

AN EPIDEMIC MODEL WITH IMMIGRATION OF
INFECTIVES AND VACCINATION

By

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Abstract

This paper is an investigation of the possible behaviors of epidemics when there is immigration with some infectives and when vaccination is in effect. Infective immigrants from outside the population may introduce communicable disease into a host population. To help controlling disease one might introduce mass vaccination. First the model of SVIS type disease is discussed to describe the behavior of an epidemic disease when spreading into a population with immigrants and when a vaccination policy is in effect. Even in this simple version of the model, backward bifurcation and multiple endemic steady states can be observed with some sets of parameter values; by mathematical analysis the condition for a stability change and for having a backward bifurcation is proved to be identical in this case. Also the sufficient condition for backward bifurcation is stated explicitly. In the case of forward bifurcation, there can be exchange of stability and Hopf bifurcation occurs in such cases - numerical examples are provided to help understanding. Next we assume a disease with no immunity gained by recovery from infection, so the model is of SVIR type. In the case of no disease fatalities several special cases are discussed; stability analysis of steady states in each case and threshold values determining existence of endemic equilibria are presented if there are any. The proof that backward bifurcation cannot occur with any set of nonnegative parameter values in SVIR model is presented. On the other hand some numerical examples of backward bifurcation with negative immigration rates, i.e. outgoing immigration from host population, are shown. When there is a backward bifurcation bringing the vaccination-reduced reproductive number down to one may not be sufficient to control the disease. Also with some parameter values stability changes can be observed even with forward bifurcation. We would be able to know the minimum portion of susceptible class to be vaccinated in order to have a control over a disease by knowing the bifurcation

point of backward bifurcation. If so we can avoid a sudden jump in the number of infectives due to an unstable middle branch of bifurcation.

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Chapter 1

Introduction and Statement of the Problem

1.1 General Overview

In this thesis we demonstrate how a mathematical model can describe epidemiological phenomena and how we can use such a model to analyze endemic states and help eradicate diseases. A model was set up using a system of nonlinear ordinary differential equations and this is analyzed mathematically, and simulated using software. Computer software gives a concrete picture of numerical predictions and indicates the direction for mathematical analysis and proof.

1.2 Research Overview

Communicable diseases may be introduced into a population through the migration of infective individuals from outside into the host population. In order to eradicate the disease, numerous efforts could be made, such as improved sanitation, antibiotics, and vaccination programs. The model is developed to describe the behavior of a disease when spreading

through population with immigration and with a vaccination policy in effect. A vaccination program could mean a program of modifying behavior to avoid risk as well as a clinical vaccination. An interesting phenomena in epidemiology is the possibility of multiple steady states and epidemiological mechanisms that produce them.

Analysis of the mathematical model shows bifurcation phenomena, usually involving a threshold parameter. The most common parameter is the basic reproductive number, R_0 , which is a dimensionless quantity demonstrating an average number of secondary infections caused by an infective individual introduced into a completely susceptible population. In epidemiology R_0 is often a threshold parameter which determines whether a disease will invade the host population or not. Such behaviour can be stated as follows in epidemiological terms: if the average number of secondary infections caused by an average infective is less than one, a disease will die out, but if it exceeds one there an epidemic will result[1].

Often this type of phenomenon involves a transcritical bifurcation, which displays an exchange of stability between the disease-free equilibrium and the endemic equilibrium. Without immigration, the disease-free equilibrium exists for all values of R_0 while an endemic equilibrium exists on only one side of the bifurcation point [10].

In the presence of forward bifurcation, an endemic equilibrium exists only when $R_0 > 1$ in the absence of infective immigration. On the other hand, when backward bifurcation is present, an endemic equilibrium also exists when $R_0 < 1$, so there can be an endemic states even when $R_0 < 1$ for some parameter sets. In a system with a backward bifurcation, when $R_0 < 1$ but is still close enough to one, there exist both stable and unstable endemic

equilibria, while for R_0 far below one there exists only stable disease-free equilibria. Thus, increasing R_0 to just above one will create a dramatic jump in the number of infectives [10]. In this case, in order to eradicate the disease, R_0 needs to be reduced far below than one until it passes a so-called saddle-node bifurcation at $R_0 < 1$, [10].

The main aims of my thesis are:

- To provide examples of backward bifurcation of an epidemic model and to explain its effect on vaccination policy;
- To show how each different model of different disease types (mainly SIS and SIR types are considered) can produce significantly different bifurcation types; and
- To demonstrate how standard and bilinear incidence can produce different types of numerical results.

In achieving these aims, I use three different models and show numerical and analytic result from each case. The computer packages I used are MATLAB (for random search of appropriate parameter sets), XPPAUT, and AUTO.

1.3 Thesis Outline

Chapter 1 covers preliminary examples that will serve as an introduction to some terminology and results already well known. I begin Chapter 2 by presenting an epidemiological model of the SVIS type when the immigration factor is included. A disease is classified as an SIS type when it confers no immunity – one can get infected later although he (or she)

has recovered from the infection previously. In this model the total population is divided into three groups – susceptibles, infectives, and vaccinated. Also there is a constant flow of immigrants from the outside into the host population. Chapter 3 covers the epidemiological model of the SVIR type when the immigration factor is considered. A disease is classified as an SIR type when it confers immunity – one will not be infected again once he (or she) recovers from infection. We focus on the different behaviour of the bifurcation diagram from the SVIS case. Various numerical results are provided.

1.4 Motivation

In 1665-1666 London suffered two epidemic disasters. In the spring and summer of 1665 an outbreak of the plague that is now identified as Bubonic Plague spread out until thousands had died. The plague indeed started in the East and invaded through Europe quickly. Bubonic Plague was called the Black Death since the victim's skin became black in patches when infected. The symptom include inflamed glands, vomiting, swollen tongue and splitting headaches. The spread of disease started slowly at first but 43 had died by May 1665. Then 6137 people died in June, 17036 in July and at its peak in August, 31159 people died. In all the total population was reduced by 15%. The characteristic features of the Great Plague were its short incubation period and the sudden emergence of the epidemic. In fact incubation took less than a week.

Since the Great Plague many scientists have paid attention to models for epidemics in mathematical terms. Also the epidemic cholera was originally isolated to India mainly, and outbreaks occurred recurrently in cyclic fashion. However, through the centuries, the range

of cholera infection spread rapidly. By the 18th and 19th centuries, in Moscow (1830), and North America (1832), cholera epidemics were reported.

Some epidemic diseases such as measles and influenza can be prevented by vaccination and many researchers have tried to study the periodic behavior of measles for instance. Table 1.1 summarizes characterizes of some disease whose infection can be prevented by vaccination.

1.5 Basic Model

To begin this section I will present one of most simplest epidemiological models of SIR type.

This model is based on a few assumptions below:

- An average infective individual make an appropriate contact sufficient to transmit infection with βN others per unit time.
- The probability that a contact of an infective individual is with a susceptible is S/N .
- A fraction γ of infectives recover per unit time.
- The demographic effect can be ignored since the epidemic time scale is very short.

Based on these assumptions Kermack and McKendrick proposed the following model in 1927:

$$S' = -\beta SI$$

$$I' = \beta SI - \gamma I$$

$$R' = \gamma I$$

Virus	Measles	Influenza A (human)	Influenza B (equine)	Influenza C (avian)
Main Species Infected	Human	Human	Equines	All avian species
Transmission	Direct respiratory	Direct respiratory	Direct respiratory	Direct respiratory and oral
Incubation Period	8-12 days	2-3 days	1-2 days	-
Infectious Period (in naive hosts)	5-8 days	< 14dd in young	7dd in large amounts, < 14dd in small amounts	Months (in wild ducks)
Infectious Period	N/A	1-3dd	1-5 days	N/A
Extent of immunity following infection/vaccination	Lifelong after natural infection	Prolonged, but strain dependent	Clinical immunity for >12 mo, but replication and transmission occurs < 12 mo	Highly variable (rapid clearance in some species, prolonged enteric infection)
Current control strategy	Infant Vaccination	Vaccination of elderly and at risk	Vaccination quarantine	Vaccination quarantine
Min population size for persistence	300,000	Probably much larger than measles for a given strain	As for human	"Small" (persistent infectious)
Epidemic dynamics	Seasonal and multi-annual epidemics	Seasonal epidemics with waves	Seasonal epidemics	-

Table 1.1: Epidemiological of characteristics of the RNA viruses (summarized in *Fields*)

In this model R can be determined once I is determined since the differential equation for R only depends on I . Hence we consider the equation for S and I first as below:

$$S' = -\beta SI$$

$$I' = (\beta S - \gamma)I$$

Since solving these equations analytically would be rather difficult one can use a qualitative approach to study the behavior of the system. This approach is well presented in [1]. We begin by dividing the equation of I' by the one of S' :

$$\frac{I'}{S'} = \frac{dI}{dS} = \frac{(\beta S - \alpha)I}{-\beta SI} = -1 + \frac{\alpha}{\beta S}$$

By integrating both sides we obtain

$$I = -S + \frac{\alpha}{\beta} \log S + c$$

and we define the function $V(S, I)$ as

$$V(S, I) = S + I - \frac{\alpha}{\beta} \log S$$

where

$$\frac{\beta}{\alpha} = \frac{\ln \frac{S_0}{S_\infty}}{K - S_\infty}$$

Now it follows that

$$I_{max} = S_0 + I_0 - \frac{\alpha}{\beta} \log S_0 - \frac{\alpha}{\beta} + \frac{\alpha}{\beta} \log \frac{\alpha}{\beta}$$

Some diseases such as measles confer immunity so recovery from such diseases provides immunity against reinfection. We shall examine a general SIR model with births and deaths

for a disease

$$\begin{aligned} S' &= \mu K - \beta SI - \mu S \\ I' &= \beta SI - (\mu + \alpha + \gamma)I \\ R' &= \gamma I - \mu R \end{aligned} \tag{1.5.1}$$

with $S + I + R = K$.

$$R_0 = \frac{\beta K}{\mu + \gamma + \alpha} = \frac{K}{S_\infty}$$

1.6 Basic SIS model

Some diseases confer immunity so recovered individuals gain immunity against the disease.

This type of disease can be modelled by SIS type where S and I stand for susceptibles and infectives respectively. Here we proposed a simple model of SIS type that includes births in the susceptible class and deaths from two classes with the rate proportional to each class.

Our model is

$$\begin{aligned} S' &= -\beta SI + \mu(K - S) + \gamma I \\ I' &= \beta SI - (\alpha + \mu + \gamma)I \end{aligned}$$

where the total population size, N , is defined as sum of population in two classes, i.e. $N(t) = S(t) + I(t)$. We assume that a disease may be fatal to some infectives so deaths due to disease can be included in a model using the disease-related death rate from infective class, α . The recovered individuals are removed from the infective class at the rate, γ , and they don't acquire immunity. The birth rate is constant and proportional to the carrying capacity, K , and the natural death rate is μ . We can start a qualitative approach by studying steady states. The equilibrium condition can be found by setting the right hand side of equation

to be zero:

$$-\beta SI + \mu(K - S) + \gamma I = 0$$

$$\beta SI - (\alpha + \mu + \gamma)I = 0$$

The second equilibrium condition factors, and we get one disease-free equilibrium, $I = 0$ and the other endemic one that satisfies $\beta S - (\alpha + \mu + \gamma) = 0$ assuming $\beta S = (\alpha + \mu + \gamma) < \beta K$. Hence by solving the two equilibrium conditions one can find the two following steady states, a disease-free and an endemic one:

$$(I^*, S^*) = (0, K)$$

$$(I^*, S^*) = \left(\frac{\mu[\beta K - (\alpha + \mu + \gamma)]}{\beta(\alpha + \mu + \gamma)}, \frac{\gamma + \mu + \alpha}{\beta} \right)$$

To study the local stability of a fixed point we linearize our system first. The Jacobian matrix is given by

$$J = \begin{pmatrix} -\mu - \beta I & -\beta S \\ \beta I & \beta S - (\gamma + \mu + \alpha) \end{pmatrix}$$

The Jacobian matrix at the disease-free equilibrium is given by

$$\begin{pmatrix} -\mu & -\beta K + \gamma \\ 0 & \beta K - (\gamma + \alpha + \mu) \end{pmatrix}$$

By looking at eigenvalues, one can easily see that the disease free equilibrium is stable if $\beta K < (\gamma + \mu + \alpha)$. Now we can turn to an endemic equilibrium and study about its stability. The Jacobian matrix evaluated at an endemic equilibrium is given by

$$\begin{pmatrix} -\frac{\mu\beta K}{(\gamma + \mu + \alpha)} & -(\mu + \alpha) \\ \frac{\mu[\beta K - (\gamma + \mu + \alpha)]}{\gamma + \mu + \alpha} & 0 \end{pmatrix}$$

We can easily see that the trace of this matrix is negative and the determinant is positive as long as $\beta K - (\gamma + \mu + \alpha) > 0$.

- If $R_0 < 1$
 - the disease-free equilibrium of 1.7.1 is stable, and
 - the endemic equilibrium does not exist.
- If $R_0 > 1$
 - the disease-free equilibrium of 1.7.1 is unstable, and
 - the endemic equilibrium exists, and is asymptotically stable.

where the basic reproductive number is defined as $R_0 = \frac{\beta K}{\mu + \gamma + \alpha}$. Note that the basic reproductive number depends on the contact rate β , carrying capacity, K , and the rates at which an infective is removed from its class.

1.7 Basic SIR model

Some diseases confer immunity so recovered individuals gain immunity against the disease. This type of disease can be modelled by SIR type where S , I , and R stands for susceptibles, infectives and the recovered respectively. The first SIR type model was proposed by H.E. Soper. He assumed that the total population size is constant and that the birth rate and death rate are constant. His model is

$$S' = -\beta SI + \mu K$$

$$I' = \beta SI - \gamma I$$

$$R' = \gamma I - \mu K$$

where β is contact rate and γ is recovery rate. However this model was criticized since there is no proper reason why one should link deaths from recovered class to births from

susceptibles, [1]. Also $R(t)$ can become negative when $R(0)$ and $I(0)$ are sufficiently small, which is another weakness of Soper's model. In 1932, Kermack and McKendrick proposed another model of SIR type that includes births in the susceptible class and deaths from all three class with the rate proportional to each class. Their model is

$$S' = -\beta SI + \mu(K - S)$$

$$I' = \beta SI - \gamma I - \mu I$$

$$R' = \gamma I - \mu R$$

where the total population size, N , is defined as the sum of the populations in the three classes, i.e. $N(t) = S(t) + I(t) + R(t)$. Their model treats only the case where there is no death due to disease. However one can assume that a disease may be fatal to some infectives so deaths due to disease can be included in the I equation. Thus in addition to the demographic effects we can also consider removal of some infectives via disease-related death. Based on this assumption we can consider a more general model that was proposed by Hethcote in 1976, [6]:

$$S' = \mu K - \beta SI - \mu S$$

$$I' = \beta SI - (\gamma + \mu + \alpha)I \tag{1.7.1}$$

$$R' = \gamma I - \mu R$$

Here we assume that α is the fraction of infectives dying from infection and γ is the rate at which infectives recover with acquired immunity. The natural death rate is μ and the birth rate, μK , is assumed to be constant. Let us start to analyze the model qualitatively

by eliminating the R variable from the system and reducing to the two-dimensional one:

$$S' = -\beta SI + \mu(K - S)$$

$$I' = \beta SI - (\gamma + \mu + \alpha)I$$

We can ignore the equation for R since R can be determined once S and I are known [1].

We can start the qualitative approach by studying steady states. The equilibrium condition can be found by setting the right hand side of the equations to be zero:

$$-\beta SI + \mu(K - S) = 0$$

$$\beta SI - (\gamma + \mu + \alpha)I = 0$$

The second equilibrium condition factors, and we get one disease-free equilibrium, $I = 0$, and the other endemic one that satisfies $\beta S - (\gamma + \mu + \alpha) = 0$ assuming $\beta S = (\gamma + \mu + \alpha) < \beta K$. Hence by solving the two equilibrium conditions one can find the following two steady states, a disease-free and an endemic one:

$$(I^*, S^*) = (0, K)$$

$$(I^*, S^*) = \left(\frac{\mu[\beta K - (\gamma + \mu + \alpha)]}{\beta(\gamma + \mu + \alpha)}, \frac{\gamma + \mu + \alpha}{\beta} \right)$$

To study the local stability of a fixed point we linearize our system first. The Jacobian matrix is given by

$$J = \begin{pmatrix} -\mu - \beta I & -\beta S \\ \beta I & \beta S - (\gamma + \mu + \alpha) \end{pmatrix}$$

The Jacobian matrix at a disease-free equilibrium is given by

$$\begin{pmatrix} -\mu & -\beta K \\ 0 & \beta K - (\gamma + \mu + \alpha) \end{pmatrix}$$

By looking at eigenvalues, one can easily see that the disease free equilibrium is stable if $\beta K < (\gamma + \mu + \alpha)$. Now we can turn to an endemic equilibrium and study its stability closely. The Jacobian matrix evaluated at an endemic equilibrium is given by

$$\begin{pmatrix} -\frac{\mu\beta K}{(\gamma+\mu+\alpha)} & -(\gamma + \mu + \alpha) \\ \frac{\mu[\beta K - (\gamma+\mu+\alpha)]}{\gamma+\mu+\alpha} & 0 \end{pmatrix}$$

The trace of this matrix is always negative and the determinant is positive as long as $\beta K - (\gamma + \mu + \alpha) > 0$, that is, the same condition as the one for existence of an endemic equilibrium. In summary there is threshold behavior in this model:

- If $R_0 < 1$
 - the disease-free equilibrium of 1.7.1 is stable, and
 - the endemic equilibrium does not exist.
- If $R_0 > 1$
 - the disease-free equilibrium of 1.7.1 is unstable, and
 - the endemic equilibrium exists, and is asymptotically stable.

where the basic reproductive number is defined as $R_0 = \frac{\beta K}{\mu + \gamma + \alpha}$. Note that the basic reproductive number depends on the contact rate, β , carrying capacity, K , and the rates at which an infective is removed from its class.

