Infectious Disease Modeling with Interpersonal Contact Patterns as a Heterogeneous Network

by

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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

In this thesis, we study deterministic compartmental epidemic models. The conventional mass-mixing assumption is replaced with infectious disease contraction occurring within a heterogeneous network. Modeling infectious diseases with a heterogeneous contact network divides disease status compartments into further sub-compartments by degree class and thus allows for the finite set of contacts of an individual to play a role in disease transmission.

These epidemiological network models are introduced as switched systems, which are systems that combine continuous dynamics with discrete logic. Many models are investigated, including SIS, SIR, SIRS, SEIR type models, and multi-city models. We analyze the stability of these switched network models. Particularly, we consider the transmission rate as a piecewise constant that changes value according to a switching signal. We establish threshold criteria for the eradication of a disease or stability of an endemic equilibrium using Lyapunov function techniques. Simulations are also conducted to support our claims and conclude conjectures.

We test constant control and pulse control schemes, including vaccination, treatment, and screening processes for the application of these infectious disease models. Necessary critical control values are determined for the eradication of the disease.

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Dedication

To my Mother and Father.

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Chapter 1

Introduction

The history of the world is intertwined with the impact of infectious diseases [10]. Infectious diseases have threatened humanity for centuries; 3000 year old Egyptian mummies were found with evidence of smallpox and art and literature dating several centuries back reference the spread of disease [10]. With scientific research and human advancements, human life expectancy has improved from approximately 30 years in 1700 to 70 years in 1970, with one of the main causes being a decline in deaths due to infectious diseases. [2]. In the 20th century, the proven effectiveness of better sanitization and the discovery of antibiotics and vaccination lead the world to believe infectious diseases would soon be eliminated [26]. However, infectious diseases continue to be one of the major causes of death and suffering in developing countries [26]. As disease agents adapt, survive, and evolve, the emergence of new diseases and re-emergence of existing diseases have become a significant worldwide problem [10, 26]. Newly identifies diseases include Lyme disease in 1975, Legionnaire's disease in 1976, toxic-shock syndrome in 1978, hepatitis C in 1989, hepatitis E in 1990 and hantavirus in 1993 [26]. The human immunodeficiency virus (HIV), which can lead to the acquired immunodeficiency syndrome (AIDS) emerged in 1981 and has become an important sexually transmitted disease as well as the fourth leading cause of death throughout the world [10, 26]. Antibiotic resistant strains of tuberculosis (TB), pneumonia and gonorrhea have evolved [26]. Malaria, dengue, and yellow fever have re-emerged and spread into new regions as climate changes occur [26]. In 2014, a major outbreak of Ebola occurred in Guinea, Sierra Leone, and Liberia [50]. Diseases such as ebola, plague, and cholera continue to erupt occasionally [26].

Human and animal invasions of new ecosystems, global warming, and environmental changes continue to provide opportunities for new and existing diseases [47]. Mass migrations, international trade and travel are notoriously effective at spreading disease to even the most remote parts of the globe [18]. While emerging and re-emerging diseases are likely to appear in poorer countires first, they can easily spread to the richer parts of the world [18]. Infectious diseases, especially when an epidemic occurs, continually make costly disruptions to trade and commerce all over the world [18]. The economic impact has many factors, including lowering productivity, reducing foreign investment, and increasing health care costs,

all which can affect the gross national product in many countries [18]. Even a relationship between disease and political stability, although indirect, exists [18]. Studies have shown a correlation between TB prevalence, an indicator of overall quality of life, and political instability [18]. Infectious diseases have an impact on the health of individuals as well as whole societies, economies and political systems [18]. Thus, the emergence and re-emergence of diseases have lead to a revived interest in infectious diseases [26].

Mathematical models are important tools in analyzing the spread and control of infectious diseases [26]. Mathematical models and computer simulations are useful to build theories, test them, assess quantitative conjectures, answer specific questions, and determine conceptual results such as thresholds, basic reproduction numbers and contact numbers [26]. The first known epidemiological model was formulated and solved by Daniel Bernoulli in 1760 to evaluate the smallpox virus [26]. In 1906, Hamer analyzed a discrete time model to understand the recurrence of measles epidemics, which may have been the first model to assume that disease incidence is related to the population densities of susceptibles and infectives [26]. Ross developed differential equation models for malaria in 1911 [26]. Starting 1926, Kermack and McKendrick published papers on epidemic models and first obtained the epidemic threshold result that if a critical value of the susceptibles density was exceeded then an epidemic outbreak would occur [26]. Deterministic epidemiological models mostly started in the 20th century, yet have grown exponentially be the middle of the 20th century [26]. Mathematical models have been formulated for diseases such as measles, rubella, chicken pox, whooping cough, diphtheria, smallpox, malaria, onchocerciasis, filariasis, rabies, gonorrhea, herpes, syphilis, and HIV/AIDS [26].

The prediction of disease evolution and social contagion processes can be conceptualized with mathematical models of spreading [8]. These models evolved from simple compartmental approaches to structured frameworks in which heterogeneities present at the community and population levels are becoming increasingly important features [3, 8]. As the case is in many models, there is an interplay between the simplicity of the models and the accuracy of its predictions [8]. A vast majority of these models assume that individuals in populations interact uniformly, which is called the "mass-mixing" assumption. While this assumption simplifies most models and allows for straightforward analysis and understanding of the dynamics, it can be beneficial to formulate models with a more realistic approach and compare the behaviour to the simpler models. The assumption that all individuals have a uniform contact pattern; that is, any person has an equal chance of contracting or transmitting the disease with any other person in the population, is oversimplified and unrealistic. One alternative to the mass-mixing assumption is the concept that each individual interacts within a network of relationship and contact patterns. It is more realistic that a person would transmit or contract the disease from their own neighbourhood of individuals which they have contact relationships with. Network analysis has been a useful explanatory tool that is relevant to epidemiology because social importance of an individual is closely linked to their role in disease spread [29]. Networks and epidemiology of directly transmitted diseases are

fundamentally linked [29].

Another convention of infectious disease models in epidemic literature assume that the parameters, such as the transmission rate, are constant in time [40]. A more realistic approach is to assume that the transmission rate is time-varying, for instance, childhood infections have been shown to peak at the start of a school year and decline significantly in the summer months [30]. There are many factors that possibly cause a seasonality effect in the spread of disease, for instance changes in host behaviour, changes in the abundance of vectors (due to weather), changes in host immunity, and changes in pathogen survivability outside their hosts [16, 21].

Many systems encountered in practice exhibit switching behaviour between different subsystems depending on various external or environmental factors [36]. Switched systems are types of hybrid systems that can model real world complex systems, such as mechanical systems, the automotive industry, aircraft and traffic control, robotics, integrated circuit design, multimedia, manufacturing, power electronics chaos generators, and chemical processes [14, 17, 22, 36, 42]. A switched system is a hybrid system consisting of a family of continuous-time subsystems and a rule that orchestrates the switching between them [36].

1.1 Contributions

The main objective of this thesis is to extend existing literature by formulating new epidemiological models with network contact patterns and time-varying transmission rates and to study the behaviour of these models. We will develop critical threshold criteria for epidemic outbreaks in network disease models with the addition of switching, the abrupt change in dynamics of the systems at certain switching times. The switching will allow for the transmission rate to vary in time and be approximated by a piecewise constant function. Although there are some studies on disease models with the network mixing assumption, there is a lack of deterministic models over networks with time-varying parameters. The switching is a new approach to combine in models with interpersonal contact patterns of disease transmission thought of as a network.

Classical models such as SIS, SIR, SIRS and SEIR models will be studied over the network mixing assumption and with a time-varying transmission rate. Further, the network approach will be considered on multi-city models, at first on a model with two cities and then with an arbitrary number of cities. Control schemes including constant and pulse control will be considered on these models. Vaccination and treatment are control schemes often found in literature. We also consider screening processes as a control for multi-city models, where infected individuals are screened and restricted of travel. We will use the control schemes and determine how they apply to switched epidemic network models.

We support our theory with simulation results.

1.2 Guide to Thesis

The thesis is structured as follows:

Chapter 2 This chapter provides necessary mathematical background including ODE theory, epidemiological modeling and switched hybrid systems.

Chapter 3 Introduction to epidemiological models using a network mixing assumption in lieu of the conventional mass mixing assumption. Stability of the disease-free and endemic equilibria is analyzed and simulations are given to back up analysis.

Chapter 4 A switching parameter is introducted to basic SIS network models including only two main disease classes, susceptible and infective (to then be divided into sub-classes by network degree). Numerical simulations are given under simple switching techniques to support analysis.

Chapter 5 Switched transmission rates are introduced to more complicated models, with 3 or more disease classes as well as multi-city models. Lyapunov techniques are used to show exponential and asymptotic stability and simulations are provided to demonstrate numerical examples.

Chapter 6 Control schemes are applied to switched SIR type network models. Constant control is first investigated where vaccination and treatment are considered. Also, screening processes where travel is restricted is studied in multi-city models. Then pulse vaccination and pulse treatment are studied and compared.

Chapter 7 Conclusions and ideas for future directions are given.

Chapter 2

Mathematical Background

In order to study epidemiological network models with switching, we first need to establish mathematical background theory covering ordinary differential equation (ODE) theory, switched systems theory, and mathematical epidemiology.

In Section 2.1, some preliminary theory will be given on ordinary differential equations, which is the backbone for all the topics covered in this thesis. It will formally provide important fundamental theories including the structure of ordinary differential equations, the existence and uniqueness of a solution to the system, and methods of proving the stability of equilibrium points using Lyapunov functions.

In Section 2.2, a brief introduction to switched systems will be given, including equilibria and stablity analysis methods using common Lyapunov functions.

In Section 2.3, mathematical epidemiological theory will be covered including the model formulation of infectious disease spread. The idea stems from compartmental models, and the use of deterministic ordinary differential equations. Important concepts such as population densities, threshold criteria, and whether or not an epidemic outbreak will occur will be discussed. Further, some background on control schemes as they apply to epidemiology is given.

2.1 Differential Equation Theory

In this section we provide some preliminary background theory on differential equations. The material in this section is taken from [38] unless stated otherwise. A general ordinary differential equation (ODE) has the form

$$x'(t) = f(t, x(t)) \tag{2.1}$$

which is a general dynamical system often used in epidemiology. This system is called *nonautonomous* because the right-hand side is dependent on the time variable t as well as

the state variable $x(t)$. The system is called an initial value problem (IVP) if we have an initial condition (IC)

$$x(t_0) = x_0$$

It is important to analyze whether this system (2.1) of differential equations has a solution, whether or not it is unique, and the stability of that solution in order to understand and predict its behaviour.

2.1.1 System of Ordinary Differential Equations

Consider a general system of automonous ordinary differential equations (ODEs) having the form:

$$x' = f(x) \tag{2.2}$$

where $x = (x_1(t), ..., x_n(t))^T$ and $f(x) = (f_1(x_1, ..., x_n), ..., f_n(x_1, ..., x_n))^T$. This system is called *autonomous* because $f(x)$ is independent of t. If an initial condition is known, $x(t_0) = x_0 \in \Omega \subset \mathbb{R}^n$, where Ω is an open subset of the n-dimensional Euclidean space, $\mathbb{R}^n$, and $t_0 \in \mathbb{R}$, then the system becomes an initial value problem (IVP) as follows:

$$\begin{cases} x' = f(x) \\ x(0) = x_0 \end{cases} \tag{2.3}$$

The solution to this IVP is a differentiable function $\phi(t; x_0)$ if $\phi'(t; x_0) = f(\phi(t; x_0))$, for all $t \in \mathbb{R}_+$. Without loss of generality, we can take $t_0 = 0$ since the IVP is autonomous. In general, there is no known method to solving system (2.3). However, it is not always necessary to know the exact solution(s) of (2.3), but rather more interesting to know whether or not a solution exists, and if that solution is unique. The following theorems explain some conditions on which a unique solution exists, starting with local uniqueness.

Theorem 2.1.1. *Let Ω be an open subset of $\mathbb{R}^n$ and assume that $f \in C^1[\Omega, \mathbb{R}^n]$. Then $\forall x_0 \in \Omega$, there exists an $\alpha > 0$ such that the IVP (2.3) has a unique solution $\phi(t; x_0)$ on the interval $[-\alpha, \alpha]$.*

The set of continuously differentiable functions that map Ω to $\mathbb{R}^n$ is denoted as $C^1[\Omega, \mathbb{R}^n]$. This theorem gives us local uniqueness in a neighbourhood of radius $\alpha > 0$ however in applications including epidemiology, it is important to know that a unique solution exists for all time $t \geq 0$. Before establishing global existence, we need the following definitions:

Definition 2.1.1. *Let $\phi(t)$ be a solution to the initial value problem (2.3) on an interval J. The interval J is called a right-maximal interval of existence for $\phi(t)$ if there does not exist an extension of $\phi(t)$ over an interval J_1 with $\phi(t)$ remaining a solution of the IVP and J is a proper subset of J_1 with different right endpoints. A left-maximal interval of existence for $\phi(t)$ can be defined similarly. A maximal interval of existence for $\phi(t)$ is an interval which is both a left-maximal and right-maximal interval.*

The following theorem and corollaries can now be stated.

Theorem 2.1.2. *Let Ω be an open subset of $\mathbb{R}^n$ and assume that $f \in C^1[\Omega, \mathbb{R}^n]$ and let $\phi(t)$ be a solution of the IVP (2.3) for some initial condition $x_0 \in \Omega$ on some interval. Then $\phi(t)$ can be extended over a maximal interval of existence, (α^*, β^*), and $\phi(t)$ tends to the boundary of Ω as $t \to \beta^*$ and $t \to \alpha^*$.*

Corollary 2.1.1. *Let $f(x)$ be continously differentiable on $\mathbb{R}^n$ and $\phi(t)$ be a solution on a right(left)-maximal interval J. Then either $J = [0, \infty)$ ($J = (-\infty, 0]$) or $J = [0, \beta^*)$ ($J = (\alpha^*, 0]$) with $\beta^* < \infty$ ($\alpha^* > -\infty$) and $||x(t)|| \to \infty$ at $t \to \beta^*$ (α^*)*

Here the Euclidean norm is assumed, so $||x(t)|| = \sqrt{x_1(t)^2 + x_2(t)^2 + ... + x_n(t)^2}$.

Corollary 2.1.2. *Let $f(x)$ be continously differentiable on $\mathbb{R}^n$ and $\phi(t)$ be a solution on a maximal interval J. Then $J = (-\infty, \infty)$ if one of the following is true*

1. *$\phi(t)$ is bounded on J,*
2. *$f(x)$ is bounded on $\mathbb{R}^n$*

The following definitions are helpful in understanding the sufficient conditions for a solution to exist for all future time, $t \geq 0$, or on a maximal interval of $J = [0, \infty)$.

Definition 2.1.2. *A subspace $D \subset \Omega$ is said to be an invariant set of (2.3) if all solutions $x(t; x_0)$ starting in D remain in D for all time $t \in \mathbb{R}$.*

Definition 2.1.3. *A subspace $D \subset \Omega$ is said to be a positively invariant set of (2.3) if all solutions $x(t; x_0)$ that start in D remain in D for all time $t \geq 0$.*

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

Corollary 2.1.3. *Let $f(x) \in C^1[\mathbb{R}^n, \mathbb{R}^n]$ and let $x(t; x_0)$ be a solution of the IVP (2.3) on a right maximal interval J. Suppose that D is a compact set that is positively invariant to the IVP (2.3). If $x_0 \in D$ then the maximal interval of existence is $J = [0, \infty)$*

Unfortunately, there is no general method for solving a nonlinear IVP analytically, and often it can be difficult to do so. However, information about the behaviour of the solution can still be gathered for many real world applications including disease modelling. For instance, finding what the long-term behaviour of the solution is, whether the solution converges to a constant value, a periodic solution, or diverges. This leads us to studying the stability of the IVP.

Suppose that $n = 2$ and the rates of growth of $x_1(t)$ and $x_2(t)$ are governed by system (2.3). We are not really interested in the exact values of $x_1(t)$ and $x_2(t)$ at every time t, but rather we are interested in the qualitative properties of $x_1(t)$ and $x_2(t)$. Do there exist specific values η_1 and η_2 such that $x_1(t) = \eta_1$ and $x_2(t) = \eta_2$ are solutions of the system and allow for both rates to co-exist and maintain their values in steady state? Such values in differential equation theory are called equilibrium values, leading us to the following definition.

Definition 2.1.5. *A point $\bar{x}$ is said to be an equilibrium point of the system (2.3) if $f(\bar{x}) = 0$.*

We introduce these stability concepts to aid in analyzing the long-term behaviour of the IVP.

Definition 2.1.6. *Assume $f(0) = 0$ and suppose there exists a solution of the IVP (2.3) $\phi(t; x_0)$ such that $\phi(0, ; x_0) = x_0$ where $x_0 \in \Omega$, then the equilibrium point $x = 0$ is said to be*

1. *stable if $\forall \epsilon > 0$, $t_0 \in \mathbb{R}_+$, there exists $\delta = \delta = \delta(t_0, \epsilon) > 0$ such that if $|x_0| < \delta$ then $||\phi(t; x_0)|| < \epsilon$ for $t \geq 0$,*

2. *asymptotically stable if (1) holds and $\forall t_0 \in \mathbb{R}_+$ there exists $\sigma(t_0) > 0$ such that if $|x_0| < \sigma(t_0)$ then $\lim_{t\to\infty} \phi(t; x_0) = 0$,*

3. *exponentially stable if $||\phi(t; x_0|| < k||x_0||e^{-\gamma t}$, $\forall t \geq 0$ where $k \geq 1$, $\gamma > 0$, for all $||x_0|| < c$ for some $c > 0$,*

4. *globally asymptotically (exponentially) stable if it is asymptotically (exponentially) stable and σ (c) is arbitrary,*

5. *unstable if (1) fails to hold.*

Also note that exponential stability implies asymptotic stability. Asymptotic stablity is useful to understand the long term behaviour of the system, while exponential stability gives more information about the rate of convergence of the solution to the origin. Stability in general is helpful in understanding whether two solutions that initially start close to each other will stay close to each other. Another useful theorem in analyzing stability is the following in regards to the linear case.

Theorem 2.1.3. *Suppose we have the system:*

$$x' = Ax \tag{2.4}$$

where $A \in \mathbb{R}^{n\times n}$ is a Hurwitz matrix (all eigenvalues have negative real part), then the origin of the system (2.4) is asymptotically stable. If there exists an eigenvalue λ of A that has positive real part, then the origin is unstable.

In the case of nonlinear IVPs, one approach is linearizing the system about an equilibrium point to obtain information about the stability of that point. We define the Jacobian matrix as the $n \times n$ matrix denoted as $Df(x)$ which represents the derivatives of $f(x) = (f_1(x_1, ..., x_n), ..., f_n(x_1, ..., x_n))$,

$$Df(x) = \frac{\partial f_i}{\partial x_j}$$

where $i, j = 1, ..., n$. If we let x be close to the equilibrium point $\bar{x}$, then by Taylor's theorem,

$$f(x) = f(\bar{x}) + Df(\bar{x}) \cdot (x - \bar{x}) + R(\bar{x}, x)$$

Because all equilibrium points can be shifted to the origin, and because $f(0) = 0$ then,

$$f(x) = Df(0) \cdot x + R(x)$$

where $R(x)/||x|| \to 0$ as $x \to 0$. Then the nonlinear system can be written as

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

which leads to the linearization of the nonlinear system.

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

This linearized system (2.5) can give information about the general nonlinear system (2.4) in the following theorem.

Theorem 2.1.4. *Suppose that $f(0) = 0$ and 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 $\phi(t; x_0)$ satisfies*

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

and the equilibrium is asymptotically stable.

Another technique to determine stability is the method of Lyapunov functions, developed by A.M. Lyapunov in 1892.

Definition 2.1.7. *Let $V : \Omega \to \mathbb{R}$ be a continuous and differentiable function. Then the derivative of V along solutions of the IVP is defined as follows:*

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

where ∇ represents the gradient operator and $\cdot$ is the dot product. This auxilary function V is often called the Lyapunov function and in many cases $V(x)$ represents the total energy of the system.

Theorem 2.1.5. *Let $f(\bar{x}) = 0$, $\Omega \subset \mathbb{R}^n$ be an open set containing $\bar{x}$, and let $V \in C^1[\Omega, \mathbb{R}]$. Assume that $V(\bar{x}) = 0$ and $V(x) > 0$ if $x \neq \bar{x}$. Then,*

1. *if $\dot{V}(x) \leq 0$, $x \in \Omega$ then $\bar{x}$ is stable.*
2. *if $\dot{V}(x) < 0$, $x \in \Omega \backslash \{\bar{x}\}$ then $\bar{x}$ is asymptotically stable.*
3. *if $\dot{V}(x) > 0$, $x \in \Omega \backslash \{\bar{x}\}$ then $\bar{x}$ is unstable.*

Lyapunov functions will be used to prove asymptotic stability of epidemic models later in the thesis.

2.1.2 Impulsive Differential Equations

Many evolution processes are characterized by the fact that at certain moments of time they experience an abrupt change of state [32]. The short-term perturbations have a duration which is negligible compared to the duration of the process [32]. This leads to a natural assumption that these perturbations act instantaneously in the form of impulses [32]. Impulsive effects are exhibited in many real-world problems, including bursting rhythm models in medicine, optimal control models in economics, and many biological phenomena involving thresholds [32]. This leads to the idea of impulsive differential equations (IDEs), differential equations involving impulsive effects.

First, we construct the Dirac delta function in order to introduce a system of impulsive differential equations. Consider the following function for any $\epsilon > 0$,

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

The Dirac delta function is defined by the integral:

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

The Dirac delta function is a generalized function, which can be regarded as the limit of the sequence of functions $\delta(t) = \lim_{\epsilon \to 0} I_\epsilon(t)$. It is possible to translate this result,

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

If we introduce the Dirac delta function to the IVP (2.3) as an input control $u(t)$ as in [22], we get

$$\begin{cases} x'(t) = f(x(t)) + u(t), \\ x(t_0) = x_0 \end{cases} \tag{2.6}$$

where

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

for some constant $c > 0$. We take $\{t_k\}_{k=1}^{\infty}$ to be a sequence of times which define the moments of impulses where $t_0 < t_1 < t_2 < ... < t_k < ... \to \infty$ as $k \to \infty$. During intervals of no impulses, $t \neq t_k$, the system acts as the ordinary differential equation system (2.3), and at the times $t = t_k$, an impulsive force with magnitude c is applied to the system. The control

acts as an impulsive force. 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 system (2.6) with the impulsive control can be re-written as [32]:

$$\begin{cases} x' = f(x), & t \in (t_{k-1}, t_k], \\ \Delta x = cx, & t = t_k, \\ x(t_0^+) = x_0, & k = 1, 2, ... \end{cases} \tag{2.7}$$

This system is called an impulsive differential equation (IDE) IVP. It models the impulsive effect by the change in the system at impulse times, shown in the second equation of the system.

To further generalize an impulsive differential system, we consider an evolution process described by the following [32]:

1. a system of differential equations, as explicitly stated in the IVP (2.3)
2. the sets $M(t)$, ($N(t) \subset \Omega$ for each $t \in \mathbb{R}_+$
3. the operator $A(t) : M(t) \to N(t)$ for $t \in \mathbb{R}_+$

With $\phi(t, x_0)$ being a solution to the IVP (2.3), the point $P_t = (t, \phi(t))$ begins its motion from the initial point, $P_{t_0}(t_0, x_0)$ and moves along the curve $\{(t, \phi) : t \geq t_0, \phi = \phi(t)\}$ until the time $t_1 > t_0$ at which the point P_t meets the set $M(t)$ [32]. At the impulse time, $t = t_1$, the operator $A(t)$ transfers the point $P_{t_1} = (t_1, \phi(t_1))$ to $P_{t_1^+} = (t_1, x_1^+) \in N(t_1)$, with $x_1^+ = A(t_1)x(t_1)$. The point continues to move along the curve with $\phi(t) = \phi(t, x_1^+)$ as the solution of (2.3) now starting at $P_{t_1} = (t_1, x_1^+)$ until $t_2 > t_1$ when it reaches the set $M(t)$ [32]. The process continues again with the point P_{t_2} and so forth, as long as the solution of (2.3) exists. The set of relations (1.), (2.), and (3.) characterizes an impulsive differential system [32]. The curve described by the point P_t, the integral curve and the function defines the solution of the impulsive differential system [32].

The impulsive differential solution may be a continuous function if the integral curve does not cross the set $M(t)$, or if it hits it at the fixed points of the operator $A(t)$ [32]. The solution may also be a piecewise continuous function with a finite number of discontinuities if the integral curve meets $M(t)$ at a finite number of points which are not fixed points of $A(t)$, or the solution could be a piecewise continuous function with a countably infinite number of discontinuities.

The impulses t_k at which the point P_t crosses the set $M(t)$ are called moments of impulsive effect [32]. Without loss of generality, we can assume the solutions of the impulsive differential system are left continuous at t_k, $k = 1, 2, ...$, that is [32]:

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

This generalization of impulsive differential systems gives rise to a variety of types of systems. We will discuss systems with impulses at fixed times. Let the set $M(t)$ represent a sequence of places $t = t_k$ where $t_k \to \infty$ as $k \to \infty$. Let $A(t)$ be defined for $t = t_k$ so the sequence of operators $\{A(k)\}$ is given by [32]

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

where $I_k : \Omega \to \Omega$. Then the set $N(t)$ is also defined only for $t = t_k$ and therefore $N(k) = A(k)M(k)$. This describes a simple impulsive differential system with impulses occurring at fixed times [32]:

$$\begin{cases} x'(t) = f(x), & t \neq t_k, k = 1, 2, ... \\ \Delta x = I_k(x), & t = t_k \\ x(t_0^+) = x_0 \end{cases} \tag{2.8}$$

The impulsive functions $I_k(x)$ provide a more general characterization than the impulsive system from (2.7) with the constant c. A solution $\phi(t, x_0)$ of the impulsive differential system (2.8) on the interval (α, β) satisfies [32]

1. $(t, \phi(t, x_0)) \in \mathbb{R} \times \Omega$ for $t \in (\alpha, \beta)$ and $(\phi(t_k^+, x_0)) = x_0$ where $x_0 \in \Omega$,
2. for $t \in (\alpha, \beta)$, $t \neq t_k$, $\phi'(t, x_0) = f(\phi(t, x_0))$, and
3. $\phi(t, x_0)$ is continuous from the left in (α, β) and if $t_k \neq \alpha \neq \beta$ then $\phi(t_k^+, x_0) = \phi(t_k, x_0) + I_k(\phi(t_k, x_0))$.

Note that if $t_0 \neq 0$, it is possible to shift the initial time to zero using $\tau = t - t_0$. Then system (2.8) becomes

$$\begin{cases} x' = f(x), & \tau \in (h_{k-1}, h_k], \\ \Delta x = px, & \tau = h_k, \\ x(0^+) = x_0 \end{cases} \tag{2.9}$$

where $h_k = t_k - t_0$ [32]. Then without loss of generality, we may take $t_0 = 0$.

Next, we establish some existence and uniqueness theorems for impulsive differential systems. The following two theorems are based on those found in [6] for the non-autonomous case. First we establish existence on a local interval.

Theorem 2.1.6. *If $f \in C^1[\Omega, \mathbb{R}^n]$ and $y + I_k(y) \in \Omega$ for each $k = 1, 2, ...$ and $y \in \Omega$, then for each $x_0 \in \Omega$ there exists a unique solution $\phi(t, x_0)$ of the IVP (2.8) which is defined in an interval of the form (t_0, ω) where ω is a constant, and is not continuable to the right.*

Now we establish conditions for global existence of a solution, also based on a theorem found in [6].

Theorem 2.1.7. *Suppose $f \in C^1[\Omega, \mathbb{R}^n]$ and $y + I_k(y) \in \Omega$ for each $k = 1, 2, ...$ and $y \in \Omega$. Let $\phi(t, x_0)$ be a unique solution of the IVP (2.8) on a maximal interval J^+. If there exists a compact set $D \subset \Omega$ such that $\phi(t, x_0) \in D$ for $t \in J^+$ then $J^+ = (t_0, \infty)$.*

Uniqueness is straightforward from the non-impulsive case [32].

Theorem 2.1.8. *Uniqueness of solutions of the IVP (2.3) for every (t_0, x_0) implies the uniqueness of solutions of the IVP (2.8).*

2.2 Switched Systems

2.2.1 Introduction

A hybrid system is a system in which continuous and discrete dynamics interact to generate the evolution of the system state [51]. Switched systems are types of hybrid systems that evolves according to mode-dependent continuous and discrete dynamics. The system experiences abrupt transitions between modes triggered by a logic-based switching rule [51]. The switching rule could be based on a vast variety of concepts, for instance by environmental, seasonal, or behavioural factors. The switching rule could be time-dependent, or state-dependent. A switched model is a family of invariant ordinary differential equations, as shown below:

$$\frac{dx}{dt} = f_i(x)$$

with $\{f_i : i \in P\}$ being a family of sufficiently regular functions and P is the index set, assumed to be finite, $P = \{1, 2, ..., m\}$. The switching signal, $\sigma(t)$ is a function which is assumed to be deterministic where $\sigma : [t_{k-1}, t_k) \to P$.. Note that $\sigma(t)$ is a piece-wise continuous function from the left. For this thesis, we denote S as the set of all possible switching signals, thus $\sigma(t) \in S$. From this we get a family of ODE systems. The set of $\{t_k\}_{k=0}^{\infty}$ are the switching times with $0 < t_1 < t_2 < ... < t_k < ...$ and $t_k \to \infty$ as $k \to \infty$. At switching time t_k the system changes from $\sigma(t_k^-)$ to $\sigma(t_k)$.

$$\sigma(t_k^-) = \lim_{h \to)^+} \sigma(t_k - h)$$

This system has a family of solutions $x(t)$ that depend on the switching signal σ and the initial conditions. Thus the switched system can be written more compactly:

$$\frac{dx}{dt} = f_\sigma(x)$$

with initial condition of $x(0) = x_0$. For a particular choice $i \in P$, $x' = f_i(x)$ is called a subsystem or mode of the switched system.

2.2.2 Equilibria and Stability

The switched system has an equilibrium point $\bar{x}$ if $f_i(\bar{x}) = 0 \ \forall i \in P$. Basically each i-th subsystem have this equilibrium point in common. The interest is in analysing the equilibria, and what the requirements are for asymptotic stability. Clearly a necessary condition for asymptotic stability under arbitrary switching is that all individual subsystems are asymptotically stable [36].

If the p-th subsystem is unstable, then by setting $\sigma(t) = p$ the switched system will be unstable. Also, this condition is not sufficient if the switching signal causes instability. One condition that guarantees that the trivial equilibrium is asymptotically stable is the existence of a common strict Lyapunov function.

Definition 2.2.1. *[4] The auxiliary 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 if V is positive definite and $\nabla V(x) \cdot f_i(x) < 0$ for all $x \in D \backslash \{0\}$ and for all subsystems i.*

Theorem 2.2.1. *[36] If the switched system has a common strict Lyapunov function $V(x)$ then the origin of the system is globally asymptotically stable for arbitrary switching.*

Another important concept is multiple Lyapunov functions. Assume that all subsystems i are stable and each of them has a Lyapunov function.

Definition 2.2.2. *[4] A switched system has multiple strict Lyapunov functions if for each subsystem i 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 $x \in D \backslash \{0\}$, $\nabla V_i(x) \cdot f_i(x) < 0$.*

Theorem 2.2.2. *[24] If the switched system has multiple strict Lyapunov functions $\{V_i : i \in P\}$ such that*

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

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

2.3 Epidemic Modelling Background

This section provides a brief overview of how infectious disease models are formulated and analyzed. We will cover some classical models which will later be further investigated by the addition of network mixing and a switched transmission rate.

2.3.1 Model Formulation

In this thesis, the continuous deterministic approach is taken where the spread of infectious disease is modelled as a system of ordinary differential equations. The simplest class of epidemic models makes the assumption that the population can be divided into different classes

or compartments depending on the stage or status of the disease [3, 5, 13, 15, 26]. Typical compartments include the susceptible class, S, for individuals that are currently healthy but able to contract the infectious disease, the infected class, I, for infected individuals that already have the disease and can pass the disease to others, and the recovered class, R, individuals who have recovered from the disease and have immunity from the disease. Occaisionally there are added classes, for instance an exposed class, E, that have experienced exposure from the disease but are not currently infectious, or perhaps a vaccinated class, V, that have received vaccination and thence also have some immunity from the disease, without having contracted the disease. The flow of individuals between classes depends on the specific disease in analysis, whether incubation periods, vaccination control schemes, short-term or life-long immunity for recovered individuals are included in the assumptions or not. Naming types of models depends on the flow of these individuals, for instance there can be SIS, SIR, SIRS, SEIR, SEIRS models to name a few.

The flow of individuals depends on model assumptions and parameter values, however in many cases the flow of individuals from the susceptible class S into the infected class I depends on a contact rate, β. Assuming the population mixes at random means that each individual has a small and equal chance of coming into contact with any other individual. This traditional assumption is called the *fully mixed* or *mass-action approximation*. The term, *mass-mixing* or *uniform mixing* is also used. The disease is transmitted when an infected person comes into contact with a susceptible person. Thus the force of infection can be calculated as broken down as in [29]:

$$\begin{aligned} \lambda = &\text{ transmission rate} \\ &\times \text{effective number of contacts per unit time} \\ &\times \text{proportion of contacts which are infectious} \\ &= \tau \times \hat{n} \times \frac{1}{N} \\ &= \beta \frac{1}{N} \end{aligned} \tag{2.10}$$

The term β consequently and conventionally represents the contact rate, which is the transmission rate times the effective number of contacts per unit time. In many cases, we consider population proportions instead of numbers of individuals, which then $N = 1$ and the contact rate is a constant term, thus the force of infection becomes $\lambda = \beta$.

This method of transmitting and contracting the disease is known as horizontal transmission. However, the disease can also be obtained by a second way: vertical transmission. Vertical incidence is usually represented in models by assuming that a fixed fraction of newborns are infected transplacentally, by a mother who has the disease and transfers it to their unborn or newborn child [26]. Both ways of obtaining the disease will be considered in the models in this thesis.

It has been discovered that in acute infections, the duration of the infecious period is distributed around a mean value [30]. The probability that an individual recovers from the infected class is dependent on how long they have been infected [30]. Conventional models assume that the infected individuals recover linearly with recovery rate $g > 0$ which corresponds to an average infectious period of $1/g$. This assumption leads to an exponentially distributed infectious period, and the fraction of infectives that are still infected after t units of time is $P(t) = e^{-gt}$ [26]. For instance, the average infectious period for having measles is about one week [26]. There are other approaches to constructing the recovery concept such as assuming individuals have a waiting time τ and then are immediately recovered which results in a delay differential equation, but the models we investigate will use the constant recovery rate assumption. The recovery incidence will be gI, which is removed from the infected class but added to another class, such as the susceptible class or the recovered class, depending on the flow of the model. More detail will be explained in the examples of classical models.

2.3.2 Threshold Values

An important threshold value in epidemiology is the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible is called the *basic reproductive number*, usually denoted as R_0 [26]. Note that R_0 is also called the *basic reproduction ratio* or the *basic reproductive rate* [26]. In many deterministic epidemiological models, an infection can get started in a fully susceptible population if and only if $R_0 > 1$ [26]. In mathematical epidemiology, it is usually the case that if the model's basic reproduction number satisfies $R_0 \leq 1$, then the disease will eventually be eradicated. If the disease is not eradicated, it is said that the disease is persistent and there is usually an endemic equilibrium. It is usually the case that $R_0 > 1$ implies that the endemic equilibrium is asymptotically stable. However, this is not always straightforward to prove, and so an alternative method of demonstrating that the disease maintains an endemic state is proving the persistence or permanence of the disease, definitions of which are found in [20].

Definition 2.3.1. *A disease is said to be persistant if there exists an $\eta > 0$ (independent of initial conditions) such that the solution of $I(t)$ of the system with initial conditions $I(0) = I_0 > 0$ satisfies*

$$\lim_{t\to\infty} inf I(t) \geq \eta$$

Definition 2.3.2. *A disease is said to be permanent if there exists a compact region Ω_0 in the interior of Ω 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*

There are two other threshold quantities, the contact number σ and the replacement number R. The contact number σ is defined as the average number of adequate contacts of a typical infective during the infectious period [26]. Here, by adequate contact we mean one that is sufficient for successful transmission of the disease, if the contact by a susceptible

R_0	Basic reproduction number
σ	Contact number
R	Replacement number

Table 2.1: Threshold Values for Epidemiology

individual is an infective [26]. The replacement number R is defined as the average number of secondary infections produced by a typical infective during the entire period of infectiousness [26].

Note that these three threshold quantities, R_0, σ, R, are all equal at the beginning of the spread of an infectious disease [26]. R_0 is only defined at the time of the disease invasion, but σ and R are defined for all time [26]. Either σ remains equal to R_0 as it does in most models, or it becomes less than the basic reproduction number, in cases where new classes of infectives with lower infectivity appear when the disease has entered the population [26]. The replacement number is the number of secondary infections from a single infective, so as time goes on and there are less susceptible people to infect, R is always less than R_0 [26]. Further, the replacement number R is always less than the contact number σ after the invasion, therefore: [26]

$$R_0 \geq \sigma \geq R$$

with all quantities equal at the time of invasion. Thresholds that dictate whether a disease eradicates or persists are very important in epidemiology [54].

2.3.3 Classical Models

The SI Model

The fully mixed susceptible-infected model (or SI model for short) is one of the most simplest versions of disease models where there are just two states, susceptible (denoted by S), and infected (denoted by I). The flow of this model is $S \to I$, which gives the name the SI model [45].

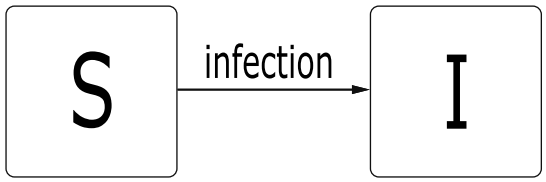


Figure 2.1: **Flow diagram of population movement in a basic SI model** (S: Susceptible, I: Infected)

Assume the total population consists of N people, and the number of people that are

susceptible and infected are denoted, respectively, as $S_c(t)$ and $I_c(t)$, thus $N = S_c + I_c$. To formulate the model, the following assumptions are made:

1. All individuals in the population mix homogeneously; every individual has an equal probability of coming into contact with any other individual in the population.

2. The rate of increase of infectives (and rate of decrease of susceptibles) by the contraction and transmission of the disease is proportional to the number of infectives and susceptibles, normalized by the total population. This calculation of the force of infection demonstrates the mass-mixing assumption, causing the incidence rate to be $\beta S_c I_c/N$ where $\beta > 0$ is the contact rate, defined as the transmission rate times the average number of contacts a person makes per unit time.

