ABSTRACT

This thesis consists a compartmental epidemiologic SIR model which is one of the useful method to understand the dynamics of the disease.

Firstly, two single models with an without vaccine are constructed. For each model two equilibrium point which are disease free and endemic are found. Basic reproduction numbers are found and using Lyapunov function stability analysis carried out. Numerical simulations give the importance of the vaccine. These two models show that vaccine has an important role for the disease.

In particular, we construct epidemic model with two strains and two vaccine. In this model we assume each strain has vaccine. Our aim in this model to see the effect of vaccine for strain one to the strain two and the vaccine to strain two to the strain one. The model consists of three equilibrium points; disease free equilibrium, endemic with respect to strain 1, endemic with respect to strain 2. Also, stability analysis carried out and two basic reproduction ratio $R_1$and R_2 are found. It is shown that there is no coexistence. However from the numerical simulations coexistences of both strain are shown. Also it is shown that the vaccine for strain one has for strain two and vaccine for strain two has negative effect for strain one.

In addition, a delayed epidemic model consisting of two strains with vaccine for each strain is formulated. The model consists of three equilibrium points; disease free equilibrium, endemic with respect to strain 1, endemic with respect to strain 2. Global stability analysis of the equilibrium points was carried out through the use of Lyapunov functions. Two basic reproduction ratios $R_1$and R_2 are found, and we have shown that, if both are less than one, the disease dies out, if one of the ratios is less than one, epidemic occurs with respect to the other. It was also shown that, any strain with highest basic reproduction ratio will automatically outperform the other strain, thereby eliminating it. Condition for the existence of endemic equilibria was also given. Numerical simulations were carried out to support the analytic results and to show the effect of vaccine for strain 1 against strain 2 and the vaccine for strain 2 against strain 1. It is found that the population for infectives to strain 2 increases when vaccine for strain 1 is absent and vice versa. And one of aim in this model to see the effect of the latent period. The latent periods τ_1 and τ_2 have positive effect on the infection of strain 1 and strain 2. For

sufficiently large latent periods τ_1 and τ_2, R_1 and R_2 becomes less than 1 respectively for the model which is given in last model.

Keywords: Global stability analysis; two strain; delay; vaccine; basic reproduction ratios; Lyapunov function

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Bu tez, hastalığın dinamiğini anlamak için en çok kullanılan gruplandırlmış SIR epdiemik modeller içermektedir.

İlk olarak, aşının etkisini iyi anlayabilmek için aşılı ve aşısız olmak üzere iki model geliştirildi. Her bir model için salgının olmadığı ve salgının olduğu iki denge noktası ve her iki model için temel bulaşma oranları $R_{0,1}$ve $R_{0,2}$ bulundu. Lyapunov fonksiyonu kullanılarak Kararlılık analizleri gösterildi. $R_{0,1} < 1$ iken salgın olmadığı ve salgın olmayan denge noktası için asimptotik kararlılık gözlemlendi. $R_{0,1} > 1$ iken toplumda salgının olduğu ve salgın olan denge noktası için asimtotik kararlılık verildi. Analitik metodları desteklemek için sayısal similasyonlar kullanıldı. Bu iki modelde aşının salgını azaltmak için önemli bir etken olduğu gözlemlenmiştir.

Özel olarak, temel iki tür salgın bölüme sahip SVIR model geliştirilmiştir. Her bir türün aşılarının var olduğu kabul edilmiştir. Bu modeldeki temel amaç, 1. tür salgın için olan aşının 2. Türe etkisi ve tam tersi olarak 2. tür için olan aşının 1. türe olan etkilerini gözlemlemektir. Model için üç tane denge noktası bulundu ve Lyapunov fonksiyonu ile kararlılık analizleri verildi. R_1ve R_2 olmak üzere iki tane temel üreme oranı bulundu. Bunlara ek olarak sayısal similasyon kullanılarak analitik sonuçlar desteklendi. Burada aşının yanlış kullanımının ters etkide bulunabileceği gözlemlendi.

Bir önceki modele ek olarak gecikme periodu eklenerek model genişletildi. Salgının olmadığı, 1. tür için salgının var olduğu 2. tür için olmadığı ve 2. tür için salgının var olduğu 1. tür için olmadığı denge noktaları olmak üzere üç tane denge noktası bulundu. R_1ve R_2 olmak üzere iki tane temel üreme oranı bulundu. Her bir denge noktası için kararlılık analizleri Lyapunov fonksiyonu kullanılarak verildi. Her iki temel üreme oranı birden küçükken iki türün de yok olduğu ve salgının olmadığı denge noktasının asimptotik kararlı olduğu gösterildi. En büyük temel üreme oranı birden büyük olan türde hastalığın çıktığı ve bu denge noktasının asimptotik kararlı olduğu gösterildi. Analitik sonuçları desteklemek için sayısal simülasyonlar verildi. Sayısal sonuçlara göre toplumda salgın varsa bireylere farklı salgın tipi için aşı verilir, bu aşı toplumda bulunan salgını artıracaktır. Modele gecikme süresi eklendiğinde salgın sayısının

düşmesi dolayısı ile bireylere bulaşma süresini uzatılmasının salgını azaltmak için bir etken olması da bu tezde verilebilecek ikinci bir sonuçtur.

Anahtar Kelimeler: Kararlılık Analizi; iki tip; delay; aşı; temel bulaşma oranı; Lyapunov fonksiyon

DYNAMICS OF TWO STRAIN EPIDEMIC MODEL WITH VACCINE AND DELAY

A THESIS SUBMITED TO THE GRADUATE SCHOOL OF APPLIED SCIENCES OF NEAR EAST UNIVERSITY

By

BİLGEN KAYMAKAMZADE

In Partial Fulfilment of the Requirements for the Doctor of Philosophy in Mathematics

NICOSIA, 2017

Bilgen KAYMAKAMZADE : DYNAMICS OF TWO STRAIN EPIDEMIC MODELS WITH VACCINE AND DELAY

Approval of Director of Graduate School of Applied Sciences

Prof. Dr. Nadire CAVUS

We certify this thesis is satisfactory for the award of the degree of Doctor of Philosophy in Mathematics

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Name, Last name: Bilgen Kaymakamzade

Signature:

Date:

To my parents...

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CHAPTER 1
INTRODUCTION

1.1 History of Pandemic

Infectious disease has been known since 165-180 AD. These diseases were known as a pandemic disease such as smallpax or measels. During this time for example in Mexico more than 30 million people has been effected from smallpox (Brauer and Castillo-Chavez, 2011).

In history we have seen more serious cases than ever the infectious disease spread between 1346-1350 more than 10000 people died in Europe. Between 1665 and 1666 Black Death (bubonic plague) affected one-sixth of the population in London. The spread of infectious disease has never been controled by the human being. In 2006 according to World Health Organization approximately 1.5 million people affected from Tubercloses. In the same year an other infectious disease namely Maleria approximately affected 40% of the whole world population. AIDS is any other disease which could Goverments should consider seriously according the UNTIL statistics 25 million people effected from AIDS (Ma and Li, 2009).

In the 20th century influenza pandemics were recorded. The 'Spanish Flu' (H1N1) is the one of the most serious pandemic which spread in the world in a short time and affected 500 million people and caused over 30 million death in 1918-1919 (Shim et al., 2017). In 1957 and 1968 Asian Flu (H2N2) and Hong Kong Flu (H3N2) were recorded respectively. The morality for these pandamics was estimated 69800 and 33800 respectively (Noble, 1982). Medical people can observe the vaccine response for endemic in many people by the late 1957. Even though they were not devastating, they killed millions of people. After these pandemics, an interesting development finding that the natural host of all influenza A viruses are waterfowl. And there was a great mutation of viruses in birds than in human.

In 1977, epidemic of influenza spread out of North-Eastern China and the former Soviet Union and it is called “Red Flu”. It was found that the effect of virus of Red Flu is nearly identical to the H1N1 virus which gives that influenza A virus mutated rapidly as they multiplied. And also it is detected that disease limited to people under the age of 25, it is explained that older individuals had antibodies from the identical virus in 1958 (Cox and Subbarao, 2000).

In 2009 next pandemic was arise from Mexico or the south- western USA, and it was again a type of H1N1 viruses which was come directly from intensively farmed pigs so called “swine Flu”. The virus had spread worldwide and in most countries there were infected people. Although the symptoms of infection was similar to seasonal influenza, the swin Flu was not as serious as had been feared. In 2009 vaccine introduced for the Swine flu but there was not enough vaccine strain of the virus. (Rybicki and Russell , 2015).

Influenza viruses are segmented, negative- sense, enveloped RNA viruses of the Orthomyxoviridae family (Zambon, 1999), and it is also called the “flu”, is a viral disease that affects humans and many animals. Influenza is a disease caused by a virus that affects mainly the nose, throat, bronchi and sometimes lungs. Through air by coughs, sneezes or from infected surfaces, and by the direct contact to infected persons casued the virus spread from person to person (Khanh, 2016).

There are three groups of influenza viruses, called type A, B, or C. Influenza A is the main group which affect both human and animals and it has antigenic variability which allows to escape neutralization from anti- bodies (Dawood, et al., 2012). Influenza B affect only human and it also exhibits antigenic variability property, but less than that of A. However this property is not common in influenza C, type C influenza causes weak infections (Bao et al., 2016), hence influenza A is more serious than B, and then C (Ju, et.al., 2016).

Influenza A virus is divided into Hemagglutinin (HA) and Neuraminidase (NA) based on the two proteins on the surface of the virus. Hemagglutinin are divided into 12 (H1– H12) and neuraminidase into nine subtypes 9 (N1–N9) (WHO, 1980). It can also be divided into

different strains, most popular strains found in people are H1N1 and H3N2 viruses (Qiu and Feng, 2010).

Antiviral treatment, Quarantine and vaccination are three important control measures for the spread of influenza. For many years anti- influenza drugs that target influenza neuraminidise have been used to prevent and treat influenza virus infectious. For example for the H1N1 influenza virus Oseltamivir drug is the most known antiviral treatment also known as Tamiflu (Ju et al., 2016). Because of the amino acid changing in neurominidase give the drug resistant strain (Shim et al., 2017). Ju et al. proposed nalidixic acid and dorzolamide which are use of drugs that are structurally similar to Oseltamivir as anti-Oseltamivir resistant influenza drugs.

Because of the high risk of the influenza pandemic and large number of death associated with influenza, understanding of spread of the influenza disease dynamics is important. The important theoric approach is Epidemic Dynamics in order to investigate the transmission dynamics of the disease.

1.2 Mathematical Model

Mathematical models play an important role to understand the dynamics of the disease. Also it gives best strategy to control the disease for a long time (Murray J. D., 2002).

The first study of mathematical models is given for smallpox which was constructed by Bernoulli in 1760 (Bernoulli, 1760). Subsequently, in 1906 Hamer formulated discrete time model for the spread of measles. In 1911, with using ordinary differential equation, the transmission of maleria betwen human and mosquitoes was given by Ross. Kermack and McKendrick are the poineer of the compartmental models. They pointed first SIR epidemic model in 1927 and they used a compartmental model with divided population into tree compartments S, I and R where S denotes the number of individuals who are Suspectible to the disease, I denotes the number of infected individuals, in this compartment individuals assumed infectious and able to spread the disease by contact with

suspectible and R denotes the number of individuals who had been infected and were removed. In their model they assumed that; There is no emigration nor imigration and neither birth nor death in the population, the number of suspectibles who are infected by an infected individual per unit of time, at a time t, is proportional to the total number of suspectibles with the proportional coefficient (transmission rate) β, so that the total number of newly infectives, at time t, is βS(t)I(t); the number removed (recoverd) individuals from the infected compartment per unit time is γI(t) at time t, where γ is the recovery rate coefficient, and recovered individuals gain permanent immunity (Kermack and McKendrick, 1927). Figure 1.1 shows the transfer diagram of the Kermack and McKendrick model.

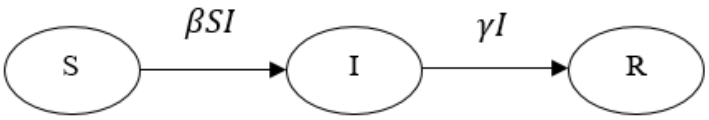

Figure 1.1: Kermack and McKendrick model.

The model is given by ordinary differential equations as follows

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI, \\ \frac{dI}{dt} &= \beta SI - \gamma I, \\ \frac{dR}{dt} &= \gamma I. \end{aligned} \tag{1.1}$$

The structure of the Kermack and McKandrick model has recovery after disease. It means any individiual after recover from the disease never become suspectible. After this model different kinds of compartmental epidemic model are introduced, depending on the disease. For example, influenza, measles, and chicken pox, usually confer immunity against reinfection therefore these kind of diseases has SIR type models (Tan et al., 2013; Coburn et al., 2009; Yang and Hsu, 2012). HIV or AIDS have no recovery after infectious than the structure of the model is SI type (Kaymakamzade, et al., 2017; Sayanet et al., 2017; Nelson and Perelson, 2002) and some diseases such as tuberculosis have no

immunity or have temporary immunity after recovery, which means individuals come back to the suspectible classes after recovery from the disease. The structures of the models of this kind of disease are SIS, SIRS, etc. (Bowong, 2010; Li et al., 1999; Zhanget et al., 2013). In addition to the above models, some diseases have expose period therefore can be added exposed compartment in the model which means all of the individuals have been infected but have not yet infectious can also be added. Then the structure of the models modified as SEI, SEIS, SEIRS, etc. (Korobeinikov and Maini, 2004; Li et al., 2006; Cheng and Yang, 2012; Yuan and Yang, 2007).

Some diseases are in the form of two (or more general, multi) strain SIR models type (Bichara et al., 2014; Muroya et al., 2016). Maleria and West Nile viruses are example for the two strain models which are transmited vector (mosquitoes, insects, etc.) to human or human to vector (Ullah, et al., 2016; Lord et al., 1996; Tchuenche et al., 2007). In addition some disease have mutation and so model consist multi strain (Kaymakamzade et al., 2016; Bianco et al., 2009). Since influenza viruses are of many forms, some researchs are on multiple strain influenza virus (Zhao et al., 2013; Gao and Zhao, 2016).

There are some methods like quarantine, treatment and vaccination to control the spread of disease. The first model with quarantine was given by Feng and Theime in 1995 and after that Wu and Feng in 2000 and Nuno et al. in 2005. The compartment Q introduced and assumed that all the infectives individuals go to the quarantine compartment before going to the recovery compartment R or suspectible compartment S. In 2002 Hethcote et al. considered a more realistic model where the part of infective individual are quarantined where the others not, eithetr enter recovery compartment or go back to the suspectible compartment. These models are given by SIQR, SIQS,SEIQR, etc. (Nuño et al., 1970). Vaidya et al. study with the H1N1 quarantine model (Vaidya et al., 2014). Nuño et al. study two- strain influenza with isolation and partial cross- immunity (Nuño et al., 2006). In 2016 Kaymakamzade et al. study with Oseltamivir resistance and non-resistance two strain model which is the one of most important influenza drug (Kaymakamzade et al., 2016). More effective to control the disease is vaccine. Any individual who takes vaccine can gain (temporary) immunity and directly can go to the recovery compartment. These kind of models assumed that vaccines have full effect but for the reality, vaccines have not

always full effect. These sort of models constructed as SIV, SVIR, SVEIR, SI etc. (McLean et al., 2006; Reynolds et al., 2014; Zaman et al., 2008).
Many researches exist for influenza virus with vaccine and immunization for influenza model (Zhao, et al., 2014; Yang and Wang, 2016; Towers and Feng, 2009).

1.3 Epidemic models with time delay

Some diseases may not be infectious until some time after becoming infected (Huang, Takeuchi, Ma, & Wei, 2010). Time delay is one of the important method can be used in epidemiology. More realistic approach includes some of the past history of the system in the models. The best way to model such processes is by incorporating time delays into the models. That is, system should be modeled by ordinary differential equation with time delay (Kuang, 1993).

Time delay can be divided into two types as discrete delay (fixed delay) and continuous (distributed) delay. In the fixed delay model the dynamic behaviour of the model at time t depends also on state at time $t-\tau$, where τ is constant. Time delay can be used to describe;

Latent or incubation period: for some diseases, the number of infectives at time t also depends on the number of infectives at a time $t-\tau$, where τ represents the latent period. Some SIR models with latent or incubation periods were studied in recent years (Takeuchi et al., 2000; Enatsu et al., 2012; Liu, 2015; Ma et al., 2004; Wang et al., 2013). SVEIR model with using delay for latent period which the vaccined class can be infected (Jiang et al., 2009; Zhang et al., 2014; Wang et al., 2011).

Immunity period: After recovery from any disease has short or long immunity against re-infectious naturally arise. This time τ represents the immunity period and after τ time later individual lose the immuinty (Xu et al., 2010; Rihan and Anwar, 2012).

Mutation Period: Some disease chance its structure in a time. And gain immunity with respect to treatement or vaccine. For these kinds of stuation delay can be represent the mutation time (Fan et al., 2010).

Above delay periods can be mixed in a model, such as two delay for latency and temproary immunity respectively (Cooke and Driessche, 1995).

1.4 Guide to the Thesis

In Chapter 2 some mathematical informations about existence and uniqueness of the system for ordinary and delay differential equations, stability criteria and next generation matrix methods are given.

In Chapter 3, two delayed modelled with and without vaccine are constructed. In subsections of Chapter 3, equilibrium points for both two models are given. Then to control the disease basic reproduction ratios for each models are found. By using Lyapunov method global stability analysis are made. Finally, the models compared numerically.

In Chapter 4, the effect of vaccine for strain 1 to the strain 2 and the effect of vaccine for strain 2 to the strain 1 are discussed. We assume that any individual which has been recovered from the infections gains immunity. That means recovered people never become susceptible. Population divided in six compartment S, V_1, V_2, I_1, I_2 and R. Stability analysis and numerical simulations have been performed for the introduced model.

Chapter 5 is concerned with delay SIR model with two strains. The model in the previous chapter is modified by adding time delay. Time delays represent the latent period for both strain. For this model, four equilibria are found and basic repruduction ratios are given. Global stabilities are studied and some simulations are given for delay model.

Chapter 6, gives the conclusion of the study.

CHAPTER 2
MATHEMATICAL PRELIMINARIES

In this chapter, some definitions and theorems are given for ordinary and delay differential equations. It is given existence and uniqueness of solution for both ordinary and delay differential equations. For the stability analysis the Lyapunov function is defined and Lyapunov stability theorem is given. Finally, for the treshold conditions of the systems next generation matrix method is given.

2.1 Ordinary Differential Equations

Consider the general ordinary differential equation (ODE)

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

with initial condition, $x(t_0) = x_0$ in the domain $|t - t_0| < \alpha$. Here $\alpha > 0$ defines the size of the region where it will be shown that a solution exist. Defining a closed rectangle

$$R = \{(t, x(t)) : |x - x_0| \leq b, |t - t_0| \leq a\},$$

centred upon the initial point (t_0, x_0). Integrating both sides of (2.1) with respect to t, gives that

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

or

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

Hence

$$x(t) = x(t_0) + \int_{t_0}^{t} f(s, x(s))ds. \quad (2.2)$$

Using the initial value and the successive approximations of the solution can be obtained as

$$x_{k+1}(t) = x_0 + \int_{t_0}^{t} f(x_k(s), s)\, ds,\ \ k = 0,1,2,3\ldots, \quad (2.3)$$

with the given x_0 of t.

2.1.1 Existence and uniqueness

Definition 2.1. (Murray and Miller, 2007). (Lipschitz Condition)
A function $f(t, x)$ is a real valued function then f is said to be satisfy a Lipschitz condition if there exists a constant K such that for any pair of point (t, x_1) and (t, x_2) in R,

$$|f(t, x_2) - f(t, x_1)| \leq K|x_2 - x_1|, \forall\, t. \quad (2.4)$$

Lemma 2.1. Suppose that $f(t, x)$ is continuously differentiable function with respect to x on a closed region R. Then there exists a positive number K such that

$$|f(t, x_2) - f(t, x_1)| \leq K|x_2 - x_1| \quad (2.5)$$

for all $(t, x_2), (t, x_1) \in R$.

Lemma 2.2. (King et al., 2003). If $\alpha = \min\left(a, \frac{b}{M}\right)$ then the succesive approximations,

$$x_0(t) = x_0,\ x_{k+1}(t) = x_0 + \int_{t_0}^{t} f\big(s, x_k(s)\big)\, ds$$

are well defined in the interval $I = \{t: |t - t_0| < \alpha\}$ and on this interval

$$|x_k(t) - x_0| < M|t - t_0| < b,$$

where $|f| < M$.

Theorem 2.1. (Perko, 2000)**.** (Existence)

If f and $\frac{\partial f}{\partial x} \in C(R)$, then the succesive approximations $x_k(t)$ converge on I to a solution of the differential equation $\dot{x} = f(t, x)$ that satisfies the initial conditions $x(t_0) = x_0$.

Lemma 2.3. (Cain and Reynolds, 2010)**.** (Gronwall's Inequality)
If $f(t)$ and $g(t)$ are nonnegative continuous functions on the interval $\alpha \leq t \leq \beta$, L is nonnegative constant and

$$f(t) \leq L + \int_{\alpha}^{t} f(s)g(s)ds \ \ for\ t \in [\alpha, \beta],$$

then

$$f(t) \leq L \exp\left\{\int_{\alpha}^{t} g(s)ds\right\} \ for\ t \in [\alpha, \beta]. \qquad (2.10)$$

Theorem 2.2 (King et al., 2003)**.** (Uniqueness)
If f and $\frac{\partial f}{\partial x}$ are continuously differentiable function on R, then the solution of the initial value problem $\dot{x}(t) = f(t, x(t))$ subject to $x(t_0) = x_0$ is unique on $|t - t_0| < \alpha$.

2.2 Delay Differential Equation

$\mathbb{R}^n$ is a n dimensional real Euclidean space with norm $|.|$, and when $n = 1$, it is denoted as $\mathbb{R}$. For $a < b$, we denote $C([a, b], \mathbb{R}^n)$ the Banach space of continuous vector functions f defined on $[a, b]$ with values $\mathbb{R}^n$. For $f \in C([a, b], \mathbb{R}^n)$, the norm of f is defined as

$$\|f\| = \sup_{a \leq t \leq b} |f(t)|,$$

where $|.|$ is a norm in $\mathbb{R}^n$. When $[a,b] = [-r,0]$ where r is positive constant, generally $C([-r,0],\mathbb{R}^n)$ denoted by C. For $\sigma \in \mathbb{R}$, $\lambda > 0$, $x \in C([\sigma - r, \sigma + \lambda],\mathbb{R}^n)$ and $t \in [\sigma, \sigma + \lambda]$, we define $x_t \in C$ as $x_t(\theta) = x(t+\theta)$, $\theta \in [-r,0]$.

Assume Ω is a subset of $\mathbb{R} \times C$, $f: \Omega \to \mathbb{R}^n$ is a given function, then delay differential equation (DDE)

$$\begin{cases} \dot{x} = f(t, x_t) & t > \sigma\,, \\ x(t) = \varphi(t) & -r \le t \le 0 \end{cases} \tag{2.12}$$

can be defined.

2.2.1 Existence and uniqueness

For each delay there exists unique solution. The existence and uniqueness theorems for constant delay are given with following theorems.

Theorem 2.3. (Kuang, 1993)**.** (Existence)
In (2.12), suppose Ω is an open subset in $\mathbb{R} \times C$ and f is continuous on Ω. If $(\sigma, \varphi) \in \Omega$, then there is a solution of (2.12) passing through (σ, φ).

Theorem 2.4 (Arino et al., 2002)**.** (Uniqueness)
Suppose Ω is an open subset in $\mathbb{R} \times C, f: \Omega \to \mathbb{R}^n$ is continuous, and $f(t, \varphi)$ is Lipschitzian with respect to φ in each compact set in Ω. If $(\sigma, \varphi) \in \Omega$, then there is a unique solution of equation (2.12) through (σ, φ).

2.3 Stability Analysis

Definition 2.2. (Verhulst , 1985)**.** An equilibrium point x^* of system (2.1) is said to be;

1. stable if, for all $\varepsilon > 0$ there exists $\delta > 0$ such that, for each x with $\|x_0 - x^*\| < \delta$ we have $\|x(t) - x^*\| < \varepsilon$ for every $t \geq 0$.

2. x^* is asymptotically stable if it is stable and $\|x(t) - x^*\| \to 0$ as $t \to \infty$.
3. We say that the equilibrium x^* is unstable if it is not stable.

Theorem 2.5. (Wiggins, 2003)**. (Liapunov Function)**
Let E be an open subset of $\mathbb{R}^n$ containing equilibrium point (x^*). Suppose V is a function such tat $f \in C^1(E)$ satisfying $V(x^*) = 0$ and $V(x) > 0$ when $x \neq x^*$. Then,
1. If $\dot{V} \leq 0$ for all $x \in E - \{x^*\}$, x^* is stable.
2. If $\dot{V} < 0$ for all $x \in E - \{x^*\}$, x^* is asymptotically stable.

In other words, an equilibrium is stable if all solutions close to it at the initial moment will not depart too far from it later on. If, additionally, all solutions initially close the equilibrium will tend to it, then we have a stronger property, called asymptotic.

2.4 Basic Reproduction Number

The basic reproduction number R_0 is the most important quantity in infectious disease epidemiology (Diekmann et al., 2009). It is the avarage number of secondary cases generated by a single infected individual during its entire period of infectiousness when introduced in to a completely suspectible population.
Alternative technique for the finding basic reproduction number is next generation matrix method which is given by Diekmann and Hesterbeek in 1990.

2.4.1 Next Genaration Matrix

To calculate R_0 to the equations of the ODE system Diekmann and Hetereebek consider the Next generating matrix method (Diekmann et al., 2009). Because of next genaration matrix method is sometimes easier then the traditional approach, it is a useful alternating method to find the basic reproduction number.

Any non-linear system of ordinary differential equation can be described as a

$$x_i(x) = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x) \qquad (2.17)$$

and $\mathcal{V}_i$ can be written

$$\mathcal{V}_i = \mathcal{V}_i^- - \mathcal{V}_i^+,$$

where $\mathcal{F}_i$ is represents the rate of appearence of new infections in to compartment i, $\mathcal{V}_i^-$ represent the rate of transfer output of the i^{th} compartment and $\mathcal{V}_i^+$ represent the rate of transfer input of the i^{th} compartment. It is assumed that all functions are continuously differentiable at least twice. Defined $\boldsymbol{x_s}$ be the set of all disease free states such that

$$\boldsymbol{x_s} = \{x \geq 0 : x_i = 0, i = 1,2, \dots, m\}$$

assuming that first m compartments correspond to infected individuals.

With the above assumption following conditions hold;

1. If $x \geq 0$, then all $\mathcal{F}_i, \mathcal{V}_i^+, \mathcal{V}_i^-$ are non-negative for all i.
2. $\mathcal{V}_i^-$ =0, when $x_i = 0$, which means that there is no any transfer of individuals of out of the compartment when the number of individuals in each compartment is equal to zero. In Particular, $\mathcal{V}_i^-$ =0 when $x_i \in \boldsymbol{x_s}$, for $i = 1,2, \dots, m$.
3. $\mathcal{F}_i = 0$, when $i > m$
4. If $x_i \in \boldsymbol{x_s}$. Then $\mathcal{F}_i = 0$ and $\mathcal{V}_i^+$ =0, for $i = 1,2, \dots, m$.
   This condition provided that the disease free subspace is invariant.
5. Let x_0 be a locally asymptotically stable disease free equilibbrium point in $\boldsymbol{x_s}$, and $Df(x_0)$ is defind as the derivative $\frac{\partial f_i}{\partial x_i}$ evaluated at the disease free equilibrium, x_0 (i.e., Jacobian matrix). The linearized equations for the disease free compartments x are decoupled from the remaining equations and can be written as
   $$\dot{x} = Df(x_0)(x - x_0).$$

Therefore, if $\mathcal{F}_i(x)$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts.

Under the above conditions, the following lemma can be given.

Lemma 2.4 (Driessche & Watmough, 2002)**:** If x_0 is a disease free equilibrium of (2.17) and $f_i(x)$ satisfies the above conditions 1-5, then the derivatives $D\mathcal{F}(x_0)$ and $D\mathcal{V}(x_0)$ are partitioned as

$$D\mathcal{F}(x_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, D\mathcal{V}(x_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}.$$

Here F and V are the $m \times m$ matrices defined by

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0)\right], \ 1 \leq i, j \leq m.$$

The derivation of the basic reproduction number is based on the linearization of the ODE model about a disease-free equilibrium.

The number of secondary infections produced by a single infected individual in a population at a disease free. It can be expressed as the product of the expected duration of the infectious period and the rate at which secondary infections occur. Let $\varphi_i(0)$ be the initial number of infected individual in each compartment i and $\varphi(t)$ be the solution of the system

$$\dot{x}_i = [F_i - V_i]x_i. \qquad (2.18)$$

Then the expected time spends in each compartment is given by the integral

$$\int_0^\infty \varphi(t)dt.$$

With $F_i(x) = 0$ and initial condition $\varphi_i(0)$ implies

$$\dot{x}_i = -V_i\, x_i,\ x_i(0) = \varphi_i(0). \qquad (2.19)$$

The solution of (2.19) is

$$x_i(t) = e^{-V_i t}\varphi_i(0).$$

Thus the expected value of new infections produced by the initially infected individuals is given by

$$\int_0^{\infty} Fe^{-Vt}\varphi_i(0) = FV^{-1}\varphi_i(0),$$

where (i,j) entry of F is the rate at which infected individuals in compartment j produce new infections in compartment i. Diekmann and Heesterbeek (2000), called K= FV^{-1} is the next generation matrix. The (i, j) entry of K is the number of secondary infections in compartment i produced by individuals initially in compartment j. In other words, the elements FV^{-1} represent the generational output of compartment i by compartment j (Hurford, Cownden, & Day, 2009). Therefore the basic reproduction ratio is given by

$$R_0 = \rho(FV^{-1}),$$

where $\rho(K)$ is denoted by spectral radius of a matrix K, which is the maximum of the modulus of the eigenvalues of K.

CHAPTER 3

SIR MODEL WITH AND WITHOUT VACCINE

In this chapter we define and constract a single strain delay model with and without vaccine to see the effect of the vaccine for the disease. The models which are constructed in this chapter modified by Chauhan models with adding delay for incubation period. Chauhan et al. studied with two model with and without vaccine models and they showed the effect of the vaccine (Chauhan et al., 2014).

In Section 3.1 the SIR model with delay is constructed, then equilibrium points, basic reproduction number and stability analysis are given for this model. In Section 3.2 the SIR model is constructed with delay and vaccine. Similarly with the previous section, equilibrium points, basic reproduction number and stability analysis are also given. In Section 3.3, numerical simulations are given for both model.

3.1 Construction of the Delay SIR Model without Vaccine

The assumptions for the model are

i. The population is fixed.
ii. The natural birth and death rates are included in the model.
iii. All birth are into suspectible class only.

The population $N(t)$ is divided tree compartment $S(t), I(t)$, and $R(t)$ which are susceptible, infected and recovery compartments respectively. The model which is constructed in this section assumed that individuals infected at time $t-\tau$ become infectious τ time later. To be a more realsitic it can be assumed that not all those infected will survive after τ times later, because of this reason survival term $e^{\mu\tau}$ is introduced. The transfer diagram of the model is given in the following Table.

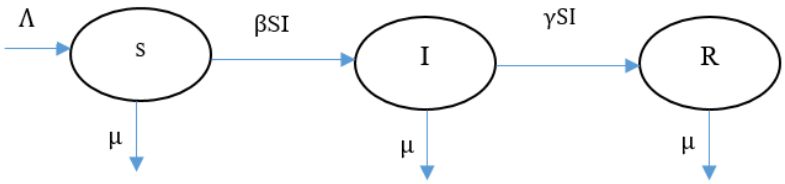

Figure 3.1: Transfer diagram of the model.

The variables and parameters are positive and their meanings are also given in Table 3.1.