1.8 Simplest immigration model without vaccination and the basic reproductive number

Let us now consider an SIS type disease in the absence of vaccination but with a constant flow of incoming immigrants. Let $S(t)$ be the number of members of the population who are susceptible to an infection at time t and let $I(t)$ be the number of members who are infective at time t . The total population size at time t is denoted by $N(t)$, with $N = S + I$ for the SIS model (the disease confers no immunity). When an infective makes contact, the probability of producing a new infection is $\frac{S}{N}$ since a new infection can be made only when a contact is made with a susceptible. Thus the rate of producing new infections is $\beta N \cdot \frac{S}{N} \cdot I = \beta SI$, where β is a constant. For simplicity, we assume that there is no disease related death. The population is replenished via two ways, the birth and immigration. We assume that newborns enter the susceptible class at a constant rate and there is a constant incoming flow of immigrants where some portion, p , of immigrants are infectives. In summary, the assumption we have in this model is as following:

- S , I and N are the number of susceptibles, infectives and total population, respectively.
- There is a constant flow of A new members into a population in unit time, where a fraction $p \geq 0$ of A is infective ($0 \leq p \leq 1$).
- There is a constant per capita natural death rate $\mu > 0$ in each class.
- A fraction $\gamma \geq 0$ of infectives recovers in unit time.

- β is the infectious contact rate per person in unit time
- Λ is the constant natural birth rate; all newborns come into the susceptible class

We can now formulate this model, dividing the total population into two classes - susceptibles (S) and infectives (I):

$$\begin{aligned} S' &= (1-p)A + \Lambda - \beta SI - \mu S + \gamma I \\ I' &= pA + \beta SI - (\mu + \gamma)I \end{aligned} \tag{1.8.1}$$

Note that the total population is the sum of two classes, susceptibles and infectives, thus

$$N(t) = S(t) + I(t)$$

It follows that

$$N' = S' + I' = A + \Lambda - \mu N$$

Since $\lim_{t \rightarrow \infty} N(t) \equiv K$, the model is asymptotically stable and we can reduce the size of model by replacing S by $K - I$, [4]. The model is now equivalent to

$$\begin{aligned} I' &= pA + \beta(K - I)I - (\mu + \gamma)I \\ &= -\beta I^2 + (\beta K - \mu - \gamma)I + pA \end{aligned} \tag{1.8.2}$$

By setting $I' = 0$, we can solve for the two equilibria when $(\beta K - \mu - \gamma)^2 - 4(-\beta)(pA) > 0$:

$$I_{1,2}^* = \frac{(\beta K - \mu - \gamma) \pm \sqrt{(\beta K - \mu - \gamma)^2 - 4(-\beta)(pA)}}{2\beta}$$

where $I_1^* \geq 0$ and $I_2^* \leq 0$. Let us consider an endemic equilibrium, I_1^* . We can rewrite I_1^* by letting $\Psi = \beta K - \mu - \gamma$, [3]:

$$\lim_{p \rightarrow 0} I_1^* = \frac{\Psi + |\Psi|}{2\beta} = \begin{cases} 0, & \text{if } \Psi < 0; \\ \frac{\Psi}{\beta}, & \text{if } \Psi > 0 \end{cases} \quad (1.8.3)$$

From this expression we obtain a threshold parameter, Ψ , and deduce the basic reproductive number, R_0 :

$$R_0 = \frac{\beta K}{\mu + \gamma}$$

Using R_0 , we can rewrite the equilibria.

$$I_{1,2}^* = \frac{(R_0 - 1)(\mu + \gamma) \pm \sqrt{(R_0 - 1)^2(\mu + \gamma)^2 + 4\beta p A}}{2\beta}$$

Note that $I_1^* \geq 0$ and $I_2^* \leq 0$ for all $R_0 \geq 0$.

Chapter 2

The SVIS model

2.1 Introduction

Let us now consider an SIS type disease when a vaccination program is in effect and there is a constant flow of incoming immigrants. Let $S(t)$ be the number of population members who are susceptible to an infection at time t , $I(t)$ be the number of members who are infective at time t , and $V(t)$ be the number of members who are vaccinated at time t . The total population size at time t is denoted by $N(t)$, with $N = S + I + V$ for the SIS model (the disease confers no immunity). Assume that each infective makes βN contacts sufficient to transmit infection in unit time, where β is a const. When an infective makes contact, the probability of producing a new infection is $\frac{S}{N}$, since the new infection can be made only when a contact is made with a susceptible. Thus, the rate of producing new infections is $\beta N \cdot \frac{S}{N} \cdot I = \beta SI$. The susceptible population is vaccinated at a constant rate, ϕ , and the rate at which the vaccine wears off is θ . We assume that there can be disease related deaths as well as natural deaths unrelated to the disease. The population is replenished in two ways, birth and immigration. We assume that all newborns enter the susceptible class at a

constant rate, Λ , and that there is a constant incoming flow (A) of immigrants where some portion of immigrants, p , is infective.

In summary, the assumptions we have in this model is as follows:

- $S(t)$, $I(t)$, $V(t)$, and $N(t)$ are the numbers of susceptibles, infectives, vaccinated, and total population at time t , respectively.
- There is a constant flow of A new members into the population per unit of time, where fraction p of immigrants is infective ($0 \leq p \leq 1$).
- The vaccine has the effect of reducing infection by a factor of σ , so that $\sigma = 0$ means that the vaccine is completely effective in preventing infection, while $\sigma = 1$ means that the vaccine is utterly ineffective.
- The rate at which the susceptible population is vaccinated is ϕ , and the rate at which the vaccine wears off is θ .
- The disease can be fatal to some infectives and we define α to be the rate of disease-related death.
- There is a constant per capita natural death rate $\mu > 0$ in each class.
- Fraction $\gamma \geq 0$ of infectives recovers in unit time.
- βN is the infectious contact rate per person in unit time.
- Λ is the constant natural birth rate, with all newborns coming into the susceptible class.

$S(t)$	Number of susceptibles at time t
$V(t)$	Number of vaccinated individuals at time t
$I(t)$	Number of infectives at time t
$R(t)$	Number of recovered people with immunity at time (t)
A	Number of immigrants
p	Portion of infectives among immigrants
Λ	Birth rate
β	Contact rate
γ	Recovery rate
ϕ	Vaccination rate
σ	Factor by which the vaccine reduces infection
θ	Rate at which the vaccine wears off
μ	Natural death rate unrelated to the disease
α	Disease related death rate
R_0	Basic reproductive number
R_ϕ	Vaccination reproductive number

Table 2.1: Summary of notation

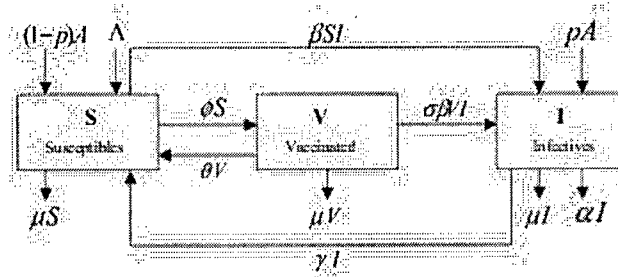


Figure 2.1: The diagram for SVIS model

We can now formulate this model, by dividing the population into three classes – susceptibles (S), vaccinated (V), and infectives (I):

$$\begin{aligned} S' &= (1-p)A + \Lambda - \beta SI - (\mu + \phi)S + \gamma I + \theta V \\ I' &= pA + \beta SI + \sigma\beta VI - (\mu + \gamma + \alpha)I \\ V' &= \phi S - \sigma\beta VI - (\mu + \theta)V \end{aligned} \tag{2.1.1}$$

Note that the total population is the sum of three classes: susceptibles, infectives, and vaccinated:

$$N(t) = S(t) + I(t) + V(t)$$

Thus, it follows that

$$N' = S' + I' + V' = A + \Lambda - \mu N - \alpha I$$

The equation 2.1.1 is the SVIS model we will use to investigate the behavior of an SIS type disease throughout this chapter. We will study first the simpler case of no disease-related death.

2.2 A model of SVIS type without disease-related death

If the disease causes no fatality ($\alpha = 0$), then we can simplify the model 2.1.1 by letting $\alpha = 0$ as follows:

$$\begin{aligned} S' &= (1-p)A + \Lambda - \beta SI - (\mu + \phi)S + \gamma I + \theta V \\ I' &= pA + \beta SI + \sigma\beta VI - (\mu + \gamma)I \\ V' &= \phi S - \sigma\beta VI - (\mu + \theta)V \end{aligned} \tag{2.2.1}$$

with

$$N' = S' + I' + V' = A + \Lambda - \mu N$$

The system is now asymptotically autonomous, so we can define the limit value of N as follows:

$$\lim_{t \rightarrow \infty} N(t) = \frac{A + \Lambda}{\mu} \equiv K$$

Definition 2.2.1. Consider the differential equation

$$\frac{dx}{dt} \equiv \dot{x} = f(x) \tag{2.2.2}$$

where $x = x(t) \in \mathbb{R}^n$ is a vector valued function of an independent variable (usually time) and $f : U \rightarrow \mathbb{R}^n$ is a smooth function defined on some subset $U \subseteq \mathbb{R}^n$. Systems of the form 2.2.2, in which the vector field does not contain time explicitly, are called *autonomous*, [12].

Definition 2.2.2. The system

$$y' = f(t, y)$$

is said to be asymptotically autonomous on the set Ω if and only if

1. $\lim_{t \rightarrow \infty} f(t, y) = h(y)$ for $y \in \Omega$ and this convergence is uniform for y in closed bounded subsets of Ω .
2. For every $\varepsilon > 0$ and every $y \in \Omega$ there exists a $\delta(\varepsilon, y) > 0$ such that $|f(t, x) - f(t, y)| < \varepsilon$, whenever $|x - y| < \delta$ for $0 \leq t < \infty$, [2].

According to *the theory of asymptotically autonomous system* we can reduce it to two-dimensional system by letting replacing S with $K - I - V$:

$$\begin{cases} I' = pA + \beta[K - I - (1 - \sigma)V]I - (\mu + \gamma)I \\ V' = \phi[K - I - V] - \sigma\beta VI - (\mu + \theta)V \end{cases} \quad (2.2.3)$$

This is the system that we will analyze in order to find the basic reproductive number. At an equilibrium, we can set the right hand side of equations 2.2.3 to be zero, which gives the equilibrium conditions:

$$\begin{aligned} \beta(1 - \sigma)V &= \frac{pA}{I} + \beta(K - I) - (\mu + \gamma) \\ \phi(K - I) &= V[\sigma\beta I + (\mu + \theta + \phi)] \end{aligned}$$

One can solve for V from the second condition and substitute V into the first one:

$$\begin{aligned} \beta(1 - \sigma)\phi(K - I) &= [\sigma\beta I + (\mu + \theta + \phi)]\left[\frac{pA}{I} + \beta(K - I) - (\mu + \gamma)\right] \\ \iff \beta\phi(1 - \sigma)(K - I)I &= [\sigma\beta I + (\mu + \theta + \phi)][pA + \beta I(K - I) - I(\mu + \gamma)] \end{aligned} \quad (2.2.4)$$

After complicated computations we omitted here, the endemic equilibrium condition, 2.2.4, becomes a cubic polynomial of I as below:

$$f(I) = EI^3 + BI^2 + CI + D = 0 \quad (2.2.5)$$

with

$$E = \beta\sigma$$

$$B = (\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K$$

$$C = -p\sigma A - K(\mu + \theta + \sigma\phi) + (\mu + \gamma)(\mu + \theta + \phi)/\beta$$

$$D = -\frac{pA(\mu + \theta + \phi)}{\beta}$$

Proposition 2.2.1. *If the system 2.2.1 has three distinct endemic steady states then two conditions on the parameters must be satisfied:*

$$(\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K < 0$$

$$\text{and } -p\sigma A - K(\mu + \theta + \sigma\phi) + (\mu + \gamma)(\mu + \theta + \phi)/\beta > 0.$$

Proof. Consider the equilibrium condition 2.2.5. Note that the sign of some coefficients of the polynomial are fixed for all nonnegative parameters: $E \geq 0$ and $D \leq 0$ for all nonnegative parameters. If $D \neq 0$, then there are either one or three positive roots since $f(0) < 0$ and $\lim_{t \rightarrow \infty} f(I) = \infty$. Through differentiating 2.2.5 with respect to I , we get $f'(I) = 3EI^2 + 2BI + C$. If $f(I) = 0$ has three positive roots, then it follows that $f'(I) = 0$ has two positive roots according to *Rolle's theorem*. Thus, $B < 0$ and $C > 0$ are the necessary conditions for the system 2.2.1 to have three endemic steady states. \square

2.2.1 Equilibria and stability analysis

Proposition 2.2.2. *The sign of the slope of the bifurcation curve, I vs β , of the system 2.2.1 is determined by the sign of $(3EI^2 + 2BI + C)$ where*

$$E = \beta\sigma$$

$$B = (\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K$$

$$C = -p\sigma A - K(\mu + \theta + \sigma\phi) + (\mu + \gamma)(\mu + \theta + \phi)/\beta$$

The slope of the bifurcation curve is positive when $(3EI^2 + 2BI + C) > 0$ and negative when $(3EI^2 + 2BI + C) < 0$.

Proof. Recall that the equilibrium condition of system 2.2.3 is the cubic equation $f(I)$, 2.2.5. We have already shown that $B < 0$ and $C > 0$ is a necessary condition that $f(I)$ has three positive equilibria using Rolle's theorem. Now consider a bifurcation diagram using β as a control parameter.

Implicit differentiation of 2.2.5 with respect to β gives:

$$\begin{aligned}
 (3EI^2 + 2BI + C) \frac{dI}{d\beta} &= -I^3 \frac{dE}{d\beta} - I^2 \frac{dB}{d\beta} - I \frac{dC}{d\beta} - \frac{dD}{d\beta} \\
 &= -I^3 \sigma + I^2 (\sigma K) + I \left(\frac{(\mu + \gamma)(\mu + \theta + \phi)}{\beta^2} \right) + \frac{pA(\mu + \theta + \phi)}{\beta^2} \\
 &= \sigma^2 I (K - I) + \frac{\mu + \theta + \phi}{\beta^2} [I(\mu + \gamma) + pA]
 \end{aligned} \tag{2.2.6}$$

We can easily see that the right hand side of implicit differentiation 2.2.6 is positive, since $K \geq I$. Thus, the sign of slope of the bifurcation curve, $\frac{dI}{d\beta}$, is determined by the sign of $(3EI^2 + 2BI + C)$. \square

The slope of the bifurcation curve of I using β as a control parameter is infinitely large when

$$\frac{dI}{d\beta} = \infty.$$

From 2.2.6 the slope becomes infinitely large when

$$3EI^2 + 2BI + C = 0. \tag{2.2.7}$$

where

$$E = \beta\sigma$$

$$B = (\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K$$

$$C = -p\sigma A - K(\mu + \theta + \sigma\phi) + (\mu + \gamma)(\mu + \theta + \phi)/\beta$$

It is easily seen that $E > 0$ for positive parameters. Hence one can easily see that there exist two distinct positive roots of equation 2.2.7 if $B < 0$, $C > 0$ and $\sqrt{B^2 - 3EC} > 0$:

$$I_{1,2}^\infty = \frac{-B \pm \sqrt{B^2 - 3EC}}{3E} \quad (2.2.8)$$

These two roots are indeed bifurcation points of 2.2.3 at which the slope of bifurcation becomes infinitely large.

