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Analysis and Simulation for Homogeneous and Heterogeneous SIR Models

Joseph Wilda
University of Central Florida

ANALYSIS AND SIMULATION FOR HOMOGENEOUS AND HETEROGENEOUS SIR MODELS

by

JOSEPH WILDA
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ABSTRACT

In mathematical epidemiology, disease transmission is commonly assumed to behave in accordance with the law of mass action; however, other disease incidence terms also exist in the literature. A homogeneous Susceptible-Infectious-Removed (SIR) model with a generalized incidence term is presented along with analytic and numerical results concerning effects of the generalization on the global disease dynamics. The spatial heterogeneity of the metapopulation with nonrandom directed movement between populations is incorporated into a heterogeneous SIR model with nonlinear incidence. The analysis of the combined effects of the spatial heterogeneity and nonlinear incidence on the disease dynamics of our model is presented along with supporting simulations. New global stability results are established for the heterogeneous model utilizing a graph-theoretic approach and Lyapunov functions. Numerical simulations confirm nonlinear incidence gives raise to rich dynamics such as synchronization and phase-lock oscillations.

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CHAPTER 1: INTRODUCTION

In mathematical epidemiology, disease transmission is commonly assumed to behave in accordance with the law of mass action, however other disease incidence terms also exist in the literature. Hethcote and van den Driessche [9] investigated a Susceptible - Exposed - Infectious - Removed - Susceptible (SEIRS) model with vital dynamics and a generalized nonlinear incidence term of the form $\beta g(I)S$ along with a delayed SIRS (Susceptible-Infectious-Removed-Susceptible) model with vital dynamics. They gave specific results concerning the stability of the disease-free equilibrium and endemic equilibria in the case that $g(I) = I^p/(1 + \alpha I^p)$. Li et. al. [12] applied a similar generalized nonlinear incidence term to an SEIR model. Conditions were established for the uniqueness and stability of the endemic equilibrium. A variety of epidemiological models (i.e. SIS, SIR, SIRS, SEIS, SEIR and SEIRS) with a nonlinear incidence term of the form $\lambda I^p S^q$ was proposed by Liu et. al. [15], [16]. The analysis was carried out rigorously to show the rich dynamics when varying the exponent p.

Once a model for a homogeneous environment is proposed, the next logical step is to investigate how the interaction between neighboring populations affect the course of a disease. Arino and van den Driessche in [3] proposed an SIS model for modeling multi-city epidemics in a constant population society. A multi-patch model was constructed by Wang and Zhao [20] in which they incorporated demographics into a society with varying population sizes. The dynamics of a different SIS epidemic patch model was developed in Allen et. al. [1]. They were able to demonstrate that if both susceptible and infected are allowed to freely move between patches, then both patches will reach an endemic state. If only infected are allowed to travel, then the disease dies out in both patches. The endemic equilibrium for a multi-patch SIR model was shown to be globally asymptotically stable in the paper by Li and Shuai [13]. This was accomplished using Lyapunov functions in conjunction with a graph-theoretic approach developed by Li and Shuai

[14]. Different forms of incidence functions were used in each of the papers discussed above.

In this thesis, a homogeneous Susceptible-Infectious-Removed (SIR) model with a generalized incidence term is presented along with analytic and numerical results concerning the effects of the generalization on the global disease dynamics. The basic reproduction number $\mathcal{R}_0$ is derived. The disease-free equilibrium (DFE) is defined and shown to be globally asymptotically stable when $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$. The existence of a unique endemic equilibrium is proven when $\mathcal{R}_0 > 1$ and a theorem is given for the globally asymptotic stability of the endemic equilibrium. Two cases for commonly used incidence terms βSI and $\beta SI/(\alpha + I)$ are presented and shown to have a globally asymptotically stable endemic equilibrium when $\mathcal{R}_0 > 1$. An example of the incidence term βSI^2 is presented as a case for the existence of multiple endemic equilibria, thus failing the assumptions in the global stability theorem. Simulations of this case are used to show the bistability as well as the co-existence of two stable limit cycles surrounding an endemic equilibrium.

The spatial heterogeneity of the metapopulation with nonrandom directed movement between populations is incorporated into the homogeneous SIR model with nonlinear incidence. The analysis of the combined effects of the spatial heterogeneity and nonlinear incidence on the disease dynamics is presented along with supporting simulations. New global stability results (Theorems 3.7.1 and 3.7.2) are established for the endemic equilibrium of the heterogeneous model utilizing a graph-theoretic approach and Lyapunov functions. Numerical simulations confirm nonlinear incidence raises rich dynamics such as synchronization and phase-lock oscillations.

CHAPTER 2: A HOMOGENEOUS SIR MODEL WITH NONLINEAR INCIDENCE

A homogeneous SIR model using a generalized incidence term is proposed in Section 2.1. The disease-free equilibrium (DFE) is discussed in Section 2.2. In Section 2.3 we establish the feasible region and verify that the DFE is the unique equilibrium on the boundary of feasible region. The basic reproduction number $\mathcal{R}_0$ is derived in Section 2.4. Sections 2.5 and 2.6 establish the local and global stability of the DFE when $\mathcal{R}_0 > 1$. We present conditions for the existence of a unique endemic equilibrium in Section 2.7. In Section 2.8, we investigate the cases for global stability and uniqueness of the endemic equilibrium, and provide examples for the cases of multiple endemic equilibria.

2.1 Basic Model

We review an SIR model with the generalized incidence term $\beta S f(I)$, in addition we included demographic terms for population dynamics. The model we will analyze is as follows

$$S' = \Lambda - \beta S f(I) - d^S S, \tag{2.1}$$

$$I' = \beta S f(I) - (d^I + \gamma) I, \tag{2.2}$$

$$R' = \gamma I - d^R R, \tag{2.3}$$

where $\Lambda > 0$ is the number of births during the period of the disease, $\beta > 0$ is the contact coefficient, d^S, d^I, d^R are the compartment specific death rates all greater than zero, and $\gamma > 0$ is the average recovery rate of an infected individual. Of course S, I and R are the populations for each respective compartment. We require that $f(I)$ be $C^1(0, \infty)$, and assume throughout that

$f(I) \geq 0$ and $f(I) = 0$ if and only if $I = 0$. Our analysis will be focusing on the following reduced system (2.4), which is comprised only of Equations (2.1) and (2.2). We leave (2.3) out since it can be considered completely determined once I is known.

$$\begin{aligned} S' &= \Lambda - \beta S f(I) - d^S S, \\ I' &= \beta S f(I) - (d^I + \gamma) I. \end{aligned} \tag{2.4}$$

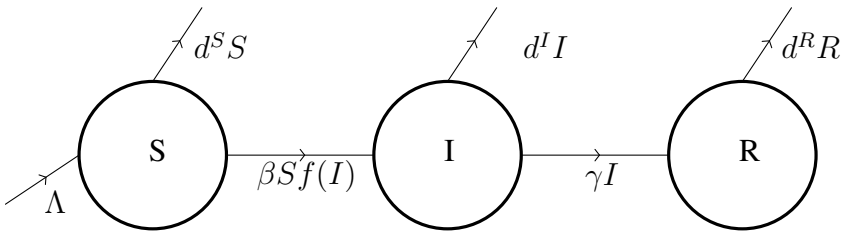


Figure 2.1: Homogeneous model flow diagram.

2.2 Disease-Free Equilibrium

Letting $S' = I' = 0 = I$, we get that $\Lambda = \beta S f(0) + d^S S$ from (2.1) and (2.2). Since $f(0) = 0$, then $S = \Lambda / d^S$. Let $S^0 := \Lambda / d^S$ and the unique disease-free equilibrium is $P^0 = (S^0, I^0)$.

2.3 Feasible Region

To establish the feasible region for our model we define $N = S + I$, where N is the total population of the people in the compartments. Let $d^* = \min\{d^S, d^I + \gamma\}$ and adding the two Equations in

(2.4) together yields

$$\begin{aligned} N' &= S' + I' \\ &= \Lambda - d^S S - (d^I + \gamma) I \\ &\leq \Lambda - d^*(S + I) = \Lambda - d^* N. \end{aligned}$$

Solving the right hand side of the last inequality, we get that $N(t) \leq \Lambda/d^* - ce^{-d^* t}$ where c is a constant depending on the initial conditions. Taking the $\limsup$ of both sides as $t \to \infty$ we get $\limsup_{t\to\infty} N(t) \leq \Lambda/d^*$. Looking further at our equation for S' we see that $\Lambda - \beta S f(I) - d^S S \leq \Lambda - d^S S$ and can achieve similar results namely, $\limsup_{t\to\infty} S(t) \leq S^0$. We can say something more, $S' \leq \Lambda - d^S S = d^S(S^0 - S)$, then if $S^0 \leq S = \Lambda/d^S$ then $S' \leq 0$ else we know it is bounded above by some positive number. The feasible region is defined as

$$\Gamma = \{(S, I) \in \mathbb{R}^2_+ \mid S + I \leq \Lambda/d^*, S \leq S^0\}.$$

From [21] and [8] we have that a region is positively invariant with respect to a system if the trajectories remain in that region for all time. Additionally it can be shown that the feasible region Γ is positively invariant with respect to the system (2.4) by a similar method used in the proof of Lemma 4.1 in [8].

2.4 Basic Reproduction Number

The basic reproduction number represents the average number of secondary infections resulting from the placement of a single infectious agent within an entirely susceptible population over the period the individual is infected, [6, Ch. 2] (also see [2]). It is also a threshold value, meaning that we expect to see at least two different behaviors when the basic reproduction number is below

or exceeds the threshold value 1. We will use the next generation method described in van den Driessche and Watmough [18] for deriving the basic reproduction number. Beginning by taking the Jacobian with respect to I of the Equation (2.2) and evaluating the result at the DFE. From [18] we split $J(I')\Big|_{(S^0,0)} = \beta S^0 f'(0) - (d^I + \gamma)$ into $F - V$, where F represents the rate of new infections appearing in the infectious compartment and V is comprised of all other terms representing transfers in or out of the infectious compartment. From Equation (4) in [18] we have the following definition for the basic reproduction number $\mathcal{R}_0 = \rho(FV^{-1})$ where ρ is the spectral radius. Solving for V^{-1}, we have that the basic reproduction number of (2.4) is

$$\mathcal{R}_0 \;=\; FV^{-1} = \frac{\beta S^0 f'(0)}{(d^I + \gamma)},$$

since F and V are scalars.