3. The incubation period of the disease is negligible; we assume when a susceptible makes adequate contact with an infective, they are immediately infectious and able to transmit the disease to a different susceptible.

4. The dynamics of the disease are short enough such that population dynamics are negligible, thus we assume a constant population.

Then we have the following system as shown in [45]:

$$\begin{cases} S_c'(t) = -\beta \dfrac{S_c I_c}{N} \\ I_c'(t) = \beta \dfrac{S_c I_c}{N} \end{cases} \tag{2.11}$$

Since $S_c'(t) + I_c'(t) = 0$, the total population remains constant and it is often convenient to normalize the variables using $S = S_c/N$ and $I = I_c/N$,

$$\begin{cases} S' = -\beta SI \\ I' = \beta SI \end{cases} \tag{2.12}$$

Population proportions will be considered in the models constructed for the remainder of the thesis. The meaningful physical domain is $D_{SI} = \{(S, I) \in \mathbb{R}^2_+ | S + I = 1\}$, which is invariant to the system since $\dot{S} + \dot{I} = 0$ and $\dot{S}|_{S=0} = 0$ and $\dot{I}|_{I=0} = 0$. Moreover, because $S + I = 1$ we can reduce the system to just one equation,

$$I' = \beta(1 - I)I$$

which takes the form of a Bernoulli differential equation which can be solved by dividing by I^2 and making the substitution $v = I^{-1}$. After plugging in the initial condition $I(0) = I_0$ we get the following solution:

$$I(t) = \frac{I_0 e^{\beta t}}{I_0 e^{\beta t} + 1 - I_0}$$

Clearly, this $I(t)$ approaches the value of 1 as $t \to \infty$. This can be seen easily by plotting this function and seeing that it produces the S-shaped logistic growth curve [45]. The disease takes over, since infected individuals remain infectious forever, causing the disease to eventually spread to every person. The curve grows exponentially at first, but then saturates as the number of susceptibles decreases and the disease has a difficult time finding new victims [45]. The SI model is a very simplified model and often can be extended to make it more realistic or appropriate for a specific disease [45].

The SIS Model

An extension of the SI model allows for *reinfection*, while remaining a simple model with just two states, is the *susceptible-infected-susceptible* model, or *SIS model* for short [45]. The SIS model assumes that susceptible individuals that contract the disease are then moved into the infected class, but once they have recovered from the disease they are immediately considered susceptible again. In other words, individuals cannot gain any sort of immunity after having the disease. Some diseases, such as gonorrhea and other sexually transmitted diseases, do not give acquired immunity to the host [54]. The SIS model has been thoroughly analyzed in literature, for example [25, 27, 30, 49]. The SIS model is predominanatly used for sexually transmitted diseases (STDs) such as chlymadia and gonorrhea, where repeat infections are common [19, 28].

We have the same assumptions as in the SI model, but additionally a fifth one,

5. Assume that the recovery rate of infectives is proportional to the number of infectives, with recovery rate g and hence the average infectious period is $1/g$.

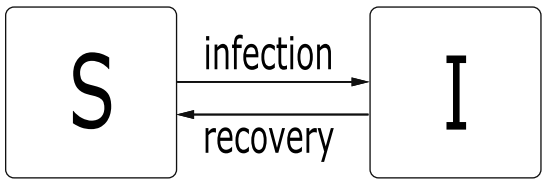


Figure 2.2: Flow diagram of population movement in a basic SIS model allowing reinfection (S: Susceptible, I: Infected)

The differential equations for the SIS model, taken from [45], are as follows:

$$\begin{cases} S' = gI - \beta SI \\ I' = \beta SI - gI \end{cases} \tag{2.13}$$

where S and I are the proportion of the population that are susceptible and infected, respectively, and the physically meaningful domain is again D_{SI} from the previous SI model.

The domain is invariant to this system since $\dot{S} + \dot{I} = 0$ and $\dot{S}|_{S=0} = gI \geq 0$ and $\dot{I}|_{I=0} = 0$. Substitute $S = 1 - I$ to reduce the system to one-dimension, we get a similar Bernoulli differential equation:

$$I' - (\beta - g)I = -\beta I^2$$

which has the solution [45]:

$$I(t) = \frac{(\beta - g)e^{(\beta-g)t}I_0}{\beta e^{(\beta-g)t}I_0 + (\beta - g) - \beta I_0}$$

Note that if $\beta < g$ then the disease will die out exponentially. However, if $\beta > g$ then the function produces a logistic growth curve but the disease never infects the entire population (i.e., $I(t)$ does not approach 1) and instead there is a limit where the system finds a stable state [45]. Another perspective of this dynamic is to consider the basic reproduction ratio, $R_0 = \beta/g$, which determines the threshold criteria. If $R_0 < 1$ then the disease is eradicated in the population, but if $R_0 > 1$ then the system reaches an endemic solution and the disease persists. $R_0 = 1$ marks an epidemic transition between a state in which the disease spreads and one in wihch it does not [45].

One assumption that could be added to epidemic model is that the duration of the disease is significantly long enough such that population dynamics become important. We can choose to incorporate the birth and death of the population. Assume that $\mu > 0$ is the birth rate, which is equal to the natural death rate. This implies that the average lifetime is $1/\mu$. It is assumed that all individuals may have children, and that the children are born healthy and thus enter the susceptible class. The SIS model with population dynamics is given as [25, 26, 30, 49]:

$$\begin{cases} S' = \mu - \beta SI - \mu S + gI \\ I' = \beta SI - gI - \mu I \end{cases} \tag{2.14}$$

where S, I represent population proportions in each class. The physically meaningful domain D_{SI} is invariant to the system as $\dot{S} + \dot{I} = 1$, $\dot{S}|_{S=0} = \mu + gI > 0$ and $\dot{I}|_{I=0} = 0$. The basic reproduction ratio is now also dependent on μ:

$$R_0 = \frac{\beta}{\mu + g}$$

This system has two equilibria, a disease-free solution $E_0 = (1, 0)$ and an endemic equilibrium $E^* = (S^*, I^*)$ where

$$S^* = \frac{\mu + g}{\beta}, \qquad I^* = \frac{\beta - \mu - g}{\beta}$$

The system can be reduced to one-dimension, and again solve the Bernoulli differential equation to get:

$$I(t) = \frac{(\beta - \mu - g)e^{(\beta-\mu-g)t}I_0}{\beta e^{(\beta-\mu-g)t}I_0 + (\beta - \mu - g) - \beta I_0}$$

If $R_0 \leq 1$ then $I(t)$ converges to zero and the disease-free solution E_0 is asymptotically stable. For $R_0 > 1$, $I(t)$ converges to the endemic value, I^* and therefore E^* is asymptotically stable [26]. This threshold criteria R_0 determines the long-term behaviour of the disease.

The SIR Model

A common extension of the SIS model is asserting the possibility of recovery from disease [45]. SIR models have been studied extensively in many literature, including Kermack and McKendrick in 1927 [25, 31, 49]. In an SIR model, people recover from the infection because their immune system fights off the agent. The infected gain life-long immunity and are moved into the recovered class and can never contract the disease again. Then infected persons recover at some constant average rate, $g > 0$.

The system of differential equations have 3 variables, with the added R class for recovered individuals [45].

$$\begin{cases} S' = -\beta SI \\ I' = \beta SI - gI \\ R' = gI \end{cases} \tag{2.15}$$

where β is the contact rate and g is the recovery rate. The physically meaningful domain is $D_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ | S + I + R = 1\}$. We assume the initial conditions are inside this domain, so $S(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$ such that $S(0) + I(0) + R(0) = 1$. To make the problem biologically interesting, often $S(0), I(0) \neq 0$. Since $\dot{S} + \dot{I} + \dot{R} = 0$ and $\dot{S}|_{S=0} = 0$, $\dot{I}|_{I=0} = 0$ and $\dot{R}|_{R=0} = gI \geq 0$, the domain is invariant to the system. Also, the model can be reduced to be two-dimensional, by omitting the equation for R. This model is well-posed, mathematically and epidemiologically, and has a unique solution for which all $t \geq 0$ given certain initial conditions [26]. For the disease-free equilibria when $I = 0$, there are infinitely many equilibrium points on the S-axis.

We have $I' = \beta SI - gI = I(\beta S - g)$. At initial time $t = 0$, then $I'|_{t=0} = I(0)(\beta S(0) - g) < 0$ if $S(0) < g/\beta$, thus $I \leq I(0)$ for all future time and $I(t)$ converges to 0. If $S(0) > g/\beta$ then $I'|_{t=0} > 0$ and I is initially increasing, thus there is an epidemic. The basic reproduction number is defined as,

$$R_0 = \frac{\beta}{g}$$

If we use $I = R'/g$ to eliminate I, we get

$$\frac{1}{S}\frac{dS}{dt} = \frac{-\beta}{g}\frac{dR}{dt}$$

which can be integrated with respect to t to get [45]:

$$S = S(0)e^{-BR/g}$$

which can be used to determine that $\lim_{t\to\infty} S(t)$ is the positive root z of the equation,

$$S(0)\exp(-\frac{\beta(1-z)}{g}) = z$$

with $0 < z \leq g/\beta$ [49]. So the disease dies out due to a lack of infectives.

If we are given the value of g then the mean infectious period if $1/g$. The probability of recovering in any time interval $\delta\tau$ is $g\,\delta\tau$ and the probability of not recovering is $1 - g\,\delta\tau$. The probability that the individual is still infected after time τ is given by

$$lim_{\delta\tau\to 0}(1 - g\,\delta\tau)^{\tau/\delta\tau} = e^{-g\tau}$$

The probability that the individual remains infected for time τ and then recovers in the interval between $\tau + d\tau$ is this quantity times $g\,d\tau$, which is a standard exponential distribution. Thus, a person is likely to recover quickly after becoming infected, however in theory they may remain infectious for a period of time that is multiple times longer than the mean infectious period, $1/g$.

This behaviour is not very realistic, but is one of the things that will improve when we look at network disease models.

The SIR Model with Population Dynamics

It may also be beneficial to consider population dynamics into the SIR model, with the assumption that the disease is long enough that population dynamics are no longer negligible. If we assume that μ is the birth and death rate, then we get the following system [25, 26, 30]:

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

The physically meaningful domain is D_{SIR} and the initial conditions are $S(0) > 0$, $I(0) > 0$, and $R(0) \geq 0$ such that the problem is biologically interesting. Note that since $S + I + R = 1$ then we have μ representing the flow of the birth of the population into the susceptible class. The basic reproduction ratio does not change, as the addition of the recovered class does not affect the rate of spread of the disease,

$$R_0 = \frac{\beta}{\mu + g},$$

which is the same as it was in the SIS case with population dynamics.

There is a disease-free solution, $S = 1$, $I = 0$, and $R = 0$. Moreover there is an endemic solution (S^*, I^*, R^*) where

$$S^* = \frac{\gamma + \mu}{\beta}, \qquad I^* = \frac{\mu}{\gamma + \mu}(1 - \frac{\gamma + \mu}{\beta}), \qquad R^* = \frac{\gamma}{\gamma + \mu}(1 - \frac{\gamma + \mu}{\beta})$$

which is in the physically meaningful domain if and only if $R_0 \geq 1$. Note when $R_0 = 1$, we get $S^* = 1$, $I^* = 0$, $R^* = 0$. This threshold criteria, R_0, dictates the long-term behaviour of R_0 [26]. It is shown in [26] that if $R_0 \leq 1$ then $(1, 0, 0)$ is globally asymptotically stable in D_{SIR} while if $R_0 > 1$ then (S^*, I^*, R^*) is globally asymptotically stable.

The SIRS Model

In SIRS models, reinfection is incorporated and the recovered individuals will move into the susceptible class again after some time of short-term immunity. A new parameter δ is introduced which represents the average rate that recovered individuals lose their immunity [45]. The equations for this model are:

$$\begin{cases} S' = \delta R - \beta SI \\ I' = \beta SI - gI \\ R' = gI - \delta R \end{cases}$$

The variables have been normalized so that $S + I + R = 1$ and each compartment represents the proportion of the population in each class. The physical domain for this system is $Q_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ | S + I + R = 1\}$ which is invariant becase $\dot{S} + \dot{I} + \dot{R} = 0$ and $\dot{S}|_{S=0} = \delta R \geq 0$, $\dot{I}|_{I=0} = 0$ and $\dot{R}|_{R=0} = gI \geq 0$. The basic reproduction number is

$$R_0 = \frac{\beta}{g}$$

where this quantity represents the threshold criteria for whether a disease will die out or persist.

The SEIR Model

Some diseases incubate inside their hosts for an amount of time before the individual becomes infectious. In the previous models, the incubating period is assumed to be negligible. This may be a poor approximation for certain diseases such as heptatitus B, Chagas' disease, HIV/AIDS and tuberculosis (TB) which have very long latent periods, in some cases which may last years [46].

In SEIR models, healthy individuals are exposed to the disease but are not yet contagious, and then when they become infectious then they are considered to be in the infected class. This leads to a fourth compartment, the exposed class, E. Assume that susceptible

individuals that make adequate contact with infectives enter the exposed class, and then leave the exposed class and become infectious at a rate $a > 0$. This leads to the following model, common in literature [30, 46].

$$\begin{cases} S' = \mu - \beta SI - \mu S \\ E' = \beta SI - aE - \mu E \\ I' = aE - gI - \mu I \\ R' = gI - \mu R \end{cases} \tag{2.17}$$

with initial conditions $S(0) > 0$, $I(0) > 0$, $E(0) > 0$, $R(0) > 0$ such that $S_0+E_0+I_0+R_0 = 1$. The flow of this model is $S \to E \to I \to R$. The physically meaningful domain is $Q_{SEIR} = \{(S, E, I, R) \in \mathbb{R}^4_+ | S + E + I + R = 1\}$. Since $\dot{S} + \dot{E} + \dot{I} + \dot{R} = 0$ and $\dot{S}|_{S=0} = \mu > 0$, $\dot{E}|_{E=0} = \beta SI \geq 0$, $\dot{I}|_{I=0} = aE \geq 0$ and $\dot{R}|_{R=0} = gI \geq 0$ then the domain is invariant to the system. For this model, the basic reproduction ratio is

$$R_0 = \frac{\beta a}{(g + \mu)(a + \mu)} \tag{2.18}$$

which is again a threshold that determines whether the disease dies out, or there is an endemic.

2.3.4 Control Schemes

Constant Control

Cohort immunization programs, also known as time-constant vaccination, have been implemented in most developed countries with varying degrees of success [1]. There have been numerous studies on constant control schemes in the mathematical epidemiology literature [41]. Under this control strategy, vaccinations are regularly given to individuals in the population who are susceptible to the disease [41]. We assume that $0 \leq p \leq 1$ is the proportion of the susceptibles that are constantly being applied the vaccination control. The vaccinated individuals then move to the removed class R with permanent or waning immunity, depending on the model. When this control scheme is applied to the SIR model, the model becomes [30]

$$\begin{cases} \dot{S} = \mu(1 - p) - \beta SI - \mu S \\ \dot{I} = \beta SI - gI - \mu I \\ \dot{R} = gI - \mu R + \mu p \end{cases} \tag{2.19}$$

with the variables normalized such that $S+I+R = 1$ and the initial conditions are biologically interesting, so $S(0) > 0$, $I(0) > 0$ and $R(0) = 1 - S(0) - I(0)$. The physically meaningful domain is $D_{SIR} = \{(S, I, R) \in \mathbb{R}^3_+ | S + I + R = 1\}$. The effect of the control scheme reduces the amount of healthy individuals to which the disease can spread, seen in the $\mu(1-p)$ term.

If we consider a change of variables where $S = (1-p)\hat{S}$, $I = (1-p)\hat{(I)}$ and $R = (1-p)\hat{R}+p$ then the system above becomes [30]:

$$\begin{cases} \hat{S}' = \mu - (1-p)\beta\hat{S}\hat{I} - \mu\hat{S} \\ \hat{I}' = (1-p)\beta\hat{S}\hat{I} - g\hat{I} - \mu\hat{I} \\ \hat{R}' = g\hat{I} - \mu\hat{R} \end{cases} \tag{2.20}$$

which gives the SIR model with population and without vaccination but with a reduced contact rate of $(1-p)\beta$. The basic reproduction ratio for this system is [30]:

$$R_0^p = \frac{(1-p)\beta}{\mu+g} = (1-p)R_0 \tag{2.21}$$

where R_0 is the basic reproduction number from the non-vaccinated model. Therefore we can make the same analytical conclusions about the asymptotic stability of the disease-free solution. The control strategy is that for successful eradication of the disease, we require $p > p_{crit}$ where

$$p_{crit} = 1 - \frac{1}{R_0}$$

In a case with no vaccination, $R_0 > 1$ would have caused an epidemic but can now be controlled by p to reduce R_0^p to become less than 1. The larger R_0 is, the greater the critical value of p_{crit} becomes.

Pulse Control

In contrast to constant control, pulse vaccination schemes are based on the strategy of applying vaccinations periodically to a large fraction of the population in a very short time period [41]. Theoretical results have shown that the critical value of p_{crit} such that $p > p_{crit}$ will achieve eradication is lowered in pulse control schemes [1]. Pulse vaccination gained prominent achievement due to its highly successful application to control poliomyelitis and measles throughout Central and South America [35]. There was also a successful program of pulse vaccination in the US for measles in 1994 [35]. Pulse vaccination is a control technique motivated by noticing that in the SIR model, $I' = \beta SI - gI - \mu I = I(\beta S - g - \mu) < 0$ if $S < (g+\mu)/\beta$.

The idea is to control the susceptible population to remain below the critical value (for example, $S_{crit} = (g+\mu)/\beta$ in the SIR model) and eradicate any epidemic by maintaining $I' < 0$. By applying this pulse control scheme, a proportion $0 \leq p \leq 1$ of the susceptible population is impulsively immunized every T time units. Vaccinated individuals enter the recovered class and gain immunity to the disease. This control scheme can be modeled by

an impulsive differential equation system [52]:

$$\begin{cases} \dot{S} = \mu - \beta SI - \mu S, & t \in ((k-1)T, kT] \\ \dot{I} = \beta SI - gI - \mu I \\ \dot{R} = gI - \mu R \\ S(t^+) = S(t) - pS(t), & t = kT \\ I(t^+) = I(t) \\ R(t^+) = R(t) + pS(t) \end{cases} \tag{2.22}$$

with $k = 1, 2, ...$ and normalized variables such that $S + I + R = 1$. The biologically interesting initial conditions are $S(0^+) > 0$, $I(0^+) > 0$ and $R(0^+) = 1 - S(0^+) - I(0^+)$ such that these belong in the physically meaningful domain D_{SIR}, which is invariant to the system.

In the model, $S(kT^+) = \lim_{h \to 0^+} S(kT + h)$ is the right hand limit, and kT^+ is the moment immediately after the k-th pulse. Here $(1, 0, 0)$ is no longer an equilibrium point but $I^* = 0$ is still an equilibrium solution for the variable $I(t)$. Under this condition, the susceptible population $S(t)$ oscillates with period T, and with $I' = 0$ the system becomes [52]:

$$\begin{cases} \dot{S} = \mu(1 - S), & t \in ((k-1)T, kT] \\ \dot{R} = -\mu R \\ S(t^+) = S(t) - pS(t), & t = kT \\ R(t^+) = R(t) + pS(t) \end{cases} \tag{2.23}$$

Assuming $I = 0$, the growth of susceptibles in the time interval $t \in ((k-1)T, kT])$, the solution of the system is

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

Immediately after pulse vaccination,

$$S(kT^+) = (1 - p)(1 + (S((k-1)T) - 1)e^{-\mu T}$$

The initial condition $S^\dagger$ may change from one pulse interval to another [52]. If we set $S^\dagger = S^\dagger(kT) = S_k$ then we can deduce a stroboscopic mapping F such that $S_k = F(S_{k-1})$ with $S_{k-1} = S((k-1)T)$. The map F has a unique fixed point,

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

Pulse vaccination yields the sequence S_k which must converge to the fixed point S^*. As the orbit converges to the fixed point, the evolution of $S(t)$ converges to the periodic disease free

solution for $t \in ((k-1)T, kT]$ [52]:

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

Notice that,

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

implying global asymptotic stability of the fixed point [37].

Floquet theory provides a well-defined framework for examining linear systems with periodic coefficients [52] (for more information about Floquet theory, see [44]). It can be shown that if $(1/T)\int_0^T \tilde{S}(t)dt < (g+\mu)/\beta$ then the periodic solution is locally asymptotically stable [52].

If we take $R_0^T = (\beta/(g+\mu))(1/T)\int_0^T \tilde{S}(t)dt$ then the condition for local asymptotic stability becomes $R_0^T < 1$. Notice that since $(1/T)\int_0^T \tilde{S}(t)dt < 1$ then $R_0^T < R_0 = \beta/(\mu+g)$. The basic reproduction number has been reduced, which is expected of the control strategy.

Chapter 3

Network Models

3.1 Introduction

One of the most important advancements of theoretical epidemiology has been the development of methods that account for realistic host population structure [33]. Models that predict disease evolution have evolved from simple compartmental approaches into structured frameworks in which heterogeneities present at community and population levels are becoming increasingly important features [3, 8] (see Figure 3.1).

The foundations of epidemiology and early models were based on population wide random-mixing, but realistically each individual has a finite set of contacts to whom they can pass infection, which forms a mixing network [29]. In order to enhance understanding and prediction of epidemic patterns and intervention measures, knowledge about the structure of mixing networks is important [29]. It is unrealistic that a population mixes randomly and that each individual has an equal chance of contacting any other individual. It is usually the case that the number of contacts an individual has is considerably smaller than the population size [45]. Models that incorporate network structure avoid the random mixing assumption by assigning to each individual a finite set of permanent contacts who they can transmit disease to and from [29]. Networks capture the permanence of interactions because it is not constantly changing as in random mixing models [29].

Basic Network Theory

The study of networks has its grounding in two disparate fields: social sciences and graph theory [29]. Some terminology in networks, depending on the field of study:

- Graph Theory: "Nodes" and "Edges"
- Social Literature: "Actors" and "Relations"
- Epidemiology: "Hosts" and "Contacts"

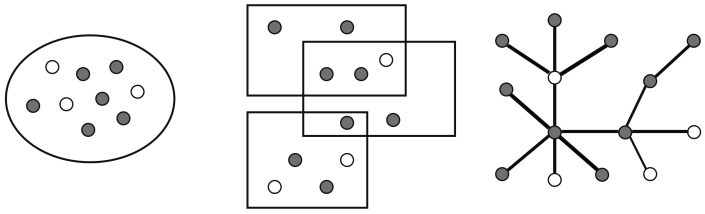


Figure 3.1: **Structures at Different Scales in Epidemic Modelling**, with different shades corresponding to different stages of the disease. Based on an image from [8]. The left-most image represents homogeneous mixing, where the population is assumed to interact homogeneously at random. The center image represents a social structure, in which people are classified by demographic information. The right-most image represents a contact network model, where a network of social interactions provide virus propagation paths.

In graph theory, the terminology used are *nodes* and *edges*, however a network is any collection of objects with connections between them [45]. A network could be used to describe people in a society or community, and the relationships between them or even the World Wide Web, descibing links between web pages. Typically in epidemiology, the nodes often represent individuals and the edges represent relationships between the individuals in which the infection can pass between [29]. Definitions in our context [29]:

Definition 3.1.1. *A neighbourhood is the set of contacts of an individual.*

Definition 3.1.2. *The degree of a contact is the size of an individual's neighbourhood. Also known as the connectivity of a node, the degree is the number of links connected to that node.*

Definition 3.1.3. *Symmetry: relationship between A and B implies a relationship between B and A*

Definition 3.1.4. *Transivity: relationship between A and B and relationship between B and C implies a relationship between A and C (in other words, whether a friend of a friend is a friend)*

These properties may be determined by social dynamics, thus the research in social sciences is relevant to epidemiology as studies about social importance of an individual and how communities interact may be linked to how disease is spread.

All networks can be represented by a matrix A, called an adjacency matrix (or sociomatrix), which may describe the connections within a population [29, 45].

$$a_{ij} = \begin{cases} 1, \text{if there is a connection such that an infection could pass from individual i to j} \\ 0, \text{otherwise} \end{cases}$$

Matrix A summarizes all connections within the network. A is sometimes symmetric but not always. Consider a situation of donated blood, then the infection can only travel one way along a link.

Definition 3.1.5. *A network is said to be an undirected graph if all connections are bidirectional.*

Definition 3.1.6. *A network is said to be a directed graph if all edges point in a direction.*

Three of the techniques to gather network information are outlined below [29]:

Infection Tracing
Field based epidemiologists determine the source of infection for each case. The networks observed are tree-like, and contain no loops. Interactions that occurred but did not result in an infection are not recorded and remain unknown.

Complete Contact Tracing
The aim is to identify all potential transmission contacts from a source individual, revealing a set of individuals who might be infected and can further be studied to trace. Problems with this type of network is defining potential transmission routes, and also is time consuming and relies on individuals sharing personal information. Contact tracing is applied as a control tool, often in the case of STDs. Asymptomatic individuals (infected persons who show no symptoms) can be treated or quarantined. Only a subset of the full mixing network will be uncovered, however it is still generally the most detailed. Example: sexual mixing networks. Snowball sampling is a non-probability sampling where existing subjects recruit future subjects from among their acquantainces.

Diary-based Studies
Diary-based studies rely on subjects to record contacts as or shortly after they occur. This shifts the workload from the researcher to the subject and allows for a larger number of individuals to be sampled. Problems include inconsistent definitions due to subject bias.

Next we list some types of networks [29]:

Random Networks
Connections are formed at random, each individual has a fixed number of contacts through which infection can spread. The random network thus usually has a lack of clustering but are homogeneous on the individual level. Dynamics of disease spread on random networks can be studied as simple branching proccesses.

$$growth\,rate\,in\,a\,random\,network = \tau(n-2) - g$$

$$growth\,rate\,with\,random\,mixing = \tau\hat{n} - g$$

where τ is the transmission rate across a contact, n is the number of contacts in a network, and $\hat{n}$ is the effective number of contacts per unit time in a random mixing model. Random networks have short path lengths, since we can have long-range links and low clustering. A common random network used is the Erdos-Renyi random network, in which we start with N finite nodes and connect every pair of nodes with the probability p, thus creating a graph

with approximately $pN(N-1)/2$ edges.

Lattices
Lattices are homogeneous at the individual level. An example of this would be the forest-fire model (see [7] for more detail). Contact between sites can be characterized as "on" or "off". Lattices can be used for SIS models (similar to forest-fire model) or SIR models (particularly with births since when trees burn, empty sites are left for recolonization). In disease transmission, there is slow growth at the beginning and the infection spreads out in a roughly circular manner, causing spatial clustering. This effect captures the wave-like progression of an infection across geographical locations. Lattices display long path lengths, that is, many steps to move between two randomly selected individuals.

Small-world Networks
Small-world networks can be formed by adding random connections to a lattice. Usually rare, long-range connections have a large effect by allowing the infection to reach all parts of the lattice relatively quickly, hence the phrase "small-world". These type of networks are characterized by long-range transmission and high clustering. Human social networks are thought to be small worlds, but neural networks and gene networks are also examples.

Spatial Networks
Spacial networks are considered one of the most "flexible" types of networks. Nodes or individuals are placed within a given area or volume and connected by a probability depending on their separation. These networks generally show a high degree of heterogeneity.

Scale-free Networks
Scale-free networks have a degree distribution which follows the power law, or at least asymptotically.

Barabasi-Albert Network
The Barabasi-Albert network is a type of network in which new nodes are added and form new links with the previously existing nodes of the network, with a higher probability of linking to a node with a greater degree [9]. A practical example of this would be the Internet, or the World Wide Web, where users are connecting to web pages and more popular webpages gain connections more rapidly.

3.2 Model Formation and Degree Distribution

Interpersonal contact patterns of disease transmission can be thought of as a network where nodes are individuals who interact with each other and edges are relations [29]. Earlier described as a "neighbourhood" of an individual, the term connectivity or degree of a node is also used, k, which is defined as the number of links connected to the node. The degree distribution, $p(k)$ is defined as the probability that a randomly chosen node in the net-

work will have degree k. Since these probabilities describe what is called the "connectivity distribution", then the expected value of k gives the average degree of the network [8,29,45].

$$\langle k \rangle = \sum_{k=1}^{n} kp\,(k)$$

In homogeneous networks, a first approximation is to consider that each node or individual has the same number of contacts, the degree $k \simeq \langle k \rangle$. This case is identitcal to the uniform mixing model where $\beta = \lambda \langle k \rangle$, where λ is the transmission rate or infection rate, defined as the probability per unit time that the infection will be transmitted between a susceptible individual and infective individual who are connected by a link in a network. However, networks that are relevant to the spread of a disease are heterogeneous, including the scale-free network, in which the degree distribution follows a power law, $p(k) \sim k^{-\sigma}$, where generally $2 \leq \sigma \leq 3$ [29]. One key assumption that is considered is a degree block approximation that assumes all nodes with the same connectivity are statistically equivalent [8,45]. Nodes can be grouped in the same class of degree k. It is assumed that individuals in the same degree class are statistically identical, thus instead of only dividing the population into classes by disease status (example: Susceptible, Infected, Recovered, etc) we also divide the population by degree. Therefore, if we have m disease classes then we will have a system of $n \times m$ dimensons, where $k = 1, ..., n$ describes the degree and n is the greatest number of links a node has in the network of analysis.

Where the term that describes the flux of susceptible individuals contracting the disease from infectious individuals is conventionally $\beta S(t) I(t)$, with β being the contact rate, the term is now $\lambda k S_k(t) \Theta(t)$, where $S_k(t)$ is the proportion of susceptible individuals in degree class k at time t [11, 34, 48, 53]. In this way, we divide the nodes in the network into groups of individuals with the same number of relations, and model that the disease will spread at an increased rate among individuals who have more contacts. Note that the value of λ is both influenced by the type of disease and the network structure. Some diseases are transmitted more easily and often than others, however the transmission rate is also a property of the network structure by the degree distribution and the social behaviours of that population. For instance, in some countries it is common etiquette to wear face masks to prevent the spread of disease but these conventions are not as widely used in other countries [29].

We assume that the connectivity of the nodes on the network is uncorrelated, thus we have an equation for the Theta function,

$$\Theta\,(t) = \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp\,(k)\, I_k\,(t)$$

which represents the probability that an arbitrary link (relation) points to an infected node [29]. With these equations, our first infectious disease model on a network can be formulated.

3.3 The SIS Network Model

We begin by adding the network mixing assumption to a simple SIS model with population dynamics, modeled after the disease models in [8, 11, 45, 53, 55, 57].

$$\begin{cases} \dot{S}_k = \mu - \lambda k S_k \Theta + g I_k - \mu S_k \\ \dot{I}_k = \lambda k S_k \Theta - g I_k - \mu I_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{3.1}$$

where μ is the birth and natural death rate of the population, λ is the transmission rate, and g is the recovery rate at which infected individuals are no longer infectious. $S_k(t)$ and $I_k(t)$ are the proportion of susceptible and infected individuals, respectively, in degree class k at time t. The physically meaningful domain is $\Omega_{SI} = \{(S_1, I_1, ..., S_n, I_n) \in \mathbb{R}^{2n}_+ | \dot{S}_k + \dot{I}_k + \dot{R}_k = 1 \, \forall k\}$. This domain is invariant to the network model (3.1) since $\dot{S}_k|_{S_k=0} = \mu + g I_k > 0$ and $\dot{I}_k|_{I_k=0} = \lambda k S_k \Theta \geq 0$, and also $\dot{S}_k + \dot{I}_k = 0$ for all k.

Note how the incidence rate of disease transmission changes from the model with uniform mixing, where it is βSI, it is now $\lambda k S_k \Theta$. If we consider a homogeneous network where all nodes (or individuals in the population) have the same given degree k, then the average degree $\sum_{j=1}^{n} jp(j)$ would then be equal to the given k. Further, $p(j)$, the probability that a randomly chosen node has degree j, becomes 0 for all $j \in \{1, ..., n\}$ with the exception of $p(k) = 1$. Then the incidence rate becomes

$$\begin{aligned} \lambda k S_k \Theta &= \lambda k S_k \frac{1}{k} \sum_{j=1}^{n} jp(j) I_j \\ &= \lambda S_k \sum_{j=1}^{n} (1 \cdot 0 \cdot I_1 + 2 \cdot 0 \cdot I_2 + ... + k \cdot 1 \cdot I_k + ... \\ &\qquad + (n-1) \cdot 0 \cdot I_{n-1} + n \cdot 0 \cdot I_n) \\ &= \lambda k S_k I_k \\ &= \beta S_k I_k \end{aligned}$$

if we take $\beta = \lambda k$ to be the contact rate (the transmission rate times the number of adequate contacts made in one time unit). Therefore if the network is homogeneous, i.e. the degree distribution is uniform, then the network model reduces to the conventional disease model with the mass mixing assumption.

This general network model can be easily solved at the early stage of the epidemics when we can assume that the number of infected individuals is a very small fraction of the total population; assume $I_k^2 << 1$ for all k. In the initial epidemic stages, we neglect terms

of order $\mathcal{O}(I_k^2)$ and then we can obtain the evolution equation for $\Theta(t)$ [8].

$$\frac{dI_k(t)}{dt} = \lambda k(1 - I_k)\Theta(t) - (g + \mu)I_k$$
$$\frac{d\Theta(t)}{dt} = [\frac{\lambda\langle k^2\rangle}{\langle k\rangle} - (g + \mu)]\Theta$$

These equations can be solved and under a uniform initial condition $I_k(0) = I_0$:

$$\Theta(t) = I_0 e^{(\lambda\langle k^2\rangle/\langle k\rangle - (g+\mu))t}$$
$$I_k(t) = I_0(1 + \frac{k\langle k\rangle}{\langle k^2\rangle}(e^{t/\tau} - 1))$$

with

$$\tau = \frac{\langle k\rangle}{\lambda\langle k^2\rangle - (g + u)\langle k\rangle}$$

The prevalence therefore increases exponentially fast, with larger degree nodes displaying larger prevalence levels [8]. The total average prevalence can be obtained as $I(t) = \sum_k p(k)I_k$,

$$I(t) = I_0(1 + \frac{\langle k\rangle^2}{\langle k^2\rangle}(e^{t/\tau} - 1))$$

Since τ represents the typical outbreak time, this leads to the crucial epidemiological concept, the epidemic threshold [8].

$$\tau^{-1} = \frac{\lambda\langle k^2\rangle}{\langle k\rangle} - (g + \mu)$$

The epidemic threshold condition can be readily written in the form

$$\tau^{-1} = (g + \mu)(R_0 - 1) > 0$$

where $R_0 = \lambda\langle k^2\rangle/(g + \mu)\langle k\rangle$ which idenitifies the basic reproductive rate, which has to be larger than 1 for spreading to occur. If the spreading rate is not large enough, (i.e. $\lambda < (g+\mu)\langle k\rangle/\langle k^2\rangle$), the epidemic outbreak will not affect a finite portion of the population and will die out in a finite time. For uncorrelated networks, this result implies the growth time scale of an epidemic outbreak is related to the heterogeneity ratio, $\kappa = \langle k^2\rangle/\langle k\rangle$, a characteristic known as graph heterogeneity. In scale-free networks with a degree exponent, $2 \leq \alpha \leq 3$, we have that $\kappa \to \infty$ as the network size $N \to \infty$. Therefore, for uncorrelated scale-free networks there is a virtually instantaneous rise of the epidemic incidence. Disease can spread very rapidly among the networks following a "cascade" of decreasing degree classes.

It is clear that there exists a disease-free equilibrium point, $E_0 = \{S_{0k}, I_{0k}\}_{k=1}^n$ where for all k, $S_{0k} = 1$ and $I_{0k} = 0$, and also a positive endemic equilibrium point under certain conditions. The endemic equilibrium point takes the form $E^* = (S_k^*, I_k^*)$ where

$$S_k^* = \frac{\mu + g}{\lambda k\Theta + \mu + g}, \qquad I_k^* = \frac{\lambda k\Theta}{\lambda k\Theta + \mu + g}$$

To impose the stationary condition we substitute $I_k = I_k^*$ into the equation for $\Theta(t)$,

$$\Theta(t) = \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k) \frac{\lambda k \Theta}{\lambda k \Theta + \mu + g} = f(\Theta) \tag{3.2}$$

Clearly $\Theta = 0$ satisfies this equation and is a fixed point. The equation is a monotonously increasing function and in order to have a solution $\Theta^* \neq 0$, the slope of $f(\Theta)$ at the point $\Theta = 0$ must be larger than or equal to 1. To allow a non-trivial solution $\Theta \in (0, 1)$ we need $df(\Theta)/d\Theta$ at $\Theta = 0$ to be greater than 1.

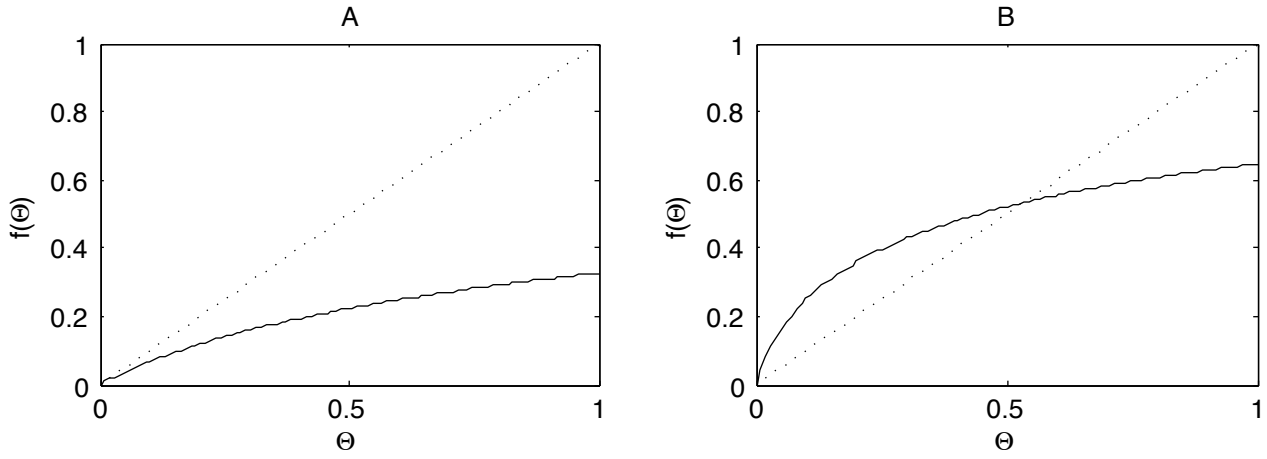


Figure 3.2: **A graphical solution of the equation** $\Theta = f(\Theta)$ **A**: If the slope of the function $f(\Theta)$ at $\Theta = 0$ is less than 1, then there is only one solution to the equation (and thus the system) at $\Theta = 0$. **B**: When the slope is larger than 1, a non-trivial solution $\Theta^* \neq 0$ exists. Based on a figure from [8]. Created in Matlab.

$$\begin{aligned}
\left.\frac{df(\Theta)}{d\Theta}\right|_{\Theta=0} &= \left.\frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k) \frac{\lambda k(\lambda k\Theta + \mu + g) - \lambda k\Theta(\lambda k)}{(\lambda k\Theta + \mu + g)^2}\right|_{\Theta=0} \\
&= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k) \frac{\lambda k(\mu + g)}{(\mu + g)^2} \\
&= \frac{1}{\langle k \rangle} \frac{\lambda}{(\mu + g)} \sum_{k=1}^{n} k^2 p(k) \\
&= \frac{\lambda \langle k^2 \rangle}{(\mu + g)\langle k \rangle} \\
&= R_0
\end{aligned}$$

If $R_0 > 1$ then there exists a positive endemic equilibrium E^*. This would suggest that if $R_0 < 1$ then only the disease-free equilibrium exists, and intuitively it would be globally asymptotically stable. This is shown in the theorem below, adapted from [11].