One can also study the stability of equilibrium from the linearization of 2.2.3:

$$J = \begin{pmatrix} -2\beta I - (1 - \sigma)\beta V - (\mu + \gamma) + \beta K & -(1 - \sigma)\beta I \\ -(\phi + \sigma\beta V) & -(\mu + \theta + \phi + \sigma\beta I) \end{pmatrix} \quad (2.2.9)$$

Using the equilibrium condition, $\frac{-pA}{I} = \beta K - \beta I - \beta(1 - \sigma)V - (\mu + \gamma)$, one can evaluate the Jacobian matrix at equilibrium:

$$J|_{I^*} = \begin{pmatrix} \frac{-pA}{I} - \beta I & -(1 - \sigma)\beta I \\ -(\phi + \sigma\beta V) & -(\mu + \theta + \phi + \sigma\beta I) \end{pmatrix} \quad (2.2.10)$$

Note that this matrix has negative trace. The determinant of this matrix is

$$\begin{aligned} \det(J) &= \sigma(\beta I)^2 + \beta I(\mu + \theta + \phi) + \frac{pA}{I}(\mu + \theta + \phi + \sigma\beta I) - (1 - \sigma)\phi\beta I - (1 - \sigma)\sigma\beta^2 V I \\ &= \beta I[\sigma\beta I + (\mu + \theta + \sigma\phi) - \beta\sigma(K - I) + (\mu + \gamma)\sigma] + \frac{pA}{I}(\mu + \theta + \phi) \end{aligned}$$

Let us further simplify the determinant using equilibrium condition,

$$\frac{pA\sigma}{I} + \beta(K - I)\sigma - \beta V\sigma(1 - \sigma) - (\mu + \gamma)\sigma = 0.$$

$$\begin{aligned}
det &= \beta I[\sigma\beta I + (\mu + \theta + \sigma\phi) - \beta\sigma(K - I) + (\mu + \gamma)\sigma] + \frac{pA}{I}(\mu + \theta + \phi) \\
&= \beta[2\sigma\beta I + (\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K] + \frac{pA}{I}(\mu + \theta + \phi) \\
&= \beta I[2EI + B] + \frac{pA}{I}(\mu + \theta + \phi) \\
&= \beta I[2EI + B] + \frac{\beta}{I}\left[\frac{pA(\mu + \theta + \phi)}{\beta}\right] \\
&= \beta I[2EI + B - \frac{D}{I^2}] \\
&= \frac{\beta}{I}[2EI^3 + BI^2 - D] \\
&= \frac{\beta}{I}[I^2(2EI + B) - D]
\end{aligned} \tag{2.2.11}$$

Recall that $D < 0$ and $E > 0$ for all positive parameters. Thus the determinant is positive if $B > 0$. Since the trace is negative, the steady states are asymptotically stable when $B > 0$ where $B = (\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \sigma\beta K$.

Proposition 2.2.3. *The exchange of stability occurs when the slope of bifurcation curve, β vs I , changes.*

Proof. Let us recall the equilibrium condition, 2.2.5. Throughout a stability analysis from above, we know that the determinant of zero indicates the threshold for stability changes:

$$det = \frac{\beta}{I}[2EI^3 + BI^2 - D] = 0 \iff 2EI^3 + BI^2 - D = 0 \tag{2.2.12}$$

Second, when the sign of the slope of the bifurcation curve changes, one can find a threshold point by letting the left hand side of equation 2.2.6 be zero and solving for I :

$$3EI^2 + 2BI + C = 0 \iff 3EI^3 + 2BI^2 + CI = 0 \tag{2.2.13}$$

Now, we can show that these two conditions are equivalent by using the equilibrium condition $EI^3 + BI^2 + CI + D = 0$.

$$(3EI^3 + 2BI^2 + CI) - (2EI^3 + BI^2 - D) = EI^3 + BI^2 + CI + D = 0 \quad (2.2.14)$$

which is the equilibrium condition. In summary, using the equilibrium condition, $EI^3 + BI^2 + CI + D = 0$, one can show that when the sign of the slope of the bifurcation curve changes, its stability changes too. \square

2.2.2 When do we get a backward bifurcation?

The idea underlying this section is that an infinite slope of the bifurcation curve signals a backward bifurcation. The slope of the bifurcation curve is infinite when $f(I) = 3EI^2 + 2BI + C = 0$. Thus if $f(I)$ has two positive distinct real roots, we get backward bifurcation. The sufficient conditions for $f(I)$ to have two positive real roots is as follows;

$$f(0) > 0, \quad \frac{-B}{3E} > 0 \quad \text{and} \quad B^2 - 3EC > 0$$

which is equivalent to

$$\begin{aligned} p &< \frac{1}{\sigma\mu\beta A} \left[\mu(\mu + \gamma)(\mu + \theta + \phi) - \beta(A + \Lambda)(1 + \sigma\phi) \right], \\ \phi &< \frac{\sigma\beta(A + \Lambda) - \sigma\mu(\mu + \gamma) - \mu(\mu + \theta)}{\sigma\mu}, \\ \text{and } p &> \frac{1}{3\sigma^2\mu\beta A} \left[-3\beta\sigma(A + \Lambda)(\mu + \theta + \sigma\phi) + 3\mu\sigma(\mu + \gamma)(\mu + \theta + \sigma\phi) \right. \\ &\quad \left. - \mu \left((\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) - \frac{\sigma\beta(A + \Lambda)}{\mu} \right)^2 \right] \end{aligned} \quad (2.2.15)$$

From Figure 2.2, one can easily notice that we lose backward bifurcation as we increase p when other parameters are fixed.

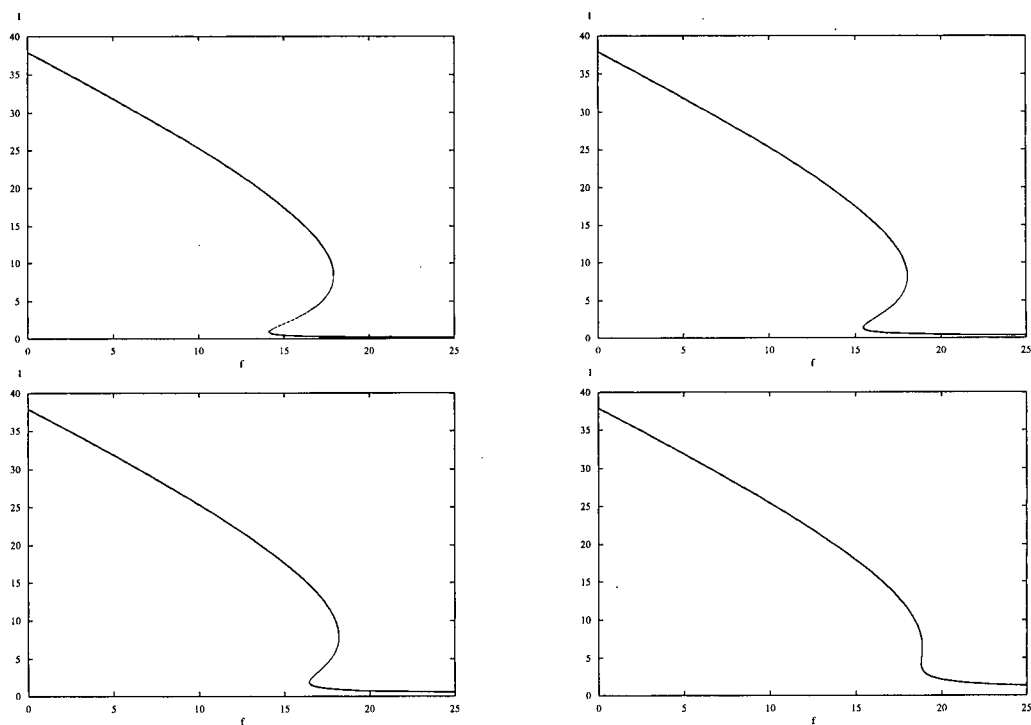


Figure 2.2: Bifurcation of SIS model when there is no disease-fatality, with various fraction infective from immigration, p . From the top left, various p values are used : $p = 0.1, p = 0.2, p = 0.7$ and $p = 0.3$ in clockwise direction respectively. Other parameters are fixed at $\Lambda = 3, \beta = 1, \sigma = 0.2, \mu = 0.1, \gamma = 12, \theta = 0.5$ and $A = 2$.

2.3 A model of SVIS type with disease-related death, i.e.

$$\alpha \neq 0.$$

We now consider the original model which includes non-zero disease-fatality. Recalling the original system of differential equation, let us remind the system of differential equations,

2.1.1:

$$\begin{aligned} S' &= (1-p)A + \Lambda - \beta SI - (\mu + \phi)S + \gamma I + \theta V \\ I' &= pA + \beta SI + \sigma\beta VI - (\mu + \gamma + \alpha)I \\ V' &= \phi S - \sigma\beta VI - (\mu + \theta)V \end{aligned}$$

Recall that the total population is the sum of three classes, susceptibles, infectives and vaccinated, i.e.

$$N(t) = S(t) + I(t) + V(t)$$

Thus it follows that

$$N' = S' + I' + V' = A + \Lambda - \mu N - \alpha I$$

We can get an alternate but yet equivalent model by replacing S by $N - V - I$. Now the model is:

$$\begin{aligned} I' &= pA + \beta I[N - I - (1 - \sigma)V] - (\mu + \gamma + \alpha)I \\ V' &= \phi(N - I) - \sigma\beta VI - (\mu + \theta + \phi)V \\ N' &= A + \Lambda - \mu N - \alpha I \end{aligned} \tag{2.3.1}$$

We can write the equilibrium conditions by letting the right-hand side of 2.3.1 be zero. The

equilibrium conditions are

$$pA + \beta I[N - I - (1 - \sigma)V] = (\mu + \gamma + \alpha)I$$

$$\phi(N - I) = (\mu + \theta + \phi + \sigma\beta I)V$$

$$\mu N + \alpha I = A + \Lambda$$

From the second and the third equilibrium conditions we can solve for N and V :

$$\begin{aligned} N &= \frac{A + \Lambda - \alpha I}{\mu} \\ V &= \frac{\phi(N - I)}{\mu + \theta + \phi + \sigma\beta I} \\ &= \frac{\phi[A + \Lambda - (\alpha + \mu)I]}{\mu(\mu + \theta + \phi + \sigma\beta I)} \end{aligned}$$

Eliminating N and V by substitution of these expressions into the first condition and simplifying, we obtain an expression involving I for the equilibrium condition of the form

$$pA + \beta I \left[\frac{A + \Lambda - \alpha I}{\mu} - I - (1 - \sigma) \frac{\phi[A + \Lambda - (\alpha + \mu)I]}{\mu(\mu + \theta + \phi + \sigma\beta I)} \right] = (\mu + \gamma + \alpha)I$$

We can further simplify by multiplying $\mu(\mu + \theta + \phi + \sigma\beta I)$ in order to get a cubic equation for the equilibrium values of I of the form

$$EI^3 + BI^2 + CI + D = 0$$

where

$$E = \beta\sigma(\alpha + \mu)$$

$$B = -(A + \Lambda)\sigma\beta + (\alpha + \mu)(\mu + \theta + \sigma\phi) + \sigma\mu(\mu + \gamma + \alpha)$$

$$C = -\mu p\sigma A - (A + \Lambda)(\mu + \theta + \sigma\phi) + \frac{\mu(\mu + \gamma + \alpha)(\mu + \theta + \phi)}{\beta}$$

$$D = \frac{-pA\mu(\mu + \theta + \phi)}{\beta}$$

In order to study the stability of steady states we start a qualitative approach by linearization of 2.3.1:

$$J = \begin{pmatrix} \beta[N - (1 - \sigma)V - I] - \beta I - (\mu + \gamma + \alpha) & -\beta(1 - \sigma)I & \beta I \\ -(\phi + \sigma\beta V) & -\sigma\beta I - (\mu + \theta + \phi) & \phi \\ -\alpha & 0 & -\mu \end{pmatrix}$$

Using the equilibrium condition, $pA + \beta I[N - I - (1 - \sigma)V] = (\mu + \gamma + \alpha)I$, we can rewrite the matrix as:

$$J|_{I^*} = \begin{pmatrix} -\frac{pA}{I} - \beta I & -\beta(1 - \sigma)I & \beta I \\ -(\phi + \sigma\beta V) & -\sigma\beta I - (\mu + \theta + \phi) & \phi \\ -\alpha & 0 & -\mu \end{pmatrix}$$

After a complicated computation, we can obtain its characteristic equation involving I in it:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$\begin{aligned} a_1 &= (1 + \sigma)\beta I + \frac{pA}{I} + 2\mu + \theta + \phi \\ a_2 &= (\beta I + \frac{pA}{I})(\mu + \theta + \phi + \sigma\beta I) + (\mu + \theta + \phi + \sigma\beta I)\mu + \mu(\beta I + \frac{pA}{I}) \\ &\quad - \beta I(1 - \sigma)(\phi + \sigma\beta V) + \alpha\beta I \\ a_3 &= \mu(\beta I + \frac{pA}{I})(\mu + \theta + \phi + \sigma\beta I) - \mu\beta I(1 - \sigma)(\phi + \sigma\beta V) \\ &\quad + \alpha\beta I(\mu + \theta + \sigma\phi + \sigma\beta I) \end{aligned}$$

By the *Routh-Hurwitz Criterion*, the steady state is globally stable if and only if

$$a_1 > 0 \quad a_3 > 0 \quad \text{and} \quad a_1a_2 > a_3.$$

The Figure 2.3 demonstrates a few cases where an equilibrium graph loses its stability as the vaccination rate, ϕ , increases and becomes stable again. At the point where it loses local

stability first, Hopf-bifurcation occurs and a periodic solution appears for some ϕ values.

Table 2.2 summarizes the explicit roots of the cubic polynomial, $\lambda^3 + A\lambda^2 + B\lambda + C = 0$ with real a_1 , a_2 and a_3 . Also the theorem about the normal form of Hopf-bifurcation and the method to detect various bifurcations in 1-dimensional space is included in Appendix.

Theorem 2.3.1. Routh-Hurwitz Theorem, [2]

Consider the characteristic equation

$$|\lambda I - A| = \lambda^n + b_1\lambda^{n-1} + \dots + b_{n-1}\lambda + b_n = 0$$

determining the n eigenvalues λ of $n \times n$ square matrix A , where I is the identity matrix.

Then the eigenvalues λ all have negative real parts if

$$\Delta_1 > 0, \quad \Delta_2 > 0, \quad \dots, \Delta_n > 0$$

where

$$\Delta_k = \begin{pmatrix} b_1 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\ b_3 & b_2 & b_1 & 1 & 0 & 0 & \dots & 0 \\ b_5 & b_4 & b_3 & b_2 & b_1 & 1 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ b_{2k-1} & b_{2k-2} & b_{2k-3} & b_{2k-4} & b_{2k-5} & b_{2k-6} & \dots & b_k \end{pmatrix}$$

2.3.1 The case where there are no infective immigrants

It is worthwhile to consider the case without infective immigrants since in this case the system will have a disease-free steady state that would not exist otherwise. This model was proposed by Kribs-Zaleta and Vekasco-Hernandezin, [10]. If there is no infective portion

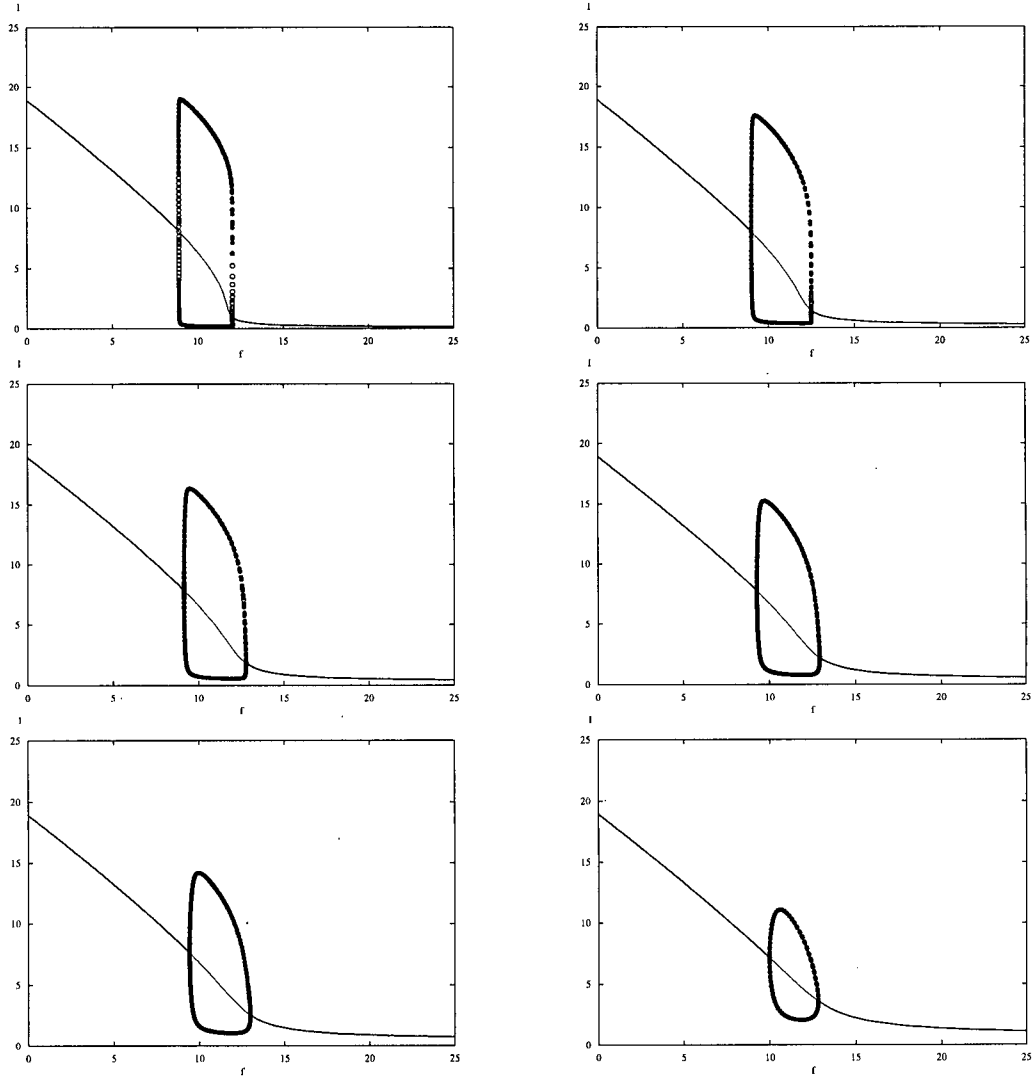


Figure 2.3: Bifurcation of SIS model with various fraction infective from immigration, p . From the top left, various p values are used : $p = 0.1, p = 0.2, p = 0.4, p = 0.48, p = 0.5$ and $p = 0.3$ respectively. Other parameters are fixed at $\Lambda = 3, \beta = 1, \sigma = 0.2, \mu = 0.1, \gamma = 12, \theta = 0.5, A = 2$