2.5 Local Asymptotic Stability of DFE

By Theorem 2 of van den Driessche and Watmough [18], if $\mathcal{R}_0 < 1$ then we have a locally asymptotically stable equilibrium point and unstable when $\mathcal{R}_0 > 1$. From this result we have the following proposition.

Proposition 2.5.1. *If $\mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable. If $\mathcal{R}_0 > 1$, then the DFE is unstable.*

2.6 Global Asymptotic Stability of DFE

Theorem 2.6.1. *Assume that $0 \leq f(I) \leq I f'(0)$ and $f(I) = 0$ iff $I = 0$. If $\mathcal{R}_0 < 1$, then the DFE is globally asymptotically stable in the feasible region Γ.*

Proof. Let $L = I$ as defined above. We differentiate it with respect our system in Γ to get

$$\begin{aligned} L' &= I' \\ &= (\beta S f(I) - (d^I + \gamma)I) \\ &\leq (\beta S^0 f(I) - (d^I + \gamma)I) \\ &= (d^I + \gamma)\left(\frac{\beta S^0 f(I)}{(d^I + \gamma)} - \frac{I f'(0)}{f'(0)}\right) \\ &= \frac{(d^I + \gamma)}{f'(0)}\left(\frac{\beta S^0 f'(0) f(I)}{(d^I + \gamma)} - I f'(0)\right) \\ &\leq \frac{(d^I + \gamma)}{f'(0)}\left(f(I) - I f'(0)\right). \end{aligned}$$

By assumption $f(I) \leq I f'(0)$, $L' \leq 0$, implying that the function L is a Lyapunov function of the system. When $L' = 0$ it implies that $0 = \beta(S - S^0)f(I)$ thus $S = S^0$ or $f(I) = 0$. Focusing on $S = S^0$ for the moment, we get that $0 = \Lambda - \beta S^0 f(I) - d^S S^0$ from (2.4) and thus $f(0) = 0$. Since $f(I) = 0$ iff $I = 0$, this tells us that P^0 is the only invariant subset. By LaSalle's Invariance Principle [10] (see also [19]), P^0 is globally asymptotically stable in Γ. □

2.7 Existence of Endemic Equilibrium

Theorem 2.7.1. *If $\mathcal{R}_0 > 1$ then there exists at least one endemic equilibrium $P^* = (S^*, I^*)$ in the interior of Γ.*

Proof. Letting S' and I' in system (2.4) be equal to zero we get

$$0 = \Lambda - \beta S f(I) - d^S S, \tag{2.5}$$

$$0 = \beta S f(I) - (d^I - \gamma)I. \tag{2.6}$$

Taking equation (2.6) we find that $S = \frac{(d^I+\gamma)I}{\beta f(I)}$. Substituting this value for S into (2.5) gets us

$$\Lambda - (d^I + \gamma)I = \frac{d^S(d^I + \gamma)I}{\beta f(I)}.$$

Define the auxiliary function $G(I)$ as follows

$$G(I) = \Phi(I) - \Psi(I) = (\Lambda - (d^I + \gamma)I) - \left(\frac{d^S(d^I + \gamma)I}{\beta f(I)}\right).$$

From the definition of the feasible region we have that $0 < I < \Lambda/d^*$. Then

$$\begin{aligned}
\lim_{I\to 0} G(I) &= \lim_{I\to 0} \Phi(I) - \lim_{I\to 0} \Psi(I) \\
&= \Lambda - \frac{d^S(d^I + \gamma)}{\beta f'(0)} \\
&= \Lambda\left(1 - \frac{d^S(d^I + \gamma)}{\Lambda\beta f'(0)}\right) \\
&= \Lambda\left(1 - \frac{1}{\mathcal{R}_0}\right) > 0,
\end{aligned}$$

and

$$\begin{aligned}
G\left(\frac{\Lambda}{d^*}\right) &= \Phi\left(\frac{\Lambda}{d^*}\right) - \Psi\left(\frac{\Lambda}{d^*}\right) \\
&= \Lambda - (d^I + \gamma)\frac{\Lambda}{d^*} - \frac{d^S(d^I + \gamma)}{\beta}\frac{\Lambda}{d^* f(\Lambda/d^*)} \\
&= \Lambda\left(1 - \frac{(d^I + \gamma)}{d^*}\right) - \frac{d^S(d^I + \gamma)}{\beta}\frac{\Lambda}{d^* f(\Lambda/d^*)} < 0.
\end{aligned}$$

Thus by the Intermediate Value Theorem there exists a $c \in [0, \Lambda/d^*]$ such that $G(c) = 0$ and hence there exists at least one endemic equilibrium for system (2.4). □

2.8 Stability of Endemic Equilibrium

In this section we assume that $\mathcal{R}_0 > 1$. Then by Theorem 2.7.1, there exists an endemic equilibrium for system (2.4), denoted by $P^* = (S^*, I^*)$.

2.8.1 Cases for Global Stability

Theorem 2.8.1. *Assume that $\mathcal{R}_0 > 1$ and $(f(I) - f(I^*))\left(\frac{f(I)}{I} - \frac{f(I^*)}{I^*}\right) \leq 0$. Then the endemic equilibrium $P^* = (S^*, I^*)$ for* (2.4) *is unique and globally asymptotically stable in the interior of* Γ.

Proof. Evaluating (2.4) at P^* we get

$$\begin{aligned} \Lambda &= \beta S^* f(I^*) + d^S S^*, \\ \beta S^* f(I^*) &= (d^I + \gamma) I^*. \end{aligned}$$

We will use the following fact $n\sqrt{\Pi_i^n a_i} - \sum_{i=1}^n a_i \leq 0$ for $a_i \geq 0$. We define $V = S - S^* - S^* \ln\left(\frac{S^*}{S}\right) + I - I^* - I^* \ln\left(\frac{I^*}{I}\right)$, then taking the derivative of V with respect to system (2.4) we get

$$\begin{aligned} V' &= S' - \frac{S^*}{S} S' + I' - \frac{I^*}{I} I' \\ &= (\beta S^* f(I^*) + d^S S^*) - d^S S - (\beta S^* f(I^*) + d^S S^*)\frac{S^*}{S} \\ &\quad + \beta S^* f(I) + d^S S - \left(\frac{\beta S^* f(I^*)}{I^*}\right) I - \beta S f(I) \frac{I^*}{I} + \beta S^* f(I^*) \end{aligned}$$

$$
\begin{aligned}
&= 2\beta S^* f(I^*) + 2d^S S^* - d^S S - d^S S^* \frac{S^*}{S} + \beta S^* f(I) \\
&\quad -\beta S^* f(I^*) \frac{S^*}{S} - \beta S^* f(I^*) \frac{I}{I^*} - \beta S f(I) \frac{I^*}{I} \\
&\leq \beta S^* f(I^*) \left(3 - 1 + \frac{f(I)}{f(I^*)} - \frac{S^*}{S} - \frac{I}{I^*} \right. \\
&\quad \left. - \frac{S f(I) I^*}{S^* f(I^*) I} - \frac{f(I^*) I}{f(I) I^*} + \frac{f(I^*) I}{f(I) I^*} \right) \\
&\leq \beta S^* f(I^*) \left(\frac{f(I)}{f(I^*)} - 1 \right) \left(1 - \frac{f(I^*) I}{f(I) I^*} \right) \\
&= \frac{\beta S^* I}{f(I)} \left(f(I) - f(I^*) \right) \left(\frac{f(I)}{I} - \frac{f(I^*)}{I^*} \right) \leq 0. \qquad (2.7)
\end{aligned}
$$

Thus, by assumption, we have that $V' \leq 0$, hence V is a Lyapunov function for system (2.4). If $V' = 0$, then $S = S^*$ and $f(I)/f(I^*) = I/I^*$. Applying $S = S^*$ to the first equation in (2.4) we get

$$
\begin{aligned}
0 = S' &= \Lambda - \beta S^* f(I) - d^S S^* \\
&= -\beta S^* (f(I) - f(I^*)),
\end{aligned}
$$

implying that $f(I) = f(I^*)$. Hence, $I/I^* = f(I)/f(I^*) = 1$. The only invariant set that makes $V' = 0$ is $\{P^*\}$, thus by LaSalle's Invariance Principle [10], P^* is globally asymptotically stable and unique. □

We will look at two cases for $f(I)$, i.e. $f(I) = I$ and $f(I) = I/(\alpha + I)$, and show that system (2.4) satisfies the conditions for Theorem 2.8.1 and thus the endemic equilibrium is globally asymptotically stable and unique.

Proposition 2.8.2. *If $f(I) = I$ and $\mathcal{R}_0 = \frac{\beta S_0}{d^I + \gamma} > 1$, then the endemic equilibrium P^* of system* (2.4) *is globally asymptotically stable and hence unique.*

Proof. If $f(I) = I$ then

$$(f(I) - f(I^*)) \left(\frac{f(I)}{I} - \frac{f(I^*)}{I^*} \right) = (I - I^*) \left(\frac{I}{I} - \frac{I^*}{I^*} \right) = 0,$$

satisfying the inequality in Theorem 2.8.1. □

Proposition 2.8.3. *If* $f(I) = \frac{I}{\alpha+I}$ *and* $\mathcal{R}_0 = \frac{\beta S_0}{\alpha(d^I+\gamma)} > 1$*, then the endemic equilibrium* P^* *of system* (2.4) *is globally asymptotically stable and hence unique.*

Proof. If $f(I) = \frac{I}{\alpha+I}$ then

$$\begin{aligned}
(f(I) - f(I^*)) \left(\frac{f(I)}{I} - \frac{f(I^*)}{I^*} \right) &= \left(\frac{I}{\alpha + I} - \frac{I^*}{\alpha + I^*} \right) \left(\frac{1}{\alpha + I} - \frac{1}{\alpha + I^*} \right) \\
&= \left(\frac{(I - I^*)\alpha}{(\alpha + I)(\alpha + I^*)} \right) \left(\frac{I^* - I}{(\alpha + I)(\alpha + I^*)} \right) \\
&= \frac{\alpha(I - I^*)(I^* - I)}{(\alpha + I)^2(\alpha + I^*)^2} \\
&\leq 0.
\end{aligned}$$

satisfying the inequality in Theorem 2.8.1. □

2.8.2 Cases for Failure of Global Stability

In the event that the conditions assumed in Theorem 2.8.1 are not satisfied, then the endemic equilibrium need not be unique and hence not globally asymptotically stable. We look at the equilibrium for the special case $f(I) = I^2$. From Equation (2.2), setting $S' = 0$ and solving for I gives us

$$I = \frac{(d^I + \gamma)}{\beta S}. \tag{2.8}$$

Taking (2.1), we get $I^2 = (\Lambda - d^S S)/(\beta S)$. Substituting (2.8) into the equation for I^2, we arrive at a quadratic equation in S

$$\beta d^s S^2 - \beta \Lambda S + (d^I + \gamma)^2 \;\; = \;\; 0. \tag{2.9}$$

Theorem 2.8.4. *Let* $f(I) = I^2$ *and* $\omega = 4d^S(d^I + \gamma)^2/(\Lambda^2\beta)$.