Table 3.1: Variables and parameter

Parameter	Description
Λ	Recruitment of individulas
$\frac{1}{\mu}$	Avarage time of life expectance
β	Transmission coefficient of susceptible individuals to the infected compartment
$\frac{1}{\gamma}$	Avarage infection period
d	Death rate from the disease
τ	Incubation period
$e^{-\mu\tau}$	Probability that an individual in the incubation period has survived

Under the above assumptions the model is given by a system of ordinary differential equations

$$\frac{dS(t)}{dt} = \Lambda - (\beta I(t) + \mu)S(t),$$

$$\frac{dI(t)}{dt} = e^{-\mu\tau}\beta S(t-\tau)I(t-\tau) - (\gamma + \mu + d)I, \qquad (3.1)$$

$$\frac{dR(t)}{dt} = \gamma I(t) - \mu R(t),$$

with the initial conditions

$$s(0) \geq 0, I(0) \geq 0, R(0) \geq 0 \ .$$

Note that, using

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

we can obtain R(t) by N(t) − S(t) − I(t). Therefore, we will study with the following system

$$\frac{dS(t)}{dt} = \Lambda - (\beta I(t) + \mu)S(t),$$

$$\frac{dI(t)}{dt} = e^{-\mu\tau}\beta S(t-\tau)I(t-\tau) - (\gamma + \mu + d)I(t). \qquad (3.2)$$

The following theorem establishes the feasible region of the system (3.2).

Theorem 3.1. The solution $\varphi \in C_2$ of the system (3.2) is unique, nonnegative and bounded and the positive invariant region is

$$\Omega = \left\{(S(t), I(t)) \in C_+^2 : H = S(t) + e^{\mu\tau}I(t+\tau) \leq \frac{\Lambda}{\mu}\right\}. \qquad (3.3)$$

Proof. For nonnegativity of solution of the system (3.2), it is needed to show solution of each equation of the system is nonnegative.

First, taking the first equation of the system (3.2), we get

$$\frac{dS}{dt} = \Lambda - (\beta I(t) + \mu)S(t) \geq -(\beta I(t) + \mu)S(t)$$

or

$$\frac{dS}{dt} + (\beta I(t) + \mu)S(t) \geq 0. \tag{3.4}$$

The integrating factor $p(t)$ of the equation (3.4)

$$p(t) = e^{\int_0^t (\beta I(u)+\mu)\, du}.$$

Therefore from (3.4), it follows

$$e^{\int_0^t (\beta I(u)+\mu)\, du} \frac{dS}{dt} + e^{\int_0^t (\beta I(u)+\mu)\, du}(\beta I(t) + \mu)S(t) \geq 0$$

or

$$\frac{d}{dt}\left[S(t)e^{\int_0^t (\beta I(u)+\mu)\, du}\right] \geq 0.$$

Taking integral with respect to s from 0 to t, we get

$$\int_0^t \frac{\mathrm{d}}{\mathrm{dt}}\left[S(s)e^{\int_0^s (\beta \mathrm{I}(\mathrm{u})+\mu)\, du}\right] dt \geq 0$$

or

$$S(t)e^{\int_0^t (\beta \mathrm{I}(\mathrm{u})+\mu)\, du}\Big|_0^t \geq 0$$

or

$$S(t)e^{\int_0^t(\beta I(u)+\mu)\,du} - S(0) \geq 0$$

or

$$S(t) \geq S(0)e^{-\int_0^t(\beta I(u)+\mu)\,du} \geq 0.$$

From the second equation of the system (3.2), it follows that

$$\frac{dI(t)}{dt} = e^{-\mu\tau}\beta S(t-\tau)I(t-\tau) - (\gamma+\mu+d)I \geq -(\gamma+\mu+d)I(t) \tag{3.5}$$

or

$$\frac{dI(t)}{dt} + (\gamma+\mu+d)I(t) \geq 0\,. \tag{3.6}$$

The integrating factor $p(t)$ of (3.6) is

$$p(t) = e^{\int_0^t(\gamma+\mu+d)\,du} = e^{(\gamma+\mu+d)t}\,.$$

Therefore from (3.6) it follows

$$e^{(\gamma+\mu+d)t}\,\frac{dI(t)}{dt} + e^{(\gamma+\mu+d)t}\,(\gamma+\mu+d)I(t) \geq 0.$$

or

$$\frac{d}{dt}\left[e^{(\gamma+\mu+d)t}\, I(t)\right] \geq 0.$$

Taking the integral with respect ot s from 0 to t, we get

$$I(t) \geq I(0)e^{-(\gamma+\mu+d)t} \geq 0.$$

Hence the solution of the system (3.2) is nonnegative.

For the proof of boundedness of the system (3.2), let us define a function

$$H = S(t) + e^{\mu\tau} I(t+\tau).$$

Therefore

$$\dot{H} = \dot{S}(t) + e^{\mu\tau}\dot{I}(t+\tau)$$

$$= \Lambda - (\beta \mathrm{I}(\mathrm{t}) + \mu)\mathrm{S}(\mathrm{t}) + e^{\mu\tau}[\mathrm{e}^{-\mu\tau}\beta \mathrm{S}(\mathrm{t})\mathrm{I}(\mathrm{t}) - (\gamma + \mu + \mathrm{d})I(t+\tau)]$$

$$= \Lambda - \mu \mathrm{S}(\mathrm{t}) - e^{\mu\tau}(\gamma + \mu + \mathrm{d})I(t+\tau)$$

$$\leq \Lambda - \mu \mathrm{S}(\mathrm{t}) - e^{\mu\tau}\mu I(t+\tau)$$

$$= \Lambda - \mu \mathrm{H}(\mathrm{t}).$$

So we have

$$\dot{H} \leq \Lambda - \mu \mathrm{H}(\mathrm{t}).$$

Since $0 \leq \dot{H}$, we get

$$0 \leq \dot{H} \leq \Lambda - \mu \mathrm{H}(\mathrm{t})$$

or

$$0 \leq \Lambda - \mu H(t). \tag{3.7}$$

Therefore, from (3.7) and for large enough t, it follows

$$H(t) \leq \frac{\Lambda}{\mu}.$$

Hence, the positive invariant region is obtained that

$$\Omega = \left\{(S(t), I(t)) \in C_+^2 : N = S(t) + e^{\mu\tau} I(t+\tau) \leq \frac{\Lambda}{\mu}\right\}.$$

Finally, we will show the uniqueness solution of the system (3.2), we define a vector function f as follows

$$f\big(\varphi(t), \varphi(t-\tau)\big) = \begin{pmatrix} f_1(\varphi(t)) \\ f_2\big(\varphi(t), \varphi(t-\tau)\big) \end{pmatrix}, \quad \varphi(t) = \begin{pmatrix} \varphi_1(t) \\ \varphi_2(t) \end{pmatrix},$$

where $f_1\big(\varphi(t)\big) = \Lambda - (\beta\varphi_2(t) + \mu)\varphi_1(t)$ and $f_2\big(\varphi(t)\big) = e^{-\mu\tau}\beta\varphi_1(t-\tau)\varphi_2(t-\tau)$ $-(\gamma + \mu + d)\varphi_2(t)$ are continuous. In order to say the system (3.2) has a unique solution it is sufficient to show that the Lipschitz condition for $f(\varphi(t), \varphi(t-\tau))$ with respect to $\varphi(t)$ holds.

For $\varphi = (\varphi_1, \varphi_2)$ and $\psi = (\psi_1, \psi_2)$, and assuming that

$$\|\psi - \varphi\| = |\psi_2 - \varphi_2| + |\psi_1 - \varphi_1|. \tag{3.8}$$

We have that

$$\|f_1(\varphi(t)) - f_1(\psi(t))\| = |(\Lambda - (\beta\varphi_2(t) + \mu)\varphi_1(t)) - (\Lambda$$
$$-(\beta\psi_2(t) + \mu)\psi_1(t))|$$

$$\leq \beta|\psi_1(t)\psi_2(t) - \varphi_1(t)\varphi_2(t)| + \mu|\psi_1(t) - \varphi_1(t)|$$

$$= \beta|\psi_1(t)\psi_2(t) - \psi_1(t)\varphi_2(t) + \psi_1(t)\varphi_2(t) - \varphi_1(t)\varphi_2(t)|$$
$$+\mu|\psi_1(t) - \varphi_1(t)|$$

$$\leq \beta|\psi_1(t)||\psi_2(t) - \varphi_2(t)| + \beta|\varphi_2(t)||\psi_1(t) - \varphi_1(t)| + \mu|\psi_1(t)$$
$$-\varphi_1(t)|$$

$$\leq K_1(|\psi_1(t) - \varphi_1(t)| + |\psi_2(t) - \varphi_2(t)|) = K_1|\psi(t) - \varphi(t)|, \qquad (3.9)$$

where

$$K_1 = \max\{\mu + \beta|\varphi_2|, \beta|\psi_1|\}$$

from the invariant set , $\varphi_1 \leq \frac{\Lambda}{\mu}$, $\varphi_2 \leq \frac{\Lambda}{\mu}$, it follows

$$K_1 = \mu + \beta\frac{\Lambda}{\mu}.$$

Furthermore, one can derive that

$$\|f_2(\varphi(t), \varphi(t-\tau)) - f_2(\psi(t), \psi(t-\tau))\| = |e^{-\mu\tau}\beta\varphi_1(t-\tau)\varphi_2(t$$
$$-\tau) - (\gamma + \mu + d)\varphi_2(t) - (e^{-\mu\tau}\beta\psi_1(t-\tau)\psi_2(t-\tau) - (\gamma + \mu$$
$$+d)\psi_2(t))|$$

$$\leq (\gamma + \mu + d)|\psi_2(t) - \varphi_2(t)|$$

$$\leq K_2|\psi(t) - \varphi(t)|, \qquad (3.10)$$

where

$$K_2 = \gamma + \mu + d.$$

Applying (3.9) and (3.10), we get

$$\|f(\varphi(t),\varphi(t-\tau))-f(\psi(t),\psi(t-\tau))\| = \|f_1(\varphi(t))-f_1(\psi(t))\|$$
$$+\|f_2(\varphi(t),\varphi(t-\tau))-f_2(\psi(t),\psi(t-\tau))\| \leq (K_1+K_2)|\psi-\varphi|,$$

where

$$K_1+K_2 = \gamma+d+2\mu+\beta\frac{\Lambda}{\mu}.$$

3.1.1 Equilibria points and Basic Reproduction Number

In this section, it will be found the equilibrium points of the system and it will be found the basic reproduction number which is the treshold condition for the system.

Theorem 3.2.

i. The system (3.2) has always disease free equilibrium $E_0 = (S_0, I_0)$, where

$$S_0 = \frac{\Lambda}{\mu} \text{ and } I_0 = 0.$$

ii. If $\frac{e^{-\mu\tau}\Lambda\beta}{(\mu+d+\gamma)\mu} \geq 1$ then system (3.2) has the endemic equilibrium $E_1 = (S^*, I^*)$, where

$$S^* = \frac{e^{\mu\tau}(\mu+d+\gamma)}{\beta} \text{ and } I^* = \frac{e^{-\mu\tau}\Lambda}{(\mu+d+\gamma)} - \frac{\mu}{\beta}.$$

Proof. Equailizing the each equation of the system (3.2) to the zero, it is obtained that

$$\Lambda-(\beta I(t)+\mu)S(t) = 0,$$

$$e^{-\mu\tau}\beta S(t-\tau)I(t-\tau)-(\gamma+\mu+d)I(t) = 0. \qquad (3.11)$$

Assume that $I(t) = 0$, then the disease free equilibrium is obtained in the first equation of (3.11) as

$$S(t) = \frac{\Lambda}{\mu},$$

then the disease free equilibrium is

$$E_0 = \left(\frac{\Lambda}{\mu}, 0\right). \tag{3.12}$$

Now assume that, $I(t) \neq 0$, from the first equation of the system (3.11), it follows

$$S(t) = \frac{\Lambda}{\beta I(t)+\mu}. \tag{3.13}$$

Putting $S(t)$ in the second equation of the system (3.11), we get

$$e^{-\mu\tau}\beta S(t-\tau)I(t-\tau) - (\gamma+\mu+d)I(t)$$

$$= e^{-\mu\tau}\beta \frac{\Lambda}{\beta I(t)-\mu} I(t-\tau) - (\gamma+\mu+d)I(t) = 0.$$

Since $I(t) \neq 0$, then

$$e^{-\mu\tau}\beta \frac{\Lambda}{\beta I(t)-\mu} - (\gamma+\mu+d) = 0$$

or

$$e^{-\mu\tau}\beta\Lambda - (\gamma+\mu+d)\beta I(t) - (\gamma+\mu+d)\mu = 0,$$

then

$$I(t) = \frac{e^{-\mu\tau}\Lambda}{\gamma+\mu+d} - \frac{\mu}{\beta}. \tag{3.14}$$

Under (3.11) and (3.14), we get

$$S(t) = \frac{\Lambda}{\beta\left(\frac{e^{-\mu\tau}\Lambda}{\gamma+\mu+d} - \frac{\mu}{\beta}\right)+\mu} = \frac{\Lambda(\gamma+\mu+d)}{\beta e^{-\mu\tau}\Lambda - \mu(\gamma+\mu+d)+\mu(\gamma+\mu+d)} = \frac{(\gamma+\mu+d)e^{\mu\tau}}{\beta}.$$

Hence the endemic equilibrium is

$$E_1 = \left(\frac{e^{\mu\tau}(\mu+d+\gamma)}{\beta}, \frac{e^{-\mu\tau}\Lambda}{(\mu+d+\gamma)} - \frac{\mu}{\beta}\right).$$

Since $S^* = \frac{e^{\mu\tau}(\mu+d+\gamma)}{\beta} \geq 0$, then E_1 is biologically meaningfull, when

$$I^* = \frac{e^{-\mu\tau}\Lambda}{(\mu+d+\gamma)} - \frac{\mu}{\beta} \geq 0.$$

or

$$\frac{e^{-\mu\tau}\Lambda\beta}{(\mu+d+\gamma)\mu} \geq 1.$$

Basic reproduction number R_0 is the number of secondary infections caused by one infectious individual in a whole susceptible population. With using the second equation of the system (3.1) the basic reproduction number is given by,

$$e^{-\mu\tau}\beta S(t-\tau)I(t-\tau) - (\gamma+\mu+d)I(t) < 0$$

or

$$\frac{e^{-\mu\tau}\beta S(t-\tau)}{(\gamma+\mu+d)} < 1.$$

The basic reproduction ratio is given at the disease free equilibrium point,

$$R_{0,1} = \frac{e^{-\mu\tau}\beta S_0}{(\gamma+\mu+d)} = \frac{e^{-\mu\tau}\Lambda\beta}{\mu(\gamma+\mu+d)}.$$

3.1.2 Stability analysis

In this section the stability analysis for both disease free and endemic equilibria are given with the method of Lyapunov function.

Theorem 3.3. The disease free equilibrium E_0 is globally asymptotically stable when $R_{0,1} < 1$.

Proof. The Lyapunov function is constructed as

$$\mathcal{V}(t) = e^{\mu\tau} I(t) + \int_{t-\tau}^{t} \beta S(u) I(u) du.$$

Since $\mathcal{V}$ is nonnegative, to show that disease free equilibrium point E_0 is globally asymptotically stable, we only need to show that $\dot{\mathcal{V}}$ negative definite. Actually,

$$\dot{\mathcal{V}}(t) = e^{\mu\tau} \dot{I}(t) + \beta S(t) I(t) - \beta S(t-\tau) I(t-\tau)$$

$$= e^{\mu\tau} [\mathrm{e}^{-\mu\tau} \beta \mathrm{S}(\mathrm{t}-\tau) \mathrm{I}(\mathrm{t}-\tau) - (\gamma + \mu + \mathrm{d}) I(t)] + \beta S(t) I(t)$$
$$-\beta S(t-\tau) I(t-\tau)$$

$$= \beta S(t) I(t) - (\gamma + \mu + \mathrm{d}) e^{\mu\tau} I(t). \qquad (3.15)$$

According form (3.3), we have $S(t) \leq \frac{\Lambda}{\mu}$, replacing this in (3.15), it is obtained

$$\dot{\mathcal{V}}(t) = \beta S(t) I(t) - (\gamma + \mu + d) e^{\mu\tau} I(t)$$

$$\leq \beta \frac{\Lambda}{\mu} I(t) - (\gamma + \mu + d) e^{\mu\tau} I(t).$$

Therefore, $\dot{\mathcal{V}}(t) < 0$, when

$$\beta \frac{\Lambda}{\mu} I(t) - (\gamma + \mu + d) e^{\mu\tau} I(t) < 0.$$

Since $I(t) > 0$, then

$$\frac{\beta\Lambda\, e^{-\mu\tau}}{\mu(\gamma+\mu+d)} < 1. \qquad (3.16)$$

The left hand side of (3.16) is the basic reproduction ratio. Hence, E_0 is globally asymptotically stable when $R_{0,1} < 1$.

Theorem 3.4. The endemic equilibrium E_1 is globaly asymptotically stable when $R_{0,1} > 1$.

Proof. The Lyapunov function is constructed as

$$\mathcal{V}(t) = S^* g\left(\frac{S(t)}{s^*}\right) + e^{\mu\tau} I^* g\left(\frac{I(t)}{I^*}\right) + \beta S^* I^* \int_{t-\tau}^{t} g\left(\frac{S(u)I(u)}{S^*I^*}\right) du,$$

where $g(x)$ defined as

$$g(x) = x - 1 - \ln x.$$

Since $g(x)$ is nonnegative function, and $I^* > 0$ when $\frac{\beta\Lambda\, e^{-\mu\tau}}{\mu(\gamma+\mu+d)} > 1$, then $\mathcal{V}(t)$ is nonnegative, to show that disease free equilibrium point E_1 is globally asymptotically stable, we only need to show that $\dot{\mathcal{V}}$ negative definite. Actually,

$$\dot{\mathcal{V}}(t) = S^*\left(\frac{\dot{S}(t)}{S^*} - \frac{\dot{S}(t)}{S(t)}\right) + e^{\mu\tau} I^*\left(\frac{\dot{I}(t)}{I^*} - \frac{\dot{I}(t)}{I(t)}\right) + \beta S^* I^*\left[\frac{S(t)I(t)}{S^*I^*} - 1\right.$$
$$\left. - \ln\left(\frac{S(t)I(t)}{S^*I^*}\right) - \frac{S(t-\tau)I(t-\tau)}{S^*I^*} + 1 + \ln\left(\frac{S(t-\tau)I(t-\tau)}{S^*I^*}\right)\right]$$

$$= \left(1 - \frac{S^*}{s(t)}\right)\left(\Lambda - (\beta \mathrm{I(t)} + \mu)\mathrm{S(t)}\right) + e^{\mu\tau}\left(1 - \frac{I^*}{I(t)}\right)(\mathrm{e}^{-\mu\tau}\beta \mathrm{S(t-\tau)I(t}$$
$$-\tau) - (\gamma + \mu + \mathrm{d})I(t)) + \beta S(t)I(t) - \beta S(t-\tau)I(t-\tau)$$
$$-\beta S^* I^*\left(\ln\left(\frac{S(t)I(t)}{S^*I^*}\right) - \ln\left(\frac{S(t-\tau)I(t-\tau)}{S^*I^*}\right)\right)$$

$$= \Lambda\left(1 - \frac{S^*}{s(t)}\right) - \beta \mathrm{I(t)S(t)} - \mu \mathrm{S(t)} + \beta \mathrm{I(t)}S^* + \mu S^* + \beta \mathrm{S(t-\tau)I(t}$$

$$- \tau) - e^{\mu\tau}(\gamma + \mu + \mathrm{d})I(t) - \frac{\beta \mathrm{S(t-\tau)I(t-\tau)}}{I(t)} I^* + e^{\mu\tau}(\gamma + \mu + \mathrm{d})I^*$$

$$+\beta S(t)I(t) - \beta S(t-\tau)I(t-\tau) - \beta S^* I^* \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)$$

$$= \Lambda\left(1 - \frac{S^*}{s(t)}\right) - \mu \mathrm{S(t)} + S^*\mu + \left(\beta S^* - e^{\mu\tau}(\gamma + \mu + \mathrm{d})\right)I(t)$$

$$-I^*\left[\frac{\beta \mathrm{S(t-\tau)I(t-\tau)}}{I(t)} - e^{\mu\tau}(\gamma + \mu + \mathrm{d}) + \beta S^* I^* \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]. \qquad (3.17)$$

From the second equation of (3.11), we have

$$\left(\beta S^* - e^{\mu\tau}(\gamma + \mu + \mathrm{d})\right)I^* = 0$$

since $I^* \neq 0$, then

$$\beta S^* - e^{\mu\tau}(\gamma + \mu + \mathrm{d}) = 0 \qquad (3.18)$$

which implies that

$$e^{\mu\tau}(\gamma + \mu + \mathrm{d}) = \beta S^*. \qquad (3.19)$$

From the endemic equilibrium is $\left(\frac{e^{\mu\tau}(\mu+d+\gamma)}{\beta}, \frac{e^{-\mu\tau}\Lambda}{(\mu+d+\gamma)} - \frac{\mu}{\beta}\right)$, we get

$$I^* = \frac{e^{-\mu\tau}\Lambda}{(\mu+d+\gamma)} - \frac{\mu}{\beta}$$

then

$$\Lambda = I^* e^{\mu\tau}(\mu + d + \gamma) + \frac{\mu e^{\mu\tau}(\mu+d+\gamma)}{\beta}$$

so

$$\Lambda = I^* e^{\mu\tau}(\mu + d + \gamma) + \mu S^* \tag{3.20}$$

replacing (3.19) in to (3.20), we get

$$\Lambda = \beta S^* I^* + \mu S^* \tag{3.21}$$

using the (3.18), (3.19) and (3.21), system (3.17) can be regarded as

$$\dot{\mathcal{V}}(t) = (\beta S^* I^* + \mu S^*)\left(1 - \frac{S^*}{s(t)}\right) + S^*\mu\left(1 - \frac{S(t)}{S^*}\right) + \big(\beta S^* - e^{\mu\tau}(\gamma + \mu + d)\big)I(t) - I^*\left[\frac{\beta S(t-\tau)I(t-\tau)}{I(t)} - \beta S^* + \beta S^* I^* \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]$$

$$= I^*\beta S^* - \beta S^* \frac{S^*}{s(t)} I^* + \mu S^*\left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) - \beta I^* S^*\left[-1 + \frac{S(t-\tau)I(t-\tau)}{I(t)S^*} + \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]$$

$$= \mu S^*\left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) + \beta I^* S^*\left[2 - \frac{S^*}{s(t)} - \frac{S(t-\tau)I(t-\tau)}{I(t)S^*} - \ln\frac{S(t)I(t)}{S(t-\tau)I(t-\tau)}\right]. \tag{3.22}$$

Since

$$g\left(\frac{S^*}{s(t)}\right) + g\left(\frac{S(t-\tau)I(t-\tau)}{I(t)S^*}\right) = \frac{S^*}{s(t)} - 1 - \ln\frac{S^*}{s(t)} + \frac{S(t-\tau)I(t-\tau)}{I(t)S^*} - 1 - \ln\frac{S(t-\tau)I(t-\tau)}{I(t)S^*}$$

$$= -2 + \frac{S^*}{s(t)} + \frac{S(t-\tau)I(t-\tau)}{I(t)S^*} + \ln\frac{S(t)}{S^*}\frac{I(t)S^*}{S(t-\tau)I(t-\tau)}$$

$$= -2 + \frac{S^*}{s(t)} + \frac{S(t-\tau)I(t-\tau)}{I(t)S^*} + \ln\frac{S(t)I(t)}{S(t-\tau)I(t-\tau)} \geq 0 \tag{3.23}$$

and

$$2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*} = -\left(S^* - S(t)\right)^2 \leq 0. \qquad (3.24)$$

Hence, because of the fact that (3.23) and (3.24), the equation (3.22) yields

$$\dot{\mathcal{V}}(t) = \mu S^* \left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) - \beta I^* S^* \left(-2 + \frac{S^*}{s(t)} + \frac{\mathrm{S(t-\tau)I(t-\tau)}}{I(t)S^*} + \ln \frac{S(t)I(t)}{S(t-\tau)I(t-\tau)}\right) \leq 0$$

which completes the proof.

3.2 Construction of the Delay SIR Model With Vaccine

In this section delay SIR model is constructed with a vaccine. Addition to the previous model vaccine compartment $V(t)$ is added and the population $N(t)$ is divided to four compartment. The variables and parameters are positive and their meanings are also given in Table 3.2.

Under these assumptions the model is given by a system of ordinary differential equations

$$\frac{dS(t)}{dt} = \Lambda - (\beta I(t) + r + \mu)S(t),$$

$$\frac{dV(t)}{dt} = rS(t) - kV(t)I(t) - (\mu + 1 - k)V(t),$$

$$\frac{dI(t)}{dt} = e^{-\mu\tau}[\beta S(t-\tau) + kV(t-\tau)]I(t-\tau) - (\gamma + \mu + d)I(t), \quad (3.25)$$

$$\frac{dR(t)}{dt} = (1-k)V(t) + \gamma I(t) - \mu R(t),$$

with the initial conditions

$$S(0) \geq 0, V(0) \geq 0, I(0) \geq 0, R(0) \geq 0 .$$

Table 3.2: Variables and parameters

Parameter	Description
Λ	Recruitment of individulas
$\frac{1}{\mu}$	Avarage time of life expectance
β	Transmission coefficient of susceptible individuals to the Infected compartment
$\frac{1}{\gamma}$	Avarage infection period
d	Infection induced death rate
τ	Incubation period
$e^{-\mu\tau}$	Probability that an individual in the incubation period has survived
r	Rate of vaccination
k	Transmission coefficient of vaccinated individuals V to I

Using

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

we can obtain $R(t)$ by

$$N(t) - S(t) - V(t) - I(t).$$

Therefore, it is sufficient to study with the following system

$$\frac{dS(t)}{dt} = \Lambda - (\beta I(t) + \lambda)S(t),$$

$$\frac{dV(t)}{dt} = rS(t) + kV(t)I(t) - (\mu + 1 - k)V(t), \tag{3.26}$$

$$\frac{dI(t)}{dt} = e^{-\mu\tau}[\beta S(t-\tau) + kV(t-\tau)]I(t-\tau) - \alpha I(t),$$

where $\lambda = r + \mu$ and $\alpha = \gamma + \mu + d$. Similary with the previous section, following theorem establishes the feasible region of the system (3.26).

Theorem 3.5. The solution of the system (3.26) exists, unique, nonnegative and bounded with the feasible region

$$\Omega = \left\{\big(S(t), V(t), I(t)\big) \in C_+^3 : H = S(t) + V(t) + e^{\mu\tau} I(t+\tau) \leq \frac{\Lambda}{\mu}\right\}$$

Proof. For nonnegativity of solution of the system (3.26), it is needed to show that the solution of each equation of the system is nonnegative.

First, taking the first equation of the system (3.2), we get

$$\frac{dS}{dt} = \Lambda - (\beta I(t) + \lambda)S(t) \geq -(\beta I(t) + \lambda)S(t)$$

or

$$\frac{dS}{dt} + (\beta I(t) + \lambda)S(t) \geq 0. \tag{3.27}$$

The integrating factor $p(t)$ of the equation (3.27)

$$p(t) = e^{\int_0^t (\beta I(u) + \lambda)\, du}.$$

Therefore, from (3.27) it follows

$$e^{\int_0^t(\beta I(u)+\lambda)\,du}\frac{dS}{dt}+e^{\int_0^t(\beta I(u)+\lambda)\,du}(\beta I(t)+\lambda)S(t)\geq 0$$

or

$$\frac{d}{dt}\left[S(t)e^{\int_0^t(\beta I(u)+\lambda)\,du}\right]\geq 0.$$

Taking the integral with respect to s from 0 to t, we get

$$S(t)e^{\int_0^t(\beta I(u)+\lambda)\,du}]_0^t\geq 0$$

or

$$S(t)e^{\int_0^t(\beta I(u)+\lambda)\,du}-S(0)\geq 0$$

or

$$S(t)\geq S(0)e^{-\int_0^t(\beta I(u)+\lambda)\,du}.$$

From the second equation of the system (3.26), it follows that

$$\frac{dV(t)}{dt}=rS(t)+kV(t)I(t)-(\mu+1-k)V(t)\geq-(\mu+1-k)V(t)$$

or

$$\frac{dV(t)}{dt}\geq-(\mu+1-k)V(t)$$

or

$$\frac{dV(t)}{dt}+(\mu+1-k)V(t)\geq 0. \qquad (3.28)$$

The integrating factor $p(t)$ of (3.28) is

$$p(t) = e^{\int_0^t (\mu+1-k)\, du} = e^{(\mu+1-k)t}.$$

Therefore, from (3.28) it follows

$$e^{(\mu+1-k)t}\, \frac{dV(t)}{dt} + e^{(\mu+1-k)t}\, (\gamma + \mu + d)V(t) \geq 0.$$

or

$$\frac{d}{dt}\left[e^{(\mu+1-k)t}\, V(t)\right] \geq 0.$$

Taking the integral with respect to s from 0 to t, we get

$$e^{(\mu+1-k)s}\, V(t)]_0^t \geq 0$$

or

$$V(t) \geq V(0)e^{-(\mu+1-k)t}.$$

Finally, from the third equation of the system (3.26), we get

$$\frac{dI(t)}{dt} = e^{-\mu\tau}[\beta S(t-\tau) + kV(t-\tau)]I(t-\tau) - \alpha I(t) \geq -\alpha I(t)$$

or

$$\frac{dI(t)}{dt} \geq -\alpha I(t) \qquad (3.29)$$

or

$$\frac{dI(t)}{dt} + \alpha I(t) \geq 0. \qquad (3.30)$$

The integrating factor $p(t)$ of (3.30) is

$$p(t) = e^{\int_0^t \alpha\, du} = e^{\alpha t}.$$

Therefore from (3.30) it follows

$$e^{\alpha t}\, \frac{dI(t)}{dt} + e^{\alpha t}\, \alpha I(t) \geq 0.$$

or

$$\frac{d}{dt}\left[e^{\alpha t}\, I(t)\right] \geq 0.$$

Taking integral with respect to s from 0 to t, we get

$$I(t) \geq I(0)e^{-\alpha t}$$

which is nonnegative. Hence the solution of the system (3.26) is nonnegative.

For the proof of boundedness of the system (3.26), let us define a function

$$H = S(t) + V(t) + e^{\mu\tau} I(t+\tau).$$

Therefore

$$\dot{H} = \dot{S}(t) + \dot{V}(t) + e^{\mu\tau}\dot{I}(t+\tau)$$

$$= \Lambda - (\beta I(t) + \lambda)S(t) + rS(t) + kV(t)I(t) - (\mu + 1 - k)V(t)$$
$$+ e^{\mu\tau}[e^{-\mu\tau}[\beta S(t) + kV(t)]I(t) - \alpha I(t+\tau)]$$
$$= \Lambda - \mu S(t) - (\mu + 1 - k)V(t) - e^{\mu\tau}\alpha I(t+\tau)$$

$$\leq \Lambda - \mu S(t) - \mu V(t) - e^{\mu\tau}\mu I(t+\tau)$$

$$= \Lambda - \mu H(t).$$

Hence, the solution of the system, is obtained from

$$\dot{H} \leq \Lambda - \mu H(t). \tag{3.31}$$

The integrating factor $p(t)$ of (3.31) is

$$p(t) = e^{\mu t}.$$

Therefore, from (3.31) it follows

$$e^{\mu t}\dot{H}(t) + e^{\mu t}\mu H(t) \leq e^{\mu t}\Lambda$$

or

$$\frac{d}{dt}\left[e^{\mu t}H(t)\right] \leq e^{\mu t}\Lambda.$$

Taking the integral with respect to s from 0 to t, we get

$$e^{\mu s}H(t)|_0^t \geq \frac{\Lambda}{\mu}e^{\mu s}\Big|_0^t$$

or

$$e^{\mu t}H(t) - H(0) \leq \frac{\Lambda}{\mu}e^{\mu t} - \frac{\Lambda}{\mu}$$

or

$$H(t) \leq e^{-\mu t}H(0) + \frac{\Lambda}{\mu}(1 - e^{-\mu t}) \leq H(0)e^{-\mu t} + \frac{\Lambda}{\mu}$$

or

$$H(t) \leq \frac{\Lambda}{\mu} + H(0)e^{-\mu t}.$$

Then

$$\lim_{t\to\infty} H(t) \leq \lim_{t\to\infty} \left(\frac{\Lambda}{\mu} + H(0)e^{-\mu t}\right) = \frac{\Lambda}{\mu}.$$

The positive invariant region is obtained that

$$\Omega = \left\{\left(S(t), V(t), I(t)\right) \in C_+^2 : H = S(t) + V(t) + e^{\mu\tau} I(t+\tau) \leq \frac{\Lambda}{\mu}\right\}.$$

Finally, we will show the uniqueness solution of the system (3.26), we define a vector function f as follows

$$f\left(\varphi(t), \varphi(t-\tau)\right) = \begin{pmatrix} f_1\left(\varphi(t)\right) \\ f_2\left(\varphi(t)\right) \\ f_2\left(\varphi(t), \varphi(t-\tau)\right) \end{pmatrix}, \quad \varphi(t) = \begin{pmatrix} \varphi_1(t) \\ \varphi_2(t) \\ \varphi_2(t) \end{pmatrix},$$

where $f_1\left(\varphi(t)\right) = \Lambda - (\beta\varphi_3(\mathrm{t}) + \lambda)\varphi_1(\mathrm{t})$, $f_2\left(\varphi(t)\right) = \mathrm{r}\varphi_1(\mathrm{t}) + \mathrm{k}\varphi_2(\mathrm{t})\varphi_3(\mathrm{t}) - (\mu + 1 - \mathrm{k})\varphi_2(\mathrm{t})$ and $f_3\left(\varphi(t)\right) = \mathrm{e}^{-\mu\tau}[\beta\varphi_1(t-\tau) + k\varphi_2(t-\tau)]\varphi_3(t-\tau) - \alpha\varphi_3(t)$ are continuous. In order to say the system (3.26) has a unique solution it is sufficient to show that the Lipschitz condition for $f(\varphi(t), \varphi(t-\tau))$, with respect to $\varphi(t)$.