$\alpha > 0$	$\beta = 0$	$\lambda_1 = -a$ $\lambda_2 = (3\alpha)^{1/2} - a$ $\lambda_3 = -(3\alpha)^{1/2} - a$
	$ \beta \leq 2\alpha^{3/2}$	$\lambda_1 = 2\alpha^{1/2} \sin \phi - a$ $\lambda_2 = -2\alpha^{1/2} \sin(\pi/3 + \phi) - a$ $\lambda_3 = 2\alpha^{1/2} \sin(\pi/3 - \phi) - a$
	$\beta > 2\alpha^{3/2}$	$\lambda_1 = -2\alpha^{1/2} \cosh \psi - a$ $\lambda_2 = \alpha^{1/2} \cosh \psi - a + i(3\alpha)^{1/2} \sinh \psi$ $\lambda_3 = \alpha^{1/2} \cosh \psi - a - i(3\alpha)^{1/2} \sinh \psi$
	$\beta < -2\alpha^{3/2}$	$\lambda_1 = 2\alpha^{1/2} \cosh \psi - a$ $\lambda_2 = -\alpha^{1/2} \cosh \psi - a + i(3\alpha)^{1/2} \sinh \psi$ $\lambda_3 = -\alpha^{1/2} \cosh \psi - a - i(3\alpha)^{1/2} \sinh \psi$
$\alpha = 0$	$-\infty < \beta < \infty$	$\lambda_1 = -\beta^{1/3} - a$ $\lambda_2 = \beta^{1/3}/2 - a + 3i\beta^{2/3}/4$ $\lambda_3 = \beta^{1/3}/2 - a - 3i\beta^{2/3}/4$
$\alpha < 0$	$-\infty < \beta < \infty$	$\lambda_1 = -2(-\alpha)^{1/2} \sinh \theta - a$ $\lambda_2 = (-\alpha)^{1/2} \sinh \theta - a + i(-3\alpha)^{1/2} \cosh \theta$ $\lambda_3 = (-\alpha)^{1/2} \sinh \theta - a - i(-3\alpha)^{1/2} \cosh \theta$

Table 2.2: Explicit roots of the cubic polynomial $p(\lambda) = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3$, with a_1, a_2 , and a_3 real. $a_1 \equiv 3a$, $a_2 \equiv 3b$, $\alpha \equiv a^2 - b$, $\beta \equiv 2a^3 - 3ab + a_3$, $\phi = (1/3) \sin^{-1} \beta/[2\alpha^{3/2}]$ ($-\pi/6 \leq \phi \leq \pi/6$), $\psi = (1/3) \cosh^{-1} \{|\beta|/[2\alpha^{3/2}]\}$ and $\theta = (1/3) \sinh^{-1} \{\beta/[2(-\alpha)^{3/2}]\}$, [11]

from immigrants, i.e. $p = 0$, then our equation becomes:

$$\begin{aligned} S' &= A + \Lambda - \beta SI - (\mu + \phi)S + \gamma I + \theta V \\ I' &= \beta SI + \sigma \beta VI - (\mu + \gamma + \alpha)I \\ V' &= \phi S - \sigma \beta VI - (\mu + \theta)V \end{aligned}$$

The total population is defined as sum of three classes: susceptibles, infectives and vaccinated, thus,

$$N(t) = S(t) + I(t) + V(t)$$

Thus it follows that

$$N'(t) = S'(t) + I'(t) + V'(t) = A + \Lambda - \mu N(t) - \alpha I(t)$$

As before we can make a similar transformation by replacing $S(t)$ by $N(t) - V(t) - I(t)$.

Now the model is:

$$\begin{aligned} I' &= \beta I[N - I - (1 - \sigma)V] - (\mu + \gamma + \alpha)I \\ V' &= \phi(N - I) - \sigma \beta VI - (\mu + \theta + \phi)V \\ N' &= A + \Lambda - \mu N - \alpha I \end{aligned} \tag{2.3.2}$$

We can write the equilibrium conditions by letting the right-hand side of 2.3.2 to be zero.

The equilibrium conditions are

$$\beta I[N - I - (1 - \sigma)V] = (\mu + \gamma + \alpha)I$$

$$\phi(N - I) = (\mu + \theta + \phi + \sigma \beta I)V$$

$$\mu N + \alpha I = A + \Lambda$$

From the second and the third equilibrium conditions we can solve for $N(t)$ and $V(t)$:

$$\begin{aligned} N(t) &= \frac{A + \Lambda - \alpha I(t)}{\mu} \\ V(t) &= \frac{\phi(N(t) - I(t))}{\mu + \theta + \phi + \sigma\beta I(t)} \\ &= \frac{\phi[A + \Lambda - (\alpha + \mu)I]}{\mu(\mu + \theta + \phi + \sigma\beta I(t))} \end{aligned}$$

Eliminating $N(t)$ and $V(t)$ by substitution of these expressions into the first condition and simplifying, we obtain an expression involving $I(t)$ for the equilibrium condition of the form

$$\beta I \left[\frac{A + \Lambda - \alpha I}{\mu} - I - (1 - \sigma) \frac{\phi[A + \Lambda - (\alpha + \mu)I]}{\mu(\mu + \theta + \phi + \sigma\beta I)} \right] = (\mu + \gamma + \alpha)I$$

We can further simplify by multiplying $\mu(\mu + \theta + \phi + \sigma\beta I)$ and factoring out a disease-free equilibrium

$$I^* = 0$$

in order to obtain an endemic condition as the quadratic equation for the equilibrium values of I of the form

$$EI^2 + BI + C = 0$$

where

$$E = \beta\sigma(\alpha + \mu)$$

$$B = -(A + \Lambda)\sigma\beta + (\alpha + \mu)(\mu + \theta + \sigma\phi) + \sigma\mu(\mu + \gamma + \alpha)$$

$$C = -(A + \Lambda)(\mu + \theta + \sigma\phi) + \frac{\mu(\mu + \gamma + \alpha)(\mu + \theta + \phi)}{\beta}$$

In order to study the stability of steady states we linearize 2.3.2, obtaining the Jacobian matrix:

$$J = \begin{pmatrix} \beta[N - (1 - \sigma)V - I] - \beta I - (\mu + \gamma + \alpha) & -\beta(1 - \sigma)I & \beta I \\ -(\phi + \sigma\beta V) & -\sigma\beta I - (\mu + \theta + \phi) & \phi \\ -\alpha & 0 & -\mu \end{pmatrix}$$

By evaluating at the disease-free equilibrium, $I^* = 0$, we can obtain three real eigenvalues:

$$\lambda_1 = \frac{\beta(\mu + \theta + \sigma\phi)(A + \Lambda)}{\mu(\mu + \theta + \phi)} - (\gamma + \alpha + \mu)$$

$$\lambda_2 = -(\phi + \theta + \mu)$$

$$\lambda_3 = -\mu$$

Note that the first eigenvalue is negative when $R(\phi) < 1$ where vaccination reproductive number is defined by

$$R(\phi) = \frac{\beta(\mu + \theta + \sigma\phi)(A + \Lambda)}{\mu(\mu + \theta + \phi)(\gamma + \alpha + \mu)}$$

Thus the disease-free equilibrium is asymptotically stable if and only of $R(\phi) < 1$. Also by using the endemic equilibrium condition, $\beta[N - I - (1 - \sigma)V] = (\mu + \gamma + \alpha)$, we can evaluate the Jacobian matrix at endemic equilibria:

$$J|_{I^*} = \begin{pmatrix} -\beta I & -\beta(1 - \sigma)I & \beta I \\ -(\phi + \sigma\beta V) & -\sigma\beta I - (\mu + \theta + \phi) & \phi \\ -\alpha & 0 & -\mu \end{pmatrix}$$

with a characteristic equation:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$a_1 = (1 + \sigma)\beta I + 2\mu + \theta + \phi$$

$$a_2 = (\beta I + \mu)(\mu + \theta + \phi + \sigma\beta I) + \beta(\mu + \alpha)I - \beta(1 - \sigma)(\phi + \sigma\beta V)$$

$$a_3 = \mu\beta I[\mu + \theta + \sigma\phi + \sigma\beta I + \sigma\beta(\sigma - 1)V] + \alpha\beta I(\mu + \theta + \sigma\phi + \sigma\beta I)$$

For this SVIS model there is a transcritical bifurcation at

$$\phi = \frac{(\mu + \theta)[\mu(\gamma + \alpha + \mu) - \beta(A + \Lambda)]}{\sigma\beta(A + \Lambda) - \mu(\gamma + \alpha + \mu)}$$

and this is demonstrated in Figure 2.4 below. One can easily see that the lower branch of the bifurcation curve is negative for $\phi < \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$, and coincides with the disease-free equilibrium value of zero at $\phi = \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$. Also the disease-free equilibrium is locally stable for $\phi > \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$ and locally unstable otherwise while the lower endemic equilibrium becomes locally unstable for $\phi > \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$. In summary these equilibria exchange stability as the endemic equilibrium moves through the disease-free equilibrium at $\phi = \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$ and there exists only one epidemiologically feasible endemic equilibrium for $\phi < \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)}$. The existence of a transcritical bifurcation at $(I, \phi) = (0, \frac{(\mu+\theta)[\mu(\gamma+\alpha+\mu)-\beta(A+\Lambda)]}{\sigma\beta(A+\Lambda)-\mu(\gamma+\alpha+\mu)})$ using the theorem by Sotomayor (1973). Also these phenomena involving transcritical bifurcation is demonstrated in Figure 2.4.

Theorem 2.3.2. (Sotomayor, 1973) Let

$$\dot{x} = f(x, \mu) \quad (2.3.3)$$

be the system of differential equations in \mathbb{R}^n depending on the singular parameter μ . When $\mu = \mu_0$, assume that there is an equilibrium x_0 , i.e. $f(x_0, \mu_0) = 0$. Suppose that the $n \times n$ matrix $A \equiv Df(x_0, \mu_0)$ has a simple eigenvalue $\lambda = 0$ with eigenvector v and that A^T has an eigenvector w corresponding to the eigenvalue $\lambda = 0$. Furthermore, suppose that A has k eigenvalues with negative real parts and $(n - k - 1)$ eigenvalues with positive real parts (counting multiplicity) and that the following conditions are satisfied

$$w^T f_\mu(x_0, \mu_0) \neq 0, \quad w^T [D^2 f(x_0, \mu_0)(v, v)] \neq 0. \quad (2.3.4)$$

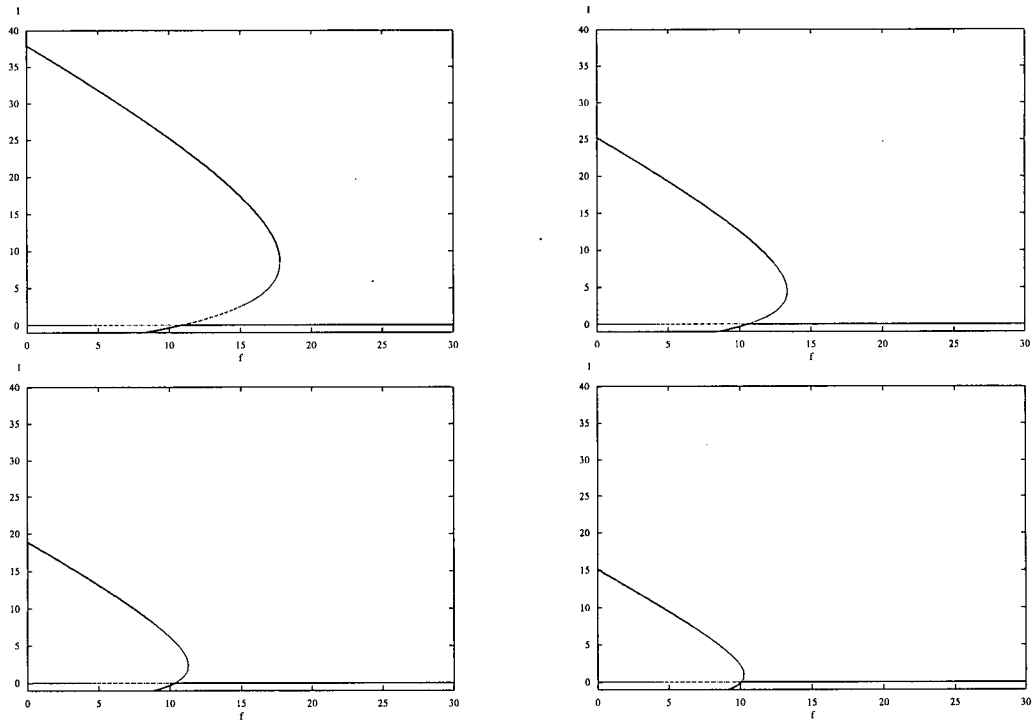


Figure 2.4: Bifurcation of SIS model when there is no disease-fatality, with various fraction infective from immigration, p . From the top left, various p values are used : $\alpha = 0, \alpha = 0.05, \alpha = 0.15$ and $\alpha = 0.1$ in clockwise direction respectively. Other parameters are fixed at $p = 0$, $\Lambda = 3$, $\beta = 1$, $\sigma = 0.2$, $\mu = 0.1$, $\gamma = 12$, $\theta = 0.5$ and $A = 2$.

Then there is a smooth curve of equilibrium points of 2.3.3 in $R^n \times R^n$ passing through (x_0, μ_0) and tangent to the hyperplane $R^n \times \{\mu_0\}$. Depending on the sign of the expressions in 2.3.4, there are no equilibrium points of 2.3.3 near x_0 when $\mu < \mu_0$ (or when $\mu > \mu_0$) and there are two equilibrium points of 2.3.3 near x_0 when $\mu > \mu_0$ (or when $\mu < \mu_0$). The two equilibrium points of 2.3.3 near x_0 are hyperbolic and have stable manifolds of dimension k and $k + 1$ respectively; i.e., the system 2.3.3 experiences a saddle-node bifurcation at the equilibrium point x_0 as the parameter μ passes through the bifurcation value $\mu = \mu_0$. The set of C^∞ -vector fields satisfying the above condition is an open, dense subset in the Banach space of all C^∞ , one-parameter, vector fields with an equilibrium point x_0 having a simple zero eigenvalue.

Corollary 2.3.3. [12] *If the conditions 2.3.4 are changed to*

$$\begin{aligned} w^T f_\mu(x_0, \mu_0) &= 0, \\ w^T [Df_\mu(x_0, \mu_0)v] &\neq 0, \text{ and} \\ w^T [D^2 f(x_0, \mu_0)(v, v)] &\neq 0, \end{aligned} \tag{2.3.5}$$

then the system 2.3.3 experiences a transcritical bifurcation at the equilibrium point x_0 as the parameter μ varies through the bifurcation value $\mu = \mu_0$.

