalle's Invariance Principle to Switched Linear Systems.* Proceedings of the 40th IEEE Conference on Decision and Control (2001). 5, 45

[25] J. P. Hespanha. *Uniform Stability of Switched Linear Systems: Extensions of LaSalle's Invariance Principle.* IEEE Transactions on Automatic Control, 49(4) (2004), pp. 470-482. 5, 40, 41, 47

[26] J. P. Hespanha and A. S. Morse. *Stability of Switched Systems with Average Dwell-Time.* Proceedings of the 38th IEEE Conference on Decision and Control, 3 (1999), pp. 2655-2660. 47

[27] H. W. Hethcote. *A Thousand and One Epidemic Models* Frontiers in Theoretical Biology, 100 (1994), pp. 504-515. 1, 2, 4, 19, 21, 59, 61, 62, 63, 86, 133, 144

[28] H. W. Hethcote. *The Mathematics of Infectious Diseases.* SIAM Review, 42 (2000), pp. 599-653. 1, 2, 3, 19, 20, 21, 22, 24, 25, 26, 28, 32, 38, 52, 77, 132, 146

[29] H. W. Hethcote. *Three Basic Epidemiological Models.* Applied Mathematical Ecology, Biomathematics, 18 (1989), pp. 119-144. 24, 26, 27, 28, 29, 34, 52, 53

[30] H. W. Hethcote and P. van den Driessche. *An SIS epidemic model with variable population size and a delay.* Journal of Mathematical Biology, 34 (1995), pp. 177-194. 21, 28, 146

[31] M. J. Keeling and P. Rohani. *Modeling Infectious Diseases in Humans and Animals.* Princeton University Press, 2008. 2, 3, 4, 18, 19, 20, 21, 24, 26, 27, 28, 30, 31, 32, 33, 34, 37, 38, 39, 51, 52, 146

[32] A. Korobeinikov. *Lyapunov functions and global properties for SEIR and SEIS epidemic models.* Mathematical Medicine and Biology, 21 (2004), pp. 75-83. 20, 31

[33] A. Korobeinikov. *Lyapunov Functions and Global Stability for SIR and SIRS Epidemiological Models with Non-linear Transmission.* Bulletin of Mathematical Biology, 30 (2006), pp. 615-626. 4, 20, 21, 59, 61, 63, 132, 133, 135, 137, 141

[34] A. Korobeinikov and P. K. Maini. *A Lyapunov Function and Global Properties for SIR and SEIR Epidemiological Models with Nonlinear Incidence.* Mathematical Biosciences and Engineering, 1(1) (2004), pp. 57-60. 21, 133

[35] A. Korobeinikov and G. C. Wake. *Lyapunov Functions and Global Stability for SIR, SIRS, and SIS Epidemiological Models*. Applied Mathematics Letters, 15 (2002), pp. 955-960. 26, 28, 30, 61

[36] C. M. Kribs-Zaleta and J. X. Velasco-Hernandez. *A simple vaccination model with multiple endemic states*. Mathematical Biosciences, 164 (2000), pp. 183-201. 33

[37] V. Lakshmikantham, D.D. Bainov, and P.S. Simeonov. *Theory of Impulsive Differential Equations*. World Scientific Publishing co. Pte. Ltd., 1989. 15, 18

[38] M. Y. Li, J. R. Graef, L. Wang, and J. Karsai. *Global dynamics of a SEIR model with varying total population size*. Mathematical Biosciences, 160 (1999), pp. 191-213. 21, 31, 32, 82, 83

[39] M. Y. Li and J. S. Muldowney. *Global Stability for the SEIR Model in Epidemiology*. Mathematical Biosciences, 125 (1995), pp. 155-164. 21, 31

[40] M. Y. Li, H. L. Smith, and L. Wang. *Global Dynamics of an Seir Epidemic Model with Vertical Transmission*. SIAM Journal on Applied Mathematics, 62 (2001), pp. 58-69. 20, 30, 31, 63, 80, 81

[41] Y. Li and J. Cui. *The effect of constant and pulse vaccination on SIS epidemic models incorporating media coverage*. Nonlinear Science and Numerical Simulation, 14 (2009), pp. 2353-2365. 3, 21, 33, 34, 91

[42] D. Liberzon and A. S. Morse. *Basic Problems in Stability and Design of Switched Systems*. Control Systems Magazine, IEEE., 19(5) (1999), pp. 59-70. 4, 5, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49

[43] S. Liu, Y. Pei, C. Li, and L. Chen. *Three kinds of TVS in a SIR epidemic model with saturated infectious force and vertical transmission*. Applied Mathematical Modelling, 33(4) (2009), pp. 1923-1932. 2, 20, 21, 33, 34, 36, 134

[44] W. Liu, H. W. Hethcote and S. A. Levin. *Dynamical behavior of epidemiological models with nonlinear incidence rates*. Journal of Mathematical Biology, 25 (1987), pp. 359-380. 21, 22, 31, 32

[45] X. Liu. *Introduction to Dynamical Systems*. University of Waterloo, 1999. 7, 11

[46] X. Liu and Y. Takeuchi. *Spread of disease with transport-related infection and entry screening*. Journal of Theoretical Biology, 242 (2006), pp. 517-528. 33, 87, 112

[47] X. Liu, Y. Takeuchi, and S. Iwami. *SVIR epidemic models with vaccination strategies*. Journal of Theoretical biology, 253 (2008), pp. 1-11. 2, 26, 33, 108, 109