1. *If* $\omega < 1$, *then system* (2.4) *has two positive endemic equilibria.*
2. *If* $\omega = 1$, *then system* (2.4) *has one positive endemic equilibrium.*
3. *if* $\omega > 1$, *then system* (2.4) *has no endemic equilibrium.*

Proof. Letting $\Delta = \Lambda^2\beta^2 - 4d^S\beta(d^I + \gamma)^2$, factoring out $\Lambda^2\beta^2$ from Δ, we get

$$\begin{aligned} \Delta &= \Lambda^2\beta^2 - 4d^S\beta(d^I + \gamma)^2 \\ &= \Lambda^2\beta^2 \left(1 - \frac{4d^S(d^I + \gamma)^2}{\Lambda^2\beta}\right) \\ &= \Lambda^2\beta^2(1 - \omega). \end{aligned} \tag{2.10}$$

Thus from (2.9) and (2.10), have

$$\begin{aligned} S &= \frac{\Lambda\beta \pm \sqrt{\Lambda^2\beta^2(1-\omega)}}{2d^S\beta} \\ &= \frac{\Lambda\beta \pm \Lambda\beta\sqrt{1-\omega}}{2d^S\beta} \\ &= \frac{\Lambda}{2d^S} \pm \frac{\Lambda}{2d^S}\sqrt{1-\omega}. \end{aligned}$$

Thus, for $\omega < 1$ we have two positive endemic equilibria since $\frac{\Lambda}{2d^S}\sqrt{1-\omega} < \frac{\Lambda}{2d^S}$. When $\omega = 1$, we have one endemic equilibrium $S = \Lambda/(2d^S)$, and when $\omega > 1$, we have no positive endemic equilibrium. □

CHAPTER 3: A HETEROGENEOUS SIR MODEL WITH NONLINEAR INCIDENCE

A heterogeneous SIR model is proposed in Section 3.1 that incorporates spatial heterogeneity and directed nonrandom movement. The disease-free equilibrium, feasible region, and the basic reproduction number $\mathcal{R}_0$ are derived for the heterogeneous model in Sections 3.2-3.4. The stability of the DFE, both locally and globally, is established in Section 3.5. The existence of the endemic equilibrium is established in Section 3.6. Two theorems are proved in Section 3.7 for establishing the global stability of the endemic equilibrium for the heterogeneous model.

3.1 Patch Model

We begin with a construction of a flow chart of the behavior we wish to model, see Figure 3.1. The indicated figure shows only two such patches, but we will analyze the n-patch case. With Figure 3.1 guiding us, we now define our n-patch SIR model as follows

$$S_i' = \Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i + \sum_{j=1}^{n} a_{ij} S_j - \sum_{j=1}^{n} a_{ji} S_i, \tag{3.1}$$

$$I_i' = \beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i, \tag{3.2}$$

$$R_i' = \gamma_i I_i - d_i^R R_i + \sum_{j=1}^{n} c_{ij} R_j - \sum_{j=1}^{n} c_{ji} R_i. \tag{3.3}$$

Here β_i is the contact coefficient of the disease in question, Λ_i is the number of births during the period of the disease, γ_i is the recovery rate of an infected individual, and d_i^S, d_i^I, and d_I^R are the compartmental death rates in the i^{th} patch. The populations for the susceptible, infectious, and recovered compartments for patch i are denoted by S_i, I_i and R_i respectively, with the corresponding

nonnegative transfer matrices denoted as $A = [a_{ij}]$, $B = [b_{ij}]$ and $C = [c_{ij}]$ with (i, j) entry representing movement from patch j to patch i. We will require that $f(I_i)$ be nonnegative for all $I \geq 0$ and f to be at least C^1. We also require β_i, γ_i, d^S, d^I, d^R, and Λ_i to be positive. As for the system (2.4) in Chapter 1, we will be focusing on a reduced system

$$\begin{aligned} S_i' &= \Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i + \sum_{j=1}^{n} a_{ij} S_j - \sum_{j=1}^{n} a_{ji} S_i, \\ I_i' &= \beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i. \end{aligned} \tag{3.4}$$

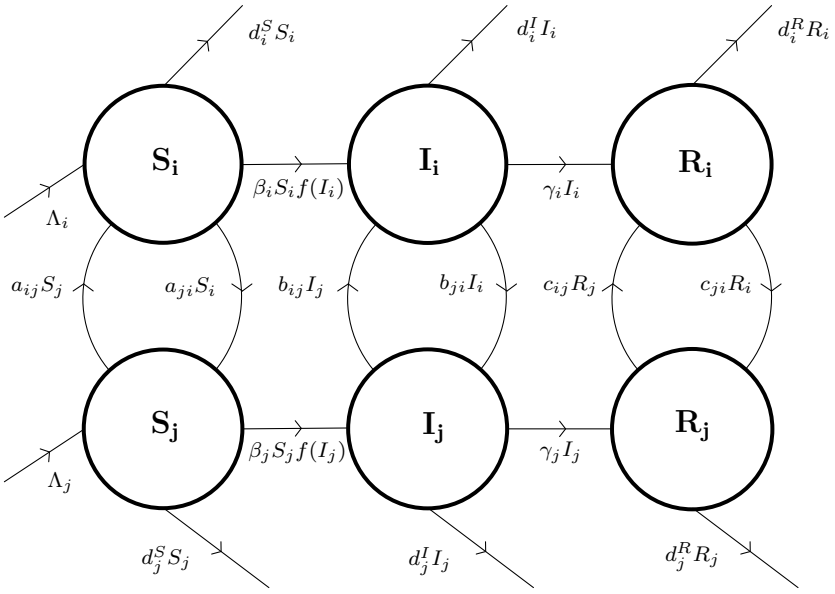


Figure 3.1: Heterogeneous model flow diagram.

3.2 Disease-Free Equilibrium

We set S_I' and I_i' equal to zero and we also assume that there are no infectious people in the population so $I_i = 0$. This gives us that (3.2) is identically equal to zero if $f(0) = 0$. Assuming

this, we get the following from (3.1):

$$0 \;=\; \Lambda_i - d_i^S S_i + \sum_{j=1}^{n} a_{ij} S_j - \sum_{j=1}^{n} a_{ji} S_i.$$

Hence,

$$\Lambda_i \;=\; \left(d_i^S + \sum_{j=1}^{n} a_{ji} \right) S_i - \sum_{j=1}^{n} a_{ij} S_j.$$

Let $\Lambda = (\Lambda_1, \Lambda_2, \ldots, \Lambda_n)$ and $S = (S_1, S_2, \ldots, S_n)$, we arrive at

$$\Lambda \;=\; \begin{bmatrix} d_1^S + \sum_{j\neq 1}^{n} a_{j1} & -a_{12} & \ldots & -a_{1n} \\ -a_{21} & d_2^S + \sum_{j\neq 2}^{n} a_{j2} & \ldots & -a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{n1} & -a_{n2} & \ldots & d_n^S + \sum_{j\neq n}^{n} a_{jn} \end{bmatrix} S.$$

Defining

$$D \;=\; \begin{bmatrix} d_1^S + \sum_{j\neq 1}^{n} a_{j1} & -a_{12} & \ldots & -a_{1n} \\ -a_{21} & d_2^S + \sum_{j\neq 2}^{n} a_{j2} & \ldots & -a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{n1} & -a_{n2} & \ldots & d_n^S + \sum_{j\neq n}^{n} a_{jn} \end{bmatrix},$$

we can then write $\Lambda = DS$. From Theorem 2.3 in Berman and Plemmons [4] we have that D is a non-singular M-matrix. This follows from the theorem, since our matrix D is column diagonally dominant and hence non-singular. It is clear that adding any non-negative diagonal matrix to D will preserve the diagonal dominance and its non-singularity. Thus D^{-1} exists and is non-negative, $S = D^{-1}\Lambda \geq 0$, and define $S^0 = (S_1^0, S_2^0, \ldots, S_n^0) = D^{-1}\Lambda$. We then denote the DFE to be $P^0 = (S_1^0, 0, S_2^0, 0, \ldots, S_n^0, 0)$.

3.3 Feasible Region

Before we can define the feasible region, we need to define a few terms. Let $\overline{\Lambda} = \sum_{i=1}^{n}(\Lambda_i)$, $d^* = \min\{d_i^S, d_i^I+\gamma_i\}$, and $N = \sum_{i=1}^{n}(S_i+I_i)$, where N represents the total population influencing the disease dynamics. It follows that

$$\begin{aligned} N' &= \sum_{i=1}^{n}(S_i' + I_i') \\ &= \sum_{j=1}^{n}\left(\Lambda_i - d_i^S S_i - (d_i^I + \gamma_i)I_i\right) \\ &\leq \sum_{j=1}^{n}\Lambda_i - d^* \sum_{j=1}^{n}(S_i + I_i) \\ &= \overline{\Lambda} - d^S N. \end{aligned}$$

Solving the differential inequality we arrive at $N(t) \leq \overline{\Lambda}/d^* - ce^{-d^*t}$, this implies that the $\limsup_{t\to\infty} N(t) \leq \overline{\Lambda}/d^*$. It follows

$$\begin{aligned} S_i' &= \Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i + \sum_{j=1}^{n} a_{ij}S_j - \sum_{j=1}^{n} a_{ij}S_i \\ &\leq \Lambda_i - d_i^S S_i + \sum_{j=1}^{n} a_{ij}S_j - \sum_{j=1}^{n} a_{ij}S_i \\ &= \Lambda_i - \left(\left(d_i^S + \sum_{j=1}^{n} a_{ij}\right) S_i - \sum_{j=1}^{n} a_{ij}S_j\right) \\ &= (DS^0 - DS)_i. \end{aligned}$$

So $S_i' \leq 0$ if $S_i^0 \leq S_i$.