2.4 Special cases

2.4.1 The case without disease fatalities in the absence of immigration, i.e. $\alpha = 0$ and $A = 0$

Assuming that there is no immigration ($A = 0$) and that there are no disease fatalities. Let us investigate the new criterion which determine the presence of a backward bifurcation. We now can formulate the revised model:

$$\begin{aligned} S' &= \Lambda - \beta SI - (\mu + \phi)S + \gamma I + \theta V \\ I' &= \beta SI + \sigma \beta VI - (\mu + \gamma)I \\ V' &= \phi S - \sigma \beta VI - (\mu + \theta)V \end{aligned} \tag{2.4.1}$$

Since $N = S + I + V$ we can add the three equations, which gives $N' = S' + I' + V' = \Lambda - \mu N$. By the theory of asymptotically autonomous systems, one can reduce the system to two dimensions by letting $N \equiv K$ and $S = K - I - V$:

$$\begin{aligned} I' &= \beta[K - I - (1 - \sigma)V]I - (\mu + \gamma)I \\ V' &= \phi[K - I - V] - \sigma \beta VI - (\mu + \theta)V \end{aligned} \tag{2.4.2}$$

One can solve for V using the first equation and substitute unto the second one to eliminate V , which yields $EI^2 + BI + C = 0$ where

$$\begin{aligned} E &= \sigma \beta \\ B &= (\mu + \theta + \sigma \phi) + \sigma(\mu + \gamma) - \sigma \beta K \\ C &= \frac{(\mu + \gamma)(\mu + \theta + \phi)}{\beta} - (\mu + \theta + \sigma \phi)K \end{aligned}$$

Implicit differentiation with respect to β gives

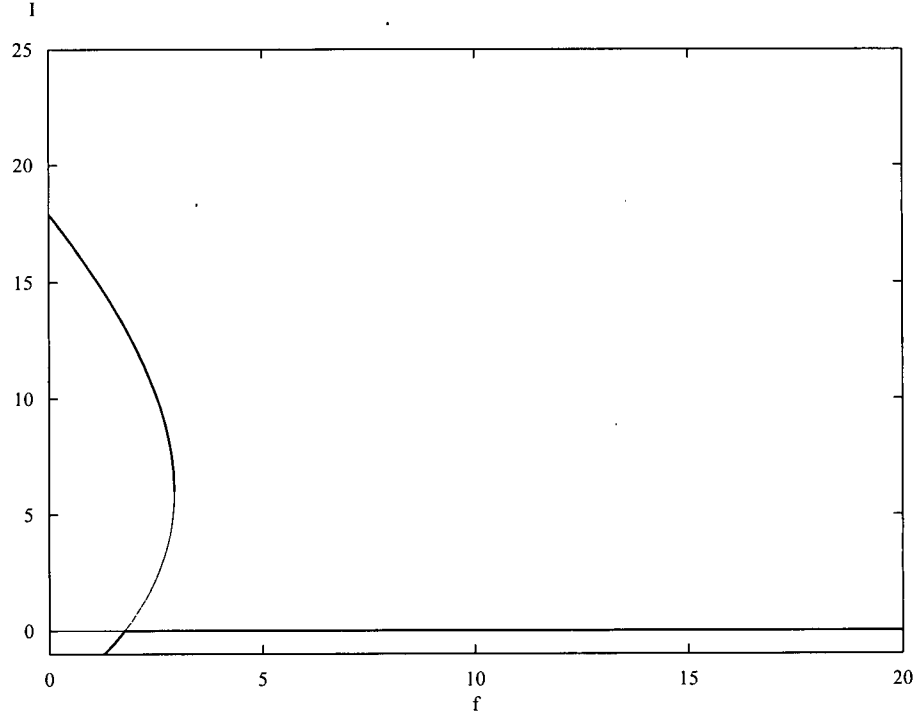


Figure 2.5: Bifurcation of SIS model in the absence of immigration and when there is no disease fatality, i.e. $\alpha = 0$, $E = 0$

$$\begin{aligned} (2EI + B) \frac{dI}{d\beta} &= -\sigma I^2 - (-\sigma K)I + \frac{(\mu + \theta + \alpha)(\mu + \theta + \phi)}{\beta^2} \\ &= \sigma I(K - I) + \frac{(\mu + \theta + \alpha)(\mu + \theta + \phi)}{\beta^2} \end{aligned}$$

The right hand side is greater than zero so we want $2EI + B > 0$ to have the positive slope of bifurcation curve, and $2EI + B < 0$ for a negative slope. Thus $2EI + B = 0$ will be critical in determining the slope of the bifurcation curve.

2.4.2 The case when all susceptibles are vaccinated immediately and vaccine does not lose its effectiveness i.e. $\theta = 0$, $\phi \rightarrow \infty$

Let us assume that there is no loss of effectiveness of vaccine, so we let $\theta = 0$. Also we assume that all the susceptibles are vaccinated immediately, i.e. $\phi \rightarrow \infty$. If there is no fatality from the disease then now we can reduce a system to one-dimensional as below:

$$\begin{aligned} I' &= pA + \sigma\beta I(K - I) - (\mu + \gamma)I \\ &= -\sigma\beta I^2 + (\sigma\beta K - \mu - \gamma)I + pA \end{aligned} \tag{2.4.3}$$

At equilibrium, $I' = 0$ and let us assume that $I_{1,2}^*$ are roots of $I' = 0$, with $I_1^* \geq 0$ and $I_2^* \leq 0$.

$$I_{1,2}^* = \frac{-(\mu + \gamma - \sigma\beta K) \pm \sqrt{(\mu + \gamma - \sigma\beta K)^2 + 4\sigma\beta pA}}{2\sigma\beta}$$

Let us define ξ as $\xi = -(\mu + \gamma - \sigma\beta K)$. Now we can rewrite the endemic equilibrium as

$$I_1^* = \frac{\xi + \sqrt{\xi^2 + 4\sigma\beta pA}}{2\sigma\beta}$$

When p gets close to zero, one can study the limit of I_1^* :

$$\lim_{p \rightarrow 0} I_1^* = \frac{\xi + |\xi|}{2\sigma\beta} = \begin{cases} 0 & \text{if } \xi < 0; \\ \frac{2\xi}{2\sigma\beta} & \text{if } \xi > 0 \end{cases}$$

Thus we can conclude that $\xi = 0$ is a threshold that determines whether there exist an endemic equilibrium when p goes to zero. Since $R_0 = \frac{\beta K}{\mu + \gamma}$, $R_0^* = \frac{\sigma\beta K}{\mu + \gamma} = \sigma R_0 \leq R_0$. Note that $R_0^* \leq R_0$. Also if p goes to zero, I_1 becomes zero, so there cannot be a backward bifurcation in this case.

The case with no infective immigrants

In this subsection we make an additional assumption about immigrants. First, we assumed already that vaccine is applied immediately to susceptibles and that the vaccine does not lose its effectiveness. In addition to that, in this subsection, we also assume that there are no infective immigrants. Then we can let $p = 0$ in the equation 2.4.3, so the revised equation is

$$\begin{aligned} I' &= \sigma\beta I(K - I) - (\mu + \gamma)I \\ &= -\sigma\beta I^2 + (\sigma\beta K - \mu - \gamma)I \end{aligned} \tag{2.4.4}$$

and its steady states are

$$I_1^* = 0 \quad I_2^* = \frac{\sigma\beta K - \mu - \gamma}{\sigma\beta} \tag{2.4.5}$$

where I_2^* is biologically relevant only when $\sigma\beta K - \mu - \gamma > 0$.

It can be shown that equation 2.4.4 exhibits a transcritical bifurcation at $I_1^* = 0$ when the contact rate, β , is used as a varying parameter. We use the theorem 2.4.1 to prove this.

Theorem 2.4.1. *Consider the function,*

$$\dot{x} = f(x, \mu) \quad , \quad x, \mu \in \mathbb{R}.$$

Let's assume that f has continuous derivatives up to third order for all (μ, x) near the

bifurcation point (μ^*, x^*) . If there is a pair (μ^*, x^*) for which

$$f(x^*, \mu^*) = 0$$

$$f_x(x^*, \mu^*) = 0$$

$$f_\mu(x^*, \mu^*) = 0$$

$$f_{x\mu}(x^*, \mu^*) \neq 0$$

$$f_{xx}(x^*, \mu^*) \neq 0$$

then $\dot{x} = f(x, \mu)$ has a (two branch) transcritical bifurcation with quadratic tangency at (μ^*, x^*) , [12].

In our equation we let

$$f(I, \beta) = -\sigma\beta I^2 + (\sigma\beta K - \mu - \gamma)I$$

Then

$$f_x(x, \beta) = -2\sigma\beta I + (\sigma\beta K - \mu - \gamma)$$

$$f_\beta(x, \beta) = -\sigma I^2 + \sigma K I$$

$$f_{x\beta}(x, \beta) = -2\sigma I + \sigma K$$

$$f_{xx}(x, \beta) = -2\sigma\beta.$$

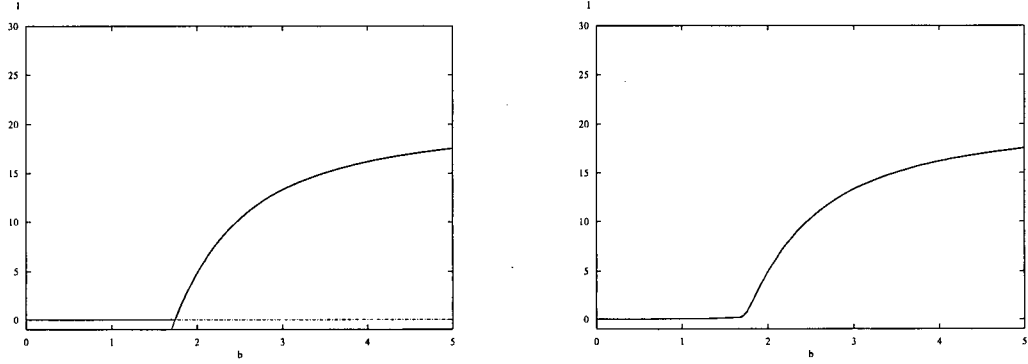


Figure 2.6: Bifurcation when all susceptibles are vaccinated immediately and vaccine does not lose its effectiveness i.e. $\theta = 0$, $\phi \rightarrow \infty$. Left: the case with no infective immigrant, i.e. $p = 0$ Right: the case with $p = 0.1$. Other parameter values are fixed at $\sigma = 0.2$, $\mu = 0.1$, $\gamma = 12$, $A = 2$, $\kappa = 20$ while a control parameter is a contact rate, β .

We can evaluate $f(I, \beta)$ and these derivatives at $(I^*, \beta^*) = (0, \frac{\mu+\gamma}{\sigma K})$:

$$f(x^*, \beta^*) = 0$$

$$f_x(x^*, \beta^*) = 0$$

$$f_\beta(x^*, \beta^*) = 0$$

$$f_{x\beta}(x^*, \beta^*) = \sigma K \neq 0$$

$$f_{xx}(x^*, \beta^*) = \frac{-2(\mu + \gamma)}{K} \neq 0$$

where other parameters are strictly positive. Hence according to the theorem 2.4.1 it follows that $\dot{I} = f(I, \beta)$ has a (two branch) transcritical bifurcation with quadratic tangency at $(I^*, \beta^*) = (0, \frac{\mu+\gamma}{\sigma K})$. This is demonstrated in Figure 2.6.

2.4.3 The case when the vaccine is utterly ineffective, i.e. $\sigma = 1$, and there are no disease fatalities, i.e. $\alpha = 0$

Let us assume that the vaccine is utterly ineffective, i.e. $\sigma = 1$, and that there is no disease-related fatality, i.e. $\alpha = 0$. One can modify the basic model, 2.1.1, based on this assumption in order to get the system:

$$\begin{aligned} I' &= pA + \beta(K - I)I - (\mu + \gamma)I \\ V' &= \phi(K - I) - \beta VI - (\mu + \theta + \phi)I \end{aligned} \tag{2.4.6}$$

Note that this is somewhat similar to the previous system for the general SIS model. At equilibrium, we have

$$-\beta I^2 + (\beta K - \mu - \gamma)I + pA = 0$$

The possible real two roots of an equation are

$$I_{1,2}^* = \frac{(\beta K - \mu - \gamma) \pm \sqrt{(\beta K - \mu - \gamma)^2 + 4\beta pA}}{2\beta}$$

From this expression, note that $I_2^* < 0$ unless $p=0$ (so $4\beta pA = 0$) and I_1^* is positive if $(\beta K - \mu - \gamma) + \sqrt{(\beta K - \mu - \gamma)^2 + 4\beta pA} > 0$

1. If $Q > 0$ then $I_1^* > 0$
2. If $Q < 0$ then $I_1^* < 0$ when $\sqrt{Q^2 + 4\beta pA} > -Q$ i.e. $4\beta pA > 0$ where $Q = \beta K - \mu - \gamma$

In summary, if $\beta K - \mu - \gamma > 0$ then there always exists an endemic equilibrium in this case and no backward bifurcation is possible.

2.4.4 The case when the vaccine is absolutely effective $\sigma = 0$ and no death is caused by the disease, i.e. $\alpha = 0$

Let us assume that the vaccine is absolutely effective and no death is caused by the disease, i.e. $\alpha = 0$. One can modify the basic model, 2.1.1, based on this assumption in order to get the system:

$$\begin{aligned} I' &= pA + \beta[K - I - V]I - (\mu + \gamma)I \\ V' &= \phi[K - I] - (\mu + \theta + \phi)V \end{aligned} \tag{2.4.7}$$

We can get equilibrium conditions by letting the equation for I' and V' to be zero.

$$\begin{aligned} pA + \beta[K - I - V]I &= (\mu + \gamma)I \\ \phi[K - I] &= (\mu + \theta + \phi)V \end{aligned}$$

From the second condition one can solve for V as following;

$$V^* = \frac{\phi K - \phi I}{\mu + \theta + \phi}$$

By substitution for V into the first condition gives

$$PI^{*2} + QI^* + R = 0$$

where

$$\begin{aligned} P &= \frac{-\beta(\mu + \theta + 2\phi)}{\mu + \theta + \phi} \\ Q &= \frac{\beta K(\mu + \theta)}{\mu + \theta + \phi} - (\mu + \gamma) \\ R &= pA \end{aligned}$$

1. The case when $p = 0$

$$\begin{aligned} I_1^* &= 0 \\ I_2^* &= \frac{-Q}{P} = \left[\frac{\beta K(\mu + \theta)}{\mu + \theta + \phi} - (\mu + \gamma) \right] \left[\frac{\mu + \theta + \phi}{-\beta(\mu + \theta + 2\phi)} \right] \end{aligned}$$

Note that $I_2^* > 0$ if and only if $\delta = \beta K(\mu + \theta) - (\mu + \gamma)(\mu + \theta + \phi) < 0$

2. The case when $p \neq 0$

Equilibrium satisfy $I' = 0$ and $V' = 0$.

$$\beta\left(\frac{\mu + \theta + 2\phi}{\mu + \theta + \phi}\right)I^2 - \left(\frac{\delta}{\mu + \theta + \phi}\right)I - pA = 0$$

$$I_{1,2}^* = \frac{\delta \pm \sqrt{\delta^2 + 4pA(\mu + \theta + \phi)\beta(\mu + \theta + 2\phi)}}{2\beta(\mu + \theta + 2\phi)}$$

$I_1^* > 0$ with

$$\lim_{p \rightarrow 0} I_1^* = \frac{\delta + |\delta|}{2\beta(\mu + \theta + 2\phi)} = \begin{cases} 0 & \text{if } \delta < 0; \\ \frac{\delta}{\beta(\mu + \theta + 2\phi)} & \text{if } \delta > 0 \end{cases}$$

Thus, $\delta = 0$ is a threshold, suggesting that there is a basic reproduction number

$$R_0 = \frac{\beta K(\mu + \theta)}{(\mu + \gamma)(\mu + \theta + \phi)}$$

Note that

$$\lim_{p \rightarrow 0} I^* = \begin{cases} 0 & \text{if } R_0 < 1; \\ > 0 & \text{if } R_0 > 1 \end{cases}$$

For $p \approx 0$ using *Taylor's series* $(1 + x)^{1/2} \approx 1 + \frac{x}{2}$,

$$2\beta(\mu + \theta + 2\phi)I^* \approx \delta + |\delta| \left[1 + \frac{2A(\mu + \theta + \phi)\beta(\mu + \theta + 2\phi)p}{\delta^2} \right]$$

If $R_0 > 1$ so that $\delta > 0$ this gives

$$I^* \approx \frac{A(\mu + \theta + \phi)}{\delta} p$$

Thus at least for p close to zero, R_0 represents a threshold.