Theorem 3.3.1. *Assume $R_0 \leq 1$, then the disease-free equilibrium E_0 is globally asymptotically stable in the meaningful domain, Ω_{SI}.*

Proof. Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^n$. Knowing that $S_k + I_k = 1$ the system can be reduced to n-dimensions.

$$S_k' = \mu - \lambda k S_k \Theta + g(1 - S_k) - \mu S_k, \qquad k = 1, 2, ..., n$$

By removing the second term which is clearly non-positive, we have that

$$S_k' \leq \mu + g(1 - S_k) - \mu S_k$$

Therefore we can consider the following auxiliary system:

$$S_k' = (\mu + g) - (\mu + g) S_k$$

which has the equilibrium point $S_k^0 = 1$. We can use a change of variables where $y = S_k - 1$:

$$\begin{aligned} y' &= S_k' \\ &= (\mu + g) - (\mu + g)(1 + y) \\ &= -(\mu + g) y \end{aligned}$$

which is a linear first order differential equation and the solution is globally asymptotically stable. □

To prove global asymptotic stability of the endemic equilibrium, we use a Lyapunov function.

Theorem 3.3.2. *Assume $R_0 > 1$. Then the endemic equilibrium E^* is globally asymptotically stable in the meaningful domain, Ω_{SI}.*

Proof. Consider a non-negative solution, $\{(S_k(t), I_k(t))\}_{k=1}^n$. Then consider the following Lyapunov function:

$$V(t) = \frac{1}{2} \sum_{k=1}^{n} \{\omega_1 (S_k - S_k^*)^2 + \omega_2 (I_k - I_k^*)^2\}$$

We calculate the derivative along the endemic equilibrium point:

$$\begin{aligned} \frac{dV(t)}{dt} &= \sum_{k=1}^{n} \{\omega_1 (S_k - S_k^*) S_k' + \omega_2 (I_k - I_k^*) I_k'\} \\ &= \sum_{k=1}^{n} \{\omega_1 (S_k - S_k^*)(\mu - \lambda k S_k \Theta + g I_k - \mu S_k) + \omega_2 (I_k - I_k^*)(\lambda k S_k \Theta - g I_k - \mu I_k)\} \end{aligned}$$

Using $S_k + I_k = 1$, $\mu - \lambda k S_k^* \Theta + g I_k^* - \mu S_k^* = 0$, and $\lambda k S_k^* \Theta - \mu I_k^* - \mu I_k^* = 0$

$$\frac{dV(t)}{dt} = \sum_{k=1}^{n} \{-\omega_1(\lambda k \Theta + \mu + g)(S_k - S_k^*)^2 - \omega_2(\lambda k \Theta + \mu + g)(I_k - I_k^*)^2\}$$

which is clearly negative definite with respect to E^*. □

3.4 The SIS Network Model with Vertical Transmission

A common modification to the SIS model is the concept of vertical transmission, in which a disease may be passed down from a mother once they give birth to a new child. If we consider that p is the probability that a mother with the disease does not pass down to the child, $0 \leq p \leq 1$, then $(1-p)$ is the probability the child gains the infection transplacentally. With μ once again representing the birth rate, then $\mu(1-p)I_k$ represents the flux entering I_k through birth and $\mu p I_k$ representing the flux entering the susceptible class as normal, for all degree values k. Then our model is:

$$\begin{cases} \dot{S}_k = \mu(S_k + pI_k) - \lambda k S_k \Theta - \mu S_k + g I_k \\ \dot{I}_k = \mu(1-p)I_k + \lambda k S_k \Theta - g I_k - \mu I_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{3.3}$$

where physically meaningful domain is Ω_{SI}. This domain is invariant to the system since $\dot{S}_k + \dot{I}_k = 0$ and $\dot{S}_k|_{S_k=0} = \mu p + g > 0$ and $\dot{I}_k|_{I_k=0} = \lambda k S_k \Theta \geq 0$, therefore the model is biologically well posed. Again, $E_0 = \{S_{0k}, I_{0k}\}_{k=1}^{n}$, where $S_{0k} = 1$, $I_{0k} = 0$ for all k is a disease-free equilibrium of the system. Setting $\dot{I}_k = 0$ and $\dot{S}_k = 0$ and applying that $S_k + I_k = 1$ then we get the following endemic equilibrium point $E^* = (S_1^*, I_1^*, ..., S_n^*, I_n^*)$ where

$$S_k^* = \frac{p\mu + g}{\lambda k \Theta + p\mu + g}, \qquad I_k^* = \frac{\lambda k \Theta}{\lambda k \Theta + p\mu + g}.$$

Using the same technique as previously to get the reproductive threshold ratio, we get that

$$R_0 = \frac{\lambda \langle k^2 \rangle}{(p\mu + g)\langle k \rangle}$$

which must be greater than 1 for a positive endemic equilibrium to exist.

At the early stage of the epidemics, we neglect terms of order $\mathcal{O}(I_k^2)$ or higher and then we can obtain the evolution equation for $\Theta(t)$:

$$\dot{I}_k = \lambda k \Theta - (p\mu + g) I_k$$
$$\dot{\Theta} = (\frac{\langle k^2 \rangle \lambda}{\langle k \rangle} - (p\mu + g))\Theta$$

Similar to the SIS model without vertical transmision, these equations can be solved such that

$$I_k(t) = I_0(1 + \frac{k\langle k\rangle}{\langle k^2\rangle}(e^{1/\tau} - 1)$$

where

$$\tau = \frac{\langle k\rangle}{\lambda\langle k^2\rangle - (p\mu + g)\langle k\rangle}.$$

Further, we have similar analysis to the previous model in that the reproductive threshold ratio decides whether the disease-free equilibrium is globally asymptotically stable or the endemic equilibrium is globally asymptotically stable.

Theorem 3.4.1. *Assume $R_0 < 1$, then the disease-free equilibrium E_0 for all k is globally asymptotically stable in the physically meaningful domain, Ω_{SI}.*

Proof. Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^n$.

$$\begin{aligned} S_k' &= \mu(S_k + pI_k) - \lambda k S_k \Theta - \mu S_k + gI_k \\ &= \mu p I_k - \lambda k S_k \Theta + gI_k \\ &= \mu p - \lambda k S_k \Theta - \mu p S_k + gI_k \end{aligned}$$

Clearly,

$$S_k' \leq \mu p + g(1 - S_k) - \mu p S_k$$

Consider the auxiliary system:

$$S_k' = (\mu p + g) - (\mu p + g)S_k$$

which has the equilibrium point $S_k^0 = 1$. We can use a change of variables by letting $y = S_k - 1$.

$$\begin{aligned} y' &= S_k' \\ &= (\mu p + g) - (\mu p + g) * 1 + y) \\ &= -(\mu p + g)y \end{aligned}$$

which is a linear first order differential equation and the solution is globally asymptotically stable. □

Theorem 3.4.2. *Assume $R_0 > 1$. Then the endemic equilibrium E^* is globally asymptotically stable in the physically meaningful domain, Ω_{SI}.*

Proof. Following the proof of Theorem 3.3.2 and using the same Lyapunov function which is clearly positive definite with respect to E^* for the system (3.3) as well, the derivative along the endemic equilibrium point is:

$$\frac{dV}{dt} = \sum_{k=1}^{n}\{-\omega_1(\lambda k\Theta + \mu p + g)(S_k - S_k^*)^2 - \omega_2(\lambda k\Theta + \mu p + g)(I_k - I_k^*)^2$$

which, assuming $R_0 > 1$, is negative definite with respect to E^*. Thus the endemic equilibrium is globally asymptotically stable. □

3.5 The SIR Network Model

In many cases, individuals who have recovered from the disease gain immunity and thus cannot contract the disease once again. Introduce the network mixing assumption into the SIR model with population dynamics. This leads to the following new SIR network model:

$$\begin{cases} \dot{S}_k = \mu - \lambda k S_k \Theta - \mu S_k \\ \dot{I}_k = \lambda k S_k \Theta - g I_k - \mu I_k \\ \dot{R}_k = g I_k - \mu R_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{3.4}$$

where $\Theta = (1/\langle k \rangle) \sum_{k=1}^{n} kp(k) I_k$, $\langle k \rangle = \sum_{k=1}^{n} kp(k)$ and μ is the birth and natural death rate and g is the recovery rate. Since there are three classes of disease status for each degree, where we had $S_k + I_k = 1$ for the SIS model we now have $S_k + I_k + R_k = 1$ for the SIR model. Also note that the physically meaningful domain $\Omega_{SIR} = \{(S_1, I_1, R_1, ..., S_n, I_n, R_n) \in \mathbb{R}_+^{3n} | S_k + I_k + R_k = 1 \, \forall k\}$ is invariant to the system, since $\dot{S}_k|_{S_k=0} = \mu > 0$, $\dot{I}_k|_{I_k=0} = \lambda k S_k \Theta \geq 0$, and $\dot{R}_k|_{R_k=0} = g I_k \geq 0$. This however does not change the picture obtained in the SIS model. Using the same approximations, the time scale for the SIR is:

$$\tau = \frac{\langle k \rangle}{\lambda \langle k^2 \rangle - (g + \mu) \langle k \rangle}.$$

Using the same technique as previously to get the reproductive threshold ratio, we get

$$R_0 = \frac{\lambda \langle k^2 \rangle}{(\mu + g) \langle k \rangle}.$$

Clearly a disease-free equilibrium E_0 point exists, where $\{S_{0k}, I_{0k}, R_{0k}\}_{k=1}^{n}$, where $S_{0k} = 1$, $I_{0k} = 0$, $R_{0k} = 0$ for all k. There is also a positive equilibrium E_* point under the condition that $R_0 > 1$, where

$$\begin{aligned} S_k^* &= \frac{\mu(g + \mu)}{(g + \mu)(\lambda k \Theta + \mu)}, \\ I_k^* &= \frac{\mu \lambda k \Theta}{(g + \mu)(\lambda k \Theta + \mu)}, \\ R_k^* &= \frac{g \lambda k \Theta}{(g + \mu)(\lambda k \Theta + \mu)} \end{aligned}$$

for all $k = 1, 2, ..., n$.

Theorem 3.5.1. *Assume $R_0 < 1$, then the disease free equilibrium E_0 is globally asymptotically stable in the meaningful physical domain, Ω_{SIR}.*

Proof. The system can be easily reduced to $2n$ dimensions, knowing that $R_k = 1 - S_k - I_k$, we only consider the first two differential equations. Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^{n}$. Clearly,

$$S_k' \leq \mu - \mu S_k, \qquad k = 1, 2, ..., n$$

Therefore we can consider the auxiliary system,

$$S_k' = \mu - \mu S_k$$

which has the equilibrium point $S_k^0 = 1$. Using a change of variables, $y = S_k - 1$,

$$\begin{aligned} y' &= S_k' \\ &= \mu - \mu(y+1) \\ &= -\mu y \end{aligned}$$

which is a linear first order differential equation. Then for any $\epsilon > 0$, $S_k(t) \leq S_k^0 + \epsilon$ for t sufficiently large. Thus,

$$I_k' \leq \lambda k(S_k^0 + \epsilon)\Theta - (g+\mu)I_k$$

Thus consider the auxiliary system:

$$I_k' = \lambda k(S_k^0 + \epsilon)\Theta - (g+\mu)I_k$$

We will prove stability by the following Lyapunov function,

$$V(t) = \sum_{k=1}^{n} b_k I_k(t)$$

where $b_k = \dfrac{kp(k)}{\langle k \rangle (g+\mu)}$. Then $b_k > 0$, $I_k > 0$ for all k thus V is positive definite.

$$\begin{aligned} V' &= \sum b_k I_k' \\ &= \sum b_k(\lambda k(S_k^0 + \epsilon)\Theta - (g+\mu)I_k) \\ &= \sum \frac{kp(k)}{\langle k \rangle (g+\mu)}(\lambda k \Theta(1+\epsilon) - (g+\mu)I_k) \\ &= \Theta(R_0 + \frac{\lambda \langle k^2 \rangle \epsilon}{\langle k \rangle (g+\mu)} - 1) \end{aligned}$$

From assumption $R_0 < 1$, fix $\epsilon > 0$ small enough so $R_0 + \lambda\langle k^2\rangle\epsilon/(\langle k\rangle(g+\mu)) < 1$. Then we have V' is negative definite with respect to $I_k = 0$ for all k. By the comparison theorem, we get global asymptotic stability for the disease-free equilibrium. □

Theorem 3.5.2. *Assume $R_0 > 1$. Then the endemic equilibrium E^* is globally asymptotically stable in the meaningful domain, Ω_{SIR}.*

Proof. Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^n$ of the reduced system, then use the following Lyapunov function:

$$V(t) = \frac{1}{2}\sum \omega_1 (S_k - S_k^*)^2 + \Theta - \Theta^* - \Theta^* \ln \frac{\Theta}{\Theta^*}$$

where $\Theta^* = \frac{1}{\langle k \rangle} \sum kp(k)I_k^*$ and ω_1 is a positive constant that depends on k. Clearly $V(t)$ is positive definite with respect to E^*. Calculating the derivative of $V(t)$:

$$\begin{aligned}
\frac{dV}{dt} &= \sum \omega_1(S_k - S_k^*)S_k' + \frac{\Theta'}{\Theta}(\Theta - \Theta^*) \\
&= \sum \omega_1(S_k - S_k^*)(\mu - \lambda k S_k \Theta - \mu S_k) - \frac{(1/\langle k \rangle)\sum kp(k)I_k'}{\Theta}(\Theta - \Theta^*) \\
&= \sum \omega_1(S_k - S_k^*)(\mu - (\lambda k\Theta + \mu)(S_k - S_k^*) - (\lambda k\Theta + \mu)S_k^*) \\
&+ \frac{(1/\langle k \rangle)\sum kp(k)(\lambda k S_k \Theta - (g+\mu)I_k)}{\Theta}(\Theta - \Theta^*) \\
&= \sum \{-\omega_1(\lambda k\Theta + \mu)(S_k - S_k^*)^2 + \omega_1(S_k - S_k^*)(\mu - \lambda k\Theta S_k^* - \mu S_k^*\} \\
&+ \frac{(\Theta/\langle k \rangle)(\sum k^2 p(k)\lambda S_k - (g+\mu))}{\Theta}(\Theta - \Theta^*) \\
&= \sum \{-\omega_1(\lambda k\Theta + \mu)(S_k - S_k^*)^2 + \omega_1(S_k - S_k^*)(\mu - \lambda k S_k^*(\Theta - \Theta^*) - \lambda k S_k^* \Theta^* - \mu S_k^*\} \\
&+ (1/\langle k \rangle)(\sum k^2 p(k)\lambda(S_k - S_k^*) + \sum k^2 p(k)\lambda S_k^* - (g+\mu))(\Theta - \Theta^*) \\
&= \sum \{-\omega_1(\lambda k\Theta + \mu)(S_k - S_k^*)^2 - \omega_1 \lambda k S_k^*(S_k - S_k^*)(\Theta - \Theta^*)\} \\
&+ (1/\langle k \rangle)\sum k^2 p(k)\lambda(S_k - S_k^*)(\Theta - \Theta^*) \\
&= \sum \{-\omega_1(\lambda k\Theta + \mu)(S_k - S_k^*)^2 + (-\omega_1 \lambda k S_k^* + \frac{1}{\langle k \rangle}k^2 p(k)\lambda)(S_k - S_k^*)(\Theta - \Theta^*)\}
\end{aligned}$$

Using the equalities $\mu - \lambda k S_k^* \Theta^* - \mu S_k^* = 0$ and $g + \mu = \lambda \langle k^2 \rangle / (\langle k \rangle) S_k^*$, then we choose $\omega_1(k) = (kp(k)/\langle k \rangle S_k^*)$ such that $V'(t) \leq 0$. Also, $V'(t) = 0$ if and only if $S_k = S_k^*$, $I_k = I_k^*$ for $k = 1, ..., n$. Thus the proof is completed. □

3.6 The SIRS Network Model

In some cases, the individuals who have recovered from the infection only have partial immunity, eventually allowing them to be susceptible to the disease again. The following model incorporates the network mixing assumption in a standard SIRS model with population dynamics.

$$\begin{cases} \dot{S_k} = \mu - \lambda k S_k \Theta + \delta R_k - \mu S_k \\ \dot{I_k} = \lambda k S_k \Theta - g I_k - \mu I_k \\ \dot{R_k} = g I_k - \delta R_k - \mu R_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{3.5}$$

Again, λ is the transmission rate, μ is the birth and death rate of the population, g is the recovery rate and lastly δ is the rate at which recovered individuals lose their immunity to the disease and move into the susceptible class once more. There is a disease-free equilibrium, $E_0 = \{S_{0k}, I_{0k}, R_{0k}\}_{k=1}^n$, where $S_{0k} = 1$, $I_{0k} = 0$, $R_{0k} = 0$ for all k for all k. There is also an endemic equilibrium point, E^*, where

$$S_k^* = \frac{(\delta+\mu)\lambda k\Theta}{\lambda(g+\delta+\mu)k\Theta + (g+\mu)(\delta+\mu)},$$
$$I_k^* = \frac{(\delta+\mu)(g+\mu)}{\lambda(g+\delta+\mu)k\Theta + (g+\mu)(\delta+\mu)},$$
$$R_k^* = \frac{g\lambda k\Theta}{\lambda(g+\delta+\mu)k\Theta + (g+\mu)(\delta+\mu)}.$$

By substituting $I_k = I_k^*$ in the equation for $\Theta = f(\Theta)$ and solving $\frac{df(\Theta)}{d\Theta} > 1$ at $\Theta = 0$ as previously we get the basic reproduction number,

$$R_0 = \frac{\lambda\langle k^2\rangle}{\langle k\rangle(g+\mu)}.$$

Notice that R_0 does not depend on δ. This is due to the disease spreading at the same rate as the SIR or the SIS model; the fact that the disease immunity is temporary does not change the basic reproduction rate.

Theorem 3.6.1. *Assume $R_0 < 1$, then the disease-free equilibrium E_0 is globally asymptotically stable in the meaningful domain, Ω_{SIR}.*

Proof. If we reduce the system to $2n$ dimensions using $R_k = 1 - S_k - I_k$, then we only consider two differential equations:

$$\begin{cases} \dot{S}_k = \mu + \delta - \lambda k S_k\Theta - \delta I_k - \delta S_k - \mu S_k \\ \dot{I}_k = \lambda k S_k\Theta - gI_k - \mu I_k, & k = 1, 2, ..., n \end{cases}$$

Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^n$. It is easy to see that

$$S_k' \leq (\mu+\delta) - (\mu+\delta)S_k, \qquad k = 1, 2, ..., n.$$

Therefore we can consider the auxiliary system,

$$S_k' = (\mu+\delta) - (\mu+\delta)S_k$$

which has the equilib-rium point $S_k^0 = 1$. Using a change of variables, $y = S_k - 1$, we can show this auxiliary system reduced to a linear first order differential equation. Then, for any $\epsilon > 0$, $S_k(t) \leq S_k^0 + \epsilon$ for t sufficiently large. Thus,

$$I_k' \leq \lambda k(S_k^0 + \epsilon)\Theta - (g+\mu)I_k.$$

Therefore we can consider the auxiliary system,

$$I_k' = \lambda k(S_k^0 + \epsilon)\Theta - (g+\mu)I_k.$$

We will prove stability by the following Lyapunov function,

$$V(t) = \sum_{k=1}^{n} b_k I_k(t)$$

where $b_k = \dfrac{kp(k)}{\langle k\rangle(g+\mu)}$. Then since $b_k > 0$, then V is positive definite with respect to the disease-free equilibrium. Further, we can show that

$$V' = \Theta(R_0 + \frac{\lambda\langle k^2\rangle\epsilon}{\langle k\rangle(g+\mu)} - 1).$$

From assumption, $R_0 < 1$, fix $\epsilon > 0$ small enough so that $R_0 + \lambda\langle k^2\rangle\epsilon/(\langle k\rangle(g+\mu)) < 1$. Then we have that V' is negative definite with respect to $I_k = 0$ for all k. By the comparison theorem, we get global asymptotic stability for the disease-free equilibrium. □

3.7 The SIRS Network Model with Vaccination

The following is an SIRS epidemic model integrating the concept of modeling contact patterns of disease transmission using networks [11]

$$\begin{cases} \dot{S}_k = -\lambda k S_k \Theta + \delta R_k - u S_k \\ \dot{I}_k = \lambda k S_k \Theta - g I_k \\ \dot{R}_k = g I_k - \delta R_k + u S_k, \qquad k = 1, 2, ..., n \end{cases} \tag{3.6}$$

where λ is the transmission rate when susceptible individuals contact with infectious individuals, g is the recovery rate from infection, the rate at which individuals move from the infected class to the recovered class, δ is the rate at which recovered individuals move into the susceptible class once again and u is the vaccination efficient (the percentage of susceptible individuals that are vaccinated and thus given short-term immunity.

In order to analyze the solutions of physical relevance, we only consider non-negative solutions of the system (2). So the initial conditions are all of the form $S_k(0) > 0, I_k(0) > 0, R_k(0) = 1 - S_k(0) - I_k(0) > 0$. The physically meaningful domain is Ω_{SIR}. Since $\dot{S}_k + \dot{I}_k + \dot{R}_k = 0$, and $\dot{S}_k|_{S_k=0} = \delta R_k \geq 0$, $\dot{I}_k|_{I_k=0} = \lambda k S_k \Theta \geq 0$ and $\dot{R}_k|_{R_k=0} = g I_k + u S_k \geq 0$ we have that this domain is invariant to system (3.6).

Futhermore, the system can be reduced into two dimensions due to the fact that $R_k(t) = 1 - S_k(t) - I_k(t)$,

$$\begin{cases} \dot{S}_k = -\lambda k S_k \Theta + \delta(1 - S_k - I_k) - u S_k \\ \dot{I}_k = \lambda k S_k \Theta - g I_k, \qquad k = 1, 2, ..., n. \end{cases}$$

Clearly there is a trivial equilibrium point $E_0 = (0, 0, ..., 0, 0)$. Another solution to solving $S_k' = 0$ and $I_k' = 0$ is E^* where:

$$S_k^* = \frac{g\delta}{g(\delta+u) + \lambda(\delta+g)k\Theta},$$

$$I_k^* = \frac{\lambda\delta k\Theta}{g(\delta+u) + \lambda(\delta+g)k\Theta}.$$

Therefore, we have another disease-free equilibrium point $E_0 = (\delta/(\delta+u), 0, ..., \delta/(\delta+u), 0)$ and an epidemic equilibrium $E^*(S_1^*, I_1^*, ..., S_n^*, I_n^*)$ with S_k^* and I_k^* as defined above.

To find the reproductive threshold ratio, we substitute I_k^* into the equation for $\Theta(t)$.

$$\Theta = \frac{1}{\langle k\rangle}\sum_{k=1}^{n} kp(k)\frac{\lambda\delta k\Theta}{g(\delta+u) + \lambda(\delta+g)k\Theta} = f(\Theta) \tag{3.7}$$

$\Theta = 0$ satisfies equation (3.7) and is a fixed point. To allow a non-trivial solution $\Theta \in (0, 1)$ we need:

$$\left.\frac{df(\Theta)}{d\Theta}\right|_{\Theta=0} > 1$$

$$\begin{aligned}
\left.\frac{df(\Theta)}{d\Theta}\right|_{\Theta=0} &= \frac{1}{\langle k\rangle}\sum kp(k)\frac{\lambda\delta(g(\delta+u) + \lambda(\delta+g)k\Theta + \lambda\delta k\Theta(\lambda(\delta+g)k)}{(g(\delta+u) + \lambda(\delta+g)k\Theta)^2} \\
&= \frac{1}{\langle k\rangle}\sum kp(k)\frac{\lambda\delta k(g(\delta+u))}{(g(\delta+u))^2} \\
&= \frac{1}{\langle k\rangle}\sum kp(k)\frac{\lambda\delta k^2}{g(\delta+u)} \\
&= \frac{\lambda\delta}{g(\delta+u)\langle k\rangle}\sum k^2p(k) \\
&= \frac{\lambda\delta\langle k^2\rangle}{g(\delta+u)\langle k\rangle} \\
&= R_0
\end{aligned}$$

If $R_0 > 1$ then $\exists$ a positive endemic equilibrium E^*. If not, then there is only one possible equilibrium: the disease-free equilibrium which brings us to the following theorems.

Theorem 3.7.1. *(modified from [11]). Assume $R_0 < 1$, then disease-free equilibrium E_0 is globally asymptotically stable in the meaningful domain, Ω_{SIR}.*

Proof. Consider a non-negative solution $\{S_k(t), I_k(t)\}_{k=1}^n$. Comparing to system (3.6), by removing the first term which is clearly less than zero, we have that

$$\frac{dS_k(t)}{dt} \leq \delta - (\delta + u)S_k(t).$$

Therefore we can consider the following auxiliary system:

$$\frac{dS_k(t)}{dt} = \delta - (\delta + u)S_k(t), \qquad k = 1, 2, ..., n \tag{3.8}$$

which has the equilibrium point $S_k^0 = \delta/(\delta + u)$. We can use an integrating factor to solve system (3.8) :

$$\begin{aligned}
\frac{dS_k(t)}{dt} + (\delta + u)S_k(t) &= \delta \\
e^{(\delta+u)t}\frac{dS_k(t)}{dt} + e^{(\delta+u)t}(\delta + u)S_k(t) &= e^{(\delta+u)t}\delta \\
(e^{(\delta+u)t}S_k(t))' &= \delta e^{(\delta+u)t} \\
\int (e^{(\delta+u)t}S_k(t))'dt &= \int \delta e^{(\delta+u)t}dt \\
e^{(\delta+u)t}S_k(t) &= \frac{\delta}{\delta + u}e^{(\delta+u)t} + C
\end{aligned}$$

Thus the solution is $S_k(t) = \delta/(\delta + u) + Ce^{-(\delta+u)t}$. Clearly, we have that $\lim_{t\to\infty} S_k(t) = \delta/(\delta+u)$, and it is the only equilibrium point in the positive quadrant and so the equilibrium is globally asymptotically stable.

Alternatively we could use a change of variables, which is much simpler and quicker. Let $y = S_k - \delta/(\delta + u)$:

$$\begin{aligned}
y' &= S_k' \\
&= \delta - (\delta + u)(y + \frac{\delta}{\delta + u}) \\
&= \delta - (\delta + u)y - \delta \\
&= -(\delta + u)y
\end{aligned}$$

which is a linear first order differential equation and the solution is globally asymptotically stable.

Then, for any $\epsilon > 0$, $S_k(t) \leq S_k^0 + \epsilon$ for t sufficiently large. Thus,

$$\frac{dI_k(t)}{dt} \leq \lambda k(S_k^0 + \epsilon)\Theta - gI_k(t)$$

Again we can consider the auxiliary system:

$$\frac{dI_k(t)}{dt} = \lambda k(S_k^0 + \epsilon)\Theta - gI_k(t), \qquad k = 1, 2, ..., n. \tag{3.9}$$

Let us consider the following Lyapunov function,

$$V(t) = \sum_{k=1}^{n} b_k I_k(t)$$

where $b_k = \dfrac{kp(k)}{g\langle k\rangle}$. We have that $b_k > 0, I_k > 0\ \forall k$ and V is positive definite.

$$\begin{aligned}
V' &= \sum b_k I_k(t)' \\
&= \sum b_k[\lambda k(S_k^0 + \epsilon)\Theta - gI_k] \\
&= \sum \frac{kp(k)}{g\langle k\rangle}[\lambda k(S_k^0 + \epsilon)\Theta - gI_k] \\
&= \sum k^2 p(k)\frac{\lambda(S_k^0 + \epsilon)}{g\langle k\rangle}\Theta - gI_k\frac{kp(k)}{g\langle k\rangle} \\
&= \sum [\frac{k^2 p(k)}{g\langle k\rangle}\lambda(\frac{\delta}{\delta + u} + \epsilon)\Theta - \frac{kp(k)I_k}{\langle k\rangle}] \\
&= \Theta(R_0 + \frac{\langle k^2\rangle\epsilon}{g\langle k\rangle} - 1)
\end{aligned}$$

From assumption we have $R_0 < 1$. We can fix $\epsilon > 0$ small enough so that $R_0 + \langle k^2\rangle\epsilon/(g\langle k\rangle) < 1$. Therefore we have $V' \leq 0$ and $dV/dt = 0$ if $I_k = 0$. Thus $\lim_{t\to\infty} I_k = 0$ as we have asymptotic stability.

By the comparison theorem, we get global asymptotic stability for the disease-free equilibrium of the original reduced system. □

Theorem 3.7.2. *[11] Assume $R_0 > 1$, and $u < g$. Then E^* is globally asymptotically stable in the meaningful domain, Ω_{SIR}.*

Proof. Consider a non-negative solution $\{S_k(t), I_k(t), R_k(t)\}_{k=1}^n$. Then use the following Lyapunov function,

$$V(t) = \frac{1}{2}\sum\{w_1(k)(S_k - S_k^*)^2 + w_2(k)(R_k - R_k^*)^2\} + (\Theta - \Theta^* - \Theta^* \ln\frac{\Theta}{\Theta^*})$$

where $R_k^* = 1 - S_k* - I_k*$, $\Theta^* = (1/\langle k\rangle)\sum kp(k)I_k^*$, and $w_1(k), w_2(k)$ are positive constants. By using the fact that $(-\lambda k S_k^*\Theta^* + \delta R_k^* - uS_k^*) = 0$, $g = \lambda\langle k^2\rangle/(\langle k\rangle)S_k^*$ and $g(1 - S_k^* - R_k^*) -$

Model	uniform mixing	network mixing
SIS	$\frac{\beta}{\mu+g}$	$\frac{\lambda\langle k^2\rangle}{(\mu+g)\langle k\rangle}$
SIR	$\frac{\beta}{\mu+g}$	$\frac{\lambda\langle k^2\rangle}{(\mu+g)\langle k\rangle}$
SIRS	$\frac{\beta\delta}{\gamma(\delta+\mu)}$	$\frac{\lambda\delta\langle k^2\rangle}{\gamma(\delta+\mu)\langle k\rangle}$

Table 3.1: Comparison of Thresholds for Uniform mixing and network mixing

$\delta R_k^* + uS_k^* = 0$ we get the following expression for dV/dt,

$$\begin{aligned}\frac{dV}{dt} = &-\sum w_1(\lambda k\Theta + u)(S_k - S_k^*)^2 - \sum w_2(g+\delta)(R_k - R_k^*)^2 \\ &+ \sum(\delta w_1 - (g-u)w_2)(S_k - S_k^*)(R_k - R_k^*) \\ &+ \sum(-\lambda k S_k^* w_1 + \ )(S_k - S_k^*)(\Theta - \Theta^*).\end{aligned}$$

We can choose w_1 and w_2 so that the last two sums are zero. That is, $w_1(k) = (kp(k)/\langle k\rangle)S_k^*$ and $w_2(k) = (\delta/(g+u))w_1(k)$. Thus we impose that $V'(t) \leq 0$ if and only if $S_k = S_k^*$, $I_k = I_k^*$ and $R_k = R_k^*$ for $k = 1, 2, ..., n$. According to the LaSalle invariance principle, we have that:

$$\lim_{t\to\infty} S_k(t) = S_k^*$$

$$\lim_{t\to\infty} I_k(t) = I_k^*$$

$$\lim_{t\to\infty} R_k(t) = R_k^*$$

Therefore, the endemic equilibrium E^* is globally asymptotically stable. □

Table 3.1 is a summary of some simple models and their respective reproductive threshold value for when the uniform mixing assumption is used and when the network mixing assumption is used.

Note the difference between β and λ, which is the contact rate and the transmission rate respectively. Recall that β is the transmission rate times the effective number of contacts per unit time. If we were to consider a given connectivity k, then $\beta = \lambda k$. However, since we are considering the entire coupled system as a whole, on average the number of contacts would be the average connectivity, $\langle k\rangle$. Therefore, we see a common theme of the reproductive threshold values for the network models being a multiple of the values for the

uniform mixing values by a factor of $\frac{\langle k^2 \rangle}{\langle k \rangle^2}$. Another way to analyze this is by the variance of the degree or connectivity. In general,

$$\begin{aligned} Var(k) &= E((k - E(k))^2) \\ &= E(k^2) - E(k)^2 \\ &= \sum_{k=1}^{n} k^2 p(k) - [\sum_{k=1}^{n} kp(k)]^2 \\ &= \langle k^2 \rangle - \langle k \rangle^2 \end{aligned}$$

This brings us to the effect of the network structure on the dynamics. The more spread the connectivity or degree distribution is, the more the reproductive threshold value increases. In general, if all individuals in the network have the exact same number of relations, then there is no change on the reproductive threshold value. However, for any $Var(k) > 0$, there will be an increase in the reproductive threshold value.

3.8 Numerical Simulations

The following simulations were completed in MATLAB, using the built-in ode solver ode45 which was used to analyze the disease models with a mixing network. A scale-free network that follows a power law degree distribution, $p(k) \sim k^{-\alpha}$ where $\alpha = 2.1$. Also we assume that $n = 50$ so the maximum number of links any single node in the network has is 50. For the parameter values, $\mu = 0.2$ and $g = 1$.

For this network we have that the average degree is $\langle k \rangle = 2.4733$ and $\langle k^2 \rangle = 24.0974$. Since the reproductive threshold for the following simulations was $R_0 = \lambda \langle k^2 \rangle / ((\mu + g)\langle k \rangle)$ then we get that the critical value of λ is $\lambda^* = 0.123$.

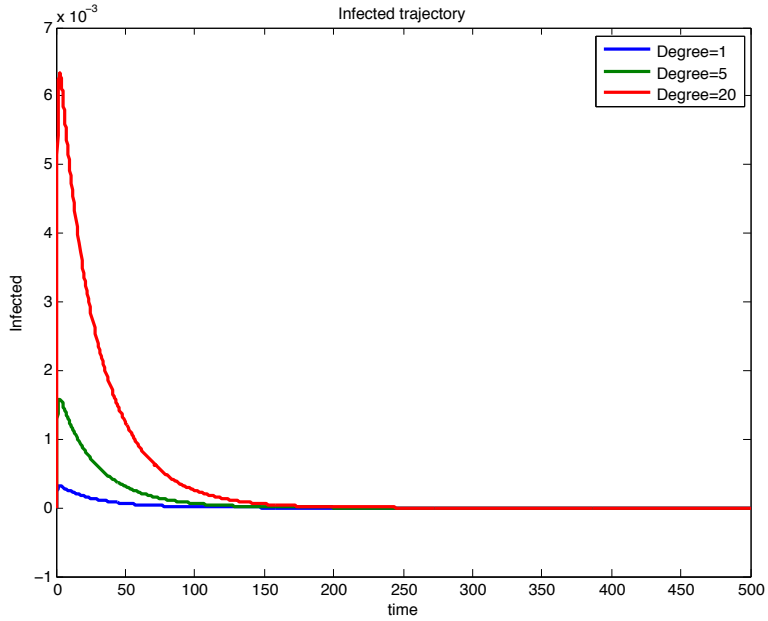


Figure 3.3: **Network SIS Model with $\lambda = 0.12$ which causes $R_0 < 1$:** the disease dies out in this simulation as expected in conjunction with Theorem 3.3.1.

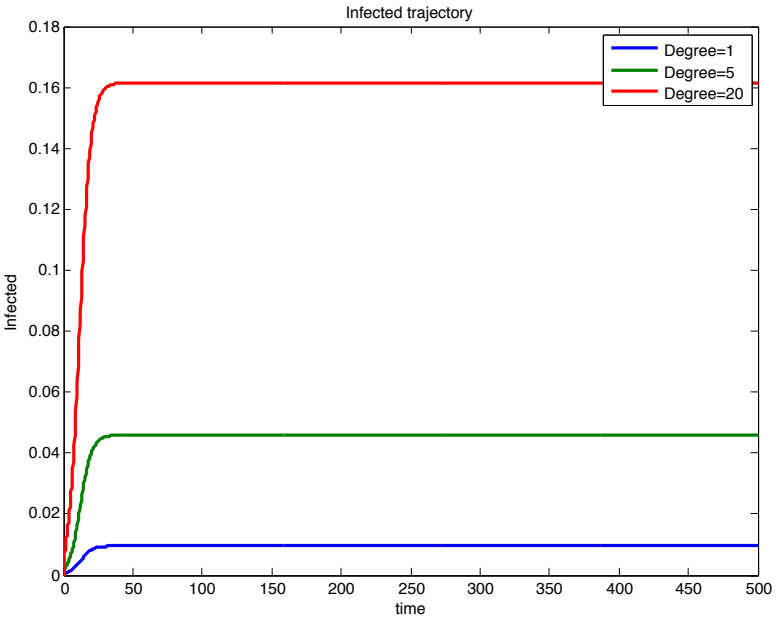


Figure 3.4: **Network SIS Model with $\lambda = 0.15$ which causes $R_0 > 1$:** and the disease persists in conjunction with Theorem 3.3.2.