For $\varphi = (\varphi_1, \varphi_2, \varphi_3)$ and $\psi = (\psi_1, \psi_2, \psi_3)$, and assuming that

$$\|\psi - \varphi\| = |\psi_3 - \varphi_3| + |\psi_2 - \varphi_2| + |\psi_1 - \varphi_1|. \qquad (3.32)$$

We have that

$$\|f_1(\varphi(t)) - f_1(\psi(t))\| = |(\Lambda - (\beta\varphi_3(t) + \lambda)\varphi_1(t)) - (\Lambda - (-\beta\psi_3(t) + \lambda)\psi_1(t))|$$

$$\leq \beta|\psi_1(t)\psi_3(t) - \varphi_1(t)\varphi_3(t)| + \lambda|\psi_1(t) - \varphi_1(t)|$$

$$= \beta|\psi_1(t)\psi_3(t) - \psi_1(t)\varphi_3(t) + \psi_1(t)\varphi_3(t) - \varphi_1(t)\varphi_3(t)| + \lambda|\psi_1(t) - \varphi_1(t)|$$

$$\leq \beta|\psi_1(t)||\psi_3(t) - \varphi_3(t)| + \beta|\varphi_3(t)||\psi_1(t) - \varphi_1(t)| + \lambda|\psi_1(t) - \varphi_1(t)|$$

$$\leq K_1(|\psi_1(t) - \varphi_1(t)| + |\psi_3(t) - \varphi_3(t)|) \leq K_1|\psi(t) - \varphi(t)|,$$

where

$$K_1 = max\{\lambda + \beta|\varphi_3|, \beta|\psi_1(t)|\}.$$

From the invariant set $\varphi_1 \leq \frac{\Lambda}{\mu}$, $\varphi_3 \leq \frac{\Lambda}{\mu}$ it follows

$$K_1 = \lambda + \beta\frac{\Lambda}{\mu}. \tag{3.33}$$

Furthermore, one can derive that

$$\|f_2(\varphi(t), \varphi(t-\tau)) - f_2(\psi(t), \psi(t-\tau))\| = |\mathrm{r}\varphi_1(\mathrm{t}) + \mathrm{k}\varphi_2(\mathrm{t})\varphi_3(\mathrm{t}) - (\mu + 1 - \mathrm{k})\varphi_2(\mathrm{t}) - \mathrm{r}\psi_1(\mathrm{t}) - \mathrm{k}\psi_2(\mathrm{t})\psi_3(\mathrm{t}) + (\mu + 1 - \mathrm{k})\psi_2(\mathrm{t})|$$

$$\leq \mathrm{r}|\varphi_1(t) - \psi_1(t)| + k|\varphi_2(t)\varphi_3(t) - \psi_2(t)\psi_3(t)| + (\mu + 1 - \mathrm{k})|\psi_2(t) - \varphi_2(t)|$$

$$\leq \mathrm{r}|\varphi_1(t) - \psi_1(t)| + k|\varphi_2(t)\varphi_3(t) - \varphi_2(t)\psi_3(t) + \varphi_2(t)\psi_3(t)$$
$$-\psi_2(t)\psi_3(t)| + (\mu + 1 - \mathrm{k})|\psi_2(t) - \varphi_2(t)|$$

$$\leq \mathrm{r}|\varphi_1(t) - \psi_1(t)| + k|\varphi_2(t)||\varphi_3(t) - \psi_3(t)| + k|\psi_3(t)||\varphi_2(t)$$
$$-\psi_2(t)| + (\mu + 1 - \mathrm{k})|\psi_2(t) - \varphi_2(t)| \leq K_2|\psi(t) - \varphi(t)|,$$

where

$$K_2 = max\{\mathrm{r}, k|\psi_3(t)| + (\mu + 1 - \mathrm{k}), k|\varphi_2(t)|\}.$$

From the invariant set $\varphi_2 \leq \frac{\Lambda}{\mu}$, $\varphi_3 \leq \frac{\Lambda}{\mu}$ it follows

$$K_2 = k\frac{\Lambda}{\mu} + (\mu + 1 - \mathrm{k})\ . \tag{3.34}$$

Finally, using the third equation of the system (3.26), we get

$$\|f_3(\varphi(t), \varphi(t-\tau)) - f_2(\psi(t), \psi(t-\tau))\| = \left|e^{-\mu\tau}\left(\beta\varphi_1(t-\tau)\varphi_3(t\right.\right.$$
$$-\tau) + k\varphi_2(t-\tau)\varphi_3(t \quad -\tau)\big) - \alpha\varphi_3(t) - \big(e^{-\mu\tau}\big(\beta\psi_1(t-\tau)\psi_3(t$$
$$\left.\left.-\tau) + k\psi_2(t-\tau)\psi_3(t \quad -\tau)\right) - \alpha\psi_3(t)\right)\Big|$$

$$\leq \alpha|\psi_3(t) - \varphi_3(t)| \leq K_3|\psi(t) - \varphi(t)|, \tag{3.35}$$

where

$$K_3 = \alpha.$$

Applying (3.33), (3.34) and (3.35), we get

$$\big\|f\big(\varphi(t), \varphi(t-\tau)\big) - f\big(\psi(t), \psi(t-\tau)\big)\big\| = \big\|f_1\big(\varphi(t)\big) - f_1\big(\psi(t)\big)\big\|$$
$$+\big\|f_2\big(\varphi(t)\big) - f_2\big(\psi(t)\big)\big\| + \big\|f_3\big(\varphi(t), \varphi(t-\tau)\big) - f_3\big(\psi(t), \psi(t-\tau)\big)\big\|$$

$$\leq (K_1 + K_2 + K_3)|\psi - \varphi|,$$

where

$$K_1 + K_2 + K_3 = (k + \beta)\frac{\Lambda}{\mu} + \mu + 1 - k + \lambda + \alpha$$

which completes the proof of Theorem 3.5.

3.2.1 Equilibrium points and basic reproduction ratio

With equalizing the each equation of the system (3.26) to the zero, then system (3.6) is recomposed as

$$\Lambda - (\beta I(t) + \lambda)S(t) = 0,$$

$$rS(t) + kV(t)I(t) - (\mu + 1 - k)V(t) = 0, \qquad (3.36)$$

$$e^{-\mu\tau}[\beta S(t - \tau) + kV(t - \tau)]I(t - \tau) - \alpha I = 0.$$

The equilibrium points are given with the following theorem.

Theorem 3.6.

i. The system (3.26) has always disease free equilibrium $E_0 = (S_0, V_0, I_0)$, where

$$E_0 = \left(\frac{\Lambda}{\mu}, \frac{r\Lambda}{\lambda(\mu+1-k)}, 0\right).$$

ii. When $\frac{e^{-\mu\tau}\Lambda}{\alpha\lambda}\left(\beta + \frac{kr}{\mu+1-k}\right) \geq 1$ the system (3.26) has endemic equilibrium $E_1 = (S^*, V^*, I^*)$, where

$$E_1 = \left(\frac{\Lambda}{\beta I^* + \lambda}, \frac{\Lambda r}{[kI^* + (\mu + 1 - k)](\beta I^* + \lambda)}, I^*\right).$$

I^* is the solution of the following equation

$$AI^{*^2} + BI^* + C = 0,$$

when

$$A = \alpha k \beta e^{\mu\tau}, B = \alpha e^{\mu\tau}[k\lambda + \beta(\mu + 1 - k)] - \beta\Lambda k, C = \lambda(\mu + 1 - k)\alpha e^{\mu\tau} - kr\Lambda - \Lambda\beta(\mu + k - 1).$$

Proof. For the disease free equilibrium, $I_0 = 0$, then the system (3.36) can be regarded as

$$\Lambda - \lambda S(t) = 0,$$

$$rS(t) - (\mu + 1 - k)V(t) = 0. \quad (3.37)$$

From the first equation of the system (3.36), S_0 is obtained as

$$S_0 = \frac{\Lambda}{\lambda}. \quad (3.38)$$

Replacing (3.38) into the second equation of the system (3.37), we get

$$r\frac{\Lambda}{\lambda} - (\mu + 1 - k)V(t) = 0$$

or

$$V_0 = \frac{r\Lambda}{\lambda(\mu + 1 - k)}. \quad (3.39)$$

In conclusion, from (3.38) and (3.39), the disease free equilibrium of the system (3.26) is obtained as

$$\left(\frac{\Lambda}{\lambda}, \frac{\mathrm{r}\Lambda}{\lambda(\mu+1-\mathrm{k})}, 0\right).$$

Now, assuming that $I \neq 0$, from the first and second equation of the system (3.36), it is easy to obtained that

$$S^* = \frac{\Lambda}{\beta I^* + \lambda} \text{ and } V^* = \frac{\Lambda r}{[kI^* + (\mu+1-k)](\beta I^* + \lambda)}.$$

Using $S^*$and V^* and the third equation of the system (3.36), we get

$$\mathrm{e}^{-\mu\tau}\left[\beta\frac{\Lambda}{\beta I^* + \lambda} + \frac{k\Lambda r}{[kI^* + (\mu+1-k)](\beta I^* + \lambda)}\right] - \alpha = 0$$

or

$$\beta\Lambda[kI^* + (\mu + 1 - k)] + \Lambda kr - \alpha\mathrm{e}^{\mu\tau}[kI^* + (\mu + 1 - k)](\beta I^* + \lambda) = 0$$

or

$$\alpha\beta k\mathrm{e}^{\mu\tau}I^{*2} + [\alpha\mathrm{e}^{\mu\tau}(\beta(\mu + 1 - k) + \lambda\mathrm{k}) - \beta\Lambda k]I^* + \lambda(\mu + 1 - k)\alpha\mathrm{e}^{\mu\tau} - \Lambda kr - \Lambda\,\beta(\mu + 1 - k) = 0.$$

Let

$$A = \alpha\beta k\mathrm{e}^{\mu\tau},\ B = \alpha e^{\mu\tau}[\lambda\mathrm{k} + \beta(\mu + 1 - k)] - \Lambda\beta k,$$

$$C = \lambda(\mu + 1 - k)\alpha\mathrm{e}^{\mu\tau} - kr\Lambda - \Lambda\beta(\mu + k - 1).$$

Then, $I^*$is the solution of

$$AI^{*^2} + BI^* + C = 0. \tag{3.40}$$

Finally, we need to show that (3. 40) has a unique positive solution. First assume that $C \geq 0$, then

$$\alpha\lambda(\mu + 1 - k)e^{\mu\tau} - kr\Lambda - \Lambda\beta(\mu + k - 1) \geq 0$$

or

$$\alpha\lambda(\mu + 1 - k)e^{\mu\tau} \geq kr\Lambda + \Lambda\beta(\mu + k - 1)$$

or

$$\alpha \geq \frac{kr\Lambda+\Lambda\beta(\mu+k-1)}{\lambda(\mu+1-k)} e^{-\mu\tau}. \tag{3.41}$$

When $C \geq 0$, the equation (3.40) has positive solution if $B < 0$. Otherwise (if $B \geq 0$) the equation (3.49) has no positive root. But when $B \leq 0$, we get

$$\alpha e^{\mu\tau}[\lambda k + \beta(\mu + 1 - k)] - \Lambda\beta k \leq 0$$

or

$$\alpha e^{\mu\tau}[\lambda k + \beta(\mu + 1 - k)] \leq k\beta\Lambda$$

or

$$\alpha \leq \frac{k\beta\Lambda e^{-\mu\tau}}{[\lambda k+\beta(\mu+1-k)]}. \tag{3.42}$$

From (3.41) and (3.42), it follows that

$$\frac{k\beta\Lambda e^{-\mu\tau}}{[\lambda k+\beta(\mu+1-k)]} \geq \alpha \geq \frac{kr\Lambda+\Lambda\beta(\mu+k-1)}{\lambda(\mu+1-k)} e^{-\mu\tau}$$

or

$$k\beta\Lambda\lambda(\mu+1-k) \geq [kr\Lambda+\Lambda\beta(\mu+k-1)][\lambda k+\beta(\mu+1-k)]$$

or

$$k\beta\Lambda\lambda(\mu+1-k) \geq k^2 r\Lambda\lambda + kr\Lambda\beta(\mu+k-1) + \Lambda\beta\lambda k(\mu+k-1) + \Lambda\beta^2(\mu+k-1)^2$$

or

$$k^2 r\Lambda\lambda + kr\Lambda\beta(\mu+k-1) + \Lambda\beta^2(\mu+k-1)^2 \leq 0.$$

Since the $\mu+k-1>0$, therefore the left side of the above inequality always positive which is a contradiction. Hence, when $C>0$ the equation (3.40) has no positive solution. Therefore C must be less than zero. Then we get

$$\alpha\lambda(\mu+1-k)e^{\mu\tau} - kr\Lambda - \Lambda\beta(\mu+k-1) < 0$$

which means that

$$\frac{\alpha\lambda(\mu+1-k)e^{\mu\tau}}{kr\Lambda+\Lambda\beta(\mu+k-1)} < 1.$$

Hence, if $\frac{\alpha\lambda(\mu+1-k)e^{\mu\tau}}{kr\Lambda+\Lambda\beta(\mu+k-1)} < 1$ is satisfied, then the system (3.26) has unique endemic equilibrium

$$E_1 = \left(\frac{\Lambda}{\beta I^*+\lambda}, \frac{\Lambda r}{[kI^*+(\mu+1-k)](\beta I^*+\lambda)}, I^*\right).$$

Here I^* is the solution of the following equation

$$AI^{*^2} + BI^* + C = 0,$$

where

$$A = \alpha k\beta e^{\mu\tau}, B = \alpha e^{\mu\tau}[k\lambda + \beta(\mu + 1 - k)] - \beta\Lambda k,$$

$$C = \lambda(\mu + 1 - k)\alpha e^{\mu\tau} - kr\Lambda - \Lambda\beta(\mu + k - 1).$$

We define the basic reproduction ratio when $I < 0$ at the disease free equilibrium. For $I < 0$, we have that

$$e^{-\mu\tau}[\beta S(t-\tau) + kV(t-\tau)]I(t-\tau) - \alpha I < 0$$

or

$$\frac{e^{-\mu\tau}\Lambda[\beta S(t-\tau)+kV(t-\tau)]}{(\gamma+\mu+d)} < 0. \qquad (3.43)$$

Substituting the disease free equilibrium into (3.43), the basic reproduction is obtained as

$$R_{0,2} = \frac{e^{-\mu\tau}\Lambda}{\alpha\lambda}\left[\beta + \frac{kr}{\mu+1-k}\right].$$

3.2.2 Global stability analysis

In this section, we study the global properties of the equilibria. We use Lyapunov function to show the global stabilities.

Theorem 3.7. The Disease free equilibrium E_0 is globally asymptotically stable if $R_{0,2} < 1$.

Proof. Consider the Lyapunov function

$$\mathcal{V} = S^0 g\left(\frac{s(t)}{S^0}\right) + V^0 g\left(\frac{V(t)}{V^0}\right) + e^{\mu\tau} I_1(t) + \int_{t-\tau}^{t} [\beta I(u)S(u) + kI(u)V(u)]du.$$

Here, $g(x) = x - 1 - \ln x$. Since $g(x)$ is positive function on $\mathbb{R}_+$. Taking the derivative of $\mathcal{V}$, we get

$$\dot{\mathcal{V}} = \left(1 - \frac{S^0}{\mathrm{S(t)}}\right)\dot{S} + \left(1 - \frac{V^0}{\mathrm{V}(t)}\right)\dot{\mathrm{V}} + e^{\mu\tau}\dot{I}(t) + \big(\mathrm{kV}(t) + \beta\mathrm{S}(t)\big)\mathrm{I}(t) - \big(\mathrm{kV}(t-\tau) + \beta\mathrm{S}(t-\tau)\big)\mathrm{I}(t-\tau)$$

$$= \left(1 - \frac{S^0}{\mathrm{S(t)}}\right)(\Lambda - (\beta\mathrm{I(t)} + \lambda)\mathrm{S(t)}) + \left(1 - \frac{V^0}{\mathrm{V}(t)}\right)(\mathrm{rS(t)} - \mathrm{kV(t)I(t)}) - (\mu + 1 - \mathrm{k})\mathrm{V(t)}) + e^{\mu\tau}(\mathrm{e}^{-\mu\tau}[\beta\mathrm{S(t-\tau)} + kV(\mathrm{t-\tau})]\mathrm{I(t-\tau)} - \alpha I(t)) + \big(\mathrm{kV}(t) + \beta\mathrm{S}(t)\big)\mathrm{I}(t) - \big(\mathrm{kV}(t-\tau) + \beta\mathrm{S}(t-\tau)\big)\mathrm{I}(t-\tau)$$

$$= \Lambda - \Lambda\frac{S^0}{\mathrm{S(t)}} - (\beta\mathrm{I(t)} + \lambda)\mathrm{S(t)} + (\beta\mathrm{I(t)} + \lambda)S^0 + \mathrm{rS(t)} - \mathrm{kV(t)I(t)} - (\mu + 1 - \mathrm{k})\mathrm{V(t)} - \mathrm{rS(t)}\frac{V^0}{\mathrm{V}(t)} + \big(\mathrm{kI(t)} + (\mu + 1 - \mathrm{k})\big)V^0 + [\beta\mathrm{S(t-\tau)} + kV(\mathrm{t-\tau})]\mathrm{I(t-\tau)} - \alpha I(t)e^{\mu\tau} + \big(\mathrm{kV}(t) + \beta\mathrm{S}(t)\big)\mathrm{I}(t) - \big(\mathrm{kV}(t-\tau) + \beta\mathrm{S}(t-\tau)\big)\mathrm{I}(t-\tau)$$

$$= \Lambda\left(1 - \frac{S^0}{\mathrm{S(t)}}\right) - \lambda\mathrm{S(t)} + (\beta\mathrm{I(t)} + \lambda)S^0 + \mathrm{rS(t)} - (\mu + 1 - \mathrm{k})\mathrm{V(t)} - \mathrm{rS(t)}\frac{V^0}{\mathrm{V}(t)} + \big(\mathrm{kI(t)} + (\mu + 1 - \mathrm{k})\big)V^0 + -\alpha I(t)e^{\mu\tau}. \qquad (3.44)$$

Since $\lambda = \mathrm{r} + \mu$ and from the disease free equilibrium point, we have

$$S_0 = \frac{\Lambda}{\lambda}$$

or

$$\Lambda = (\mathrm{r} + \mu)S_0 \tag{3.45}$$

and

$$V_0 = \frac{\mathrm{r}\Lambda}{\lambda(\mu+1-\mathrm{k})}$$

or

$$(\mu + 1 - \mathrm{k}) = \frac{\mathrm{r}\Lambda}{\lambda V_0}. \tag{3.46}$$

Replacing (3.45) in to (3.46), we get

$$(\mu + 1 - \mathrm{k}) = \frac{\mathrm{r}}{V_0}S_0. \tag{3.47}$$

Using the (3.44) and (3.45), (3.47) can be regarded as

$$\dot{\mathcal{V}} = (\mathrm{r} + \mu)S_0\left(1 - \frac{S_0}{\mathrm{S(t)}}\right) - (\mathrm{r} + \mu)\mathrm{S(t)} + \big(\beta\mathrm{I(t)} + (\mathrm{r} + \mu)\big)S_0$$
$$+ \mathrm{rS(t)} - \frac{\mathrm{r}}{V_0}S_0\mathrm{V(t)} - \mathrm{rS(t)}\frac{V^0}{\mathrm{V}(t)} + \left(\mathrm{kI(t)} + \frac{\mathrm{r}}{V_0}S_0\right)V^0 - \alpha I(t)e^{\mu\tau}$$

$$= \mu S_0\left(1 - \frac{S_0}{\mathrm{S(t)}}\right) + rS_0\left(1 - \frac{S_0}{\mathrm{S(t)}}\right) - \mathrm{rS(t)} - \mu\mathrm{S(t)} + \mathrm{r}S_0 + \mu S_0$$
$$+\beta\mathrm{I(t)}S_0 + \mathrm{rS(t)} - \frac{\mathrm{r}}{V_0}S_0\mathrm{V(t)} - \mathrm{rS(t)}\frac{V^0}{\mathrm{V}(t)} + \mathrm{kI(t)}V^0 + \frac{\mathrm{r}}{V_0}S_0V^0$$
$$-\alpha I(t)e^{\mu\tau}$$

$$= \mu S_0\left(2 - \frac{S_0}{\mathrm{S(t)}} - \frac{\mathrm{S(t)}}{S_0}\right) + rS_0\left(3 - \frac{S_0}{\mathrm{S(t)}} - \frac{\mathrm{V(t)}}{V_0} - \frac{\mathrm{S(t)}}{S_0}\frac{V^0}{\mathrm{V}(t)}\right) + I(t)(\mathrm{k}V^0$$
$$+\beta S_0 - \alpha e^{\mu\tau}). \tag{3.48}$$

Since we have that

$$2 - \frac{S_0}{\mathrm{S(t)}} - \frac{\mathrm{S(t)}}{S_0} = -\frac{\left(S_0 - \mathrm{S(t)}\right)^2}{S_0 \mathrm{S(t)}} < 0. \tag{3.49}$$

We will prove that

$$3 - \frac{S_0}{\mathrm{S(t)}} - \frac{\mathrm{V(t)}}{V_0} - \frac{\mathrm{S(t)}}{S_0}\frac{V^0}{\mathrm{V}(t)} < 0. \tag{3.50}$$

We assume $\frac{S_0}{\mathrm{S(t)}} = x$, $\frac{\mathrm{V(t)}}{V_0} = y$, then $\frac{\mathrm{S(t)}}{S_0}\frac{V^0}{\mathrm{V}(t)} = \frac{1}{x}\frac{1}{y}$, from the arithmetic and geometric meaning of x, y and $\frac{1}{x}\frac{1}{y}$, we have

$$\frac{x+y+\frac{1}{x}\frac{1}{y}}{3} > \sqrt[3]{xy\frac{1}{x}\frac{1}{y}} \Rightarrow x + y + \frac{1}{x}\frac{1}{y} > 3.$$

From that it follows (3.50).

$$3 - \frac{S_0}{\mathrm{S(t)}} - \frac{\mathrm{V(t)}}{V_0} - \frac{V^0}{\mathrm{V}(t)} < 0.$$

From the fact that (3.49) and (3.50), to satisfied $\dot{\mathcal{V}} < 0$, we need to satisfied

$$\mathrm{k}V^0 + \beta S_0 - \alpha e^{\mu\tau} < 0$$

or

$$\frac{\mathrm{k}V^0 + \beta S_0}{\alpha} e^{-\mu\tau} = R_0 < 1$$

Hence E_0 is globally asymptotically stable iff $R_0 < 1$.

Theorem 3.8. The endemic equilibrium E_1 is globaly asymptotically stable when $R_{0,2} > 1$.

Proof. The Lyapunov function is constructed as

$$\mathcal{V}(t) = S^* g\left(\frac{S(t)}{s^*}\right) + V^* g\left(\frac{V(t)}{V^*}\right) + e^{\mu\tau} I^* g\left(\frac{I(t)}{I^*}\right)$$
$$+ \int_{t-\tau}^{t} \left(\beta S^* I^* g\left(\frac{S(u)I(u)}{S^*I^*}\right) + kV^* I^* g\left(\frac{V(u)I(u)}{V^*I^*}\right)\right) du,$$

where $g(x)$ defined as

$$g(x) = x - 1 - \ln x.$$

Since, $g(x)$ is nonnegative function, $\mathcal{V}(t)$ is nonnegative, to show that disease free equilibrium point E_1 is globally asymptotically stable, we only need to show that $\dot{\mathcal{V}}$ negative definite. Actually,

$$\dot{\mathcal{V}}(t) = S^*\left(\frac{\dot{S}(t)}{S^*} - \frac{\dot{S}(t)}{S(t)}\right) + V^*\left(\frac{\dot{V}(t)}{V^*} - \frac{\dot{V}(t)}{V(t)}\right) + e^{\mu\tau} I^*\left(\frac{\dot{I}(t)}{I^*} - \frac{\dot{I}(t)}{I(t)}\right)$$
$$+\beta S^* I^*\left[\frac{S(t)I(t)}{S^*I^*} - 1 - \ln\left(\frac{S(t)I(t)}{S^*I^*}\right) - \frac{S(t-\tau)I(t-\tau)}{S^*I^*} + 1 + \ln\left(\frac{S(t-\tau)I(t-\tau)}{S^*I^*}\right)\right]$$
$$+ kV^* I^*\left[\frac{V(t)I(t)}{V^*I^*} - 1 - \ln\left(\frac{V(t)I(t)}{V^*I^*}\right) - \frac{V(t-\tau)I(t-\tau)}{V^*I^*} + 1 + \ln\left(\frac{V(t-\tau)I(t-\tau)}{V^*I^*}\right)\right]$$

$$= \left(1 - \frac{S^*}{s(t)}\right)(\Lambda - (\beta \mathrm{I(t)} + \lambda)\mathrm{S(t)}) + \left(1 - \frac{V^*}{V(t)}\right)(\mathrm{rS(t)} - \mathrm{kV(t)I(t)}$$
$$-(\mu + 1 - \mathrm{k})\mathrm{V(t)}) + e^{\mu\tau}\left(1 - \frac{I^*}{I(t)}\right)(\mathrm{e}^{-\mu\tau}[\beta \mathrm{S(t-\tau)} + kV(\mathrm{t-\tau})]\mathrm{I(t}$$
$$-\tau) - \alpha I(t)) + \beta S(t)I(t) - \beta S(t-\tau)I(t-\tau) + kV(t)I(t)$$
$$-kV(t-\tau)I(t-\tau) - \beta S^* I^*\left(\ln\left(\frac{S(t)I(t)}{S^*I^*}\right) - \ln\left(\frac{S(t-\tau)I(t-\tau)}{S^*I^*}\right)\right)$$
$$-kV^* I^*\left(\ln\left(\frac{V(t)I(t)}{V^*I^*}\right) - \ln\left(\frac{V(t-\tau)I(t-\tau)}{V^*I^*}\right)\right)$$

$$= \Lambda\left(1 - \frac{S^*}{s(t)}\right) - \beta \mathrm{I(t)S(t)} - \lambda \mathrm{S(t)} + \beta \mathrm{I(t)}S^* + \lambda S^* + \mathrm{rS(t)}\left(1 - \frac{V^*}{V(t)}\right)$$
$$-\mathrm{kV(t)I(t)} - (\mu + 1 - \mathrm{k})\mathrm{V(t)} + \mathrm{kI(t)}V^* - (\mu + 1 - \mathrm{k})V^*$$
$$+\beta \mathrm{S(t-\tau)I(t-\tau)} + kV(\mathrm{t-\tau})\mathrm{I(t-\tau)} - e^{\mu\tau}\alpha I(t) - \frac{\beta \mathrm{S(t-\tau)I(t-\tau)}}{I(t)} I^*$$
$$-\frac{\mathrm{kV(t-\tau)I(t-\tau)}}{I(t)} I^* + e^{\mu\tau}\alpha I^* + \beta S(t)I(t) + kV(t)I(t) - \beta S(t-\tau)I(t$$

$$-\tau) - kV(t-\tau)I(t-\tau) - \beta S^* I^* \ln\left(\frac{S(t)I(t)}{S(t-\tau)I(t-\tau)}\right)$$
$$-kV^* I^* \ln\left(\frac{V(t)I(t)}{V(t-\tau)I(t-\tau)}\right)$$

$$= \Lambda\left(1 - \frac{S^*}{s(t)}\right) - \lambda \mathrm{S(t)} + \lambda \mathrm{S}^*\mathrm{(t)} + rS(t) - (\mu + 1 - \mathrm{k})\mathrm{V(t)}$$
$$-\mathrm{rS(t)}\frac{V^*}{V(t)} + (\mu + 1 - \mathrm{k})V^* + (\beta S^* + \mathrm{kV}^* - \alpha e^{\mu\tau})I(t)$$
$$-I^*\left[\frac{\beta \mathrm{S(t-\tau)I(t-\tau)}}{I(t)} + \frac{\mathrm{kV(t-\tau)I(t-\tau)}}{I(t)} - \alpha e^{\mu\tau} + \beta S^* I^* \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right.$$
$$\left.+\beta S^* I^* \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]. \qquad (3.51)$$

From the second equation of (3.30) it follows

$$\mathrm{e}^{-\mu\tau}[\beta \mathrm{S}^* + \mathrm{k}V^*]\mathrm{I}^* - \alpha I^* = 0.$$

Since $I^* \neq 0$, then

$$\beta \mathrm{S}^* + \mathrm{k}V^* - \mathrm{e}^{\mu\tau}\alpha = 0 \qquad (3.52)$$

which implies that

$$\mathrm{e}^{\mu\tau}\alpha = \beta \mathrm{S}^* + \mathrm{k}V^*. \qquad (3.53)$$

From the endemic equilibrium we have $\left(\frac{\Lambda}{\beta I^* + \lambda}, \frac{\Lambda r}{[kI^* + (\mu + 1 - k)](\beta I^* + \lambda)}, I^*\right)$, and from $\lambda = \mathrm{r} + \mu$ it follows

$$S^* = \frac{\Lambda}{\beta I^* + \lambda} \Rightarrow \Lambda = S^*(\beta I^* + \lambda) \Rightarrow \Lambda = S^*(\beta I^* + \mathrm{r} + \mu) \qquad (3.54)$$

and

$$V^* = \frac{\Lambda r}{[kI^* + (\mu + 1 - k)](\beta I^* + \lambda)} \Rightarrow \mu + 1 - k = \frac{rS^*}{V^*} - kI^* \qquad (3.55)$$

According (3.54) and (3.55), formula (3.51) can be regarded as

$$\dot{\mathcal{V}}(t) = S^*(\beta I^* + \mathrm{r} + \mu)\left(1 - \frac{S^*}{s(t)}\right) + (\mathrm{r} + \mu)S^*\left(1 - \frac{S(t)}{S^*}\right) + rS(t)$$
$$-\mathrm{rS(t)}\frac{V^*}{V(t)} - (\mu + 1 - \mathrm{k})\mathrm{V(t)} + (\mu + 1 - \mathrm{k})V^* + +(\beta S^* + \mathrm{kV}^*$$
$$-\alpha e^{\mu\tau})I(t) - I^*\left[\frac{\beta\mathrm{S(t-\tau)I(t-\tau)}}{I(t)} + \frac{\mathrm{kV(t-\tau)I(t-\tau)}}{I(t)} - (\beta\mathrm{S}^* + \mathrm{k}V^*)\right.$$
$$\left.+\beta S^*I^*\ln\left(\frac{S(t)I(t)}{S(t-\tau)I(t-\tau)}\right) + \beta S^*I^*\ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]$$

$$= I^*\beta S^* - \beta S^*\frac{S^*}{s(t)}I^* + \mu S^*\left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) + \mathrm{r}S^*\left(2 - \frac{S^*}{s(t)}\right.$$
$$\left.-\frac{\mathrm{S(t)}}{S^*}\frac{V^*}{V(t)}\right) + \left(\frac{rS^*}{V^*} - kI^*\right)V^*\left(1 - \frac{\mathrm{V(t)}}{V^*}\right) - \beta I^*S^*\left[-1 + \frac{\mathrm{S(t-\tau)I(t-\tau)}}{I(t)S^*}\right.$$
$$\left.+\ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right] - kI^*V^*\left[-1 + \frac{\mathrm{V(t-\tau)I(t-\tau)}}{I(t)V^*} + \ln\left(\frac{V(t)I(t)}{V(t-\tau)I(t-\tau)}\right)\right]$$

$$= \mu S^*\left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) + \mathrm{r}S^*\left(3 - \frac{S^*}{s(t)} - \frac{\mathrm{V(t)}}{V^*} - \frac{\mathrm{S(t)}}{S^*}\frac{V^*}{V(t)}\right)$$
$$-\beta I^*S^*\left[-2 + \frac{S^*}{S(t)} + \frac{\mathrm{S(t-\tau)I(t-\tau)}}{I(t)S^*} + \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]$$
$$-kI^*V^*\left[-2 + \frac{V^*}{V(t)} + \frac{\mathrm{V(t-\tau)I(t-\tau)}}{I(t)V^*} + \ln\left(\frac{V(t)I(t)}{V(t-\tau)I(t-\tau)}\right)\right]. \qquad (3.56)$$

From, (3.20) and (3.21) it follows

$$2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*} \leq 0.$$

We will study

$$-2 + \frac{S^*}{S(t)} + \frac{\mathrm{S(t-\tau)I(t-\tau)}}{I(t)S^*} + \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right) > 0.$$

It can be written as

$$g\left(\frac{V^*}{V(t)}\right) + g\left(\frac{V(t-\tau)I(t-\tau)}{I(t)V^*}\right) = \frac{V^*}{V(t)} - 1 - \ln\frac{V^*}{V(t)} + \frac{V(t-\tau)I(t-\tau)}{I(t)V^*} - 1$$

$$-\ln\frac{V(t-\tau)I(t-\tau)}{I(t)V^*} = -2 + \frac{V^*}{V(t)} + \frac{V(t-\tau)I(t-\tau)}{I(t)V^*} + \ln\frac{V(t)}{V^*}\frac{I(t)V^*}{V(t-\tau)I(t-\tau)}$$

$$= -2 + \frac{V^*}{V(t)} + \frac{V(t-\tau)I(t-\tau)}{I(t)V^*} + \ln\frac{V(t)I(t)}{V(t-\tau)I(t-\tau)} \geq 0. \qquad (3.57)$$

-

Hence, because of the fact that (3.20) and (3.21), and (3.57) the equation (3.56) yields

$$\dot{\mathcal{V}}(t) = \mu S^*\left(2 - \frac{S^*}{s(t)} - \frac{S(t)}{S^*}\right) + \mathrm{r}S^*\left(3 - \frac{S^*}{s(t)} - \frac{\mathrm{V(t)}}{V^*} - \frac{\mathrm{S(t)}}{S^*}\frac{V^*}{V(t)}\right)$$

$$-\beta I^* S^*\left[-2 + \frac{S^*}{S(t)} + \frac{\mathrm{S(t-\tau)I(t-\tau)}}{I(t)S^*} + \ln\left(\frac{S(t)I(t)}{(t-\tau)I(t-\tau)}\right)\right]$$

$$-kI^*V^*\left[-2 + \frac{V^*}{V(t)} + \frac{\mathrm{V(t-\tau)I(t-\tau)}}{I(t)V^*} + \ln\left(\frac{V(t)I(t)}{V(t-\tau)I(t-\tau)}\right)\right] \leq 0.$$

Therefore, the endemic equilibrium E_1 is globaly asymptotically stable.