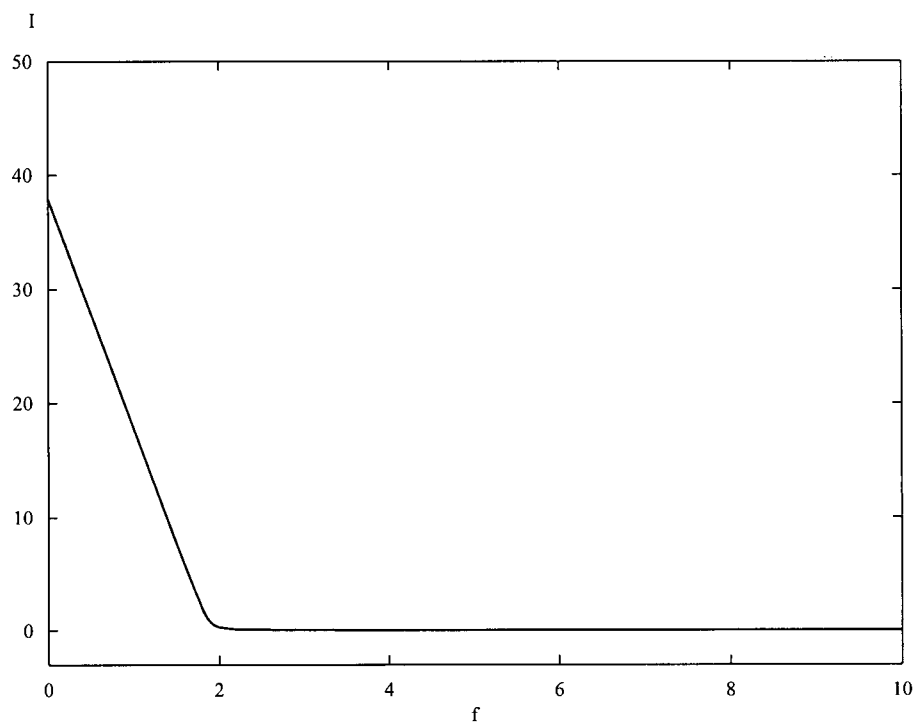


Figure 2.7: Bifurcation when vaccine is absolutely effective $\sigma = 0$ and no death is caused by the disease, i.e. $\alpha = 0$

Chapter 3

The SVIR model

3.1 The general SVIR Model

Let us now consider an SIR type disease when a vaccination program is in effect and there is a constant flow of incoming immigrants. We define S , V , I , R and N as the number of susceptibles, vaccinated, infectives and recovered individuals and total population respectively. We model new infections using the simple mass-action law, so that in general there are βSI new infections in unit time when β is the rate of contact that is sufficient to transmit the disease. We also assume a constant recovery rate, γ . The vaccine has the effect of reducing the susceptibility to infection by a factor of σ , so that $\sigma = 0$ means that the vaccine is completely effective in preventing infection, while $\sigma = 1$ means that the vaccine is utterly ineffective [10]. The rate at which the susceptible population is vaccinated is ϕ , and the rate at which the vaccine wears off is θ . We assume that there can be disease related death and define α to be the rate of disease-related death, while μ is the rate of natural death that is not related to the disease. The population is replenished in two ways, birth and immigration. We assume that all newborns enter the susceptible class at the constant

rate of Λ and there is a constant incoming flow of immigrants, A , where some portion, p , of immigrants are infectives.

We can now formulate this model, dividing the population into four classes - susceptibles (S), vaccinated (V), infectives (I) and recovered (R):

$$\begin{aligned}
 S' &= \Lambda + (1-p)A - \beta SI - (\mu + \phi)S + \theta V \\
 V' &= \phi S - \sigma \beta VI - (\mu + \theta)V \\
 I' &= pA + \beta SI + \sigma \beta VI - (\mu + \gamma + \alpha)I \\
 R' &= \gamma I - \mu R
 \end{aligned}
 \tag{3.1.1}$$

with $S(t) + V(t) + I(t) + R(t) = N(t)$. Thus it follows that $N' = A + \Lambda - \alpha I - \mu N$.

We can get an alternate but equivalent model by replacing S by $N - V - I - R$. Now the model is

$$\begin{aligned}
 V' &= \phi(N - I - R) - \sigma \beta VI - (\phi + \theta + \mu)V \\
 I' &= pA + \beta I[N - I - (1 - \sigma)V - R] - (\alpha + \gamma + \mu)I \\
 R' &= \gamma I - \mu R \\
 N' &= A + \Lambda - \alpha I - \mu N
 \end{aligned}
 \tag{3.1.2}$$

We can write the equilibrium conditions by letting the right-hand side of 3.1.2 to be

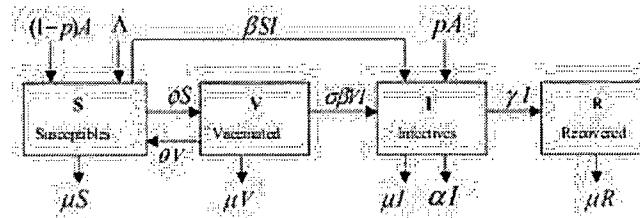


Figure 3.1: The diagram for SVIR model

$S(t)$	Number of susceptibles at time t
$V(t)$	Number of vaccinated individuals at time t
$I(t)$	Number of infectives at time t
$R(t)$	Number of recovered people with immunity at time t
A	Immigrants
p	Portion of infectives among immigrants
Λ	Birth rate
β	Contact rate
γ	Recovery rate
ϕ	Vaccination rate
σ	Factor by which the vaccine has the effect of reducing the infection
θ	Rate at which the vaccine wears off
μ	Natural death rate that is not related to the disease
α	Disease-related death rate
R_0	Basic reproductive number
R_ϕ	Vaccination reproductive number

Table 3.1: Summary of notation

zero. The equilibrium conditions are

$$\mu N = A + \Lambda - \alpha I$$

$$\mu R = \gamma I$$

$$[\sigma\beta I + (\phi + \theta + \mu)]V = \phi(N - I - R)$$

$$(\alpha + \gamma + \mu)I = pA + \beta I[N - I - R - (1 - \sigma)V]$$

We can solve the first and the second conditions for the equilibrium values

$$N^* = \frac{A + \Lambda - \alpha I^*}{\mu}$$

$$R^* = \frac{\gamma I^*}{\mu}$$

Solving for V from the third condition and substituting for N^* and R^* gives

$$\begin{aligned} V^* &= \frac{\phi(N - I - R)}{\sigma\beta I(\mu + \theta + \phi)} \\ &= \frac{\phi\left(\frac{A + \Lambda - \alpha I}{\mu} - I - \frac{\gamma I}{\mu}\right)}{\sigma\beta I(\mu + \theta + \phi)} \\ &= \frac{\phi[A + \Lambda - (\alpha + \gamma + \mu)I]}{\mu[\sigma\beta I + (\mu + \theta + \phi)]} \end{aligned}$$

Eliminating N , V , and R by substitution of these expressions into the last condition and simplifying, we obtain a cubic equation for the equilibrium values of I of the form

$$EI^3 + BI^2 + CI + D = 0 \quad (3.1.3)$$

with

$$E = \beta^2\sigma(\alpha + \gamma + \mu)$$

$$B = \sigma\beta\mu(\alpha + \gamma + \mu) - \beta^2\sigma(\Lambda + A) + \beta(\alpha + \gamma + \mu)(\mu + \theta + \sigma\phi)$$

$$C = -pA\sigma\mu + \mu(\alpha + \gamma + \mu)(\mu + \theta + \phi) - \beta(\mu + \theta + \sigma\phi)(A + \Lambda)$$

$$D = -pA\mu(\mu + \theta + \sigma\phi)$$

Let us first consider the basic reproductive number in the absence of vaccination. The basic reproductive number of the model without vaccination is

$$\dot{R}_0 = \frac{\beta(A + \Lambda)}{\mu(\alpha + \gamma + \mu)} \quad (3.1.4)$$

The reproductive number of the model with vaccination is

$$R(\phi) = \frac{\beta(A + \Lambda)(\mu + \theta + \sigma\phi)}{\mu(\alpha + \gamma + \mu)(\mu + \theta + \phi)} \quad (3.1.5)$$

3.1.1 The vaccine reproductive number, $R(\phi)$

Let us consider the case when there are no infective immigrants, i.e. $p = 0$. Now we consider the special case when $p = 0$ from the model 3.1.2.

$$\begin{aligned} V' &= \phi(N - I - R) - \sigma\beta VI - (\phi + \theta + \mu)V \\ I' &= \beta SI + \sigma\beta VI - (\alpha + \gamma + \mu)I \\ R' &= \gamma I - \mu R \\ N' &= A + \Lambda - \alpha I - \mu N \end{aligned} \quad (3.1.6)$$

We can write the equilibrium conditions by letting the right-hand side of 3.1.6 be zero.

The equilibrium conditions are

$$\begin{aligned} \sigma\beta VI + (\phi + \theta + \mu)V &= \phi(N - I - R) \\ \beta I[N - I - R - (1 - \sigma)V] &= (\alpha + \gamma + \mu)I \\ \mu R &= \gamma I \\ \mu N &= A + \Lambda - \alpha I \end{aligned}$$

We can solve the third and the fourth conditions for the equilibrium values

$$R^* = \frac{\gamma I^*}{\mu} \quad (3.1.7)$$

$$N^* = \frac{A + \Lambda - \alpha I^*}{\mu} \quad (3.1.8)$$

From the second condition we can easily see that there is disease-free equilibrium, $I_1^* = 0$.

At disease-free equilibrium we can evaluate the other equilibrium values of R and N using 3.1.7 and 3.1.8

$$R_1^* = 0, \quad N_1^* = \frac{A + \Lambda}{\mu}.$$

Solving for V from the first condition and substituting for N^* and R^* gives

$$\begin{aligned} V^* &= \frac{\phi(N - I - R)}{\sigma\beta I(\mu + \theta + \phi)} \\ &= \frac{\phi(\frac{A + \Lambda - \alpha I}{\mu} - I - \frac{\gamma I}{\mu})}{\sigma\beta I(\mu + \theta + \phi)} \\ &= \frac{\phi[A + \Lambda - (\alpha + \gamma + \mu)I]}{\mu[\sigma\beta I + (\mu + \theta + \phi)]} \end{aligned}$$

Submitting the values of R , S and I at disease-free we find

$$V_1^* = \frac{\phi(A + \Lambda)}{\mu(\mu + \theta + \phi)}$$

The Jacobian matrix of the system 3.1.6 is

$$J = \begin{pmatrix} -\phi - \sigma\beta V & -\sigma\beta I - (\mu + \theta + \phi) & -\phi & \phi \\ -2\beta I + \beta[N - R - (1 - \sigma)V] - (\gamma + \alpha + \mu) & -\beta I(1 - \sigma) & -\beta I & \beta I \\ \delta & 0 & -\mu & 0 \\ -\alpha & 0 & 0 & -\mu \end{pmatrix}.$$

Now we can evaluate this Jacobian at the disease-free equilibrium

$$J|_{I_1^*=0} = \begin{pmatrix} -\phi[1 + \frac{\sigma\beta(A+\Lambda)}{\mu(\mu+\theta+\phi)}] & -(\mu+\theta+\phi) & -\phi & \phi \\ \frac{\beta(A+\Lambda)}{\mu}[1 - \frac{(1-\sigma)\phi}{\mu+\theta+\phi}] - (\gamma+\alpha+\mu) & 0 & 0 & 0 \\ \delta & 0 & -\mu & 0 \\ -\alpha & 0 & 0 & -\mu \end{pmatrix}.$$

The characteristic equation of the Jacobian matrix above is reduced to

$$\left[\frac{\beta(A+\Lambda)(\mu+\theta+\sigma\phi)}{\mu(\mu+\theta+\phi)} - (\gamma+\alpha+\mu) - \lambda \right] [-(\mu+\theta+\phi+\lambda)(\mu+\lambda)^2] = 0$$

Thus,

$$\lambda_1 = \frac{\beta(A+\Lambda)(\mu+\theta+\sigma\phi)}{\mu(\mu+\theta+\phi)} - (\gamma+\alpha+\mu)$$

$$\lambda_2 = -(\mu+\theta+\phi)$$

$$\lambda_{3,4} = -\mu$$

Since λ_2 and $\lambda_{3,4}$ are negative, the only condition required to ensure the stability of disease-free equilibrium is

$$\frac{\beta(A+\Lambda)(\mu+\theta+\sigma\phi)}{\mu(\mu+\theta+\phi)} - (\gamma+\alpha+\mu) < 0$$

Thus now we define a vaccine reproductive number

$$R(\phi) = \frac{\beta(A+\Lambda)(\mu+\theta+\sigma\phi)}{\mu(\gamma+\alpha+\mu)(\mu+\theta+\phi)}$$

and the disease-free equilibrium is locally asymptotically stable if $R(\phi) < 1$.

In the absence of vaccination, i.e. $\phi = 0$, we define a dimensionless basic reproductive number, R_0 as

$$R_0 = \frac{\beta(A+\Lambda)}{\mu(\gamma+\alpha+\mu)}$$

Note that $R(0) = R_0$ and that $R(\phi) \leq R_0$ and also that $\sigma R_0 \leq R(\phi)$ for all $\phi \geq 0$ since $0 \leq \sigma \leq 1$ with

$$\lim_{\phi \rightarrow \infty} R(\phi) \equiv \sigma R_0.$$

3.2 Endemic equilibria and bifurcations when there are no infective immigrants, $p = 0$.

Let us first consider the two extreme cases in order to investigate endemic equilibria for the model 3.1.2. The first case is when the vaccine is useless and there is no infective immigrant, i.e. $\sigma = 1$ and $p = 0$. Our system becomes

$$S' = \Lambda + A - \beta SI - (\mu + \phi)S + \theta V$$

$$V' = \phi S - \beta VI - (\mu + \theta)V$$

$$I' = \beta SI + \beta VI - (\mu + \gamma + \alpha)I$$

$$R' = \gamma I - \mu R$$

with $S(t) + V(t) + I(t) + R(t) = N(t)$. Note that $R(\phi)$ reduces to R_0 when $\sigma = 1$. By substitution and using the equilibrium conditions, one can find there is an endemic equilibrium,

$$I^* = \frac{\beta(A + \Lambda) - \mu(\alpha + \gamma + \mu)}{\beta(\alpha + \gamma + \mu)}$$

which exists only when $R_0 > 1$.

If instead we suppose that the vaccine is completely effective and that there are no

infective immigrants, i.e. $\sigma = 0$ and $p = 0$, then the model becomes

$$S' = \Lambda + A - \beta SI - (\mu + \phi)S + \theta V$$

$$V' = \phi S - (\mu + \theta)V$$

$$I' = \beta SI - (\mu + \gamma + \alpha)I$$

$$R' = \gamma I - \mu R$$

with $S(t) + V(t) + I(t) + R(t) = N(t)$. After complicated calculation which we omit we find that there is one endemic equilibrium,

$$I^* = \frac{\beta(A + \Lambda)(\theta + \mu) - \mu(\phi + \theta + \mu)(\alpha + \mu + \gamma)}{\beta(\alpha + \mu + \gamma)(\theta + \mu)}$$

which exists only for $R(\phi) > 1$ when $\sigma = 0$.

Now we wish to consider the more general case when the vaccine is partially ineffective and when there are no infectives immigrant, i.e. $0 < \sigma < 1$ and $p = 0$.

$$S' = \Lambda + A - \beta SI - (\mu + \phi)S + \theta V$$

$$V' = \phi S - \sigma\beta VI - (\mu + \theta)V$$

$$I' = \beta SI + \sigma\beta VI - (\mu + \gamma + \alpha)I$$

$$R' = \gamma I - \mu R$$

(3.2.1)

with $S(t) + V(t) + I(t) + R(t) = N(t)$. From equilibrium condition 3.1.3, we know that there is a disease-free equilibrium regardless of different parameter values. After factoring out this disease-free equilibrium, I , we get an equilibrium condition as a quadratic polynomial of I .

$$EI^2 + BI + C = 0 \quad (3.2.2)$$

with

$$E = \beta^2 \sigma (\alpha + \gamma + \mu)$$

$$B = \sigma \beta \mu (\alpha + \gamma + \mu) - \beta^2 \sigma (\Lambda + A) + \beta (\alpha + \gamma + \mu) (\mu + \theta + \sigma \phi)$$

$$C = \mu (\alpha + \gamma + \mu) (\mu + \theta + \phi) - \beta (\mu + \theta + \sigma \phi) (A + \Lambda)$$

Now an endemic equilibrium corresponds to a positive real solution of equation 3.2.2. Note that $E > 0$ and that $C < 0$ precisely when $R(\phi) > 1$. Note also that $B^2 - 4EC > 0$ when $C < 0$. One can easily deduce that there is precisely one endemic equilibrium when $R(\phi) > 1$ since there are two real roots and the product of those two roots is negative. On the other hand we can see that $C > 0$ if $R(\phi) < 1$. Note that there are exactly two changes in the sign of coefficients of equation 3.2.2 if coefficient $B < 0$ and none when $B > 0$. By *Descartes' rule of signs* one can conclude that the maximum number of endemic equilibria is two when $R(\phi) < 1$ and $B < 0$, and that there is no endemic equilibrium when $R(\phi) < 1$ and $B > 0$. However it is shown that it is always the case that the system does not have any endemic equilibrium when $R(\phi) < 1$.