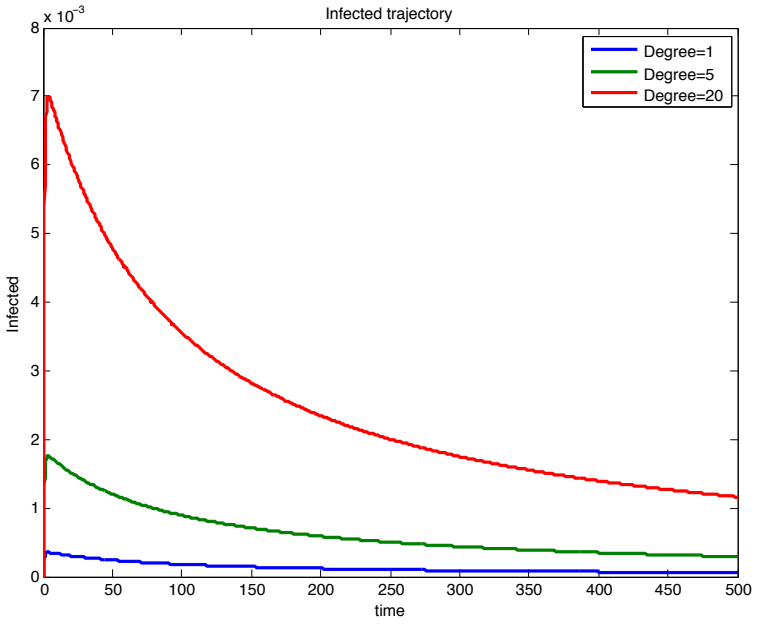


Figure 3.5: **Network SIS Model with $\lambda = \lambda^*$ so $R_0 = 1$:** the disease dies out in this simulation as expected in conjunction with Theorem 3.3.1.

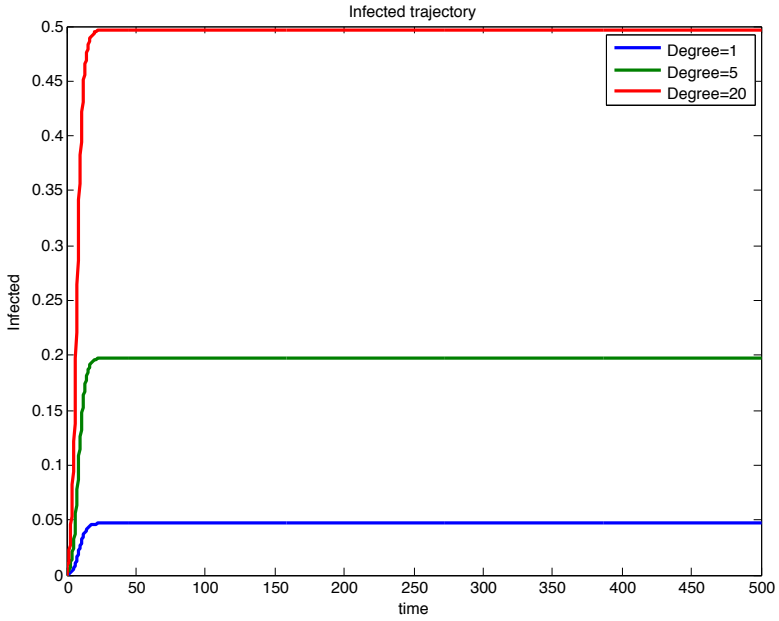


Figure 3.6: **Network SIS Model with Vertical Transmission with $\lambda = 0.12$ and $p = 0.4$:** The addition of vertical transmission causes the disease to persist instead of die out.

Chapter 4

Network SIS Models with Switching

In this chapter, we begin to investigate the addition of switching to a parameter, the transmission rate, to network epidemic models that first only have two main compartments. We start with models that only have two main compartments because they can typically be reduced to n-dimensions which will be represented by one single equation based on the degree distribution, k, which goes from 1 to n.

We will analyze three SIS type models, first the basic SIS model with population dynamics in Section 4.1, then the SIS model with population dynamics and vertical transmission in Section 4.2, and finally the SIS model with switched transmission, recovery, and birth rate in Sectio 4.3. At the end of the chapter we support our results with computer simulations.

4.1 The SIS Network Model with Switched Transmission Rate

We start with an SIS Model in which individuals who contract the disease and recover are immediately susceptible to the disease repeatedly; there is no immunity. We want to introduce switching to the SIS model by assuming that the transmission rate, λ, is a parameter that varies over time. Assume a simple way for λ to vary; assume that it is a piecewise constant that switches value at switching times, t_l, with $t_0 = 0 < t_1 < t_2 < ... < t_l \to \infty$ as $l \to \infty$. We can assume without loss of generality that the initial time is zero. Assume there are m different transmission rates that λ_i can take on. Then the switching signal $\sigma(t)$ is a function which maps the set of all positive real numbers $\mathbb{R}_+$ to the set of integers from 1 to m, $\{1, 2, ..., m\}$. We assume that $\sigma(t)$ is piecewise continuous from the left, and that i follows this switching rule σ. The system of differential equations are given as follows,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta + g I_k - \mu S_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k, \qquad k = 1, 2, ..., n \end{cases} \tag{4.1}$$

with $k \in \{1, ..., n\}$ where n is the highest degree in the network and $i \in \{1, 2, ..., m\}$ following the switching rule $\sigma(t)$. As before, $0 < \mu \leq 1$ is the birth and natural death rate and

$0 < g \leq 1$ is the recovery rate. The variables S_k, I_k are the proportion of susceptible and infected individuals with degree k, respectively. The meaningful physical domain for this system is $\Omega_{SI} = \{(S_1, I_1, S_2, I_2, ..., S_n, I_n) \in \mathbb{R}_+^{2n} | S_k + I_k = 1 \, \forall \, k \in \{1, ..., n\}\}$. Since we have that $S_k + I_k = 1$ then $\dot{S}_k + \dot{I}_k = 0$. Also, $\dot{S}_k|_{S_k=0} = \mu + gI_k > 0$, and $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta > 0$. Therefore the physically meaningful domain is invariant to the switched system. For each subsystem, define the basic reproduction number, from the non-switched case,

$$R_{0i} = \frac{\lambda_i \langle k^2 \rangle}{(\mu + g)\langle k \rangle}$$

which is the average number of secondary infections produced by a single infected individual in a wholly susceptible population. Each subsystem has its own basic reproductive number, due to switching the transmission rate. All subsystems have a disease-free equilibrium in common, $E_0 = (S_{01}, I_{01}, S_{02}, I_{02}, ..., S_{0n}, I_{0n})$ where $(S_{0k}, I_{0k}) = (1, 0) \, \forall k = 1, ..., n$. Each subsystem has a unique endemic equilibrium, $E^* = (S_1^*, I_1^*, S_2^*, I_2^*, ..., S_n^*, I_n^*)$ where

$$S_k^* = \frac{\mu + g}{\lambda_i k \Theta + \mu + g}, \qquad I_k^* = \frac{\lambda_i k \Theta}{\lambda_i k \Theta + \mu + g}$$

which exist in the meaningful domain if $R_{0i} > 1$ for all k.

The overall switched system has only one equilibrium, which is the disease-free equilibrium E_0, since it is an equilibrium point of all subsystems. Therefore, we can study E_0 using a common Lyapunov function. This leads us to the following theorem on global asymptotic stability of the disease-free equilibrium.

Since $S_k = 1 - I_k$, we can reduce this system into n-dimensions and write the system with one differential equation for each value of k:

$$\frac{dI_k(t)}{dt} = \lambda_i k \Theta(t) - (\lambda_i k \Theta + g + \mu) I_k(t)$$

Theorem 4.1.1. *Assume that for all subsystems $i \in \sigma$ we have the following inequality*

$$\frac{\lambda_i \langle k^2 \rangle}{(\mu + g)\langle k \rangle} < 1$$

then we have that the equilibrium point $E_0 = (S_{01}, I_{01}, S_{02}, I_{02}, ..., S_{0n}, I_{0n})$ where $(S_{0k}, I_{0k}) = (1, 0) \, \forall k = 1, ..., n$ is globally asymptotically stable in the meaningful domain Ω_{SI}, and thus the disease dies out.

Proof. Consider the following common Lyapunov function

$$V(t) = \frac{1}{2} \sum_{k=1}^{n} \omega_1(k) I_k^2 + \langle k \rangle \Theta$$

where $\omega_1(k)$ is a positive constant that depends on k and is to be determined suitably. The auxiliary function V is clearly positive definite for all $i \in \sigma$. Calculating the derivative of $V(t)$ along the disease-free solution of the switched system, it follows that

$$\frac{dV}{dt} = \sum_{k=1}^{n} \{-\omega_1(\lambda_i k\Theta + \mu + g)I_k^2 + \lambda_i k(\omega_i - kp(k))I_k\Theta\} + (\lambda_i\langle k^2\rangle - (\mu+g)\langle k\rangle)\Theta$$

To make the second term in the sum zero, we choose $\omega_1(k) = kp(k)$. Then since we assume that $\lambda_i\langle k^2\rangle/((\mu+g)\langle k\rangle) < 1$ then $dV/dt \leq 0$ and $dV/dt = 0$ if and only if $I_k = 0$ for all values of k. Then the disease-free solution is globally asymptotically stable. □

This criterion that all the basic reproductive numbers for each subsystem is less than 1 makes logical sense biologically, since an infected person on average infects at most one other person, then the disease dies out. To broaden this condition, we consider the average of the reproductive numbers. Define the time-weighted mean of R_0 as follows,

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

Define $T_i(t)$ to be the total activation time for the i-th subsystem in the interval $(0, t]$. This way we can calculate the time-weighted mean of R_0 as a summation of the m subsystems,

$$\langle R_\sigma\rangle = \frac{1}{t}\sum_{i=1}^{m} R_i T_i(t).$$

Use this definition in determining stability of the disease-free equilibrium based on the average R_0, thus allowing for $R_i > 1$ in some subsystems, as long as $R_i < 1$ in other subsystems to balance it out.

Lemma 4.1.1. *(adapted from theorem 2.1 in [40]) Consider a general switched epidemiology system with basic reproductive numbers $R_i = A_i/B$ for $i = 1, 2, ..., m$ where $A_1, ..., A_m, B > 0$ are positive constants. If*

$$\langle R_\sigma\rangle < 1 - \epsilon$$

for $t \leq h$, with constants $\epsilon > 0$, $h \geq 0$ and switching rule $\sigma \in S$, 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.

$$\begin{aligned}
\langle R_\sigma\rangle &< 1 - \epsilon \\
\frac{1}{t}\int_0^t \frac{A_{\sigma(s)}}{B}ds &< 1 - \epsilon \\
\frac{1}{t}\int_0^t (A_{\sigma(s)} - B)ds &< -\epsilon B
\end{aligned}$$

Let $c = \epsilon B$, then

$$\begin{aligned}
\int_0^t (A_{\sigma(s)} - B)ds &< -ct \\
\int_0^{T_1(t)} (A_1 - B)ds + ... + \int_0^{T_m(t)} (A_m - B)ds &< -ct \\
\sum_{i=1}^{m} \int_0^{T_i(t)} (A_i - B)ds &< -ct \\
\sum_{i=1}^{m} (A_i - B)T_i(t) &< -ct
\end{aligned}$$

for $t \geq h$. □

This Lemma will be used to prove exponential stability of the disease-free equilibrium in many theorems, including the following one, motivated by [22].

Theorem 4.1.2. *If $\langle R_\sigma \rangle < 1 - \epsilon$ for all $t \geq 0$ and $\epsilon > 0$, with switching rule $\sigma \in S$, then the disease-free solution is exponentially stable in the meaningful domain, Q_{SI}.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned}
\Theta'(t) &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k) I_k'(t) \\
&= \frac{1}{\langle k \rangle} \sum kp(k)(\lambda_{i_l} k\Theta - \lambda_{i_l} k\Theta I_k - (\mu + g)I_k \\
&\leq \frac{1}{\langle k \rangle} \sum kp(k)(\lambda_{i_l} k\Theta - (\mu + g)I_k) \\
&= \frac{1}{\langle k \rangle} (\lambda_{i_l} \Theta \sum k^2 p(k) - (\mu + g) \sum kp(k) I_k) \\
&= (\frac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle} - (\mu + g))\Theta \\
&= C_{i_l} \Theta
\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle} - \mu - g$. Then for $(t_{l-1}, t_l]$,

$$\Theta(t) \leq \Theta(t_{l-1}) \exp[C_{i_l}(t - t_{l-1})] \tag{4.2}$$

Since $\Theta \geq 0$ for all $t \geq 0$, Θ is bounded in the 1-norm, based on the effects of the switching rule. Apply this onto each subinterval. For $t \in (0, t]$:

$$\begin{aligned}
\Theta(t) &\leq \Theta(0) \exp[C_{i_1} t], \\
so \quad \Theta(t_1) &\leq \Theta(0) \exp[C_{i_1} t_1]
\end{aligned}$$

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

$$\begin{aligned}\Theta(t) &\leq \Theta(t_1)\exp[C_{i_2}(t-t_1)] \\ &\leq \Theta(0)\exp[C_{i_1}t_1 + C_{i_2}(t-t_1)] \\ &\vdots\end{aligned}$$

For $(t_{l-1}, t_l]$:

$$\begin{aligned}\Theta(t) &\leq \Theta(0)\exp[C_{i_1}t_1 + C_{i_2}(t_2-t_1) + ... + C_{i_l}(t_l - t_{l-1})] \\ &= \Theta(0)\exp[\sum_{i=1}^{m} C_i T_i(t)]\end{aligned}$$

It then follows with the previous Lemma with $A_i = \lambda_i\langle k^2\rangle/\langle k\rangle$ and $B = \mu + g$ that $\Theta \leq \Theta(0)\exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Then if $\Theta(t)$ converges to 0 exponentially and $\Theta = (1/\langle k\rangle)\sum kp(k)I_k$, then for all k, I_k must be converging to 0 exponentially and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

It becomes clear that we can produce the following corollary to note that convergence to the disease-free equilibrium applies for all future time, $t \geq h$ for some $h > 0$ constant. In other words, even if the $\langle R_\sigma\rangle$ is not less than $1 - \epsilon$ currently, the system will still converge to the disease-free solution as long as $\langle R_\sigma\rangle < 1 - \epsilon$ eventually.

Corollary 4.1.1. *If $\langle R_\sigma\rangle < 1 - \epsilon$ for $t \geq h$ where $\epsilon > 0$, $h \geq 0$ are constants and $\sigma \in S$ is the switching rule, then the solution converges to the disease-free solution in the meaningful domain Ω_{SI}.*

Proof. We have $\Theta(t) \leq \Theta(0)\exp[\sum C_i T_i(t)]$ for $t \geq h$, then $\Theta(t) \leq \Theta(0)\exp(-ct)$ for some $c > 0$ and $t \geq h$. Since $\Theta = (1/\langle k\rangle)\sum kp(k)I_k$ then each I_k is converging to 0 and since $S_k = 1 - I_k$, the solution is converging to the disease-free equilibrium. □

It could be impractical or difficult to approximate R_0. Suppose that

$$R_1, ..., R_r < 1 \quad \textit{and} \quad R_{r+1}, ..., R_m \geq 1$$

and define

$$R^- = \max_{i=1,...,r} R_i \quad \textit{and} \quad R^+ = \max_{i=r+1,...,m} R_i$$

where, without loss of generality, subsystems $1, ..., r$ are stable and subsystems $r+1, ..., m$ are unstable, and $T^-(t)$ is the total activation time of the all the stable subsystems and $T^+(t)$ is the total activation time of all the unstable subsystems during the interval $(0, t]$, thus $T^-(t) + T^+(t) = t$. With these definitions, we can introduce a special case of periodic switching. Suppose $\tau_l = t_l - t_{l-1}$ is the activation time of subsystem l in one period, where the length of one period is $T = \tau_1 + ... + \tau_m$. Then, motivated by [22], we get the following result.

Corollary 4.1.2. *If $\langle R_\sigma \rangle < 1$ and the switching rule is periodic, then the disease-free solution is asymptotically stable in the meaningful domain, Ω_{SI}.*

Proof. First show that if $\langle R_\sigma \rangle < 1$ then $(R_1 - 1)\tau_1 + ...(R_m - 1)\tau_m < 0$.

$$\begin{aligned}
&\langle R_\sigma \rangle < 1 \\
\iff &\frac{1}{t}\int_0^t R_{\sigma(s)} ds < 1 \\
\iff &\frac{1}{t}\int_0^t (R_{\sigma(s)} - 1) ds < 0 \\
\iff &\int_0^t (R_{\sigma(s)} - 1) ds < 0 \\
\iff &\int_0^{T_1} (R_1 - 1) ds + ... + \int_0^{T_m} (R_m - 1) ds < 0 \\
\iff &(R_1 - 1)T_1 + ... + (R_m - 1)T_m < 0
\end{aligned}$$

Then show convergence. For $t \in (0, T]$,

$$\Theta(t) \leq \Theta(0) \exp[C_1\tau_1 + ... + C_m(t - (T - \tau_m))]$$

where $C_i = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (\mu + g)$ as before.

$$\begin{aligned}
\Theta(t) &\leq \Theta(0) \exp[C_1\tau_1 + ... + C_m\tau_m] \\
&= \Theta(0) \exp[(\mu + g)((R_1 - 1)\tau_1 + ... + (R_m - 1)\tau_m)]
\end{aligned}$$

Let $\eta = \exp[(\mu+g)((R_1-1)\tau_1+...+(R_m-1)\tau_m)]$. Since $(R_1-1)T_1+...+(R_m-1)T_m < 0$ then $\eta < 1$. Thus we have,

$$\Theta(t) \leq \eta\Theta(0) \leq \Theta(0).$$

Then consider $\Theta(hT)$, where h is an integer, $h = 1, 2, ...$ Then it can be shown similarly that

$$\Theta(hT) \leq \eta\Theta((h - 1)T)$$

for any h. Inductively,

$$\begin{aligned}
\Theta(hT) &\leq \eta\Theta((h - 1)T) \\
&\leq \eta^2\Theta((h - 2)T) \\
&\leq ... \\
&\leq n^h\Theta(0).
\end{aligned}$$

Since $\eta < 1$, then as $h \to \infty$, we have $\eta^h \to 0$. Thus as h approaches infinity, the sequence $\{\Theta(hT)\}$ converges to 0. Without loss of generality, for some $t \in (t_{l-1}, t_l]$ and with $hT < t_l \leq (h+1)T$,

$$\Theta(t) \leq \Theta(hT) \exp[C_1\tau_1 + ... + C_l(t - t_l)] \leq \Theta(hT)e^M$$

where M is a constant, $M > 0$. Then since the sequence $\{\Theta(hT)\}$ is converging to 0 as $k \to \infty$ and $h \to \infty$, then $\Theta(t)$ is converging to 0. □

We can also use the same definitions of activation times of the stable and unstable subsystems to introduce the following theorem motivated by [23].

Theorem 4.1.3. *If $T^+(t) \leq qT^-(t)$ for some constant $q \geq 0$ then $(R^- - 1) + q(R^+ - 1) < 0$ implies that the disease-free solution is exponentially stable.*

Proof. Note that $t = T^- + T^+ \leq (1+q)T^-$.

$$\begin{aligned}
\Theta(t) &\leq \Theta(0) \exp[C_{i1}t_1 + ... + C_{il}(t - t_{l-1})] \\
&= \Theta(0) \exp[(\mu+g)(R_{i1} - 1)t_1 + ... + (\mu+g)(R_{il} - 1)(t - t_{l-1})] \\
&= \Theta(0) \exp[(\mu+g)(R^- - 1)T^-(t) + (\mu+g)(R^+ - 1)T^+(t)] \\
&\leq \Theta(0) \exp[(\mu+g)((R^- - 1)T^-(t) + (R^+ - 1)qT^-(t))] \\
&\leq \Theta(0) \exp[(\mu+g)((R^- - 1) + q(R^+ - 1))T^-(t)] \\
&\leq \Theta(0) \exp[(\mu+g)((R^- - 1) + q(R^+ - 1))\frac{t}{q+1}]
\end{aligned}$$

Then we have that $\Theta \leq \Theta(0) \exp[-ct]$ with $-c = (\mu+g)((R^- - 1) + q(R^+ - 1)) < 0$ and for all $t \geq 0$. Then if $\Theta(t)$ converges to 0 exponentially then for all k, I_k must be converging to 0 exponentially and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

Note that previously we showed that the endemic equilibrium point exists for each subsystem under certain conditions, but we did not fully solve for the equilbrium point since Θ is a function of t. We now consider the evolution equation for Θ.

$$\begin{aligned}
\frac{d\Theta}{dt} &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k) \frac{dI_k}{dt} \\
&= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)(\lambda_i k\Theta - (\lambda_i + \mu + g)I_k) \\
&= \frac{1}{\langle k \rangle} (\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k) I_k - (\mu+g)\langle k \rangle)\Theta
\end{aligned}$$

Impose the stationary condition in order to solve for the value of $\Theta^*(t) = (1/\langle k \rangle) \sum kp(k)I_k^*$ when $\Theta'(t) = 0$. Clearly $\Theta^* = 0$ is a solution so we only consider the endemic solution.

$$\begin{aligned}
\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k) I_k^* - (\mu + g)\langle k \rangle &= 0 \\
\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k) \frac{\lambda_i k \Theta}{\lambda_i k \Theta + \mu + g} - (\mu + g)\langle k \rangle &= 0 \\
\sum_{k=1}^{n} (\lambda_i k^2 p(k) - (\mu + g) k p(k) - \frac{\lambda_i^2 k^3 p(k)}{\lambda_i k \Theta^* + \mu + g} \Theta^*) &= 0
\end{aligned}$$

After allowing an equal denominator for all three terms and setting the numerator to 0, we get that

$$\begin{aligned}
\Theta^* &= \frac{\lambda_i \langle k^2 \rangle - (\mu + g)\langle k \rangle}{\lambda_i \langle k^2 \rangle} \\
\Theta^* &= 1 - \frac{(\mu + g)\langle k \rangle}{\lambda_i \langle k^2 \rangle} \\
\Theta^* &= 1 - \frac{1}{R_i}
\end{aligned}$$

which yields the endemic equilibrium equations:

$$S_k^* = \frac{(\mu + g)\langle k^2 \rangle}{(\lambda_i \langle k^2 \rangle - (\mu + g)\langle k \rangle)k + (\mu + g)\langle k^2 \rangle},$$

$$I_k^* = \frac{(\lambda_i \langle k^2 \rangle - (\mu + g)\langle k \rangle)k}{(\lambda_i \langle k^2 \rangle - (\mu + g)\langle k \rangle)k + (\mu + g)\langle k^2 \rangle}$$

Conjecture 4.1.1. *If $\langle R_\sigma \rangle > 1 - \epsilon$ for all $t \geq h$ for some $h \geq 0$ and with switching rule $\sigma \in S$ then the disease of the system will be persistent.*

See simulations of when $\langle R_\sigma \rangle > 1$ and the result is the persistence of the disease which is often an oscillating solution due to the switching.

4.2 The SIS Network Model with Vertical Transmission and Switched Transmission Rate

We modify the previous model to add the concept of vertical transmision, to compare the changes with the previous SIS Network Model without switching. The system equations are,

$$\begin{cases} \dot{S}_k = \mu(S_k + pI_k) - \lambda_i k S_k \Theta - \mu S_k + gI_k \\ \dot{I}_k = \mu(1 - p)I_k + \lambda_i k S_k \Theta - gI_k - \mu I_k, \end{cases} \tag{4.3}$$

where $k = 1, 2, ..., n$.

The transmission rate, λ_i, is a piece-wise constant function where i follows the switching signal, $\sigma(t) \in S$. Again, μ is the birth/death rate and g is the recovery rate from the disease. The addition of vertical transmission intoduces the parameter p, where $0 \leq p \leq 1$, which represents the proportion of newborns with infected mothers that do not get infected. Therefore, $(1 - p)$ is the proportion of newborns with infected mothers that get the disease via vertical transmission. The physically meaningful domain is the same as in system (4.1), denoted by Ω_{SI}. Clearly since $S_k + I_k = 1$ then $\dot{S}_k + \dot{I}_k = 0$. Further, we have that $\dot{S}_k|_{S_k=0} = (\mu p + g)I_k \geq 0$ and $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0$, thus Ω_{SI} is invariant to the system (4.2).

There is a disease-free equilibrium, E_0 which is defined the same as in section 4.1, where $S_k = 1$ and $I_k = 0$ for all $k \in \{1, ..., n\}$. Also there is an endemic equilibrium unique for each i-th subsystem, where

$$S_k^* = \frac{g + \mu p}{\lambda_i k \Theta + g + \mu p}, \qquad I_k^* = \frac{\lambda_i k \Theta}{\lambda_i k \Theta + g + \mu p}$$

for $k = 1, 2, ..., n$. The endemic value of Θ for these equilibria, calculated in a similar manner as in section 4.1, is found to be

$$\Theta^* = 1 - \frac{1}{R_i}$$

where R_i, the basic reproduction number, for system (4.2) is

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{(p\mu + g)\langle k \rangle}$$

for $i \in \{1, ..., m\}$. Clearly, we have the same result where if all the subsystems' basic reproductive number meets certain criteria, then we have global asymptotic stability of the disease free equilibrium.

Theorem 4.2.1. *Assume that for all $i \in \sigma$ we have the following inequality*

$$\frac{\lambda_i \langle k^2 \rangle}{(p\mu + g)\langle k \rangle} < 1$$

then we have that the equilibrium point $E_0 = (S_{01}, I_{01}, S_{02}, I_{02}, ..., S_{0n}, I_{0n})$ where $(S_{0k}, I_{0k}) = (1, 0)$ for all $k = 1, ..., n$ is globally asymptotically stable, and thus the disease dies out.

Proof. The proof follows using the common Lyapunov function

$$V(t) = \frac{1}{2} \sum_{k=1}^{n} \omega_1(k) I_k^2 + \langle k \rangle \Theta$$

where $\omega_1(k)$ is a positive constant that depends on k and is to be determined suitably. The auxiliary function V is clearly positive definite for all $i \in \sigma$. Calculating the derivative of $V(t)$ along the disease-free solution of the system, it follows that

$$\frac{dV}{dt} = \sum_{k=1}^{n} \{-\omega_1(\lambda_i k\Theta + p\mu + g)I_k^2 + \lambda_i k(\omega_1 - kp(k))I_k\Theta\} + (\lambda_i\langle k^2\rangle - (p\mu + g)\langle k\rangle)\Theta$$

To make the second term in the summation zero, we choose $\omega_1(k) = kp(k)$. Then since we assume that $\dfrac{\lambda_i\langle k^2\rangle}{(p\mu + g)\langle k\rangle} < 1$ then $\dfrac{dV}{dt} \leq 0$ and $\dfrac{dV}{dt} = 0$ if and only if $I_k = 0$ for all k. Then the disease-free solution is globally asymptotically stable. □

Again, a less strict condition is desired here, in order to allow some subsystems to be considered unstable but overall average out by the time-weighted mean of R_i given by $\int_0^t R_{\sigma(s)}ds$.

Theorem 4.2.2. *If $\langle R_\sigma\rangle < 1 - \epsilon$ for all $t \geq 0$ and $\epsilon > 0$ with switching rule $\sigma \in S$, then the disease-free solution is exponentially stable in the meaningful domain, Q_{SI}. If $\langle R_\sigma\rangle < 1$ and the switching rule is periodic then the disease-free equilibrium is asymptotically stable in the domain Q_{SI}.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\Theta'(t) = (\frac{\lambda_{il}\langle k^2\rangle}{\langle k\rangle} - (p\mu + g))\Theta(t) = C_{i_l}\Theta(t)$$

where $C_{i_l} = \dfrac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle} - p\mu - g$. Then beginning with equation (4.2) and following the proof of Theorem 4.1.2. and Lemma 4.1.1. where $A_i = \dfrac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle}$ and $B = p\mu + g$ that the disease-free equilibrium is exponentially stable. If the switching rule is periodic then the proof follows from Corollary 4.1.2. □

4.3 The SIS Network Model with Switched Transmission, Recovery, Birth and Death Rate

The following SIS Model allows for the recovery rate and the birth and death rate as well as the transmission rate to be a piece-wise parameter that follows a switching signal. Perhaps it is not just the transmission rate that in reality exhibits seasonality, but even the birth rate and recovery rate could change due to environmental changes [46]. Consider the model,

$$\begin{cases} \dot{S}_k = \mu_i - \lambda_i k S_k\Theta + g_i I_k - \mu S_k \\ \dot{I}_k = \lambda_i k S_k\Theta - g_i I_k - \mu_i I_k \end{cases} \tag{4.4}$$

for $k = 1, 2, ..., n$ and with $i \in \{1, 2, ..., m\}$ following the switching rule $\sigma(t)$. As before, λ_i is the switched transmission rate. Moreover, μ_i is the birth rate for subsystem i and g_i is the recovery rate for subsystem i, both also switched parameters. The meaningful physical domain for this system is $\Omega_{SI} = \{(S_1, I_1, ..., S_n, I_n) \in \mathbb{R}^{2n}_+ | S_k + I_k = 1 \; \forall \; k\}$. Note that $S_k + I_k = 1$ so $\dot{S}_k + \dot{I}_k = 0$. Also, $\dot{S}_k|_{S_k=0} = \mu_i + g_i I_k > 0$, $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0$, therefore the domain Ω_{SI} is invariant to the system. For each subsystem, define the basic reproduction number as,

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{(\mu_i + g_i)\langle k \rangle}.$$

Each subsystem has its own basic reproduction number, now varying by three different parameters. Similarly, each subsystem as a unique endemic equilibrium point,

$$S_k^* = \frac{\mu_i + g_i}{\lambda_i k \Theta + \mu_i + g_i},$$
$$I_k^* = \frac{\lambda_i k \Theta}{\lambda_i k \Theta + \mu_i + g_i}$$

which exist in the meaningful domain if $R_{0i} > 1$. Also note that again, $\Theta^* = 1 - 1/R_i$ is the endemic value of Θ. Since these endemic equilibrium points vary for each subsystem, the overall switched system has only one equilibrium, the disease-free equilibrium $E_0 = (1, 0, ..., 1, 0)$, since it is common to all subsystems. Since $S_k = 1 - I_k$, we can reduce this system into n-dimensions and write the system with one differential equation for each degree class k,

$$\dot{I}_k = \lambda_i k \Theta - (\lambda_i k \Theta + g_i + \mu_i) I_k.$$

Theorem 4.3.1. *Assume that for all subsystems $i \in \sigma$ we have the following inequality*

$$\frac{\lambda_i \langle k^2 \rangle}{(\mu_i + g_i)\langle k \rangle} \leq 1$$

then we have that the equilibrium point $E_0 = (S_{01}, I_{01}, S_{02}, I_{02}, ..., S_{0n}, I_{0n})$ where $(S_{0k}, I_{0k}) = (1, 0)$ for all k is globally asymptotically stable, and thus the disease dies out.

Proof. Considering the common Lyapunov function,

$$V(t) = \frac{1}{2} \sum_{k=1}^{n} \omega(k) I_k^2 + \langle k \rangle \Theta$$

where $\omega_1(k)$ is a positive constant. The auxiliary function V is clearly positive definite for all $i \in \sigma$. Calculating the derivative of $V(t)$ along the disease-free solution of the switched system, it follows that

$$\frac{dV}{dt} = \sum_{k=1}^{n} \{-\omega_1(\lambda_i k \Theta + \mu_i + g_i) I_k^2 + \lambda_i k (\omega_i - k p(k)) I_k \Theta\} + (\lambda_i \langle k^2 \rangle - (\mu_i + g_i)\langle k \rangle)\Theta.$$

To make the second term in the sum zero, we choose $\omega_1(k) = kp(k)$. Then since we assume that $\frac{\lambda_i\langle k^2\rangle}{(\mu_i+g_i)\langle k\rangle} < 1$ then $\frac{dV}{dt} \leq 0$ and $\frac{dV}{dt} = 0$ if and only if $I_k = 0$ for all values of k. Then the disease-free solution is globally asymptotically stable. □

This condition, however, is very strict and thus a more broad condition is desirable.

Theorem 4.3.2. *If* $\sum_{i=1}^{m}(A_i - B_i)T_i(t) < -ct$ *where* $A_i = \frac{\lambda_i\langle k^2\rangle}{\langle k\rangle}$ *and* $B_i = \mu_i + g_i$ *and* $c > 0$ *is a constant and for all* $t \geq 0$ *and if* $\langle R_\sigma\rangle < 1 - \epsilon$ *for all* $t \geq 0$ *and* $\epsilon > 0$ *with switching rule* $\sigma \in S$*, then the disease-free solution is exponentially stable in the meaningful domain,* Ω_{SI}*.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$ we have that

$$\begin{aligned}\Theta'(t) &= \frac{1}{\langle k\rangle}\sum kp(k)(\lambda_{i_l}k\Theta - (\lambda_{i_l}k\Theta I_k + \mu_i + g_i)I_k)\\ &\leq (\frac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle} - (\mu_i + g_i))\Theta\\ &= C_{i_l}\Theta\end{aligned}$$

where $C_{i_l} = A_i - B_i$ and $A_i = \frac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle}$ and $B_i = (\mu_i + g_i)$. Then it follows from Theorem 4.1.2. starting with equation (4.2) that $\Theta(t) \leq \Theta(0)\exp[\sum_{i=1}^{m}(A_i - B_i)T_i(t)]$. From the assumption, we get that $\Theta \leq \Theta(0)\exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Then Θ converges to 0 exponentially as for all k, I_k is converging to 0 exponentially and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

4.4 Numerical Simulations

In MATLAB, the built-in ode solver ode45 was used to analyze the switched network models from this chapter on a scale-free network that follows a power law degree distribution, $p(k) \sim k^{-\alpha}$ where $\alpha = 2.1$. Also, we assume that $n = 50$ so the maximum number of links any single node in the network has is 50. For the parameter values, $\mu = 0.2$ and $g = 1$. Then for simplicity, there are two subsystems $i = \{1, 2\}$ and λ_1 and λ_2 varied to change the value of R_0.

In such a network that follows the aforementioned power law distribution, we have that the average degree is $\langle k\rangle = 2.4733$, also signifying the mean number of contacts an individual in the network is linked to that which the infectious disease may be transmitted. Further, another notable value is $\langle k^2\rangle = 24.0974$. In such a case, we get that $R_i < 1$ if and only if $\lambda_i < 0.123 = \lambda^*$. We assume a simple switching rule between 2 subsystems where switching occurs after every 5 time steps. Also, the simulation is run for 100 time steps or more to get

a picture of the stability of the system. The initial values were set by setting $I_{n-1} = 1$, thus providing the population with a superspreader (an infectious individual with 49 contacts).

Since $S_k + I_k = 1$, the SIS model can be reduced to one dimension and only the Infected, I_k, is drawn on the curves of the graphs. In this particular system, we have:

$$\frac{dI_k(t)}{dt} = \lambda_i k(1 - I_k(t))\Theta(t) - \mu I_k(t) - gI_k(t)$$

where $\Theta(t) = \dfrac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)I_k(t)$ and $\langle k \rangle = \sum_{k=1}^{n} kp(k)$. Three varying degrees, 1, 5, and 20 are displayed on the graphs for comparative purposes in blue, green and red continuous curves respectively. Note that the higher the degree, the more the disease spreads and the longer it remains.

From Figure 4.1, if both the reproductive numbers are greater than 1, then the disease-free equilibrium is unstable, as we see that the disease persists in a periodic solution. This periodic motion is attributed to the switching effect between two subsystems. In Figure 4.3, we test to see what happens when one subsystem's reproductive number is greater than 1, while the overall average between the two R_i values maintains greater than 1. As one might predict, the disease also persists and has a periodic solution.

A similar observation is made in Figures 4.2 and 7.4. In Figure 4.2, both reproductive threshold values are below 1, and thus while the disease spreads initially, as $t \to \infty$ the disease dies out. In Figure 4.4, the disease-free equilibrium is also asymptotically approached in this case where the average R_0 is less than 1. However, we do have one subsystem's reproductive threshold value above 1, and thus we see an initial spread of the infectious disease, as well as a continual 'spike' that decreases in amplitude as time goes on and as the disease eventually gets eradicated.

Figure 4.1: **Network SIS Switched Model** with $\lambda_1 = 0.13$ and $\lambda_2 = 0.15$ so both $\lambda_1, \lambda_2 > \lambda^*$ and $R_1 = 1.055, R_2 = 1.218 > 1$: On average, $\langle R_\sigma \rangle = 1.137$ and the disease persists, as Theorem 4.1.1. would suggest.

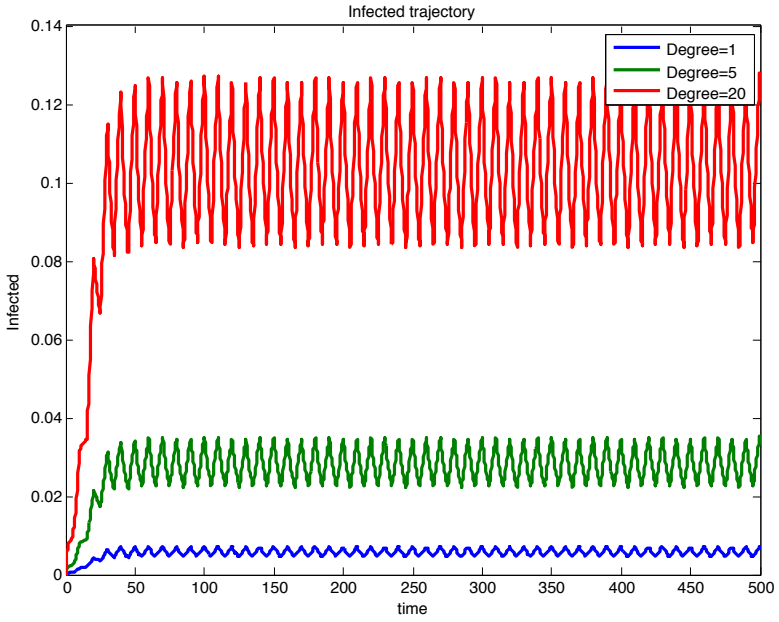


Figure 4.2: **Network SIS Switched Model** $\lambda_1 = 0.1$ and $\lambda_2 = 0.015$, so both $\lambda_1, \lambda_2 < \lambda^*$ and $R_1 = 0.839, R_2 = 0.126 < 1$: On average, $\langle R_\sigma \rangle = 0.483$ and the disease dies out in conjunction with Theorem 4.1.1.