3.3 Numerical Simulations

In this section, the results of both models are discussed with numerically. The parameters of the model was evaluated by (Kaymakamzade and Hınçal, 2017) and some of the parameters are estimated. Figure 3.2 and Figure 3.3 are given for the first model which has no vaccine. Figure 3.2 shows the disease free equilibrium with the parameters $\Lambda = 200, \beta = 0.00003,\ \gamma = 0.07, \mu = 0.02,\ d = 0.2,$ and $\tau = 4$ then $R_{0,1} = 0.01909896$. Figure 3.3 shows the endemic equilibrium with the parameters $\Lambda = 200, \beta = 0.00003,$ $\gamma = 0.07, \mu = 0.02,\ d = 0.2,$ and $\tau = 4$ then the basic reproduction number is $R_{0,1} = 9.5494794$ which shows that endemic occure. In addition to these parameters it is assume that $r = 0.1$ and $k = 0.0001$ for Figure 3.4, and $r = 0.4$ and $k = 0.0001$ for Figure 3.5. which are for the second model then the basic reproduction ratios are found $R_{0,2} = 1.6435974$ and $R_{0,2} = 0.5141857$ respectively.

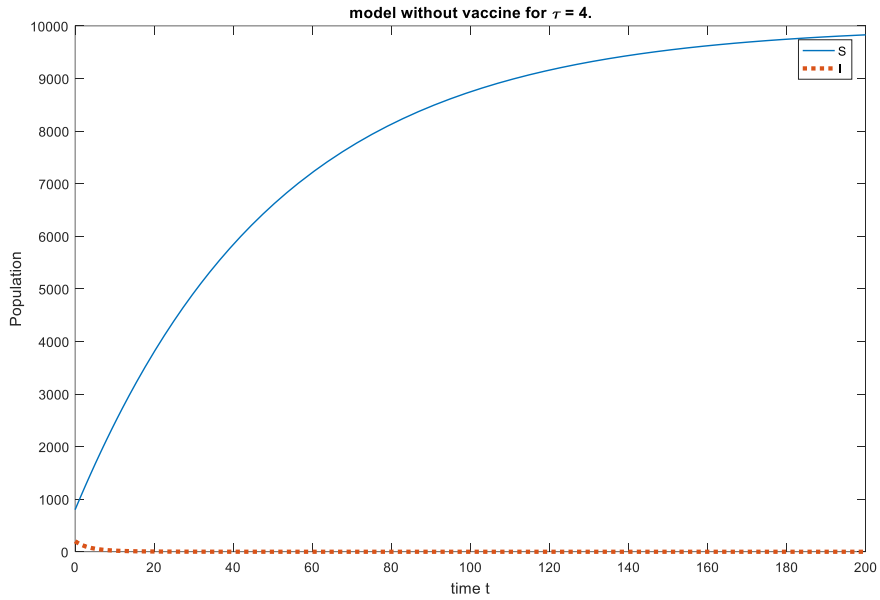

Figure 3.2: Disease free equilibrium for the model without vaccine, the parameters are, $\Lambda = 200, \beta = 0.00003, \gamma = 0.07, \mu = 0.02, d = 0.2, R_{0,1} = 0.01909896$

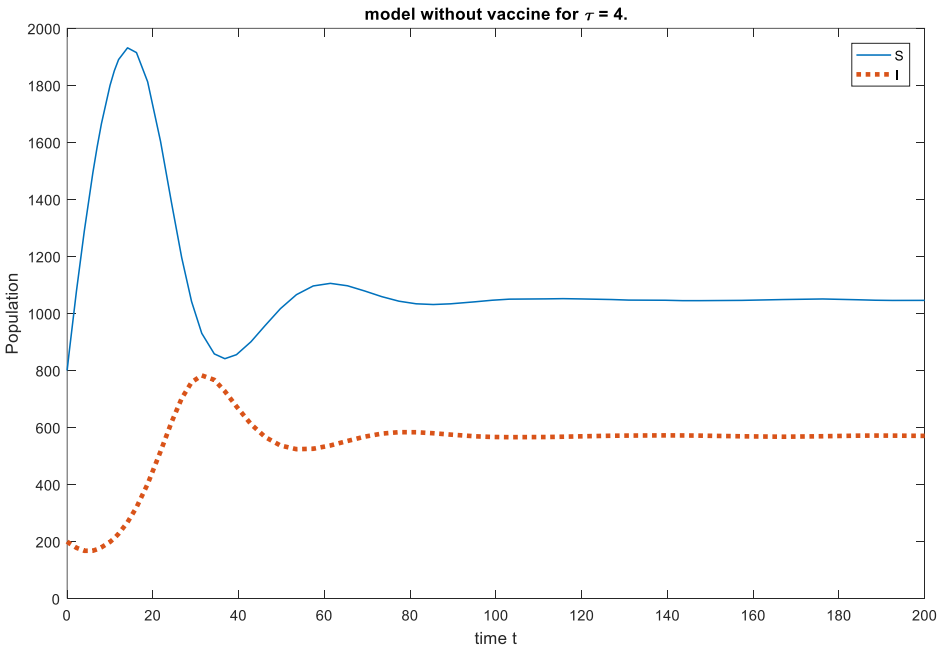

Figure 3.3: Model without vaccine, the parameters are, $\Lambda = 200, \beta = 0.0003,$ $\gamma = 0.07, \mu = 0.02, d = 0.2, R_{0,1} = 9.5494794$

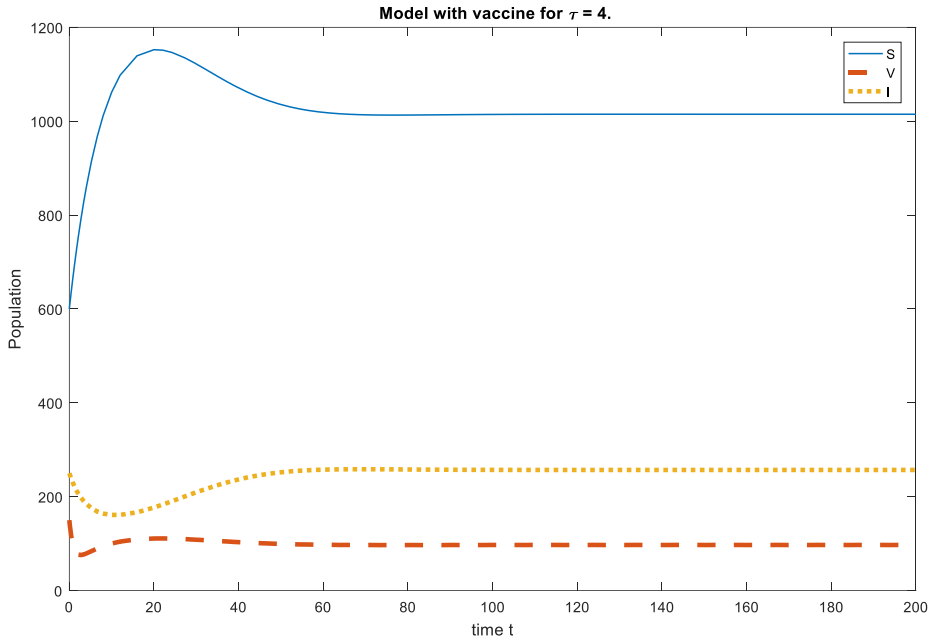

Figure 3.4: Model with vaccine, the parameters are, $\Lambda = 200, \beta = 0.0003,$ $\gamma_1 = 0.07, \mu = 0.02, d = 0.2, k = 0.0001, r = 0.1, R_{0,2} = 1.6435974.$

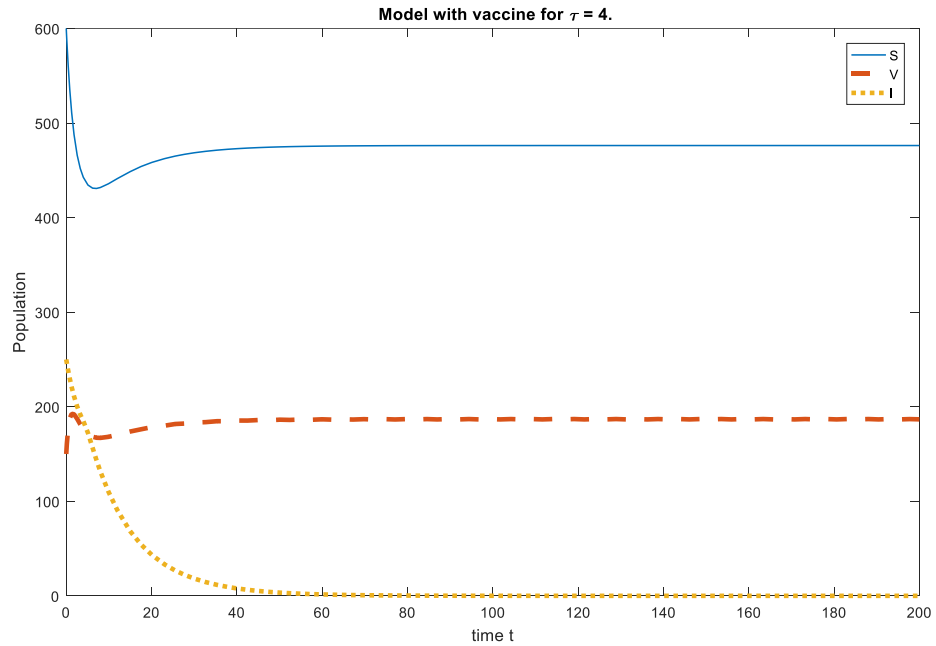

Figure 3.5: Model with vaccine, the parameters are, $\Lambda = 200, \beta = 0.0003,$ $\gamma_1 = 0.07, \mu = 0.02,\ d = 0.2, k = 0.0001, r = 0.4, R_{0,2} = 0.5141857$.

3.4 Conclusion

In this chapter, two models with and without vaccine are constucted.Two equilibria which are disease free and endemic equilibriums are found and with using Lyapunov function it is shown that the global stabilities of each equilibria for both model. For the first model it is found that disease free equilibrium E_0 is globally asymptotically stable when $R_{0,1} < 1$ and endemic equilibrium E_1 is always asymptotically stable. With using similar method it is shown that E_0 is asymptotically stable when $R_{0,2} < 1$ and E_1 is always global asymptotically stable for model 2. In last section numerical simulations are given for both models. The transmission rate taken the same for both models to see the effect of the vaccine and from the Figure 3.2 and Figure 3.4 it can be seen that when individuals take vaccine enough the infected population decrease. Therefore vaccine play an important role for control the disease.

CHAPTER 4

TWO- STRAIN EPIDEMIC MODEL WITH TWO VACCINES

In this chapter, we consider two strain influenza model with two vaccination in which strain 2 is the mutation of strain 1. A mutation is the sudden change in the genetic makeup that occurs either due to mistakes when DNA is copied or as a result of environmental factors. Here strain 2 was assumed to be as a result of changes in the proteins that made up strain 1. Proper vaccine administration is a critical component of a successful influenza control program. It is a key part of ensuring that vaccination is as safe and effective as possible. Unfortunately, it is easy to make vaccine administration error. Although some improperly administered vaccines may be valid, sometimes such errors open the possibility of patients being unprotected against the disease. In this paper we want to study the effects of administering vaccine for strain 1 (V_1) against strain 2, and administering vaccine for strain 2 (V_2) against strain 1.

This chapter is organized as follows: In Section 4.1 we formulate the two strain influenza model with vaccination compartments with respect to strain1 and strain 2. In Section 4.2, all possible equilibria, basic reproduction ratios and the global stabilities for the equilibrium points are determined. In Section 4.3, Numerical Simulations are given to support the analytic results. Finally, in Section 4.4, conclusions and discussions are given.

4.1. Structure of the Model

The population N is divided into six compartments by modifying the model of (Rahman and Zou, 2011). The compartments are S, V_1, V_2, I_1, I_2 and R, which denotes the sizes of suspectible, immunized with the vaccination for strain 1, immunized with the vaccination for strain 2, infected with strain 1, infected with strain 2 and recovered compartments respectively.

Table 4.1: Variables and Parameters

Parameter	Description
Λ	Recruitment of individulas
$\frac{1}{\mu}$	Avarage time of life expectance
r_1	Rate of vaccination with strain 1
r_2	Rate of vaccination with strain 1
k_1	Transmission coefficient of vaccinated individuals V_1 to strain 2
k_2	Transmission coefficient of vaccinated individuals V_2 to strain 1
β_1	Transmission coefficient of susceptible individuals to strain 1
β_2	Transmission coefficient of susceptible individuals to strain 2
$\frac{1}{\gamma_1}$	Average infection period for strain 1
$\frac{1}{\gamma_2}$	Average infection period for strain 2
ν_1	Infection induced death rate of strain 1
ν_2	Infection induced death rate of strain

In the model it is assumed that there is a constant recruitment into susceptible class through birth and immigration, and it is assumed that there is no double infection. The variables and parameters are positive and their meanings are given in Table 4.1, also the transfer diagram of the model is given in Figure 4.1.

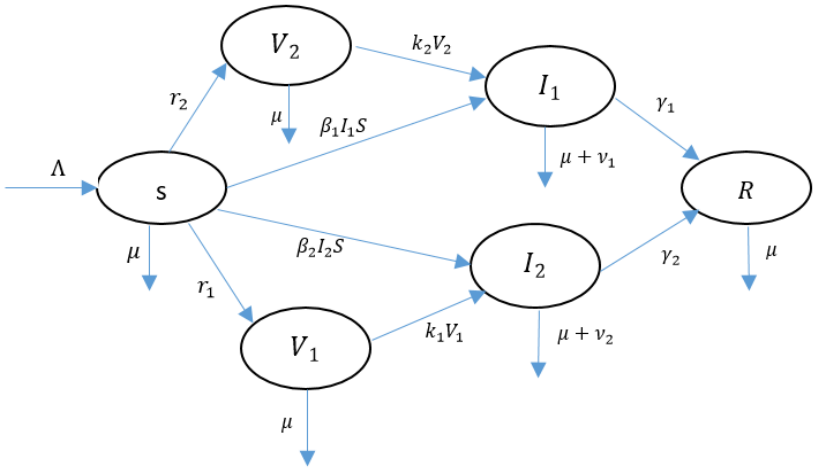

Figure 4.1: Transfer diagram of model (4.1).

With these assumptions the model is given by a system of ordinary differential equations

$$\frac{dS(t)}{dt} = \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t),$$

$$\frac{dV_1(t)}{dt} = r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t),$$

$$\frac{dV_2(t)}{dt} = r_2 S(t) - (k_2 I_1(t) + \mu)V_2(t), \qquad (4.1)$$

$$\frac{dI_1(t)}{dt} = \big(k_2 V_2(t) + \beta_1 S(t)\big)I_1(t) - \alpha_1 I_1(t),$$

$$\frac{dI_2(t)}{dt} = \big(k_1 V_1(t) + \beta_2 S(t)\big)I_2(t) - \alpha_2 I_2(t),$$

$$\frac{dR(t)}{dt} = \gamma_1 I_1(t) + \gamma_2 I_2(t) - \mu R(t),$$

where $\lambda = r_1 + r_2 + \mu$, $\alpha_1 = \mu + \nu_1 + \gamma_1$ and $\alpha_2 = \mu + \nu_2 + \gamma_2$, With the initial values $S(0) = \phi_1$, $V_1(0) = \phi_2$, $V_2(0) = \phi_3$, $I_1(0) = \phi_4$, $I_2(0) = \phi_5$ and $R(0) = \phi_6$.

Since $S(t) + V_1(t) + V_2(t) + I_1(t) + I_2(t) + R(t) = N(t)$, the system (4.1) can be rewritten as

$$\frac{dS(t)}{dt} = \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t),$$

$$\frac{dV_1(t)}{dt} = r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t),$$

$$\frac{dV_2(t)}{dt} = r_2 S(t) - (k_2 I_1(t) + \mu)V_2(t), \qquad (4.2)$$

$$\frac{dI_1(t)}{dt} = \big(k_2 V_2(t) + \beta_1 S(t)\big)I_1(t) - \alpha_1 I_1(t),$$

$$\frac{dI_2(t)}{dt} = (k_1 V_1(t) + \beta_2 S(t))I_2(t) - \alpha_2 I_2(t).$$

4.2 Disease Dynamics

Theorem 4.1. The solution $(S(t), V_1(t), V_2(t), I_1(t), I_2(t), R(t))$ of the system is nonnegative and bounded and the feasible region of the system (4.1) is

$$\Omega = \Big\{(S(t) + V_1(t) + V_2(t) + I_1(t) + I_2(t) + R(t)): S(t) > 0, V_1(t) > 0, I_1(t) > 0, I_2(t) > 0, R(t) > 0, S(t) + V_1(t) + V_2(t) + I_1(t) I_2(t) + R(t) \leq \frac{\Lambda}{\mu}\Big\}.$$

Proof. First, it is shown that the the solution of the system nonnegative, from the first equation of the system (4.1), we have

$$\frac{dS(t)}{dt} = \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t) \geq -(\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t)$$

or

$$\frac{dS(t)}{dt} + (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t) \geq 0. \tag{4.3}$$

The integrating factor $p(t)$ of the equation (4.3)

$$p(t) = e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du}.$$

Therefore, from (4.3) it follows

$$e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} \frac{dS(t)}{dt} + e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t) \geq 0$$

or

$$\frac{d}{dt}\left[e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} S(t)\right] \geq 0.$$

Taking the integral with respect to s from 0 to t, we get

$$e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} S(s)\Big|_0^t \geq 0$$

or

$$e^{\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} S(t) - S(0) \geq 0.$$

Therefore the solution of (4.3) is obtain as

$$S(t) \geq \Phi_1 e^{-\int_0^t (\beta_1 I_1(u) + \beta_2 I_2(u) + \lambda)\, du} \geq 0.$$

Form the second equation of the system, we get

$$\frac{dV_1(t)}{dt} = r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t) \geq -(k_1 I_2(t) + \mu)V_1(t)$$

or

$$\frac{dV_1(t)}{dt} + (k_1 I_2(t) + \mu)V_1(t) \geq 0 \qquad (4.4)$$

The integrating factor $p(t)$ of the equation (4.4)

$$e^{\int_0^t (k_1 I_2(u)+\mu)du}.$$

Therefore, from (4.4) it follows

$$e^{\int_0^t (k_1 I_2(u)+\mu)du}\frac{dV_1(t)}{dt} + e^{\int_0^t (k_1 I_2(u)+\mu)du}(k_1 I_2(t) + \mu)V_1(t) \geq 0$$

or

$$\frac{d}{dt}\left[e^{\int_0^t (k_1 I_2(u)+\mu)du} V_1(t)\right] \geq 0.$$

Taking the integral with respect to s from 0 to t, we get

$$e^{\int_0^t (k_1 I_2(u)+\mu)du} V_1(s)\Big|_0^t \geq 0$$

or

$$e^{\int_0^t (k_1 I_2(u)+\mu)du} V_1(t) - V_1(0) \geq 0$$

or

$$V_1(t) \geq \phi_2 e^{-\int_0^t (k_1 I_2(u)+\mu)du} \geq 0$$

with using third equation of the system (4.1), similarly with V_1 the solution of V_2 can be found as

$$V_2(t) \geq \phi_3 e^{\int_0^t (k_2 I_1(u)+\mu)du} \geq 0 .$$

The forth equation gives that

$$\frac{dI_1(t)}{dt} = (k_2 V_2(t) + \beta_1 S(t))I_1(t) - \alpha_1 I_1(t) \geq -\alpha_1 I_1(t)$$

or

$$\frac{dI_1(t)}{dt} + \alpha_1 I_1(t) \geq 0$$

then the solution is obtained as

$$I_1(t) \geq \phi_4 e^{-\alpha_1 t} \geq 0.$$

From the fifth and the last equation of the system, the solutions of I_2 and R are obtained, $I_2 \geq \phi_5 e^{-\alpha_2 t} \geq 0$ and $R \geq \phi_6 e^{-\mu t} \geq 0$ respectively. Hence, all of the solutions of the system (4.1) are positive.

Now, it is shown that the system is bounded. Since

$$N(t) = S(t) + V_1(t) + V_2(t) + I_1(t) + I_2(t) + R(t)$$

taking derivative of both sides of the system, we get

$$\dot{N}(t) = \dot{S}(t) + \dot{V}_1(t) + \dot{V}_2(t) + \dot{I}_1(t) + \dot{I}_2(t) + \dot{R}(t).$$

It follows that

$$N\dot{(t)} = \Lambda - \mu\big(\mathrm{S}(t) + V_1(t) + V_2(t) + I_1(t) + I_2(t) + R(t)\big)$$
$$-\nu_1 I_1(t) - \nu_2 I_2(t)$$

or

$$\dot{N}(t) = \Lambda - \mu\mathrm{N}(t) - \nu_1 I_1(t) - \nu_2 I_2(t).$$

Since $I_1(t) \geq 0$ and $I_2(t) \geq 0$, then

$$\dot{N}(t) \leq \Lambda - \mu\mathrm{N}(t). \qquad (4.5)$$

Since $0 \leq \dot{N}(t)$, we have

$$0 \leq \Lambda - \mu\mathrm{N}(t)$$

or

$$\mathrm{N}(t) \leq \frac{\Lambda}{\mu}.$$

Hence, for sufficient large t, the feasible region is obtain as

$$\Omega = S\left\{(t), V_1(t), V_2(t), I_1(t), I_2(t), R(t) \in C_+^5 : N = S(t) + V_1(t)\right.$$
$$\left. + V_2(t) + I_1(t) + I_2(t) + R(t) \leq \frac{\Lambda}{\mu}\right\}.$$

Theorem 4.2. There exists a unique solution of system (4.2).

Proof. System (4.2) can be written as

$$f(\varphi(t)) = \begin{pmatrix} f_1(\varphi(t)) \\ f_2(\varphi(t)) \\ f_3(\varphi(t)) \\ f_4(\varphi(t)) \\ f_5(\varphi(t)) \end{pmatrix}, \ \varphi(t) = \begin{pmatrix} \varphi_1(t) \\ \varphi_2(t) \\ \varphi_3(t) \\ \varphi_4(t) \\ \varphi_5(t) \end{pmatrix},$$

where

$$f_1\big(\varphi(t)\big) = \Lambda - (\beta_1\varphi_4(t) + \beta_2\varphi_5(t) + \lambda)\varphi_1, f_2\varphi(t) = r_1\varphi_1(t)$$
$$-(k_1\varphi_5(t) + \mu)\varphi_2(t), f_3\varphi(t) = r_2\varphi_1(t) - (k_2I_1(t)$$
$$+\mu)\varphi_3(t), f_4\big(\varphi(t)\big) = \big(k_2\varphi_3(t) + \beta_1\varphi_1(t)\big)\varphi_4(t)$$
$$-\alpha_1\varphi_4(t), f_5(\varphi(t)) = (k_1\varphi_2(t) + \beta_2\varphi_1(t))\varphi_5(t) - \alpha_2\varphi_5(t)$$

are continuous. In order to say the system (4.2) has a unique solution it is sufficient to show that the Lipschitz condition for $f(\varphi(t))$ with respect to $\varphi(t)$ holds.

For $\varphi(t) = (\varphi_1(t), \varphi_2(t), \varphi_3(t), \varphi_4(t), \varphi_5(t))$ and $\psi(t) = (\psi_1(t), \psi_2(t), \psi_3(t), \psi_4(t), \psi_5(t))$, and assuming that

$$|\psi - \varphi| = \sum_{i=1}^{5} |\psi_i - \varphi_i|. \qquad (4.6)$$

Then

$$\|\mathrm{f}_1(\varphi(t)) - \mathrm{f}_1(\psi(t))\| = |\Lambda - (\beta_1\varphi_4(t) + \beta_2\varphi_5(t) + \lambda)\varphi_1(t)$$
$$-(\Lambda - (\beta_1\psi_4(t) + \beta_2\psi_5(t) + \lambda)\psi_1(t))|$$

$$\leq \beta_1|\psi_4(t)\psi_1(t) - \varphi_4(t)\varphi_1(t)| + \beta_2|\psi_5(t)\psi_1(t) - \varphi_5(t)\varphi_1(t)|$$
$$+\lambda|\psi_1(t) - \varphi_1(t)|$$

$$= \beta_1|\psi_4(t)\psi_1(t) - \psi_1(t)\varphi_4(t) + \psi_1(t)\varphi_4(t) - \varphi_4(t)\varphi_1(t)|$$
$$+\beta_2|\psi_5(t)\psi_1(t) - \psi_1(t)\varphi_5(t) + \psi_1(t)\varphi_5(t) - \varphi_5(t)\varphi_1(t)|$$
$$+\lambda|\psi_1(t) - \varphi_1(t)|$$

$$\leq \beta_1|\psi_1(t)||\psi_4(t) - \varphi_4(t)| + \beta_1|\varphi_4(t)||\psi_1(t) - \varphi_1(t)|$$
$$+\beta_2|\psi_1(t)||\psi_5(t) - \varphi_5(t)| \quad +\beta_2|\varphi_5(t)||\psi_1(t) - \varphi_1(t)|$$
$$+\lambda|\psi_1(t) - \varphi_1(t)|$$

$$= (\beta_1|\psi_4(t)| + \beta_2|\varphi_5(t)| + \lambda)|\psi_1(t) - \varphi_1(t)| + \beta_1|\psi_1(t)||\psi_4(t)$$
$$-\varphi_4(t)| + \beta_2|\psi_1(t)||\emptyset_5(t) - \varphi_5(t)| \leq K_1|\psi(t) - \varphi(t)|, \qquad (4.7)$$

where

$K_1 = \max\{\beta_1|\psi_4(t)| + \beta_2|\varphi_5(t)| + \lambda, \beta_1|\psi_1(t)|, \beta_2|\psi_1(t)|\}.$

From the invariant set , $\varphi_1(t) \leq \frac{\Lambda}{\mu}$, $\varphi_4(t) \leq \frac{\Lambda}{\mu}$ and $\varphi_5(t) \leq \frac{\Lambda}{\mu}$, it follows

$K_1 = (\beta_1 + \beta_2)\frac{\Lambda}{\mu} + \lambda.$

Furthermore, one can derive that

$$\|f_2(\varphi(t)) - f_2(\psi(t))\| = |r_1\varphi_1(t) - (k_1\varphi_5(t) + \mu)\varphi_2(t)$$
$$-(r_1\psi_1(t) - (k_1\psi_5(t) + \mu)\psi_2(t))|$$

$$\leq r_1|\varphi_1(t) - \psi_1(t)| + \mu|\psi_2(t) - \varphi_2(t)| + k_1|\psi_5(t)\psi_2(t)$$
$$-\varphi_5(t)\varphi_2(t)|$$
$$\leq r_1|\varphi_1(t) - \psi_1(t)| + \mu|\psi_2(t) - \varphi_2(t)| + k_1|\psi_5(t)||\psi_2(t)$$
$$-\varphi_2(t)| + k_1|\varphi_2(t)||\psi_5(t) - \varphi_5(t)|$$
$$= r_1|\varphi_1(t) - \psi_1(t)| + (\mu + k_1|\psi_5(t)|)|\psi_2(t) - \varphi_2(t)|$$
$$+k_1|\varphi_2(t)||\psi_5(t) - \varphi_5(t)| \leq K_2|\psi(t) - \varphi(t)|, \qquad (4.8)$$

where

$$K_2 = \max\{r_1, (\mu + k_1|\psi_5(t)|), k_1|\varphi_2(t)|\}.$$

From the invariant set , $\varphi_1(t) \leq \frac{\Lambda}{\mu}$, $\varphi_2(t) \leq \frac{\Lambda}{\mu}$ and $\varphi_5(t) \leq \frac{\Lambda}{\mu}$, it follows

$$K_2 = \mu + k_1 \frac{\Lambda}{\mu}.$$

For the fourth equation of the system (4.2), we have

$$\begin{aligned}
&\|f_3(\varphi(t)) - f_3(\psi(t))\| = |r_2\varphi_1(t) - (k_2\varphi_4(t) + \mu)\varphi_3(t) \\
&-(r_2\psi_1(t) - (k_2\psi_4(t) + \mu)\psi_3(t))| \\
&\leq r_2|\varphi_1(t) - \psi_1(t)| + \mu|\psi_3(t) - \varphi_3(t)| + k_2|\psi_5(t)\psi_3(t) \\
&-\varphi_4(t)\varphi_3(t)| \\
&\leq r_2|\varphi_1(t) - \psi_1(t)| + \mu|\psi_3(t) - \varphi_3(t)| + k_2|\psi_4(t)||\psi_3(t) \\
&-\varphi_3(t)| + k_2|\varphi_3(t)||\psi_4(t) - \varphi_4(t)| \\
&= r_2|\varphi_1(t) - \psi_1(t)| + (\mu + k_2|\psi_4(t)|)|\psi_3(t) - \varphi_3(t)| \\
&+k_2|\varphi_3(t)||\psi_4(t) - \varphi_4(t)| \leq K_3|\psi(t) - \varphi(t)|, \qquad (4.9)
\end{aligned}$$

where,

$$K_3 = \max\{r_2, (\mu + k_2|\psi_4(t)|), k_2|\varphi_3(t)|\}.$$

From the invariant set , $\varphi_1(t) \leq \frac{\Lambda}{\mu}$, $\varphi_3(t) \leq \frac{\Lambda}{\mu}$ and $\varphi_4(t) \leq \frac{\Lambda}{\mu}$, it follows

$$K_3 = \mu + k_2 \frac{\Lambda}{\mu}.$$

The forth equation gives that

$$\|f_4(\varphi(t)) - f_4(\psi(t))\| = \left|\left(k_2\varphi_3(t) + \beta_1\varphi_1(t)\right)\varphi_4(t) - \alpha_1\varphi_4(t)\right.$$
$$\left.-\left((k_2\psi_3(t) + \beta_1\psi_1(t))\psi_4(t) - \alpha_1\psi_4(t)\right)\right|$$

$$\leq \alpha_1|\psi_4(t) - \varphi_4(t)| + \beta_1|\varphi_1(t)\varphi_4(t) - \psi_1(t)\psi_4(t)|$$
$$+k_2|\varphi_3(t)\varphi_4(t) - \psi_3(t)\psi_4(t)|$$

$$\leq \alpha_1|\psi_4(t) - \varphi_4(t)| + \beta_1|\varphi_1(t)||\varphi_4(t) - \psi_4(t)| + \beta_1|\psi_4(t)||\varphi_1(t)$$
$$-\psi_1(t)| + k_2|\varphi_3(t)||\varphi_4(t) - \psi_4(t)| + k_2|\psi_4(t)||\varphi_3(t) - \psi_3(t)|$$
$$= \beta_1|\psi_4(t)||\varphi_1(t) - \psi_1(t)| + k_2|\psi_4(t)||\varphi_3(t) - \psi_3(t)|$$
$$+(\alpha_1 + \beta_1|\varphi_1(t)| + k_2|\varphi_3(t)|)|\varphi_4(t) - \psi_4(t)| \leq K_4|\psi(t) - \varphi(t)|, \quad (4.10)$$

where

$$K_4 = \max\{\beta_1|\psi_4(t)|, k_2|\psi_4(t)|, \alpha_1 + \beta_1|\varphi_1(t)| + k_2|\varphi_3(t)|\}.$$