We call our feasible region Γ and define it as

$$\Gamma \;=\; \left\{ (S_1, I_1, \ldots, S_n, I_n) \in \mathbb{R}^{2n}_{+} \,\middle|\, \sum_{i=1}^{n} (S_i + I_i) \leq \frac{\overline{\Lambda}}{d^*}; S_i \leq S_i^0 \right\}.$$

Now, we need to verify that there do not exist any other equilibria on the boundary of Γ.

Theorem 3.3.1. *We assume that the movement matrix $B = [b_{ij}]$ is irreducible and that $I_i = 0$ for some $i = 1, \ldots, n$, then $I_j = 0$ for all $j \neq i$. It then follows P^0 is the only equilibrium point on the boundary of Γ.*

Proof. Let $I_i = 0$ for some i and $I_j \neq 0$ for all $j \neq i$ then (3.2) becomes

$$0 \;=\; \sum_{j \neq i}^{n} b_{ij} I_j, \tag{3.5}$$

if $b_{ij} > 0$ then $I_j = 0$. This tell us that if $I_i = 0$ and $b_{ij} > 0$, then $I_j = 0$ for some j. Using our irreducibility assumption on (b_{ij}), we know that there exists a path from I_i to I_j. Then applying (3.5) we see

$$0 \;=\; b_{ie_1} I_{e_1} + b_{e_1 e_2} I_{e_2} + \cdots + b_{e_{m-1} e_m} I_m + b_{e_m j} I_j,$$

which implies that

$$I_{e_1} = 0, I_{e_2} = 0, \ldots, I_m = 0.$$

We then have that $I_j = 0$ for all j, so when (b_{ij}) is irreducible and $I_i = 0$ for some i, then $I = 0$ for all I_i for $i = 1, \ldots, n$. Thus P^0 is the only equilibrium point on the boundary. □

3.4 Basic Reproduction Number

We will utilize the next generation method as described in the paper by van den Driessche and Watmough [18]. We take the derivative of (3.2) with respect to I_i and evaluate the result at the DFE,

$$J(I_i')\Big|_{P^0} = \begin{bmatrix} \beta_1 S_1^0 f'(0) - (d_1^I + \gamma_1) - \sum_{j\neq 1}^{n} b_{j1} & b_{12} & \dots & b_{1n} \\ b_{21} & \beta_2 S_2^0 f'(0) - (d_2^I + \gamma_2) - \sum_{j\neq 2}^{n} b_{j2} & \dots & b_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ b_{n1} & b_{n2} & \dots & \beta_n S_n^0 f'(0) - (d_n^I + \gamma_n) - \sum_{j\neq n}^{n} b_{jn} \end{bmatrix}.$$

Performing a splitting, we define the new disease matrix

$$F = \begin{bmatrix} \beta_1 S_1^0 f'(0) & 0 & \dots & 0 \\ 0 & \beta_2 S_2^0 f'(0) & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \beta_n S_n^0 f'(0) \end{bmatrix}$$

and disease transfer matrix

$$V = \begin{bmatrix} (d_1^I + \gamma_1) + \sum_{j\neq 1}^{n} b_{j1} & -b_{12} & \dots & -b_{1n} \\ -b_{21} & (d_2^I + \gamma_2) + \sum_{j\neq 2}^{n} b_{j2} & \dots & -b_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -b_{n1} & -b_{n2} & \dots & (d_n^I + \gamma_n) + \sum_{j\neq n}^{n} b_{jn} \end{bmatrix}.$$

Then the basic reproduction number is $\mathcal{R}_0 = \rho(FV^{-1})$, where F represents the rate of appearance of new infected individuals and V is comprised of the number of infected transferred between patches.

3.5 Stability of DFE

By Theorem 2 from van den Driessche and Watmough [18], we have that the DFE is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable otherwise. Furthermore, the following results show the DFE is globally asymptotically stable when $\mathcal{R}_0 < 1$.

Theorem 3.5.1. *Assume $\mathcal{R}_0 < 1$, $[b_{ij}]$ is irreducible, $0 \leq f(I_i) \leq f'(0)I_i$ and $f(I) = 0$ iff $I = 0$. Then the DFE is globally asymptotically stable in the interior of Γ and unique.*

Proof. We have that V is column diagonally dominant, then by similar reasoning used to establish that D is a non-singular m-matrix we have the V is a non-singular m-matrix as well. Thus $V^{-1} \geq 0$. From Theorem 1.3d in Plemmons and Berman [4], we have that V^{-1} is irreducible. Similarly, we can show that $V^{-1}F$ is irreducible, thus by Perron-Frobenius theorem, there exists a left eigenvector ω of $V^{-1}F$ that is strictly positive. The corresponding eigenvalue $\nu = \rho(V^{-1}F) = \rho(FV^{-1}) = \mathcal{R}_0$. We then have the following

$$\begin{aligned} \omega V^{-1}F &= \omega\mathcal{R}_0, \\ \frac{\omega}{\mathcal{R}_0} &= \omega F^{-1}V. \end{aligned}$$

Define $c_i = \omega_i/(\beta_i S_i^0 f'(0))$ and $L = \sum_{j=1}^{n} c_i I_i$. Taking the derivative of L with respect to t we get

$$\begin{aligned} L' &= \sum_{j=1}^{n} c_i I_i' \\ &= \sum_{j=1}^{n} c_i \left(\beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i \right) \\ &\leq \sum_{j=1}^{n} c_i \left(\beta_i S_i^0 f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i \right). \end{aligned}$$

Applying our assumption that $f(I_i) \leq f'(0)I_i$, we have

$$\begin{aligned} L' &\leq \sum_{j=1}^{n} c_i \left(\beta_i S_i^0 f'(0) I_i - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i \right) \\ &= c(F - V)I \\ &= (\omega - \omega F^{-1} V)I \\ &= \omega \left(1 - \frac{1}{\mathcal{R}_0} \right) I. \end{aligned}$$

Thus, $L' \leq 0$ when $\mathcal{R}_0 < 1$. Namely, L is a Lyapunov function of (3.1) & (3.2). If $L' = 0$, this implies that $S_i = S_i^0$ or $I_i = 0$. Assume that $S_i = S_i^0$. Looking back at (3.1) we get $\beta_i S_i^0 f(I_i) = 0$ which implies that $f(I_i) = 0$. Thus, the invariant set where $L' = 0$ is $\{P^0\}$. By LaSalle Invariance Principle [10], the DFE, P^0, is globally asymptotically stable. □

3.6 Existence of Endemic Equilibrium

Theorem 3.6.1. *If $\mathcal{R}_0 > 1$, then there exists at least one endemic equilibrium $P^* = (S_1^*, I_1^*, \ldots, S_n^*, I_n^*)$ for the system* (3.4) *in the interior of* Γ.

Proof. Take $c_i = \omega_i / (\beta_i S_I^0 f'(0))$ and $L = \sum_{j=1}^{n} c_i I_i$ as defined in the proof of Theorem 3.5.1. Then,

$$\begin{aligned} L' &= \sum_{j=1}^{n} c_i \left(\beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i \right) \\ &= \sum_{j=1}^{n} c_i \left(\left(\frac{\beta_i S_i f(I_i)}{I_i} - (d_i^I + \gamma_i) - \sum_{j=1}^{n} b_{ji} \right) I_i + \sum_{j=1}^{n} b_{ij} I_j \right) \\ &= c(\widetilde{F} - V)I. \end{aligned}$$

Here $\widetilde{F_{ij}} = \frac{\beta_i S_i f(I_i)}{I_i}$ when $i = j$, $\widetilde{F_{ij}} = 0$ for $i \neq j$, and $\lim_{(S_i,I_i)\to(S_i^0,0)} \widetilde{F} = F$. Taking the limit of L' we get

$$\begin{aligned}
\lim_{(S_i,I_i)\to(S_i^0,0)} L' &= \lim_{(S_i,I_i)\to(S_i^0,0)} c(\widetilde{F} - V)I \\
&= c(F - V) \lim_{(S_i,I_i)\to(S_i^0,0)} I \\
&= \omega \left(1 - \frac{1}{\mathcal{R}_0}\right) \lim_{(S_i,I_i)\to(S_i^0,0)} I \geq 0.
\end{aligned}$$

Thus, if $\mathcal{R}_0 > 1$, then $L' > 0$ for some neighborhood $N_\epsilon(P^0)$ about P^0. This implies P^0 is unstable and all trajectories that start close enough to the DFE will leave $N_\epsilon(P^0)$. Hence the system (3.4) is uniformly persistent by [7, Theorem 4.3] and a similar argument in [11, Proposition 3.3]. Uniform persistence and uniform boundedness of solutions in the interior of Γ implies the existence of at least one endemic equilibrium (see Theorem D.3 in [17] or Theorem 2.8.6 in [5]). □

3.7 Stability of Endemic Equilibrium

Theorem 3.7.1. *Assume that* $[a_{ij}] = 0$, $[b_{ij}]$ *is irreducible, and* $(f(I_i) - f(I_i^*)) \left(\frac{f(I_i)}{I_i} - \frac{f(I_i^*)}{I_i^*}\right) \leq 0$. *If* $\mathcal{R}_0 > 1$, *then the endemic equilibrium* P^* *of system* (3.4) *is globally asymptotically stable and unique in the interior of* Γ.