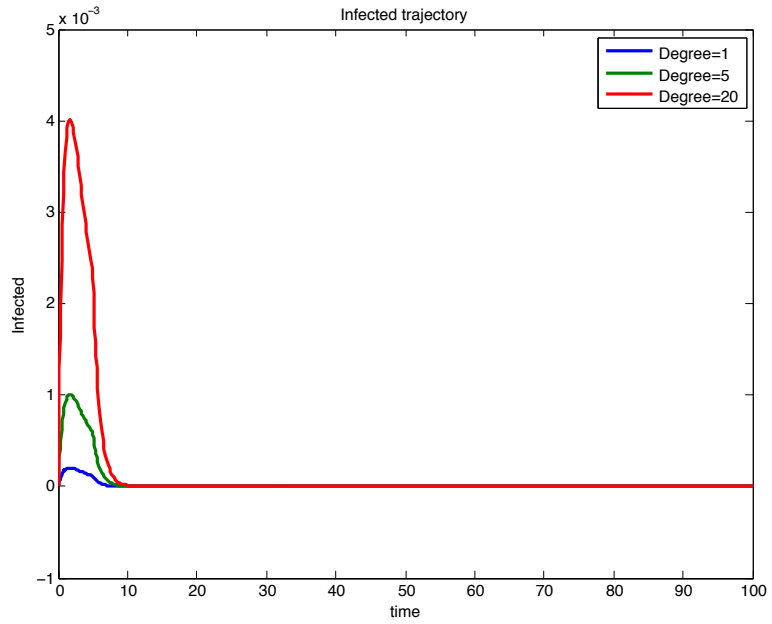


Figure 4.3: **Network SIS Switched Model** with $\lambda_1 = 0.3$ and $\lambda_2 = 0.015$ resulting in an average $\bar{\lambda} > \lambda^*$, $R_1 = 2.518$ and $R_2 = 0.126$ thus on average $\langle R_\sigma \rangle = 1.322 > 1$ and the disease persists as expected from Theorem 4.1.2.

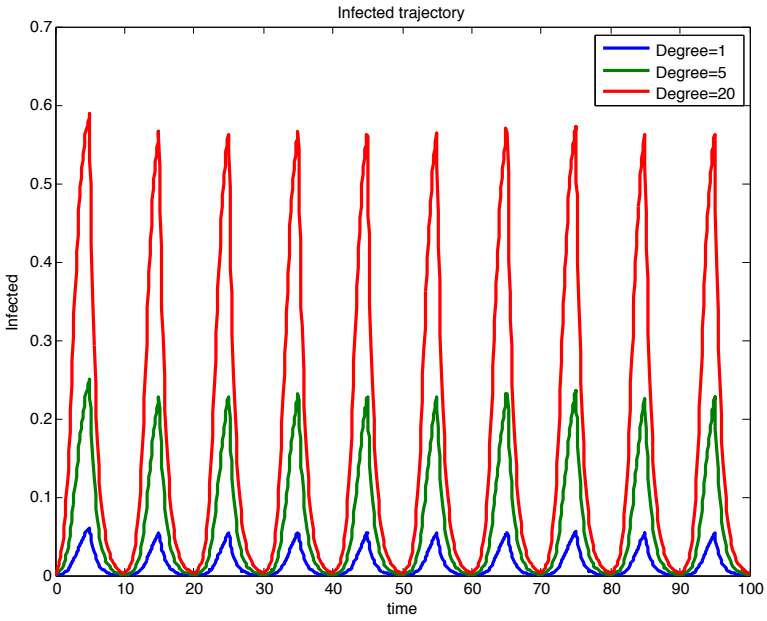


Figure 4.4: **Network SIS Switched Model** with $\lambda_1 = 0.13$ and $\lambda_2 = 0.09$, $R_{01} = 1.091$ and $R_{02} = 0.755$ resulting in an average $\bar{\lambda} < \lambda^*$, thus on average $R_0 = 0.923 < 1$ and the disease dies out in this simulation as expected from Theorem 4.1.2.

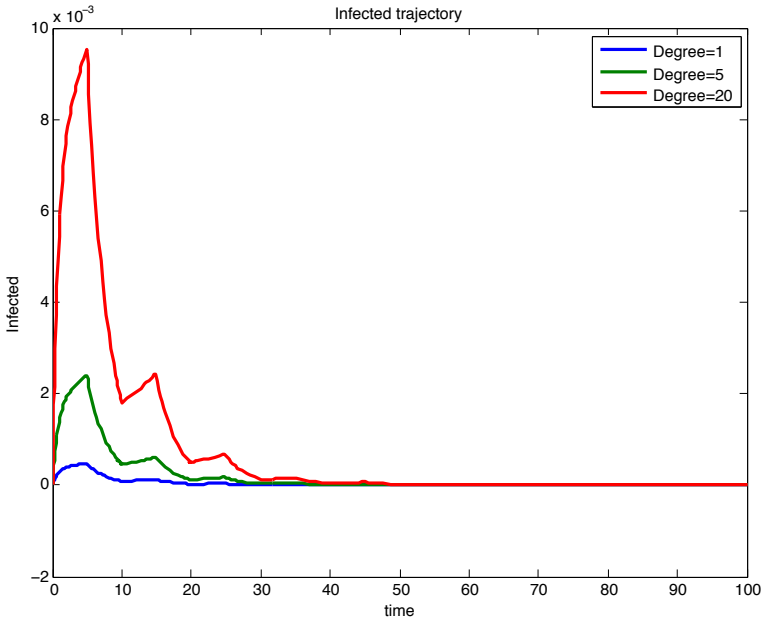


Figure 4.5: **Network SIS Switched Model** with $\lambda_1 = 0.22$ and $\lambda_2 = 0.015$, also resulting in an average $\bar{\lambda} < \lambda^*$, $R_1 = 1.846$ and $R_2 = 0.126$ thus on average $\langle R_\sigma \rangle = 0.986 < 1$ and the disease dies out in this simulation as expected from Theorem 4.1.2., but persists longer due to the greater difference between the two transmission rates.

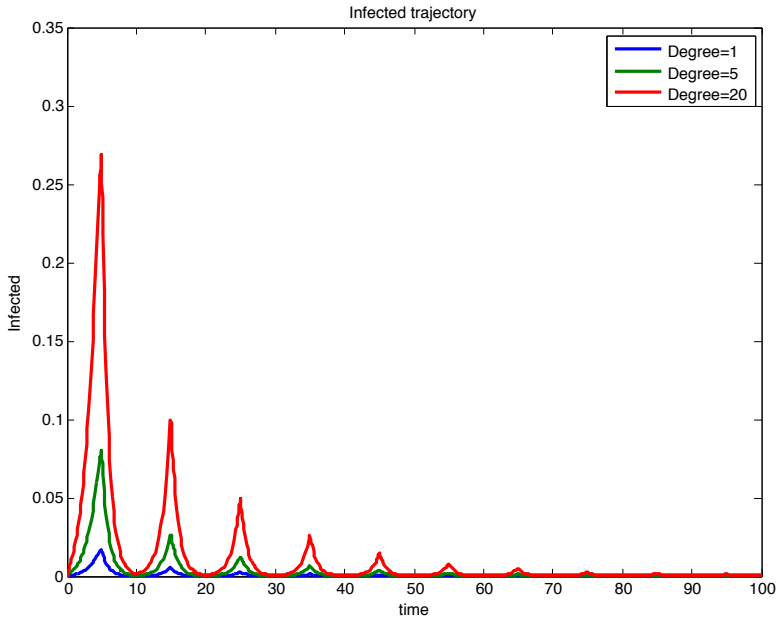


Figure 4.6: **Network SIS Switched Model** with $\lambda_1 = 0.15$ and $\lambda_2 = 0.11$, which give $R_{01} = 1.218$ and $R_{02} = 0.893$. This time different time intervals were chosen for each subsystem and the weighted average $\langle R_\sigma \rangle = 0.974 < 1$ and the disease dies out, in conjunction with Theorem 4.1.2.

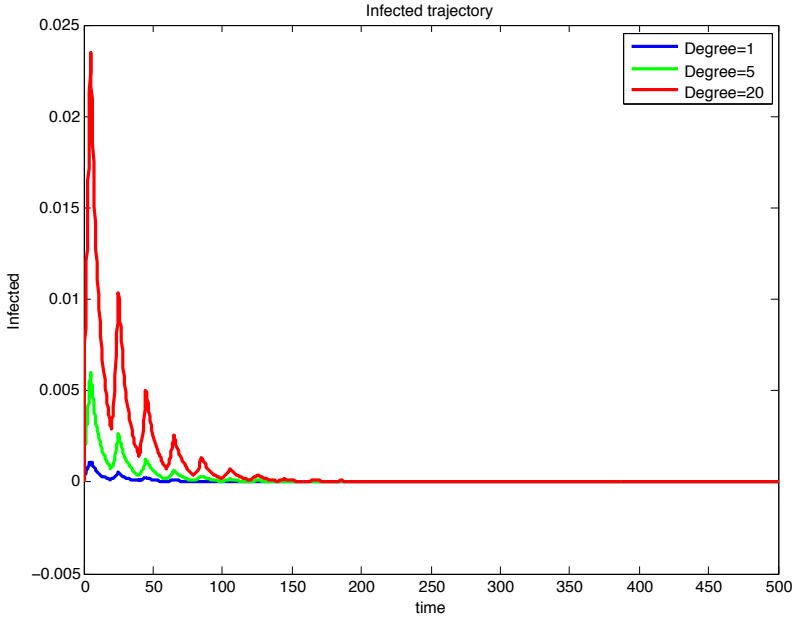


Figure 4.7: **Network SIS Switched Model** with $\lambda_1 = 0.11$ and $\lambda_2 = 0.13$, which give $R_1 = 0.893$ and $R_2 = 1.055$. This time different time intervals were chosen for each subsystem and the weighted average $\langle R_\sigma \rangle = 1.015$ and the disease dies out in conjunction with Theorem 4.1.2.

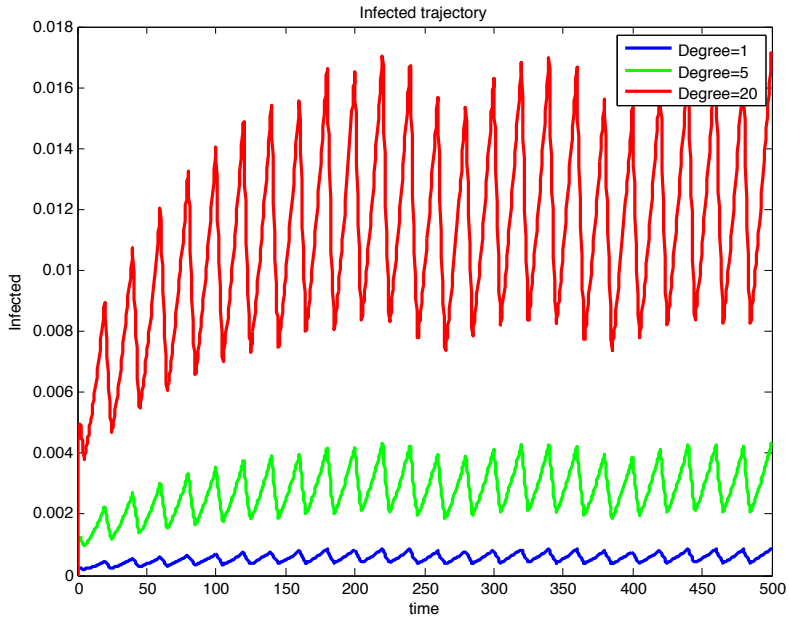


Figure 4.8: **Network SIS Switched Model with Vertical Transmission** where $\lambda_1 = 0.22$ and $\lambda_2 = 0.015$, and $p = 0.4$ which give $R_1 = 2.051$ and $R_2 = 0.140$. On average $\langle R_\sigma \rangle = 1.096$ and the disease persists in conjunction with Theorem 4.2.2. Note that the addition of vertical transmission results in the persistence of the disease.

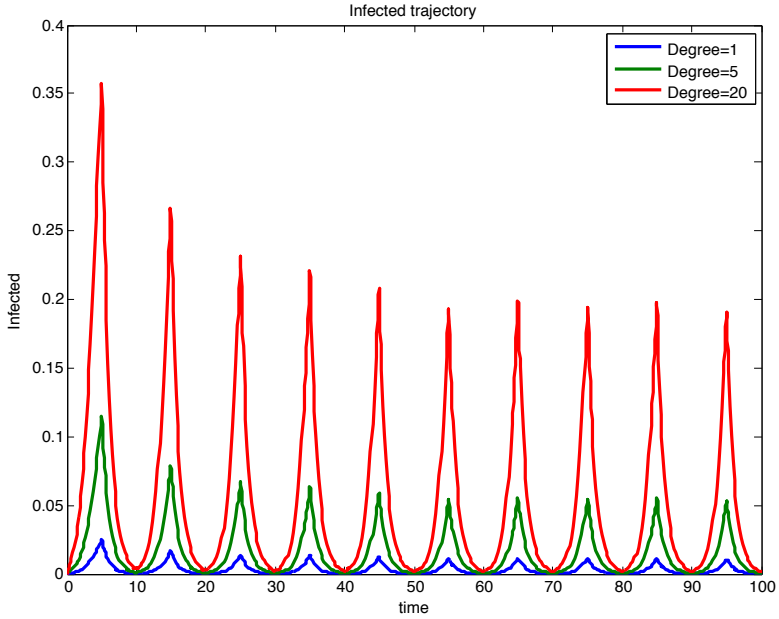
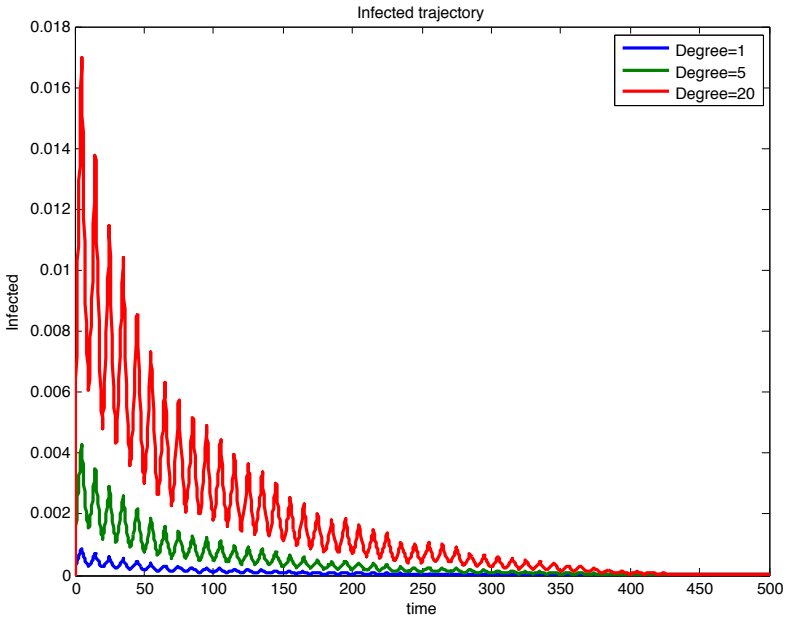


Figure 4.9: **Network SIS Switched Model with Vertical Transmission** where $\lambda_1 = 0.13$ and $\lambda_2 = 0.09$, and $p = 0.4$ which give $R_1 = 0.812$ and $R_2 = 1.173$. On average $\langle R_\sigma \rangle = 0.9925$ and the disease dies out in conjunction with Theorem 4.2.2. but persists longer than without vertical transmission.



Chapter 5

Network SIR, SIRS, SEIR and Multi-City Models with Switching

We have established that the mixing network assumption is far more realistic than the uniform mixing assumption, and that it is necessary to investigate switched systems that account for changes in environment and other external factors. The alternative approach to the previous network models is to approximate the transmission rate as a piecewise constant, which is applied to models with 3 or more disease status compartments in this chapter.

In Section 5.1, we apply the time-varying transmission rate to the SIR Network Model. The switched SIR network model without population dynamics is studied in Section 5.2, and then the switched SIR network model with vertical transmission is studied in Section 5.3. In Section 5.4, the addition of waning immunity extends the switched network model into an SIRS model. In Section 5.5, we study an SEIR model to account for the incubation period. Finally, Section 5.6 studies the addition of switching to multi-city network models. At the end of the chapter, numerical simulation results are given.

5.1 The SIR Network Model with Switched Transmission Rate

In some cases, it is necessary to include the recovered compartment, R, in order to portray partial or life-long immunity. We add a switched transmission rate to the SIR model with the network mixing assumption,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k \\ \dot{R}_k = g I_k - \mu R_k, \qquad\qquad k = 1, 2, ..., n. \end{cases} \tag{5.1}$$

The physically meaningful domain is $\Omega_{SIR} = \{(S_1, I_1, R_1, ..., S_n, I_n, R_n) \in \mathbb{R}^{3n}_+ | S_k + I_k + R_k = 1 \, \forall k = 1, 2, ..., n\}$. We have $\dot{S}_k + \dot{I}_k + \dot{R}_k = 0$ since $S_k + I_k + R_k = 1$. Also,

$$\dot{S}_k|_{S_k=0} = \mu > 0, \qquad \dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0, \qquad \dot{R}_k|_{R_k=0} = gI_k \geq 0$$

therefore Ω_{SIR} is invariant to the system.

Due to the third compartment, the system is $3n$-dimensional, although with the fact that $S_k + I_k + R_k = 1$, the system can intrinsically be reduced to $2n$-dimensions. Clearly there is a disease-free equilibrium E_0 for all $i \in \sigma$ where $S_k = 1$, $I_k = 0$, and $R_k = 0$, and an endemic disease free equilibrium E^* where,

$$\begin{aligned} S_k^* &= \frac{\mu(g+\mu)}{(\lambda_i k\Theta + \mu)(g+\mu)}, \\ I_k^* &= \frac{\lambda_i k\Theta\mu}{(\lambda_i k\Theta + \mu)(g+\mu)}, \\ R_k^* &= \frac{\lambda_i k\Theta g}{(\lambda_i k\Theta + \mu)(g+\mu)} \end{aligned}$$

which is unique for the i-th subsystem. Recall from the non-switched case, the basic reproductive number for the i-th subsystem is,

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{(\mu+g)\langle k \rangle}.$$

Then we can also solve the evolution equation for $\Theta(t)$, impose stationary conditions by setting $\dfrac{d\Theta}{dt} = 0$ and $I_k = I_k^*$ and $S_k = S_k^*$ to solve for the stationary Theta equation, Θ^* at the endemic equilibrium,

$$\begin{aligned} \frac{d\Theta}{dt} &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} k p(k) \frac{dI_k}{dt} \\ &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} k p(k) (\lambda_i k (1 - I_k - R_k)\Theta - (g+\mu) I_k) \\ &= \frac{1}{\langle k \rangle} (\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k)(I_k + R_k) + (\mu+g)\langle k \rangle)\Theta \end{aligned}$$

$$\begin{aligned} \frac{1}{\langle k \rangle} (\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k)(I_k^* + R_k^*) + (\mu+g)\langle k \rangle)\Theta = 0 \\ \frac{1}{\langle k \rangle} (\lambda_i \langle k^2 \rangle - \lambda_i \sum k^2 p(k) \frac{\lambda_i k\Theta}{\lambda_i k\Theta + \mu} + (\mu+g)\langle k \rangle)\Theta = 0 \\ \sum (\lambda_i k^2 p(k) - (g+\mu) k p(k) - \frac{k^3 p(k) \lambda_i^2 \Theta}{\lambda_i k\Theta + \mu}) = 0 \end{aligned}$$

After allowing an equal denominator for all terms and setting the numerator to 0, we get that

$$\begin{aligned}\Theta^* &= \frac{\mu(\lambda_i\langle k^2\rangle - (g+\mu)\langle k\rangle)}{\lambda_i\langle k^2\rangle(g+\mu)} \\ &= \frac{\mu}{g+\mu}(1-\frac{1}{R_i}).\end{aligned}$$

Since $R_k = 1 - S_k - I_k$, we can reduce this system into $2n$-dimensions.

Theorem 5.1.1. *Assume that for all subsystems $i \in \sigma$ we have the following inequality*

$$\frac{\lambda_i\langle k^2\rangle}{(g+\mu)\langle k\rangle} < 1$$

then we have that the disease-free equilibrium point is globally asymptotically stable, and thus the disease dies out.

Proof. Consider the following common Lyapunov function,

$$V(t) = \frac{1}{2}\sum_{k=1}^{n}\{\omega_1(k)(S_k-1)^2\} + \langle k\rangle\Theta$$

where $\omega_1(k)$ is positive constants that depend on k and are to be determined suitably. The auxiliary function V is clearly positive definite for all $i \in \sigma$. Calculating the derivative of $V(t)$ along the disease-free solution of the switched system, it follows that

$$V'(t) = \sum_{k=1}^{n}\{-\omega_1(\lambda_i k\Theta+\mu)(S_k-1)^2 + \lambda_i k(kp(k)-\omega_1)S_k\Theta\} + (\sum_{k=1}^{n}\lambda_i\omega_1 k - \langle k\rangle(g+\mu))\Theta$$

To make the second term zero, we choose $\omega_1(k) = kp(k)$. Then the coefficient for Θ in the third term becomes $(\lambda_i\langle k^2\rangle - \langle k\rangle(g+\mu))$ and due to the inequality assumed for all i we get that $V'(t) \leq 0$ and $V'(t) = 0$ if and only if $S_k = 1$, $I_k = 0$ for all values of k. Then the disease-free solution is globally asymptotically stable. □

Theorem 5.1.2. *Assume $\langle R_\sigma\rangle < 1-\epsilon$ for all $t > 0$ and $\epsilon > 0$ with switching rule $\sigma \in S$, then the disease-free solution is exponentially stable in the meaningful domain, Q_{SI}.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned}\Theta'(t) &= \frac{1}{\langle k\rangle}\lambda_i\langle k^2\rangle\Theta - \frac{1}{\langle k\rangle}\sum k^2p(k)(I_k+R_k)\Theta - (g+\mu)\Theta \\ &\leq [\frac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (g+\mu)]\Theta \\ &= C_{i_l}\Theta\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g+\mu)$. Then starting with equation (4.2) using the proof of Theorem 4.1.2. and Lemma 4.1.2. where $A_i = \dfrac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle}$ and $B = g+\mu$ that $\Theta \leq \Theta(0)\exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Then if $\Theta(t)$ converges to 0 exponentially and $\Theta = \dfrac{1}{\langle k \rangle} \sum kp(k)I_k$ then for all k, I_k must be converging to 0 exponentially and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

Based on the simulations, we can make a conjecture about the endemic equilibrium.

Conjecture 5.1.1. *Assume $\langle R_\sigma \rangle > 1$ for all $t \geq 0$ and switching signal $\sigma \in S$, then the disease persists and there will be an epidemic.*

5.2 The SIR Network Model with Switched Transmission Rate without Population Dynamics

Introduce switching into the SIR model without population dynamics. It is assumed that the time scale of the disease is short and thus any change in the population size can be ignored (the birth and death rate is removed from the previous model). Assume the transmission rate switches between m subsystems, $\lambda_1, ..., \lambda_m > 0$:

$$\begin{cases} \dot{S}_k = -\lambda_i k S_k \Theta \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k \\ \dot{R}_k = g I_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{5.2}$$

with $i \in \{1, 2, ..., m\}$ following the switching rule $\sigma(t)$. The physically meaningful domain is Ω_{SIR}. This domain is invariant to the system because $\dot{S}_k + \dot{I}_k + \dot{R}_k = 0$ and $\dot{S}_k|_{S_k=0} = 0$, $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0$ and $\dot{R}_k|_{R_k=0} = g I_k \geq 0$. All subsystems have a basic reproduction number depending on the piece-wise constant λ_i,

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{g \langle k \rangle}$$

By setting each of the differential equations in the system to 0, it is clear that for all $k \in \{1, 2, ..., n\}$, $I_k^* = 0$. $S_k^* + R_k^* = 1$, with $S_k^*, R_k^* \geq 0 \in \mathbb{R}$. There are an infinite number of disease-free equilibrium points however there is no endemic equilibrium point. Therefore, we consider two questions:

1. Will the disease die out?
2. Will an epidemic occur?

From the system equations, it is clear that $S_k(t) \leq S_k(0)$ for all time $t \geq 0$. Thus, $\Theta'(t) = \frac{1}{\langle k \rangle} \sum kp(k)(\lambda_i k S_k(t)\Theta(t) - gI_k(t)) \leq [\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} S_k(0) - g]\Theta$. If $\frac{\lambda_i \langle k^2 \rangle}{g\langle k \rangle} < \frac{1}{\max\limits_{k \in \{1,...,n\}} S_k(0)}$ for all i, then $\Theta'(t) < 0$ hence $\Theta \leq \Theta(0)$ for $t \geq 0$. Therefore, the disease dies out.

Theorem 5.2.1. *If* $\langle R_\sigma \rangle < \frac{1}{\max\limits_{k \in \{1,...,n\}} S_k(0)} - \epsilon$ *for all* $t \geq 0$ *and* $\epsilon > 0$ *and switching rule* $\sigma \in S$*, then the disease will be eradicated and there will be no epidemic.*

Proof. Let i_l follow the switching rule $\sigma \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$, we have that:

$$\Theta' \leq (\frac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle} - g)\Theta$$

Then, using that $\Theta' \leq C_{i_l}\Theta$ with $C_{i_l} = \frac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle} - g$ then we can use Theorem 4.1.2. starting with equation (4.2) and Lemma 4.1.1. with $A_i = \frac{\lambda_{i_l} \langle k^2 \rangle}{\langle k \rangle}$ and $B = g$ to show that $\Theta'(t) \leq \Theta(0)\exp[-ct]$. This concludes that $\Theta(t) \leq \Theta(0)$ and there will not be an epidemic. Further, this also shows that $\lim_{t \to \infty} \Theta(t) = 0$ which shows the disease will be eradicated. □

5.3 The SIR Network Model with Switched Transmission Rate and Vertical Transmission

Now introduce switching into an SIR network model with vertical transmission as well as horizontal transmission. In this scenario, not only does the infection spread through contact, but the infection may also be passed down from mother to child. If we let p be the proportion of newborns with infected mothers that do not catch the disease, then the model is as follows:

$$\begin{cases} \dot{S_k} = \mu(S_k + R_k + pI_k) - \lambda_i k S_k \Theta - \mu S_k \\ \dot{I_k} = \mu(1-p)I_k + \lambda_i k S_k \Theta - gI_k - \mu I_k \\ \dot{R_k} = gI_k - \mu R_k \end{cases} \tag{5.3}$$

with $k = 1, 2, ..., n$.

The physically meaningful domain is $\Omega_{SIR} = \{(S_1, I_1, R_1, ..., S_n, I_n, R_n) \in \mathbb{R}^{3n}_+ | S_k + I_k + R_k = 1 \, \forall k\}$. Clearly $\dot{S_k} + \dot{I_k} + \dot{R_k} = 0$, and

$$\dot{S_k}|_{S_k=0} = \mu(R_k + pI_k) \geq 0, \qquad \dot{I_k}|_{I_k=0} = \lambda_i k S_k \Theta \geq 0, \qquad \dot{R_k}|_{R_k=0} = gI_k \geq 0$$

therefore, the domain is invariant to the system. There are 2 equilibrium values, clearly the disease-free equilibrium E_0 where $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k. The endemic equilibrium

is $E^* = (S_1^*, I_1^*, R_1^*, ..., S_n^*, I_n^*, R_n^*)$ where

$$S_k^* = \frac{\mu(g+\mu p)}{\lambda_i k\Theta(\mu+g)+\mu(g+\mu p)}$$
$$I_k^* = \frac{\lambda_i k\Theta\mu}{\lambda_i k\Theta(\mu+g)+\mu(g+\mu p)}$$
$$R_k^* = \frac{\lambda_i k\Theta g}{\lambda_i k\Theta(\mu+g)+\mu(g+\mu p)}$$

for each i-th subsystem. Moreover, we can use the substitution of $I_k = I_k^*$ into the equation for Θ to solving similarly as previously for the basic reproduction number, which gives:

$$R_i = \frac{\lambda_i\langle k^2\rangle}{(g+\mu p)\langle k\rangle}$$

for each i-th subsystem. Notice how the basic reproduction number is the same as before, the addition of vertical transmission does not change the rate of spread of the disease.

We can solve the evolution equation for $\Theta(t)$ by imposing stationary conditions $I_k = I_k^*$, $S_k = S_k^*$, $R_k = R_k^*$ and setting $d\Theta/dt = 0$ and we get the endemic value of Θ:

$$\begin{aligned}\Theta^* &= \frac{\mu(\lambda_i\langle k^2\rangle - (g+\mu p)\langle k\rangle)}{\lambda_i\langle k^2\rangle(g+\mu)}\\ &= \frac{\mu}{g+\mu}(1-\frac{1}{R_i})\end{aligned}$$

Theorem 5.3.1. *Assume that for all subsystems $i \in \sigma$ we have the following inequality:*

$$\frac{\lambda_i\langle k^2\rangle}{(g+\mu p)\langle k\rangle} < 1$$

then the disease-free equilibrium is globally asymptotically stable and the disease dies out.

Proof. Consider the following common Lyapunov function

$$V(t) = \frac{1}{2}\sum_{k=1}^{n}\omega_1(k)(S_k-1)^2 + \langle k\rangle\Theta$$

where $\omega_1(k)$ is a positive constant that depends on k and is to be determined suitably. The auxiliary function V is positive definite for all $i \in \sigma$. Calculating the deriviative of $V(t)$ along the disease-free solution of the switched system, it follows that

$$\begin{aligned}V'(t) =& \sum_{k=1}^{n}\{-\omega_1(\lambda_i k\Theta+\mu)(S_k-1)^2 + \omega_1\mu(1-p)(S_k-1)I_k + \lambda_i k(kp(k)-\omega_1)S_k\Theta\}\\ &+\sum_{k=1}^{n}(\omega_1\lambda_i k - kp(k)(g+\mu p))\Theta.\end{aligned}$$

The first and second term will be less than or equal to zero, where $S_k = 1$ or $p = 1$ gives equality. Then, to make the third term zero, we select $\omega_1(k) = kp(k)$. This causes the last term to become $(\lambda_i\langle k^2\rangle - \langle k\rangle(g + \mu p))\Theta$ and by the inequality in the assumption of this theorem, this term is negative as well. Then for all i we get that $V'(t) \leq 0$ and $V'(t) = 0$ if and only if $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k. Therefore the disease-free equilibrium is globally asymptotically stable, and the disease dies out. □

However, once again a less strict condition is desired for the eradication of the disease.

Theorem 5.3.2. *Assume $\langle R_\sigma\rangle < 1 - \epsilon$ for all $t > 0$ and $\epsilon > 0$ with switching rule $\sigma \in S$, then the disease-free equilibrium is exponentially stable in the meaningful domain, Ω_{SIR}.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned}\Theta'(t) &= \frac{1}{\langle k\rangle}\sum_{k=1}^{n}\{\lambda_i k^2 p(k)\Theta(1 - I_k - R_k) - (g + \mu p)kp(k)I_k\}\\ &\leq (\frac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (g + \mu p))\Theta\\ &= C_{i_l}\Theta\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (g + \mu p)$. Then the proof follows using the proof of Theorem 4.1.2. starting at equation (4.2) and Lemma 4.1.1. where $A_i = \dfrac{\lambda_i\langle k^2\rangle}{\langle k\rangle}$ and $B = g + \mu p$ that $\Theta(t) \leq \Theta(0)\exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Then if $\Theta(t)$ converges to 0 exponentially then I_k must be converging to 0 exponentially for all k and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

Conjecture 5.3.1. *If the dwell-time average of the basic reproduction ratio is greater than 1, $\langle R_\sigma\rangle > 1$, then the disease persists and there will be an epidemic.*

5.4 The SIRS Network Model with Switched Transmission Rate

We now introduce switching into the SIRS Network Model, which allows for the loss of immunity to the disease at a rate $\delta > 0$. Infected individuals who recover gain partial immunity, but then become susceptible to the disease once again. The system equations for the model are as follows,

$$\begin{cases}\dot{S}_k = \mu - \lambda_i k S_k\Theta + \delta R_k - \mu S_k\\ \dot{I}_k = \lambda_i k S_k\Theta - gI_k - \mu I_k\\ \dot{R}_k = gI_k - \delta R_k - \mu R_k, \qquad k = 1, 2, ..., n.\end{cases} \tag{5.4}$$

The physically meaningful domain is Ω_{SIR}. There are 2 equilibrium values, clearly the disease-free equilibrium E_0 where $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k. The endemic equilibrium is $E^* = (S_1^*, I_1^*, R_1^*, ..., S_n^*, I_n^*, R_n^*)$ where

$$\begin{aligned} S_k^* &= \frac{(g+\mu)(\delta+\mu)}{(\delta+g+\mu)\lambda_i k\Theta + (g+\mu)(\delta+\mu)}, \\ I_k^* &= \frac{(\delta+\mu)\lambda_i k\Theta}{(\delta+g+\mu)\lambda_i k\Theta + (g+\mu)(\delta+\mu)}, \\ R_k^* &= \frac{g\lambda_i k\Theta}{(\delta+g+\mu)\lambda_i k\Theta + (g+\mu)(\delta+\mu)} \end{aligned}$$

for each i-th subsystem. Further, the basic reproduction number for the i-th subsystem is the same as in the SIS and SIR case,

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle (g+\mu)}$$

as the rate of spread of the disease remains the same, regardless of partial immunity to the infection. Solving the evolution equation for $\Theta(t)$ by imposing stationary conditions and setting $d\Theta/dt = 0$ we get the endemic value of Θ:

$$\begin{aligned} \Theta^* &= \frac{(\delta+\mu)(\lambda_i\langle k^2\rangle - (g+\mu)\langle k\rangle)}{(\delta+g+\mu)\lambda_i\langle k^2\rangle} \\ &= \frac{\delta+\mu}{\delta+g+\mu}(1 - \frac{1}{R_i}). \end{aligned}$$

Theorem 5.4.1. *Assume $\langle R_\sigma \rangle < 1 - \epsilon$ for all $t > 0$ and $\epsilon > 0$ with switching rule $\sigma \in S$, then the disease-free equilibrium is exponentially stable in the meaningful domain, Ω_{SIR}.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned} \Theta'(t) &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} \{\lambda_i k^2 p(k) \Theta(1 - I_k - R_k) - (g+\mu) k p(k) I_k\} \\ &\leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g+\mu))\Theta \\ &= C_{i_l}\Theta \end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g+\mu)$. Then it follows using the proof of Theorem 4.1.2. and Lemma 4.1.1. where $A_i = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle}$ and $B = g + \mu p$ that $\Theta(t) \leq \Theta(0)\exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Then if $\Theta(t)$ converges to 0 exponentially then I_k must be converging to 0 exponentially for all k and the disease-free equilibrium is exponentially stable in the physically meaningful domain. □

5.5 The SEIR Network Model with Switched Transmission Rate

In many infectious diseases, it is more realistic to account for the incubation period, which is the time it takes from first being exposed to the disease to start showing symptoms and becoming infectious. In this case, another disease class called Exposed (E_k) will represent individuals with degree k who have contracted the disease but not yet contagious. The parameter, $a > 0$, represents the rate at which exposed individuals become infectious. Then $1/a$ represents the average incubating period. The system equations are as follows

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k \\ \dot{E}_k = \lambda_i k S_k \Theta - a E_k - \mu E_k \\ \dot{I}_k = a E_k - g I_k - \mu I_k \\ \dot{R}_k = g I_k - \mu R_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{5.5}$$

with μ being the birth/death rate and g is the recovery rate as usual. Also, $\Theta(t) = (1/\langle k \rangle) \sum_{k=1}^{n} kp(k)I_k$ as usual since even though the exposed class have been exposed to the disease, only the infectious class can transmit the disease. The physically meaningful domain is $\Omega_{SEIR} = \{(S_1, E_1, I_1, R_1, ..., S_n, E_n, I_n, R_n) \in \mathbb{R}_+^{4n} | S_k + E_k + I_k + R_k = 1 \, \forall k\}$. We have $\dot{S}_k + \dot{E}_k + \dot{I}_k + \dot{R}_k = 0$ and,

$$\dot{S}_k|_{S_k=0} = \mu > 0, \quad \dot{E}_k|_{E_k=0} = \lambda_i k S_k \Theta \geq 0, \quad \dot{I}_k|_{I_k=0} = a E_k \geq 0, \quad \dot{R}_k|_{R_k=0} g I_k \geq 0$$

so the physically meaningful domain is positively invariant to the system. There are two equilibrium values; the disease-free equilibrium E_0 is common to all subsystems where $S_k = 1$, $E_k = 0$, $I_k = 0$, $R_k = 0$ for all k. The endemic equilibrium E^* for the i-th subsystem is:

$$\begin{aligned} S_k^* &= \frac{\lambda_i k \Theta \mu}{\lambda_i k \Theta + \mu}, \\ E_k^* &= \frac{\lambda_i k \Theta \mu}{(\lambda_i k \Theta + \mu)(a + \mu)}, \\ I_k^* &= \frac{\lambda_i k \Theta a \mu}{(\lambda_i k \Theta + \mu)(a + \mu)(g + \mu)}, \\ R_k^* &= \frac{\lambda_i k \Theta g}{(\lambda_i k \Theta + \mu)(a + \mu)(g + \mu)} \end{aligned}$$

Further, the basic reproduction number for the i-th subsystem is:

$$R_i = \frac{\lambda_i a \langle k^2 \rangle}{(a + \mu)(g + \mu)\langle k \rangle}$$

Solving the for endemic stationary value of Theta:

$$\Theta^* = \frac{a\mu}{(a+\mu)(g+\mu)}(1 - \frac{1}{R_i})$$

Note that here, the same argument to prove stability for when $\langle R_\sigma \rangle < 1 - \epsilon$ for some $\epsilon > 0$ cannot be used, since $I_k' = aE_k - gI_k - \mu I_k$ and thus it is not easily shown that $\Theta' \leq C(R_i - 1)\Theta$ where C is some positive constant. Note that if positive sums of E_k and I_k are grouped, convergence is also not easily shown. However, we can prove that if for all subsystems $i \in \{1, ..., m\}$, $R_i < 1$, and the solution of the system converges to the disease-free equilibrium.

Theorem 5.5.1. *If $R_1, ..., R_m < 1$ then the solution of system (5.5) converges to the disease-free equilibrium E_0, which is globally asymptotically stable in the meaningful domain, Ω_{SEIR} under arbitrary switching.*

Proof. Consider the Lyapunov function $V(t) = \sum_{k=1}^{n} \{akp(k)\ E_k + (a+\mu)k\ p(k)\ \Theta\}$. We have that $V = 0$ when $E_k = 0$ and $I_k = 0$ for all k, and $V > 0$ for all trajectories in the physically meaningful domain excluding the disease-free equilibrium. The derivative of V along the disease-free solution is

$$\frac{dV}{dt} = (\lambda_i a \sum_{k=1}^{n} k^2 p(k) S_k - (a+\mu)(g+\mu) \sum_{k=1}^{n} kp(k))\Theta$$

Using $S_k \leq 1$, it is clear that

$$\frac{dV}{dt} \leq (\lambda_i a \langle k^2 \rangle - (a+\mu)(g+\mu))\Theta = (a+\mu)(g+\mu)(R_i - 1)\Theta.$$

Therefore, if $R_i < 1$ for all $i \in \{1, .., m\}$, then $V' \leq 0$ and thus $V(t)$ is a common strict Lyapunov function. Then the disease-free equilibrium is globally asymptotically stable for arbitrary switching. □

5.6 Network Multi-City Models with Switching

Many infectious diseases can be transmitted from one region to another due to people travelling [39]. For example, in 2003 SARS which had started in one area of China spread to most of China and other cities in the world due to infected individuals traveling [43]. In 2009, the H1N1 influenza which appeared first in Mexico soon spread to countries all over the world [56]. In many developing countries, the travelling conditions such as sanitization in mass transit can be relatively poor, leading to an increase in the spread of disease while traveling [12]. We will study multi-city models to try to understand the geographic spread of disease.