Therefore

$$K_4 = \alpha_1 + (\beta_1 + k_2)\frac{\Lambda}{\mu}.$$

Finally,

$$\|f_5(\varphi(t)) - f_5(\psi(t))\| = \left|\left(k_1\varphi_2(t) + \beta_2\varphi_1(t)\right)\varphi_5(t) - \alpha_2\varphi_5(t)\right.$$
$$\left.-\left((k_1\psi_2(t) + \beta_2\psi_1(t))\psi_5(t) - \alpha_2\psi_5(t)\right)\right|$$

$$\leq \alpha_2|\psi_5(t) - \varphi_5(t)| + \beta_2|\varphi_1(t)\varphi_5(t) - \psi_1(t)\psi_5(t)|$$
$$+k_2\left|\varphi_2(t)\varphi_5(t) - \psi_{2(t)}\psi_5(t)\right|$$

$$\leq \alpha_2|\psi_5(t) - \varphi_5(t)| + \beta_2|\varphi_1(t)||\varphi_5(t) - \psi_5(t)| + \beta_2|\psi_5(t)||\varphi_1(t) - \psi_1(t)| + k_1|\varphi_2(t)||\varphi_5(t) - \psi_5(t)| + k_1|\psi_5(t)||\varphi_2(t) - \psi_2(t)|$$

$$= \beta_2|\psi_5(t)||\varphi_1(t) - \psi_1(t)| + k_1|\psi_5(t)||\varphi_2(t) - \psi_2(t)| + (\alpha_2 + \beta_2|\varphi_1(t)| + k_1|\varphi_2(t)|)|\varphi_5(t) - \psi_5(t)| \leq K_5|\psi(t) - \varphi(t)|, \tag{4.11}$$

where

$$K_5 = \max\{\beta_2|\psi_5(t)|, k_1|\psi_5(t)|, \alpha_2 + \beta_2|\varphi_1(t)| + k_1|\varphi_2(t)|\}.$$

From the invariant set, it follows that

$$K_5 = \alpha_2 + (\beta_2 + k_1)\frac{\Lambda}{\mu}.$$

Applying (4.7), (4.8), (4.9), (4.10) and (4.11), we get

$$\|f(\varphi(t)) - f(\psi(t))\| = \|f_1(\varphi(t)) - f_1(\psi(t))\| + \|f_2(\varphi(t)) - f_2(\psi(t))\| + \|f_3(\varphi(t)) - f_3(\psi(t))\| + \|f_4(\varphi(t)) - f_4(\psi(t))\| + \|f_5(\varphi(t)) - f_5(\psi(t))\| \leq (K_1 + K_2 + K_3 + K_4 + K_5)\,|\psi(t) - \varphi(t)|,$$

where

$$K_1 + K_2 + K_3 + K_4 + K_5 = (2\beta_1 + 2\beta_2 + 2k_1 + 2k_2)\frac{\Lambda}{\mu} + \lambda + 2\mu + \alpha_1 + \alpha_2.$$

Hence the system (4.2) has a unique solution.

4.3 Equilibrium and Stability Analysis

4.3.1 Equilibria of the system

Theorem 4.3.

1. System (4.2) has a disease free equilibrium $E_0 = \left(\frac{\Lambda}{\lambda}, \frac{r_1\Lambda}{\lambda\mu}, \frac{r_2\Lambda}{\lambda\mu}, 0,0\right)$.

2. When $\left(\frac{k_2 r_2}{\alpha_1\mu} + \frac{\beta_1}{\alpha_1}\right)\frac{\Lambda}{\lambda} \geq 1$ then the system (4.2) has the single strain (strain 1) infectious equilibrium $E_1 = (\bar{S}, \bar{V}_1, \bar{V}_2, \bar{I}_1, 0)$, where

$$\bar{S} = \frac{\Lambda}{\beta_1 I_1^1 + \lambda}, \bar{V}_1 = \frac{r_1\Lambda}{\mu(\beta_1 I_1 + \lambda)}, \bar{V}_2 = \frac{r_2\Lambda}{(\beta_1 I_1 + \lambda)(\mu + k_2 I_1)}, \bar{I}_1 = 0.$$

3. When, $\left(\frac{k_1 r_1}{\alpha_2\mu} + \frac{\beta_2}{\alpha_2}\right)\frac{\Lambda}{\lambda} \geq 1$, the system (4.2) has the single strain (strain 2) infectious equilibrium $E_2 = \left(\hat{S}, \hat{V}_1, \hat{V}_2, 0, \hat{I}_2\right)$, where

$$\hat{S} = \frac{\Lambda}{\beta_2 I_2 + \lambda}, \hat{V}_1 = \frac{r_1\Lambda}{(\beta_2 I_2 + \lambda)(\mu + k_1 I_2)}, \hat{V}_2 = \frac{r_2\Lambda}{\mu(\beta_2 I_2 + \lambda)}, \hat{I}_1 = 0.$$

4. System (4.2) has no double strain infection equilibrium.

Proof. Setting the each equation in (4.2) equal to zero, we get

$$\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S = 0,$$

$$r_1 S - (k_1 I_2 + \mu)V_1 = 0,$$

$$r_2 S - (k_2 I_1 + \mu)V_2 = 0, \qquad (4.12)$$

$$(k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1 = 0,$$

$$(k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2 = 0.$$

1. Since, $I_1 = 0$ and $I_2 = 0$, then we obtain

$$\Lambda - \lambda S = 0\ ,$$

$$r_1 S - \mu V_1 = 0, \qquad (4.13)$$

$$r_2 S - \mu V_2 = 0.$$

From the first equation of the system (4.13), it follows that

$$S = \frac{\lambda}{\Lambda}.$$

Using the value of S and second equation of system (4.13), then V_1 is obtained that

$$V_1 = \frac{r_1}{\mu}\frac{\lambda}{\Lambda}.$$

Finally, using the value of S and the third equation of the sysem (4.13), it is given that

$$V_2 = \frac{r_2}{\mu}\frac{\lambda}{\Lambda}.$$

Therefore, the disease free equilibrium is

$$E_0 = \left(\frac{\lambda}{\Lambda}, \frac{r_1}{\mu}\frac{\lambda}{\Lambda}, \frac{r_2}{\mu}\frac{\lambda}{\Lambda}, 0,0\right).$$

Since all the coordinates of E_0 are positive, then it is biologically meaningful.

2. For the Strain 2 disease free equilibrium (strain 1 infection equilibrium) E_1, $\bar{I}_2 = 0$ and $\bar{I}_1 \neq 0$. Then with using the system (4.9) we have

$$\Lambda - (\beta_1 I_1 + \lambda)S = 0,$$

$$r_1 S - \mu V_1 = 0,$$

$$r_2 S - (k_2 I_1 + \mu) V_2 = 0, \tag{4.14}$$

$$(k_2 V_2 + \beta_1 S) - \alpha_1 = 0.$$

The first three equations of system (4.14), gives that

$S = \frac{\Lambda}{\beta_1 I_1 + \lambda}$, $V_1 = \frac{r_1 S}{\mu}$, and $V_2 = \frac{r_2 S}{k_2 I_1 + \mu}$

or

$S = \frac{\Lambda}{\beta_1 I_1 + \lambda}$, $V_1 = \frac{r_1}{\mu} \frac{\Lambda}{\beta_1 I_1 + \lambda}$, $V_2 = \frac{r_2}{k_2 I_1 + \mu} \frac{\Lambda}{\beta_1 I_1 + \lambda}$.

Putting S, and V_2 in the fourth equation of the system (4.14), we get

$$\left(k_2 \frac{r_2}{k_2 I_1 + \mu} \frac{\Lambda}{\beta_1 I_1 + \lambda} + \beta_1 \frac{\Lambda}{\beta_1 I_1 + \lambda}\right) - \alpha_1 = 0$$

or

$$\Lambda k_2 r_2 + \Lambda \beta_1 (k_2 I_1 + \mu) - \alpha_1 (k_2 I_1 + \mu)(\beta_1 I_1 + \lambda) = 0$$

or

$$(\alpha_1 \beta_1 k_2) I_1^2 + (\alpha_1 k_2 \lambda + \alpha_1 \beta_1 \mu - \Lambda \beta_1 k_2) I_1 + (\alpha_1 \lambda \mu - \Lambda k_2 r_2 - \Lambda \beta_1 \mu) = 0. \tag{4.15}$$

Choosing, $A = \alpha_1 \beta_1 k_2$,$B = \alpha_1 k_2 \lambda + \alpha_1 \beta_1 \mu - \Lambda \beta_1 k_2$, and $C = \alpha_1 \lambda \mu - \Lambda k_2 r_2 - \Lambda \beta_1 \mu$. System (4.12) can be written as

$$A I_1^2 + B I_1 + C = 0. \tag{4.16}$$

Since $\bar{S}, \bar{V}_1$ and $\bar{V}_2$ are all positive, in order to check the biologically meaningfulness of E_1 we need to show that the equation (4.16) has only one positive root. To prove it, first we assume that, $C \geq 0$ (in this case $B < 0$) then

$$\alpha_1 \lambda \mu - k_2 r_2 \Lambda - \beta_1 \Lambda \mu \geq 0$$

or

$$\alpha_1 (r_1 + r_2 + \mu)\mu \geq k_2 r_2 \Lambda + \beta_1 \Lambda \mu$$

or

$$\alpha_1 \geq \frac{k_2 r_2 \Lambda + \beta_1 \Lambda \mu}{(r_1 + r_2 + \mu)\mu}. \qquad (4.17)$$

When C $\geq$ 0, B must be less than zero otherwise (if B $\geq$ 0) equation (4.16) has no positive root. However, when B $\leq$ 0, we have

$$\alpha_1 \beta_1 \mu - k_2 \beta_1 \Lambda + \alpha_1 \lambda k_2 \leq 0$$

or

$$\alpha_1 (\beta_1 \mu + \lambda k_2) \leq k_2 \beta_1 \Lambda$$

or

$$\frac{1}{\alpha_1} \geq \frac{\beta_1 \mu + (r_1 + r_2 + \mu) k_2}{k_2 \beta_1 \Lambda}$$

$$\alpha_1 \leq \frac{k_2 \beta_1 \Lambda}{\beta_1 \mu + (r_1 + r_2 + \mu) k_2}. \qquad (4.18)$$

From (4.14) and (4.15), we get,

$$\frac{k_2 r_2 \Lambda + \beta_1 \Lambda \mu}{(r_1 + r_2 + \mu)\mu} \leq \alpha_1 \leq \frac{k_2 \beta_1 \Lambda}{\beta_1 \mu + (r_1 + r_2 + \mu) k_2}$$

or

$$\frac{k_2 r_2 \Lambda + \beta_1 \Lambda \mu}{(r_1 + r_2 + \mu)\mu} \frac{\beta_1 \mu + (r_1 + r_2 + \mu) k_2}{k_2 \beta_1 \Lambda} \leq 1 \qquad (4.19)$$

or

$$\Lambda \beta_1 k_2 r_2 \mu + \beta_1^2 \Lambda \mu^2 + k_2^2 r_2 \Lambda (r_1 + r_2 + \mu) + \Lambda \beta_1 k_2 \mu (r_1 + r_2 + \mu)$$

$$\leq \Lambda \beta_1 k_2 \mu (r_1 + r_2 + \mu)$$

or

$$(k_2 r_2 \Lambda + \beta_1 \mu \Lambda) \beta_1 \mu + (r_1 + r_2 + \mu) k_2^2 r_2 \Lambda \leq 0. \qquad (4.20)$$

It is a contradiction, since all coefficients in equation (4.20) are positive. Hence when $C \geq 0$, B must be greater than zero, it means there is no positive solution of equation (4.13) and so E_1 is meaningless when $C \geq 0$.

It can be seen that, when $C < 0$ we have

$$\alpha_1 \lambda \mu - k_2 r_2 \Lambda - \beta_1 \Lambda \mu < 0$$

so

$$\left(\frac{k_2 r_2}{\alpha_1 \mu} + \frac{\beta_1}{\alpha_1}\right) \frac{\Lambda}{\lambda} \geq 1.$$

Therefore, the equation has a unique positive solution $\bar{I}_1$ when $C < 0$. Hence E_1 is biologically meaningfull iff

$$\left(\frac{k_2 r_2}{\alpha_1 \mu} + \frac{\beta_1}{\alpha_1}\right) \frac{\Lambda}{\lambda} \geq 1.$$

3. For the Strain 1 disease free equilibrium (strain 2 infection equilibrium) E_2, $\hat{I}_1 = 0$ and $\hat{I}_2 \neq 0$. Again using the system (4.11) we have

$$\Lambda - (\beta_2 I_2 + \lambda)S = 0,$$

$$r_1 S - (k_1 I_2 + \mu)V_1 = 0,$$

$$r_2 S - \mu V_2 = 0, \qquad (4.21)$$

$$(k_1 V_1 + \beta_2 S) - \alpha_2 = 0.$$

From the first three equations of system (4.21), we obtained that

$$S = \frac{\Lambda}{\beta_2 I_2 + \lambda}, V_1 = \frac{r_1 S}{k_1 I_2 + \mu}, V_2 = \frac{r_2 S}{\mu},$$

then

$$S = \frac{\Lambda}{\beta_1 I_1 + \lambda}, V_1 = \frac{r_1}{k_1 I_2 + \mu}\frac{\Lambda}{\beta_2 I_2 + \lambda}, V_2 = \frac{r_2}{\mu}\frac{\Lambda}{\beta_2 I_2 + \lambda}.$$

Putting S, and V_1 in the fourth equation of the system (4.21), we get

$$\left(k_1 \frac{r_1}{k_1 I_2 + \mu}\frac{\Lambda}{\beta_2 I_2 + \lambda} + \beta_2 \frac{\Lambda}{\beta_1 I_1 + \lambda}\right) - \alpha_1 = 0$$

or

$$\Lambda k_1 r_1 + \Lambda\beta_2(k_1 I_2 + \mu) - \alpha_2(k_1 I_2 + \mu)(\beta_2 I_2 + \lambda) = 0$$

or

$$(\alpha_2\beta_2 k_1)I_2^2 + (\alpha_2 k_1\lambda + \alpha_2\beta_2\mu - \Lambda\beta_2 k_1)I_2 + (\alpha_2\lambda\mu - \Lambda k_1 r_1 - \Lambda\beta_2\mu) = 0. \qquad (4.22)$$

Let, $A = \alpha_2\beta_2 k_1$, $B = \alpha_2 k_1\lambda + \alpha_2\beta_2\mu - \Lambda\beta_2 k_1$, and $C = \alpha_2\lambda\mu - \Lambda k_1 r_1 - \Lambda\beta_2\mu$, then the system (4.19) can be written as

$$AI_2^2 + BI_2 + C = 0. \qquad (4.23)$$

Since $\hat{S}, \hat{V}_1$ and $\hat{V}_2$ are all positive, in order to check the biologically meaningfulness of E_2 we need to show that the equation (4.23) has only one positive root. As in the previous case $E_2$is biologically meaningfull, when

$$\left(\frac{k_1 r_1}{\alpha_2 \mu} + \frac{\beta_2}{\alpha_2}\right)\frac{\Lambda}{\lambda} \geq 1.$$

4. From the first three equations of the system (4.11) it can be obtained that

$$S^* = \frac{\Lambda}{\beta_1 I_1 + \beta_2 I_2 + \lambda}, V_1^* = \frac{r_1 \Lambda}{(\beta_1 I_1 + \beta_2 I_2 + \lambda)(\mu + k_1 I_2)}, V_2^* = \frac{r_2 \Lambda}{(\beta_1 I_1 + \beta_2 I_2 + \lambda)(\mu + k_2 I_1)}.$$

Replacing them into the last two equation of the system (4.11), it will be obtained the following system

$$a_1 I_1^2 + b_1 I_1 I_2 + c_1 I_1 + d_1 I_2 + e_1 = 0,$$
$$a_2 I_2^2 + b_2 I_1 I_2 + c_2 I_1 + d_2 I_2 + e_2 = 0$$

where,

$$a_1 = -\alpha_1\beta_1 k_2,\ b_1 = -\alpha_1\beta_2 k_2,\ c_1 = \beta_1\Lambda k_2 - \alpha_1\lambda k_2 - \alpha_1\beta_1\mu,$$
$$d_1 = -\alpha_1\beta_2\mu,\ e_1 = k_2 r_2\Lambda + \beta_1\Lambda\mu - \alpha_1\lambda\mu,\ a_2 = -\alpha_2\beta_1 k_1,$$
$$b_2 = -\alpha_2\beta_1 k_1,\ c_2 = -\alpha_2\beta_1\mu,\ d_2 = \beta_2\Lambda k_1 - \alpha_2\lambda k_1 - \alpha_2\beta_2\mu,$$
$$e_2 = k_1 r_1\Lambda + \beta_2\Lambda\mu - \alpha_2\lambda\mu.$$

Therefore analytically there is no co-existence of the disease.

4.3.2 Basic Reproduction Number

Basic reproduction ratio (R_0) is the number of secondary infections caused by one infectious individual in a whole susceptible population. To find the basic reproduction ratio we use the next genaration matrix method whics is given in the Chapter 2.

$$\mathcal{F} = \begin{bmatrix} (k_2 V_2 + \beta_1 S) I_1 \\ (k_1 V_1 + \beta_2 S) I_2 \end{bmatrix}, \text{ and } \mathcal{V} = \begin{bmatrix} \alpha_1 I_1 \\ \alpha_2 I_2 \end{bmatrix}$$

taking the partial derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the equilibrium point, follows that

$$F(E_0) = \begin{bmatrix} \beta_1 S^0 + k_2 {V_2}^0 & 0 \\ 0 & \beta_2 S^0 + k_1 {V_1}^0 \end{bmatrix}, V(E_0) = \begin{bmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{bmatrix}$$

matrix F is nonnegative and is responsible for new infections, while V is invertible and is reffered to as the transmission matrix for the model (4.2). It follows that the inverse matrix of V is

$$V^{-1}(E_0) = \begin{bmatrix} \frac{1}{\alpha_1} & 0 \\ 0 & \frac{1}{\alpha_2} \end{bmatrix},$$

then the multiplication of F and V^{-1} is

$$FV^{-1} = \begin{bmatrix} \frac{\beta_1 S^0 + k_2 {V_2}^0}{\alpha_1} & 0 \\ 0 & \frac{\beta_2 S^0 + k_1 {V_1}^0}{\alpha_2} \end{bmatrix}.$$

The Jacobian matrix of FV^{-1} is obtained as

$$\begin{bmatrix} \frac{\beta_1 S^0 + k_2 {V_2}^0}{\alpha_1} - \lambda & 0 \\ 0 & \frac{\beta_2 S^0 + k_1 {V_1}^0}{\alpha_2} - \lambda \end{bmatrix} = 0$$

it follows that

$$\lambda^2 - \left(\frac{\beta_1 S^0 + k_2 {V_2}^0}{\alpha_1} + \frac{\beta_2 S^0 + k_1 {V_1}^0}{\alpha_2}\right)\lambda + \frac{\beta_1 S^0 + k_2 {V_2}^0}{\alpha_1}\frac{\beta_2 S^0 + k_1 {V_1}^0}{\alpha_2} = 0$$

$$\lambda_1 = \frac{\beta_1 S^0 + k_2 {V_2}^0}{\alpha_1}, \lambda_1 = \frac{\beta_2 S^0 + k_1 {V_1}^0}{\alpha_2}$$

Since the dominant eigenvalue is the basic reproduction ratio, therefore the basic reprodiction ratio is

$$R_0 = max\{R_1, R_2\},$$

where

$$R_1 = \frac{\beta_1}{\alpha_1}\frac{\Lambda}{\lambda} + \frac{k_2}{\alpha_1}\frac{r_2}{\mu}\frac{\Lambda}{\lambda},\ R_2 = \frac{\beta_2}{\alpha_2}\frac{\Lambda}{\lambda} + \frac{k_1}{\alpha_2}\frac{r_1}{\mu}\frac{\Lambda}{\lambda}.$$

4.3.3 Global stability of equilibria

In this section, the global properties of the equilibria are studied. Lyapunov function is used to show the global stabilities.

Theorem 4.3. The DFE E_0 is globally asymptotically stable if $R_0 < 1$.

Proof. Consider the Lyapunov function

$$V(S, V_1, V_2, I_1, I_2) = g\left(\frac{S}{S^0}\right) + g\left(\frac{V_1}{{V_1}^0}\right) + g\left(\frac{V_2}{{V_2}^0}\right) + I_1 + I_2, \qquad (4.24)$$

where $g(x) = x - 1 - ln\, x$, which is positive function in $\mathbb{R}_+$. And since $I_1 > 0$ and $I_2 > 0$, therefore $V > 0$ and

$$V(S^0, V_1^0, V_2^0, I_1^0, I_2^0) = g\left(\frac{S^0}{S^0}\right) + g\left(\frac{V_1^0}{{V_1}^0}\right) + g\left(\frac{V_2^0}{{V_2}^0}\right) + I_1^0 + I_2^0 = 0.$$

To show that E_0 is globally asymptotically stable, it is sufficient to show that $\dot{V}$ is negative definite. Taking the derivative of equation (4.24), it is obtained that

$$\dot{V} = \left(\dot{S} - \frac{\dot{S}}{\frac{S}{S^0}}\right) + \left(\dot{V}_1 - \frac{\dot{V}_1}{\frac{V_1}{{V_1}^0}}\right) + \left(\dot{V}_2 - \frac{\dot{V}_2}{\frac{V_2}{{V_2}^0}}\right) + \dot{I}_1 + \dot{I}_2$$

or

$$\dot{V} = \left(1 - \frac{S^0}{S}\right)\dot{S} + \left(1 - \frac{{V_1}^0}{V_1}\right)\dot{V}_1 + \left(1 - \frac{{V_2}^0}{V_2}\right)\dot{V}_2 + \dot{I}_1 + \dot{I}_2$$

$$= \left(1 - \frac{S^0}{S}\right)(\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S) + \left(1 - \frac{{V_1}^0}{V_1}\right)(r_1 S - (k_1 I_2 + \mu)V_1) + \left(1 - \frac{{V_2}^0}{V_2}\right)(r_2 S - (k_2 I_1 + \mu)V_2) + (k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1 + \left((k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2\right)$$

$$= \Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S - \Lambda\frac{S^0}{S} + (\beta_1 I_1 + \beta_2 I_2 + \lambda)S^0 + r_1 S - (k_1 I_2 + \mu)V_1 - r_1 S\frac{{V_1}^0}{V_1} + (k_1 I_2 + \mu){V_1}^0 + r_2 S - (k_2 I_1 + \mu)V_2 - r_2 S\frac{{V_2}^0}{V_2} + (k_2 I_1 + \mu){V_2}^0 + \left((k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1\right) + ((k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2) + (k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1 + \left((k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2\right). \quad (4.25)$$

From the disease free equilibrium, we have

$$\Lambda = \lambda S^0,\ \mu = r_1\frac{S^0}{{V_1}^0} \text{ and } \mu = r_2\frac{S^0}{{V_2}^0} - k_2{I_1}^0.$$

Putting them in (4.25), we get

$$\dot{V} = \lambda S^0\left(2 - \frac{S^0}{S}\right) + I_1\left(-\alpha_1 + k_2{V_2}^0 + \beta_1 S^0\right) + I_2(-\alpha_2 + k_1{V_1}^0$$

$$+\beta_2 S^0) - \mu S + \mu\left({V_1}^0 - V_1\right) + \mu\left({V_2}^0 - V_2\right) - r_1 S\frac{{V_1}^0}{V_1} - r_2 S\frac{{V_2}^0}{V_2}$$

$$= (r_1 + r_2 + \mu)S^0\left(2 - \frac{S^0}{S}\right) - \mu S - \alpha_1 I_1\left(1 - \left(\frac{k_2}{\alpha_1}{V_2}^0 + \frac{\beta_1}{\alpha_1}S^0\right)\right)$$

$$-\alpha_2 I_2\left(1 - \left(\frac{k_1}{\alpha_2}{V_1}^0 + \frac{\beta_2}{\alpha_2}S^0\right)\right) + \frac{r_1 S^0}{{V_1}^0}\left({V_1}^0 - V_1\right) + \frac{r_2 S^0}{{V_2}^0}\left({V_2}^0 - V_2\right)$$

$$= \mu S^0\left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + r_1 S^0\left(3 - \frac{S^0}{S} - \frac{V_1}{{V_1}^0} - \frac{S}{S^0}\frac{{V_1}^0}{V_1}\right)$$

$$+r_2 S^0\left(3 - \frac{S^0}{S} - \frac{V_2}{{V_2}^0} - \frac{S}{S^0}\frac{{V_2}^0}{V_2}\right) + \alpha_1 I_1(R_1 - 1) + \alpha_2 I_2(R_2 - 1).$$

The relation between arithmetic and geometric mean gives that

$$2 - \frac{S^0}{S} - \frac{S}{S^0} < 0,\ 3 - \frac{S^0}{S} - \frac{V_1}{{V_1}^0} - \frac{S}{S^0}\frac{{V_1}^0}{V_1} < 0 \text{ and } 3 - \frac{S^0}{S} - \frac{V_2}{{V_2}^0} - \frac{S}{S^0}\frac{{V_2}^0}{V_2} < 0.$$

Therefore $\dot{V} < 0$ if $R_1 < 1$ and $R_2 < 1$. Hence E_0 is globally asymptotically stable if $\mathrm{R}_0 < 1$.

Theorem 4.4. E_1 is globally asymptotically stable if $R_2 < 1$.

Proof: Consider the Lyapunov function

$$V(S, V_1, V_2, I_1, I_2) = g\left(\frac{S}{\bar{S}}\right) + g\left(\frac{V_1}{\bar{V_1}}\right) + g\left(\frac{V_2}{\bar{V_2}}\right) + g\left(\frac{I_1}{\bar{I_1}}\right) + I_2$$

where, $g(x) = x - 1 - \ln x$, which is positive function. And since $I_1 > 0$, therefore $V \geq 0$. We need to show that $\dot{V}$ is negative definite.

$$\dot{V} = \left(1 - \frac{\bar{S}}{S}\right)\dot{S} + \left(1 - \frac{\bar{V_1}}{V_1}\right)\dot{V_1} + \left(1 - \frac{\bar{V_2}}{V_2}\right)\dot{V_2} + \left(1 - \frac{\bar{I_1}}{I_1}\right)\dot{I_1} + \dot{I_2}$$

$$= \left(1 - \frac{\bar{S}}{S}\right)(\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S) + \left(1 - \frac{\bar{V_1}}{V_1}\right)(r_1 S - (k_1 I_2 + \mu)V_1)$$

$$+\left(1-\frac{\bar{V}_2}{V_2}\right)(r_2S-(k_2I_1+\mu)V_2)+\left(1-\frac{I_1}{I_1}\right)\left((k_2V_2+\beta_1S)I_1-\alpha_1I_1\right)$$
$$+(k_1V_1+\beta_2S)I_2-\alpha_2I_2$$

$$=\Lambda-(\beta_1I_1+\beta_2I_2+\lambda)S-\Lambda\frac{\bar{S}}{S}+(\beta_1I_1+\beta_2I_2+\lambda)\bar{S}+r_1S$$
$$-(k_1I_2+\mu)V_1-r_1S\frac{\bar{V}_1}{V_1}+(k_1I_2+\mu)\bar{V}_1+r_2S-(k_2I_1+\mu)V_2-r_2S\frac{\bar{V}_2}{V_2}$$
$$+(k_2I_1+\mu)\bar{V}_2+(k_2V_2+\beta_1S)I_1-\alpha_1I_1-(k_2V_2+\beta_1S)\bar{I}_1+\alpha_1\bar{I}_1$$
$$+(k_1V_1+\beta_2S)I_2-\alpha_2I_2$$
$$=\beta_1\bar{S}\bar{I}_1\left(1-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+\lambda\bar{S}\left(2-\frac{\bar{S}}{S}\right)+(r_1+r_2)S-\lambda S+\mu\bar{V}_1\left(1-\frac{V_1}{\bar{V}_1}\right)$$
$$+\mu\bar{V}_2\left(1-\frac{V_2}{\bar{V}_2}\right)-\ r_1S\frac{\bar{V}_1}{V_1}-r_2S\frac{\bar{V}_2}{V_2}-\ I_1(-\alpha_1+k_2\bar{V}_2+\beta_1\bar{S})$$
$$+I_2(-\alpha_2+k_1\bar{V}_1+\beta_2\bar{S})-\mu S+\mu(\bar{V}_1-V_1)+\mu(\bar{V}_2-V_2)-r_1S\frac{\bar{V}_1}{V_1}$$
$$-r_2S\frac{\bar{V}_2}{V_2}-k_2V_2\bar{I}_1-\alpha_1\bar{I}_1$$

$$=\beta_1\bar{S}\bar{I}_1\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+\mu\bar{S}\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+r_1\bar{S}\left(3-\frac{\bar{S}}{S}-\frac{V_1}{\bar{V}_1}-\frac{S}{\bar{S}}\frac{\bar{V}_1}{V_1}\right)$$
$$+r_2\bar{S}\left(3-\frac{\bar{S}}{S}-\frac{V_2}{\bar{V}_2}-\frac{S}{\bar{S}}\frac{\bar{V}_2}{V_2}\right)-\bar{I}_1(-k_2\bar{V}_2-\beta_1\bar{S}+\alpha_1)+I_1(-\alpha_1+k_2\bar{V}_2$$
$$+\beta_1\bar{S})+I_2(-\alpha_2+k_1\bar{V}_2+\beta_2\bar{S}).$$

Since $-k_2\bar{V}_2-\beta_1\bar{S}+\alpha_1=0$, then we have

$$\dot{V}=\beta_1\bar{S}\bar{I}_1\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+\mu\bar{S}\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+r_1\bar{S}\left(3-\frac{\bar{S}}{S}-\frac{V_1}{\bar{V}_1}-\frac{S}{\bar{S}}\frac{\bar{V}_1}{V_1}\right)$$
$$+r_2\bar{S}\left(3-\frac{\bar{S}}{S}-\frac{V_2}{\bar{V}_2}-\frac{S}{\bar{S}}\frac{\bar{V}_2}{V_2}\right)+I_2(R_2-1).$$

From the relation between arithmetic and geometric means, it follows

$$2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}<0,\ 2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}<0 \text{ and } 3-\frac{\bar{S}}{S}-\frac{V_1}{\bar{V}_1}-\frac{S}{\bar{S}}\frac{\bar{V}_1}{V_1}<0.$$

Therefore $\dot{V}<0$ if $R_2<1$. Hence E_1 is globally asymptotically stable if $R_2<1$.