Proof. Evaluating system (3.4) at P^* gives us,

$$\begin{aligned}
\Lambda_i &= \beta_i S_i^* f(I^*) + d_i^S S^*, \\
(d_i^I + \gamma_i) &= \frac{\beta_i S_i^* f(I_i^*)}{I_i^*} + \sum_{j=1}^{n} b_{ij} \frac{I_j^*}{I_i^*} - \sum_{j=1}^{n} b_{ji}.
\end{aligned}$$

We will utilize $n\sqrt{\Pi_i^n x_i} - \sum_{i=1}^n x_i \leq 0$ for $x_i \geq 0$ and $1 - x + \ln(x) \leq 0$ for $x > 0$. Let

$V_i = S_i - S_i^* - S_i^* \ln\left(\frac{S_i^*}{S_i}\right) + I_i - I_i^* - I_i^* \ln\left(\frac{I_i^*}{I_i}\right)$, differentiating with respect to (3.4) we get,

$$\begin{aligned}
V_i' &= \Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i - \frac{S_i^*}{S_i}\left(\Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i\right) \\
&\quad + \beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i \\
&\quad - \frac{I_i^*}{I_i}\left(\beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i + \sum_{j=1}^{n} b_{ij} I_j - \sum_{j=1}^{n} b_{ji} I_i\right) \\
&= d_i^S S_i^* \left(2 - \frac{S_i}{S_i^*} - \frac{S_i^*}{S_i}\right) \\
&\quad + \beta_i S_i^* f(I_i^*) \left(2 - \frac{S_i^*}{S_i} + \frac{f(I_i)}{f(I_i^*)} - \frac{I_i}{I_i^*} - \frac{S_i f(I_i) I_i^*}{S_i^* f(I_i^*) I_i}\right) \\
&\quad + \sum_{j=1}^{n} b_{ij} I_j^* \left(\frac{I_j}{I_j^*} - \frac{I_i}{I_i^*} - \frac{I_j I_i^*}{I_j^* I_i} + 1\right) \\
&\leq \beta_i S_i^* f(I_i^*) \left(2 - \frac{S_i^*}{S_i} + \frac{f(I_i)}{f(I_i^*)} - \frac{I_i}{I_i^*} - \frac{S_i f(I_i) I_i^*}{S_i^* f(I_i^*) I_i}\right) \\
&\quad + \sum_{j=1}^{n} b_{ij} I_j^* \left(\frac{I_j}{I_j^*} - \frac{I_i}{I_i^*} - \frac{I_j I_i^*}{I_j^* I_i} + 1\right) \\
&\leq \sum_{j=1}^{n} b_{ij} I_j^* \left(\left[\frac{I_j}{I_j^*} - \ln\left(\frac{I_j}{I_j^*}\right)\right] - \left[\frac{I_i}{I_i^*} - \ln\left(\frac{I_i}{I_i^*}\right)\right]\right) \\
&= \sum_{j=1}^{n} b_{ij} I_j^* \left(H_j(I_j) - H_i(I_i)\right),
\end{aligned}$$

where $H_i(I_i) = \frac{I_i}{I_i^*} - \ln\left(\frac{I_i}{I_i^*}\right)$. We define the weighted digraph $\mathcal{D}$ with the associated weight matrix $\mathcal{W}$ as the ordered pair $(\mathcal{D}, \mathcal{W})$ and let entries $(w_{ij}) = b_{ij} I_j^*$. Furthermore we define $c_i = \sum_{\mathcal{T} \in \mathbb{T}} w(\mathcal{T}) \geq 0$, then by Theorem 2.3 in [14], we have the following:

$$\sum_{i=1, j=1}^{n} c_i b_{ij} I_j^* \left(H_j(I_j) - H_i(I_i)\right) = 0.$$

We then define $V(S_1, I_1, \ldots, S_n, I_n) = \sum_{i=1}^{n} c_i V_i(S_i, I_i)$, with $c_i > 0$ if $(\mathcal{D}, \mathcal{W})$ is irreducible,

giving us that

$$\begin{aligned} V' &= \sum_{i=1}^{n} c_i V_i'(S_i, I_i) \\ &\leq \sum_{i=1}^{n} c_i \left(\sum_{j=1}^{n} b_{ij} I_j^* \left(H_j(I_j) - H_i(I_i) \right) \right) \\ &= 0 \end{aligned}$$

for all $(S_1, I_1, S_2, I_2, \ldots, S_n, I_n) \in \Gamma$, thus V is a Lyapunov function for system (3.4). Since we have that B is irreducible, then c_i is irreducible, and thus $c_i > 0$ for all i. Thus, $V' = 0$ implies that $S_i = S_i^*$ and $f(I_i)/f(I_i^*) = I_i/I_i^*$ for all i. Substituting S_i^* for S_i in (3.1), we get that

$$0 \quad = (S_i)' = (S_i^*)' = \Lambda_i - \beta_i S_i^* f(I_i^*) - d_i^S S_i^* + \textstyle\sum_{j=1}^{n} a_{ij} S_j^* - \sum_{j=1}^{n} a_{ji} S_i^*$$

implying that $f(I_i^*) = f(I_i)$ for all i. Hence, $I_i/I_i^* = f(I_i)/f(I_i^*) = 1$. The only invariant set that makes $V' = 0$ is $\{P^*\}$, thus by LaSalle Invariance Principle [10], P^* is globally asymptotically stable and unique. □

Theorem 3.7.2. *Assume* $[b_{ij}] = 0$, $[a_{ij}]$ *is irreducible, and* $(f(I_i) - f(I_i^*)) \left(\frac{f(I_i)}{I_i} - \frac{f(I_i^*)}{I_i^*} \right) \leq 0$. *If* $\mathcal{R}_0 > 1$, *then the endemic equilibrium* P^* *of system* (3.4) *is unique and globally asymptotically stable in the interior of* Γ.

Proof. Evaluating system (3.4) at P^* gives us,

$$\begin{aligned} d_i^S &= \frac{\Lambda_i}{S_i^*} - \frac{\beta_i S_i^* f(I^*)}{S_i^*} + \sum_{j=1}^{n} a_{ij} \frac{S_j^*}{S_i^*} - \sum_{j=1}^{n} a_{ji}, \\ (d_i^I + \gamma_i) &= \frac{\beta_i S_i^* f(I_i^*)}{I_i^*}. \end{aligned}$$

We will utilize $n\sqrt{\Pi_i^n x_i} - \sum_{i=1}^{n} x_i \leq 0$ for $x_i \geq 0$ and $1 - x + \ln(x) \leq 0$ for $x > 0$. Let

$V_i = S_i - S_i^* - S_i^* \ln\left(\frac{S^*}{S}\right) + \int_{I_i^*}^{I_i} \frac{f(\xi)-f(I_i^*)}{f(\xi)} d\xi$, differentiating with respect to (3.4) we get,

$$\begin{aligned}
V_i' &= \Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i + \sum_{j=1}^{n} a_{ij} S_j - \sum_{j=1}^{n} a_{ji} S_i \\
&\quad -\frac{S_i^*}{S_i}\left(\Lambda_i - \beta_i S_i f(I_i) - d_i^S S_i + \sum_{j=1}^{n} a_{ij} S_j - \sum_{j=1}^{n} a_{ji} S_i\right) \\
&\quad +\beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i - \frac{f(I_i^*)}{f(I_i)}\left(\beta_i S_i f(I_i) - (d_i^I + \gamma_i) I_i\right) \\
&= \Lambda_i \left(2 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\right) \\
&\quad +\beta_i S_i^* f(I_i^*)\left(\frac{f(I_i)}{f(I_i^*)} - 1 - \frac{I_i}{I_i^*} + \frac{f(I_i^*) I_i}{f(I_i) I_i^*}\right) \\
&\quad +\sum_{j=1}^{n} a_{ij} S_j^* \left(\frac{S_j}{S_j^*} + 1 - \frac{S_i}{S_i^*} - \frac{S_j S_i^*}{S_i S_j^*}\right) \\
&\leq \sum_{j=1}^{n} a_{ij} S_j^* \left(\left[\frac{S_j}{S_j^*} - \ln\left(\frac{S_j}{S_j^*}\right)\right] - \left[\frac{S_i}{S_i^*} - \ln\left(\frac{S_i}{S_i^*}\right)\right]\right) \\
&= \sum_{j=1}^{n} a_{ij} S_j^* \left(K_j(S_j) - K_i(S_i)\right),
\end{aligned}$$

where $K_i(S_i) = \frac{S_i}{S_i^*} - \ln\left(\frac{S_i}{S_i^*}\right)$. We define the weighted digraph $\mathcal{D}$ with the associated weight matrix $\mathcal{W}$ as the ordered pair $(\mathcal{D}, \mathcal{W})$ and let entries $(w_{ij}) = a_{ij} S_j^*$. Furthermore, we define $c_i = \sum_{\mathcal{T}\in\mathbb{T}} w(\mathcal{T}) \geq 0$, then by Theorem 2.3 in [14] we have

$$\sum_{i=1,j=1}^{n} c_i a_{ij} S_j^* \left(K_j(S_j) - K_i(S_i)\right) = 0.$$

We then define $V(S_1, I_1, S_2, I_2, \ldots, S_n, I_n) = \sum_{i=1}^{n} c_i V_i(S_i, I_i)$, with $c_i > 0$ if $(\mathcal{D}, \mathcal{W})$ is irreducible, giving us

$$V' = \sum_{i=1}^{n} c_i V_i'(S_i, I_i) \leq \sum_{i=1}^{n} c_i \left(\sum_{j=1}^{n} a_{ij} S_j^* \left(K_j(S_j) - K_i(S_i)\right)\right) = 0$$

for all $(S_1, I_1, S_2, I_2, \ldots, S_n, I_n) \in \Gamma$. Thus V is a Lyapunov function for system (3.4). Since we have A is irreducible, then c_i is irreducible, and thus $c_i > 0$ for all i. Thus, $V' = 0$ implies that $S_i = S_i^*$ and $f(I_i)/f(I_i^*) = I_i/I_i^*$ for all i. Substituting S_i^* for S_i in (3.1) we get that

$$0 \quad = (S_i)' = (S_i^*)' = \Lambda_i - \beta_i S_i^* f(I_i^*) - d_i^S S_i^* + \sum_{j=1}^n a_{ij} S_j^* - \sum_{j=1}^n a_{ji} S_i^*$$

implying that $f(I_i^*) = f(I_i)$ for all i. Hence, $I_i/I_i^* = f(I_i)/f(I_i^*) = 1$. The only invariant set that makes $V' = 0$ is $\{P^*\}$, thus by LaSalle Invariance Principle [10], P^* is globally asymptotically stable and unique. □

CHAPTER 4: SIMULATIONS

In this chapter, we present simulations supporting and complementing our analysis in Chapters 2 and 3. Specifically, we choose $f(I) = I^2$ in the previous models (2.4) and (3.4), as it gives more interesting dynamical behavior. Simulations for the homogeneous model (2.4) are carried out in Section 4.2 while the simulations for the heterogeneous model (3.4) are in Section 4.3.