5.6.1 Two Cities

For simplicity, assume there are two cities and that only healthy members from both populations may travel between the two cities at a rate $\alpha > 0$. While this assumption is not realistic, it allows for the model to remain simple enough to first analyze before considering more realistic models. For the multi-city systems, assume that both cities have the same type of degree distribution network and switched transmission rate, λ_i, which follows a switching rule $\sigma \in S$. Assume the birth and death rate is $\mu > 0$ and the recovery rate is $g > 0$ for both cities. The system equations are,

$$\begin{cases} \dot{S}_{c1,k} = \mu(S_{c1,k} + I_{c1,k}) - \lambda_i k S_{c1,k}\Theta_{c1} - \mu S_{c1,k} + gI_{c1,k} - \alpha S_{c1,k} + \alpha S_{c2,k} \\ \dot{I}_{c1,k} = \lambda_i k S_{c1,k}\Theta_{c1} - gI_{c1,k} - \mu I_{c1,k} \\ \dot{S}_{c2,k} = \mu(S_{c2,k} + I_{c2,k}) - \lambda_i k S_{c2,k}\Theta_{c2} - \mu S_{c2,k} + gI_{c2,k} - \alpha S_{c2,k} + \alpha S_{c1,k} \\ \dot{I}_{c2,k} = \lambda_i k S_{c2,k}\Theta_{c2} - gI_{c2,k} - \mu I_{c2,k} \end{cases} \tag{5.6}$$

where $k = 1, 2, ..., n$. Also, $\Theta_{c1,k} = 1/\langle k\rangle \sum_{k=1}^{n} kp(k)I_{c1,k}$ and $\Theta_{c2,k} = 1/\langle k\rangle \sum_{k=1}^{n} kp(k)I_{c2,k}$.

Note that $\dot{S}_{c1,k} + \dot{I}_{c1,k} + \dot{S}_{c2,k} + \dot{I}_{c2,k} = 0$ as they are proportions of a constant population. Suppose that $S_{c1,k} + I_{c1,k} = n_1$ and $S_{c2,k} + I_{c2,k} = n_2$ and that $n_1 + n_2 = 1$. The physically meaningful domain is $Q_{SISI} = \{(S_{c1,1}, I_{c1,1}, S_{c2,1}, I_{c2,1}, ..., S_{c1,n}, I_{c1,n}, S_{c2,n}, I_{c2,n}) \in \mathbb{R}_+^{4n} | S_{c1,k} + I_{c1,k} + S_{c2,k} + I_{c2,k} = 1\ \forall k\}$. We have that $\dot{S}_{c1,k} + \dot{I}_{c1,k} + \dot{S}_{c2,k} + \dot{I}_{c2,k} = 0$ and

$$\dot{S}_{c1,k}|_{S_{c1,k}=0} = (\mu + g)I_{c1,k} + \alpha S_{c2,k} \geq 0, \qquad \dot{I}_{c1,k}|_{I_{c1,k}=0} = \lambda_i k S_{c1,k}\Theta_{c1} \geq 0,$$
$$\dot{S}_{c2,k}|_{S_{c2,k}=0} = (\mu + g)I_{c2,k} + \alpha S_{c1,k} \geq 0, \qquad \dot{I}_{c2,k}|_{I_{c2,k}=0} = \lambda_i k S_{c2,k}\Theta_{c2} \geq 0.$$

Thus, the domain Q_{SISI} is invariant to the multi-city switched system. For each i-th subsystem, the basic reproduction number is

$$R_i = \frac{\lambda_i \langle k^2\rangle}{(\mu + g)\langle k\rangle}$$

and there is a disease-free equilibrium point, $E_0 = (S_{c1,k}^0, I_{c1,k}^0, S_{c2,k}^0, I_{c2,k}^0)_{k=1}^n$ where $S_{c1,k}^0 = 1/2$, $I_{c1,k}^0 = 0$, $S_{c2,k}^0 = 1/2$, $I_{c1,k}^0 = 0$.

Theorem 5.6.1. *If $\langle R_\sigma\rangle < 1 - \epsilon$ for all $t \geq 0$ with constant $\epsilon > 0$ and switching rule $\sigma \in S$ then the disease-free equilibrium is exponentially stable.*

Proof. Let i_l follow the switching rule $\sigma \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$, we have that

$$\begin{aligned} \frac{\Theta_{cj}}{dt} &= \frac{1}{\langle k\rangle} \sum_{k=1}^{n} kp(k)(\lambda_{i_l} k S_{cj,k} - gI_{cj,k} - \mu I_{cj,k}) \\ &\leq (\frac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle} - (g + \mu))\Theta_{cj} \\ &= C_{i_l}\Theta_{cj} \end{aligned}$$

with $C_{i_l} = \dfrac{\lambda_{i_l}\langle k^2\rangle}{\langle k\rangle} - (g+\mu)$ which applies to both $j=1$ and $j=2$. Starting with equation (4.2) and following the proof of Theorem 4.1.2. and using Lemma 4.1.1. then we have that $\Theta'_{cj} \leq \Theta_{cj}(0)\exp[-c_j t]$ for $j=1,2$ and $c_j > 0$ for all $t \geq 0$. Then $I_{c1,k}$ and $I_{c2,k}$ are exponentially converging to 0 for all k. □

Note that if we assume different degree distribution networks for the two cities, the dynamics remain mostly the same except for the expected value of the degree, and the variance of the degree for both networks. In this case, the threshold value is re-calculated to take in a maximum or minimum of these two values, based on the system.

Now assume both susceptible and infected individuals are allowed to travel between the two cities, and that individuals can contract the disease while traveling. Instead of the network mixing, it makes more sense for a uniform mixing assumption during travel. If we introduce another parameter, $\gamma > 0$, which is the contact rate for catching the disease amongst traveling individuals, the model is as follows:

$$\begin{cases} \dot{S}_{c1,k} = \mu(S_{c1,k}+I_{c1,k}) - \lambda_i k S_{c1,k}\Theta_{c1} - \mu S_{c1,k} + gI_{c1,k} - \alpha S_{c1,k} + \alpha S_{c2,k} - \alpha\gamma S_{c2,k}I_{c2,k} \\ \dot{I}_{c1,k} = \lambda_i k S_{c1,k}\Theta_{c1} - gI_{c1,k} - \mu I_{c1,k} - \alpha I_{c1,k} + \alpha I_{c2,k} + \alpha\gamma S_{c2,k}I_{c2,k} \\ \dot{S}_{c2,k} = \mu(S_{c2,k}+I_{c2,k}) - \lambda_i k S_{c2,k}\Theta_{c2} - \mu S_{c2,k} + gI_{c2,k} - \alpha S_{c2,k} + \alpha S_{c1,k} - \alpha\gamma S_{c1,k}I_{c1,k} \\ \dot{I}_{c2,k} = \lambda_i k S_{c2,k}\Theta_{c2} - gI_{c2,k} - \mu I_{c2,k} - \alpha I_{c2,k} + \alpha I_{c1,k} + \alpha\gamma S_{c1,k}I_{c1,k} \end{cases} \tag{5.7}$$

where $k = 1, 2, ..., n$.

Again the physically meaningful domain is

$$Q_{SISI} = \{(S_{c1,1}, I_{c1,1}, S_{c2,1}, I_{c2,1}, ..., S_{c1,n}, I_{c1,n}, S_{c2,n}, I_{c2,n}) \in \mathbb{R}_+^{4n} | S_{c1,k}+I_{c1,k}+S_{c2,k}+I_{c2,k} = 1 \forall k\}$$

Then $\dot{S}_{c1,k} + \dot{I}_{c1,k} + \dot{S}_{c2,k} + \dot{I}_{c2,k} = 0$ for all k. Moreover since $0 \leq \gamma \leq 1$ then,

$$\begin{aligned} \dot{S}_{c1,k}|_{S_{c1,k}=0} &= \mu I_{c1,k} + gI_{c1,k} + \alpha S_{c2,k}(1-\gamma I_{c2,k}) \geq 0, \\ \dot{I}_{c1,k}|_{I_{c1,k}} &= \lambda_i k S_{c1,k}\Theta_{c1} + \alpha I_{c2,k}(1+\gamma S_{c2,k}) \geq 0, \\ \dot{S}_{c2,k}|_{S_{c2,k}=0} &= \mu I_{c2,k} + gI_{c2,k} + \alpha S_{c1,k}(1-\gamma I_{c1,k}) \geq 0, \\ \dot{I}_{c2,k}|_{I_{c2,k}=0} &= \lambda_i k S_{c2,k}\Theta_{c2} + \alpha I_{c1,k}(1+\gamma S_{c1,k}) \geq 0, \end{aligned}$$

thus Q_{SISI} is invariant to the multi-city system (5.7). There is a disease-free equilibrium that is common to all subsystems, $E_0 = (S^0_{c1,k}, I^0_{c1,k}, S^0_{c2,k}, I^0_{c2,k})_{k=1}^n$ where $S^0_{c1,k} = 1/2$, $I^0_{c1,k} = 0$, $S^0_{c2,k} = 1/2$, $I^0_{c1,k} = 0$ for all k.

Theorem 5.6.2. *If* $\langle \dfrac{\lambda_\sigma\langle k^2\rangle + \alpha\gamma\langle k\rangle}{\langle k\rangle(g+\mu)} \rangle < 1-\epsilon$ *for all* $t \geq 0$ *with constant* $\epsilon > 0$ *and switching rule* $\sigma \in S$ *then the disease-free equilibrium is exponentially stable in* Q_{SISI}.

Proof. Let i_l follow the switching rule, $\sigma(t)$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$, we have that

$$\begin{aligned}
(\Theta_{c1} + \Theta_{c2})' &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)(I_{c1,k} + I_{c2,k})' \\
&= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)(\lambda_i k S_{c1,k}\Theta_{c1} + \lambda_i k S_{c2,k}\Theta_{c2} - (g+\mu)(I_{c1,k} + I_{c2,k}) \\
&+ \alpha\gamma(S_{c1,k}I_{c1,k} + S_{c2,k}I_{c2,k})) \\
&\leq \frac{1}{\langle k \rangle} \sum_{k=1}^{n} (\lambda_i k^2 p(k)(\Theta_{c1} + \Theta_{c2}) - (g+\mu)kp(k)(I_{c1,k} + I_{c2,k}) \\
&+ \alpha\gamma(I_{c1,k} + I_{c2,k})) \\
&= (\frac{\lambda_i \langle k^2 \rangle + \alpha\gamma\langle k \rangle}{\langle k \rangle} - (g+\mu))(\Theta_{c1} + \Theta_{c2}) \\
&= C_{i_l}(\Theta_{c1} + \Theta_{c2})
\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle + \alpha\gamma\langle k \rangle}{\langle k \rangle} - (g+\mu)$. Then following the proof of Theorem 4.1.2. and Lemma 4.1.1., with $A_i = \dfrac{\lambda_i \langle k^2 \rangle + \alpha\gamma\langle k \rangle}{\langle k \rangle}$ and $B = g + \mu$, we can show that $(\Theta_{c1} + \Theta_{c2}) \leq (\Theta_{c1}(0) + \Theta_{c2}(0)) \exp[-ct]$ for some $c > 0$ and for all $t \geq 0$. Since Θ_{c1}, Θ_{c2} are converging to zero, then $I_{c1,k}$, $I_{c2,k}$ must be converging to 0 for all k. Then, the limiting equations for $S_{c1,k}$ and $S_{c2,k}$ are

$$\begin{cases} \dot{S}_{c1,k} = -\alpha S_{c1,k} + \alpha S_{c2,k} \\ \dot{S}_{c2,k} = -\alpha S_{c2,k} + \alpha S_{c1,k} \end{cases}$$

which implies that both $S_{c1,k}$ and $S_{c2,k}$ are converging to $1/2$. Therefore the solution converges to the disease-free equilibrium in the meaningful domain Q_{SISI}. □

Another idea is to incorporate media coverage into the multi-city models. We suppose that as information gets spread throughout the city about the disease the citizens gain awareness and can take preventative measures which then reduces the transmissibility of the disease. If $c_1, c_2 < 0$ represent the rate of media coverage throughout city 1 and city 2 respectively, then the transmission rate becomes $\lambda_i - c_1$ and $\lambda_i - c_2$, respectively. We assume here that c_1, c_2 are both small enough so that $\lambda_i - c_1 \geq 0$ and $\lambda_i - c_2 \geq 0$. Here we also choose to have different birth/death rates, recovery rates and travelling rates for each city.

$$\begin{cases}
\dot{S}_{c1,k} = \mu_1(S_{c1,k} + I_{c1,k}) - (\lambda_i - c_1)kS_{c1,k}\Theta_{c1} - \mu_1 S_{c1,k} + g_1 I_{c1,k} \\
\qquad\qquad -\alpha_1 S_{c1,k} + \alpha_2 S_{c2,k} - \alpha_2\gamma S_{c2,k}I_{c2,k} \\
\dot{I}_{c1,k} = (\lambda_i - c_1)kS_{c1,k}\Theta_{c1} - g_1 I_{c1,k} - \mu_1 I_{c1,k} - \alpha_1 I_{c1,k} + \alpha_2 I_{c2,k} + \alpha_2\gamma S_{c2,k}I_{c2,k} \\
\dot{S}_{c2,k} = \mu_2(S_{c2,k} + I_{c2,k}) - (\lambda_i - c_2)kS_{c2,k}\Theta_{c2} - \mu_2 S_{c2,k} + g_2 I_{c2,k} \\
\qquad\qquad -\alpha_2 S_{c2,k} + \alpha_1 S_{c1,k} - \alpha_1\gamma S_{c1,k}I_{c1,k} \\
\dot{I}_{c2,k} = (\lambda_i - c_2)kS_{c2,k}\Theta_{c2} - g_2 I_{c2,k} - \mu_2 I_{c2,k} - \alpha_2 I_{c2,k} + \alpha_1 I_{c1,k} + \alpha_1\gamma S_{c1,k}I_{c1,k}
\end{cases} \tag{5.8}$$

with $k = 1, 2, ..., n$. The physically meaningful domain is Q_{SISI}. We have that

$$\begin{aligned}
\dot{S}_{c1,k}|_{S_{c1,k}=0} &= \mu_1 I_{c1,k} + g_1 I_{c1,k} + \alpha_2 S_{c2,k}(1 - \gamma I_{c2,k}) \geq 0, \\
\dot{I}_{c1,k}|_{I_{c1,k}=0} &= (\lambda_i - c_1) k S_{c1,k} \Theta_{c1} + \alpha_2 I_{c2,k}(1 + \gamma S_{c2,k}) \geq 0, \\
\dot{S}_{c2,k}|_{S_{c2,k}=0} &= \mu_2 I_{c2,k} + g_2 I_{c2,k} + \alpha_1 S_{c1,k}(1 - \gamma I_{c1,k}) \geq 0, \\
\dot{I}_{c2,k}|_{I_{c2,k}=0} &= (\lambda_i - c_2) k S_{c2,k} \Theta_{c2} + \alpha_1 I_{c1,k}(1 + \gamma S_{c1,k}) \geq 0
\end{aligned}$$

therefore this domain is invariant to the switched system. There is a disease-free equilibrium that is common to all subsystems, where $S_{c1,k} = \alpha_2/(\alpha_1 + \alpha_2)$, $I_{c1,k} = 0$,$S_{c2,k} = \alpha_1/(\alpha_1 + \alpha_2)$, and $I_{c2,k} = 0$ for all k. The non-physical basic reproduction number is

$$R_i^{non} = \frac{(\lambda_i - c_{min})\langle k^2 \rangle + \alpha_{max}\gamma\langle k \rangle}{\langle k \rangle (g_{min} + \mu_{min})}$$

Theorem 5.6.3. *If $\langle R_\sigma^{non} \rangle < 1 - \epsilon$ with $\epsilon > 0$ a constant for all $t \geq 0$ and switching rule $\sigma \in S$ then the solution of the system converges to the disease-free equilibrium which is exponentially stable.*

Proof. Let i_l follow the switching rule, $\sigma(t)$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ we have that

$$\begin{aligned}
\Theta'_{c1} &= \frac{1}{\langle k \rangle}(\lambda_i - c_1)\langle k^2 \rangle \Theta_{c1} - (g_1 + \mu_1 + \alpha_1)\Theta_{c1} + (\alpha_2 + \alpha_2\gamma)\Theta_{c2} \\
&\leq [\frac{(\lambda_i - c_1)\langle k^2 \rangle}{\langle k \rangle} - (g_1 + \mu_1 + \alpha_1)]\Theta_{c1} + [\alpha_2(1 + \gamma)]\Theta_{c2}
\end{aligned}$$

and similarly

$$\begin{aligned}
\Theta'_{c2} &= \frac{1}{\langle k \rangle}(\lambda_i - c_2)\langle k^2 \rangle \Theta_{c2} - (g_2 + \mu_2 + \alpha_2)\Theta_{c2} + (\alpha_1 + \alpha_1\gamma)\Theta_{c1} \\
&\leq [\frac{(\lambda_i - c_2)\langle k^2 \rangle}{\langle k \rangle} - (g_2 + \mu_2 + \alpha_2)]\Theta_{c2} + [\alpha_1(1 + \gamma)]\Theta_{c1}
\end{aligned}$$

therefore,

$$\begin{aligned}
(\Theta_{c1} + \Theta_{c2})' &\leq [\frac{(\lambda_i - c_1)\langle k^2 \rangle + \alpha_1\gamma\langle k \rangle}{\langle k \rangle} - (g_1 + \mu_1)]\Theta_{c1} + [\frac{(\lambda_i - c_2)\langle k^2 \rangle + \alpha_2\gamma\langle k \rangle}{\langle k \rangle} - (g_2 + \mu_2)]\Theta c2 \\
&\leq [\frac{(\lambda_i - c_{min}\langle k^2 \rangle + \alpha_{max}\gamma\langle k \rangle}{\langle k \rangle} - (g_{min} + \mu_{min})](\Theta_{c1} + \Theta c2) \\
&\leq C_{i_l}(\Theta_{c1} + \theta_{c2})
\end{aligned}$$

where $C_{i_l} = \dfrac{(\lambda_{i_l} - c_{min}\langle k^2 \rangle + \alpha_{max}\gamma\langle k \rangle}{\langle k \rangle} - (g_{min} + \mu_{min})$. Then following the proof of Lemma 4.1.1. and Theorem 4.1.2., with $A_i = \dfrac{(\lambda_i - c_{min}\langle k^2 \rangle + \alpha_{max}\gamma\langle k \rangle}{\langle k \rangle}$ and $B = g_{min} + \mu_{min}$ we

can show that $(\Theta_{c1} + \Theta_{c2}) \leq (\Theta_{c1}(0) + \Theta_{c2}(0)) \exp[-ct]$ for all $t \geq 0$ where $c > 0$ is some constant. This further implies that Θ_{c1} and Θ_{c2} are exponentially converging to 0, and since both functions are composed of the sum of non-negative multiples of $I_{c1,k}$ and $I_{c2,k}$, then for all k, $I_{c1,k}$ and $I_{c2,k}$ are both converging to 0 exponentially. Then, the limiting equations for $S_{c1,k}$ and $S_{c2,k}$ are

$$\begin{aligned}\dot{S}_{c1,k} &= -\alpha_1 S_{c1,k} + \alpha_2 S_{c2,k},\\ \dot{S}_{c2,k} &= -\alpha_2 S_{c2,k} + \alpha_1 S_{c1,k}\end{aligned}$$

which implies that both $S_{c1,k}$ and $S_{c2,k}$ are converging to $\alpha_2/(\alpha_1 + \alpha_2)$ and $\alpha_1/(\alpha_1 + \alpha_2)$. Therefore the solution converges to the disease-free equilibrium in the meaningful domain, which is exponentially stable. □

5.6.2 η Cities

The next model extends the multi-city concept to an arbitrary number of cities. If we have η cities, each modelled as an SIS-model with susceptible and infectives traveling at a rate $0 \leq \alpha \leq 1$ and transport-related infections at a rate $0 \leq \gamma \leq 1$:

$$\begin{cases}
\dot{S}_{c1,k} = \mu(S_{c1,k} + I_{c1,k}) - \lambda_i k S_{c1,k}\Theta_{c1} - \mu S_{c1,k} + gI_{c1,k} - \alpha S_{c1,k} \\
\qquad\qquad + \dfrac{\alpha}{\eta - 1}[\sum_{l=2}^{\eta} S_{cl,k} - \gamma \sum_{l=2}^{\eta} S_{cl,k} I_{cl,k}] \\
\dot{I}_{c1,k} = \lambda_i k S_{c1,k}\Theta_{c1} - gI_{c1,k} - \mu I_{c1,k} - \alpha I_{c1,k} + \dfrac{\alpha}{\eta - 1}[\sum_{l=2}^{\eta} I_{cl,k} + \gamma \sum_{l=2}^{\eta} S_{cl,k} I_{cl,k}] \\
\vdots \\
\dot{S}_{cj,k} = \mu(S_{cj,k} + I_{cj,k}) - \lambda_i k S_{cj,k}\Theta_{cj} - \mu S_{cj,k} + gI_{cj,k} - \alpha S_{cj,k} \\
\qquad\qquad + \dfrac{\alpha}{\eta - 1}[\sum_{l=1,l\neq j}^{\eta} S_{cl,k} - \gamma \sum_{l=1,l\neq j}^{\eta} S_{cl,k} I_{cl,k}] \\
\dot{I}_{cj,k} = \lambda_i k S_{cj,k}\Theta_{cj} - gI_{cj,k} - \mu I_{cj,k} - \alpha I_{cj,k} + \dfrac{\alpha}{\eta - 1}[\sum_{l=1,l\neq j}^{\eta} I_{cl,k} + \gamma \sum_{l=1,l\neq j}^{\eta} S_{cl,k} I_{cl,k}] \\
\vdots \\
\dot{S}_{c\eta,k} = \mu(S_{c\eta,k} + I_{c\eta,k}) - \lambda_i k S_{c\eta,k}\Theta_{c\eta} - \mu S_{c\eta,k} + gI_{c\eta,k} - \alpha S_{c\eta,k} \\
\qquad\qquad + \dfrac{\alpha}{\eta - 1}[\sum_{l=1}^{\eta-1} S_{cl,k} - \gamma \sum_{l=1}^{\eta-1} S_{cl,k} I_{cl,k}] \\
\dot{I}_{c\eta,k} = \lambda_i k S_{c\eta,k}\Theta_{c\eta} - gI_{c\eta,k} - \mu I_{c\eta,k} - \alpha I_{c\eta,k} + \dfrac{\alpha}{\eta - 1}[\sum_{l=1}^{\eta-1} I_{cl,k} + \gamma \sum_{l=1}^{\eta-1} S_{cl,k} I_{cl,k}]
\end{cases} \tag{5.9}$$

The physically meaningful domain is

$$\Omega_{(SI)_\eta} = \{(S_{c1,1}, I_{c1,1}, ..., S_{c\eta,1}, I_{c\eta,1}, ..., S_{c1,n}, I_{c1,n}, ..., S_{c\eta,n}, I_{c\eta,n}) | \sum_{j=1}^{\eta} (S_{cj,k} + I_{cj,k}) = 1 \; \forall k\}$$

Since $0 \leq \gamma \leq 1$ then $\dot{S}_{cj,k}|_{S_{cj,k}=0} \geq 0$ and $\dot{I}_{cj,k}|_{I_{cj,k}=0} \geq 0$ hence the domain is invariant to this switched system.

Theorem 5.6.4. *If $\langle R_\sigma \rangle < 1 - \epsilon$ with $\epsilon > 0$ a constant for all $t \geq 0$ and switching rule $\sigma \in S$ then the solution of the system converges to the disease-free equilibrium which is exponentially stable.*

Proof. Let i_l follow the switching rule, $\sigma(t)$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ we have that

$$\begin{aligned}\Theta'_{cj} &= \frac{1}{\langle k \rangle}[\lambda_i \sum k^2 p(k) \Theta_{cj}(1 - I_{cj,k}) - (g + \mu + \alpha)\langle k \rangle \Theta_{cj} + \frac{\alpha}{\eta - 1}(\sum \langle k \rangle \Theta_{cl} + \gamma \sum I_{cl,k}(1 - S_{cl,k}))] \\ &\leq \frac{1}{\langle k \rangle}[\lambda_i \langle k^2 \rangle \Theta_{cj} - (g + \mu + \alpha)\langle k \rangle \Theta_{cj} + \frac{\alpha}{\eta - 1}(1 + \gamma) \sum_{l=1, l \neq j}^{\eta} \Theta_{cl}]\end{aligned}$$

thus

$$\begin{aligned}(\sum_{j=1}^{\eta} \Theta_{cj})' &\leq [\frac{\lambda_i \langle k^2 \rangle + \alpha \langle k \rangle (1 + \gamma)}{\langle k \rangle} - (g + \mu + \alpha)](\sum_{j=1}^{\eta} \Theta_{cj}) \\ &= C_{il}(\sum_{j=1}^{\eta} \Theta_{cj})\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle + \alpha \langle k \rangle (1 + \gamma)}{\langle k \rangle} - (g + \mu + \alpha)$. Then following the proof of Theorem 4.1.2. and Lemma 4.1.1. with $A_i = \dfrac{\lambda_i \langle k^2 \rangle + \alpha \langle k \rangle (1 + \gamma)}{\langle k \rangle}$ and $B = g + \mu + \alpha$ we can show that $(\sum_{j=1}^{\eta} \Theta_{cj}) \leq (\sum_{j=1}^{\eta} \Theta_{cj}(0)) \exp[-ct]$ for all $t \geq 0$ where $c > 0$ is some constant. This further implies that all Θ_{cj} for $j = 1, ..., \eta$ are exponentially converging to 0, and since all Θ functions are composed of the sum of non-negative multiples of $I_{cj,k}$, then for all j, k, $I_{cj,k}$ is converging to 0 exponentially. Then, the limiting equations for $S_{cj,k}$:

$$\dot{S}_{cj,k} = -\alpha S_{cj,k} + \frac{\alpha}{\eta - 1} \sum_{l=1, l \neq j}^{\eta} S_{cl,k}$$

which implies that $S_{cj,k}$ is converging to $1/(\eta - 1)$. Therefore the solution converges to the disease-free equilibrium in the meaningful domain, which is exponentially stable. □

5.7 Numerical Simulations

In MATLAB, the built-in ode solver ode45 was used to analyze the switched network models in this chapter on a scale-free network that follows a power law degree distribution,

$p(k) \sim k^{-\alpha}$ where $\alpha = 2.1$. Also, we assume that $n = 50$ so the maximum number of links any single node in the network has is 50. For the parameter values, $\mu = 0.2$ and $g = 1$. Then for simplicity, there are two subsystems $i = \{1, 2\}$ and λ_1 and λ_2 varied to change the value of R_0.

In such a network that follows the aforementioned power law distribution, we have that the average degree is $\langle k \rangle = 2.4733$, also signifying the mean number of contacts an individual in the network is linked to that which the infectious disease may be transmitted. Further, another notable value is $\langle k^2 \rangle = 24.0974$. In such a case, we get that $R_{0i} < 1$ if and only if $\lambda_i < 0.123 = \lambda^*$. We assume a simple switching rule between 2 subsystems where switching occurs after every 5 time steps. The initial values were set by setting $I_{n-1} = 1$, thus providing the population with a superspreader (an infectious individual with 49 contacts).

Figure 5.1: **Network SIR Switched Model** with $\lambda_1 = 0.13$ and $\lambda_2 = 0.15$ so both $\lambda_1, \lambda_2 > \lambda^*$ and $R_1 = 1.055, R_2 = 1.218 > 1$: On average, $\langle R_\sigma \rangle = 1.137$ and the disease persists in conjunction with Theorem 5.1.1.

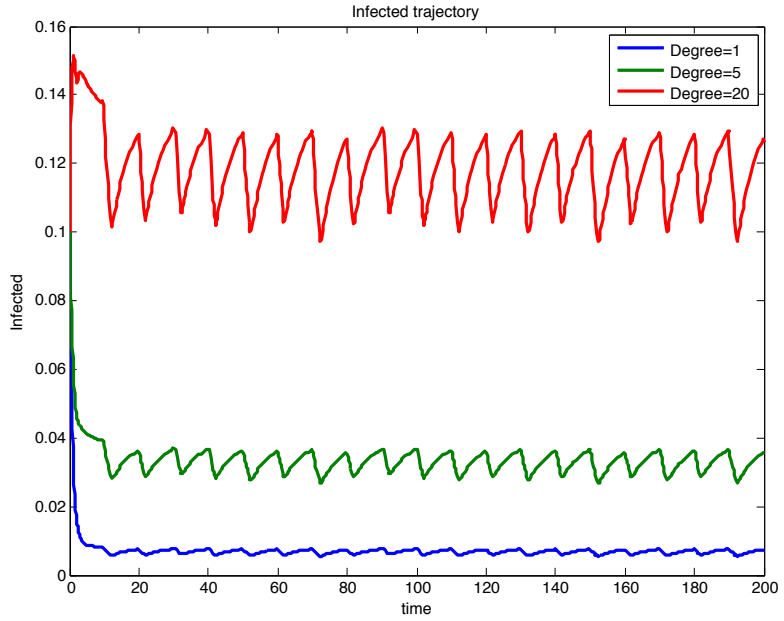


Figure 5.2: **Network SIR Switched Model** with $\lambda_1 = 0.1$ and $\lambda_2 = 0.09$ so both $\lambda_1, \lambda_2 < \lambda^*$ and $R_1 = 0.812, R_2 = 0.731 < 1$: On average, $\langle R_\sigma \rangle = 0.772$ and the disease dies out in conjunction with Theorem 5.1.1.

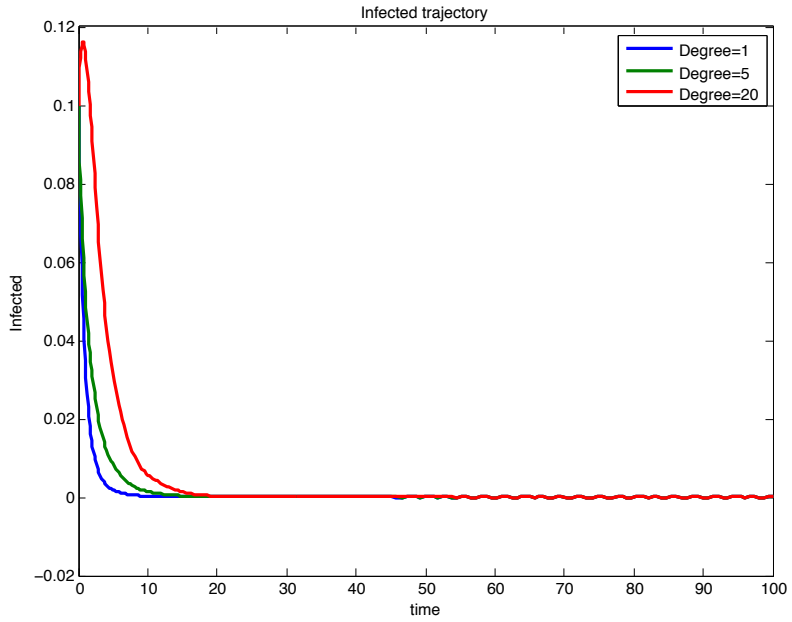


Figure 5.3: **Network SIR Switched Model** with $\lambda_1 = 0.09$ and $\lambda_2 = 0.15$ so $R_1 = 0.731, R_2 = 1.218 > 1$: On average, $\langle R_\sigma \rangle = 0.975$ and the disease dies out in conjunction with Theorem 5.1.2.

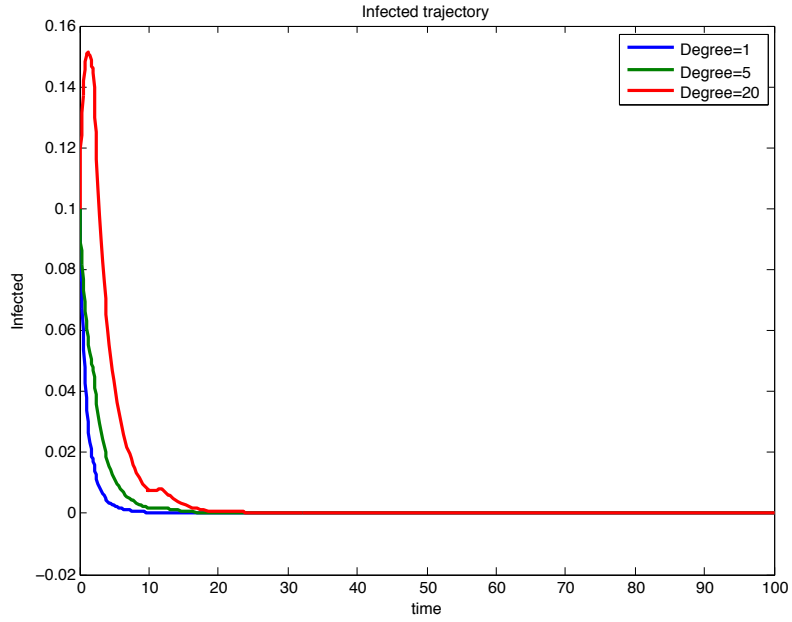


Figure 5.4: **Network SIR Switched Model** with $\lambda_1 = 0.3$ and $\lambda_2 = 0.09$ so $R_1 = 2.436 and R_2 = 0.731 > 1$ but on average, $\langle R_\sigma \rangle = 1.584 > 1$ and the disease persists leading to Conjecture 5.1.1.

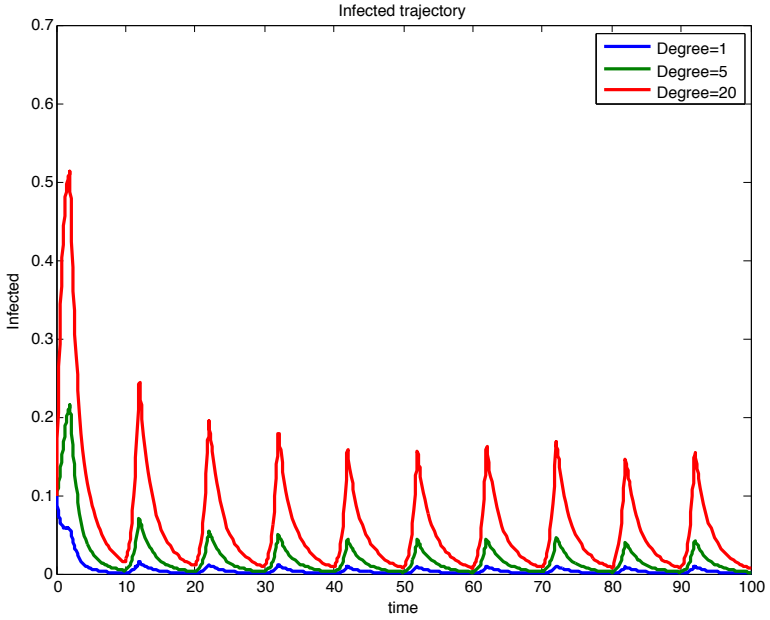


Figure 5.5: **Network SIR Switched Model with Vertical Transmission** with $\lambda_1 = 0.13$ and $\lambda_2 = 0.15$ so both $\lambda_1, \lambda_2 > \lambda^*$ and $R_1 = 1.055, R_2 = 1.218 > 1$: On average, $\langle R_0 \rangle = 1.137$ and the disease persists as expected from Theorem 5.3.2.

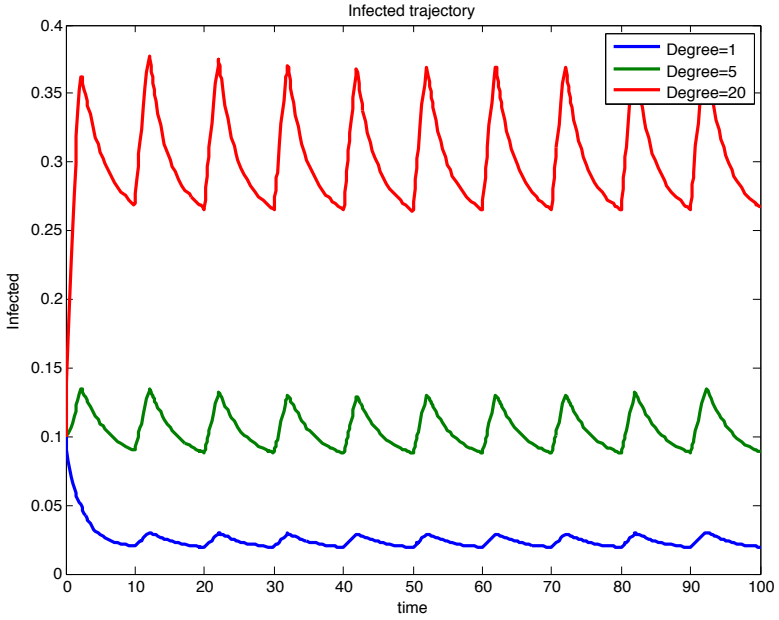


Figure 5.6: **Network SIRS Switched Model with $\lambda_1 = 0.13$ and $\lambda_2 = 0.09$**, on average $\langle R_\sigma \rangle = 0.975 < 1$ and the solution converges to the disease-free equilibrium as expected from Theorem 5.4.1.