Theorem 4.5. E_2 is globally asymptotically stable if $R_1 < 1$.

Proof. Consider the Lyapunov function

$$V(S, V_1, V_2, I_1, I_2) = g\left(\frac{S}{\hat{S}}\right) + g\left(\frac{V_1}{\hat{V}_1}\right) + g\left(\frac{V_2}{\hat{V}_2}\right) + I_1 + g\left(\frac{I_1}{\hat{I}_2}\right),$$

where, $g(x) = x - 1 - \ln x$, which is positive function. And since $I_1 > 0$, therefore $V \geq 0$. We need to show that $\dot{V}$ is negative definite.

$$\dot{V} = \left(1 - \frac{\hat{S}}{S}\right)\dot{S} + \left(1 - \frac{\hat{V}_1}{V_1}\right)\dot{V}_1 + \left(1 - \frac{\hat{V}_2}{V_2}\right)\dot{V}_2 + + \dot{I}_1 + \left(1 - \frac{\hat{I}_1}{I_2}\right)\dot{I}_2$$
$$= \left(1 - \frac{\hat{S}}{S}\right)(\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S) + \left(1 - \frac{\hat{V}_1}{V_1}\right)(r_1 S - (k_1 I_2 + \mu)V_1)$$
$$+ \left(1 - \frac{\hat{V}_2}{V_2}\right)(r_2 S - (k_2 I_1 + \mu)V_2) + (k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1$$
$$+ \left(1 - \frac{\hat{I}_1}{I_2}\right)\left((k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2\right)$$

$$= \Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S - \Lambda\frac{\hat{S}}{S} + (\beta_1 I_1 + \beta_2 I_2 + \lambda)\hat{S} + r_1 S$$
$$-(k_1 I_2 + \mu)V_1 - r_1 S\frac{\hat{V}_1}{V_1} + (k_1 I_2 + \mu)\hat{V}_1 + r_2 S - (k_2 I_1 + \mu)V_2 - r_2 S\frac{\hat{V}_2}{V_2}$$
$$+(k_2 I_1 + \mu)\hat{V}_2 + (k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1 + (k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2$$
$$-(k_1 V_1 + \beta_2 S)\hat{I}_1 + \alpha_2 \hat{I}_1$$
$$= \beta_2 \hat{S}\hat{I}_1\left(1 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}}\right) + \lambda\hat{S}\left(2 - \frac{\hat{S}}{S}\right) + (r_1 + r_2)S - \lambda S + \mu\hat{V}_1\left(1 - \frac{V_1}{\hat{V}_1}\right)$$
$$+\mu\hat{V}_2\left(1 - \frac{V_2}{\hat{V}_2}\right) - r_1 S\frac{\hat{V}_1}{V_1} - r_2 S\frac{\hat{V}_2}{V_2} - I_1\left(-\alpha_1 + k_2\hat{V}_2 + \beta_1\hat{S}\right)$$
$$+I_2\left(-\alpha_2 + k_1\hat{V}_1 + \beta_2\hat{S}\right) - \mu S + \mu\left(\hat{V}_1 - V_1\right) + \mu\left(\hat{V}_2 - V_2\right) - r_1 S\frac{\hat{V}_1}{V_1}$$
$$-r_2 S\frac{\hat{V}_2}{V_2} - k_1 V_1 \hat{I}_2 - \alpha_2 \hat{I}_2$$

$$= \beta_2 \hat{S}\hat{I}_2\left(2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}}\right) + \mu\hat{S}\left(2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}}\right) + r_1\hat{S}\left(3 - \frac{\hat{S}}{S} - \frac{V_1}{\hat{V}_1} - \frac{S}{\hat{S}}\frac{\hat{V}_1}{V_1}\right)$$
$$+r_2\hat{S}\left(3 - \frac{\hat{S}}{S} - \frac{V_2}{\hat{V}_2} - \frac{S}{\hat{S}}\frac{\hat{V}_2}{V_2}\right) + I_1\left(-\alpha_1 + k_2\hat{V}_2 + \beta_1\hat{S}\right) + I_2\left(-\alpha_2 + k_1\hat{V}_1\right.$$
$$\left.+\beta_2\hat{S}\right) - \hat{I}_2\left(-k_1\hat{V}_1 - \beta_2\hat{S} + \alpha_2\right).$$

Since $-k_1\hat{V}_1 - \beta_2\hat{S} + \alpha_2 = 0$, then we have

$$\dot{V} = \beta_1\hat{S}\hat{I}_2\left(2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}}\right) + \mu\hat{S}\left(2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}}\right) + r_1\hat{S}\left(3 - \frac{\hat{S}}{S} - \frac{V_1}{\hat{V}_1} - \frac{S}{\hat{S}}\frac{\hat{V}_1}{V_1}\right)$$
$$+r_2\hat{S}\left(3 - \frac{\hat{S}}{S} - \frac{V_2}{\hat{V}_2} - \frac{S}{\hat{S}}\frac{\hat{V}_2}{V_2}\right) + I_1(R_1 - 1) < 0$$

By the relation between arithmetic and geometric means, we have

$$2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}} < 0,\ 2 - \frac{\hat{S}}{S} - \frac{S}{\hat{S}} < 0,\ \ 3 - \frac{\hat{S}}{S} - \frac{V_1}{\hat{V}_1} - \frac{S}{\hat{S}}\frac{\hat{V}_1}{V_1} < 0 \text{ and}$$
$$3 - \frac{\hat{S}}{S} - \frac{V_2}{\hat{V}_2} - \frac{S}{\hat{S}}\frac{\hat{V}_2}{V_2} < 0.$$

Therefore $\dot{V} < 0$ if $R_1 < 1$. Hence E_2 is globally asymptotically stable if $R_1 < 1$.

4.4. Numerical Simulations

This section is carried out of the numerical simulations of the model (4.2) with using ode45 suite in Matlab which use the Runge-Kutta numerical method to support the analytic results. The parameters were calculated by the previous study (Rahman & Zou, 2011) and some of the parameter estimated.

In Fig 4.1 both strains (I_1 and I_2) die out, this is because the basic reproduction ratios for the strains are both less than one ($R_1 = 0.2966$ and $R_2 = 0.2765$). In Fig 4.2 strain1 (I_1) dies out and strain2 (I_2) persists ($R_1 = 0.2966$ and $R_2 = 2.350$), and in Fig 4.3 strain2 (I_2) dies out and strain1 (I_1) persists ($R_1 = 2.5979$ and $R_2 = 0.2765$). Lastly in Fig 4.4 both the two strains (I_1 and I_2) persist, this is because the basic reproduction ratios are both greater than one ($R_1 = 2.5979$ and $R_2 = 2.3501$).

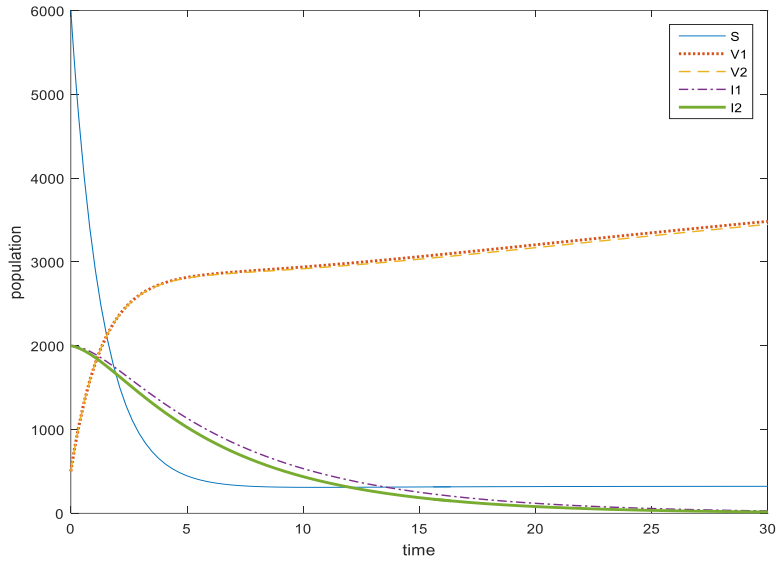

Figure 4. 2: Disease Free equilibrium: both strain die out. Parameter values are,

$\beta_1 = 0.00003, \beta_1 = 0.00003, k_1 = 0.00001, k_2 = 0.00001,$

$r_1 = 0.3, r_2 = 0.3, v_1 = 0.1, v_2 = 0.1, \gamma_1 = 0.07, \gamma_2 = 0.09,$

$\mu = 0.02, \Lambda = 200,\ R_1 = 0.2966$ and $R_2 = 0.2765.$

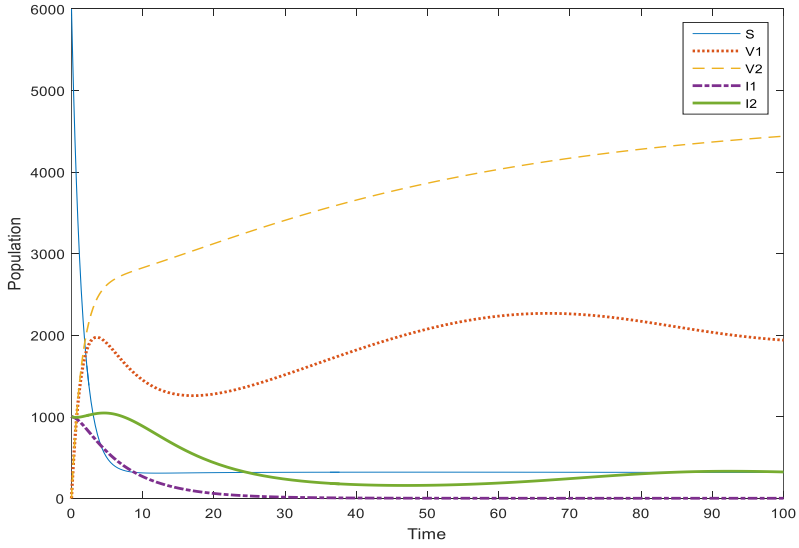

Figure 4.3: Endemic for strain 2: Parameter values are $\beta_1 = 0.00003,$

$\beta_2 = 0.00003, k_1 = 0.0001, k_2 = 0.00001, r_1 = 0.3,$

$r_2 = 0.3, v_1 = 0.1, v_2 = 0.1, \gamma_1 = 0.07, \gamma_2 = 0.09, \mu = 0.02,$

$\Lambda = 200, R_1 = 0.2966$ and $R_2 = 2.350.$

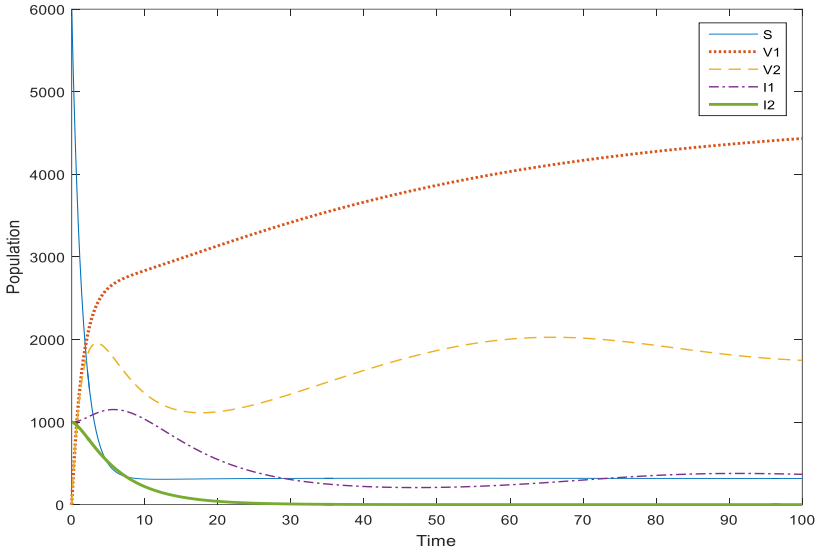

Figure 4.4: Endemic for strain 1: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.00001$, $k_2 = 0.0001$, $r_1 = 0.3$, $r_2 = 0.3$, $\nu_1 = 0.1$, $\nu_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_2 = 0.09$, $\mu = 0.02$, $\Lambda = 200$, $R_1 = 2.5979$ and $R_2 = 0.2765$.

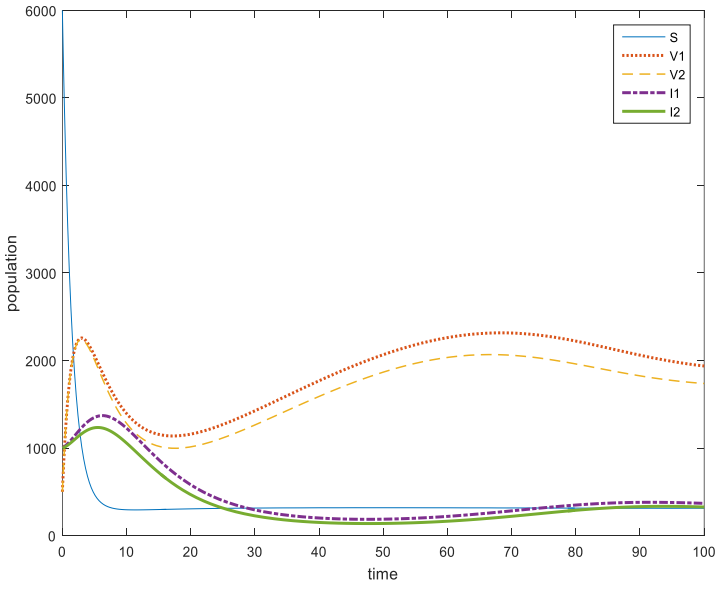

Figure 4. 5: both endemic: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.0001$, $k_2 = 0.0001$, $r_1 = 0.3$, $r_2 = 0.3$, $\nu_1 = 0.1$, $\nu_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_2 = 0.09$, $\mu = 0.02$, $\Lambda = 200$, $R_1 = 2.5979$ and $R_2 = 2.3501$.

To show the effect of vaccine for strain1 against strain 2 and the vaccine for strain 2 against strain1, we carried out the following numerical simulations as can be seen in Figure 4.5 and Figure 4.6.

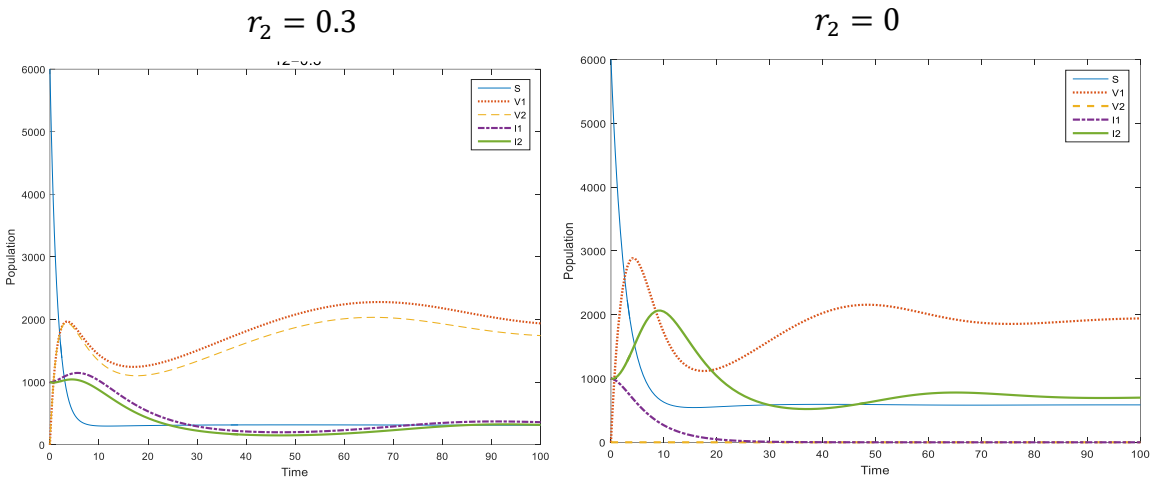

Figure 4.6: both endemic: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.0001$, $k_2 = 0.0001$, $r_1 = 0.3$, $\nu_1 = 0.1$, $\nu_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_2 = 0.09$, $\mu = 0.02$ and $\Lambda = 200$.

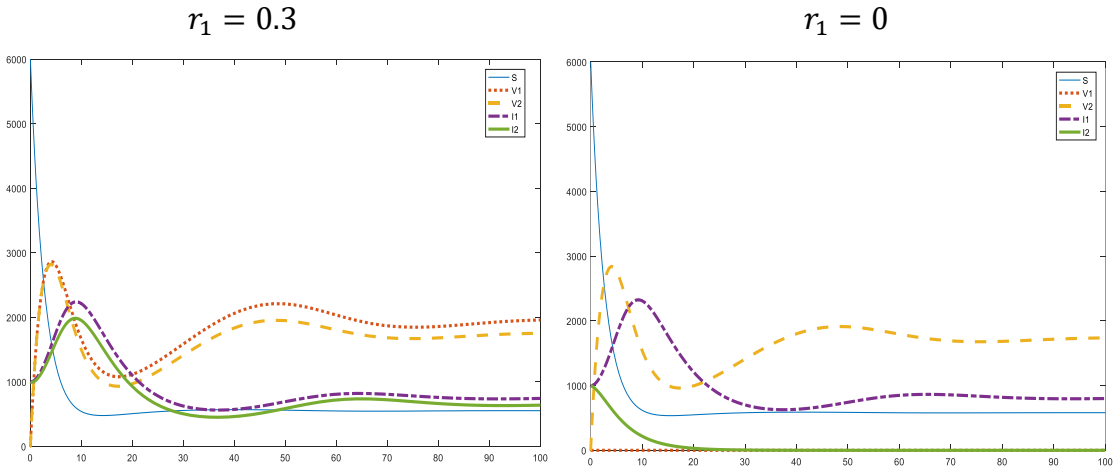

Figure 4.7: both endemic: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.0001$, $k_2 = 0.0001$, $r_2 = 0.3$, $\nu_1 = 0.1$, $\nu_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_2 = 0.09$, $\mu = 0.02$ and $\Lambda = 200$.

4.5 Conclusion

In this chapter, we have studied the dynamics of a two strain epidemic model with two vaccinations. The associated reproduction ratio for each strain is obtained. Moreover, we show that if the reproductions of both strains are less than one, the disease free equilibrium is globally asymptotically stable, and so the disease dies out. Otherwise there exist a unique strain 1 only or strain 2 only boundary equilibrium. The global stability of each boundary equilibrium point is also derived under some threshold conditions. We also stated some conditions that ensure the existence of endemic equilibrium. Several numerical simulations were carried out to support the analytic results

The basic reproduction ratios are R_1 and R_2 which are the threshold quantities of the population dynamics are determined as

$$R_1 = \frac{\beta_1}{\alpha_1}\frac{\Lambda}{\lambda} + \frac{k_2}{\alpha_1}\frac{r_2}{\mu}\frac{\Lambda}{\lambda}, \quad R_2 = \frac{\beta_2}{\alpha_2}\frac{\Lambda}{\lambda} + \frac{k_1}{\alpha_2}\frac{r_1}{\mu}\frac{\Lambda}{\lambda}$$

It can be seen that the global stabilities of each equilibrium point depend on their magnitude. However, to avoid epidemics it sufficient to reduce the magnitude of the basic reproduction ratio below the threshold value (one). This can be achieved simply by reducing the incidence or recruitment rate.

Numerical simulations were carried out to support the analytic results and to show the effect of vaccine for strain 1 against strain 2 and the vaccine for strain 2 against strain1. We have also shown that the population for infectives to strain 2 increases when vaccine for strain 1 is absent and vice versa.

In figure 4.5 it was shown that when vaccine for strain 2 is absent strain 1 dies out, but when there is 30% vaccine for strain 2, strain persists. This shows that vaccine 2 has negative effect on strain 1. Similarly in figure 4.6 it was shown that vaccine 1 has negative effect on strain 2.

Chauhan proposed two models and showed effective of vaccine to the population. In their results disease can be controlled with vaccine (Chauhan et al., 2014). In 2010 Rahman and Zou constructed two strain model with one vaccine for strain one and they study the dynamics of strain two. In our study we add vaccine for strain 2 and we studied with two strain and two vaccine. We observed that vaccine for strain 1 has negative effect to vaccine 2.

CHAPTER 5

TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS AND TWO TIME DELAY

In this chapter, in addition to the previous chapter, it is added incubation time period for both strains which makes the model more realistic and constructed two strain influenza model with two vaccines in which the strain 2 is the mutation of strain 1.

Time between infection of strain 1 (or 2) produce a new virus. So study with the effect of time delay on vaccine-induced immunity is crucial. In this chapter, we present a mathematical model to describe the dynamics of a two-strain flu model with two delays.We targeted on the effects of vaccine for strain one opposed to strain 2 and the vaccine for strain 2 opposed to strain 1.

This chapter organized as follows: In Section 5.1 formulated a two strain influenza model with delay and vaccination compartments regarding to strain 1 and strain 2. In Section 5.2 all possible equilibria and basic reproduction ratios are given, and using Lyapunov functional global stabilities are studied for each equilibrium. In Section 5.3, some Numerical Simulations are given to reinforcement the theoretical results. Finally, in Section 5.4, conclusions and discussions are given.

5.1 Stracture of Model

The epidemic model which is constructed in this chapter consists of two strains and two vaccines with two delays (τ_1 and τ_2). Similarly to the previous chapter the population N(t) is divided into suspectible, immunized with the vaccination for strain 1, immunized with the vaccination for strain 2, infected with strain 1, infected with strain 2 and recovered compartments with $S, V_1, V_2, I_1, I_2$and R, respectively.

Assuming that infected at time $t-\tau_1$ and $t-\tau_2$ become infectious τ_1 and τ_2 times later respectively. To be a more realistic it can be assumed that not all of those infected will

survive after τ_1 (τ_2) times later, because of this reason survival term $e^{\mu\tau_i}$ ($i = 1,2$) is introduced.

Here it is assumed that there is a constant recruitment into susceptible class through birth and immigration and there is no double infection. The average life expectancy is μ and $d_i(i = 1, 2)$ are infection death rates of strain1 and 2 respectively. The avarage time spent in class I_1 and I_2 become recovery $\frac{1}{\gamma_1}$ and $\frac{1}{\gamma_2}$ respectively. The suspectible individuals are vaccined with constant rate r_1 for strain 1 and r_2 for strain 2. The vaccinated individual V_1 can also be infected by strain 2 at a rate k_1 and the vaccinated individual V_2 can also be infected by strain 1 at a rate k_2. β_1 and β_2 are transmission coefficients of susceptible individuals to strain 1 and strain 2 respectively. The variables and parameters are positive. With these assumptions the model is given by a system of 6 ordinary differential equations

$$\frac{dS(t)}{dt} = \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t),$$

$$\frac{dV_1(t)}{dt} = r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t),$$

$$\frac{dV_2(t)}{dt} = r_2 S(t) - (k_2 I_1(t) + \mu)V_2(t), \qquad (5.1)$$

$$\frac{dI_1(t)}{dt} = e^{-\mu\tau_1}\big(k_2 V_2(t-\tau_1) + \beta_1 S(t-\tau_1)\big)I_1(t-\tau_1) - \alpha_1 I_1(t),$$

$$\frac{dI_2(t)}{dt} = e^{-\mu\tau_2}\big(k_1 V_1(t-\tau_2) + \beta_2 S(t-\tau_2)\big)I_2(t-\tau_2) - \alpha_2 I_2(t),$$

$$\frac{dR(t)}{dt} = \gamma_1 I_1(t) + \gamma_2 I_2(t) - \mu R(t),$$

wehere $\lambda = r_1 + r_2 + \mu$, $\alpha_1 = \mu + \nu_1 + \gamma_1$ and $\alpha_2 = \mu + \nu_2 + \gamma_2$, with the condition $\mathrm{S} + \mathrm{V_1} + \mathrm{V_2} + \mathrm{I_1} + \mathrm{I_2} + \mathrm{R} = \mathrm{N}$. Since R does not appear in the equations for $\frac{dS(t)}{dt}$, $\frac{dV_1(t)}{dt}$, $\frac{dV_2(t)}{dt}$, $\frac{dI_1(t)}{dt}$, $\frac{dI_2(t)}{dt}$ analizing the behaviour of solutions of the following system is sufficient.

$$\frac{dS(t)}{dt} = \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t),$$

$$\frac{dV_1(t)}{dt} = r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t),$$

$$\frac{dV_2(t)}{dt} = r_2 S(t) - (k_2 I_1(t) + \mu)V_2(t), \qquad (5.2)$$

$$\frac{dI_1(t)}{dt} = e^{-\mu\tau_1}(k_2 V_2(t-\tau_1) + \beta_1 S(t-\tau_1))I_1(t-\tau_1) - \alpha_1 I_1(t),$$

$$\frac{dI_2(t)}{dt} = e^{-\mu\tau_2}\big(k_1 V_1(t-\tau_2) + \beta_2 S(t-\tau_2)\big)I_2(t-\tau_2) - \alpha_2 I_2(t).$$

The initial conditions of system (2) is given as

$$S(\theta) = \phi_1(\theta), V_1(\theta) = \phi_2(\theta), V_2(\theta) = \phi_3(\theta), I_1(\theta) = \phi_4(\theta),$$
$$I_2(\theta) = \phi_5(\theta), \theta \in [-\tau, 0], \phi_i(0) > 0, \phi_i(\theta) \in C_+^5([-\tau, 0], \mathbb{R}_+^5),$$
$$i = 1, \dots, 5, \tau = max\{\tau_1, \tau_2\}.$$

Here $C = C([-\tau, 0]; \mathbb{R})$ denotes the Banach space with norm

$$\|\phi\| = sup_{-\tau \le \theta \le 0}|\phi(\theta)| \text{ for } \phi \in C.$$

The nonnegative cone for C is defined by $C_+ = C([-\tau, 0], \mathbb{R}_+)$, where $\mathbb{R}_+ = [0, \infty)$.

Theorem 5.1. The feasible region of the model (5.2) with above initial conditions is given by

$$\Omega = \Big\{S(t), V_1(t), V_2(t), I_1(t), I_2(t), R(t) \in C_+^5 : S(t) + V_1(t) + V_2(t)$$
$$+ e^{\mu\tau_1} I_1(t+\tau_1) + e^{\mu\tau_2} I_2(t+\tau_2) \le \frac{\Lambda}{\mu}\Big\}.$$

Proof. To find the feasible region, define

$$H = S(t) + V_1(t) + V_2(t) + e^{-\mu\tau_1} I_1(t+\tau_1) + e^{-\mu\tau_2} I_2(t+\tau_2),$$

then

$$\dot{H}(t) = \dot{S}(t) + \dot{V}_1(t) + \dot{V}_2(t) + e^{-\mu\tau_1}\dot{I}_1(t+\tau_1) + e^{-\mu\tau_2}\dot{I}_2(t+\tau_2)$$

$$\begin{aligned}
&= \Lambda - (\beta_1 I_1(t) + \beta_2 I_2(t) + \lambda)S(t) + r_1 S(t) - (k_1 I_2(t) + \mu)V_1(t) \\
&+ r_2 S(t) - (k_2 I_1(t) + \mu)V_2(t) + \big(k_2 V_2(t) + \beta_1 S(t)\big)I_1(t) \\
&- e^{\mu\tau_1}\alpha_1 I_1(t+\tau_1) + \big(k_1 V_1(t) + \beta_2 S(t)\big)I_2(t) - e^{-\mu\tau_2}\alpha_2 I_2(t+\tau_2)
\end{aligned}$$

$$\begin{aligned}
&= \Lambda - \mu S(t) - \mu V_1(t) - \mu V_2(t) - e^{\mu\tau_1}(\mu + \gamma_1 + d_1)I_1(t) \\
&- e^{-\mu\tau_2}(\mu + \gamma_2 + d_2)I_2(t)
\end{aligned}$$

$$\leq \Lambda - \mu\big(S(t) + V_1(t) + V_2(t) + I_1(t) + e^{-\mu\tau_2} I_2(t)\big) = \Lambda - \mu H$$

or

$$0 \leq \dot{H} \leq \Lambda - \mu H.$$

Thus

$$\text{limsup}_{t\to\infty}\ \text{H} \leq \frac{\Lambda}{\mu}.$$

Hence $H(t)$ is bounded. Therefore all compartments of S, V_1, V_2, I_1, I_2 are bounded with $\frac{\Lambda}{\mu}$.

Theorem 5.2. There exists a unique solution of system (5.2).

Proof. System (5.2) can be written as

$$f(\varphi(t),\varphi(t-\tau))=\begin{pmatrix} f_1(\varphi(t)) \\ f_2(\varphi(t)) \\ f_3(\varphi(t)) \\ f_4(\varphi(t),\varphi(t-\tau)) \\ f_5(\varphi(t),\varphi(t-\tau)) \end{pmatrix},\ \varphi(t)=\begin{pmatrix} \varphi_1(t) \\ \varphi_2(t) \\ \varphi_3(t) \\ \varphi_4(t) \\ \varphi_5(t) \end{pmatrix},$$

where

$f_1\big(\varphi(t)\big)=\Lambda-(\beta_1\varphi_4(t)+\beta_2\varphi_5(t)+\lambda)\varphi_1, f_2\varphi(t)=r_1\varphi_1(t)-(k_1\varphi_5(t)$
$+\mu)\varphi_2(t), f_3\varphi(t)=r_2\varphi_1(t)-(k_2I_1(t) \quad +\mu)\varphi_3(t), f_4\big(\varphi(t),\varphi(t-\tau)\big)$
$=\big(k_2\varphi_3(t-\tau)+\beta_1\varphi_1(t-\tau)\big)\varphi_4(t \quad -\tau)-\alpha_1\varphi_4(t-\tau), f_5(\varphi(t),\varphi(t$
$-\tau))=(k_1\varphi_2(t-\tau)+\beta_2\varphi_1(t \quad -\tau))\varphi_5(t-\tau)-\alpha_2\varphi_5(t-\tau)$ are continuous.
In order to say the system (4.2) has a unique solution it is sufficient to show that the Lipschitz condition for $f(\varphi(t),\varphi(t-\tau))$ with respect to $\varphi(t)$ holds.