Proposition 3.2.1. *For model 3.2.1, with $R(\phi)$ as defined in 3.1.5, there is no endemic equilibrium when $R(\phi) < 1$.*

Proof. We first assume that $R(\phi) < 1$ and $B < 0$:

$$R(\phi) < 1 \quad \Leftrightarrow \quad \beta (\mu + \theta + \sigma \phi) (A + \Lambda) < \mu (\alpha + \gamma + \mu) (\mu + \theta + \phi)$$

$$B < 0 \quad \Leftrightarrow \quad \beta \sigma \mu (\alpha + \gamma + \mu) + \beta (\alpha + \gamma + \mu) (\mu + \theta + \sigma \phi) < \beta^2 \sigma (A + \Lambda)$$

Combining these two conditions one can get the following relation:

$$\sigma \mu (\alpha + \gamma + \mu) + (\alpha + \gamma + \mu) (\mu + \theta + \sigma \phi) < \frac{\sigma \mu (\alpha + \gamma + \mu) (\mu + \theta + \phi)}{\mu + \theta + \sigma \phi}$$

Factoring out $\alpha + \gamma + \mu$ it reduces to

$$\sigma\mu + \mu + \theta + \sigma\phi < \frac{\sigma\mu(\mu + \theta + \phi)}{\mu + \theta + \sigma\phi}$$

Multiplying $\mu + \theta + \sigma\phi$ on both sides of equation gives

$$[(\sigma + 1)\mu + \theta + \sigma\phi](\mu + \theta + \sigma\phi) < \sigma\mu(\mu + \theta + \phi)$$

After expansion and some calculations which we omit we get an expression,

$$(\theta + \sigma\phi)(\mu + \theta + \sigma\phi) + \mu(\mu + \theta) + \sigma^2\mu\phi < 0$$

which is a contradiction for all nonzero parameters. Therefore we can rule out the case where $R(\phi) < 1$ and $B < 0$. Note that $R(\phi) < 1$ corresponds to $C > 0$ where B and C are defined as in 3.2.2. One can deduce that when $R(\phi) < 1$ B is always positive for nonzero parameters, thus we cannot have any endemic equilibrium in this case by *Descartes' rule of signs*. \square

Theorem 3.2.2. *Descartes' rule of signs*

The number of positive real roots of an equation with real coefficients,

$$f(x) = a_0x^n + a_1x^{n-1} + \dots + a_n = 0,$$

is never greater than the number of variations in the sequences of its coefficients

$$a_0, a_1, \dots, a_n$$

and, if less, then always by an even number

We can now summarize the results as follows:

Lemma 3.2.3. *For model 3.2.1, with $R(\phi)$ as defined in 3.1.5,*

1. *When $R(\phi) > 1$, there is precisely one endemic equilibrium.*

2. When $R(\phi) < 1$, there is no endemic equilibrium.

3.3 The general SVIR case: Non-existence of backward bifurcation

Now we return to more general case of the SVIR model, 3.1.1 and we wish to study on the types of its bifurcation. We recall the endemic equilibrium condition as a cubic equation of I :

$$EI^3 + BI^2 + CI + D = 0$$

with

$$E = \beta^2\sigma(\alpha + \gamma + \mu)$$

$$B = \sigma\beta\mu(\alpha + \gamma + \mu) - \beta^2\sigma(\Lambda + A) + \beta(\alpha + \gamma + \mu)(\mu + \theta + \sigma\phi)$$

$$C = -pA\sigma\mu + \mu(\alpha + \gamma + \mu)(\mu + \theta + \phi) - \beta(\mu + \theta + \sigma\phi)(A + \Lambda)$$

$$D = -pA\mu(\mu + \theta + \sigma\phi)$$

Note that it is clear that $E > 0$ and $D < 0$. As the vaccination rate $\phi \rightarrow \infty$, the reproductive number approaches σR_0 . A backward bifurcation is signalled by an interval for ϕ on which there are three positive roots of 3.1.3. In order to have a backward bifurcation at $R(\phi) = 1$, it is necessary to have

$$R_0 > 1 \quad \sigma R_0 < 1 \quad R(\phi) < 1$$

Under the assumption $\sigma R_0 < 1$ we have

$$\begin{aligned}
 B &= \sigma\beta\mu(\alpha + \mu + \gamma) - \beta^2\sigma(A + \Lambda) + \beta(\alpha + \mu + \gamma)(\mu + \theta + \sigma\phi) \\
 &> \sigma\beta\mu(\alpha + \mu + \gamma) - \beta\mu(\alpha + \mu + \gamma) + \beta(\alpha + \mu + \gamma)(\mu + \theta + \sigma\phi) \\
 &= \beta(\alpha + \mu + \gamma)(\sigma\mu + \theta + \sigma\phi) \\
 &> 0
 \end{aligned}$$

Thus regardless of the sign of C there is only one sign change in the coefficients of 3.1.3. By Descartes' rule of signs the equation 3.1.3 can have at most one positive root. Thus there cannot be a backward bifurcation.

3.4 Outgoing immigrants and backward bifurcations

In previous section we showed that there cannot be a backward bifurcation for all nonnegative parameter values including immigration rate. However, from numerical simulation using XPPAUT, it was found that there can be backward bifurcation if we allow the rate of immigration to be negative, i.e. $A < 0$. In other words, if there is a constant outgoing immigration flow from the host population, backward bifurcation can occur with some parameter sets. Some exemplary figures are shown below with indication of Hopf bifurcation and its stability. For instance, in Figure 3.3, Hopf bifurcation occurs at $\phi = 0.4727$ with period 4.557 and bifurcation loses stability at that point to become unstable as ϕ increases through $\phi = 0.4727$.

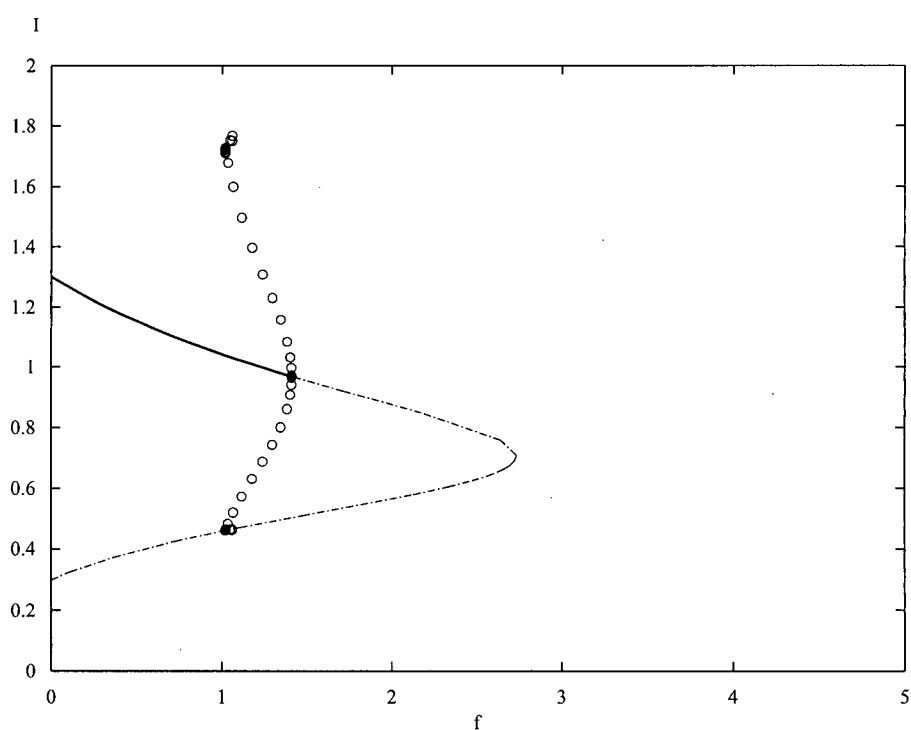


Figure 3.2: Outgoing immigrants and Hopf bifurcation 1: Other parameters are fixed at $A = -5.55$, $p = 0.50$, $\alpha = 0.43$, $\beta = 2.92$, $\sigma = 0.34$, $\mu = 0.68$, $\gamma = 0.53$, $\theta = 0.36$

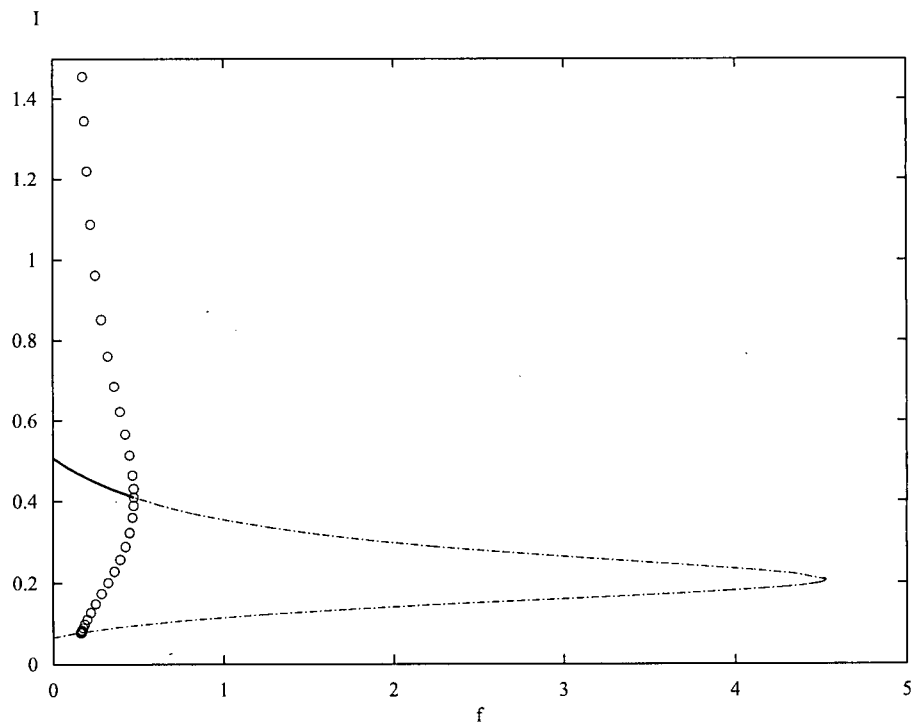


Figure 3.3: Outgoing immigrants and Hopf bifurcation 2: Other parameters are fixed at $A = -7.65$, $p = 0.10$, $\alpha = 0.73$, $\beta = 3.77$, $\sigma = 0.18$, $\mu = 0.37$, $\gamma = 0.92$, $\theta = 0.52$

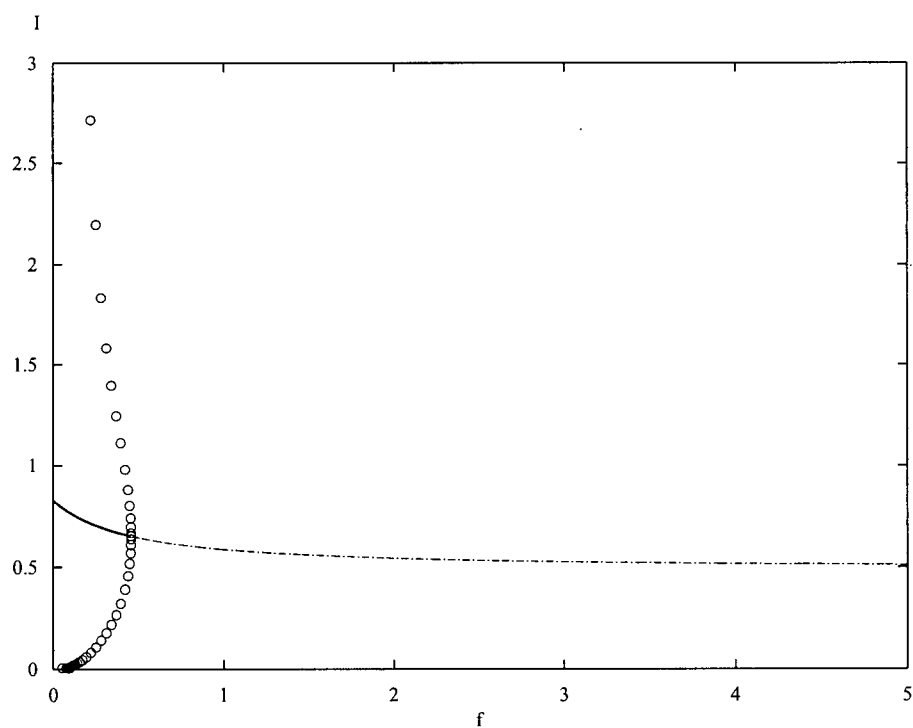


Figure 3.4: Outgoing immigrants and Hopf bifurcation 3: Other parameters are fixed at $A = -2.73$, $p = 0.47$, $\alpha = 0.90$, $\beta = 6.26$, $\sigma = 0.06$, $\mu = 0.09$, $\gamma = 2.71$, $\theta = 0.41$

3.5 Special case: The SVIR model when there are no disease fatalities but with infective immigrants, i.e. $p \neq 0$ and $\alpha = 0$

In this section we assume that there is a constant flow of infective immigrants into host population and no disease fatality. Based on this assumption, we have the system of ODE's below:

$$S' = \Lambda + (1 - p)A - \beta SI - (\mu + \phi)S + \theta V$$

$$I' = pA + \beta SI + \sigma \beta VI - (\mu + \gamma)I$$

$$V' = \phi S - \sigma \beta VI - (\mu + \theta)V$$

$$R' = \gamma I - \mu R$$

The total population is the sum of population of each class, i.e. $N = S + I + V + R$. Thus $N' = S' + I' + V' + R' = A + \Lambda - \mu N$. By theory of autonomous system, it follows that $\lim_{t \rightarrow \infty} N \equiv K = \frac{A + \Lambda}{\mu}$. Replacing S with $K - I - V - R$, we have reduced system of ODE's here:

$$I' = pA + \beta(K - I - V - R)I + \sigma \beta VI - (\mu + \gamma)I$$

$$V' = \phi(K - I - V - R) - \sigma \beta VI - (\theta + \mu)V \quad (3.5.1)$$

$$R' = \gamma I - \mu R$$

Equilibrium Condition

Endemic equilibrium conditions are

$$\begin{aligned}\frac{pA}{I} - \beta I &= -\sigma\beta V + (\mu + \gamma) - \beta(K - V - R) \\ \phi(K - I - V - R) &= \sigma\beta VI + (\theta + \mu)V \\ \gamma I &= \mu R\end{aligned}$$

One can reduce these endemic equilibrium conditions into one cubic equation of I by substituting for K, V and R :

$$f(I) \equiv EI^3 + BI^2 + CI + D = 0 \quad (3.5.2)$$

where

$$\begin{aligned}E &= \beta^2\sigma(\mu + \gamma) \\ B &= \beta[-\beta\sigma(A + \Lambda) + (\mu + \gamma)(\theta + \mu + \sigma\phi + \sigma\mu)] \\ C &= [-pA\mu\sigma\beta - \beta(A + \Lambda)(\theta + \mu + \sigma\phi) + \mu(\mu + \gamma)(\theta + \mu + \phi)] \\ D &= -pA\mu^2(\theta + \mu + \phi)\end{aligned}$$

Since 3.5.2 $f(0) < 0$ and $\lim_{I \rightarrow \infty} f(I) = \infty$ there exist either one or three positive roots, I^* . Now let us consider $f'(I) = 3EI^2 + 2BI + C$. By *Rolle's theorem*, if $f(I)$ has three distinctive positive roots then $f'(I)$ must have two positive roots. Thus $B < 0$ and $C > 0$ is a necessary condition to three positive endemic equilibria.

3.5.1 Stability analysis

Linearization of 3.5.1 will lead to

$$\begin{pmatrix} \beta(K - V - R) - 2\beta I + \sigma\beta V - (\mu + \gamma) & -\beta I + \sigma\beta I & -\beta I \\ -\phi - \sigma\beta V & -\phi - \theta - \mu - \sigma\beta I & -\phi \\ \gamma & 0 & -\mu \end{pmatrix} \quad (3.5.3)$$

3.5.3 can be reduced using equilibrium condition, $\frac{pA}{I} + \beta I = \beta(K - I - R) + \sigma\beta V - (\mu + \gamma)$,

to the following:

$$\begin{pmatrix} -\frac{pA}{I} - \beta I & \beta(\sigma - 1)I & -\beta I \\ -\phi - \sigma\beta V & -(\phi + \theta + \mu) - \sigma\beta I & -\phi \\ \gamma & 0 & -\mu \end{pmatrix} = \begin{pmatrix} A & B & C \\ D & E & F \\ G & 0 & I \end{pmatrix}$$

The characteristic equation is

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$a_1 = -(A + E + I)$$

$$a_2 = (EI + AE + AI - CG - BD)$$

$$a_3 = (BDI + CGE - AEI - BFG)$$

For global stability, it is required that

$$a_1 > 0$$

$$a_3 > 0$$

$$a_1a_2 - a_3 > 0$$

Chapter 4

Conclusion and Discussion

The purpose of this paper is to take a close look at the endemic behavior of the diseases of SIS and SIR type. To a simple SIS model with vaccination we added the immigration of infectives and the rate of the disease-related death rate. As to the contact between infectives and susceptibles we assume a bilinear incidence. The result of our mathematical analysis indicate that a vaccination campaign ϕ has an effect of reducing a reproductive number, which means that the average number of secondary infection caused by an average infective becomes smaller when vaccination is in effect. Furthermore, in SVIS model, a vaccination campaign meant to reduce a disease's reproductive number below one may fail to control disease when there is a backward bifurcation. If one aims to eradicate the disease that is already established, he needs to make sure the vaccination rate is far greater than the one corresponding to the vaccination reproductive number, $R(\phi) = 1$. Bringing down the vaccination reproductive number just below one may not be good enough to eradicate the disease in such a case. Also if there is no immigration of infective, a typical transcritical bifurcation may be observed. The disease-free equilibrium and endemic one coincide at $R(\phi) = 1$ and they exchange the stability at that point. Also we found that there is possible forward

bifurcation with exchange of stability using some parameter sets.