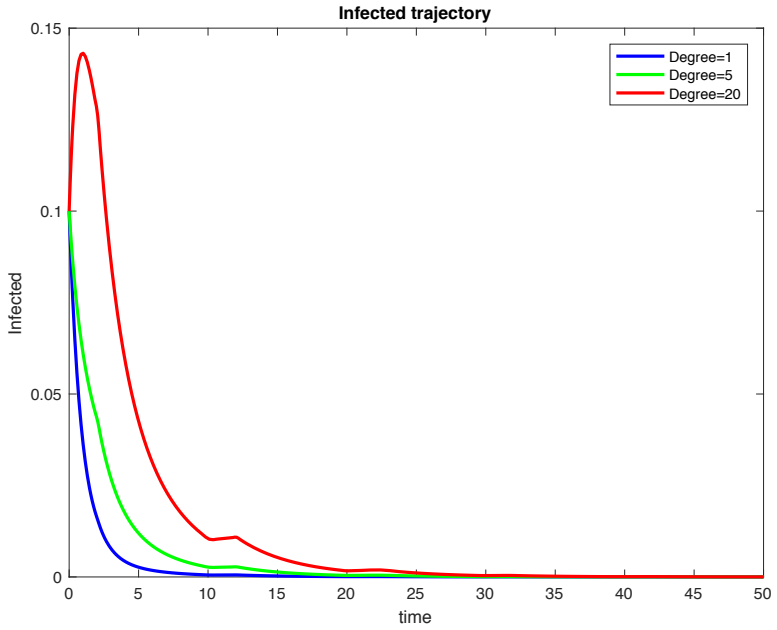


Figure 5.7: **Network SEIR Switched Model with $\lambda_1 = 0.13$ and $\lambda_2 = 0.16$**, on average $\langle R_0 \rangle = 1.299$ and the solution converges to the endemic equilibrium as expected from Theorem 5.5.1.

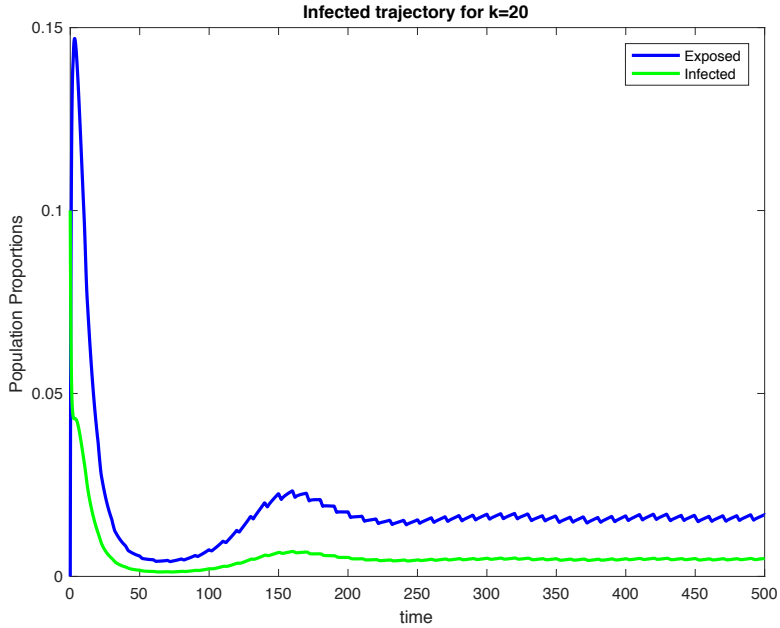


Figure 5.8: **Network SEIR Switched Model with** $\lambda_1 = 0.13$ **and** $\lambda_2 = 0.09$, on average $\langle R_0 \rangle = 0.985$ and the solution converges to the disease-free equilibrium in conjunction with Theorem 5.5.1.

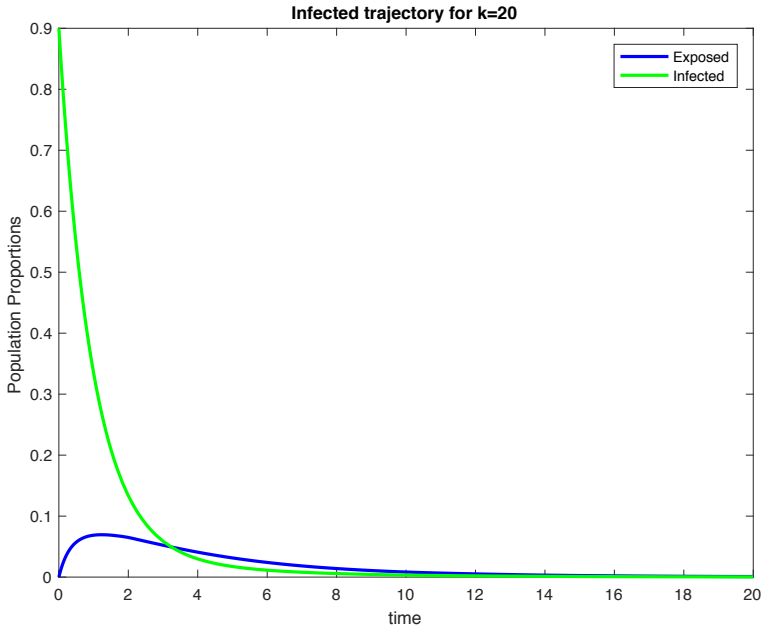


Figure 5.9: **Network Multi-City Switched Model with** $\lambda_1 = 0.13$ **and** $\lambda_2 = 0.16$, then $\langle R_\sigma \rangle = 1.177 > 1$ and the disease persists as expected.

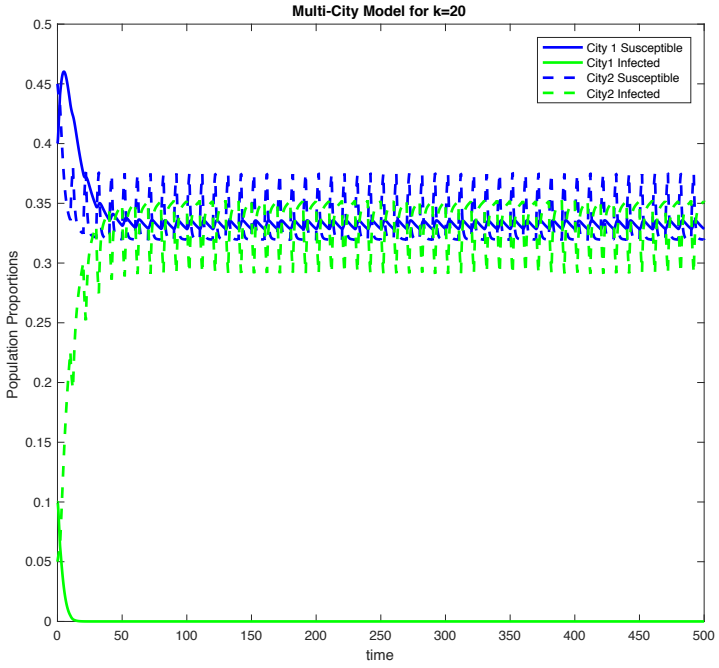
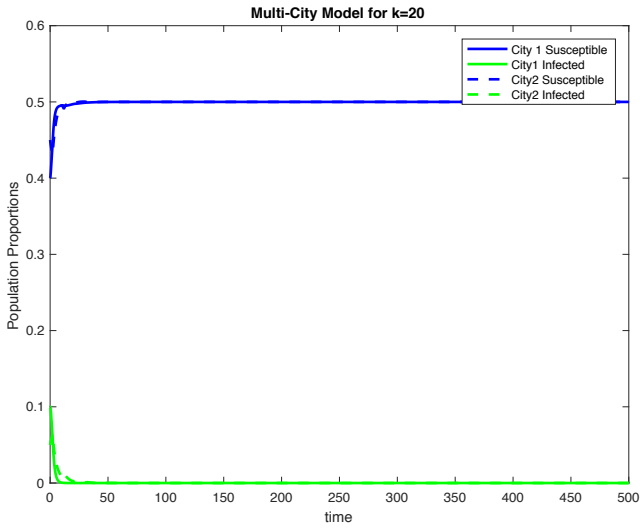


Figure 5.10: **Network Multi-City Switched Model with** $\lambda_1 = 0.13$ **and** $\lambda_2 = 0.08$, then $\langle R_\sigma \rangle = 0.852 < 1$ and the disease dies out as expected.



Chapter 6

Control Schemes for Switched Network Epidemiological Models

Control schemes are very important tools in the application of mathematical epidemiology. In Section 6.1, we will investigate constant control strategies including treatment of infectives, vaccination of newborns, and vaccination of susceptibles. We will also consider a constant control for multi-city models, where the travel of infected individuals is restricted due to a screening process. In Section 6.2, pulse control schemes will be investigated. Simulations will be presented at the end of the chapter.

6.1 Constant Control Schemes

6.1.1 Switched SIR Network Model with Treatment of Infectives

The first control strategy we will investigate is to provide treatment to the infectives and reduce the transmissibility of the disease. A proportion $0 \leq p \leq 1$ of all infectives will receive constant treatment which is assumed to be successful and then these treated individuals will enter the recovered class. This control scheme is implemented in the SIR network model with switching, given by the differential equations below,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k - p I_k \\ \dot{R}_k = g I_k - \mu R_k + p I_k, \qquad\qquad k = 1, 2, ..., n. \end{cases} \tag{6.1}$$

where the initial conditions follow $S_k(0) > 0$, $I_k(0) > 0$ and $R_k(0) = 1 - S_k(0) - I_k(0) > 0$ and the physically meaningful domain is Ω_{SIR}. Since $\dot{S}_k|_{S_k=0} = \mu > 0$, $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0$, $\dot{R}_k|_{R_k=0} = (g+p) I_k \geq 0$ and $\dot{S}_k + \dot{I}_k + \dot{R}_k = 0$ for all $k = 1, 2, ..., n$ then the meaningful domain is invariant to the system (6.1). The reproductive threshold ratio for each subsystem i of this switched system is:

$$R_i^p = \frac{\lambda_i \langle k^2 \rangle}{(g+\mu+p)\langle k \rangle}.$$

There is a disease-free equilibrium E_0 that is common to all subsystems, $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k, and an endemic equilibrium E^* that is unique for every subsystem i

$$\begin{aligned} S_k^* &= \frac{\mu}{\lambda_i k \Theta + \mu}, \\ I_k^* &= \frac{\lambda_i k \Theta \mu}{(\lambda_i k \Theta + \mu)(g+\mu+p)}, \\ R_k^* &= \frac{\lambda_i k \Theta (g+p)}{(\lambda_i k \Theta + \mu)(g+\mu+p)} \end{aligned}$$

and the stationary value of Theta is:

$$\Theta^* = \frac{\mu}{g+\mu+p}(1 - \frac{1}{R_i}).$$

Theorem 6.1.1. *If $\langle R_\sigma^p \rangle < 1 - \epsilon$ for all $t \geq 0$ and some constant $\epsilon > 0$ with switching rule $\sigma \in S$, then the disease-free equilibrium is exponentially stable in the physically meaningful domain. If the switching rule is periodic then the solution of the system converges to the disease-free equilibrium E_0 asymptotically in the meaningful domain Ω_{SIR}.*

Proof. Let i_l follow the switching rule, $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned} \Theta' &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)(\lambda_i k S_k \Theta - g I_k - \mu I_k - p I_k) \\ &\leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g+\mu+p))\Theta \\ &= C_{i_l} \Theta \end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g+\mu+p)$. Then, following the proof of Theorem 4.1.2. and Lemma 4.1.1. where $A_i = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle}$ and $B = g+\mu+p$, we have that $\Theta(t) \leq \Theta(0)\exp[-ct]$ for all $t \geq 0$ and for some constant $c > 0$. If the switching signal is periodic, then it follows Corollary 4.1.2. that the solution converges to the disease-free solution which is asymptotically stable in the meaningful domain. □

This control strategy allows for more straightforward analysis than the constant vaccination models since the treatment is being applied to the infected population directly, and the dynamics of the system are similar to the switched SIR network model without treatment.

However, treating infectives may be more difficult to conduct realistically, it is not always simple to identify infected individuals and then provide the effective treatment, rather than to vaccinate a healthy individual and prevent them from contracting the disease. Further, the inequality $\langle R_\sigma^p \rangle < 1 - \epsilon$ defines a critical treatment proportion, $p \geq p_{crit}$ in order to achieve disease eradication,

$$p_{crit} = (g + \mu)(\frac{\langle R_\sigma \rangle}{1 - \epsilon} - 1)$$

6.1.2 Switched SIR Network Model with Vaccination of Newborns

The next control strategy is constant vaccination of newborns, which will be applied onto the SIR network model with switching. Here, a fraction $0 \leq p \leq 1$ of all newborns are continuously vaccinated and will be considered as recovered since they are not susceptible to the disease and have gained some kind of immunity against contracting the disease. Switching will be considered by approximating the transmission rate as a piecewise constant, again motivated by varying in time due to seasonality.

$$\begin{cases} \dot{S}_k = \mu(1-p) - \lambda_i k S_k \Theta - \mu S_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k \\ \dot{R}_k = g I_k - \mu R_k + \mu p, \qquad\qquad k = 1, 2, ..., n. \end{cases} \tag{6.2}$$

In this model, the control strategy is to vaccination a proportion p of all newborns. This is a straightforward method but can easily get expensive, especially when the required proportion p to eradicate the disease is very high.

The reproductive threshold ratio for each subsystem i of this switched system is:

$$R_i^p = \frac{(1-p)\lambda_i \langle k^2 \rangle}{(g + \mu)\langle k \rangle}.$$

There is a disease-free equilibrium E_0 that is common to all subsystems, where $S_k = (1-p)$, $I_k = 0$, $R_k = p$ for all k. There is also an endemic equilibrium E^* which is unique for each i-th subsystem where,

$$\begin{aligned} S_k^* &= \frac{\mu(1-p)}{\lambda_i k \Theta^* + \mu}, \\ I_k^* &= \frac{\mu(1-p)\lambda_i k \Theta^*}{(g+\mu)(\lambda_i k \Theta^* + \mu)}, \\ R_k^* &= \frac{g(1-p)\lambda_i k \Theta^* + \mu p}{(g+\mu)(\lambda_i k \Theta^* + \mu)} \end{aligned}$$

for all $k = 1, 2, ..., n$. The stationary value of Theta is

$$\Theta^* = \frac{\mu}{g + \mu}(1-p)(1 - \frac{1}{R_i}).$$

If we implement a change of variables, $S_k = \hat{S}_k(1-p)$, $I_k = \hat{I}_k(1-p)$, $R_k = \hat{R}_k(1-p)+p$, the system transforms into the switched SIR network model without vaccination. The system is identical to the model without vaccination if $p = 0$. Motivated by the analysis of that system, we conclude with the following conjecture,

Conjecture 6.1.1. *If $\langle R_\sigma^p \rangle < 1 - \epsilon$ with constant $\epsilon > 0$ for all $t \geq 0$ and switching rule $\sigma \in S$, then the solution of the system converges to the disease-free equilibrium, which is exponentially stable in the physically meaningful domain. If the switching rule is periodic and $\langle R_\sigma^p \rangle < 1$ then the solution of the system converges asymptotically to the disease-free equilibrium.*

If we denote $\langle R_\sigma \rangle$ as the time-weighted average of the reproductive threshold ratios for the switched SIR network model without vaccination, then $\langle R_\sigma^p \rangle = (1-p)\langle R_\sigma \rangle$. The conjecture leads us to a critical value for p, the minimum vaccination proportion that will eradicate the disease (that is, if $p > p_{crit}$ then the disease will die out).

$$p_{crit} = 1 - \frac{1-\epsilon}{\langle R_\sigma \rangle}$$

In many cases, p_{crit} may be a large value close to 1, which makes the control strategy very expensive.

6.1.3 Switched SIR Network Model with Vaccination of Susceptibles

Here we implement the vaccination of all susceptibles instead of newborns, with $0 \leq p \leq 1$ represnting the proportion of successful vaccinations that continuously occur. The system equations are as follows,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k - p S_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k \\ \dot{R}_k = g I_k - \mu R_k + p S_k, \qquad\qquad k = 1, 2, ..., n. \end{cases}$$

The reproductive threshold ratio for each i-th subsystem is

$$R_i^p = \frac{\lambda_i \langle k^2 \rangle \mu}{(g+\mu)\langle k \rangle (\mu + p)}.$$

Again, there is a disease-free equilibrium E_0 that is common to all subsystems, where $S_k = \mu/(\mu+p)$, $I_k = 0$, and $R_k = p/(\mu+p)$ for all k. There is also an endemic equilibrium point E^* unique for each i-th subsystem where,

$$S_k^* = \frac{\mu}{\lambda_i k\Theta + \mu + p},$$
$$I_k^* = \frac{\lambda_i k\Theta\mu}{(g+\mu)(\lambda_i + \mu + p)},$$
$$R_k^* = \frac{\lambda_i k\Theta g + (g+\mu)p}{(g+\mu)(\lambda_i k\Theta + \mu + p)}$$

for all $k = 1, 2, ..., n$ where the stationary value of Theta is

$$\Theta^* = \frac{\mu}{g+\mu}(1 - \frac{1}{R_i^p}).$$

Note that $R_i^p \leq R_i$ if R_i is the reproductive threshold ratio from the switched SIR network model without vaccination.

Conjecture 6.1.2. *If $\langle R_\sigma^p \rangle < 1 - \epsilon$ with constant $\epsilon > 0$ for all $t \geq 0$ and switching rule $\sigma \in S$, then the solution of the system converges to the disease-free equilibrium E_0, which is exponentially stable in the physically meaningful domain. If the switching rule is periodic and $\langle R_\sigma^p \rangle < 1$ then the solution of the system converges to the disease-free equilibrium.*

The conjecture leads us to a critical value for p, the minimum vaccination proportion that will eradicate the disease, that is, if $p > p_{crit}$ then the disease will die out.

$$p_{crit} = \mu(\frac{\langle R_\sigma \rangle}{1-\epsilon} - 1)$$

with $R_i = \lambda_i \langle k^2 \rangle / ((\mu + g)\langle k \rangle)$.

6.1.4 Switched SIR Network Model with Constant Treatment of Infectives and Waning Immunity

Now consider the control scheme of constant treatment of the infectives being applied to the switched SIR network model. Suppose that the immunity gained from the treatment or from recovery from the disease is temporary. If δ represents the waning rate of the immunity, then we have the model system equations as follows,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k + \delta R_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k - p I_k \\ \dot{R}_k = g I_k + p I_k - \mu R_k - \delta R_k, \qquad k = 1, 2, ..., n \end{cases} \tag{6.3}$$

with $i \in \{1, ..., m\}$ that follows the switching rule $\sigma(t) \in S$, and $S_k(0) > 0$, $I_k(0) > 0$, $R_k(0) > 0$ for all $k \in \{1, ..., n)$. The physically meaningful domain for this system is Ω_{SIR}. There is a disease-free equilibrium E_0 that is common for all subsystems, $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k. There is also an endemic equilibrium unique for each i-th subsystem,

$$S_k^* = \frac{(\mu+\delta)(g+\mu p)}{\lambda_i k\Theta(g+p+\mu+\delta)+(\mu+\delta)(g+\mu+p)}$$
$$I_k^* = \frac{\lambda_i k\Theta(\mu+\delta)}{\lambda_i k\Theta(g+p+\mu+\delta)+(\mu+\delta)(g+\mu+p)}$$
$$R_k^* = \frac{\lambda_i k\Theta(g+p)}{\lambda_i k\Theta(g+p+\mu+\delta)+(\mu+\delta)(g+\mu+p)}$$

Then the basic reproduction ratio for the i-th subsystem is:

$$R_i^p = \frac{\lambda_i\langle k^2\rangle}{(g+\mu+p)\langle k\rangle} \tag{6.4}$$

In this case, $R_i^p = R_i(g+\mu)/(g+\mu+p)$, thus $R_i^p \leq R_i$ with equality when $p = 0$, or there is no treatment.

Theorem 6.1.2. *If $\langle R_\sigma^p\rangle < 1-\epsilon$ with $\epsilon > 0$ a constant and for all $t \geq 0$ with switching rule $\sigma \in S$, then the solution of the system converges to the disease-free equilibrium, which is exponentially stable in the physically meaningful domain. If the switching rule is periodic and $\langle R_\sigma^p\rangle < 1$ then the solution of the system converges to the disease-free equilibrium.*

Proof. Let i_l follow the switching rule, $\sigma(t) \in S$. Then for $t \in [t_{l-1}, t_l)$, $i_l \in \sigma(t)$, we have that

$$\begin{aligned}\Theta' &= \frac{1}{\langle k\rangle}\sum_{k=1}^{n} kp(k)(\lambda_i k S_k\Theta - (g+\mu+p)I_k)\\ &\leq [\frac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (g+\mu+p)]\Theta\\ &= C_{i_l}\Theta\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (g+\mu+p)$. Then, following the Theorem 4.1.2. and Lemma 4.1.1. with $A_i = \dfrac{\lambda_i\langle k^2\rangle}{\langle k\rangle}$ and $B = g+\mu+p$, we have that Θ converges exponentially to 0 since $\Theta(t) \leq \Theta(0)\exp[-ct]$ for some constant $c > 0$ and for all $t \geq 0$. Since Θ is a sum of all non-negative multiples of I_k, each I_k is converging exponentially to 0. Therefore we have that the disease-free equilibrium is exponentially stable, and the disease dies out. Further, if the switching signal is periodic, then it follows that the solution converges to the disease-free solution which is asymptotically stable in the meaningful domain. □

From this inequality from the theorem, we can determine the critical value p_{crit} such that if $p > p_{crit}$ then eradication is achieved.

$$p_{crit} = (g + \mu)(\frac{\langle R_\sigma \rangle}{1 - \epsilon} - 1)$$

where $\langle R_\sigma \rangle$ is the activation time weighted mean of the basic reproductive ratios from the switched SIR network model without control.

6.1.5 Switched SIR Network Model with Constant Vaccination of Susceptibles and Waning Immunity

Consider the constant vaccination control of the susceptibles to be applied to a switched SIR network model, but now suppose that the immunity gained from the vaccination or from recovery is temporary. If $0 \leq \delta \leq 1$ is the waning rate of the immunity, then the immune period is $1/\delta$. The model is represented by the following system of equations,

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k - p S_k + \delta R_k \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k \\ \dot{R}_k = g I_k + p S_k - \mu R_k - \delta R_k, \qquad\qquad k = 1, 2, ..., n \end{cases} \tag{6.5}$$

with $i \in \{1, ..., m\}$ that follows the switching rule $\sigma(t) \in S$, and $S_k(0) > 0$, $I_k(0) > 0$, $R_k(0) > 0$ for all $k \in \{1, ..., n)$. The physically meaningful domain for this system is $\Omega_{SIR} = \{(S_1, I_1, R_1, ..., S_n, I_n, R_n) \in \mathbb{R}^{3n}_+ | S_k + I_k + R_k = 1 \, \forall k\}$.

There is a disease-free equilibrium that is common to all m subsystems, where $S_k = (\mu + \delta)/(\mu + \delta + p)$, $I_k = 0$, and $R_k = p/(\mu + \delta + p)$ for all $k \in \{1, ..., n\}$. Each subsystem also has a unique endemic equilibrium, where

$$\begin{aligned} S_k^* &= \frac{(g + \mu)(\mu + \delta)}{\lambda_i k \Theta(\mu + \delta + g) + (g + \mu)(\mu + \delta + p)}, \\ I_k^* &= \frac{\lambda_i k \Theta(\mu + \delta)}{\lambda_i k \Theta(\mu + \delta + g) + (g + \mu)(\mu + \delta + p)}, \\ R_k^* &= \frac{\lambda_i k \Theta g + (g + \mu)p}{\lambda_i k \Theta(\mu + \delta + g) + (g + \mu)(\mu + \delta + p)}. \end{aligned}$$

The basic reproductive ratio for the i-th subsystem is:

$$R_i^p = \frac{\lambda_i \langle k^2 \rangle (\mu + \delta)}{(g + \mu)\langle k \rangle (\mu + \delta + p)}. \tag{6.6}$$

Since $R_i^p = R_i(\mu + \delta)/(\mu + \delta + p)$ then $R_i^p \leq R_i$ with equality when $p = 0$, with R_i representing the basic reproduction number of the i-th subsystem from the switched SIR network model without control.

Conjecture 6.1.3. *If $\langle R_\sigma^p \rangle < 1 - \epsilon$ with constant $\epsilon > 0$ for all $t \geq 0$ and switching rule $\sigma \in S$, then the solution of the system converges to the disease-free equilibrium E_0, which is exponentially stable in the phsyically meaningful domain. If the switching rule is periodic and $\langle R_\sigma^p \rangle < 1$ then the solution of the system converges to the disease-free equilibrium.*

The conjecture leads us to a critical value for p, the minimum vaccination proportion that will eradicate the disease, that is, if $p > p_{crit}$, then the disease will die out.

$$p_{crit} = (\mu + \delta)(\frac{\langle R_\sigma \rangle}{1 - \epsilon} - 1) \tag{6.7}$$

6.1.6 Screening Process Control Scheme in a Multi-City Model

In the multi-city models, an idea for a control scheme is restricting travel as a means to control the disease spread. This can be difficult to implement, as the main problem is first identifying the infected individuals. SARS was an example of using a screening process to restrict travel and trying to contain the disease, which was effective due to the global awareness of SARS and the seriousness of the disease. As individuals were traveling, visual inspections, thermal scanning, and administering questionnaires were helpful in identifying infected individuals.

To demonstrate the screening process control scheme, we first assume that there are two cities, and that susceptible and infective individuals are travelling between the cities. Suppose that $\alpha_1 > 0$ is the rate of travel of people from city 1 to city 2, and similarly α_2 is the rate of travel of people from city 2 to city 1. Then suppose that the screening process has a success rate of identifying infected individuals of $0 \leq p \leq 1$, and assume that there are no false positives in the test (i.e., none of the people identified as infected are actually not infected). The individuals who are screened then enter a separate class, $V_{c1,k}$ and $V_{c2,k}$, placed in isolation in city 1 and city 2 respectively for treatment, and further sub-categorized by their network degree k. The parameter $f > 0$ is the rate at which individuals leave the screened class by successfully receiving treatment and enter the susceptible class once more. Also assume a standard incidence rate for the infection of the disease while individuals are traveling, with contact rate $0 \leq \gamma \leq 1$. Then the model is represented by,

$$
\begin{cases}
\dot{S}_{c1,k} = \mu(S_{c1,k} + I_{c1,k}) - \lambda_i k S_{c1,k}\Theta_{c1} - \mu S_{c1,k} + gI_{c1,k} + fV_{c1,k} \\
\qquad -\alpha_1 S_{c1,k} + \alpha_2 S_{c2,k} - \alpha_2\gamma S_{c2,k} I_{c2,k} \\
\dot{I}_{c1,k} = \lambda_i k S_{c1,k}\Theta_{c1} - gI_{c1,k} - \mu I_{c1,k} - \alpha_1 I_{c1,k} + (1-p)\alpha_2 I_{c2,k} \\
\qquad +(1-p)\alpha_2\gamma S_{c2,k} I_{c2,k} \\
\dot{V}_{c1,k} = p\alpha_2 I_{c2,k} + p\alpha_2\gamma S_{c2,k} I_{c2,k} - fV_{c1,k} \\
\dot{S}_{c2,k} = \mu(S_{c2,k} + I_{c2,k}) - \lambda_i k S_{c2,k}\Theta_{c2} - \mu S_{c2,k} + gI_{c2,k} + fV_{c2,k} \\
\qquad -\alpha_2 S_{c2,k} + \alpha_1 S_{c1,k} - \alpha_1\gamma S_{c1,k} I_{c1,k} \\
\dot{I}_{c2,k} = \lambda_i k S_{c2,k}\Theta_{c2} - gI_{c2,k} - \mu I_{c2,k} - \alpha_2 I_{c2,k} + (1-p)\alpha_1 I_{c1,k} \\
\qquad +(1-p)\alpha_1\gamma S_{c1,k} I_{c1,k} \\
\dot{V}_{c2,k} = p\alpha_1 I_{c1,k} + p\alpha_1\gamma S_{c1,k} I_{c1,k} - fV_{c2,k}
\end{cases}
\tag{6.8}
$$

with $k = 1, 2, ..., n$. Here, $i \in \{1, ..., m\}$ follows a switching rule, $\sigma(t) \in S$. Furthermore we have that $S_{c1,k} + I_{c1,k} + V_{c1,k} + S_{c2,k} + I_{c2,k} + V_{c2,k} = 1$, as these represent proportions of the population in each class. The initial conditions are $S_{c1,k}(0) > 0$, $S_{c2,k}(0) > 0$, $I_{c1,k}(0) > 0$, $I_{c2,k}(0) > 0$. The physically meaningful domain for this system is:

$$
\begin{aligned}
\Omega_{SIVSIV} = &\{(S_{c1,1}, I_{c1,1}, V_{c1,1}, S_{c2,1}, I_{c2,1}, V_{c2,1}, ..., S_{c1,n}, I_{c1,n}, V_{c1,n}, S_{c2,n}, I_{c2,n}, V_{c2,n}) \in \mathbb{R}_+^{6n} \\
&|S_{c1,k} + I_{c1,k} + V_{c1,k} + S_{c2,k} + I_{c2,k} + V_{c2,k} = 1 \forall k\}
\end{aligned}
$$

Since we have that $0 \leq \gamma \leq 1$, then

$$
\begin{aligned}
&\dot{S}_{c1,k}|_{S_{c1,k}=0} = \mu I_{c1,k} + gI_{c1,k} + fV_{c1,k} + \alpha_2 S_{c2,k}(1 - \gamma I_{c2,k}) \geq 0 \\
&\dot{I}_{c1,k}|_{I_{c1,k}=0} = \lambda_i k S_{c1,k}\Theta_{c1} + (1-p)\alpha_2 I_{c2,k}(1 + \gamma S_{c2,k}) \geq 0 \\
&\dot{V}_{c1,k}|_{V_{c1,k}=0} = p\alpha_2 I_{c2,k}(1 + \gamma S_{c2,k}) \geq 0 \\
&\dot{S}_{c2,k}|_{S_{c2,k}=0} = \mu I_{c2,k} + gI_{c2,k} + fV_{c2,k} + \alpha_1 S_{c1,k}(1 - \gamma I_{c1,k}) \geq 0 \\
&\dot{I}_{c2,k}|_{I_{c2,k}=0} = \lambda_i k S_{c2,k}\Theta_{c2} + (1-p)\alpha_1 I_{c1,k}(1 + \gamma S_{c1,k}) \geq 0 \\
&\dot{V}_{c2,k}|_{V_{c2,k}=0} = p\alpha_1 I_{c1,k}(1 + \gamma S_{c1,k}) \geq 0
\end{aligned}
$$

which implies that the physically meaningful domain Ω_{SIVSIV} is invariant to the switched system. There is a disease-free equilibrium that is common to all subsystems where

$$
\begin{aligned}
S_{c1,k} &= \frac{\alpha_2}{\alpha_1 + \alpha_2} \\
I_{c1,k} &= 0 \\
V_{c1,k} &= 0 \\
S_{c2,k} &= \frac{\alpha_1}{\alpha_1 + \alpha_2} \\
I_{c2,k} &= 0 \\
V_{c2,k} &= 0
\end{aligned}
$$

For this model, we define the non-physical basic reproduction number for the i-th subsystem,

$$R_i^{p,non} = \frac{\lambda_i \langle k^2 \rangle + (1-p)(1+\gamma)\alpha_{max}\langle k \rangle}{\langle k \rangle (g + \mu + \alpha_{min})} \tag{6.9}$$

where $\alpha_{max} = \max\{\alpha_1, \alpha_2\}$, and $\alpha_{min} = \{\alpha_1, \alpha_2\}$. The use of the max and min functions mean these basic reproduction numbers are not physically meaningful but they still take into account the screening process probability p. The theorems established are sufficient but perhaps not necessary.

Theorem 6.1.3. *If $\langle R_\sigma^{p,non} \rangle < 1 - \epsilon$ for all $t \geq 0$, with constant $\epsilon > 0$ and switching rule $\sigma(t) \in S$, then the solution of the system converges to the disease-free equilibrium which is exponentially stable in the meaningful domain. If the switching rule is periodic and $\langle R_\sigma^{p,non} \rangle < 1$ then the solution of the system converges to the disease-free equilibrium, which is asymptotically stable.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$,

$$\begin{aligned}
\dot{\Theta}_{c1} &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)[\lambda_i k S_{c1,k}\Theta_{c1} - (g + \mu + \alpha_1)I_{c1,k} + (1-p)\alpha_2 I_{c2,k} + (1-p)\alpha_2\alpha_2\gamma S_{c2,k}I_{c2,k}] \\
&\leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g + \mu + \alpha_1))\Theta_{c1} + (1-p)\alpha_2(1+\gamma)\Theta_{c2}
\end{aligned}$$

and

$$\begin{aligned}
\dot{\Theta}_{c2} &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)[\lambda_i k S_{c2,k}\Theta_{c2} - (g + \mu + \alpha_2)I_{c2,k} + (1-p)\alpha_1 I_{c1,k} + (1-p)\alpha_1\alpha_1\gamma S_{c1,k}I_{c1,k}] \\
&\leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g + \mu + \alpha_2))\Theta_{c2} + (1-p)\alpha_1(1+\gamma)\Theta_{c1}.
\end{aligned}$$

Thus we have that

$$(\Theta_{c1} + \Theta_{c2})' = (\frac{\lambda_i \langle k^2 \rangle + (1-p)\alpha_{max}(1+\gamma)\langle k \rangle}{\langle k \rangle} - (g + \mu + \alpha_{min}))(\Theta_{c1} + \Theta_{c2}). \tag{6.10}$$

Therefore we have that

$$(\Theta_{c1} + \Theta_{c2})' \leq C_{i_l}(\Theta_{c1} + \Theta_{c2})$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle + (1-p)\alpha_{max}(1+\gamma)\langle k \rangle}{\langle k \rangle} - (g + \mu + \alpha_{min})$.

Following the proof of the Theorem 4.1.2. and Lemma 4.1.1. where

$$A_i = \frac{\lambda_i \langle k^2 \rangle + (1-p)\alpha_{max}(1+\gamma)\langle k \rangle}{\langle k \rangle}$$

and $B = g + \mu + \alpha_{min}$, we have that $\Theta_{c1} + \Theta_{c2} \leq (\Theta_{c1}(0) + \Theta_{c2}(0)) \exp[-ct]$ for all $t \geq 0$ and for some constant $c > 0$. Therefore, if $\langle R_\sigma^{p,non} \rangle < 1 - \epsilon$ we have that the solution is exponentially converging to the disease-free equilibrium of the overall switched system. Further, if the switching signal is periodic, then the disease-free equilibrium is asymptotically stable. □

The condition for the theorem $\langle R_\sigma^{p,non} \rangle < 1 - \epsilon$ above leads us to the critical value p_{crit} such that if $p > p_{crit}$ then eradication of the disease will be achieved. Since we used max and min functions and this basic reproduction number is non-physically meaningful, then this critical value will likely be higher than necessary for eradication.

6.2 Pulse Control Schemes

6.2.1 Switched SIR Network Model with Pulse Treatment of the Infectives

Now we implement a pulse control strategy, where instead of applying a constant treatment to the infectives, we impulsively treat a proportion of the infectives. Assume a certain fraction of the infected population is given treatment then cured of the disease at certain times t_l. It may seem non-physically acceptable that infected individuals are cured instantaneously, but it is sometimes reasonable to assume that the time scale of the treatment is very short compared to the time scale of the dynamics of the disease.

Suppose that there are m different pulses, and $0 \leq p_1, ..., p_m \leq 1$, and at the pulse times, t_l with $l = 1, 2, ...$, it is possible to apply one of the pulses. The switching times are $t_1 = 0 < t_1 < t_2 < ... < t_l < ... \to \infty$. At each switching time, t_l, an impulsive cure is applied to a fraction $0 \leq p_i \leq 1$ of the infected individuals in the population. We also introduce switching the transmission rate $\lambda_1, ..., \lambda_m > 0$ so that this parameter is time-varying. Then we have the model as follows:

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k \Theta - \mu S_k, & t \in (t_{l_1}, t_l] \\ \dot{I}_k = \lambda_i k S_k \Theta - g I_k - \mu I_k & \\ \dot{R}_k = g I_k - \mu R_k & \\ S_k(t^+) = S_k(t), & t = t_l \\ I_k(t^+) = I_k(t) - p_i I_k(t) & \\ R_k(t^+) = R_k(t) + p_i I_k(t) & \end{cases} \tag{6.11}$$

Here $k \in \{1, 2, ..., n\}$ is the degree as before, and $i \in \{1, ..., m\}$ follows the switching rule and there are m subsystems that the system switches between. Also $l = 1, 2, ...$ indicates the switching and impulsive times, t_l. We assume that solutions are continuous from the left at

t_l, thus

$$\begin{aligned}\{(S_k(t_l), I_k(t_l), R_k(t_l))\}_{k=1}^n &= \{(S_k(t_l^-), I_k(t_l^-), R_k(t_l^-))\}_{k=1}^n \\ &= \lim_{h\to 0^+} \{(S_k(t_l - h), I_k(t_l - h), R_k(t_l - h))\}_{k=1}^n\end{aligned}$$

and

$$\{(S_k(t_l^+), I_k(t_l^+), R_k(t_l^+))\}_{k=1}^n = \lim_{h\to 0^+} \{(S_k(t_l + h), I_k(t_l + h), R_k(t_l + h))\}_{k=1}^n.$$

We also assume that there is no impulsive effect at the initial time t_0, and we take $t_0 = 0$ without loss of generality. The initial conditions, $S_k(0^+) = S_{k,0} > 0$, $I_k(0^+) = I_{k,0} > 0$, $R_k(0^+) = R_{k,0}$. The basic reproduction number for the i-th subsystem is

$$R_i = \frac{\lambda_i \langle k^2 \rangle}{(\mu + g)\langle k \rangle} \tag{6.12}$$

Clearly there is a disease-free equilibrium point that is common to all subsystems from $1, ..., m$ where $S_k = 1$, $I_k = 0$, $R_k = 0$ for all k. Recall that $T_i(t)$ is the total activation time of subsystem i in the interval $(0, t]$.

Theorem 6.2.1. *If we have that* $(m-1)\ln(1-p) + \sum_{i=1}^{m} C_i T_i(t) \leq -ct$ *then the solution converges to the disease-free equilibrium, which is exponentially stable in the physically meaningful domain.*

Proof. Let i_l follow the switching rule $\sigma(t) \in S$. Then for $t \in (t_{l-1}, t_l]$, $i_l \in \sigma(t)$ and

$$\begin{aligned}\Theta' &= \frac{1}{\langle k \rangle} \sum_{k=1}^{n} kp(k)(\lambda_i k S_k \Theta - g I_k - \mu I_k) \\ &\leq [\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g + \mu)]\Theta \\ &= C_{i_l} \Theta\end{aligned}$$

where $C_{i_l} = \dfrac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g + \mu)$.

For $t \in (t_{l-1}, t_l]$:

$$\Theta(t) \leq \Theta(t_{l-1}^+) \exp[C_{i_l}(t - t_{l-1})].$$

Since for all k, $I_k(t) \geq 0$ for all $t \geq 0$ and since Θ is a sum of positive multiples of I_k then $\Theta(t) \geq 0$ for $t \geq 0$ as well. Then $\Theta(t)$ is bounded.