For $\varphi(t)=(\varphi_1(t),\varphi_2(t),\varphi_3(t),\varphi_4(t),\varphi_5(t))$ and $\psi(t)=(\psi_1(t),\ \psi_2(t),\psi_3(t),\psi_4(t),$ $\psi_5(t))$, and assuming that

$$|\psi-\varphi|=\textstyle\sum_{i=1}^{5}|\psi_i-\varphi_i|. \qquad (5.3)$$

Then

$$\|\mathrm{f}_1(\varphi(t))-\mathrm{f}_1(\psi(t))\|=|\Lambda-(\beta_1\varphi_4(t)+\beta_2\varphi_5(t)+\lambda)\varphi_1(t)$$
$$-(\Lambda-(\beta_1\psi_4(t)+\beta_2\psi_5(t)+\lambda)\psi_1(t))|$$

$$\leq\beta_1|\psi_4(t)\psi_1(t)-\varphi_4(t)\varphi_1(t)|+\beta_2|\psi_5(t)\psi_1(t)-\varphi_5(t)\varphi_1(t)|$$
$$+\lambda|\psi_1(t)-\varphi_1(t)|$$

$$=\beta_1|\psi_4(t)\psi_1(t)-\psi_1(t)\varphi_4(t)+\psi_1(t)\varphi_4(t)-\varphi_4(t)\varphi_1(t)|$$
$$+\beta_2|\psi_5(t)\psi_1(t)-\psi_1(t)\varphi_5(t)+\psi_1(t)\varphi_5(t)-\varphi_5(t)\varphi_1(t)|$$
$$+\lambda|\psi_1(t)-\varphi_1(t)|$$

$$\leq \beta_1|\psi_1(t)||\psi_4(t)-\varphi_4(t)|+\beta_1|\varphi_4(t)||\psi_1(t)-\varphi_1(t)|$$
$$+\beta_2|\psi_1(t)||\psi_5(t)-\varphi_5(t)| \quad +\beta_2|\varphi_5(t)||\psi_1(t)-\varphi_1(t)|$$
$$+\lambda|\psi_1(t)-\varphi_1(t)|$$

$$=(\beta_1|\psi_4(t)|+\beta_2|\varphi_5(t)|+\lambda)|\psi_1(t)-\varphi_1(t)|+\beta_1|\psi_1(t)||\psi_4(t)$$
$$-\varphi_4(t)|+\beta_2|\psi_1(t)||\emptyset_5(t)-\varphi_5(t)|\leq K_1|\psi(t)-\varphi(t)|, \qquad (5.4)$$

where

$$K_1=\max\{\beta_1|\psi_4(t)|+\beta_2|\varphi_5(t)|+\lambda,\beta_1|\psi_1(t)|,\beta_2|\psi_1(t)|\}.$$

From the invariant set , $\varphi_1(t)\leq\frac{\Lambda}{\mu}$, $\varphi_4(t)\leq\frac{\Lambda}{\mu}$ and $\varphi_5(t)\leq\frac{\Lambda}{\mu}$, it follows

$$K_1=(\beta_1+\beta_2)\frac{\Lambda}{\mu}+\lambda.$$

Furthermore, one can derive that

$$\|f_2(\varphi(t))-f_2(\psi(t))\|=|r_1\varphi_1(t)-(k_1\varphi_5(t)+\mu)\varphi_2(t)$$
$$-(r_1\psi_1(t)-(k_1\psi_5(t)+\mu)\psi_2(t))|$$

$$\leq r_1|\varphi_1(t)-\psi_1(t)|+\ \mu|\psi_2(t)-\varphi_2(t)|+k_1|\psi_5(t)\psi_2(t)$$
$$-\varphi_5(t)\varphi_2(t)|$$
$$\leq r_1|\varphi_1(t)-\psi_1(t)|+\ \mu|\psi_2(t)-\varphi_2(t)|+k_1|\psi_5(t)||\psi_2(t)$$
$$-\varphi_2(t)|+k_1|\varphi_2(t)||\psi_5(t)-\varphi_5(t)|$$
$$=r_1|\varphi_1(t)-\psi_1(t)|+\ (\mu+k_1|\psi_5(t)|)|\psi_2(t)-\varphi_2(t)|$$
$$+k_1|\varphi_2(t)||\psi_5(t)-\varphi_5(t)|\leq K_2|\psi(t)-\varphi(t)|, \qquad (5.5)$$

where

$$K_2=max\{r_1,(\mu+k_1|\psi_5(t)|),k_1|\varphi_2(t)|\}.$$

from the invariant set , $\varphi_1(t) \leq \frac{\Lambda}{\mu}$, $\varphi_2(t) \leq \frac{\Lambda}{\mu}$ and $\varphi_5(t) \leq \frac{\Lambda}{\mu}$, it follows

$$K_2 = \mu + k_1 \frac{\Lambda}{\mu}.$$

For the fourth equation of the system (5.2), we have

$$\begin{aligned}
&\|\mathrm{f}_3(\varphi(t)) - \mathrm{f}_3(\psi(t))\| = |\mathrm{r}_2\varphi_1(t) - (\mathrm{k}_2\varphi_4(t) + \mu)\varphi_3(t) \\
&-(\mathrm{r}_2\psi_1(t) - (\mathrm{k}_2\psi_4(t) + \mu)\psi_3(t))| \\
&\leq \mathrm{r}_2|\varphi_1(t) - \psi_1(t)| + \mu|\psi_3(t) - \varphi_3(t)| + \mathrm{k}_2|\psi_5(t)\psi_3(t) \\
&-\varphi_4(t)\varphi_3(t)| \\
&\leq \mathrm{r}_2|\varphi_1(t) - \psi_1(t)| + \mu|\psi_3(t) - \varphi_3(t)| + \mathrm{k}_2|\psi_4(t)||\psi_3(t) \\
&-\varphi_3(t)| + \mathrm{k}_2|\varphi_3(t)||\psi_4(t) - \varphi_4(t)| \\
&= \mathrm{r}_2|\varphi_1(t) - \psi_1(t)| + (\mu + \mathrm{k}_2|\psi_4(t)|)|\psi_3(t) - \varphi_3(t)| \\
&+\mathrm{k}_2|\varphi_3(t)||\psi_4(t) - \varphi_4(t)| \leq K_3|\psi(t) - \varphi(t)|, \qquad (5.6)
\end{aligned}$$

where,

$$K_3 = \max\{\mathrm{r}_2, (\mu + \mathrm{k}_2|\psi_4(t)|), \mathrm{k}_2|\varphi_3(t)|\}.$$

From the invariant set , $\varphi_1(t) \leq \frac{\Lambda}{\mu}$, $\varphi_3(t) \leq \frac{\Lambda}{\mu}$ and $\varphi_4(t) \leq \frac{\Lambda}{\mu}$, it follows

$$K_3 = \mu + k_2 \frac{\Lambda}{\mu}.$$

The forth equation gives that

$$\begin{aligned}
&\|f_4(\varphi(t), \varphi(t-\tau)) - f_4(\psi(t), \psi(t-\tau))\| = \big|(k_2\varphi_3(t-\tau) \\
&+\beta_1\varphi_1(t-\tau))\varphi_4(t-\tau) - \alpha_1\varphi_4(t) - \big((k_2\psi_3(t-\tau) + \beta_1\psi_1(t \\
&-\tau))\psi_4(t-\tau) - \alpha_1\psi_4(t)\big)\big|
\end{aligned}$$

$$\leq \alpha_1|\psi_4(t) - \varphi_4(t)| \leq K_4|\psi(t) - \varphi(t)|, \tag{5.7}$$

where

$$K_4 = \alpha_1.$$

Finally,

$$\|f_5(\varphi(t), \varphi(t-\tau)) - f_5(\psi(t), \psi(t-\tau))\| = \big|(k_1\varphi_2(t-\tau) + \beta_2\varphi_1(t-\tau))\varphi_5(t-\tau) - \alpha_2\varphi_5(t) - \big((k_1\psi_2(t-\tau) + \beta_2\psi_1(t-\tau))\psi_5(t-\tau) - \alpha_2\psi_5(t)\big)\big|$$

$$\leq \alpha_2|\psi_5(t) - \varphi_5(t)| \leq K_5|\psi(t) - \varphi(t)|, \tag{5.8}$$

where

$$K_5 = \alpha_2.$$

Applying (5.4), (5.5), (5.6), (5.7) and (5.8), we get

$$\|f(\varphi(t)) - f(\psi(t))\| = \|f_1(\varphi(t)) - f_1(\psi(t))\| + \|f_2(\varphi(t)) - f_2(\psi(t))\| + \|f_3(\varphi(t)) - f_3(\psi(t))\| + \|f_4(\varphi(t)) - f_4(\psi(t))\| + \|f_5(\varphi(t)) - f_5(\psi(t))\| \leq (K_1 + K_2 + K_3 + K_4 + K_5)\,|\psi(t) - \varphi(t)|,$$

where

$$K_1 + K_2 + K_3 + K_4 + K_5 = (\beta_1 + \beta_2 + k_1 + k_2)\frac{\Lambda}{\mu} + \lambda + 2\mu + \alpha_1 + \alpha_2.$$

Hence the system (5.2) has a unique solution.

5.2 Equilibrium and Stability Analysis

5.2.1 Equilibrium points

Theorem 5.3.

1. System (5.2) has a disease free equilibrium $E_0 = \left(\frac{\Lambda}{\lambda}, \frac{r_1\Lambda}{\lambda\mu}, \frac{r_2\Lambda}{\lambda\mu}, 0,0\right)$.

2. When $\left(\frac{k_2 r_2}{\alpha_1\mu} + \frac{\beta_1}{\alpha_1}\right)\frac{\Lambda}{\lambda}e^{-\mu\tau_1} \geq 1$ then the system (5.2) has strain 1 endemic (strain 2 disease free) equilibrium $E_1 = (\bar{S}, \bar{V}_1, \bar{V}_2, \bar{I}_1, 0)$, where

$$\bar{S} = \frac{\Lambda}{\beta_1 I_1^1 + \lambda}, \bar{V}_1 = \frac{r_1\Lambda}{\mu(\beta_1 I_1 + \lambda)}, \bar{V}_2 = \frac{r_2\Lambda}{(\beta_1 I_1 + \lambda)(\mu + k_2 I_1)}, \bar{I}_2 = 0$$

and $\bar{I}_1$ is the root of

$$AI_1^2 + BI_1 + C = 0,$$

where $A = \alpha_1\beta_1 k_2\, e^{\mu\tau_1}$, $B = \alpha_1(\beta_1\mu + \lambda k_2)e^{\mu\tau_1} - k_2\beta_1\Lambda$, $C = \alpha_1\lambda\mu e^{\mu\tau_1} - (k_2 r_2\Lambda + \beta_1\Lambda\mu)$.

3. When, $\left(\frac{k_1 r_1}{\alpha_2\mu} + \frac{\beta_2}{\alpha_2}\right)\frac{\Lambda}{\lambda}e^{-\mu\tau_2} \geq 1$, the system (5.2) has the single strain 2 endemic (strain 1 disease free) equilibrium $E_2 = \left(\hat{S}, \hat{V}_1, \hat{V}_2, 0, \hat{I}_2\right)$, where

$$\hat{S} = \frac{\Lambda}{\beta_2 I_2 + \lambda}, \hat{V}_1 = \frac{r_1\Lambda}{(\beta_2 I_2 + \lambda)(\mu + k_1 I_2)}, \hat{V}_2 = \frac{r_2\Lambda}{\mu(\beta_2 I_2 + \lambda)}, \hat{I}_1 = 0$$

and $\hat{I}_2$ is the root of

$$AI_2^2 + BI_2 + C = 0$$

where $A = \alpha_2\beta_2 k_1\, e^{\mu\tau_2}$, $B = \alpha_2(\beta_2\mu + \lambda k_1)e^{\mu\tau_2} - k_1\beta_2\Lambda$, $C = \alpha_2\lambda\mu e^{\mu\tau_2} - (k_1 r_1\Lambda + \beta_2\Lambda\mu)$.

4. System (5.2) has no double strain infection equilibrium.

Proof. Setting the each equation in (5.2) equals to zero, it follows

$$\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S = 0,$$

$$r_1 S - (k_1 I_2 + \mu)V_1 = 0,$$

$$r_2 S - (k_2 I_1 + \mu)V_2 = 0, \qquad (5.9)$$

$$e^{-\mu\tau_1}(k_2 V_2 + \beta_1 S)I_1 - \alpha_1 I_1 = 0,$$

$$e^{-\mu\tau_2}(k_1 V_1 + \beta_2 S)I_2 - \alpha_2 I_2 = 0.$$

1. Since, $I_1 = 0$ and $I_2 = 0$, then from the first three equations of the system (5.9), it is obtained that

$$S = \frac{\lambda}{\Lambda}, V_1 = \frac{\mathrm{r}_1}{\mu}\frac{\lambda}{\Lambda}, V_2 = \frac{\mathrm{r}_2}{\mu}\frac{\lambda}{\Lambda}.$$

Therefore, the disease free equilibrium is

$$E_0 = \left(\frac{\lambda}{\Lambda}, \frac{r_1}{\mu}\frac{\lambda}{\Lambda}, \frac{r_2}{\mu}\frac{\lambda}{\Lambda}, 0,0\right).$$

Since all the coordinates of E_0 are positive, then it is biologically meaningful.

2. For the Strain 2 disease free equilibrium (strain 1 infection equilibrium) E_1, $\bar{I}_2 = 0$ and $\bar{I}_1 \neq 0$. Then with using the system (5.3) we have

$$\Lambda - (\beta_1 \mathrm{I}_1 + \lambda)\mathrm{S} = 0,$$

$$\mathrm{r}_1 \mathrm{S} - \mu \mathrm{V}_1 = 0,$$

$$r_2 S - (k_2 I_1 + \mu) V_2 = 0, \tag{5.10}$$

$$e^{-\mu\tau_1}(k_2 V_2 + \beta_1 S) - \alpha_1 = 0.$$

The first three equations of system (5.10), gives that

$$S = \frac{\Lambda}{\beta_1 I_1 + \lambda}, V_1 = \frac{r_1 S}{\mu}, \; V_2 = \frac{r_2 S}{k_2 I_1 + \mu}.$$

or

$$S = \frac{\Lambda}{\beta_1 I_1 + \lambda}, V_1 = \frac{r_1}{\mu}\frac{\Lambda}{\beta_1 I_1 + \lambda}, V_2 = \frac{r_2}{k_2 I_1 + \mu}\frac{\Lambda}{\beta_1 I_1 + \lambda}.$$

Putting S, and V_2 in the fourth equation of the system (5.10), we get

$$\left(k_2 \frac{r_2}{k_2 I_1 + \mu}\frac{\Lambda}{\beta_1 I_1 + \lambda} + \beta_1 \frac{\Lambda}{\beta_1 I_1 + \lambda}\right) - e^{\mu\tau_1}\alpha_1 = 0$$

or

$$\Lambda k_2 r_2 + \Lambda\beta_1(k_2 I_1 + \mu) - \alpha_1(k_2 I_1 + \mu)(\beta_1 I_1 + \lambda) = 0$$

or

$$e^{\mu\tau_1}(\alpha_1\beta_1 k_2) I_1^2 + (e^{\mu\tau_1}\alpha_1 k_2\lambda + e^{\mu\tau_1}\alpha_1\beta_1\mu - \Lambda\beta_1 k_2) I_1$$
$$+(e^{\mu\tau_1}\alpha_1\lambda\mu - \Lambda k_2 r_2 - \Lambda\beta_1\,\mu) = 0. \tag{5.11}$$

Choosing, $A = e^{\mu\tau_1}\alpha_1\beta_1 k_2$,$B = e^{\mu\tau_1}(\alpha_1 k_2\lambda + \alpha_1\beta_1\mu) - \Lambda\beta_1 k_2$, and $C = e^{\mu\tau_1}\alpha_1\lambda\mu$ $\Lambda k_2 r_2 - \Lambda\beta_1\mu$, system (5.11) can be rewritten as

$$AI_1^2 + BI_1 + C = 0 \tag{5.12}$$

Since $\bar{S}, \bar{V}_1$ and $\bar{V}_2$ are all positive, in order to check the biologically meaningfulness of E_1 we need to show that the equation (5.12) has only one positive root. Following with equation (4.16), we can see that (5.12) has only one positive root when

$$\frac{\Lambda e^{-\mu\tau_1}}{\alpha_{-1}\lambda}\left(\beta_1 + \frac{k_2 r_2}{\mu}\right) \geq 1.$$

3. For the strain 1 disease free equilibrium (strain 2 infection equilibrium) E_2, $\hat{I}_1 = 0$ and $\hat{I}_2 \neq 0$ Again using the system (5.10), it can be obtained

$$\hat{S} = \frac{\Lambda}{\beta_2 I_2 + \lambda}, \hat{V}_1 = \frac{r_1 \Lambda}{(\beta_2 I_2 + \lambda)(\mu + k_1 I_2)}, \hat{V}_2 = \frac{r_2 \Lambda}{\mu(\beta_2 I_2 + \lambda)}, \hat{I}_1 = 0$$

and

$$AI_2^2 + BI_2 + C = 0, \qquad (5.13)$$

where $A = e^{\mu\tau_2}\alpha_2\beta_2 k_1$, $B = e^{\mu\tau_2}(\alpha_2 k_1\lambda + \alpha_2\beta_2\mu) - \Lambda\beta_2 k_1$ and $C = e^{\mu\tau_2}\alpha_2\lambda\mu - \Lambda k_1 r_1 - \Lambda\beta_2\mu$. (5.13) has a unique positive solution when

$$\frac{\Lambda e^{-\mu\tau_2}}{\alpha_2\lambda}\left(\beta_2 + \frac{k_1 r_1}{\mu}\right) \geq 1.$$

4. From the equations of the system (5.10) it can be obtained

$$S^* = \frac{\Lambda}{\beta_1 I_1 + \beta_2 I_2 + \lambda}, V_1^* = \frac{r_1 \Lambda}{(\beta_1 I_1 + \beta_2 I_2 + \lambda)(\mu + k_1 I_2)}, V_2^* = \frac{r_2 \Lambda}{(\beta_1 I_1 + \beta_2 I_2 + \lambda)(\mu + k_2 I_1)},$$

when they are replaced into the last two equation of the system (5.10), it will obtained the following system

$$a_1 I_1^2 + b_1 I_1 I_2 + c_1 I_1 + d_1 I_2 + e_1 = 0,$$

$$a_2 I_2^2 + b_2 I_1 I_2 + c_2 I_1 + d_2 I_2 + e_2 = 0, \qquad (5.14)$$

where

$$a_1 = -\alpha_1\beta_1 k_2, \quad b_1 = -\alpha_1\beta_2 k_2, \quad c_1 = e^{-\mu\tau_1}\beta_1\Lambda k_2 - \alpha_1\lambda k_2 - \alpha_1\beta_1\mu,$$
$$d_1 = -\alpha_1\beta_2\mu, \quad e_1 = e^{-\mu\tau_1}(k_2 r_2\Lambda + \beta_1\Lambda\mu) - \alpha_1\lambda\mu, \qquad a_2 = -\alpha_2\beta_1 k_1,$$
$$b_2 = -\alpha_2\beta_1 k_1, \qquad c_2 = -\alpha_2\beta_1\mu, \quad d_2 = e^{-\mu\tau_2}\beta_2\Lambda k_1 - \alpha_2\lambda k_1 - \alpha_2\beta_2\mu,$$
$$e_2 = e^{-\mu\tau_2}(k_1 r_1\Lambda + \beta_2\Lambda\mu) - \alpha_2\lambda\mu.$$

However, (5.8) has no solution.

5.2.2 Basic Reproduction Number

Basic reproduction ratio (R_0) is the number of secondary infections which is caused by one infectious individual in a wholly susceptible population. We use the next generation matrix

$$F = \begin{bmatrix} \left(\beta_1 S^0 + k_2 {V_2}^0\right) e^{-\mu\tau_1} & 0 \\ 0 & \left(\beta_2 S^0 + k_1 {V_1}^0\right) e^{-\mu\tau_2} \end{bmatrix}, \; V = \begin{bmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{bmatrix},$$

the matrix F is non-negative and is responsible for new infections, while V is invertible and is reffered to as the transmission matrix for the model (2), It follows that

$$FV^{-1} = \begin{bmatrix} \frac{\left(\beta_1 S^0 + k_2 {V_2}^0\right) e^{-\mu\tau_1}}{\alpha_1} & 0 \\ 0 & \frac{\left(\beta_2 S^0 + k_1 {V_1}^0\right) e^{-\mu\tau_2}}{\alpha_2} \end{bmatrix}$$

then the basic reproduction ratio

$$R_0 = \max\{R_1, R_2\},$$

where

$$R_1 = \frac{\Lambda e^{-\mu\tau_1}}{\alpha_1\lambda}\left(\beta_1 + \frac{k_2 r_2}{\mu}\right),\ R_2 = \frac{\Lambda e^{-\mu\tau_2}}{\alpha_2\lambda}\left(\beta_2 + \frac{k_1 r_1}{\mu}\right).$$

5.2.3 Global Stability Analysis

In this section, we study the global properties of the equilibria. Lyapunov function is used to show the global stabilities.

Theorem 5.4. The DFE E_0 is globally asymptotically stable if $R_0 < 1$.

Proof: Consider the Lyapunov function

$$\mathcal{V} = S^0 g\left(\frac{s(t)}{S^0}\right) + V_1{}^0 g\left(\frac{V_1(t)}{V_1{}^0}\right) + V_2{}^0 g\left(\frac{V_2(t)}{V_2{}^0}\right) + e^{\mu\tau_1} I_1(t)$$
$$+ \int_{t-\tau_1}^{t} [\beta_1 I_1(u)S(u) + k_2 I_1(u) V_2(u)]du + e^{\mu\tau_2} I_2(t)$$
$$+ \int_{t-\tau_2}^{t} [\beta_2 I_2(u)S(u) + k_1 I_2(u) V_1(u)]du$$

$$\dot{\mathcal{V}} = \left(1 - \frac{S^0}{S(t)}\right)\dot{S} + \left(1 - \frac{V_1{}^0}{V_1(t)}\right)\dot{V}_1 + \left(1 - \frac{V_2{}^0}{V_2(t)}\right)\dot{V}_2 + e^{\mu\tau_1}\dot{I}_1(t)$$
$$+\big(k_2V_2(t) + \beta_1 S(t)\big)I_1(t) - \big(k_2V_2(t-\tau_1) + \beta_1 S(t-\tau_2)\big)I_1(t-\tau_1)$$
$$+e^{\mu\tau_2}\dot{I}_2(t) + \big(k_1V_1(t) + \beta_2 S(t)\big)I_2(t) - \big(k_1V_1(t-\tau_2) + \beta_2 S(t$$
$$-\tau_2)\big)I_2(t-\tau_2)$$

$$= \left(1 - \frac{S^0}{S(t)}\right)(\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S) + \left(1 - \frac{V_1{}^0}{V_1(t)}\right)(r_1 S$$
$$-(k_1 I_2 + \mu)V_1) + \left(1 - \frac{V_2{}^0}{V_2(t)}\right)(r_2 S - (k_2 I_1 + \mu)V_2)$$
$$+e^{\mu\tau_1}\left(e^{-\mu\tau_1}\big(k_2V_2(t-\tau_1) + \beta_1 S(t-\tau_1)\big)I_1(t-\tau_1) - \alpha_1 I_1(t)\right)$$
$$+\big(k_2V_2(t) + \beta_1 S(t)\big)I_1(t) - \big(k_2V_2(t-\tau_1) + \beta_1 S(t-\tau_2)\big)I_1(t-\tau_1)$$
$$+e^{\mu\tau_2}\big[e^{-\mu\tau_2}\big(k_1V_1(t-\tau_2) + \beta_2 S(t-\tau_2)\big)I_2(t-\tau_2) - \alpha_2 I_2(t)\big]$$
$$+\big(k_1V_1(t) + \beta_2 S(t)\big)I_2(t) - \big(k_1V_1(t-\tau_2) + \beta_2 S(t-\tau_2)\big)I_2(t-\tau_2)$$

making some simplification and using $\mu = r_1 \frac{S^0}{{V_1}^0}$ and $\mu = r_2 \frac{S^0}{{V_2}^0}$, we have

$$\dot{\mathcal{V}} = \mu S^0 \left(2 - \frac{S^0}{S(t)} - \frac{S(t)}{S^0}\right) + r_1 S^0 \left(3 - \frac{S^0}{S(t)} - \frac{V_1}{{V_1}^0} - \frac{S(t)}{S^0}\frac{{V_1}^0}{V_1}\right)$$
$$+ r_2 S^0 \left(3 - \frac{S^0}{S(t)} - \frac{V_2}{{V_2}^0} - \frac{S(t)}{S^0}\frac{{V_2}^0}{V_2}\right) I_1\left(\beta_1 S^0 + k_2 {V_2}^0 - \alpha_1 e^{\mu\tau_1}\right)$$
$$+ I_2\left(\beta_2 S^0 + k_1 {V_1}^0 - \alpha_2 e^{\mu\tau_2}\right)$$

then, $\dot{\mathcal{V}} < 0$ when $R_2 < 1$.

Theorem 5.5. The First strain endemic equilibrium E_1 is globally asymptotically stable if $R_2 < 1$.

Proof. Consider the Lyapunov function

$$\mathcal{V} = \bar{S} g\left(\frac{S(t)}{\bar{S}}\right) + \bar{V}_1 g\left(\frac{V_1(t)}{\bar{V}_1}\right) + \bar{V}_2 g\left(\frac{V_2(t)}{\bar{V}_2}\right) + e^{\mu\tau_1} g\left(\frac{I_1(t)}{\bar{I}_1}\right)$$
$$+ \int_{t-\tau_1}^{t} \left[\beta_1 \bar{I}_1 \bar{S} g\left(\frac{I_1(u)S(u)}{\bar{I}_1 \bar{S}}\right) + k_2 \bar{I}_1 \bar{V}_2 g\left(\frac{I_1(u)V_2(u)}{\bar{I}_1 \bar{V}_2}\right)\right] du + e^{\mu\tau_2} I_2(t)$$
$$+ \int_{t-\tau_2}^{t} [\beta_2 I_2(u)S(u) + k_1 I_2(u) V_1(u)] du.$$

Where $g(x) = x - 1 - \ln x$. Since $g(x)$ is positive function. And since $I_1 > 0$ and $I_2 > 0$, therefore $\mathcal{V} \geq 0$. We need to show that $\dot{\mathcal{V}}$ is negative definite.

$$\dot{\mathcal{V}} = \left(1 - \frac{\bar{S}}{S(t)}\right)(\Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S) + \left(1 - \frac{\bar{V}_1}{V_1(t)}\right)(r_1 S$$
$$-(k_1 I_2 + \mu)V_1) + \left(1 - \frac{\bar{V}_2}{V_2(t)}\right)(r_2 S - (k_2 I_1 + \mu)V_2)$$
$$+ e^{\mu\tau_1}\left(1 - \frac{\bar{I}_1}{I_1(t)}\right)(e^{-\mu\tau_1}\left(k_2 V_2(t-\tau_1) + \beta_1 S(t-\tau_1)\right)I_1(t-\tau_1)$$
$$-\alpha_1 I_1(t)) + \beta_1 \bar{I}_1 \bar{S}\left[\frac{I_1(t)S(t)}{\bar{I}_1 \bar{S}} - \ln\left(\frac{I_1(t)S(t)}{\bar{I}_1 \bar{S}}\right) - \frac{I_1(t-\tau_1)S(t-\tau_1)}{\bar{I}_1 \bar{S}}\right.$$
$$\left. + ln\left(\frac{I_1(t-\tau_1)S(t-\tau_1)}{\bar{I}_1 \bar{S}}\right)\right] + k_2 \bar{I}_1 \bar{V}_2\left[\frac{I_1(t)V_2(t)}{\bar{I}_1 \bar{V}_2} - ln\left(\frac{I_1(t)V_2}{\bar{I}_1 \bar{V}_2}\right)\right.$$
$$\left. - \frac{I_1(t-\tau_1)V_2(t-\tau_1)}{\bar{I}_1 \bar{V}_2} + \ln\left(\frac{I_1(t-\tau_1)V_2(t-\tau_1)}{\bar{I}_1 \bar{V}_2}\right)\right] + e^{\mu\tau_2}[e^{-\mu\tau_2}(k_1 V_1(t-\tau_2)$$

$$+\beta_2 S(t-\tau_2))I_2(t-\tau_2) - \alpha_2 I_2(t)] + \big(k_1 V_1(t) + \beta_2 S(t)\big)I_2(t)$$
$$-\big(k_1 V_1(t-\tau_2) + \beta_2 S(t-\tau_2)\big)I_2(t-\tau_2).$$

After some simplifications we get

$$\dot{\mathcal{V}} = \mu\bar{S}\left(2 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{S(t)}{\bar{S}}\right) + \mathrm{r}_1\bar{S}\left(3 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{V_1}{\bar{V}_1} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_1}{V_1}\right) \quad + \mathrm{r}_2\bar{S}\Big(3$$
$$- \frac{\bar{S}}{\mathrm{S(t)}} - \frac{V_2}{\bar{V}_2} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_2}{V_2}\Big) + \beta_1\bar{I}_1\bar{S}\Big(2 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{I_1(t-\tau_1)S(t-\tau_1)}{I_1(t)\bar{S}}$$
$$+ \ln\Big(\frac{I_1(t-\tau_1)S(t-\tau_1)}{I_1(t)S(t)}\Big)\Big) + k_2\bar{I}_1\bar{V}_2\Big(2 - \frac{\bar{V}_2}{\mathrm{V}_2(t)} - \frac{I_1(t-\tau_1)\,V_2(t-\tau_1)}{I_1(t)\bar{V}_2}$$
$$- \ln\Big(\frac{I_1(t-\tau_1)\,V_2(t-\tau_1)}{I_1(t)\,V_2(t)}\Big)\Big) + \ I_1(\beta_1\bar{S} + k_2\,\bar{V}_2 - \alpha_1 e^{\mu\tau_1}) + \ I_2(\beta_2\bar{S}$$
$$+ k_1\,\bar{V}_1 - \alpha_2 e^{\mu\tau_2})$$

$$= \mu\bar{S}\left(2 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{S(t)}{\bar{S}}\right) + \mathrm{r}_1\bar{S}\Big(3 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{V_1}{\bar{V}_1} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_1}{V_1}\Big) + \mathrm{r}_2\bar{S}\Big(3 - \frac{\bar{S}}{\mathrm{S(t)}}$$
$$- \frac{V_2}{\bar{V}_2} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_2}{V_2}\Big) - \beta_1\bar{I}_1\bar{S}\left(\mathrm{g}\Big(\frac{\bar{S}}{\mathrm{S(t)}}\Big) + g\left(\frac{I_1(t-\tau_1)S(t-\tau_1)}{I_1(t)\bar{S}}\right)\right)$$
$$- k_2\bar{I}_1\,\bar{V}_2\left(\mathrm{g}\Big(\frac{\bar{V}_2}{\mathrm{V}_2(t)}\Big) + g\left(\frac{I_1(t-\tau_1)\,V_2(t-\tau_1)}{I_1(t)\bar{V}_2}\right)\right) + \ I_2\left(\beta_2\frac{\Lambda}{\beta_1\bar{I}_1+\lambda}\right.$$
$$\left. + k_1\,\frac{\Lambda}{\mu(\beta_1\bar{I}_1+\lambda)} - \alpha_2 e^{\mu\tau_2}\right)$$

$$\leq \mu\bar{S}\left(2 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{S(t)}{\bar{S}}\right) + \mathrm{r}_1\bar{S}\Big(3 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{V_1}{\bar{V}_1} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_1}{V_1}\Big) + \mathrm{r}_2\bar{S}\Big(3 - \frac{\bar{S}}{\mathrm{S(t)}}$$
$$- \frac{V_2}{\bar{V}_2} - \frac{S(t)}{\bar{S}}\frac{\bar{V}_2}{V_2}\Big) - \beta_1\bar{I}_1\bar{S}\left(\mathrm{g}\Big(\frac{\bar{S}}{\mathrm{S(t)}}\Big) + g\left(\frac{I_1(t-\tau_1)S(t-\tau_1)}{I_1(t)\bar{S}}\right)\right)$$
$$- k_2\bar{I}_1\,\bar{V}_2\left(\mathrm{g}\Big(\frac{\bar{V}_2}{\mathrm{V}_2(t)}\Big) + g\left(\frac{I_1(t-\tau_1)\,V_2(t-\tau_1)}{I_1(t)\overline{V_2}}\right)\right) + \ I_2\alpha_2 e^{\mu\tau_2}\left(\frac{\Lambda e^{-\mu\tau_2}}{\alpha_2\lambda}\Big(\beta_2\right.$$
$$\left. + \ \frac{k_1}{\mu}\Big) - 1\right).$$

Since

$$2-\frac{\bar{S}}{\mathrm{S(t)}}-\frac{S(t)}{\bar{S}}<0,\ 3-\frac{\bar{S}}{\mathrm{S(t)}}-\frac{V_1}{\bar{V}_1}-\frac{S(t)}{\bar{S}}\frac{\bar{V}_1}{V_1}<0,\ 3-\frac{\bar{S}}{\mathrm{S(t)}}-\frac{V_2}{\bar{V}_2}-\frac{S(t)}{\bar{S}}\frac{\bar{V}_2}{V_2}<0$$

and $\beta_1\bar{S}+k_2\,\bar{V}_2-\alpha_1 e^{\mu\tau_1}=0$.

Therefore, $\dot{\mathcal{V}}<0$ when $R_2<1$.

Theorem 5.6. The second strain endemic equilibrium E_2 is globally asymptotically stable if $R_1<1$.