4.1 Parameter Values

For our simulations we took the birth rate in the United States to be 13.42 births / 1,000 population, the death rates d^S and d^I were assumed equal and given the value 8.15 deaths/ 1,000 populations. Both of the death rate and birth rate were found online at the CIA's World FactBook and is an estimate for 2014. In addition, we assumed an infectious period $1/\gamma$ of 15 days for a single infected individual.

4.2 Homogeneous Model

Consider the homogeneous model (2.4) with $f(I) = I^2$. We have

$$\begin{aligned} S' &= \Lambda - \beta S I^2 - d^S S, \\ I' &= \beta S I^2 - (d^I + \gamma) I. \end{aligned} \tag{4.1}$$

Define $\sigma := \frac{4d^S(d^I+\gamma)^2}{\Lambda^2}$, rewriting Δ from (2.10) so that the sign is dependent on the difference of β and σ we get $\Delta = \Lambda^2\beta(\beta - \sigma)$. Using the parameter values defined in section 4.1, the calculated the value of $\sigma = \frac{4d^S(d^I+\gamma)^2}{\Lambda^2} \approx 2.4 \times 10^{-9}$. For our simulations, we will take β to be greater than σ,

then by Table 4.1 we can expect two endemic equilibrium to be present.

Table 4.1: Number of equilibria based on β relative to σ.

$\beta < \sigma$	0 positive equilibrium
$\beta = \sigma$	1 positive equilibrium
$\beta > \sigma$	2 positive equilibria

The nullclines of (4.1) are shown in Figures 4.1(a)-(d) for different β values. When $\beta < \sigma$, we have the case depicted in Figure 4.1(a), where the S nullcline intersects the I nullclines only on the boundary, meaning that we have no endemic equilibrium, only the disease-free equilibrium. When $\beta = \sigma$, Figure 4.1(b) shows that there is exactly one intersection between the S nullcline and the I nullcines in the interior of Γ, thus we have a single endemic equilibrium. Once $\beta > \sigma$ the S nullcline intersects the I nullclines in two places in the interior of the feasible region (see Figure 4.1(c)), demonstrating that there will be two endemic equilibrium. As β increases the lower endemic equilibrium (EE1) gets closer to the DFE, while the upper endemic equilibrium (EE2) approaches the I axis (Figure 4.1(d)).

From the vector field overlaid the nullclines in Figure 4.1(c) and (d), we see that the flow undergoes significant changes in the vicinity of the nullclines. This was investigated further by looking at the end behavior of solutions curves starting from different initial conditions. We were able to demonstrate that (4.1) exhibits bistability, see Figure 4.2(a)-(f). The behavior of the infected population vs time can be seen in Figure 4.2(a)-(c), where (b) and (c) are the respective closer views of the upper and lower endemic equilibria. We selected five initial conditions, labeled I.C. 1, ..., I.C. 5 in Figure 4.2, two points around the upper (I.C. 5, I.C. 4), two points around the lower endemic equilibrium (I.C. 3, I.C. 2), and one point near the DFE (I.C. 1). Looking at the Figure 4.2(b), we see that I.C. 4 and 5 experience sustained oscillation at different amplitudes throughout the duration of the simulation, Figure 4.2(e) shows that the solutions settle into two distinct limit

cycles about EE2. The solution resulting from I.C. 3 has the curve leaving the vicinity of EE1 and entering into a limit cycle about EE2. This is shown in the fact that the solution curve leaves the plot area of Figure 4.2(c), enters Figure 4.2(b) from the bottom and then enters orbit about EE2 (this can also be seen in (e) and (f)). While for I.C. 1 and 2, they end up in a disease free state, Figure 4.2(c) and (f).

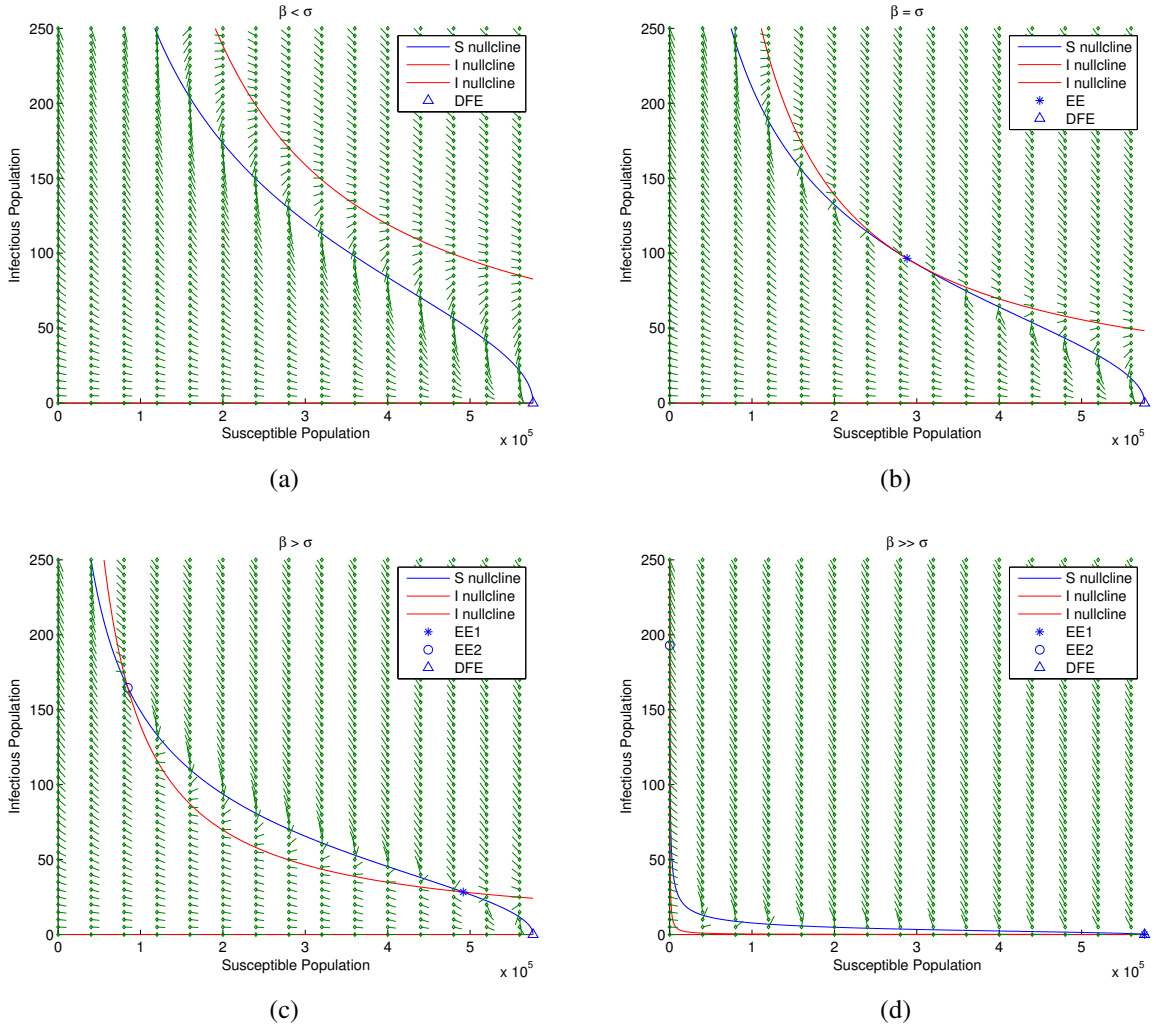


Figure 4.1: Nullclines of system (4.1) with vector field overlaid for different values of β relatively to σ.

For the final simulation involving the homogeneous model, we looked at how the behavior of a solution changed for a fixed initial condition as β was varied. Figure 4.3(a)-(f) shows our results from this simulation. We found that for the chosen initial condition the behavior changed significantly based on the β value. For the initial β value, the disease would die out in the population after invoking an epidemic. As β was increased, the infected population experienced sustained oscillations, Figure 4.3(b)-(d), before going to an endemic state (Figure 4.3(e) and (f)).