Immediately after t_l:

$$I_k(t_l^+) = (1-p)I_k(t_l)$$

$$\begin{aligned}\Theta(t_l^+) &= \frac{1}{\langle k\rangle}\sum_{k=1}^{n} kp(k)(1-p)I_k(t_l) \\ &= (1-p)\Theta(t_l)\end{aligned}$$

Then we consider each subinterval. For $t \in (0, t]$:

$$\begin{aligned}\Theta(t) &\leq \Theta(0)\exp[C_{i_1}t] \\ \Theta(t_1) &\leq \Theta(0)\exp[C_{i_1}t_1] \\ \Theta(t_1^+) &= (1-p)\Theta(t_1) \\ \Theta(t_1^+) &\leq (1-p)\Theta(0)\exp[C_{i_1}t_1]\end{aligned}$$

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

$$\begin{aligned}\Theta(t) &\leq \Theta(t_1^+)\exp[C_{i_l}(t-t_1)] \leq \Theta(0)(1-p)\exp[C_{i_l}t_1 + C_{i_2}(t-t_1)] \\ \Theta(t_2^+) &= (1-p)\Theta(t_2) \\ \Theta(t_2^+) &\leq (1-p)^2\Theta(0)\exp[C_{i_1}t_1 + C_{i_2}(t_2-t_1)]\end{aligned}$$

$\vdots$

For $t \in (t_{l-1}, t_l]$:

$$\begin{aligned}\Theta(t) &\leq \Theta(t_{l-1}^+)\exp[C_{i_l}(t-t_{l-1})] \\ &\leq \Theta(0)(1-p)^{l-1}\exp(C_{i_1}t_1 + C_{i_2}(t_2-t_1) + ... + C_{i_l}(t-t_{l-1}))\end{aligned}$$

$$\begin{aligned}\Theta(t_l^+) &= (1-p)\Theta(t_l) \\ \Theta(t_l^+) &\leq (1-p)^l\Theta(0)\exp[C_{i_1}t_1 + C_{i_2}(t_2-t_1) + ... + C_{i_l}(t_l-t_{l-1})] \\ \Theta(t_l^+) &\leq \Theta(0)(1-p)e^{C_{i_1}t_1}(1-p)e^{C_{i_2}(t_2-t_1)}\ldots(1-p)e^{C_{i_l}(t_l-t_{l-1})} \\ \Theta(t_l^+) &\leq \Theta(0)e^{\ln(1-p)}e^{C_{i_1}t_1}\ldots e^{\ln(1-p)}e^{C_{i_l}(t-t_{l-1})} \\ \Theta(t_l^+) &\leq \Theta(0)\exp(\sum_{i=1}^{m}(\ln(1-p) + C_iT_i(t)))\end{aligned}$$

$$\Theta(t) \leq \Theta(0)\exp[(m-1)\ln(1-p) + \sum_{i=1}^{m} C_iT_i(t)] \leq \Theta(0)\exp[-ct]$$

Therefore, if we have that $(m-1)\ln(1-p)+\sum_{i=1}^{m} C_i T_i(t) \leq -ct$ then the solution converges to the disease free equilibrium which is exponentially stable in the physically meaningful domain. □

The unfortunate thing is that this condition that $(m-1)\ln(1-p)+\sum_{i=1}^{m} C_i T_i(t) \leq -ct$ is not easily verified. Consider if for all i, $R_i \geq 1$. We will define S_{dwell} as the set of all switching signals considered to have a dwell time, meaning there exists an $\eta > 0$ such that $t_l - t_{l-1} \geq \eta$ for all $l = 1, 2, ...$ in the switching signal. The idea is that the transmission rate does not switch too quickly, and each λ_{i_l} dwells for a long enough time.

Theorem 6.2.2. *Suppose that $0 \leq p_i \leq 1$ for all $i = 1, ..., m$ and $R_1, ..., R_m \geq 1$. If the switching signal is considered to have a dwell time, that is $\sigma(t) \in S_{dwell}$ and there exists a constant $\alpha > 1$ such that $\ln(\alpha(1-p_i)) + \eta(\mu+g)(R_i - 1) \leq 0$ for all i, then the solution asymptotically converges to the disease-free equilibrium.*

Proof. Let $i_l \in \sigma(t) \in S_{dwell}$. Then for $t \in (t_{l-1}, t_l]$ and $\sigma(t) \in S$ and

$$\Theta'(t) \leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (\mu+g))\Theta = C_{i_l}\Theta$$

with $C_{i_l} = \frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle}$. Note that since we assume for all i, $R_i \geq 1$ then $C_{i_l} \geq 0$. Also, since $\Theta(t) \geq 0$ and $\Theta'(t) \leq C_{i_l}\Theta$ then Θ is bounded.

For $t \in (t_{l-1}, t_l]$:

$$\Theta(t) \leq \Theta(t_{l-1}^+)\exp[C_{i_l}(t - t_{l-1})].$$

Immediately after each t_l:

$$\Theta(t_l^+) = (1 - p_{i_l})\Theta(t_l).$$

We will use these equations to apply to each sub-interval:

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

$$\begin{aligned}
\Theta(t) &\leq \Theta(0)\exp(C_{i_l}t) \\
\Theta(t_1) &\leq \Theta(0)\exp(C_{i_l}t_1) \\
\Theta(t_1^+) &= (1 - p_{i_l})\Theta(t_1) \\
\Theta(t_1^+) &\leq (1 - p_{i_l})\Theta(0)\exp(C_{i_l}t_1)
\end{aligned}$$

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

$$\begin{aligned}
\Theta(t) &\leq \Theta(t_1^+)\exp[C_{i_2}(t-t_1)] \\
\Theta(t) &\leq (1-p_{i_1})\Theta(0)\exp[C_{i_l}t_1 + C_{i_2}(t-t_1)] \\
\Theta(t_2^+) &= (1-p_{i_2})\Theta(t_2) \\
\Theta(t_2^+) &\leq (1-p_{i_1})(1-p_{i_2})\Theta(0)\exp(C_{i_1}t_1 + C_{i_2}(t_2-t_1)) \\
&\vdots
\end{aligned}$$

For $t \in (t_{l-1}, t_l]$:

$$\begin{aligned}
\Theta(t) &\leq \Theta(0)(1-p_{i_1})\dots(1-p_{i_{l-1}})\exp(C_{i_1}t_1 + \dots + C_{i_l}(t-t_{l-1})) \\
&\leq \Theta(0)(1-p_{i_1})\dots(1-p_{i_{l-1}})\exp(C_{i_1}\eta + \dots + C_{i_l}\eta) \\
&\leq \Theta(0)\frac{1}{\alpha^l(1-p_{i_l})}\alpha(1-p_{i_1})e^{(C_{i_1}\eta)}\alpha(1-p_{i_2})e^{(C_{i_2}\eta)}\dots\alpha(1-p_{i_l})e^{(C_{i_l}\eta)} \\
&\leq \Theta(0)\frac{1}{\alpha^l(1-p_{i_l})}\alpha(1-p_{i_1})e^{(\mu+g)(R_{i_1}-1)\eta}\alpha(1-p_{i_2})e^{(\mu+g)(R_{i_2}-1)\eta}\dots\alpha(1-p_{i_l})e^{(\mu+g)(R_{i_l}-1)\eta} \\
&\leq \Theta(0)\frac{1}{\alpha^l(1-p_{i_l})}
\end{aligned}$$

Then we have the disease-free equilibrium is asymptotically stable. □

What about the case where the switching signal is periodic? If we have that $\tau_l = t_l - t_{l-1}$ and for m subsystems, $\tau_{l+m} = \tau_l$, then the switching signal is said to be periodic. We assume that if $R_l = R_i$ on $(t_{l-1}, t_l]$ then $R_{l+m} = R_l$ and $p_i = 0$ unless $t = lT$ with $T = \tau_1 + \dots + \tau_m$ being the period, then $p_i = p$. In other words, the pulses are applied at the end of each period. Denote the set of all periodic switching signals as $S_{periodic} \subset S$. This leads us to the following theorem:

Theorem 6.2.3. *If the switching rule is periodic, that is $\sigma(t) \in S_{periodic}$, and if we have the following inequality:*

$$\ln(1-p) + (\mu+g)((R_1-1)\tau_1 + \dots + (R_m-1)\tau_m) < 0$$

then the solution converges to the disease-free solution which is asymptotically stable.

Proof. First show convergence. For $(0, T]$:

$$\Theta(t) \leq \Theta(0)\exp[C_1\tau_1 + \dots + C_m(t-(T-\tau_m)]$$

with $C_i = \dfrac{\lambda_i\langle k^2\rangle}{\langle k\rangle} - (\mu+g)$.

Immediately after T, the first impulse is applied:

$$\begin{aligned}
\Theta(T^+) &\leq \Theta(0)(1-p)\exp[C_1\tau_1 + \dots + C_m\tau_m] \\
&= \Theta(0)\exp[\ln(1-p) + C_1\tau_1 + \dots + C_m\tau_m] \\
&= \eta\Theta(0)
\end{aligned}$$

where $\eta = \exp[\ln(1-p) + C_1\tau_1 + ... + C_m\tau_m] < 1$. Similarly we can show that $\Theta(hT^+) \leq \eta\Theta((h-1)T^+)$ for any integer $h = 1, 2, ...$ Then,

$$\begin{aligned}\Theta(hT^+) &\leq \eta\Theta((h-1)T^+) \\ &\leq \eta(\eta\Theta((h-2)T^+)) \\ &\leq ... \\ &\leq \eta^h\Theta(0)\end{aligned}$$

Then it becomes clear that the sequence $\{\Theta(hT^+)\}_{h=1}^{\infty}$ is converging to zero. Therefore, as $h \to \infty$, $\Theta(T^+)$ is converging to zero.

Then show stability. Suppose that $R_1, ..., R_r \geq 1$ and $R_{r+1}, ..., R_m < 1$. Then we have that $C_1, ..., C_r \geq 0$ and $C_{r+1}, ..., C_m < 0$. Then during the first period, $(0, T]$, the maximum vvalue of Θ is:

$$\Theta_{max} = \Theta(0)e^{C_1\tau_1+...+C_r\tau_r} = \Theta(0)B$$

For any $\epsilon > 0$, choose $\delta = \epsilon/B$. Then if $\Theta(0) < \delta$ in the interval $(0, T]$,

$$\Theta \leq \Theta_{max} = \Theta(0)B < \delta B = \delta\epsilon/\delta = \epsilon$$

which completes the definition of stabilty. More generally for any interval $(t_{l-1}, t_l]$, and $hT < t_l \leq (h+1)T$ then $\Theta(t) \leq \Theta(hT^+)(1-p)^h B < \Theta(0)(1-p)^h B < \delta B = \epsilon$. Then the solution is asymptotically stable. □

From this theorem, we can use the inequality condition to determine the critical value p_{crit} such that if $p > p_{crit}$, and the switching signal is periodic, $\sigma(t) \in S_{periodic}$, then the eradication of the disease is achieved.

$$p_{crit} = 1 - e^{-(\mu+g)((R_1-1)\tau_1+...+(R_m-1)\tau_m)}$$

6.2.2 Switched SIR Network Model with Pulse Vaccination of the Susceptibles

We can also consider pulse vaccination into the model with pulse treatment. Then the switched SIR network model becomes:

$$\begin{cases} \dot{S}_k = \mu - \lambda_i k S_k\Theta - \mu S_k, & t \in ((l-1)T, lT] \\ \dot{I}_k = \lambda_i k S_k\Theta - gI_k - \mu I_k & \\ \dot{R}_k = gI_k - \mu R_k & \\ S_k(t^+) = S_k(t) - pS_k(t), & t = lT \\ I_k(t^+) = I_k(t) - pI_k(t) & \\ R_k(t^+) = R_k(t) + pS_k(t) + pI_k(t) & \end{cases} \tag{6.13}$$

for $k = 1, 2, ..., n$.

Assume that the switching signal is periodic, $\sigma \in S_{periodic}$, and the pulses occur at the end of each period which are $T = \tau_1 + ... + \tau_m$ long. The initial conditions are $S_k(0^+) = S_{k,0} > 0$, $I_k(0^+) = I_{k,0} > 0$, $R_k(0^+) = R_{k,0}$ for all $k \in \{1, ..., n\}$, with n being the highest degree in the network. We assume that $S_k(t) + I_k(t) + R_k(t) = 1$ for all k and for all $t \geq 0$, thus these represent proportions of the population. The meaningful domain is $\Omega_{SIR} = \{(S_1, I_1, R_1, ..., S_n, I_n, R_n) \in \mathbb{R}^{3n}_+ | S_k + I_k + R_k = 1 \, \forall k\}$.

We have that $\dot{S}_k + \dot{I}_k + \dot{R}_k = 0$ since $S_k + I_k + R_k = 1$. Also, $\dot{S}_k|_{S_k=0} = \mu > 0$, $\dot{I}_k|_{I_k=0} = \lambda_i k S_k \Theta \geq 0$, $\dot{R}_k|_{R_k=0} = gI_k \geq 0$. Therefore the physically meaningful domain is invariant to the switched system. The impulsive differene equations do not move the solution outside the domain. The basic reproduction ratio for the i-th subsystem is

$$R_i = \frac{\lambda_i \langle k \rangle}{(\mu + g)\langle k \rangle}$$

as it is in the non-pulse switched SIR network model. The disease-free equilibrium from the non-pulse model where $S_k = 1$, $I_k = 0$, $R_k = 0$ is no longer an equilibrium for this pulse switched system, due to the pulse vaccination which moves the subsystem even when $I_k = 0$. However $I_k = 0$ is still an equilibrium solution, and since $I_k = 1 - S_k - R_k$, we can reduce this system to

$$\begin{cases} \dot{S}_k = \mu - \mu S_k, & t \in ((l-1)T, lT] \\ \dot{R}_k = -\mu R_k & \\ S_k(t^+) = S_k(t) - pS_k(t), & t = lT \\ R_k(t^+) = R_k(t) + pR_k(t) & \end{cases} \tag{6.14}$$

for $k = 1, 2, ..., n$.

This reduced system is no longer a switched system as it does not depend on the piecewise parameter, the transmission rate, λ_i.

Theorem 6.2.4. *If the switching rule is periodic, $\sigma \in S_{periodic}$, and we have that*

$$\ln(1-p) + (\mu + g)((R_1 - 1)\tau_1 + ... + (R_m - 1)\tau_m) \leq 0$$

then the periodic disease-free equilibrium is globally asymptotically stable.

Proof. If the switching rule is periodic, $\sigma \in S_{periodic}$, and $t \in (t_{l-1}, t_l]$, $i_l = \sigma(t)$ and

$$\begin{aligned} \Theta'(t) &= \frac{1}{\langle k \rangle}(\lambda_i k S_k \Theta - gI_k - \mu I_k) \\ &\leq (\frac{\lambda_i \langle k^2 \rangle}{\langle k \rangle} - (g + \mu))\Theta \\ &= C_{i_l}\Theta \end{aligned}$$

with $C_{il} = \lambda_i \langle k^2 \rangle / \langle k \rangle - \mu - g$. After each period $\Theta(lT^+)\Theta(lT) - p\Theta(lT)$. Using the proof from Corollary 4.1.2, then the periodic disease-free solution is asymptotically stable. The limiting system becomes

$$\begin{cases} \dot{S}_k = \mu - \mu S_k \\ \dot{R}_k = -\mu R_k \\ S_k(t^+) = S_k(t) - pS_k(t) \\ R_k(t^+) = R_k(t) + pS_k(t) \end{cases} \tag{6.15}$$

For $(l-1)T < t \leq lT$, integrate and solve the equation between pulses:

$$\begin{cases} S_k(t) = 1 + (S_k((l-1)T) - 1)e^{-\mu(t-(l-1)T)} \\ R_k(t) = 1 - S_k(t) \end{cases} \tag{6.16}$$

Then, immediately after pulse vaccination:

$$\begin{aligned} S_k(lT^+) &= (1-p)S_k(lT) \\ &= (1-p)(1 + (S_k((l-1)T) - 1)e^{-\mu T}) \\ &= F(S_k((l-1)T)) \end{aligned}$$

which defines a stroboscopic mapping which has a fixed point where

$$\hat{S}_k = \frac{(1-p)(1-e^{-\mu T})}{1-(1-p)e^{-\mu T}} \tag{6.17}$$

and

$$\left.\frac{dF(S_k(lT))}{dS_k(lT)}\right|_{S_k(lT)=\hat{S}_k} = (1-p)e^{-\mu T} < 1.$$

Therefore this fixed point is globally asymptotically stable. □

Again, the restraint given by the theorem provides the critical value p_{crit} where if $p > p_{crit}$ then eradication is achieved.

$$p_{crit} = 1 - e^{-(\mu+g)((R_1-1)\tau_1 + \ldots + (R_m-1)\tau_m)}$$

6.3 Numerical Simulations

In MATLAB, the built-in ode solver ode45 was used to analyze the SIR and SIRS switched network models on a scale-free network that follows a power law degree distribution, $p(k) \sim k^{-\alpha}$ where $\alpha = 2.1$. Also, we assume that $n = 50$ so the maximum number of links any single node in the network has is 50. For the parameter values, $\mu = 0.1$ and $g = 1$. Then for simplicity, there are two subsystems $i = \{1, 2\}$ and λ_1 and λ_2 varied to change the value of R_0.

Figure 6.1: **Constant Vaccination of Newborns in an SIR Model** with $\lambda_1 = 0.85$ and $\lambda_2 = 0.50$ so both and $R_1 = 7.53, R_2 = 4.42 > 1$ with R_i representing the basic reproduction ratio of the non-vaccinated system. Here $p = 0.3$ is still not strong enough to eradicate the disease, and there is an epidemic and the disease persists.

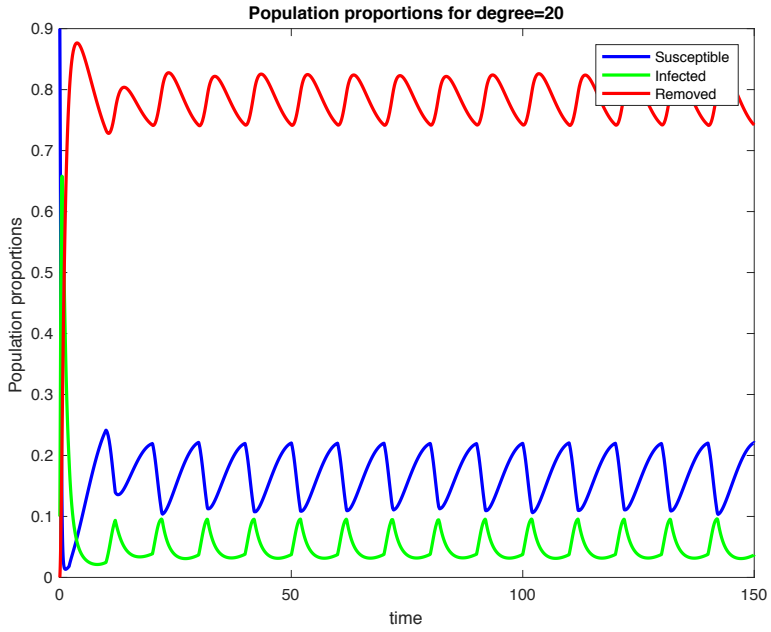


Figure 6.2: **Constant Vaccination of Newborns in an SIR Model** with $\lambda_1 = 0.85$ and $\lambda_2 = 0.50$ so both and $R_1 = 7.53, R_2 = 4.42 > 1$ with R_i representing the basic reproduction ratio of the non-vaccinated system. Here $p = 0.83$ eradicates the disease, since $p_{crit} = 0.82$.

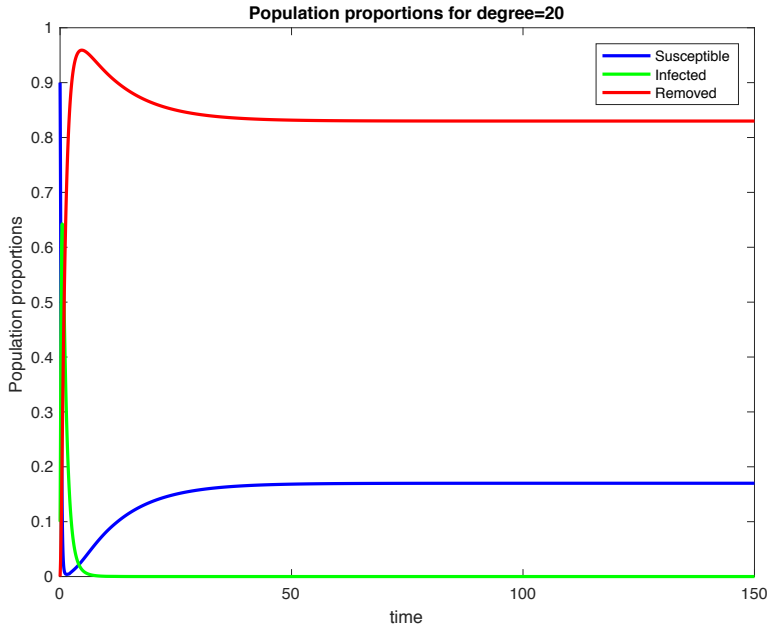


Figure 6.3: **Constant Vaccination of Susceptibles in an SIR Model** with $\lambda_1 = 0.85$ and $\lambda_2 = 0.50$ so both and $R_1 = 7.53, R_2 = 4.42 > 1$ with R_i representing the basic reproduction ratio of the non-vaccinated system. Here $p = 0.3$ does not eradicate the disease, and there is an epidemic.

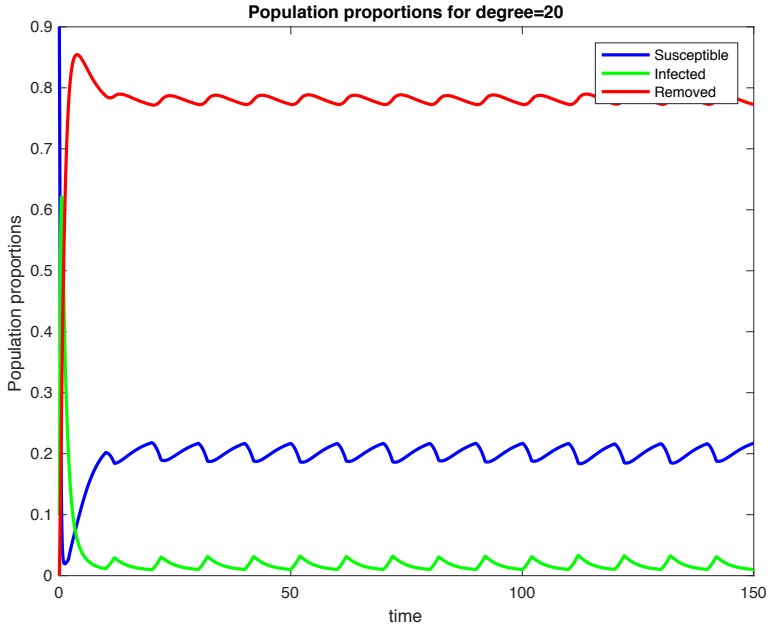


Figure 6.4: **Constant Vaccination of Susceptibles in an SIR Model** with the same parameter values as above. Here $p = 0.5$ eradicates the disease, since $p_{crit} = 0.4972$. Vaccinating the susceptible appears to be a better control scheme than vaccination of the newborns.

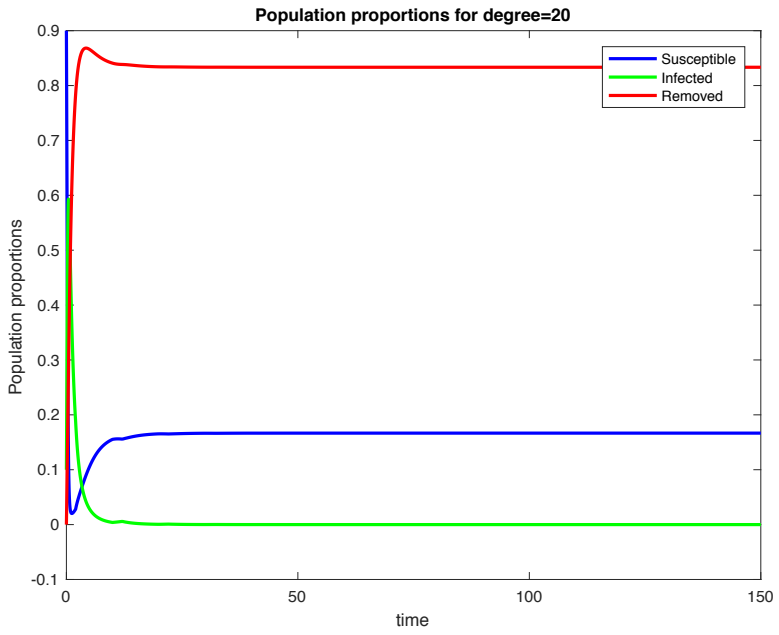


Figure 6.5: **Constant Treatment of Infectives in an SIR Model** with the same parameter values as above. Treating the infected individuals is a less effective control scheme, since even with $p = 1$ eradication is impossible.

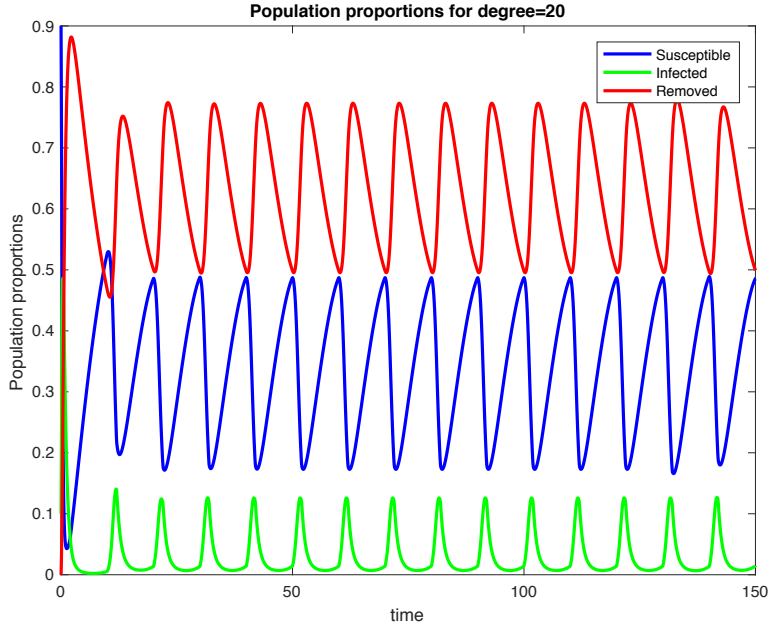


Figure 6.6: **Constant Treatment of Infectives in an SIR Model** with $\lambda_1 = 0.15$ and $\lambda_2 = 0.20$ so both and $R_1 = 1.329, R_2 = 1.771 > 1$ have been reduced. When $p = 0$ we get the usual switched SIR network model where the disease persists.

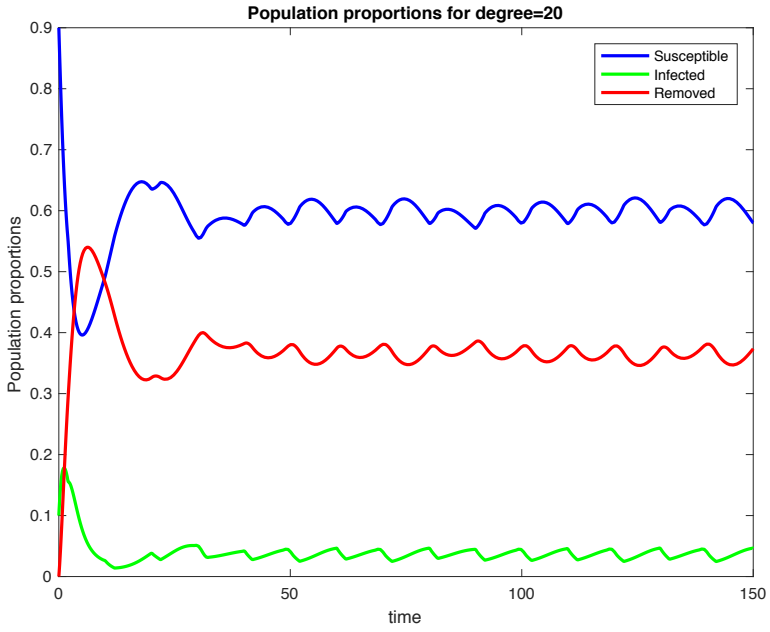


Figure 6.7: **Constant Treatment of Infectives in an SIR Model** with the same parameter values as above. Now with the reduced transmission rates and $p = 1$ eradication is achieved.

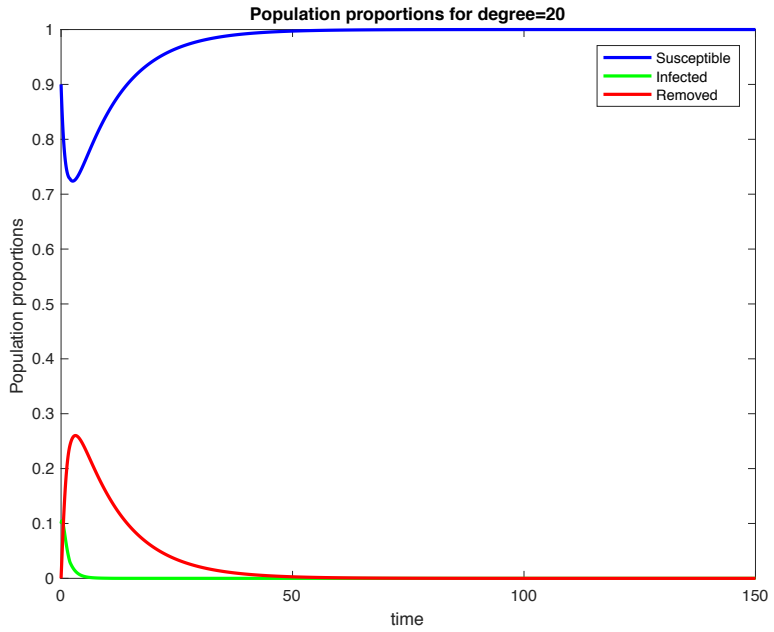


Figure 6.8: **Constant Vaccination of Susceptibles with Waning Immunity in an SIR Model** with $\delta = 0.1$ and $\lambda_1 = 0.85$, $\lambda_2 = 0.5$. Here $p = 0.5$ is no longer effective.

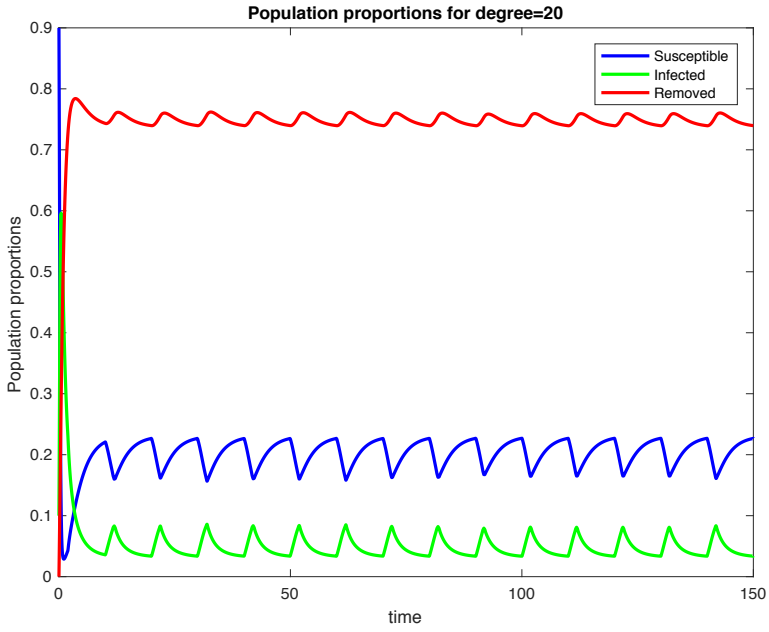


Figure 6.9: **Constant Vaccination of Susceptibles with Waning Immunity in an SIR Model** with $\delta = 0.1$ and $\lambda_1 = 0.85$, $\lambda_2 = 0.5$. Due to the waning immunity, the $p_{crit} = 0.9944$. In this figure, $p = 1$ demonstrates the eradication of the disease.

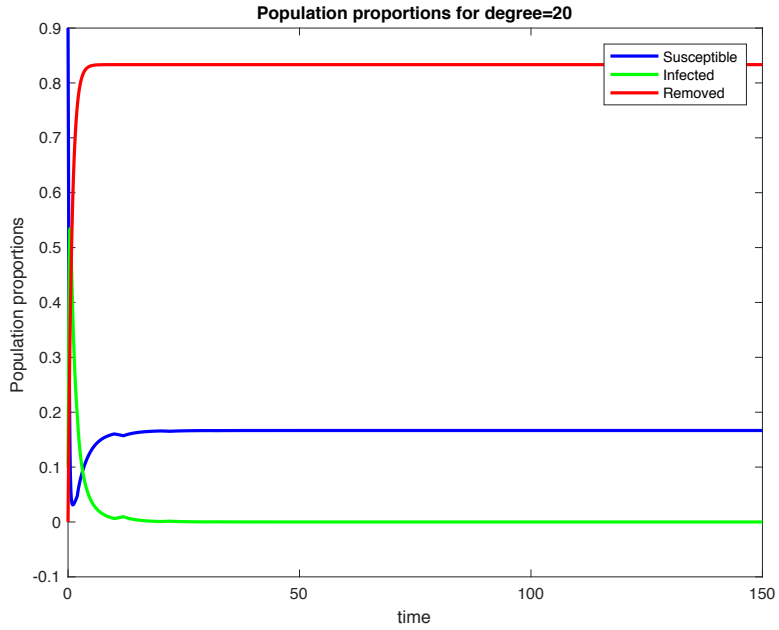
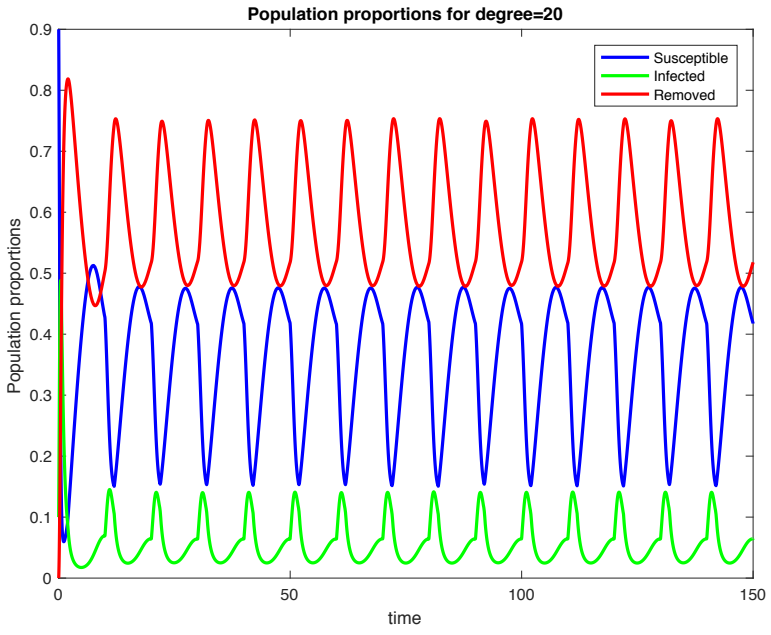


Figure 6.10: **Constant Treatment of Infectives with Waning Immunity in an SIR Model** with $\delta = 0.1$ and $\lambda_1 = 0.85$, $\lambda_2 = 0.5$. Even with $p = 1$ eradication is not achieved again, again showing that treatment is less effective.



Chapter 7

Conclusions and Future Directions

In this thesis, we have extended the mathematical epidemiological literature on models that consider interpersonal contact patterns as networks by the addition of time-varying transmission rates. We have introduced switching into these network type models, motivated by differences in seasons, by modeling the transmission rates and other parameters as a piecewise constant function.

In Chapter 4, we first investigate n-dimensional disease network models consisting of two main disease classes, susceptible and infective. We first introduce switching into the basic network SIS type model with population dynamics, then compare the results to a model with vertical transmission, as well as a model that includes switching for more than one parameter. We show that if the activation time weighted basic reproduction rate, $\langle R_\sigma \rangle$, is less than $1 - \epsilon$ for any small $\epsilon > 0$, then the disease will be eradicated and the disease-free solution is exponentially stable. We have also shown that if the switching signal is periodic and $\langle R_\sigma < 1$ then the solution converges to the disease-free equilibrium, which is asympotically stable. These results were then supported with numerical examples and computer simulations which also lead to conjectures about the permanence of the disease when $\langle R_\sigma \rangle > 1$.

In Chapter 5, we introduce switching into more complicated infectious disease network models, that consist of at least three or more main disease classes. These models include the SIR type models, with and without population dynamics, with vertical transmission, SEIR model, and multi-city models (first with two cities and then with η number of cities). We establish stability results for these models as well, and provide numerical examples and simulations as evidence to the results.

In Chapter 6, we implement a few constant control strategies involving vaccination and treatment, with and without waning immunity, and determine critical $0 \leq p \leq 1$ values that eradicate the disease or allow the disease to survive. We also consider pulse control and determine critical p values.

In the future, there are many more types of models that could be investigated, as well

as a variety of control schemes that could be investigated to further the application of these network models. One popular type of disease modeling to consider would be using delay differential equations to describe an latent period, and how the network mixing assumption affects these models. There were also some concepts in disease modeling that were not discussed in this thesis, such as disease mortality and a varying population size.

The stability analysis of this thesis can be improved upon, for instance, the stability of the endemic equilibria for each subsystem of the switched network model. The interest would be to find sufficient and necessary conditions that will cause the disease to persist, and what the endemic solution of a switched system is, whether it follows an oscillation between all i-th endemic equilibria, $i = 1, 2, ..., m$, or perhaps moves outside the convex hull of the endemic equilibria.

More theory could be expanded on the network mixing assumption, how this is modeled beyond the use of the Theta function that sums and averages the probability of transmission from an infected individual proportional to the number of links that a node has. Types of networks other than the scale-free network could be considered, such as a growing network with preferential attachment. In this thesis we considered networks that do not change over time, but one idea would be to investigate dynamic networks, where nodes and links are continually added or removed over time.

Another variation to consider is the flexibility of the switching signal. It would be of interest to investigate state-dependent switching, as opposed to time-dependent switching. That is, the parameters would change based on the values of the proportions of epidemiological compartments. This leads to another class of control schemes, considering the switching signal as a control and what are necessary conditions that the switching rule should have to achieve disease eradication. Some switching control ideas might be media coverage or other types of public disease awareness that will be implemented as a control strategy to reduce the transmission rate, dependent on time or the state of the system.

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