Proof. Consider the Lyapunov function

$$\mathcal{V}=\hat{S}g\left(\frac{s(t)}{\hat{S}}\right)+\hat{V}_1 g\left(\frac{V_1(t)}{\hat{V}_1}\right)+\hat{V}_2 g\left(\frac{V_2(t)}{\hat{V}_2}\right)+e^{\mu\tau_1}\,I_1(t)$$
$$+\int_{t-\tau_1}^{t}[\beta_1\,I_1(u)S(u)+k_2\,I_2(u)\,V_2(u)]du+e^{\mu\tau_2}g\left(\frac{I_2(t)}{\hat{I}_2}\right)$$
$$+\int_{t-\tau_2}^{t}\left[\beta_2\hat{I}_2\bar{S}g\left(\frac{I_2(u)S(u)}{\hat{I}_2\hat{S}}\right)+k_1\,\overline{I_2}\;\overline{V_1}g\left(\frac{I_2(u)\,V_1(u)}{\hat{I}_2\hat{V}_1}\right)\right]du,$$

where $g(x)=x-1-\ln x$. Since $g(x)$ is positive function. And since $\mathrm{I}_1>0$ and $\mathrm{I}_2>0$, therefore $\mathcal{V}\geq 0$. We need to show that $\dot{\mathcal{V}}$ is negative definite. Actually,

$$\dot{\mathcal{V}}=\left(1-\frac{\hat{S}}{\mathrm{S(t)}}\right)(\Lambda-(\beta_1\mathrm{I}_1+\beta_2\mathrm{I}_2+\lambda)\mathrm{S})+\left(1-\frac{\widehat{V_1}}{\mathrm{V}_1(t)}\right)(\mathrm{r}_1\mathrm{S}$$
$$-(\mathrm{k}_1\mathrm{I}_2+\mu)\mathrm{V}_1)+\left(1-\frac{\widehat{V_2}}{\mathrm{V}_2(t)}\right)(\mathrm{r}_2\mathrm{S}-(\mathrm{k}_2\mathrm{I}_1+\mu)\mathrm{V}_2)$$
$$+e^{\mu\tau_1}\left[e^{-\mu\tau_1}\left(\mathrm{k}_1\mathrm{V}_2(t-\tau_1)+\beta_1\mathrm{S}(t-\tau_1)\right)\mathrm{I}_1(t-\tau_1)-\alpha_1\mathrm{I}_1(t)\right]$$
$$+\left(\mathrm{k}_2\mathrm{V}_2(t)+\beta_1\mathrm{S}(t)\right)\mathrm{I}_1(t)-\left(\mathrm{k}_2\mathrm{V}_2(t-\tau_1)+\beta_1\mathrm{S}(t-\tau_1)\right)\mathrm{I}_1(t-\tau_1)$$
$$+e^{\mu\tau_2}\left(1-\frac{\hat{I}_2}{I_2(t)}\right)\left(e^{-\mu\tau_2}\left(\mathrm{k}_1\mathrm{V}_1(\mathrm{t}-\tau_2)+\beta_2\mathrm{S}(\mathrm{t}-\tau_2)\right)\mathrm{I}_2(\mathrm{t}-\tau_2)\right.$$
$$\left.-\alpha_2\mathrm{I}_2(t)\right)+\beta_2\hat{I}_2\bar{S}\left[\frac{I_2(t)S(t)}{\hat{I}_2\hat{S}}-\ln\left(\frac{I_2(t)S(t)}{\hat{I}_2\,\hat{S}}\right)-\frac{I_2(t-\tau_2)S(t-\tau_2)}{\hat{I}_2\,\hat{S}}\right.$$
$$\left.+\ln\left(\frac{I_2(t-\tau_2)S(t-\tau_2)}{\hat{I}_2\,\hat{S}}\right)\right]+k_1\,\overline{I_2}\;\widehat{V_1}\left[\frac{I_2(t)\,V_1(t)}{\hat{I}_2\,\hat{V}_1}-\ln\left(\frac{I_2(t)\,V_1}{\hat{I}_2\;\hat{V}_1}\right)\right.$$
$$\left.-\frac{I_2(t-\tau_2)\,V_1(t-\tau_2)}{\hat{I}_2\,\hat{V}_1}+\ln\left(\frac{I_2(t-\tau_2)\,V_1(t-\tau_2)}{\hat{I}_2\,\hat{V}_1}\right)\right].$$

After some simplifiction we get

$$\dot{\mathcal{V}} = \mu\hat{S}\left(2 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{S(t)}{\hat{S}}\right) + \mathrm{r}_1\bar{S}\left(3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_1}{\hat{V}_1} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_1}{V_1}\right) + \mathrm{r}_2\hat{S}\left(3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_2}{\hat{V}_2} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_2}{V_2}\right) + \beta_2\hat{I}_2\hat{S}\left(2 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{I_2(t-\tau_2)S(t-\tau_2)}{I_2(t)\hat{S}} + \ln\left(\frac{I_2(t-\tau_2)S(t-\tau_2)}{I_2(t)S(t)}\right)\right) + k_1\hat{I}_1\,\hat{V}_1\left(2 - \frac{\hat{V}_1}{\mathrm{V}_1(t)} - \frac{I_2(t-\tau_2)\,V_1(t-\tau_2)}{I_2(t)\,\hat{V}_1} - \ln\left(\frac{I_2(t-\tau_2)\,V_1(t-\tau_2)}{I_2(t)\,V_1(t)}\right)\right) + I_1\left(\beta_1\bar{S} + k_2\,\hat{V}_2 - \alpha_1 e^{\mu\tau_1}\right) + I_2\left(\beta_2\bar{S} + k_1\,\hat{V}_1 - \alpha_2 e^{\mu\tau_2}\right)$$

$$= \mu\hat{S}\left(2 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{S(t)}{\hat{S}}\right) + \mathrm{r}_1\bar{S}\left(3 - \frac{\bar{S}}{\mathrm{S(t)}} - \frac{V_1}{\hat{V}_1} - \frac{S(t)}{\bar{S}}\frac{\hat{V}_1}{V_1}\right) + \mathrm{r}_2\hat{S}\left(3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_2}{\hat{V}_2} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_2}{V_2}\right) - \beta_2\,\hat{I}_2\hat{S}\left(\mathrm{g}\left(\frac{\hat{S}}{\mathrm{S(t)}}\right) + g\left(\frac{I_2(t-\tau_2)S(t-\tau_2)}{I_2(t)\hat{S}}\right)\right) - k_1\hat{I}_2\;\hat{V}_1\left(\mathrm{g}\left(\frac{\hat{V}_1}{\mathrm{V}_1(t)}\right) + g\left(\frac{I_2(t-\tau_2)\,V_1(t-\tau_2)}{I_2(t)\;\hat{V}_1}\right)\right) + I_1\left(\beta_1\frac{\Lambda}{\mu(\beta_2\hat{I}_2+\lambda)} + k_2\,\frac{\Lambda}{(\beta_2\hat{I}_2+\lambda)} - \alpha_1 e^{\mu\tau_1}\right)$$

$$\leq \mu\hat{S}\left(2 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{S(t)}{\hat{S}}\right) + \mathrm{r}_1\,\hat{S}\left(3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_1}{\hat{V}_1} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_1}{V_1}\right) + \mathrm{r}_2\hat{S}\left(3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_2}{\hat{V}_2} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_2}{V_2}\right) - \beta_1\hat{I}_1\hat{S}\left(\mathrm{g}\left(\frac{\hat{S}}{\mathrm{S(t)}}\right) + g\left(\frac{I_1(t-\tau_1)S(t-\tau_1)}{I_1(t)\hat{S}}\right)\right) - k_2\hat{I}_1\,\hat{V}_2\left(\mathrm{g}\left(\frac{\hat{V}_2}{\mathrm{V}_2(t)}\right) + g\left(\frac{I_1(t-\tau_1)\,V_2(t-\tau_1)}{I_1(t)\hat{V}_2}\right)\right) + I_1\alpha_1 e^{\mu\tau_1}\left(\frac{\Lambda e^{-\mu\tau_1}}{\alpha_1\lambda}\left(\beta_1 + \frac{k_2}{\mu}\right) - 1\right).$$

Since,

$2 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{S(t)}{\hat{S}} < 0$, $3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_1}{\hat{V}_1} - \frac{S(t)}{\bar{S}}\frac{\hat{V}_1}{V_1} < 0$, $3 - \frac{\hat{S}}{\mathrm{S(t)}} - \frac{V_2}{\hat{V}_2} - \frac{S(t)}{\hat{S}}\frac{\hat{V}_2}{V_2} < 0$ and $\beta_2\hat{S} + k_1\,\hat{V}_1 - \alpha_2 e^{\mu\tau_2} = 0$.

Therefore, $\dot{\mathcal{V}} < 0$ when $R_1 < 1$.

5.3 Numerical Simulation

Numerical simulations were carried out to support the analytic results. In Figure 5.1 it is shown that if $R_1 < 1$ and $R_2 < 1$, both the two strains die out. If $R_2 < 1$, strain 1 persists and the second dies out (Figure 5.2), whereas if $R_1 < 1$, strain 2 persists and the first dies out (Fig 5.3). In figure 5.4 it was shown that if $R_1 > 1$ and $R_2 > 1$, then the two strains persist. To see the effect of incubation perod we give

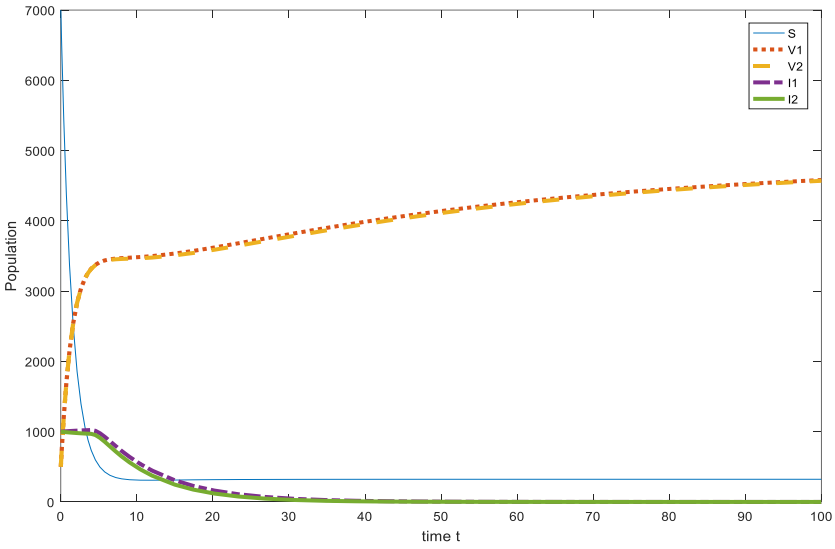

Figure 5. 1: Disease Free: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.00001$, $k_2 = 0.00001$, $r_1 = 0.3$, $r_2 = 0.3$, $d_1 = 0.1$, $d_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_2 = 0.09$ $\mu = 0.02, \Lambda = 200$, $\tau_1 = \tau_2 = 4$, $R_1 = 0.2821$ and $R_2 = 0.2552$.

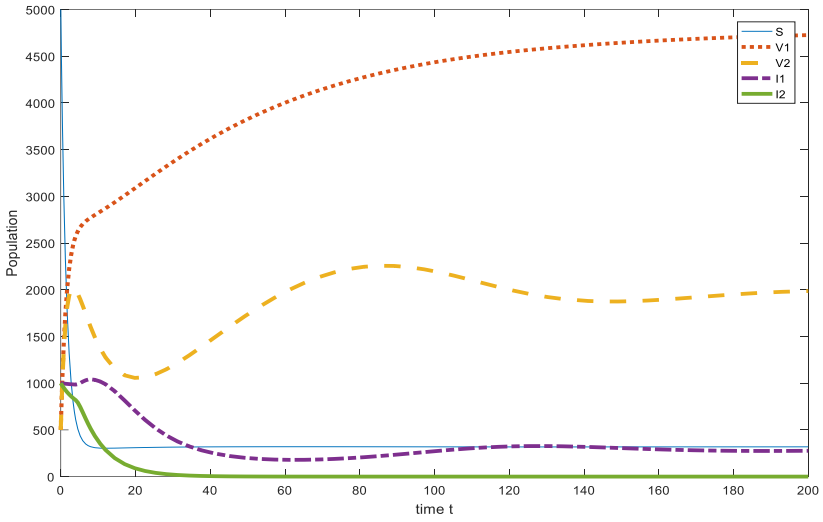

Figure 5.2: First strain endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.00001, k_2 = 0.0001, r_1 = 0.3, r_2 = 0.3, d_1 = 0.1, d_2 = 0.1,$ $\gamma_1 = 0.07, \gamma_2 = 0.09\ \mu = 0.02, \Lambda = 200, \tau_1 = \tau_2 = 4,$ $\mathrm{R}_1 = 2.3979$ and $\mathrm{R}_2 = 0.2552$.

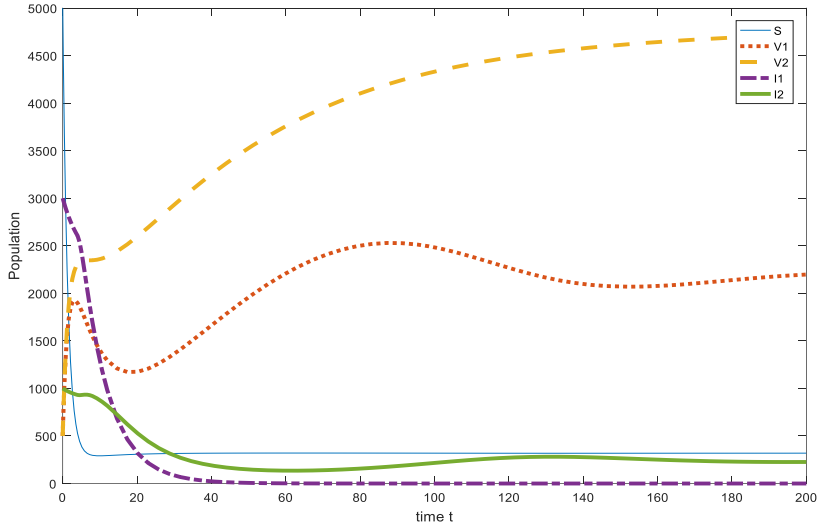

Figure 5.3: Second Strain endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.0001, k_2 = 0.00001, r_1 = 0.3, r_2 = 0.3, d_1 = 0.1, d_2 = 0.1,$ $\gamma_1 = 0.07, \gamma_2 = 0.09\ \mu = 0.02, \Lambda = 200, \tau_1 = \tau_2 = 4,$ $\mathrm{R}_1 = 0.2821$ and $\mathrm{R}_2 = 2.1695$.

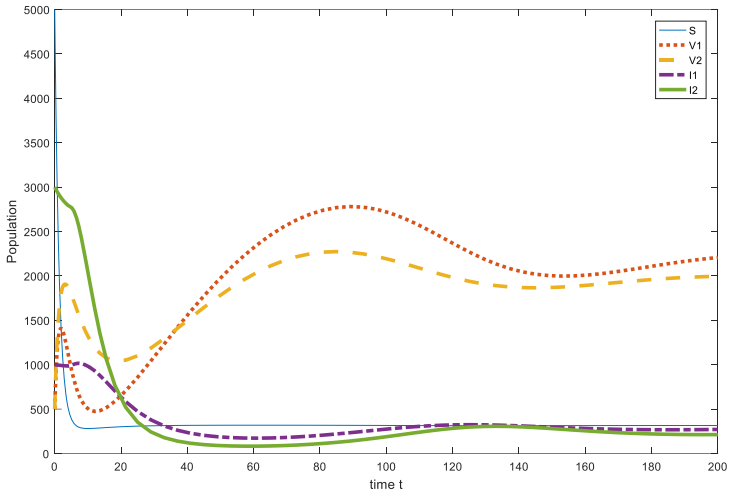

Figure 5.4: Both endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.0001, k_2 = 0.0001, r_1 = 0.3, r_2 = 0.3, d_1 = 0.1, d_2 = 0.1,$ $\gamma_1 = 0.07, \gamma_2 = 0.09\, \mu = 0.02, \Lambda = 200, \tau_1 = \tau_2 = 4,$ $\mathrm{R}_1 = 2.3979$ and $\mathrm{R}_2 = 2.1695.$

To show the effect of vaccine for strain1 against strain 2 and the vaccine for strain 2 against strain1, we carried out the following numerical simulations as can be seen in Figure 5.5 and Figure 5.6.

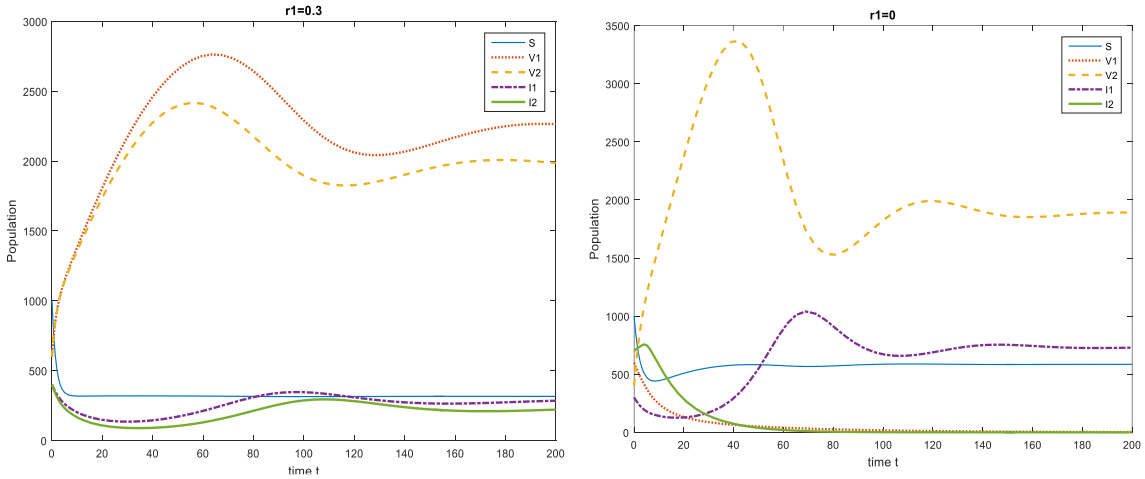

Figure 5.5: Both endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.0001, k_2 = 0.0001, r_2 = 0.3, d_1 = 0.1, d_2 = 0.1, \gamma_1 = 0.07,$ $\gamma_2 = 0.09, \mu = 0.02$ and $\Lambda = 200, \tau_1 = \tau_2 = 4.$

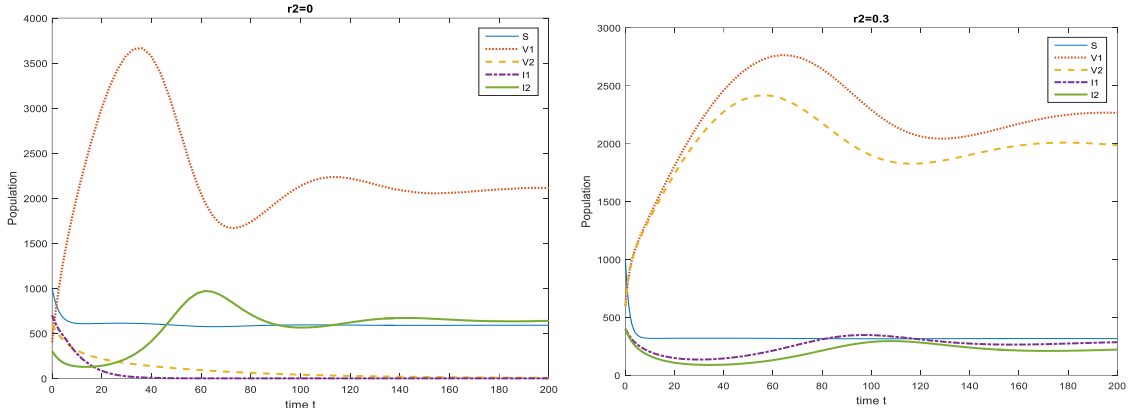

Figure 5.6: Both endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.0001, k_2 = 0.0001, r_1 = 0.3, d_1 = 0.1, d_2 = 0.1, \gamma_1 = 0.07,$ $\gamma_2 = 0.09, \mu = 0.02$ and $\Lambda = 200, \tau_1 = \tau_2 = 4$

In Figure 5.7, it is given the effect of the incubation period. We assume the incubation period of both strain increase from 4 to 15 and we see that disease decrease. In Figure 5.8 and 5.9 given the effect of vaccine for both strains seperately. Firstly, incubation period increased 15 then 30.

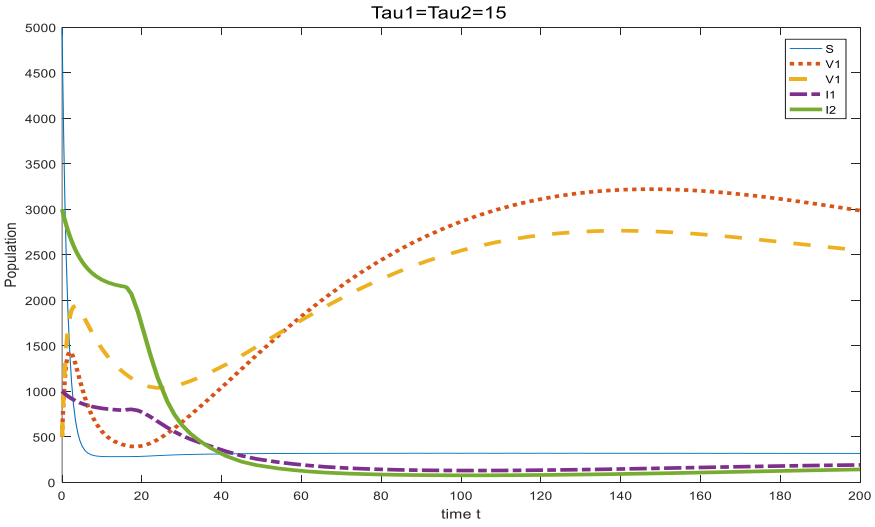

Figure 5.7: Both endemic: Parameter values are $\beta_1 = 0.00003, \beta_2 = 0.00003,$ $k_1 = 0.0001, k_2 = 0.0001, r_1 = 0.3, r_1 = 0.3, d_1 = 0.1, d_2 = 0.1,$ $\gamma_1 = 0.07, \gamma_1 = 0.09, \mu = 0.02, \Lambda = 200, \tau_1 = \tau_2 = 15.$

$\tau_2 = 15$ $\tau_2 = 30$

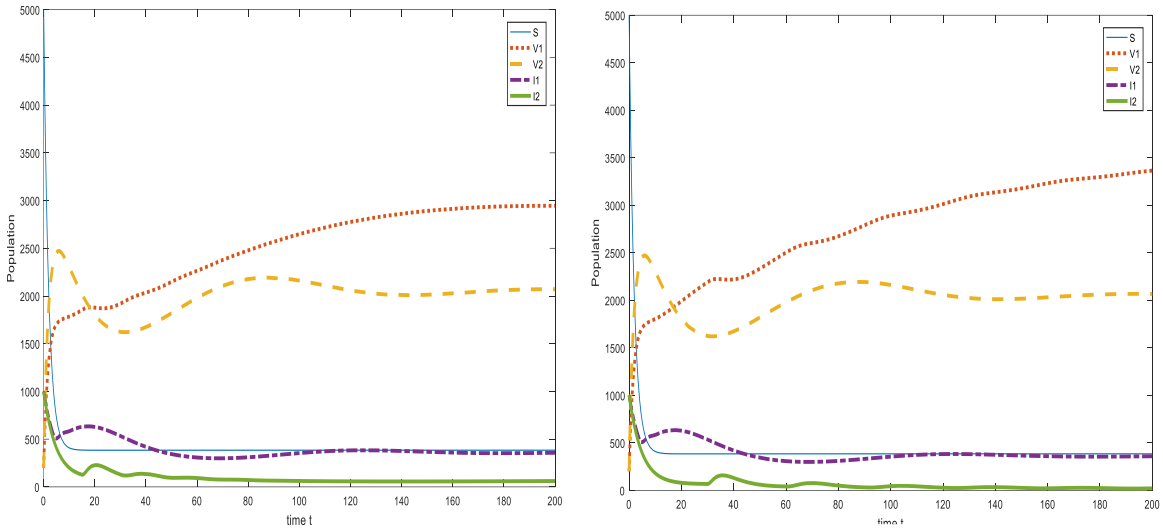

Figure 5.8: Both endemic: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.0001$, $k_2 = 0.0001$, $r_1 = 0.2$, $r_1 = 0.3$, $d_1 = 0.1$, $d_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_1 = 0.09$, $\mu = 0.02$, $\Lambda = 200$, $\tau_1 = 4$.

$\tau_1 = 15$ $\tau_1 = 30$

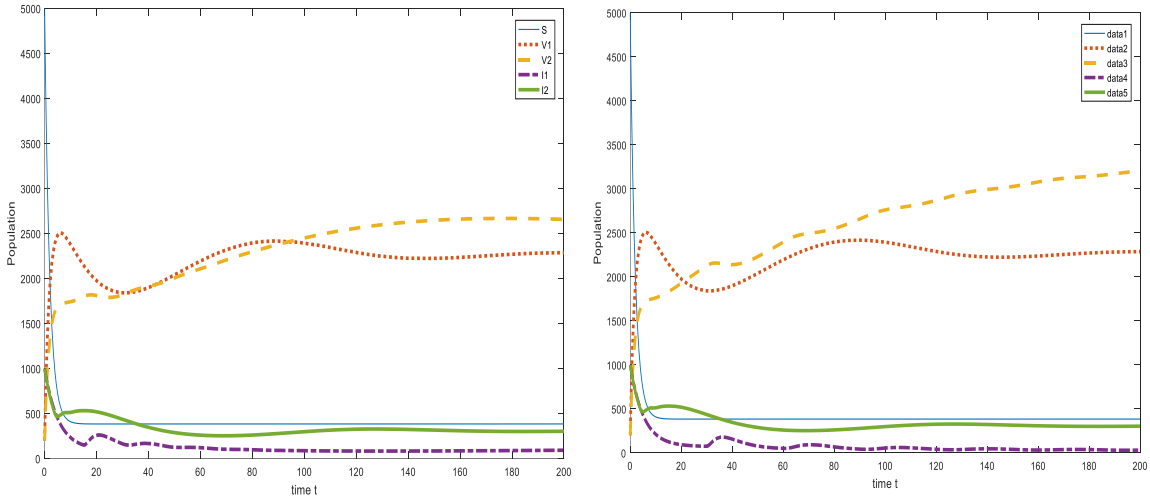

Figure 5.9: Both endemic: Parameter values are $\beta_1 = 0.00003$, $\beta_2 = 0.00003$, $k_1 = 0.0001$, $k_2 = 0.0001$, $r_1 = 0.3$, $r_1 = 0.2$, $d_1 = 0.1$, $d_2 = 0.1$, $\gamma_1 = 0.07$, $\gamma_1 = 0.09$, $\mu = 0.02$, $\Lambda = 200$, $\tau_2 = 4$.

5.4 Conclusion

In this chapter, we study an epidemic model with two vaccine and two time delay. We have studied equilibrium points and under some threshold conditions the global stability of each boundary equilibrium point is derived. The global stability analysis of each equilibria are established by constructing Lyapunov functionals and using Lyapunov- Laselle invariance principle. We found two basic reproduction ratios R_1 and R_2. When both $R_1 < 1$ and $R_2 < 1$ then the disease free equilibrium exists and globally asymptotically stable and disease dies out. Moreover when R_1>1 then strain one endemic equilibrium E_1exists and under the condition $R_2 < 1$ it is globally asymptotically stable. Furhermore when $R_2 > 1$, strain two endemic equilibrium E_2 exists and it is globally asymptotically stable provided that $R_1 < 1$.

R_1 is a decreasing function on time delay τ_1 then the latent period τ_1 has positive effect on the infection of strain 1 and sufficiently large latent period τ_1, R_1 becomes less than one (assuming all other parameters are fixed). Similarly, R_2 is a decreasing function on time delay τ_2 then the latent period τ_2 has positive effect on the infection of strain 1 and sufficiently large latent period τ_2, R_2 becomes less than 1 (assuming all other parameters are fixed). The numerical sumulations give the adoption of vaccination 1 does influence the disease dynamics of strain 2 and similarly vactination for strain 2 dose influence the disease dynamics of strain 1. As we can see figure5.6 and 5.7 the vaccine for strain 1 caused by endemic for strain 2 and similarly vaccine 2 caused endemic for strain 1. Figure 5.8 and Figure 5.9 shows the effect of latent (incubation) period. As we can see in Figure 5.8 when incubation period increse to 15 for strain 2, disease decrease and when it increase 30 then disease can be diese out. Similary for strain1.

If, $\tau_1 = \tau_2 = 0$, then this becomes the previous model which is studied in Chapter 4. Therefore, all theorems which are given in this chapter consists the theorems which are given in Chapter 4. Thus this chapter is generalization of Chapter 4.

CHAPTER 6
CONCLUSION

This thesis consists single strain and two strain models which the second strain is the mutation of the first strain. First two SIR model with and without vaccintion. Some analytical and numerical method used to see the effect of the vaccine. Basic reproduction ratios are found for both model. Stability analysis with using Lyapunov's idea are given for disease free and endemic equilibria points for each model. And in the last section some numerical results are given to support the analytical part. As it can be seen from the figures when the rate of the vaccinated individuals increase then the disease starts to die out. In the result of this chapter, the importance of vaccine arrise.

In Chapter 4 and 5 two strain SIR models are constructed, the model which is given in Chapter 5 is more realistic and extention of the model in Chapter 4. Three equilibriums are found for both models and Stability analysis are studied. Several numerical simulations were carried out to support the analytic results. In analytically there is no co-existence equilibrium point. However from the numerical simulations we have shown the coexistence. In detailed analytic stability remains a challenging problem to us. In summary, the two vaccines not only can have effects on the stability of the boundary equilibria, but can also allow the existence of the coexistence equilibrium.

Numerical simulations were carried out to support the analytic results and to show the effect of vaccine for strain1 against strain 2 and the vaccine for strain 2 against strain1. We have also shown that the population for infectives to strain 2 increases when vaccine for strain 1 is absent and vice versa. And it is observed that when there is no incubation for disease then infection individual increase therefore if incubation (latent) period can be increased then disease can dies out.

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EDUCATION

Degree	Institution	Year of Graduation
M.Sc.	NEU, Department of Mathematics	2014
B. Sc.	NEU, Department of Mathematics	2011

WORK EXPERIENCE

Year	Place	Enrollment
Feb, 2012- Present	Department of Mathematics	Lecturer
2011-2012	Department of Mathematics	Teaching Assistant

FOREIGN LANGUAGES

English, fluently spoken and written

PUBLICATIONS IN INTERNATIONAL REFEREED JOURNALS (IN COVERAGE OF SSCI AND SCI – EXPANDED):

- Kaymakamzade, B., Sanlidag, T., Hincal, E., Sayan, M., Saad, F.T. & Baba, IA. (2017). Role of awareness in controlling HIV/AIDS: A mathematical model. *Quality and Quantity*, DOI 10.1007/s11135-017-0640-2

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- Sayan, M., Hincal, E., Sanlidag, T., Kaymakamzade, B., Saad, F.T. & Baba, IA. (2017). Dynamics of HIV/AIDS in Turkey from 1985 to 2016. *Quality and Quantity*, DOI 10.1007/s11135-017-0648-7

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BULLETIN PRESENTED IN INTERNATIONAL ACADEMIC MEETINGS AND PUBLISHED IN PROCEEDING BOOKS:

- Kaymakamzade, B., Baba, IA. & Hincal E. (2016). Global stability analysis of oseltamivir–resistant influenza virus model . 12th International Conference on Application of Fuzzy Systems and Soft Computing, ICAFS 2016, 29-30 August 2016, Vienna, Austria. *Procedia Computer Science* 102 (2016) 333 – 341

THESISES

Master

- Kaymakamzade, B. (2014). Hyperbolic Geometry and Complex Analysis. Unpublished Master Thesis, Near East University, Faculty of Arts and Sciences, Nicosia, Cyprus

COURSES GIVEN (*from 2012 to 2017*)

Undergraduate:

- Calculus
- Abstract Mathematics I
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- Differential Equations
- Real Analysis

- Complex Analysis I
- Complex Analysis II
- Algebra I
- Algebra II
- Analytic Geometry I
- Analytic Geometry II
- Differential Geometry I
- Differential Geometry II
- Partial Differential Equations I
- Orthogonal Polynomials
- Mathematics for Business Students I
- Mathematics for Business Students II
- Basic Mathematics for Architecture

HOBBIES

- Reading, Listen to Music, Folk Dancing, Studying Mathematics, Learning Languages