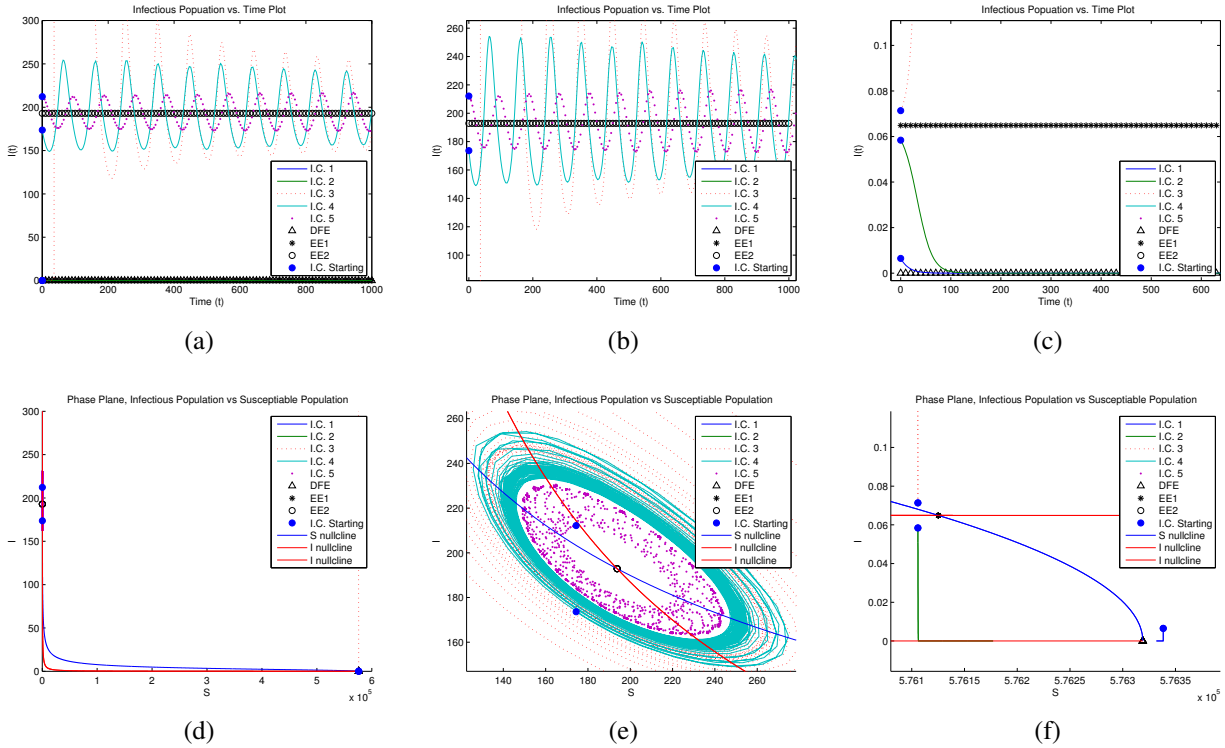
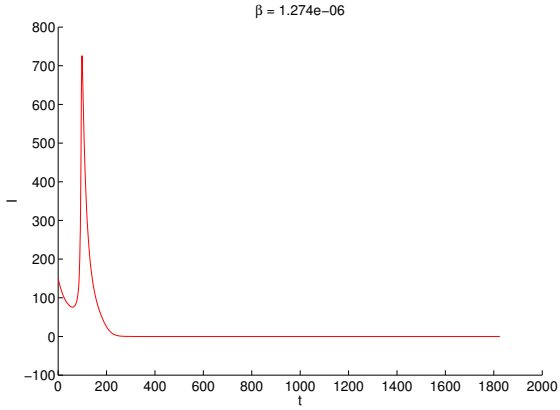
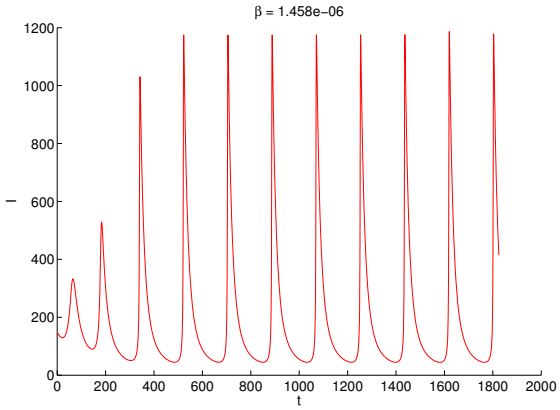


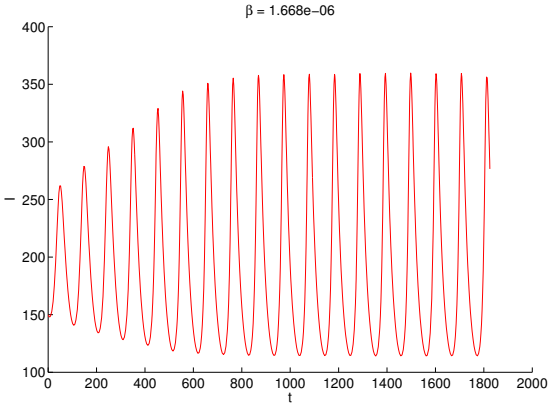
Figure 4.2: Bistability of system (4.1) with $\beta = 1.784 \times 10^{-6} > \sigma$. Subplot (b) corresponds with a closer look of EE2 in (a), (c) corresponds with a closer look of EE1 in (a). While (e) is a closer look at EE2 in (d) and (f) is a closer look at EE1 in (d).



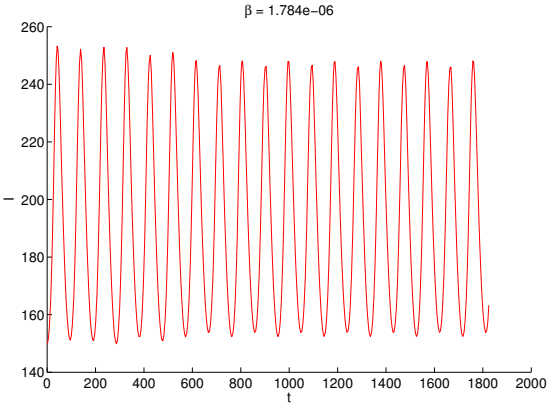
(a) $\beta = 1.274 * 10^{-6}$



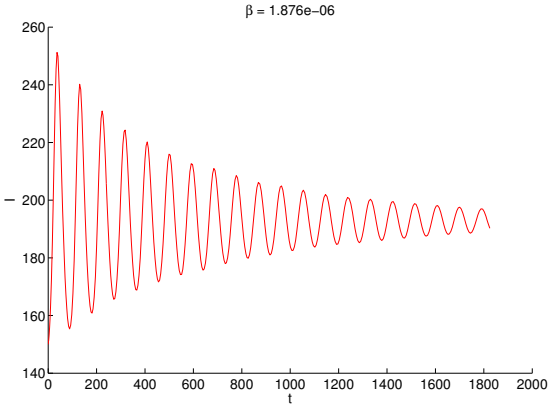
(b) $\beta = 1.458 * 10^{-6}$



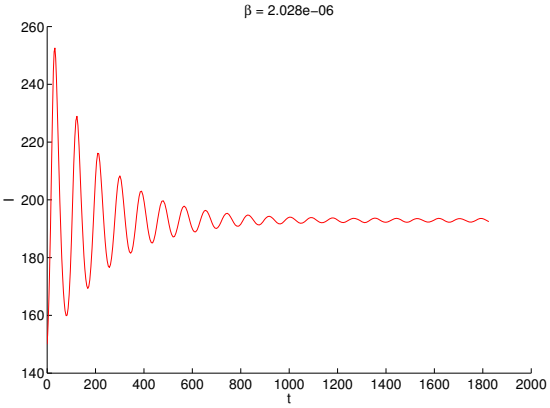
(c) $\beta = 1.668 * 10^{-6}$



(d) $\beta = 1.784 * 10^{-6}$



(e) $\beta = 1.876 * 10^{-6}$



(f) $\beta = 2.028 * 10^{-6}$

Figure 4.3: Behavior of system (4.1) near EE2 with $1.274 \times 10^{-6} \leq \beta \leq 2.028 \times 10^{-6}$.

4.3 Heterogeneous Model

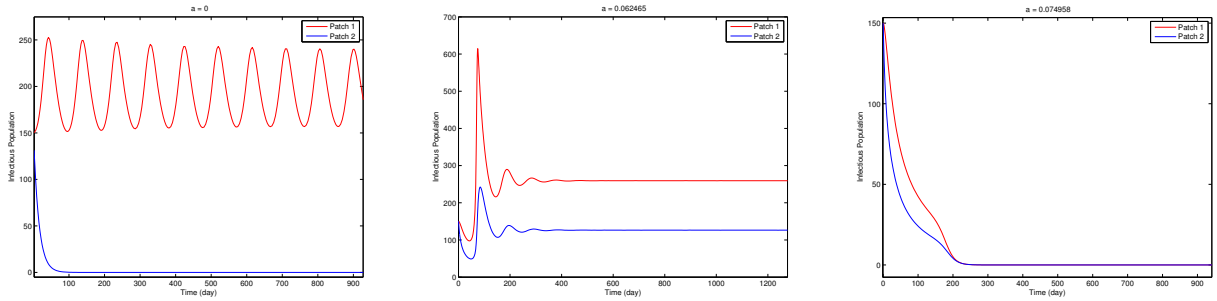
For our simulations of the the heterogeneous mode,l we consider the special case of (3.4) with 2 patches [n=2] and $f(I) = I^2$. Namely, we consider

$$\begin{aligned} S_1' &= \Lambda_1 - \beta_1 S_1 I_1^2 - d_1^S S_1 + a_{12} S_2 - a_{21} S_1, \\ S_2' &= \Lambda_2 - \beta_2 S_2 I_2^2 - d_2^S S_2 + a_{21} S_1 - a_{12} S_2, \\ I_1' &= \beta_1 S_1 I_1^2 - (d_1^I + \gamma_1) I_1 + b_{12} I_2 - b_{21} I_1, \\ I_2' &= \beta_2 S_2 I_2^2 - (d_2^I + \gamma_2) I_2 + b_{21} I_1 - b_{12} I_2. \end{aligned} \tag{4.2}$$

We also assumed all movement rates are the same, i.e. $a_{12} = a_{21} = b_{12} = b_{21} = a$, with a being a positive constant. In our simulations of the heterogeneous model, we varied the contact coefficients between the patches and held all other parameter values fixed (i.e. $\beta_1 \neq \beta_2$, but $d_1^I = d_2^I = d_1^S = d_2^S$ and $\gamma_1 = \gamma_2$).

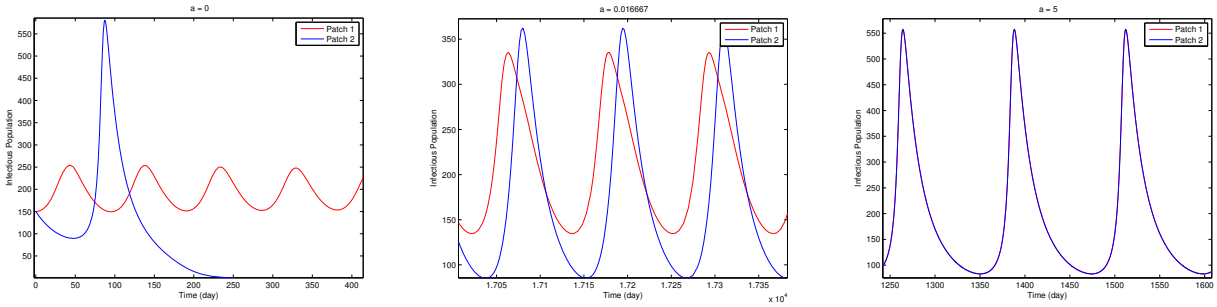
For our first simulation, we chose β_1 and β_2 such that in isolation patch 1 would be experiencing sustained oscillations in the population while the disease in patch 2 dies out, see Figure 4.4(a). Once movement is initiated, we see in Figure 4.4(b) that both patches enter into an endemic state until the movement rate surpasses a threshold value, resulting in both patches becoming disease free, Figure 4.4(c).