The main results from the SVIS model is that a backward bifurcation is possible if the vaccination is partially but not completely effective and for the SVIR model backward bifurcation is not possible. Note that both SVIS and SVIR model are set up based on bilinear incidence and that standard and more general incidence is not covered, but if there are no disease deaths so that the total population size is (asymptotically) constant, all incidence forms are equivalent.

From SVIR model we proved that there cannot be a backward bifurcation and only forward one is possible with incoming infective immigrants. However in very rare cases there is possible backward bifurcation only with outgoing immigration of infectives.

The model can be more significant when transformed to adjust to specific transmittable diseases; using specific parameter values and adding some extra terms into a model would do this. If we can get a real clinical data then we will be even able to compare one to the results. Furthermore exposed periods of infection can be also considered to improve a model. Regarding infective periods, I can improve it by making it non-fixed but arbitrary; some studied on exponentially distributed one, for example. Also the contact rate with saturation may be used in some cases.

Speaking of tools for this study, I mainly dealt with a system of nonlinear ordinary differential equations and understand it by looking at equilibrium, phase plane and bifurcation diagram. Stability analysis is critical in this study since we would be able to know whether endemic equilibrium would be stable so the disease would persist or not. By setting up a good epidemic model and understanding well we can have many advantages of preventing invasion of infection to population. One of the most important result may be knowing the possible endemic equilibrium. To prevent it, it will certainly be helpful for us to plan vaccination policy better. Knowing bifurcation point of backward bifurcation we would know the minimum portion of susceptible class to be vaccinated in order to have a control over a disease. Also having sufficient condition for having backward bifurcation would help us to avoid sudden jump in number of infectives due to unstable branch of bifurcation [10].

Appendix A

Bifurcation

A.1 Hopf Bifurcation

Theorem A.1.1. (Hopf [1942]). Suppose that the system $\dot{x} = f_\mu(x)$, $x \in \mathbb{R}^n$, $\mu \in \mathbb{R}$ has an equilibrium (x_0, μ_0) at which the following properties are satisfied:

(H1) $Df(x_0)$ has a simple pair of pure imaginary eigenvalues and no

Then (H1) implies that there is a smooth curve of equilibria $(x(\mu), \mu)$ with $x(\mu_0) = x_0$. The eigenvalues $\lambda(\mu)$, $\bar{\lambda}(\mu)$ of $D_x f_{\mu_0}(x(\mu))$ which are imaginary at $\mu = \mu_0$ vary smoothly with μ . If, moreover,

$$\frac{d}{d\mu}(\operatorname{Re}\lambda(\mu))|_{\mu=\mu_0} = d \neq 0,$$

then there is a unique three-dimensional center manifold passing through (x_0, μ_0) in $\mathbb{R}^n \times \mathbb{R}$ and a smooth system of coordinates (preserving the planes $\mu = \text{const.}$) for which the Taylor expansion of degree 3 on the center manifold is given by

$$\begin{aligned}\dot{x} &= (d\mu + a(x^2 + y^2))x - (\omega + c\mu + b(x^2 + y^2))y, \\ \dot{y} &= (\omega + c\mu + b(x^2 + y^2))x + (d\mu + a(x^2 + y^2))y.\end{aligned}\tag{A.1.1}$$

If $a \neq 0$ there is a surface of periodic solutions in the center manifold which has quadratic tangency with the eigenspace of $\lambda(\mu_0)$, $\bar{\lambda}(\mu_0)$ agreeing to second order with the paraboloid $\mu = -(a/d)(x^2 + y^2)$. If $a < 0$, then these periodic solutions are stable limit cycles, while if $a > 0$, the periodic solutions are repelling.

Theorem A.1.2. Suppose that system with $x \in \mathbb{R}^n$ and $\mu \in \mathbb{R}$ has a critical point x_0 for $\mu = \mu_0$ and that $Df(x_0, \mu_0)$ has a simple pair of pure imaginary eigenvalues with zero

real part. Then there is a smooth curve of equilibrium points $x(\mu)$ with $x(\mu_0) = x_0$ and the eigenvalues, $\lambda(\mu)$ and $\bar{\lambda}(\mu)$ of $Df(x(\mu), \mu)$, which are pure imaginary at $\mu = \mu_0$, vary smoothly with μ . Furthermore, if

$$\frac{d}{d\mu}[\operatorname{Re}\lambda(\mu)]_{\mu=\mu_0} \neq 0,$$

then there is a unique two-dimensional center manifold through the point (x_0, μ_0) and a smooth transformation of coordinates such that the system on the center manifold is transformed into the normal form

$$\dot{x} = -y + ax(x^2 + y^2) - by(x^2 + y^2) + O(|x|^4)$$

$$\dot{y} = x + bx(x^2 + y^2) + ay(x^2 + y^2) + O(|x|^4)$$

in a neighborhood of the origin which, for $a \neq 0$, has a weak focus of multiplicity one at the origin and

$$\dot{x} = \mu x - y + ax(x^2 + y^2) - by(x^2 + y^2)$$

$$\dot{y} = x + \mu y + bx(x^2 + y^2) + ay(x^2 + y^2)$$

is a universal unfolding of this normal form in a neighborhood of the origin on the center manifold.

Here we summarize theorem for some types of bifurcations, saddle-node, transcritical, and pitchfork bifurcation of

$$\dot{x} = f(x, \mu) \quad , \quad x, \mu \in \mathbb{R}.$$

Theorem A.1.3. Consider the function,

$$\dot{x} = f(x, \mu) \quad , \quad x, \mu \in \mathbb{R}.$$

Let's assume that f has continuous derivatives up to third order for all (μ, x) near the

bifurcation point (μ^*, x^*) . If there is a pair (μ^*, x^*) for which

$$\begin{aligned} f(x^*, \mu^*) &= 0 \\ f_x(x^*, \mu^*) &= 0 \\ f_\mu(x^*, \mu^*) &\neq 0 \\ f_{xx}(x^*, \mu^*) &\neq 0 \end{aligned}$$

then $\dot{x} = f(x, \mu)$ has a saddle-node bifurcation with quadratic tangency at (μ^*, x^*) .

Theorem A.1.4. Consider the function,

$$\dot{x} = f(x, \mu) \quad , \quad x, \mu \in \mathbb{R}.$$

Let's assume that f has continuous derivatives up to third order for all (μ, x) near the bifurcation point (μ^*, x^*) . If there is a pair (μ^*, x^*) for which

$$\begin{aligned} f(x^*, \mu^*) &= 0 \\ f_x(x^*, \mu^*) &= 0 \\ f_\mu(x^*, \mu^*) &= 0 \\ f_{x\mu}(x^*, \mu^*) &\neq 0 \\ f_{xx}(x^*, \mu^*) &\neq 0 \end{aligned}$$

then $\dot{x} = f(x, \mu)$ has a (two branch) transcritical bifurcation with quadratic tangency at (μ^*, x^*) .

Theorem A.1.5. Consider the function,

$$\dot{x} = f(x, \mu) \quad , \quad x, \mu \in \mathbb{R}.$$

Let's assume that f has continuous derivatives up to fourth order for all (μ, x) near the

bifurcation point (μ^*, x^*) . If there is a pair (μ^*, x^*) for which

$$f(x^*, \mu^*) = 0$$

$$f_x(x^*, \mu^*) = 0$$

$$f_\mu(x^*, \mu^*) = 0$$

$$f_{xx}(x^*, \mu^*) = 0$$

$$f_{x\mu}(x^*, \mu^*) \neq 0$$

$$f_{xxx}(x^*, \mu^*) \neq 0$$

then $\dot{x} = f(x, \mu)$ has a pitchfork bifurcation with quadratic tangency at (μ^*, x^*) .

Appendix B

Transcritical bifurcation of SVIS model with $p = 0$

Our system of SVIS type with no infective immigrant is

$$I' = \beta I[N - I - (1 - \sigma)V] - (\mu + \gamma + \alpha)I$$

$$V' = \phi(N - I) - \sigma\beta VI - (\mu + \theta + \phi)V$$

$$N' = A + \Lambda - \mu N - \alpha I$$

with

$$N(t) = S(t) + I(t) + V(t)$$

and

$$N'(t) = S'(t) + I'(t) + V'(t) = A + \Lambda - \mu N(t) - \alpha I(t).$$

In the notation of Theorem by Sotomayor, we have

$$\begin{aligned} A &= Df(I = 0, \phi = \phi_0) \\ &= \begin{pmatrix} 0 & 0 & 0 \\ -\phi_0 - \frac{\sigma\beta(A+\Lambda) - \sigma\mu(\gamma+\alpha+\mu)}{\mu(1-\sigma)} & -(\mu + \theta + \phi_0) & \phi_0 \\ -\alpha & 0 & -\mu \end{pmatrix} \end{aligned} \quad (\text{B.0.1})$$

where

$$\begin{aligned}
 \phi_0 &= \frac{(\mu + \theta)[\mu(\gamma + \alpha + \mu) - \beta(A + \Lambda)]}{\sigma\beta(A + \Lambda) - \mu(\gamma + \alpha + \mu)}. \\
 f_\phi(I = 0, \phi = \phi_0) &= \begin{pmatrix} 0 \\ \frac{-\sigma\beta(A + \Lambda) + \mu(\gamma + \alpha + \mu)}{\mu\beta(1 - \sigma)} \\ 0 \end{pmatrix} \\
 w &= (1, 0, 0)^T \\
 v &= \left(1, \frac{-\phi_0}{\mu + \theta + \phi_0} \left(\frac{(\mu + \alpha)(\mu + \theta + \phi_0) + \sigma\beta(A + \Lambda)}{\mu(\mu + \theta + \phi_0)} \right), -\frac{\alpha}{\mu} \right)^T
 \end{aligned} \tag{B.0.2}$$

Appendix C

Derivation of Stability Formula of two-dimensional Hopf bifurcation [5]

If the reduced system has a purely imaginary pair of eigenvalues $\lambda = \pm i\omega$, then we can represent it as a single complex expression,

$$\dot{z} = \lambda z + h(z, \bar{z}), \quad (\text{C.0.1})$$

where

$$z = x + iy \quad \text{and} \quad \lambda = i\omega$$

At $\mu = 0$, the normal form,

$$\begin{aligned} \dot{x} &= (d\mu + a(x^2 + y^2))x - (\omega + c\mu + b(x^2 + y^2))y, \\ \dot{y} &= (\omega + c\mu + b(x^2 + y^2))x + (d\mu + a(x^2 + y^2))y \end{aligned}$$

becomes

$$\dot{w} = \lambda w + c_1 w^2 \bar{w} + c_2 w^3 \bar{w}^2 + \cdots + c_k w^{k+1} \bar{w}^k + O(|w|^{2k+3}) \quad (\text{C.0.2})$$

$$\equiv \lambda w + \hat{h}(w, \bar{w}), \quad (\text{C.0.3})$$

where the coefficients are of them form

$$c_j = a_j + ib_j.$$

Note that in polar coordinates we have

$$\dot{r} = a_1 r^3 + a_2 r^5 + \cdots,$$

$$\dot{\theta} = \omega + b_1 r^2 + b_2 r^4 + \cdots,$$

and the first nonzero coefficients a_j, b_j determine the stability of the periodic orbit and the amplitude dependent modification to its period. We use the near identity transformation,

$$z = w + \psi(w, \bar{w}), \quad \psi = O(|w|^2), \quad (\text{C.0.4})$$

, in order to transform C.0.1 into C.0.2. Substituting C.0.4 into C.0.1 and using C.0.2, we obtain

$$\lambda(w\psi_w - \psi) + \bar{\lambda}\bar{w}\psi_{\bar{w}} = h(w + \psi, \bar{w} + \bar{\psi}) - \hat{h}(w, \bar{w})(1 + \psi_w) - \hat{h}(w, \bar{w})\psi_{\bar{w}}. \quad (\text{C.0.5})$$

We proceed by expressing ψ as a Taylor series

$$\psi(w, \bar{w}) = \sum_{2 \leq j+k \leq 3} \psi_{jk} \frac{w^j \bar{w}^k}{j!k!} + O(|w|^4). \quad (\text{C.0.6})$$

where

$$\psi_{jk} = \partial \psi^{j+k} / \partial w^j \partial \bar{w}^k.$$

Now let's use the normal form, $\hat{h}(w, \bar{w}) = c_1 w^2 \bar{w} + O(|w|^5)$, and substitute C.0.6 into C.0.5 in order to get

$$\begin{aligned} \lambda \psi_{ww} \frac{w^2}{2} + \bar{\lambda} \psi_{w\bar{w}} w \bar{w} + (2\bar{\lambda} - \lambda) \psi_{\bar{w}\bar{w}} \frac{\bar{w}^2}{2} &= h_{ww} \frac{w^2}{2} + h_{w\bar{w}} w \bar{w} + h_{\bar{w}\bar{w}} \frac{\bar{w}^2}{2} \\ &+ O(|w|^3). \end{aligned}$$

Equating coefficients yields the leading terms in the transformation

$$\psi_{ww} = \frac{h_{ww}}{\lambda} = -\frac{ih_{ww}}{\omega}, \quad (\text{C.0.7})$$

$$\psi_{w\bar{w}} = \frac{h_{w\bar{w}}}{\bar{\lambda}} = \frac{ih_{w\bar{w}}}{\omega}, \quad (\text{C.0.8})$$

$$\psi_{\bar{w}\bar{w}} = \frac{h_{\bar{w}\bar{w}}}{(2\bar{\lambda} - \lambda)} = \frac{ih_{\bar{w}\bar{w}}}{3\omega}. \quad (\text{C.0.9})$$

We do expansion to one higher order and equate the coefficients of the normal form term $w^2 \bar{w}$. For this term, the coefficient on the left-hand side of C.0.5 vanishes and the right-hand side becomes

$$h_{ww} \psi_{w\bar{w}} + h_{w\bar{w}} \left(\frac{\psi_{ww}}{2} + \bar{\psi}_{w\bar{w}} \right) + h_{\bar{w}\bar{w}} \frac{\psi_{\bar{w}\bar{w}}}{2} + \frac{h_{ww\bar{w}}}{2} - c_1 = 0,$$

or, using C.0.7

$$c_1 = \frac{i}{2\omega} (h_{ww} h_{w\bar{w}} - 2|h_{w\bar{w}}|^2 - \frac{1}{3}|h_{\bar{w}\bar{w}}|^2) + \frac{h_{ww\bar{w}}}{2}. \quad (\text{C.0.10})$$

Thus it follows that

$$2a_1 = 2\text{Re}(c_1) = h_{ww\bar{w}}^R - \frac{1}{\omega} (h_{ww}^R h_{w\bar{w}}^I + h_{w\bar{w}}^R h_{ww}^I), \quad (\text{C.0.11})$$

where R and I denote real and imaginary parts, respectively.

Expanding f and g in Taylor series and taking real and imaginary parts of the complex

valued function h it follows that the relevant terms in C.0.11 may be expressed as

$$\begin{aligned}
 h_{ww\bar{w}}^R &= \frac{1}{8}(f_{xxx} + f_{xyy} + g_{xxy} + g_{yyy}), \\
 h_{ww}^R &= \frac{1}{4}(f_{xx} - f_{yy} + 2g_{xy}), \\
 h_{ww}^I &= \frac{1}{4}(g_{xx} - g_{yy} - 2f_{xy}), \\
 h_{w\bar{w}}^R &= \frac{1}{4}(f_{xx} + f_{yy}), \\
 h_{w\bar{w}}^I &= \frac{1}{4}(g_{xx} + g_{yy}).
 \end{aligned} \tag{C.0.12}$$

We can derive the stability formula C.0.13 by substitution of C.0.12 into C.0.11:

$$\begin{aligned}
 16a_1 &= (f_{xxx} + f_{xyy} + g_{xxy} + g_{yyy}) \\
 &+ \frac{1}{\omega}[f_{xy}(f_{xx} + f_{yy}) - g_{xy}(g_{xx} + g_{yy}) - f_{xx}g_{xx} + f_{yy}g_{yy}].
 \end{aligned}$$

or,

$$\boxed{
 \begin{aligned}
 a_1 &= \frac{1}{16}[f_{xxx} + f_{xyy} + g_{xxy} + g_{yyy}] \\
 &+ \frac{1}{16\omega}[f_{xy}(f_{xx} + f_{yy}) - g_{xy}(g_{xx} + g_{yy}) - f_{xx}g_{xx} + f_{yy}g_{yy}].
 \end{aligned}
 } \tag{C.0.13}$$

Also note that the normal form for the parameterized Hopf bifurcation is neatly expressed in complex variables as

$$\dot{w} = \lambda w + c_1 w^2 \bar{w} + O(|w|^5), \tag{C.0.14}$$

where $\lambda = \mu + i\omega$.

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