[48] Z. Lu, X. Chi, and L. Chen. *The Effect of Constant and Pulse Vaccination on SIR Epidemic Model with Horizontal and Vertical Transmission.* Mathematical and Computer Modelling, 36 (2002), pp. 1039-1057. 3, 20, 33, 34, 59, 68

[49] J. Ma and Z. Ma. *Epidemic Threshold Conditions for Seasonally Forced SEIR Models.* Mathematical Biosciences and Engineering, 3(1) (2006), pp. 161-172. 4, 21, 31, 32, 51, 63, 66, 99

[50] J.D. Meiss. *Differential Dynamical Systems.* Society for Industrial and Applied Mathematics, 2007. 36

[51] X. Meng and L. Chen. *The dynamics of a new SIR epidemic model concerning pulse vaccination strategy.* Applied Mathematics and Computation, 197 (2008), pp. 582-597. 20, 23, 33, 34, 38

[52] H. N. Moreira and W. Yuquan. *Global Stability in an SIRI Model.* SIAM, 39(3) (1997), pp. 496-502. 21

[53] Y. Mori, T. Mori, and Y. Kuroe. *A Solution to the Common Lyapunov Function Problem for Continuous-Time Systems.* Proceedings of the 36th Conference on Decision & Control (1997). 5

[54] E. Moulay, R. Bourdais, and W. Perruquetti. *Stabilization of nonlinear switched systems using control Lyapunov functions.* Nonlinear analysis: Hybrid Systems, 1 (2007), pp. 482-490. 5

[55] J.D. Murray. *Mathematical Biology.* Springer-Verlag, 1989. 2, 19, 24, 25, 26, 28, 146

[56] K. S. Narendra and J. Balakrishnan. *A Common Lyapunov Function for Stable LTI Systems with Commuting A-Matrices.* IEEE Transactions on Automatic Control, 39(12) (1994), pp. 2469-2471. 5

[57] A. d'Onofrio. *On pulse vaccination strategy in the SIR epidemic model with vertical transmission.* Applied Mathematics Letters, 18 (2005), pp. 729-737. 20, 51, 59

[58] A. d'Onofrio *Pulse Vaccination Strategy in the SIR Epidemic Model: Global Asymptotic Stable Eradication in Presence of Vaccine Failures* Mathematical and Computer Modelling, 36 (2002), pp. 473-489. 21, 34, 51, 122, 124, 139

[59] A. d'Onofrio. *Stability properties of pulse vaccination strategy in SEIR epidemic model.* Mathematical Biosciences, 179 (2002). pp. 57-72. 51

[60] A. d'Onofrio. *Vaccination policies and nonlinear force of infection: generalization of an observation by Alexander and Moghadas (2004).* Applied Mathematics and Computation, 168 (2005), pp. 613-622. 3, 4, 21, 38, 51, 132, 133

[61] G. Pang and L. Chen. *A delayed SIRS epidemic model with pulse vaccination.* Chaos, Solitons and Fracticals, 34 (2007), pp. 1629-1635. 3, 4, 21, 34, 134, 146

[62] S. Pettersson and B. Lennartson. *Stability and Robustness for Hybrid Systems.* Proceedings of the 35th Conference on Decision and Control (1996). 5, 47, 48

[63] I. B. Schwartz. *Multiple stable recurrent outbreaks and predictability in seasonally forced nonlinear epidemic models.* Journal of Mathematical Biology, 21 (1985), pp. 247-361. 3, 31, 51

[64] R. Shorten, F. Wirth, O. Mason, K. Wulff, and C. King. *Stability Criteria for Switched and Hybrid Systems.* SIAM Review, 49 (2007), pp. 545-592. 4, 5, 40, 45, 46, 47

[65] R.N. Shorten, F. O. Cairbre, and P. Curran. *On the dynamic instability of a class of switching system.* International Journal of Control, 79(6) (2006), pp. 630-635. 5

[66] B. Shulgin, L. Stone, and Z. Agur. *Pulse Vaccination Strategy in the SIR Epidemic Model.* Bulletin of Mathematical Biology, 60 (1998), pp. 1123-1148. 4, 33, 34, 35, 36, 37, 38, 39, 51, 97, 127

[67] L. Stone, B. Shulgin, and Z. Agur. *Theoretical Examination of the Pulse Vaccination Policy in the SIR Epidemic Model.* Mathematical and Computer Modelling, 31 (2000), pp. 207-215. 3, 33, 34, 37, 38

[68] Y. Takeuchi, X. Liu, and J. Cui. *Global dynamics of SIS models with transport-related infection.* Journal of Mathematical Analysis and Applications, 329 (2007), pp. 1460-1471. 33, 87, 112

[69] H. R. Thieme. *Uniform persistence and permanence for non-autonomous semiflows in population biology.* Mathematical Biosciences, 166 (2000). pp. 173-201. 23

[70] V. I. Vorotnikov. *Partial Stability and Control.* Birkhauser, 1998. 14, 15

[71] E.R. Vrscay. *Differential Equations II.* University of Waterloo, 2005. 15

[72] W. Wang and G. Mulone. *Threshold of disease transmission in a patch environment.* Journal of Mathematical Analysis and Applications, 285 (2003), pp. 321-335. 22, 28, 87, 92

[73] Y. Zhou and H. Liu. *Stability of Periodic Solutions for an SIS Model with Pulse Vaccination.* Mathematical and Computer Modelling, 38 (2003), pp. 299-308. 33, 34, 104