We then kept β_1, but chose a different β_2 value for patch 2, such that in isolation an epidemic would occur before the disease died out. With population movement taking place between patches, we see in Figure 4.5(b) that both patches experience periodic epidemics, but with the epidemics in patch 1 preceding those in patch 2. When the movement rates increases enough, the epidemics experienced by both patches are synchronized and have equal magnitude.



(a) No movement (b) $a = 0.062465$ (c) $a = 0.074958$

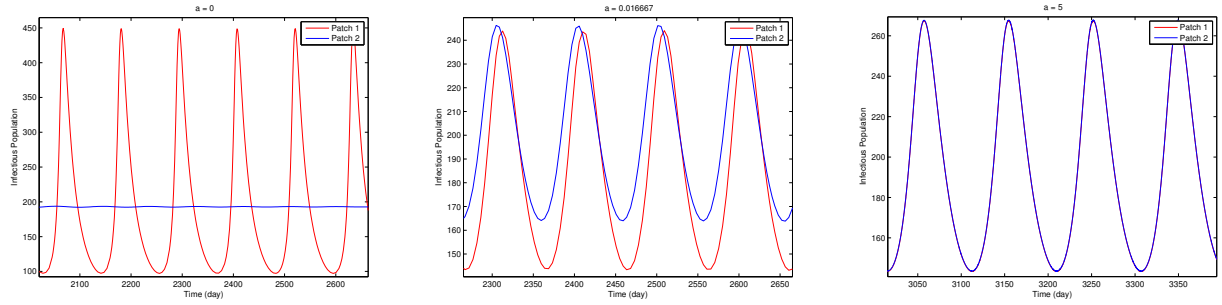
Figure 4.4: Simulations of (4.2) with $\beta_1 = 1.784 \times 10^{-6}$, $\beta_2 = 1.784 \times 10^{-8}$ and increasing movement.



(a) No movement (b) $a = 0.016667$ (c) $a = 5$

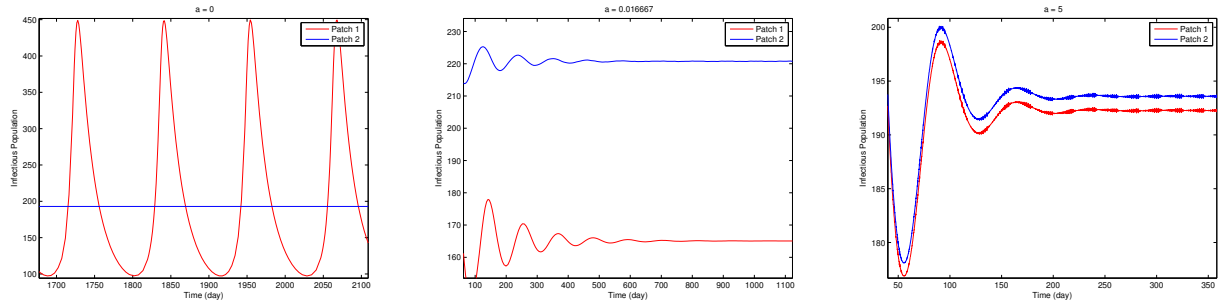
Figure 4.5: Simulations of (4.2) with $\beta_1 = 1.784 \times 10^{-6}$, $\beta_2 = 1.3 \times 10^{-6}$ and increasing movement.

Next we look at when there is no movement between patch 1 and 2, patch 2 is in an endemic state, and patch 1 experiences periodic epidemics, Figure 4.6(a). Once movement is allowed, 4.6(b) shows that both exhibit periodic epidemics. As movement increases, the phase shift between the epidemics of each patch diminishes resulting in the synchronization of the epidemics as seen in Figure 4.6(c). For a larger β_2 value we see a completely different result. With movement between the patches both go to endemic equilibrium, and any further increases results in both patches approaching the same endemic equilibrium, see Figure 4.7.



(a) No movement (b) $a = 0.016667$ (c) $a = 5$

Figure 4.6: Simulations of (4.2) with $\beta_1 = 1.6 \times 10^{-6}$, $\beta_2 = 1.9 \times 10^{-6}$ and increasing movement.



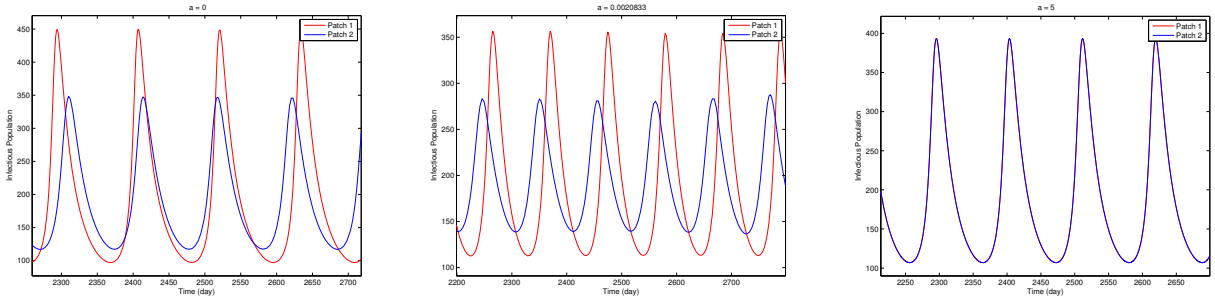
(a) No movement (b) $a = 0.016667$ (c) $a = 5$

Figure 4.7: Simulations of (4.2) with $\beta_1 = 1.6 \times 10^{-6}$, $\beta_2 = 5 \times 10^{-6}$ and increasing movement.

When both patches are experiencing periodic epidemics in isolation, as seen in Figure 4.8(a), and the populations are allowed to travel between the patches, the only outcome we were able to show was that both patches would equalize and have periodic epidemics, Figure 4.8(c). Prior to synchronization of the patches the oscillation periods match although with differing amplitudes, Figure 4.8(b).

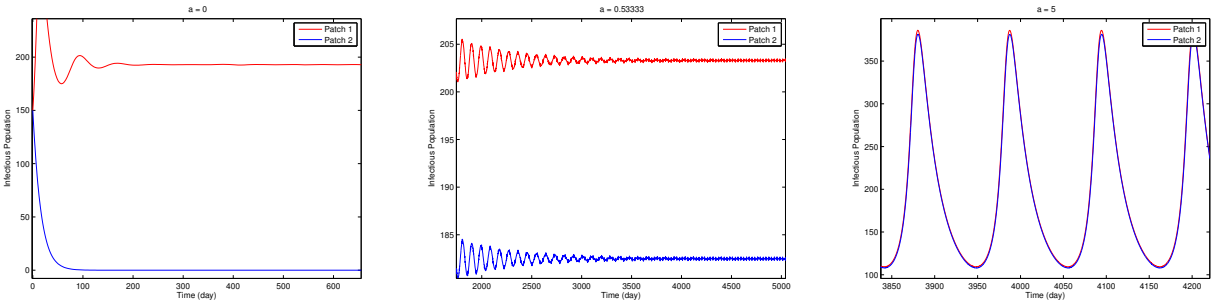
The final experiment was to investigate the case when, for no movement between the patches, patch 1 was in an endemic state while the disease died out for patch 2, Figure 4.9(a). From Figure

4.9(b) we see that with movement between the patches both go to an endemic equilibrium. Further increases in the movement gave rise to both patches experiencing periodic epidemics, Figure 4.9(c).



(a) No movement (b) $a = 0.0020833$ (c) $a = 5$

Figure 4.8: Simulations of (4.2) with $\beta_1 = 1.6 \times 10^{-6}$, $\beta_2 = 1.68 \times 10^{-6}$ and increasing movement.



(a) No movement (b) $a = 0.53333$ (c) $a = 5$

Figure 4.9: Simulations of (4.2) with $\beta_1 = 3.1 \times 10^{-6}$, $\beta_2 = 1.5 \times 10^{-7}$ and increasing movement.

CHAPTER 5: CONCLUSIONS AND FUTURE STUDIES

An SIR model with spatial heterogeneity was investigated to understand the effects of movement between isolated communities (patches) at various degrees of infection. Our initial consideration of the homogeneous SIR model was to establish the behaviors of the individual patches before allowing population movement between patches. We were able to establish conditions for the stability of the disease-free equilibrium and endemic equilibrium for the homogeneous model with generalized incidence, as well as for the heterogeneous SIR model that incorporates the nonrandom, directed movement among the patches. In the case of the homogeneous model, we looked at two incidence terms common to the literature and showed that the endemic equilibrium is globally asymptotically stable in both cases. When these conditions are not met, we can expect interesting dynamical behavior to occur; specifically, we established the presence of bistability as well as multiple endemic equilibria. For the heterogeneous model, we established the uniqueness and global stability of the endemic equilibrium when either susceptible or infectious populations are allowed to move freely between patches.

In our simulations, we were able to confirm the existence of the multiple endemic equilibrium for a single patch, the existence of two limit cycles, and bistability. When we looked at the two patch case of our heterogeneous model it was seen that different behaviors can be observed for different movement rates for a given contact coefficient. This is seen when coupling a patch experiencing periodic epidemics with one in which the disease dies out, the result is that for sufficiently small movement rates both patches will go to endemic equilibrium, while for larger movement rates the disease dies out in both patches. Another example is when a particular disease is endemic in a given patch is coupled with a patch in which the disease died out, the result was that both went to an endemic state. For larger movement rates the two patches developed oscillations. In all simulations conducted, as movement between patches was increased the effective difference

between the populations diminished.

In the future, we plan on continuing to work towards establishing the global stability of the endemic equilibrium for the heterogeneous model when both the susceptible and infectious populations are allowed to move freely. In addition to performing the simulations for the case when the initial conditions are not equal, we plan on investigating the instance when the interpatch movement is not symmetric. We also plan on performing numerical investigations where the rate of transfer of the susceptible population differs from the infectious population. In addition, further numerical investigation into the dynamics of multi-patch models would be of interest.

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